Abstracts

001 RENIN CAUSES RELAXATION OF RAT RENAL ARTERIES

S Becker, A Ferro. King’s College London, London, UK

Renin is generally regarded to be monospecific for the activation of angiotensinogen to angiotensin I, which is subsequently converted by angiotensin conversion enzyme (ACE) to angiotensin II, a potent vasoconstrictor. ACE inhibition effectively lowers blood pressure and has been repeatedly shown to prevent cardiovascular events in clinical trials. Treatment with ACE inhibitors elevates plasma renin activity and concentration and, although much is known about the role of renin in vascular control mediated by the renin–angiotensin–aldosterone system, the direct effects of renin on vascular reactivity and blood pressure have not been reported to date. In the present study, we therefore examined the acute effect of renin on vascular contractility.

Rat renal arteries (200–600 µm) were isolated and mounted on a Muvany–Halpern myograph in order to measure tension. Arteries were subsequently constricted with a submaximal concentration of prostaglandin F2α and cumulative concentrations of renin (10⁻¹¹–10⁻⁵ mol) or vehicle were applied. Intracellular Ca²⁺ ([Ca²⁺]i) was estimated by fluorescence microscopy using the intracellular Ca²⁺ fluorophore fura PE 3-AM.

Renin, at concentrations up to 4 nmol did not cause contraction of rat renal arteries. On the other hand, following prostaglandin F2α (15–20 µmol) preconstriction, renin (0.01–1 nmol) induced concentration-dependent vasorelaxation, which was dependent on its protease activity, because it was found to be blocked by the protease inhibitor pepstatin A (10 µmol). Renin-induced relaxation was not inhibited by mechanical removal of the endothelium, by treatment with the cyclooxygenase inhibitor indomethacin (10 µmol) in combination with the nitric oxide (NO) synthase inhibitor N⁵-nitro-L-arginine methyl ester (300 µmol), or by the NO scavenger carboxy-PTIO (300 µmol), arguing against any involvement of NO or of prostaglandins in this effect. However, renin-induced relaxation was abolished by the soluble guanylyl cyclase inhibitor ODQ (50 µmol, fig 1) and by the inactive cyclic GMP analogue and antagonist Rp-8-bromo-cGMPS (10 µmol), but was unaffected by protein kinase G inhibition with KT5823 (1–3 µmol). [Ca²⁺]i, initially decreased to a small extent and quickly returned to initial levels, despite continuing relaxation to renin (fig 2).

These findings suggest that renin causes relaxation of the rat renal artery through a pathway that is dependent on soluble guanylyl cyclase and on cyclic GMP elevation, which is independent of protein kinase G; this may involve cyclic GMP-dependent phosphodiesterase inhibition and consequent accumulation of cyclic AMP and resultant Ca²⁺ desensitisation, as has previously been described. Our findings demonstrate a novel, hitherto undescribed, action of renin on the vasculature, which is likely to be of physiological and pathophysiological importance.

002 GENOME-WIDE ASSOCIATION STUDY IDENTIFIES MLXIPL AS A NOVEL DETERMINANT OF TRIGLYCERIDE LEVELS IN MAN

JC Chambers, P Elliott, J Scott, JS Kooper. Imperial College London, London, UK

Background: The metabolic syndrome and its component phenotypes of obesity, dyslipidaemia, hypertension, impaired glucose tolerance and diabetes are major risk factors for heart disease and stroke. To identify common genetic variants underlying these metabolic disturbances, we performed a three-stage association study, genotyping 12 344 individuals from three ethnic groups.

Methods: Stage one consisted of two genome-wide scans of over 240 000 single nucleotide polymorphisms (SNP) in 1006 Indian Asian and 1005 European men. Analyses of these scans were used to select 5764 SNP for a second stage of genotyping in 4569 Europeans, Indian Asians and Mexicans. Replication of 40 SNP was performed in a third stage in 5968 individuals of European ancestry.

Results: We observed and replicated a highly significant association between triglycerides and a non-synonymous SNP in a glucose-sensitive transcriptional factor that regulates lipogenesis, triglyceride synthesis and very low-density lipoprotein secretion (p<10⁻⁷ in replication phase). Median triglyceride levels were 2.07, 1.96, and 1.75 mmol/l in subjects with CC, CG and GG genotypes, respectively, and the SNP conferred an odds ratio for hypertriglyceridaemia of 1.29 per copy of the high-risk allele. The SNP accounts for 0.48% of the variance in log triglyceride levels. We separately confirmed associations with genes previously reported to be associated with triglyceride levels including LPL, LIPC, ABCA1, and an apolipoprotein cluster.

Conclusion: We have identified a novel genetic variant determining plasma triglyceride levels in man. The polymorphism identified underscores the importance of pathways involved in channeling glucose into lipogenesis and fat storage.
UNRAVELLING THE MOLECULAR PHENOTYPE BEHIND FAMILIAL DILATED CARDIOMYOPATHIES: THE FIRST REPORTED HUMAN FUNCTIONAL STUDY OF A UNIQUE TROPONIN C MUTATION, GLU159ASP

The genetics of familial cardiomyopathies are well established but studies of underlying molecular mechanisms using recombinant proteins and animal models of disease have often given conflicting results. Unravelling the links between genotype and phenotype now demands the study of human cardiac tissue. The missense mutation Gly159Asp (G159D) in cardiac troponin C (TnC) is associated with dilated cardiomyopathy (DCM). We have obtained biopsy material from a patient genotyped with the G159D mutation during cardiac transplantation. Troponin isolated from human DCM tissue will have the post-translational modifications and mutant to wild-type ratios characteristic of this DCM phenotype. The functional properties of troponin isolated from this biopsy sample were compared with control troponin isolated from non-failing donor heart muscle using an in-vitro motility assay. Our strategy has been to reconstitute human cardiac partner proteins into the thin filament to replicate a human system accurately. Thin filaments were reconstituted with skeletal rabbit actin (the same amino acid sequence as human ACTA1), human troponin (from non-failing or mutant G159D heart) and human cardiac alpha tropomyosin (β1g). Measurements in sodium dodecyl sulphate–polyacrylamide gel electrophoresis using Pro-Q Diamond phosphoprotein gel stain showed that troponin I and troponin T phosphorylation levels were not significantly different between dephosphorylated non-failing troponin compared with native non-failing troponin (EC50 NF/NF.dp = 4.7 ± 0.29). We report two main effects of the G159D TnC mutation: a reduced response to troponin phosphorylation levels, and a higher Ca²⁺ sensitivity of G159D troponin in the percentage motility parameter. When G159D troponin was dephosphorylated with 1.4 units/ml acid phosphatase, the Ca²⁺ sensitivity was similar to that of G159D troponin in its native phosphorylation state (EC₅₀ G159D/G159D.dp = 1.24 ± 0.17). This can be directly compared with the characteristic increase in Ca²⁺ sensitivity of dephosphorylated non-failing troponin compared with native non-failing troponin (EC₅₀ NF/NF.dp = 4.8 ± 2.05). Comparisons of the G159D troponin with non-failing troponin when both dephosphorylated show that G159D troponin has a slightly raised Ca²⁺ sensitivity compared with non-failing troponin (EC₅₀ NF.dp/G159D.dp = 1.77 ± 0.29). We report two main effects of the G159D TnC mutation: a reduced response to troponin phosphorylation levels, and a higher Ca²⁺ sensitivity, especially when phosphorylated. We conclude that the reduced response to troponin phosphorylation levels, likely to alter beta-adrenergic modulation of the myofilament, could on its own cause a DCM phenotype. The higher Ca²⁺ sensitivity does not correspond with previous reports of other DCM mutations studied in less physiological systems. This, however, is the first report using human cardiac DCM tissue, by reconstituting natively modified thin filament proteins the human system is more accurately represented than previous studies.

004 DOWNREGULATION OF TISSUE INHIBITOR OF METALLOPROTEINASES (TIMP)-3 DEFINES A SUBPOPULATION OF HIGHLY INVASIVE FOAM-CELL MACROPHAGES

Atherosclerotic plaque rupture is the underlying cause of cardiovascular disease, the world’s number one killer. Advanced plaques contain a high proportion of foam-cell macrophages, which secrete higher levels of matrix metalloproteinases than non-foamy macrophages and thus are thought to contribute to plaque development and rupture. We investigated the expression of the endogenous tissue inhibitor of metalloproteinases (TIMP) 3 during foam-cell formation, and its effects on macrophage and foam-cell behaviour.

Foam cells derived from cholesterol-fed rabbits demonstrated a significant decrease in TIMP-3 mRNA (49%; p < 0.05) and protein expression (84%; p < 0.001) compared with control macrophages. Adding back TIMP-3 to foam cells significantly inhibited migration (51%; p < 0.05), proliferation (70%; p < 0.05) and apoptosis (36%; p < 0.05), but had no effect on non-foamy macrophages. Dual immunocytochemistry demonstrated that a significantly higher proportion of TIMP-3-negative foam-cell macrophages exhibited signs of apoptosis (76 ± 7%; p < 0.05) compared with TIMP-3-positive cells (25 ± 7%). Immunocytochemistry for TIMP-3 on foam cells revealed a subset of these cells (28%) that were TIMP-3 negative. Furthermore, only cells negative for TIMP-3 invaded a synthetic basement membrane using an in-vitro invasion assay. In early rabbit atherosclerotic plaques, TIMP-3 expression was associated with macrophages. However, in advanced plaques, foam cells with little or no TIMP-3 protein expression were found in the deeper layers of the plaque. Similarly, a mixture of foam-cell macrophages with intense TIMP-3 protein expression and with little or no TIMP-3 expression were also observed in advanced human atherosclerotic plaques. TIMP-3-positive and negative foam-cell macrophages were intermingled at the shoulder regions towards the lipid core of these advanced human lesions.

These results demonstrate that TIMP-3 is downregulated when macrophages become lipid loaded and this causes increased migration, proliferation and susceptibility to apoptosis. Furthermore, a distinct highly invasive subset of macrophage foam cells exists with very low TIMP-3 expression. We conclude that TIMP-3-positive and negative foam-cell macrophages were intermingled at the shoulder regions towards the lipid core of these advanced human lesions.

These results demonstrate that TIMP-3 is downregulated when macrophages become lipid loaded and this causes increased migration, proliferation and susceptibility to apoptosis. Furthermore, a distinct highly invasive subset of macrophage foam cells exists with very low TIMP-3 expression. We conclude that the loss of TIMP-3 from foam cells dramatically alters their potential to destabilise atherosclerotic plaques. Therefore, the demonstration of divergent foam-cell macrophage phenotypes in atherosclerotic lesions and their differing proteolytic potential may aid the further elucidation of therapies to promote atherosclerotic plaque stability.

005 IDIOPATHIC RESTRICTIVE CARDIOMYOPATHY IN CHILDREN IS CAUSED BY MUTATIONS IN CARDIAC SARCOMERE PROTEIN GENES

Aim: To determine the prevalence of sarcomere protein gene mutations in children with idiopathic restrictive cardiomyopathy (RCM).

Methods and Results: 12 patients (nine females, mean age 5.1 years) with idiopathic RCM referred between 1991 and August 2006 underwent detailed clinical and genetic evaluation. Nine had received cardiac transplants at the time of the study. The
entire coding sequences of the genes encoding eight cardiac sarcomere proteins and desmin were screened for mutations. Familial evaluation was performed on first-degree relatives. Four patients (35%) had a family history of cardiomyopathy: RCM (n = 2); dilated cardiomyopathy (n = 1) and left ventricular non-compaction (n = 1). Sarcomere protein gene mutations were identified in four patients (35%): two in the cardiac troponin I gene (TNNIS) and one each in the troponin T (TNNT2) and α-cardiac actin (ACTC) genes. Two were de novo mutations and three were novel mutations. All mutations occurred in functionally important and conserved regions of the genes.

Conclusions: Sarcomere protein gene mutations are an important cause of idiopathic RCM in childhood. We describe the first mutation in ACTC in familial RCM. These findings represent a novel disease paradigm in paediatric cardiac practice. The identification of RCM in a child should prompt consideration of sarcomere protein disease as a possible cause and warrants clinical evaluation of the family.

HETEROGENEOUS SERCA2A TRANSFECTION REDUCES SPONTANEOUS AND INDUCIBLE VENTRICULAR ARRHYTHMIAS IN THE RAT MODEL OF HEART FAILURE

AR Lyon, AH Sephempour, S Dubb, K Macleod, PA Poole-Wilson, NS Peters, SE Harding, Imperial College, London, UK

SERCA2a gene therapy improves myocardial contractile function and will be assessed in a clinical gene therapy trial for heart failure. However, there are theoretical concerns regarding SERCA2a and arrhythmogenesis. The effect of heterogeneous SERCA2a gene therapy upon ventricular arrhythmias was studied in a rat heart failure model.

Adult male rats underwent coronary ligation to induce large myocardial infarction (MI). 16 weeks post-MI, left ventricular function was measured using in-vivo pressure–volume analysis. Serum BNP and infarct size were measured. Sham ligation served as a control for the heart failure model.

The in-vivo arrhythmia phenotype was measured using implantable ECG telemetry transmitters. Spontaneous arrhythmias were recorded for 24 hours, followed by in-vivo arrhythmia provocation with 0.5 mg/kg isoprenaline injection. Rats with heart failure received cardiac gene therapy with 3.75 × 10^7 Ad.SERCA2a.GFP particles via three direct myocardial injections, or Ad.GFP control. Sham MI rats received Ad.GFP control. Spontaneous and isoprenaline-induced arrhythmias were recorded 6 days after gene therapy. Hearts were explanted and studied ex vivo on Langendorff apparatus with ECG analysis. Ventricular arrhythmia thresholds were measured using programmed electrical stimulation and isoprenaline perfusion (10^−7 mol).

Pressure–volume analysis demonstrated significant left ventricular impairment at 16 weeks post-MI compared to sham controls: left ventricular ejection fraction (%) 56.5 (4) versus 75.7 (2), left ventricular end-diastolic pressure (mm Hg) 17.2 (2.2) versus 7.9 (0.4), end-systolic pressure–volume relationship (mm Hg/ml) 0.53 (0.11) versus 1.87 (0.29) p < 0.01. Serum BNP levels (pg/ml) were increased in the heart failure model 251 (38) versus undetectable in sham MI (p < 0.001).

SERCA2a gene therapy reduced both total ventricular arrhythmias and sustained ventricular arrhythmias (couplets, triplets, ventricular tachycardia) in vivo in the heart failure (HF) model. Log total spontaneous ventricular arrhythmias: sham 0.3 (0.1), HF 2.6 (1.2), HF-SERCA 1.8 (0.4), HF-GFP 3.5 (0.2) p < 0.01. Log total isoprenaline-induced ventricular arrhythmias: sham 1.2 (0.2), HF 2.0 (0.1), HF-SERCA 1.6 (0.2), HF-GFP 2.2 (0.2) p < 0.05. Log spontaneous sustained ventricular arrhythmias: sham 0.0 (0.0), HF 1.1 (0.2), HF-SERCA 0.54 (0.23), HF-GFP 0.96 (0.41) p < 0.05. SERCA2a completely protected against isoprenaline-induced ventricular tachycardia in vivo (cases ventricular tachycardia/total): sham 0/8, HF 15/18, HF-SERCA 0/8, HF-GFP 5/8 p < 0.01. SERCA2a reduced programmed electrical stimulation-induced ventricular tachycardia in heart failure hearts: SERCA (37%) versus GFP (86%) p < 0.05. The S2 cycle length (ms) at which programmed electrical stimulation-induced ventricular tachycardia was shortened after SERCA gene therapy: SERCA 62 (5) versus GFP 73 (5) (sham 48 (3)). SERCA demonstrated a trend towards protection against isoprenaline-induced ventricular tachycardia ex vivo 1.4 (0.5) versus 3.5 (1.9).

Heterogeneous SERCA2a gene transfection protected against both spontaneous and inducible ventricular arrhythmias in vivo and ex vivo in the post-MI rat failing heart. No increase in arrhythmia susceptibility was detected in the setting of heterogeneous gene delivery to the impaired left ventricle, and the mechanism of benefit may lead to novel antiarrhythmic strategies to treat arrhythmias in heart failure.

LOWER MORTALITY WITH DRUG-ELUTING STENT IN THE "REAL WORLD"

1AE Alahmar, 1RH Stables, 1M Andron, 1M Egred, 2AA Rahman, 1K Albouaini, 1B Patel, 1M Shaw, 1AD Grayson, 2RA Perry, 1Cardiothoracic Centre Liverpool, Liverpool, UK; 2Leeds General Hospital, Leeds, UK; 3Royal Liverpool University Hospital, Liverpool, UK

Background: Long-term mortality following drug-eluting stent (DES) implantation in daily practice is still a concern.

Methods: We carried out retrospective analysis of prospectively collected data on all patients undergoing percutaneous coronary intervention with stent implantation at our institution between January 2005 and December 2004. To account for differences in patient characteristics, logistic regression was used to produce a propensity score for DES group membership using age, smoking status, New York Heart Association class, diabetes, priority, left main stem, restenotic lesion, vessel diameter, and length of lesion. Patients receiving DES were then matched to patients receiving bare metal stents (BMS) with identical propensity scores using the greedy match technique. We were able to match 777 patients in each group (DES and BMS) (table), which were then compared with respect to the incidence of death.

Results: During the study period 995 patients received DES. Of these, 82 patients had combined DES and BMS use and were therefore excluded, leaving 913 DES patients compared with 2105 BMS patients. Patients who received DES were more likely to have diabetes (p < 0.001), restenotic lesions (p < 0.001), left main stem interventions (p < 0.001), long lesions (p < 0.001), small diameter lesions (p < 0.001), and American Heart Association C-type lesions (p < 0.001). Two years mortality was lower in the DES group before (2.0% versus 4.1% p = 0.003), and after (1.8% versus 4.0% p = 0.01) matching (fig).

Conclusions: In our "real world" series, DES implantation was associated with lower mortality compared with BMS.

Abstract 007

<table>
<thead>
<tr>
<th></th>
<th>DES (n = 777)</th>
<th>BMS (n = 777)</th>
<th>p Value</th>
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</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>60.6 ± 10.7</td>
<td>60.6 ± 10.0</td>
<td>0.84</td>
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<tr>
<td>Diabetes (%)</td>
<td>21.2</td>
<td>20.6</td>
<td>0.76</td>
</tr>
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<td>Non-elective (%)</td>
<td>28.0</td>
<td>25.2</td>
<td>0.11</td>
</tr>
<tr>
<td>GPIIb IIIa inhibitors (%)</td>
<td>62.9</td>
<td>60.9</td>
<td>0.40</td>
</tr>
<tr>
<td>LMS lesion (%)</td>
<td>1.7</td>
<td>1.2</td>
<td>0.39</td>
</tr>
<tr>
<td>Vessel diameter &lt;2.5 mm (%)</td>
<td>43.8</td>
<td>44.0</td>
<td>0.92</td>
</tr>
<tr>
<td>Lesion length &gt;20 mm (%)</td>
<td>51.2</td>
<td>54.1</td>
<td>0.26</td>
</tr>
<tr>
<td>CTO &gt;3 months (%)</td>
<td>9.8</td>
<td>9.9</td>
<td>0.93</td>
</tr>
<tr>
<td>AHA C-type lesion (%)</td>
<td>58</td>
<td>61</td>
<td>0.23</td>
</tr>
</tbody>
</table>

AHA, American Heart Association; CTO, chronic total occlusion; LMS, left main stem.
Background and Purpose: There is increasing evidence of a reciprocal interrelationship between chronic heart failure (CHF) and insulin resistance (IR) such that IR may be pathophysiologically linked to the evolution of the disease in CHF. However, the prevalence of IR in the CHF population has not been fully defined. The purpose of this study was to establish the prevalence of IR among non-diabetic CHF patients and to assess its relation to disease severity.

Methods: The homeostatic model of insulin resistance was assessed in a cohort of 129 CHF patients; mean age 69.2 ± 10.4 years, range 30–90 years, males 76%, CHF of ischaemic aetiology 82.2% and BMI (27.4 ± 4.4 kg/m²). All were on regular CHF medication. Patients underwent cardiopulmonary exercise testing and peripheral endothelial function testing by reactive hyperaemia peripheral arterial tonometry.

Results: The prevalence of IR as defined by a fasting insulin resistance index >2.7 was 61% in CHF. The degree of IR was not related to the aetiology of CHF and to the left ventricular ejection fraction. There was a significant correlation between IR and serum triglyceride (r = 0.33, p<0.01), high-density lipoprotein cholesterol (r = −0.275, p<0.01), leptin (r = 0.39, p = 0.03) and central obesity (r = 0.232, p<0.01). The degree of IR was related to the exercise capacity and peak oxygen consumption (VO₂). The mean of IR increased significantly with worsening functional New York Heart Association classes I, II, III and IV (2.1, 2.9, 4.8, 8.9, r = 0.437, p<0.01). The IR patients had a significantly lower exercise duration (340 ± 168.3 versus 601 ± 265.9 seconds, p<0.01) and peak VO₂ (6.4 ± 2.3 versus 14.5 ± 1.7 ml/kg per minute, p<0.05). Exercise peak cardiac output determined by the inert gas re-breathing method was lower in patients with IR (5.2 ± 1.2 versus 9.2 ± 0.89 l/minute, p<0.05). In addition, endothelial function as measured by reactive hyperaemia peripheral arterial tonometry decreased significantly in patients with IR compared with patients with normal insulin sensitivity (1.64 ± 0.36 versus 2.0 ± 0.53, p<0.05).

Conclusion: These findings suggest that IR is highly prevalent among CHF patients and is associated with decreased exercise effort and capacity in patients with CHF. Targeting IR might represent a new strategy in the treatment of CHF.

Abstract 007
Abstract 010

The presence of left atrial thrombus despite anticoagulation in patients undergoing left atrial ablation for atrial fibrillation cannot be predicted by clinical risk factors


Conventionally, the use of warfarin for thromboprophylaxis in patients with atrial fibrillation is based upon clinical risk factors, such as the CHAD2 scoring system. Guidelines also recommend that all patients undergoing elective cardioversion are anticoagulated before the procedure. Left atrial thrombus is an absolute contraindication to left atrial catheter ablation (LACA) for atrial fibrillation as catheter manipulation is likely to result in embolisation. The incidence of thrombus in low-risk patients without anticoagulation and high-risk patients with therapeutic anticoagulation is not known. Transoesophageal echocardiography (TOE) is a very sensitive technique for detecting left atrial thrombus. This study examines whether therapeutic anticoagulation for a minimum of 1 month in all patients undergoing LACA is effective in preventing left atrial thrombus formation.

Methods: We analyzed the records and preoperative TOE images of 160 consecutive patients undergoing LACA (age 56 ± 11 years, 76% male). All patients were therapeutically anticoagulated with warfarin for at least 1 month before admission. Warfarin was stopped 2 days before admission and TOE was performed on the day of the procedure. All the echocardiograms were reviewed for evidence of left atrial appendage thrombosis. The presence or absence of thrombus was confirmed by two independent cardiologists.

Results: Four patients were found to have left atrial thrombus despite therapeutic preoperative anticoagulation, leading to cancellation of their procedure. Three had paroxysmal atrial fibrillation and one persistent atrial fibrillation. The presence of thrombus was not predicted by CHAD2 scores (0, 1, 2 and 4) or age (42, 62, 72 and 61 years). One patient had severe left ventricular dysfunction, none had valvular disease. Left atrial thrombus reduced in size but still persisted in the two patients with the lowest CHAD2 score despite increased intensity of anticoagulation.

Conclusion: There is a 2.5% incidence of left atrial thrombus detected by TOE in patients presenting for LACA despite anticoagulation with warfarin. This cannot be predicted from the patients arrhythmia burden, age or risk factors. These clots are frequently resistant to more intensive anticoagulation. TOE is mandatory in all patients before LACA to exclude left atrial thrombus.

Abstract 012

Percutaneous aortic valve replacement in severe aortic stenosis: first UK experience

H Jhala, T Spy, D Chin, E Logtens, J-L Laborde, I Kovac. Glenfield Hospital, Leicester, UK; Clinique Pasteur, Toulouse, France

Introduction: Significant aortic stenosis is common in the elderly. However, such patients are often declined for or refuse surgery due to perceived risk. We report the first clinical experience in the United Kingdom of percutaneous aortic valve replacement (PAVR) via the femoral route implanted in a high-risk elderly population.

Methods: All patients treated had severe symptomatic aortic stenosis (aortic valve area (AVA) <1 cm²) and were considered by cardiologists and a cardiac surgeon to be at high risk for conventional surgery although not necessarily surgical rejects. Case selection was based on a number of clinical, echocardiographic and angiographic parameters. Among these, femoral arteries had to be at least 6 mm in size to accommodate the valve delivery system. If required, percutaneous coronary revascularisation was performed pre-procedure. We used the third generation CoreValve aortic revalving system, an 18 French system consisting of a porcine pericardial valve mounted on a self-expanding nitinol stent frame for percutaneous transfemoral delivery. Transthoracic echocardiography was used to assess valve function before and after the procedure.

Results: Between 30 January and 23 November 2007, PAVR was attempted in 24 patients. The mean age was 85.0 ± 5.1 years with a mean logistic Euroscore of 21.4 ± 14.3% (SD). 39.1% were male. Baseline ejection fraction calculated by standard biplane echocardiographic methods was 49.0 ± 11.1%. Peak and mean atrioventricular gradients at baseline were 76.6 ± 28.1 mm Hg and 45.5 ± 18.5 mm Hg, respectively, with AVA 0.73 ± 0.19 cm². Four cases were performed under local anaesthesia with sedation and the remainder under general anaesthesia. One borderline suitable case had sub-6 mm femoral arteries and so the 18 F femoral sheath could not be inserted. In the remainder, there was 100% procedural success with no procedural mortality. The mean total procedure time was 124 ± 30 minutes with actual valve replacement time of 12 ± 12 minutes. Average post-procedural time to discharge was 5.9 ± 4.0 days. Predischarge echocardiography revealed a peak gradient of 16.3 ± 7.5 mm Hg and a mean of

CCA, common carotid artery; HDL, high-density lipoprotein; IMT, intima-media thickness.
LONG-TERM SAFETY OF BARE-METAL AND DRUG-ELUTING STENTS FOR ON VERSUS OFF-LABEL INDICATIONS

N Kukreja, J Daemen, Y Onuma, P van Twisk, R van Domburg, E Boersma, P de Jaegere, PW Serruys. Erasmus MC, Rotterdam, The Netherlands

Background: Sirolimus and paclitaxel-eluting stents (SES and PES, respectively) produce a sustained reduction in repeat revascularisation compared with bare-metal stents (BMS), accompanied by a comparable safety profile after up to 4 years when used for recommended indications (on-label use). There are still limited data on the long-term safety and efficacy of drug-eluting stents (DES) for off-label indications.

Methods: Between 1 January 2000 and 31 December 2005 a total of 6129 consecutive patients were treated during three sequential periods with either BMS (n = 2428; January 2000 to April 2002), SES (n = 866; April 2000 to February 2003) or PES (n = 2835; February 2003 to December 2005). The rate of off-label use was 75.8% in the BMS cohort, 74.5% in the SES cohort and 81.0% in the PES cohort. Four-year follow-up data on the occurrence of death, myocardial infarction, repeat revascularisation and stent thrombosis were collected. Survival information was obtained from municipal civil registries and causes of death are classified according to the International Classification of Diseases and Related Health Problems, 10th Revision.

Results: Baseline clinical and procedural complexity increased over time. Survival rates were lower in the off-label compared with the on-label cohorts (BMS 84.2% versus 93.3%; p < 0.001), (DES 85.3% versus 91.8%; p < 0.001) (fig 1). There were no differences in mortality between DES and BMS when stratified by on or off-label use. In the DES group, target vessel revascularisation was more common in the off-label group (12.8% versus 9.5%, p = 0.037), whereas there were no differences among the BMS group irrespective of on or off-label indication. The off-label DES group had a higher incidence of late stent thrombosis (2.2% off-label versus 1.0% on-label) (fig 2).

Conclusion: All-cause mortality is significantly higher after off-label use irrespective of the type of stent. DES are superior to BMS in reducing target vessel revascularisation in both on and off-label indications and the DES benefit is similar for both on and off-label indications. Late stent thrombosis occurs more often after off-label DES use, whereas there was no difference in stent thrombosis between on and off-label BMS use.

TRANSITION CARE: EVALUATION OF THE INPATIENT NEEDS OF ADULTS WITH CONGENITAL HEART DISEASE

S Arif, L Hudsmith, S Hawkesford, S Bowater, P Cift, S Thorne. Worcester Royal Hospital, Worcester, UK; *University Hospitals Birmingham, Birmingham, UK

As a result of advances in paediatric cardiac surgery, catheter interventions, medical and perioperative management and imaging techniques, the number of adults with congenital heart disease (CHD) surviving into adulthood is ever-increasing and currently exceeds the number of children. A fundamental aspect of patient care is the smooth transition from paediatric to adulthood, as outlined in the Department of Health guidance—a commissioning guide for services for young people and grown-ups with congenital heart disease (May 2006). This important aspect of care was identified as the main outstanding area that required improvement.

In our Trust (a tertiary referral centre for adults with CHD), young patients are managed frequently on an inpatient basis on mixed adult wards, alongside patients with other cardiological conditions.

Methods: We assessed the needs of young people with adult CHD (n = 50) admitted onto a mixed adult ward using a detailed questionnaire to evaluate patient expectations, experiences and suggestions. The questionnaire was distributed to all inpatients admitted with adult CHD. The uptake was 100%. The majority of patients had experience of inpatient stay on paediatric cardiology wards.

Results: The mean age of the participants was 26.4 ± 6.0 years (16–38 years). The important features to note were as follows (and will be shown in detail on the day): (1) 90% of patients found the general ward environment to be at least satisfactory, but 64% of patients had no access to a lounge. (2) 58% of patients felt that there was not sufficient access to a lounge.
privacy with bathroom facilities. (3) Although more than 90% of patients had access to payable TV monitors providing access to internet, telephone and games, this was deemed expensive. (4) More than half of patients had no access to reading material. (5) Only 28% of patients had contact with the Grown Up Congenital Heart (GUCH) nurse. Of these patients all found this contact beneficial. This reflects the limited time available with the current resources.

**Conclusions:** The smooth transition of patients with CHD into adult services improves long-term care. We identified that these patients have particular needs that are not currently met in a conventional mixed adult cardiology ward. We hope to improve services for these patients and aim to achieve this generic process with specialist transition nurses, wards and collaboration with other medical subspecialties.

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**015 EVALUATION OF A NEW DEVICE FOR THE TRANSMISSION OF ELECTROCARDIOGRAMS BY E-MAIL**

SJ Leslie, PS Potts, P Macfarlane, JL Barclay, Raigmore Hospital, Inverness, UK; Portree Medical Centre, Portree, UK

**Background:** The electrocardiogram (ECG) is an essential diagnostic test in the assessment of a variety of cardiac conditions. However, confidence and skill in ECG interpretation varies between general practitioners (GP). Access to specialist assessment of an ECG is often useful to ensure good patient care. Recent developments in ECG encryption allow secure digital transmission by e-mail.

**Aims:** The aims of this study were to establish the practicalities of ECG transmission using the Dan Medical system and to assess the real-time delays inherent in using traditional methods of communication compared with digital transmission via e-mail.

**Methods:** Simulated ECG and patient scenarios (n = 10) were sent from a remote island GP simultaneously by post, fax or by e-mail to the consultant cardiologist at the local district general hospital. The consultant was blinded to the clinical scenario and the mode of transmission.

**Results:** One e-mail was unanswered and one fax and one postal referral were not received by the GP surgery giving a 10% loss of communication in each of the three groups. In a further fax referral the ECG was not received by the consultant cardiologist. The generation of a typed letter and return of response by post resulted in a considerable delay. The average total time for an e-mail response was much shorter (0.7 days) compared with the faxed referral (19.9 ± 11.5 days, p<0.001) or post (20.4 ± 2.6 days, p<0.001). The quality of the faxed ECG were more variable and of low quality compared with either hard copy by post or by e-mail (6.1 ± 1.2 versus 10 ± 0 versus 9 ± 0, both p<0.001). E-mail responses were considerably shorter (average 54 ± 8 words) than either fax response (95 ± 32, p<0.001) or postal response (87 ± 28, p<0.001) (fig).

**Conclusions:** Safe and secure electronic transmission of ECG using the Dan Medical system is possible and reduced the significant time delays when compared with more traditional methods of communication. The use of e-mail resulted in fewer words used in correspondence. The exact effect on clinical decision making by changing mode of communication is not known.
audit of guideline implementation on the prevention of cardiovascular disease in clinical practice in coronary patients.

Methods: 75 hospitals in 22 countries participated in the survey. Consecutive patients with acute myocardial infarction, ischaemia, coronary artery bypass grafting and percutaneous transluminal coronary angioplasty were identified retrospectively through hospital medical records and were invited for interview and physical examination (weight, waist, blood pressure, lipid profile and blood glucose). Current smoking status was validated by breath carbon monoxide \( > 10 \text{ ppm} \).

Results: 8966 (73% of identified eligible) patients were interviewed under age 80 years with a mean age of 63.1 years; 25.3% were women. The prevalence of smoking at interview was 17.2% overall and 38% in those under 50 years. 51.9% of patients smoking in the month before their event were still smoking at interview. Information on smoking habit is available for most patients in the medical notes with verbal advice to quit in 90.7%. 20.1% of smokers reported being advised to use nicotine replacement therapy and 11.6% of smokers used nicotine replacement therapy. Self-reported dietary changes include the following: 82.1% reducing fat, 73.5% changing fat type, 77.9% increasing fruit and vegetable consumption and 42.3% eating more oily fish. 69.9% of patients reported either no physical activity or only light activity weekly. One third reported having a long-standing illness, disability or infirmity. One half of patients reported having no intention to take regular exercise to increase physical fitness. 81.8% of patients were overweight (BMI \( > 25 \text{ kg/m}^2 \)), 35.3% were obese (BMI \( > 30 \text{ kg/m}^2 \)), 78% were abdominally overweight (waist circumference \( > 94 \text{ cm} \) in men, \( > 80 \text{ cm} \) in women) and 52.7% were centrally obese (waist circumference \( > 102 \text{ cm} \) in men, \( > 88 \text{ cm} \) in women). Among overweight (obese) patients at interview, 37.9% (50.9%) had attempted to lose weight in the past month. 44.9% of patients reported being advised to follow a cardiac rehabilitation programme within 3 months of discharge from hospital. Of these 69.8% attended. Overall, 33.9% of all patients accessed a programme.

Conclusions and Implications: Only half of all smokers had stopped smoking after their event and few reported receiving professional support or drug therapy. Most patients reported adopting elements of a cardioprotective diet although less than half said they increased their consumption of oily fish. Two-thirds of patients reported sedentary habits with only half intending to increase their physical fitness. Overweight and obesity is very prevalent in these patients with only half or less attempting to lose weight. Only one-third of the interviewed patients accessed a cardiac rehabilitation programme. A professional comprehensive multidisciplinary ambulatory preventive cardiology programme should be available for all coronary patients.

### Abstract 018 Table 1

<table>
<thead>
<tr>
<th>Partner</th>
<th>Current</th>
<th>Ex</th>
<th>Never</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient</td>
<td>O</td>
<td>E</td>
<td>O/E</td>
</tr>
<tr>
<td>Current</td>
<td>69</td>
<td>39.5</td>
<td>1.75</td>
</tr>
<tr>
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<tr>
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</tr>
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</tr>
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</table>

E = expected; O = observed.

### Abstract 018 Table 2

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<th>Patients</th>
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<th>1 Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient only smoked</td>
<td>71.1% (69/97)</td>
<td>73.6% (53/72)</td>
</tr>
<tr>
<td>Both smoked</td>
<td>55.8% (29/52)</td>
<td>57.6% (19/33)</td>
</tr>
<tr>
<td>Partners</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Partner only smoked</td>
<td>19.5% (8/41)</td>
<td>27.8% (10/36)</td>
</tr>
<tr>
<td>Both smoked</td>
<td>23.5% (8/34)</td>
<td>39.4% (13/33)</td>
</tr>
<tr>
<td>Patients/partners</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Only one smoker</td>
<td>55.8% (77/138)</td>
<td>60.1% (63/101)</td>
</tr>
<tr>
<td>Both smoked</td>
<td>43.0% (37/86)</td>
<td>48.2% (32/66)</td>
</tr>
</tbody>
</table>

### 019 CARDIAC MISCONCEPTIONS IN HOSPITAL STAFF

SJ Leslie, E Mackean, F Patience, H Corrigall, Raigmore Hospital, Inverness, UK

Background: There are approximately two million people with chronic stable angina in the United Kingdom, many of whom remain symptomatic despite medical therapy. Angina patients’ beliefs about their condition can influence their symptoms and effective rehabilitation. In particular, cardiac misconceptions have a detrimental effect on the frequency of angina and functional status. Misconceptions may have their origin in a patient’s preconceived ideas about their condition or come from well-meaning friends and family. Cardiac misconception may be worsened by inconsistent advice from healthcare staff. Inexperienced and non-specialist nurses may have more cardiac misconceptions, whereas the cardiac beliefs of doctors are not known. An accurate and consistent
Cardiac misconceptions (n = 177)

Abstract 019

approach to patient information is important from all staff. This is especially important as, due to bed and staffing shortages within the NHS, cardiac patients may be treated on general medical wards.

Aims: The aim of this survey was to determine if staff who care for cardiac patients have personal cardiac misconceptions that could be potentially damaging to patients’ recovery.

Methods: Healthcare staff (n = 157) who provided inpatient care for cardiac patients were invited to complete the York Angina Beliefs Questionnaire, which is a sensitive tool for eliciting an individual’s cardiac misconceptions. This questionnaire is now part of the Angina Plan, which is a brief cognitive behavioural intervention for patients who suffer from angina. A cohort of primary school teachers were used as a control group (n = 20). Data are presented as (mean ± SEM) and analyzed using Student’s t-test (Excel, 2002).

Results: On average, doctors had the lowest cardiac misconception score and medical students had the highest (19.2 ± 1.9 versus 27.0 ± 2.0, p<0.001). Primary school teachers (n = 20) had a slightly lower score than either nursing students or fifth year medical students, although this did not reach statistical significance (26.1 ± 1.7 versus 27.0 ± 2.0 and 26.2 ± 1.0, respectively, fig).

Scores within staff varied considerably depending on ward and previous education in cardiac rehabilitation. Nurses working in coronary care units with previous cardiac rehabilitation training had the lowest overall scores (17.1 ± 2.1).

Conclusions: Cardiac misconceptions are common in hospital staff and variable within staff groups. As expected, staff who care for cardiac patients have lower misconceptions than students or a control group of non-healthcare professionals (primary school teachers) all who had similar levels of cardiac misconception. This suggests that the education of medical and nursing students is suboptimal in the area of cardiac knowledge about angina and myocardial infarction. Given that both nursing and medical students have access to patients, this could have detrimental effects on patients. More effort should be made to ensure that students and staff have consistent and correct cardiac knowledge.

020 TELEMONITORING IN HEART FAILURE, ACCESSIBILITY AND ACCEPTABILITY: THE HOME–HF STUDY

J Riley, O Dar, C Chapman, S Dubrey, J Gabe, MA Cowie, Royal Brompton Hospital/Imperial College, London, UK; Imperial College, London, UK; West Middlesex University Hospital, Middlesex, UK; Hillingdon Hospital NHS Trust, Middlesex, UK; Ealing Hospital NHS Trust, Middlesex, UK; Royal Holloway College, University of London, London, UK

Background: Whereas evidence supports the effectiveness of disease management programmes in heart failure, their current provision in the United Kingdom is inadequate for the growing population with heart failure. This has prompted the development of remote monitoring. Recently published studies of telemonitoring have demonstrated a reduction in mortality in patients with advanced heart failure. However, its effect in a less selected patient population of more elderly patients with comorbidity has not yet been tested. This paper reports our experiences with the Home–HF study, a multicentre randomised controlled trial evaluating home telemonitoring in a general heart failure population in the United Kingdom.

Method: Patients hospitalised with a new diagnosis of heart failure or following acute decompensation were eligible for inclusion into the study. Patients randomly assigned to telemonitoring monitored their weight, blood pressure, oxygen saturation and heart failure symptoms daily. Through their home phone line this information was transmitted for review by a heart failure nurse who decided upon subsequent management. Using purposive sampling, 15 patients using telemonitoring were interviewed about their views and experiences and the data were analyzed using qualitative research analysis techniques.

Results: Over 13 months, 457 patients from three hospitals in north-west London were screened for participation and 182 (65% men, average age 72 years, 51% living alone) were recruited. Adherence to daily telemonitoring was good. Eight patients required repeat education in the use of the telemonitoring, two failed to transmit vital signs and one patient asked for the monitoring to be removed. On 166 occasions and in 54 patients the telemonitoring data and subsequent nurse telephone assessment identified clinical deterioration. This led to four major responses: patient advice regarding the management of their diuretic therapy on 72 (43%) occasions, early review in secondary care on 32 (19%) occasions and a recommendation to contact primary care on 14 (8%) occasions. On 48 (30%) occasions the reinforcement of self-care information was the major focus of the intervention. Preliminary analysis of patient interviews suggests that telemonitoring facilitates a new route for communication that fits the patients’ daily self-care routines. It provides physical and emotional support to them in their homes and enables education for self-care and access to specialist help when needed. The final analysis will be available for presentation at the British Cardiovascular Society conference.

Conclusion: This study indicates that telemonitoring enables the early detection of deterioration and that patients can adapt their daily self-care routines. This has important implications for the future delivery of effective heart failure management at a time and location convenient to the patient.

021 NURSE-LED CHEST PAIN ASSESSMENT: DOES IT ADD QUALITY?

A Roebeck. City Hospitals Sunderland NHS Foundation Trust/Sunderland, UK

Introduction: Patients presenting with acute undifferentiated chest pain are responsible for between 20% and 30% of all emergency department (ED) contacts. They require rapid accurate assessment and risk stratification to identify acute coronary syndromes (ACS). Patients with ACS benefit from reductions in mortality and morbidity (physical and psychological) plus reduced length of hospital stay if they receive the appropriate evidence-based therapies early after the onset of symptoms. However, national research indicates that care in the ED is not standardised and there are wide variations in admission rates and access to diagnostic technologies. Evidence suggests that up to 8% of patients who present at the ED with symptoms of ACS are discharged home inappropriately. This paper discusses the development of a nurse-led chest pain assessment unit (CPAU) in a large district general hospital in the north of England. The paper focuses on the advances made within cardiovascular nursing, including the implementation
of nurse-led history-taking and physical assessment and independent nurse prescribing. The paper concludes with the presentation of previously unpublished data (both quantitative and qualitative) that support the changes made in the patient pathway and the development of the nursing role within chest pain assessment.

Results: Length of stay analysis (LOS) suggests: LOS for angina has been reduced by 76%; LOS for non-cardiac chest pain has been reduced by 51%. This equates to a 27-bed medical ward being empty for one year. Domiciliary patient journey interviews indicate that patients have high levels of satisfaction with their care (n = 110). Partnership working between the CPAU and the local ambulance trust resulted in 94% of patients suffering from a heart attack receiving their thrombolysis within 60 minutes of phoning for professional help (call to needle time) in 2007. The national average is 64% (MINAP, 2007). The use of cardiac biochemical markers has reduced by approximately 150 per month since the CPAU opened. This equates to less patient phlebotomy with associated pain, discomfort and risk of hospital-acquired infection. A cost saving of £1.5K per month was also achieved. The prescribing of antiplatelet therapies has become more selective and evidence based. This equates to optimum patient benefit with justified (evidence-based) risk and a cost saving of £4K per month. 90% more patients are now treated in line with European Society of Cardiology Guidelines.

Discussion: This paper demonstrates that nurse-led chest pain assessment can improve the quality of the ACS patient journey by aiding early, evidence-based identification and management. Moreover, this paper also demonstrates that the patient journey can be improved within existing funding facilitating further improvements in patient care.

022 PMCA4B MODULATES BETA-ADRENERGIC RESPONSE THROUGH REGULATION OF PHOSPHOAMBAN PHOSPHORYLATION
T Mohamed, S Prehar, M Zi, T Mohamed, PJ Stanley, EJ Cartwright, N Alatwi, L Neyses. University of Manchester, Manchester, UK

Heart failure is one of the major causes of death in western Europe. Alteration in cardiac homeostasis has been recognised as an associated factor with heart failure. In contrast to most other known cardiac transporters in the myocardium, little is known about the role of the sarcoplasmic calcium pump (plasma membrane calcium ATPase; PMCA), which ejects calcium from the cytosol into the interstitium. We have previously suggested a novel function for PMCA isoform 4 as a modulator of neuronal nitric oxide synthase (nNOS) activity. However, the physiological consequences of PMCA4b-mediated nNOS regulation in the heart remain unknown. Recently, we have shown that transgenic mice overexpressing PMCA4b in the heart have a reduced β-inotropic response compared with wild-type (WT) mice, which is probably caused by nNOS regulation. In this current work we aim to investigate the relationship between PMCA4 nNOS modulation and β-adrenergic stimulation in the heart. PMCA4b transgenic animal hearts showed a 75% reduction in nNOS activity compared with their WT littermates as well as 25% reduction in cGMP levels compared with WT littermates (n = 8, p<0.05). In contrast, PMCA4b transgenic animal hearts showed a 30% elevation in cAMP levels compared with their WT littermates (n = 8, p<0.05). Phospholamban is one of the key end-targets of β-adrenergic signalling and has been linked to the nNOS/cGMP pathway. Further analysis using adult cardiomyocytes isolated from PMCA4b transgenic mice demonstrated that they showed threefold higher Ser16-phospholamban phosphorylation at baseline compared with WT myocytes. In addition, the relative response to β-adrenergic stimulation was significantly reduced in PMCA4b transgenic mice (1.21 ± 0.19-fold induction after 2 mol isoproterenol stimulation in PMCA4b transgenic mice, versus 3.14 ± 0.7 in WT mice, n = 5, p<0.05). These results are in line with the previous in-vivo finding that PMCA4b transgenic mice demonstrated an attenuated response to the β-adrenergic agonist. To dissect the mechanism further we conducted a study using neonatal rat cardiomyocytes (NRCM) overexpressing PMCA4b or LacZ (control) using a recombinant adenovirus expression system. NRCM overexpressing PMCA4b showed a significant reduction by 21.4 ± 5.11% in nitric oxide levels and 24 ± 5.09% in cGMP levels compared with control cells (n = 6 each and p<0.05). In addition, PMCA4b overexpression increased cAMP levels by 94.4 ± 8.17% compared with control (n = 6, p<0.05). In keeping with the data from transgenic animals, the overexpression of PMCA4 in NRCM increased Ser16-phospholamban phosphorylation by 65.5 ± 17.1% compared with control at baseline. nNOS inhibition in control cardiomyocytes simulates the effect of PMCA4b overexpression on Ser16-phospholamban phosphorylation (n = 5, p<0.05). These findings show that PMCA4b has a relevant physiological function in the heart through the modulation of nNOS signalling, i.e. PMCA4b inhibits nNOS-mediated nitric oxide production and cGMP, which leads to cAMP elevation and increased Ser16-phospholamban phosphorylation, which modulates the β-inotropic response in the heart.

023 THE PLASMA MEMBRANE CALCIUM/CALMODULIN-DEPENDENT ATPASE 4 IS A NOVEL MODULATOR OF MYOCARDIAL HYPERTROPHY
D Oceandy, S Prehar, M Zi, T Mohamed, PJ Stanley, EJ Cartwright, N Alatwi, L Neyses. University of Manchester, Manchester, UK

Myocardial hypertrophy is an important pathological process that can lead to left ventricular dysfunction and eventually heart failure. A growing body of knowledge on the elucidation of the regulator of cardiac hypertrophy has been documented, including factors that promote hypertrophy and molecules that inhibit cardiac hypertrophy. Here we report a novel regulator of cardiac hypertrophy; the isoform 4 of plasma membrane calcium ATPase (PMCA4), which tightly interacts with and modulates neuronal nitric oxide synthase (nNOS) activity in the heart.

We used PMCA4 knockout (PMCA4−−) mice and wild-type (WT) littermates and subjected them to transverse aortic constriction (TAC) or a sham-operated procedure. Five weeks after TAC, PMCA4−− mice showed a reduced hypertrophic response compared with WT as indicated by left ventricular mass/tibia length ratio (PMCA4−−: 5.51 ± 0.42 mg/mm; WT: 7.85 ± 0.98 mg/mm; p<0.05, n > 10). Haemodynamic and echocardiography assessments revealed that TAC-operated PMCA4−− mice displayed a significant increase in contractility index (preload recruitable stroke work) compared with WT, whereas the left ventricular chamber dimension (LVEDD and EDV) was maintained at the range of sham-operated animals. However, TAC-operated WT animals showed reduced contractility as well as enlargement of left ventricular chamber dimensions, indicating a progression towards heart failure. Histological analysis demonstrated a significantly reduced cardiomyocyte cross-sectional area in TAC-operated PMCA4−− compared with WT. The activation of fetal gene programmes such as ANP, BNP and βMHC was also blunted in PMCA4−− mice. We then analyzed the molecular pathway that might be modified by PMCA4 ablation. Whereas nNOS activity was significantly increased in PMCA4−− mice, we found that Akt activation was reduced in TAC-operated PMCA4−− compared with TAC-operated WT mice.

Our results suggest that PMCA4 is a novel and important regulator of myocardial hypertrophy and further strengthens the notion that PMCA4 is part of a novel signalling pathway in the heart.
ENDOTHELIAL OVEREXPRESSION OF NOX4 ENHANCES VASO-LAXATION AND LOWERS BLOOD PRESSURE IN MICE IN VIVO

R Ray, M Zhang, A Ouattara, A Cave, A Brewer, A Shah. King’s College London, London, UK

Oxidative stress, arising from the relative overproduction of reactive oxygen species (ROS), is implicated in the genesis of cardiovascular diseases through the inactivation of nitric oxide and the modulation of redox-sensitive signalling pathways. NADPH oxidases (Noxs) are a family of enzymes that are an important source of vascular ROS, with the Nox2 and Nox4 isoforms being the major sources of endothelial ROS. Although convincing evidence supports the involvement of Nox2 in endothelial dysfunction, the role of Nox4 is unclear, with recent data suggesting that Nox4 is distinctly regulated. This study aimed to investigate the role of Nox4 in the endothelium in vivo. We generated transgenic mice with endothelial-targeted overexpression of Nox4 using a Tie2 promoter construct, and backcrossed into a C57Bl6/J background. Transgenic mice had twofold greater Nox4 mRNA expression in coronary microvascular endothelial cells (CMEC) and threefold greater aortic Nox4 protein compared with wild-type (WT) littermates (p < 0.001). Transgenic CMEC had increased NADPH-dependent superoxide production (237.6 ± 2.7 versus 186.5 ± 7.1 integrated relative light unit; n = 3, p < 0.01) and increased hydrogen peroxide generation (homovanillic acid assay) compared with WT (7.60 ± 0.70 versus 3.22 ± 0.42 μmol H2O2/106 cells; n = 3, p < 0.01). There were no changes in the expression of p22phox, SOD1-3 or catalase mRNA. In-vivo systolic and diastolic blood pressure measured by telemetry was significantly lower in transgenic mice compared with WT (systolic 117.4 ± 19 versus 125.5 ± 2.1 mm Hg and diastolic 90.1 ± 2.0 versus 98.1 ± 2.1 mm Hg; n = 5, p < 0.05). Isolated preconditioned aortic rings from transgenic mice revealed enhanced acetylcholine-induced vasorelaxation compared with WT (−log EC50 7.76 ± 0.07 versus 7.20 ± 0.05; n = 12, p < 0.001) and a difference that was abolished by catalase (1500 U/ml). Similarly, coronary microvascular resistance in isolated Langendorff-perfused transgenic hearts was reduced to a greater extent than in WT (−log EC50 5.59 ± 0.27 versus 4.80 ± 0.48; n = 5, p < 0.05), an effect also abolished by catalase (1500 U/ml). Chronic 7-day administration of the superoxide dismutase and catalase-mimetic, EUK-8, in vivo abolished the difference in blood pressure between transgenic and WT (difference 11.7 ± 1.6 mm Hg pre versus 1.6 ± 4.3 mm Hg post-EUK-8). These results indicate that endothelial overexpression of Nox4 has an unexpected beneficial effect on vasomotor tone and blood pressure, possibly via the generation of hydrogen peroxide. Taken together with earlier studies on Nox2, our results suggest that endothelial Nox4 and Nox2 have distinct and contrasting actions in vivo.

REPEATED REPLICATION AND META-ANALYSIS OF THE ASSOCIATION BETWEEN CHROMOSOME 9P21.3 AND CORONARY ARTERY DISEASE

NJ Samani, A Götz, P Braund, R McGinnis, D-A Tregouet, M Mangino, P Linsel-Nitschke, F Cambien, H Bengtsson, K Stark, S Blankenberg, L Tietz, P Ducimetiere, A Kenny, MUR Ghori, S Schreiber, NE B Mokhtari, AS Hall, RJ Dixon, AH Goodall, H Liptau, H Pollard, DF Schwartz, LA Hethom, JE Wichmann, K König, M Fischer, C Messinger, W Duwehband, P Deloukas, J Thompson, J Erdmann, A Ziegler, H Schunkert, U University of Leicester, Leicester, UK; University of Leipzig, Leipzig, Germany; Wellcome Trust Sanger Institute, Hinxton, UK; INSERM, UMR S 525, Paris, France; Université de Regensburg, Regensburg, Germany; Johannes Gutenberg University, Mainz, Germany; Unilever INSERM 780, Paris, France; UK-SH, Centre Kiel, Kiel, Germany; University of Leeds, Leeds, UK; Ludwig Maximilians University, Munich, Germany; GSF Nationales Forschungszentrum für Umwelt und Gesundheit, Neuherberg, Germany; University of Cambridge, Cambridge, UK

Recently, genome-wide association studies identified variants on chromosome 9p21.3 to affect the risk of coronary artery disease (CAD). We investigated the association of this locus with CAD in seven case–control studies and undertook a meta-analysis. A single nucleotide polymorphism (SNP), rs1333049, representing the 9p21.3 locus was genotyped in a total of 4645 patients with myocardial infarction (MI) or CAD and 5177 controls. The mode of inheritance was determined. In addition, in five of the seven studies we genotyped three additional SNP to assess a risk-associated haplotype (ACAC). Finally a meta-analysis of the present data and all previously published samples was conducted. The risk allele (C) of the lead SNP rs1333049 was uniformly associated with CAD in each study (p < 0.05). In a pooled analysis the odds ratio per copy of the risk allele was 1.29 (95% CI 1.22 to 1.37, p = 0.001). The ACAC haplotype was likewise associated with CAD (odds ratio 1.25, 95% CI 1.15 to 1.33, p < 0.10). An autosomal additive mode of inheritance best explained the underlying association. The meta-analysis in 12 004 cases and 28 949 controls increased the overall level of evidence for association with CAD to p = 6.04 x 10^-10 (odds ratio 1.24, 95% CI 1.20 to 1.29). This broad replication provides unprecedented evidence for the association between genetic variants at chromosome 9p21.3 and the risk of CAD.

INVESTIGATION OF ENDOTHELIAL PROGENITOR CELL RESPONSES FOLLOWING ELECTIVE PERCUTANEOUS CORONARY INTERVENTION

HE Thomas, HM Arthur, BD Keavney. University of Newcastle, Newcastle upon Tyne, UK

Introduction: Endothelial progenitor cells (EPC) are circulating mononuclear cells that participate in vascular repair and regeneration. A small number of studies have investigated whether a mobilisation of EPC occurs after the vascular injury occurring in percutaneous coronary intervention (PCI), with very variable results. There are many differences between these studies in terms of the methods of EPC detection, the definition of EPC used, timing of samples and the patients included. Most critically, these studies have in general not accounted for possible non-specific inflammatory responses consequent on myocardial necrosis after PCI. We sought to establish whether there is a vascular injury-specific mobilisation of EPC after PCI by carrying out a comprehensive flow cytometry assessment of all the commonly used EPC phenotypes, in patients undergoing PCI that is not complicated by myocardial necrosis.

Methods: We carried out quantification of EPC from 20 patient volunteers without diabetes, immediately before elective PCI and at 6 and 24 hours after their procedure, using flow cytometry analysis of whole blood, following the acquisition of 60 000 events in the lymphocyte gate. We measured absolute counts (using fluorescent beads) of cells expressing all the surface marker combinations of CD34, CD133 and kinase domain receptor (KDR), which have previously been used to define EPC. CD45 expression was used as an additional gating criterion for CD34+ cells. Patients were excluded from the analysis if the post-procedure troponin I measurement suggested myocardial damage had occurred. Two-way analysis of variance and paired t-tests were used to analyze the results.

Results: 20 patients (16 men) aged 58.6 ± 10.9 years (mean ± SD) received treatment to a vessel of mean ± SD length 32.5 ± 19.3 mm. EPC with the phenotypes CD34+, CD34+CD45+, CD134+, CD34+CD134+, CD34+KDR+ and CD134+KDR+ all exhibited significant changes after PCI. Overall, the pattern was of a fall of 7–15% in EPC numbers between pre-procedure and 6 hours post-procedure (significant in all the above phenotypes except CD34+CD45+ and a significant subsequent rise (5–18%) at the 24 hour sample in all the above phenotypes to levels similar to post-procedure.

The figure shows representative plots of the CD34+CD134+ and CD34+KDR+ EPC counts during the study.
Conclusions: The specific vascular injury induced by PCI did not lead to early mobilisation of EPC despite a careful assessment of multiple EPC phenotypes. Previous studies suggesting a rise in EPC after PCI have included a large proportion of patients with significant elevation of troponin post-procedure. As tissue necrosis can lead to EPC mobilisation, these previous studies may have been confounded. It is possible that the consumption of EPC at sites of vascular injury is responsible for the slight drop in EPC at 6 hours.

ISCHAEMIC PRECONDITIONING IS NOT DEPENDENT UPON GSK-3B INHIBITION

IG Webb, Y Nishino, JE Clark, MS Marber. The Rayne Institute, St Thomas’ Hospital, Kings College, London, UK

GSK-3b inactivation by phosphorylation is proposed to be the strategic point of convergence for multiple upstream pathways triggered by ischaemic preconditioning. Supportive data, however, are largely based on pharmacomodulation strategies with agents lacking selectivity. We set out to clarify the role of GSK-3b inhibition in preconditioning using a targeted mouse line with inactivation-resistant GSK-3a/b.

Methods: Ischaemic preconditioning: Isolated Langendorff-perfused hearts of 25–30 g C57BL/6 mice were subjected to 30 minutes of global ischaemia and 120 minutes of reperfusion. Hearts were randomly assigned to ischaemic preconditioning (4 × 4 minutes ischaemia/6 minutes reperfusion) or uninterrupted perfusion (CON) just before index ischaemia. Left ventricular end-diastolic (LVEDP) and developed pressures (LVDP) were recorded throughout. Infarct size was determined by planimetry of TTC-stained sections. LVDP (mm Hg) LVEDP (mm Hg)

Abstract 027

BIO, 6-bromomoiindirubin-3'-oxime; CON, uninterrupted perfusion; IP, ischaemic preconditioning; KI, knock-in; SB, SB216763; WT, wild-type.

Results: Ischaemic preconditioning resulted in significant improvements in haemodynamics during the reperfusion phase and a reduction in infarct size (fig). GSK-3b, but not GSK-3a, was phosphorylated after ischaemic preconditioning and then dephosphorylated during ischaemia to a level similar to that of controls. GSK-3b phosphorylation was abolished in GSK-3a/b knock-in mice (KI) in KI control hearts appeared protected against ischaemia compared with WT. Ischaemic preconditioning remained protective in both KI and WT hearts. LVEDP and LVDP in C57BL/6, GSK-3ab KI and WT hearts subjected to 30 minutes ischaemia/120 minutes reperfusion (control) with or without preconditioning with ischaemia, SB or BIO (table).

Conclusion: Ischaemic preconditioning results in only modest GSK-3b phosphorylation in the isolated perfused murine heart. Pretreatment with two alternative GSK-3 inhibitors failed to reduce infarct size. However, GSK-3a/b knock-in mice (KI) have targeted Ser-to-Ala mutations at these residues, preventing phosphorylation and, thus, kinase inactivation. Isolated hearts of KI and wild-type (WT) littermates were subjected to infarction with or without ischaemic preconditioning.

Abstract 027

<table>
<thead>
<tr>
<th>Treatment</th>
<th>60 min reperfusion</th>
<th>120 min reperfusion</th>
<th>Baseline</th>
<th>60 min reperfusion</th>
<th>120 min reperfusion</th>
</tr>
</thead>
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<tr>
<td>C57BL/6 CON</td>
<td>66.3 ± 1.5</td>
<td>11.9 ± 2.1</td>
<td>12.9 ± 1.9</td>
<td>6.6 ± 0.3</td>
<td>50.6 ± 3.8</td>
</tr>
<tr>
<td>IP</td>
<td>65.9 ± 1.9</td>
<td>22.5 ± 2.5*</td>
<td>22.6 ± 2.3*</td>
<td>4.3 ± 0.6</td>
<td>27.3 ± 3.4*</td>
</tr>
<tr>
<td>C57BL/6 SB</td>
<td>70.1 ± 3.8</td>
<td>14.5 ± 1.3*</td>
<td>16.4 ± 1.3</td>
<td>6.7 ± 0.7</td>
<td>65.9 ± 1.6*</td>
</tr>
<tr>
<td>BIO</td>
<td>64.6 ± 2.5</td>
<td>15.0 ± 6.4</td>
<td>13.0 ± 5.3</td>
<td>6.1 ± 0.6</td>
<td>55.9 ± 9.0</td>
</tr>
<tr>
<td>GSK3ab Ki CON</td>
<td>66.3 ± 2.7</td>
<td>32.3 ± 3.6*</td>
<td>28.3 ± 2.7*</td>
<td>5.7 ± 0.5</td>
<td>34.6 ± 4.4*</td>
</tr>
<tr>
<td>IP</td>
<td>69.7 ± 3.6</td>
<td>13.7 ± 4.3</td>
<td>14.4 ± 10.7</td>
<td>6.8 ± 0.4</td>
<td>14.1 ± 2.1*</td>
</tr>
<tr>
<td>GSK3abWT CON</td>
<td>69.8 ± 3.6</td>
<td>13.7 ± 4.3</td>
<td>14.4 ± 10.7</td>
<td>6.8 ± 0.4</td>
<td>57.6 ± 6.1</td>
</tr>
<tr>
<td>IP</td>
<td>86.8 ± 2.6</td>
<td>19.4 ± 4.3</td>
<td>21.9 ± 4.2</td>
<td>5.4 ± 0.6</td>
<td>43.3 ± 7.1</td>
</tr>
</tbody>
</table>

BIO, 6-bromomoiindirubin-3’-oxime; CON, uninterrupted perfusion; IP, ischaemic preconditioning; LVDP, left ventricular developed pressure; LVEDP, left ventricular end-diastolic pressure; SB, SB216763; WT, wild type. *p < 0.05 versus CON; †p < 0.05 versus WT.

Abstract 027

BIO, 6-bromomoiindirubin-3’-oxime; CON, uninterrupted perfusion; IP, ischaemic preconditioning; KI, knock-in; SB, SB216763; WT, wild-type.
provide cardioprotection against lethal ischaemia. Furthermore, ischaemic preconditioning remained protective in inactivation-resistant GSK-3α/b mice. Together, these data suggest that GSK-3β inhibition is unlikely to be the key determinant of cardioprotective signalling in ischaemic preconditioning in the mouse.

### Abstract 028

**RELATIONSHIPS BETWEEN PROGNOSTIC, SYMPTOMATIC AND ECHOCARDIOGRAPHIC OUTCOMES AFTER CARDIAC RESYNCHRONISATION THERAPY**

1PWX Foley, 1S Chalil, K Khadjooi, 2B Stegemann, 3MF Frenneaux, 1REA Smith, 1KF Leyva. 1Good Hope Hospital, University of Birmingham, Heart of England NHS Foundation Trust, Sutton Coldfield, UK; 2Bakken Research Centre, Medtronic Inc, Maasstricht, The Netherlands; 3University of Birmingham, Birmingham, UK

**Introduction:** Some clinical guidelines distinguish between indications for improving mortality and indications for improving symptoms. It is generally assumed that, after cardiac resynchronisation therapy (CRT), a prognostic response parallels a symptomatic response. It is also assumed that these clinical outcomes relate to reverse left ventricular remodelling. We have explored long-term mortality in relation to the symptomatic and echocardiographic response after CRT.

**Methods:** 238 patients with heart failure (aged 68.7 ± 10.7 years, mean ± SD) underwent a 6-minute walk test, a quality of life assessment and echocardiography before and at 1, 3 and every 6 months after CRT device implantation. Events were quantified for up to 7 years.

**Results:** Non-survivors derived similar symptomatic benefits to survivors, in terms of New York Heart Association class (−1.21 ± 0.8 versus −1.25 ± 0.5), 6 minutes walking distance (66.2 ± 89.2 versus 93.3 ± 123.3 m) and quality of life scores (−18.8 ± 24.4 versus −21.3 ± 26.7, all p = NS). A >10% reduction in left ventricular end-systolic volume (LVESV) predicted the composite endpoint of cardiovascular mortality or heart failure hospitalisations (heart rate (HR) 1.74, p = 0.0135), cardiovascular (HR 1.76, p = 0.0227) and total mortality (HR 1.86, p = 0.0085) (table). Receiver operator characteristic curves, however, revealed that a ≥10% reduction in LVESV had a sensitivity of 52% and a specificity of 60% in predicting total (area under curve (AUC) 0.59) or cardiovascular (AUC 0.56) mortality. Univariate Cox proportional hazards analyses of changes in LVESV (the independent variable is a ≥10% reduction) in LVESV at follow-up in relation to clinical endpoints (fig).

**Conclusions:** Patients who die early after CRT derive similar symptomatic benefits to patients who survive longer. Reverse left ventricular remodelling, assessed using two-dimensional transthoracic echocardiography, is a poor predictor of long-term survival after CRT. This raises doubts as to the use of reductions in LVESV as a surrogate measure of mortality in research studies.

### Abstract 029

**THE PATHOPHYSIOLOGICAL EFFECTS OF LEFT BUNDLE BRANCH BLOCK: IMPLICATIONS FOR MYOCARDIAL CONTRAST ECHOCARDIOGRAPHY VERSUS RADIONUCLIDE PERFUSION IMAGING FOR THE DETECTION OF CORONARY ARTERY DISEASE**

S Hayat, G Dwivedi, A Jacobsen, TK Lim, C Kinsey, R Senior. Northwick Park Hospital, Harrow, UK

**Background:** We aimed to investigate the cardiac effects of left bundle branch block (LBBB) using myocardial contrast echocardiography (MCE), to ascertain the value of MCE for the detection of coronary artery disease (CAD) in such patients and to uncover the mechanism that affects the accuracy of single-photon emission tomography (SPECT) in these patients.

**Methods:** Accordingly, 63 LBBB patients (group A), 10 left ventricular ejection fraction (LVEF) matched controls without both LBBB and CAD (group B) and 10 normal controls (group C) underwent resting echocardiography. Rest and vasodilator MCE and SPECT were undertaken in LBBB patients. Septal and posterior wall thickness, thickening, quantitative myocardial blood flow (MBF) and MBF reserve were measured.

**Results:** SW/PW thickness and thickening, respectively, were smaller (p = 0.03 and p<0.001) in group A compared with both groups B and C, but resting septal/posterior wall MBF and MBF reserve ratios were similar in all three groups. MBF reserve not MBF was reduced in groups A and B (2.2 ± 0.8 versus 2.2 ± 0.2, p = 0.98) compared with group C (3.1 ± 0.5, p<0.005). Septal wall thickness was an independent predictor (p = 0.006) of SPECT defects in LBBB patients without CAD. MCE (92%) had similar sensitivity to SPECT (92%), but the specificity of MCE (95%) was superior (p<0.001) to SPECT (47%) for the detection of CAD.

**Conclusions:** Despite asymmetric reduction in septal wall thickness and function, MBF is preserved and MBF reserve is homogeneously reduced in LBBB patients. As a result of the partial volume effect, the accuracy of SPECT for the detection of CAD was significantly compromised compared with MCE.

### Abstract 030

**LOCAL PROVIDION OF PRIMARY PERCUTANEOUS CORONARY INTERVENTION IN A DISTRICT GENERAL HOSPITAL SETTING: EXTENSION TO 24/7 PROVISION DRAMATICALLY REDUCES THE NEED FOR RESCUE PERCUTANEOUS CORONARY INTERVENTION WITH ACCEPTABLE DOOR-TO-BALLOON TIMES**

PK Kong, D Connolly, R Ahmad. Sandwell General Hospital, Sandwell and West Birmingham Hospitals NHS Trust, Birmingham, UK

**Background:** Most hospitals providing a daily 24-hour (24/7) primary percutaneous coronary intervention (PPCI) service for ST elevation myocardial infarction are large tertiary centres. The provision of a 24/7 PPCI service by district general hospitals (DGH) has not been fully evaluated.

**Aims:** To assess the feasibility and outcomes of local DGH provision of a 24/7 PPCI service.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hazard ratio (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular death or hospitalisation for HF</td>
<td>1.74 (1.11 to 2.70)</td>
<td>0.0135</td>
</tr>
<tr>
<td>Death from any cause or hospitalisation for MCE</td>
<td>1.49 (1.00 to 2.23)</td>
<td>0.0563</td>
</tr>
<tr>
<td>Cardiovascular death</td>
<td>1.76 (1.08 to 2.87)</td>
<td>0.0227</td>
</tr>
<tr>
<td>Death from any cause</td>
<td>1.86 (1.17 to 2.96)</td>
<td>0.0085</td>
</tr>
</tbody>
</table>

HF, heart failure; MCE, major cardiovascular events.
Methods: A retrospective audit of hospital databases was carried out on consecutive patients receiving PPCI at Sandwell General Hospital, a DGH serving a population of 250,000. The hospital has two interventional cardiologists with additional after-hours cover by three interventionists from its sister hospital, City Hospital, Birmingham. In particular, changes in door-to-balloon times and rescue percutaneous coronary intervention (RPCI) were examined in relation to extension to a 24/7 service.

Results: Between April 2003 and November 2007, there were 198 PPCI, with door-to-balloon times ascertainable in 137 PPCI (figs 1 and 2). The mean age was 65 years (range 26–100), 70% patients were men and 14% had diabetes. Four phases were audited: phase 1 (April 2003 to June 2005) when PPCI was performed for thrombolysis contraindication; phase 2 (July 2005 to January 2006) when PPCI was provided during 08:00–16:00 hours on weekdays; phase 3 (February 2006 to December 2006) when PPCI was provided during 08:00–20:00 hours daily; phase 4 (January 2007 to November 2007) when 24/7 PPCI was provided. From phases 2 to 4, median door-to-balloon times increased from 54 to 75 minutes, the proportion of door-to-balloon times under 90 minutes decreased from 89% to 61%, the proportion of PPCI occurring 20:00–08:00 after-hours increased from 0% to 52%, the proportion of PPCI with door-to-balloon times greater than 90 minutes that occurred after-hours increased from 0% to 47%, PPCI as a proportion of PPCI and RPCI increased from 58% to 99%, and inpatient mortality decreased from 11% to 7% (table 1). During phase 4, 74% PPCI were performed by the two in-house interventionists. Overall, 15% (29 patients) had cardiogenic shock, of which 41% (12 patients) died. 19 of the patients with cardiogenic shock required intraaortic balloon pump (IABP) out of 20 IABP used. The 12 patients with cardiogenic shock contributed 80% to the 15 inpatient deaths (table 2).

Conclusions: This audit demonstrates that it was feasible for a DGH to deliver a 24/7 PPCI service with favourable door-to-balloon times. The rolling out from office hours to 24/7 increased the median door-to-balloon times. There was a dramatic reduction in the need for RPCI. Inpatient mortality appeared to improve but the numbers were too small to conclude firmly. During the 24/7 phase, the small number of in-house interventionists was able to perform 74% of the PPCI as a result of most of the PPCI (68%) occurring during hours and the indispensable cross-site additional cover by the sister hospital. We believe that good provision of a 24/7 PPCI service by a DGH is feasible with organisational will and should be an alternative or complementary model of care to provision in large infarct centres.

<table>
<thead>
<tr>
<th>Abstract 030 Table 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase</td>
</tr>
<tr>
<td>All</td>
</tr>
<tr>
<td>April 2003–June 2005</td>
</tr>
<tr>
<td>July 2005–January 2006</td>
</tr>
<tr>
<td>February 2006–December 2006</td>
</tr>
<tr>
<td>January 2007–November 2007</td>
</tr>
</tbody>
</table>

D2B, door-to-balloon times; PPCI, primary percutaneous coronary intervention.

<table>
<thead>
<tr>
<th>Abstract 030 Table 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase</td>
</tr>
<tr>
<td>All</td>
</tr>
<tr>
<td>April 2003–June 2005</td>
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<tr>
<td>July 2005–January 2006</td>
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<tr>
<td>February 2006–December 2006</td>
</tr>
<tr>
<td>January 2007–November 2007</td>
</tr>
</tbody>
</table>

PPCI, primary percutaneous coronary intervention; RPCI, rescue percutaneous coronary intervention.
Background: Targeting specific antihypertensive therapy to phenotypes who will best respond is an attractive concept. Relative aldosterone excess, characterised by a raised aldosterone to renin ratio (ARR), is a common subtype in hypertension (up to 15% of patients) that is often associated with poor response to therapy. Moreover, it is well known that aldosterone exerts various deleterious effects on the cardiovascular system. Patients with a high ARR have aldosteronism or aldosterone-sensitive hypertension is debated. However, it is important to know whether spironolactone is superior to other diuretics such as bendroflumethiazide in this setting. We hypothesised that patients with a high ARR (HR) would show a better hypotensive response to specific aldosterone receptor blockade with spironolactone than conventional low-dose thiazide diuretic therapy with bendroflumethiazide in comparison with patients with a low ARR (LR).

Methods: We conducted a double-blind, randomised, crossover, trial in hypertensive patients (systolic ambulatory blood pressure (SABP) >140 mm Hg) with either a HR (≥750 and a plasma aldosterone >250 pmol/l) or LR (<300 and a plasma renin activity <10 ng/ml per hour). Each stratum underwent 12 weeks of treatment each with spironolactone 50 mg per day and bendroflumethiazide 2.5 mg per day in random order separated by a 2-week washout. The primary endpoint was the difference (Δ) in mean SABP comparing the HR with the LR (ΔStrata). Secondary endpoints were mean diastolic, day and night time ambulatory blood pressure differences (spironolactone – bendroflumethiazide) in comparison with patients at a low ARR (LR).

Results: 111 subjects (60 HR and 51 LR) completed the study. The mean age in the HR group was 55.6 years versus 58.4 years in the LR group. There was a male predominance of 65% in the HR group. Mean ARR was 4.35 (CI 2.15 to 7.55, p<0.001). In the LR group ARR was 0.51 (CI 0.27 to 0.75, p<0.001). The ΔStrata (HR versus LR) was −1.58 mm Hg (CI (−2.08, −1.08) mm Hg, p<0.001). In the LR group SABP was 129.7 mm Hg on spironolactone versus 133.1 mm Hg on bendroflumethiazide (Δ=−3.43 (CI −4.33 to −2.52) mm Hg, p<0.001). In the HR group SABP was 129.4 mm Hg on spironolactone versus 134.4 mm Hg on bendroflumethiazide (Δ=−5.01 (CI −7.51 to −2.52) mm Hg, p<0.001). The ΔStrata (HR versus LR) was −1.58 mm Hg (CI (−2.08, −1.08) mm Hg, p=0.0394). Results were similar for the secondary endpoints. Moreover neither renin nor aldosterone levels independently predicted the response to spironolactone. The results were also independent of concomitant angiotensin-converting enzyme inhibitor or angiotensin receptor blocker use (figs 1 and 2).

Conclusion: In the doses used, over 3 months duration, ARR does not predict the therapeutic response to the mineralocorticoid antagonist spironolactone. Spironolactone 50 mg was significantly more effective than bendroflumethiazide 2.5 mg irrespective of ARR, renin or aldosterone.

Abstract 031 Table 1 Blood pressure differences (spironolactone–bendroflumethiazide) in low ARR

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean</th>
<th>SD</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SABP</td>
<td>−5.01</td>
<td>9.66</td>
<td>0.001</td>
</tr>
<tr>
<td>Clinic SBP</td>
<td>−4.50</td>
<td>11.95</td>
<td>0.0042</td>
</tr>
<tr>
<td>Day SABP</td>
<td>−5.46</td>
<td>9.75</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Night SABP</td>
<td>−4.30</td>
<td>11.87</td>
<td>0.0068</td>
</tr>
<tr>
<td>DABP</td>
<td>−2.56</td>
<td>6.32</td>
<td>0.0027</td>
</tr>
<tr>
<td>Clinic DBP</td>
<td>−1.68</td>
<td>6.90</td>
<td>0.0065</td>
</tr>
<tr>
<td>Day DABP</td>
<td>−3.01</td>
<td>6.24</td>
<td>0.0014</td>
</tr>
<tr>
<td>Night DABP</td>
<td>−1.85</td>
<td>8.62</td>
<td>0.1015</td>
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</table>

ARR, ratio of aldosterone to renin; DABP, diastolic ambulatory blood pressure; DBP, diastolic blood pressure; SABP, systolic ambulatory blood pressure; SBP, systolic blood pressure.

Abstract 031 Table 2 Blood pressure differences (spironolactone–bendroflumethiazide) in high ARR

<table>
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<tr>
<th>Variable</th>
<th>Mean</th>
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<tbody>
<tr>
<td>SABP</td>
<td>−3.43</td>
<td>9.79</td>
<td>0.0157</td>
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<tr>
<td>Clinic SBP</td>
<td>−3.20</td>
<td>15.76</td>
<td>0.1537</td>
</tr>
<tr>
<td>Day SABP</td>
<td>−3.28</td>
<td>10.91</td>
<td>0.0157</td>
</tr>
<tr>
<td>Night SABP</td>
<td>−3.15</td>
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<td>0.0032</td>
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<tr>
<td>DABP</td>
<td>−2.22</td>
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<td>0.0030</td>
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<td>Clinic DBP</td>
<td>−1.54</td>
<td>7.49</td>
<td>0.1486</td>
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<tr>
<td>Day DABP</td>
<td>−2.32</td>
<td>5.97</td>
<td>0.0077</td>
</tr>
<tr>
<td>Night DABP</td>
<td>−2.35</td>
<td>5.73</td>
<td>0.0051</td>
</tr>
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</table>

ARR, ratio of aldosterone to renin; DABP, diastolic ambulatory blood pressure; DBP, diastolic blood pressure; SABP, systolic ambulatory blood pressure; SBP, systolic blood pressure.
ACCURATE DETECTION OF CORONARY ARTERY DISEASE BY ECHOCARDIOGRAPHY USING PERFLUBUTANE POLYMER MICROSPHERES, A NOVEL CONTRAST AGENT: COMPARISON WITH NUCLEAR PERFUSION IMAGING IN TWO PHASE III MULTICENTRE CLINICAL TRIALS

1R Senior, 2M Zabalgoitia, 3M Monaghan, 4M Main, 5JL Zamorano, 6K Tiemann, 7L Agati, 8NJ Weissman, 9AL Klein, 10TH Marwick, 11M Ahmad, 12AN DeMaria, 13H Becher, 14S Kaul, 15JE Udelson, 16FJ Wackers, 17RC Walovitch, 18MH Picard.

Northwick Park Hospital, Harrow, UK; 2University of Texas Health Science Centre, San Antonio, Texas, USA; 3King’s College Hospital, London, UK; 4University of California–San Diego, San Diego, California, USA; 5Mid America Heart Institute, Kansas City, Missouri, USA; 6University Clinic San Carlos, Madrid, Spain; 7University of Bona, Bona, Germany; 8La Sapienza University of Rome, Rome, Italy; 9Cardiovascular Research Institute, Washington, DC, USA; 10Cleveland Clinic, Cleveland, Ohio, USA; 11Princess Alexandra Hospital, Brisbane, Australia; 12University of Texas, Galveston, Texas, USA; 13University of California–San Diego, San Diego, California, USA; 14Oregon Health Sciences University, Portland, Oregon, USA; 15Yale University School of Medicine, New Haven, Connecticut, USA; 16Accusphere Inc, Watertown, South Dakota, USA; 17Massachusetts General Hospital, Boston, Massachusetts, USA

Background: Real-time assessment of myocardial perfusion (RAMP) imaging 1 and 2 are phase III trials conducted to determine whether perflubutane polymer microspheres (PPM) injectable suspension (formerly AI-700), a synthetic biodegradable ultrasound contrast agent, can assess myocardial perfusion and detect coronary disease in patients being evaluated for inducible ischaemia.

Methods: Among RAMP-1 and RAMP-2 angina patients from 28 international sites, those who underwent PPM echocardiography (ECHO) imaging (real-time and triggered) as well as 99mTc quantitative myocardial perfusion imaging (nuclear) at rest and at dipyridamole stress comprised the efficacy population (n = 662). Images were interpreted for the presence of a defect (wall motion and/or perfusion) by independent blinded readers (three ECHO and/or nuclear). Disease was defined using quantitative coronary angiography (>70% stenosis), if available, or 90-day outcome with clinical history and nuclear assessment. Primary efficacy endpoints (accuracy followed by sensitivity and specificity) were evaluated using non-inferiority and superiority analysis (one-sided alpha = 0.025) compared with nuclear. The median performing nuclear reader was the comparator in RAMP-2.

Results: RAMP-1 and RAMP-2 consisted of 285 patients (125 disease positive, 44%) and 377 patients (220 disease positive, 58%), respectively. Compared with nuclear, six, four and three of six ECHO readers were non-inferior for accuracy, sensitivity and specificity, respectively. Moreover, two and three ECHO readers also demonstrated superiority for specificity and sensitivity, respectively (table). The majority of adverse events (headache, chest pain or discomfort, nausea and flushing) occurred after dipyridamole dosing, were mild, transient and required no treatment.

Conclusions: PPM ECHO imaging was well tolerated and has similar diagnostic performance compared with nuclear perfusion in chest pain patients being evaluated for inducible ischaemia.

ECG AND REPERFUSION: DO WE KNOW WHAT WE ARE DOING?

RJ Trent, H Raju, JD Jones, FM Christopherson. Wrexham Maelor Hospital, Wrexham, UK

Background: Resolution of ST segment elevation is the principal method employed to assess coronary reperfusion in patients with ST elevation myocardial infarction (STEMI), and will thus inform decisions about the necessity of rescue percutaneous coronary intervention. Variation in the ST segment is reported with changes in frequency response settings, ie, use of ECG filters (fig 1). Therefore, the inconsistent use of ECG filter settings may influence the assessment of coronary reperfusion. UK guidelines exist for standard 12-lead ECG acquisition (Society for Cardiological Science and Technology (SCST), 2006); however, their effect on UK practice re ST shift monitoring is undetermined.

Objectives: To measure adherence to current ECG acquisition guidelines with respect to the interpretation of ST segment shift in STEMI patients in UK practice. To examine the consistency of ECG recordings in individual units within the same hospital.

Methods: Acute NHS Trusts in England and Wales were surveyed. Individual emergency departments (ED), medical admissions units (MAU) and coronary care units (CCU) were contacted by phone; a standard proforma was sent by fax or e-mail for completion by a senior nurse in each department. Anonymised ECG were also requested from individual units to establish standard and filtered settings.

Results: A total of 221 acute NHS Trusts were approached. Completed returns were received from 97 (43.9%) hospitals, equating to a total of 133 departments, of which 99 (74.4%) administer thrombolysis or monitor patients postlysis. In the vast majority of units (132/133, 99.2%) ECG are performed by nursing staff. Nearly half of all departments surveyed (64/133, 48.1%) routinely use filtered ECG recordings, with a minority (52/133, 39.1%) regularly labelling filtered ECG. A majority of senior nurses (83/133, 62.4%) believe that the use of the filter assisted with interpretation of ECG changes. Just over half of respondents (78/133, 58.5%) believe that the use of the filter assisted with interpretation of ECG changes.

Abstract 032

<table>
<thead>
<tr>
<th>RAMP-1</th>
<th>RAMP-2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ECHO (%) (95% CI)</strong></td>
<td><strong>Nuclear (%) (95% CI)</strong></td>
</tr>
<tr>
<td>Accuracy</td>
<td></td>
</tr>
<tr>
<td>Reader 1</td>
<td>66 (61 to 72)*</td>
</tr>
<tr>
<td>Reader 2</td>
<td>67 (61 to 72)*</td>
</tr>
<tr>
<td>Reader 3</td>
<td>71 (68 to 76)*</td>
</tr>
<tr>
<td>Sensitivity</td>
<td></td>
</tr>
<tr>
<td>Reader 1</td>
<td>77 (68 to 84)*</td>
</tr>
<tr>
<td>Reader 2</td>
<td>57 (48 to 68)</td>
</tr>
<tr>
<td>Reader 3</td>
<td>50 (41 to 59)</td>
</tr>
<tr>
<td>Specificity</td>
<td></td>
</tr>
<tr>
<td>Reader 1</td>
<td>58 (50 to 66)</td>
</tr>
<tr>
<td>Reader 2</td>
<td>75 (68 to 82)*</td>
</tr>
<tr>
<td>Reader 3</td>
<td>88 (82 to 93)*</td>
</tr>
</tbody>
</table>

ECHO, echocardiography; RAMP, real-time assessment of myocardial perfusion. *non-inferior; †superior; p<0.025.
133, 54.9%) were able to supply data regarding their specific filter settings. Of these, 16/73 (21.9%) use correct SCST settings with the filter on (fig 2A), whereas only 3/73 (4.1%) use the corresponding SCST recommendations for unfiltered ECG recordings (fig 2B).

When thrombolysis is delivered “front of house”, 12 hospitals provided paired data from either ED or MAU and CCU. Only 7/12 of these paired sites recorded filter frequency settings, all of which differed between ED/MAU and CCU.

**Conclusion:** ECG are not being performed as recommended by the SCST 2006 guidelines in the majority of acute trusts analyzed in this audit. Notably, there is a lack of conformity in the use of ECG filters between departments within individual hospitals, with a variety of settings being used nationally. Given the importance of ST resolution as a measure of reperfusion for STEMI patients, it is paramount that filter frequency response settings are standardised for all ECG machines in order to facilitate objective comparison.

---

**Abstract 033 Figure 1**

![Diagram A: Non-compliant 78% (Compliant 22%)](image1)

**Abstract 033 Figure 2**

![Diagram B: Non-compliant 96% (Compliant 4%)](image2)

133, 54.9%) were able to supply data regarding their specific filter settings. Of these, 16/73 (21.9%) use correct SCST settings with the filter on (fig 2A), whereas only 3/73 (4.1%) use the corresponding SCST recommendations for unfiltered ECG recordings (fig 2B). When thrombolysis is delivered “front of house”, 12 hospitals provided paired data from either ED or MAU and CCU. Only 7/12 of these paired sites recorded filter frequency settings, all of which differed between ED/MAU and CCU.

**Conclusion:** ECG are not being performed as recommended by the SCST 2006 guidelines in the majority of acute trusts analyzed in this audit. Notably, there is a lack of conformity in the use of ECG filters between departments within individual hospitals, with a variety of settings being used nationally. Given the importance of ST resolution as a measure of reperfusion for STEMI patients, it is paramount that filter frequency response settings are standardised for all ECG machines in order to facilitate objective comparison.

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**Abstract 034**

**ECHO IDENTIFICATION AND QUANTIFICATION OF INFLAMMATORY MOLECULES IN THE HEART**

1JSM Yeh, 2C Sennoga, 3E McConnell, 4R Eckersley, 5M Tang, 6D Dawson, 7JJ Boyle, 8JM Saddon, 9A Stepney, 10DO Haskard, 11P Nihoyannopoulos. 1National Heart and Lung Institute, Imperial College, London, UK; 2Imaging Sciences Department, Imperial College, London, UK; 3Department of Bioengineering, Imperial College, London, UK; 4Echocardiography, Hammersmith Hospital, London, UK; 5Histopathology Department, Imperial College, London, UK; 6Chemistry Department, Imperial College, London, UK; 7Central Biomedical Services, Imperial College, London, UK

**Background:** Inflammation underlies important cardiovascular diseases such as coronary heart disease, myocarditis and heart transplantation rejection. The ability to detect the extent and degree of inflammation in the heart at the molecular level has potential diagnostic, prognostic and patient management values. E-selectin is an inflammatory molecule expressed on activated endothelial cells, involved in the recruitment of leucocytes to sites of inflammation. We designed targeting microbubbles as contrast agents for real-time imaging and quantification of E-selectin expressions in the heart using echo.

**Methods:** Phospholipid microbubbles targeting E-selectin were prepared by conjugating reduced anti-E-selectin F(ab’2) onto the microbubble surface using maleimide. Microbubbles were examined microscopically and size distribution determined using electrozone sensing; specific binding was confirmed on E-selectin coated plates. Lipopolysaccharide (a bacterial endotoxin) was used to induce global E-selectin expression in the mouse heart. Quantification of E-selectin mRNA in the heart at different time points post-lipopolysaccharide induction using real-time reverse transcription PCR correlated with the quantification of E-selectin protein using radiolabelled antibodies published elsewhere. Targeted microbubble echo to detect and quantify E-selectin in the heart was done on anaesthetised adult male C57Bl6 mice (wild-type) at 4–5 hours or 5–6 hours post-lipopolysaccharide induction, when the levels of E-selectin expression differed by approximately twofold between these two time points. Targeting microbubbles (9 x 10^7) were injected as a bolus via the tail vein. Acuson Sequoia 512 with the 15L8-S transducer in contrast pulse sequencing (a bubble-specific mode) at 14 MHz, low power (mechanical index = 0.22–0.26) and fixed gain were used. Lipopolysaccharide-treated homozygote E-selectin knock-out mice on C57Bl6 genetic background were used as negative controls. Ultrasound image signal intensities were log-decompressed and quantified off-line using dedicated YABCO software.

**Results:** Targeting microbubbles were stable; their mean and maximum diameters were 2 and 6 μm, respectively, allowing non-obstructed flow in the microvasculature. Targeted microbubble

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**Abstract 034 Figure 1**

KO, knock-out; LPS, lipopolysaccharide; MB, microbubble; WT, wild-type.
Patients stratified by QRS duration and left ventricular ejection fraction (LVEF) were grouped according to LVEF and QRS duration. Consecutive patients (n = 336) who were admitted with a diagnosis of MI from the period April 2006 to October 2007 were grouped according to LVEF and QRS duration (see table). A total of 27% patients had an LVEF less than 35% and 10% had a QRS greater than 120 ms. On the basis of LVEF and QRS alone, 15/336 (4%) were eligible for ICD and 77/336 (23%) required a Holter with a view to VT stimulation test. Assuming 60 499 ST or non-ST elevation MI per year for England and Wales, this equates to an additional 2420 ICD and 13 915 Holter tests per year.

Conclusions: Implementation of current NICE guidance on ICD therapy for primary prevention after MI demands a substantial increase in the provision of ICD and Holter monitoring.

Abstract 036 Table 1

<table>
<thead>
<tr>
<th></th>
<th>Patients not treated who should have been</th>
<th>Patients treated appropriately</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender male : female</td>
<td>10 : 12</td>
<td>64 : 29</td>
</tr>
<tr>
<td>% Diabetic</td>
<td>36</td>
<td>12.9</td>
</tr>
<tr>
<td>Age, years (median and range)</td>
<td>70.2 (52–87)</td>
<td>59.5 (34–83)</td>
</tr>
<tr>
<td>Weight, kg (median and range)</td>
<td>72.2 (49–118)</td>
<td>81.8 (45–120)</td>
</tr>
<tr>
<td>Serum creatinine, mmol (median and range)</td>
<td>119 (59–516)</td>
<td>92.8 (52–550)</td>
</tr>
<tr>
<td>GFR (median and range)</td>
<td>81.6 (14–120)</td>
<td>92.1 (11–218)</td>
</tr>
</tbody>
</table>

GFR, glomerular filtration rate.
Background Purpose: Recent problems related to the use of thiazolidinediones highlight the difficulties in managing diabetes in patients with congestive heart failure (CHF). An alternative and cheaper approach is to use the insulin sensitiser, metformin. Previous concerns of lactic acidosis with biguanides have generally not been a problem with metformin. On the contrary, observational data suggest that metformin may actually be beneficial for CHF through its insulin sensitising properties. This study aimed to evaluate the safety of metformin and to explore any evidence of benefit of its use in CHF in a large population prescription database study.

Methods: The Health Informatics Centre dispensed prescribing database for the population of Tayside, Scotland (400 000 people) was employed. Patients with incident CHF (n = 774) between 1994 and 2003 were identified through administrative medical records based on International Classification of Diseases (ICD) version 9 code 428, ICD-10 code-50 and through the use of combined CHF medications of loop diuretics and angiotensin-converting enzyme inhibitors. Subjects were grouped according to oral hypoglycaemic agents into three study cohorts: metformin monotherapy (n = 90), sulfonylurea monotherapy (n = 381) and combination (n = 303). The Cox regression model was used to assess differences in all-cause mortality, all-cause hospitalisation and a combination of all-cause hospitalisation or mortality by estimation of relative risks.

Results: The average age of subjects was 75 ± 9.79 years (range 42–99), 55% were men and follow-up was for 10 years. Compared with sulfonylurea monotherapy, fewer deaths occurred in patients receiving metformin only: 295 (77.4%) for sulfonylurea monotherapy versus 54 (60.0%) for metformin monotherapy, unadjusted risk ratio (RR) 0.78, 95% CI 0.57 to 1.06. After adjusting for differences between groups (age, sex, creatinine and medication) the RR was 0.90 (95% CI 0.63 to 1.28) and 201 (66.3%) for combination therapy (RR 0.72, 95% CI 0.58 to 0.88). One year mortality was also observed: fewer deaths occurred in the metformin and combination group compared with sulfonylurea monotherapy; the adjusted RR for metformin was 0.48 (95% CI 0.24 to 0.96) and RR 0.66 (95% CI 0.46 to 0.96) for the combination group. A reduction in hospitalisations was also observed: 346 (90.8%) for sulfonylurea monotherapy versus 70 (77.8%) for metformin (RR 0.74, 95% CI 0.57 to 0.96) and 264 (87.1%) for sulfonylurea monotherapy versus 70 (77.8%) for metformin (RR 0.72, 95% CI 0.58 to 0.88). One year mortality was also observed: fewer deaths occurred in the metformin and combination group compared with sulfonylurea monotherapy; the adjusted RR for metformin was 0.48 (95% CI 0.24 to 0.96) and RR 0.66 (95% CI 0.46 to 0.96) for the combination group. Combined endpoints (all-cause hospitalisation or mortality) were lower in the metformin group compared with sulfonylurea monotherapy (RR 0.74, 95% CI 0.56 to 0.99) and RR 0.92 (95% CI 0.77 to 1.10) for the combination group.

Conclusion: In this large observational study of CHF patients treated with oral hypoglycaemic agents, those treated with metformin alone or in combination were associated with a markedly lower risk of morbidity and mortality when compared with those receiving sulfonylurea alone. A clinical trial of metformin in CHF is warranted.
it is unknown whether adding BNP would enhance risk prediction over and above the GRACE score.

**Methods:** We recruited 449 consecutive ACS patients and measured the admission GRACE score and bedside BNP levels. The main outcome measure was either all-cause mortality, re-admission with ACS or congestive heart failure (defined as a cardiovascular event) at 10 months from presentation.

**Results:** Of the 449 patients, 120 patients presented with ST elevation myocardial infarction (27%). There were 90 cardiovascular events at 10 months. Both higher GRACE terciles and higher BNP terciles predicted cardiovascular events. There was a significant but partial correlation between the GRACE score and log BNP (R = 0.552, p = 0.001). On multivariate analyses, after adjusting for the GRACE score itself, increasing BNP terciles independently predicted cardiovascular events (second BNP tercile adjusted relative risk (RR) 2.28 (95% CI 1.15 to 4.51) and third BNP tercile adjusted RR 4.91 (95% CI 2.62 to 9.22)). Patients with a high GRACE score and high BNP were more likely to experience cardiovascular events at 10 months (RR 6.00, 95% CI 2.40 to 14.83) compared with those with high GRACE scores and low BNP (RR 2.40, 95% CI 0.76 to 7.56).

**Conclusion:** In ACS, BNP predicts cardiovascular events over and above the GRACE score. In addition, the combined use of both the GRACE score and BNP further identifies a subset of ACS patients at particularly high risk. This implies that both the GRACE score and BNP reflect somewhat different risk attributes when predicting adverse prognosis in ACS and their synergistic use can enhance risk stratification in ACS, if these data can be confirmed by other studies.

**Abstract 039**

**ADDITION OF B-TYPE NATRIURETIC PEPTIDE TO THE THROMBOLYSIS IN MYOCARDIAL INFARCTION RISK SCORE ENHANCES RISK STRATIFICATION IN ACUTE CORONARY SYNDROME**

DSC Ang, L Wei, CC Lang, AD Struthers. University of Dundee, Dundee, UK

**Background:** In acute coronary syndrome (ACS), both the thrombolysis in myocardial infarction (TIMI) risk score and B-type natriuretic peptide (BNP) predict adverse prognosis. However, it is unknown whether the addition of BNP to the TIMI risk score would enhance risk stratification in ACS.

**Methods:** We recruited 329 consecutive non-ST elevation ACS patients and measured admission TIMI risk scores and bedside BNP levels. The main outcome measure was either all-cause mortality, re-admission with ACS or congestive heart failure (defined as a cardiovascular event) at 10 months from presentation.

**Results:** Of the 329 patients, 93 patients presented with unstable angina (28%) (fig). There were 72 cardiovascular events at 10 months. Both higher TIMI risk terciles and higher BNP terciles predicted cardiovascular events. There was a significant but partial correlation between the TIMI risk score and log BNP (R = 0.439, p < 0.001). On multivariate analyses, after adjusting for the TIMI risk score itself, increasing BNP terciles independently predicted cardiovascular events (second BNP tercile adjusted relative risk (RR) 2.28 (95% CI 1.15 to 4.51) and third BNP tercile adjusted RR 4.91 (95% CI 2.62 to 9.22)). Patients with a high TIMI score and high BNP were more likely to experience cardiovascular events at 10 months (RR 6.00, 95% CI 2.40 to 14.83) compared with those with high TIMI scores and low BNP (RR 2.40, 95% CI 0.76 to 7.56).

**Conclusion:** In ACS, BNP predicts cardiovascular events over and above the TIMI risk score. This suggests that both methods reflect different risk attributes when predicting adverse prognosis in ACS. In addition, the combined use of both the TIMI risk score and BNP further identifies a subset of ACS patients at particularly high risk. Therefore the synergistic use of both modalities has the potential to enhance risk stratification in ACS.
of groin haematoma and large groin haematoma (>5 cm diameter) after PCI was more frequent and the overall length of hospital stay longer for patients receiving heparin (haematoma 43/148 versus 16/207; p<0.001; large haematoma 13/148 versus 3/207; p<0.001; length of stay 14 ± 7 days versus 11 ± 1; p<0.05). The incidence of any bleeding events by TIMI or GUSTO criteria was also more frequent in the heparin group (17/148 versus 5/207; p<0.001). Although major adverse cardiac event-free survival by Kaplan-Meier estimates at 12 months did not differ between cohorts (89.9% versus 91.8%; p = ns), overall event-free survival favoured those treated with bivalirudin (78.4% versus 89.4%; p<0.01).

Conclusions: In a high-risk population of patients undergoing PCI after presentation with troponin-positive ACS, these data suggest that a primary strategy of bivalirudin use during PCI will reduce the use of glycoprotein IIb/IIIa inhibitors and subsequent bleeding events, facilitating early post-procedural discharge without a compromising incidence of major adverse cardiac events at 1 year.

041 THE PREVALENCE OF ABSOLUTE AND RELATIVE CONTRAINDICATIONS TO STATIN THERAPY AFTER ACUTE CORONARY SYNDROME

1KM Bailey, 1The Space Rocket investigators. 1Leeds University, Leeds, UK; 2NHS, UK

Objective: To explore the incidence of absolute or relative contraindications to statin therapy in patients after acute coronary syndrome (ACS).

Design: Screening data from a multicentre clinical trial comparing statin regimes to heparin in 11 305 patients were screened, of whom 7941 were confirmed as having ACS (fig). Of these no information was collected on statin contraindications in 2461 patients because of individual characteristics to be considered when prescribing. Fortunately, serious adverse events with statins are rare, but a large proportion of these events occur in patients with concomitant conditions or contraindications. Clinicians need to be aware of the caution advised when prescribing statins to ensure there is no increase in the risk of serious adverse events. Patients should then be prescribed either an alternative agent or be commenced at a lower starting dose.

042 ASSESSMENT OF PERCUTANEOUS CORONARY INTERVENTION PRACTICE: RESULTS OF A NETWORK-WIDE PEER REVIEW AUDIT ASSESSMENT

MWH Behan, GF Dixon, L Blows, D Hildick-Smith, S Holmberg, A deBelder. Sussex Cardiac Centre, Brighton, UK

Background: Cardiac network collective governance is increasingly difficult with the expansion of percutaneous coronary intervention (PCI) services. Tools for assessing PCI are usually based on adverse outcomes; however, we have developed an inclusive mechanism to audit individual PCI operator case selection, technical and strategic skill on a network-wide basis. We report here on our 16-month experience.

Methods and Results: Our network consists of a tertiary centre and two district general hospitals (DGH) performing PCI, with 10 interventionists and over 2000 PCI are performed annually. Over a 16-month period, a monthly review meeting was held, in which 10% of cases from throughout the network (n = 326), were randomly selected (at least one case per operator) and examined by three reviewers (one tertiary and one DGH interventionalist and one cardiac surgeon) on a rotational basis. The appropriateness of intervention, strategy and outcome were evaluated and recorded. Results were made available for the network overall but were also broken down for individual operators. Operator volume varied so results were presented as percentages to preserve anonymity. Our overall network results are shown in the table. An example of individual breakdown for appropriateness of strategy is shown in the figure. From this figure it can be seen that individual operators 5, 6 and 8 were adopting appropriate strategies less often than their colleagues.

Conclusion and Discussion: This tool has demonstrated that appropriate standards of care are maintained across the network. In this model feedback to individual operators allows debate and provokes thought about PCI decisions. It provides an equitable review system—as the committee changes each month, and all interventionists are involved in the process. Individual operators are made aware of how they are performing and therefore trends have been identified that have helped improve practice. This audit tool

Abstract 042

<table>
<thead>
<tr>
<th>Assessment</th>
<th>% (n = 326)</th>
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</thead>
<tbody>
<tr>
<td>Anatomy suitable for PCI</td>
<td>94.2</td>
</tr>
<tr>
<td>Lesion sufficiently severe for treatment</td>
<td>96</td>
</tr>
<tr>
<td>Strategy chosen appropriate</td>
<td>86.2</td>
</tr>
<tr>
<td>Satisfactory outcome</td>
<td>90.8</td>
</tr>
</tbody>
</table>

PCI, percutaneous coronary intervention.
Several primary cardiac arrhythmia syndromes are known to have a genetic basis and are caused by mutations in ion channel genes. These mutations cause abnormal ionic currents which can lead to ECG abnormalities and cardiac arrhythmias. These syndromes, known as cardiac channelopathies, include long QT syndrome (LQTS), short QT syndrome, Brugada syndrome and catecholaminergic polymorphic ventricular tachycardia (CPVT), and are responsible for up to 40% of all cases of sudden unexplained cardiac deaths in those under the age of 35 years.

Methods: All patients attending the inherited cardiac clinic at the Royal Victoria Hospital were reviewed and patients referred for investigation of, or diagnosed with, a cardiac channelopathy were included in the analysis.

Results: To date, 32 families have been genetically diagnosed with LQTS. In these families, 250 individuals have been genetically screened; 141 (56%) carry a mutation for LQTS and 95 (38%) are non-carriers (results pending in 14 (6%) of these 32 families. 19 have LQTS type 1, six have LQTS type 2, two have LQTS type 3, one has LQTS type 5 and a further four families have pathogenic mutations in two different genes. These families were identified following: investigation of syncope (35.4%); routine ECG (19.3%); screening following sudden death in family (16.1%); successful resuscitation of cardiac arrest (15%); investigation of palpitations (13%) and investigation after a near drowning episode (3.2%). In the largest LQTS family in northern Ireland to date, a total of 49 individuals have been genetically screened and 29 have been found to carry the pathogenic mutation. In the cohort of 32 families with genetically diagnosed LQTS, 28.3% of affected individuals have a normal corrected QT interval on ECG. A further 10 families have a clinical diagnosis of LQTS with no gene mutation identified at present. Nine families have been referred for investigation of likely Brugada syndrome with three having mutations in SCN5A detected by genetic screening. One family has been diagnosed with CPVT on genetic screening and CPVT is a likely clinical diagnosis in one further family. To date no short QT syndrome families have been identified.

Conclusion: Cardiac channelopathies are important primary cardiac arrhythmia syndromes that are not uncommon and remain undiagnosed in a significant number of individuals. Genetic testing aids in the identification of individuals carrying these gene mutations so that appropriate preventative measures and tailored therapeutic management can be implemented.

Background: Although the prognostic importance of angiographic progression/regression of coronary artery disease is well established, the importance of coronary artery remodelling is less certain. To explore this subject further, we analyzed the intravascular ultrasound (IVUS) data derived from a contemporary clinical trial population.

Methods: Single-vessel IVUS was performed in a standardised fashion and all data underwent central laboratory analyses. Patient follow-up was performed by questionnaire, and all cardiovascular events were verified by case record review by two cardiologists. A cardiovascular event was taken to represent one of the following: cardiovascular death; angina requiring hospitalisation; myocardial infarction; stroke; percutaneous coronary intervention (PCI); coronary artery bypass surgery. Hospitalisation for angina was defined as a hospital admission for typical chest pain without associated cardiac biomarker elevation. Myocardial infarction was defined as hospitalisation for symptoms attributed to acute cardiac ischaemia, biomarker elevation and changes on the electrocardiogram.

Results: Eighty-six patients (mean age 58 years (SD 8); 63 (73%) men; nine (10%) with diabetes) were included. Four patients refused follow-up angiography and IVUS. With the exception of one of these patients, complete 5-year follow-up of vital status and morbid events were available for all patients. During this period, 24 subjects (28%) experienced at least one cardiovascular event and four (5%) non-cardiac deaths occurred (table). Reduction in mean (SD) total vessel volume (~2.27 ± 6.47 mm³) was less in patients who underwent percutaneous coronary intervention (PCI) during follow-up, compared with patients who did not undergo PCI (~14.03 ± 38.83 mm³; p = 0.003). Reduction in median (range) vessel volume tended to be less in patients who had cardiac events (~6.62 mm³, range ~88.47 to 89.99 mm³) compared with patients who did not experience a cardiac event during follow-up (~14.85 mm³, range ~92.03 to 117.71 mm³, p = 0.1032). Reduction in total lumen volume (median, range) was less in patients who experienced a cardiac event (~1.23 mm³, ~42.06 to 49.48 mm³) compared with patients who did not experience a cardiac event (~13.53 mm³, ~50.63 to 107.59 mm³; p = 0.0474).

Conclusions: IVUS-derived measures of coronary artery remodelling were associated with cardiovascular events. Positive (outward) remodelling is associated with an adverse long-term cardiovascular prognosis. The possibility that positive remodelling could represent a surrogate biomarker merits investigation in other IVUS cohorts.
045 RE-PROCESSING ELECTROPHYSIOLOGY CATHETERS
SE Bowater, D Jones, S Flannigan, H Marshall, MJ Griffith. Queen Elizabeth Hospital, Birmingham, UK

Introduction: Single-use catheters have become standard practice in the United Kingdom over the past 25 years, largely due to concerns about infection and prion transmission. The re-use of catheters designed for single use is controversial but is performed in many countries including the United States and Germany. Studies have shown that re-processing single-use electrophysiology catheters had no effect on procedure time, fluoroscopy time, radiofrequency deliveries, complication rates or recurrence rates. We have looked at the potential costs and savings involved in re-processing electrophysiology catheters at the Queen Elizabeth Hospital Birmingham through a certified company (Vanguard AG Medical Services, Germany). The catheters are cleaned, tested individually for electrical and mechanical functionality and then sterilised. The reprocessing company are liable for any events arising from this process.

Methods: We retrospectively examined all electrophysiology cases performed in 2006 at the Queen Elizabeth Hospital, Birmingham. Procedures were divided into arrhythmia type and a standard protocol for catheter use in each type of procedure was used. Some catheters were not able to be reprocessed and this was accounted for. We made the assumption, on information from the company, that each catheter could be re-processed an average of nine times (out of a maximum of 12 times). Total costs for the year were subsequently calculated for single use only or re-processing.

Results: 466 procedures were performed in 2006 (83 atrial fibrillation, 103 flutter, 252 supraventricular tachycardia and 48 others including ablate and pace and ventricular tachycardia). The total spent on single-use catheters in 2006 was £560 856. A change to re-processing our catheters would reduce this cost to £189 279. The potential savings for each arrhythmia type is shown in the figure. Extrapolated to the population mean age and mean age at electrophysiology procedures for Herefordshire patients compared with other areas was between 92 and 115 pmp. The rate in Worcestershire was 155 pmp. However, in Herefordshire it was 202 pmp (fig) and this trend is still seen if private sector procedures are excluded. There are proportionately higher numbers of atrioventricular nodal re-entry tachycardia ablations for Herefordshire and Worcestershire patients and more atrial fibrillation ablation and “ablate and pace” procedures for Herefordshire patients compared with other areas.

Conclusion: Re-processing catheters would lead to large savings for the health service and these savings would be expected to increase as the number of procedures increase. Evidence does not back up concerns about the usability of re-processed catheters or complications including infection. It is imperative to use a certified company for the re-processing to ensure the same safety and performance as new devices.

046 THE EFFECTS OF CLINIC STYLE ON ACCESS RATES TO CATHETER ABLATION IN THE MIDLANDS
1 SE Bowater, 2 L Tapp, 1 A Price, 1 H Marshall, 2 N Prasad, 2 J Glancy, 1 MJ Griffith. 1 Queen Elizabeth Hospital, Birmingham, UK; 2 Good Hope Hospital, Sutton Coldfield, UK; 3 Hereford County Hospital, Hereford, UK

Introduction: The demand for catheter ablation for arrhythmias is growing but very few data have been published on access rates in the United Kingdom. Within the Midlands region there are only three hospitals that provide this service: University Hospital Birmingham (UHB), University Hospital of North Staffordshire and University Hospital Leicester. Hereford County Hospital is a district general hospital in the Midlands that runs a joint electrophysiology clinic in partnership between UHB and the local cardiology department. Each patient is first reviewed by the local cardiology team and subsequently discussed with the electrophysiology consultant who then continues the consultation in conjunction with the local team. To determine the effect this joint style of working has for Herefordshire patients, we have examined the data for electrophysiology studies and catheter ablation procedures within the Midlands region.

Methods: Information was gathered retrospectively from the finance and information departments of the three trusts, an electronic database at UHB and from paper records in the private sector for 2005–2006. We analyzed the access rates from the different primary care trusts grouped together by area. Results are expressed as number per million population (pmp).

Results: The total access rates for ablation procedures in most areas was between 92 and 115 pmp. The rate in Worcestershire was 155 pmp. However, in Herefordshire it was 202 pmp (fig) and this trend is still seen if private sector procedures are excluded. There are proportionately higher numbers of atrioventricular nodal re-entry tachycardia ablations for Herefordshire and Worcestershire patients and more atrial fibrillation ablations and “ablate and pace” procedures for Herefordshire patients compared with other areas.

Access rates to electrophysiology ablation are higher for all age groups in Herefordshire. 6622 ablation procedures in England were looked at the potential costs and savings involved in re-processing electrophysiology catheters at the Queen Elizabeth Hospital Birmingham through a certified company (Vanguard AG Medical Services, Germany). The catheters are cleaned, tested individually for electrical and mechanical functionality and then sterilised. The reprocessing company are liable for any events arising from this process.

Methods: We retrospectively examined all electrophysiology cases performed in 2006 at the Queen Elizabeth Hospital, Birmingham. Procedures were divided into arrhythmia type and a standard protocol for catheter use in each type of procedure was used. Some catheters were not able to be reprocessed and this was accounted for. We made the assumption, on information from the company, that each catheter could be re-processed an average of nine times (out of a maximum of 12 times). Total costs for the year were subsequently calculated for single use only or re-processing.

Results: 466 procedures were performed in 2006 (83 atrial fibrillation, 103 flutter, 252 supraventricular tachycardia and 48 others including ablate and pace and ventricular tachycardia). The total spent on single-use catheters in 2006 was £560 856. A change to re-processing our catheters would reduce this cost to £189 279. The potential savings for each arrhythmia type is shown in the figure. Extrapolated to the population mean age and mean age at electrophysiology procedures for Herefordshire patients compared with other areas was between 92 and 115 pmp. The rate in Worcestershire was 155 pmp. However, in Herefordshire it was 202 pmp (fig) and this trend is still seen if private sector procedures are excluded. There are proportionately higher numbers of atrioventricular nodal re-entry tachycardia ablations for Herefordshire and Worcestershire patients and more atrial fibrillation ablations and “ablate and pace” procedures for Herefordshire patients compared with other areas.

Conclusion: Re-processing catheters would lead to large savings for the health service and these savings would be expected to increase as the number of procedures increase. Evidence does not back up concerns about the usability of re-processed catheters or complications including infection. It is imperative to use a certified company for the re-processing to ensure the same safety and performance as new devices.

Abstract 045
AF, atrial fibrillation; SVT, supraventricular tachycardia.
population of 50.5 million for England, this gives an access rate of 120 pmp. The access rate for the Midlands region appears to be close to the national average, with a much higher access rate in Herefordshire.

**Conclusion:** Access to catheter ablations is higher in Herefordshire than all other areas in the Midlands, including the area local to the tertiary electrophysiology centre. These differences in access rates cannot be explained by demographics alone. The clinic style adopted by Hereford County Hospital optimises access to tertiary centre electrophysiology expertise for local patients. The access rate in Herefordshire may reflect the true demand for catheter ablations in the United Kingdom. If the access rates achieved there were to be replicated nationally by the wider use of this clinic style, there would be a requirement for 11 000 ablations in England annually.

### Abstract 046

<table>
<thead>
<tr>
<th>Age at AF procedure</th>
<th>Population mean age (years)</th>
<th>Patient mean age AF (years)</th>
<th>Access rate pmp AF ablation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pan Birmingham</td>
<td>36.1</td>
<td>56.8</td>
<td>25</td>
</tr>
<tr>
<td>Herefordshire</td>
<td>40.3</td>
<td>60.1</td>
<td>133</td>
</tr>
<tr>
<td>Worcestershire</td>
<td>38.9</td>
<td>58.2</td>
<td>49</td>
</tr>
<tr>
<td>Shropshire</td>
<td>38.3</td>
<td>57.3</td>
<td>41</td>
</tr>
</tbody>
</table>

*AF, atrial fibrillation; pmp, per million population.*

### Abstract 047 Table 1

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Number (%)</th>
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</thead>
<tbody>
<tr>
<td>Pat foramen ovale closure</td>
<td>58 (29.4)</td>
</tr>
<tr>
<td>Atrial septal defect closure</td>
<td>18 (9.1)</td>
</tr>
<tr>
<td>Coarctation stenting</td>
<td>7 (3.6)</td>
</tr>
<tr>
<td>Ventricular septal defect closure</td>
<td>6 (3.0)</td>
</tr>
<tr>
<td>Other intervention</td>
<td>13 (6.6)</td>
</tr>
<tr>
<td>Left and right heart catheterisation</td>
<td>78 (40.0)</td>
</tr>
<tr>
<td>Right heart catheterisation</td>
<td>12 (6.1)</td>
</tr>
<tr>
<td>Left heart catheterisation</td>
<td>5 (2.5)</td>
</tr>
</tbody>
</table>

### Abstract 047 Table 2

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Entire group Number (%) n = 197</th>
<th>Complication group Number (%) n = 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average age, years</td>
<td>41.7</td>
<td>50.0</td>
</tr>
<tr>
<td>Mean weight, kg</td>
<td>73.2</td>
<td>70.6</td>
</tr>
<tr>
<td>Female</td>
<td>106 (53.8)</td>
<td>6 (85.7)</td>
</tr>
<tr>
<td>Previous catheterisation</td>
<td>44 (22.3)</td>
<td>2 (28.6)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>5 (2.5)</td>
<td>1 (14.3)</td>
</tr>
<tr>
<td>History of smoking</td>
<td>27 (13.7)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Warfarin</td>
<td>42 (21.3)</td>
<td>3 (42.9)</td>
</tr>
<tr>
<td>Received heparin</td>
<td>107 (54.3)</td>
<td>5 (71.4)</td>
</tr>
<tr>
<td>Closure device</td>
<td>3 (1.5)</td>
<td>0 (0.0)</td>
</tr>
</tbody>
</table>

### Abstract 047

**FEMORAL VASCULAR ACCESS COMPLICATIONS IN ADULT CONGENITAL HEART DISEASE PATIENTS: AUDIT FROM A SINGLE TERTIARY CENTRE**

1CD Chue, 1LE Hudsmith, 2O Stumper, 3J De Giovanni, 1SA Thorne, 1P Clift. 1Queen Elizabeth Hospital Birmingham, Birmingham, UK; 2Birmingham Children’s Hospital, Birmingham, UK

**Introduction:** Vascular complications are a major cause of morbidity after cardiac catheterisation. The incidence of complications after catheterisation and percutaneous intervention in patients with adult congenital heart disease (ACHD) is poorly documented.

**Methods:** All vascular access complications after ACHD procedures in a single large tertiary centre over a 12-month period were retrospectively studied. Complications were defined as haematoma, pseudoaneurysm, arteriovenous fistula or bleeding resulting in the need for imaging, transfusion, vascular or radiological intervention or delayed discharge.

**Results:** Of 197 procedures (102 interventions, 95 catheterisations, table 1), a complication rate of 3.6% was identified with the main complications being femoral artery pseudoaneurysm (three) and haematoma (two), resulting in delayed discharge by a mean of 2.7 days (range 1–4). Ultrasound scanning was diagnostic and mechanical compression was sufficient as treatment. No blood transfusions were required, there were no cases of infection associated with haematomas or false aneurysms and no vascular surgery input was required. Predictors of risk for the development of complications include female sex, history of diabetes and antidepressant use. Risk factors for complications include female sex, history of diabetes and antidepressant use. Risk factors for complications include female sex, history of diabetes and antidepressant use. Risk factors for complications include female sex, history of diabetes and antidepressant use.

**Discussion:** Our complication rate is low and is comparable to the complication rate in adults undergoing diagnostic coronary angiography and percutaneous coronary intervention despite the use of larger sheaths and the combination of arterial and venous sheaths in the majority of patients. Over a third of patients (patient foramen ovale and atrial septal defect device closures) were preloaded with dual antplatelet therapy as well as a large number of patients receiving 50–70 units/kg of heparin before the procedure, mirroring coronary interventional practice.

**Conclusion:** ACHD patients represent a unique and ever-growing population with a higher incidence of catheterisation as children, surgical cut-down scars and anatomical variants. Some patients with risk factors for the development of vascular complications should be considered for device closure of the venous access site.

### Abstract 048

**PALPITATIONS AND PSYCHOLOGICAL MORBIDITY**

1J Cooke, 2A Shiner, 3D Sandler, 4L O’Toole. 1Chesterfield Royal Hospital Foundation Trust, Chesterfield, UK; 2Derbyshire County PCT, Chesterfield, UK; 3Royal Hallamshire Hospital, Sheffield, UK

**Purpose:** High levels of psychiatric morbidity have been reported in patients referred for 24-hour tapes. We explored the extent of psychological disorder in patients referred for the investigation of palpitations and compared them with patients referred to a cardiology clinic for other indications.

**Methods:** Consecutive patients referred to our cardiology service primarily for the investigation of palpitations were enrolled into the study. Immediately before their outpatient visit the patients were invited to fill in a hospital anxiety and depression scale (HADS) questionnaire. This is a well-validated screening tool designed to reveal depression and anxiety. Scores range from 0 to 21 for each diagnosis. A score of 12 or greater is compatible with clinically relevant disorder and a score of 8–11 with borderline disorder. The cardiological diagnosis was divided into two groups: clinically significant dysrhythmia ((paroxysmal) atrial fibrillation or flutter, supraventricular tachycardia, ventricular tachycardia) or clinically non-significant dysrhythmia (ectopic beats) or no dysrhythmia. Subsequently, a second set of patients referred to the same clinic for other indications other than the investigation of palpitations were invited to fill in HADS questionnaires. Palpitations patients were followed up by notes review after 3 years.

**Results:** 167 patients were studied, 78 in the palpitations group and 89 in the non-palpitations group. Palpitations patients were younger and more likely to be female. Clinical anxiety was significantly more common in palpitations patients (χ² test p = 0.04). Depression appeared to be more prevalent in the...
non-palpitations patients. 4 (19%) patients with clinical anxiety had clinically significant dysrhythmia (two paroxysmal atrial fibrillation, two supraventricular tachycardia). Clinically significant dysrhythmia was present in 9/38 (24%) of patients with normal anxiety scores. In the majority of patients 43/78 (55%) ectopic beats were felt to be the cause of the presenting symptom. There was no ventricular tachycardia and only one death was noted after 3 years (in a 62-year-old woman with ischaemic heart disease).

Conclusions: Anxiety is common in patients referred to cardiologists with palpitations. It does not necessarily discriminate between clinically significant and non-significant dysrhythmia. Cardiologists are trained to recognise dysrhythmia rather than psychological disorder. Patients with palpitations would be better served if event recorders were used to identify the relevant dysrhythmia in primary care, and if psychological morbidity was recognised and addressed in the same setting.

CLINICAL ACUMEN AND THE TREADMILL IN THE RAPID ACCESS CHEST PAIN CLINIC: CAN WE DO BETTER? SIGNIFICANT MAJOR ADVERSE CARDIAC EVENT RATE AT 1-YEAR FOLLOW-UP IN PATIENTS DISCHARGED TO THEIR GP

SH Dorman, J Barry, P Jeetley, AK Nightingale. United Bristol Healthcare Trust, Bristol, UK

Introduction: The efficacy of a rapid access chest pain clinic (RACPC) in the diagnosis and early treatment of patients with stable angina is well established. Recent studies have, however, shown a small but significant cardiac event rate in patients discharged from a RACPC with a diagnosis of non-cardiac chest pain. Exercise testing, despite its limited sensitivity and specificity remains the default stress test with only limited use of alternative functional imaging techniques. Now, however, new serological and non-invasive anatomical assessment by 64-slice cardiac computed tomography are being proposed as offering incremental value with low and intermediate risk patients. We set out to evaluate whether current practice with clinical assessment and exercise testing provided adequate risk stratification to ascertain what role, if any, these new technologies might play in the future.

Methods: We analyzed 680 consecutive attendees at a RACPC to assess their pretest probability of coronary artery disease by Diamond Forrester criteria, outcome of exercise testing and subsequent disposal and management. Furthermore, of the 470 (69%) patients who were discharged to their general practitioner (GP) for ongoing management, we undertook 1-year follow-up for major adverse cardiac events.

Results: 113 (17%), 423 (62%), and 144 (21%) had a high, intermediate and low/very low Diamond Forrester risk of significant major adverse cardiac events, respectively. 663 (98%) patients who were discharged from a RACPC with a diagnosis of non-cardiac chest pain; PCI, percutaneous coronary intervention. Of the 680 patients, eight (1%) were admitted, 96 (14%) had outpatient angiography, 41 (6%) stress echo or myocardial perfusion imaging, 75 (11%) echo or other tests and 470 (69%) were discharged to their GP for ongoing management. At 1-year follow-up of the 470 patients discharged, seven (1.5%) were later admitted with an acute coronary syndrome of whom five had inpatient percutaneous coronary intervention and one later died. A further four (1%) had elective revascularisation (two percutaneous coronary intervention, two coronary artery bypass grafting). Of these, 11 (2%) patients discharged to their GP with a subsequent adverse cardiac event, six (55%) were high risk and five (45%) were intermediate risk; four (40%) had a positive exercise test, three (30%) were indeterminate and three (30%) were negative (see table, figs 1 and 2).

Conclusion: In a large cohort of patients discharged from a RACPC to their GP for ongoing management, there was a small but significant major adverse cardiac event rate that could not have been easily predicted based on clinical assessment and exercise testing alone. Although the limited use of non-invasive functional imaging may have been contributory there is clearly still scope for improved risk stratification in a small proportion of patients. Further research is now required into the role of adjunctive serological and non-invasive anatomical assessment in this setting to see if this small but significant adverse event rate can be reduced.
**050** LIPID LOWERING WITH SIMVASTATIN 40 MG AFTER ACUTE CORONARY SYNDROMES ACHIEVES NATIONAL NSF/GMS AUDIT STANDARDS BUT NOT JBS2 TARGETS FOR SECONDARY PREVENTION

1SH Dorman, 2TW Johnson, 3NEJ West. 1United Bristol Healthcare Trust, Bristol, UK; 2Swindon and Marlborough NHS Trust, Swindon, UK; 3Papworth Hospital NHS Trust, Papworth, UK.

Introduction: Patients presenting with acute coronary syndromes (ACS) are at high risk of recurrent events and benefit from aggressive lipid-lowering therapy. Despite this, the monitoring of lipid treatment goals across primary and secondary care is variable and uncertainty remains over whether these patients are achieving optimal secondary prevention. Given the financial constraints of a publicly funded National Health Service, we used a standard policy of simvastatin 40 mg per day for ACS patients and aimed to assess monitoring and the attainment of national and European lipid targets in a real-world population.

Methods: We evaluated a cohort of ACS patients (n = 158) undergoing an invasive strategy between June and December 2004. Baseline assessment included cardiovascular risk factors, medication and lipid profile. Default lipid-lowering strategy was simvastatin 40 mg per day, instituted during inpatient stay. Alternative statins were considered if patients were simvastatin intolerant or unsatisfactory lipid levels were obtained during simvastatin pretreatment. We evaluated when and by whom the first lipid check had been arranged after discharge, and whether the patient had achieved NSF/GMS (total cholesterol <5 mmol/l), ESC (total cholesterol <4.5 mmol/l) and JBS2 targets (total cholesterol <4 mmol/l). Further assessment was made of the most recent lipid profile, providing follow-up at 2 years post-ACS.

Results: Follow-up was available in 138/158 (87%) patients at 600 ± 151 days, of whom 100 (72%) were men, 71 (51%) were hypertensive, 13 (9%) had diabetes, 65 (46%) were known to be hyperlipidaemic, 43 (32%) were current smokers and with a mean age of 66 ± 11 years. 95 (69%) patients were statin naive on admission, but by discharge 126 (91%) of patients were statin treated, 99 (76%) taking simvastatin 40 mg per day. The mean time to first lipid profile check after discharge was 121 ± 110 days; 119/138 (89%) cases performed in primary care. At late follow-up only 7/138 (5%) of patients had no further lipid profile measured. Fasting lipid levels were seldom performed, preventing accurate low-density lipoprotein estimation. For ACS patients admitted on statins 45/138 (31%), mean initial total cholesterol decreased from 4.4 ± 1.1 to 4.1 ± 0.9 mmol/l at first follow-up and 4.0 ± 0.9 mmol/l at late follow-up. For statin-naive patients 95/138 (69%) mean initial total cholesterol decreased from 5.9 ± 1.4 to 4.2 ± 1 mmol/l at first follow-up and 3.9 ± 0.8 mmol/l at late follow-up. Failure to reach JBS2 targets (total cholesterol <4 mmol/l) at 2 years was observed in 49% of those patients on statins before index admission and 40% of the statin-naive patients (fig).

Conclusion: The use of a default strategy for lipid lowering with simvastatin 40 mg per day in ACS provides a cost-effective alternative to more aggressive lipid-lowering regimes. Although NSF/GMS targets are met, it remains to be seen whether clinical outcomes mirror those seen with more aggressive lipid lowering.

**051** HIGH PREVALENCE OF ABNORMAL GLUCOSE METABOLISM IN PATIENTS PRESENTING FOR ROUTINE CORONARY ANGIOGRAPHY

C English, J Hastings, S Dineen, K Daly, P Nash, J Crowley. University College Hospital Galway, Galway, Ireland.

Background: Abnormal glucose metabolism is a known risk factor for coronary artery disease and is frequently unrecognised even in patients with acute coronary syndrome. Patients with stable coronary symptoms frequently have multiple risk factors and yet have no assessment of glucose regulation. The purpose of this study was to assess the prevalence of impaired glucose tolerance and diabetes mellitus in a group of patients with stable symptoms presenting for coronary angiography.

Methods: An oral glucose tolerance test was performed according to World Health Organisation (WHO) guidelines on 139 unselected patients undergoing elective angiography for suspected angina. Patients with known diabetes mellitus were excluded. Demographic data including cardiovascular risk factors, body mass index (BMI), history of coronary artery disease were recorded.

Results: 159 patients (45% women, 55% men) with a mean age of 62.8 years were studied. 46% of patients had an elevated fasting total cholesterol and 17% had a BMI over 25 kg/m2. 11 years. 95 (69%) patients were statin naive on admission, but by discharge 126 (91%) of patients were statin treated, 99 (76%) taking simvastatin 40 mg per day. The mean time to first lipid profile check after discharge was 121 ± 110 days; 119/138 (89%) cases performed in primary care. At late follow-up only 7/138 (5%) of patients had no further lipid profile measured. Fasting lipid levels were seldom performed, preventing accurate low-density lipoprotein estimation. For ACS patients admitted on statins 45/138 (31%), mean initial total cholesterol decreased from 4.4 ± 1.1 to 4.1 ± 0.9 mmol/l at first follow-up and 4.0 ± 0.9 mmol/l at late follow-up. For statin-naive patients 95/138 (69%) mean initial total cholesterol decreased from 5.9 ± 1.4 to 4.2 ± 1 mmol/l at first follow-up and 3.9 ± 0.8 mmol/l at late follow-up. Failure to reach JBS2 targets (total cholesterol <4 mmol/l) at 2 years was observed in 49% of those patients on statins before index admission and 40% of the statin-naive patients (fig).

Conclusion: The use of a default strategy for lipid lowering with simvastatin 40 mg per day in ACS provides a cost-effective alternative to more aggressive lipid-lowering regimes. Although NSF/GMS targets are met, it remains to be seen whether clinical outcomes mirror those seen with more aggressive lipid lowering.

**052** CORONARY ARTERY BYPASS GRAFTING AND PERCUTANEOUS CORONARY INTERVENTION FOR LEFT MAIN STEM CORONARY ARTERY DISEASE: SYNERGY IN A REAL-WORLD REGISTRY

1J Gunn, 2N Briffa. 1University of Sheffield, Sheffield, UK; 2Northern General Hospital, Sheffield, UK.

Background: Revascularisation for left main stem (LMS) disease is often portrayed as percutaneous coronary intervention (PCI) versus coronary artery bypass grafting (CABG), a philosophy perpetuated by randomised controlled trials, which, by their nature, pit one mode of revascularisation against another and, because the patients in those studies must be suitable for both modalities, many patients are excluded. In the real world, however, patients must be allocated to one or other treatment. There is, therefore, a strong argument for robust outcome data from registries.

Aim: To perform a retrospective analysis of prospectively collected data for all patients with an unprotected LMS stenosis who underwent revascularisation in Sheffield in the era of drug-eluting stents.
Methods: We examined the Sheffield operating theatre and catheter laboratory database (Infobrix) for the period March 2004 to June 2007 to determine the number of patients undergoing CABG and PCI for coronary artery disease including a significant LMS stenosis. Angiograms were viewed by JG to ensure that only patients with a significant LMS stenosis were included. Patients undergoing valve surgery were excluded. The logistic EuroSCORE was calculated for both groups. The primary outcome was inhospital and late mortality and this was determined by a data clerk from national statistics.

Results: Of 7258 patients revascularised, 680 had an LMS stenosis (168/million per year; 9.4% of the total). 72% were treated with CABG and 28% with PCI. The proportions presenting as emergency/urgent/elective were 3/35/62% (CABG) and 12/23/65% (PCI) (p<0.01 for emergency). The mean logistic EuroSCORE estimation of in-hospital death was 5.5% (CABG) and 9.2% (PCI) (p<0.005). The proportion in a catastrophic state was 1.4% (CABG) and 9.0% (PCI) (p<0.001). 41% of the PCI patients were deemed unfit for CABG. The 1-month mortality was 3% (CABG) and 6% (PCI) (p = ns). The (median) 20-month mortality was 7% (CABG) and 15% (PCI) (p<0.005). For the patients who died, the EuroSCORE was 13.1% (CABG) and 25.2% (PCI) (p<0.05). For elective patients, the 20-month mortality was 3.8% (CABG) and 5% (PCI) (p = ns); and for those with an EuroSCORE less than 5, 2.9% (CABG) and 5.6% (PCI) (p = ns). For the PCI patients who would have been fit for CABG, 20-month mortality was 4.9%.

Conclusions: Even in a centre with a LMS PCI programme in the era of drug-eluting stents, CABG is three times more commonly recommended than PCI. The preoperative risk for patients undergoing CABG is lower than for those undergoing PCI, and the PCI cohort contains a high percentage of patients turned down for CABG. The proportion of patients treated as an emergency and in a catastrophic state is lower for CABG than for PCI. The overall mortality is, therefore, lower for CABG than for PCI. Patients who are suitable for CABG or PCI do very well with both. CABG and PCI are useful complementary strategies for a mixed population of patients presenting to a tertiary centre with a LMS stenosis.

Abstract 053

<table>
<thead>
<tr>
<th>% Correct</th>
<th>COC</th>
<th>Cerazette Mirena IUS</th>
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</thead>
<tbody>
<tr>
<td>Mechanical mitral valve</td>
<td>45</td>
<td>65</td>
</tr>
<tr>
<td>Paroxysmal atrial fibrillation</td>
<td>35</td>
<td>71</td>
</tr>
<tr>
<td>Ischaemic heart disease</td>
<td>44</td>
<td>67</td>
</tr>
<tr>
<td>Dilated cardiomyopathy</td>
<td>21</td>
<td>67</td>
</tr>
<tr>
<td>Pulmonary hypertension</td>
<td>57</td>
<td>49</td>
</tr>
</tbody>
</table>

COC, combined oral contraceptive pill; IUS, intrauterine system.

Conclusion: A large number of women are not being given adequate advice regarding effective and appropriate contraception by their medical professionals. As a result some women may be incorrectly denied effective hormonal contraceptive products, leading to unplanned and potentially high-risk pregnancies, whereas other patients may be inappropriately prescribed oestrogen-containing products, exposing them to increased cardiovascular risk. It is the responsibility of all cardiologists to have an understanding of the range and efficacy of available contraceptive methods.

054 ELECTIVE CARDIOVERSION UNDER CONSCIOUS SEDATION: 6-YEAR EXPERIENCE OF MORE THAN 2000 PROCEDURES

Introduction: Certain international guidelines recommend elective DC cardioversion (DC-CV) to be carried out under general anaesthesia. In 2001, a new service for day case DC-CV was initiated at our institution. A doctor and nurse team administers conscious sedation with intravenous midazolam without an attending anaesthetist. A database was generated at conception of our service that now includes more than 2000 procedures to date. A previously published 12-month review involving 368 patients from our institution has suggested that this may be safe, effective and well tolerated. We reviewed our current database to study the efficacy and safety of this service spanning more than 6 years in this much larger cohort of patients.

Methods: We examined our database for information on age, gender, medication, dose of midazolam, number of shocks delivered, total energy used, success at restoration (and maintenance thereof) of sinus rhythm and complications. Patients who had sinus rhythm restored were invited for repeat ECG at 4 weeks.

Results: A total of 2099 DC-CV procedures were performed on 1653 patients electively between January 2001 and October 2007 (1178 men, 475 women; mean age 66.2 years (SD 10.3)). Drug therapy (N; %) included beta blockers (1318; 62.8%), amiodarone (390; 18.6%), calcium blockers (567; 18.6%), digoxin (705;33.5%), flecainide (70; 3.3%) angiotensin-converting enzyme inhibitor (776; 36.9%), angiotensin II receptor blocker (104; 4.9%). Information on sedation/anaesthetic method was available on 1896 procedures. Of these, 1824 (96%; 1294 men, mean age 66.4 years (SD 10.1)) used
conscious sedation with intravenous midazolam (median dose (range) 6 mg (2–20 mg). In this cohort, sinus rhythm was restored and maintained to discharge in a total of 1694 patients (95%) following delivery of a mean 1.55 shocks (mean energy 164.6 J; 1.2% monophasic). Of 72 patients (3.8%; 60 men, mean age 60.6 years (SD 10.5)) who underwent general anaesthesia receiving an average of 2.2 shocks (mean energy 373 J; 27% monophasic), data on success at immediate restoration of sinus rhythm were available for 68 procedures (94%); this was achieved in 50 cases (74%). Of 1555 patients in the sedation group attending for follow-up ECG at 4 weeks, 826 patients (61%) remained in sinus rhythm. There were two (≤0.1%) instances of respiratory arrest requiring anaesthetic support, both non-fatal and occurring in the initial 2 years of the service. Complete heart block needing pacing complicated two cases. No neurological complications occurred. **Conclusion:** This study confirms the findings of smaller registries and studies that DC–CV under nurse and physician-led sedation is safe and effective. The lower success of DC–CV in our general anaesthesia cohort should be interpreted in the context of the smaller numbers and higher use of monophasic shock waveforms in this group.

**055 ACCURACY OF AMBULANCE STAFF DIAGNOSIS OF ACUTE CARDIOGENIC PULMONARY OEDEMA: A PROSPECTIVE DIAGNOSTIC STUDY OF 1334 PATIENTS**

E Jenkinson, M Woollard, I Robertson-Steel, F Newcombe. Heartlands Hospital/ West Midlands Ambulance Service, Birmingham, UK; 2Faculty of Pre-hospital Care Research Unit, Middlesborough, UK; 3West Midlands Ambulance Service, Birmingham, UK. 4University of Cardiff, Cardiff, UK

**Background:** There is evidence that early recognition and treatment of acute cardiogenic pulmonary oedema offers a survival benefit. This study evaluated the accuracy of UK ambulance staff diagnosis of pulmonary oedema.

**Methods:** Data were collected prospectively for 1334 patients with respiratory distress who were transported to a UK emergency department (ED) by ambulance. ED discharge diagnosis data were collected by a researcher blinded to the prehospital diagnosis. Ambulance crew diagnosis was compared against the ED diagnosis for each patient. Ethical approval was not required for this audit but it was registered with the research and development departments of the relevant trusts.

**Results:** 1155 patients were suitable for inclusion in the data analysis. The prevalence of pulmonary oedema in the study population was 6.41% (95% CI 5.06% to 7.98%). Sensitivity of diagnosis was 32.43% (22.0% to 44.32%) and specificity was 96.76% (95.53% to 97.73%). The likelihood ratio for a positive diagnosis was 10.02% (6.25% to 15.68%) and for a negative diagnosis 0.70% (0.52% to 0.80%). 704 patients were attended to by paramedic crews and the remainder by technician crews. There was no significant difference in prevalence between the two groups. The sensitivity of paramedic diagnosis was significantly higher than technician diagnosis (42.6% versus 11.1%, respectively, p = 0.005) but there was no significant difference in specificity or likelihood ratio of a positive result between the two groups.

**Limitations:** Previous studies have shown that ED diagnosis of pulmonary oedema is inaccurate and the preferred gold standard would have been hospital discharge diagnosis. The study was published before data collection and this may have led to the introduction of bias.

**Conclusions:** The specificity of ambulance crew diagnosis was high, suggesting that if a patient was treated for pulmonary oedema then this was likely to have been appropriate. Sensitivity was low, with only one third of patients with pulmonary oedema identified. Additional training is required so that the correct patients are identified for treatment.

**056 IMPLANTABLE CARDBIOVER DEFIBRILLATOR IMPLANTATION IN NORTHWEST LONDON: AN AUDIT OF NICE GUIDELINE ADHERENCE**

M Koa-Wing, C Gardner, S Schofield, DW Davies, NS Peters, P Kanagaratnam. 1Imperial College Healthcare NHS Trust, London, UK; 2The Audit, Information and Analysis Unit for London, Kent, Surrey and Sussex, Beekley, UK; 3Specialised Services Commissioning NW London, Hillingdon Primary Care Trust, Middlesex, UK

**Introduction:** Implantable cardioverter defibrillator (ICD) implantation for the prevention of sudden cardiac death is increasing. We audited the adherence of implantation practices to National Institute for Health and Clinical Excellence (NICE) guidelines in the northwest London region.

**Methods:** A prospective audit of all patients referred for ICD implantation at four northwest London implanting centres was performed from October 2005 to April 2006, collecting data by independent questionnaire. Indications for implantation of new ICD were compared with the NICE guidelines (2000) as well as clinical trial entry criteria, in particular MADIT II and SCD-HeFT.

**Results:** A total of 235 ICDs were implanted. 193 (82%) were male and 42 (18%) female. Primary prevention ICD were implanted in 79 (34%), secondary prevention ICD in 87 (37%) and generator replacements were performed in 66 (28%). No documented indication was found in three (1%) patients. (Table shows number of ICD implants and their indications). The mean age for a primary prevention ICD was 58 ± 16 years and for secondary prevention was 61 ± 17 years. Indications adherent to NICE occurred in 83 (95%) secondary prevention ICD patients and in 10 (13%) primary prevention implants, with only one primary prevention ICD meeting the criteria for postinfarction patients. To explain the large number of primary prevention ICD not meeting with NICE criteria, this group was broken down by aetiology, risk stratification tools used and type of device. Aetiologies included ischaemic heart disease in 44 (56%) patients, dilated cardiomyopathy in 16 (20%), hypertrophic cardiomyopathy in six (7.5%), long QT syndrome in four (5%), congenital heart disease in two (2.5%) and other/unknown in seven (9%) patients. Holter monitors were used in 41 (52%) cases and electrophysiological studies were performed in four patients.

**Abstract 056**

<table>
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<th>Indication</th>
<th>No of implants</th>
<th>% of Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary prevention ICD</td>
<td></td>
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</tr>
<tr>
<td>*Previous MI, nsVT, EF &lt;35%, positive EPS</td>
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<td>1.3</td>
</tr>
<tr>
<td>*Familial disorder at risk of sudden cardiac death</td>
<td>9</td>
<td>11.4</td>
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<tr>
<td>nsVT with previous MI and EF &lt;35%</td>
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<td>13.9</td>
</tr>
<tr>
<td>Previous MI with EF ≤30% (MADIT II trial criteria)</td>
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</tr>
<tr>
<td>NYHA class III/IV with EF &lt;35% (SCD-Heft trial criteria)</td>
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<td>20.3</td>
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</tr>
<tr>
<td>*VF cardiac arrest</td>
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<tr>
<td>*Asymptomatic sustained VT with previous MI and EF &lt;35%</td>
<td>2</td>
<td>2.3</td>
</tr>
<tr>
<td>*Symptomatic VT (syncpe/haemodynamic compromise</td>
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<td>4</td>
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</table>

**EF:** ejection fraction; **EPS:** electrophysiology studies; MI, myocardial infarction; nsVT, non-sustained ventricular tachycardia; NYHA, New York Heart Association; VF, ventricular fibrillation; VT, ventricular tachycardia.

*Indication in keeping with NICE recommendations.
(5%) cases. Single chamber ICD were implanted in four (5%) patients, dual chamber ICD in 24 (30%) patients and biventricular ICDs in 51 (65%) patients. A large number of primary prophylactic implants 38 (48%) met with clinical trial entry criteria for MADIT II and SCD-HeFT. NICE guidance on primary prevention ICD was updated during the audit in 2006 to include postinfarction patients with ejection fraction less than 30% and QRS greater than 120 ms (MADIT II subgroup). Assuming the MADIT II patients with a biventricular pacing ICD qualify (n = 17) this potentially would mean 36% of primary devices met NICE guidance on primary prevention.

Conclusion: In northwest London, NICE guidelines are being followed in secondary prevention; however, primary prevention ICD implant practices are exceeding guidelines. A lack of specific guidance for non-infarct-related aetiologies, as well as the implantation of biventricular pacing ICD for the main indication of cardiac resynchronisation are potential reasons for this finding. Risk stratification tools are being underutilised, whereas clinical trial data appear to be influencing physicians’ practice.

**057 EUROASPIRE III: LIFESTYLE AND RISK FACTOR MANAGEMENT AND USE OF DRUG THERAPIES IN CORONARY PATIENTS FROM 22 COUNTRIES IN EUROPE**

1K Kotseva, 1C Jennings, 2D De Bacquer, 2G De Backer, 3U Keil, 1D Wood. 1NHLL, Imperial College London, London, UK; 2University of Ghent, Ghent, Belgium; 3University of Munster, Munster, Germany

**Objectives:** EUROASPIRE I and II surveys, conducted by the European Society of Cardiology in 1995–1996 (nine countries) and 1999–2000 (15 countries) showed a high prevalence of modifiable risk factors in coronary patients in Europe and a real potential to reduce coronary heart disease morbidity and mortality further. The aim of the EUROASPIRE III survey was to determine in patients with coronary heart disease whether the 2005 Joint European Societies guidelines on cardiovascular disease prevention are being followed in clinical practice.

**Methods:** The EUROASPIRE III survey was undertaken in 2006–2007 in selected geographical areas and hospitals in 22 European countries. Consecutive patients, men and women under 80 years of age at the time of the index event or procedure, and with one or more of the following diagnoses: coronary artery bypass graft, percutaneous transluminal coronary angioplasty, acute myocardial infarction and acute myocardial ischaemia, were identified retrospectively. Data collection was based on a review of hospital medical records and a prospective interview and examination at least 6 months after the index event or procedure.

**Results:** A total of 13 935 medical records (27.4% women) were reviewed and 8966 patients were interviewed on average 1.24 years after their index event (participation rate 73.0%). At interview, 17.2% of patients smoked cigarettes, 81.8% were overweight (BMI >25 kg/m²), 35.3% were obese (BMI ≥30 kg/m²), 52.7% had central obesity (waist circumference ≥102 cm in men or ≥88 cm in women), 50.0% had raised blood pressure (≥140/90 mm Hg; ≥130/80 mm Hg for patients with diabetes), 34.2% had elevated total cholesterol ≥5.0 mmol/l and 34.8% had diabetes (self-reported or fasting plasma glucose ≥7 mmol/l). The use of prophylactic drug therapies was as follows: aspirin or other antiplatelet drugs 90.5%, beta-blockers 79.8%, angiotensin-converting enzyme inhibitors 59.9%, angiotensin II receptor blockers 12.0%, statins 78.1%, anticoagulants 5.6%. Only 58.3% of patients using blood pressure-lowering medication were controlled (<140/90 mm Hg; <130/80 mm Hg for patients with diabetes). 27.7% patients on lipid-lowering medication had not achieved the total cholesterol goal of less than 5 mmol/l (45.0% <4.5 mmol/l). The therapeutic control of diabetes was poor, with only 10.4% of patients with self-reported diabetes having a fasting plasma glucose less than 6.1 mmol/l.

**Conclusions:** EUROASPIRE III shows that a large majority of coronary patients have adverse lifestyles and many do not achieve the blood pressure, lipid and diabetes goals. So a wide gap continues to exist in the implementation of evidence-based medicine in cardiological practice in both hospital and primary care. There is a considerable potential to raise the standard of preventive care in Europe through preventive cardiology programmes involving multidisciplinary teams of healthcare professionals helping patients achieve the lifestyle, risk factors and therapeutic targets for cardiovascular disease prevention.

**058 CLINICAL REALITY OF CORONARY PREVENTION IN EUROPE: A COMPARISON OF EUROASPIRE I, II AND III SURVEYS**

1K Kotseva, 1C Jennings, 2D De Bacquer, 2G De Backer, 3U Keil, 1D Wood. 1NHLL, Imperial College London, London, UK; 2University of Ghent, Ghent, Belgium; 3University of Munster, Munster, Germany

**Objectives:** Three EUROASPIRE surveys of coronary patients have been conducted over 12 years in eight countries—Czech Republic, Finland, France, Germany, Hungary, Italy, The Netherlands, Slovenia—to describe time trends in the risk factor and therapeutic management in the prevention of cardiovascular disease.

**Methods:** 8547 patients with coronary artery disease—coronary artery surgery (coronary artery bypass grafting), angioplasty (percutaneous transluminal coronary angioplasty), myocardial infarction or ischaemia—have been interviewed and examined over this period.

**Results:** The prevalence of smoking remained unchanged overall in the three surveys (20.5%, 21.2%, 18.2%) but has increased in younger patients and especially in women. The prevalence of obesity (BMI >30 kg/m²) and central obesity (waist circumference >102 cm in men and >88 cm in women) has increased (25.0%, 32.6%, 38.0%) and (42.2%, 53.0%, 54.9%), respectively. The proportions with high blood pressure ≥140/90 mm Hg ≥130/90 mm Hg in diabetes) were similar (58.1%, 58.3%, 60.9%). Therapeutic control of blood pressure had deteriorated from 41% in the first to 38.7% in the third survey. However, the management of blood lipids has improved considerably and the proportions with elevated total cholesterol ≥5.0 mmol/l and low-density lipoprotein cholesterol ≥5.0 mmol/l have decreased substantially: total cholesterol, 87.0%, 59.6%, 28.5%; low-density lipoprotein cholesterol, 88.7%, 60.5%, 24.7%. The proportion of patients on lipid-lowering medication achieving the total cholesterol target of less than 5.0 mmol/l increased from 19.5% to 75.3%. The prevalence of diabetes has increased (17.4%, 20.1%, 28.0%) and the prevalence of undetected diabetes increased with 14.8% in the third survey, making a total of 42.8% of all patients with diabetes. Prescriptions for cardioprotective medications have increased across the three surveys for antiplatelet therapies (80.8%, 83.6%, 93.2%), beta-blockers (56.0%, 69.0%, 85.5%), angiotensin-converting enzyme/angiotensin II receptor blockers (31.0%, 49.2%, 74.6%), statins (18.1%, 57.3%, 87.0%) and diuretics (15.3%, 18.8%, 31.1%).

**Conclusions:** The adverse lifestyle trends among European coronary patients, with increased smoking in younger patients and alarming increases in both obesity and central obesity are a cause for concern. So is the lack of any improvement in blood pressure management. Lipid management continues to improve, but a substantial proportion of patients still remain above the recommended lipid targets. The rising prevalence of diabetes is a growing concern, with almost half of all coronary patients with this diagnosis, a third of whom are undetected. The use of drug therapies is increasing but pharmacotherapy is not sufficient. Patients require a professional lifestyle intervention through a preventive cardiology programme to help them achieve the lifestyle, risk factors and therapeutic targets for cardiovascular disease prevention.
EXTERNAL VALIDATION OF ESTABLISHED RISK ADJUSTMENT MODELS FOR PROCEDURAL COMPLICATIONS AFTER PERCUTANEOUS CORONARY INTERVENTION ON AN INDEPENDENT DATASET IN A UK SETTING

B Kunadian, J Dunning, R Das, AP Roberts, R Motley, AJ Turley, D Twomey, JA Hall, RA Wright, AGC Sutton, D Muir, MA de Belder. The James Cook University Hospital, Middlesbrough, UK

Objectives: There is a pressing need for workable risk models for patients undergoing percutaneous coronary intervention (PCI). A few risk models have been proposed, but to be applicable to a national audit process, they must be validated not only on the local populations from which they were derived but also on other geographical populations (internal versus external validation). We sought to validate two proposed risk adjustment models (Mayo Clinic, USA and North West Quality Improvement Programme, UK models) for in-hospital PCI complications on an independent dataset of relatively high-risk patients undergoing PCI.


Methods: Between September 2002 and August 2006, 5034 consecutive PCI procedures (validation set) were performed on a patient group characterised by a high incidence of acute myocardial infarction (MI; 16.1%) and cardiogenic shock (1.7%). Two external models, one developed by the North West Quality Improvement Programme (NWQIP model, UK) and the other by the Mayo Clinic Risk Score (MC model, USA) were externally validated.

Main Outcome Measure: Major adverse cardiovascular and cerebrovascular events, which were in-hospital mortality, Q wave MI, emergent coronary artery bypass grafting and cerebrovascular accidents.

Results: In this patient group, an overall in-hospital complication rate of 2% was observed. Multivariate regression analysis identified risk factors for in-hospital complications that were similar to the risk factors identified by the two external models. When fitted to the dataset, both external models had an area under the receiver operating characteristic curve greater than 0.85 (c index (95% CI), NWQIP; 0.86 (0.82 to 0.9), MC; 0.87 (0.84 to 0.9)) indicating overall excellent model discrimination and calibration (Hosmer–Lemeshow test, p > 0.05). The NWQIP model was accurate in predicting in-hospital complications in different patient subgroups (age groups, cardiogenic shock, diabetes, women, previous MI, previous coronary artery bypass grafting) (see fig).

Conclusions: We have externally validated both models. Despite differences in variable selection, both these predictive models yield comparable results that provided excellent model discrimination and calibration when applied to patient groups in a different geographical population other than the one on which the original model was developed.

CHANGES IN THE USE OF DRUG-ELUTING STENTS FOR PERCUTANEOUS CORONARY INTERVENTION

S Nadar, C Varma, T Millane, G Lip, R Watson. City Hospital, Birmingham, UK

Background and Aim: The use of intracoronary stents has revolutionised the treatment of coronary artery disease. Drug eluting stents (DES) in particular appeared to have a very low complication rate compared with bare metal stents. However, by August 2006 there was a series of highly publicised data pertaining to the increased risk of late stent thrombosis associated with the use of DES. We aimed to determine the impact of these data on our use of DES and compare it with the guidelines issued by the National Institute for Health and Clinical Excellence (NICE).

Design: A retrospective observational study over an 18-month period from September 2005 to February 2007. Period 1 was defined as the first 12 months (September 2005 to August 2006) and period 2 as the last 6 months (September 2007 to February 2007) in the setting of a teaching hospital serving a population of 600 000. Main outcome measures were the change in DES use between period 1 and period 2 and the comparison of DES use with the NICE guidelines (DES use recommended if lesion length > 15 mm and/or diameter < 3 mm), between the two periods.

Results: Data were retrieved from the British Cardiovascular Interventional Society (BCIS) database. A total of 1446 patients with 2208 stents was studied. Baseline clinical measures and lesion characteristics were similar between the two periods. Similar numbers of lesions in the two periods were eligible to receive a DES as per NICE guidelines (49% of lesions in period 1 and 47% in period 2, p = ns). There was an overall significant reduction in the use of DES from period 1 compared with period 2 (66% versus 56%, p < 0.001). For lesions fulfilling NICE criteria for DES there was no difference in DES use (period 1 82% versus period 2 80%, p = 0.01). For lesions not fulfilling NICE criteria there was a significant reduction in DES use between periods (51% versus 35%, p < 0.001). There remained a high level of DES use for complicated lesions (bifurcation lesions, chronic total occlusions, saphenous vein grafts and in-stent restenosis). However, on comparison between the two periods, there was a statistically significant reduction in the number of patients who received a DES for in-stent restenosis (96% versus 80%, p = 0.02) and for saphenous vein graft PCI (80% versus 57%, p = 0.001) but not for bifurcation lesions (77% versus 72%, p = ns) and chronic total occlusions (66% versus 58%, p = ns) between the two periods.

Conclusions: There has been a significant reduction in the overall use of DES, driven by a reduction in non-NICE criteria fulfilling the use of DES. Use of DES for all complex cases, however, remains high.

ADVERSE RISK PROFILE AND MANAGEMENT DELAYS IN PATIENTS WITHOUT A DIAGNOSTIC EXERCISE TEST: LIMITATIONS OF THE RAPID ACCESS CHEST PAIN SERVICE MODEL

BS Nair, T Harrid, S Chacko, W Turkie, I Diab, P Arumugam, RS Khattar. Manchester Royal Infirmary, Manchester, UK

The provision of diagnostic services is challenged by the 18 weeks referral to treatment target. The rapid access chest pain (RACP) service model aims to fast-track the diagnostic evaluation of suspected cardiac chest pain with the aid of exercise electrocardiography (ECG). However, approximately 25%–30% of patients either have an equivocal exercise ECG or are unable to exercise. The aim of this study was to compare the demographic factors, risk profile and
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<table>
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<tr>
<th>Demographic factors</th>
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<th>Group 2 (n = 494)</th>
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<td>Hypertension (%)</td>
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</tr>
<tr>
<td>Smoking (%)</td>
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<td>24.8</td>
<td>NS</td>
</tr>
<tr>
<td>Previous CAD (%)</td>
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<tr>
<td>Pre-test probability of CAD (%)</td>
<td>41.0</td>
<td>58.2</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Management plan

Angiography (%) | 13.6 | 13.8 | NS
Stress imaging (%) | 5.3 | 70.1 | <0.001
Discharge (%) | 78.2 | 11.8 | <0.001
Other (%) | 2.9 | 4.3 | NS

CAD, coronary artery disease.

management pathway of those with and without a diagnostic exercise ECG following RACP clinic assessment. We performed a retrospective analysis of the RACP service from January 2004 to December 2006. The parameters analyzed included age, sex, ethnicity, diabetes, hypertension, hypercholesterolaemia, smoking, previous coronary artery disease (CAD) and management plan. A total of 2199 patients attended the RACP clinic during the study period. Of these, 316 patients were inappropriate referrals and were therefore excluded from the analysis. The study cohort consisted of 1883 patients who were considered eligible for ischaemia testing. The patients were divided into two groups; group 1 consisted of those with a diagnostic exercise ECG (either positive or negative) and group 2 were those without a diagnostic test (either an equivocal result or unable to exercise). Comparative data of the two groups are shown in the table.

Group 2 patients were significantly older, had a higher proportion of women, higher prevalence of diabetes, hypertension and hypercholesterolaemia and a higher pre-test probability of CAD. Approximately 70% of these patients were referred for pharmacological stress imaging, incurring a delay of 20.6 ± 10.1 weeks before a diagnosis could be made. In conclusion, patients leaving the RACP clinic without a diagnostic exercise ECG have a potentially higher risk of CAD and greater management delays than those with a diagnostic test. This study highlights the need to improve access to pharmacological stress imaging in order to manage this high-risk group of patients appropriately and to facilitate compliance with the 18-week target.

Methods: An observational population-based study of all patients on statin therapy within an average sized (5800 patients) suburban general practice.

Results: A total of 540 patients were identified to have been on a statin. 72 were excluded from the study (23 had no recent cholesterol results, 49 were not currently taking statins). Indications for therapy included hypertension 58% (271/468), ischaemic heart disease 30.3% (142/468), diabetes 27.8% (130/468), hypercholesterolaemia 17.9% (84/468), transient ischaemic attack/cerebrovascular accident 12.2% (57/468), family history 6% (28/468) and peripheral vascular disease 2.1% (10/468). The average total cholesterol was 4.7 mmol/l (range 2.4–8.2). Statin therapy taken included simvastatin 65.7% (298/468), atorvastatin 31.8% (149/468), rosuvastatin 1.9% (9/468), pravastatin 0.8% (4/468) and fluvastatin 0.6% (3/468). Only 1.3% (6/468) were taking dual ezetimibe and statin therapy. 81.5% of patients had had no changes to their therapy within the previous 6 months. As per NICE guidelines, 70.3% (329/468) reached target compared with only 30.8% (144/468) as per the JBS2 guidelines.

Conclusion: On current statin therapy less than a third of patients are reaching target according to JBS2 guidelines. Tighter cholesterol control as suggested by JBS2 guidelines is likely to require higher doses of statins or the use of add-on therapies, which in turn may have a significant financial impact on primary care budgets or result in an increase in statin-induced side effects experienced by patients.

063 LEFT VENTRICULAR IMPAIRMENT AND LONG-TERM MORTALITY FROM ACUTE CORONARY SYNDROMES: ANALYSIS BY HAEMOGLOBIN CONCENTRATION

Introduction: Anaemia is an important determinant of heart failure and death after ST elevation myocardial infarction (STEMI) and may contribute to the cumulative risk of death from an acute coronary syndrome (ACS).

Methods: We examined data from 833 consecutive patients with a diagnosis of ACS between April 2004 and September 2005 and stratified them by quartiles of admission haemoglobin concentration (Hb): Q1 = 6.3 to 12.9 g/dl, Q2 = 13 to 14.2 g/dl, Q3 = 14.3 to 15.1 g/dl and Q4 = 15.2 to 18.4 g/dl. Mortality data were collected in October 2006 and the degree of left ventricular impairment by echocardiography was analyzed. Data were expressed as means ± SD or as median and interquartile ranges. Discrete or categorical data were summarized using frequencies and percentages. An independent t-test and ANOVA with Bonferroni correction were used for comparison of normally distributed data. Differences in proportions of data were analyzed using the χ² test.

Results: There were 162 (19.3%) STEMI, 474 (56.7%) non-STEMI/troponin-positive ACS and 197 (23.8%) troponin-negative ACS patients. 397 (47.7%) of the cohort underwent left ventricular function assessment by echocardiography, of which 183 (46.1%) had normal left ventricular systolic function. The mean (SD) Hb for STEMI, non-STEMI/troponin-positive ACS, and troponin-negative ACS was 14.4 g/dl (SD 1.9), 13.7 g/dl (SD 1.9) and 14.0 g/dl (SD 1.5), respectively. Rates of STEMI increased across (Hb) quartile groups from (Q1) to (Q4), as rates of non-STEMI/troponin-positive ACS decreased from (Q1) to (Q4) (p = 0.001) (table 1). Rates of severe left ventricular impairment were inversely related to Hb for patients with STEMI and non-STEMI/troponin-positive ACS (table 2). There were 19 (11.7%) STEMI deaths, 45 (9.4%) non-STEMI/troponin-positive ACS deaths, and seven (3.5%) troponin-negative ACS deaths. The proportions of deaths corresponded to the degree...
of anaemia (p<0.001) and there was a significant difference in the mean (SD) time to death between Q1 and Q4 (72.3 days (SD 109.6) and 185.4 days (SD 204.1), p = 0.041). Each increase in Hb quartile reduced the risk of death by 28% (odds ratio 0.72, 95% CI 0.54 to 0.89, p = 0.02).

Conclusion: In our study population, in patients admitted to hospital with ACS, anaemia was common and was associated with increased long-term mortality. For those with STEMI or non-STEMI/troponin-positive ACS, anaemia was associated with the degree of left ventricular impairment.

PATIENTS WITH METABOLIC SYNDROME PRESENT WITH NON-ST ELEVATION MYOCARDIAL INFARCTION AT A YOUNGER AGE AND HAVE WORSE ANGIOGRAPHIC FINDINGS

GK Rao, B Noronha, AL Innasimuthu, GK Davis. University Hospital Aintree, Liverpool, UK

Introduction: Metabolic syndrome (MS) is a major risk factor for ischaemic heart disease. The influence of MS on the outcome of acute coronary syndrome is not well defined. We investigate the influence of metabolic syndrome on angiography findings in patients presenting with non-ST elevation myocardial infarction (NSTEMI).

Methods: In this prospective case–control study over 12 months, we included unselected consecutive patients presenting with NSTEMI (diagnosed by typical chest pain suggestive of angina, elevation of troponin T >0.01 ng/l, with or without ECG changes). International Diabetes Federation criteria were used to identify the patients with MS. Patients with MS (group 1) were compared with patients without (group 2) for several variables. All patients underwent diagnostic left heart catheterisation. Left ventricular systolic function was assessed by left ventriculogram or echocardiogram (by an experienced technician, eyeballing method). A stenosis of greater than 50% of left main or greater than 75% of epicardial coronary arteries was considered significant. Statistical analysis was done by χ² and Student’s t-test and a p value less than 0.05 was accepted as significant.

Results: 94 patients were screened for MS. 74 (79%) satisfied the inclusion criteria. Patients with MS had significantly lower high-density lipoprotein levels, higher triglyceride levels, larger waist circumference and higher diastolic blood pressure (figs 1 and 2). They were also younger by 7 years at the time of the NSTEMI and were more likely to have impaired left ventricular function (table 1). 28 (37%) patients had lesions amenable for revascularisation by coronary artery bypass grafting in group 1 compared with
one (5%) in group 2 (p = 0.005). Other variables were comparable between the two groups including male/female ratio, normal ECG at admission, mean creatinine kinase and troponin T levels, systolic blood pressure, number of significant stenotic lesions and number of epicardial coronary arteries involved.

Conclusions: A very high proportion (79%) of patients with NSTEMI have MS. Patients with MS are likely to be younger at the time of presentation, have impaired left ventricular function and angiographically severe disease requiring coronary artery bypass grafting. This implicates more aggressive management of MS and further research into the effects of treatment on these outcomes.

065 CLINICAL OUTCOMES IN PRE-HOSPITAL THROMBOLYSIS IN A RURAL SETTING
1P Salahshouri, 1L Mccormick, 2P Murray, 1S Khan, 2J Scott, 2L Sharples, 1PM Schofield. 1Papworth NHS Trust, Cambridge, UK; 2East Anglian Ambulance Trust, Cambridge, UK; 2East of England Ambulance NHS Trust, Cambridge, UK; 4MRC Biostatistics Unit, Cambridge, UK

Background: Prompt reperfusion treatment with thrombolysis for ST elevation myocardial infarcts (STEMI) is associated with better prognosis. In rural areas prehospital thrombolysis (PHT) plays a particular role. In East Anglia, before the commencement of PHT, less than 25% of STEMI received thrombolysis within 60 minutes of call-to-needle time.

Method: Between November 2003 and February 2007, 1062 patients received PHT with Tienaplatel for a presumed diagnosis of STEMI. Data obtained prospectively for each patient included demographic characteristics, cardiovascular risk factors, ECG characteristics (at baseline and 90 minutes post-thrombolysis), administration times of lytic therapy, bolus heparin and heparin infusion, the need for rethrombolysis and rescue percutaneous coronary intervention, as well as figures on cardiac arrest, haemorrhagic stroke and mortality.

Results: We analyzed the data on 872 patients (mean age 64.0 years (10.6), 652 men). Of these, 705 (81%) received PHT with call-to-needle time less than 60 minutes. There were 57 (5.7%) cardiac arrests in this group, with 17 of these occurring in hospital. There were 52 deaths in this group with actuarial survival of 93.3% (SE 0.9%) at 30 days, 91.7% (SE 1.0%) at 6 months and 90.8% (SE 1.1%) at 12 months after treatment. In-hospital complications included cardiogenic shock 1.6%, gastrointestinal bleed 0.9%, and in-hospital death 1.1% at 12 months after treatment. In-hospital complications included cardiogenic shock 1.6%, gastrointestinal bleed 0.9%, and in-hospital death 1.1% at 12 months after treatment.

Conclusion: PHT has an important role to play in the treatment of STEMI in rural areas. It is safe and effective, with good clinical outcomes.

066 IS RATE OR REGULARITY THE MORE IMPORTANT RISK PREDICTOR IN POST-MYOCARDIAL INFARCTION ATRIAL FIBRILLATION?
1R Sankaranarayanan, 2MA James, 2H Gonna, 2S Burtscheill, 3R Holloway, 1Royal Blackburn Hospital, Blackburn, UK; 2Taunton and Somerset Hospital, Taunton, UK

Objectives: It is well known that atrial fibrillation (AF) is associated with increased mortality and a higher complication rate post-myocardial infarction (MI). In a previous study we showed that a significant proportion of this increased mortality is due to an increased incidence of ventricular fibrillation (VF). We postulated that this VF may be induced by the rapid irregular stimulation of the ventricle at a vulnerable time. We have now further analyzed patients with AF by evaluating their heart rate and regularity to assess which is more predictive of VF.

Methods: From among 500 consecutive patients admitted to our coronary care unit with acute MI we identified 124 with AF, who were monitored for in-hospital arrhythmias. We analyzed the ventricular rate during AF, ie, the ventricular rate on admission in patients with AF on admission and ventricular rate at AF onset in patients with new-onset AF. We also calculated the degree of irregularity by using a ratio of the longest RR interval to the shortest RR interval (irregularity index) on the ECG.

Results: Of the 124 patients with AF, 67 were already in AF on admission and 57 developed AF subsequent to admission (new onset). The results showed that during their admission, patients with AF had a significantly higher incidence of VF compared with the non-AF group (15% versus 6%, p = 0.05). The increased risk of VF was largely confined to the group with AF on admission (16%, p = 0.01), whereas the incidence of VF in the new-onset AF group was 9% (p = 0.57). The median heart rate was 90 beats per minute (range 54–150) for patients with AF on admission and 140 beats per minute (range 50–160) for the new-onset AF group (p<0.01). The mean irregularity index was 4.1 ± 1.5 for patients with AF on admission compared with 2.1 ± 0.7 for patients with new-onset AF (p<0.001). The group at highest risk of VF thus had a slower but more irregular heart rhythm.

Conclusions: In our study, AF on admission in postinfarct patients seems to be associated with an increased incidence of VF. Although these patients have a well-controlled ventricular rate in comparison with patients with new-onset AF, they also have a more irregular rhythm, possibly potentiating short–long–short sequences, thereby predisposing them to develop VF.

067 APPROPRIATENESS ASSESSMENT OF CARDIAC MAGNETIC RESONANCE IMAGING UTILISATION AND THE ROLE OF VIABILITY IMAGING IN THE PATIENT CARE ALGORITHM
M Schmitt, D Das, G McCann. Glenfield Hospital, Leicester, UK

Background: As a result of technological progress and widening clinical indications associated with increasing therapeutic options, cardiovascular imaging has seen a decade of enormous growth. However, cardiovascular imaging as a specialty largely lacks the same strong evidence base that has distinguished therapeutic cardiovascular medicine and surgery from other specialties. Consequently, the role of cardiovascular imaging within the patient care algorithm has come under scrutiny. Against this background the ACCF/ACR/SCCT/SCMR/ASNC/NASCI/SCAI/SIR published their 2006 appropriateness criteria consensus document for cardiac computed tomography and cardiac magnetic resonance imaging (CMRI) in order to ensure the efficient and equitable allocation of healthcare resources in imaging.

Objectives: First, we sought to audit our own clinical utilisation of CMRI against the appropriateness criteria over the initial 12 months since their publication. Second, we attempted to determine the impact of the imaging results on patient care using the example of viability imaging.

Methods: We retrospectively analyzed all request forms and referral letters of patients who attended for CMRI in our department between 26 September 2006 and 30 September 2007. In addition, we reviewed all case notes of patients predominantly referred for viability imaging. All original requests had been coded before acceptance by an imaging consultant (three radiologists plus one cardiologist) and were additionally retrospectively classified by two further physicians; according to the appropriateness criteria scoring system and according to clinical indication groups. When there was uncertainty (or disagreement between the two physicians) the request was deemed unclassified. In all patients referred for viability assessment, the impact of the imaging result on patient care was determined by review of the medical records.
Results: We performed a total of 699 (non-stress perfusion) CMRI in the 12 months after publication of the appropriateness criteria. A total of 639 scans (92.7%) were scored appropriate (338 ± 9×A, 290 ± 8×A, 11 ± 7×A), 11 scans were scored uncertain (U4–6), eight scans were scored inappropriate (I1–3) and 41 were scored unclassified. The breakdown of all scans according to clinical indications is shown in the figure. Patients referred for viability imaging comprised a high-risk group with 8/105 patients dying during the average follow-up of 255 ± 75 days. Viability imaging was readily and appropriately incorporated into clinical decision making with 25/27 revascularisation procedures deemed appropriate on the basis of CMRI report and clinical findings.

Conclusion: We were able to demonstrate “appropriate” usage of CMRI in a large UK tertiary centre setting. The results of viability imaging are readily used for important clinical decision making and resource allocation in a high-risk population.

068 DECLINING LIPID LEVELS IN PATIENTS ADMITTED WITH MYOCARDIAL INFARCTION TO A REGIONAL CARDIOLOGY CENTRE 2000–2006
PJ Scott, V Kodoth, R Noad, JR Bennett, JC Murphy, G Manoharan, AAJ Adgey. Royal Victoria Hospital, Belfast, UK

Background: Hypercholesterolaemia is a major risk factor for coronary artery disease. Revised Joint British Society Guidelines 2005 (JBS2) have recommended lower low-density lipoprotein (LDL) and total cholesterol with higher high-density lipoprotein (HDL) cholesterol targets for both primary and secondary prevention. We reviewed trends in fasting lipid levels of patients admitted with myocardial infarction (MI) to our centre and assessed compliance with these guidelines.

Methods: Fasting lipid profiles were analyzed in patients admitted with an MI from January 2000 to December 2006 (n = 1346). For patients admitted in 2005, lipid profile values were re-evaluated at least 6 months after admission to determine whether JBS2 target lipid values had been achieved.

Results: On admission, average total cholesterol decreased from 5.2 mmol/l in 2000 to 4.65 mmol/l in 2006 (p = 0.026) and LDL cholesterol from 3.1 mmol/l to 2.5 mmol/l (p = 0.009). HDL cholesterol rose from 1.1 mmol/l in 2000 to 1.3 mmol/l in 2006 (p = 0.006). STElevation myocardial infarction (STEMI) patients had significantly higher total cholesterol (5.12 mmol/l versus 5.04 mmol/l; p = 0.019), LDL (3.0 mmol/l versus 2.75 mmol/l; p = 0.0001) and lower HDL (1.20 mmol/l versus 1.24 mmol/l; p = 0.161) when compared with those admitted with non-ST elevation myocardial infarction (NSTEMI). The number of STEMI patients fell from 221 in 2000 to 72 in 2006 (p < 0.001). Six months after their admission in 2005, 74% had achieved LDL 71% HDL and 69% total cholesterol JBS2 targets (total cholesterol <4 mmol/l, LDL <2 mmol/l and HDL >1.0 mmol/l (men) or >1.2 mmol/l (women)).

Conclusion: Our study reveals a reduction in lipid profile values on admission from 2000 to 2006. We also noted that patients admitted with STEMI had a higher total cholesterol, LDL and lower HDL than NSTEMI. Current guidelines for the primary and secondary prevention of coronary heart disease have led to more fastidious usage of antilipid medications and have had a significant impact on the reduction of cholesterol in patients admitted with MI. The previously documented fall in patients admitted with STEMI is further highlighted in our study, which may be linked with the associated fall in average cholesterol levels.

069 INFLAMMATORY PROCESSES ARE ASSOCIATED WITH INSULIN RESISTANCE AMONG UK INDIAN ASIANS, AND NOT ACCOUNTED FOR BY OBESITY
JS Sehmi, JC Chambers, JS Kooner. Imperial College, London, UK

Background: Inflammation plays a key role in the development of atherosclerosis. Previous studies have shown that C-reactive protein (CRP), a sensitive marker of inflammation, is increased among Indian Asians and is closely associated with obesity. We investigated the relationships between CRP and metabolic risk factors in Indian Asians and European whites to identify the determinants of elevated CRP in UK Indian Asians.

Methods: We investigated 1025 healthy male participants (518 Indian Asian, 507 European white), aged 45–60 years, recruited at random from general practitioner lists in West London. Participants were characterised for conventional coronary heart disease (CHD) risk factors, insulin resistance and related metabolic disturbances, and for high-sensitivity CRP. Insulin resistance was determined from paired measurements of fasting glucose and insulin using the homeostasis model assessment–estimated insulin resistance (HOMA–IR).

Results: CRP concentrations were higher in Indian Asians, compared with European whites (p < 0.001). CRP values were strongly associated with the waist-to-hip ratio, HDL cholesterol, triglycerides, blood pressure and HOMA–IR, in both racial groups (table). In multivariate analysis, CRP showed independent associations with central obesity and insulin resistance, but not with other metabolic risk factors. Comparisons between the ethnic groups showed that increased CRP in Indian Asians

Abstract 069 Characteristics of participants

<table>
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<tr>
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<th>Indian Asians (N = 518)</th>
<th>European whites (N = 507)</th>
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<tr>
<td>Current smoking</td>
<td>6.4%</td>
<td>37.0%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HOMA–IR</td>
<td>2.9 ± 3.4</td>
<td>2.0 ± 1.9</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

CRP, C-reactive protein; HDL, high-density lipoprotein; HOMA–IR, homeostasis model assessment–estimated insulin resistance.
Comparison with Europeans was not affected by adjustment for conventional CHD risk factors, but could be accounted for completely by adjustment for the higher level of obesity and insulin resistance in Asians.

Discussion: CRP concentrations are higher in healthy Indian Asians than in European whites, and are independently associated with obesity and insulin resistance in both populations. Elevated CRP in Indian Asians is accounted for by their increased prevalence of insulin resistance, compared with Europeans. Our results suggest that inflammation and insulin resistance are closely associated among Indian Asians, and may contribute to their increased CHD risk.

Audit of Cardiac Resynchronisation Therapy

SL Smithson, MM Tynan, K Neville Smith, JM McComb. Freeman Hospital, Newcastle upon Tyne, UK

Introduction: The National Institute for Health and Clinical Excellence (NICE) issued guidance for cardiac resynchronisation therapy (CRT) in 2007, recognising that this overlapped with its previous guidance on defibrillator therapy (2005). The European Society of Cardiology (ESC) also issued guidance on device therapy in 2007. The Department of Health requires that NICE recommendations are audited, so we reviewed the indications for device implantation in consecutive patients treated with CRT at a single centre during one year.

Methods: 87 patients received CRT devices during the year 1 July 2006 to 20 August 2007. Notes were available in 86 and were reviewed. Indications for CRT and/or defibrillator therapy were defined using NICE technology appraisals: 95 (defibrillator therapy), 120 (CRT) and ESC guidelines as audit standards. 46 patients received pacemakers (CRT-P) and 40 received CRT with defibrillation capacity (CRT-D).

Results: Compliance with NICE guidance and ESC recommendations is shown in the table. CRT was indicated in 26/46 (56%) CRT-P patients using NICE and in 98% using ESC guidance. The main reasons for this difference were atrial arrhythmia in four and previous pacing in six. CRT-D was indicated in nine CRT-P patients, who did not receive it: the indication was primary prevention in ischaemic heart disease in six; two patients declined it. CRT was indicated in 27/40 (67%) CRT-D patients using NICE criteria and in 85% using ESC. The commonest reason for failure to meet criteria was symptom status, New York Heart Association I or II. Three patients did not fulfil NICE criteria for implantable cardioverter defibrillator implantation and one did not fulfil ESC criteria.

Conclusion: The vast majority of patients who received CRT-P or CRT-D fulfilled ESC criteria, but a significant minority failed to meet NICE guidance, both for CRT and for defibrillator therapy (but rarely for both). The discrepancy between the two sets of criteria and the lower proportion of patients fulfilling the more stringent NICE guidance suggest that the ESC criteria more accurately reflect clinical opinion.

Abstract 070

<table>
<thead>
<tr>
<th>Device received</th>
<th>Therapy indicated</th>
<th>NICE</th>
<th>ESC</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRT-P (n = 46)</td>
<td>Pacing</td>
<td>26</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>Defibrillator</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>CRT-D (n = 40)</td>
<td>Pacing</td>
<td>27</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>Defibrillator</td>
<td>37</td>
<td>39</td>
</tr>
</tbody>
</table>

CRT-D, cardiac resynchronisation therapy with defibrillation capacity; CRT-P, cardiac resynchronisation therapy with pacemaker; ESC, European Society of Cardiology; NICE, National Institute for Health and Clinical Excellence.
Abstract 072 Figure 1

Abstract 072 Figure 2

and four (5.2%) of 11 low-risk patients from post undergoing a stress test for further risk stratification (fig 1). Applying a generalised linear model to the length of in-hospital stay for ACS patients revealed a mean of 8.87 (CI 8.39 to 9.37) bed-days for pre and 6.04 (CI 5.55 to 6.56) bed-days for post ACS service introduction years (p, 0.001) (fig 2).

Conclusion: The establishment of a dedicated ACS service was shown to maintain similar clinical management outcomes but significantly reduce the in-hospital stay of ACS patients with consequent large cost savings (£50 000/annum). A dedicated exercise testing facility for further risk stratification of low-risk ACS patients has been established following this audit cycle.

Background: Fast rotational angiography (RA) is a new technique in which the C-arm rotates through a 120° arc over 4 seconds during a single injection of contrast medium, producing a panoramic view of the coronary arteries. Planning a percutaneous coronary intervention (PCI) is based upon scrutiny of the original diagnostic angiogram supplemented by new images obtained before the PCI.

Aim: We compared RA with conventional single-plane angiography (SPA) for pre-PCI planning.

Methods: We studied elective patients attending for PCI to non-occluded coronary arteries in a catheter laboratory equipped with a Philips Allura FD10 system. The operator selected RA or SPA for the preprocedural runs. The operator and, offline, an independent observer, scored the quality of the imaging of overall disease burden and individual stenoses, their level of confidence in assessing those parameters and their planned procedure with each modality. The x ray dose, volume of contrast, procedure time, addition or subtraction of target lesions, runs and procedure details were recorded.

Results: 120 patients were recruited, 60 for RA and 60 for SPA. The two groups were well matched for age, sex, weight, number of target lesions and equipment used. A mean 26 runs were recorded for both groups. The mean number of preprocedural runs was 3.7 (RA group; 57% of RA were supplemented with SPA) and 4.3 (SPA group) (p = 0.11). For the operator and the independent observer (respectively), RA gave greater improvement in confidence scores than SPA in the assessment of the number of target lesions (p = 0.02 and 0.06), lesion length (p = 0.01 and 0.01), degree of stenosis (p = 0.01 and 0.02) and tortuosity (p = 0.02 and 0.04). For the operators, it also gave greater confidence in lesion irregularity (p = 0.01), eccentricity (p = 0.01), branch involvement (p = 0.08 overall, and 0.03 for the left anterior descending artery/diagonal) and angulation (p = 0.06). Unplanned target lesions were added or subtracted during the PCI in 8% in the RA group versus 14% in the RA group (p = 0.18). There was no significant difference between the groups in contrast usage or x ray dose. The mean procedure time was 67 minutes (RA) versus 58 minutes (SPA) (p = 0.17).

Conclusions: RA has incremental value over SPA when recording the pre-PCI angiograms, notably in giving the operator confidence in planning the details of the intended procedure and particularly in the assessment of the number of significant lesions, percentage stenosis of intermediate lesions and bifurcations of the left anterior descending artery. Supplementation with extreme cranial and caudal and lateral views is required for selected lesions. It does not save time, contrast or x ray dose and has no extra value in simple cases.

SAFETY OF EARLY AEROMEDICAL REPATRIATION FOLLOWING ACUTE CORONARY SYNDROME

Introduction: UK residents make over 64 million visits abroad each year, with Europe accounting for 70% of destinations. Unfortunately, taking a holiday is associated with an increased risk of having a myocardial infarction. Current guidelines recommend a delay of up to 21 days after myocardial infarction before commercial air travel. The main concern for transporting cardiac patients is the effect of hypoxia at altitude and its associated reduction in ischaemic threshold. Earlier repatriation may have beneficial medical, economic and social outcomes when patients are returned to their home country. We

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Abstract 074

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group A (n = 144)</th>
<th>Group B (n = 242)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>62.7 (1.02)</td>
<td>64.8 (0.71)</td>
<td>0.09</td>
</tr>
<tr>
<td>Male/female</td>
<td>121/23</td>
<td>185/57</td>
<td>0.08</td>
</tr>
<tr>
<td>Flight time (minutes)</td>
<td>243.8 (18)</td>
<td>325.6 (18.1)</td>
<td>0.003</td>
</tr>
<tr>
<td>Distance (km)</td>
<td>2599.4 (234.0)</td>
<td>3699.7 (238.2)</td>
<td>0.002</td>
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<tr>
<td>STEMI/NSTEMI</td>
<td>97/47</td>
<td>169/73</td>
<td>0.65</td>
</tr>
<tr>
<td>PCI</td>
<td>117</td>
<td>88</td>
<td>0.0001</td>
</tr>
<tr>
<td>CABG</td>
<td>0</td>
<td>19</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention; NSTEMI, non-ST elevation myocardial infarction; STEMI, ST elevation myocardial infarction.

Methods: A retrospective analysis of the comprehensive transportation medical records of all aeromedical repatriations of patients after an acute coronary syndrome via a commercial airline undertaken by Healix International, a medical repatriation company based in Hampton, UK, from 1 April 2004 to 1 September 2007.

Results: During the study period, 386 patients were transported with a doctor escort following an acute coronary syndrome. ST elevation myocardial infarction (STEMI) was diagnosed in 266 (68.9%) patients and non-ST elevation myocardial infarction (NSTEMI) in 120 (31.1%) patients. Patients were transported 4–38 days (mean 12.5) from initial presentation. A total of 144 patients (37.3%) were repatriated <10 days (mean 8.8) from presentation (group A) and 242 (62.7%) more than 10 days (mean 15.2) from presentation (group B). There was no difference in the ratio of STEMI/NSTEMI between groups. Patients in group A were more likely to have had percutaneous coronary intervention before repatriation. Flight times and distance travelled were significantly higher in group B (table). No serious complications occurred during repatriation: no significant hypotension, arrhythmias or myocardial infarction were observed during flight. Asymptomatic hypoxia with pulse oximetry less than 92% at altitude was more common in repatriation: no significant hypotension, arrhythmias or myocardial infarction were observed during flight. Asymptomatic hypoxia with pulse oximetry less than 92% at altitude was more common in

Conclusions: Aeromedical transportation of patients following acute coronary syndrome can be safely undertaken earlier than 10 days after initial presentation with an appropriately trained medical escort.

Abstract 075

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group A (n = 144)</th>
<th>Group B (n = 242)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
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<td>0.002</td>
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<tr>
<td>STEMI/NSTEMI</td>
<td>97/47</td>
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<tr>
<td>PCI</td>
<td>117</td>
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<td>0.0001</td>
</tr>
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<td>CABG</td>
<td>0</td>
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</tr>
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Abstract 075 Figure 1

Abstract 075

Does MINAP accurately record medical practice: A comparison of MINAP data and hospital information concerning secondary prevention medication

Introduction: Recent government initiatives have set targets that allow comparison of practice across England and treatment of myocardial infarction (MI) including secondary prevention as a key feature. The Myocardial Infarction National Audit Project (MINAP) is the main tool used to measure the achievement of targets. The MINAP has defined items of data, there is not a nationally standardised form and local variances in layout and entry exist. Our analysis and MINAP stems from several sources. Although MINAP has defined items of data, there is not a nationally standardised form and local variances in layout and entry exist. Our data are entered by specialist nurses and may be done before the

Methods: Using the local database we were able to identify patients from the first (n = 65) and third (n = 58) quarters of 2006 who had received a discharge diagnosis of MI or troponin-positive acute coronary syndrome. We reviewed cases to identify those that should be excluded by MINAP criteria. Review of discharge letter and case notes (in cases in which treatment was not prescribed or clearly contraindicated) generated our most accurate “true” value. We compared this value with the MINAP report and national average (see table).

Results: Local MINAP reports suggested that prescribing was below national standards. We identified several exclusions (inpatient deaths, myopericarditis and acute transfers) from the discharge prescription analysis. There were instances in which MINAP data were incomplete or unknown. The presence of asepsis disease accounted for most cases in which β-blockers were not prescribed (25% of admissions in one month). Many patients did not achieve a normal, stable blood pressure to allow ACE inhibition, β-blockade or both within the duration of admission. Concerns about renal function and contrast use accounted for further cases in which ACE inhibitors were not given. The medical notes confirmed that doctors sometimes fail to state treatment contraindications on the discharge summary (see figs 1 and 2).

Conclusion: Our results suggest potential misreporting and dilution of nationally reported data. Therefore, MINAP may not accurately reflect acute coronary syndrome and prescribing outcomes without local quality control checks. Discrepancy between our analysis and MINAP stems from several sources. Although MINAP has defined items of data, there is not a nationally standardised form and local variances in layout and entry exist. Our data are entered by specialist nurses and may be done before the

Abstract 075

<table>
<thead>
<tr>
<th>1st quarter 2006</th>
<th>2nd quarter 2006</th>
<th>3rd quarter 2006</th>
</tr>
</thead>
<tbody>
<tr>
<td>True value (n = 65)</td>
<td>77.3 (71.2)</td>
<td>93.6 (86.3)</td>
</tr>
<tr>
<td>MINAP (n = 78)</td>
<td>77.3 (71.2)</td>
<td>93.6 (86.3)</td>
</tr>
<tr>
<td>National average</td>
<td>92.1 (89.9)</td>
<td>91.3 (91.1)</td>
</tr>
</tbody>
</table>

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II blocker; MINAP, Myocardial Infarction National Audit Project.
Abstract 076 Summary of key cardiac network responses from the questionnaire

<table>
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<th></th>
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<tbody>
<tr>
<td>Clinical CR subgroup</td>
<td>27</td>
<td>2</td>
</tr>
<tr>
<td>NSF standards met</td>
<td>12</td>
<td>17</td>
</tr>
<tr>
<td>Designated cardiologist</td>
<td>20</td>
<td>9</td>
</tr>
<tr>
<td>Increased BHF/NOF CR/heart failure grant funding</td>
<td>20</td>
<td>9</td>
</tr>
<tr>
<td>National audit data entry</td>
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<td>23</td>
</tr>
<tr>
<td>Following defined standards</td>
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<td>5</td>
</tr>
<tr>
<td>Home-based option</td>
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<td>23</td>
</tr>
<tr>
<td>NICE post-MI guidelines met</td>
<td>10</td>
<td>19</td>
</tr>
<tr>
<td>Patient involvement</td>
<td>23</td>
<td>6</td>
</tr>
</tbody>
</table>

BHF, British Heart Foundation; CR, cardiac rehabilitation; MI, myocardial infarction; NICE, National Institute for Health and Clinical Excellence; NOF, national outcome framework; NSF, National Service Framework.

Discharge letter. The data show that our prescription of secondary prevention medication in appropriate cases is close to 100%. Prescription of secondary prevention medication is affected by contraindications and side effects suggesting there would be benefit from capturing this information in MINAP records beyond simply dichotomising data. Greater clarity might be achieved by using a special discharge template to reflect national standards and when deviation has occurred.

076 AUDIT OF CARDIAC REHABILITATION ACROSS THE ENGLISH CARDIAC NETWORKS

A Varghese, A Moqshi, L Binder, R Tipson, M Walsh, EJ Flint, Dudley Group of Hospitals, Dudley, UK; NHS Heart Improvement Programme, London, UK; British Cardiac Network, London, UK; Black Country Cardiac Network, Dudley, UK.

Introduction: Cardiac rehabilitation (CR) is an evidence-based intervention in the reduction of mortality and morbidity that accompanies the global epidemic of heart disease. However, within the United Kingdom, provision of this essential aspect of management has been shown to be patchy and poor. In order to redress this deficiency, a national campaign was launched by the British Heart Foundation (BHF), the British Association for Cardiac Rehabilitation, and the BHF Care and Education Research Group at the University of York to support CR patients and service providers in conjunction with guidelines outlined within the National Service Framework (NSF). Cardiac networks are ideally placed to coordinate improvement across their health communities. We present details of the current state of development of CR across the English cardiac networks.

Method: A 16-part questionnaire was developed and distributed jointly by the Black Country Cardiac Network and the Heart Improvement Programme. Twenty-nine of the 30 cardiac networks sent this questionnaire by electronic mail in July 2007, completing responses for provisional analysis by September 2007 to inform the “Shaping the Future of Cardiology” perspective in October.

Results: Twenty-nine of the 30 cardiac networks reported on their efforts to deliver cardiac rehabilitation according to BHF/NHS standard and NICE post-MI guidelines. A designated lead CR cardiologist in 69% of the networks, with the same percentage declaring that they had received increased BHF/national outcome framework CR/heart failure grant funding. Entry of data to the National Audit of Cardiac Rehabilitation was performed by only 21% of the networks as a whole, but 90% expressed commitment to do so. 83% followed defined standards of service provision, and most of these (16 out of 24) also audited these to inform commissioning. Only 34% reported a robust commissioning link, 41% access to choice revascularisation pathway monies, but 10% were already revisiting this pathway approach with the introduction of primary percutaneous coronary intervention. A viable home-based CR option was provided by 21% of the networks, the NICE post-myocardial infarction guidelines were being met by 54% and beneficial patient involvement in cardiac networks was 79% (45% cardiac networks being specifically encouraged towards improving cardiac rehabilitation by their public and patient involvement approach).

Conclusion: This operational survey has supported cardiac networks in developing their cardiac rehabilitation work plans by sharing practice experience, finding majority commitment to the National Audit of Cardiac Rehabilitation audit longer term, identifying commissioning challenges and demonstrating the tremendous patient appreciation of valuable cardiac rehabilitation services.

077 DÉBLOCAGE, OFF-SITE PERCUTANEOUS CORONARY INTERVENTION IMPROVES ACCESS TO REVASCULARISATION IN ACUTE CORONARY SYNDROMES: RESULT OF THE STUDY OF ANGIOGRAPHY AND REVASCULARISATION IN SWINDON (STARS) AUDIT

TA Hyde, SV Venkatachalapathy, C Cannon, KDS Pannu, R Gopal, S Tholoor, C Keen, S Kuram, C Wretham. The Great Western Hospital, Swindon, UK.

Aims: Off-site percutaneous coronary intervention (PCI) started locally in April 2006. We aimed to assess the effect of this service on the care of acute coronary syndrome (ACS) patients.

Setting: A medium-size district general hospital with a single catheter laboratory without primary PCI.

Methods: Using the chest pain register and MINAP database, all patients admitted with ACS in July 2005 were identified retrospectively. All patients admitted with chest pain in July 2007 were identified prospectively. Data regarding baseline characteristics and in-hospital care were collated and compared.

Results: Of the 120 patients identified in 2005, 70 had definite ACS: ST elevation myocardial infarction (STEMI) 17; non-STEMI 23 and unstable angina n = 30. In 2007, 200 patients were admitted with chest pain, 69 of whom had definite ACS: STEMI 16; non-STEMI 22 and unstable angina n = 31. Among ACS patients the rates of angiography and revascularisation have increased in 2007 (see table). The length of stay has fallen considerably,

Abstract 075 Figure 2
ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; MINAP, Myocardial Infarction National Audit Project.
/particularly for patients who underwent inpatient angiography, mean 13 versus 21 days (see fig). In-hospital mortality was lower in 2007, 7.2% versus 14%.

Conclusion: At the Great Western Hospital the introduction of the PCI service has been associated with an improvement in the care of ACS patients.

Abstract 078
COMPLEMENT C3 IS INCORPORATED INTO FIBRIN CLOTS AND RESULTS IN IMPAIRED FIBRINOLYSIS

Background: The development of obstructive coronary artery disease is related to inflammatory atherothrombotic changes in the vessel wall. We have previously reported the importance of both inflammatory (C-reactive protein and C3) and thrombotic (plasminogen activator inhibitor 1, fibrinogen and fibrin) components in this process; however, less is known about how inflammation and thrombosis interact in disease. The main protein component of a plasma clot is fibrinogen; however, clots formed from purified fibrinogen differ substantially in structure to those formed from plasma, suggesting that other plasma proteins may be crosslinked into the clot, which significantly influence clot structure/function.

Aim: To analyze the protein components of in-vitro formed plasma clots and determine the influence of novel proteins on fibrin structure and function.

Methods: Perfused solubilised plasma clots were separated by two-dimensional gel electrophoresis and proteins were identified by matrix-assisted laser desorption/ionisation mass spectroscopy. Functional analyses included ELISA-based binding assays and turbidimetric assays of clot formation, morphology and lysis.

Results: A number of novel clot proteins were identified, including complement C3. C3 is the central component of the complement system and has previously been shown to predict the development of cardiovascular disease. This protein was therefore selected for further functional analyses. In ELISA-based binding assays, C3 bound to immobilised fibrinogen and fibrin in a dose-dependent manner, with Kds of 49.6 nM and 75.0 nM, respectively, as shown in the figure (A and B). In turbidity and lysis assays, C3 prolonged the tissue plasminogen activator-induced lysis time of fibrin clots in a dose-dependent manner in the presence and absence of crosslinking by factor XIII, as shown in the figure (C). We analyzed the association between clot lysis times and C3 in the Leeds Family Study and found that C3 was correlated with 50% lysis time (r = 0.27, p<0.001). C3 remained independently associated with lysis time after accounting for age, sex, fibrinogen, factor XIII and plasminogen activator inhibitor 1.

Conclusions: This study has shown that two-dimensional gel electrophoresis analysis of plasma clots identifies novel clot components that influence fibrin structure and function. Complement C3 binds to both fibrinogen and fibrin and prolongs tissue plasminogen activator-induced lysis time suggesting that C3 interacts with thrombotic mechanisms to influence outcome. The results provide further insights into mechanisms whereby enhanced inflammatory responses dictate disease development.

Abstract 079
NOX2 MODULATION OF CELL CYCLE INHIBITORY PROTEIN P21CIP1 IN ENDOTHELIAL CELLS
1LM Fan, 2G Viniq, 3G Brooks, 3JM Li. 1Addenbrookes Hospital, Cambridge, UK; 2University of Surrey, Guildford, UK; 3University of Reading, Reading, UK

The abilities of endothelial cells to proliferate, to be quiescent and to undergo apoptosis during remodelling are important determinants relating to angiogenesis, wound healing and many cardiovascular diseases. Endothelial cells express constitutively a NADPH oxidase, which is a major source of superoxide production. The catalytic subunit of NADPH oxidase has several isoforms (Nox1–5). However, their individual roles in endothelial function remain
unknown. In this study, we investigated the role of Nox2 in nutrient deprivation-induced cell cycle arrest and apoptosis.

In proliferating human dermal microvascular endothelial cells, Nox2 mRNA expression was low, but was upregulated 24 hours after starvation and increased to 8 ± 3.5-fold at 36 hours of starvation as detected by quantitative real-time PCR. Accompanying the upregulation of Nox2, there was a 2.28 ± 0.18-fold increase in O$_2^-$ production detected by lucigenin-chemiluminescence inhibition by tiron (O$_2^-$ scavenger), a dramatic induction of p21$^{\text{cip1}}$ and p53 protein expression detected by immunoblotting, cell cycle arrest and the onset of cell apoptosis detected by propidium-iodide FACS analysis (all p < 0.05). All these changes were inhibited significantly by adding apocynin (NADPH oxidase inhibitor), or by in-vitro deletion of Nox2 expression using full-length antisense Nox2 cDNA, or in coronary microvascular endothelial cells isolated from Nox2 knockout mice. In Nox2 knockout cells, neither O$_2^-$ production nor the p21$^{\text{cip1}}$ and p53 expressions were increased significantly after 36 hours of starvation and only 0.46% of cells were apoptotic compared with approximately 12% found in wild-type controls.

In conclusion, Nox2 is involved in the modulation of p21$^{\text{cip1}}$ and p53 expression and endothelial cell cycle regulation.

### 080 LOW-DENSITY LIPOPROTEIN CONTROLS IL-8 PRODUCTION IN MONOCYTES VIA TRIBBLES-2


**Introduction:** Inflammatory activation of monocytes is key both in physiologic innate immune responses and in pathological conditions, such as atherosclerosis and acute coronary syndromes. However, the mechanisms that modulate the responsiveness of monocytes to inflammatory stimuli are still poorly understood.

**Basic Methods:** The human samples were obtained under the ethical approval granted by the North Sheffield Research Committee. THP-1 and RAW264.7 cells were maintained and used with standard protocols. siRNA SmartPool against human Trb-2, Mkk4, Mkk7 and MeK1 were purchased from Dharmacon and used according to the manufacturer’s recommendation. Fluorescent probe Dil (Invitrogen) was used for studying acetylated low-density lipoprotein (LDL) uptake by monocytes. Western blotting, cell transfection and real-time PCR were undertaken following the standard protocol or the instructions from manufacturers. Protein-fragment complementation assay was used to study the interactions between Trb-2 and Mkk, in which the Trb-2 and Mkk were tagged with a half fragment of yellow fluorescent protein, respectively.

**Results:** Here we report that acetylated LDL potentiates lipopro- lyasacharide-induced IL-8 production in these cells. The expression of tribbles-2, a novel regulator of mitogen-activated protein kinase activation, is selectively downregulated by acetylated LDL in vitro, which results in enhanced expression of IL-8. We also demonstrate that tribbles-2 is a binding partner and a negative regulator of selected mitogen-activated protein kinase kinases. Overexpression of tribbles-2 leads to reduced activation of the ERK and JNK pathway upon lipopolysaccharide challenge. By contrast, downregulation of the expression of tribbles-2 leads to enhanced activation of these pathways and an increase in IL-8 production. Analysis of primary monocytes showed that the level of tribbles-2 expression is inversely correlated with the cell’s ability to produce IL-8. Furthermore, downregulation of trb-2 was observed in peripheral blood mononuclear cells of individuals with acute coronary syndromes, compared with samples from patients with chronic stable angina, suggesting that trb-2 may contribute to the development of acute coronary syndrome.

**Conclusion:** Taken together, our results define trb-2 as a novel key regulator of monocyte biology, which determines the capacity of these cells to produce IL-8, in inflammatory settings.

### 081 GLYCEMIC STATUS UNDERLIES THE INCREASED ARTERIAL STIFFNESS AND IMPAIRED ENDOTHELIAL FUNCTION IN SOUTH ASIAN STROKE SURVIVORS COMPARED WITH EUROPEAN CAUCASIAN COUNTERPARTS IN THE UNITED KINGDOM

A Gunaratne, J Patel, B Gammon, R Potluri, R Butt, N Panja, E Hughes, G Lip. University Department of Medicine, Birmingham, UK; 2University Department of Medicine, City Hospital, Birmingham, UK

**Background:** The pathophysiology of excessive premature cerebrovascular disease mortality among South Asian stroke survivors living in Britain remains unclear. Indices of arterial stiffness and endothelium dysfunction are accepted as independent markers of cerebrovascular disease having a positive prognostic and diagnostic impact. We hypothesised that indices of arterial stiffness and endothelial dysfunction are higher in South Asian stroke survivors compared with European Caucasians.

**Methods:** Using a representative sampling approach (West Midlands, United Kingdom) we determined arterial stiffness (SI) and endothelial-dependent vessel function (post salbutamol) and independent (post-glyceryltrinitrate) administration by digital volume pulse photoplethysmography in 100 South Asian stroke survivors and compared with 60 age and gender-matched European Caucasians in a temperature-controlled environment using a direct, standardised approach.

**Results:** Both ethnic groups were comparable for cardiovascular risk profiles (table 1), except for a higher prevalence of diabetes mellitus in South Asians (54.1% versus 10.3%; p < 0.001) and atrial fibrillation in European Caucasians (17.2% versus 3.8%; p = 0.01). South Asians had higher arterial stiffness (mean (ms$^{-1}$) (SD)) (11.06 (2.07) versus 9.78 (1.36); p = 0.008) and impaired endothelial-dependent vascular function (%). (3.68 (3.0) versus 6.53 (4.1); p = 0.007). On univariate analysis, fasting plasma glucose was negatively related to endothelial function (R = −0.57; p < 0.001) and hypertension (3.7 (0.8 to 6.5); p = 0.01) independently associated with endothelial function.

**Conclusion:** South Asian stroke survivors have an impaired endothelial-dependent vascular function and increased arterial stiffness compared with European Caucasians but this appears to explain the disproportional impact of glycaemic status and blood pressure on the vascular endothelium and aberrant remodelling of the vessel wall characteristics. Further work is warranted to determine the prognostic implications.

**Abstract 081**

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>South Asian</th>
<th>European Caucasian</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>100</td>
<td>60</td>
<td></td>
</tr>
<tr>
<td>Age, years (SD)</td>
<td>62.53 (13.1)</td>
<td>60.9 (9.02)</td>
<td>0.51</td>
</tr>
<tr>
<td>Male (%)</td>
<td>70.4%</td>
<td>69%</td>
<td>0.53</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>54.1</td>
<td>10.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>84.8</td>
<td>93.1</td>
<td>0.25</td>
</tr>
<tr>
<td>Atrial fibrillation, n (%)</td>
<td>3.8</td>
<td>17.2</td>
<td>0.01</td>
</tr>
<tr>
<td>Hyperlipidemia, n (%)</td>
<td>83.5</td>
<td>93.1</td>
<td>0.23</td>
</tr>
<tr>
<td>Smoking, n (%)</td>
<td>20.3</td>
<td>62.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td>141.2</td>
<td>135.8</td>
<td>0.19</td>
</tr>
<tr>
<td>Diastolic blood pressure</td>
<td>79.6</td>
<td>78.35</td>
<td>0.62</td>
</tr>
<tr>
<td>Serum cholesterol (mmol/l)</td>
<td>3.86 (0.77)</td>
<td>3.40 (0.53)</td>
<td>0.08</td>
</tr>
<tr>
<td>Serum HDL (mmol/l)</td>
<td>1.34 (0.38)</td>
<td>1.35 (0.37)</td>
<td>0.97</td>
</tr>
<tr>
<td>Fasting plasma glucose (mmol/l)</td>
<td>6.25 (2.31)</td>
<td>5.38 (0.51)</td>
<td>0.06</td>
</tr>
<tr>
<td>Waist-hip ratio</td>
<td>0.94 (0.11)</td>
<td>0.96 (0.12)</td>
<td>0.44</td>
</tr>
<tr>
<td>Body mass index (kg/m$^2$)</td>
<td>33.2 (4.8)</td>
<td>29.97 (5.8)</td>
<td>0.7</td>
</tr>
</tbody>
</table>

HDL, high-density lipoprotein.
Dietary-induced obesity results in metabolic and vascular insulin-like growth factor 1 resistance via disturbance of the IGF-1/insulin signalling pathway

H Imrie, H Viswanthanaran, A Rajwani, A Abbas, M Kahn, SB Wheatcroft, MT Kearney, University of Leeds, Leeds, UK

Endothelial cell dysfunction, characterised by a reduction in the bioavailability of nitric oxide (NO), plays an important role in the initiation of atherosclerosis. Insulin-like growth factor 1 (IGF-1) may be involved in the regulation of NO production via the phosphatidylinositol-3-kinase/Akt/endothelial nitric oxide synthase (eNOS) pathway. In this study we have investigated whether dietary-induced obesity leads to disturbances of this pathway.

C57/Blk6 mice fed a high fat diet for 20 weeks (n = 12) showed a significant increase in body weight and fat pad size when compared with Chow fed controls (n = 12). Blood pressure measurement showed an age-related increase in systolic blood pressure in high fat fed (19.2% from baseline) versus Chow fed mice (7.6% from baseline). Blood glucose levels increased from 13.5 to 20 mmol/l at 120 minutes in high fat fed mice, versus 5.7–7.3 mmol/l in the Chow fed group (p = 0.009) by tolerance testing. In response to insulin, blood glucose fell by 72% in the Chow fed mice, versus 5.7–6.0 mmol/l in high fat fed mice (p = 0.001). The high fat fed mice were less sensitive to IGF-1 stimulation than the Chow fed mice by IGF-1 tolerance testing (p = 0.046 at 30 minutes). The basal protein level of phosphorylated eNOS in the aortae of the high fat fed mice was 24.2% less than that of the Chow fed mice. Upon IGF-1 stimulation levels of phosphorylated eNOS increased by 45.1% in the Chow fed mice compared with a slight decrease of 5% in the high fat fed mice after normalisation to eNOS protein levels. eNOS activity in the aortae of Chow fed mice, measured by an ex-vivo l-citrulline assay, showed an increase of 1.6-fold in response to IGF-1 (100 nmol/l; 10 minutes) compared with the high fat fed mice (n = 5; p < 0.01). Phenoxyphrine-induced constriction was blunted by IGF-1, causing vasorelaxation in Chow fed mice. This relaxation effect was blocked in high fat fed mice.

These data suggest that dietary-induced obesity results in resistance to IGF-1 at both a metabolic and vascular level via an endothelial/phosphatidylinositol-3-kinase/NO-dependent mechanism.

Low-dose intravenous nitrite dilates both peripheral and central vessels in hypoxia: A potential new therapy for ischaemia

TE Ingram, AG Pinder, DM Bailey, AG Fraser, PE James. Cardiff University, Cardiff, UK; University of Glamorgan, Pontypridd, UK

Background: The initial discoveries surrounding nitric oxide (NO) physiology suggested a linear model of kinetics. Recently, this one-way model of NO metabolism has been challenged. It has been demonstrated in vitro that under favourable conditions, such as a low pH or hypoxia, nitrite (NO2) can be reduced back to NO. This being the case then the well-established but weak vasodilator effect of nitrite would be potentiated by a hypoxic environment; making it a targeted NO donor. We investigated this hypothesis by examining the effect that a low-dose nitrite infusion has under both normoxic and hypoxic conditions.

Methods: 12 healthy volunteers were studied in a controlled environmental chamber. Under room air fractional inspired oxygen (FiO2; 21%) transthoracic echocardiography, strain gauge plethysmography to measure forearm blood flow (FFB) in the non-dominant arm and ipsilateral venous blood sampling were undertaken. The chamber was then reduced to a FiO2 of 12%. After a 3-hour equilibration period repeat measurements were taken and an intravenous infusion of sodium nitrite (1000 nmol/minute) was given into the contralateral arm for 30 minutes. Next, a further peak set of measurements was taken and one final set was subsequently performed at 1 hour post-infusion. As a control the protocol was repeated on a separate occasion in six subjects during normoxia, without the 3-hour equilibration period. A variety of ECHO markers of pulmonary arterial pressure were analyzed, the most reproducible of which was the pulmonary acceleration time.

Results: Normoxia: Plasma (nitrite) was doubled by the infusion (pre-infusion 178 nmol/l; peak 596 nmol/l). At 1 hour post-infusion levels had returned to near baseline. Both FBF and pulmonary acceleration time remained unchanged during the study. Hypoxia: A similar profile of plasma (nitrite) was observed (pre-infusion 213 nmol/l; peak 424 nmol/l; 1 hour post 261 nmol/l). There was a small, non-significant, increase in FBF during the hypoxia equilibration period (pre-hypoxia 2.01 ml/100 ml per minute; pre-infusion 2.16 ml/100 ml per minute) consistent with a drop in systemic vascular resistance and an increase in cardiac output due to hypoxia. There was a significant increase in FBF in response to the infusion of nitrite (peak 3.06 ml/100 ml per minute; t-test p < 0.05), which had reduced by 1 hour post-infusion. Pulmonary acceleration time was significantly shortened in response to the infusion of nitrite.

Abstract 083

<table>
<thead>
<tr>
<th>Normoxia (mean ± SEM)</th>
<th>Pre-infusion</th>
<th>Peak</th>
<th>1 Hour post-infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Forearm blood flow (ml/100 ml/min)</td>
<td>1.54 (± 0.18)</td>
<td>1.47 (± 0.24)</td>
<td>1.38 (± 0.07)</td>
</tr>
<tr>
<td>Pulmonary acceleration time (ms)</td>
<td>230 (± 17)</td>
<td>224 (± 17)</td>
<td>225 (± 16)</td>
</tr>
<tr>
<td>Plasma (nitrite) (nmol/l)</td>
<td>178 (± 34)</td>
<td>396 (± 80)</td>
<td>222 (± 45)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hypoxia (mean ± SEM)</th>
<th>Pre-hypoxia</th>
<th>Pre-infusion</th>
<th>Peak</th>
<th>1 Hour post-infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Forearm blood flow (ml/100 ml/min)</td>
<td>2.01 (± 0.31)</td>
<td>2.16 (± 0.14)</td>
<td>3.06 (± 0.35)</td>
<td>2.76 (± 0.56)</td>
</tr>
<tr>
<td>Pulmonary acceleration time (ms)</td>
<td>252 (± 9)</td>
<td>192 (± 6)</td>
<td>211 (± 7)</td>
<td>204 (± 5)</td>
</tr>
<tr>
<td>Plasma (nitrite) (nmol/l)</td>
<td>185 (± 16)</td>
<td>213 (± 20)</td>
<td>424 (± 47)</td>
<td>261 (± 20)</td>
</tr>
</tbody>
</table>
initial 3-hour hypoxia exposure reflecting an increase in pulmonary vascular resistance (pre-hypoxia 252 ms; pre-infusion 192 ms; \(p<0.05\)). There was a significant reversal of this trend after the infusion of nitrite (peak 211 ms; \(p<0.05\)). This effect was reduced at 1 hour post-infusion (see table and fig).

**Discussion:** Our in-vivo model demonstrates that the vasodilator effects of nitrite are enhanced by hypoxia and that this difference is observed at low levels of supplementation. This feature of nitrite pharmacokinetics could have therapeutic implications in the fields of coronary ischaemia and pulmonary hypertension.

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**Abstract 084**

**INDICES OF APOPTOSIS IN PATIENTS WITH IMPAIRED GLUCOSE TOLERANCE AFTER ACUTE MYOCARDIAL INFARCTION**

S Jassiani, VJ Karthikeyan, T Millane, OYH Lip. City Hospital, Birmingham, UK

**Background:** Impaired glucose tolerance (IGT) after acute myocardial infarction (AMI) is largely ignored despite evidence of an increased cardiac event rate in such patients. We hypothesised that apoptotic cell death following AMI measured by an increase in soluble Fas and Fas ligand, two transmembrane glycoproteins involved in apoptosis, would be more pronounced in IGT patients compared with those with normal glucose tolerance (NGT).

**Method:** Consecutive non-diabetic patients presenting with AMI underwent standard oral glucose tolerance testing 3–5 days after admission. Apoptosis was assessed by measuring soluble Fas and Fas ligand levels in the fasting state and after 75 g glucose load. Soluble Fas and Fas ligand levels were measured by ELISA.

**Results:** 125 patients (mean age 59 years (SD 12.5); 107 (86%) men) were studied. Baseline levels of soluble Fas were higher in IGT patients compared with NGT patients (\(p<0.01\), with a significant increase in soluble Fas levels in response to glucose challenge in the IGT and diabetes mellitus groups (table). There was no significant difference in soluble Fas ligand levels between the groups both pre and post-glucose challenge.

**Conclusion:** IGT post-AMI is associated with significantly higher levels of soluble Fas when compared with NGT. Interestingly, the levels of soluble Fas in the IGT group are comparable with those with frank diabetes. A further increase in soluble Fas appears to occur in response to a rise in plasma glucose levels. The increase in soluble Fas may play an important role in the pathophysiological mechanisms of IGT post-AMI and its associated poor clinical outcome in such patients. Is it time actively to seek and manage IGT post-AMI?

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**Abstract 085**

**A PORCINE ENDOVASCULAR MODEL OF A CHRONIC TOTAL CORONARY ARTERY OCCLUSION**

1DJS Kelly, 2AC Morton, 3T Raina, 4H Lupton, 5P Arnold, 6J Gunn, 7AH Gershlick.
1Glentfield General Hospital, Leicester, UK; 2University of Sheffield, Sheffield, UK; 3Brivant Ltd, Galway, Ireland

**Background:** Chronic total coronary artery occlusion (CTO) remains a significant clinical challenge for percutaneous coronary intervention. There is a need for a reliable, simple, endovascular model to test new therapies.

**Aim:** To produce a survivable CTO in a normal pig coronary artery using endovascular means.

**Methods:** 34 pigs (38 vessels) underwent endovascular intervention to their coronary arteries in a sequential, “block”, evolutionary, experimental design of three to four animals in each group, in which different potential methods were tested in each group. Three devices were studied: a suture-constricted, balloon-expandable, PTFE-coated, stainless steel stent graft; a suture-constricted, self-expanding, nitinol, PTFE-coated stent graft; and a copper-plated, stainless steel, balloon-expandable stent (fig). Two pig sizes were tested: 18 and 50 kg. Four deployment sites were tested: proximal and mid-left anterior descending artery and right coronary artery. Two stent–artery ratios were tested: 1 : 1 and 1.25 : 1. Two antiplatelet strategies were tested: aspirin alone for 5 days and aspirin and clopidogrel for 5 weeks. The endpoint was animal survival with angiographic and histological evidence of a CTO at 28 days.

**Results:** The best results (100% survival with angiographic and histological evidence of a CTO) was obtained in 50 kg pigs, with deployment of a copper-plated, balloon-expandable stent in mid-right coronary artery, at a stent–artery ratio of 1 : 1, with 5 weeks dual antiplatelet therapy.

**Conclusions:** A reliable, simple, endovascular model of CTO is possible in the pig coronary artery using a copper-plated stent. It would lend itself to the testing of new recanalisation and revascularisation strategies.

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**Abstract 086**

**EVIDENCE FOR A POTENTIAL NEW METHOD OF THERAPEUTIC ANGIOGENESIS: INCREASED ENDOTHELIAL CELL MOBILITY AND TUBULE FORMATION IN CELL CULTURE AFTER STABILISATION OF HYPOXIA-INDUCIBLE FACTOR**

1DJK Kelly, 2VJ Mecinovic, 3CJ Schofield, 4J Gunn, 5AH Gershlick, 6Glenfield Hospital, Leicester, UK; 7University of Oxford, Oxford, UK; 8Northern General Hospital, Sheffield, UK

**Introduction:** Chronic total coronary occlusions are often resistant to treatment by percutaneous intervention. Clinical trials of therapeutic angiogenesis with the systemic administration of single-protein growth factors such as vascular endothelial growth factor (VEGF) have been negative. Hypoxia-inducible factor (HIF) binds DNA sequences within the hypoxia response elements of several target genes involved in angiogenesis, and thus the
upregulation of HIF is potentially a more physiological pro-angiogenic therapy than the addition of growth factors such as VEGF. In humans the proteolytic stability of HIF is regulated via oxygen-dependent hydroxylases. Endothelial cells coalesce into tubule structures when cultured on the basement membrane extract, matrigel. We tested whether a prolyl-4-hydroxylase inhibitor, di-methyl oxalyl glycine (DMOG), could accelerate endothelial cell mobility and tubule formation in an in-vitro angiogenesis model.

**Method:** EHy926 human umbilical vein endothelial cells were cultured in DMEM with 2% HAT and 2% FBS. 72 wells of a 96-well plate were inoculated with 40,000 cells per well, passage 4/5, over 50 μl of reduced growth-factor matrigel. 100 μl of culture medium was added with 125 μmol DMOG, 250 μg VEGF or 125 μmol glycine (control). 160 μmol of a specific VEGF receptor inhibitor was added to alternate wells. Wells were photographed at 4, 8, 16, 24, 36 and 48 hours for evidence of cell migration. Blinded off-line digital image analysis using a 10 x 10 overlay-grid was performed to measure the percentage proportion of grid squares containing one or more branching tubule structure (tubule coverage). Statistical analysis was by paired t-test.

**Results:** Minimal tube formation was present at 8 hours. By 16 hours DMOG culture produced similar tubule coverage to VEGF but more than control, mean (SD) DMOG 38.7 (3.6), VEGF 33.4 (4.6), p = 0.60; control 4 (1.7), p = 0.012. The addition of a VEGF receptor inhibitor reduced mean tubule coverage at 16 hours in DMOG culture to 30.3 (2.5), p = 0.038 and essentially abolished migration under VEGF culture, tubule coverage 0.5 (0.7). Cell migration was complete in all cultures by 36 hours (fig).

**Conclusions:** The addition of DMOG to endothelial cells in matrigel culture accelerates endothelial cell migration and tubule formation. This effect is partly mediated via VEGF. HIF-stabilising compounds may promote collateral vessel formation in vivo. We are currently investigating their use as stent-based therapy in a novel porcine percutaneous model of coronary occlusion.

**Abstract 087**

**In-vivo Observations on Angiogenesis: Dose-Dependent Effects of the Prolyl-4-Hydroxylase Inhibitor, Di-Methyl Oxalyl-Glycine, on Arterial Development in Embryonic Zebrafish**

1DJ Kelly, 1DJ Mecinovic, 1CJ Schofield, 1J Gunn, 1AH Gershlick, 1T Chico, 1Glenfield Hospital, Leicester, UK; 2University of Oxford, Oxford, UK; 3Northern General Hospital, Sheffield, UK; 4University of Sheffield, Sheffield, UK

**Introduction:** Hypoxia-inducible factor (HIF) binds DNA sequences within the hypoxia response elements of several target genes involved in angiogenesis. The manipulation of HIF is a potential target for therapeutic angiogenesis. In humans the proteolytic stability of HIF is regulated via oxygen-dependent hydroxylases. We tested whether a prolyl-4-hydroxylase inhibitor, di-methyl oxalyl glycine (DMOG) was active in-vivo using a zebrafish model of arteriogenesis and collateral vessel formation.

**Method:** The zebrafish (*Danio rerio*) embryo, by virtue of its translucency, is used as a model of arteriogenesis. Gridlock mutant embryos (GM), n = 320, were produced by insertional mutagenesis and expressed a phenotype with occluded proximal aorta in association with a variable degree of distal collateral formation via intersegmental vessels. GM embryos, 3 days post-fertilisation were exposed to a range of DMOG concentrations in E3 medium and the proportion of embryos displaying distal aortic flow via collateral vessels was quantified by light microscopy. Transgenic zebrafish embryos (Fly 1 mutants, fig 1) expressing green fluorescent protein as an endothelial cell marker (n = 956), were collected 3 hours post-fertilisation and exposed to increasing doses of DMOG up to 100 μmol. The effect upon arteriogenesis was observed with fluorescent confocal microscopy.

**Results:** DMOG did not affect the rate of collateral recruitment among GM embryos. At day 5 post-fertilisation, there was no difference in the rate of collateral recruitment between the embryos exposed to DMOG 100 μmol and control GM embryos: distal aortic flow was seen in 38.5% of those in DMOG and 49.5% of embryos in control medium, p = 0.38. A dose-dependent relationship was observed between DMOG concentration and altered arteriogenesis in the Fly-1 mutant embryos. At 27 hours post-fertilisation 5.7% of control embryos displayed evidence of alteration in development of
the aorta or intersegmental vessels with ectopic vasculature and arteriovenous fistulation. In DMOG 50 μmol 41.4% displayed altered vasculature, p = 0.003; rising to 96.8% of embryos exposed to DMOG 100 μmol, p < 0.001. Structural changes were observed in the aorta and in the adjacent notochord, a structure that is known to signal embryonic artemogenesis via vascular endothelial growth factor (fig 2).

Conclusions: DMOG affects embryonic zebrafish artemogenesis in a dose-dependent manner. Initial published data suggest that HIF-stabilising compounds may play a role in promoting collateral vessel formation in vivo. We are currently investigating their use as stent-based therapy in a novel porcine percutaneous model of coronary occlusion.

**088 ATORVASTATIN ACTIVATES A NOVEL NBS1-DEPENDENT MECHANISM OF ACCELERATING DNA REPAIR IN ATHEROSCLEROSIS**

MM Mahmoudi, I Gorenne, JR Mercer, N Figg, MR Bennett. Addenbrooke’s Hospital, Cambridge, UK

There is evidence that reactive oxygen species (ROS) and DNA damage promote the development and complications of atherosclerosis. Although treatment with the HMG-CoA reductase inhibitors (statins) is beneficial in both primary and secondary prevention studies, many of these effects may be independent of their cholesterol-lowering properties. We have studied the role of oxidative stress and its modulation by statins in the DNA damage response and repair pathways of normal and plaque human vascular smooth muscle cells (VSMC). Using dual immunohistochemistry, human plaque VSMC showed increased expression of the DNA damage markers P-ATM/ATR substrate and P-H2AX with increasing disease severity. Cultured plaque VSMC showed a 1.5-fold increase in oxidative stress, a 4.4-fold increase in double-stranded DNA breaks using a COMET assay and the expression of P-ATM and P-H2AX by Western blots. ROS analogues induced a robust DNA damage response in VSMC, characterised by lengthening of tails on COMET assay and activation of ATM and NBS1, with completion of repair by 6 hours. Atorvastatin pretreatment did not reduce ROS or initial DNA damage, but accelerated DNA repair and the kinetics of induction of NBS1 and P-ATM. Atorvastatin could also markedly reduce telomere shortening in culture induced by oxidative stress. Atorvastatin induced phosphorylation of Hdm2 and delayed the degradation of NBS1 siRNA knockdown of Hdm2 replicated the effect of atorvastatin on NBS1, confirming that the effect of atorvastatin required Hdm2. The ability of atorvastatin to accelerate repair was also completely dependent on NBS1, as atorvastatin could not accelerate P-ATM or DNA repair in cells either null or expressing constitutively active NBS1. To examine the effects of atorvastatin administration on other organs and cell types after DNA damage, we administered atorvastatin to mice for 2 weeks before sublethal total body irradiation and harvested organs 0–24 hours later. Atorvastatin pretreatment reduced P-H2AX expression indicating more rapid double-strand break repair. Finally, we treated rabbits with pre-existing neointimal lesions transferred from a high fat to a low fat diet with either statin or control. Statin treatment markedly reduced the expression of P-ATM/ATR substrate and 8-Oxo-G. In both irradiated mice and rabbits the effects of statin treatment were independent of any effect on serum lipids. In summary, we have identified a novel mechanism of accelerating DNA repair. Statins accelerate DNA repair via the phosphorylation of Hdm2, stabilisation of NBS1 and more rapid phosphorylation of ATM and H2AX. Acceleration of DNA repair results in faster recovery of DNA integrity, limiting tissue toxicity after irradiation or oxidant damage, suggesting that statins may be useful adjunctive treatment to radiotherapy. Furthermore, acceleration of DNA repair and amelioration of cellular senescence may be important mechanisms by which statins stabilise atherosclerotic plaques.

**089 L-ARGININE SUPPLEMENTATION IN HYPERCHOLESTEROLAEMIC PATIENTS WITH THE ASP298 ENOS VARIANT**

RK Nair, 1AM Dart, 1JF Chin-Dusting, 2NN Huynh, 2NN Huynh. 1Hull Royal Infirmary, Hull, UK; 2Alfred Hospital, Melbourne, Australia; 3Baker Heart Research Institute, Melbourne, Australia

Background: A single nucleotide polymorphism in the endothelial nitric oxide synthase (eNOS) gene, resulting in glutamate (Glu) to aspartate (Asp) substitution at amino acid position 298 is associated with endothelial dysfunction, systemic hypertension1 and vascular disease.2

Aim and Hypothesis: This prompted us to examine whether individuals at high cardiovascular risk carrying such a mutation display a phenotypic profile of worse endothelial dysfunction and can respond better to therapy. We thus investigated whether the nitric oxide parent compound L-arginine can revert endothelial dysfunction more effectively in hypercholesterolaemic patients with the Asp298 eNOS variant.

Methods: Hypercholesterolaemic patients with no other cardiovascular risk factors were identified from the Alfred and Baker Gene Bank database. The eNOS gene fragment was amplified by standard PCR from gDNA and genotyping was performed by restriction enzyme digest. The study group, homozygous for the Asp298 eNOS variant (Asp/Asp; n = 5) were age and sex matched with controls homozygous for the Glu298 eNOS variant (Glu/Glu; n = 6). In a randomised crossover study design, forearm vascular responses to intra-arterial acetylcholine (ACh) at 18.5 and 37 μg/l and sodium nitroprusside (SNP) at 4 and 8 μg/l were obtained in the absence and presence of either L-arginine or its inert isomer D-arginine 5 mg/kg per minute (delivered in a double blind protocol) using venous occlusion plethysmography. Plasma nitrate (NO3) levels were determined by Griess reaction.

Results: Baseline forearm blood flow was similar in both groups (Asp/Asp versus Glu/Glu; 3.07 ± 0.54 and 4.03 ± 0.41 ml/100 ml per minute; p = 0.18). Neither responses to ACh nor SNP differed between the two groups. Both L- and D-arginine increased baseline forearm blood flow levels significantly but neither augmented the vasodilatory responses to ACh (L-arginine p = 0.77) nor SNP. Basal plasma NO3 levels were similar in both groups (p = 0.07) although a decreasing trend in the Asp/Asp group was observed.

Conclusions: Hypercholesterolaemic patients with Asp298 eNOS polymorphism do not exhibit greater impairment of endothelial function as assessed by vasodilatory response to acetylcholine nor respond better to L-arginine therapy. We have shown that hypercholesterolaemic patients with the Asp298 gene do not display a greater impairment of endothelial function compared with patients homozygous for the Glu298 gene. To our knowledge this is the first vascular functional study in patients with eNOS gene polymorphisms in a population at high risk of developing atherosclerosis. It demonstrates that the genetic mutation does not translate to an impaired vascular phenotype.


**090 THE CONTRIBUTION OF ENDOTHELIAL-DERIVED HYPERPOLARISING FACTOR AND NITRIC OXIDE TO BASAL AND STIMULATORY VASODILATOR TONE IN METABOLIC SYNDROME**

M Ozkor, J Murrow, N Kavtaradze, A Sheikh, J Jorgensen, K Pohlel, A Manatunga, A Qayyum. Emory University, Atlanta, Georgia, USA

Background: Vasodilator tone in humans is modulated by a variety of endothelium-derived factors including nitric oxide (NO) and endothelium-derived hyperpolarising factor (EDHF). EDHF contributes to vasodilation by stimulating calcium-dependent potassium channels (KCa) that can be inhibited by tetraethylammonium.

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In vivo application of rapamycin-eluting microbeads inhibits vein graft disease in a porcine model

T Rajathurai, SIA Rizvi, AC Newby, GJ Murphy. Bristol Heart Institute, Bristol, UK.

Introduction: Failure of human aortocoronary vein grafts due to neointima formation is a result of smooth muscle cell proliferation. Rapamycin is a known antiproliferative agent that is effective when delivered locally from drug-eluting stents. We investigated the effects of gradual release rapamycin-eluting microbeads applied in vivo to the adventitial surface of experimental pig vein grafts of similar calibre to human vein grafts.

Methods: Rapamycin-eluting polyvinyl alcohol (PVA) microbeads suspended in vehicle (pluronic gel) were applied to the adventitial surface of porcine saphenous vein to carotid artery interposition grafts. Morphometric and immunocytochemical analyses were performed at 4 weeks post-grafting. Values are expressed as mean ± standard error.

Results: Neointimal thickness (102 ± 15 μm rapamycin versus 210 ± 29 μm control, n = 8, p = 0.005), medial thickness (231 ± 18 μm versus 308 ± 38 μm, p = 0.09) and overall wall thickness (334 ± 27 μm versus 518 ± 65 μm, p = 0.02) were reduced by low-dose rapamycin-eluting microbead application in 4-week vein grafts. There was no difference between treated and control groups at the higher dose, possibly as a result of a systemic effect of rapamycin release. Immunocytochemical staining for Dolichos biflorus agglutinin lectin demonstrated no loss of endothelium in the microbead-treated grafts at any dose when compared with controls.

Conclusion: Rapamycin-eluting microbeads, when applied in vivo, reduced neointima formation in porcine vein grafts at 4 weeks without significant endothelial denudation. These results demonstrate that microbeads may be used as a delivery vehicle for antiproliferative agents at the time of aortocoronary bypass grafting. Ultimately, this may help in reducing the incidence of vein graft failure in cardiac surgery patients.
abdominal aorta (distal descending aorta 8.4 ± 1.8 versus 11.4 ± 2.3 mm Hg⁻¹ × 10⁻³; p<0.05).

Conclusion: Acute elevation of FFA in healthy subjects results in a significant reduction in aortic distensibility. More distal aortic regions were associated with relatively larger reductions in aortic distensibility compared with more proximal regions; a pattern similar to that seen in obesity. Elevation of FFA is associated with oxidative stress and has been shown to impair endothelium-dependent relaxation in isolated rabbit aorta and human studies of leg blood flow in obese subjects using a similar infusion to our study. This suggests that our observed aortic changes may be due to similar mechanisms.

093 WEIGHT LOSS REVERSES AORTIC DISTENSIBILITY CHANGES IN SUBJECTS WITH SEVERE OBESITY BUT NO IDENTIFIABLE CARDIAC RISK FACTORS: A 1-YEAR FOLLOW-UP STUDY


Introduction: Obesity has been linked to reduced aortic elastic function but studies of central aortic distensibility in obesity are limited. Our hypothesis was that aortic distensibility changes in severe obesity are at least partly reversible over one year after significant weight loss.

Method: Seventy-one subjects, all with no identifiable cardiac risk factors, (46 obese BMI 38.4 ± 7.2, 25 normal weight BMI 21.9 ± 1.8) underwent magnetic resonance imaging of the aorta at 1.5 T. Aortic distensibility was assessed at three levels; the ascending (Ao) and proximal descending aorta (PDA) at the level of the pulmonary artery and the abdominal aorta (DDA). There were no significant differences in fasting glucose (5.2 ± 0.6 versus 4.9 ± 0.4 mmol/l, p = 0.10), cholesterol (5.0 ± 0.8 versus 5.3 ± 0.9 mmol/l, p = 0.27), systolic blood pressure (122 ± 13 versus 115 ± 10 mm Hg, p = 0.10) or diastolic blood pressure (76 ± 8 versus 75 ± 8 mm Hg, p = 0.09) between obese and normal weight subjects, with all measurements remaining in the normal range. Twenty obese subjects have undergone repeat imaging after one year of significant weight loss (21 ± 17 kg; 19% body weight).

Results: Obesity was associated with a significant decrease in aortic distensibility at all three levels of the aorta (Ao 4.6 ± 2.0 versus 5.3 ± 3.2 mm Hg⁻¹ × 10⁻³, p<0.01; PDA 4.1 ± 1.3 versus 5.8 ± 2.2, p<0.001; DDA 5.6 ± 2.2 versus 7.9 ± 3.2, p<0.001). More distal aortic regions were associated with relatively larger reductions in aortic distensibility compared with more proximal regions. After a one year period of weight loss, there was a significant increase in aortic distensibility in the DDA (7.0 ± 2.6 versus 4.9 ± 1.7, p = 0.002), aortic distensibility improvements in proximal sections did not reach statistical significance (Ao 3.9 ± 1.6 versus 5.0 ± 3.2, p = 0.12; PDA 4.4 ± 1.3 versus 4.9 ± 2.1, p = 0.24) (fig).

Conclusion: Using regional magnetic resonance imaging measurements of the aorta, significant reductions in regional mechanical function have been shown in obese individuals in the absence of hypertension, hypercholesterolaemia or diabetes when compared with lean age and sex-matched controls. The pattern of this reduction shows a relatively greater reduction in compliance and distensibility in more distal (proximal descending and abdominal) segments of the aorta as opposed to the more proximal segment (ascending aorta). After one year of substantial weight loss aortic elastic properties are improved. Distal aortic elastic function appears to be more sensitive to changes in BMI than more proximal regions.

094 LONG-TERM ORAL TETRAHYDROBIOPTERIN SUPPLEMENTATION REDUCES ATHEROSCLEROSIS IN APOLIPOPROTEIN E KNOCKOUT MICE

1TS Schmidt, 1MJ Crabtree, 1AHB Hale, 2CA O’Neill, 1NJ Alp. 1Department of Cardiovascular Medicine, Oxford University, Oxford, UK; 2BioMarin Pharmaceutical Inc, Novato, California, USA

The balance between nitric oxide (NO) production by “coupled” endothelial nitric oxide synthase (eNOS) and pathological superoxide production by “uncoupled” eNOS depends on the availability of its cofactor tetrahydrobiopterin (BH4). Previous research suggests that BH4 supplementation may restore eNOS coupling in vascular disease. We tested a novel stable pharmaceutical formulation of BH4 as an oral therapeutic agent to reduce atherosclerosis in male apolipoprotein E knockout (ApoE-KO) mice. Single oral dose pharmacokinetic studies (10, 50, 500 mg/kg) revealed rapid BH4 uptake from the gastrointestinal tract into plasma and organs. Although in most organs BH4 levels increased at 24 hours, suggesting active mechanisms for BH4 absorption, BH4 levels in the aorta remained markedly reduced at 8 hours or 12 weeks in ApoE-KO mice fed a standard chow diet had no effect on heart rate, blood pressure, or lipid profile at any dose. Oral BH4 treatment at 10 mg/kg per day resulted in reduced aortic root plaque area (45% reduction at both time points) compared with placebo (p<0.05) (figs 1 and 2). At higher doses (50 and 100 mg/kg) BH4 showed no effect on aortic root plaques in ApoE-KO mice, compared with placebo (p>0.05) (figs 1 and 2).
500 mg/kg per day) we observed a trend towards decreased lesion size, but there was significantly impaired weight gain in these two groups. In conclusion, these data indicate a marked reduction in atherosclerosis by low-dose BH4 supplementation in ApoE-KO mice, highlight important tissue-specific differences in BH4 uptake and retention and indicate possible toxicity at higher BH4 doses. These results will guide translational studies of this novel stable BH4 formulation as a potential therapy for vascular disease.

095 THE ROLE OF THE FIBRINOGEN ALPHA CHAIN IN CONTROLLING THE RATE OF FXIII ACTIVATION: IMPLICATIONS FOR CORONARY ARTERY THROMBUS FORMATION


Background: The development of an obstructive arterial thrombus is dependent on the generation of a platelet-rich fibrin mesh secondary to plaque rupture. Fibrin itself is formed by the cleavage of fibrinogen by thrombin with subsequent fibrin cross-linking by factor XIII B subunit (FXIIIB); however, the mechanisms for this dissociation of coagulation factor XIII A subunit (FXIIIA) from the B subunit in the presence of 1.5 mmol calcium, compared with 10 mmol calcium required to cause the same degree of FXIII activation in the absence of the α-chain.

Conclusions: The binding of both FXIII A and B subunits to this area of the fibrinogen α-chain plays a crucial role in controlling the amount of activated FXIII generated for clot stabilisation and presents a potential target for therapeutic intervention.

Funding: This work was supported by British Heart Foundation Programme grant RG/03/004.

096 ALDOSTERONE ANTAGONISM FOR POORLY CONTROLLED HYPERTENSION IN TYPE 2 DIABETES: CONFLICTING EFFECTS ON BLOOD PRESSURE, ENDOTHELIAL FUNCTION, GLYCAEMIC CONTROL AND HORMONAL PROFILES

K Swaminathan, J Davies, J George, NS Rajendra, AD Struthers. Ninewells Hospital and Medical School, Dundee, UK

Abstract 096 Table 1

<table>
<thead>
<tr>
<th>Age</th>
<th>62.6 years (48–78)</th>
</tr>
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<tr>
<td>BMI</td>
<td>30.6 (3.8)</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>162.7 (17.2)</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>88.9 (9.2)</td>
</tr>
<tr>
<td>Sodium, mmol/l</td>
<td>140.1 (2.6)</td>
</tr>
<tr>
<td>Potassium, mmol/l</td>
<td>4.3 (0.3)</td>
</tr>
<tr>
<td>Urea, mmol/l</td>
<td>6.1 (1.8)</td>
</tr>
<tr>
<td>Creatinine, μmol/l</td>
<td>94.4 (18.3)</td>
</tr>
<tr>
<td>Male (female)</td>
<td>28 (10)</td>
</tr>
<tr>
<td>ACEI/ARB</td>
<td>100% (29/9)</td>
</tr>
</tbody>
</table>

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; BMI, body mass index.
Abstract 096

Introduction: The human cardiac troponin I (hTnIc) gene shows cardiac-specific and developmentally regulated expression, with TnIc mRNA expression increasing towards birth in both rodents and man. An electrophoretic mobility shift analysis (EMSA) showed that four proteins present in cardiac muscle extracts bind a novel CACC/Sp1 element within the hTnIc proximal promoter. Two of these proteins were identified as Sp1 and Sp3. The other two proteins appeared to be novel heart-enriched CACC-box binding proteins 1 and 2. We hypothesised that HCB1 and HCB2 might be important tissue-restricted regulators of cardiac gene expression and employed yeast one-hybrid screening in order to identify them.

Methods: A rat neonatal cardiac myocyte (NCM) cDNA library was screened in yeast with the hTnIc CACC/Sp1 element, and library proteins that bind this element were identified by DNA sequencing.

Results: Several transcription factor clones were obtained, one of which encoded nuclear factor 1-A (NF1-A). Inspection of the hTnIc CACC-box, which is present in the EMSA and yeast one-hybrid probes, revealed a potential NF1 binding site overlapping the CACC-box. Using competition and supershift EMSA we showed that HCB1 and HCB2 represent NF1-A protein–DNA complexes. Cardiac NF1-A transcripts are abundantly expressed in both myocytes and fibroblasts and at time points consistent with the expression pattern of TnIc. The NF1-A gene is subject to alternative splicing and we found that NF1-A represses the hTnIc promoter in primary rat NCM cultures. Moreover, mutation of the NF1 binding site in the hTnIc promoter leads to a six to eightfold increase in promoter output in transfected NCM. However, a splice variant that has a different C-terminus acted as an activator in this system, suggesting that different NF1-A isoforms can up or downregulate hTnIc expression. Preliminary in-situ hybridisation data indicate that in the early mouse embryo (E10.5), NF1-A is expressed widely in the heart (pericardial sac, endocardial cushions and endocardium) but is absent from the myocyte. A genome-wide microarray study indicates that levels of NF1-A expression correlate with NF1-B expression. Current work is testing whether NF1-A forms functional heterodimers with this close family member.

Conclusions: In summary, we have identified an NF1 binding site within the hTnIc promoter and shown that it binds NF1-A. Different NF1-A isoforms may regulate TnIc expression in the adult cardiac myocyte and prevent TnIc expression in non-myocytes. We hypothesise therefore that NF1-A expression is dynamically regulated during development, and speculate that it may contribute to targeting TnIc expression to the cardiac myocyte at certain developmental stages by preventing aberrant TnIc expression in other myocardial cell types.

Funding: This work was supported by the British Heart Foundation and an NHLI PhD studentship.
Objective and Methods: To identify the atrial protein changes in CHF, we applied high-throughput proteomic analysis to left atrial cardiomyocytes harvested from sham (n = 5) and ventricular-tachycardia-paced (VTP, 240 bpm × 2 weeks, n = 4) CHF dogs. Protein extracts were subjected to two-dimensional gel electrophoresis using differential in-gel electrophoresis technology. Proteins that were found to be differentially expressed between the groups (p < 0.05) were excised for identification using tandem mass spectrometry.

Results: From our protein extracts, 1105 proteins were resolved using two-dimensional gel electrophoresis, and 225 proteins were significantly altered between the groups (152 increased, 93 decreased in VTP). To date, 166 of these have been identified by mass spectrometry. Groups of proteins that may be functionally important in the development of atrial fibrillation in this model of CHF were identified. Among the significantly upregulated atrial proteins in CHF were heat shock proteins (HSP; α-B crystallin, HSP70 and CRTF78) and numerous structural proteins (including desmin, filamin C, tubulin and vimentin). An increase was seen in fragments of both desmin and filamin C. Downregulated proteins included antioxidants (superoxide dismutase and peroxiredoxin 3), key enzymes involved in metabolism (pyruvate dehydrogenase E1 component α subunit, malate dehydrogenase, isocitrate dehydrogenase 1, H+ transporting ATP synthase mitochondrial F0 complex and ubiquinol-cytochrome C reductase core protein 1) and contractile proteins (myosin light chains 1 and 2 and cardiac troponin T). Interestingly, an atrial to ventricular switch was observed, with decreased expression of the atrial myosin light chain 2 and a corresponding increase in the ventricular isoform.

Conclusions: VTP-induced CHF substantially alters the atrial protein expression profile. Upreregulated HSP may reflect autoprotective mechanisms, whereas increased fragmentation of desmin and filamin C suggests structural damage. Downregulated contractile proteins probably account for thrombosis-promoting stunning, antioxidants reflect oxidative stress and decreased metabolic proteins suggest adaptations to increased metabolic needs. The myosin light chain 2 switch observed may be an adaptive response to contractile dysfunction. All protein changes observed may be important in the pathogenesis of atrial fibrillation. This first large-scale proteomic analysis of CHF-induced atrial remodelling provides novel insights into molecular mechanisms underlying an atrial remodelling paradigm of substantial clinical relevance.

MYOCARDIAL WALL MOTION IN ZEBRAFISH EMBRYOS ASSESSED BY VIDEO EDGE DETECTION: INFLUENCE OF NOREPINEPHRINE, MS-222 AND TEMPERATURE

MA Denvir, CS Tucker, JJ Mullins. University of Edinburgh, Edinburgh, UK

Background: Zebrafish are increasingly used to study the influences of gene mutation and manipulation on cardiac development, structure and function. In this study, a video edge detection system was used to characterise, continuously, cardiac ventricle wall motion in 2–5-day-old zebrafish embryos embedded in 0.6% agar and examined under light microscopy at room temperature (22 °C). Using video edge detection software (IonOptix Inc), the motion of a small region of the cardiac ventricle wall (see fig) was converted to a continuous chart trace allowing analysis of wall motion amplitude (WMA) and myocardial wall velocity during systole (MWVs) and diastole (MWVd).

Results: Cardiac wall motion characteristics changed progressively from day 2 to 5 (WMA, 2 days, 17.6 ± 4.4 μm versus 5 days, 24.6 ± 4.7 μm, p < 0.01). MWVd was more rapid than MWVs at all developmental time points. Embryonic hearts were also assessed after increasing concentrations of norepinephrine and the anaesthetic agent MS222 (tricaine) were added to the bathing water. In response to norepinephrine, WMA increased significantly more in 4-day embryos compared with 2-day embryos (change in WMA, 13.6 ± 8.2 μm versus 4.0 ± 8.8 μm, p = 0.01, respectively), whereas the decrease in WMA in response to MS222 was similar in both 2 and 4-day embryos. Heart rate, MWVs and MWVd were significantly higher at 28 °C compared with 22 °C.

Conclusions: Video edge detection appears sufficiently sensitive to detect subtle changes in diastolic and systolic cardiac function during development and changes resulting from pharmacological and environmental interventions. Such measurements could be valuable in the assessment of altered cardiac function after genetic manipulation.

ROLE OF THE KLF15 TRANSCRIPTION FACTOR IN AN ANTI-HYPERTROPHIC PATHWAY INVOLVING GSK3β

S Hussain, E Lara-Pezzi, N Brand. Heart Science Centre, Imperial College London, Harefield, UK

Introduction: Members of the Krüppel-like factor (KLF) family of transcription factors function as transcriptional activators and/or repressors depending on cell and gene context. KLF15, which is expressed in the cardiac myocyte, has been shown to be downregulated in cardiac hypertrophy and may be an inhibitor of cardiac hypertrophy and the progression to heart failure. The aim of our study was to map domains of KLF15 that interact with co-activators or repressors and identify signalling pathways that target this factor.

Methods: In order to identify co-activators for KLF15, fusions of full-length or truncated KLF15 open reading frame attached to the GAL4 DNA-binding domain were created and transfected into cultured cells along with a luciferase reporter containing five copies of the GAL4 binding site. Co-immunoprecipitation, GST-pulldown assays and Western blotting were used to confirm activity and changes in signalling pathways affected by KLF15.

Results: We identified two activation domains, a weak one (aa 1–100) and a second potent domain (aa 100–200). We found that the transactivation abilities of GAL4-KLF15 are enhanced by CREB-binding protein (CBP), suggesting that KLF15 transactivates via recruitment of CBP. An interaction between KLF15 and CBP was shown both in vitro and in vivo and mapped to the first activation domain (AD1) of KLF15. This region contains an LxxLL motif.
(where X is any amino acid) that has been shown to mediate protein–protein interactions between CBF and other transcription proteins, such as nuclear receptors and the co-activator PGC-1α. Mutation of the LxxLL motif to LxxAA not only abolished the interaction between KLF15 and CBF but also the activity of AD1. Comparative proteomics identified several binding sites for GSK3β, which has been shown to inactivate prohypertrophic transcription factors such as Nfat or GATA-4 by phosphorylation and we show here that GSK3β positively activates KLF15. We also found that KLF15 inhibits the activity of NFAT through a novel mechanism that involves PTEN and GSK3β. In addition, we have shown that KLF15 is negatively regulated by the histone deacetylase HDAC1 through direct interaction with the first zinc finger of the KLF15 DNA-binding domain. This suggests that HDAC1 is able to modulate the transcriptional activity of KLF15 by regulating its interaction with CBF and/or other co-activator proteins.

**Conclusions:** KLF15 is a key anti-hypertrophic factor that exerts its effect through multiple mechanisms involving GSK3β and chromatin remodelling proteins.

**Funding:** This work was supported by the British Heart Foundation (PG 05/116) and the Magdi Yacoub Institute.

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**101 IS DEPRESSED MYOCYTE CONTRACTILITY AN EARLY EVENT IN THE NATURAL HISTORY OF HEART FAILURE?**

1WO Idigo, 1YH Zhang, 1C Lygate, 1R Carnicer, 1D Dawson, 1B Casadei, 1John Radcliffe Hospital, University of Oxford, Oxford, UK; 2Edinburgh Royal Infirmary, A54 Heart

After myocardial infarction (MI), the heart undergoes a process of remodelling characterised by progressive dilatation, impaired systolic and diastolic function, and reduced β-adrenergic reserve. Studies in explanted failing human hearts have shown a similar impairment in myocyte function and a suppressed activity of the SR calcium pump (SERCA2a), leading to the conclusion that restoring SERCA2a function may be sufficient to prevent or reverse heart failure in humans. However, other data have indicated that the functional status of left ventricular myocytes does not always parallel the degree of heart failure in vivo and that, rather than being the initial mechanism responsible for left ventricular dysfunction, altered myocyte contraction and calcium handling may be the hallmark of advanced/end-stage heart failure. To test this hypothesis, we compared the contractile and calcium handling properties of left ventricular myocytes isolated from C57BL/6 mice 12 weeks after left anterior descending artery ligation or sham surgery.

Infarct size (35–50%) and left ventricular function were evaluated by three-dimensional echocardiography. Contraction and [Ca2+]i transients (Fura-2 AM) were measured in field-stimulated myocytes (3 Hz, 55°C) under basal conditions and in response to increasing doses of isoproterenol (10–100 nmol). The left ventricular ejection fraction was significantly reduced in infarcted mice compared with shams (23% versus 55%, p < 0.001, n = 9 in each group) and the heart weight to body weight ratio was significantly increased (11.7 ± 0.6 versus 7.5 ± 0.3, p = 0.001). In line with these findings, left ventricular myocytes isolated from infarcted hearts were significantly larger than those from sham operated hearts (7073 ± 234 μm² versus 4136 ± 146 μm², p = 0.001, n = 108 and 79 cells). These findings, confirming the presence of left ventricular myocyte dysfunction and adverse remodelling post-MI, were not mirrored in isolated left ventricular myocytes. In particular, basal cell shortening was enhanced in myocytes from infarcted hearts (3.58 ± 0.42 μm versus 6.74 ± 0.38 μm in shams, p = 0.001, n = 136 and 80 cells), as was the amplitude of the [Ca2+]i transient (0.46 ± 0.02 versus 0.34 ± 0.03, p < 0.001, n = 76 and 85 cells) and the SR calcium content (10 mm caffeine spritz, 0.66 ± 0.06 versus 0.51 ± 0.04, p = 0.04, n = 14 and 21 cells). Furthermore, a larger proportion of the SR calcium was released with each contraction in myocytes isolated from infarcted hearts. The rate of decay of [Ca2+]i was faster both in field-stimulated (90.0 ± 3.6 ms versus 115.7 ± 5.0 ms, p < 0.001, n = 52 and 36 cells) and caffeine-induced [Ca2+]i transients, suggesting the upregulation of the sodium/calcium exchanger activity. The myocyte inotropic response to increasing doses of isoproterenol was similar, although the dose–response curve was shifted upwards in the infarcted group.

In summary, our findings indicate that left ventricular dysfunction post-MI is not necessarily associated with impaired myocyte contraction, both under basal conditions and in response to inotropic challenges and suggest that altered SERCA2a activity may not be an early event in the natural history of heart failure.

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**102 ACE2 OVEREXPRESSION IN THE MYOCARDIUM OF STROKE-PRONE SPONTANEOUSLY HYPERTENSIVE RATS LEADS TO FIBROSIS**

1R Masson, 1MA Craig, 1SA Nicklin, 1K Gilday, 1MW McBride, 2P Gregorevic, 1JM Allen, 1JS Chamberlain, 1D Graham, 1A Dominiczak, 1AH Baker, 1University of Glasgow, Glasgow, UK; 2University of Washington, Seattle, Washington, USA

The function of angiotensin-converting enzyme 2 (ACE2), a recently identified homologue of angiotensin-converting enzyme, in the regulation of cardiac structure and function as well as the maintenance of systemic blood pressure remains unclear. ACE2 primarily hydrolyses angiotensin (Ang) II and less efficiently Ang I, resulting in Ang 1–9 and Ang 1–7 production. ACE2 may thus play a pivotal role in the renin–angiotensin system (RAS) by reducing concentrations of the profibrotic, proproliferative vasoconstrictor Ang II and raising levels of the antiﬁbrotic, antiproliferative vasodilatory peptide Ang 1–7. Here we assess the effect of ACE2 overexpression in vivo on heart function and blood pressure.

To assess the effect of ACE2 overexpression in SHRSP, four groups of animals (n = 6 per group) were included in the study; enalapril, PBS, rAAV6-alkaline phosphatase (control reporter gene) and rAAV6:ACE2. ACE2 was shown to be overexpressed selectively in the rAAV6:ACE2-injected animals. Blood pressure was monitored by tail cuff and was significantly lower (p < 0.001) in the rAAV6:ACE2 group in weeks 9, 10 and 11 post-infusion compared with PBS and control virus-infused animals. Echocardiography was used to assess cardiac function and showed substantial systolic dysfunction in ACE2-treated animals compared with all controls. Rats treated with rAAV6:ACE2 exhibited a significant (28%) reduction in ejection fraction and a 20% reduction in fractional shortening over the duration of the study. We also quantified endothelial function in peripheral resistance vessels (mesentery) by wire myography. Myography demonstrated increased basal nitric oxide in the vessels from rAAV6:ACE2 transduced animals compared with the rAAV6:AF group, indicative of an improved peripheral endothelial function. Haematoxylin and eosin staining was used to assess cardiac structure and revealed an abnormal phenotype. Masson’s trichrome and picrosirius red indicated cardiac fibrosis that was absent from all other treatment groups. To assess activation of potential profibrotic pathways we performed gene expression profiling using Illumina expression arrays at 4 weeks. Profiling of differentially expressed genes was performed on RNA extracted from the heart. Micro-array analysis revealed the upregulation of fibrosis-associated genes and the downregulation of apelin, myosin heavy chain 11 (MYH11) and GATA binding protein 6 (GATA6).

In summary, we found that the overexpression of ACE2 in SHRSP myocardium led to severe cardiac fibrosis and cardiac abnormalities. Gene expression analysis revealed early activation of fibrosis-associated genes.
**103 ABNORMAL ELECTRICAL FUNCTION AND HYPERTROPHY OF THE HEART CAUSED BY LOSS OF INTEGRIN ALPHA 7**

R Nadif, M Emerson, U Mayer, L Neyes, EJ Cartwright. University of Manchester, Manchester, UK; Imperial College, London, UK; University of East Anglia, Norwich, UK

It is relatively common for cardiovascular complications, including cardiac hypertrophy, arrhythmias and sudden death to be associated with muscular dystrophies. Null-mutations in integrin alpha 7, a member of a family of transmembrane proteins that mediate interactions between cells and extracellular matrix proteins, have been linked to myopathy in humans. Our integrin alpha 7-deficient mouse model (α7−/−), which faithfully replicates this myopathy, dies prematurely at one year of age; however, it is clear that their sudden death is not directly attributable to the dystrophic phenotype. We therefore analyzed the cardiac structure, contractile and electrical functions in integrin alpha 7-deficient mice to determine whether their sudden death is associated with altered cardiac function.

ECG analysis revealed delayed electrical conduction in γγ7−/− hearts at 6 months of age, with α7−/− mice exhibiting both long QTe duration (γ7−/−: 0.08 ± 0.008 seconds, α7+/−: 0.06 ± 0.01 seconds; n = 10; p<0.01) and a prolonged PR interval (γ7−/−: 0.04 ± 0.001 seconds, α7+/−: 0.03 ± 0.001 seconds; n = 10; p<0.05). α7−/− mice were more susceptible to drug-induced arrhythmias: treatment with ouabain (2 mg/kg body weight) in combination with isoprenaline (2.5 mg/kg body weight) induced ventricular tachycardia and fibrillation and subsequently death in α7−/−, but not in wild-type mice (fig). Interestingly, γ7−/− also displayed a concentric pattern of ventricular hypertrophy characterised by increased septal wall thickness and reduced left ventricular end-diastolic diameter starting from 6 months of age. These structural changes were accompanied by a 30% increase in myocyte size and increased ANP gene expression, which is a molecular marker of hypertrophy.

In conclusion, in addition to muscular dystrophy, deletion of the integrin alpha 7 gene in mice leads to abnormal electrical conduction, a marked predisposition to lethal arrhythmias, as well as cardiac hypertrophy. The integrin alpha 7 null mice may thus provide a model for studying aspects of arrhythmogenesis and lethal arrhythmias.

**104 DIFFERENT SOURCES OF OXIDANT STRESS IN THE EARLY AND LATE STAGE OF ATRIAL FIBRILLATION**

SN Reilly, NJ Alp, B Casadei. University of Oxford, Department of Cardiovascular Medicine, John Radcliffe Hospital, Oxford, UK

**Background:** Atrial fibrillation is associated with electrical and structural remodelling of the atria and with increased myocardial oxidative stress, leading to reduced nitric oxide bioavailability and nitric oxide synthase (NOS) uncoupling. To date, it remains unclear whether oxidative stress is an early event in atrial fibrillation-induced myocardial remodelling or a consequence of this process. To address this issue, we evaluated the time course and sources of superoxide (O2−) production in the right atrial (RA) and left atrial (LA) myocardium of a goat model of pacing-induced atrial fibrillation.

**Methods:** Atrial O2− was assessed by lucigenin-enhanced chemiluminescence and 2-OH ethidium detection by high-performance liquid chromatography (HPLC) 14 days after the onset of atrial fibrillation (ie, in the presence of electrical but not of significant structural remodelling) and after 6 months (both electrical and structural remodelling present). The NOS cofactor tetrahydrobiopterin (BH4) measured by HPLC and NOS activity ([14C]-l-arginine and HFLC) were also assessed.

**Results:** Early atrial fibrillation was associated with a significant increase in O2− release in the LA only (fig, n = 5). Inhibition of NADPH oxidases normalised O2− production in the fibrillating LA but had no significant effect in the RA or in control animals in sinus rhythm. Atrial BH4 levels and NOS activity were unaffected after 14 days of atrial fibrillation. After 6 months of atrial fibrillation, O2− release was significantly increased in both atria. NADPH oxidase inhibition did not affect O2− production significantly, whereas inhibition of NOS or mitochondrial oxidases decreased O2− by 16 ± 3.1% and 38 ± 4.1%, respectively (p<0.05). Atrial BH4 was significantly reduced (p<0.05 versus sinus rhythm).

**Conclusions:** An NADPH oxidase-dependent increase in LA O2− production is an early event in the history of atrial fibrillation-induced remodelling. In contrast, in late atrial fibrillation, increased atrial O2− release is generated by mitochondrial oxidases and by uncoupled NOS activity. These findings indicate that NADPH oxidases may play an important role in triggering myocardial remodelling in atrial fibrillation but may no longer be a valuable target for therapeutic intervention once this process is established.

**105 THE DELTA AND EPSILON ISOFORMS OF PROTEIN KINASE C HAVE OPPOSING ACTIONS IN HUMAN ATRIAL MUSCLE DURING SIMULATED ISAHEMIA–REPERFUSION INJURY**

V Sivaraman, DJ Hausenloy, DM Yellon. Hatter Cardiovascular Institute, University College London and Royal Free Hospitals Medical School, London, UK

Protein kinase C (PKC) has been demonstrated to play a key role in cardioprotection in animal models of myocardial ischaemia–reperfusion injury. Ten isoforms of PKC have been identified, of which the PKC-δ and PKC-ε isoforms appear to play divergent roles...
Heart studies suggest that the activation of PKC-\(\varepsilon\) in the setting of ischaemia–reperfusion injury. Experimental animal postconditioning; WT, wild-type. *\(p\) CON, uninterrupted reperfusion; CsA, ciclosporin A; KI, knock-in; PostC, the activation of PKC-\(\varepsilon\). However, the role of these individual PKC isoforms in human myocardium is unknown. We hypothesised that pharmacological inhibition of PKC-\(\delta\) and the activation of PKC-\(\varepsilon\) at the time of myocardial reperfusion would protect human atrial muscle subjected to simulated ischaemia–reperfusion injury.

Human atrial trabeculae were isolated from atrial appendage tissue harvested from patients undergoing cardiac surgery and subjected to 90 minutes of hypoxia followed by 120 minutes of reoxygenation, at the end of which the recovery of baseline contractile function was determined. Atrial trabeculae were randomly assigned to: (1) control; (2) carrier control (in which only the carrier peptide was present); (3) a standard hypoxic preconditioning (HPC) protocol comprising 4 minutes of hypoxia followed by 16 minutes of reoxygenation before the index hypoxic period; (4) a specific peptide inhibitor of PKC-\(\delta\) (0.5 \(\mu\)mol) (KAI Pharmaceuticals Inc) given at the onset of reoxygenation; (5) a specific peptide activator of PKC-\(\varepsilon\) (0.5 \(\mu\)mol) (KAI Pharmaceuticals) given at the onset of reperfusion.

Treatment with HPC, the PKC-\(\delta\) inhibitor and PKC-\(\varepsilon\) activator, all improved the recovery of baseline contractile function (51.7 \(\pm\) 4.6\%, 50.1 \(\pm\) 2.8\%, 40.7 \(\pm\) 2.1\%, respectively; versus 24.2 \(\pm\) 2.7\% with carrier control; \(p<0.05; N>5\) per group). In conclusion, we report for the first time that either inhibiting PKC-\(\delta\) or activating PKC-\(\varepsilon\) at the time of myocardial reperfusion is cardioprotective in human atrial muscle. These findings provide novel treatment strategies for reducing myocardial injury in patients presenting with an acute myocardial infarction, which can be administered at the time of myocardial reperfusion.

### Abstract 106

GSK-3B IS NOT A NECESSARY SIGNALLING INTERMEDIATE IN POSTCONDITIONING

IG Webb, Y Nishino, JE Clark, MS Marber. The Rayne Institute, St Thomas’ Hospital, Kings College, London, UK

Postconditioning after lethal ischaemia is cardioprotective. GSK-3b is reported as an important intermediate of protective signalling through its inhibition of mitochondrial permeability transition pore (mPTP) opening. We set out to clarify the role of GSK-3b inhibition in postconditioning using a targeted mouse line with inactivation-resistant GSK-3a/b.

**Methods:** Ischaemic postconditioning (PostC): Isolated Langendorff-perfused hearts of C57BL/6 mice were subjected to 30 minutes global ischaemia and 120 minutes reperfusion. Hearts underwent PostC (10 \(\times\) 5 seconds reperfusion/5 seconds ischaemia) or uninterrupted reperfusion (CON) after index ischaemia. Left ventricular end-diastolic and developed pressures were recorded throughout. Infarct size was determined by planimetry of TTC-stained myocardium. Other heart preparations were snap-frozen in liquid nitrogen at various times for assessment of GSK-3 activation.

**Results:** Treatment with HPC, the PKC-\(\delta\) inhibitor and PKC-\(\varepsilon\) activator, all improved the recovery of baseline contractile function (51.7 \(\pm\) 4.6\%, 50.1 \(\pm\) 2.8\%, 40.7 \(\pm\) 2.1\%, respectively; versus 24.2 \(\pm\) 2.7\% with carrier control; \(p<0.05; N>5\) per group). In conclusion, we report for the first time that either inhibiting PKC-\(\delta\) or activating PKC-\(\varepsilon\) at the time of myocardial reperfusion is cardioprotective in human atrial muscle. These findings provide novel treatment strategies for reducing myocardial injury in patients presenting with an acute myocardial infarction, which can be administered at the time of myocardial reperfusion.

**Abstract 106**

**LVDP (mm Hg)**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Baseline</th>
<th>60 mins reperfusion</th>
<th>120 mins reperfusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>C57BL/6 CON</td>
<td>86.8 (\pm) 1.4</td>
<td>10.3 (\pm) 1.7</td>
<td>10.4 (\pm) 1.6</td>
</tr>
<tr>
<td>C57BL/6 PostC</td>
<td>87.0 (\pm) 2.2</td>
<td>20.7 (\pm) 4.0*</td>
<td>21.5 (\pm) 3.1*</td>
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<tr>
<td>C57BL/6 SB15</td>
<td>88.4 (\pm) 2.4</td>
<td>10.3 (\pm) 3.3</td>
<td>11.5 (\pm) 2.5</td>
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<tr>
<td>C57BL/6 SB120</td>
<td>67.1 (\pm) 2.1</td>
<td>18.9 (\pm) 1.7</td>
<td>10.0 (\pm) 2.0</td>
</tr>
<tr>
<td>GSK-3ab KI CON</td>
<td>66.3 (\pm) 2.7</td>
<td>32.3 (\pm) 3.6†</td>
<td>28.3 (\pm) 2.7†</td>
</tr>
<tr>
<td>GSK-3ab KI PostC</td>
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<td>44.4 (\pm) 3.5†</td>
<td>38.1 (\pm) 2.9†</td>
</tr>
<tr>
<td>GSK-3ab WT CON</td>
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<td>13.7 (\pm) 4.3</td>
<td>14.4 (\pm) 10.7</td>
</tr>
<tr>
<td>GSK-3ab WT PostC</td>
<td>65.4 (\pm) 1.3</td>
<td>30.3 (\pm) 3.4*</td>
<td>28.4 (\pm) 2.5*</td>
</tr>
</tbody>
</table>

CON, uninterrupted reperfusion; KI, knock-in; LVDP, left ventricular developed pressure; LVEDP, left ventricular end-diastolic pressure; PostC, 10 \(\times\) 5 seconds reperfusion/5 seconds ischaemia; SB15, SB216763 for 15 minutes; SB120, SB216763 for 120 minutes; WT, wild-type.

---

**LVEDP (mm Hg)**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Baseline</th>
<th>60 mins reperfusion</th>
<th>120 mins reperfusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>C57BL/6 CON</td>
<td>4.2 (\pm) 0.7</td>
<td>41.6 (\pm) 2.7</td>
<td>29.3 (\pm) 2.8</td>
</tr>
<tr>
<td>C57BL/6 PostC</td>
<td>4.3 (\pm) 0.5</td>
<td>29.5 (\pm) 6.0*</td>
<td>21.8 (\pm) 5.2*</td>
</tr>
<tr>
<td>C57BL/6 SB15</td>
<td>4.0 (\pm) 0.5</td>
<td>47.4 (\pm) 5.1</td>
<td>38.8 (\pm) 4.6</td>
</tr>
<tr>
<td>C57BL/6 SB120</td>
<td>4.0 (\pm) 0.4</td>
<td>47.4 (\pm) 3.7</td>
<td>34.5 (\pm) 5.4</td>
</tr>
<tr>
<td>GSK-3ab KI CON</td>
<td>5.7 (\pm) 0.5</td>
<td>34.6 (\pm) 4.4†</td>
<td>29.3 (\pm) 3.6†</td>
</tr>
<tr>
<td>GSK-3ab KI PostC</td>
<td>5.2 (\pm) 0.7</td>
<td>22.4 (\pm) 4.2</td>
<td>18.9 (\pm) 3.5</td>
</tr>
<tr>
<td>GSK-3ab WT CON</td>
<td>6.6 (\pm) 0.4</td>
<td>57.6 (\pm) 6.1</td>
<td>49.6 (\pm) 6.0</td>
</tr>
<tr>
<td>GSK-3ab WT PostC</td>
<td>6.1 (\pm) 0.7</td>
<td>31.4 (\pm) 5.2*</td>
<td>24.8 (\pm) 4.1*</td>
</tr>
</tbody>
</table>

CON, uninterrupted reperfusion; KI, knock-in; LVDP, left ventricular developed pressure; LVEDP, left ventricular end-diastolic pressure; PostC, 10 \(\times\) 5 seconds reperfusion/5 seconds ischaemia; SB15, SB216763 for 15 minutes; SB120, SB216763 for 120 minutes; WT, wild-type.
achieved by treatment of hearts at the point of reperfusion with SB216763 (3 μmol/l) for 15 minutes or 120 minutes. Effect of inactivation-resistant GSK-3 on ischaemic postconditioning: GSK-3 activity is inhibited by Ser9 (GSK-3b) and Ser21 (GSK-3a) phosphorylation. GSK-3a/b knock-in mice (KI) have targeted Ser-to-Ala mutations at these residues, preventing phosphorylation and, thus, kinase inactivation. Isolated hearts of KI and wild-type (WT) littermates were subjected to infarction with or without PostC at the point of reperfusion. Direct mPTP inhibition in GSK-3a/b KI mice: KI and WT hearts subjected to infarction were perfused with 0.2 μmol/l ciclosporin A (CsA) for 10 minutes at the moment of reperfusion or normal buffer (CON).

Results: PostC resulted in significant haemodynamic improvements and reduction in infarct size in C57BL/6 hearts. GSK-3 was dephosphorylated during ischaemia and partly re-phosphorylated at reperfusion. There was no significant difference between control and PostC. Treatment with SB216763 for 15 or 120 minutes at reperfusion provided no cardioprotection. KI control hearts appeared intrinsically protected against ischaemia compared with WT. PostC remained cardioprotective in both KI and WT hearts. Direct mPTP inhibition with CsA reduced infarct size in both genotypes to levels comparable with PostC in respective groups (see table and fig).

Conclusion: PostC does not alter GSK-3 phosphorylation during early reperfusion, and pharmacological inhibition of GSK-3 at the point of reperfusion is not beneficial. Both PostC and direct mPTP modulation remain cardioprotective in GSK-3a/b activation-resistant mice, suggesting that protection is achieved independent of GSK-3 inhibition. Together, these data suggest that GSK-3b inhibition is unlikely to be the key determinant of cardioprotective signalling in ischaemic postconditioning in the mouse.

RAS-ASSOCIATION FACTOR 1, A NOVEL REGULATOR OF CARDIAC HYPERTROPHY

M Zl, D Oceandy, S Prehar, A Pickard, EJ Cartwright, L Neyses. University of Manchester, Manchester, UK

Ras, a small GTP binding protein, regulates a number of important processes in cardiomyocytes including cell growth and apoptosis. Patients with Costello syndrome, in which the H-Ras gene is mutated, display severe hypertrophic cardiomyopathy. We have recently demonstrated that Ras-association factor 1 isoform A (RASSF1A), a novel effector of Ras, is expressed in the adult mouse heart and regulates adrenergic-induced cellular hypertrophy in neonatal rat cardiomyocytes. Here we used RASSF1A knock-out mice to investigate further whether RASSF1A regulates cardiac hypertrophy.

Cardiac hypertrophy was induced in 3-month-old RASSF1A knock-out mice and wild-type littermates, respectively, by treatment for 7 days with isoprenaline (10 mg/kg body weight/day) or vehicle using a mini-osmotic pump (fig).

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RASSF1A−/− mice exhibited a significantly reduced hypertrophic response compared with wild type as indicated by the heart weight to tibia length ratio (HW/TL, WT-Iso, 8.0 ± 0.2 mg/mm, RASSF1−/− Iso, 6.9 ± 0.3 mg/mm, p = 0.01, n = 7). As RASSF1A has been demonstrated to interact with and regulate an apoptosis modulator, the kinase Mst1, we investigated whether this molecule was differently regulated in RASSF1A−/− mice. We found that Mst1 phosphorylation was reduced in isoprenaline-treated RASSF1A−/− mice compared with wild-type littermates. Our findings suggest that RASSF1A is a regulator of adrenergic-induced cardiac hypertrophy acting on the Mst1 pathway.

THE "CYPSTAT" GENETIC SUBSTUDY OF THE SECONDARY PREVENTION OF ACUTE CORONARY EVENTS: REDUCTION OF CHOLESTEROL TO KEY EUROPEAN TARGETS (SPACE ROCKET) TRIAL

KM Bailey, Leeds University, Leeds, UK

Background: Genetic and other individual factors influence the efficacy and tolerability of cholesterol lowering with statins, possibly including a common genetic variant that determines the presence or absence of the drug metabolising enzyme isoform, cytochrome P450 3A5 (CYP3A5), which has an allele frequency of 5% in African Americans, 50% in south Asians and 15% in white Europeans. We tested the hypothesis that the presence of the CYP3A5 isoform would be associated with attenuated lowering of cholesterol after treatment with simvastatin 40 mg due to increased drug metabolism via this metabolic route.

Methods: The study was conducted prospectively in the context of an independent, open-label, blinded-endpoint, multicentre, randomised controlled, parallel group trial randomly selecting patients with myocardial infarction (MI) to receive either simvastatin 40 mg or rosuvastatin 10 mg for 3 months. In 672 patients the presence or absence of the cytochrome P450 3A5 (CYP3A5) isoform was determined using a TaqMan PCR assay that identified CYP3A5*1 and CYP3A5*3 alleles. The main outcome of interest reported here was the attainment at 3 months of the ACC, AHA and ESC optimal treatment target for patients with MI of low-density lipoprotein cholesterol of less than 1.81 mmol/l according to randomised statin based on the presence (CYP3A5*1/*1 plus CYP3A5*1/*3) or absence (CYP3A5*3/*3) of the cytochrome P450 3A5 isoform. Observed differences were assessed by binary logistic regression analysis initially without covariate adjustment and then also with adjustment for previous statin use, age at time of MI and also prandialisation low-density lipoprotein cholesterol.

Results: Patients who were CYP3A5 positive (13.3%) or CYP3A5 negative (86.6%) were comparable at the time of index MI with regard to mean low-density lipoprotein cholesterol (3.15 mmol/l versus 3.23 mmol/l) and other factors such as age (61.9 versus 61.5 years). In the CYP3A5-positive group at 3 months 26.8% simvastatin versus 59.6% rosuvastatin patients had achieved an optimal low-density lipoprotein cholesterol of less than 1.81 mmol/l (unadjusted odds ratio (OR) 4.02; 95% CI 1.63 to 9.92; p = 0.003; adjusted OR 3.78; 95% CI 1.22 to 11.67; p = 0.021), whereas 41.0% simvastatin versus 46.3% rosuvastatin patients in the CYP3A5-negative group had achieved an optimal low-density lipoprotein cholesterol of less than 1.81 mmol/l (unadjusted OR 1.24; 95% CI 1.04 to 1.47; p = 0.01) and for CYP3A5-negative patients 2.05 mmol/l (SD 0.69) versus 1.97 mmol/l (SD 0.62; p = 0.15).

Conclusion: For a minority of patients with genetic variants that permit expression of the drug metabolising cytochrome P450 isoform CYP3A5, we observed significantly lower effectiveness for
simvastatin 40 mg compared with rosuvastatin 10 mg, whereas for a majority not having this variant we observed a smaller difference that was not statistically significant.

### 109 TELOMERE LENGTH IS SHORTER IN HEALTHY OFFSPRING OF INDIVIDUALS WITH CORONARY ARTERY DISEASE: SUPPORT FOR THE TELOMERE HYPOTHESIS

**SW Brouilette, A Whittaker, SE Stevens, P van der Harst, AH Goodall, NJ Samani.**

1Department of Cardiovascular Sciences, University of Leicester, Leicester, UK; 2Department of Experimental Cardiology, University of Groningen, Groningen, The Netherlands

Telomeres are shorter in individuals with coronary artery disease (CAD) and may indicate premature biological ageing. However, whether shorter telomeres in such individuals are a primary abnormality or secondary to the disease is unclear. To investigate this, we compared telomere lengths in healthy young adults with contrasting familial risk of CAD. Mean telomere restriction fragment (TRF) length in DNA from circulating leucocytes was determined in 45 healthy offspring of individuals with premature CAD (case offspring) and 59 offspring from families without such a history (control offspring). Correlation in mean TRF length was also assessed in 67 offspring–parent pairs. We found independent effects of age (p = 0.012) and offspring status (p = 0.004), but not BMI (p = 0.168) or smoking status (p = 0.652) on mean TRF length. The adjusted difference in mean TRF between case and control offspring was 0.47 kb (95% CI 0.25 to 0.69 kb, p<0.001), equivalent to more than 25 years of age-related attrition in telomere length. Furthermore, a significant positive correlation in mean TRF length was observed between parents and offspring (r = 0.37, p = 0.002). These findings suggest that inheritance of shorter telomeres is associated with an increased familial risk of CAD. The findings support the hypothesis that telomere length is a primary abnormality involved in the pathogenesis of CAD.

### 110 CIRCULATING NEPRILYSIN AND CARDIOVASCULAR RISK: ASSOCIATIONS WITH INSULIN RESISTANCE AND THE METABOLIC SYNDROME


**Introduction:** Neprilysin cleaves several bioactive peptides involved in the regulation of vascular function. In human microvascular endothelial cells, fatty acids and glucose increase neprilysin activity, and inhibition of neprilysin in animal studies results in increased insulin sensitivity, suggesting that neprilysin may be related to the metabolic syndrome.

**Aim:** To test formally the hypothesis that circulating neprilysin is associated with the metabolic syndrome, insulin resistance and associated cardiovascular risk.

**Methods:** Plasma neprilysin was measured by activity assay in 318 healthy white men of European origin characterised for the presence of the metabolic syndrome according to International Diabetes Federation (IDF) criteria (MetS IDF).

**Results:** Neprilysin was significantly higher in subjects with MetS IDF (0.384 nmol/l (0.235–0.798)) compared with those without (0.198 nmol/l (0.071–0.387), p<0.001). Neprilysin was also significantly higher in subjects possessing subcomponents of the MetS IDF and increased progressively with the increasing number of MetS IDF components, being approximately eightfold higher in those with five MetS IDF components compared with those with no MetS IDF components, as shown in the figure. Neprilysin was also correlated with insulin resistance and haemostatic cardiovascular risk factors. In logistic regression analyses neprilysin was independently associated with raised triglyceride (odds ratio (OR) for neprilysin in the upper tertile versus lowest tertile: 3.04 (1.49 to 6.19) p = 0.001), decreased high-density lipoprotein (OR for neprilysin in the upper tertile versus lowest tertile: 2.89 (1.25 to 6.67) p = 0.013); and hypertension (OR for neprilysin in the upper tertile versus lowest tertile: 2.09 (1.10 to 3.95) p = 0.024), defined according to IDF criteria.

**Conclusion:** These results indicate that raised circulating neprilysin may be an independent risk factor or marker for the development of cardiovascular disease associated with insulin resistance and the metabolic syndrome.

### 111 DOES GENETIC VARIATION IN FTO ACCOUNT FOR THE INCREASED RISK OF OBESITY AND TYPE 2 DIABETES IN UK INDIAN ASIANS?

**JC Chambers, W Zhang, D Zabaneh, D Balding, MI McCarthy, P Scott, P Elliott, JS Kramer. Imperial College London, London, UK; Oxford University, Oxford, UK**

**Background:** Obesity and type-2 diabetes (T2D) are major risk factors for cardiovascular disease. Central obesity and T2D are more common in Indian Asians and may account for up to 70% of their excess cardiovascular disease compared with white European individuals. Recent studies have identified genetic variation in the FTO gene as a novel cause of obesity and T2D in north American and European populations. We examined whether FTO contributes to the increased risk of obesity and T2D among UK Indian Asians.

**Material and Methods:** We investigated 2694 Indian Asian men, aged 35–75 years, recruited from the lists of general practitioners in west London, as part of the London Life Sciences Population Study. A history of diabetes, weight, BMI, waist–hip ratio (WHR) and fasting glucose were recorded for all subjects. There were 600 subjects with T2D. Participants were genotyped using the Illumina 317K Beadchip array, which includes two single nucleotide polymorphisms (SNP), rs8050136 and rs7581812, in the FTO gene that are in complete linkage disequilibrium with rs9999609, the SNP previously reported as strongly associated with obesity in European populations. The array also includes 652 SNP in the 5 Mb genomic
region spanning the FTO gene. SNP were examined for association with BMI, WHR and T2D, using PLINK and CHROMSCAN software.

**Results:** SNP rs8050136 and rs3751812, perfect proxies for rs9939609, were both associated with weight (table), with an approximate 1 kg increase in weight per copy of the high-risk allele. However, neither SNP showed association with BMI, WHR, or T2D in Indian Asians (rs8050136: BMI p = 0.07, WHR p = 0.15, T2D p = 0.97; rs3751812: BMI p = 0.08, WHR p = 0.15, T2D p = 0.97). Multilocus testing combining information from multiple markers also did not detect any significant association of FTO with BMI, WHR or T2D in Indian Asians. For both SNP, comparison with HapMap data shows that the allele associated with increased weight is less common in Indian Asians than the reference CEU population of European white ancestry (33% versus 45% at both SNP).

**Conclusions:** Variants in the FTO gene are associated with weight in Indian Asians, but not with central obesity or T2D. The high-risk allele is less common in Indian Asians than Europeans. Our findings indicate that FTO does not account for increased obesity/T2D in Indian Asians.

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**Abstract 112**

**TRANSCRIPTION FACTOR 7-LIKE 2, INSULIN ACTION AND RISK OF TYPE 2 DIABETES AMONG INDIAN ASIAN AND WHITE EUROPEAN MEN**

JC Chambers, J Scott, K Meeran, P Jain, S Bloom, JS Kooner. Imperial College London, London, UK

**Background:** Transcription factor 7-like 2 (TCF7L2) polymorphisms are associated with type 2 diabetes (T2D) in north American and European populations. We investigated whether TCF7L2 accounts for the increased risk of T2D in Indian Asians and examined the mechanisms underlying the relationship between TCF7L2 and T2D.

**Methods:** We genotyped 1006 Indian Asian and 1005 white European men for single nucleotide polymorphism rs4506565 in TCF7L2. We examined the relationship of rs4506565 with T2D, insulin sensitivity and pancreatic beta-cell function (using homeostatic model assessment; HOMA). In 123 subjects we investigated relationships between rs4506565 and plasma glucagon-like peptide 1 (GLP-1).

**Results:** We found that the rs4506565 T allele was associated with an increased risk of impaired fasting glucose and T2D among Indian Asians and white Europeans (p<0.01). The frequency of rs4506565 T allele was similar and the population-attributable risk of rs4506565 to T2D was 23% in Indian Asians and Europeans. rs4506565 was associated with reduced HOMA-B (p<0.05) but not HOMA-S (p>0.1). The TCF7L2 genotype was not associated with fasting or post-glucose load plasma GLP-1

**Conclusions:** The TCF7L2 rs4506565 polymorphism is associated with impaired fasting glucose and T2D in Indian Asians and Europeans. The relationship of TCF7L2 with T2D is mediated via reduced pancreatic beta-cell function, but this is not the result of reduced plasma GLP-1. TCF7L2 makes an important contributor to the risk of T2D in both populations, but does not account for increased T2D in Asians compared with Europeans.

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**Abstract 113**

**A PROSPECTIVE COMPARISON OF TWO-DIMENSIONAL ECHOCARDIOGRAPHY AND N-TERMINAL PRO-BNP IN THE PREDICTION OF ADVERSE OUTCOMES AFTER ACUTE MYOCARDIAL INFARCTION**

D Kelly, S Khan, L Ng, I Squire. University Hospitals Leicester, Leicester, Leicester, UK

**Introduction:** Identification of subjects at risk of adverse prognosis after acute myocardial infarction (AMI) is essential in the planning of management strategies. Both echocardiographic left ventricular dysfunction and elevated plasma B-type natriuretic peptide (BNP) are associated with adverse outcomes after AMI; however, no previous study has prospectively compared these methods. We aimed to compare the ability of echocardiographic markers (left ventricular ejection fraction (LVEF), wall motion index score (WMIS), left ventricular end-systolic volume (LVESV) and left ventricular end-diastolic volume (LVEDV)) with N-terminal pro-brain natriuretic peptide (NT proBNP) to predict adverse outcomes post-AMI.

**Methods:** We studied 404 patients with AMI. Plasma NT proBNP was measured before discharge and all subjects underwent transthoracic echocardiography at this time. Our primary endpoint was the occurrence of the combination of death or heart failure; secondary endpoints included death, heart failure and the composite of death, heart failure or recurrent myocardial infarction.
outcomes included the individual components of the primary and re-infarction over a median period of 313 days (range 1–619).

**Results:** LVEF was lower, WMIS higher, LVESV higher and NT proBNP higher in subjects who reached the primary endpoint and in those who suffered a heart failure episode (all \( p < 0.001 \)). LVEF was lower, WMIS higher, and NT proBNP higher in those who died (all \( p < 0.001 \)). WMIS was higher in those who had a re-infarction (\( p = 0.028 \)). On multivariate analysis WMIS (\( p = 0.017 \)) and NT proBNP (\( p = 0.009 \)) retained independent association with our primary endpoint. Receiver operator characteristic curves revealed an area under the curve for the prediction of death or heart failure of 0.747 for WMIS, 0.789 for NT proBNP and 0.820 for a logistic model combining the two factors. Receiver operator characteristic curves were used to identify cut-off concentrations to give the optimum sensitivity and specificity for the detection of our endpoint (WMIS 1.45, NTproBNP 1472 pmol/l). Subjects with WMIS above 1.45 (odds ratio (OR) 5.36, 95% CI 2.72 to 10.57; \( p < 0.001 \)) or NT proBNP greater than 1472 pmol/l (OR 6.33, 95% CI 3.55 to 11.29; \( p < 0.001 \)) had a markedly increased risk of death or heart failure. A combination of the two markers gave additional prognostic data over either alone (fig).

**Conclusion:** WMIS and NT proBNP are robust markers of adverse prognosis post-AMI and have similar predictive ability for the identification of patients at risk of death or heart failure. The use of both markers in combination gives additional information above either alone.

**115 MID-REGIONAL PRO-ATRIAL NATRIURETIC PEPTIDE PREDICTS RISK OF DEATH IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION: LEICESTER ACUTE MYOCARDIAL INFARCTION PEPTIDE STUDY**

**Introduction:** Multimarker strategies may assist risk stratification after acute myocardial infarction (AMI). Midregional pro-atrial natriuretic peptide (MR-proANP) is a newly described stable peptide.
fragment of N-terminal pro-atrial natriuretic peptide. We compared the prognostic value of MR-proANP and an established marker N-terminal pro-B-type natriuretic peptide (NT-proBNP) post-AMI.

**Methods:** We recruited 983 consecutive post-AMI patients (720 men, median age 65 years, range 24–95) in a prospective study with follow-up over 345 days (0–764). Plasma measurements were made 3–5 days after chest pain onset. The plasma concentration of NT-proBNP was determined using an in-house non-competitive chemiluminescent immunoassay and MR-proANP was detected using a novel commercial assay (Brahms Ag, Germany).

**Results:** Plasma MR-proANP was raised in patients who died (n = 101) compared with survivors (median pmol/l, 310 (range 48–1150) versus 108 (4.9–1210), p < 0.001 (fig)). Using Cox modelling log₁₀ MR-proANP (hazard ratio (HR) 4.25) and log₁₀ NT-proBNP (HR 5.55) were significant independent predictors of death. In patients stratified by NT-proBNP in the highest quartile (>5900 pmol/l), MR-proANP in the top quartile (>550 pmol/l) was associated with poorer outcomes (p < 0.001). Findings were similar for heart failure as an individual endpoint. However, neither marker predicted recurrent myocardial infarction.

**Conclusions:** The A and B-type natriuretic systems are activated post-AMI. MR-proANP is a powerful predictor of adverse outcome especially in those with an elevated NT-proBNP. MR-proANP may represent a clinically useful marker of prognosis after an AMI as part of a multimarker strategy targeting the natriuretic neurohormonal pathway.

**MONOCYTE GENE EXPRESSION PROFILING IN INDIVIDUALS WITH CONTRASTING FAMILIAL RISK FOR PREMATURE MYOCARDIAL INFARCTION**

1U Krishnan, 1JR Wright, 2R Farrugia, 3P Ellis, 4NA Watkins, 5WH Duvehand, 1AH Goodall, 1NJ Samani. 1Department of Cardiovascular Sciences, University of Leicester, Leicester, UK; 2Department of Haematology, University of Cambridge and NBS, Cambridge, UK; 3Wellcome Trust Sanger Institute, Cambridge, UK.

**Introduction:** Coronary artery disease (CAD) and myocardial infarction (MI) have a strong genetic basis, which may manifest as differences in expression of genes in key cells. Monocytes play an important role in atherothrombosis and their stimulation by platelets is an important step. The aim of this project was to compare monocyte gene expression profiles in healthy subjects with contrasting familial risk of CAD/MI at baseline and after stimulation with platelets.

**Methods:** Six healthy men (18–40 years) with a family history of premature MI and six healthy controls were recruited. Circulating monocytes were isolated using CD14 antibody-coated magnetic beads. RNA was extracted at baseline (t0) and after incubation of whole blood for 4 hours (t4) with cross-linked collagen-related peptide (CRP-XL) to simulate monocyte activation via platelets.

**Results:** Transcriptome profiling of monocytes has identified genes that are differentially expressed between subjects with differing inheritance profiles for MI, both at baseline and following stimulation of monocytes by platelets. CYP27A1, a cholesterol efflux enzyme in monocyte-derived macrophages showed the greatest difference between groups at both time points. Previous studies suggest that this enzyme co-localises with macrophages at the shoulder regions of atherosclerotic plaques and point mutations in the gene have been linked to premature atherosclerosis. Further delineation of the cellular and genetic regulation of this enzyme pathway may reveal potential targets for early risk stratification and/or targeted therapy.

**Abstract 116 Table 1**

<table>
<thead>
<tr>
<th>Demographic data</th>
<th>Offspring of MI (n = 6)</th>
<th>Controls (n = 6)</th>
<th>p Value (Mann–Whitney test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>28.83</td>
<td>32.16</td>
<td>0.19</td>
</tr>
<tr>
<td>BMI</td>
<td>26.01</td>
<td>27.66</td>
<td>0.69</td>
</tr>
<tr>
<td>Waist to hip ratio</td>
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<td>0.89</td>
<td>0.22</td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>133.6</td>
<td>124.3</td>
<td>0.1</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>79.3</td>
<td>76.3</td>
<td>0.37</td>
</tr>
<tr>
<td>Smokers</td>
<td>2/6</td>
<td>1/6</td>
<td>N/A</td>
</tr>
<tr>
<td>Total cholesterol : HDL (mmol/l)</td>
<td>6.08</td>
<td>4.78</td>
<td>0.29</td>
</tr>
<tr>
<td>LDL (mmol/l)</td>
<td>3.54</td>
<td>3.44</td>
<td>0.91</td>
</tr>
<tr>
<td>Fasting glucose (mmol/l)</td>
<td>5.1</td>
<td>4.7</td>
<td>0.14</td>
</tr>
</tbody>
</table>

BMI, body mass index; DBP, diastolic blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein; MI, myocardial infarction; SBP, systolic blood pressure.

**Abstract 116 Table 2**

<table>
<thead>
<tr>
<th>Comparisons</th>
<th>Upregulated genes</th>
<th>Downregulated genes</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Offspring of MI versus controls (t0)</td>
<td>5</td>
<td>15</td>
<td>20</td>
</tr>
<tr>
<td>Offspring of MI versus controls (t4)</td>
<td>28</td>
<td>35</td>
<td>63</td>
</tr>
<tr>
<td>Offspring of MI (t0 versus t4)</td>
<td>121</td>
<td>46</td>
<td>167</td>
</tr>
<tr>
<td>Controls (t0 versus t4)</td>
<td>140</td>
<td>34</td>
<td>174</td>
</tr>
</tbody>
</table>

MI, myocardial infarction.
CIRCULATING ENDOTHELIAL PROGENITOR CELLS FROM HEALTHY INDIVIDUALS EXHIBIT DIURNAL VARIATION

HE Thomas, RE Redgrave, MS Cunnington, BD Keavney, HM Arthur. University of Newcastle, Newcastle upon Tyne, UK

Introduction: Endothelial progenitor cells (EPC) have been implicated in the pathophysiology of cardiovascular diseases and the level of circulating EPC may be a useful new biomarker of cardiovascular risk. Leucocytes and several EPC mobilising factors exhibit diurnal variation, with peak values in the evening, and we aimed to assess whether EPC exhibit a similar circadian rhythm. If this were the case, it would have important implications not only for their biology but also for interpreting previous and conducting future clinical studies.

Methods: We carried out quantification of EPC from 15 healthy adult male volunteers at 08:00, 15:00 and 22:00 hours. EPC were measured using flow cytometry analysis of whole blood, following the acquisition of 60,000 events in the lymphocyte gate. We measured absolute counts of cells expressing all the surface marker combinations of CD34, CD133 and kinase domain receptor (KDR), which have been used to define EPC. CD45 expression was used as an additional gating criterion for CD34+ cells. Our methods identified seven EPC phenotypes, which includes all those commonly measured and we have previously demonstrated that they are highly reproducible. Two-way analysis of variance and paired t-tests were used to analyze the results.

Results: EPC counts of cells with the phenotype CD34+, CD34+CD45+, CD133+, CD34+CD133+, CD133+KDR+ and CD34+CD133+KDR+ all exhibited significant diurnal variation during the study period (see table), with a fall in EPC numbers between 08:00 and 15:00 hours and a subsequent rise to an overall peak value at 22:00 hours. The cell counts at 22:00 hours were significantly higher than at 15:00 hours in all the above phenotypes (increases of 17% to 42%). In addition, the CD34+ EPC counts were 16% higher at 08:00 than at 15:00 hours (p = 0.031) and the CD34+CD133+KDR+ EPC were 38% higher at 22:00 than at 08:00 hours (p = 0.037). The figure shows representative plots (CD34+ and CD34+CD133+) of the EPC counts during the study.

Conclusions: EPC showed substantial diurnal variation and the reasons for this remain incompletely understood, although diurnal variation in glucocorticoids and EPC mobilising cytokines is likely to contribute. An understanding of the molecular mechanisms controlling this previously undescribed diurnal variation of EPC would improve our understanding of EPC kinetics following the acquisition of 60,000 events in the lymphocyte gate.

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EPC, endothelial progenitor cell.

<table>
<thead>
<tr>
<th>Cell population</th>
<th>ANOVA across 3 study time points p value</th>
<th>Time points between which significant differences seen</th>
<th>Paired t-test p value</th>
<th>Fold increase in EPC count</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD34+</td>
<td>0.003</td>
<td>22:00-&gt;15:00</td>
<td>&lt;0.001</td>
<td>1.28</td>
</tr>
<tr>
<td>CD34+</td>
<td>0.003</td>
<td>08:00-&gt;15:00</td>
<td>0.031</td>
<td>1.16</td>
</tr>
<tr>
<td>CD34+CD45+</td>
<td>0.046</td>
<td>22:00-&gt;15:00</td>
<td>0.013</td>
<td>1.17</td>
</tr>
<tr>
<td>CD133+</td>
<td>0.023</td>
<td>22:00-&gt;15:00</td>
<td>0.001</td>
<td>1.24</td>
</tr>
<tr>
<td>CD34+CD133+</td>
<td>0.015</td>
<td>22:00-&gt;15:00</td>
<td>0.006</td>
<td>1.23</td>
</tr>
<tr>
<td>CD133+KDR+</td>
<td>0.027</td>
<td>22:00-&gt;15:00</td>
<td>0.009</td>
<td>1.39</td>
</tr>
<tr>
<td>CD34+CD133+KDR+</td>
<td>0.016</td>
<td>22:00-&gt;08:00</td>
<td>0.037</td>
<td>1.38</td>
</tr>
<tr>
<td>CD34+CD133+KDR+</td>
<td>0.016</td>
<td>22:00-&gt;15:00</td>
<td>0.012</td>
<td>1.42</td>
</tr>
</tbody>
</table>

CD34+ and CD34+ CD133+ EPC counts during the study period

p = 0.031 p < 0.001

p = 0.006

EPC, endothelial progenitor cell.
and allow us to develop strategies to mobilise these cells. The timing of blood sampling is neither specified nor standardised in most of the existing studies of EPC and variations in this could potentially influence the results. The effects of diurnal variation seen here are of a similar magnitude to the differences in EPC numbers previously shown between cardiac patients and controls and we suggest that the time of sampling should be included in future studies to avoid potential confounding. Diurnal changes in EPC numbers may be relevant to the diurnal variation in the acute coronary syndrome.

**Abstract 119 Figure 1**

HFABP, heart-type fatty acid binding protein; Trop, troponin.

12–24 hours from symptom onset. A “positive troponin” was defined as ≥0.05 µg/l, based on the 99th centile value in an apparently healthy population. Additional serum and plasma samples were collected on all patients at the time of their routine troponin test. Of these, 957 patients had serum samples suitable for HFABP measurement (after excluding missing/insufficient/unsuitable samples) and have been included in the analysis. Mortality was monitored through the Office of National Statistics. Median follow-up was for 542 days (11 months) with a minimum follow-up duration of 6 months.

**Results:** All-cause mortality in “troponin-positive” patients was 8.6% (25/268). 72% of patients had “negative” troponin measured 12–24 hours from symptom onset (689/957). Among these patients who had “negative” troponin, 39 had HFABP ≥0.5 µg/l (being the 99th centile value for an apparently healthy population with a mean age similar to the population under study). The unadjusted mortality in these patients was 12.8% (5/39) as against 1.7% (11/918) in those with HFABP less than 0.5 µg/l (p = 0.001). Across the entire cohort of patients, troponin did not significantly predict mortality at 11 months. However, HFABP was a significant predictor of mortality on univariate analysis (p<0.001). After adjusting for age and serum creatinine using a Cox proportional

**Objective:** To evaluate the role of heart-type fatty acid binding protein (HFABP) in risk stratifying patients with suspected acute coronary syndrome (ACS), particularly those who are identified as “troponin negative”.

**Design:** A consecutive cohort of 1083 patients with suspected ACS recruited from a single teaching hospital at Leeds.

**Methods:** The FAB study recruited consecutive consenting patients admitted with “suspected” (and “confirmed”) ACS during a 10-month period (15 May 2006 to 31 March 2007). Baseline clinical data including ECG were collected at the time of recruitment. All patients had troponin I measured routinely using the new high-sensitivity Bayer ultra-troponin I assay on a serum sample collected

**Abstract 119 Figure 2**

ROC curve
- Troponin I (12 h)
- HFABP (12 h)

**Figure 2**

ROC, receiver operator characteristic.
BRAIN-NATRIURETIC PEPTIDE IS THE BEST SINGLE MARKER FOR LONG-TERM MORTALITY IN ACUTE CORONARY SYNDROME

1K Viswanathan, PhD; 2M Batterham; 3M Mooney; 4S Thistlethwaite; 5AS Hall.
1University of Leeds, Leeds, UK; 2Leeds General Infirmary, Leeds, UK

Objective: We aimed to evaluate the role of brain-natriuretic peptide (BNP) in risk stratifying patients with suspected acute coronary syndrome (ACS), especially among those identified as “troponin negative”.

Design: A consecutive cohort of 1083 patients with suspected ACS recruited from a single teaching hospital in Leeds.

Methods: The FAB study recruited consecutive consenting patients admitted with “suspected” (and “confirmed”) ACS during a 10-month period (15 May 2006 to 31 March 2007). Baseline clinical data including ECG were collected at the time of recruitment. All patients had troponin I measured routinely using the new high-sensitivity Bayer ultra-troponin I assay on a serum sample collected 12–24 hours from symptom onset. A “positive troponin” was defined as >0.05 μg/l, based on the 99th centile value in an apparently healthy population. Additional serum and plasma samples were collected at the time of the routine troponin test. Of these, 959 patients had plasma samples suitable for BNP measurement (after excluding missing/insufficient/unsuitable samples) and have been included in the analysis. Mortality was monitored through the Office of National Statistics. Median follow-up for long-term mortality was for 342 days (11 months) with a minimum follow-up duration of 6 months.

Results: Overall all-cause mortality was 3.9% (99/959). 72.1% of patients had “negative” troponin measured 12–24 hours from symptom onset (691/959). The unadjusted mortality for “troponin-positive” patients was 7.8% as against 2.3% in “troponin-negative” patients. The mean BNP measured was 59.2 pmol/l (SD 35.4). Cut-offs for tertiles of BNP in pmol/l were 5.35 and 24.8. Unadjusted mortality across tertiles of BNP are shown in fig 1 (T1 0.5%, T2 1.6%, T3 9.8%). Across the entire cohort of patients, troponin did not significantly predict long-term mortality. However, BNP was a significant predictor of mortality on univariate analysis (p<0.001). After adjusting for age, serum creatinine and high-sensitivity C-reactive protein (hsCRP) using a Cox proportional hazards multivariate model, BNP was an independent predictor of mortality (hazard ratio 1.002, 95% CI 1.001 to 1.004, p = 0.001; using BNP as a continuous variable measured in μl/l). Using receiver operator characteristic curves, BNP was superior to age, serum creatinine, hsCRP and troponin in predicting long-term mortality. The area under the curve for BNP, age, serum creatinine, hsCRP and TnI was 0.86, 0.82, 0.69 and 0.67, respectively (see fig 2). When the receiver operator characteristic curve analysis was confined to patients who were “troponin negative”, BNP remained the most useful marker in predicting long-term mortality with an area under the curve of 0.81.

Conclusion: We have shown that BNP is valuable as a predictor of long-term mortality across patients with suspected ACS, independent of age, creatinine, troponin and hsCRP. BNP is the single most useful marker for predicting long-term mortality, including patients with troponin-negative chest pain.

MMP3: A PREDICTOR OF VENTRICULAR FUNCTION AFTER ACUTE MYOCARDIAL INFARCTION?

1RAP Weir, PhD; 1A Murphy, PhD; 1S Clements, PhD; 1T Steedman, PhD; 1JJV McMurray, MD; 2LL Ng, PhD; 3B Square, PhD; 4U Dargie, MD.
1Western Infirmary, Glasgow, UK; 2Leicester Royal Infirmary, Leicester, UK

Introduction: Matrix metalloproteinase 3 (MMP3) plays a potential mechanistic role in adverse ventricular remodelling after acute myocardial infarction (AMI) in echocardiographic studies. Cardiac magnetic resonance imaging (CMRI) is a more accurate and reproducible imaging modality in patients with left ventricular systolic dysfunction. We measured MMP3 in a cohort of AMI patients with left ventricular systolic dysfunction and analyzed its influence on left ventricular function and its relationship with neurohormones.

Methods: 100 patients with AMI (left ventricular ejection fraction (LVEF) <40% on screening echocardiography) underwent screening sample MMP3, brain natriuretic peptide (BNP) and N-terminal pro-brain natriuretic peptide (NT proBNP) sampling at a mean 2.8 days after...
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| Variable | Baseline, mean (SD) | 6 months, mean (SD) | p Value  
|----------|---------------------|---------------------|-----------
| MMP3 (mg/ml) | 6.20 (3.10) | 6.57 (3.10) | 0.249 |
| BNP (pg/ml) | 242.5 (180.0) | 120.1 (199.1) | <0.001 |
| NT proBNP (pg/ml) | 2587 (2732) | 841 (1983) | <0.001 |
| LVESVI (ml/m²) | 43.6 (15.2) | 43.1 (20.7) | 0.771 |
| LVEDVI (ml/m²) | 83.9 (18.0) | 88.1 (23.0) | 0.011 |
| LVMi (g/m²) | 74.4 (15.3) | 67.1 (14.3) | <0.001 |
| LVEF (%) | 48.9 (18.8) | 53.0 (12.0) | <0.001 |
| Infarct volume (g/m²) | 34.0 (21.2) | 20.9 (12.9) | <0.001 |

BNP, brain natriuretic peptide; LVEDVI, left ventricular end-diastolic volume index; LVESVI, left ventricular ejection fraction; LVMi, left ventricular end-systolic volume index; LVEDVI, left ventricular mass index; MMP3, matrix metalloproteinase 3; NT proBNP, N-terminal pro-brain natriuretic peptide.

AMI, followed by CMRI at a mean 4.2 days. CMRI and bloods were repeated at 6 months.

Results: Mean age was 58.9 years (SD 12.0) (77% male). 92% of infarcts were ST-elevation myocardial infarction, with 8% non-ST-elevation myocardial infarction. Infarct site was anterior in 55% and inferior/posterior in 45%. Blood results and CMRI parameters are shown in the table. MMP3 correlated with age (r = 0.24, p = 0.018) and was higher in men (6.7 ± 3.2 versus 4.9 ± 2.8 units, p = 0.015). MMP3 was weakly but significantly associated with baseline (r = −0.25, p = 0.014) and 6-month (r = 0.32, p = 0.002) LVEF, and with baseline (r = 0.28, p = 0.005) and 6-month (r = 0.31, p = 0.003) infarct volumes, but not with left ventricular volumes. There was a significant relationship between MMP3 and baseline BNP (r = 0.35, p = 0.001) and NT proBNP (r = 0.44, p<0.001). The change in MMP3 over time also correlated significantly but weakly with the change in NT proBNP over time (p = 0.32, p = 0.002).

Conclusion: An association exists between MMP3 levels and LVEF, both acutely and at 6 months after AMI. Elevated MMP3 levels also appear to have an association with neurohormones of known prognostic importance in this condition. Further studies are merited to determine whether MMP3 may ultimately be considered a prognostic marker of ventricular function and outcomes after AMI.

Abstract 122 Multidimensional scaling (MDS) showing population clustering. CEU, European; CHB–JPT, Chinese and Japanese; YRI, African.

1W Zhang, D Zabaneh, D Balding, Mi McCarthy, P Elliott, J Scott, JS Kooser, JF Chambers. Imperial College London, London, UK; 2Oxford University, Oxford, UK

Background: Indian Asians (persons originating from India, Pakistan, Bangladesh and Sri Lanka) are at increased risk of obesity, type 2 diabetes and coronary heart disease. Genome-wide association studies are in progress to identify genetic variants underlying these common traits in Indian Asians. Although the risks of obesity, diabetes and coronary heart disease are increased in each of the Indian Asian subgroups, it remains unknown whether these groups are genetically homogeneous. Unsuspected genetic structure may confound the analysis and interpretation of association studies. The purpose of the present study was to examine genetic homogeneity among Indian Asians.

Materials and Methods: We investigated 2694 Indian Asian men aged 35–75 years, recruited from the lists of general practitioners in west London, as part of the London Life Sciences Population Study. Country of birth and religion were recorded for allocation of subgroups. Genotyping was performed using the Illumina 317K Beadchip. We examined the genome-wide data using principal components analysis and multidimensional scaling (MDS) to identify population structure. Genotype data from the north European (CEU), African (YRI) and Chinese and Japanese (CHB–JPT) populations from HapMap were used to establish reference points.

Results: Population structure revealed by MDS is presented graphically (fig). Indian Asians were genetically closest to the north European population, but showed a greater genetic diversity than observed in the HapMap reference populations. Both principal components analysis and MDS showed clear evidence of population structure. Genetic heterogeneity was evident for both geographical groupings, with a prominent north–south axis (fig), as well as for the major religious subgroups (Sikh, Hindu, Muslim).

Conclusions: The Indian Asian population is genetically most similar to the north European HapMap population, but shows significant genetic diversity. Population genetic structure is evident based on both geographical as well as religious groupings. This population structure has important implications for the design, conduct, analysis and interpretation of genome-wide and other genetic association studies among Indian Asians.

123 SAFETY OF CONTRAST AGENTS IN STRESS ECHO CARDIOGRAPHY FOR EVALUATING PATIENTS WITH KNOWN OR SUSPECTED CORONARY ARTERY DISEASE

B Anantharam, V Bhatia, N Chahal, F Gani, R Senior. Northwick Park Hospital, Harrow, UK

Aim: The aim of the study is to assess the safety of the contrast agents used in stress echocardiography in patients with known or suspected coronary artery disease.

Background: Several previous studies had proved the safety of commercially available contrast agents in stress echocardiography. However, there have been recent reports of serious cardiopulmonary reactions (including four deaths) in patients in relation to the used contrast agent. Subsequently, the US Food and Drug Administration has issued a black box warning regarding the use of contrast agents in patients with unstable cardiac conditions. Therefore, we sought to assess the safety record of contrast agents used within our institution.

Methods: Over a 2-year period, 2372 patients underwent stress echocardiography (exercise, dobutamine). Of these patients 659 (27.7%) had presented within 24 hours of chest pain with a non-diagnostic ECG but negative 12-hour troponin. In patients who underwent stress echocardiography, contrast was used in 510 (21.5%). Sonovue (Bracco, Milan, Italy) was used in 51%, Luminy (Bristol Myers Squibb Medical Imaging Inc, North Billerica, Massachusetts, USA) was used in 48% and Optison (GE-Amersham, Princeton, New Jersey, USA) was used in 0.19%. The haemodynamic and adverse effects of contrast agents were compared with 1862 patients who underwent conventional stress echocardiography without contrast.
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<table>
<thead>
<tr>
<th>Complications</th>
<th>Without contrast (1862)</th>
<th>Without contrast (510)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Acute myocardial infarction</td>
<td>3 (0.16%)</td>
<td>0</td>
<td>0.83</td>
</tr>
<tr>
<td>Arrhythmias</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Supraventricular tachycardia</td>
<td>8 (0.42%)</td>
<td>0</td>
<td>0.24</td>
</tr>
<tr>
<td>Atrial fibrillation/flutter</td>
<td>1 (0.05%)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Non-sustained tachycardia</td>
<td>1 (0.05%)</td>
<td>0</td>
<td>0.48</td>
</tr>
<tr>
<td>Hypotension</td>
<td>10 (0.50%)</td>
<td>1 (0.20%)</td>
<td>0.52</td>
</tr>
<tr>
<td>Complete heart block</td>
<td>1 (0.05%)</td>
<td>0</td>
<td>0.48</td>
</tr>
<tr>
<td>Allergy</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

Combined p value 0.27.

Results: There were no deaths in patients with or without contrast. There was no incidence of non-fatal myocardial infarction with contrast agents. However, three cases of non-fatal myocardial infarction occurred post-stress echocardiography without contrast (0.16%, p = 0.83). Hypotension occurred in one (0.20%) patient at rest after the injection of contrast, which responded immediately to intravenous fluids; however, in patients without contrast there were 10 cases of hypotension (0.50%, p = 0.52). There was no incidence of arrhythmias with contrast, whereas nine cases of supraventricular tachycardia and one case of non-sustained ventricular tachycardia were observed in patients who underwent stress echocardiography without contrast. No allergic reaction was observed with contrast agents (table).

Conclusions: Within our institutional practice contrast agents were shown to be safe when used in stress echocardiography for evaluating patients with known or suspected coronary artery disease.

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COMPARISON OF ADENOSINE STRESS CONTRAST ECHOCARDIOGRAPHY WITH CARDIOVASCULAR MAGNETIC RESONANCE IN PATIENTS WITH SUSPECTED CORONARY ARTERY DISEASE

1JR Arnold, 1TD Karamitsos, 1JM Francis, 1TJ Pegg, 1N Searle, 1S Neubauer, 2H Becher, 3JB Selvanayagam. 1University of Oxford Centre for Clinical Magnetic Resonance Research, Oxford, UK; 2Department of Cardiology, John Radcliffe Hospital, Oxford, UK; 3University Department of Cardiovascular Medicine, John Radcliffe Hospital, Oxford, UK

Introduction: Several imaging modalities are available for the non-invasive assessment of coronary artery disease (CAD), but cardiovascular magnetic resonance (CMR) and echocardiography benefit from the absence of ionising radiation. Myocardial stress perfusion imaging with CMR is now well established in the assessment of CAD and a multiparametric approach combining perfusion and infarction imaging further augments its diagnostic performance. Despite the widespread use of dobutamine stress echocardiography (SE) in clinical practice, adenosine SE is not routinely used because of reduced accuracy when wall motion assessment alone is used to evaluate ischaemia. However, the recent advent of second-generation contrast agents now enables a multiparametric approach for echocardiography, involving simultaneous myocardial perfusion and wall motion analysis. We sought to compare two optimised diagnostic strategies in patients with suspected CAD: (1) a combined perfusion and infarct imaging algorithm by CMR and (2) combined perfusion and wall motion analysis by adenosine SE.

Methods: Thirty-one patients with suspected CAD were studied pre-angiography with SE and 3 Tesla CMR, at stress (140 μg/kg per minute intravenous adenosine) and rest. For CMR, first-pass perfusion and delayed enhancement images were acquired in the short-axis plane after intravenous gadolinium-DTPA bolus injections (0.05 mmol/kg). For the SE study, two, three and four-chamber long-axis images were acquired during intravenous Sonovue infusion. CMR and SE images were interpreted visually by two observers blinded to clinical and angiographic data. For CMR, the diagnosis of CAD was determined by the presence of reversible perfusion defects or delayed enhancement, and for SE by reversible perfusion or wall motion abnormalities. OCA served as the reference standard: CAD was defined as one or more stenoses of ≥50% reference diameter in vessels of diameters ≥2 mm.

Results: The prevalence of CAD was 71%. All CMR and SE images were visually interpretable. Compared with SE, CMR provided higher diagnostic accuracy (94% versus 81%) and sensitivity (96% versus 78%), but similar specificity (82% versus 82%) for the detection of CAD. CMR also identified disease location with greater sensitivity (left anterior descending (LAD) 88% versus 76%, circumflex (LCx) 75% versus 65%, right coronary artery (RCA) 100% versus 62%) but similar specificity (LAD 93% versus 86%, LCx 96% versus 100%, RCA 89% versus 100%). CMR was superior to SE in identifying single-vessel and multivessel disease (area under the receiver operator characteristic curve 0.88 ± 0.07 versus 0.74 ± 0.10 and 0.91 ± 0.06 versus 0.75 ± 0.10). However, there was no significant difference in the overall detection of CAD (area under the receiver operator characteristic curve: 0.88 ± 0.08 SE versus 0.92 ± 0.05 CMR; p = 0.32, fig).

Conclusion: CMR provides higher sensitivity by virtue of its high spatial resolution, whereas the combination of wall motion and perfusion analysis with SE confers high specificity. The diagnostic performance of adenosine SE approaches that of CMR; therefore adenosine SE may be clinically useful for the evaluation of patients with suspected CAD.

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TWO-DIMENSIONAL SPECKLE TRACKING: CAN IT RELIABLY MEASURE THE INOTROPIC EFFECT OF INCREASING DOSES OF DOBUTAMINE, IN NORMAL LEFT VENTRICULAR SEGMENTS?

A Bhan, S Kapetanakis, BS Rana, F Casella, MJ Monaghan. King’s College Hospital, London, UK

Background: The use of two-dimensional speckle tracking derived strain is emerging as a useful tool in the functional assessment of
myocardium, both at rest and stress. We set out to see if this technique could reliably document the inotropic effect of dobutamine, in normal left ventricular segments, during the different stages of a stress echo.

**Methods:** We studied 27 patients (16 men), with a low pre-test probability of coronary artery disease, who had been referred for dobutamine stress echo and who had normal tests. Standard stress protocol images were acquired at baseline (0 μg/kg per minute), low dose (10 μg/kg per minute), intermediate (30 μg/kg per minute) and peak (40 μg/kg per minute). The standard images were reported by an experienced operator and the speckle analysis was performed by an independent observer, using the American Society of Echo 17 segment model. Peak radial strain was calculated for each segment at each stage. These results were then combined to give a mean peak radial strain and SD per coronary artery territory per stage.

**Results:** At baseline mean peak strain in the left anterior descending (LAD) was 25% (SD 9). This increased to 32% (10.5) at low dose, 57% (18.4) at intermediate and 74% (18.4) at peak. The circumflex (LCx) results were 27% (12.4), 33% (6.3), 49% (14.4) and 73% (18.4), respectively, and for the right coronary (RCA) they were 10% (5.5), 24% (8.5), 26% (7.5) and 55% (18.2). ANOVA revealed a statistically significant escalation in strain with increasing doses of dobutamine in all territories (p<0.001 for all coronaries). Post-hoc t-testing revealed that the only individual stages not to reach statistical significance were the LCx from rest to low dose and the RCA from low dose to intermediate. We then looked at the percentage of the global strain that was contributed by each coronary artery at each stage. For the LAD this was 38% at rest, 40% at low dose, 45% at intermediate and 38% at peak. For the LCx the values were 41%, 36%, 58%, 33% and for the RCA 21%, 15% and 29%. ANOVA of all the stages demonstrated no statistically significant change in any territory.

**Conclusion:** This is the first study in humans to demonstrate that speckle tracking can reliably measure increasing myocardial strain with increasing doses of dobutamine in normal left ventricular segments. Figures for the RCA are lower than for the LAD and LCx with slightly higher variability. Regardless of increases in global left ventricular strain, the percentage of this contributed by an individual artery remains relatively constant. This technique has the potential to be an objective aid in the interpretation of dobutamine stress echo. However, further study is required in both normal and ischaemic segments.

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**Abstract 126**

**PERCUTANEOUS AORTIC VALVE REPLACEMENT: IS THERE A DIFFERENCE BETWEEN TWO AND THREE-DIMENSIONAL TRANSOESOPHAGEAL ECHOCARDIOGRAPHY WHEN ASSESSING AORTIC ANNULAR DIAMETER?**

A Bhan, S Kapetanakis, K Wilson, P Pearson, O Wendler, A El-Gamel, P McCarthy, MR Thomas, MJ Monaghan. King’s College Hospital, London, UK

**Background:** Percutaneous aortic valve replacement (PAVR) is a relatively new procedure currently aimed at those deemed too high risk for conventional surgery. Preliminary data have been very encouraging and a number of clinical trials are ongoing. Accurate imaging is mandated for all aspects of this procedure, not least in the assessment of aortic annular size. The valves come in different sizes and undersizing has potential implications regarding post-procedure paraprosthetic aortic regurgitation. We are currently utilising three-dimensional (3D) transoesophageal echo (TOE) in our PAVR programme and wanted to see if there was a discrepancy between annular measurements made using two-dimensional (2D) and 3D TOE.

**Methods:** Measurements on 13 patients (five men) who underwent successful valve deployment were made. Annular diameters were taken on 2D and 3D images by two independent observers. The distance between the insertion points of the leaflets was taken in a mid-systolic frame. 2D measurements were made using the mid-oesophageal long axis view. 3D measurements were taken from a full volume or live 3D acquisition, and a 3D multiplane reconstruction (MPR) viewer was used to line the valve up in orthogonal planes.

**Results:** Annular measurements were possible using both 2D and 3D in all patients. Interobserver agreement was very good for both techniques with a correlation coefficient of 0.85 for 2D and 0.86 for 3D TOE.
Intraobserver correlation was 0.86 for 2D and 0.87 for 3D. When the annular measurements between the two readers were combined the mean obtained by 3D was larger than that obtained using 2D: 20.7 mm (SD 2.4) for 2D and 21.5 mm (SD 2.4) for 3D. This difference (0.8 mm) was statistically significant (p = 0.02).

Conclusion: Aortic annular measurements using both 2D and 3D TOE show very good reliability and reproducibility. However, 2D TOE appears to underestimate aortic annular diameter when compared with 3D. As this procedure becomes more prevalent and the variety of valve sizes grows this discrepancy may become important in the sizing process.

127 LEFT ATRIAL SIZE DETERMINED BY HAND-HELD ECHOCARDIOGRAPHY PREDICTS LONG-TERM ADVERSE CARDIAC OUTCOME IN PATIENTS SCREENED FOR HEART FAILURE IN THE COMMUNITY

G Dwivedi, GI Galasko, A Banfield, TK Lim, R Senior. Northwick Park Hospital, Harrow, UK

Background: It has previously been shown that hand-held echocardiography (HE) performed by a trained sonographer is an accurate screening modality for heart failure in the community. However, its prognostic significance compared with clinical and electrocardiographic (ECG) variables is unknown.

Objective: To evaluate the prognostic significance of HE with other clinical and electrocardiographic variables in community subjects screened for heart failure.

Methods: Accordingly, a total of 1392 members of the general population and 928 higher risk subjects were randomly selected from seven community practices. A total of 563 consecutive subjects underwent HE. Left ventricular wall thickness (interventricular septum and posterior wall in diastole), left ventricular ejection fraction, left atrial size in parasternal long axis view and left ventricular internal dimensions were noted. All of these patients also underwent complete clinical assessment including pulmonary function tests and ECG (abnormal ECG was defined as the presence of atrial fibrillation or flutter, ventricular arrhythmia, conduction defects, ST or T-wave abnormalities, pathological Q wave, paced rhythm or left ventricular hypertrophy). The patients were subsequently followed up for all-cause mortality and heart failure admissions.

Results: Of the total 563 subjects recruited, 537 were available for the follow-up (mean of 63 ± 16 months). There were 45 (8%) all-cause mortality and 15 (3%) admissions with heart failure. Among the clinical variables (diabetes, hypertension, peripheral vascular disease, cerebrovascular disease and body mass index), pulmonary function tests and ECG; left atrial size on HE was a multivariate predictor for both mortality (p < 0.01) as well as mortality or heart failure (p < 0.01). Age (p < 0.01 and p < 0.001) and abnormal ECG (p < 0.01) were the other multivariable predictors for mortality and mortality or heart failure admissions.

Conclusions: Left atrial size, a marker of left ventricular filling pressure, assessed by HE predicted long-term adverse outcomes in community subjects screened for heart failure independent of clinical prognostic variables.

128 MYOCARDIAL VIABILITY ASSESSMENT USING RESTING MYOCARDIAL CONTRAST ECHOCARDIOGRAPHY AND NOT BY TECNETIUM-SESTAMIBI SPECT INDEPENDENTLY PREDICTS HARD CARDIAC OUTCOME AFTER ACUTE MYOCARDIAL INFARCTION AND REPERFUSION THERAPY

G Dwivedi, R Janardhanan, SA Hayat, JA Swinburn, R Senior. Northwick Park Hospital, Harrow, UK

Introduction: Assessment of myocardial viability, an important marker for outcome, depends largely on myocardial microvascular volume with technetium-sestamibi single photon emission computed tomography (SPECT). However, myocardial viability assessment is more accurate using myocardial contrast echocardiography (MCE) as it assesses both microvascular volume as well as myocardial blood flow. We hypothesised that after acute myocardial infarction (AMI) and reperfusion therapy, myocardial viability assessment using MCE and not SPECT independently predicts hard cardiac events.

Methods: Accordingly, 99 patients with AMI underwent resting low-power MCE and SPECT after reperfusion therapy. MCE (0, normal; 1, reduced; 2, absent) perfusion was assessed over 15 cardiac cycles after the destruction of microbubbles with high-energy pulses. Both SPECT (0, normal; 1, mildly reduced; 2, moderately reduced; 3, severely reduced; 4, absent tracer uptake)
and MCE perfusion were scored on a 16-segment left ventricular model. Contrast perfusion index and SPECT perfusion index were calculated by adding the respective scores in the 16 left ventricular segments divided by 16. Contrast perfusion index and SPECT perfusion index were used as a measure of myocardial viability on MCE and SPECT, respectively. The patients were subsequently followed up for cardiac death and AMI.

**Results:** Of the 99 patients recruited, 95 were available for the follow-up (mean 46 ± 16 months). There were eight cardiac deaths and seven AMI. Areas under the receiver operator characteristic curves for predicting cardiac death and cardiac death or AMI with MCE (0.72 and 0.68) were higher compared with SPECT (0.68 and 0.45). Among the clinical, biochemical and echocardiographic markers of prognosis, only myocardial viability determined by MCE and age were independent predictors of cardiac death (p = 0.04) and cardiac death or AMI (p = 0.002) (fig).

**Conclusion:** Myocardial viability assessment using resting MCE and not SPECT independently predicts hard cardiac outcome after AMI and reperfusion therapy.

### 129 SUBCLINICAL ABNORMALITIES OF REGIONAL LEFT VENTRICULAR MYOCARDIAL DEFORMATION IN EARLY STAGE CHRONIC KIDNEY DISEASE: THE PRECURSOR OF URAEMIC CARDIOMYOPATHY?

**1**NC Edwards, **A** Hirth, **CJ** Ferro, **JN** Townend, **RP** Steeds. **1University of Birmingham, Birmingham, UK; 3Institute of Clinical Medicine, University of Bergen and Department of Heart Disease, Haukeland University Hospital, Bergen, Norway; 3University Hospital Birmingham, Birmingham, UK

**Background:** Abnormal left ventricular deformation is an independent predictor of a poor prognosis in end-stage chronic kidney disease (CKD) and is thought to reflect the extensive interstitial fibrosis and myocyte abnormalities found in uraemic cardiomyopathy on left ventricular biopsy. Studies of left ventricular function have not previously been performed in early stage CKD despite the fact that there is a graded inverse relationship between cardiovascular events and glomerular filtration rates (GFR) below 80 ml/min per 1.73 m². The aim of this study was to examine left ventricular systolic function using tissue Doppler and regional deformation imaging in early CKD compared with a healthy control population.

**Methods:** 40 patients (aged 48 ± 9 years, male 61%) with early stage CKD (GFR 56 ± 13 ml/min per 1.73 m², mean creatinine 126 mmol/l) were compared with 30 healthy age and sex-matched controls. The aetiology of CKD was determined by clinical investigation and/or renal biopsy (glomerulonephritis 40%, vasculitis 25%, undetermined 17%, reflux 8%, adult polycystic disease 8%, other 4%). All subjects were normotensive (mean 125 ± 1/76 ± 1 mm Hg) with no history of cardiovascular disease. Transthoracic echocardiography including tissue Doppler velocities and longitudinal deformation (strain/strain rate) in the basal and mid-segments of the septal and lateral left ventricular walls was performed in all subjects.

**Results:** There were no differences in left ventricular dimensions (internal diameter 4.9 ± 0.4 cm versus 5.0 ± 0.4 cm), left ventricular ejection fraction (65 ± 6% versus 64 ± 5%) or basal systolic velocities (mean 6.1 ± 1.4 cm/s versus 6.2 ± 1.5 cm/s). Basal lateral, basal septal and mid-septal peak systolic strain were reduced in CKD (p<0.05) with pronounced post-systolic shortening (p<0.01) (table). Peak systolic sinus rhythm was reduced in the basal lateral, mid-lateral and mid-septal walls (p<0.05). Left ventricular mass index was increased in CKD (85 ± 16 g/m² versus 96 ± 19 g/m², p<0.05) but subgroup analysis of patients with CKD and left ventricular hypertension revealed no differences in strain and strain rate compared with patients with CKD and normal left ventricular mass. There was no correlation with blood pressure.

**Conclusion:** Systolic deformation is abnormal early in CKD, preceding the major alterations in left ventricular size and function that are characteristic of uraemic cardiomyopathy. These data suggest that regional myocardial fibrosis, myocyte disarray and capillary density are present early in CKD and may contribute to increased rates of cardiovascular morbidity and mortality observed at all stages of CKD.

### 130 IMPAIRED DIASTOLIC FUNCTION IN EARLY STAGE CHRONIC KIDNEY DISEASE: THE PRECURSOR TO URAEMIC CARDIOMYOPATHY?

**1NC Edwards, **CJ Ferro, **JN Townend, **RP Steeds. **1University of Birmingham, Birmingham, UK; 3University Hospital Birmingham, Birmingham, UK

**Introduction:** A quarter of deaths in chronic kidney disease (CKD) occur as a result of heart failure and sudden cardiac death. Adverse prognostic abnormalities of left ventricular geometry and function are characteristic of uraemic cardiomyopathy but are present in early CKD. The aim of this study was to determine whether subclinical ventricular abnormalities are present in early stage CKD.

**Methods:** 117 patients with non-diabetic early stage 2 and stage 3 CKD (mean GFR 51 ml/min, mean creatinine 136 mmol/l) were compared with 40 age and sex-matched controls. All subjects were normotensive (mean 125 ± 1/76 ± 1 mm Hg) and had no history of cardiovascular disease. Cardiac magnetic resonance imaging (1.5 T) and transathoracic echocardiography (GE Vingmed Vivid 7) were performed to assess systolic and diastolic ventricular function using standard techniques.

**Results:** Patients with early CKD had preserved left ventricular longitudinal systolic velocities and ejection fraction. There was marked impairment in resting diastolic function and left ventricular relaxation in early CKD compared with controls (table). A quarter of patients with CKD had left ventricular hypertrophy despite no difference in blood pressure (126 ± 11/77 ± 8 mm Hg, LVH versus no LVH 124 ± 12/77 ± 9 mm Hg). In these cases, there was an additional, progressive impairment in diastolic function and also reduced ejection fraction (64.4 ± 9.5% versus 71.2 ± 6.7% p<0.01) compared both with controls and with patients with CKD and normal left ventricular mass.

**Conclusion:** Impaired left ventricular relaxation is present in early stage CKD, before a rise in plasma creatinine may be detected and at a stage when systolic function is preserved. These changes

<table>
<thead>
<tr>
<th>Abstract 129</th>
<th>Controls (n = 30)</th>
<th>CKD (n = 40)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak basal lateral/medial-lateral strain (%)</td>
<td>−17.9 ± 5.5/−14.9 ± 3.8</td>
<td>−14.0 ± 5.3/−13.9 ± 5.7</td>
</tr>
<tr>
<td>Peak basal septal/medial-septal strain (%)</td>
<td>−18.8 ± 4.7/−18.7 ± 4.7</td>
<td>−17.2 ± 5.1/−16.1 ± 4.8*</td>
</tr>
<tr>
<td>Post-systolic shortening basal lateral/medial septal (%)</td>
<td>8 ± 3/7 ± 2</td>
<td>23 ± 6/16 ± 27†</td>
</tr>
<tr>
<td>Peak basal lateral/medial-lateral strain rate (s⁻¹)</td>
<td>−1.38 ± 0.68/−0.91 ± 0.25</td>
<td>−0.89 ± 0.41/−0.75 ± 0.27†</td>
</tr>
<tr>
<td>Peak basal septal/medial-septal strain rate (s⁻¹)</td>
<td>−1.00 ± 0.22/−1.09 ± 0.18</td>
<td>−0.95 ± 0.25/−0.98 ± 0.26*</td>
</tr>
</tbody>
</table>

*p<0.05; †p<0.01 chronic kidney disease (CKD) versus controls.
Abstract 130

<table>
<thead>
<tr>
<th>Controls (n = 40)</th>
<th>CKD stage 2 (n = 29)</th>
<th>CKD stage 3 (n = 88)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEF (%) CMR</td>
<td>71.6 ± 5.9</td>
<td>69.9 ± 6.2</td>
</tr>
<tr>
<td>Left ventricular mass index (g/m²) CMR</td>
<td>55.1 ± 9.4</td>
<td>64.2 ± 15.2*</td>
</tr>
<tr>
<td>LVH (%)</td>
<td>0</td>
<td>9 (36†)</td>
</tr>
<tr>
<td>Lateral annular Em (cm/s)</td>
<td>12.1 ± 3.1</td>
<td>10.5 ± 2.4†</td>
</tr>
<tr>
<td>E/Em</td>
<td>5.6 ± 1.1</td>
<td>7.4 ± 1.8†</td>
</tr>
<tr>
<td>Colour flow propagation velocity (cm/s)</td>
<td>62.9 ± 11.0</td>
<td>54.6 ± 15.3*</td>
</tr>
<tr>
<td>LA volumes/BSA (m³/m²)</td>
<td>19.2 ± 4.0</td>
<td>25.2 ± 6.3*</td>
</tr>
<tr>
<td>Left ventricular Tei Index</td>
<td>0.38 ± 0.04</td>
<td>0.48 ± 0.11†</td>
</tr>
</tbody>
</table>

BSA, body surface area; CMR, cardiac magnetic resonance; LA, left atrial; LVEF, left ventricular ejection fraction; LVH, left ventricular hypertension.

*p<0.05, †p<0.01 chronic kidney disease (CKD) versus controls.

precede the occurrence of LVH and deteriorate further once left ventricular mass is abnormal. We speculate that diastolic dysfunction is the first marker of uraemic cardiomyopathy and may predicate the high levels of cardiovascular morbidity and mortality in patients at all stages of CKD.

131 ISCHAEMIC LEFT VENTRICULAR DYSFUNCTION IS ASSOCIATED WITH INCREASED DYSSYNCHRONY

1SKH, 2PM Heck, 3SP Hoole, 4DP Dutka. 1Papworth Hospital, Cambridge, UK; 2Addenbrooke’s Hospital, Cambridge, UK.

Background: Global left ventricular dyssynchrony is common in the setting of ischaemic heart disease and has prognostic significance in the group with impaired left ventricular function. However, in some patients significant dyssynchrony may only become apparent under conditions of increased demand. We postulated that ischaemic left ventricular dysfunction is associated with increased dyssynchrony.

Methods: 55 patients with angiographically documented coronary artery disease and normal left ventricular function at rest underwent dobutamine stress echocardiography with tissue Doppler data acquisition using a standard clinical protocol. The dyssynchrony index was calculated as the standard deviation of the time to peak systolic velocity of eight basal and mid-segments obtained from the apical two and four-chamber views at rest, peak stress and recovery using Bazett’s formula to correct for changes in heart rate.

Results: There was significant dyssynchrony at rest with a mean (SD) dyssynchrony index of 48 (22) msec. At peak stress this increased to 52 (35) msec (p<0.05) and increased further at recovery (58 (43) msec, p<0.05). Ischaemia was confirmed by deterioration in wall motion score index from a mean of 0 at baseline to 1.5 at peak stress. There were no significant differences between those patients with multi-vessel versus single vessel coronary artery disease (p = 0.46).

Conclusions: Global left ventricular dyssynchrony increases as ischaemic dysfunction develops. We speculate that the clinical importance of this observation may be that some patients may need dyssynchrony assessment to be performed under conditions of increased demand.

132 ASSESSMENT OF REGIONAL LEFT VENTRICULAR SYSTOLIC FUNCTION USING STRAIN AND STRAIN RATE ECHOCARDIOGRAPHY IN ADULT PATIENTS WITH MARFAN SYNDROME

A Kotsiakoglou, GR Sutherland, V Kapetanakis, J Moggridge, DK Nassiri, AJ Carrm, AH Child. St George’s, University of London, London, UK

Background: Marfan syndrome (MFS) is a connective tissue disorder caused by mutations in the gene that encodes for the protein fibrillin-1. Recently published studies demonstrated primary systolic myocardial impairment in MFS using conventional echocardiography. Strain and strain rate echocardiography constitute a validated technique in quantifying regional changes in myocardial deformation. We sought to investigate the spatial distribution of left ventricular systolic abnormalities seen in MFS using ultrasound-based strain rate imaging.

Methods: Seventeen unoperated MFS patients, 10 men and seven women (mean age 36.4 ± 3.0 years) and 19 normal controls without significant differences in age, sex and body surface area, were examined by one observer. None of these patients had more than trivial valvular disease. All the study subjects were in sinus rhythm. A comprehensive echocardiographic examination was performed in all participants at rest, using a Vivid 7 Vingmed-General Electric ultrasound scanner equipped with a 45-MHz probe. Ejection fraction was measured by Simpson’s biplane method. Real-time two-dimensional colour Doppler myocardial imaging data were recorded using standard parasternal and apical four, two and three-chamber views to evaluate radial and longitudinal left ventricular systolic function, respectively. Digitally stored images were analyzed offline using the Echopac version 6.0.0 (GE Systems). All measurements were averaged over three consecutive cardiac cycles.

Results: Ejection fraction was significantly lower in MFS patients when compared with controls (64.60 ± 1.53% versus 71.73 ± 0.85%, p = 0.001). Velocity datasets were obtained from all participants (n = 36). Post-processing of the colour tissue data to extract peak systolic strain rate (SRSYS) and systolic strain (eSYS) curves showed that all the obtained deformation traces were interpretable. Values were presented as mean ± SE. Regional radial SRSYS was significantly reduced in the basal and mid-left ventricular posterior wall segments when compared with controls (3.38 ± 0.22 s⁻¹ versus 4.0 ± 0.14 s⁻¹, p = 0.02 and 3.08 ± 0.13 s⁻¹ versus 3.95 ± 0.18 s⁻¹, p = 0.001, respectively). eSYS was also significantly reduced in the same posterior wall segments (72.23 ± 4.50% versus 93.62 ± 2.48%, p = 0.001 and 66.57 ± 5.47% versus 95.94 ± 3.11%, p = 0.001, respectively). Both longitudinal SRSYS and eSYS were significantly reduced in the basal, mid and apical segments of the interventricular septum and in the lateral, inferior, anterior and posterior left ventricular walls in MFS patients. In a multiple regression analysis including age, sex and systolic blood pressure, MFS was strongly correlated with reduced regional systolic left ventricular deformation (p<0.001).

Conclusions: Our preliminary data showed a uniform reduction in regional left ventricular systolic deformation in MFS patients. This could be attributed to fibrillin-1 deficiency in the cardiac extracellular matrix. Treatment may need to be tailored to prevent further deterioration by supporting left ventricular function.
Abstract 133 Figure 1

Abstract 133 Figure 2

Abstract 134 Figure 1

133 ASSESSMENT OF CAROTID COMPLIANCE USING A REAL-TIME VASCULAR ULTRASOUND IMAGE ANALYSIS SYSTEM IN ADULT PATIENTS WITH MARFAN SYNDROME


Background: The functional abnormalities in the aortic root in patients with Marfan syndrome (MFS) reflect a reduced content of fibrillin-1 (FBN1), dysregulated cytokine transforming growth factor beta and increased collagen deposition related to FBN-1 gene mutations. In MFS, the carotid arteries that originate from the aortic arch, an area that often becomes aneurysmal, may also contain diminished FBN1, which would predispose them to impaired carotid compliance and potential aneurysm formation. For this purpose, we sought to investigate carotid compliance using a real-time vascular image analysis system.

Methods: Thirty-one unoperated MFS patients, 20 men and 11 women (mean age 34.3 ± 12.2 years) and 29 normal controls with no significant differences in age, sex and body surface area (BSA) to the patient group were examined. The entire length of each carotid system was initially scanned longitudinally using a 14 MHz linear array transducer. A stereotactic clamp was used to hold the transducer in contact with the carotid artery (fig 1). Changes in arterial size during the cardiac cycle were continually recorded for 1 minute from the right common carotid artery (RCCA) and left common carotid artery (LCCA) separately using the vascular image analysis system (fig 2).

Results: Carotid compliance measurements obtained from the RCCA and LCCA showed statistically significant differences between MFS patients and normal controls (RCCC: 0.126 ± 0.008 mm².mm Hg⁻¹ versus 0.173 ± 0.007 mm².mm Hg⁻¹, p < 0.001 and LCCC: 0.152 ± 0.007 mm².mm Hg⁻¹ versus 0.158 ± 0.007 mm².mm Hg⁻¹, p = 0.007). RCCA and LCCA intima-media thickness did not differ between patients and normal controls (RCCA: 0.050 ± 0.001 cm versus 0.050 ± 0.001 cm, p > 0.05 and LCCA: 0.050 ± 0.001 cm versus 0.047 ± 0.001 cm, p > 0.05). In a multiple regression analysis after adjusting for age, sex, BSA and systolic blood pressure, MFS was associated with reduced carotid compliance (RCCC: p < 0.001 and LCCC: p = 0.019). Sex, BSA and β-blockade showed no effect on carotid compliance, whereas age was negatively associated with carotid compliance (RCCC: p = 0.001 and LCCC: p = 0.001). Systolic blood pressure measurements did not differ between the two groups (119 ± 2.09 mm Hg versus 114 ± 1.57 mm Hg, p > 0.05).

Conclusions: Despite normal intima-media thickness, carotid compliance was significantly reduced in patients with MFS. This could be attributed to FBN1 deficiency and dysregulated cytokine transforming growth factor beta in the carotid walls. Treatment with angiotensin II type 1 inhibitors may prove beneficial in preserving not only the aortic wall structure but also the carotid arteries.

134 PRIMARY IMPAIRMENT OF RIGHT VENTRICULAR FUNCTION IN ADULT PATIENTS WITH MARFAN SYNDROME

A Kiotsekoglou, GR Sutherland, V Kapetanakis, AJ Moggridge, MM Mullen, DK Nassiri, AJ Camm, AH Child. St George’s, University of London, London, UK; Royal Brompton Hospital, London, UK

Background: The right ventricle deals with the cardiac output in the same way as the left ventricle. Mild left ventricular systolic and diastolic impairment has been demonstrated in Marfan syndrome (MFS). However, little attention has been paid to the functioning of the right ventricle. The aim of this study was to assess right ventricular function in unoperated MFS patients without significant valvular disease.

Methods: Sixty-six unoperated patients with MFS, 37 men and 29 women (mean age 31.9 ± 1.5 years) and 61 normal controls with no significant differences in age, sex and body surface area to the patient group were studied using conventional echocardiography and tissue Doppler imaging (TDI). Tricuspid annular motion (TAM) was obtained by placing in the long axis an M-mode sounding beam across the lateral tricuspid annular region with measurements made 60 msec after the beginning of QRS (fig 1). Tricuspid regurgitation was also recorded to assess the rate of pressure rise (Dp/DT) in the right ventricle (fig 2). Systolic and diastolic tricuspid annular velocities were calculated by tracking colour tissue Doppler images.

Results: Basal and mid-cavity end-diastolic right ventricular diameters obtained from a true non-foreshortened apical...
Introduction: Hepatopulmonary syndrome (HPS) is characterised by platypnoea (dyspnoea induced by the upright position and relieved by recumbency) and orthodeoxia (arterial deoxygenation accentuated in the upright position and relieved by recumbency). Orthodeoxia is thought to be caused by preferential perfusion of intrapulmonary vascular dilatations in the lung bases so that a right–left shunt is increased when the patient is upright leading to hypoxia. HPS is associated with an adverse outcome in end-stage liver disease and leads to urgent transplantation (orthotopic liver transplantation; OLT). Agitated saline bubble contrast echocardiography is a major method used for detection of intrapulmonary shunting, but is almost always performed with the patient lying supine. The aim of this study was to investigate prospectively the incidence of HPS diagnosed by contrast echocardiography and to assess the relative efficacy of injection in the standing compared with the lying position in detecting right–left intrapulmonary shunting in these patients.

Methods: Arterial blood gas in the lying and standing position, lung-function tests and contrast echocardiography were performed in 50 consecutive patients with cirrhosis (men, 60%; median age 53 years) referred for OLT assessment. All patients were randomly assigned to receive 10 ml agitated saline contrast (1 ml room air; 1 ml venous blood; 8 ml saline) first either in the lying or standing position. A total of four injections, two in the lying and two in the standing position, were performed with and without the Valsalva manoeuvre. All echocardiograms were recorded and reviewed by an observer blinded to the order of injection. HPS was defined by arterial hypoxaemia or a fall in oxygen saturation greater than 20% from the lying to the standing position, decreased carbon monoxide diffusing capacity, and the passage of contrast after three cardiac cycles.

Results: Arterial blood gas and decreased carbon monoxide diffusing capacity were diagnostic of HPS in 16% and 22% of patients, respectively. Contrast injection showed late right–left shunting in 13 patients (26%). Only 14% of patients met all three HPS criteria, whereas 12% were considered to have HPS based on late positive contrast echocardiography alone. Intrapulmonary shunts were more common in patients with hypoxaemia (87.5% versus 14.3%, p < 0.001), low decreased carbon monoxide diffusing capacity (69.2% versus 10.8%, p < 0.001) and dyspnoea (77.8% versus 14.6%, p < 0.001) than in those without. Intrapulmonary shunting was detected more frequently in patients receiving contrast first in the standing position than in the lying position (84.6% versus 15.4%, p = 0.003). Among those patients with positive contrast echocardiography in both positions, there was a consistent increase in the size of shunt when standing compared with lying.

Conclusions: Injection of agitated saline contrast in the standing position increases the sensitivity of shunt detection consistent with HPS in patients undergoing OLT compared with the lying position. Standing contrast injections may be preferable in all situations in which platypnoea–orthodeoxia and intrapulmonary shunting is suspected.

BCS abstracts

LYING AND STANDING CONTRAST ECHOCARDIOGRAPHY FOR THE DIAGNOSIS OF HEPATOPULMONARY SYNDROME IN PATIENTS UNDERGOING LIVER TRANSPLANTATION

I Lenci, A Akhri, T Manzia, L Toti, J Neuberger, R Steeds. University Hospital (Queen Elizabeth), Birmingham, UK

Introduction: Hepatopulmonary syndrome (HPS) is characterised by platypnoea (dyspnoea induced by the upright position and relieved by recumbency) and orthodeoxia (arterial deoxygenation accentuated in the upright position and relieved by recumbency). Orthodeoxia is thought to be caused by preferential perfusion of intrapulmonary vascular dilatations in the lung bases so that a right–left shunt is increased when the patient is upright leading to hypoxia. HPS is associated with an adverse outcome in end-stage liver disease and leads to urgent transplantation (orthotopic liver transplantation; OLT). Agitated saline bubble contrast echocardiography is a major method used for detection of intrapulmonary shunting, but is almost always performed with the patient lying supine. The aim of this study was to investigate prospectively the incidence of HPS diagnosed by contrast echocardiography and to assess the relative efficacy of injection in the standing compared with the lying position in detecting right–left intrapulmonary shunting in these patients.

Methods: Arterial blood gas in the lying and standing position, lung-function tests and contrast echocardiography were performed in 50 consecutive patients with cirrhosis (men, 60%; median age 53 years) referred for OLT assessment. All patients were randomly assigned to receive 10 ml agitated saline contrast (1 ml room air; 1 ml venous blood; 8 ml saline) first either in the lying or standing position. A total of four injections, two in the lying and two in the standing position, were performed with and without the Valsalva manoeuvre. All echocardiograms were recorded and reviewed by an observer blinded to the order of injection. HPS was defined by arterial hypoxaemia or a fall in oxygen saturation greater than 20% from the lying to the standing position, decreased carbon monoxide diffusing capacity, and the passage of contrast after three cardiac cycles.

Results: Arterial blood gas and decreased carbon monoxide diffusing capacity were diagnostic of HPS in 16% and 22% of patients, respectively. Contrast injection showed late right–left shunting in 13 patients (26%). Only 14% of patients met all three HPS criteria, whereas 12% were considered to have HPS based on late positive contrast echocardiography alone. Intrapulmonary shunts were more common in patients with hypoxaemia (87.5% versus 14.3%, p < 0.001), low decreased carbon monoxide diffusing capacity (69.2% versus 10.8%, p < 0.001) and dyspnoea (77.8% versus 14.6%, p < 0.001) than in those without. Intrapulmonary shunting was detected more frequently in patients receiving contrast first in the standing position than in the lying position (84.6% versus 15.4%, p = 0.003). Among those patients with positive contrast echocardiography in both positions, there was a consistent increase in the size of shunt when standing compared with lying.

Conclusions: Injection of agitated saline contrast in the standing position increases the sensitivity of shunt detection consistent with HPS in patients undergoing OLT compared with the lying position. Standing contrast injections may be preferable in all situations in which platypnoea–orthodeoxia and intrapulmonary shunting is suspected.
Tissue Doppler analysis of right ventricular function. Tissue Doppler analysis of right ventricular function was at the lateral aspect of the tricuspid valve. From left to right above, the deflections represent: (1) Isovolumetric contraction; (2) S’ (systole), E’ (early diastole) and A’ (late diastole). Tissue Doppler imaging velocities were measured at the lateral aspect of the tricuspid valve (right ventricle; RV), septal and lateral aspects of the mitral annular ring (left ventricle; LV).

Abstract 136 Table 1 Bioimpedance analysis changes in response to acute water load

<table>
<thead>
<tr>
<th>Parameter</th>
<th>n</th>
<th>Control Baseline</th>
<th>Maximal change</th>
<th>Oral water Baseline</th>
<th>Maximal change</th>
<th>Intravenous saline Baseline</th>
<th>Maximal change</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Z 5 KHz (Ω)</td>
<td>24</td>
<td>613 (90)</td>
<td>620 (91)</td>
<td>614 (86)</td>
<td>605 (85)</td>
<td>613 (80)</td>
<td>566 (67)</td>
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<tr>
<td>Z 50 KHz (Ω)</td>
<td>24</td>
<td>528 (62)</td>
<td>531 (63)</td>
<td>528 (78)</td>
<td>520 (78)</td>
<td>528 (74)</td>
<td>495 (65)</td>
<td>&lt;0.001</td>
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<tr>
<td>Z 100 KHz (Ω)</td>
<td>24</td>
<td>496 (79)</td>
<td>497 (78)</td>
<td>496 (74)</td>
<td>487 (74)</td>
<td>495 (71)</td>
<td>465 (62)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Z 200 KHz (Ω)</td>
<td>24</td>
<td>468 (75)</td>
<td>469 (78)</td>
<td>467 (70)</td>
<td>459 (70)</td>
<td>466 (68)</td>
<td>439 (60)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Baseline and maximal change presented as mean (SD); Z, impedance; 5–200 KHz, current frequency.

Abstract 136 Table 2 Echocardiographic changes in response to acute volume load

<table>
<thead>
<tr>
<th>Parameter</th>
<th>n</th>
<th>Control Baseline</th>
<th>Maximal change</th>
<th>Oral water Baseline</th>
<th>Maximal change</th>
<th>Intravenous saline Baseline</th>
<th>Maximal change</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MV E (m/s)</td>
<td>30</td>
<td>0.72 (0.12)</td>
<td>0.69 (0.14)*</td>
<td>0.69 (0.14)</td>
<td>0.72 (0.14)*</td>
<td>0.72 (0.13)</td>
<td>0.82 (0.15)*</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MV E (m/s)</td>
<td>29</td>
<td>0.65 (0.14)</td>
<td>0.62 (0.11)*</td>
<td>0.64 (0.12)</td>
<td>0.67 (0.12)*</td>
<td>0.66 (0.12)</td>
<td>0.75 (0.14)*</td>
<td>0.0007</td>
</tr>
<tr>
<td>MV E (m/s)</td>
<td>18</td>
<td>5.8 (1.6)</td>
<td>4.9 (1.3)*</td>
<td>5.3 (1.3)</td>
<td>5.9 (1.1)</td>
<td>5.8 (1.8)</td>
<td>6.2 (1.4)*</td>
<td>0.0001</td>
</tr>
<tr>
<td>MV E (m/s)</td>
<td>18</td>
<td>7.2 (1.8)</td>
<td>6.3 (1.4)**</td>
<td>6.9 (1.9)</td>
<td>7.5 (1.5)**</td>
<td>7.0 (1.8)</td>
<td>7.7 (1.9)**</td>
<td>0.013</td>
</tr>
<tr>
<td>IVCD(e) (cm/m²)</td>
<td>29</td>
<td>1.20 (0.21)</td>
<td>1.15 (0.19)</td>
<td>1.18 (0.19)</td>
<td>1.19 (0.17)*</td>
<td>1.16 (0.19)</td>
<td>1.24 (0.21)*</td>
<td>0.036</td>
</tr>
<tr>
<td>IVCD(m) (cm/m²)</td>
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<td>0.80 (0.10)</td>
<td>0.81 (0.15)</td>
<td>0.79 (0.19)</td>
<td>0.80 (0.16)*</td>
<td>0.82 (0.14)</td>
<td>0.88 (0.14)*</td>
<td>0.036</td>
</tr>
</tbody>
</table>

Baseline and maximal change presented as mean (SD); e, expiration; E, early peak velocity; Ea, tissue Doppler early peak velocity; IVCD, inferior vena cava diameter corrected for body surface area; l, lateral wall; mi, maximal inspiration; MV, transmitral; s, septal wall; v, valsalva manoeuvre.

Significant change with oral water compared with other interventions.

Significant change with intravenous saline compared with other interventions.

Significant change with oral water compared with other interventions.

### Abstract 137

**Relative Right Ventricle Versus Left Ventricle Function in Patients Who Have Either Had or Not Had Coronary Artery Bypass Graft Surgery: A Cross-Sectional Study**

H Yadav, M Fontana, B Unsworth, G Biller, A Kyriacou, BS Wasan, A Sharp, J Mayet, DP Francis. International Centre for Circulatory Health, St Mary’s Hospital and National Heart and Lung Institute, Imperial College, London, UK.

**Introduction:** Emerging evidence suggests right ventricular function may be compromised following coronary artery bypass graft surgery (CABG). We tested this hypothesis of selective right ventricular impairment of function by CABG in a cross-sectional cohort of subjects with heart failure, with and without a history of CABG. Pulsed-wave tissue Doppler imaging was used as a sensitive assay of ventricular function.

**Methods:** Myocardial peak systolic (S’), early diastolic (E’), and late diastolic (A’) velocities were measured at the septal and lateral aspects of the mitral annulus and at the tricuspid annulus, using tissue Doppler echocardiography in 101 patients with established heart failure, 40 of whom had undergone previous CABG and 61 of whom had not. To adjust for varying degrees of overall cardiac impairment, we calculated the ratio between the velocities of the right and left ventricle.

**Results:** There was a significant difference in the right ventricular to left ventricular (RV : LV) velocity ratios between patient groups. For S’, the RV : LV ratio was 32% lower in CABG patients compared with the non-CABG group (p<0.001). For E’, the RV : LV ratio was 39% lower in the CABG group compared with the non-CABG group (p<0.001). For A’, the RV : LV ratio was 34% lower in the CABG group compared with the non-CABG group.
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Figure 2 Selective impairment of right ventricular function ratio between right ventricular (RV) and left ventricular (LV) peak systolic (S') and early diastolic (E') and late diastolic (A') velocities recorded at the tricuspid annulus and lateral aspect of the mitral annulus. Results expressed as mean (± SE). CABG, coronary artery bypass grafting.

(p<0.001). Even when only non-CABG heart failure patients with ischaemic aetiology were considered, a similar relative impairment was seen: by 27% in S' (p<0.005), 37% in E' (p<0.005) and by 52% in A' (p<0.01) (figs 1 and 2).

Conclusions: The significantly lower RV : LV ratio in heart failure patients who have undergone a CABG procedure supports the hypothesis of a specific permanent impairment of right ventricle function after CABG surgery. These changes cannot be explained simply by some general feature of ischaemia, because the difference persisted even when non-ischaemic patients were removed.

Abstract 138

Cardiac Magnetic Resonance-Determined Infarct Size in Diabetic Versus Non-Diabetic Patients After First Acute Myocardial Infarction

1 N Abidin, 1 N Maredia, 2 G Bainbridge, 2 S Ball, 2 S Plein, 2 J P Greenwood. 1 Academic Unit of Cardiovascular Medicine, University of Leeds, Leeds, UK; 2 Leeds General Infirmary, Leeds, UK

Background: Patients with diabetes mellitus (DM) have higher mortality after myocardial infarction (MI) than those without diabetes. Infarct size and its impact on left ventricular function is known to be a major determinant of outcome after acute MI. Late gadolinium hypertrophy cardiac magnetic resonance (CMR) imaging is the most accurate in-vivo imaging modality for the determination of infarct size.

Objectives: The aim was to determine if patients with DM had a larger infarct size after their first presentation of acute MI, using late gadolinium hypervascularity CMR imaging.

Methods: Ninety-three patients with a first acute MI were studied. Of these, 23 patients had a previous history of DM or glucose intolerance. MI was defined on the basis of the clinical presentation and the presence of cardiac ischemic ECG changes. CMR was performed in all patients within 7 days of the index event. The CMR protocol included standard cine imaging as well as late gadolinium hyperenhancement imaging. Left ventricular function parameters were determined semiautomatically using standard software.

Results: There were no significant differences in age (non-DM 57.7 ± 10.8 versus DM 60.7 ± 10.9; p = 0.56), gender (male: non-DM 82.9% versus DM 91.3%; p = 0.33), clinical cardiovascular risk factors (smoker: non-DM 60% versus DM 52.2%; p = 0.68; family history of premature coronary artery disease: non-DM 41.4% versus DM 43.5%; p = 0.68; body mass index: non-DM 26.2 ± 3.7 versus DM 26.6 ± 3.2; p = 0.61) or location of myocardial infarction (anterior: non-DM 44.3% versus DM 47.8%; p = 0.42) between the two groups. There was a higher peak creatinine kinase rise after acute MI in the DM group compared with the non-DM group (2649 ± 1833 versus 1660 ± 1200; p = 0.02). In comparison with the non-DM group, the DM group had significantly larger infarct size and lower ejection fraction (see table and fig).

Conclusion: Compared with non-DM, patients with DM have a larger infarct size and lower ejection fraction as determined by CMR. A significant adverse prognosis is associated with DM.


Characterisation and Initial Validation of Area-At-Risk Derived by T2-Magnetic Resonance Imaging in Acute Myocardial Infarction

C Berry, P Kellman, AH Aletras, C Mancini, M Chen, L Hsu, RJ Lederman, AE Arai. National Institutes of Health, Bethesda, Maryland, USA

Introduction: Myocardial area-at-risk (AAR) is a determinant of the size of acute myocardial infarction (MI) and prognosis in patients with chronic coronary disease. Whereas non-invasive evaluation of AAR by magnetic resonance imaging (MRI) is

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An example of infarct planimetry for quantification.
potentially useful, its application has been problematical. Late enhancement by gadolinium may not be representative of AAR in reperfused MI, and T2-derived oedema imaging can be confounded by surface coil intensity problems and signal drop-off. Using novel T2 methods developed to overcome these limitations, we investigated whether measurement of AAR in human MI would correlate with two validated angiographic AAR risk scores.

Methods: Eleven acute MI patients who underwent emergent percutaneous coronary intervention (PCI) and who consented to inpatient MRI were included in the study. The APPROACH angiographic jeopardy score has been validated against infarct size by late gadolinium enhancement (LGE). MVO was defined as a dark zone within the LGE infarct. Dark zones within T2 segments that co-located with MVO were considered haemorrhagic. Results are expressed as mean ± SD.

Results: Ten men and one woman (58 ± 11 years); 36% type 2 diabetes; 9% previous MI; 9% previous PCI underwent MRI within one week of emergent PCI (April–September 2007) at a community hospital. According to LGE, four (36%) patients had an anterior MI and seven (64%) patients had a non-anterior MI. Ten (91%) patients had transmural LGE and MVO was evident in 8 (73%) of these cases (fig). T2 dark zones consistent with haemorrhage were evident in all patients with MVO, except one patient with non-transmural MI. Haemorrhage appeared transmural in four (50%) affected patients. The mean AAR by T2-prepared MRI was 36.2 ± 10.7% of total left ventricular area. The mean APPROACH and DUKE jeopardy scores were 44.5 ± 12.2% and 27 ± 15.3%, respectively. MRI-derived AAR correlated with the APPROACH (R = 0.58) and DUKE (R = 0.61) jeopardy scores.

Conclusion: Qualitative evaluation of AAR by true FISP MRI and late enhancement imaging revealed that haemorrhage is common in MVO. Quantitative estimates of AAR by true FISP MRI correlate well with reference angiographic AAR scores, despite heterogeneity in patient presentation and management. Whether or not the angiographic jeopardy scores may underestimate AAR merits further investigation.

Introduction: Microvascular obstruction (MVO), as revealed by cardiac magnetic resonance imaging (MRI), is an adverse prognostic sign following acute myocardial infarction (AMI). The pathophysiology of MVO initially involves intracellular and interstitial oedema leading to microvascular obstruction and haemorrhage. We hypothesised that ischaemic preconditioning might attenuate the infarct cascade and inhibit the occurrence of MVO.

Methods: In order to mimic human index AMI, we used a porcine model of reperfused AMI induced by sustained intracoronary balloon inflation (90 minutes, n = 16). Animals were assigned to a preconditioning protocol (6 × 2 minute serial balloon inflations separated by 5 minute intervals of reperfusion versus no preconditioning; immediate and sustained balloon inflation). Collateral supply (CFIp = (distal coronary pressure during balloon occlusion – Pv)/(mean arterial pressure – Pv); Pv, central venous pressure) was quantified using a pressure-sensitive coronary guidewire. In-vivo imaging was performed at 48 hours and 8 weeks post-myocardial infarction (MI) at 1.5 Tesla. Using state-of-the-art techniques, myocardial water and mobility were imaged by T2-prepared steady-state free-precession (T2P-SSFP) coupled with automated proton density surface coil intensity correction. T2-infarct imaging was performed at 48 hours and 8 weeks post-myocardial infarction (MI) with MVO in all animals, except one, which had a non-transmural MI (fig). T2 dark zones consistent with haemorrhage occurred in all LGE MVO areas. At the 8-week follow-up MRI (n = 4 to 30 November 2007), there was evidence of wall thinning greater than 50% and akinesis in the infarct territory of animals that had transmural MI/MVO/haemorrhage at 48 hours (n = 3). Alternatively, in the animal that had non-transmural MI/no MVO/haemorrhage at 48 hours, wall thickness and contractility were normal and there was no LGE at the 8-week follow-up MRI.

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MVO, microvascular obstruction.

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PRECONDITIONING DOES NOT INFLUENCE THE OCCURRENCE OF MICROVASCULAR OBSTRUCTION OR HEMORRHAGE REVEALED BY MAGNETIC RESONANCE IMAGING IN A PRE-CLINICAL MODEL OF ACUTE REPERFUSED MYOCARDIAL INFARCTION

C Berry, P Kellman, AE Aletras, W Schenke, L Hsu, V Wright, A Faranesh, RJ Lederman, AE Arai. National Institutes of Health, Bethesda, Maryland, USA
Abstract 141

<table>
<thead>
<tr>
<th></th>
<th>ΔPCr/ATP = 0.3</th>
<th>ΔPCr/ATP = 0.4</th>
<th>ΔPCr/ATP = 0.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Independent groups</td>
<td>σ = 0.38</td>
<td>σ = 0.40</td>
<td>σ = 0.50</td>
</tr>
<tr>
<td>Power 95%</td>
<td>N = 43</td>
<td>N = 25</td>
<td>N = 16</td>
</tr>
<tr>
<td>Power 90%</td>
<td>N = 35</td>
<td>N = 20</td>
<td>N = 13</td>
</tr>
<tr>
<td>Power 80%</td>
<td>N = 26</td>
<td>N = 15</td>
<td>N = 10</td>
</tr>
<tr>
<td>Paired groups</td>
<td>σ = 0.35</td>
<td>σ = 0.38</td>
<td>σ = 0.35</td>
</tr>
<tr>
<td>Power 95%</td>
<td>N = 20</td>
<td>N = 12</td>
<td>N = 9</td>
</tr>
<tr>
<td>Power 90%</td>
<td>N = 16</td>
<td>N = 10</td>
<td>N = 7</td>
</tr>
<tr>
<td>Power 80%</td>
<td>N = 13</td>
<td>N = 8</td>
<td>N = 6</td>
</tr>
</tbody>
</table>

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REPRODUCIBILITY OF 31-PHOSPHORUS CARDIAC MAGNETIC RESONANCE SPECTROSCOPY AT 3 TESLA

1-2Y Emmanuel, 1DJ Tyler, 1LE Cochlin, 1CJ Holloway, 1LE Hudsmith, 2K Clarke, 1S Neubauer, 1MD Robson. 1OCMR, University of Oxford, Oxford, UK; 2CMRG, University of Oxford, Oxford, UK.

Aim: Phosphorus (31P) magnetic resonance spectroscopy provides the only technique for in-vivo assessment of tissue energy metabolism. As well as giving unique insights into metabolic processes that may underlie pathologies such as heart failure and hypertrophic cardiomyopathy, it also offers a tool for the evaluation of therapeutic interventions. The most widely used measure is the ratio of phosphocreatine (PCr) to adenosine triphosphate (ATP). The phosphorus signal is inherently weak and cardiac studies to date have suffered from poor spatial resolution, limiting sensitivity in the detection of myocardial alterations. Previous studies used a variety of spatial localisation and analysis methods, leading to marked variation in reported normal values for the PCr/ATP ratio with few studies on reproducibility. Our objective was to develop an acquisition method utilising the increased field strength of 3 Tesla to improve myocardial specificity within a feasible scan time. Furthermore, we wished to develop an analysis method dependent purely on anatomical location of spectra and, as such, free from the well-known bias caused by the use of criteria based on spectral quality in the selection of data for analysis.

Methods: 20 healthy male subjects were scanned on two separate occasions using an optimised chemical shift imaging protocol at 3 T. Strict anatomical criteria were used to select three voxels covering the septal myocardium at the level of the papillary muscle on the short axis view (see fig). Data were analyzed for intra- and inter-subject, and intra and inter-observer variability. No data were excluded.

Results: The average PCr/ATP value across subjects for scan 1 was 2.07 ± 0.38 and scan 2 was 2.14 ± 0.46 (p = 0.59, NS). Intra-subject variability was 0.43 ± 0.35 (percentage difference 20%) and inter-subject coefficient of variation was 18%. The intra-observer variability, assessed as the absolute difference between analyses by a single observer, was 0.14 ± 0.24, showing no significant difference between analyses. The inter-observer variability showed no significant differences between four different observers, demonstrated by an intra-class correlation coefficient of 0.765. Robust data on the reproducibility of the technique are essential to determine the power and sample sizes required in planning future studies. Using data from this study, calculations are given for paired and unpaired studies (see table).

Conclusion: 31P magnetic resonance spectroscopy offers an invaluable method for the investigation of myocardial metabolism but has previously suffered from inherent signal quality limitations. Using the increased signal available at 3 T we present a technique that provides data with improved myocardial specificity. Furthermore, we have developed robust analysis methods that are free from potential bias and suitable for widespread application both across research groups and across disease models. Within the constraints of the technique, we provide a framework for future studies with feasible cohort sizes.

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VALUE OF COMBINING TISSUE SYNCHRONISATION MAPPING WITH SCAR IMAGING IN PREDICTING MORTALITY AND MORBIDITY AFTER CARDIAC RESYNCHRONISATION THERAPY

1PWX Foley, 1F Leyva, 1S Challi, 1B Stegemann, 1K Khadjooi, 1MP Frenneaux, 1REA Smith. 1Good Hope Hospital, University of Birmingham, Heart of England NHS Foundation Trust, Sutton Coldfield, UK; 2Bakken Research Centre, Medtronic Inc, Maastricht, The Netherlands; 3University of Birmingham, Birmingham, UK.

Introduction: Cardiac dyssynchrony and the presence of a posterolateral left ventricular scar, identified using cardiovascular magnetic resonance (CMR), have independently been shown to predict outcome after cardiac resynchronisation therapy (CRT).

Methods: 141 patients with heart failure (aged 66.8 ± 10.1 years, mean ± SD, NYHA class III or IV, left ventricular ejection fraction <35%) treated with CRT underwent pre-implant assessments of myocardial scarring (late gadolinium enhancement CMR) and dyssynchrony. The latter was quantified in terms of the CMR–tissue synchronisation index (CMR–TSI; SD of time-to-peak inward radial motion for up to 60 myocardial segments). These variables were assessed in relation to clinical outcome.

Results: After 5.3 years, patients with a CMR–TSI of 110 ms or greater and a posterolateral myocardial scar had a higher risk of cardiovascular death or hospitalisation for heart failure (hazard ratio (HR) 11.8; 95% CI 3.99 to 35.0, p < 0.001) as well as death from any cause or hospitalisation from major cardiovascular events (HR 12.6; 95% CI 4.69 to 35.7, both p < 0.001) than patients with a
Abstract 142 Clinical endpoints for patients undergoing cardiac resynchronisation therapy, grouped according to degree of dyssynchrony and presence or absence of posterolateral scar

<table>
<thead>
<tr>
<th>No of patients</th>
<th>CMR-TSI &lt;110 ms, no PL scar</th>
<th>CMR-TSI &gt;110 ms, no PL scar</th>
<th>CMR-TSI &lt;110 ms, PL scar</th>
<th>CMR-TSI &gt;110 ms, PL scar</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total mortality or hospitalisation for MCE</td>
<td>43 (30%)</td>
<td>5 (8%)</td>
<td>7 (25%)</td>
<td>11 (46%) ***</td>
</tr>
<tr>
<td>Cardiovascular mortality or hospitalisation for MCE</td>
<td>36 (20%)</td>
<td>4 (6%)</td>
<td>4 (14%)</td>
<td>10 (42%) ***</td>
</tr>
<tr>
<td>Cardiovascular mortality</td>
<td>20 (21%)</td>
<td>3 (5%)</td>
<td>5 (18%)</td>
<td>7 (29%) **</td>
</tr>
<tr>
<td>Total mortality</td>
<td>33</td>
<td>4 (6%)</td>
<td>6 (21%)*</td>
<td>8 (33%)**</td>
</tr>
</tbody>
</table>

CMR–TSI, cardiac magnetic resonance–tissue synchronisation index; MCE, major cardiovascular events; PL, posterolateral.

p Values refer to differences between the groups and the group with a CMR–TSI less than 110 msec and no posterolateral scar, denoted as: *p<0.05, **p<0.01, ***p<0.001.

Conclusions: The combination of CMR–TSI and scar location provides a powerful, independent predictor of mortality and morbidity after CRT.

143 CORONARY ARTERY CALCIFICATION AS A PREDICTOR OF INCREASED CORONARY HEART DISEASE RISK IN UK INDIAN ASIANS

1P Jain, 1JC Chambers, 1P Elliott, 2ED Williams, 2B Kraly, 3S Muscat, 3A Lahiri, 1JS Kmoer. 1Imperial College, London, UK; 2University College London, London, UK; 3Cardiac Imaging and Research Centre, Wellington Hospital, London, UK

Background: Coronary heart disease (CHD) mortality is 70% higher among UK Indian Asian than white Europeans. Currently available risk stratification tools and biomarkers do not allow the accurate identification of Indian Asians at increased risk of CHD. Coronary artery calcification (CAC) is highly correlated with coronary plaque burden and is an independent predictor of future CHD events in north American and European white populations. We hypothesised that CAC is increased in Indian Asians compared with white Europeans and may provide a non-invasive tool for the assessment of CHD risk in Indian Asians.

Methods: We investigated 2398 Indian Asian and white European men and women, aged 35–75 years (Indian Asians: 837 men, 530 women; white European: 722 men, 309 women). Participants were recruited from the practice lists of 58 general practitioners in west London, as part of the London Life Sciences Population (LOLIPOP) study and were all free from clinical cardiovascular disease. CAC was measured for all participants using an electron beam computed tomography scanner (Imatron C-150 (modified), General Electric).

Participants were also characterised for cardiovascular risk factors. Participants were also characterised for cardiovascular risk factors.

Results: In comparison with Europeans, Indian Asians had an approximately twofold higher prevalence of hypertension and type 2 diabetes, higher waist–hip ratio and triglycerides, and lower high-density lipoprotein cholesterol (table). Cigarette smoking and cholesterol levels were lower in Indian Asians compared with white Europeans. CAC was more common in men than women, and CAC scores were closely associated with cardiovascular risk factors including age, cigarette smoking, hypertension, diabetes, total cholesterol and metabolic syndrome (all p<0.05). In contrast, there was no difference in CAC prevalence or mean levels of CAC between Indian Asians and Europeans either before or after adjustment for the measured cardiovascular risk factors (fig).

Summary: CAC is not increased in Indian Asians compared with white Europeans, in any age group or in either gender. Similar CAC in Indian Asians and Europeans contrasts with an almost twofold higher risk of myocardial infarction and CHD mortality in Asians. CAC does not predict or identify the excess CHD risk in Indian Asians.

Abstract 143 Characteristics of participants

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Indian Asians</th>
<th>White Europeans</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cigarette smoking (%)</td>
<td>18</td>
<td>1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Waist–hip ratio</td>
<td>0.95 ± 0.07</td>
<td>0.92 ± 0.08</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>38</td>
<td>20</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Type 2 diabetes (%)</td>
<td>18</td>
<td>7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fasting glucose (mmol/l)</td>
<td>5.8 ± 1.8</td>
<td>5.4 ± 1.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total cholesterol (mmol/l)</td>
<td>5.3 ± 1</td>
<td>5.6 ± 1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HDL cholesterol (mmol/l)</td>
<td>1.3 ± 0.3</td>
<td>1.4 ± 0.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Triglycerides (mmol/l)</td>
<td>1.7 ± 1.2</td>
<td>1.54 ± 1.1</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

HDL, high-density lipoprotein.
COMPARISON OF TWO-DIMENSIONAL AND MULTI-SLAB THREE-DIMENSIONAL MAGNETIC RESONANCE TECHNIQUES FOR MEASURING CAROTID WALL VOLUMES

NG Keenan, A Grasso, D Locca, M Roughton, PD Gatehouse, DN Firmin, DJ Pennell.
CMR Unit, Royal Brompton Hospital, London, UK

Purpose: The purpose of this study was to compare a multi-slab three-dimensional (3D) volume selective fast spin echo (FSE) magnetic resonance sequence with a routine two-dimensional (2D) FSE sequence for the quantification of carotid wall volume.

Introduction: Cardiovascular magnetic resonance (CMR) can image the arterial wall at high resolution. It has been used to characterise atherosclerotic plaque and to measure plaque response to statin therapy. However, scan times of over one hour limit its applicability to large studies and acceptability to patients. The conventional sequence is a 2D FSE sequence. Each slice may take 1–2 minutes to acquire and numerous slices are required. A 3D multi-slab volume selective FSE sequence developed at our institution is faster. It has been validated in several technical studies, but not in a larger study of clinical performance.

Methods: 100 normal subjects (50 men, mean age 44.6 years) had carotid arterial wall CMR using 2D and 3D techniques. A 1.5 T scanner (Siemens Sonata) and a purpose-built carotid surface coils (Machnet BV, The Netherlands) were used. The resolution of both sequences was identical (pixel size 0.43 x 0.43 mm, interpolated to 0.21 x 0.21 mm during reconstruction). Planimetry of the carotid artery was performed to measure total vessel volume, lumen volume and wall volume over 20 contiguous slices. The 2D results were compared with 3D using scatterplots with line of identity, Bland–Altman plots and lines of best fit (fig). Institutional review board permission was obtained, and all subjects provided written informed consent.

Results: The scan time needed to acquire 20 slices by the 2D technique was 1560 RR intervals. By comparison, the scan time to acquire 24 slices in three slabs by the 3D technique was 609 RR intervals. This is a 55% reduction in scan time. If 24 slices were to be acquired by both techniques, there would have been a 63% reduction in scan time with the 3D technique. 100% of datasets by both techniques, there would have been a 63% reduction in scan time with the 3D technique. 100% of datasets by both techniques.

Conclusions: Multi-slab volume selective 3D FSE carotid arterial wall imaging performs similarly to a conventional 2D technique, but with substantially reduced scan time. The values for total vessel volume are very similar. The 3D technique yields values for lumen volume that are 4.9% less and wall volume that are 4.7% greater than those from the 2D technique. These discrepancies may result from greater blood flow artifact in 3D images being contoured as vessel wall. The difference is not due to resolution as this is identical for 2D and 3D. Overall, the reduction in scan time with the 3D technique significantly improves the clinical performance of CMR carotid imaging.

INTEGRATED CARDIAC AND VASCULAR ASSESSMENT IN TAKAYASU’S ARTERITIS AND SYSTEMIC LUPUS ERYTHEMATOSUS BY CARDIOVASCULAR MAGNETIC RESONANCE

NG Keenan, JC Mason, A Maceira, M Roughton, R Assomull, R O’Hanlon, J Andrews, PD Gatehouse, DN Firmin, DO Haskard, DJ Pennell. CMR Unit, Royal Brompton Hospital, London, UK; Hammersmith Hospital, London, UK; Royal Brompton Hospital, London, UK; Imperial College, London, UK

Background: Takayasu’s arteritis (TA) is a disease of vascular inflammation and systemic lupus erythematous (SLE) is a multi-system inflammatory disorder in which vasculitis is common and accelerated atherosclerosis is typical. Cardiovascular magnetic resonance (CMR) can be used to perform an integrated assessment of vascular and cardiac disease. The purpose of this study was to investigate the utility of CMR in TA and SLE.

Methods: 16 patients with TA, 11 patients with SLE and two populations comprising 110 normal volunteers were prospectively recruited. All subjects with TA and SLE underwent a three-stage CMR protocol: (1) carotid artery study; (2) endothelial function; (3) cardiac study. Indices of carotid arterial morphology including the wall/outer wall (W/OW) ratio (a measure of vascular thickening) were derived. Endothelial function was measured by brachial artery reactivity after 5 minutes of distal ischaemia. The cardiac study included assessment of left ventricular volumes, mass, systolic function and imaging in the late phase after gadolinium-DTPA for myocardial fibrosis and infarction.

Results: The vessel wall volume and W/OW ratio were highest in TA and higher in SLE compared with normal controls. The differences between all groups were statistically significant. Z scores (a measure of variation) were derived (table and fig). Endothelial function was severely impaired in TA and SLE. Mean flow-mediated dilatation was 6.5% for patients with TA (CI 2.4% to 10.2%) and 4.0% for SLE patients (CI 3.4% to 11.4%), significantly below published normal values using an identical technique (15.5%, CI 11.6 to 19.4)1 (SLE p = 0.011, TA p = 0.004). Body surface area-indexed left ventricular volumes were lower at endystole in both TA and SLE (TA 19 ± 4 ml/m², p<0.001; SLE 20 ± 4 ml/m²; normals 25 ml/m², p<0.05) and this was reflected in more dynamic left ventricular function in TA (ejection fraction 74 ± 5% versus normals 67 ± 1%, p<0.001) and a trend towards higher ejection fraction in SLE (71 ± 5%, p = 0.09). Late gadolinium enhancement (LGE) was seen in five of 15 TA patients (33%) and in six of 10 SLE patients (60%). The pattern of LGE included midwall fibrosis, subendocardial infarction and insertion point fibrosis in both patient groups.

Abstract 145

<table>
<thead>
<tr>
<th>Wall volume left/mm³</th>
<th>TA</th>
<th>SLE</th>
<th>Normals</th>
<th>p Value (TA vs SLE vs normals)</th>
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<td>Wall volume right/mm³</td>
<td>1059</td>
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<td>655</td>
<td>&lt;0.05</td>
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<tr>
<td>W/OW right (%)</td>
<td>45</td>
<td>36</td>
<td>32</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>W/OW left (%)</td>
<td>51</td>
<td>35</td>
<td>31</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

SLE, systemic lupus erythematous; TA, Takayasu’s arteritis; W/OW, wall/outer wall ratio. Box plot of Z scores for vessel wall volume for TA, SLE and normal subjects, left and right carotid arteries. Z score, standard deviation.
Conclusion: CMR identifies significant vessel wall thickening and endothelial dysfunction in TA and SLE compared with normal controls. The W/OW ratio is helpful as a measure of vessel wall thickening. Reduced end-systolic volumes indicate more dynamic systolic function, which may occur as a response to reduced vascular compliance. There is a high prevalence of LGE of all patterns in these patients that warrants further study. Overall, an integrated method of cardiovascular assessment by CMR has a high diagnostic yield in TA and SLE.


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Background and Aims: Right ventricular function predicts outcome in patients with advanced heart failure but little is known about the prognostic significance of right ventricular morphology and function in patients with mild to moderate heart failure.

Methods: 123 normal subjects and 383 patients with left ventricular ejection fraction less than 45% underwent cardiac magnetic resonance imaging. The left ventricular and right ventricular borders were drawn manually. Left ventricular and right ventricular mass and volumes measured at end-diastole and end-systole were indexed to body surface area and were used to calculate the left ventricular and right ventricular ejection fraction (EF). Right ventricular dilatation was defined as mean right ventricular end-systolic volume + 2SD in normal subjects.

Statistics: Continuous variables are presented as median and interquartile ranges. Categorical variables were presented as absolute values and proportions. Comparison of continuous variables was performed using the Kruskal–Wallis test and χ² test for categorical variables. A p value greater than 0.05 was considered statistically significant.

Results: The median patient age was 71 years (64–77), 86% were men, 22% had NYHA III/IV breathlessness, 77% ischaemic heart disease and 52% renal dysfunction. The median left ventricular EF was 33% (27%–40%) and the right ventricular EF was 44% (35%–53%). 289 patients had an undilated right ventricle and 94 had right ventricular dilatation. Patients with right ventricular dilatation were more likely to be NYHA III/IV (50% versus 19%, p = 0.006), have lower systolic blood pressure (120 versus 129, p = 0.004), higher brain natriuretic peptide (343 versus 135, p = 0.001) and were less likely to have ischaemic heart disease (65% versus 83%, p<0.001) or tolerate β-blockers (79% versus 91%, p = 0.002). These patients had lower left ventricular EF (31% versus 35%, p = 0.018) and larger left ventricular end-diastolic volumes (137 ml/m² versus 115 ml/m², p<0.001). 108 (28%) patients died over 44 ± 22 months (35 (37%) from the dilated right ventricle group and 69 (24%) from the non-dilated right ventricle group, log-rank 8.228, p = 0.004). In multiple Cox regression analysis only right ventricular dilatation and age were independent predictors of mortality (hazard ratio (HR) 1.948, 95% CI 1.232 to 3.078, p = 0.004 and HR 1.032, 95% CI 1.005 to 1.060, p = 0.020, respectively).

Conclusions: Right ventricular volumes are important predictors of mortality in patients with moderate heart failure when assessed by an accurate method such as cardiac magnetic resonance imaging.

MEASUREMENT OF LEFT VENTRICULAR DIMENSIONS WITH CONTRAST-ENHANCED THREE-DIMENSIONAL CINE MAGNETIC RESONANCE IMAGING FACILITATED BY K–T SENSE

N Maredia, S Kozerke, N Abidin, A Langhat, J P Greenwood, P Boesiger, S Plein. University of Leeds, Leeds, UK; Institute for Biomedical Engineering, University and ETH Zurich, Zurich, Switzerland

Introduction: Cardiovascular magnetic resonance (CMR) is the most accurate and reproducible method for determining left ventricular volumes and mass. Conventionally, volumetric measurements are derived from contiguous two-dimensional (2D) slices.
The recently proposed k-t SENSE method allows substantial acceleration of data acquisition by applying sparse sampling along the spatial frequency (k) and temporal (t) encoding axes. This work compares volumetric measurements derived from three-dimensional (3D) k-t SENSE-accelerated cine imaging against standard 2D acquisition, before and after contrast administration.

**Method:** 14 volunteers and 12 patients underwent CMR imaging (Philips 1.5 T). A 2D dataset was acquired, covering the left ventricle in 10–12 short axis slices from apex to base (balanced steady-state free-precession (SSFP), TR 2.8 ms, TE 1.4 ms, flip angle 55°, spatial resolution 2.0 x 2.0 x 10 mm, one slice per breath-hold). A k-t SENSE accelerated 3D dataset was then acquired, with scan orientation and spatial coverage identical to the 2D reference study (3D balanced SSFP, TR 3.2 ms, TE 1.6 ms, flip angle 50°, spatial resolution 2 x 2 x 10 mm, single 14-second breath-hold, k-t acceleration factor 5). Acquisition was repeated after intravenous injection of 0.1 mmol/kg gadobutrolum. Left ventricular end-diastolic and end-systolic volumes (EDV, ESV), ejection fraction (EF) and mass were calculated for each dataset. Lin’s concordance coefficient was used to assess agreement between measurements.

**Results:** Left ventricular EDV, ESV, mass and EF measurements were mostly underestimated by the 3D method but levels of bias were small. The 3D k-t SENSE technique demonstrated moderate agreement with 2D imaging for the estimation of EDV and EF (both concordance coefficients 0.92), and substantial agreement for ESV and left ventricular mass (concordance coefficients 0.95 and 0.97, respectively) before contrast administration. After contrast administration, agreement improved for all parameters (see table and figs 1 to 3).

**Conclusion:** k-t SENSE-accelerated 3D CMR cine imaging can be reliably used to assess left ventricular volumes and mass. Using 5 x k-t SENSE acceleration, a full left ventricular study, with temporal and spatial resolution equivalent to the 2D reference, could be acquired with a single 14-second breathhold followed by a 4-second breathhold for training data. By comparison, a conventional 2D approach can take several minutes. Contrast administration improves the agreement between 2D and 3D acquisitions. The differences observed between left ventricular parameters derived from 2D and 3D k-t accelerated images in this study are small enough to be irrelevant in most clinical scenarios.

<table>
<thead>
<tr>
<th></th>
<th>2D mean ± SD</th>
<th>3D pre-Gd mean ± SD</th>
<th>3D post-Gd mean ± SD</th>
<th>Bias (95% CI)</th>
<th>Lin’s coefficient (95% CI)</th>
<th>Bias versus 2D (95% CI)</th>
<th>Lin’s coefficient versus 2D (95% CI)</th>
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</thead>
<tbody>
<tr>
<td>LVEDV (ml)</td>
<td>149.0 ± 40.2</td>
<td>142.9 ± 35.4</td>
<td>144.3 ± 37.4</td>
<td>6.1 (−20.9 to 33.2)</td>
<td>0.92 (0.87 to 0.98)</td>
<td>4.7 (−12.7 to 22.1)</td>
<td>0.97 (0.94 to 0.99)</td>
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<tr>
<td>LVESV (ml)</td>
<td>70.6 ± 33.7</td>
<td>70.0 ± 28.8</td>
<td>71.4 ± 32.3</td>
<td>0.6 (−19.0 to 20.3)</td>
<td>0.95 (0.92 to 0.98)</td>
<td>−0.8 (−10.8 to 9.2)</td>
<td>0.99 (0.98 to 1.00)</td>
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<tr>
<td>LVM (g)</td>
<td>111.7 ± 33.1</td>
<td>108.2 ± 31.1</td>
<td>110 ± 32.2</td>
<td>3.5 (−11.3 to 18.4)</td>
<td>0.97 (0.94 to 0.99)</td>
<td>−1.7 (−11.0 to 14.4)</td>
<td>0.98 (0.96 to 1.00)</td>
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<tr>
<td>LVEF (%)</td>
<td>54.0 ± 8.3</td>
<td>52.0 ± 8.1</td>
<td>52.0 ± 8.4</td>
<td>2.0 (−3.5 to 7.4)</td>
<td>0.92 (0.86 to 0.98)</td>
<td>2.0 (−3.1 to 7.1)</td>
<td>0.93 (0.87 to 0.96)</td>
</tr>
</tbody>
</table>

Gd, gadobutrolum; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; LVESV, left ventricular end-systolic volume; LVM, left ventricular mass.
Background: The extent of damage after acute myocardial infarction is closely related to the prognosis so it is of clinical importance to make an accurate in-vivo estimate of infarct size. Routinely available data include cardiac biomarkers and the 12-lead ECG. This study investigates the relationship between troponin I (TnI), the ECG-derived Selvester score (SS) and contrast-enhanced magnetic resonance imaging (ceMRI) measures of infarct size.

Methods: 80 consecutive patients with first acute coronary syndrome underwent ceMRI at a mean (SD) of 64 hours (23) from chest pain on a Siemens Sonata 1.5T system using a phased array chest coil. ceMRI was performed 15 minutes after peripheral injection of 0.2 mmol/kg gadolinium-DTPA using a breath-hold segmented gradient-echo inversion-recovery sequence. The scans were reviewed by two experienced observers and the area of delayed enhancement (DE) was planimetered manually. 25 patients were excluded based on ceMRI findings: 11 had DE in more than one coronary territory; three had subendocardial sparing pattern of DE and nine were Tnl positive with no evidence of DE. 57 patients (43 men) of mean (SD) age 59.8 years (12.5) were included in the final analysis. Serum TnI was measured 8–12 hours after the onset of chest pain. The complete 50-criteria, 31-point Selvester QRS scoring system was performed at the time of initial ceMRI by the Duke ECG core laboratory.

Results: Infarct size by ceMRI is moderately correlated with TnI (r = 0.69, p<0.001) and SS (r = 0.59, p<0.001). When admission TnI or SS are compared with the final infarct size (mean 38 days) then there is a trend towards improved correlation (TnI r = 0.75, p = 0.001), (SS r = 0.69, p = 0.001). When admission TnI is combined with SS in an ANOVA model the correlation is significantly improved (r = 0.80, p<0.001). When TnI is not collateral supply. Potentially, this relatively simple wire-based technique could be used at the time of PCI as a marker of MVO and myocardial damage.

Conclusions: Both TnI and SS correlate with acute infarct size by ceMRI and this correlation is enhanced when they are used in combination. Improved correlation of standard biomarkers with final infarct size suggests that the optimal time for acquiring ceMRI images may be once the acute injury process has settled down, ie, at least 2 weeks after acute myocardial infarction.

THE INDEX OF MICROVASCULAR OBSTRUCTION BUT NOT CORONARY COLLATERAL SUPPLY IS ASSOCIATED WITH MICROVASCULAR OBSTRUCTION REVEALED BY CONTRAST ENHANCED MAGNETIC RESONANCE IMAGING

Background: The status of the coronary microvasculature is known to influence outcome independently in patients with acute myocardial infarction. The pathophysiological significance of microvascular obstruction (MVO) as revealed by magnetic resonance imaging is unknown. The index of microcirculatory resistance (IMR) is a straightforward, novel pressure wire-derived measure of microvascular function. We investigated the relationships between IMR with MVO and left ventricular volume assessment by gadolinium contrast-enhanced magnetic resonance imaging (ceMRI).

Methods: Forty-three consecutive ST elevation acute myocardial infarction patients who gave informed consent were included. During percutaneous coronary intervention (PCI), a coronary pressure/temperature tipped guidewire was advanced into the culprit artery and baseline means transit times (Tmn) were obtained after the bolus intracoronary injection of 3 ml saline. Tmn and distal coronary pressure (Pd) were obtained under conditions of peak hyperaemia achieved by intravenous adenosine infusion (140 μg/kg per minute). IMR was calculated using these data (IMR = Pd × Tmn). Patients underwent gadolinium contrast-enhanced coronary magnetic resonance 24–48 hours later. Left ventricular dimensions were assessed using retrograded (true FISP) cineangiographic breath-hold sequences and MVO was defined as a dark core of hypoenhancement within the area of hyperenhanced infarcted tissue using breath-hold turboFLASH sequences after an intravenous bolus of gadolinium (0.1 mmol/kg).

Results: Physiological measurements were successfully achieved in all consenting patients and all had contrast-enhanced coronary magnetic resonance scans at 24–48 hours post-PCI without complication. The median IMR (interquartile range) was 34.3 (22.7–48.7) and the range was 9.9–114. Nineteen (44%) of 43 patients had MVO. IMR (median interquartile range) was higher in patients with MVO (38.8 (30.2–56.2)) compared with in patients without MVO (27.4 (19.5–37.5), p = 0.008). Coronary collateral supply was 0.26 (0.18–0.35) in patients with MVO and 0.26 (0.2–0.35) in patients without MVO. IMR also correlated significantly with left ventricular ejection fraction (r = –0.53, p<0.001) and with left ventricular end-diastolic volume (r = 0.466, p = 0.002) but not with coronary collateral supply (p = 0.5). In addition, IMR correlated significantly with peak troponin I (r = 0.56, p<0.001).

Conclusions: IMR is considerably higher in those patients with MVO as assessed by ceMRI. IMR correlates with left ventricular dimensions, ejection fraction, peak troponin I concentration, but not collateral supply. Potentially, this relatively simple wire-based technique could be used at the time of PCI as a marker of MVO and myocardial damage.
### Abstract 150 Table 2

<table>
<thead>
<tr>
<th>ICA</th>
<th>CAC score (ASE)</th>
<th>Stenosis</th>
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<td>N (%)</td>
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<td>N (%)</td>
</tr>
<tr>
<td></td>
<td>10 (42%)</td>
<td>7 (25%)</td>
<td>14 (36%)</td>
<td>3 (23%)</td>
<td></td>
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<tr>
<td></td>
<td>101–400</td>
<td>10 (42%)</td>
<td>4 (14%)</td>
<td>14 (36%)</td>
<td>0 (0%)</td>
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<tr>
<td></td>
<td>401+</td>
<td>4 (17%)</td>
<td>17 (61%)</td>
<td>11 (28%)</td>
<td>10 (17%)</td>
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<tr>
<td>p Value</td>
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ASE, Agatston score equivalent; CAC, coronary artery calcification; ICA, conventional invasive angiography.

**Aim:** The primary aim of this study was to investigate whether coronary calcification is a sensitive predictor of significant CAD in patients with an intermediate to high likelihood of CAD.

**Methods:** 52 consecutive patients (18 women, mean age 66 ± 11 years) with an intermediate to high likelihood of CAD referred for ICA underwent coronary calcium scores as the preliminary part of a research CTA. Coronary artery stenoses were assessed visually for CTA and using quantitative coronary angiography (QCA) for ICA.

**Results:** There was good agreement between CTA and ICA for the detection of significant stenosis (see tables 1 and 2). Using the ASE to stratify this cohort would have led to 7/52 (14%) patients being falsely reassured (QCA >50%; 3/7 (45%) of these had subsequent stenoses >70% on QCA), whereas 4/52 (8%) patients would have undergone unnecessary ICA (QCA <50%) using the ICA stenosis as gold standard.

**Conclusions:** A low coronary calcium score does not accurately exclude significant stenosis in patients with an intermediate to high likelihood of CAD. ICA and CTA have similar efficacy in the detection of significant stenoses in patients with an intermediate ASE; however, this study supports the hypothesis that ICA should be used in patients with a high ASE as CTA tends to underestimate the severity of significant coronary stenoses in these patients.

### 151 64-MDCT CORONARY ANGIOGRAPHY COMPARED WITH MYOCARDIAL PERFUSION SCINTIGRAPHY FOR DIAGNOSIS OF FUNCTIONALLY SIGNIFICANT STENOSIS IN PATIENTS WITH LOW TO INTERMEDIATE LIKELIHOOD OF CORONARY ARTERY DISEASE

**Background:** 64-MDCT coronary angiography (CTA) has been proposed as a method of investigating possible coronary artery disease (CAD) in patients who present with chest pain but with a low to intermediate likelihood of CAD. We compared 64-MDCT coronary angiography with 99mTc-tetrofosmin myocardial perfusion scintigraphy (MPS) prospectively for the detection of functionally significant CAD.

**Methods:** 52 consecutive patients with a low to intermediate likelihood of coronary artery disease referred for MPS also underwent CTA. CTA datasets were analyzed by two experienced, blinded observers and coronary artery segments were reported as <50%, 50–69%, 70–99% stenoses or occluded. MPS images were similarly analyzed for inducible perfusion abnormalities and coronary territories were identified.

**Results:** At patient level agreement between CTA and MPS for CTA lesions >50% was 87% (sensitivity 100%, specificity 84%, positive predictive value (PPV) 50%, negative predictive value (NPV) 100%). For CTA lesions >70% agreement was 96% (sensitivity 86%, specificity 98%, PPV 86%, NPV 98%). At the coronary artery level, CTA lesions of >50% compared with MPS, only 7/20 coronary arteries with identified lesions correlated with a perfusion defect in the corresponding vascular territory on MPS (four reversible and three mixed). Eight segmental MPS perfusion defects were identified in areas subtended by arteries with lesions of <50% stenoses on MDCT. For CTA lesions of >70% compared with MPS data, there were eight coronary arteries with identified lesions; however, only six correlated with a perfusion defect in the corresponding vascular territory on MPS (three reversible and three mixed). Two coronary arteries with stenoses of >70% on CTA had no associated perfusion defect on MPS. 10 segmental MPS perfusion defects were identified in areas subtended by arteries with lesions of <70% stenoses on MDCT.

**Conclusions:** In patients with a low to intermediate likelihood of CAD there is good correlation between MPS and CTA for the detection of functionally significant coronary artery stenoses when CTA detects a narrowing of >70% severity. CTA stenoses of >70% should be used to determine functional significance, not >50% as is currently usual practice. Correlation of vascular territory between CTA and MPS, however, is less robust.

**Introduction:** Magnetic resonance (MR) scanning at a field strength of 3.0 Tesla (3 T) has been shown to generate improvements in signal-to-noise ratio (SNR), contrast enhancement and diagnostic accuracy when compared with 1.5 Tesla (1.5 T). k-t SENSE has already been used to accelerate data acquisition in first pass perfusion studies performed at 1.5 T, through the exploitation of temporal data correlations and spatial undersampling. Applying this method to higher field strength produces a synergistic effect, whereby undersampling corrects for some of the unwanted effects of the higher static magnetic field, whereas the higher field strength compensates for the SNR loss associated with spatial undersampling.

**Aim:** To evaluate high spatial resolution k-space and time sensitivity encoding (k-t SENSE) accelerated myocardial perfusion–MR imaging at 3.0 T in comparison with 1.5 T.

**Methods:** Perfusion–MR was carried out at 1.5 T and 3.0 T with a saturation recovery gradient echo pulse sequence (repetition time msec/echo time msec 3.0/1.0, flip angle 15°) combined with k-t SENSE (5× acceleration, 11 interleaved training profiles, spatial resolution 1.8 × 1.8 × 10 mm³). 14 volunteers were studied at rest and 37 patients during adenosine stress. In volunteers, comparison was also made with 3.0 T 2× SENSE-accelerated perfusion–MR imaging at 3.0 T in comparison with 1.5 T.

**Data:**

<table>
<thead>
<tr>
<th>CAC score (ASE)</th>
<th>N (%)</th>
<th>N (%)</th>
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<tr>
<td>p Value</td>
<td>0.004</td>
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</table>

ASE, Agatston score equivalent; CAC, coronary artery calcification; ICA, conventional invasive angiography.

**Abstract 152** 3.0 and 1.5 Tesla k-t SENSE-accelerated stress perfusion–magnetic resonance studies in a patient with three-vessel coronary artery disease. Four short axis slices from base (left) to apex (right) are shown. Both datasets have similar diagnostic content but image quality at 3.0 T is superior.
Low-dose dobutamine adds incremental value to delayed enhancement cardiac magnetic resonance for the prediction of adverse remodelling following acute myocardial infarction

AE Scott, SIK Semple, T Redpath, G Small, G Hillis. Aberdeen University, Aberdeen, UK

Background: An increase in left ventricular end-diastolic volume (LVEDV) following acute myocardial infarction (AMI) is known as ‘adverse remodelling’ and is established as a poor prognostic factor. In the early post-infarct period infarct size, as determined by delayed enhancement cardiac magnetic resonance (DE CMR), has been shown to predict changes in LVEDV 6 months post-AMI. The utility of low-dose dobutamine CMR for predicting remodelling post-AMI is not established. We hypothesised that a comprehensive CMR scan would yield a model more predictive of adverse remodelling than data from the DE component alone. We examined variables from a combined low-dose dobutamine and DE CMR to delineate the model most predictive of adverse remodelling post-AMI. We examined the relative value of data from the DE and the low-dose dobutamine components alone.

Methods: 55 patients with AMI and a new akinetic segment were recruited. CMR scans were performed on a GE 1.5 T Signa CVi scanner 2–6 days post-AMI and at 6 months. LVEDV at baseline and follow-up was measured using the validated “sum of discs” method. Baseline variables were recorded in five categories: (1) baseline dimensions; (2) contractile response to dobutamine; (3) extent of delayed enhancement; (4) extent of persistent microvascular obstruction; (5) first pass perfusion kinetics. Quantitation was performed using MEDIS 6.0.1 software.

Results: Examining all variables from low-dose dobutamine and DE components of the scan with forwards linear regression revealed a combination of six parameters (volume of persistent microvascular obstruction, end-systolic wall thickness (ESWT) in the infarct zone, improvement in quantitative wall motion with dobutamine, improvement in ESWT in the infarct territory with dobutamine, improvement in thickening in the infarct territory with dobutamine and average transmurality of DE in the infarct zone) most accurately predicted changes in LVEDV between baseline and follow-up ($r = 0.881, r^2 = 0.777$). The most predictive univariable was the volume of persistent microvascular obstruction ($r = 0.62, r^2 = 0.384$). Linear regression using variables only from the DE component derived a model encompassing the volume of DE and average transmurality of DE in the infarct territory, which predicted changes in LVEDV ($r = 0.66, r^2 = 0.435$) but with less accuracy than the combined model. Linear regression using variables only from the low-dose dobutamine component derived a model encompassing the percentage change in LVEDV with dobutamine, improvement in ejection fraction with dobutamine, improvement in ESVW with dobutamine, quantitative wall motion in the infarct territory with dobutamine and visual wall motion score with dobutamine, predicted changes in LVEDV with a similar accuracy to the optimal combined model ($r = 0.875, r^2 = 0.766$).

Conclusions: A comprehensive CMR examination accurately predicts adverse remodelling post-AMI. Low-dose dobutamine significantly increases the predictive power of DE CMR and is independently predictive of adverse remodelling. Low-dose dobutamine CMR may be effectively utilised alone or in combination with DE CMR for the accurate prediction of remodelling post-AMI.

Combined low-dose dobutamine and delayed enhancement cardiac magnetic resonance is more predictive of infarct zone and left ventricular functional recovery than either element alone

AE Scott, SIK Semple, G Small, T Redpath, G Hillis. Aberdeen University, Aberdeen, UK

Background: In the setting of acute myocardial infarction (AMI), delayed enhancement cardiac magnetic resonance (CMR) has been shown to predict segmental functional recovery. Predictive accuracy in this setting may be increased by the use of low-dose dobutamine. Data regarding the relative and combined utility of these techniques to predict infarct zone and global left ventricular functional recovery are sparse and conflicting.

Methods: 55 patients with AMI and a new akinetic segment on a screening echocardiogram were recruited. CMR scans were performed on a GE 1.5 T Signa CVi scanner 2–6 days post AMI and at 6 months. Resting dimensions, contractile response to dobutamine, extent of delayed enhancement, extent of persistent microvascular obstruction and first pass perfusion kinetics were measured at baseline. Quantitation was performed with MEDIS 6.0.1 software. Infarct zone functional recovery was determined by changes in quantitative wall motion, visual wall motion and average end-systolic wall thickness in the infarct zone. Global functional recovery was determined by changes in left ventricular ejection fraction and average end-systolic wall thickness over the entire left ventricle. Forward linear regression was used to derive the optimal predictive models.
Abstract 154

<table>
<thead>
<tr>
<th>Infarct zone functional recovery</th>
<th>LDD CMR</th>
<th>DE CMR</th>
<th>Combined</th>
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<tr>
<td></td>
<td>r</td>
<td>r²</td>
<td>r</td>
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<tr>
<td>Average quantitative</td>
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<td>NM</td>
</tr>
<tr>
<td>Average visual wall motion</td>
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<tr>
<td>Global functional recovery</td>
<td>0.566</td>
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<tr>
<td>Ejection fraction</td>
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<tr>
<td>Average ESWT</td>
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</table>

CMR, cardiac magnetic resonance; DE, delayed enhancement; ESWT, end-systolic wall thickness; LDD, low-dose dobutamine; NM, no model.

Results: The table shows the relative and combined utility of low-dose dobutamine and delayed enhancement CMR in predicting functional recovery within the infarct zone and globally. Regardless of the definition of infarct zone/global functional recovery, a combined scan provides superior predictive power.

Conclusion: A comprehensive CMR examination with both delayed enhancement and low-dose dobutamine allows more accurate prediction of infarct zone and global functional recovery than either component alone.

156 CHRONICALLY ISAEMIC HIBERNATING MYOCARDIUM REDUCES PREDICTION OF RECOVERY BY DELAYED ENHANCEMENT CARDIAC MAGNETIC RESONANCE IMAGING IN HEART FAILURE SECONDARY TO CORONARY DISEASE WITH NO SYMPTOMS OF ANGINA

Purpose: The objective of this study was to evaluate cardiac magnetic resonance (CMR) in patients with heart failure secondary to ischaemic heart disease (IHD) and no symptoms of angina.

Methods: 21 consecutive patients were recruited from a randomised controlled trial comparing best medical treatment with revascularisation in chronic heart failure secondary to IHD. All patients underwent comprehensive CMR assessment after randomisation, including functional cines, rest/stress myocardial perfusion and delayed enhancement imaging. Follow-up CMR was repeated after 6 months of optimised medical treatment or 6 months post-revascularisation. Each left ventricle was divided into 16 segments and qualitatively and quantitatively assessed for wall motion, perfusion abnormalities and late gadolinium enhancement (LGE).

Results: 13 patients were randomly assigned to medical treatment and eight to revascularisation. Three patients in the revascularisation group and one patient in the medical group had an absolute improvement in left ventricular ejection fraction (LVEF) of >5% on follow-up in comparison with baseline, with the same numbers in each respective group also demonstrating a deterioration in LVEF of >5%. The three revascularisation patients who demonstrated an absolute improvement in LVEF had the shortest duration of failure, but this did not reach statistical difference to those who did not (13 versus 39 months, p = 0.1). There was no significant difference between LVEF or LGE between the two groups individually or versus each other on either initial or follow-up scans, but there was a significant improvement in the left ventricular end-diastolic volume index in the medical cohort (133.7 versus 123 ml/m², p = 0.001). Myocardial perfusion as measured by mean perfusion reserve index (MPRI) improved between initial and follow-up studies in the revascularisation (1.27 versus 1.69, p<0.001) but not in the medical (1.49 versus 1.41, p = 0.33) cohort. Comparing groups there was no significant difference on initial scan, but on follow-up the MPRI was significantly higher in the revascularisation cohort (p<0.001). On subanalysis, the mean MPRI in segments that subsequently demonstrated improved wall motion showed a significant difference from segments that did not on the initial scan in the revascularisation group (1.52 versus 1.22, p = 0.02), but not in the medical group (1.59 versus 1.47). The only variable that reached statistical significance on logistic regression analysis for the prediction of recovery was duration of failure in the medical cohort (p = 0.02).

Conclusion: In chronic heart failure secondary to IHD, the predictive value of LGE for functional recovery is reduced. This is probably related to chronic ischaemia leading to ultrastructural cellular changes and the downregulation of contractile function in hibernating myocardium. Given the maintenance of cell membrane integrity, these changes will not be evident on gadolinium-based delayed enhancement imaging.
Wilcoxon signed-ranks test was used. A p value of 0.05 or less was considered statistically significant.

**Results:** The right ventricular inferior wall (median (interquartile range) 46% (35–67%)) was significantly thinner than the septum (86% (80–110%) p < 0.001), and the minimum thickness was 2.5 mm (fig 1). The right coronary artery was dominant in 11 (65%), whereas the remaining six had left dominance (fig 2). In six hearts with right dominance, the right coronary artery gave rise to the branch before reaching the crux of the heart. This ‘early take-off’ caused the entire branch to be deviated rightward. On the contrary, in two hearts with left dominance, the left circumflex artery ran beyond the crux and then gave rise to the branch, again resulting in a similar rightward deviation. These deviations allow the branch to run on the thin walled part of the right ventricle where stitches are placed during typical “vertical” plication.

**Conclusions:** Rightward deviation of the posterior descending branch was frequently observed in hearts with Ebstein malformation. Together with the thinness of the ventricular wall, care should be taken to the branch when a surgeon places stitches for the plication.

---

**Abstract 156 Figure 1**

Wilcoxon signed-ranks test was used. A p value of 0.05 or less was considered statistically significant.

**Results:** The right ventricular inferior wall (median (interquartile range) 46% (35–67%)) was significantly thinner than the septum (86% (80–110%) p < 0.001), and the minimum thickness was 2.5 mm (fig 1). The right coronary artery was dominant in 11 (65%), whereas the remaining six had left dominance (fig 2). In six hearts with right dominance, the right coronary artery gave rise to the branch before reaching the crux of the heart. This ‘early take-off’ caused the entire branch to be deviated rightward. On the contrary, in two hearts with left dominance, the left circumflex artery ran beyond the crux and then gave rise to the branch, again resulting in a similar rightward deviation. These deviations allow the branch to run on the thin walled part of the right ventricle where stitches are placed during typical “vertical” plication.

**Conclusions:** Rightward deviation of the posterior descending branch was frequently observed in hearts with Ebstein malformation. Together with the thinness of the ventricular wall, care should be taken to the branch when a surgeon places stitches for the plication.

---

**Abstract 156 Figure 2**

**Role of Platelet Receptor Polymorphisms and Culture Media on Staphylococcus Aureus-Induced Platelet Aggregation: Implications for the Pathogenesis of Infective Endocarditis**

S Daga, JGS Callaghan, JG Shepherd, DE Newby, JR Fitzgerald. University of Edinburgh, Edinburgh, UK

**Background:** Staphylococcus aureus–platelet interactions are important in the pathogenesis of infective endocarditis (IE) and may be mediated by platelet FcγRIIa, GPIIb/IIIa and GPIb receptors.

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**Abstract 157**

**157 ROLE OF PLATELET RECEPTOR POLYMORPHISMS AND CULTURE MEDIA ON STAPHYLOCOCCUS AUREUS-INDUCED PLATELET AGGREGATION: IMPLICATIONS FOR THE PATHOGENESIS OF INFECTIVE ENDOCARDITIS**

S Daga, JGS Callaghan, JG Shepherd, DE Newby, JR Fitzgerald. University of Edinburgh, Edinburgh, UK

**Background:** Staphylococcus aureus–platelet interactions are important in the pathogenesis of infective endocarditis (IE) and may be mediated by platelet FcγRIIa, GPIIb/IIIa and GPIb receptors.
Polymorphisms of these receptors influence susceptibility to cardiovascular, cerebrovascular and autoimmune diseases but their relevance to the outcome of IE is unknown. The aims of the current study were to investigate ex vivo the role of platelet receptor polymorphisms and growth conditions on S aureus-induced platelet aggregation.

Methods: FcyRIIa H131R, GPIIb/IIIa PIa and the Kozak, VNTR and HPA-2 polymorphisms of GPIb were determined in 21 patients with IE and 168 healthy volunteers. S aureus strains were isolated from patients with IE, patients with bacteremia and nasal commensals from healthy individuals. They were grown in heparinised whole human blood or nutrient broth and used to induce platelet aggregation. Lag time to the induction of platelet aggregation and percentage maximal aggregation were determined.

Results: There were no differences in the ability of IE, bacteremia or commensal isolates to induce platelet aggregation (p = ns). However, compared with bacterial growth in brain–heart infusion (a nutrient-rich growth medium commonly used for in-vitro studies but poorly representing the nutrient-depleted in-vivo state), all strains grown in blood were able to induce platelet aggregation. There were no differences in the prevalence of platelet receptor polymorphisms in patients with IE compared with healthy volunteers (p = ns). The GPIb Kozak T/C genotype in individuals homozygous for the FcyRIIa H/H variant was associated with increased lag time to S aureus-induced platelet aggregation (7.81 ± 0.64 minutes versus 5.53 ± 1.28 minutes; p = 0.035) with a trend towards increased percentage aggregation (76.2 ± 6.6% versus 64.6 ± 3.9%; p = 0.059). There were no associations between other polymorphisms, either individually or in combination, with susceptibility to platelet aggregation induced by S aureus or the pharmacological agonists ADP, ristocetin or PAR-1 (p = ns for all). However, there was evidence of donor variation in susceptibility to S aureus-induced platelet aggregation that was not explained by platelet polymorphisms alone.

Conclusions: We have shown for the first time that the growth of S aureus in whole blood stimulates the expression of bacterial factors that induce platelet aggregation. Donor variation in susceptibility to S aureus-induced platelet aggregation may also be due to varying titres of antibodies against S aureus surface proteins such as MSCRAMM. Finally, the Kozak C allele may represent a novel risk factor for the development of IE.
Conclusions: BNP levels correlate with non-invasive parameters of disease severity in children with HCM, including measures of elevated left ventricular filling pressures. In a group of patients in whom the evaluation of symptoms is difficult, BNP may be a useful additional tool in the assessment of disease severity.

OUTCOME OF SEVERE SYMPTOMATIC AORTIC STENOSIS IN PATIENTS AGED 80 YEARS AND OVER: BENEFITS OF AORTIC VALVE REPLACEMENT

1J. Kojodjojo, 1N. Gohil, 1D. Barker, 1P. Youssaf, 2A. Choong, 2M. Koa-Wing, 1J. Bayliss, 1D. Hackett, 1M. Khan. 1Hemel Hempstead General Hospital, Hemel Hempstead, UK; 2Imperial College London, London, UK

Introduction: Results from high volume tertiary centres have shown that aortic valve replacement (AVR) can be performed safely in elderly patients with symptomatic, severe aortic stenosis. It is also clear that the majority of elderly aortic stenosis patients are not referred for surgery and therefore these figures are likely to be subject to referral bias. The survival benefits of AVR over conservative treatment have not been convincingly demonstrated in patients aged above 80 years. The aim of our study is to provide real-world data on the outcomes of patients aged 80 years and over with severe symptomatic aortic stenosis and determine the survival benefits of AVR.

Methods: Hemel Hempstead General Hospital is the sole provider of echocardiographic services to a population of 256,000 in Hertfordshire. Individuals aged 80 years and over with severe symptomatic aortic stenosis were divided into three groups: subjects who underwent AVR (group A); patients who were eligible for AVR but declined surgery due to personal choice (group B) and those who were not fit for surgery and were managed conservatively (group C). Follow-up was conducted by outpatient attendances, review of medical records and telephone interviews. Operative risks were assessed by the use of the logistic European System for Cardiac Operative Risk Evaluation (EuroSCORE). The severity of aortic stenosis and left ventricular function was assessed by transthoracic echocardiography. The primary endpoint was all-cause mortality and survival was analyzed by the Kaplan–Meier method.

Results: From 2001 to 2006, 103 patients aged 80 years and over (mean age 86.0 ± 4.2 years, 41% male) were diagnosed with severe, symptomatic aortic stenosis. Complete follow-up was available for all 103 patients and averaged 1.6 ± 1.4 years (maximum of 5.9 years). Groups A and B were similar in terms of age, operative mortality risks averaged 1.6 ± 1.4 years (mean age 86.0 ± 3.0 years). In group A (n = 17), all 15 patients were alive after 3.6 ± 1.3 years and assessed by the EuroSCORE and echocardiographic parameters. In group A (n = 17), all 15 patients were alive after 3.6 ± 1.4 years and assessed by the EuroSCORE and echocardiographic parameters. Group B had a better chance of survival compared with group C, with the median survival times of 20.6 and 12.2 months, respectively (p = 0.04). Among patients fit for AVR (groups A and B), refusal to undergo surgery (hazard ratio 12.61, p = 0.001) was the only predictor of mortality in a multivariate model.

Conclusions: In elderly aortic stenosis patients fit for surgery, AVR is associated with a low operative risk and refusal to undergo surgery is associated with a 12-fold increase in mortality risk. These findings have significant implications for informed decision-making when managing the fit, elderly patient with aortic stenosis.

THE PROGNOSTIC ABILITY OF AORTIC REGURGITATION QUANTIFICATION WITH CARDIOVASCULAR MAGNETIC RESONANCE

1SG. Myerson, 1TD. Karamitos, 1JM. Francis, 2AP. Banning, 3S. Neubauer. 1University of Oxford, Oxford, UK; 2John Radcliffe Hospital, Oxford, UK

Background: Asymptomatic patients with aortic regurgitation can present a management challenge. Current indications for surgery in aortic regurgitation focus on symptoms, left ventricular dilation or left ventricular dysfunction. Quantifying aortic regurgitation has not previously been used to guide management, due to the difficulty in achieving this with echocardiography. Cardiovascular magnetic resonance imaging (CMR) can accurately quantify aortic regurgitation and left ventricular volumes/function, and we examined whether these could predict symptom development and in particular whether quantifying regurgitation was superior to left ventricular indices in predicting the need for aortic valve surgery.

Methods: We followed 50 patients with aortic regurgitation over 30 ± 20 months using serial CMR measurements of aortic regurgitation and left ventricular volumes and function. The best predictors for progression to symptoms and surgery were identified.

Results: Aortic regurgitant fraction correctly predicted the progression to symptoms/surgery in the 33 initially asymptomatic patients: survival without surgery was 100% for the 20 subjects with regurgitant fraction < 33% compared with 37% for the 13 subjects with regurgitant fraction > 33% (p < 0.001 by log rank; fig).
It also accurately identified symptomatic patients requiring surgery in the whole group (including 17 initially symptomatic patients planned for surgery)—area under the curve on receiver operating characteristics 0.87 (p<0.001), with greater predictive value than all left ventricular volume/function indices and was the only independent predictor on multiple logistic regression analysis. Left ventricular end-systolic volume index >47 ml/m² (area under the curve 0.73; p = 0.002) and left ventricular ejection fraction <63% (area under the curve 0.71; p = 0.005) had lower discriminatory ability and were not independent predictors.

Conclusions: Aortic regurgitation quantification with CMR accurately predicted the progression to symptoms/surgery and was superior to indices of left ventricular volume or function. Its use in patients with aortic regurgitation should be encouraged.

**162 PHYSIOLOGICAL CHANGES WITH DOBUTAMINE STRESS IN TETRALOGY OF FALLOT: A PROSPECTIVE MAGNETIC RESONANCE IMAGING PILOT STUDY**

1V Parish, 1G Greil, 1A Bell, 2C Head, 2J Hancock, 1P Beerbaum. 1King’s College, London, UK; 2St Thomas’ Hospital, London, UK

Introduction: In tetralogy of Fallot (TOF), surgical repair is undertaken in childhood but standard repair techniques result in pulmonary regurgitation. With time this induces right ventricular dilation and dysfunction resulting in exercise intolerance and cardiac arrhythmias associated with an increased risk of sudden death. Although pulmonary valve replacement has been shown to improve symptoms, appropriate timing for this procedure continues to be debated. This study aims to evaluate the role of dobutamine stress magnetic resonance imaging (MRI) in the assessment of right ventricular contractile reserve in post-repair TOF with significant pulmonary regurgitation.

Methods: Patients with repaired TOF and pulmonary regurgitation referred for cardiac MRI were invited to participate. In addition to morphological assessment, ventricular volumes (two-dimensional cine MRI) and pulmonary artery and aortic flows (phase-contrast MRI) were obtained at baseline and during dobutamine infusion at 10 and 20 µg/kg per minute. Comparison of volumetric data at baseline, 10 and 20 µg of dobutamine was performed using Student’s t-test (significance p<0.05).

Results: To date 14 TOF patients were prospectively enrolled in the study. Four patients were excluded from the analysis due to either poor image quality or incomplete image acquisition. The mean age at MRI was 32.6 ± 15 years, with mean age of surgical repair of 6.1 ± 5.8 years. Preliminary data revealed at baseline, mean right ventricular end-diastolic volume (RVEDV) 133 ± 19 ml/m², mean right ventricular ejection fraction 53 ± 6% and mean pulmonary artery regurgitant fraction 45 ± 9%. During stress imaging, heart rate (cardiac index) increased from 67 ± 9 bpm (2.9 ± 0.4 l/minute per m²) at baseline to 89 ± 19 bpm (5.9 ± 1.1 l/minute per m²) at 10 µg dobutamine and 120 ± 25 bpm (4.7 ± 1.1 l/minute per m²) at 20 µg dobutamine (p<0.01). In the left ventricle, there is a clear decrease in left ventricular end-diastolic volume (LVEDV) and left ventricular end-systolic volume (LVESV) at 10 and 20 µg dobutamine. In contrast, for the right ventricle there is little decrease in RVEDV and right ventricular end-systolic volume (RVESV) from baseline to 10 µg dobutamine, and no significant further reduction in end-systolic volume is seen at 20 µg dobutamine. Graphical representation of individual LVESV shows a decrease in volumes with increasing dobutamine concentrations. The RVESV may paradoxically increase in some patients at high dobutamine concentrations (table and figs 1 and 2).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline (mean ± SD, n = 10)</th>
<th>Dobutamine 10 µg (mean ± SD, n = 10)</th>
<th>Dobutamine 20 µg (mean ± SD, n = 7)</th>
<th>p Value 0 versus dobutamine 10 µg</th>
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<tr>
<td>Heart rate, bpm</td>
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<td>89.1 ± 18.9</td>
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<td>45.3 ± 13.4</td>
<td>39.8 ± 9.5</td>
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<td>LVCO, l/min/m²</td>
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<td>RVEDV, ml/m²</td>
<td>132.8 ± 19.4</td>
<td>124.3 ± 25.3</td>
<td>112.7 ± 23.4</td>
<td>NS</td>
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<td>RVESV, ml/m²</td>
<td>63.1 ± 6.4</td>
<td>53.7 ± 22.3</td>
<td>47.9 ± 15.6</td>
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<tr>
<td>RVSV, ml/m²</td>
<td>68.7 ± 7.7</td>
<td>70.6 ± 12.7</td>
<td>64.9 ± 11.7</td>
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<td>RVCO, l/min/m²</td>
<td>4.67 ± 1.0</td>
<td>6.1 ± 1.2</td>
<td>7.6 ± 1.0</td>
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LVCO, left ventricular contractile reserve; LVEDV, left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume; LVSV, left ventricular systolic volume; RVCO, right ventricular contractile reserve; RVEDV, right ventricular end-diastolic volume; RVESV, right ventricular end-systolic volume; RVSV, right ventricular systolic volume.
Conclusions: Although preliminary, the study demonstrates the diagnostic potential of dobutamine stress MRI in patients with TOF and severe pulmonary regurgitation. Whereas the left ventricle clearly reduced end-diastolic and end-systolic volumes at each dobutamine level, the right ventricle showed much less response at 10 μg dobutamine and failed to reduce or even increased RVESV at 20 μg dobutamine. RVESV under stress may thus become a discriminative parameter in post-repair TOF patients with relevant pulmonary regurgitation if confirmed in a larger population. Through further study we hope to determine which combination of cardiac volumetric and flow parameters and their response to stress are most suited to guide clinical decisions regarding the timing of pulmonary valve replacement.

Abstract 163 Neonatal outcomes.

mothers (64.7%) with structural heart disease. Four neonates were small for gestational age, of which three mothers (75%) had structural heart disease. All mothers with babies with congenital heart defects had structural cardiac defects.

Discussion: Maternal MDT (obstetrician, cardiologist and obgyny anaesthetist) are vital for the management of this small group of patients who have a high morbidity (60%) but low mortality (1%). Neonatal complications (predominantly prematurity) are significant, highlighting the need for prepgregnancy counselling in patients with existing structural heart disease. The caesarean section rate for cardiac reasons is high and will be reviewed. Database audit suggests the need for more assiduous recording of NYHA class and mode of delivery. Ischaemic heart disease events are low due to failure of capture of data through an MDT, because they are usually acute events. An intranet-based register of management plans (including postpartum) to which new acute problems can be added is suggested.

Abstract 163

<table>
<thead>
<tr>
<th>GUCH</th>
<th>Cardiomyopathy</th>
<th>Arrhythmias</th>
<th>Ischaemic heart disease</th>
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<td>n = 24</td>
<td>n = 2</td>
<td>n = 1</td>
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<td>SVT (22)</td>
<td>Coronary artery spasm (1)</td>
<td>Traumatic aortic dissection (1)</td>
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<td>ARVC (1)</td>
<td>VT (1)</td>
<td>Coronary thrombus (1)</td>
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<tr>
<td>Right heart defects (4)</td>
<td>Fabry’s (1)</td>
<td>Ventricular bigemini (1)</td>
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<tr>
<td>Complex GUCH (11)</td>
<td>Peripartum (4)</td>
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</table>

ARVC, arrhythmogenic right ventricular cardiomyopathy; GUCH, grown-up congenital heart disease; SVT, supraventricular tachycardia; VT, ventricular tachycardia.
A NOVEL LOW TILT WAVEFORM FOR THE INTERNAL DEFIBRILLATION OF VENTRICULAR FIBRILLATION

1JR Bennett, 1KM Darragh, 2SJ Walsh, 1JD Allen, 1A AJ Adgey, 1G Manoharan. 1Royal Victoria Hospital, Queen’s University, Belfast, UK; 2Royal Victoria Hospital, Belfast, UK. 1SM Darragh, 1KM Darragh, 2JD Allen, 1A AJ Adgey, 1G Manoharan. 1Royal Victoria Hospital, Queen’s University, Belfast, UK; 2Royal Victoria Hospital, Belfast, UK.

Method: Randomly assessed at four monophasic pulse width settings (5, 7, 10 25% (p < 0.016) and than pulse widths 6/6 ms at 400 V (S 11%, p<0.001) and at 450 V (S 0.001). Greater than a 50% success rate (E50) was achieved by pulse width 8/4 ms at 550 V (S 77%; mpV 342.6 V; mpA 6.711 A; mpΩ 0.49 Ω; ml 27.8 J).

Conclusion: This low tilt waveform is effective in defibrillating ventricular fibrillation in large pigs with high defibrillation thresholds. The low tilt biphasic waveform with first pulse two-thirds of total pulse width improves defibrillation efficacy significantly. Comparison studies with standard waveforms are in progress. These preliminary results are promising in the development of novel waveform technology.

The burden of atrial fibrillation in patients with chronic heart failure is substantial; the recent Euroheart heart failure survey described a prevalence of 25% in 11 527 patients, whereas other studies have shown the prevalence to be as high as 50%. Studies investigating the prevalence of atrial fibrillation in heart failure patients often rely on detecting the arrhythmia via electrocardiograms performed at different timepoints. This approach often fails to detect paroxysms of atrial fibrillation thus underestimating the true burden of atrial fibrillation in heart failure patients. Atrial fibrillation has been shown to increase all-cause mortality and hospitalisation in heart failure patients, thus the identification of these at-risk patients is of paramount importance.

We retrospectively studied the prevalence of atrial fibrillation in 162 heart failure patients with a mean ejection fraction of 25.1 ± 3.7% treated with cardiac resynchronisation therapy (CRT) devices followed up at the Manchester Heart Centre for a mean of 435 days (range 1–1277 days) to determine whether patients thought not to have atrial fibrillation have a significant, albeit underrecognised burden of atrial fibrillation. Significant paroxysms of atrial fibrillation were defined as mode switching episodes on the CRT devices with an atrial rate greater than 200 for at least 30 seconds. Patient notes were reviewed to ascertain whether patients were documented to have either chronic or paroxysmal atrial fibrillation.

The demographics of the study population are shown in the table.

Of the 162 patients studied, 43 were found to have a history of chronic atrial fibrillation (26.5%), 18 of paroxysmal atrial fibrillation (11.1%) and 101 patients (62.3%) had no previous history of atrial fibrillation and were in sinus rhythm at their last appointment. Of the 101 patients not previously known to have atrial fibrillation, 27 (26.7%) were found to have significant episodes of atrial fibrillation on CRT mode switching analysis (fig A). In addition, there was a significant difference in anticoagulation rates between those patients newly diagnosed with paroxysmal atrial fibrillation and previously not known to have atrial fibrillation.
fibrillation compared with those with existing paroxysmal atrial fibrillation (13.5% and 83.3%, respectively, p < 0.01, fig B).

No significant difference in the mean ejection fraction of these two groups of patients was observed (22.8% versus 23.4%, respectively)

In summary, analysis of data from CRT devices in a population of heart failure patients identified an additional 27% of patients with atrial fibrillation in a group in which atrial fibrillation was not previously diagnosed. Furthermore, these individuals had markedly lower rates of anticoagulation than those with known paroxysmal atrial fibrillation. Further studies are warranted to assess the true burden of atrial fibrillation in these at-risk heart failure patients, which at present appears to be underrecognised, and to identify whether these patients warrant anticoagulation.

Abstract 167
MORBIDITY ASSOCIATED WITH DELAYS TO PERMANENT PACING
MS Cunningham, CJ Plummer, JM McComb. Freeman Hospital, Newcastle upon Tyne, UK

Introduction: We have previously demonstrated failure to refer for pacing in a significant proportion of patients after initial documentation of a permanent pacing indication. We have now studied the morbidity associated with the delays caused by this.

Methods: 95 consecutive patients undergoing permanent pacemaker (PPM) implantation for bradycardia indications at a single implanting centre between 1 June 2006 and 31 August 2006 were studied. Hospital records (from referring and implanting centres) were reviewed. Pacing indications (defined by ACC/AHA 2002 guidelines) were assessed by two cardiologists with an interest in pacing, based on ECG and clinical data. Data relating to symptoms, hospital admissions, investigations, referral date and PPM implantation were recorded.

Results: 33 patients (35%) had a class I/IIa pacing indication that did not trigger referral for pacing. These patients experienced a significantly longer overall delay from symptom onset to PPM implantation: median 562 days (range 9–7332) versus 50 days (range 0–3228), p < 0.001* (see table). 18 (55%) of the “missed” indications occurred while patients were taking rate-limiting drugs for the control of previous tachyarrhythmia (10), hypertension (6), ischaemic heart disease (1), unknown (1). 26 (79%) patients with “missed” indications experienced adverse clinical events between the time of the initial documented pacing indication and PPM implantation: 23 had ongoing symptoms (syncope 10, dizziness/dyspnoea 12, asystolic arrest 1); 18 were hospitalised (on one to five occasions) with bradycardia, or tachyarrhythmia related to the withdrawal of rate-limiting medication; three received temporary pacing wires. 28 patients had additional unnecessary investigations: Holter recording (19); R-test/reveal (5); tilt-room assessment (6). The “missed” indications occurred under the care of general physicians/geriatricians (23), cardiologists (7) and surgeons (3).

Conclusions: 35% of patients who received PPM had a previously documented pacing indication that did not trigger a pacing referral. These patients have significant delays to PPM implantation, ongoing symptoms, hospitalisations and unnecessary procedures/investigations. Significant morbidity may be avoided by the prompt recognition and treatment of pacing indications.

Abstract 168
DIAGNOSTIC INVESTIGATIONS LEADING TO PERMANENT PACEMAKER IMPLANTATION
MS Cunningham, CJ Plummer, JM McComb. Freeman Hospital, Newcastle upon Tyne, UK

Introduction: Permanent pacemaker (PPM) implantation rates are lower in the United Kingdom than in most other European countries, the reasons for which are unclear. Restricted access to

<table>
<thead>
<tr>
<th>Delay</th>
<th>Urgently paced (n = 48)</th>
<th>Electively paced (n = 47)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Recognised (n = 34)</td>
<td>Missed (n = 14)</td>
</tr>
<tr>
<td>Pacing indication to</td>
<td>0 (0–11)</td>
<td>153 (6–7332)*</td>
</tr>
<tr>
<td>pacing referral</td>
<td></td>
<td></td>
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<tr>
<td>&lt;1 day</td>
<td>24</td>
<td>0</td>
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<tr>
<td>1–7 days</td>
<td>8</td>
<td>2</td>
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<tr>
<td>1–4 weeks</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>4–26 weeks</td>
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<td>3</td>
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<tr>
<td>&gt;26 weeks</td>
<td>0</td>
<td>7</td>
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<tr>
<td>Symptom onset to</td>
<td>11 (0–2856)</td>
<td>401 (9–7332)*</td>
</tr>
<tr>
<td>PPM implant</td>
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</tr>
</tbody>
</table>

PPM, permanent pacemaker.

*p < 0.001.
Abstract 168

<table>
<thead>
<tr>
<th>Investigations performed</th>
<th>Diagnostic investigation</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Urgent (n = 48)</td>
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<tr>
<td>12-lead ECG</td>
<td>48 (100%)</td>
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<tr>
<td>24–48 hour Holter monitoring</td>
<td>21 (44%)</td>
</tr>
<tr>
<td>Event recorder</td>
<td>2 (4)</td>
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<tr>
<td>Implantable loop recorder</td>
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<tr>
<td>Documented telemetry</td>
<td>24 (50%)</td>
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<tr>
<td>Tilt service assessment or carotid sinus massage</td>
<td>5 (10)</td>
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<td>Other or undetermined</td>
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Abstract 169

<table>
<thead>
<tr>
<th>Patients</th>
<th>Sex (N males)</th>
<th>Genotype</th>
<th>Genotype</th>
<th>Genotype</th>
<th>Negative genotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICD</td>
<td>26 (52)</td>
<td>0</td>
<td>7</td>
<td>4</td>
<td>18</td>
</tr>
<tr>
<td>Non-ICD</td>
<td>12/30</td>
<td>18</td>
<td>21</td>
<td>5</td>
<td>56</td>
</tr>
</tbody>
</table>

ICD, implantable cardiac defibrillator.

OUTCOME OF DEFIBRILLATOR IMPLANTATION IN PATIENTS REFERRED FOR LONG QT SYNDROME GENETIC TESTING

Abstract 169

Methods: 95 consecutive patients undergoing PPM implantation for bradycardia indications at a single UK implanting centre between 1 June 2006 and 31 August 2006 were studied. Hospital records (from referring and implanting centres) were reviewed. Data relating to symptoms, investigations, documented pacing indications (defined by ACC/AHA 2002 guidelines), referral date and PPM implantation were recorded.

Results: 48 patients were referred for pacing urgently as inpatients (U), and 47 electively as outpatients (E). ECG indications for pacing were: complete heart block (U 17, E 4), Mobitz II (U 4, E 11), sinus node disease (U 18, E 17), atrial fibrillation with pauses (U 5, E 4), carotid sinus hypersensitivity (U 0, E 7), bifascicular block with syncope (U 4, E 5), other (U 0, E 1). Patients’ symptoms were: syncope (U 26, E 25), dizziness (U 13, E 10), other (U 9, E 12). For 46 (48%) of the 95 patients, 12-lead ECG was the diagnostic test that identified the pacing indication (see table). However, 77 patients (81%) had other investigations/monitoring of heart rhythm. In 33 (48%) of the 95 patients the first documented pacing indication did not trigger a pacing referral and 28 of these patients went on to have additional investigations.

Conclusion: A high proportion (81%) of patients who receive a PPM undergo specialised rhythm investigation/monitoring, but half of all pacing indications are diagnosed by 12-lead ECG alone. A third of patients undergo additional investigation once a pacing indication has already been documented. Limitations in the interpretation of relevant investigations, rather than restricted access to them, may contribute to low UK pacing rates.

LEFT VENTRICULAR DYSFUNCTION IN PATIENTS REFERRED FOR PACEMAKERS: IMPLICATIONS FOR PACEMAKER SELECTION

Abstract 170

<table>
<thead>
<tr>
<th>Patients without LV dysfunction</th>
<th>Patients with LV dysfunction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age</td>
<td>74</td>
</tr>
<tr>
<td>Male sex (%)</td>
<td>60</td>
</tr>
<tr>
<td>Atrial fibrillation (%)</td>
<td>18</td>
</tr>
<tr>
<td>Sinus node dysfunction (%)</td>
<td>30</td>
</tr>
<tr>
<td>AV node disease (%)</td>
<td>47</td>
</tr>
</tbody>
</table>

AV, atrioventricular; LV, left ventricular.
outcomes are associated with an increased frequency of RVP (more than 40%) and the degree of ventricular dyssynchrony induced. Recent European Society of Cardiology (ESC) guidelines for cardiac pacing (August 2007) recommend biventricular pacing to avoid chronic RVP in heart failure patients with bradyarrhythmia indications. However, this has significant healthcare implications. The aim of this study was to determine the prevalence of left ventricular dysfunction among patients referred for permanent pacemakers.

Methods and Results: Pacemaker referrals over 12 months (October 2006 to October 2007) were retrospectively analyzed in three tertiary referral centres and a comparative cost analysis of pacemaker selection was determined. 574 patients (65% male), mean age 74 ± 14 years (SD) (range 24–96), were referred for permanent pacemaker implantation. 317 (55%) had a previous determination of left ventricular function by echocardiography, although only 242 (42%) had an echo within the past 2 years. Of the patients with previous echocardiography, 53 (17%) had left ventricular dysfunction, defined by moderate to severe left ventricular systolic dysfunction, or left ventricular ejection fraction less than 35%. Bradyarrhythmia indications are shown in the table. After implantation, 80% of pacemaker patients with left ventricular dysfunction were found to have more than 40% RVP, a level associated with worsened outcomes. By comparative cost analysis, applying ESC guidelines would cost an additional £3000 per patient, but would be offset by reduced heart failure morbidity and mortality.

Conclusion: Moderate to severe left ventricular dysfunction was found in 17% of patients referred with bradyarrhythmia indications for pacemakers, and most require frequent RVP for concomitant atrioventricular node disease. These patients should be considered for biventricular pacing according to the latest ESC guidelines. Routine assessment of left ventricular function before pacemaker implantation is necessary. Our data suggest that implementation of these recommendations have significant healthcare cost and service implications.

In younger patients this represents a lot of monitoring cost for very little return, whereas in older patients the implant rate suggests that simply implanting a pacemaker in the first place would be more cost-effective, avoiding the cost of the initial reveal, while being safer for those who experience potentially fatal asystole during monitoring. Obviously, in young patients, one would not wish to subject them to pacing when the likelihood of ultimately requiring it is so low. However, for older patients (certainly those over the age of 70 years) it would seem entirely reasonable to implant a simple VVI device with a low back-up rate for diagnosis (and life saving) and upgrade to a DDD device if appropriate. This would certainly be far more cost-effective and safer. Complications from pacing would be slightly higher than reveal implant but not a lot. During a 3-month audit period in the past year, a similar number of pacemakers (57) were implanted, with no deaths or major complications. Two patients developed a haematoma, but there were no wound infections. In general, there is no reason why the infection rate should not be similar between the two procedures.

However, in cost terms if we were to compare the cost of a reveal (£1400) and implant (£1105) plus pacemaker when indicated, against the cost of a VVI (£610) and implant (£1286) with upgrade to DDD when DDD pacemakers were implanted, based on the numbers obtained from this retrospective analysis, the cost saving would be £31 315 in total (£666 per patient). If the policy was restricted to using the VVI approach only in older patients the cost savings are still considerable, for example using an age cut-off of 60 years, the savings would be £21 923 and with an age cut-off of 70 years, the savings would be £12 869.

We believe that the majority of implanted reveal devices at their current price are not cost-effective and carry a slightly higher mortality risk, this hypothesis should be tested in a randomised controlled trial.

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### 171 ARE REVEAL DEVICES REALLY COST-EFFECTIVE?

M James, H Gonna. Musgrove Park Hospital, Taunton, UK

Having experienced two deaths in patients while using reveal devices we decided to review our overall experience with their use. Although the reveal is excellent for providing a diagnosis, it is not therapeutic and there is always the possibility that the diagnosis will be posthumous. We reviewed the outcome of all our implants since 2000, in which monitoring had been concluded or there was at least 2 years follow-up since implant. The results showed that 47 implants met these criteria. The mean age was 61 years (range 20–90). Eleven patients went on to receive a pacemaker implant (10 DDD, one VVI), an overall implant rate of 23%. No patient was identified with ventricular tachycardia. The implant rate was related to age such that only 10% were implanted under the age of 50 years (age 48 years). Unsurprisingly, the highest implant rate was in the over 70 year age group (7/17, 41%).

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### 172 FIVE-YEAR EXPERIENCE OF DEVICE LEAD EXTRACTIONS IN A UK TERTIARY CENTRE

1MS Hamid, 1A Arujuna, 1S Khan, 1A Ladwiniec, 1N Patel, 1C Bucknall, 1CA Rinaldi. 1St Thomas’ Hospital, London, UK; 2Eastbourne District General Hospital, Eastbourne, UK

Introduction: Device therapy is being increasingly utilised in the management of heart rhythm disturbances and heart failure therapy. This has entailed the use of more complex devices, leads with coils and placement in the coronary sinus. This rise in implantation rates has also led to a concomitant increase in device system extractions.

Methods: We are a referral centre for lead extractions. These were performed in the cardiac catheter laboratory with onsite cardiothoracic cover. The methods used were manual traction with locking stylets and Excimer laser, a system in which a sheath is positioned over the lead and surrounding fibrosis is vaporised while advancing the sheath.

Results: Between 2003 and 2007, 183 consecutive cases were referred for lead extraction. The average age was 65 years (range 28–83), 76% men and 24% women. The mean implantation time was 75 months (range 4–312). The indications for extraction were as follows: pocket infection 51%, non-functioning lead 22%, erosion 21%, endocarditis/septicaemia 5%, superior vena cava thrombosis 0.5% and painful lead 0.5%. Type of device: single chamber 10%, dual chamber 63%, implantable cardio defibrillator 17%, cardiac resynchronisation therapy 5% and cardiac resynchronisation therapy defibrillator 5%. The total number of leads extracted was 369: atrial 157 (57%), right ventricular 175 (47%), implantable cardio defibrillator 40 (11%) and coronary sinus 19 (5%). A superior approach was used in 99.4%, femoral in 0.6% and laser was utilised in 44% of cases. Complete removal was achieved in 90.7%, partial...
removal in 7.6% and failure in 1.7%. Surgical extraction was necessary in 2%, all with endocarditis. Major complications were death one day post-explant in one patient with septicaemia and three cases (1.6%) of tamponade.

**Conclusion:** As the number and complexity of devices increases, the necessity for device explantations is also likely to rise. Our experience suggests that this procedure can be performed both successfully and safely with the use of a percutaneous approach in the majority of patients, including those with coronary sinus leads. With the advent of the laser sheath, cases that would previously have required a surgical approach can be performed.

**EXPERIENCE OF CORONARY SINUS LEAD EXTRACTIONS IN A UK TERTIARY CENTRE**

1 MS Hamid, 1 A Arujuna, 1 S Khan, 1 A Ladwiniec, 1 N Patel, 1 C Bucknall, 1 CA Rinaldi. 1 St Thomas’ Hospital, London, UK; 2 Eastbourne General Hospital, Eastbourne, UK

**Introduction:** Cardiac resynchronisation therapy (CRT) is an established therapy for heart failure and the increasing number of implants is likely to result in a concomitant need for explantation. There is a broad evidence base for the percutaneous extraction of right sided leads but coronary sinus lead placement brings new challenges to explantation due to placement in often complex and fragile venous anatomy.

**Methods:** We are a referral centre for lead extractions and we report our experience over a 4-year period, with the information reviewed from a cardiac procedures database. The extractions were performed in the cardiac catheter laboratory with onsite cardiothoracic cover. The methods used were manual traction with locking stylets and Excimer laser, a system utilising a sheath enabling advancement of the sheath. All device explants at our centre are performed by three experienced operators.

**Results:** Between 2004 and 2007, 19 cases were referred for coronary sinus lead extraction consisting of 10 CRT pacemakers and nine CRT defibrillators. The average age was 68.4 years (range 59–76), 18 (95%) were men. The mean implantation time was 25.5 months (range 1–62). Indications for extraction were: pocket infection, eight (42%); high coronary sinus lead threshold/displacement, five (26%); erosion, four (21%) and endocarditis, two (11%). The total number of leads extracted was 68: atrial 17 (25%), right ventricular 22 (32%), defibrillator 10 (15%) and coronary sinus 19 (28%). A superior approach was used in all cases, with an average procedure time of 85 minutes. All 19 coronary sinus leads were removed with manual traction, with laser utilised in four cases (21%) to mobilise the non-coronary sinus leads. Complete removal of all leads was achieved in 100% of cases and no complications of coronary sinus laceration, pericardial effusion or emergency surgery occurred.

**Conclusion:** Our experience suggests that the removal of coronary sinus leads percutaneously is a viable option when CRT systems need to be explanted. An experienced operator and cardiothoracic back-up should be available to minimise the attendant risk. The leads were extracted safely by the use of gentle traction but it is likely that as these systems are in patients for longer periods, laser therapy may be necessary.

**CHANGES IN CARDIAC CONDUCTION AFTER PERCUTANEOUS AORTIC VALVE REPLACEMENT IN SEVERE AORTIC STENOSIS**

1 H Jallaihawi, 1 D Chin, 1 J-L Laborde, 1 E Logten, 1 T Spyt, 1 J Kovac. 1 Glenfield Hospital, Leicester, UK; 2 Clinique Pasteur, Toulouse, France

**Introduction:** Changes in atrioventricular conduction are a recognised complication after open aortic valve replacement, with requirement for a permanent pacemaker in the region of 10%. We studied changes in atrioventricular conduction and requirements for permanent pacing after percutaneous aortic valve replacement (pAVR) with the CoreValve porcine stented bioprosthesis in patients with severe calcific aortic stenosis.

**Methods:** In patients receiving pAVR, we recorded changes in electrocardiographic variables as well as the incidence of permanent pacing. Potential clinical, electrocardiographic and echocardiographic predictors of permanent pacing requirement were studied in a univariate binary logistic model with requirement for pacemaker as the dependent variable. In addition, in those who were permanently paced, the frequency of pacing at 1 month was evaluated.

**Results:** Between January and November 2007, 25 patients underwent pAVR in our centre with the CoreValve stented bioprosthesis. 6/25 (26.1%) were in atrial fibrillation at baseline and 5/25 (15%) were already paced at baseline. 17/25 were in sinus rhythm at baseline; of this group, PR interval did not prolong significantly post-procedure (185 ± 61 ms pre-procedure versus 180 ± 43 ms post-procedure, p = 0.6). Of the 20 unpaced patients at baseline, 6/20 required a permanent pacemaker post-procedure (30%) and in this was for high-grade atrioventricular block in two cases and a junctional rhythm in the remainder. Three patients had VVIR pacemakers and three DDR, all were set to rate 80–120. A slight prolongation of the QRS duration was observed in those not requiring pacing (102 ± 30 ms pre-procedure versus 111 ± 28 ms post-procedure, p = 0.049). Baseline predictors for the need for a permanent pacemaker were studied in those unpaced at baseline. The need for a pacemaker was unrelated to age (p = 0.933), sex (p = 0.09), peak troponin (p = 0.38), baseline ejection fraction (p = 0.26), left ventricular outflow tract dimension at baseline (p = 0.67) and calculated aortic valve area at baseline (p = 0.9). Pacemaker requirement was also unrelated to PR interval pre-procedure (p = 0.9), the presence of atrial fibrillation (p = 0.68) and QRS duration pre-procedure (p = 0.58). It did not appear to be related to previous percutaneous coronary intervention or coronary artery bypass grafting. At 1 month follow-up, of the six who were paced, two required ventricular pacing <10% of the time, suggesting a temporal improvement in atrioventricular conduction and that the absolute pacemaker requirement after pAVR is approximately 20%.

**Conclusion:** Changes in normal atrioventricular conduction are observed after pAVR, including prolongation of QRS duration and an absolute requirement for permanent pacing in approximately 20% of patients. Requirement for permanent pacing appears difficult to predict using baseline variables. Of those paced, there appears to be a temporal relationship in terms of the recovery of normal atrioventricular conduction in a significant proportion of patients, which requires further study. Contemporised data for approximately 50 cases will be presented at the meeting.

**ELECTIVE DAY-CASE PERMANENT PACEMAKER IMPLANTATION IS SAFE AND COST-EFFECTIVE: EXPERIENCE FROM A LARGE UK TERTIARY CENTRE**

S Krishnamoorthy, A Nadir, P Mullin, A Morley-Davies, J Creamer, F Osman. University Hospital of North Staffordshire, Stoke on Trent, UK

**Introduction:** An increasing number of patients are undergoing permanent pacemaker implantation. Patients often stay in hospital overnight following implantation, placing an increasing burden on hospital services, which has a major cost implication for the NHS. This is more evident in the target-driven culture that prevails within the NHS. Day-case procedures could be effective in alleviating some of this strain. We have been performing elective permanent pacemaker implantation as day-case procedures since 1997 at the University Hospital of North Staffordshire, Stoke on Trent.
Methods: We retrospectively evaluated our day-case permanent pacemaker procedures for the time period April 2002 to December 2006. We collected data on baseline patient characteristics, procedure numbers and immediate complications. We identified those who required in-hospital stay and why. We also evaluated whether those who were discharged the same day had a readmission into hospital within 6 weeks for a pacemaker complication. We also performed a cost analysis to identify cost savings to the NHS of adopting this policy of day-case permanent pacemaker implantation.

Results: A total of 780 patients were implanted with a permanent pacemaker intended as a day-case procedure during the period of study; of these 41 patients (5.3%) had an overnight stay. The mean age ± SE of the entire cohort was 78.3 ± 0.4 years, 464 men (59.5%) and 316 women (40.5%). Single-chamber devices were implanted in 272 patients (34.9%) and dual-chamber devices in 508 (65.1%). Of those with a single-chamber pacemaker 27 had atrial-based and 245 ventricular-based devices. The route of vascular access was the subclavian vein in 451 (55.5%) and the cephalic vein in 549 (44.7%). Pre-implant intravenous antibiotics were not administered routinely to any patients but gentamicin was given into the pocket during the procedure. All patients were given a 5-day course of oral antibiotics. Forty-one patients (5.3%) required an overnight stay in hospital following implantation. The reasons for this included haematoma formation (n = 12), pneumothorax (n = 2), social reasons (n = 7), observation post-implant at the physician’s request but no complication (n = 13), subclavian vein thrombosis (n = 1), angina (n = 3), arrhythmia (n = 1) and patient on warfarin therapy (n = 2). An overnight stay at the University Hospital of North Staffordshire is currently estimated to cost £203.60. During the past year (November 2005 to November 2006) 109 patients had a day-case permanent pacemaker procedure resulting in a cost saving of £22 192.40 for adopting the day-case strategy. None of those discharged the same day had a readmission into hospital within 6 weeks with a pacemaker complication.

Conclusions: Permanent pacemaker implantation performed as a day-case procedure is safe and cost-effective. The prevalence of complications is low and only a small minority require admission into hospital for an overnight stay. Expanding this policy to other hospitals in the NHS has the potential for huge cost savings.

### 176 THE RELATIONSHIP BETWEEN RIGHT VENTRICULAR PACING AND ATRIAL FIBRILLATION BURDEN IN PATIENTS WITH PAROXYSMAL ATRIAL FIBRILLATION

RA McIntosh, RA Veasey, PSG Hong, JC Silberbauer, G Lloyd, N Patel, N Sulke. Eastbourne General Hospital, Eastbourne, UK

Introduction: In the short or medium term right ventricular pacing has no effect on atrial fibrillation burden in patients with paroxysmal atrial fibrillation (PAF). The effects of right ventricular pacing on PAF in the long term are unknown (unlike persistent atrial fibrillation). We evaluated the effect of right ventricular pacing on atrial fibrillation burden in patients with symptomatic drug-resistant PAF.

Methods: Short and long-term pacing data from 62 patients with Vitatron Selection 9000, Vitatron T70, Medtronic Enrhythm or Symphony DR2550 pacemakers were analyzed. These pacemakers have sophisticated atrial fibrillation diagnostic Holters that accurately demonstrate atrial fibrillation burden. The devices also record the quantity of sensed sinus and ventricular activity as well as the percentage of ventricular and atrial pacing delivered. By analyzing implanted pacemaker data at short and long-term follow-up the effect of ventricular pacing on atrial fibrillation burden was assessed.

Results: 62 patients (age 74 ± 8 years, 46.8% male) underwent Holter interrogation following an induction period of one month and again after long-term follow-up of at least one year (mean 1020 ± 573 days). No significant increase in delivered ventricular pacing over time was observed (52.7 ± 35% to 51.8 ± 39%, \(p = 0.9\)). Atrial fibrillation burden increased slightly over time (13.1 ± 16.2% to 18.0 ± 28.8%); however, this change was not significant (\(p = 0.1\)). There was no statistically significant correlation between the amount of ventricular pacing delivered and the change in atrial fibrillation burden (\(r = 0.155, p = 0.2\)) (fig).

Conclusion: In patients with symptomatic pre-implant PAF, increased right ventricular apical pacing does not affect arrhythmia burden in either the short or long term. This is in contradistinction to persistent atrial fibrillation studies and suggests different arrhythmia mechanisms.

### 177 A SINGLE DEFIBRILLATION SAFETY MARGIN TEST IS SUFFICIENT IN MOST PATIENTS AT IMPLANTATION OF AN IMPLANTABLE CARDIOVERTER DEFIBRILLATOR

F Osman, M Jeilan, A Habib, S Kundu, JH Tuan, R Mantravadi, PJ Stafford, R Pathmanathan, GA Ng. Glenfield Hospital, Leicester, UK

Introduction: As implantable cardioverter defibrillators (ICD) are designed to treat arrhythmias with the potential to cause sudden death, it is important that efficacy can be assured at the time of implantation. A defibrillation safety margin (DSM) is determined at implant typically with a protocol of two defibrillations at a minimum of 10 J below the maximum output of the device. With the advent of transvenous leads and high energy devices, this strategy of double DSM testing may not be necessary.

Methods: We retrospectively examined our ICD implant database at Glenfield Hospital, Leicester, from September 2006 to October 2007 to examine data on DSM testing and recorded baseline patient characteristics, indications, implant data of right ventricular lead and procedure times. We evaluated whether the DSM tests were successful and how many were performed. Logistic regression analysis was performed to identify predictors of success for two consecutive successful DSM tests with a minimum 10 J safety margin.

Results: During the period of study 264 devices were implanted. The mean age of the cohort was 65.6 ± 0.8 years (mean ± SE). 115 patients (44%) had ICD implantation for primary prevention and 149 (56%) for secondary prevention. 156 (59%) patients had ischaemic cardiomypathy and 108 (41%) non-ischaemic cardiomypathy. The prevalence of poor left ventricular function (ejection fraction <30%) was 75.9%, moderate left ventricular function (ejection fraction 30–50%) was 15.0% and good left ventricular function (ejection fraction ≥50%) was 7.4%. The prevalence of a DSM test that was successful was 94.6%. We found that a single DSM test was successful in most patients (97%).
ventricular function (ejection fraction >50%) was 11.1%. The mean QRS duration on ECG was 130.2 ± 3.0 msec. The mean implantation procedure time was 89.8 ± 3.6 minutes. The mean implant data for the right ventricular lead were: R-wave 15.2 ± 0.4 mV, impedance 732.1 ± 13.8 ohms and threshold 0.66 ± 0.03 V at 0.5 msec. The ICD were single chamber in 118, dual chamber in 146 (including 71 cardiac resynchronisation therapy ICD). The median energy for the first DSM test was 25 J (range 21–30) and 25 J (range 21–40) for the second test. The prevalence of successful DSM with a 10 J safety margin was 97.6% for the first and 96.0% for the second test. Of those who had a successful first DSM test (with a 10 J safety margin), 97.9% had a successful second DSM with a 10 J safety margin. The remaining 2.1% had a successful DSM at maximum output for the device; no patients who had successful first DSM (with a 10 J safety margin) failed the second DSM test. Successful first DSM with a 10 J safety margin was found to be an independent predictor for a successful 10 J safety margin for two consecutive DSM tests (p<0.001).

Conclusions: Most patients had a successful first DSM test with a 10 J safety margin with modern transvenous leads and high energy devices. All patients who had a successful first DSM test with a 10 J safety margin had a successful second DSM (the vast majority with a 10 J safety margin). This suggests that a second DSM test is unnecessary in the majority, especially given that a second test prolongs the procedure and could be associated with complications, especially in those with severe left ventricular impairment.

### COST-EFFECTIVENESS OF BI-ATRIAL PACING FOR REFRACTORY ATRIAL FIBRILLATION

R Sankaranarayanan, MA James, H Gonna, S Butchael, R Holloway. Taunton and Somerset Hospital, Taunton, UK

Objective: We have previously reported the long-term successful results of bi-atrial pacing in the management of drug-resistant atrial fibrillation by alleviating symptoms and atrial fibrillation duration. This current study analyses whether our bi-atrial pacing strategy has also been cost-effective.

Methods: 31 patients with drug-resistant atrial fibrillation (mean of 59 months from first diagnosis), who were considered suitable for atrioventricular node ablation and pacing, underwent bi-atrial pacemaker implantation as an alternative management strategy, with a view to proceeding to atrioventricular node ablation and pacing (“ablate and pace” strategy) if bi-atrial pacing alone was unsuccessful. We evaluated hospital admissions, requirement for DC cardioversions and anti-arrhythmic drug usage during an equal time period pre and post-implant for each patient and subjected these to economic analysis.

Results: During the pre-implant study period there were 46 hospitalisations for atrial fibrillation (excluding elective day-case cardioversion) and 362 hospital bed-days; post-implant, there were eight hospitalisations and 38 bed-days. A similar reduction was seen for DC cardioversions, which reduced from 34 pre-implant to 15 post-implant. Our results are summarised in the table. The saving of 4.82 bed-days per patient per year was reflected in a cost saving of £1421 per patient per year. The reduction in DC cardioversions (cost of each procedure £430) resulted in a total reduction in cost of £54 per patient per year. This translated into a total saving of £7227 of £1475 per patient per year. This would result in further cost saving. One patient had to undergo atrioventricular node ablation due to poor control of atrial fibrillation post-bi-atrial pacing and including the cost of this procedure, the implant cost of our bi-atrial pacing strategy is £153 293 compared with a procedural cost of £191 177, which would have accrued if we had originally adopted an “ablate and pace” strategy. We cannot make a direct comparison between the total costs of these two strategies because we have no data on what the follow-up admission rates would have been for the “ablate and pace” strategy.

Conclusions: Our study has shown that bi-atrial pacing for the long-term management of drug-resistant atrial fibrillation is cost-effective and may be more cost-effective than an “ablate and pace” strategy.

### OPTIMISATION OF CARDIAC RESYNCHRONISATION THERAPY IMPROVES LEFT VENTRICULAR DIASTOLIC FUNCTION

DE Thomas, V Vintila, AG Fraser, ZR Yousef. University Hospital of Wales, Cardiff, UK

There are many physiological mechanisms through which biventricular pacing benefits patients with severe heart failure. To assess the contribution of an improvement in diastolic function, we studied the effects of cardiac resynchronisation therapy on left ventricular filling pressure estimated from the ratio of the velocity of mitral inflow (E) to the velocity of annular motion (e’). This ratio is a validated non-invasive correlate of pulmonary capillary wedge pressure: E/e’ >10, where e’ is measured from the lateral mitral annulus using pulsed tissue Doppler and detects a pulmonary capillary wedge pressure >15 mm Hg with a sensitivity of 97% and a specificity of 78%.

Methods: 17 patients undergoing biventricular pacemaker implantation for conventional indications (ejection fraction <40%, QRS >140 ms) were recruited. Before, 3 months after implantation and 6 months after implantation, they underwent functional assessment (by peak oxygen consumption on exercise (VO2 max), and 6-minute hall walk test (6 mwt)), quality of life assessment and detailed transthoracic echocardiography. At the 3-month visit, patients had optimisation of atrioventricular and interventricular delays, guided by changes in left ventricular stroke volume (estimated from the velocity time integral of systolic flow in the left ventricular outflow tract). Transmitial Doppler and pulsed wave lateral mitral annular velocities were averaged from three consecutive heart beats. A positive response to biventricular pacing was defined as an improvement of >25% in the 6 mwt distance from baseline to 3 months. Values are expressed as mean ± SD.

Results: Of the 17 patients recruited, nine were responders and eight were non-responders. E/e’ was similar between groups at baseline; at 3 months it had fallen by a mean of 21% in responders (p<0.05) compared with 15% in non-responders (NS); at 6 months it had fallen by a further 29% in responders but was unchanged in non-responders (see table). Stroke volume increased by 42% in responders compared with 27% in non-responders (NS). Conventional diastolic indices (E/A ratio, deceleration time, isovolumetric relaxation time, filling time) showed no differences.
Abstract 179

### Results:

The beneficial effects of atrial pacing on paroxysmal atrial fibrillation (PFAF) may be negated by increased ventricular pacing. This was a prospective randomised study evaluating the effect of pacing algorithms that minimise ventricular pacing (managed ventricular pacing, MVP) with and without anti-atrial fibrillation algorithms, on atrial fibrillation burden in patients with PAF.

### Methods:

Using a single blind three-way crossover design, patients with atrial fibrillation burden 1–70%, implanted with pacemakers with MVP capability were enrolled. Three devices and the differing algorithms for reducing ventricular pacing were assessed: Vitatron T70 (refined ventricular pacing (RVP)), Ela Symphony (AAsafeR2) and Medtronic Enhythm (MVF, minimised ventricular pacing). Patients were randomly assigned to MVP with or without preventive atrial fibrillation algorithms or DDDR (atrioventricular delay 150 ms) for 2 months per phase. The primary outcome measure was atrial fibrillation burden. Secondary outcome measures examined the effect of ventricular and atrial pacing on atrial fibrillation burden.

### Results:

84 patients were enrolled, of these 51 (mean age 73.8 ± 8.1, 62.5% men) had an atrial fibrillation burden of 1–70% during the induction phase and completed all study phases. Overall, there was no significant difference in atrial fibrillation burden between the control phase DDDR, 14.1 ± 17.9% and MVP, 13.4 ± 16.6%, or MVP + atrial fibrillation algorithms, 12.1 ± 15.6%, 4.3, p = 0.58. Mean ventricular pacing was significantly higher during the control phase, 83.5 ± 19.6%, than in MVP 14.5 ± 24.5% and MVP + algorithms 20.2 ± 28.3%, p < 0.001. Atrial pacing was greater during MVP + algorithms, 68.9 ± 26.9% versus 51.8 ± 28.9% in DDDR and 48.4 ± 32.2% in MVP alone, p < 0.01. There was no significant correlation between V pacing and atrial fibrillation burden. In the MVP and MVP + algorithms phases there were significant differences in the median values of ventricular pacing between individual devices (see table) Median ventricular pacing for the T70, Symphony and EnRhythm was 13.0%, 3.0% and 1.0%, respectively, in the MVP phase (p = 0.05). Median ventricular pacing for the T70, Symphony and EnRhythm was 14.0%, 5.5% and 2.1%, respectively, in the MVP + algorithms phase (p = 0.04).

Conclusion: MVP algorithms are highly effective in reducing ventricular pacing with significant differences between the available algorithms. Combined, and individually, there is no significant reduction in atrial fibrillation burden with minimal ventricular pacing algorithms. No additional benefit or adverse outcome was found with preventative anti-atrial fibrillation algorithms in combination with minimal ventricular pacing algorithms.


Abstract 180

<table>
<thead>
<tr>
<th></th>
<th>All patients (n = 18)</th>
<th>Responders (n = 10)</th>
<th>Non-responders (n = 8)</th>
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<td>Baseline</td>
<td>14.9 ± 4.9</td>
<td>15.3 ± 5.5</td>
<td>14.4 ± 4.4</td>
</tr>
<tr>
<td>3 Months</td>
<td>12.2 ± 4.5*</td>
<td>12.1 ± 4.3*</td>
<td>12.3 ± 5.0</td>
</tr>
<tr>
<td>6 Months</td>
<td>10.4 ± 3.7††</td>
<td>9.1 ± 3.1††</td>
<td>12.0 ± 4.1††</td>
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</tbody>
</table>

*p < 0.05 baseline versus 3 months, †p < 0.05 baseline versus 6 months, ††p < 0.05 3 months versus 6 months.

Background: Implantable cardioverter defibrillators (ICD) are used for the primary and secondary prevention of sudden cardiac death in high-risk populations. However, very few data exist about the determinants of long-term outcome after ICD implantation.

Aims: To identify predictors of mortality after ICD implantation, to identify predictors of inappropriate shocks due to malignant ventricular arrhythmias and to estimate the incidence of adverse effects and inappropriate shocks.

Methods: 211 patients with an ICD were invited to participate in a heart failure programme and 165 were recruited after written consent. Investigations included 12-lead ECG, signal-averaged ECG, two-dimensional echo, routine blood tests, N-terminal pro-brain natriuretic peptide, 6-minute walking test, ICD interrogation, clinical examination and review of medical therapy. These variables were analyzed by logistic regression and odds ratios calculated, predicting the risk of shocks and mortality.

Results: The patients were followed for a mean of 68 ± 34 months. Mean age was 67 ± 10 years and 83% were men. 76% had coronary disease and 43% had had percutaneous coronary intervention or coronary artery bypass grafting. At implantation, mean ejection fraction was 33 ± 15%. 35% had severe left ventricular impairment and 88% were in NYHA class II or III. 61% were on aspirin/clopidogrel, 32% on warfarin, 47% on amiodarone, 82% on angiotensin-converting enzyme inhibitor/angiotensin receptor blocker, 67% on statins and 86% were taking beta-blockers during the follow-up period. The prevalence of arrhythmias detected on ICD interrogation was as follows: atrial fibrillation in 59 (36%), frequent ventricular extrasystoles in 28 (17%), non-sustained ventricular tachycardia in 61 (37%) and supraventricular tachycardia (SVT) in 36 (22%). 16 (10%) patients

AF, atrial fibrillation; MVP, managed ventricular pacing.
Cardiac autonomic changes are detectable immediately after PVI. The use of short time segments to calculate HRV indices from the surface ECG may allow on-line assessment of autonomic function during ablation and provide an endpoint for such procedures.

Conclusions: Cardiac autonomic changes are detectable immediately after PVI. The use of short time segments to calculate HRV indices from the surface ECG may allow on-line assessment of autonomic function during ablation and provide an endpoint for such procedures.

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**Abstract 182**

**IMMEDIATELY DETECTABLE HEART RATE VARIABILITY CHANGES FOLLOWING ABLATION FOR ATRIAL FIBRILLATION MAY BE AN INDICATION OF VAGAL INJURY**

1PB Lim, 1T Stuber, 1M Koa-Wing, 1M Wright, 1P Kojodjojo, 1NS Peters, 1DW Davies, 1DP Francis, 1P Kanagaratnam. 1St Mary’s Hospital and Imperial College, London, UK; 2St Mary’s Hospital, London, UK

Introduction: Vagal denervation has been suggested to contribute to improved outcome after atrial fibrillation ablation with changes in heart rate variability (HRV) indices from 24-hour ECG recordings cited as a measure of altered autonomic tone. The prolonged recording period precludes the use of HRV indices as an on-line measure of vagal denervation. We hypothesised that HRV alterations should be immediately apparent in short recording segments following ablation at known sites of high vagal innervation such as pulmonary vein ostia.

Methods: Patients undergoing pulmonary vein isolation (PVI) were compared with those having slow pathway ablation for atrioventricular nodal re-entrant tachycardia (AVNRT). Five segments (each 45 seconds) of sinus rhythm from surface ECG recordings were sampled at 1000 Hz (Bard EP, Lowell, USA) and analyzed pre and post-ablation. Using software that calculated RR intervals and RR intervals (by 67.8%) and HF (by 65.1%) despite no change in the RR interval (see table). There were no significant differences in HRV indices after slow pathway ablation for AVNRT (n = 7).

Conclusions: Cardiac autonomic changes are detectable immediately after PVI. The use of short time segments to calculate HRV indices from the surface ECG may allow on-line assessment of autonomic function during ablation and provide an endpoint for such procedures.

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**Abstract 183**

**ELECTROGRAM ANALYSIS USING CARDIAC RIPPLE MAPPING: A NOVEL METHOD FOR THREE-DIMENSIONAL VISUALISATION OF INTRACARDIAC SIGNALS**

NWF Linton, M Koa-Wing, P Kojodjojo, NS Peters, DW Davies, DP Francis, P Kanagaratnam. Imperial College Healthcare NHS Trust, London, UK

Introduction: Isochronal activation mapping of cardiac arrhythmias can be susceptible to errors from the assignment of local activation time and subsequent interpolation between points. We sought to develop a method of three-dimensional (3D) visualisation of “raw” electrograms, incorporating electrogram amplitude that would allow temporospatial appreciation of the quality of intracardiac signals without the assignment of activation times or interpolating data into unmapped regions.

Methods: Mapping algorithms were developed using Matlab software. A 3D surface reconstruction algorithm creates a smooth shell that intersects the imported electrogram locations, using an ellipsoid as a basis for piecemeal bicubic spline interpolation. Electrograms are time-gated using the surface ECG and then displayed at their corresponding coordinates as dynamic moving surface-bars that change in length and colour according to the electrogram voltage–time relationships.

Electro-anatomical data from patients with CARTO maps were imported into the program for validation.

Results: Sinus rhythm activation maps were used to validate sequences in both atria. Unlike isochronal mapping, which only assigns a single timing to each signal (which can lead to misinterpretation of the interpolated map, see fig 1), ripple mapping facilitates interpretation of more complex electrograms with multiple deflections. Figure 2 illustrates a simple example of ripple mapping revealing a far-field ventricular signal. The point of earliest activation is clearly seen.

Conclusions: Ripple mapping allows activation of the myocardium to be tracked visually without previous assignment of local activation times or interpolation into unmapped regions. It is potentially a unique method for displaying double and fractionated electrograms.

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<table>
<thead>
<tr>
<th>AF</th>
<th>AF post</th>
<th>p Value</th>
<th>AVNRT</th>
<th>AVNRT post</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RR (ms)</td>
<td>831.32 ± 175.80</td>
<td>752.86 ± 199.88</td>
<td>0.14</td>
<td>600.65 ± 132.74</td>
<td>661.44 ± 178.04</td>
</tr>
<tr>
<td>SDNN (ms)</td>
<td>21.27 ± 9.43</td>
<td>11.59 ± 6.56</td>
<td>0.036</td>
<td>29.16 ± 8.57</td>
<td>33.59 ± 16.83</td>
</tr>
<tr>
<td>RMSSD (ms)</td>
<td>18.51 ± 12.36</td>
<td>11.44 ± 8.91</td>
<td>0.21</td>
<td>22.83 ± 11.79</td>
<td>18.86 ± 10.97</td>
</tr>
<tr>
<td>Triangular index (ms)</td>
<td>66.45 ± 18.86</td>
<td>43.73 ± 12.01</td>
<td>0.014</td>
<td>85.09 ± 14.09</td>
<td>90.61 ± 38.06</td>
</tr>
<tr>
<td>LF (ms2)</td>
<td>42.55 ± 44.37</td>
<td>13.72 ± 18.87</td>
<td>0.033</td>
<td>137.34 ± 63.89</td>
<td>214.64 ± 159.25</td>
</tr>
<tr>
<td>HF (ms2)</td>
<td>41.77 ± 39.60</td>
<td>14.59 ± 18.86</td>
<td>0.005</td>
<td>71.31 ± 30.31</td>
<td>72.18 ± 51.46</td>
</tr>
</tbody>
</table>

AF, atrial fibrillation; AVNRT, atrioventricular nodal re-entrant tachycardia; HF, high frequency; LF, low frequency; RMSSD, root mean square of successive differences; SDNN, standard deviation normal to normal.
REPOLARISATION RESERVE AND PHYSIOLOGICAL RESTITUTION BY SYMPATHETIC NERVE STIMULATION IN LONG QT MODELS

1R Mantravadi, 2G Salama, 3GA Ng. 1Department of Cardiovascular Sciences, University of Leicester, Leicester, UK; 2Department of Cell Biology Physiology, University of Pittsburgh, Pittsburgh, Pennsylvania, USA; 3University Hospitals of Leicester, Glenfield Hospital, Leicester, UK

Introduction: Restitution kinetics, reduction in repolarisation reserve and dispersion of repolarisation are linked to arrhythmogenesis. However, due to technical difficulties, physiological restitution curves (PRK) have not yet been shown to be linked to repolarisation reserve, a mechanism shown to be involved in the arrhythmogenesis in long QT syndromes.

Methods: We developed a novel neurocardiological model combining isolated innervated Langendorff perfused rabbit heart preparation and optical mapping. Action potential duration (APD) characteristics over 256 sites over the left ventricle were mapped using voltage-sensitive dye di-4ANEPPS. We compared PRK with sympathetic nerve stimulation (SNS) and PRK by pacing alone (without SNS). Both pacing and SNS had identical beat-to-beat changes in activation intervals to correct for rate influence on APD adaptation. Then, we repeated this protocol after creating long QT type repolarisation disorders by treating the hearts with specific ion channel inhibitors HMR1556 (0.5 μmol), E4031 (0.01 μmol), APA (10 nmol), for IKs, IKr, INa inactivation, respectively, in three different experimental subsets. All data were expressed as mean ± SEM and were compared against respective controls for statistical significance, in paired samples using paired t-tests.

Results: With SNS (and pacing), the activation intervals decreased from 407 ± 18 to 269 ± 9 ms and returned to baseline. For exactly the same activation intervals change the APD adaptation was significantly more with SNS compared with pacing alone (ΔAPD% SNS versus pace: 29 ± 1 versus 19 ± 1; p<0.05). ΔAPD SNS versus pace: 64 ± 8 versus 49 ± 7 ms; p<0.05. This difference was due to increased APD adaptation at peak heart rates by SNS over and above that achieved by pacing alone. At the highest plateau heart rates, the slope of the restitution curve was negative in both groups. After ion channel inhibition, SNS driven hearts could not increase the APD adaptation any more than pacing and the PRK loops were similar at the same sites, where differences were seen earlier in the same hearts as controls (ΔAPD% SNS versus pace under HMR1556, E4031 and APA were: 32 ± 2 versus 31 ± 2, 22 ± 4 versus 18 ± 5 and 29 ± 6 versus 28 ± 6, respectively; with all having p = NS). Furthermore, all hearts treated with ion channel inhibitors also showed a dramatic increase in spatial dispersion of repolarisation measured as APD base minus APD apex (control versus ion channel inhibition 16 ± 1 versus −25 ms; p<0.05).

Conclusion: These new neurocardiological studies suggest that the differences between the SNS and pacing PRK loops and their loss with ion channel inhibition points to a possible link between physiological restitution and reduction of repolarisation reserve, suggesting a unified mechanism of vulnerability to arrhythmias in three different long QT syndromes.
MEASUREMENT OF HUMAN VENTRICULAR REPOLARISATION USING NON-CONTACT MAPPING: VALIDATION USING CONTACT UNIPOLAR ELECTROGRAMS

DC Murday, NG Turner, AM Yue, PR Roberts, JM Morgan. Southampton University Hospitals NHS Trust, Southampton, UK

Introduction: Non-contact mapping (NCM) is a potential method of assessing cardiac repolarisation. It provides high density virtual electrogram recordings from the endocardium. The use of NCM to measure activation recovery intervals (ARI) has previously been validated against monophasic action potential recordings. It is suggested that NCM may be more prone to far-field signals. Comparison of ARI using NCM against contact unipolar recordings has not been described.

Methods: Activation times, activation recovery intervals (ARI) and T-wave morphologies were recorded from ventricular contact unipolar electrograms and same-site reconstructed virtual electrograms (using the Ensite 3000 NCM system) in two patients. Recordings during sinus rhythm, ventricular pacing and ventricular ectopic beats were assessed. Measurements were made off-line using a custom-made semi-automated computer program (MatLab 2007a, The Mathworks, Inc), which provides ARI measurements using both the Wyatt and alternative methods. T-wave morphology was categorised as positive, negative or biphasic. For the Wyatt method, ARI was measured between times of dV/dt\textsubscript{min} of the QRS and the dV/dt\textsubscript{max} of the T-wave for all T-wave morphologies. In the alternative method, recovery was determined at the dV/dt\textsubscript{max} of the T-wave for negative T-wave, at the dV/dt\textsubscript{min} of the T-wave for positive T-wave, and at the mean time between dV/dt\textsubscript{max} and dV/dt\textsubscript{min} for biphasic T-wave.

Results: 155 beats were analysed from 19 different ventricular sites. The T-wave morphology category was identical for all beats in both contact and NCM recordings. The difference between contact and NCM activation time was 8 ± 1 ms (mean ± SE). Activation times were correlated (r = 0.72, p < 0.01). Differences between contact ARI and NCM ARI using the Wyatt and alternative method were 0 ± 1 ms and 2 ± 1 ms, respectively. ARI times using either the Wyatt (r = 0.97, p < 0.01) or alternative method (r = 0.93, p < 0.01) were correlated (see table and fig).

Conclusion: There was correlation and a high level of agreement between contact and NCM measurements for all T-wave morphologies. NCM provides results equivalent to contact catheter techniques without evidence of timing errors due to far-field signals. The high density of electrograms available via NCM makes it an ideal tool to examine global ventricular repolarisation and arrhythmogenic potential in humans.

<table>
<thead>
<tr>
<th>T-wave morphology (n)</th>
<th>Timing differences using Wyatt method (ms)</th>
<th>Timing differences using alternative method (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive (49)</td>
<td>-4 ± 3</td>
<td>2 ± 2</td>
</tr>
<tr>
<td>Negative (77)</td>
<td>0.5 ± 1</td>
<td>N/A</td>
</tr>
<tr>
<td>Biphasic (27)</td>
<td>12 ± 3</td>
<td>12 ± 3</td>
</tr>
<tr>
<td>All (153)</td>
<td>0 ± 1</td>
<td>2 ± 1</td>
</tr>
</tbody>
</table>

Abstract 185

ARI, activation recovery interval; NCM, non-contact mapping.
Abstract 187 Table 1

<table>
<thead>
<tr>
<th></th>
<th>PVMC isolated</th>
<th>PVMC conducting</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ablation isolated</td>
<td>19</td>
<td>4</td>
<td>23</td>
</tr>
<tr>
<td>Ablation conducting</td>
<td>1</td>
<td>24</td>
<td>25</td>
</tr>
<tr>
<td>Total</td>
<td>20</td>
<td>28</td>
<td>48</td>
</tr>
</tbody>
</table>

PVMC, pulmonary vein multipolar catheter.

Abstract 187 Table 2

<table>
<thead>
<tr>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>95%</td>
<td>86%</td>
<td>83%</td>
<td>98%</td>
<td>90%</td>
</tr>
</tbody>
</table>

NPV, negative predictive value; PPV, positive predictive value.

Abstract 187

COMPARISON OF SINGLE ABLATION CATHETER VERSUS MULTIPOLAR MAPPING CATHETER FOR ASSESSMENT OF PULMONARY VEIN CONDUCTION


Introduction: Electrical isolation of the pulmonary veins is believed to be a fundamental component of procedural success in left atrial ablation for atrial fibrillation. Confirmation of this may be performed with either a separate pulmonary vein multipolar catheter (PVMC) or simply with the ablation catheter itself. The PVMC is perceived as being more accurate but requires either a separate transseptal puncture or the interchange of catheters through a single sheath. We present data comparing the performance of ablation catheter alone against the gold standard of PVMC for assessment of pulmonary vein conduction.

Methods: 48 assessments were made on 32 pulmonary veins in eight patients (four de novo, four redo) aged 63 ± 4.7 years undergoing left atrial circumferential ablation for atrial fibrillation. For de-novo cases the first assessments of pulmonary vein conduction were made after the initial empiric wide area circumferential ablation. If conduction persisted (according to the PVMC findings) repeat encirclement was performed followed by a second assessment. For repeat procedures the initial assessment was made before any ablation and the second assessment was made after empiric circumferential ablation. PVMC electrograms were not displayed during ablation. Assessment was performed by two electrophysiologists reaching consensus on each occasion with the ablation catheter used first and then PVMC. PVMC recordings were treated as gold standard, any discordance was therefore treated as an error of ablation catheter assessment.

Results: PVMC assessments demonstrated isolation on 20 occasions and conduction in 28 (table 1). Ablation catheter assessments correctly identified conduction in 24/28 and isolation in 19/20. Assessments took place in atrial fibrillation in 20, coronary sinus pacing in seven and sinus rhythm in 21; in this small sample discorances occurred in atrial fibrillation and sinus rhythm but not coronary sinus pacing. Overall, this represents a 10% error rate, a 95% sensitivity and 86% specificity, a positive predictive value of 83% and a negative predictive value of 96% for detecting isolation in pulmonary veins (table 2).

Conclusions: Assessment of pulmonary vein conduction using an ablation catheter alone is inferior to a dedicated PVMC, as a single catheter will miss failure to isolate in 14% of veins. Given the importance of confirming pulmonary vein isolation in treating these patients the additional accuracy of the PVMC justifies the modest degree of added complexity and cost its use brings to the procedure.

Abstract 188

INTERATRIAL SEPTAL THICKNESS AND DIFFICULTY WITH TRANSSEPTAL PUNCTURE DURING CATHETER ABLATION OF ATRIAL FIBRILLATION

DR Tomlinson, N Sabharwal, MJK Yousefzei, Y Bashir, TR Betts. John Radcliffe Hospital, Oxford, UK

Background: A significant proportion of patients require redo procedures for recurrent atrial arrhythmias following left atrial catheter ablation for atrial fibrillation. There are no data on the long-term effects of serial single or multiple transseptal puncture (TSP) on the intra-atrial septum (IAS) structure. On the one hand, instrumentation may result in fibrosis and thickening of the IAS, making future attempts at TSP more difficult and prone to complication; conversely, it may leave IAS defects that facilitate subsequent procedures.

Methods: Retrospective analysis of all patients with transoesophageal echocardiograms (TOE) immediately before first and redo atrial fibrillation ablation procedures undertaken at the John Radcliffe Hospital between September 2004 and November 2007. Ease of TSP was recorded prospectively in the ablation report; once the transseptal sheath had been positioned at the fossa any procedures requiring excessive force or conversion to TOE guidance were reported as difficult. A single observer (NS) assessed IAS thickness using offline analysis of stored TOE images. Measurements from the central IAS point (fossa) were taken at the same point in the cardiac cycle and at a similar insonating angle. Interatrial shunting was assessed using colour flow Doppler.

Results: The study population comprised 40 patients (36 men, four women) with a mean age of 55 years (SD 9). The mean difference in insonating TOE angle between studies was 5° (SD 4). Four patients had a patent foramen ovale (PFO) on both TOE, one had PFO on the first TOE only. The mean change in fossa thickness was +0.3 mm (SD 1.4), range –2.1 to +6.2 mm. Difficulty with TSP was encountered in 10 patients; two during first TSP alone (fossa thickness 1.9 and 1.4 mm), one during first and redo TSP (fossa thickness 2.4 and 3.0 mm) and seven during redo TSP procedures alone. Of this latter group, there was no significant change in fossa thickness and no difference from those patients with straightforward TSP (see fig). TSP difficulty was also not associated with gender, age and hypertension, nor paroxysmal versus persistent atrial fibrillation. However, of the seven patients with difficult TSP during redo procedures, two had diabetes; there were no diabetic patients in the group with straightforward TSP (p = 0.004). One pericardial effusion requiring drainage occurred in a patient with difficult redo TSP.

Conclusions: TSP for left atrial ablation had no effect on the IAS thickness. Although de novo TSP was relatively straightforward, during 20% of repeat procedures there was considerable resistance and difficulty in crossing the IAS; these patients were more likely to have diabetes. Following TSP, structural changes may occur in the IAS, resulting in fibrosis but without significant thickening. During redo TSP, particularly in patients with diabetes, TOE guidance may reduce procedural difficulty and complications.
Methods: 42 consecutive patients (age 73 ± 7.8 years, 29 men) who had atrial RFA for atrial fibrillation at the time of concomitant elective cardiac surgery were assessed. Patients were reviewed at 6 weeks postoperatively and were monitored with 7-day Holters with full disclosure, allowing beat-to-beat analysis, at 6 months post-surgery. Holters were inspected manually and atrial fibrillation recurrence was defined as greater than 30 seconds of atrial fibrillation (ie, sustained atrial fibrillation). Patients accurately documented time and duration of any symptoms and this was correlated with device Holter atrial fibrillation episodes.

Results: 6 months postoperatively and before 7-day Holter monitoring, 31 patients (73.8%) did not demonstrate any evidence of atrial fibrillation recurrence. Holter analysis revealed that the mean atrial fibrillation burden for all patients was 35.8 ± 48.9%, with a mean number of atrial fibrillation episodes per patient of 1.2 ± 2.7. No evidence of atrial fibrillation recurrence was actually observed in 25 patients (59.5%) with 7-day monitoring (p<0.05). Six patients had significant episodes of asymptomatic paroxysmal atrial fibrillation, with a mean atrial fibrillation burden of 14.0%.

Conclusions: Surgical RFA for the treatment of atrial fibrillation, performed at the time of concomitant cardiac surgery, is a highly successful procedure. However, prolonged cardiac monitoring demonstrates a significant number of patients to have asymptomatic episodes of atrial fibrillation not detected by other means. This has important implications for decisions regarding postoperative anti-arrhythmic and anticoagulant usage.

Abstract 190 Table 1

<table>
<thead>
<tr>
<th>QRS duration (msec)</th>
<th>No of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;120</td>
<td>87</td>
</tr>
<tr>
<td>120–149</td>
<td>10</td>
</tr>
<tr>
<td>&gt;150</td>
<td>3</td>
</tr>
</tbody>
</table>

The efficacy of pulmonary vein isolation for atrial fibrillation in patients with implanted permanent pacemakers: the previously paced pulmonary vein isolation (P3VI) study

Introduction: The practice of catheter ablation for atrial fibrillation is increasing rapidly. At present, the efficacy of this procedure is assessed by means of ECG recording, intermittent Holter monitoring and the evaluation of patient symptoms. We sought to evaluate the true efficacy of this procedure in patients with permanent pacemakers capable of continuous cardiac rhythm monitoring.

Methods: 17 patients (aged 62.9 ± 9.2 years, 13 men) underwent an average of 1.5 pulmonary vein isolation procedures in three major UK centres. All patients had previously been implanted with a pacemaker or atrial defibrillator device. Data from the device Holters was downloaded before catheter ablation and at 2 months, 4 months and 6 months post-procedure. The primary outcome measure was atrial fibrillation burden.

Results: Initial atrial fibrillation burden was 30.1 ± 27.9%. After catheter ablation this was significantly reduced at 2 months to 9.0 ± 16.7% (p = 0.03), at 4 months to 6.1 ± 13.2% and at 6 months to 9.4 ± 21.4% (p = 0.05). Only seven of 17 (41%) patients demonstrated no significant recurrence of arrhythmia during follow-up. Quality of life measures showed significant improvement post-ablation. One patient had a pericardial effusion post-procedure requiring pericardiocentesis. Five patients had brief admissions within 30 days of ablation due to arrhythmia recurrence.

Conclusions: Catheter ablation for atrial fibrillation significantly reduces atrial fibrillation burden as assessed by implanted cardiac pacemaker and defibrillator devices. However, at present only a minority of patients are rendered completely arrhythmia free. This has important implications for the use of anti-arrhythmic drugs and anticoagulant usage.
failure patients be more cost-effective? Considering they are in NYHA class III/IV heart failure and on optimal medical therapy.

**Abstract 192**

**REDUCED TWISTING OF THE LEFT VENTRICLE IN PATIENTS WITH SYMPTOMATIC NON-OBSTRUCTIVE HYPERTROPHIC CARDIOMYOPATHY: A STUDY USING TWO-DIMENSIONAL SPECKLE TRACKING IMAGING**

K Abozguia, 1G Nallur Shivu, 1T Phan, 1AR Maher, 1M Nassimizadeh, 2Z Yousef, 1W McKenna, 2H Watkins, 3P Elliott, 1M Frenneaux. 1University of Birmingham, Birmingham, UK; 2University Hospital of Wales, Cardiff, UK; 3The Heart Hospital, London, UK; 4University of Oxford, Oxford, UK

**Introduction:** Speckle tracking echocardiography (STE) is an angle-independent technique that allows the measurements of left ventricular rotation and twist. The aim of this study was to compare left ventricular twisting and untwisting in symptomatic non-obstructive hypertrophic cardiomyopathy (HCM) patients with age-matched controls using STE.

**Methods:** 39 symptomatic non-obstructive HCM patients (27 men, mean age 52 years) and 20 age-matched controls were enrolled. We measured maximal oxygen consumption (VO2 max) and acquired basal, mid and apical left ventricular short-axis images in all patients. STE values were measured and the peak value of left ventricular rotation and rotational rate were obtained at each plane. Left ventricular twisting was defined as the net difference in peak left ventricular torsional velocity between apical and base rotation during systole, whereas left ventricular untwisting was measured in the same manner during diastole.

**Results:** All results were expressed as (mean ± SD). Patients exhibited marked exercise limitation (mean VO2 max 22.1 ml/kg per minute, which was 63 ± 11% of the age and gender predicted maximum), mean left ventricular ejection fraction was 68% (range 55–80%). Left ventricular twisting was significantly lower in HCM patients compared with controls (peak torsion velocity 93.6 ± 60.2 μm/s versus 106.3 ± 38.9 μm/s, p = 0.02; fig 1). Peak torsion was significantly higher in HCM patients (13.2 ± 7.9 μm versus 11 ± 5.6 μm, p = 0.006; fig 2). However, the left ventricular untwisting rate in HCM patients was similar to controls (282.5 ± 47.1 versus 280.6 ± 31.7 p = NS).

**Conclusion:** Despite normal ejection fraction, left ventricular twisting during systole was significantly lower in symptomatic non-obstructive HCM patients compared with controls. However, left ventricular untwisting was not reduced in HCM patients.
Abstract 193 Comparison of aerobic exercise capacity of growth hormone deficient (GHD) patients (grey points) versus healthy controls (black points). LVM, left ventricular mass; VO2max, maximum oxygen consumption.

The results of resting and peak exercise parameters in GHD patients versus healthy controls are detailed in Table 1. Compared with healthy controls, there was no significant difference in aerobic exercise capacity (see fig) or peak cardiac power output (CPO) between the two groups. However, the AGHDA score significantly correlated with peak exercise cardiac index and serum IGF-1 levels correlated with aerobic exercise capacity. Whether GHD is an independent determinant of symptoms and exercise intolerance in heart failure patients requires a direct study by assessing the cardiovascular functional effects of rhGH therapy.

Abstract 193 Results of resting and peak exercise parameters in GHD patients versus healthy controls

<table>
<thead>
<tr>
<th>Parameter</th>
<th>GHD patients</th>
<th>Healthy controls</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>45.8 ± 13.4</td>
<td>48.0 ± 10.1</td>
<td>0.29</td>
</tr>
<tr>
<td>Resting heart rate (bpm)</td>
<td>74.0 ± 9.1</td>
<td>66.5 ± 10.0</td>
<td>0.36</td>
</tr>
<tr>
<td>Resting MAP (mm Hg)</td>
<td>99.3 ± 12.5</td>
<td>96.6 ± 8.1</td>
<td>0.26</td>
</tr>
<tr>
<td>RER</td>
<td>1.06 ± 0.08</td>
<td>1.13 ± 0.07</td>
<td>0.98</td>
</tr>
<tr>
<td>Peak heart rate (bpm)</td>
<td>151.7 ± 21.2</td>
<td>171.1 ± 11.1</td>
<td>0.001</td>
</tr>
<tr>
<td>Peak MAP (mm Hg)</td>
<td>110.5 ± 15.7</td>
<td>123.1 ± 12.6</td>
<td>0.28</td>
</tr>
<tr>
<td>Peak cardiac output ([l/min])</td>
<td>17.9 ± 3.9</td>
<td>16.7 ± 3.5</td>
<td>0.09</td>
</tr>
<tr>
<td>Peak cardiac power (Watts)</td>
<td>4.37 ± 1.05</td>
<td>4.61 ± 1.0</td>
<td>0.25</td>
</tr>
<tr>
<td>Peak VO2max/kg (ml/min/kg)</td>
<td>28.0 ± 7.5</td>
<td>30.4 ± 8.0</td>
<td>0.54</td>
</tr>
</tbody>
</table>

GHD, growth hormone deficient; MAP, mean arterial pressure; RER, respiratory exchange ratio. Results are reported as mean ± SD.

Cardiac history have a reduced quality of life. A hallmark of heart failure is exercise intolerance. Whether growth hormone deficiency is causally related to heart failure symptoms is unknown. As a first step to examine this possibility, we hypothesised that the reduced quality of life in GHD patients relates to impaired cardiovascular performance and reduced levels of cardiorespiratory fitness.

Methods: 18 adult patients with severe GHD awaiting recombinant human growth hormone (rhGH) therapy and without heart failure underwent transthoracic echocardiography and cardiopulmonary exercise testing. Cardiac output was measured non-invasively, using the carbon dioxide-rebreathing method. Cardiac power output was calculated from cardiac output multiplied by mean arterial pressure. Age, BMI and sex-matched sedentary healthy volunteers (110 women and 54 men) served as normal controls.

Results: All patients had severe GHD based on high assessment of growth hormone deficiency in adults quality of life (AGHDA) scores (mean 20, range 12–25). NICE (2003) recommended that high AGHDA scores be the selection criteria for rhGH therapy. Echocardiographic measurements including left ventricular mass, ejection fraction, left and right ventricular diastolic and systolic measurements and the E/A ratio were within the normal reference ranges. Compared with healthy controls, there was no significant difference in aerobic exercise capacity (see fig) or peak cardiac functional capacity (see table). The AGHDA score correlated with the peak exercise cardiac index (R = −0.50, p = 0.03) but no other measure of cardiac performance. There was a significant correlation between serum insulin-like growth factor 1 (IGF-1) and maximum oxygen consumption (VO2max: R = 0.64, p = 0.004), VO2max/body weight (R = 0.78, p = 0.001) and VO2max/lean body mass (R = 0.65, p = 0.003). There was also a significant correlation between the IGF-1 Z score and VO2max/kg (R = 0.52, p = 0.02).

Conclusion: Despite markedly impaired AGHDA scores, our cohort of GHD patients had normal aerobic exercise capacity and cardiorespiratory fitness. However, within the GHD cohort, AGHDA score significantly correlated with peak exercise cardiac index and serum IGF-1 levels correlated with aerobic exercise capacity. Whether GHD is an independent determinant of symptoms and exercise intolerance in heart failure patients requires a direct study by assessing the cardiovascular functional effects of rhGH therapy.
Most sarcomeric mutations that cause hypertrophic cardiomyopathy (HCM) are missense mutations that act as dominant negative alleles by encoding ‘poison polypeptides’. The potential exceptions are mutations in myosin-binding protein C (MyBPC), which frequently encode truncated proteins, suggesting that they may act as null alleles resulting in haploinsufficiency. Distinguishing between these possibilities will be important for understanding the role of this important regulatory protein. However, the limited studies to date on human heart samples have neither detected truncated protein nor documented altered MyBPC stoichiometry. To resolve this we have studied left ventricular muscle samples from patients undergoing surgical myectomy for obstructive HCM and compared these with samples from non-failing (donor) heart muscle. Seven out of 27 myectomy samples were found to contain mutations in MyBPC, with convincing evidence that they were responsible for HCM: two previously described missense alleles (Glu258Lys, Arg502Trp) and five premature terminations (truncating in domains C3, C5, C7 (x2), C10). Western blots were performed using an antibody shown to recognise specifically the N-terminal region (C0–C2) of MyBPC. The MyBPC content was quantified by densitometry and normalised to staining with an anti-actin antibody. No truncated peptides were detected in whole muscle homogenates or the myofibrillar fraction of HCM tissue (including in overloaded gels). However, the overall level of MyBPC in myofibrils was reduced by 24 ± 4% in myofibrils from tissue containing a MyBPC mutation: 0.76 ± 0.04 (n = 59) versus 1.00 ± 0.05 in non-failing (n = 19; p = 0.001) and 1.01 ± 0.05 (n = 24) in non-MyBPC mutant myectomies. Four of the myectomy samples individually showed statistically significant differences from the non-failing group; these included both truncation and missense samples. The absence of detectable lower molecular weight protein suggests that the truncated MyBPC proteins are degraded, arguing against their incorporation in the myofibre and any dominant negative effect. In contrast, the lowered relative level of full-length MyBPC in the myofibre argues strongly for haploinsufficiency as the disease mechanism (potentially for missense as well as truncation alleles). Previous work on the partial extraction of MyBPC suggests that lowered MyBPC stoichiometry would be expected to alter muscle function.

Abstract 196 Table 1

<table>
<thead>
<tr>
<th>Patient demographics and medical history</th>
<th>N = 19</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), median (IQR)</td>
<td>73 (56–78)</td>
</tr>
<tr>
<td>Male</td>
<td>16 (84%)</td>
</tr>
<tr>
<td>NYHA class 3</td>
<td>18 (95%)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>10 (52%)</td>
</tr>
<tr>
<td>Conventional pacemaker (DDD or VVI)</td>
<td>10 (52%)</td>
</tr>
<tr>
<td>Ischaemic heart disease</td>
<td>9 (47%)</td>
</tr>
<tr>
<td>QRS width (ms) mean (SD)</td>
<td>105 (37)</td>
</tr>
<tr>
<td>MDRO GFR (ml/min/1.73 m2) mean (SD)</td>
<td>51 (15.8)</td>
</tr>
<tr>
<td>CKD class 3–5</td>
<td>15 (79%)</td>
</tr>
</tbody>
</table>

CKD, chronic kidney disease; GFR, glomerular filtration rate; IQR, interquartile range; MDRO, modification of diet in renal disease equation; NYHA, New York Heart Association.

Abstract 196 Table 2

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>6 Months</th>
<th>Change, mean (95% CI)</th>
<th>p Value</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEF (%), mean (SD)</td>
<td>23 (8.3)</td>
<td>30 (10.8)</td>
<td>7 (3.7 to 10.7)</td>
<td>&lt;0.001</td>
<td>19</td>
</tr>
<tr>
<td>LVSV (ml), mean (SD)</td>
<td>283 (94)</td>
<td>227 (84)</td>
<td>−56 (−86 to −24)</td>
<td>&lt;0.002</td>
<td>19</td>
</tr>
<tr>
<td>SD LV phase (µ), mean (SD)</td>
<td>89 (27)</td>
<td>61 (29)</td>
<td>−27 (−44 to −12)</td>
<td>&lt;0.002</td>
<td>19</td>
</tr>
<tr>
<td>BNP (pmol/l), mean (SD)</td>
<td>101.6 (72.4)</td>
<td>64.6 (47.7)</td>
<td>−37 (−78.1 to −0.73)</td>
<td>&lt;0.05</td>
<td>18</td>
</tr>
<tr>
<td>MLWHF score, mean (SD)</td>
<td>51 (20)</td>
<td>35 (17)</td>
<td>−16 (−7 to −25)</td>
<td>&lt;0.01</td>
<td>18</td>
</tr>
<tr>
<td>6MWD (m), mean (SD)</td>
<td>243 (68)</td>
<td>302 (85)</td>
<td>59 (28 to 90)</td>
<td>&lt;0.002</td>
<td>16</td>
</tr>
</tbody>
</table>

BNP, brain natriuretic peptide; LVEF, left ventricular ejection fraction; LVSV, left ventricular systolic volume; MLWHF, Minnesota living with heart failure questionnaire; 6MWD, 6-minute walk distance; SD LV, standard deviation of left ventricular phase.
Methods: We studied prospectively 19 patients with systolic dysfunction, NYHA class III symptoms and a prolonged QRS who underwent CRT implantation. All patients had radionuclide ventriculography, a 6-minute walk test, Minnesota living with heart failure questionnaires and plasma brain natriuretic peptide measurements at baseline and after 6 months follow-up. Pacing was adjusted to obtain optimal left ventricular filling and aortic velocity time integral at 1 month using transthoracic echocardiography. Analysis was on an intention to treat basis.

Results: The baseline characteristics of the cohort are detailed in table 1. This is an elderly population with a median age of 75 years and 42% were over 75 years. Fifteen (79%) had moderate renal dysfunction (chronic kidney disease class 3–5). Ten patients (52%) had upgrades of chronic right ventricular pacing and 12 patients (63%) had CRT with an implantable defibrillator. More than half the patients had atrial fibrillation at baseline and one patient required ablation for atrial flutter at the time of implant. Patients were on maximum tolerated medical therapy that included: angiotensin-converting enzyme inhibitors or angiotensin receptor antagonists (100%), beta-blockers (65%), aldosterone antagonists (84%) and high dose diuretics (47%). Left ventricular ejection fraction (LVEF) increased, as did quality of life and 6-minute walk distance. Systolic volume and the standard deviation of left ventricular phase, which is a marker of left ventricular dyssynchrony, decreased (table 2). 13 patients (68%) had an increase of >5% in LVEF as evidence of reverse left ventricular remodelling. There was no significant difference between patients with atrial fibrillation and sinus rhythm or those who had an upgrade from conventional to biventricular pacing. However, the six patients who had atrial fibrillation and an upgrade of chronic right ventricular pacing had a greater mean increase in LVEF at 6 months (12% (1.6) versus 4% (5.6); p<0.001) (see fig).

Conclusions: CRT results in favourable left ventricular remodelling and a reduction in left ventricular dysynchrony in advanced heart failure patients with a prolonged QRS duration. Patients with atrial fibrillation and conventional pacing also derive substantial symptomatic benefit and improvement in left ventricular function with CRT.
on the number of days alive and out of hospital and the cost-effectiveness of home telemonitoring relative to usual care will also be analyzed.

**Results:** A total of 182 patients has been randomly selected with the following baseline demographics: 120 (66%) men, 62 (34%) women, mean age 71 years (SD ± 12 years), 49 (27%) from an ethnic background, 61 (34%) with a measurable ejection fraction have preserved systolic function, 65% were in NYHA class II and 35% in NYHA class III, with no patients being NYHA class I or IV. To date there have been 22 (12%) deaths and 50 (50%) of the patients have had 720 readmissions, of which 50 were non-elective. Follow-up will complete in December 2007 with results available in January 2008.

**Conclusion:** We will present the results of a large UK study of telemonitoring in heart failure, among a typical elderly urban multiethnic population. The event rate overall is high, with the potential relative benefit of telemonitoring considerable. The results of this study will have important implications for the way heart failure care is delivered in the United Kingdom.

### Abstract 198 Table 1

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years (SD)</td>
<td>71.3 (10.5)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>209 (51.6)</td>
</tr>
<tr>
<td>Weight, kg (SD)</td>
<td>76.5 (21.0)</td>
</tr>
<tr>
<td>Sodium, mmol/l (SD)</td>
<td>138.1 (4.5)</td>
</tr>
<tr>
<td>BNP, ng/l (IQR)</td>
<td>887 (413–1671)</td>
</tr>
<tr>
<td>Creatinine, mmol/l (IQR)</td>
<td>112 (91–144)</td>
</tr>
<tr>
<td>eGFR, ml/min (SD)</td>
<td>52.2 (19.1)</td>
</tr>
<tr>
<td>Urea, mmol/l (IQR)</td>
<td>8.3 (6.2–11.9)</td>
</tr>
</tbody>
</table>

BNP, brain natriuretic peptide; eGFR, estimated glomerular filtration rate; IQR, interquartile range.

### Abstract 198 Table 2

<table>
<thead>
<tr>
<th>eGFR (per 10 ml/min change)</th>
<th>HR (± 95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Univariate analysis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>log(urea) (per unit change)</td>
<td>0.82 (0.72 to 0.94)</td>
<td>0.005</td>
</tr>
<tr>
<td>&gt;median urea (versus &lt;median urea)</td>
<td>2.42 (1.55 to 3.80)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Model 1 gFR (per 10 ml/min change)</td>
<td>0.99 (0.81 to 1.22)</td>
<td>0.96</td>
</tr>
<tr>
<td>Model 2 gFR (per 10 ml/min change)</td>
<td>2.37 (1.18 to 4.78)</td>
<td>0.02</td>
</tr>
<tr>
<td>Model 3 gFR (per 10 ml/min change)</td>
<td>0.92 (0.78 to 1.10)</td>
<td>0.36</td>
</tr>
<tr>
<td>Model 4 gFR (per 10 ml/min change)</td>
<td>1.79 (1.08 to 2.97)</td>
<td>0.003</td>
</tr>
</tbody>
</table>

eGFR, estimated glomerular filtration rate; HR, hazard ratio.

**Subjects and Methods:** Consecutive patients admitted between 1 December 2006 and 10 October 2007 with suspected decompen-sated heart failure to the Royal and Western Infirmaries in Glasgow were invited to participate in an ongoing observational study. A confirmed diagnosis of heart failure required typical clinical findings and a brain natriuretic peptide (BNP) level greater than 100 pg/ml. Urea and eGFR were available for all patients. All-cause mortality was the primary outcome measure. Patients were censored if death occurred or at the end of follow-up. Variables were analyzed as continuous when normal distribution assumptions held; otherwise appropriate transformations were applied or data were analyzed as binary (median versus < median). Proportional hazard models were used to calculate hazard ratios for the risk of death. First, both urea and eGFR were analyzed univariately. Second, both variables were entered together to assess the relative importance of each factor on outcome. Finally, the analyses were adjusted for age, sex and BNP with a backwards stepwise method employed for term removal (p > 0.10). Multicollinearity was assessed.

**Results:** 405 patients with clinical and BNP criteria for heart failure were recruited. Follow-up was available for a mean of 162 days (range 2–325) and 63 deaths occurred during this time. eGFR was normally distributed and was analyzed as a linear variable; urea was positively skewed and was analyzed in a linear fashion as log(urea), or as a binary variable. Baseline characteristics are shown in table 1. Univariate analysis demonstrated increasing eGFR associated with a reduced risk of death (table 2). Both >median urea and increases in log(urea) predicted a poor outcome (table 2). Multivariate analysis using both linear covariates demonstrated that log(urea), but not eGFR, predicted mortality (model 1, table 2). A correlation matrix statistic of 0.76 suggested the variables were sufficiently distinct to test within a single model. When the urea concentration was analyzed as a binary variable alongside eGFR, >median urea predicted mortality, with eGFR no longer significantly associated with the outcome (model 2, table 2). Finally, when the analyses were adjusted for age, sex and BNP, log(urea) (model 3) or >median urea (model 4) remained within the multivariate model, whereas eGFR was non-significant and was thus removed from the equation.

**Conclusion:** Elevated urea concentration was more powerful than eGFR at predicting an increased risk of early mortality following admission with heart failure and may be useful at identifying which patients would benefit from intensive monitoring and treatment after discharge from hospital.
term. Whether this represents cardiac deterioration or pump inadequacy in the face of increasing cardiovascular demands is unknown. Hitherto, it was unclear how pregnancy affected peak cardiac function. One way of resolving this issue is by measuring cardiac pump function directly through cardiopulmonary exercise testing.

**Methods:** We performed a longitudinal assessment of 30 healthy women (mean age 33 years) during their third trimester of pregnancy (mean gestation 34 weeks) and 3 months postpartum (non-pregnant state). Central hemodynamic indices, including mean arterial pressure (MAPpk), peak oxygen uptake (VO2pk) and peak cardiac output (COPpk), were measured during symptom-limited maximal cardiopulmonary exercise on a treadmill (weight-bearing exercise). Peak cardiac function was represented by peak exercise cardiac power output, (COPpk = product of COPpk and MAPpk).

**Results:** All participants exercised to cardiopulmonary limits, exceeding their ventilatory threshold (respiratory exchange ratio >1). There were no adverse events secondary to exercise testing. During pregnancy there were highly significant reductions in VO2pk (from 2211 to 2019 ml/m²/min, p<0.001) and exercise duration (from 11.0 to 9.5 minutes, p<0.01). Despite these reductions, there were no significant reduction in COPpk, COPpk and MAPpk (all p>0.05, fig).

**Conclusion:** Maximal cardiopulmonary exercise testing can be safely conducted during pregnancy. Comparing the pregnant and non-pregnant states longitudinally, the reduced exercise ability and aerobic capacity near term was dissociated from preserved cardiac pumping capacity. This illustrates a principle that changes in VO2pk do not necessarily reflect parallel changes in cardiac function.

**200 PEAK CARDIAC POWER, MEASURED NON-INVASIVELY, IS A POWERFUL PREDICTOR OF OUTCOME IN CHRONIC HEART FAILURE**

1TK Lim, 2DM Mancini, 3P Karlin, 2J Haythe, 2W Levy, 1CC Lang. Ninewells Hospital, Dundee, UK; 2Columbia University, New York, New York, USA; 3University of Washington, Washington, DC, USA

**Objectives:** Invasive determination of haemodynamically derived variables (cardiac output response, left ventricular stroke work index (LVSWI), cardiac power) have been described to be better prognostic indicators than peak VO2. Using non-invasive measurements of cardiac output during exercise, we compared the prognostic value of peak cardiac output response, LVSWI and cardiac power to peak VO2 in heart failure patients referred for heart failure and transplant evaluation.

**Methods and Results:** Accordingly, 171 heart failure patients (119 men, aged 53 ± 14 years) underwent bicycle exercise with non-invasive estimation of cardiac output using an inert gas rebreathing method (Innocor, Copenhagen, Denmark). The ejection fraction averaged 24 ± 12%. In 148 patients, an accurate measure of peak cardiac output response was achieved. Peak cardiac power was derived from the product of the peak mean blood pressure and cardiac output divided by 451. LVSWI was derived using an assumed peak pulmonary capillary wedge of 30 mm Hg. Endpoints consisted of death, urgent transplant or left ventricular assisted device implantation. Follow-up averaged 24 months (range 9–36 months). LVSWI was derived using an assumed peak pulmonary capillary wedge of 30 mm Hg. Endpoints consisted of death, urgent transplant or left ventricular assisted device implantation. Follow-up averaged 24 months (range 9–36 months).

Peak cardiac power, measured non-invasively, is an independent predictor of outcome that can enhance the prognostic power of peak VO2 in the evaluation of heart failure patients.

**201 BIOMEPEDANCE ANALYSIS IS MORE SENSITIVE THAN BODY WEIGHT AT DETECTING ASYMPTOMATIC DIURETIC-INDUCED VOLUME CHANGES IN STABLE PATIENTS WITH LEFT VENTRICULAR SYSTOLIC DYSFUNCTION**

MJ Ng Kam Chuen, GYH Lip, RJ MacFadyen. City Hospital, Birmingham, UK

**Background:** Detecting asymptomatic trends to volume overload or dehydration could avoid hospital admission before decompensation in left ventricular systolic dysfunction (LVSD). Current means of volume assessment in LVSD are insensitive and there is a need for better non-invasive methods.

**Methods:** 26 patients (23 men; aged 70.4 ± 7.4 years, range 55–82; left ventricular ejection fraction 24.7 ± 7.3%, range 10–36; New York Heart Association class I–III; body mass index 26.7 ± 5.6 kg/m², range 17.9–38.6; 17 on furosemide 40 mg daily, nine on furosemide 80 mg daily) with stable LVSD were studied over a 7-day protocol. Patients took normal oral diuretic on day 1; diuretic was omitted on days 2, 3, and 4 and was followed by an intravenous injection of 50 mg furosemide on day 4. Normal oral furosemide was resumed on days 5, 6 and 7. Whole body, trunk and right lung bioimpedance analysis (Bodystat Quadscan 4000) and body weight were measured on days 1, 2, 3, 4 and 7.

**Results:** All patients remained asymptomatic throughout the protocol (table). Body weight increased non-significantly from day 1 to day 4 and fell from day 4 to day 7 (p = 0.225). In contrast, whole body, trunk and right lung impedance (Z) reduced significantly during the diuretic withdrawal phase and increased following the resumption of diuretics.

**Conclusion:** Bioimpedance analysis is more sensitive than body weight in defining volume changes in response to diuretic cessation and diuretic-induced volume loss in stable LVSD. Larger studies to assess its use in the practical management of chronic LVSD patients are justified.

**202 DETECTION OF "OCCULT" LEFT VENTRICULAR THROMBUS USING CONTRAST-ENHANCED CARDIAC MAGNETIC RESONANCE IN PATIENTS WITH IMPAIRED VENTRICULAR FUNCTION UNDERGOING CORONARY ARTERY BYPASS SURGERY**

1TJ Pegg, 2D Karamitoss, 1JR Arnold, 1J Francis, 2D Taggart, 2S Neubauer, 2JB Selvanayagam. 1University of Oxford, Oxford, UK; 2Flinders Medical Centre, Adelaide, Australia

**Background:** Left ventricular systolic dysfunction is associated with a two to threefold increase in the risk of stroke. Although the pathophysiology underlying this association is complex, the presence of left ventricular thrombus (LVT) is thought to contribute at least partly to this increased risk. More recently, changes in body weight and impedance to 5 KHz current (Z 5 KHz) in response to diuretic-induced volume changes in stable patients with left ventricular systolic dysfunction

**Abstract 201** Changes in body weight and impedance to 5 KHz current (Z 5 KHz) in response to diuretic-induced volume changes in stable patients with left ventricular systolic dysfunction

<table>
<thead>
<tr>
<th>Parameter</th>
<th>n</th>
<th>Day 1 (baseline) mean (SD)</th>
<th>Day 4 (diuretic withdrawal) mean (SD)</th>
<th>Day 7 (diuretic resumption) mean (SD)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td>26</td>
<td>81.2 (19.0)</td>
<td>82.9 (19.0)</td>
<td>82.1 (19.0)</td>
<td>0.225</td>
</tr>
<tr>
<td>d Z 5 KHz (Ci)</td>
<td>25</td>
<td>537 (81)</td>
<td>518 (81)</td>
<td>533 (84)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>p Z 5 KHz (Ci)</td>
<td>25</td>
<td>121 (16)</td>
<td>117 (12)</td>
<td>118 (13)</td>
<td>0.001</td>
</tr>
<tr>
<td>n Z 5 KHz (Ci)</td>
<td>25</td>
<td>54 (8)</td>
<td>50 (9)</td>
<td>55 (11)</td>
<td>0.009</td>
</tr>
</tbody>
</table>

d, whole body; p, trunk; n, right lung.
contrast-enhanced cardiac magnetic resonance imaging (CE-CMR) has emerged as an important non-invasive tool for the assessment of heart failure and has the capability to diagnose LVT with greater ease than transthoracic echocardiography (TTE).

**Aims:** To examine the prevalence of LVT as detected by CE-CMR in a consecutive series of patients with chronic left ventricular dysfunction referred for coronary artery bypass surgery (CABG). To compare the rates of detection of LVT between CMR and TTE/ventriculography in this population of patients.

**Methods:** 44 patients with impaired ventricular function (CMR ejection fraction <50%) scheduled for isolated elective CABG underwent conventional left ventricular assessment (TTE and left ventricular angiography) as part of the clinical preoperative assessment and CMR as part of a research protocol. CE-CMR images were acquired by a 1.5 Tesla Siemens Sonata scanner in three long axis planes using steady state free precession imaging (flip angle 60° TE/TR 1.6/700 TI 450 ms) or ultrafast gradient echo imaging (flip angle 25° TE/TR 4.3/750 TI 450 ms) following a bolus injection of Omniscan 0.1/mmol/kg body weight. The CMR images were analyzed for the presence of LVT by two blinded observers working in consensus. LVT was defined as a filling defect characteristically present at the apex, or associated with an area of wall motion abnormality that was seen in two image planes. Artefact was characterised by a filling defect seen within the wall of the myocardium (no-reflow phenomenon) or was visualised in only one plane.

**Results:** The overall mean age was 66 ± 8 years and 93% were men. Eight out of 44 patients (18%) had LVT identified by CE-CMR. Patients with LVT tended to have a lower ejection fraction and increased left ventricular volumes; however, none of these comparisons were statistically significant, see table. Patients with LVT were significantly younger (61 ± 10 years) than patients in whom thrombus was not identified (67 ± 7 years) p = 0.03, table. Logistic regression analysis demonstrated age to be the only predictor for LVT, with younger age indicating a higher risk. Conventional imaging identified the presence of LVT by two blinded observers working in consensus. LVT was defined as a filling defect characteristically present at the apex, or associated with an area of wall motion abnormality that was seen in two image planes. Artefact was characterised by a filling defect seen within the wall of the myocardium (no-reflow phenomenon) or was visualised in only one plane.

**Conclusions:** LVT is difficult to diagnose by conventional imaging techniques and CE-CMR may play a role in the preoperative assessment of this group, both for viability assessment and LVT detection. LVT was more likely to be present in younger patients presenting with heart failure and factors that are associated with premature ischaemic heart disease may also influence the prevalence of LVT.

### Abstract 202

<table>
<thead>
<tr>
<th></th>
<th>LVT-positive</th>
<th>LVT-negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>61 ± 10</td>
<td>67 ± 7*</td>
</tr>
<tr>
<td>Male %</td>
<td>100 (8/8)</td>
<td>92 (33/36)</td>
</tr>
<tr>
<td>Smoking %</td>
<td>25 (2/8)</td>
<td>8 (6/36)</td>
</tr>
<tr>
<td>Diabetes %</td>
<td>38 (3/8)</td>
<td>33 (12/36)</td>
</tr>
<tr>
<td>LVEF %</td>
<td>37 ± 14</td>
<td>39 ± 11</td>
</tr>
<tr>
<td>LVEDV (ml/m²)</td>
<td>136 ± 40</td>
<td>114 ± 31</td>
</tr>
<tr>
<td>LVESV (ml/m²)</td>
<td>89 ± 41</td>
<td>72 ± 31</td>
</tr>
<tr>
<td>Warfarin</td>
<td>25 (2/8)</td>
<td>6 (2/36)</td>
</tr>
<tr>
<td>EURO score</td>
<td>7.9 ± 4.6</td>
<td>10.3 ± 9</td>
</tr>
</tbody>
</table>

LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; LVESV, left ventricular end-systolic volume; LVT, left ventricular thrombus.

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**Abstract 203**

**LEFT AND RIGHT VENTRICULAR TISSUE VELOCITIES ARE REDUCED IN HYPERTROPHIC CARDIOMYOPATHY BUT NOT IN ATHLETE’S HEART**

1SE Petersen, 1LE Hudsmith, 1M Ali, 1JM Francis, 1M Jerosch-Herold, 1M Markl, 1AA Young, 2MD Robson, 2H Watkins, 2S Neubauer. 1Department of Cardiovascular Medicine, John Radcliffe Hospital, Oxford, UK; 2Brigham and Women’s Hospital, Department of Radiology, Cardiovascular Imaging Section, Boston, Massachusetts, USA; 3University Hospital Freiburg, Department of Radiology, Medical Physics, Freiburg, Germany; 4University of Auckland, Department of Anatomy, Auckland, New Zealand

**Introduction:** Left ventricular hypertrophy due to athlete’s heart and hypertrophic cardiomyopathy (HCM) can be difficult to distinguish clinically and can affect both ventricles. Cine phase contrast velocity magnetic resonance imaging (tissue phase
Abstract 203 Myocardial velocities adjusted for covariates. White, control; light grey, athlete’s heart; dark grey, hypertrophic cardiomyopathy. LV, left ventricle; RV, right ventricle. * and # denote statistical significance for hypertrophic cardiomyopathy versus controls and hypertrophic cardiomyopathy versus athlete’s heart, respectively, with the number of symbols representing the significance level p<0.05, **/#/# p<0.01, ***/###/## p<0.001.

segmented gradient echo sequence for the analysis of myocardial velocities with high spatial resolution at 1.5 Tesla. Peak systolic and diastolic radial and longitudinal velocities in both the left and right ventricle were determined. Velocities were averages of a mid-ventricular short axis slice with the exception of left ventricular longitudinal velocities, which are based on averages of basal short axis slices. Left and right ventricular masses and volumes were determined with standard steady state free precession cine imaging. A univariate general linear model with fixed effects for group and covariates, including age, heart rate, and appropriate end-diastolic ventricular or right ventricular dimensions was used.

**Results:** Myocardial mass indexed to body surface area (g/m²) was significantly higher in HCM (80 ± 26, p<0.001) and athletes (83 ± 17, p<0.001) when compared with controls (61 ± 11) in the left ventricle, but the right ventricular mass index was only significantly increased in athletes (26 ± 4 versus controls: 21 ± 4, p = 0.009). In HCM, but not in athletes, radial and longitudinal left ventricular peak diastolic velocities were significantly reduced when compared with controls (fig). There was a 27% lower right ventricular peak longitudinal diastolic velocity in HCM compared with controls (p<0.001), but systolic radial and longitudinal and diastolic radial right ventricular myocardial velocities were not different among the groups.

**Conclusions:** Left ventricular hypertrophy leads to reduced diastolic left ventricular myocardial velocities in HCM, but not athletes. TPM also allows an assessment of right ventricular myocardial velocities and in HCM the right ventricular relaxation pattern was abnormal even in the absence of significant right ventricular hypertrophy. TPM may help differentiate athlete’s heart from HCM in clinically difficult cases.

### 204 DIAGNOSTIC YIELD IN FIRST DEGREE RELATIVES OF VICTIMS OF SUDDEN ADULT DEATH SYNDROME FOLLOWING SYSTEMATIC CLINICAL EVALUATION IN AN EXPERT SETTING

**Objectives:** Sudden adult death syndrome (SADS) accounts for at least 4% of all sudden cardiac deaths in the United Kingdom. Most causal disorders are potentially inherited. However, routine genetic assessment of relatives of victims of SADS is not widely available in the United Kingdom. Given the genetic heterogeneity and incomplete understanding of conditions implicated in SADS, a negative genetic test cannot exclude a familial disorder. The aim of this study was to identify the prevalence of familial cardiac disorders in first degree relatives of SADS victims based on systematic, purely clinical evaluation.

**Methods:** Between March 2006 and September 2007, 22 families of victims of SADS were evaluated in a tertiary inherited cardiac clinic. All victims’ hearts were examined by an expert cardiac pathologist and a structural cause was excluded. A total of 71 individuals underwent comprehensive cardiac clinical evaluation, consisting of 12-lead ECG, echocardiography, exercise stress testing, 24-hour Holter and, when applicable, an Amilase provocation test and/or cardiac magnetic resonance scan. All investigations were interpreted by a cardiac expert in SADS.

**Results:** All family members had a structurally normal heart. Of the 22 families, 14 (64%) had objective evidence of an ion channel. In particular, 11 (79%) had clinical evidence of the Brugada phenotype either on resting ECG or after amilase provocation and three (21%) demonstrated clinical manifestation of the long QT syndrome. A total of 23 of 71 (32%) asymptomatic family members were identified with an ion channel disorder.

**Conclusions:** Systematic clinical evaluation of families of victims of SADS in an expert setting is associated a high diagnostic yield (64%). In our series, ion channel disorders account for almost
two-thirds of all cases of SADS. The potential role of genetic testing further increasing diagnostic yield remains to be elucidated.

**205 VENTRICULAR HYPERTROPHIC RESPONSE PRECEDES VENTRICULAR CAVITY DILATATION IN RESPONSE TO INCREASING BODY MASS INDEX**


**Introduction:** Cardiovascular magnetic resonance (CMR) imaging is a modality ideally suited to the study of the cardiovascular system in the setting of obesity, as it is not subject to the same restrictions of acoustic window that occur in echocardiography. We used CMR to investigate the traditional hypothesis that in obesity compensatory ventricular hypertrophy occurs as a result of increased wall stress imposed by cavity dilatation in response to increased blood volume. We tested the alternative hypothesis that leptin, an adipokine known to cause ventricular hypertrophy, may initiate the cascade of events leading to a hypertrophic response.

**Methods:** 88 female subjects without identifiable cardiovascular risk factors (BMI range 18.7–59.2 kg/m²), were separated into quartiles; normal (BMI 21.2 ± 1.6), overweight (BMI 28.3 ± 2.2), obese (BMI 34.7 ± 2.0) and severely obese (BMI 45.0 ± 4.7). All subjects underwent CMR at 1.5 Tesla to determine left and right ventricular mass, end-diastolic volume and ejection fraction. Fasting blood samples for glucose (mmol/l), cholesterol (mmol/l), insulin (IU/l) and leptin (ng/ml) were taken on the day of scanning.

**Results:** All quartiles were well matched for age, height, blood pressure, glucose and cholesterol. All subjects were normotensive (systolic blood pressure 121 ± 11 mm Hg, diastolic blood pressure 74 ± 8 mm Hg), normoglycaemic (5.0 ± 0.6 mmol/l) and normocholesterolaemic (5.0 ± 0.7 mmol/l) on the day of scanning. As expected, BMI correlated positively with left and right ventricular mass as well as left and right ventricular end-systolic and end-diastolic volumes. However, on transition from normal to overweight, a significant left and right ventricular hypertrophic response (left ventricular: 78 ± 11 g versus 103 ± 16, p < 0.001; right ventricular: 26 ± 7 g versus 40 ± 11 g, p < 0.001) was observed in the absence of cavity dilatation (left ventricular end-diastolic volume: 119 ± 15 versus 121 ± 21 ml, p > 0.99; right ventricular end-diastolic volume: 131 ± 17 versus 130 ± 24; p > 0.99). Furthermore, significant increases in serum leptin levels occurred at this pre-obese stage (15.6 ± 19 versus 36.5 ± 22 ng/ml; p = 0.015) (see fig).

**Conclusion:** In a cohort of healthy female subjects with a wide range of BMI, left and right ventricular hypertrophy precedes cavity dilatation in pre-obese individuals, whereas in manifest obesity, both cavity dilatation and ventricular hypertrophy ensue. Elevated leptin levels may be responsible for this early effect on ventricular mass in response to increased body weight. This suggests that left and right ventricular adaptive changes to increasing fat mass occur in two phases, an early, predominantly leptin-mediated, hypertrophic response with modest weight gain, and a later mixed endocrine-volumetric response characterised by cavity dilatation and wall stress-induced eccentric hypertrophy. Cardiovascular mortality has been shown to be higher in overweight pre-obese individuals than normal weight individuals, and leptin-induced left and right ventricular hypertrophy may be one potential mechanism for this.

**Abstract 205**

BMI, body mass index; EDV, end-diastolic volume; LV, left ventricular; RV, right ventricular.

**206 VENTRICULAR STRUCTURAL CHANGES IN SUBJECTS WITH SEVERE OBESITY IN THE ABSENCE OF CARDIOVASCULAR RISK FACTORS ARE REVERSIBLE WITH SIGNIFICANT WEIGHT LOSS: A 1-YEAR FOLLOW-UP STUDY**


**Introduction:** The obesity epidemic is escalating worldwide and if present trends continue is set to become the primary cause of cardiovascular disease. Studies have shown that ventricular hypertrophy is a prominent feature of the cardiometabolic syndrome and is associated with increased cardiovascular risk. However, it is unclear whether ventricular hypertrophy in severe obesity is reversible with significant weight loss. This study aimed to investigate the reversibility of ventricular hypertrophy in severe obesity with significant weight loss.

**Methods:** 20 subjects with severe obesity (BMI > 35 kg/m²) and without identifiable cardiovascular risk factors were included in this study. All subjects underwent CMR at baseline and after 1 year of significant weight loss (≥ 10% of initial body weight). Left and right ventricular mass, end-diastolic volume and ejection fraction were determined at baseline and follow-up.

**Results:** All subjects were normotensive (systolic blood pressure 121 ± 11 mm Hg, diastolic blood pressure 74 ± 8 mm Hg), normoglycaemic (5.0 ± 0.6 mmol/l) and normocholesterolaemic (5.0 ± 0.7 mmol/l) at baseline and follow-up. BMI correlated positively with left and right ventricular mass as well as left and right ventricular end-systolic and end-diastolic volumes. However, on transition from normal to overweight, a significant left and right ventricular hypertrophic response (left ventricular: 78 ± 11 g versus 103 ± 16, p < 0.001; right ventricular: 26 ± 7 g versus 40 ± 11 g, p < 0.001) was observed in the absence of cavity dilatation (left ventricular end-diastolic volume: 119 ± 15 versus 121 ± 21 ml, p > 0.99; right ventricular end-diastolic volume: 131 ± 17 versus 130 ± 24; p > 0.99). Furthermore, significant increases in serum leptin levels occurred at this pre-obese stage (15.6 ± 19 versus 36.5 ± 22 ng/ml; p = 0.015) (see fig).

**Conclusion:** In a cohort of healthy female subjects with a wide range of BMI, left and right ventricular hypertrophy precedes cavity dilatation in pre-obese individuals, whereas in manifest obesity, both cavity dilatation and ventricular hypertrophy ensue. Elevated leptin levels may be responsible for this early effect on ventricular mass in response to increased body weight. This suggests that left and right ventricular adaptive changes to increasing fat mass occur in two phases, an early, predominantly leptin-mediated, hypertrophic response with modest weight gain, and a later mixed endocrine-volumetric response characterised by cavity dilatation and wall stress-induced eccentric hypertrophy. Cardiovascular mortality has been shown to be higher in overweight pre-obese individuals than normal weight individuals, and leptin-induced left and right ventricular hypertrophy may be one potential mechanism for this.

Abstract 206

BMI, body mass index; EDV, end-diastolic volume; LV, left ventricular; RV, right ventricular.
morbidity and mortality in the next decade. Obesity has been linked to a spectrum of cardiovascular abnormalities from subclinical changes in cardiac structure to overt heart failure and has been linked to increased cardiovascular mortality. Obesity without associated co-morbidity has been shown to cause increased ventricular mass and cavity dilatation and is associated with increased mortality. Our hypothesis was that these changes are, at least partly, reversible following significant weight loss over one year.

**Method:** Forty-four obese (average BMI 38.6 ± 7.2 SD) and 25 age and sex-matched controls with no cardiac risk factors (BMI 21.9 ± 1.8 SD) underwent cardiac magnetic resonance imaging at 1.5 Tesla to determine left ventricular and right ventricular mass, volumes and ejection fraction. No difference in fasting glucose, cholesterol or blood pressure was seen between normal and obese subjects. There were no significant differences in fasting glucose (5.2 ± 0.6 versus 4.9 ± 0.4 mmol/l, p = 0.10), cholesterol (5.0 ± 0.8 versus 5.3 ± 0.9 mmol/l, p = 0.27), systolic blood pressure (122 ± 13 versus 115 ± 10 mm Hg, p = 0.10) or diastolic blood pressure (76 ± 8 versus 73 ± 8 mm Hg, p = 0.09) between obese and normal weight subjects, with all measurements remaining in the normal range. Twenty obese subjects underwent repeat imaging after a one-year period of weight loss (14 supervised diet, six R-en-Y gastric bypass, average weight loss 21 ± 17 kg, 19% of total body weight).

**Results:** Obesity was associated with elevated left and right ventricular mass (left ventricular 126 ± 28 versus 91 ± 24 g; p<0.001; right ventricular 54 ± 11 versus 25 ± 7; p<0.001), elevated end-diastolic volume (left ventricular 146 ± 20 versus 120 ± 22 ml; p<0.001; right ventricular 159 ± 22 versus 133 ± 28; p<0.001), elevated end-systolic volume (left ventricular 47 ± 11 ml versus 57 ± 10; p<0.01; right ventricular 61 ± 13 ml versus 51 ± 15; p<0.01). Left ventricular and right ventricular ejection fraction were similar between control and obese groups (left ventricular p = 0.43, right ventricular p = 0.72). After weight loss, there was a significant reduction in left and right ventricular mass (left ventricular by 14 ± 10 g; p<0.001; right ventricular by 21 ± 9 g; p<0.001) and both left and right ventricular end-diastolic volume (left ventricular by 15 ± 10 ml; p<0.001; right ventricular by 10 ± 15 ml; p = 0.01) and end-systolic volume (left ventricular by 6 ± 10 ml; p = 0.02). Ejection fraction was unchanged with weight loss (left ventricular p = 0.26, right ventricular p = 0.52) (see fig).

**Discussion:** Left ventricular hypertrophy is linked to increased morbidity and all-cause mortality; therefore understanding the various mechanisms responsible for reversal of left ventricular hypertrophy is of great clinical importance. Cardiovascular mortality has been shown to be higher in obese individuals than normal weight individuals, and left ventricular hypertrophy may be one potential mechanism for this. Here we have shown in subjects with obesity, in the absence of identifiable cardiac risk factors, that ventricular hypertrophy and ventricular dilatation were partly reversible after a one year period of significant weight loss.

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**DO CHOLESTEROL LEVELS INFLUENCE LONG-TERM HEART FAILURE OUTCOME IN POST-INFARCT PATIENTS WITH MODERATE TO SEVERE LEFT VENTRICULAR SYSTOLIC DYSFUNCTION?**

1R Sankaranarayanan, 2M A James, 3H Gonna, 2S Burtchaell, 2R Holloway. 1Royal Blackburn Hospital, Blackburn, UK; 2Taunton and Somerset Hospital, Taunton, UK

**Objective:** Although statins are known to have beneficial effects in ischaemic heart disease through pleiotropic mechanisms, their influence on heart failure is not clearly defined. It also remains to be established whether excessive cholesterol lowering could actually be detrimental to heart failure outcome. We therefore conducted this study to analyze the effects of statins and cholesterol levels on long-term heart failure outcome in post myocardial infarction (MI) patients with moderate to severe heart failure.

**Methods:** We enrolled 500 consecutive patients (358 men,142 women) admitted to our coronary care unit with a diagnosis of acute MI between March 2000 and March 2002. Patients with a left ventricular ejection fraction (LVEF) of <40% were retrospectively analyzed according to whether they were on a statin or not. Their heart failure outcome excluding further ischaemic events, ie, heart failure admissions and death due to heart failure, as well as annual cholesterol levels were evaluated. Follow-up was between 4.5 and 6.4 years with a mean follow-up of 5.5 years.

**Results:** 339/500 patients (68%) had LVEF of <40%. Of these, 249 were on a statin and 90 were not on a statin. Patients discharged on a statin were younger with a mean age of 67 years compared with the non-statins (mean age 75 years; p<0.001). Mean baseline cholesterol levels were significantly higher in the statin group (p<0.001), whereas the non-statin group had a significantly higher mean cholesterol level at 1 year (p<0.001) and subsequent years as shown in table 1. Patients with heart failure events (heart failure admissions or deaths) had higher mean cholesterol (p = 0.05) in the

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Statin Group</th>
<th>Non-Statin Group</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean cholesterol (mmol/l)</td>
<td>6.4 ± 1.1</td>
<td>5.8 ± 1.0</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

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EDV, end-diastolic volume; LV, left ventricular; LVEF, left ventricular ejection fraction; RV, right ventricular; RVEF, right ventricular ejection fraction.
Abstract 207 Table 1

<table>
<thead>
<tr>
<th>Time</th>
<th>Mean cholesterol level in statin group</th>
<th>Mean cholesterol level in no-statin group</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>5.76</td>
<td>4.68</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>1 Year</td>
<td>4.17</td>
<td>4.76</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2 Years</td>
<td>4.32</td>
<td>4.55</td>
<td>0.10</td>
</tr>
<tr>
<td>3 Years</td>
<td>4.42</td>
<td>4.62</td>
<td>0.27</td>
</tr>
<tr>
<td>4 Years</td>
<td>4.38</td>
<td>4.43</td>
<td>0.76</td>
</tr>
<tr>
<td>5 Years</td>
<td>4.21</td>
<td>4.42</td>
<td>0.25</td>
</tr>
</tbody>
</table>

Abstract 207 Table 2

<table>
<thead>
<tr>
<th>Time</th>
<th>Mean cholesterol level in patients with heart failure events</th>
<th>Mean cholesterol level in patients without heart failure events</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>5.3</td>
<td>5.6</td>
<td>0.22</td>
</tr>
<tr>
<td>1 Year</td>
<td>4.6</td>
<td>4.2</td>
<td>0.05</td>
</tr>
<tr>
<td>2 Years</td>
<td>4.4</td>
<td>4.4</td>
<td>0.8</td>
</tr>
<tr>
<td>3 Years</td>
<td>4.7</td>
<td>4.4</td>
<td>0.15</td>
</tr>
<tr>
<td>4 Years</td>
<td>4.7</td>
<td>4.4</td>
<td>0.26</td>
</tr>
<tr>
<td>5 Years</td>
<td>4.5</td>
<td>4.2</td>
<td>0.19</td>
</tr>
</tbody>
</table>

Background: The main symptom in patients with heart failure and normal ejection fraction is breathlessness on exertion but there is little information on the functional abnormalities that may develop on exercise and that may be underlying the symptoms. We hypothesised that exercise-induced derangements are more relevant to the genesis of symptoms and diagnosis than any resting echocardiographic values and therefore have conducted exercise echocardiography studies with full tissue Doppler imaging (TDI) and two-dimensional (2D) echocardiography to assess systolic and diastolic function both at rest and on exercise.

Methods: Patients with a clinical diagnosis of heart failure and normal ejection fraction patients on exercise, with a failure to increase both systolic longitudinal function and early diastolic filling. Exercise echocardiography adds valuable information for the management and diagnosis of these patients.

Conclusions: This study demonstrates that statins improve long-term heart failure outcome in post-MI patients with left ventricular ejection fraction <40% and this effect seems to be independent of serum cholesterol levels after the first year post-MI.

ABNORMAL LEFT VENTRICULAR SYSTOLIC AND DIASTOLIC FUNCTION ON EXERCISE IN PATIENTS WITH HEART FAILURE AND NORMAL EJECTION FRACTION

YI Tan, 2WG Wenzelburger, 2ESP Lee, 2G Hetlile, 2G Mahadavain, 1UK Williams, 2F Leyva, 2MP Frenneaux, 2JE Sanders. 1University of Birmingham, Birmingham, UK; 2University Hospital of North Staffordshire, Stoke on Trent, UK; 3Good Hope Hospital, Birmingham, UK

Background: The main symptom in patients with heart failure and normal ejection fraction is breathlessness on exertion but there is little information on the functional abnormalities that may develop on exercise and that may be underlying the symptoms. We hypothesised that exercise-induced derangements are more relevant to the genesis of symptoms and diagnosis than any resting echocardiographic values and therefore have conducted exercise echocardiography studies with full tissue Doppler imaging (TDI) and two-dimensional (2D) echocardiography to assess systolic and diastolic function both at rest and on exercise.

Methods: Patients with a clinical diagnosis of heart failure and normal ejection fraction and treated with diuretics were examined. Standard mitral valve inflow velocities (E and A), TDI measurements of mitral annular velocities in systole (Sm) and early diastole (Em) were taken at rest and exercise (submaximal to onset of dyspnoea). Both Sm and Em are reliable indices of longitudinal systolic and diastolic function, which are a major component of global function and normally increase on exercise. E/Em an index of left ventricular filling pressures was derived. These measurements were compared with age-matched asymptomatic controls. Images were analyzed off-line.

Results: 21 patients (12 women, aged 71 ± 7 years, BMI 31 ± 4, left ventricular ejection fraction 61 ± 5%) and 18 controls (14 women, aged 67 ± 6 years, BMI 26 ± 4, left ventricular ejection fraction 61 ± 8%) who had adequate images and satisfactory heart rate response (100 bpm) were included for analysis. Sm was comparable in both groups at rest; however, during exercise Sm increased by only 15% in patients compared with 48% in controls, a statistically significant difference (p = 0.019). Similarly, although both E and Em at rest were similar in both groups Em increased by 51% in patients and 89% in controls (difference p = 0.005). The estimated filling pressure, E/Em, increased more on exercise in the patients than in controls (11 ± 4 versus 9 ± 2, p = 0.059).

Conclusions: Exercise echocardiography revealed significant abnormalities of both systolic and diastolic function in heart failure and normal ejection fraction patients on exercise, with a failure to increase both systolic longitudinal function and early diastolic filling. Exercise echocardiography adds valuable information for the management and diagnosis of these patients.

208 INVESTIGATION OF RELATIONSHIPS BETWEEN CIRCULATING ENDOTHELIAL PROGENITOR CELL NUMBERS, CARDIAC ALLOGRAFT VASCULOPATHY AND DONOR HEART AGE IN CARDIAC TRANSPLANT RECIPIENTS

HE Thomas, 2G Parry, 1JD Dark, 1HM Arthur, 1BD Keavney. 1University of Newcastle, Newcastle upon Tyne, UK; 2Freeman Hospital, Newcastle upon Tyne, UK

Introduction: Cardiac allograft vasculopathy (CAV) is the principal reason for cardiac transplant failure in the long term and is the leading cause of death after the first year. Endothelial progenitor cells (EPC) are circulating bone marrow-derived mononuclear cells that have the capacity to differentiate into endothelial cells and contribute to vascular repair. A single small previous study (15 patients) suggested that CAV may be associated with reduced EPC, but that study took no account of donor heart age, a major risk factor for CAV. We have studied this relationship in a larger cohort, with more precise matching of patients for factors known to affect EPC and utilising a comprehensive flow cytometry-based EPC detection method.

Methods: We identified cardiac transplant patients with and without CAV (17 pairs) who were matched for factors known to influence EPC numbers: recipient sex, recipient age (within 5 years), time since transplant (within 3 years), aetiology of pretransplant disease, statin or angiotensin-converting enzyme inhibitor therapy, smoking, renal impairment (creatinine >250 µmol/l) and diabetes mellitus. CAV was defined angiographically as >20% stenosis of a main branch epicardial artery. We also identified 64 patients (32 pairs), similarly matched who had discordant donor heart ages by at least 20 years. EPC were quantified in these patients using flow cytometry analysis of whole blood, following the acquisition of 60 000 events in the lymphocyte gate. We measured absolute counts (using fluorescent beads) of cells expressing all the surface marker combinations of CD34, CD133 and kinase domain receptor (KDR), which have previously been used to define EPC. EPC counts were analyzed using paired t-tests following logarithmic transformation.

Results: The baseline clinical and laboratory characteristics of the study patients were similar in each group with no statistically significant differences (see table). There were no significant
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CAV  
(n = 17)  
No CAV  
(n = 17)  
Old donor  
(n = 32)  
Young donor  
(n = 32)

Age, years (mean ± SD)  
55.6 ± 14  
56.2 ± 14  
57.5 ± 13.6  
58.3 ± 12.9
Male sex, no (%) of patients  
16 (94)  
16 (94)  
31 (97)  
31 (97)
Aetiology, no (%) of patients  
HD  
10 (59)  
10 (59)  
21 (66.7)  
21 (66.7)
Aetiology cardiomyopathy, no (%) of patients  
7 (41)  
7 (41)  
11 (33.3)  
11 (33.3)
Time since transplantation, years (mean ± SD)  
11.5 ± 3.8  
10.4 ± 3.6  
9.7 ± 4.7  
9.4 ± 4.4
Systolic blood pressure, mm Hg (mean ± SD)  
132.9 ± 9.8  
122.5 ± 35.6  
132.4 ± 16.3  
128.9 ± 12.5
Serum creatinine, μmol/l (mean ± SD)  
148.1 ± 30  
139.8 ± 50  
155.7 ± 48.1  
149.3 ± 10.4
Serum cholesterol, mmol/l (mean ± SD)  
5 ± 1.2  
4.9 ± 1.8  
4.7 ± 0.9  
4.9 ± 1.1
Lymphocyte count, x10⁹  
2.1 ± 1  
1.7 ± 0.7  
2.2 ± 0.9  
1.8 ± 0.9

CAV, cardiac allograft vasculopathy; HD, ischaemic heart disease.

differences in the absolute numbers of the seven EPC populations in patients with and without CAV. There were also no significant differences in circulating EPC numbers in patients with discordant donor heart age.

Conclusions: This study of patients with and without CAV was over twice the size of the only previous work in this area and it suggests little if any role for circulating EPC in susceptibility to CAV. There are no previously published data regarding donor heart age and EPC; our study suggests that the increased susceptibility to CAV with older donor hearts is not mediated via circulating EPC. Our results are also consistent with the theory that the age-related decline in EPC numbers seen in normal individuals relates to bone marrow ageing rather than the failure of ageing target tissues to induce EPC mobilisation.

210 ACUTE HAEMODYNAMIC EFFECTS OF CARDIAC RESYNCHRONISATION THERAPY IN HEART FAILURE WITH A NARROW QRS DURATION

Aims: Cardiac resynchronisation therapy (CRT) is currently restricted to those patients with a QRS duration >120 ms. We hypothesised that CRT would result in an acute haemodynamic benefit in patients with heart failure, a narrow QRS duration and no dyssynchrony (Yu dyssynchrony index <32).

Patients and Methods: Twenty-eight patients with an ejection fraction <35%, in sinus rhythm, and with NYHA class III/IV heart failure underwent pressure volume studies at the time of pacemaker implantation. External constraint, left ventricular stroke work, maximum +dp/dt and the slope of the preload recruitable stroke work relation (a load-independent measure of left ventricular contractility), were measured from the end-diastolic pressure–volume relation recorded during inferior vena cava occlusion, at baseline, during biventricular pacing (BIVP) and during left ventricular pacing (LVP).

Results: External constraint was present in 15 of the 28 patients and was reduced from 5.3 to 0.8 mm Hg (p < 0.01) during BIVP, and from 5.3 to 0.9 mm Hg (p < 0.01) in response to LVP. The slope of the preload recruitable stroke work relation increased in response to both BIVP (11.5–15.2; p < 0.01) and LVP (11.3–15.3; p < 0.01). Left ventricular stroke work increased in response to both BIVP (2450–3123; p < 0.01) and LVP (2450–3403; p < 0.01). Maximum +dp/dt increased from 977 to 997 (p = 0.20) with BIVP, and from 977 to 1014 (p < 0.01) with LVP.

Conclusion: Both BIVP and LVP result in an improvement in acute haemodynamic variables in heart failure patients with a narrow QRS duration, suggesting that CRT could be extended for use in this patient population.

211 METOPROLOL IMPROVES IRREGULARITY OF VENTRICULAR RATE IN PATIENTS WITH PERMANENT ATRIAL FIBRILLATION


Background: Ventricular rate-control is an established therapeutic strategy in patients with permanent atrial fibrillation. Currently available criteria for effective rate-control are not well defined and are based solely on the average heart rate. Increased irregularity of the ventricular rate (HRirr) during atrial fibrillation has been shown to have a deleterious haemodynamic effect that is independent of the average heart rate. The effect of drugs currently used for rate-control during atrial fibrillation on HRirr has not been investigated so far.

Methods: We studied 22 patients (mean age 68 ± 12 years) with permanent atrial fibrillation. All patients had preserved left ventricular systolic function (ejection fraction >50%) measured over 15 consecutive cycles). Each patient was consecutively treated with digoxin, diltiazem and metoprolol in random sequence for a period of 6 weeks on each therapy, with doses adequate to achieve a resting heart rate of 80 ± 10 bpm. HRirr was measured by the percentage of RR intervals (PNN) >50–250 ms in 25 ms increments (PNN50, PNN75, ..., PNN250) over a period of 30 minutes. Within-patient comparisons were made for PNN50–250 between the three drug regimens using repeated measures ANOVA with Tukey post-hoc comparisons.

Results: HRirr was decreased at rest during treatment with diltiazem compared with digoxin and was further decreased on treatment with metoprolol, but statistically significant differences were only seen between metoprolol and digoxin using PNN75 (mean ± SE, 48.1 ± 1.7% versus 53.6 ± 1.8%, p = 0.049) and PNN250 (34 ± 1.7% versus 39.6 ± 2.0%, p = 0.044). The average resting heart rates were similar during the three treatment regimens (digoxin: 82 ± 7, diltiazem: 78 ± 6, metoprolol: 80 ± 6 bpm; p > 0.05).

Conclusion: In patients with permanent atrial fibrillation, treatment with metoprolol significantly improves the regularity of the resting ventricular rhythm independently of the average heart rate compared with digoxin. Heart rate irregularity should be included in the criteria to assess the adequacy of effective pharmacological rate-control of atrial fibrillation in addition to the average heart rate.

212 PERIPHERAL PULSATILE ARTERIAL PRESSURE IS DETERMINED BY THE CENTRAL RESERVOIR, WHICH IS SIMILAR ACROSS DIFFERENT ARTERIAL SITES

ASN Malaweera, JE Davies, N Hadjiloizou, C Manisty, J Aguado-Sierra, A Zambanini, J Mayet, DP Francis, KH Parker, AD Hughes. International Centre for Circulatory Health, Imperial College, London, UK

Introduction: There is a large variation in the pulse pressure waveform in systole throughout the arterial system; however, the
of p47phox (a major regulatory subunit of NADPH oxidase) and a marked increase in the levels of ERK1/2 and p38 MAPK activation.

In conclusion, chronic cocaine administration causes severe cardiac oxidative stress through the upregulation of NADPH oxidase and p47phox phosphorylation. Increased ROS production from NADPH oxidase contributes to MAPK (ERK1/2 and p38 MAPK) activation and subsequent cardiac complications.

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CARDIOVASCULAR RISK AND PERIPHERAL PULSEWAVE MEASUREMENT IN A POPULATION-BASED STUDY

C Hajat, MD Tobin, J Gracey, T Smith, PR Burton, NJ Samani. University of Leicester, Leicester, UK

Increased large arterial stiffness is associated with greater cardiovascular risk. Large arterial stiffness, conventionally measured using carotid-femoral pulse wave velocity (cfPWV), is well established as a measure of cardiovascular risk. An alternative is that of digital volume pulse measurement, which is simpler and less observer-dependent. The stiffness index obtained, SIDVP, correlates significantly with cfPWV (r = 0.65) but is less well established as a predictor of cardiovascular risk. The study aims are to investigate SIDVP in relation to cardiovascular risk factors, Framingham risk scores and heritability. As part of the Genetic Regulation of Arterial Pressure of Humans in the Community (GRAPHIC) population-based study in Leicestershire, UK, 657 subjects received digital volume pulse measurements (Pulse Trace; Micro Medical, UK). Generalised estimating equations were used for association testing to account for familial relationships. Age and sex were included as covariates in all analyses. Variance components analysis in WinBUGS was used to determine heritability. Cardiovascular and stroke risk were determined using Framingham risk scores. Of 657 subjects, all had one, 654 had two, 647 had three and 21 had four pulse wave recordings. There were 357 (51%) men, 320 (49%) women, 338 (51%) from the parental and 319 (49%) from the offspring generation. The mean age was 59.2 years (SD 14.3, range 18–60). Mean SIDVP was 8.02 m/s (range 2.06–17.77, 95% CI 7.64 to 8.40) and was 8% lower for women (7.85 m/s) than men (8.65 m/s) (p=0.001) and 22% lower for offspring (7.18 m/s) than parents (9.16 m/s) (p=0.001). Each increasing year of age was associated with a 0.076 m/s increase in SIDVP. The proportion of the variance in SIDVP attributable to additive polygenic effects (narrow sense heritability (h2N)) was 10.1% (95% CI 0.006 to 0.295) (see table).

Factors associated with SIDVP. The diastolic, but not systolic, blood pressure level was associated with an increase in SIDVP. Duration of hypertension was associated with a higher SIDVP with borderline significance. High blood pressure during pregnancy was associated with SIDVP and this persisted after adjusting for those diagnosed as being hypertensive. Measures of left ventricular mass (Sokolov–Lyon and Cornell voltages), the absence of nocturnal dipping and 24-hour mean pulse pressure were not associated with SIDVP. Subjects with >10% 10-year risk of coronary heart disease

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<table>
<thead>
<tr>
<th>Covariate</th>
<th>SIDVP coefficient (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean 24-hour DBP</td>
<td>0.043 (0.010 to 0.076)</td>
<td>0.010</td>
</tr>
<tr>
<td>High BP during pregnancy</td>
<td>1.789 (0.214 to 3.364)</td>
<td>0.026</td>
</tr>
<tr>
<td>Blood glucose level</td>
<td>0.133 (0.008 to 0.259)</td>
<td>0.037</td>
</tr>
<tr>
<td>Waist-hip ratio</td>
<td>2.793 (0.051 to 5.535)</td>
<td>0.046</td>
</tr>
<tr>
<td>CHD risk score (&gt;10% 10-year risk)</td>
<td>0.917 (0.213 to 1.621)</td>
<td>0.011</td>
</tr>
<tr>
<td>CVD risk score (&gt;10% 10-year risk)</td>
<td>0.838 (0.132 to 1.545)</td>
<td>0.020</td>
</tr>
<tr>
<td>Hypertension duration (years)</td>
<td>0.083 (0.009 to 0.138)</td>
<td>0.088</td>
</tr>
</tbody>
</table>

BP, blood pressure; CHD, coronary heart disease; CVD, cardiovascular disease; DBP, diastolic blood pressure.
had a 0.9 m/s (p = 0.01) higher SIDVP and those with >10% 10-year risk of cardiovascular disease had a 0.8 m/s higher SIDVP (p = 0.02) compared with those with <10% 10-year risk scores. Random blood glucose levels, but not a history of diabetes mellitus, waist–hip ratio, but not waist circumference or body mass index, were associated with increased SIDVP. This study has shown that variation in SIDVP is influenced more by environmental than genetic factors. SIDVP demonstrates the same associations with cardiovascular and cerebrovascular risk factors as cfPWV and other measures of large arterial stiffness. This study highlights the potential for the use of SIDVP as a marker of end-organ damage, as a predictor of risk of cardiovascular disease and as an intermediate phenotype.

### CIRCULATING ENDOTHELIAL CELLS AND CIRCULATING PROGENITOR CELLS IN HYPERTENSION IN PREGNANCY: A BALANCE BETWEEN ENDOTHELIAL DAMAGE AND REPAIR?

YJ Karthikeyan, T Watson, DA Lane, S Baghdadi, DG Bevers, GYH Lip. University Department of Medicine, City Hospital, Birmingham, UK

**Introduction:** Endothelial damage has been implicated in the pathogenesis of hypertension in pregnancy. Circulating endothelial cells (CEC) reflect endothelial damage whereas circulating progenitor cells (CPC) regulate and maintain the vasculature. We hypothesised that the CPC : CEC ratio is altered in (hypertensive) pregnant women compared with non-pregnant healthy controls.

**Methods:** Hypertensive pregnant women (n = 30), >20 weeks gestation attending the antenatal hypertension clinic (blood pressures >140/90 mm Hg untreated or <140/90 mm Hg treated) were recruited. CEC were measured by immunomagnetic separation using anti-CD146 monoclonal antibody coated beads. CPC were defined using flow cytometry as CD133+/CD34+/CD45– lymphocytes. Controls included normotensive pregnant (n = 59) and non-pregnant healthy women (n = 43); the CPC : CEC ratio was expressed in the three groups.

**Results:** We recruited 112 women (mean age 30 years (SD 7)). CEC were markedly raised in the hypertensive pregnant women (p<0.001). CPC were raised in the normotensive pregnant group compared with the healthy controls (p<0.05); the CPC : CEC ratio was lower in hypertensive pregnant women compared with healthy controls (p<0.05). A strong negative correlation was noted between the CPC : CEC ratio and blood pressure.

**Conclusion:** Whereas our findings confirm the association of endothelial damage in hypertensive compared with normotensive pregnancies, low CPC : CEC ratios in the former and high CPC in the latter suggest a complex pathophysiological relationship involving endothelial damage and regeneration attempts by CPC mobilisation to restore vascular haemostasis.

### FEASIBILITY STUDY OF A VIRTUAL APPROACH TO CARDIOVASCULAR RISK MANAGEMENT

1BJR Singer, 2ME Edmunds, 3FP Cappuccio. 1Clinical Sciences Research Institute, University of Warwick Medical School, Coventry, UK; 2University Hospital, UHCW NHS Trust, Coventry, UK; 3Clinical Sciences Research Institute, Coventry, UK

**Background:** Blood pressure in primary care remains above conservative UK General Medical Services (GMS) contract audit thresholds in approximately 30% of hypertensive patients. We assessed a virtual clinic approach to improving the management of this large number of patients at high cardiovascular risk.

**Design:** Phase 1: An electronic record review in early 2006 of patients above GMS target blood pressure. Phase 2: January to March 2007—proforma-based, cost-free GP referral to the University Hospital for telephone consultation. Three hypertension specialists reviewed 99/344 records of patients with blood pressures >150/90 mm Hg for essential hypertension, >140/80 mm Hg for diabetes mellitus (DM) in two general practices (list size 14 000). Phase 3: In the previous 2 months, all local GPs were informed about the virtual clinic by e-mail, letter, educational sessions and practice visits. A hypertension nurse practitioner helped GPs to identify patients likely to benefit from structured telephone advice. An electronic proforma was designed for virtual referrals. Outcomes of virtual consultations were recorded on electronic detailed care records.

**Results:** Of the 99 (42 women) records reviewed, 26 patients (38% DM) had GP action pending. In 34 (44% DM), outpatient referral was indicated based on BHS/NICE guidelines. In 39 (53% DM) electronic telephone consultation was considered advisable. There were 13 virtual consultations (age 63 years (95% CI 57 to 69 years); five women: blood pressure 167 (158 to 176)/90 (85 to 95) mm Hg; BMI 33.7 (30.5 to 36.9) kg/m²). In five patients, formal outpatient referral for investigation or management of secondary hypertension was indicated (primary hyperaldosteronism in two, renal artery stenosis in two and coarctation of aorta in one). In eight of the 13 virtual referrals, GP treatment did not conform to BHS/NICE
guidelines. Undertreated hypothyroidism was identified in one virtual hypertension referral. One new finding of atrial fibrillation was identified in a patient intended for virtual referral, who was also referred by the GP through the Choose and Book system to our standard outpatient cardiovascular clinic.

Conclusions: Previously undetected important co-morbidity and secondary hypertension were identified. Further work is needed to address primary care shortcomings in the effective management of hypertension. Virtual cardiovascular clinics provide a new option for improving patient management and therefore reducing preventable cardiovascular risk and associated cost pressures on primary and secondary care services.

**Abstract 218**

**THE IMPACT OF DIABETES ON 2-YEAR MORTALITY FOLLOWING PERCUTANEOUS CORONARY INTERVENTION IN THE CURRENT ERA**

M Andron, RA Perry, AE Alahmar, M Egred, AD Grayson, M Shaw, ND Palmer, RH Stables. Cardiothoracic Centre, Liverpool, UK

**Background:** Previous studies have shown a significant increased risk of follow-up mortality after percutaneous coronary intervention (PCI) in diabetic patients compared with their non-diabetic counterparts. It is not clear, however, whether the improvement in interventional techniques and adjunctive pharmacotherapy in recent years has altered this risk.

**Objective:** To examine the effect of diabetes as a risk factor on 2-year mortality after PCI in “real world” clinical practice.

**Methods:** We performed retrospective analysis and data review of all patients undergoing PCI at our tertiary centre between 1 January 2000 and 31 December 2004. During this period, our institution performed a consecutive series of 6160 PCI procedures involving stent implantation. These procedures were performed in 5759 patients of whom 801 patients had diabetes (13.9%) and 4958 did not have diabetes (86.1%). The primary outcome measure of the study was death, which was obtained from the National Strategic Tracing Service. All patients were followed up for a period of 2 years. Multivariate logistic regression analysis was used to determine risk factors for follow-up mortality. Cumulative event rates at 1 and 2 years, stratified by diabetes status, were calculated by the Kaplan–Meier method and compared using log-rank statistics.

**Results:** The crude (unadjusted) mortality rates at 1 and 2 years for the diabetic cohort showed a trend towards higher mortality, although this did not reach statistical significance (3.2% and 5.1%, respectively, for those with diabetes, and 2.4% and 3.8%, respectively, for those without diabetes, log rank p = 0.12, fig). This trend has disappeared after adjustment for risk factors for mortality (fig). Other independent predictors of mortality were increasing age, renal dysfunction, peripheral vascular disease, NYHA class >2, urgent PCI, left main stem PCI, vessel diameter ≤2.5 mm and three-vessel disease (table). Drug-eluting stent (DES) use was associated with reduced mortality at 2 years in the entire cohort (odds ratio (OR) 0.43; 95% CI 0.26 to 0.71; p = 0.001), therefore we performed an interaction test, which suggested little evidence that the impact of DES use on mortality differed between diabetic and non-diabetic patients (OR 0.51; 95% CI 0.21 to 1.26; p = 0.146).

**Conclusion:** In our large series, diabetes does not appear to be an independent predictor for 2-year mortality following PCI. The conditions associated with diabetes have been shown to be more important risk factors when deciding revascularisation strategy in such patients. Furthermore, the use of DES appeared safe in this group of patients.

**Abstract 219**

**PERCUTANEOUS AORTIC VALVE REPLACEMENT: WHAT IS THE LIKELY DEMAND IN THE ELDERLY? A 1-YEAR AUDIT OF ADMISSIONS TO A BUSY DISTRICT GENERAL HOSPITAL**

JO Baker, K Wong, T Jackson, RA Swallow, JR Radvan. Royal Bournemouth and Christchurch NHS Trust, Bournemouth, UK

**Introduction:** European literature suggests that 2–3% of the population over the age of 65 years has aortic stenosis, and one third of elderly patients with significant symptomatic aortic stenosis is not offered surgical intervention. The very elderly comprise a fast growing segment of the UK population and this group of patients is traditionally never offered surgery by virtue of their co-morbidity. Recently, two case-series of percutaneous aortic valve replacement (PAVR) have shown encouraging results in this group. We therefore sought to assess the number of patients who might benefit from PAVR, presenting to a large district general hospital, with a catchment population of 350 000.

**Methods:** From the 29 131 patients admitted on the medical take from the period of October 2006 to September 2007, we retrospectively identified 150 patients over the age of 85 years who had a diagnosis of aortic stenosis on their discharge summary. In these patients the following data were collected: NYHA class, patient demographics, aortic valve area, valve gradient, left ventricular function, other medical co-morbidities. An individual EuroSCORE mortality for surgical valve replacement was calculated. Moderate to severe aortic stenosis was defined as a valve area of less than 1 cm² and/or valve gradient of greater than 30 mm Hg and severe renal disease by a creatinine of greater than 200. Patient mortality was assessed to one year.

**Results:** Complete data have been collected in 50 patients to date (38%). Of these, 70% of patients were women. Approximately 30% had moderate to severe aortic stenosis. The average log mortality EuroSCORE in this group was 15% if treated with surgical valve replacement. 50% had NYHA class II symptoms and 15% had
LONG-TERM SAFETY OF DRUG-ELUTING STENTS IN THE ELDERLY

MWH Behan, G Winder, GF Dixon, D Hillick-Smith, S Holmberg, A deBelder. Sussex Cardiac Centre, Brighton, UK

Introduction: There are increasing numbers of patients over the age of 75 years being treated with percutaneous coronary intervention (PCI). In this elderly group there are high rates of co-morbidity and complex coronary anatomy. This anatomy is more suitable for drug-eluting stents (DES) than bare metal stents (BMS) but these elderly patients are more likely to have complications as a result of long-term dual antiplatelet therapy. Limited data are available for the use of DES compared with BMS in the elderly population.

Methods: Details of all patients treated at a single, high volume, tertiary centre by PCI between 1 November 2002 and 31 October 2006 were prospectively collected by being entered onto a database at the time of the procedure by the primary operator. Patients presenting with cardiogenic shock were excluded. Three groups were defined according to age and type of stent deployed: age >75 years treated with BMS, >75 years treated with DES and <75 years treated with DES. Subgroup analysis was performed. Baseline clinical and angiographic characteristics were recorded. Patients were evaluated for procedural success, major adverse events and were followed up at 30 days, 1 year and 3 years for all-cause mortality using data from the NHS Strategic Tracing Service.

Results: A total of 1149 patients was identified. 551 patients were over the age of 75 years (age range 75–92). The results are shown in tables 1 and 2.

Conclusion: The use of DES in elderly patients is as safe as BMS and this is maintained at 1 and 3 years. There were no significant differences in outcomes between the older groups; however, there was a trend towards a decrease in mortality at both one year and at 3-year follow-up in the DES group. In the elderly are used more for elective cases with more complex anatomy. The DES <75 year group’s mortality was less than half than that of the older group. This is likely to be due to increased co-morbidity and coronary anatomy complexity in the older group.

Abstract 220 Table 1 Patient characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>BMS (417) patients</th>
<th>DES (114) patients</th>
<th>DES (618) patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&gt;75 years</td>
<td>&gt;75 years</td>
<td>&lt;75 years</td>
</tr>
<tr>
<td>Age (years (mean))</td>
<td>78.8 (3.2)</td>
<td>78.8 (2.9)</td>
<td>61.2 (8.9)</td>
</tr>
<tr>
<td>Sex (% male)</td>
<td>59.6</td>
<td>58.8</td>
<td>72.1</td>
</tr>
<tr>
<td>Elective (%)</td>
<td>38.8*</td>
<td>53.8</td>
<td>59.5</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>9.5*</td>
<td>11.8</td>
<td>15</td>
</tr>
<tr>
<td>LV function &lt;30% (%)</td>
<td>6.7</td>
<td>6.6</td>
<td>3</td>
</tr>
<tr>
<td>% With multivessel disease</td>
<td>47</td>
<td>40</td>
<td>42</td>
</tr>
<tr>
<td>Lesion calcification (%)</td>
<td>22.8</td>
<td>27</td>
<td>12.3</td>
</tr>
<tr>
<td>AHA grade (% A/B/C)</td>
<td>32/43/25*</td>
<td>26/38/36</td>
<td>29/40/31</td>
</tr>
</tbody>
</table>

NHHA, American Heart Association; BMS, bare metal stent; DES, drug-eluting stent; LV, left ventricular.

*Represents a significant difference (p<0.05) when compared with patients >75 years with DES.

Abstract 220 Table 2 Patient outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>BMS (417) patients &gt;75 years</th>
<th>DES (114) patients &gt;75 years</th>
<th>DES (618) patients &lt;75 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedural success (%)</td>
<td>98.6</td>
<td>99.1</td>
<td>98.6</td>
</tr>
<tr>
<td>MACE in hospital (%)</td>
<td>1.4</td>
<td>0</td>
<td>0.5</td>
</tr>
<tr>
<td>MACE 30 days (%)</td>
<td>1.9</td>
<td>0.9</td>
<td>0.5</td>
</tr>
<tr>
<td>Death 30 days (%)</td>
<td>1.7</td>
<td>0.9</td>
<td>0.2</td>
</tr>
<tr>
<td>Death 1 year (%)</td>
<td>7.2</td>
<td>3.5</td>
<td>1.3*</td>
</tr>
<tr>
<td>Death 3 year (%)</td>
<td>15.8</td>
<td>9.6</td>
<td>4.4*</td>
</tr>
</tbody>
</table>

BMS, bare metal stent; DES, drug-eluting stent; MACE, major adverse cardiac event.

*Represents a significant difference (p<0.05) when compared with patients >75 years with DES.

RECRUITABLE CORONARY COLLATERAL SUPPLY AND LEFT VENTRICULAR STIFFNESS ARE LINKED IN ACUTE MYOCARDIAL INFARCTION IN SWINE

C Berry, W Schenke, AH Aletas, L Hsu, V Wright, A Faranesh, RJ Lederman, AE Arai. National Institutes of Health, Bethesda, Maryland, USA

Introduction: The haemodynamic regulation of collateral supply in acute myocardial infarction (AMI) is incompletely understood. We investigated this subject in a preclinical AMI model.

Methods: A swine model was adopted because the heart of this species is similar to man. Animals were anaesthetised and ventilated. A pressure-sensitive coronary wire and central venous pressure (Pv) were used to calculate collateral flow index (CFIp = distal coronary pressure – Pv/MAP – Pv). Study 1: A preconditioning protocol (6 x 2 minutes coronary balloon inflations separated by 5 minute rest intervals) also aimed to recruit collaterals acutely. Study 2: Steady-state calibrated left ventricular pressure–volume relationships were derived during caval balloon occlusion and respiratory arrest. The end-diastolic pressure–volume relationship (EDPVR, mm Hg/ml) was measured and the steady-state slope (n > 7 heart beats) was taken to represent left ventricular stiffness.

Results: In 16 swine, the median (interquartile range; IQR) CFIp at baseline was 0.045 (0, 0.12). Insignificant (CFIp >0.10) and significant (CFIp ≥0.10) collateral supplies were evident in 10 (60%) and 6 (40%) swine respectively. Study 1: Twelve swine entered the pre-conditioning protocol (n = 10, circumflex; n = 2, left anterior descending) and 11 survived with complete data. After six inflations, median CFIp remained similar to baseline (0.105; IQR 0.02, 0.26; p = 0.23). On an individual basis, CFIp increased in six (55%) swine (+ACFIp, median 0.13; IQR 0.09, 0.19), and fell or was unchanged in five (45%) swine (–ACFIp, median –0.05; IQR –0.05, –0.0). Mean arterial pressure (MAP) remained fairly constant (+ΔMAP 1.0 (5.6) mm Hg) in swine with a recruitable collateral supply whereas MAP fell in swine with no recruitable collateral supply (mean (SD) +ΔMAP –8.3 (7.4) mm Hg; p = 0.04). ΔACFIp was predicted by +ΔMAP (R² = 0.39; p = 0.055). Study 2: Seven swine (n = 5 from study 1; n = 2, no-preconditioning) survived with complete data at 60 minutes. The mean (SD) EDPVR slope (0.17 (0.03)) was less in swine with an enhanced collateral supply (CFIp <median 0.11; n = 3) compared with the EDPVR slope in swine with reduced collateral (CFIp ≥0.11; mean (SD) EDPVR slope 0.57 (0.09); p = 0.019; n = 4). The EDPVR slope was less (mean (SD) 0.18 (0.04)) in swine with recruitable collaterals at 60 minutes (ΔCFIp >1) at 60 minutes versus baseline, n = 4) compared with the EDPVR slope in swine with a ΔCFIp 60 minutes <1 (0.42 (0.04); p = 0.001; n = 3; fig). The EDPVR slope was
inversely related to CFIp (CFIp = 0.28–0.58 EDPVR slope; \( R^2 = 0.56, p = 0.049, n = 7 \)). The mean LVEDP at baseline (8 (5) mm Hg) and at 60 minutes (12 (6)) were similar (\( p = 0.25 \)). LVEDP, the time constant of left ventricular relaxation and the end-systolic pressure–volume relationship slope were unrelated to CFIp. Similar findings occurred at 90 minutes of balloon occlusion (\( n = 6 \)).

**Conclusions:** Consistent with coronary autoregulation, the propensity to augment collateral supply is influenced by MAP. In AMI, recruitable collateral supply is associated with reduced left ventricular wall stiffness. Equally, increased left ventricular stiffness (eg, secondary to severe ischaemia) may inhibit collateral recruitment.

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**Abstract 222**

**Gender, Body Mass and the Risk of Periprocedural Bleeding Following Percutaneous Coronary Intervention: Insights from the British Columbia Cardiac Registry**

1J Byrne, 2M Spence, 3A Chase, 4R Mildenberger, 5B Berry, 6D Pi, 7E Fretz, 4D Hilton. 1King’s College Hospital, London, UK; 2The Royal Hospitals, Belfast, UK; 3Morriston Hospital, Swansea, UK; 4Royal Jubilee Hospital, Victoria, Canada; 5Vancouver Island Health Authority, Victoria, Canada; 6University of British Columbia, Vancouver, Canada; 7St Paul’s Hospital, Vancouver, Canada

**Background:** Recent data have suggested that bleeding following percutaneous coronary intervention (PCI) is relatively common and is associated with an adverse prognosis, particularly in high-risk subgroups. We sought to investigate further the relationship between body mass, bleeding and outcome following PCI using a large provincial registry. This study examined major bleeding rates and mortality after PCI in a cohort of 39 386 patients over a 6-year period, using postprocedural transfusion as a surrogate for major PCI-related bleeding.

**Methods:** Data were collected from three large provincial databases; the British Columbia Cardiac and Transfusion Registries were cross-referenced from 1999 to 2005, using transfusions (non-coronary artery bypass graft related) within a 9-day window after PCI as a surrogate for major bleeding. Data were cross-referenced with vital statistics to determine patient status (alive/dead) at 1 year. The \( \chi^2 \) test was used for comparisons of categorical data, and the two-tailed Student’s \( t \)-test was used to compare continuous variables. Forward and backward stepwise logistical regression was used to identify independent predictors of outcome following PCI, with the final models including only those covariates with a \( p \leq 0.05 \).

**Results:** A clear bi-modal (U-shaped) relationship was seen between BMI and mortality, with a decreased survival in lean patients with a BMI of \( \leq 18.5 \), and in patients with class 3 obesity. Overweight patients and those with milder degrees of obesity had lower mortality when compared with patients with a normal BMI. 978 (2.5%) patients required transfusion. Mortality in the transfused group was 22.7% (transfused) cf 3.2% (non-transfused) at 1 year. Periprocedural transfusion was associated with a 3.8-fold (hazard ratio (HR) 3.9, 95% CI 1.89 to 8) increase in risk of one-year mortality across the entire cohort and was more common in women across the body mass spectrum. Furthermore, transfusion itself adopted the same bimodal distribution across the entire cohort, with increased frequency in both the grossly obese and the very lean cohort (see figs 1 and 2).

**Conclusion:** Major bleeding confers an adverse long-term prognosis after PCI. In our cohort, transfusion, as a surrogate for periprocedural bleeding, was the most powerful independent predictor of outcome at 1 year following PCI across all BMI groups, with an almost fourfold increased risk of death across the entire cohort, with increased frequency in both the grossly obese and the very lean cohort (see figs 1 and 2).

Identifying demographic and procedural factors that increase risk will facilitate more accurate risk scoring of patients undergoing PCI and allow targeted bleeding avoidance strategies. Body mass and female sex identifies subgroups at far higher risk of bleeding after PCI, an observation that merits further study.

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**Abstract 223**

**Renal Impairment in Heart Attack Centre Patients: A Real World Experience**

NG Campbell, R De Palma, K Ahuja, N Salahuddin, MT Rothman, C Knight. London Chest Hospital, Bonner Road, London, UK

**Introduction:** Contrast induced nephropathy (CIN) is one of a number of causes of renal dysfunction in post-myocardial infarction patients who have undergone coronary angiography or angioplasty. Pre-existing renal impairment is a risk factor for CIN in patients...
undergoing invasive cardiac management and prophylactic measures are used electively. The renal function of patients brought directly to heart attack centres (HAC) is unknown at the time of procedure, so prophylactic measures are not used. We investigated the incidence of pre and post-procedure renal impairment in the population of patients presenting to a HAC with the aim of identifying which patients are at higher risk of nephropathy post-procedure.

Methods: We identified all of the patients who were admitted via the HAC at the London Chest Hospital who underwent coronary angiography angioplasty between April 2006 and March 2007. We defined pre-existing renal dysfunction as an estimated glomerular filtration rate of <50 ml/min, according to the Modification of Diet in Renal Disease equation. The definition of (all-cause) post-procedure nephropathy was an increase in serum creatinine (SCr) >44.2 μmol/l (0.5 mg/dl) from baseline or an increase of 25% in SCr from baseline during hospital admission.

Results: 581 patients were taken to the cardiac catheter laboratory who had been admitted via the HAC between April 2006 and March 2007. The mean age was 61.3 years; men 77%. 49 patients (8.4%) had renal dysfunction before the procedure. 74 patients (12.7%) developed post-procedure nephropathy and the incidence of post-procedure nephropathy in those with previous renal dysfunction was significantly increased (35.8%, p<0.001). Patients who received >580 ml contrast were significantly more likely to develop post-procedure nephropathy than those who received ≤ 350 ml (26.8% versus 11.3%, p=0.01).

Conclusion: HAC patients who undergo coronary angiography angioplasty should receive CIN prophylaxis if they have a known or suspected history of baseline renal impairment, or if they receive a high contrast load.

225 SHORT AND MEDIUM-TERM MORTALITY IN PATIENTS UNDERGOING LEFT MAIN STEM PERCUTANEOUS CORONARY INTERVENTION

JR Dalzell, ST Jadhav, K Robertson, J Kelly, MM Lindsay, SD Robb, WS Hills, KG Oddy, Department of Cardiology, Western Infirmary, Glasgow, UK

Background: Revascularisation for patients with left main stem (LMS) coronary disease has traditionally been with coronary artery bypass grafting (CABG). Although prospective data from randomised controlled trials comparing percutaneous coronary intervention (PCI) with CABG are awaited, patients commonly undergo PCI for LMS coronary disease in the “real world” most commonly having been declined for CABG due to excessive risk. We reviewed all cases of LMS PCI at the Western Infirmary, Glasgow, a large tertiary cardiology centre serving the west of Scotland, over a 45-month period.

Methods: All LMS PCI undertaken at the Western Infirmary between January 2003 and October 2006 were reviewed. Cases were identified from the hospital’s catheterisation laboratory database and case notes were then reviewed.

Results: Patient characteristics: 107 cases were identified. 71/107 (66%) were men with a mean age of 70 years (range 16–90), comorbidities included. The case mix breakdown was as follows: elective 42%, urgent 48%, emergency 10%. 71 patients (67%) had unprotected LMS PCI and 45 patients (42%) had some form of previous coronary revascularisation. The majority of these patients (60%) had LMS PCI as a result of being declined for CABG for either excessive per-operative risk (54%) or having had a previous CABG (26%). Predicted surgical mortality was calculated using logistic EuroSCORE and ranged from 1.22% to 69.9% with a mean of 26.59%. Procedural data: Vascular access was by the radial artery in 50% of cases. Glycoprotein IIb/IIIa inhibitors were used in 46% of cases. An intra-aortic balloon pump was inserted pre-procedure in 50% of cases. The majority of these patients were women (60%). There was 3.7% on-table mortality and 5.6% 24-hour mortality. In-hospital mortality was 9.3% and these patients had a mean predicted mortality rate. In-hospital mortality was 9.3% and these patients had a mean predicted mortality rate by logistic EuroSCORE of 38.1% (nine out of 10 of these patients were in the top tertile of predicted mortality rate). There was an overall 87% survival at 1 year (fig).

Abstract 225

In patients with myocardial infarction complicated by cardiogenic shock (MI-CS) the use of intra-aortic balloon pumping (IABP) is recommended. MI-CS causes a systemic inflammatory response syndrome leading to further impaired haemodynamics and multi-organ dysfunction syndrome (MODS). This inflammatory response could be improved (by improvement of shock haemodynamics) or worsened (by exposure of the circulation to foreign material) with IABP use. No randomised clinical trial has examined the use of IABP in treating MODS and inflammation in primary percutaneous coronary intervention (PCI)-treated MI-CS.

Methods: 40 consecutive patients with acute MI-CS were randomly assigned to receive therapy with or without IABP (for >48 hours) in addition to PCI-centred care. APACHE II scores and inflammatory markers (leucocyte count, IL-6, tumour necrosis factor alpha, and C-reactive protein levels) were measured at enrolment and daily for 4 days.

Results: The mean age of the study population was 64 ± 1.9 years, 52% were mechanically ventilated, the mean left ventricular ejection fraction was 27 ± 2.1% and 28 day survival was 67%. The global mean APACHE II score was 20.4 ± 2.7 (illustrating the severity of disease) but was not significantly affected by the use of IABP. IL-6 levels were raised in both groups, illustrating systemic inflammatory activation in MI-CS but levels remained elevated (500 ng/ml mean) and were not affected by IABP use. Similarly, the other markers of inflammation were unaffected by the implementation of IABP therapy.

Conclusion: Although IABP therapy may exert pro or anti-inflammatory influences; given the present data, we conclude that IABP use does not significantly improve markers of systemic inflammation or the development of systemic inflammatory response syndrome/MODS in PCI-treated MI-CS patients.
Conclusions: LMS PCI carries a very low mortality risk in those patients undergoing elective revascularisation. Even in high-risk patients undergoing LMS PCI in the acute setting, the medium-term outcomes are acceptable and the vast majority of deaths occur in those with the highest predicted risk before discharge in the index admission. Until prospective randomised data comparing CABG and PCI in patients with LMS disease are available, LMS PCI seems to be an acceptable form of revascularisation in terms of short-term and medium-term mortality, especially in those with excessive predicted surgical mortality and those presenting acutely.

226 MICROcirculatory-OriGINATING PRESSURE Predominantly DETERMINES CORONARY BLOOD FLOW IN HUMANS: EVALUATION USING WAVE INTENSITY ANALYSIS

JE Davies, ZI Whinnett, NH Hadjiloizou, CH Manisty, AD Hughes, KH Parker, DP Francis, JM Mayet. International Centre for Circulatory Health, St Mary’s Hospital and Imperial College, London, UK; 2Physiological Flow Laboratory, Department of Bioengineering, Imperial College, London, UK

Background: Blood flow to the myocardium is controlled by the delicate balance between aortic and microcirculatory-originating pressure. However, until recently it was not possible to separate the pressure waveform to quantify these components. Using wave intensity analysis we separated coronary pressure to explore this balance, and explain why the coronary flow profile differs markedly from that in the proximal aorta.

Method and Results: In 18 subjects simultaneous pressure and Doppler velocity were measured in the proximal left main stem, left anterior descending, circumflex artery and proximal aorta. Wave intensity analysis was used to separate pressure into its proximal and distal-originating components. In the aorta more than 70% intensity analysis was used to separate pressure into its proximal anterior descending, circumflex artery and proximal aorta. Wave Doppler velocity were measured in the proximal left main stem, left ascending coronary arteries, only 48% of the increase in pressure came from a proximally originating pressure. In contrast, in the coronary arteries, only 48% of the increase in pressure came from a proximal origin and the remainder from a distal (microcirculatory) origin (31.3 ± 11.5 versus 33.7 ± 8.4 mm Hg, p = 0.47). Distal-originating pressure rises before proximal-originating pressure (41 ± 28 ms after the peak of the R-wave on the ECG versus 104 ± 25 ms, p<0.001). This excess distal-originating pressure attenuates the rise of coronary flow velocity (0.2 ± 0.23 m/s), which is only reversed during cardiac relaxation when distal-originating pressure falls rapidly and coronary flow velocity peaks (0.58 ± 0.49 m/s) (see figs 1 and 2).

Conclusion: Aortic flow velocity is largely driven by the proximally originating aortic pressure. In contrast, coronary blood flow velocity is heavily regulated by the coronary microcirculation. During cardiac contraction distal coronary pressure exceeds proximal-originating pressure—restricting blood flow. Only after cardiac relaxation begins does distal pressure fall, allowing coronary flow velocity to rise rapidly.

227 CORONARY ARTERY DISEASE IN ASYMPTOMATIC RENAL TRANSPLANT ASSESSMENT PATIENTS

GIW Galasko, A Frankel, CSR Baker. Cardiology Department, Hammersmith Hospital, London, UK; 2Renal Department, Hammersmith Hospital, London, UK

Background: Coronary artery disease (CAD) is the commonest cause of death in end-stage renal failure (ESRF) and may be asymptomatic. Although transplantation eventually reduces cardiac mortality, the perioperative event rate is high. The role of diagnostic angiography and/or intervention before renal transplantation is unclear. This study was undertaken to establish the prevalence of significant CAD in asymptomatic renal transplant assessment patients and to evaluate the effect of revascularisation.

Methods: A retrospective review of consecutive asymptomatic patients with ESRF undergoing coronary angiography from 2003 before renal transplantation. Significant CAD was defined as a stenosis ≥70% in a major epicardial coronary artery on visual inspection. Patients were followed up for death or major adverse cardiac events (MACE) (new cerebrovascular accident, myocardial infarction, non-ST elevation myocardial infarction or hospitalisation with pulmonary oedema). Mean follow-up was 419 days.

Results: 258 patients with ESRF underwent angiography (174 men (67%), mean age 56 years, 121 with diabetes (47%)). Significant CAD occurred in 125 patients (48%), 55% diabetics versus 45% non-diabetics (p = 0.07) and 56% male versus 32% female (p = 0.001). Multivessel disease was seen in 36% of patients with diabetes versus 23% of non-diabetic patients (p = 0.02). 85 patients (33%) were referred for revascularisation before transplantation. 41 patients (16%) underwent renal transplantation, 14 (34%) with significant CAD, five (12%) were managed medically and nine (22%) following revascularisation. 14 patients died and 39 patients died or had a MACE at follow-up. There was no significant difference in mortality between those with significant CAD and those free from CAD (94.2 versus 92.8%, p = 0.20). Patients with significant CAD had significantly higher rates of death or MACE than those free from CAD (p = 0.007) with 12-month rates of 82.8% and 94.5%, respectively. Multivariate predictors of death or MACE were significant CAD at angiography (odds ratio (OR) 2.3, p = 0.014) and not undergoing renal transplantation (OR 3.8, p = 0.05).

Conclusions: Despite an absence of symptoms, CAD is extremely common in the renal transplant assessment population, especially in male diabetic patients. The presence of significant CAD independently predicts death or MACE. Diagnostic angiography ± revascularisation should be considered in chronic ESRF patients before renal transplantation.
LONG-TERM FOLLOW-UP OF PATIENTS WITH FOUR OR MORE DRUG-ELUTING STENTS: IMPLICATIONS FOR CONTEMPORARY INTERVENTIONAL PRACTICE

1RT Gerber, 2A Ielasi, 2C Godino, 2A Latib, 2E Airoldi, 2A Chieffo, 2M Montorfano, 2R Rogacka, 2V Magni, 2M Carlino, 2I Michev, 1A Colombo.

1EMO Centro Cuore Columbus and San Raffaele Hospital, Milan, Italy; 2San Raffaele Hospital, Milan, Italy; 3EMO Centro Cuore Columbus, Milan, Italy

Introduction: Ever more frequently patients undergoing percutaneous coronary intervention (PCI) present with more complex disease and associated multiple co-morbidities. Therefore the need for multivessel procedures with multiple stent insertion is expanding. Stent thrombosis and restenosis are always a concern when implanting several stents. There is limited evidence concerning clinical outcomes for multiple stent insertion in the drug-eluting stent (DES) era. We therefore present 3-year clinical and angiographic follow-up data from two centres for patients who had four or more DES implanted between April 2002 and 2004.

Methods: Clinical follow-up (38 ± 16 months) was performed in all patients, with 77% having angiographic follow-up. Patients were included from the point that the fourth stent was inserted whether this was during the index procedure or any further procedures. Data were entered prospectively in institutional databases. Indications for PCI were symptomatic myocardial ischaemia or evidence of reversible myocardial ischaemia from perfusion or stress testing. Data are expressed as mean ± SD and definitions of stent thrombosis are according to the Academic Research Consortium criteria.

Results: 266 patients were identified comprising 1086 lesions with a mean number of stents implanted of 5.7 per patient. Patients were 63 ± 10 years old (male, 94%), hypertension 73%, diabetes 30%, family history 41%, smoker 15%. Patients had unstable angina 25%, previous PCI 50%, previous coronary artery bypass grafting 21%, previous myocardial infarction (MI) 45% and a mean ejection fraction of 53%. Complete revascularisation was performed in 158 (59%). At follow-up the total mortality was 18 (6.8%); 12 (4.5%) deaths were cardiac, six (2.3%) were non-cardiac (five due to neoplasia and one stroke). Of the cardiac deaths, five were out of hospital cardiac arrests, five were in-hospital cardiac arrests; two being during cardiac procedures, one of which was an acute stent thrombosis (0.38%). Restenosis was seen in 186/844 lesions (22%) with a target lesion revascularisation (TLR) of 151/1086 (13.9%) and a TLR per patient of 105/266 (39%). There were three (1.1%) definite stent thrombosis; one was acute, one late and one very late. The acute stroke thrombosis was related to a vessel rupture and tamponade and the patient subsequently died in intensive care. The late stent thrombosis occurred 7 months after the index procedure and was within the distal portion of the previous stent. This patient then presented 3 years later with a further stent thrombosis (very late) in the same vessel, all these events occurred on dual antiplatelet therapy. The combined composite endpoint of major adverse cardiac event (TLR, MI and cardiac death) at follow-up was 122 (46%).

Conclusions: This study demonstrates an acceptable occurrence of MI and death, with a low incidence of definite and probable stroke thrombosis. The high incidence of TLR appears to be related to the complex cohort of patients.
**229 LONG-TERM FOLLOW-UP OF THE SUBINTIMAL TRACKING AND RE-ENTRY TECHNIQUE FOR CHRONIC TOTAL OCCLUSIONS**

1RT Gerber, 1M Carlino, 1C Godino, 1A Latib, 1F Airoldi, 2A Qasim, 2R Romagnoli, 2A Chieffo, 3M Montorfano, 3R Rogacka, 3V Magni, 3J Cosgrave, 2G Melz, 1I Michev, 1A Colombo. EMO Centro Cuore Columbus and San Raffaele Hospital, Milan, Italy; 2EMO Centro Cuore Columbus, Milan, Italy; 3San Raffaele Hospital, Milan, Italy; 1Royal Brompton and St Mary’s Hospital and Imperial College London, London, UK; 2University of Mainz, Mainz, Germany; 3Washington Mitchell, 1C Di Mario, 2R Erbel, 3R Waksman, 1M Dalby. Chieffo, 2M Montorfano, 2R Rogacka, 2V Magni, 3J Cosgrave, 2G Melz, 1I Michev, 1A Colombo.

**Introduction:** Since the inception of percutaneous coronary intervention (PCI) as a successful treatment for coronary stenosis its application to chronic total occlusions (CTO) has always yielded disappointing results. This has been due to low procedural success and high restenosis rates. Novel techniques to cross CTO have improved procedural success and we have shown that recanalisation of a CTO with the subintimal tracking and re-entry (STAR) technique is feasible and relatively safe. Therefore, the question of long-term safety with the STAR needs to be addressed. We present here the long-term clinical and angiographic outcomes for all patients who underwent the STAR procedure in two separate institutions.

**Methods:** 108 patients underwent attempted recanalisation with the STAR between November 2002 and 2004. Indications for PCI were symptomatic myocardial ischaemia or evidence of reversible myocardial ischaemia from perfusion or stress testing. Data were entered prospectively in institutional databases. Clinical follow-up was performed in 104 patients (96%) and angiographic follow-up in 74 patients (68%). Data are expressed as mean ± SD.

**Results:** Patients were 63 ± 10 years old (male; 95%), hypertension 66%, hyperlipidaemia 74%, diabetes 21%, family history 48%, smoker 15%. Patients had unstable angina 11%, previous PCI 57%, previous coronary artery bypass grafting 34%, previous myocardial infarction (MI) 54% and a mean ejection fraction of 51%. There was immediate procedural success in 85 patients (79%). Follow-up was performed at 572 days (interquartile range 113–541) from the index procedure. The target vessel was the right coronary artery 76%, circumflex 17.6%, left anterior descending 6.4%. In total 190 stents were implanted (2.11 per patient) with a mean length of 51 ± 3.1 mm and 134 being drug-eluting stents (DES; 70%) and 56 bare metal stents (BMS; 30%). Overall, major adverse cardiac event at follow-up was 44 (40%), which comprised 42 repeat PCI, one coronary artery bypass grafting and two cardiac deaths. One cardiac death was an out of hospital cardiac arrest 8 months postprocedure and the other was sudden death at 28 months postprocedure. There was one non-cardiac death from neoplasia. Target vessel revascularisation was performed in 45 (40%) and target lesion revascularisation in 36 (35%). Restenosis was seen in 40 patients (54%) with a focal pattern in 14 (19%), diffuse in eight (11%) and occlusive in 18 (24%). Restenosis was recorded in 23 DES (17%) and 17 BMS (51%) stents. There were no episodes of definite or probable late stent thrombosis during the follow-up period but there was one episode of acute stent thrombosis that was treated successfully by repeat PCI during the index hospital stay.

**Conclusions:** In this large cohort of patients with extended follow-up there was acceptable outcome from the STAR technique in terms of procedural success, mortality and stent technique during follow-up. There is, however, a high rate of re-intervention that reflects the complexity of the disease and of the procedure.

**230 CORONARY ARTERY VASOMOTION MAY BE POSSIBLE IN SEGMENTS PREVIOUSLY TREATED WITH BIOABSORBABLE MAGNESIUM ALLOY CORONARY STENTS**

1G Ghimire, 1J Sprio, 2R Kharbanda, 1M Roughton, 1P Barlis, 1M Mason, 1C Isley, 1A Mitchell, 1C Di Mario, 1R Erbel, 1W Waksman, 1M Dalby, 1Royal Brompton and Harefield NHS Trust, London, UK; 2University of Mainz, Mainz, Germany; 3Washington Hospital Centre, Washington, DC, USA

**Introduction:** Permanent metallic stents (PMS) prevent early complications of coronary angioplasty but prevent normal vasomotion, which may have short and long-term deleterious effects. Bioabsorbable stents may allow vessel healing and permit vasodilatation.

**Methods:** We investigated endothelium independent smooth muscle vasodilator function at 4 months after implantation of magnesium alloy absorbable metal stents (AMS) as part of the Progress-AMS clinical trial (n = 5) compared with a control group of PMS (n = 10) patients undergoing follow-up angiography but who were free from angiographic restenosis. Quantitative coronary angiography using an automated edge detection system was performed before and after the administration of 2 mg intracoronary isosorbide dinitrate. The diameter of the vessel was measured at 0.2 mm intervals throughout the stented segments and a 1 cm proximal reference segment. The cross-sectional area was calculated (πr²) and averaged before and after the isosorbide dinitrate injection and the percentage change calculated. The Mann–Whitney test was used to compare the percentage change in the groups (see fig).

**Results:** Reference segments demonstrated preserved vasomotor function in all cases: +15.28% (AMS) versus +17.15% (PMS), p = 0.59. The mean percentage increase in the cross-sectional area for the stented segment was +6.78% for the AMS versus −1.30% for the PMS, p = 0.003.

**Conclusions:** These data demonstrate that 4 months after AMS stent implantation vasomotor function in reference segments is no different to that observed with reference segments of PMS. However, in contrast to PMS, within the previously AMS-stented segments there is demonstrable vasodilatation. These observations may have important implications for vessel healing after percutaneous coronary interventions and future stent design.

**231 THE IMPORTANCE OF THE MICROVASCULATURE IN DETERMINING THE SHAPE OF THE LEFT AND RIGHT CORONARY ARTERY FLOW VELOCITY WAVEFORM**

N Hadjiioannou, J Davies, AJ Baks, R Barah, I Malik, R Faole, K Parker, A Hughes, D Francis, J Mayet, St Mary’s Hospital and Imperial College London, London, UK

**Background:** Despite having almost identical origins and similar perfusion pressures, the flow velocity waveforms in the left and right coronary arteries are strikingly different. We speculate that pressure differences originating from the distal (microcirculatory)
Coronary perforation is one of the most feared complications of coronary intervention. Published series have analyzed procedures performed before the widespread utilization of drug-eluting stents (DES). The Ellis classification has been used to grade the severity of coronary perforations. Ellis class I perforations are defined as extraluminal crater without extravasation and do not adversely affect outcome. Ellis class II–IV coronary perforations have been associated with a mortality of 10–20%. The incidence of class II–IV coronary perforation in these studies varies from 0.1% to 0.48%. The introduction of DES has enabled cardiologists to tackle more complex and higher risk coronary lesions. We postulated therefore, that in contemporary practice with the ability to treat more complex disease, the incidence of coronary perforation may be increasing.

**Methods:** We carried out a retrospective analysis of all coronary interventions following the widespread adoption of DES in our centre from May 2004 to October 2007 to determine the incidence of coronary perforation. This involved a detailed analysis of all percutaneous coronary intervention cases in our angioplasty database during this period followed by angiographic and case note review of patients identified with suspected class II–IV coronary perforation. We examined associations between demographic and lesion characteristics with the occurrence of class II–IV coronary perforation and factors leading to poor outcome after perforation.

**Results:** During the study period, 11,097 lesions were treated in 6766 patients. DES usage was 77%. The incidence of class II–IV coronary perforation was 0.56% (n = 57) overall, with an incidence of 0.66% in the second half of the study. Female sex was strongly associated with coronary perforation (p = 0.001) as was increasing age and lesion calcification (p < 0.001, p = 0.005, respectively). Diabetes, renal failure (creatinine >200 μmol/l) and bifurcation lesion were not associated with a greater risk of perforation. Coronary perforation was associated with balloon predilation in five patients, cutting balloon predilation in four patients, stent deployment in 13 patients and wire tip trauma in 10 patients. The mortality rate after perforation was 16.2%. 58% of perforations (n = 23) were of Ellis class IV, with a mortality rate of 30% in this group. The factors associated with death after perforation were Ellis class IV severity (p = 0.037), preprocedure thrombolysis (p = 0.004) and non-elective procedure (p = 0.014).

**Conclusion:** This study suggests that in the DES era, the incidence of coronary perforation is increasing. To minimise the occurrence of this potentially fatal complication, particular caution should be exercised in those at highest risk, which include the elderly, female patients and those in whom calcified lesions are treated.

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**Abstract 231**

LMS, left main stem; RCA, right coronary artery.

We applied wave intensity analysis to separate and quantify proximal and distal-originating pressures, to explore the differences in these velocity waveforms.

**Methods:** In 20 subjects with unobstructed coronary arteries, sensor-tipped intra-arterial wires were used to measure simultaneous pressure and Doppler velocity in the proximal left main stem (LMS) and proximal right coronary artery (RCA). Wave intensity analysis was applied to derive proximal and distal-originating waves and we examined them with respect to structural and anatomical differences between the two arteries.

**Results:** The diastolic–systolic ratio of peak flow velocity in the RCA was significantly less than the LMS (1.00 ± 0.32 versus 1.79 ± 0.48, p < 0.001). The cause was a lower diastolic flow velocity in the RCA than in the LMS (35.1 ± 21.4 cm/s versus 56.4 ± 32.5 cm/s, p < 0.002), which is explicable by the lower distal-originating suction wave velocity (2.8 ± 6.6 × 10⁶ Wm⁻²/s versus 16.0 ± 12.2 × 10⁶ Wm⁻²/s, p < 0.01). The suction wave in the LMS positively correlated with left ventricular pressure (r = 0.6, p < 0.01) and in the RCA with estimated right ventricular systolic pressure (r = 0.7, p = 0.05) but not with the respective diameter in these arteries (fig).

**Conclusion:** In contrast to the LMS, where coronary flow velocity was predominantly diastolic, in the proximal RCA coronary flow velocity in systole and diastole was similar. This difference was accounted for by the lower diastolic flow velocity in the RCA than the LMS. This is due to a smaller distal-originating ‘suction wave’ in the RCA, which can be explained by the lower pressure generated in the right than the left ventricle.

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**232 INCREASING INCIDENCE OF CORONARY PERFORATION IN THE DRUG-ELUTING STENT ERA**

C Hendry, M Eisenberger, M Mamas, M El-Omar, F Fath-Ordoubadi, DG Fraser. Manchester Heart Centre, Manchester Royal Infirmary, Manchester, UK

Coronary perforation is one of the most feared complications of coronary intervention. Published series have analyzed procedures performed before the widespread utilisation of drug-eluting stents (DES). The Ellis classification has been used to grade the severity of coronary perforation in these studies. Ellis class I perforations are defined as extraluminal crater without extravasation and do not adversely affect outcome. Ellis class II–IV coronary perforations have been associated with a mortality of 10–20%. The incidence of class II–IV coronary perforations in these series varies from 0.1% to 0.48%. The introduction of DES has enabled cardiologists to tackle more complex and higher risk coronary lesions. We postulated therefore, that in contemporary practice with the ability to treat more complex disease, the incidence of coronary perforation may be increasing.

**Methods:** We carried out a retrospective analysis of all coronary interventions following the widespread adoption of DES in our centre from May 2004 to October 2007 to determine the incidence of coronary perforation. This involved a detailed analysis of all percutaneous coronary intervention cases in our angioplasty database during this period followed by angiographic and case note review of patients identified with suspected class II–IV coronary perforation. We examined associations between demographic and lesion characteristics with the occurrence of class II–IV coronary perforation and factors leading to poor outcome after perforation.

**Results:** During the study period, 11,097 lesions were treated in 6766 patients. DES usage was 77%. The incidence of class II–IV coronary perforation was 0.56% (n = 57) overall, with an incidence of 0.66% in the second half of the study. Female sex was strongly associated with coronary perforation (p = 0.001) as was increasing age and lesion calcification (p < 0.001, p = 0.005, respectively). Diabetes, renal failure (creatinine >200 μmol/l) and bifurcation lesion were not associated with a greater risk of perforation. Coronary perforation was associated with balloon predilation in five patients, cutting balloon predilation in four patients, stent deployment in 13 patients and wire tip trauma in 10 patients. The mortality rate after perforation was 16.2%. 58% of perforations (n = 23) were of Ellis class IV, with a mortality rate of 30% in this group. The factors associated with death after perforation were Ellis class IV severity (p = 0.037), preprocedure thrombolysis (p = 0.004) and non-elective procedure (p = 0.014).

**Conclusion:** This study suggests that in the DES era, the incidence of coronary perforation is increasing. To minimise the occurrence of this potentially fatal complication, particular caution should be exercised in those at highest risk, which include the elderly, female patients and those in whom calcified lesions are treated.

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**233 EVALUATION OF SAFETY AND EFFICACY OF TRANSRADIAL PRIMARY ANGIOPLASTY FOR ST SEGMENT ELEVATION MYOCARDIAL INFARCTION: A UK TERTIARY CENTRE’S EXPERIENCE**

S Hetherington, R Morley, M De Belder, J Hall, D Mair, A Sutton, R Wright. The James Cook University Hospital, Middlesbrough, UK

**Background:** Primary percutaneous coronary intervention (PPCI) is the preferred reperfusion strategy for patients presenting with ST segment elevation myocardial infarction (STEMI). The frequent use of GPIIb–IIIa antagonists in the PPCI setting is associated with an important increase in bleeding risk. The transradial approach for elective coronary intervention is an effective alternative to the femoral approach with a lower risk of bleeding complications and shortened hospital stays. We examined the safety and efficacy of emergency transradial PPCI in a high volume UK regional centre.

**Methods:** An analysis of prospectively collected data on 610 consecutive patients presenting with STEMI in the absence of preprocedural cardiogenic shock and treated by PPCI, between January 2003 and August 2007. Patients transferred for rescue angioplasty were not included. Clinical, procedural and in-hospital mortality data were compared. Data are presented as n (%), mean (SD) or median (interquartile range) when appropriate.

**Results:** The initial choice of access route was radial in 209 cases (34.3%) and femoral in 401 cases (65.7%). 15 radial cases (7.2%) required concomitant femoral artery access for an intra-aortic balloon pump (IABP). The mean age of subjects was 62 years and 71% were men. There were no significant differences in baseline demographics or angiographic severity of coronary artery disease between the groups. A variable preference for radial access was observed among the five lead operators (between 5.9% and 87.3%). Use of radial access was associated with significantly lower contrast...
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<table>
<thead>
<tr>
<th>Outcome</th>
<th>Radial approach, n = 209</th>
<th>Femoral approach, n = 01</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dual access required (radial + femoral or bifemoral)</td>
<td>30 (14.4%)</td>
<td>12 (3.0%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Failed initial access</td>
<td>15 (7.2%)</td>
<td>4 (1.0%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Vascular complications requiring intervention</td>
<td>3 (1.4%)</td>
<td>5 (1.2%)</td>
<td>NS</td>
</tr>
<tr>
<td>Needle to balloon time, minutes</td>
<td>17 (12–27)</td>
<td>17 (12–23)</td>
<td>NS</td>
</tr>
<tr>
<td>TIMI 3 flow at procedure end</td>
<td>184 (88%)</td>
<td>357 (89%)</td>
<td>NS</td>
</tr>
<tr>
<td>In-hospital MACCE</td>
<td>8 (3.8%)</td>
<td>23 (5.7%)</td>
<td>NS</td>
</tr>
<tr>
<td>Time to discharge, days</td>
<td>2.9 (2.2–4.5)</td>
<td>3.6 (2.4–6.3)</td>
<td>0.001</td>
</tr>
<tr>
<td>Glycoprotein IIb–IIIa use</td>
<td>182 (87%)</td>
<td>355 (89%)</td>
<td>NS</td>
</tr>
<tr>
<td>IABP insertion (all femoral)</td>
<td>15 (7.2%)</td>
<td>43 (7.0%)</td>
<td>NS</td>
</tr>
</tbody>
</table>

IABP, intra-aortic balloon pump; MACCE, major cardiac or cerebrovascular event.

load (222 versus 270 ml, p<0.001) and length of hospital stay post-
procedure (2.9 versus 3.6 days, p = 0.001), and a trend towards
lower radiation dosage (36.5 versus 40.5 Gy/cm², p = 0.092). Initial
access failure was significantly more common in the radial group
(7.2% versus 1.0%, p<0.001). There were no differences in needle to
balloon times (17 versus 17 minutes, NS), procedural success, in-
hospital mortality (1.9% versus 2.5%, NS), major cardiac or
cerebrovascular event, IABP and GPIIb–IIIa use or major vascular
complications (table).

Conclusions: In the setting of acute STEMI without cardiogenic
shock, PPCI via an initial transradial approach is safe, with
comparable needle to balloon times, procedural success and in-
hospital outcomes to a femoral approach. The transradial approach
is also associated with earlier hospital discharge.

Abstract 234

ANTI-PLATELET EFFECTS OF ASPIRIN ARE MODIFIED BY
CLOPIDOGREL: ASSESSMENT OF A CLINICALLY RELEVANT
INTERACTION USING SHORT THROMBELASTOGRAPHY

1AR Hobson, 2Z Qureshi, 3P Banks, 4NP Curzen. 1Wessex Cardiac Unit, Southampton University Hospital, Southampton, UK; 2Southampton University Medical School, Southampton, UK

Introduction: Clopidogrel acts by irreversible blockade of platelet
P2Y12 receptors, inhibiting adenosine diphosphate (ADP)-induced
aggregation. Despite additional mechanisms of action, including
anti-inflammatory effects, being suggested the “gold standard”
method of assessing response to clopidogrel, optical aggregometry
with ADP stimulation, only measures the effect of clopidogrel on
ADP-induced platelet aggregation. This may partly explain the
disparity between rates of “resistance” and subsequent event rates.
We have used a novel modification of thrombelastography “short
TEG” to investigate whether clopidogrel has synergistic effects with
aspirin on arachidonic acid (AA)-stimulated clot formation.

Methods: 36 patients with coronary artery disease on aspirin
75 mg were recruited. Exclusion criteria were: smoking, antplatelet
medication other than aspirin within 14 days, and history of peptic
ulceration, bronchial asthma or bleeding. Blood tests were
performed before and 6 hours after witnessed administration of a
clopidogrel 600 mg loading dose. Analysis was performed using the
area under the curve at 15 minutes (AUC15) of the TEG traces
obtained with ADP, AA and kaolin stimulation. The percentage
clotting inhibition (%CIn) for both aspirin and clopidogrel was
obtained with ADP, AA and kaolin stimulation. The percentage
area under the curve at 15 minutes (AUC15) of the TEG traces
clopidogrel 600 mg loading dose. Analysis was performed using the
performed before and 6 hours after witnessed administration of a

Results: As expected there was a 34.2 ± 9.2% reduction in the
AUC15 of the ADP channel from 1074 ± 58 to 700 ± 99
(p<0.001) after clopidogrel with a corresponding increase in %CIn
due to clopidogrel (p<0.001). There was also a 35.0 ± 8.2%
decrease in the AUC15 of the AA channel from 401 ± 71 to
234 ± 33 (p<0.001) and a corresponding increase in %CIn due to
aspirin (p<0.001). The number of patients “resistant” to aspirin
was 10 of 36 at baseline and two of 36 after clopidogrel (p = 0.02)
(fig).

Conclusions: Using short TEG we have demonstrated that in CAD
patients on maintenance aspirin therapy, clopidogrel not only
significantly reduces the response to ADP stimulation, but also
significantly reduces the response to AA stimulation and decreases
the number of patients “resistant” to aspirin. This mechanism of
action may be clinically important, particularly in the context of
clopidogrel cessation, when conceivably it could contribute to the
increased risk of stent thrombosis observed in percutaneous
coronary intervention patients shortly after stopping clopidogrel.
The use of assays that solely identify the effect of clopidogrel on
ADP-induced platelet aggregation may be suboptimal, ignoring
additional mechanisms of action including a synergistic effect with
aspirin. Response to clopidogrel assessed with the AUC15: as well as
the expected response observed in the ADP channel there is a
significant reduction in the AA channel.
**BCS abstracts**

### 235 REDUCTION IN POST-PROCEDURAL STAY IN PERCUTANEOUS RELATIVE TO OPEN AORTIC VALVE REPLACEMENT IN SEVERE AORTIC STENOSIS IN OCTOGENARIANS

H Jilaihawi, I Spyt, LC Laborde, E Logtens, D Chin, J Kovac. Glenfield Hospital, Leicester, UK; Clinique Pasteur, Toulouse, France

**Introduction:** Significant aortic stenosis is common in the elderly. However, such patients are often considered high risk for surgery and when accepted for open surgery they often experience prolonged periods of in-hospital recovery from an open cardiac operation. We report the first clinical experience in the United Kingdom of percutaneous aortic valve replacement (AVR) via the femoral route implanted in 23 elderly patients using a self-expanding nitinol frame for percutaneous transfemoral delivery. Transthoracic echocardiography was used to assess valve function before and after the procedure. Time from procedure to discharge was recorded and compared with a local surgical cohort.

**Results:** Mean age was 85 years (SD 5.1) with mean logistic EuroSCORE of 21.4 (SD 14.3). 8/23 cases (34.7%) were surgical “rejects” and the remainder “high-risk” cases as assessed by a cardiologist and a cardiac surgeon. 19 cases were performed under general and four under local anaesthesia. The peak aortic valve pressure gradient was reduced from 74.8 mm Hg (SD 31.1) to 16.0 mm Hg (SD 6.4) (p < 0.001). The calculated effective orifice area increased from 0.7 cm² (SD 0.14) to 1.5 cm² (SD 0.22) (p < 0.001). Only one patient had grade 2 paraprosthetic aortic regurgitation close to the time of discharge, the remainder having grade 1 or less. Mean post-procedural stay was 5.8 days (SD 3.7). For comparison, we audited the total post-procedural stay of a Leicester series of 1756 conventional open AVR surgery patients with mean age of 66.5 years (SD 12.6). The average postoperative stay for all patients after open surgery was 12.3 days (SD 11.2). This was significantly longer than in the octogenarian percutaneous group (p = 0.001).

**Conclusion:** Our initial experience suggests that percutaneous AVR via the retrograde approach, using the self-expanding aortic valve system, is an effective treatment associated with a considerable shortening of inpatient stay following surgery, even in very elderly patients. Data will be contemporised at the time of the meeting for approximately 50 cases.

*ReValving is a trademark of CoreValve Inc.

### 236 RESCUE PERCUTANEOUS CORONARY INTERVENTION: HOW DO THE OUTCOMES FROM “REAL-WORLD” PATIENTS COMPARE WITH PUBLISHED TRIALS?

DJ Kelly, K Fairbrother, K Chitkara, AH Gershlick. Glenfield Hospital, Leicester, UK

**Introduction:** Following the publication of trial data, rescue percutaneous coronary intervention (PCI) has become standard therapy for patients suffering lytic failure after ST-segment elevation myocardial infarction. As randomised trials inevitably recruit a selected patient population, we have conducted a retrospective analysis of outcomes in 185 consecutive patients undergoing rescue PCI for primary lytic failure, treated between April 2005 and August 2007 and paying particular attention to the impact of delay from symptom onset to rescue PCI and the requirement for interhospital transfer.

**Method:** 185 consecutive patients undergoing rescue PCI were identified from the hospital database of 4487 patients undergoing PCI during the study period. Case notes of all patients were examined to collect in-hospital complications and longer term follow-up. Repeat cardiac catheterisation episodes were identified and case notes interrogated for those episodes. Definition of endpoints was as in the previously published REACT trial. Deaths were confirmed with the Office of National Statistics.

**Results:** Patient demographics are outlined in table 1. The mean delay (SD) from symptom onset to rescue PCI was 501 (229) minutes (8.35 hours), range 145–2240 minutes. Clinical outcomes at a mean follow-up period of 4.5 months are summarised in table 2. All-cause mortality at this time was 7%. Follow-up was available for a mean of 9.2 months for local patients and 1.2 months for transferred patients. The mean delay from symptom onset to PCI was significantly longer in patients undergoing inter-hospital transfer (525 versus 438 minutes, p = 0.001). However, while this trended to a higher mortality outcome (8.4% versus 3.7%, p = 0.42) and composite of death, recurrent myocardial infarction, stroke, or severe heart failure (11.5% versus 9.5%, p = 0.322) these differences did not reach significance. Patients subject to the longest delay before PCI (tertile range 560–2240 minutes, mean 694 minutes) had an increased incidence of death (15.1% versus 3.2%) compared with those with the shortest delay (tertile range 145–405 minutes, mean 290 minutes), although this did not reach statistical significance, p = 0.09. The mortality rate in the mid tertile of delay (tertile range 405–560 minutes, mean 485 minutes) was intermediate at 4.5%.

**Abstract 236 Table 1** Demographic data for patients undergoing rescue PCI

<table>
<thead>
<tr>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, years (SD)</td>
</tr>
<tr>
<td>Male gender</td>
</tr>
<tr>
<td>Cardiogenic shock</td>
</tr>
<tr>
<td>Previous MI</td>
</tr>
<tr>
<td>Previous CABG</td>
</tr>
<tr>
<td>Previous PCI</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td>Hypertension</td>
</tr>
<tr>
<td>Renal creatine &gt;200</td>
</tr>
<tr>
<td>Current smoker</td>
</tr>
<tr>
<td>Anterior MI</td>
</tr>
<tr>
<td>Culprit bypass graft</td>
</tr>
<tr>
<td>DES</td>
</tr>
<tr>
<td>GPIIb/IIIa</td>
</tr>
<tr>
<td>Atherectomy device</td>
</tr>
<tr>
<td>IABP</td>
</tr>
</tbody>
</table>

CABG, coronary artery bypass grafting; DES, drug-eluting stent; IABP, intra-arterial balloon pump; MI, myocardial infarction; PCI, percutaneous coronary intervention.

**Abstract 236 Table 2** Clinical outcomes at longer-term follow-up (mean 4.5 months) following rescue PCI

<table>
<thead>
<tr>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause death*</td>
</tr>
<tr>
<td>Recurrent MI*</td>
</tr>
<tr>
<td>Stroke*</td>
</tr>
<tr>
<td>Severe heart failure*</td>
</tr>
<tr>
<td>Staged or planned PCI</td>
</tr>
<tr>
<td>Target vessel revascularisation</td>
</tr>
<tr>
<td>Acute renal failure</td>
</tr>
<tr>
<td>Emergency CABG</td>
</tr>
<tr>
<td>Major bleed</td>
</tr>
<tr>
<td>Minor bleed</td>
</tr>
</tbody>
</table>

*Major adverse cardiac events 10.3

CABG, coronary artery bypass grafting; MI, myocardial infarction; PCI, percutaneous coronary intervention.
Conclusions: In a “real-world” cohort of unselected patients undergoing rescue PCI, clinical outcomes appear favourable and similar to those seen in the rescue PCI arm of the REACT trial. Rescue PCI should be considered in all patients with failed thrombolysis. Furthermore, our data support the need for prompt reperfusion, although the time constraints appear less important than for primary PCI.

**Abstract 237 Table 1** Rates of death, myocardial infarction or stroke following PCI with stents or CABG

<table>
<thead>
<tr>
<th>Stent type (follow-up)</th>
<th>PCI (%) n = 1518</th>
<th>CABG (%) n = 1533</th>
<th>Relative risk</th>
<th>95% CI</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMS (1 year)</td>
<td>9.5</td>
<td>10</td>
<td>0.94</td>
<td>0.81 to 1.09</td>
<td>0.60</td>
</tr>
<tr>
<td>BMS (5 years)</td>
<td>18.7</td>
<td>18.4</td>
<td>1.02</td>
<td>0.85 to 1.22</td>
<td>0.853</td>
</tr>
<tr>
<td>DES (1 year)</td>
<td>3.6</td>
<td>9.8</td>
<td>0.68</td>
<td>0.49 to 0.93</td>
<td>0.017</td>
</tr>
<tr>
<td>Combined BMS + DES (1 year)</td>
<td>7.1</td>
<td>9.7</td>
<td>0.73</td>
<td>0.60 to 0.89</td>
<td>0.034</td>
</tr>
</tbody>
</table>

BMS, bare metal stent; CABG, coronary artery bypass grafting; DES, drug-eluting stent; PCI, percutaneous coronary intervention.

**Abstract 237 Table 2** Rates of the secondary endpoints (mortality and repeat revascularisation) following PCI with stents or CABG

<table>
<thead>
<tr>
<th>Stent type (follow-up)</th>
<th>PCI (%) n = 1518</th>
<th>CABG (%) n = 1533</th>
<th>Relative risk</th>
<th>95% CI</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMS (1 year)</td>
<td>3.5</td>
<td>3.3</td>
<td>1.07</td>
<td>0.73 to 1.56</td>
<td>0.732</td>
</tr>
<tr>
<td>BMS (5 years)</td>
<td>9.3</td>
<td>9.5</td>
<td>0.98</td>
<td>0.75 to 1.28</td>
<td>0.866</td>
</tr>
<tr>
<td>DES (1 year)</td>
<td>2.9</td>
<td>5.8</td>
<td>0.50</td>
<td>0.31 to 0.80</td>
<td>0.004</td>
</tr>
<tr>
<td>Combined BMS + DES (1 year)</td>
<td>3.3</td>
<td>4.1</td>
<td>0.79</td>
<td>0.49 to 1.34</td>
<td>0.112</td>
</tr>
<tr>
<td>Revascularisation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMS (1 year)</td>
<td>17.5</td>
<td>4.1</td>
<td>4.26</td>
<td>3.27 to 5.55</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMS (5 years)</td>
<td>30.3</td>
<td>7.6</td>
<td>4.01</td>
<td>3.18 to 5.07</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DES (1 year)</td>
<td>7.5</td>
<td>4.0</td>
<td>1.88</td>
<td>1.28 to 2.75</td>
<td>0.001</td>
</tr>
</tbody>
</table>

BMS, bare metal stent; CABG, coronary artery bypass grafting; DES, drug-eluting stent; PCI, percutaneous coronary intervention.
Abstract 238

<table>
<thead>
<tr>
<th></th>
<th>CTO success</th>
<th>CTO failure</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>340</td>
<td>161</td>
<td></td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>52.9</td>
<td>60.9</td>
<td>0.06</td>
</tr>
<tr>
<td>Previous CABG (%)</td>
<td>4.4</td>
<td>9.9</td>
<td>0.02</td>
</tr>
<tr>
<td>Occluded length (mm, mean ± SD)</td>
<td>23.3 ± 18.4</td>
<td>17.2 ± 12.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Functional occlusion (%)</td>
<td>14.7</td>
<td>4.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Moderate–severe calcification (%)</td>
<td>26.5</td>
<td>47.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CTO involving bifurcations (%)</td>
<td>29.2</td>
<td>18.1</td>
<td>0.005</td>
</tr>
<tr>
<td>Bridging collaterals (%)</td>
<td>34.4</td>
<td>44.1</td>
<td>0.024</td>
</tr>
<tr>
<td>Tapered morphology of stump (%)</td>
<td>40.1</td>
<td>29.4</td>
<td>0.015</td>
</tr>
</tbody>
</table>

CABG, coronary artery bypass grafting; CTO, chronic total occlusion.

Results: Patients were aged 63 ± 12 years, 84% male, 28% diabetic, 21%, 6.2% and 32% had a previous myocardial infarction, coronary artery bypass graft surgery and percutaneous coronary intervention, respectively. Mean length and median duration of occlusion was 19 ± 15 mm and 5 (3, 12) months, respectively. Contralateral injections, parallel wire, anchoring balloon technique, retrograde wiring and CTO-specific wires (>3 g tip load) were employed in 25%, 21%, 6%, 5% and 75% of cases, respectively. Angiographic success was obtained in 68% and in-hospital major adverse cardiac events were 2.4%. Angiographic or clinical features with significant associations (or strong trends) to procedural success are illustrated in the table. Occlusion duration was not significant on univariate analysis (median (interquartile range) duration 4 (3, 12) months with procedural success versus 5 (3, 12) months with procedural failure, p = 0.6). By multiple logistic regression analysis the only independent predictors of failure were moderate to severe calcification (p = 0.001; odds ratio (OR) 2.9; CI 1.9 to 4.5) and occlusion length (p = 0.008; OR 1.5; CI 1.1 to 1.9 per 20 mm increase in occlusion length), whereas functional occlusion (p = 0.007; OR 3.3; CI 1.4 to 7.8) and CTO involving bifurcation (p = 0.009; OR 2.1; CI 1.2 to 3.7) predicted success.

Conclusion: With novel techniques and specific equipment occlusion length and moderate to severe lesion calcification are the only factors that predict failure of CTO revascularisation. Previously identified predictors such as bridging collaterals or blunt stump morphology are no longer independently predictive of failure and should not in themselves preclude an attempt at percutaneous revascularisation.

FOUR-YEAR CLINICAL FOLLOW-UP OF THE RAPAMYCIN-ELUTING STENT EVALUATED AT ROTTERDAM CARDIOLOGY HOSPITAL (RESEARCH) REGISTRY

N Kukreja, J Daemen, P van Twisk, Y Onuma, P de Jaegere, R van Domburg, PW Sarma, Erasmus MC, Rotterdam, The Netherlands

Background: Although the safety of drug-eluting stents has been under considerable scrutiny, limited real-world follow-up data extending up to 4 years are available. The randomised clinical trials carefully selected patients and are not reflective of everyday practice.

Methods: From April to October 2002, we enrolled 508 consecutive patients treated with sirolimus-eluting stents (SES). The control group consisted of 450 patients treated with bare metal stents (BMS) treated in the preceding 6 months. Follow-up survival data for all patients were obtained from municipal civil registries. The causes of death were classified according to the International Classification of Diseases and Related Health Problems, 10th Revision. A health questionnaire was subsequently sent to all living patients with specific enquires on rehospitalisation and major adverse cardiac events. For patients who suffered an adverse event, medical records or discharge summaries were systematically reviewed. General practitioners, referring cardiologists and patients were contacted as necessary if further information was required.

Results: After 4 years of follow-up, we found that the incidence of composite major adverse clinical events (all-cause death, myocardial infarction or target vessel revascularisation) was significantly lower in the SES group (25.0% versus 28.7%, adjusted hazard ratio (HR) 0.66, 95% CI 0.51 to 0.86), as were rates of target vessel revascularisation (12.2% versus 17.8%, adjusted HR 0.57, 95% CI 0.39 to 0.83) (fig). There were no differences in all-cause mortality (10.5% SES versus 10.6% BMS, p = 0.9) or in the rates of cardiac death (4.5% versus 6.9%, p = 0.1). The independent predictors of mortality were cardiogenic shock (HR 5.79, 95% CI 2.46 to 13.6), left main treatment (HR 2.17, 95% CI 1.00 to 4.17), diabetes mellitus (HR 1.78, 95% CI 1.11 to 2.65), age (per 10-year increment HR 1.42, 95% CI 1.16 to 1.74) and angiographic success (HR 0.43, 95% CI 0.19 to 0.98). Although there was no difference in overall stent thrombosis (2.3% versus 2.2%, p = 1.0), SES had a higher rate of very late stent thrombosis (1.4% versus 0%, p = 0.02), balanced by a lower rate of early stent thrombosis (0.4% versus 1.8%, p = 0.05) (tables 1 and 2).

Conclusion: After 4 years, we found that SES remained safe and effective compared with BMS. Nevertheless, the higher rate of very late stent thrombosis remains a concern: longer-term follow-up will be required to determine the extent of this problem.

Abstract 239 Table 1 Cumulative incidence of adverse events

<table>
<thead>
<tr>
<th></th>
<th>BMS</th>
<th>SES</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>48 (10.6%)</td>
<td>53 (10.5%)</td>
<td>0.9</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>23 (5.2%)</td>
<td>21 (4.2%)</td>
<td>0.5</td>
</tr>
<tr>
<td>Target vessel revascularisation</td>
<td>78 (17.8%)</td>
<td>60 (12.2%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Composite MACE</td>
<td>127 (28.7%)</td>
<td>115 (23.0%)</td>
<td>0.05</td>
</tr>
<tr>
<td>Stent thrombosis</td>
<td>10 (2.2%)</td>
<td>12 (2.3%)</td>
<td>1.0</td>
</tr>
</tbody>
</table>

BMS, bare metal stent; MACE, major adverse cardiac event; SES, sirolimus-eluting stent.
LONG-TERM CLINICAL FOLLOW-UP OF 6129 CONSECUTIVE ALL-COMERS TREATED WITH BARE METAL, SIROLIMUS OR PACLITAXEL-ELUTING STENTS

N Kukreja, J Daemen, P van Twisk, Y Onuma, R van Domburg, E Boersma, P de Jaegere, PW Serruys. Erasmus MC, Rotterdam, The Netherlands

Introduction: Sirolimus and paclitaxel-eluting stents (SES and PES, respectively) produce a sustained reduction in repeat revascularisations compared with bare metal stents (BMS). However, there have been recent concerns regarding the long-term safety and risk of stent thrombosis in drug-eluting stents (DES).

Methods: Between 1 January 2000 and 31 December 2005 a total of 6129 consecutive patients were treated during three sequential periods with either BMS (n = 2428; January 2000 to April 2002), SES (n = 866; April 2000 to February 2003) or PES (n = 2835; February 2003 to December 2005). Four-year follow-up on the occurrence of death, myocardial infarction, repeat revascularisation and stent thrombosis was collected. Survival information was obtained from municipal civil registries and causes of death were classified according to the International Classification of Diseases and Related Health Problems, 10th Revision.

Results: Patients treated with SES had better survival rates than those treated with PES and a non-significant trend towards improved survival compared with BMS. There were no differences in survival between BMS and PES (fig 1). Target vessel revascularisation (TVR) rates were lower with both types of DES compared with BMS, with no differences between SES and PES (fig 2). After 4 years, the rates of definite stent thrombosis were 1.6% for BMS patients, 2.6% with SES and 3.2% with PES (SES versus BMS, p = 0.11; SES versus PES p = 0.32, PES versus BMS p = 0.003). TVR rates were lower in the DES patients after 1 year (hazard ratio (HR) 0.57, 95% CI 0.46 to 0.71, p < 0.001) and 4 years (HR 0.74, 95% CI 0.63 to 0.88, p < 0.001). The beneficial effects on TVR were seen across all subgroups.

Conclusion: All-cause mortality was lower following SES implantation, although both SES and PES remain superior to BMS in reducing TVR. However, a clear decrease in the adjusted treatment effect (TVR) between 1 and 4 years of follow-up was observed. Very late stent thrombosis occurs more often after DES use.

BIODEGRADABLE POLYMER-BASED, SIROLIMUS-ELUTING SUPRALIMUS STENT: 6-MONTH ANGIOGRAPHIC AND 30-MONTH CLINICAL FOLLOW-UP RESULTS FROM THE SERIES I PROSPECTIVE STUDY

1N Kukreja, S Dani, P Parikh, H Joshi, J Prajapati, S Jain, S Thanvi, B Shah, JP Dutta. 1Erasmus MC, Rotterdam, The Netherlands; 2SAL Hospital and Medical Institute, Ahmedabad, India; 3Sheth Vadilal Sarabhai General Hospital, Ahmedabad, India; 4Sahajanand Medical Technologies Pvt Ltd, Surat, India

Background: There have been recent concerns regarding the long-term safety of the first generation of drug-eluting stents, which utilised a permanent polymer coating for drug delivery. SERIES I is a prospective, non-randomised, first-in-man open label study with the biodegradable polymer-based Supralimus sirolimus-eluting stent (Sahajanand Medical Technologies Pvt Ltd, India) for the treatment of patients with coronary artery lesions.

Methods: The Supralimus stent consists of a stainless steel stent platform (Matrix; Sahajanand Medical Technologies) coated with a biodegradable polymer and sirolimus. 100 patients were treated with 126 Supralimus stents (mean lesion length 10.5 ± 4.3 mm, mean reference vessel diameter 2.66 ± 0.62 mm). The prespecified primary endpoints were major adverse clinical events (MACE; defined as a composite of cardiac death, non-fatal myocardial infarction (Q-wave and non-Q wave), or clinically justified target vessel revascularisation) at 30 days and angiographic binary instant restenosis at 6 months. The secondary endpoint was MACE at 9 months. All the patients were clinically followed up at 30 days, 6, 9, 24 and 30 months (fig).

Results: There were no in-hospital complications and no adverse clinical events at 30 days follow-up. MACE rates were 6% at 9-month follow-up and 7% after 30 months follow-up.
follow-up in a prespecified subgroup of 60 patients at 6 months showed binary angiographic restenosis rates of 0% (in-stent) and 1.7% (in-segment). The in-stent late loss was 0.09 ± 0.37 mm.

**Conclusion:** The biodegradable-polymer-based sirolimus-eluting stent (Supralimus) demonstrates favourable angiographic results, while maintaining an excellent safety profile.

**DO WE HAVE THE COURAGE TO DEFER CORONARY INTERVENTION? A REAL-WORLD ANALYSIS**

TPE Lockie, D Perera, P O’Kane, S Hartley, S Khan, S Pattinson, SR Redwood. St Thomas’ Hospital, London, UK

**Background:** Myocardial fractional flow reserve (FFR) has become a clinically accepted standard for the invasive detection of ischaemia. The DEFER study has shown that patients with a single moderate coronary stenosis on angiography can be safely treated medically if the FFR is >0.75. It has also been suggested that FFR can be used to guide revascularisation strategies in multivessel disease.

**Methods:** 300 consecutive patients who had coronary pressure wire assessments between 2005 and 2007 were included in the analysis. FFR was calculated as (Pd–Pv)/(Pa–Pv), where Pa, Pv and Pd are simultaneous aortic, right atrial and distal coronary pressures measured during an intravenous infusion of adenosine at 140 μg/kg per minute. We assessed the influence of the FFR result on subsequent lesion revascularisation, the long-term outcome of patients who had intervention deferred and performed on the basis of an FFR threshold of 0.75 and the impact of multivessel FFR assessment on revascularisation strategy. Outcome data were collected through patient questionnaires and analysis of the cardiothoracic database at St Thomas’ Hospital. Data are presented as mean ± standard deviation.

**Results:** Of the 300 patients, 264 were included in the analysis. 14 study patients were excluded; nine patients’ FFR measurement was unsuccessful (four unable to wire vessel, three adenosine-induced heart block, two adenosine-induced bronchospasm); 13 patients’ data were not available. Patients included were 62 ± 11 years old and 1.3 ± 0.5 vessels were examined in each case. 92% of lesions with a FFR < 0.75 underwent revascularisation and 94% of lesions with a FFR > 0.75 had intervention deferred. Of those who underwent revascularisation, 12 patients had coronary artery bypass surgery and 96 had percutaneous intervention. The FFR was 0.71 ± 0.07 in those who had revascularisation performed and 0.86 ± 0.06 in those who were deferred (p < 0.001). At 1.32 ± 0.56 years, the composite endpoint of death, myocardial infarction or target vessel revascularisation occurred in 5.6% in the ‘perform’ group versus 9.0% in the ‘defer’ groups (p = 0.45) see fig 1 for individual endpoints, all NS. Overall, 77% of patients avoided revascularisation of at least one vessel (1.3 ± 0.5) on the basis of the FFR measurement see fig 2.

**Conclusions:** Deferring revascularisation of intermediate coronary lesions on the basis of a dichotomous FFR threshold of 0.75 appears to be a safe strategy. FFR can be used to classify multivessel disease further and to tailor revascularisation strategies to avoid unnecessary interventions.
comparable outcomes to unfractionated heparin (UFH) or enoxaparin with glycoprotein IIb/IIIa inhibitors in patients with acute cardiac syndrome (ACS) treated with PCI. Anticoagulation with bivalirudin alone suppressed adverse ischaemic events similar to other regimens, while significantly lowering the risk of haemorrhagic complications. Another promising synthetic coagulation inhibitor, fondaparinux (Arixtra), studied in the OASIS-V trial, was unexpectedly associated with an increase in the development of a rare, potentially dangerous event, guide catheter thrombosis. To our knowledge, this adverse event has not been examined in bivalirudin trials. We studied the development of catheter thrombosis with bivalirudin, UFH and enoxaparin in a controlled environment using an in-vitro model.

Methods: Seven healthy volunteers pretreated with aspirin (500 mg) gave 50 ml blood, collected into sample tubes containing anticoagulant. Seven anticoagulant combinations were tested and the volunteers donated blood seven times and acted as their own controls. The groups were: group 1 UFH 0.8 U/ml (10); group 2 UFH + integrilin 1.7 µg/ml (10); group 3 enoxaparin 0.6 U/ml (10); group 4 enoxaparin + integrilin (10); group 5 bivalirudin 0.3 µg/ml (10); group 6 bivalirudin + integrilin (10); group 7 bivalirudin + continuous infusion of bivalirudin. The blood/anticoagulant mix was kept at 37°C and continuously circulated through a 6 French multipurpose guiding catheter (Cordis) for 60 minutes or until the catheter became blocked with thrombus. Thrombus development was assessed by weighing each catheter before and after the procedure. The activated clotting time (ACT) of the perfusate was measured at the end of each experiment.

Results: Following anticoagulation with bolus dose bivalirudin, the catheter was invariably occluded with thrombus after 45 minutes of circulation. Similar results were obtained with bolus bivalirudin alone or in combination with integrilin. Catheter occlusion by thrombosis was associated with a perfusate ACT of 200 s. However, a continuous infusion of bivalirudin, (resulting in an ACT consistently in the range of 350–400 s) prevented the development of occlusive catheter thrombosis. Mean thrombus weight was significantly greater in group 5 (bivalirudin) than in group 2 (UFH + integrilin), group 3 (enoxaparin), group 4 (enoxaparin + integrilin) and group 7 (bivalirudin bolus + continuous infusion).

Conclusion: Bolus bivalirudin was not sufficient to prevent cardiac catheter thrombosis in our in-vitro study. However, a continuous infusion of bivalirudin had similar antithrombotic efficacy compared with other treatment strategies. The ready development of catheter thrombosis with bolus bivalirudin underlines the importance of using recommended dosing regimes for bivalirudin with a bolus followed by infusion in patients undergoing PCI.

Abstract 244

Demographics

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Age</th>
<th>Sex (male)</th>
<th>Previous MI</th>
<th>Gp 2b/3a</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risks</td>
<td>Diabetes</td>
<td>Hypertension</td>
<td>Smoker</td>
<td>Cr &gt;200</td>
</tr>
<tr>
<td></td>
<td>57 ± 0.7 years</td>
<td>236 (82.5%)</td>
<td>53 (18.5%)</td>
<td>232 (72%)</td>
</tr>
<tr>
<td></td>
<td>34 (11.8%)</td>
<td>85 (29.6%)</td>
<td>105 (36.6%)</td>
<td>1 (0.4%)</td>
</tr>
<tr>
<td>Infarct artery</td>
<td>LAD</td>
<td>LCX</td>
<td>RCA</td>
<td>Other</td>
</tr>
<tr>
<td></td>
<td>115 (40%)</td>
<td>43 (15%)</td>
<td>103 (36%)</td>
<td>26 (9%)</td>
</tr>
</tbody>
</table>

Cr, creatinine; Gp, glycoprotein; LAD, left anterior descending; LCX, left circumflex; MI, myocardial infarction; RCA, right coronary artery.

244 REAL WORLD BLEEDING COMPLICATIONS DURING RESCUE PERCUTANEOUS CORONARY INTERVENTION: THE MANCHESTER HEART CENTRE EXPERIENCE

MA Mamas, M Zi, B Clarke, M El-Ormar, F Fath-Orudabadi, R Khattar, C Appleby, M Anwar, L Nancy, D Fraser. Department of Cardiology, Manchester University, Manchester, UK; Manchester Heart Centre, Manchester, UK

Rescue percutaneous coronary intervention (PCI) performed as an emergency procedure in patients with ST elevation myocardial infarction has been widely adopted in the United Kingdom in patients in whom there is poor ST resolution following thrombolysis. This strategy has been investigated in the UK-based REACT (n = 144 patients) and MERLIN (n = 153 patients) trials. Coronary angioplasty in this setting has been associated with an increased risk of bleeding complications. In the REACT study, 26% of patients had overt bleeding and in the MERLIN study 11% required transfusion. We postulated that bleeding complications performed in a “real world” setting could be higher than those observed in the setting of these clinical trials in which many high-risk patients are excluded.

We therefore retrospectively studied 287 patients admitted to Manchester Heart Centre for rescue PCI from January 2004 to August 2007 to assess bleeding complications in a “real-world” cohort of patients and identify those groups at risk from bleeding complications.

The demographics of these 287 patients are presented in the table.

There was a total of nine deaths during the inpatient stay (3.1%) of which two were during the procedure (0.7%). A total of 48 bleeding complications (16.7%) were noted, three of which were intracranial bleeds (1%), three retroperitoneal bleeds (1%), 27 had a haematoma >2 cm (9.4%) of which three required blood transfusion. Four patients had haematemesis (1.4%) and a further three patients (1%) had a significant drop in haemoglobin necessitating a blood transfusion in which the source of bleeding was not identified. In total, in this cohort nine patients required a blood transfusion (3.1%). Of the nine in-hospital deaths only one (11.1%) occurred as a consequence of a major bleed (intracranial haemorrhage). The mean age of patients with a bleed was significantly greater at 60.2 ± 1.8 years than the mean age of patients who did not suffer a bleeding complication, 56 ± 0.7 years (p<0.05). There was a significantly greater proportion of women in the bleeding group (28%) compared with the non-bleeding group (14.5%) p<0.05. No significant difference between the two cohorts of patients in percentage hypertension (19.5% versus 16.4%), smokers (15.4% versus 18.9%), diabetes (14.5% versus 8.8%) or percentage glycoprotein 2b/3a inhibitors used (85.4% versus 74.4%) in the bleeding versus non-bleeding cohort was observed.

In summary, in one of the largest published series of patients undergoing rescue PCI, close to the combined size of the MERLIN and REACT trial cohort (287 patients versus 297 patients) we have demonstrated a low risk from serious bleeding complications that was lower than in the randomised trials. This is despite the inclusion of higher risk patients excluded from the MERLIN and REACT trials and our greater rates of glycoprotein 2b/3a inhibitor usage (72%) compared with MERLIN (3.3%) and REACT (43.4%), which would have been expected to increase our bleeding complications further. We have demonstrated that age and female sex in particular represent an increased risk of potential bleeding complications.

245 A COMPARISON OF FRACTIONAL FLOW RESERVE AND MIBI-SPECT TO DETECT ISCHAEMIC TERRITORIES IN PATIENTS WITH MULTIVESSEL CORONARY ARTERY DISEASE

N Melikian, P De Bondt, T Cusset, E Wyffels, J Bartunek, G Heyndrickx, W Wijns, B De Bruyne. Cardiovascular Division, King’s College School of Medicine, London, UK; Cardiovascular Center Aalst, Aalst, Belgium

Introduction: MIBI-single photon emission computed tomography (MIBI) can underestimate the number of ischaemic territories in patients with multivessel coronary disease (MVCD), with only 29% of patients with angiographic three-vessel disease having perfusion defects in all territories. However, the association
Abstract 245 Per-patient and per-vascular territory comparison of MIBI-single-photon emission computed tomography and FFR in patients with multivessel coronary disease

<table>
<thead>
<tr>
<th></th>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Per-patient</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FFR ≤ 0.80</td>
<td>15</td>
<td>8</td>
</tr>
<tr>
<td>&gt; 0.80</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Per-vascular territory</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FFR ≤ 0.80</td>
<td>22</td>
<td>17</td>
</tr>
<tr>
<td>&gt; 0.80</td>
<td>15</td>
<td>30</td>
</tr>
</tbody>
</table>

FFR, fractional flow reserve.

between physiological evidence for ischaemia per vessel derived from coronary fractional flow reserve (FFR) and MIBI in MVCD is unknown.

Methods: In 84 vascular territories in 28 patients (mean age 63.9 ± 9.8 years, left ventricular ejection fraction 69 ± 12%) with angiographic MVCD (>50% stenosis in ≥2 vessels) results of MIBI (rest/stress adenosine) were compared with FFR measurements in each coronary vessel. The AHA semiquantitative five-point scoring system using a 17-segment model was used to report MIBI scans. A FFR <0.80 was taken as evidence of ischaemia.

Results: MIBI was positive in at least one territory in 19 (67%) patients both MIBI and FFR detected identical ischaemic territories, MIBI: 0.3 ± 0.7, FFR: 1.0 ± 0.1; <0.001) or overestimated (11 (39%) patients—mean number of ischaemic territories, MIBI: 2.0 ± 0.0, FFR: 1.0 ± 0.1; p = 0.02) the number of ischaemic territories. There was a weak correlation between the severity of ischaemia as assessed by MIBI in each vascular territory and the actual FFR value (r = 0.34, p = 0.001).

Conclusion: Although MIBI is positive for ischaemia in a proportion of patients with MVCD it has poor concordance with FFR and under or overestimates the number of ischaemic territories in 71% of patients in comparison with FFR.

247 TREATMENT OF INTERNAL MAMMARY ARTERY GRAFT STENOSIS WITH DRUG-ELUTING STENTS COMPARED WITH BARE METAL STENTS

A Qasimi, J Cosgrave, A Latib, F Airoldi, A Colombio. EMO Centro Cuore Columbus, Milan, Italy

Introduction: Coronary artery bypass grafting with internal mammary arteries (IMA) is effective, with a low failure rate. The relative infrequency of flow limiting IMA graft stenosis means that there are a paucity of data regarding the safety and benefits of percutaneous intervention for IMA stenosis. This study examines the outcome of bare metal stents (BMS) compared with drug-eluting stents (DES) for IMA graft stenosis.

Methods: This retrospective study examined patients treated for IMA graft stenosis between April 1999 and April 2005. BMS were used from 1999 to 2001 and DES from 2001 to 2005. Patient and follow-up data were collected for a minimum of 12 months. The follow-up period for BMS implantation was curtailed to match the follow-up period for DES. The endpoints examined were in-hospital outcome and follow-up target lesion revascularisation, target vessel revascularisation, myocardial infarction, death and major adverse clinical events (MACE). MACE was a combined endpoint of target vessel revascularisation, myocardial infarction and death.

Results: The study examined 70 patients: 28 with BMS (1999–2001) and 42 with DES (2001–2005) implantation. There were no significant differences in patient characteristics between the two groups. The rates of procedural complications were low with no significant differences between BMS and DES. In-hospital myocardial infarction (BMS 3.6% versus DES 2.3%). There were no available and suitable. A single stent approach was generally used for disease of the ostium or body and a “shotgun” approach for disease of the bifurcation. Maximum revascularisation of other significant disease was performed. Reopro and intra-aortic balloon pumping were used liberally. Dual antiplatelet therapy was given for double stent patients for life. The patients were followed clinically, without routine repeat angiography. The outcomes were death and repeat revascularisation.

Results: To December 2007, 250 consecutive patients were treated. The mean age was 67 years and 70% were men. The logistic New York PCI risk score estimated mortality was median 0.59%, range 0.12–64.46%. Treatment was as an emergency in 12%, urgent in 26% and elective in 65%. 50% were unsuitable for CABG and 11% had a “protected” LMS. 10% were in cardiogenic shock, a balloon pump was used in 20% and Reopro in 48%. A mean 2.0 other main vessels were diseased and 1.7 were treated. 71% of the lesions involved the bifurcation. A single LMS stent was used in 42% and two in 55%. Drug-eluting stents were used in 59%. The procedure was technically successful in 99.2%. Overall 24-month mortality was 10% (median NY score of the dead patients was 12.5%, EuroSCORE 21.3%). 6.5% died within 7 days (NY score 7.05%, EuroSCORE 15.56%) and 3.2% late (NY score 0.81%, EuroSCORE 4.99%). The median time of death was 5 days (range 0–300). 24-month mortality was 38% (emergency), 12.5% (urgent) and 3.8% (elective). 24-month mortality did not differ for bifurcation/non-bifurcation lesions. 24-month mortality of patients who were suitable for CABG was 4%. Overall, repeat revascularisation was required in 4% (six PCI and three CABG).

Conclusions: PCI to the LMS is a safe and effective resource for a typical population of patients presenting to a major centre, including a high proportion of acutely ill patients, those with significant co-morbidity and surgical rejects. The outcomes depend upon the clinical presentation, with 2-year survival of 62% for emergency, 67.5% for urgent and 96.2% for elective patients. For patients suitable for CABG, PCI and CABG offer equivalent 2-year mortalities.
episodes of in-hospital death or acute stent thrombosis. There was a single episode of subacute stent thrombosis with BMS use, and none with DES. There was one episode of late stent thrombosis in the BMS group according to the ARC research criteria and none in the DES group. The rate of target lesion revascularisation was significantly higher for BMS (17.9% versus 119%, p = 0.01), as was target vessel revascularisation (BMS 28.6% versus 16.6%, p = 0.01). There were no significant differences in death or myocardial infarction at follow-up (myocardial infarction BMS 7.2% versus DES 2.5%; death BMS 7.2% versus DES 2.5%). The MACE rate was 42.8% for BMS and 21.4% for DES (p = 0.001).

Conclusions: The findings in this study showed that stent implantation was a safe and effective treatment for IMA graft stenosis with low event rates over long-term follow-up. Treatment with DES was significantly better than BMS in terms of procedural outcome and long-term follow-up.

248 NOVEL TREATMENT OF CLOPIDOGREL INTOLERANCE

U Rao, S Talwar, R Swallow. Royal Bournemouth Hospital, Bournemouth, UK

Introduction: There is substantial trial evidence for using clopidogrel and aspirin as the main therapy in atherothrombotic disease (CURE, CAPRIE) and in percutaneous coronary interventions (PCI) (PCI-CURE). However, approximately 4% of patients develop allergic reactions within 1–72 days of initiating clopidogrel. Discontinuation is not an option as it is associated with an increased risk of mortality and morbidity. The treatments available include substituting with ticlopidine and anti-coagulation, which although effective have potentially life-threatening side effects and more recently desensitisation therapy. We also experienced a similar problem in our setting, which prompted us to conduct this study and evaluate a novel treatment option.

Methods: This prospective study, including patients who underwent single or multivessel PCI at Royal Bournemouth Hospital (RBCH) and subsequently developed an allergic reaction to clopidogrel, was carried out over a period of 23 months (January 2006 to November 2007). These patients were identified either via their local general practitioners or from direct contact with the RBCH PCI service as advised at the time of PCI. Patients with a rash felt to be secondary to clopidogrel were treated with a course of prednisolone and chlorpheniramine for 7 days and advised to continue clopidogrel. A telephone survey was performed to evaluate the following parameters: procedures performed, onset of rash, details of the rash, treatment given or changed, improvement in rash, any recurrence, hospital admissions and history of discontinuation of clopidogrel.

Results: Of the 2701 patients admitted for PCI, only 20 patients developed allergic reaction and 19 were available for survey (nine men and 10 women). The average patient age was 67.2 years (29–120). The majority of the patients had drug-eluting stents and two had bare-metal stents. In these patients the rash developed between 1 and 21 days (average 4.5) after commencing clopidogrel. It was generalised in 89% (17) of the patients and localised (hands and chest) in two patients. They were all treated with oral steroids and antihistamines except two cases who responded to topical steroid cream and chlorpheniramine only. There were no hospital admissions. There was complete resolution of rash in 17 (89%) patients within 1–14 days (average 3.2) following treatment, one patient had partial response but was able to continue clopidogrel and another had no response. No recurrence or any side effects to the treatment were reported.

Conclusion: In our series of 2701 patients only 0.7% developed allergic reaction to clopidogrel. Antiplatelet agent inducing allergic reaction is an issue of concern especially in the era of drug-eluting stents and stent thrombosis. We propose a novel, safe and effective way of managing this problem without stopping or substituting clopidogrel.

249 EVALUATION OF THE CLINICAL PERFORMANCE OF THE MEDTRONIC ENDEAVOR ABT-578 ELUTING CORONARY STENT SYSTEM IN PATIENTS UNDERGOING PRIMARY PERCUTANEOUS CORONARY INTERVENTION FOR ACUTE MYOCARDIAL INFARCTION: THE ENDEAVOR PRIMARY PCI STUDY (E-PPCI)


Background: Primary percutaneous coronary intervention (PCI) is superior to thrombolysis in patients with ST elevation acute myocardial infarction (STEMI). Furthermore, drug-eluting stents (DES) have been shown to be superior to bare metal stents (BMS) for reduction in clinical restenosis rates. Data on late stent thrombosis (>30 days) raise concern about DES placement in a patient with an acute coronary syndrome. Recent studies using sirolimus (TYPHOON) and paclitaxel (PASSION)-eluting stents in the PCI setting have been published and suggest equivalence or superior outcomes compared with BMS. We report the first evaluation of the Medtronic Endeavor ABT-578 eluting coronary stent system in patients undergoing PCI.

Methods: A prospective, single-centre registry of consecutive patients admitted with STEMI who underwent PCI was performed. All subjects were within 12 hours of onset of symptoms when the clinical decision was made to undergo PCI and each received one or more Endeavor stents in one or more target lesions. Clopidogrel 600 mg and aspirin 300 mg preprocedure followed by 75 mg daily maintenance of each for 12 months was given universally. All subjects received Reopro (abciximab) and unfractionated heparin (70 IU/kg).

Results: 102 STEMI patients (76 men, 26 women) received 162 Endeavor stents; age range 37–84 years (mean 62 ± 12 years). Risk factor profile on presentation in percentages comprised 29% hypertension, 25% hyperlipidaemia, 11% diabetes, 48% current smokers and 33% positive family history. Major adverse cardiovascular event rate (MACE) was defined as the composite endpoint of death, recurrent myocardial infarction and target lesion revascularisation (repeat percutaneous coronary intervention or coronary artery bypass grafting). The primary endpoint of 30-day MACE was seen in four patients and comprised two deaths (days 1 and 14) and two target lesion revascularisations as a result of early stent thrombosis (days 9 and 11). One of these early stent thromboses was a presumed result of aspirin and clopidogrel non-compliance. Follow-up at 6 months has resulted in one further MACE of target lesion revascularisation on day 107 for late stent thrombosis.

Conclusion: This is the first report of the use of the Endeavor stent in an unselected, consecutive PCI population. The low occurrence of the primary endpoint in only 4.9% of the study population at 6 months follow-up suggests that this DES platform is safe and comparable to other DES platforms in STEMI. However, longer-term follow-up is necessary.

250 MYOCARDIAL INFARCTION AFTER PERCUTANEOUS CORONARY INTERVENTION: A META-ANALYSIS OF TROPTONIN ELEVATION APPLYING THE NEW UNIVERSAL DEFINITION

1L Testa, 2WJ van Gaal, 3R Bhindi, 3I Porto, 3AP Banning, 3John Radcliffe Hospital, Oxford, UK; 2Northern Hospital, Melbourne, Australia; 3Catholic University, Rome, Italy

Background: Elevation of troponin after scheduled percutaneous coronary intervention (PCI) is a recognised consequence. Recently, a new definition of PCI-related myocardial infarction (MI) has been suggested. We sought to evaluate the incidence, prognostic significance and impact of this new definition.
Any Tn elevation

<table>
<thead>
<tr>
<th>Event</th>
<th>Hydrophilic-coated sheath (%)</th>
<th>Non-hydrophilic-coated sheath (%)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MACE</td>
<td>25</td>
<td>33</td>
<td>0.49</td>
</tr>
<tr>
<td>Death</td>
<td>20</td>
<td>50</td>
<td>0.15</td>
</tr>
<tr>
<td>AMI</td>
<td>33</td>
<td>50</td>
<td>0.18</td>
</tr>
<tr>
<td>Re-PCI</td>
<td>10</td>
<td>25</td>
<td>0.12</td>
</tr>
<tr>
<td>CABG</td>
<td>3</td>
<td>3</td>
<td>0.12</td>
</tr>
</tbody>
</table>

Abstract 250

CABG, coronary artery bypass grafting; MACE, major adverse cardiac event; PCI, percutaneous coronary intervention; ULN, upper limit of normal.

Methods: Search of BioMed Central, CENTRAL, mRCT, and PubMed (updated October 2007). Outcomes of interest were: major adverse cardiac events (MACE; the composite of all-cause death, MI, repeat target vessel PCI and coronary artery bypass grafting (CABG)); single endpoints were also assessed.

Results: Fifteen studies have been included totalling 7891 patients. Average follow-up was 17.7 months. Troponin elevation, regardless of its extent, occurred in 28.7% of patients. It was associated with an increased risk of MACE (odds ratio (OR) 1.48 (1.12 to 1.96), number needed to harm (NNH) 20), death (OR 2.19 (1.59 to 3.00), NNH 50), and MI (OR 3.19 (2.71 to 6.31), NNH 33), and repeat target vessel PCI (OR 1.47 (1.06 to 2.03), NNH 25). No significant differences were observed for the risk of CABG. Four studies, totalling 2539, reported data about patients with different extents of troponin elevation. The incidence of PCI-related MI according to the new definition was 14.5%. Using this definition, the risk of MACE was further increased: OR 2.25 (1.26 to 4.00), NNH 3. An increase in the troponin level below the prespecified arbitrary cutoff was not associated with a significantly increased risk of MACE (see fig).

Conclusion: Small increases in troponin do not appear to confer an adverse prognosis at 18 months; however, a diagnosis of MI according to the new guidelines applies to 15% of patients undergoing PCI and these patients are at high risk of further adverse events.

Abstract 251

Background: Outcomes following percutaneous coronary intervention (PCI) are increasingly becoming the focus of attention, particularly with the adoption of drug-eluting stents (DES). However “real-world” data are lacking. We therefore analyzed outcomes in a registry of consecutive patients undergoing PCI in a contemporary setting.

Methods: All patients who underwent PCI between January 2005 and January 2006 were included in the registry. Adverse outcomes, defined as cardiac death, myocardial infarction (ST elevation myocardial infarction and non-ST elevation myocardial infarction) and target vessel revascularisation, were obtained from electronic patient records and case note review. A Cox proportional hazard regression model was used to analyze event-free survival.

Results: 518 consecutive patients (69.3% male, 30.7% female, mean age 66 years) were included in the registry. A total of 907 stents (78% DES, 10% non-DES, 12% hybrid) were inserted for 747 lesions (35% class A, 56% class B, 9% class C). Median follow-up was 53 weeks (range 29–79 weeks). All patients received clopidogrel therapy for 12 months. The following factors were not associated with an adverse outcome: age, clinical syndrome, lesion type, multivessel PCI, multiple stents, stent type (DES, non-DES, hybrid), stent length >30 mm (single or overlapping). However, female gender appeared to be an independent predictor of adverse outcome, with a significantly lower event-free survival compared with male gender (p = 0.009; hazard ratio 0.53; CI 0.145 to 0.756; fig).

Conclusion: Female gender is associated with an adverse outcome after PCI in a contemporary setting with high percentage DES use. These adverse events are predominantly driven by an increased risk in mainly (78.1%) from their general practitioner. Twenty-four patients (1.9%) were prescribed antibiotics for a presumed infective abscess; 31.5% of patients who reported problems were women, compared with 19.7% of patients who did not report problems (p<0.001). There was no age difference between those who did (64.6 years (SD 11.1)) and did not (65.6 years (SD 10.2)) report adverse events (p = 0.27). Of the 1283 patient population, 856 had had a HCS used, 427 a non-hydrophilic sheath. The use of HCS was associated with a significant excess of patient-reported adverse outcomes (see table). A logistic regression analysis confirmed that the use of a hydrophilic sheath (odds ratio (OR) 1.5, 1.05 to 2.26) and female gender (OR 1.9, 1.4 to 2.8) were independent predictors of self-reported adverse outcomes after controlling for possible confounders.

Conclusion: These data suggest that use of HCS for radial artery cannulation is associated with an increase in adverse reactions at the site of arterial access, compared with a non-hydrophilic sheath.

Abstract 252

FEMALE GENDER IS ASSOCIATED WITH SIGNIFICANTLY ADVERSE OUTCOME FOLLOWING PERCUTANEOUS CORONARY INTERVENTION: DATA FROM A CONTEMPORARY “REAL-WORLD” REGISTRY

V Venugopal, D Aher, DP Lipkin, JG Coghlan, RD Rakhit. Royal Free Hampstead NHS Trust, London, UK

Background: Outcomes following percutaneous coronary intervention (PCI) are increasingly becoming the focus of attention, particularly with the adoption of drug-eluting stents (DES). However “real-world” data are lacking. We therefore analyzed outcomes in a registry of consecutive patients undergoing PCI in a contemporary setting.

Methods: All patients who underwent PCI between January 2005 and January 2006 were included in the registry. Adverse outcomes, defined as cardiac death, myocardial infarction (ST elevation myocardial infarction and non-ST elevation myocardial infarction) and target vessel revascularisation, were obtained from electronic patient records and case note review. A Cox proportional hazard regression model was used to analyze event-free survival.

Results: 518 consecutive patients (69.3% male, 30.7% female, mean age 66 years) were included in the registry. A total of 907 stents (78% DES, 10% non-DES, 12% hybrid) were inserted for 747 lesions (35% class A, 56% class B, 9% class C). Median follow-up was 53 weeks (range 29–79 weeks). All patients received clopidogrel therapy for 12 months. The following factors were not associated with an adverse outcome: age, clinical syndrome, lesion type, multivessel PCI, multiple stents, stent type (DES, non-DES, hybrid), stent length >30 mm (single or overlapping). However, female gender appeared to be an independent predictor of adverse outcome, with a significantly lower event-free survival compared with male gender (p = 0.009; hazard ratio 0.53; CI 0.145 to 0.756; fig).

Conclusion: Female gender is associated with an adverse outcome after PCI in a contemporary setting with high percentage DES use. These adverse events are predominantly driven by an increased risk
of cardiac death. The reasons for this increased mortality remain unclear and are being investigated.

**Abstract 252**

**INVESTIGATING THE EFFECTS OF ASPIRIN ON BLOOD CLOT STRUCTURE USING A NOVEL CELLULAR IN-VITRO SYSTEM**

RA Ajjan, KF Standeven, M Khanbhai, F Phoenix, MT Kearney, PJ Grant. University of Leeds, Leeds, UK

Blood clot structure plays a role in determining predisposition to atherothrombotic events as clots formed from thin fibres and small pores are associated with premature and more severe cardiovascular disease. Aspirin, used for both primary and secondary cardiovascular protection, acetylates and inhibits cyclo-oxygenase-1, consequently leading to decreased platelet aggregation. Another potential mode of action of aspirin is related to the effects of acetylation of fibrin(ogen) to modulate clot structure, thereby contributing to cardiovascular protection through an alternative mechanism. The aim of the present work was to investigate the direct effects of aspirin on fibrinogen and clot structure using a novel system that employs recombinant techniques. Chinese hamster ovary cell lines stably transfected with the three chains of fibrinogen were grown in the absence (0) and presence of increasing concentrations (1, 10 and 100 mg/l) of aspirin. Fibrinogen was purified from the media using affinity chromatography and clots were made from recombinant protein by the addition of 0.5 U/ml thrombin in the presence of 2.5 mmol CaCl₂. Clot structure was studied using turbidity measurements, permeation analysis and electron microscopy. Fibrinolysis rates were determined by turbidity measurements after the addition of 10 nmol/ml tissue plasminogen activator and 0.1 mg/ml plasminogen. Mean final turbidity (optical density, ± SEM) of the fibrin clot was 0.083 (±0.03), 0.093 (±0.002), 0.101 (±0.005) and 0.125 (±0.003) in the presence of 0, 1, 10 and 100 mg/l aspirin in culture media, respectively (p<0.05). Permeation analysis showed a permeability coefficient (Ks cm² 10⁻²) of 1.68 (±0.29) and 4.13 (±0.33) comparing fibrinogen produced from cells grown without aspirin and in the presence of 100 mg/l aspirin. The above data indicate the formation of clots with thicker fibres and bigger pores in the presence of aspirin, a finding confirmed using scanning electron microscopy, which showed a looser three-dimensional clot structure with increased fibre thickness (147.9 (± 4.7) nm) when clots were made from aspirin-treated fibrinogen compared with non-aspirin-treated protein (66.3 (±4.2) nm; p<0.05). Fibrinolysis experiments demonstrated a time to 50% (±5%) lysis of 300, 270, 255 and 240 seconds with the presence of 0, 1, 10 and 100 mg/l aspirin in culture media, respectively. In summary, using a novel Chinese hamster ovary cell system we have shown that aspirin directly alters clot structure, resulting in the formation of clots with thicker fibres, bigger pores, which are easier to lyse and are less thrombotic. This study confirms an alternative mode of action for aspirin, which should be considered in studies evaluating the biochemical efficacy of this agent.

**Abstract 254**

**THE ICONS RISK SCORE: PREDICTORS OF 1-YEAR MORTALITY IN PATIENTS WITH ACUTE CORONARY SYNDROME WITHOUT PERSISTENT ST-SEGMENT ELEVATION, RESULTS FROM THE IMPROVING CARDIOVASCULAR OUTCOMES IN NOVA SCOTIA DATABASE**

1M Engd, 2R Townley, 3A Mitnitski, 3B Chan, 3Y Song, 3Y Wang, 3B Brownell, 3JL Cox, 3MP Love. 1Queen Elizabeth II Health Sciences Centre, Halifax Infirmary, Halifax, Canada; 2Kelowna Hospital, British Columbia, Kelowna, Canada

**Aim:** Early risk stratification of patients presenting with acute coronary syndrome (ACS) is used to guide therapeutic strategy. Several risk scores have been developed to predict short-term events: in hospital for the GRACE risk score, 14 days for the TIMI, and 30 days for the PURSUIT. However, a significant proportion of events, including death, occur after 30 days. We sought to develop a non-ST elevation ACS admission risk score to predict one-year mortality in a real-world Canadian setting.

**Method:** We assessed data on 1442 patients admitted with an index ACS (unstable angina, non-ST elevation myocardial infarction) event between 1998 and 2002 from the Improving Cardiovascular Outcomes in Nova Scotia (ICONS) database. Patients with cardiogenic shock, cardiac arrest, or death within 24 hours of admission were excluded. The primary endpoint was one-year mortality. A linear multivariate discrimination model was used to select variables that were independent predictors of 1-year mortality. These variables were entered into logistic regression in order to calculate the 1-year prediction score. Receiver operator characteristic analyses and area under the curve (C-statistic) were used for assessment of the predictive accuracy of the score and bootstrapping for internal validation.

**Results:** Ten variables independently predicted 1-year mortality. After testing to ensure there was no interaction, an adjusted score was assigned to each variable based on its logistic regression coefficient. Age >70 years, 3 points; history of coronary heart failure, 3 points; history of renal failure or creatinine >133 µmol/l, 3

<table>
<thead>
<tr>
<th>Variable</th>
<th>Score</th>
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<tbody>
<tr>
<td>Age &gt;70 years</td>
<td>3</td>
</tr>
<tr>
<td>History of CHF</td>
<td>3</td>
</tr>
<tr>
<td>History of renal failure or admission creatinine &gt;133</td>
<td>3</td>
</tr>
<tr>
<td>NSTEMI rather than UA</td>
<td>3</td>
</tr>
<tr>
<td>History of stroke</td>
<td>2</td>
</tr>
<tr>
<td>History of atrial fibrillation</td>
<td>2</td>
</tr>
<tr>
<td>Admission haemoglobin &lt;100</td>
<td>2</td>
</tr>
<tr>
<td>Admission diastolic BP &lt;50 or HR &gt;100</td>
<td>2</td>
</tr>
<tr>
<td>History of MI</td>
<td>1</td>
</tr>
<tr>
<td>History of diabetes or admission glucose &gt;11</td>
<td>1</td>
</tr>
</tbody>
</table>

**Total risk score**

- 1-Year mortality
  - 0–3: 2%
  - 4–6: 8%
  - 7–9: 19%
  - 10–13: 37%
  - >13: 58%

BP, blood pressure; CHF, coronary heart failure; HR, heart rate; MI, myocardial infarction; NSTEMI, non-ST elevation myocardial infarction; UA, unstable angina.
Background: There is a rigorous UK policy to treat >80% (NHS "statin productivity metric target") of heart patients with generic statin to achieve an audited total cholesterol of <5.0 mmol/l (Quality and Outcomes Framework target CHD8 worth 16 points). General Practitioners and Primary Care Trusts receive financial incentives for applying this policy, which differs from the optimal strategy cited by leading professional societies such as the American Heart Association (AHA), American College of Cardiology (ACC) and European Society of Cardiology (ESC).

Methods: The Space Rocket Trial was an independent, prospective open-label, blinded-endpoint, multicentre, randomised controlled, parallel group trial recruiting patients admitted to UK hospitals with myocardial infarction. Patients were randomly assigned to receive either simvastatin 40 mg or rosuvastatin 10 mg and were followed up for 3 months. The primary outcome was the attainment of 3 months of one or both of the 2004 ESC lipid targets of total cholesterol <4.5 mmol/l, low-density lipoprotein (LDL) cholesterol <2.5 mmol/l. We also conducted a post-hoc assessment using the subsequently (2006/2007) published ACC, AHA and ESC optimal treatment target for patients with myocardial infarction <1.81 mmol/l.

Results: 1263 consenting patients were randomly assigned to the two treatment arms and were well matched at baseline. At the time of the index myocardial infarction mean age was 62.5 versus 62.1 years; mean total cholesterol was 5.38 mmol/l versus 5.36 mmol/l; mean LDL-cholesterol was 3.22 mmol/l versus 3.32 mmol/l. After 3 months 77.6% simvastatin versus 79.9% rosuvastatin patients had achieved one or both of the 2004 European lipid targets (odds ratio (OR) 1.16; 95% CI 0.90 to 1.53; p = 0.29) representing an absence of superiority of one treatment over the other despite statistically significant but otherwise small differences in mean total cholesterol of 3.58 mmol/l versus 3.75 mmol/l (p = 0.005) and mean LDL-cholesterol of 2.08 mmol/l versus 1.94 mmol/l (p = 0.009). Of note, 37.8% simvastatin versus 45.0% rosuvastatin patients had achieved the ESC, ACC and AHA recommended optimal LDL-cholesterol for acute coronary syndrome patients of <1.81 mmol/l (OR 1.37; 95% CI 1.09 to 1.72; p = 0.007).

Conclusion: We observed no superiority of one treatment over the other with regard to the percentage of patients with either total cholesterol <4.5 mmol/l or LDL-cholesterol <2.5 mmol/l. There were differences in the mean lipid values and also the percentage achieving the ESC, ACC and AHA optimal targets of <1.81 mmol/l at 3 months.
ASSOCIATIONS BETWEEN METHODS OF MEASUREMENT OF ASPIRIN RESISTANCE AND THEIR TEMPORAL VARIATIONS IN PATIENTS WITH ISCHAEMIC HEART DISEASE

1AR Muir, 1MF McMullin, 1C Patterson, 1PP McKeown, 1Royal Victoria Hospital, Belfast, UK; 2Queen’s University, Belfast, UK

Background: The Antiplatelet Trialists’ Collaboration highlighted a 25% reduction of cardiac events in patients treated with aspirin. Aspirin’s antiplatelet effects are variable as events still occur despite therapy (“clinical aspirin resistance”). There is no agreed laboratory definition of aspirin resistance; various tests, including optical platelet aggregometry (OPA), platelet function analyzer (PFA-100TM), and quantitative analysis of serum and urine TXB2 metabolites have been used. This study aimed to characterise the prevalence of aspirin resistance in a northern Irish cohort, to investigate the associations between various methods of assessment of response to aspirin and to evaluate their variability on a temporal basis.

Methods: Patients with stable ischaemic heart disease, taking 150 mg aspirin daily, had platelet function assessment (by OPA and PFA-100TM) and quantitative analysis of serum and urine TXB2 at two visits 2 weeks apart. The prevalences of resistance by each method and associations between methods and time points were assessed.

Results: 175 patients (aged 62.7 ± 8.7 years, 82.9% men) were enrolled. The prevalence of aspirin resistance by OPA was 1.7% and 4.6% at the first and second visits, respectively, whereas 63.4% and 68.0% were aspirin semiresponders. By PFA-100TM, 21.7% and 20.0% were aspirin non-responders at each visit. There were poor associations between PFA-100TM and OPA and between TXB2 metabolites and both PFA-100TM and OPA. There were no associations between visits in OPA resistance or TXB2 metabolites, but there was a significant weak association for PFA-100TM response.

Conclusion: The prevalence of aspirin resistance is highly dependent on the method of platelet function testing used. The gold standard method of OPA cannot reliably be predicted by PFA-100TM testing or the measurement of TXB2 metabolites. Aspirin response varies on a temporal basis, indicating that one method of testing on a single occasion is not adequate to diagnose aspirin resistance reliably or guide antiplatelet therapy in a clinical setting.

REPLACEMENT OF THE PRECORDIAL LEADS OF THE 12-LEAD ELECTROCARDIOGRAM MAY IMPROVE DETECTION OF ST SEGMENT ELEVATION MYOCARDIAL INFARCTION

P Scott, P McKavanagh, N McKeog, JC Murphy, JR Bennet, G Manoharan, AAJ Adighe, Royal Victoria Hospital, Belfast, UK

Background: The 12-lead electrocardiogram (ECG) is the initial investigation of choice for the assessment of patients with chest pain. Major management decisions are based on these ECG findings alone. Utilising body surface mapping (BSM) technology, the aim of this study was to determine if the current six precordial leads (V1–V6) are indeed optimally located for the detection of ST segment elevation in ST elevation myocardial infarction (STEMI).

Methods: We analyzed 528 (38% anterior, 44% inferior and 18% lateral) cases of STEMI and 279 controls (normal ECG with normal cardiac markers). Eighty-lead BSM (Prime ECG) and 12-lead ECG were recorded simultaneously on all patients initially, before revascularisation. Mean ST segment elevation for each lead (1–80) on the BSM was compared with the corresponding 12-lead precordial leads (V1–V6). An optimised lead set was developed and sensitivity and specificity calculated. Logistic regression analysis of the ST segment was also used to compare both sets, shown as a receiver operator characteristic (ROC) c-statistic (area under the ROC curve).

Results: For anterior and lateral STEMI, leads V1, V2, 32, 42, 51 and 57 had the greatest mean ST elevation. These leads are located in the same horizontal plane as that of V1 and V2. Lead 32 had a significantly greater mean ST elevation than the corresponding precordial lead V3 (p = 0.012) and leads 42, 51 and 57 were also significantly greater than corresponding leads V4, V5 and V6 (p<0.001). For inferior myocardial infarction, the limb leads (II, III and aVF) were significantly superior to the inferior located leads of the BSM (p<0.001). The sensitivity and specificity of this new lead set was 71% and 99%, respectively, compared with 61% and 99% for the 12-lead ECG. ROC c-statistics were similar, the new set: 0.839 (CI 0.811 to 0.866) and the 12-lead ECG 0.841 (CI 0.814 to 0.868).

Conclusion: Leads placed on a horizontal strip, in line with leads V1 and V2, provided the optimal placement for the diagnosis of STEMI and appear superior to leads V3, V4, V5 and V6. This is of significant clinical interest, not only in terms of ease and replication of lead placement but may also lead to the increased recruitment of patients eligible for revascularisation with borderline ST segment elevation on the initial 12-lead ECG.

DO PATIENTS DIAGNOSED WITH NON-ST ELEVATION MYOCARDIAL INFARCTION BY NEW ESC CRITERIA HAVE THE SAME LONG-TERM OUTCOME AS OTHER MYOCARDIAL INFARCTS?

1M Teoh, 1S Dubrey, 1M Roughton, 1R Grocott-Mason. 1Hillingdon Hospital, Uxbridge, UK; 2Royal Brompton NHS Trust, London, UK

In 2000 new diagnostic criteria for the diagnosis of acute myocardial infarction (MI) were introduced by ESC/ACC. This meant that patients who would previously have been labelled as unstable angina (no enzyme rise) were now, due to a troponin rise, classified as MI. This doubled the number of non-ST elevation myocardial infarctions (STEMI) at our institution.

Aims: To investigate whether patients, whose MI only fulfils the new ESC criteria (ischaemic troponin rise) (group A), would have a similar long-term outcome to those with a twofold increase in creatinine kinase (CK) (WHO criteria) (group B).

Methods: 790 consecutive patients with MI admitted to Hillingdon Hospital between January 2001 and December 2002 were retrospectively analyzed, using medical notes, patient questionnaires and GP data. Mortality data were provided by the Office of National Statistics.

Results: There were 258 with non-STEMI only by ESC criteria, ie, positive troponin but normal CK (group A); 223 patients with non-STEMI by WHO criteria (group B) and 309 patients with STEMI. Patients in group A were older (71.1 ± 12.9 versus 68.7 ± 13.3 years; p<0.05) and were more likely to be hypertensive (53.3% versus 44%; p<0.05) compared to those in group B. There were no differences in treatments and discharge medications between groups A and B. All-cause mortality was similar between groups A and B at all time points (18.2% versus 20.2% at 30 days; 32.2% versus 34.5% at 1 year and 38% versus 39.5% at 2 years, respectively; fig 1). In contrast, STEMI patients (n = 309) were younger (65.1 years) and were more likely to be male and a current smoker, but were less likely to be hypertensive or to have had previous angina, than the non-STEMI groups. Long term all-cause mortality was better after STEMI than non-STEMI at 1 and 2 years (16.2% at 1 year and 19.4% at 2 years, p<0.05) (fig 2).

Conclusions: These data show: (1) the new ESC criteria identify twice as many patients with non-STEMI compared with the old WHO criteria; (2) the long-term outcome after non-STEMI in a “real world” population is poor, with a one in three all-cause mortality by 2 years; (3) this outcome is identical, irrespective of the diagnostic criteria used; (4) as previously known, long-term survival is worse after non-STEMI than STEMI, a difference that is
likely to be increased by the increased use of primary angioplasty. The study highlights the need for aggressive secondary prevention treatments and the assessment of all patients after an ischaemic troponin rise, even those with only a small increase.

260 30-DAY MORTALITY RATES FOR PATIENTS ADMITTED WITH ACUTE CORONARY SYNDROME: CUMULATIVE FUNNEL PLOTS FOR TWO CARDIAC CENTRES WITHIN THE NORTH-EAST OF ENGLAND

AJ Turley, R Das, AP Roberts, R Morley, S Jamieson, MA de Belder, I Haq. James Cook University Hospital, Middlesbrough, UK; Royal Victoria Infirmary Hospital, Newcastle, UK

Introduction: The evaluation of methods and management of acute coronary events (EMMACE) risk score is a validated and reproducible risk model that predicts 30-day all-cause mortality in patients with acute coronary syndromes (ACS). The model was developed based on age on admission, heart rate and systolic blood pressure. Temporal hospital performance may be examined with cumulative funnel plots that allow a meaningful visual comparison of observed and predicted mortality. A retrospective analysis of prospectively collected data investigating two regional cardiac centres’ ACS cohort. Mortality for both centres fell below control limits of the national mean.

Methods: We identified 1810 consecutive patients admitted to the James Cook University Hospital, Middlesbrough (JCUH) and the Royal Victoria Infirmary Hospital, Newcastle (RVI), with a discharge diagnosis of ACS, between April 2004 and March 2007.

Patients’ clinical characteristics and reference data were taken from the Myocardial Infarction National Audit Programme (MINAP) dataset. Cumulative funnel plots (Spiegelhalter) of observed and predicted mean performance on a case-series basis were generated. Upper and lower control limits calculated at 3 sigma around the mean predicted mortality were derived.

Results: For the combined cohort: mean age 67.9 years (± 13.7), mean heart rate 82.2 bpm (± 23.1) and mean systolic blood pressure 140.7 mm Hg (± 32.8). Overall 15.6% of patients had diabetes (n = 283). Hospital mortality was 7% (126 patients). The 30-day all-cause mortality was 7.7% (140 patients). Results are expressed as mean ± SD (see table). The observed and predicted mortality was clearly visualised in the funnel plots and allowed comparison of the observed and expected quality of care. Figure 1 depicts cumulative mortality in the two cardiac centres’ ACS cohort. Mortality for both centres fell below control limits of the national mean.

Conclusions: Cumulative hospital performance can easily be visualised using funnel plots (fig 2). Real-time monitoring of performance is possible. This promotes transparency and openness in the delivery of healthcare and an early assessment of observed variations. Crude 30-day mortality at the RVI was higher than at JCUH, but the plots demonstrate that the rate was below expected, most likely due to the higher risk of the patients.

Abstract 260

<table>
<thead>
<tr>
<th>JCUH (n = 510)</th>
<th>RVI (n = 1300)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes mellitus</td>
<td>69 (13.5%)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>65 (± 13)</td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>144 (± 32)</td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td>80 (± 20)</td>
</tr>
<tr>
<td>Hospital mortality</td>
<td>29 (5.7%)</td>
</tr>
<tr>
<td>30-Day mortality</td>
<td>31 (6.1%)</td>
</tr>
</tbody>
</table>

JCUH, James Cook University Hospital, Middlesbrough; RVI, Royal Victoria Infirmary Hospital, Newcastle; SBP, systolic blood pressure.

Abstract 260 Figure 1

LCL, lower control limit; UCL, upper control limit.
IS THE INCREASED CARDIOVASCULAR MORTALITY IN SOUTH ASIANS A RESULT OF INCREASED INCIDENCE OR CASE FATALITY? FOUR NEW STUDIES AND A META-ANALYSIS


Introduction: The relative contribution of incidence and case fatality to the high cardiovascular mortality rates observed in South Asians in high-income countries throughout the world is not known. We sought to report four new studies and systematically evaluate the published evidence on both the incidence of disease and case fatality in South Asians compared with majority populations.

Methods: We contribute three new prognostic studies with 14,244 events in acute coronary syndrome patients, 651 events in an angiographic cohort of stable coronary disease and 287 events in an incident angina cohort, and one new aetiological study contributing 101 events. A systematic literature review was carried out using Medline 1966–2007 and citations from references. We calculated pooled odds ratios (OR) and 95% CI using a random effects model.

Results: In addition to our own Whitehall II study, we found only one other study on incidence. South Asians had higher rates of incident coronary events (pooled OR 2.02, 95% CI 1.23 to 1.81). For prognosis, we identified six additional studies; survival after presentation with coronary disease was better in South Asians (pooled OR 0.81, 95% CI 0.74 to 0.87) (fig).

Conclusion: We found a higher incidence of disease in South Asians than in their white counterparts, but once they presented with disease their prognosis was better. The dissociation between the aetiological and prognostic findings has implications for the understanding of disease progression and suggests that public health efforts to reduce disparities in mortality should focus on primary prevention rather than the provision of healthcare to those with disease.

EUROACTION: CHANGES IN SMOKING, DIET AND PHYSICAL ACTIVITY OVER ONE YEAR IN A FAMILY-BASED PREVENTIVE CARDIOLOGY PROGRAMME IN HOSPITAL AND GENERAL PRACTICE

JL Jones, CJ Jennings, A Holden, SB Connolly, K Kotseva, T Collier, G De Backer, DA Wood. National Heart and Lung Institute, Imperial College, London, UK; Department of Epidemiology and Population Health, London School of Hygiene and Tropical Medicine, London, UK

Purpose: EUROACTION is a cluster randomised controlled trial of a multidisciplinary family-based preventive cardiology programme aimed at managing coronary patients, high-risk individuals and their families in the European lifestyle, risk factor and therapeutic targets for cardiovascular prevention.

Methods: In each of six European countries, pairs of general hospitals and general practices were randomly assigned to the EUROACTION programme or usual care. Intervention patients were invited to attend a comprehensive risk factor and lifestyle management programme. All patients were assessed for changes over 1 year in smoking, diet and physical activity. Measurement tools included breath carbon monoxide, anthropometric measures, a food habit questionnaire and 7-day physical activity recall.

Results: 1965 (71% of all eligible) patients in the intervention and 1999 (81% of all eligible) patients in usual care attended the final assessment. Using random effects meta-analysis, smoking, dietary and physical activity changes from initial screening to 1 year in the intervention were compared with usual care (table). There were significantly more quit attempts in smokers within the intervention arm but no significant differences overall in the prevalence of smoking, with a low use of pharmacological therapies to support smoking cessation.<%.

Conclusions: The EUROACTION preventive cardiology programme helped more patients achieve healthier lifestyle changes for diet and physical activity, together with reductions in weight.

Abstract 261

<table>
<thead>
<tr>
<th>Study ID</th>
<th>Lower risk in South Asians</th>
<th>Higher risk in South Asians</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of events/no. of patients</td>
<td>ES (95% CI)</td>
</tr>
<tr>
<td>Forouhi 2006</td>
<td>94/1787 108/1420</td>
<td>3.75 (2.27 to 6.19)</td>
</tr>
<tr>
<td>Whitehall II</td>
<td>80/9184 21/577</td>
<td>1.68 (1.21 to 2.94)</td>
</tr>
<tr>
<td>INCIDENCE (1-squared 62.3%, p = 0.070)</td>
<td>20/50 20/23</td>
<td>2.17 (0.97 to 4.88)</td>
</tr>
<tr>
<td>Hughes 1996</td>
<td>236/5605 51/2189</td>
<td>0.82 (0.29 to 2.61)</td>
</tr>
<tr>
<td>Wilkinson 1996</td>
<td>32/313 23/149</td>
<td>1.44 (0.79 to 2.61)</td>
</tr>
<tr>
<td>Gupta 2001</td>
<td>39/553 45/553</td>
<td>1.26 (0.82 to 1.92)</td>
</tr>
<tr>
<td>ACRE (coronary angiogram)</td>
<td>587/2974 64/502</td>
<td>0.80 (0.47 to 1.36)</td>
</tr>
<tr>
<td>Lew 2003</td>
<td>56/469 19/303</td>
<td>0.78 (0.45 to 1.34)</td>
</tr>
<tr>
<td>Fischbaker 2006</td>
<td>2967/21306 40/105</td>
<td>0.59 (0.43 to 0.81)</td>
</tr>
<tr>
<td>MINAP (acute coronary)</td>
<td>13924/74216 320/3223</td>
<td>0.83 (0.73 to 0.95)</td>
</tr>
<tr>
<td>Mak 2003</td>
<td>2942/7102 593/2224</td>
<td>0.81 (0.72 to 0.91)</td>
</tr>
<tr>
<td>PROGNOSIS (1-squared 30.5, p = 0.174)</td>
<td>5</td>
<td>1</td>
</tr>
</tbody>
</table>

(Illustriors=our data)
Abstract 262 Changes and difference in change in diet and physical activity over 1 year: EUROACTION intervention versus usual care

<table>
<thead>
<tr>
<th>Coronary patients INT</th>
<th>Coronary patients UC</th>
<th>A change over 1-year INT versus UC (95% CI)</th>
<th>High CVD risk patients INT</th>
<th>High CVD risk patients UC</th>
<th>A change over 1-year INT versus UC (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change over 1 year in proportion achieving fruit and vegetables &gt;400 g/day (%)</td>
<td>25</td>
<td>9</td>
<td>+15.8% (+2.2 to +29.3)*</td>
<td>27</td>
<td>4</td>
</tr>
<tr>
<td>Change over 1 year in proportion achieving fish &gt;20 g/week (%)</td>
<td>24</td>
<td>10</td>
<td>+11.8% (-2.1 to +25.6)</td>
<td>20</td>
<td>4</td>
</tr>
<tr>
<td>Change over 1 year in proportion achieving oily fish 3+ times/week (%)</td>
<td>14</td>
<td>3</td>
<td>+11.4% (0.6 to 22.1)*</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Change over 1 year in proportion participating in moderate intensity activity &gt;4 ×/week &gt;30 minutes (%)</td>
<td>27</td>
<td>0.2</td>
<td>+28.1% (+13.9 to +42.3)*</td>
<td>24</td>
<td>10</td>
</tr>
<tr>
<td>Mean change over 1 year in BMI of those &gt;25 kg/m²</td>
<td>–0.3</td>
<td>0.4</td>
<td>–0.7 kg/m² (–1.0 to –0.3)*</td>
<td>–0.5</td>
<td>0.13</td>
</tr>
<tr>
<td>Mean change over 1 year in waist circumference in men &gt;94 cm and women &gt;80 cm</td>
<td>–1.5</td>
<td>–0.8</td>
<td>–0.8 cm (–3.7 to +2.1)</td>
<td>–1.7</td>
<td>0.2</td>
</tr>
</tbody>
</table>

CVD, cardiovascular disease; INT, intervention; UC, usual care.
*p<0.05; †subsample in usual care.

and central adiposity, thereby reducing the risk of cardiovascular disease in everyday clinical practice.

263 A COMPARISON OF EMERGENCY NURSES’ EMERGENCY NURSE PRACTITIONERS’ AND EMERGENCY CARE PRACTITIONERS’ USE OF HEURISTICS IN THEIR CLINICAL REASONING AND DECISION MAKING ABILITY TO MANAGE/TRIAGE PATIENTS PRESENTING WITH CHEST PAIN CORRECTLY

1H Cox, J Alibaran, R Hoskins, S Moyle, T Quinn, A Gray, L Lockyer, 1University of the West of England, Bristol, UK, 2Coventry University, Coventry, UK

Background: Chest pain is considered the commonest reason for emergency department (ED) attendance. Ensuring that patients with acute coronary syndrome are appropriately triaged and effectively managed is a key expectation of service providers and users. However, the inappropriate discharge of patients with evidence of ischaemic heart disease remains an area of concern.1,2 Previous research has reported the use of electrocardiograph (ECG) and clinical vignettes to assess coronary care unit3 and ED4 nurses’ ability to recognise ECG and clinical characteristics of ST elevation myocardial infarction. In recent years, the ED staff and emergency care practitioners (ECP) have been more engaged in the management of patients presenting with chest pain. However, whether the ED nurses and ECP are competent in correctly interpreting ECG and other clinical information in relation to the initial management of the patient with acute chest pain is an area not previously studied.

Aim: To investigate the accuracy between emergency nurse practitioners, emergency nurses, and ECP in relation to accuracy of assessment for patients presenting with acute chest pain.

Methods: A convenience sample composed of all students attending the emergency care programmes across two university sites within the southwest and midland region from November 2006 to May 2007 was recruited. Data collection utilised a series of six online case studies including typical and atypical examples of chest pain with the use of ECG vignettes; face and content validity for each case study was verified by a panel of experts. Through the use of clinical reasoning and diagnostic ability participants selected diagnostic and treatment options for the appropriate management of the patient case studies. The study conformed to ethical standards, consent and approval was sought and gained.

Results: The sample consisted of 46 emergency staff, N = 29 (south-west study site) and N = 14 (midlands study site). 83% of participants received on-the-job cardiac training, with only 4% of participants having undertaken formal cardiac training and education. Ongoing analysis identifies that a majority of the respondents (87%) correctly identified acute coronary syndrome through the initial history and 12-lead ECG. However, this figure fell to 46% correctly diagnosing a chest infection, 35% oesophagitis and 19% aortic dissection. Participants’ confidence in managing patients with chest pain was neutral to very confident in 81%, with only 19% feeling unsure or very unsure of their abilities.

Conclusion: The initial results appear to show that the participants from the groups performed well in patients presenting with an acute coronary syndrome. However, further analysis of the results is required to link the accuracy of assessment, confidence level and diagnostic ability to the education received and differing emergency care roles.


264 DO HEART FAILURE SPECIALIST NURSES REALLY MAKE A DIFFERENCE TO HEALTH-RELATED QUALITY OF LIFE, ANXIETY AND DEPRESSION LEVELS AND SELF-CARE BEHAVIOURS IN THEIR PATIENTS?

JF Pattenden, SCoulton, KSplilsbury, RJP Lewin. University of York, York, UK

Introduction: In recognition of the increasing prevalence of heart failure, 76 heart failure specialist nurses were funded for 3 years with charitable funding and employed in primary care trusts.

Methods: As part of the evaluation to assess the impact of these nurses, patients and carers were invited to complete a set of measures. 954 patients and 342 carers were recruited and completed baseline surveys. Patients completed the Minnesota Living with Heart Failure (MLHF), the Hospital Anxiety and Depression Scale (HAD) and the European Heart Failure Self-Care Behaviour scale (HFSC). Both patients and carers completed the SF12 generic health-related quality of life measure and a satisfaction with care questionnaire.

Results: Good follow-up rates of >70% were seen at both 6 months and 12 months. Patients recruited were mostly men (70%) with a mean age of 72 years and were similar to patients who were not recruited but had fewer co-morbidities and more contacts with their nurse. Scores on the MLHF improved significantly; at 12 months an absence of co-morbidities was related to a significant reduction in score. There was a small but significant improvement in the HFSC score, but a low level of self-care is still indicated. The SF12 physical component score improved significantly but was poor compared with the population average, whereas the mental health...
component improved and was similar to the population average. The proportion of patients with confirmed anxiety disorder increased at 12 months, as did the proportion with borderline depressive disorder. Patient and carer satisfaction with care measured across four domains was high but decreased by small amounts at 12 months, apart from the depth of relationship, which improved for carers. Carers’ SF12 physical component scores worsened over 12 months and are poor compared with population norms but better than those of patients. The SF12 mental health component score did not change and was similar to patient scores. Conclusions: There were small but significant changes in most measures, implying that the nurses had a positive impact on the health-related quality of life of their patients. It may be that comorbidities play a larger part in quality of life than heart failure in some patients. Levels of anxiety and depression may be underestimated. Self-care improved but only for certain behaviours. There were very high levels of satisfaction with care in patients and their informal carers, but carer quality of life did not improve. Data will be presented and implications discussed at the conference.

**265 PATIENT, CARER AND PUBLIC INVOLVEMENT IN SUPPORTING PATIENTS WITH CHRONIC HEART FAILURE**

L Peardon, R Pratt, D Yellowlees, J Reid, SJ Leslie, MA Denyer, Chest, Heart and Stroke, Scotland, Edinburgh, UK; University of Edinburgh, Edinburgh, UK; St Johns Hospital Livingstone, Edinburgh, UK; Royal Infirmary Of Edinburgh, Edinburgh, UK; Raigmore Hospital, Inverness, UK

Background: Involving patients, their relatives and the general public in the delivery of a healthcare service has been recommended in a number of government directives but putting these recommendations into practice is challenging. A number of services have achieved this in the United Kingdom; notably in cancer care. Here we report the development of two elements of non-medical care developed by a clinical network for patients with chronic heart failure (CHF) involving patients, their carers and public lay-volunteers.

Methods: A lay-volunteer programme was developed in conjunction with a medical charity (Chest, Heart and Stroke, Scotland; CHSS), which included training in befriending skills, moving and handling, first-aid and raising awareness of CHF. Following consultation with patients/carers, CHSS also arranged quarterly forum meetings for patients and their carers at community-based locations including church halls and community centres around the region and commenced the circulation of a patient/carer newsletter.

Results: Over the course of 3 years, 35 volunteers (age range 17–76 years), supported by a dedicated coordinator and working closely with a heart failure nurse service in selecting clients, visited 43 CHF clients in their homes. The volunteers encouraged clients to renew interests they had before their diagnosis to reintegrate into the local community and once again to enjoy everyday activities, for example going to the library, the post office, out for a coffee or for a walk, with the physical and emotional support of the volunteer. Comments from patients and families receiving visits include: “this takes the strain off the family…”, “sharing good conversation and being able to go out and leave my home area”, and some patients admitted “looking forward to seeing someone” for simple companionship. 12 patient-carer meetings have been held over a 3-year period. The average attendance is 42, including both patients and carers. Topics at forum meetings have included diet, relaxation, pacing activity, advice from the Citizen’s Advice Bureau, “question-time” using an expert panel made up of a consultant, GP and pharmacist, with dedicated carers’ sessions running concurrently every second meeting. Comments have included “I felt that someone was listening” and “found answers”.

Conclusions: Public, patient and carer involvement is possible in the NHS setting as part of a clinical network for CHF. In our experience, support from the voluntary sector is important in not only providing financial support but also allowing a shift in focus from medicalisation to innovative community and social partnership support for CHF clients and their families.

**266 AGGRESSIVE PHARMACOINVASIVE THERAPY FOR ST ELEVATION MYOCARDIAL INFARCTION MAY DELIVER COMPARABLE OUTCOMES TO PRIMARY PERCUTANEOUS CORONARY INTERVENTION IN A UK SETTING**

D Adlam, J Ehtisham, CJ McKenna, N Spyrou, J Swinburn, WP Orr. Royal Berkshire Hospital, Reading, UK

Background: The treatment of ST elevation myocardial infarction in the United Kingdom is changing rapidly and there is huge momentum behind a policy of primary percutaneous coronary intervention (PCI) for all. Many trials have shown outcome benefits for primary PCI over thrombolysis-based strategies, but no randomised trials truly compare modern primary PCI with rapid thrombolysis/mandated rescue/early angiography and PCI. The STREAM trial may go some way to answering this question.

Method: Analysis of treatment and outcomes for all patients presenting with STEMI to a large district general hospital with on-site PCI. Primary therapy thrombolysis, but with mandatory rescue at 60 minutes, primary PCI for patients ineligible for thrombolysis and early subsequent angiography with PCI were used when appropriate. Data from audited Myocardial Infarction National Audit Programme (MINAP) returns and a local catheter laboratory database were used to assess outcomes.

Results: See table.

Conclusions: A pharmacoinvasive strategy with back-up PCI available on-site round the clock may provide, particularly away from major cities, at least equivalent outcomes to transfer for primary PCI. Such an approach reduces by at least 70% the volume of out-of-hours catheter laboratory work and may therefore have an important beneficial effect on staff retention and the ability to maintain steady elective schedules.

**267 PRIMARY ANGIOPLASTY FROM THE RADIAL ROUTE IS SAFE AND EFFECTIVE AND DOES NOT SIGNIFICANTLY INCREASE DOOR TO BALLOON TIME**

A Shahzad, AP Worrall, MS Norell, SS Khogali, M Cusack, M Banks, JM Cotton. New Cross Hospital, Wolverhampton, UK

Background: The gold standard acute therapy for ST segment elevation myocardial infarction is timely reperfusion with primary percutaneous intervention (PCI). Patients are often elderly with associated co-morbidity. Patients receive aggressive antiagulation/antiplatelet therapy before primary PCI and so choice of arterial access site may have an important impact on outcome. The radial approach for PCI is becoming increasingly popular but is considered by some to be more time-consuming and/or complex in unstable patients.

Methods: We analyzed data on all patients admitted for primary PCI in the first 6 months of our network-wide 24-hour primary PCI programme. Data were collected prospectively on a dedicated
Database and cross referenced with the Myocardial Infarction National Audit Programme (MINAP) and case record review when required. Door to balloon time, procedure start time to balloon, procedural radiation dose, fluoroscopy time and contrast use were assessed for cases performed via the femoral and radial routes. Continuous variables are expressed as median (range) and the groups were compared using appropriate non-parametric tests taking \( p < 0.05 \) as significant. Two of five of the operators in the programme favour the radial approach for all primary PCI.

**Results:** In 6 months, the primary PCI service was activated 258 times. Of these, 207 patients required primary PCI. 157 (75.8%) were performed via the femoral route and 50 radially (24.2%). Results are shown in the table. Access site failure occurred in two (4%) of the radial and two (1.3%) of the femoral cases (NS, \( 95\% \) CI 0.7 to 14.9). The procedure start to balloon time was significantly longer for radial versus femoral cases (28 versus 22 minutes, \( p = 0.001 \)) but this did not significantly affect the overall door to balloon times (60 versus 64 minutes, \( p = 0.65 \)). The radiation dose for the radial route was higher than the femoral cases (103.9 versus 90 Gy cm\(^2\), \( p = 0.03 \)), but the fluoroscopy times were not (9:48 versus 9:12 minutes, \( p = 0.96 \)). Contrast use was similar in the two groups. Two vascular complications occurred in the femoral group (one significant haematoma, one pseudo-aneurysm) and none in the radial group.

**Conclusions:** The radial approach is safe and effective for PPCI when performed by appropriately trained operators with a high level of success. The importance of increased radiation dose and procedure to balloon time in the radial group needs careful assessment over a longer period, but in our cohort the door to balloon times were not significantly increased and complication rates were very low.

**Abstract 268**

**INCIDENCE OF TAKO-TSUBO CARDIOMYOPATHY IN PATIENTS UNDERGOING PRIMARY ANGIOPLASTY FOR ST ELEVATION MYOCARDIAL INFARCTION**


**Background:** Tako-tsubo cardiomyopathy (TTCM) is a stress-induced cardiomyopathy characterised by reversible ventricular apical dysfunction in the absence of significant epicardial coronary disease. Its presentation mimics that of an acute myocardial infarction (MI) and is being increasingly recognised as a result of early coronary angiography and primary coronary intervention (PCI). We aimed to determine the incidence of TTCM in patients with ST elevation myocardial infarction (STEMI) referred for PCI.

**Methods and Results:** The Yorkshire Heart Centre provides a 24-hour PCI service to over 1.2 million people within west Yorkshire. 486 patients with chest pain (<12 hours duration) and ST elevation referred for PCI between September 2006 and September 2007 were identified. During this period six (1.4%) patients were diagnosed with TTCM. All were post-menopausal women with a mean age of 73 ± 10 years. Troponin I levels were elevated in all cases (14.4 ± 12.9 \( \mu \)g/l). Echocardiography (all patients) and cardiac magnetic resonance imaging (five patients) was performed at baseline and during follow-up (within 6 months of presentation). Both imaging modalities demonstrated significant improvement in left ventricular size and function. Urine catecholamines were estimated in all, without abnormality. There were no deaths at the initial follow-up visit (6–8 weeks) (see fig).

**Conclusions:** TTCM represents a reversible cardiomyopathy seen in approximately 1.4% of patients undergoing PCI for STEMI. This finding highlights the importance of performing left ventriculography in all STEMI patients in the absence of significant coronary disease.
Background: Timely primary PCI is the gold standard therapy for acute ST segment elevation myocardial infarction. An increasing number of centres in the United Kingdom are now offering this treatment option. Setting up a primary PCI programme is complex, involving multidisciplinary cooperation and careful costing exercises. We have been offering this service to our local population in working hours for 3 years and to our full network population round the clock for the past 6 months. The aim of this study is to identify whether starting a primary PCI programme in the United Kingdom uncovers extra revascularisation procedures in addition to the index primary PCI and how these extra cases are identified.

Methods: 167 patients from our local catchment (population approximately 0.3 million) underwent primary PCI for acute myocardial infarction between January 2005 and September 2007. We excluded patients from our wider network area so as to have robust clinical follow-up data. Cases were identified from our prospective primary PCI database and angiogram results and follow-up information was confirmed by assessment of the case records and angiographic images. Survivors were scheduled for follow-up at our dedicated post-myocardial infarction clinic (PMIC) one month after discharge. Coronary lesions >50% of the luminal calibre were considered significant.

Findings: Of the 167 patients treated with primary PCI, 94 patients had single vessel disease (SV group, 56%) and 73 multivessel (MV group, 44%). Overall 30-day mortality was 4.2% with the majority of cases in the multivessel group. Mortality in the MV group was 8.2% (n = 6, five with cardiogenic shock) and in the SV group 1% (n = 1). Following the index procedure 27 patients underwent repeat revascularisation procedures (16.2%). Of these, 18 were by PCI (10.8%) and nine by coronary artery bypass surgery (CABG, 5.4%). Three of the repeat revascularisation procedures were in the SV group and 24 in the MV group. Of the 66 survivors in the MV group, 15 were booked for revascularisation directly after discharge. Coronary lesions >50% of the luminal calibre were considered significant.

Conclusions: Our findings suggest that if setting up a primary PCI service, departments should consider the need for repeat(extra revascularisation procedures in approximately 16% of cases, with a 2 : 1 split between PCI and CABG. A dedicated PMIC and non-invasive testing at follow-up are useful in determining which patients should be offered repeat procedures.

Abstract 270 Table 1

<table>
<thead>
<tr>
<th>Baseline characteristics (% unless otherwise specified)</th>
<th>MI (n = 431)</th>
<th>Aborted MI (n = 42)</th>
<th>p Value</th>
<th>Masquerading MI (n = 17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean years)</td>
<td>62</td>
<td>61</td>
<td>0.49</td>
<td>501</td>
</tr>
<tr>
<td>Male</td>
<td>72</td>
<td>59</td>
<td>0.08</td>
<td>88</td>
</tr>
<tr>
<td>Diabetes</td>
<td>8.6</td>
<td>14</td>
<td>0.22</td>
<td>5.9</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>4.2</td>
<td>9.5</td>
<td>0.12</td>
<td>0</td>
</tr>
<tr>
<td>Previous angina</td>
<td>14</td>
<td>29</td>
<td>0.02</td>
<td>11</td>
</tr>
<tr>
<td>Previous MI</td>
<td>13</td>
<td>24</td>
<td>0.05</td>
<td>0</td>
</tr>
<tr>
<td>Median symptom to door time (mins)*</td>
<td>122</td>
<td>136</td>
<td>0.42</td>
<td>92</td>
</tr>
<tr>
<td>Median symptom to balloon time (mins)**</td>
<td>205</td>
<td>210</td>
<td>0.47</td>
<td>N/A</td>
</tr>
<tr>
<td>Symptom to balloon under 90 mins†</td>
<td>4.5</td>
<td>13</td>
<td>0.02</td>
<td>N/A</td>
</tr>
</tbody>
</table>

*23 patients excluded as in hospital at time of symptom onset.
†Statistically different from true myocardial infarction (MI) group.
‡17 patients excluded from MI/aborted MI group because did not have percutaneous coronary intervention.
were generally younger and had less co-morbidity. There were no deaths in this group (see fig).

Conclusion: Aborted infarcts were more likely to be women and have a previous history of ischaemic heart disease. They were more likely to have a door to balloon time of less than 90 minutes and have pre-PCI TIMI 3 flow. This group had a higher rate of emergency coronary artery bypass grafting but had no deaths in-hospital or at 30 days.

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### Abstract 270 Table 2

<table>
<thead>
<tr>
<th>Outcomes (%)</th>
<th>MI (n = 431)</th>
<th>Aborted MI (n = 42)</th>
<th>p Value</th>
<th>Masquarading MI (n = 17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emergency CABG</td>
<td>0.5</td>
<td>4.8</td>
<td>&lt;0.01</td>
<td>0</td>
</tr>
<tr>
<td>Refractory ischaemia/reinfarction</td>
<td>1.6</td>
<td>0</td>
<td>0.4</td>
<td>0</td>
</tr>
<tr>
<td>Moderate to severe LV impairment</td>
<td>45</td>
<td>44</td>
<td>0.88</td>
<td>13.3*</td>
</tr>
<tr>
<td>Pre-PCI TIMI 3 flow</td>
<td>6.1</td>
<td>40</td>
<td>&lt;0.001</td>
<td>100*</td>
</tr>
<tr>
<td>Shock</td>
<td>4.4</td>
<td>0</td>
<td>0.2</td>
<td>0</td>
</tr>
<tr>
<td>Cardiac arrest</td>
<td>6.0</td>
<td>0</td>
<td>0.1</td>
<td>0</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.2</td>
<td>2.4</td>
<td>0.14</td>
<td>0</td>
</tr>
<tr>
<td>In-hospital mortality</td>
<td>1.9</td>
<td>0</td>
<td>0.37</td>
<td>0</td>
</tr>
</tbody>
</table>

CABG, coronary artery bypass grafting; LV, left ventricular; MI, myocardial infarction; PCI, percutaneous coronary intervention.

*Statistically different from true MI group.

### Abstract 271

#### VALIDATION OF RISK ADJUSTMENT MODELS FOR MORTALITY FOLLOWING PRIMARY PERCUTANEOUS INTERVENTION USING A UK-BASED DATASET

**DJ Twomey, B Kunadian, S Khan, R Morley, AC Sutton, RA Wright, JA Hall, D Muir, MA de Belder. James Cook University Hospital, Middlesbrough, UK**

**Introduction:** Risk models for elective and emergency percutaneous coronary intervention (PCI) can be used to risk stratify patients and aid decision making on the basis of individual risk. They can also be used to assess individual centres or operators and improve quality of care. In primary PCI, risk scores have been shown to predict in-hospital, 30-day and 6-month mortality. They have been internally validated, using the population from which they were derived and individual scores have also been externally validated. However, no study has used the same population to validate all four scores and a UK-based population has not previously been used for validation.

**Methods:** We used data compiled from 543 consecutive primary PCI procedures performed at our centre between September 2002 and April 2007. We evaluated CADILLAC, Stent-PAMI, TIMI, and Zwolle primary PCI risk scores. The accuracy of individual scores was evaluated using the area under the receiver operator curve (c-index) (see fig).

**Results:** All risk scores demonstrated good discrimination of mortality: c-index, 95% CI; CADILLAC (30-day mortality) 0.807, 0.723 to 0.892; Stent-PAMI (in-hospital) 0.825, 0.724 to 0.926; Stent-PAMI (6-month) 0.816, 0.734 to 0.898; TIMI (30-day) 0.792, 0.680 to 0.903; Zwolle (30-day) 0.824, 0.724 to 0.911. There were no statistical differences between the scores when used to predict 30-day mortality. The CADILLAC graph not shown as it excluded shock patients.

**Conclusion:** The risk scores performed well using a real-life dataset based in the United Kingdom. All scores have a similar predictive value.

### Abstract 272

#### USING STATISTICAL PROCESS CONTROL TO PLOT THE DOOR-TO-BALLOON TIME FOR DATA FEEDBACK AND ANALYSIS IN PATIENTS PRESENTING WITH ACUTE MYOCARDIAL INFARCTION

**D Twomey, B Kunadian, AP Roberts, R Morley, JA Hall, AGC Sutton, RA Wright, DF Muir, MA de Belder. The James Cook University Hospital, Middlesbrough, UK**

**Background:** Reducing symptom to reperfusion times is an essential part of delivering effective reperfusion for ST elevation myocardial infarction. Reducing door to balloon (DTB) times can
help to reduce the overall time to treatment. Continuous review of local data helps to improve DTB times.

**Methods:** We have used statistical process control (SPC) charts to plot the door-to-balloon times for individual patients admitted to our department with ST elevation myocardial infarction. These were used for feedback and analysis of individual and overall DTB times. We then used these to assess the impact of implementing a coronary care nurse coordinator as a single point of contact utilising electronic ECG transmission for activation of the catheterisation laboratory on door-to-balloon times.

**Results:** The SPC plot shows two intervals; one before the introduction of a single point of contact for activation of the catheterisation laboratory (from April 2004 to August 2005) and one after the introduction of the new system (from September 2005 to December 2006). The upper control limit is a statistically defined boundary approximately equivalent to the 99% confidence limit. Median DTB times fell from 94 minutes to 56.5 minutes with an associated change in the upper control limit (see fig). This was statistically significant. Outliers can easily be evaluated.

**Conclusion:** SPC provides a statistically robust mechanism for assessing the effect of systematic changes, as well as a clear visual representation of door-to-balloon times for individual patients. It allows the easy identification of significant outliers for the investigation of any variation with a special cause. The introduction of a coronary care unit coordinator as a single point of contact reduced the median DTB time by 37 minutes.