**NON-RESTRICTIVE EXTERNAL STENTING REDUCES MEDIAL AND NEOINTIMAL THICKENING IN A PIG MODEL OF ARTERIOVENOUS BYPASS GRADING**

Bristol Heart Institute, University of Bristol, Bristol, United Kingdom

The long-term clinical success of coronary artery bypass grafting with autogenous venous saphenous vein is limited by progressive medial and neointimal thickening in the graft and superimposed atherosclerosis.

We sought to reduce wall thickening by applying an external to experimental grafts in pigs. The diameter of an external stent was designed to allow unrestricted initial expansion of the vein in response to arterial pressure and was highly porous so as to minimise adventitial damage.

Four weeks after graft implantation, stented grafts had a larger lumen (11.28±2.2 SD mm² vs 7.63±2.4 mm², p<0.05, n=9) and an almost 4 fold thinner media (0.145±0.08 vs 0.35±0.24, p<0.001) than paired unstented grafts in the same animals. Cell proliferation, detected by immunohistochemistry for proliferating cell nuclear antigen, was significantly reduced by stenting in the neointimal and medial layers. Furthermore, stented grafts showed a significant upregulation of cAMP, cGMP and PGJ2-synthesises and reduced release of LTβ, compared to unstented grafts.

This data shows that external stenting of saphenous vein bypass grafts reduces smooth muscle cell proliferation and wall thickening, and maintains the integrity of several biochemical systems which are important in preventing vein graft failure. Because wall thickness and final luminal size are thought to be of paramount importance in maintaining long-term patency, non-restrictive external stenting is likely to be of benefit.

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**ENDOTHELIN-1 PLAYS A FUNCTIONAL ROLE IN NORDRENALEN-INDUCED VENTRICULAR HYPERTROPHY IN VIVO AND IN VITRO**

S Kadoura, National Heart & Lung Institute, London

Endothelin-1 (ET-1) has potent effects upon cell growth. We tested the hypothesis that endogenous ET-1 plays a functional role in noradrenaline (NE)-induced ventricular hypertrophy by studying physical indices and molecular markers of hypertrophy, ventricular and non-cardiac expression of ET-1 mRNA, and the effects of bosentan, an orally-active competitive ETα and ETβ receptor antagonist without adrenocortical antagonism. Experiments were performed on a rat model of hypertrophy and cultured myocytes. Male Sprague Dawley (150g, n=70) were divided into 4 groups: 1. Sham-operated, 2. NE-infused (600g/kg by subcutaneous osmotic pumps up to 7 days). 3. Sham-operated given bosentan (100mg/kg/day by gavage), 4. NE-infused given bosentan. NE caused a 35-fold increase in ventricular ET-1 mRNA within 1 day (ET-1:GAPDH mRNA at 1 day 0.01±0.01 for sham, n=8, vs 0.13±0.08 for NE, n=8, P<0.01), an effect seen not only in lung, kidney or skeletal muscle. NE also caused significant increases in ventricular mass, RNA and protein content, and expression of mRNA for atrial and ventricular myocyte-specific sarcomeres (see table for detail).

Myocyte protein content and [3H]-phenylalanine incorporation also increased, effects attenuated by 10μM bosentan (fig.B). ET-1 plays a direct role in myocyte proliferation and hypertrophy with cross-talk between these systems in vivo and in vitro.

**THE RENIN-ANGIOTENSIN SYSTEM AND LEFT VENTRICULAR HYPERTROPHY: RAT AND HUMAN STUDIES**

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Myocardial renin-angiotensin-systems(RAS) may regulate left ventricular (LV) growth (LVH). We tested this hypothesis in the rat and human Introduction 1: The transgenic TGR(mRen-2)27 rat expresses the renin converting enzyme gene. Their hypertensive phenotype may be a stimulus for LVH.

Methods/Results 1: Blood pressure(BP) was recorded weekly in 4 groups: heterozygote TGR(un-treated) and RisACE-inhibitor ramipril 1μg/kg/day had similar blood pressures, as did Ris(rapamitin) 1mg/kg/day and control-transgenic(C). LV mass and collagen content were assessed by HPLC at 4 months.

Results were as follows:

<table>
<thead>
<tr>
<th>Group</th>
<th>LV Mass (g)</th>
<th>LV Collagen (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TGR</td>
<td>1.10±0.4</td>
<td>6.38±5</td>
</tr>
<tr>
<td>R1</td>
<td>1.53±0.5</td>
<td>7.4±6.4</td>
</tr>
<tr>
<td>R2</td>
<td>1.44±0.6</td>
<td>4.28±2.2</td>
</tr>
<tr>
<td>TGR + Ris</td>
<td>7.10±2.8</td>
<td></td>
</tr>
</tbody>
</table>

Conclusion 1: ACE-inhibition limits hypertensive LVH in the TGR by a non-hypotensive mechanism

Introduction 2: The absence (deletion, D) rather than presence (insertion, I) of a 287 base-pair marker in the angiotensin-converting enzyme (ACE) gene may be associated with raised tissue ACE levels. If renin-angiotensin systems regulate LV growth, then the LVH response to a hypertensive stimulus may be greater in DD than II individuals.

Methods/Results 2: Male military recruits were studied pre- and post 10 weeks physical training LVH was assessed echocardiographically(n=134), electrocardiographically (n=121), and by plasma beta-natriuretic peptide (BNP) assay(n=49). Mean LV mass altered by -1.7g ±4.7g and +5.6g (II LD and DIAN, p=0.009 for heterogeneity<0.0001). ECG LVH prevalence increased in DD genotype (10/37 pre-training vs 18/37 post-p<0.05), and was unchanged in II. Plasma BNP levels rose by 11.4pg/ml and 50.2pg/ml (II vs DD p<0.01). Finally, mortality in human LVH may be partly mediated by renin-angiotensin systems.
THROMBIN - MORE THAN A THROMBOGENIC MEDIATOR: ACTIVATION OF THE CARDIAC SARCOLEMMA Na+/H+ EXCHANGER VIA THE CLOSED THROMBIN RECEPTOR

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Cardiovascular Research, The Rayne Institute, St Thomas' Hospital, London

We have studied whether thrombin activates the sarcomemlal Na+/H+ exchanger (NHE) in freshly-isolated adult rat ventricular myocytes and the signalling mechanism of any such effect. Reverse transcription polymerase chain reaction analysis revealed thrombin receptor mRNA expression in a myocyte-enriched cell preparation. As an index of NHE activity, intracellular pH (pHi) versus acid flux rate (d(pH)/dt) relationships were determined in single myocytes (n=5-11/group) loaded with the pH-sensitive fluorophore C-SNARF-1, after 2 consecutive intracellular acid pulses (induced by transient exposure to 20 mM NH4Cl) in bicarbonate-free medium. In control cells, the percent change in pHi (ΔpHi) after the second acid pulse (relative to the first) was ±10%, at an identical pHi of 6.9. When the second acid pulse occurred in the presence of 0.2, 1 or 5 U/ml thrombin, ΔpHi was increased to 45±22, 64±23 and 110±24% (p<0.05 vs control). A hexameric thrombin receptor activating peptide (SFLRN, 25 μM) mimicked the effect of 5 U/ml thrombin (ΔpHi=93±31%, p<0.05 vs control), while an inactive control peptide (FLLRN, 25 μM) was without effect (ΔpHi=±6%). In cells pretreated with 100 μM G109203X (selective protein kinase C inhibitor), ΔpHi was similar in the control group (94±4%) and the groups exposed to 5 U/ml thrombin (-4±14%) or 25 μM SFLRN (-4±20%). Following treatment with 10 μM HOE694 (selective NHE inhibitor), pHi did not recover after an acid load, even in the presence of thrombin, confirming that NHE was the primary acid efflux mechanism under the conditions employed. We conclude that adult rat ventricular myocytes express a functional thrombin receptor, whose stimulation results in activation of the sarcomemlal Na+/H+ exchanger through a protein kinase C-mediated mechanism.

COMPARISON OF ISCHAEMIC PRECONDITIONING AND A HIGHLY SELECTIVE ATP-DEPENDENT POTASSIUM CHANNEL OPENER IN ISOLATED HUMAN ATRIAL MUSCLE

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The aim of this study was to compare the protective effects of ischaemic preconditioning and a highly selective ATP-dependent potassium (KATP) channel opener in human myocardium. The KATP channel opener BMS 180448 was used alone and in conjunction with the KATP channel blocker glibenclamide (Glib). Methods: Individual human atrial trabeculae were suspended in an organ bath and superfused with oxygenated Tyrode's solution at 37°C and paced at 1 Hz before entering the protocols. 4 experimental groups were studied (n=6 in each group): 1) C/G - 90 minutes hypoxic substrate-free perfusion at 3Hz (stimulated ischaemia), followed by 120 minutes of reoxygenation with substrate at 1Hz (reperfusion). 2) Preconditioning - 9 minutes simulated ischaemia and 7 minutes reperfusion, followed by the 90 min. simulated ischaemia and 120 min. reperfusion. 3) BMS 180448 (3 μM) was added to the superfusate for 5 minutes followed by the 90 min. simulated ischaemia and 120 min. reperfusion. 4) BMS 180448 (30 μM) + Glib. (1 μM) - Glib was added to the superfusate for 10 minutes, and BMS 180448 was added for only 5 minutes prior to the 90 min. simulated ischaemia. This was followed by 120 min. reperfusion. The endpoint was percentage recovery of contractile function (%R) measured at the end of 120 min. reperfusion. Results: mean ± standard error of mean.

Group | %R
--- | ---
Control | 20.8 ± 3.5
Preconditioning | 50.5 ± 3.6
BMS 180448 | 59.2 ± 8.6
BMS 180448 + Glib | 50.5 ± 2.7

The BMS compound and preconditioning both resulted in a similar degree of protection, which was significantly different to controls (p<0.05, ANOVA). This protection was prevented when the KATP channel blocker glibenclamide was added prior to the BMS 180448. Conclusion: This shows that in an in vitro human atrial muscle preparation, BMS 180448, a specific KATP channel opener, is able to mimic the protective effects of ischaemic preconditioning.

DD GENOTYPE OF THE ANGIOTENSIN-CONVERTING ENZYME (ACE) GENOME IS ASSOCIATED WITH ABNORMAL DIASTOLIC FUNCTION IN ESSENTIAL HYPERTENSION

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An insertion/deletion polymorphism in the ACE gene accounts for 50% of the variation in serum ACE activity. ACE is responsible for the generation of angiotensin II which has not only pressor and mitogenic activity but also impairs active myocardial relaxation. We investigated the contribution of genetic polymorphisms of the ACE gene to the development of diastolic functional abnormalities in 100 patients with essential hypertension. All patients underwent echocardiographic assessment of left ventricular mass index ((LVMI) and diastolic function indices of peak and integrals of early to late filling (E/Ap and E/A respectively), and determination of ACE genotype groups. Analysis of covariance (ANCOVA) modelled for indices of diastolic function, adjusting for age, sex, heart rate and LVMI demonstrated the E/Ap interacted with age (p<0.0001), heart rate (r=0.0001) and ACE genotype (p=0.018), and the E/A interacted with age (p=0.001). heart rate (p=0.025) and ACE genotype (p=0.047). There was a strong correlation between E/Ap and LVMI in the DD group (r=0.81, p<0.0001) but not in heterozygotes (r=0.23, p=0.23).

These findings suggest that the DD genotype of the ACE gene is associated with impairment of left ventricular diastolic filling in patients with essential hypertension.

DIFFERENTIAL LEFT VENTRICULAR RELAXANT EFFECTS OF -SH AND NON-SH CONTAINING ACE INHIBITORS

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Cardiovascular Sciences Group, UWCM, Cardiff.

ACE inhibitors are beneficial in heart failure and left ventricular (LV) hypotropy. ACE increases angiotensin II, and inactivates bradykinin which releases nitric oxide from endothelial cells. We have previously shown that both exogenous and endogenous nitric oxide enhance LV relaxation. We studied the effects of the SH-containing ACE inhibitors captopril and zofenaprilat and the non-SH-containing ACE inhibitors lisinopril and quinaprilat on LV function in isolated guinea-pig hearts (constant loading and rate; Krebs' buffer; 37°C; indomethacin, 1μM). LV pressure (LVp) was measured using a 2F Millar catheter, and LV relaxation assessed by an exponential time constant (Tg). Captopril (1μM) accelerated early LV relaxation (i.e. reduced Tg; -15.2±1.6% at 16min; n=9; p<0.05) without affecting LVP, dp/dt or coronary flow. This effect was significantly reduced by haemoglobin (1μM) or HOE140 (10μM), which inactivates nitric oxide and inhibit BKc receptors respectively (-1.7±1.2% and -7±2.5% respectively at 16min; both p<0.05 cf captopril alone). Zofenaprilat had similar effects, reducing Tg by -10.1±1% at 16min (n=5; p<0.05) and this was also inhibited by haemoglobin and HOE140 in a similar manner to captopril. Neither lisinopril nor quinaprilat had any effect on Tg (-4.8±2.1% and +3.4±1.9% at 16min; both n=6; both p>NS) or on LVP, dp/dt and coronary flow. Concurrent administration of lisinopril either with the oxygen free-radical scavenger, superoxide dismutase (60U/ml) or the SH-containing compound, n-acetyl cysteine (1μM) also had no effect on LV relaxation.

Thus, (1) Both captopril and zofenaprilat exert selective LV relaxant effects, with attenuation by haemoglobin and HOE140 suggesting involvement of endogenous nitric oxide and bradykinin, (2) the lack of effect of lisinopril and quinaprilat suggests that the presence of an -SH group is essential for this effect, (3) the results with superoxide dismutase and n-acetyl cysteine suggest that neither the anti-oxidant nor an SH-group forming activity of the -SH group is involved in this mechanism of action, (4) the lack of vasodilator activity of captopril or zofenaprilat may reflect the site of bradykinin/nitric oxide release, (5) the direct LV relaxant actions of captopril and zofenaprilat may be beneficial in "diastolic dysfunction".
PREVIOUSLY-REPORTED MITOCHONDRIAL DNA MUTATIONS ARE NOT A COMMON CAUSE OF IDIOPATHIC DILATED CARDIOMYOPATHY

LJ Turner*, S. Kadavath*, JF Cooper+, AHV Schapira†, PA Poole-Wilson†. †Royal Free Hospital School of Medicine and *National Heart & Lung Institute, London

The cardiomyopathies constitute a heterogeneous group of diseases, usually of unknown aetiology, in which cardiac muscle is primarily involved. There is increasing evidence that point mutations of mitochondrial DNA (mtDNA) are responsible for a number of cardiomyopathies occurring in the presence of skeletal myopathy. We investigated the occurrence of 7 previously-reported pathogenic mtDNA mutations, in patients with dilated cardiomyopathy (DCM; blood samples n=29, myocardial tissue n=8), and compared these with individuals with ischaemic heart disease (blood n=29, myocardium n=13), hypertrophic cardiomyopathy (blood n=4, myocardium n=1) and controls (transplant donor myocardium from individuals without known cardiac disease, n=3). Total DNA or whole cell lysates were subjected to PCR amplification and restriction enzyme digestion for the identification of the following mtDNA point mutations:

<table>
<thead>
<tr>
<th>mtDNA mutation</th>
<th>associated clinical syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>3243, A to G</td>
<td>exophalangomyopathy with lactic acidosis and stroke-like symptoms</td>
</tr>
<tr>
<td>3252, A to G</td>
<td>exophalangomyopathy with diabetes mellitus</td>
</tr>
<tr>
<td>3260, A to G</td>
<td>maternally-inherited skeletal myopathy with cardiomyopathy</td>
</tr>
<tr>
<td>4269, A to G</td>
<td>exophalangomyopathy and progressive cardiac failure</td>
</tr>
<tr>
<td>8344, A to G</td>
<td>myoclonic epilepsy with ragged red fibres</td>
</tr>
<tr>
<td>8993, T to G/C</td>
<td>neurological muscle weakness, ataxia and retinal pigmentation; also Leigh’s disease and cardiomyopathy</td>
</tr>
<tr>
<td>9997, T to C</td>
<td>maternally-inherited hypertrophic cardiomyopathy</td>
</tr>
</tbody>
</table>

None of these mtDNA point mutations were detected in the blood or myocardium of any of the individuals with DCM, or in the other groups tested. This suggests that although these mutations are associated with some forms of cardiomyopathy, they are not a common cause of idiopathic DCM.

THE AETIOLOGY OF IDIOPATHIC DILATED CARDIOMYOPATHY (DCM): FAMILIAL PREVALENCE AND HLA-TYPES

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The cause of DCM is by definition unknown. The most popular hypothesis is that the disease is an autoimmune response. Prospective studies of DCM have identified a familial incidence of roughly 20%. Many studies since have searched in vain for a marker to predict families at risk of developing DCM.

Methods and Results: to date, 85 probands with DCM have been entered in the study. All had normal coronary arteries by angiography, as well as the other usual exclusions. 168 relatives from 50 of these proband families have been screened for DCM by echocardiography. The probands were HLA-typed and compared with 9000 normal controls from the Blood Transfusion Service. The disease was defined as definitively familial if at least one first-degree relative fulfilled both ECHO criteria (LVEF < 57% and LVEDD > 57mm) and LVEF < 50%, and possibly familial if only one of the ECHO criteria was met. A reported unexplained sudden death in a first-degree relative before the age of 50 years was included in the possible group.

The familial incidence of DCM in this patient group was definite in 18% and possible in a total of 40%. The HLA-DR4 frequency in controls and the non-familial DCM probands was the same (32% vs 31%). However, the DR4 frequency in the familial cases was significantly higher (65% vs 90% p < 0.01).

Conclusions: the familial incidence of DCM in this patient group is a definite 18% and possible 40%. It is cases of DCM which in DR4-linked, implying an autoimmune inherited predisposition in this subgroup of patients. The DR4 haplotype identifies two-thirds of the families with a tendency to the disease.

DIFFERENCES IN SHORT-TERM OUTCOME FOR ACUTE MI BETWEEN GERMANY AND THE UK: THE ROLE OF CLINICAL TRIAL DATA IN THE RESOURCE UTILISATION DEBATE

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In several recent multi-national clinical trials of thrombolysis for acute myocardial infarction it has been noted that overall mortality rates differ significantly with country often to a greater extent than that seen between the agents under investigation. As these same studies also provide insight as to differences with respect to in-hospital management and resource utilisation, it is tempting to use such studies as evidence in the continuing debate on the level of resource required in the UK for the treatment of myocardial infarction.

This paper argues, using data from the INJECT trial, that headline mortality rates should be used with extreme caution. The INJECT Trial recruited 2280 patients in the UK and 1909 patients in Germany. Overall 35 day mortality in the two countries was 10.2% and 7.4% respectively. Mean length of hospital stay was 7.4 days, UK, and 20.8 days, Germany. Some 37.5% of patients in Germany received a coronary angiogram during the index admission compared with 2.6% of UK admissions, with 35 day CARG/PTCA rates being 13.6% for Germany and 0.5% for the UK. However, the data available also show clearly that there are differences between the two countries with respect to demography and prior morbidity, despite the fact that all patients were entered under a common protocol.

After a multivariate analysis correcting for differences between the two countries with respect to prognostic variables available at entry to the study, there is no evidence from the INJECT trial that mortality depends on country and no evidence of any association between outcome and management.

Clinical trials do have a major role to play when determining the value of alternative management strategies as prospective studies such as SWIFT and RITA have shown. Similarly, the large randomised trials of thrombolysis provide evidence of the value of the therapy but they cannot provide comparable insight into the appropriateness of other non-randomised management strategies.

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(205) MODERATED POSTER

CALL-TO-NEEDLE TIMES IN GRAMPIAN: THE PIVOTAL ROLE OF THE GENERAL PRACTITIONER IN ACHIEVING EARLY THROMBOLYSIS

J Rawles, C Sinclair, N Waugh, Medicines Assessment Research Unit, University of Aberdeen, and Grampian Health Board

A British Heart Foundation guideline proposed that, ideally, patients with acute myocardial infarction should receive thrombolysis within 60 minutes of seeking medical assistance: a target "call-to-needle time" of 90 minutes was adopted as being attainable.

We have audited the call-to-opiate and call-to-thrombolysis times in patients referred to Aberdeen Royal Infirmary from the city and suburbs of Aberdeen, and from peripheral practices in Grampian >15 miles from the hospital. All times are medians [95% confidence intervals].

Call-to-opiate times were significantly shorter for patients receiving opiates from their general practitioners (GPs) (30 [25-30] minutes) than for those receiving it in the accident and emergency department (56 [41-90] minutes).

All 117 patients from Aberdeen city and suburbs who were given thrombolysis were given it in hospital, and patients with suspected acute myocardial infarction either rang 999 (n=89) or called their GPs (n=193). Call-to-thrombolysis times were not significantly different (93 [75-125] vs 105 [95-135] minutes) for the two routes of admission: although patients who were seen by their GPs arrived at hospital later than those who rang 999, they were referred directly to the coronary care unit where the door-to-needle time (36 [28-42] minutes) was shorter than for patients taken to the accident and emergency department (62 [56-80] minutes).

In peripheral practices all referrals were seen first by their GPs: 66 patients with acute myocardial infarction were given thrombolysis by their GPs, and 143 in hospital; the call-to-thrombolysis times were 45 [40-48] minutes and 160 [133-180] minutes, respectively.

Conclusion The British Heart Foundation target call-to-thrombolysis time of 90 minutes is readily attainable if thrombolysis is given by general practitioners.

(206) MODERATED POSTER

POST MORTEM FINDINGS IN ASSESSING SUCCESS OF OUT OF HOSPITAL RESUSCITATION


The true value of community resuscitation programs for acute cardiac events may have been underestimated in the past because of the inclusion of irreversible cases of sudden death. In those cases where resuscitation is unsuccessful, the inclusion of post-mortem data allows accurate distinction of reversible and irreversible cardiac deaths, as well as allowing the elimination of irreversible non-cardiac causes of death from the data.

To address these issues, all out of hospital resuscitation attempts involving the ambulance service between 1989-1992 on the island of Jersey were studied retrospectively. 152 cases were identified of which 132 were witnessed collapses. There were 95 (62.5%) males and 57 (37.5%) females. Mean age was 63.4 (SD=16.6). The average interval between receiving an emergency call at the control room and a vehicle arriving on the scene was 5.5 mins (SD=3, n=111). 32 patients achieved a spontaneous cardiac output as a result of resuscitation but only 19 survived to be discharged from hospital. If unwitnessed collapses are excluded this represents an initial survival rate of 24.2% and a survival rate at discharge of 14.4%. Of the 133 deaths, post mortem results were available in 82 (61.7%). Of these, 58 (70.7%) patients had evidence of an acute atheromatous occlusion of a coronary vessel. 4 (4.9%) had an irreversible cardiac cause of death, namely LV rupture and 30 (20.4%) had non cardiac deaths of which the main cause was ruptured abdominal aortic aneurysm. Therefore, non cardiac and irreversible cardiac causes of death constitute a sizeable group (29.3%). If these data are excluded, the survival rate at discharge was 17.9%.

In conclusion, taking post mortem results into account is likely to improve the survival to discharge rates of out of hospital resuscitation programs and thus reflect the true beneficial impact of such programs on acute cardiac events in the community.

(207) MODERATED POSTER

LOW-COST TRANSMISSION OF CARDIAC ANGIGRAMS BETWEEN SECONDARY & TERTIARY CARDIAC UNITS

D Chin, S Gaughan*, M Higan**, R Wray*, A Mclead**, M J Monaghan, King's College Hospital, London, Conquest Hospital, Hastings*, and Eastbourne Hospital**

The proliferation of cardiac angiographic facilities in secondary (DGH) cardiac units has enabled local provision of invasive diagnostic services. However, specialist advice and referral of the patient for interventional/surgical procedures requires transport of the angio film to a tertiary specialist unit, incurring delays, cost and inconvenience. Recent advances in desktop computer (PC) processing power and the availability of a fibre-optic (ISDN) high data capacity telephone network, has made the transtelephonic transmission of high quality moving video images possible. PC workstations (cost £3,500) using a 75MHz pentium processor, 16MB RAM, 1.2GBYTE hard disc, real time MPEP compression frame grabber board, high resolution monitor and SVHS video recorder were established in two DGH and one tertiary unit. The two DGH workstations were linked to the tertiary unit using twin channel ISDN connections (cost = £400 installation + £250 p.a.). Specially written Windows based software "Video Mail" allows capture of real-time SVHS video and angiographic recordings at 25 frames/sec and 30:1 compression ratio direct to the Hard Disc. The software also permits editing of the angiogram prior to transmission and creation of an accompanying text file. Connection to the ISDN network, dial-up of the remote workstation and the entire data transfer takes just 10 minutes, meaning automatic transfer at both ends with the received angio "pigeon hole" for an identified Consultant or user. Average transmission time for a complete angiogram study is 20 mins. Other video image based investigations, such as echocardiograms have also been successfully transferred. On this newly established system, 50 studies have been transmitted to date, over distances of >80 miles. All studies have been judged to be of appropriate diagnostic quality.

In conclusion, these recent technological advances will enhance the efficiency of patient data transfer between cardiac units and make cardiac telemedicine a low-cost possibility.

(208) MODERATED POSTER

FACTORS AFFECTING UPTAKE OF CARDIAC REHABILITATION IN GLASGOW

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1Public Health Department, Greater Glasgow Health Board, Glasgow; 2Cardiology Department, Stobhill Hospital, Glasgow; 3Cardiology Department, Western Infirmary, Glasgow.

Cardiac rehabilitation has been shown to significantly improve prognosis following MI, reducing total and cardiovascular mortality, and fatal reinfarction rate. However, many patients do not attend rehabilitation. The aim of this study was to determine which factors influenced uptake of cardiac rehabilitation. Routine discharge data were used to identify all patients discharged following MI over a six month period from the four hospitals in Glasgow offering rehabilitation. Postcodes were used to attribute Carstairs deprivation scores to patients. Of the 1120 patients discharged following MI, 59% were male. The median age was 66 years (IQR 57-74); 21% died prior to discharge and 59% were under the care of a cardiologist. Three hundred and fifteen (36%) patients discharged alive were invited to rehabilitation. Of these, 187 (59%) started the programme and, 109 (34%) completed it. On stepwise logistic regression analysis hospital (p<0.0001), age (p<0.0001), sex (p<0.05) and admission under a cardiologist (p<0.05) were significant independent determinants of whether patients were invited to rehabilitation. Uptake of rehabilitation following invitation was significantly associated with admission under a cardiologist (p<0.05), hospital (p<0.005) and deprivation (p<0.001). Once rehabilitation had been started, the only determinant of completion was deprivation (p<0.05). Questionnaires were sent to patients to ascertain problems with attendance. The most frequent reasons cited were cost and lack of transport, and parking problems. Of those attending no charge, 39% reported that they would find it easier to attend a community-based programme. A pilot community-based rehabilitation service has been established in a deprived area in Glasgow.

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(209) MODERATED POSTER

Audit of Physician Training in temporary cardiac pacing from District General Hospitals in the North West Region

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Competence in temporary pacing is an important part of the training of junior physicians. There has been increasing reports regarding the high complication rate of this procedure. We report the results of a questionnaire survey assessing the level of technical skill and experience (including radiation practices) among Senior House Officers (SHO’s [n=33]) and Registrars (RegS [n=11]) working in District General Hospitals (DGH’s) in the North West Region. The mean number of years worked since qualification was 3 for SHO’s and 8.5 for Registrars. 39% of SHO’s and 10(90%) of Registrars had obtained the MRCP. 33(75%) had performed less than 5 pacemakers and none had performed 5 or more procedures in the preceding 12 months. The subclavian route was the commonly used approach (38/44) but 19% of doctors frequently needed help for successful cannulation. 60% could not perform internal jugular venous cannulation. 30% had frequent problems with lead positioning with 50% "learning to position" at least once in the preceding twelve months. 50% did not keep or have a record kept of there screening times or wear a radiation badge. 43% had not attended radiation protection training. 74% could not perform post-implant threshold measurements. All doctors entered further training.

Conclusions: Junior medical staff in DGH’s have very limited experience in temporary pacing and require a formal training program.

(211) MODERATED POSTER

HELCOBACTER PYLORI INFECTION AND CORONARY HEART DISEASE IN MIDDLE-AGED MEN: PROSPECTIVE RELATIONS IN A NESTED CASE-CONTROL STUDY

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Department of Primary Care and Population Sciences, Royal Free Hospital School of Medicine, London and Departments of Medicine and Public Health Sciences, St George’s Hospital Medical School, London.

Helicobacter pylori, a chronic bacterial infection often acquired in childhood, has been implicated as a risk factor for coronary heart disease (CHD) in retrospective studies. We have examined the prospective relationship between helicobacter pylori infection and CHD, using a nested case-control study within a prospective investigation of cardiovascular disease in British men from 24 towns aged 40-59 years at entry (1978-80). Serum samples stored at entry were analysed by ELISA for the presence of H. pylori specific IgG antibodies. Incident cases of myocardial infarction (N =135) and controls (N =136), frequency matched to towns by age and group, were identified. Ninety-five of the myocardial infarction cases (70%) were seropositive for H. pylori compared with 78 (57%) of the controls (odds ratio 1.77, 95% CI 1.06 to 2.95, p = 0.03). Helicobacter pylori infection was associated with manual social class, residence in Northern England or Scotland, cigarette smoking, higher systolic pressure and blood pressure and a lower height-standardized FEV1. Adjustment for these factors attenuated the relationship between H. pylori and myocardial infarction (odds ratio = 1.31, 95% CI 0.70 to 2.43, p = 0.40). The relation between Helicobacter infection and fatal myocardial infarction was slightly stronger (odds ratio 2.41, 95% CI 1.13 to 5.12) but was also markedly attenuated after adjustment (1.56, 95% CI 0.68 to 3.61). In this prospective study, the association between Helicobacter pylori infection and increased risk of myocardial infarction is substantially explained by adult social class and major cardiovascular risk factors, making a causal association less likely.

(210) MODERATED POSTER

ALTERATIONS IN THE MANAGEMENT OF CARDIAC FAILURE: EVIDENCE OF IMPROVEMENT.

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We have previously shown that patients with cardiac failure are often inadequately treated in hospital. In order to assess whether the management has improved since audited in 1992 we analysed the cases of consecutive patients discharged from Aberdeen Royal Infirmary on or after 1/95 with a diagnosis of cardiac failure (International Classification of Diseases 9th revision codings 428.0, 428.1 and 428.9).

At discharge from hospital the cardiac function of 73.1% had been assessed by echocardiography and/or radionuclide scanning or left ventriculography. This represents a significant increase since 1992 (73.1% of 39.7% in 1992; p=0.0001). Similarly 56% (140/250) of patients were being treated with an angiotensin converting enzyme (ACE) inhibitor; once again this represents a significant improvement (56% of 40% in 1992; p=0.001). The doses of ACE inhibitors prescribed at discharge had also increased significantly, with 45% (63/140) of patients now treated with >75mg captopril, 20mg enalapril or equivalent. Of those not on an ACE inhibitor 28 (25.5%) had clear contraindications to such therapy. As before, patients discharged on an ACE inhibitor were significantly younger (mean age 68.8 years of 74.0 years; 2p<0.001). They were also more often on a specialist cardiac unit though this fell short of statistical significance (15% vs 7%; p=0.08).

The investigation and treatment of cardiac failure appears to have improved since 1992, presumably because of greater awareness of the condition and the potential to improve prognosis with the use of ACE inhibition. However, the management of a sizable proportion of patients remains sub-optimal.

(212) MODERATED POSTER

HELCOBACTER PYLORI INFECTION AND CORONARY HEART DISEASE IN NORTH GLASGOW.

TA McDonagh, CE Morrison, M Woodward, JLV McMurray, BJ Tuatall-Pedoe, KEI McColl, GD Low, JDargie.
Departments of Cardiology and Medicine, Western Infirmary, MONICA Project and Department of Medicine, Royal Infirmary, Glasgow.

Recent evidence has suggested that Helicobacter pylori infection is associated with coronary heart disease(CHD). We investigated whether H. pylori infection is related to prevalent coronary heart disease, in a random sample of 1428 men and women aged 25-74, in North Glasgow. CHD was assessed by self reported myocardial infarction (MI), self reported angina, and electrocardiography (ECG). Standard risk factors for CHD, fibrinogen concentration and serum concentrations of H. pylori specific IgG antibody were measured. H. pylori seropositivity increased with age(p<0.001), and was significantly more prevalent in men than women. Rising from 50% in women aged 25-34 up to 70% of men over 65 yrs. Infection with H. pylori was strongly associated with social class(p<0.001) being four or more times more common in the most socioeconomically deprived group compared with the most affluent. H. pylori was significantly associated with current smoking, expired air carbon monoxide levels and a higher systolic blood pressure in men. There was no significant increase in the odds ratio in those seropositive for H. pylori with regards to any manifestation of CHD(0.89 for men,0.95 for women, previous MI(1.47 for men,1.09 for women),self reported angina (0.91 for men,0.82 for women) or ECG abnormalities(0.85 for men,1.31 for women), after adjustment for age, standard cardiovascular risk factors and social class. Plasma fibrinogen was no higher in seropositives. Seropositivity to H. pylori is associated with a trend towards a greater prevalence of CHD, However, that association is likely to be spurious and can be adequately explained by the much stronger association of H. pylori infection with age and social class , both of which are linked with CHD.
ATRIOVEN TRICULAR NODE ABLATION AND IMPLANTATION OF DUAL CHAMBER MODE: SWITCHING PACEMAKERS FOR PAROXYSMAL ATRIAL FIBRILLATION - EFFECTS ON QUALITY OF LIFE, EXERCISE CAPACITY AND LEFT VENTRICULAR SYSTOLIC FUNCTION

HJ Marshall, Z Harris, MJ Griffith, MD Gammage.
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Atrioventricular (AV) node ablation and implantation of a dual chamber mode-switching (DDDR/M) pacemaker is becoming accepted as treatment for refractory paroxysmal atrial fibrillation (PAF). To date, however, there are few data available to assess its efficacy. We have, therefore, assessed the effects of this procedure on quality of life, exercise capacity and left ventricular (LV) systolic function. We studied 18 consecutive patients presenting to us with drug refractory PAF (age range 39–77 years). A full drug history was taken and quality of life was assessed before and after the procedure using the Psychological General Well Being Index (PGWB), the McMaster Health Index (MHI) and a visual analogue scale for cardiac symptoms. Nine of the patients also underwent symptom-limited exercise tests using the CAD protocol and echocardiography to assess LV systolic function, measured as fractional shortening (FS%). A mean of 5.3 antiarrhythmic drugs or combinations of drugs had been tried before intervention. Mean values for parameters measured are shown below.

<table>
<thead>
<tr>
<th>PGWB</th>
<th>MHI</th>
<th>Symptom Score</th>
<th>Number of Drugs *</th>
<th>FS%</th>
<th>Exercise Time (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre</td>
<td>59.44</td>
<td>14.11</td>
<td>56.44</td>
<td>1.38</td>
<td>34.47 (11)</td>
</tr>
<tr>
<td>Post</td>
<td>77.22</td>
<td>15.22</td>
<td>21.58</td>
<td>0.06</td>
<td>31.56 (3)</td>
</tr>
</tbody>
</table>

* = antiarrhythmic drugs and | = number of patients in AF at time of testing.

The study demonstrates that AV node ablation and implantation of a DDDR/M pacemaker is an effective treatment for drug refractory PAF. In this group of patients it produced a significant improvement in quality of life, whilst allowing a reduction in antiarrhythmic drug burden. There was no significant change in exercise capacity or LV systolic function. We conclude, therefore, that the popularity of this treatment is justified, but that further studies are needed to determine its optimum timing.

DO PATIENTS PREFER MODE SWITCHING?

A history of paroxysmal atrial tachyarrhythmias (PAT) has been a relative contraindication to implantation of dual chamber pacemakers. The aim of this study was to compare single chamber rate responsive ventricular pacing (VR) to dual chamber rate responsive pacing with mode switch on (DM) or off (DR), in patients (pts) with a history of PAT and heart block. Pts were randomised to each pacing mode for a period of 1 month. All kept a diary, sent trans-telephonic ECGs when symptomatic, and underwent 24hr ambulatory cardiac monitoring in each mode. At the end of each period, they performed an exercise test (CAEP protocol), and completed 3 different symptom questionnaires. 36 pts aged 65+/−13 years (19M,17F) have been recruited. Diagnoses were heart block (42%), sinus node disease (39%), or both (19%). Pacemakers were Diamond (7), Vigor DR (12), Thera DR (10), Chronos RM (4), and Meta DR 1254 (3).

In 5 pts the atrial arrhythmia became chronic and they were excluded. Perceived exercise capacity was significantly greater in DM compared to VR (P=0.02), but did not differ from DR (P=ns). Perceived general well-being was significantly greater in DM than either VR (P=0.006), or DR (P=0.03). Pts were less likely to have symptoms suggestive of pacemaker syndrome, as assessed by Specific Symptom Prevalence Questionnaire, in DM compared to VR (P=0.05). 33% of pts programmed to VR terminated their mode early due to unacceptable symptoms, as compared to 17% in DR and 3% in DM. The overall preferred pacing mode was DM in 52%, DR in 22%, VR in 10%, and no preference in 16%. In 12 pts with moderate to frequent PAT, the preferred mode was DM 67%, VR 17%, DM/VR 8%, and DR 8% 60% of pts with ‘fast’ MS pacemakers preferred the DM mode, compared to 40% with ‘medium’ and 50% with ‘slow’ MS devices (P=ns). The exercise time was significantly longer in DM (8.5min) compared to VR (7.6min) (P=0.02). There were no cases of rapid ventricular tracking of a PAT in DM mode, and only one case of inappropriate MS during exercise. Thus, in pts with PAT, DM is the preferred mode and VR is least acceptable. Pts with moderate to frequent PAT tolerate DR poorly. Inappropriate MS and tracking of PAT in DM mode was very uncommon.

IS MODE SWITCHING DDDR PACING SUPERIOR TO VVIR PACING FOLLOWING ATRIOVENTRICULAR NODE ABLATION FOR REFRACTORY ATRIAL FIBRILLATION?
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Wessex Cardiothoracic Centre, Southampton University Hospital, Southampton.

Mode switching (MS) DDDR pacing may be superior to VVIR pacing in patients (pts) following atrioventricular node ablation (AVNA) but is more costly and complex. We performed a prospective randomised double blind study to compare MS DDDR pacing with VVIR pacing in 15 pts (6 females) mean age 56 ± 7 years following AVNA for atrial fibrillation (AF) refractory to drug treatment. 3 pts had concomitant heart disease (2 ischaemic and 1 idiopathic dilated cardiomyopathy). Study Design: At recruitment pacemakers were reprogrammed, using predetermined settings, to MS DDDR or VVIR for 2 weeks then crossed over for the final 2 weeks. Atrial rhythm was documented at each of 5 visits. Pts kept analogue scale symptom diaries (modified Borg) for awareness of i) missed beats, ii) prolonged irregular heart beat, iii) fatigue, iv) dizziness, v) shortness of breath and vi) general well-being. Pts performed Bruce protocol exercise tests at the end of weeks 1 and 3. Results: 5 pts had normal sinus rhythm and 2 pts had AF at each visit; the remainder had AF at one or more visits. Prolonged irregular heart beat had a higher symptom score (0.01 vs 0.8; p<0.01) in the MS DDDR mode. But other symptom scores and general well-being scores were not significantly different. As expected, exercise duration was greater (488sec vs 380sec p<0.05) in those pts (m²?) with sinus rhythm on the day of exercise in MS DDDR. Conclusion: To best select pts for MS DDR an assessment of the frequency of AF paroxysms should be part of the work-up before AVNA and pacemaker implantation. The improved exercise tolerance associated with MS DDR may be offset by an increased awareness of palpitation (presumably related to the mode switching algorithm) in pts with frequent bouts of AF.

INTRAMYOCARDIAL CONDUCTION ABNORMALITIES IN IDIOPATHIC DILATED CARDIOMYOPATHY MAY REFINE RISK ASSESSMENT.
Department of Cardiological Sciences St George’s Hospital Medical School, London.

Ventricular arrhythmias carry an adverse prognosis in idiopathic dilated cardiomyopathy (DCM) yet programmed ventricular stimulation remains controversial. We used a new electrophysiological technique, initially developed in hyperkalaemic cardiomyopathy, in 21 patients with DCM (mean age 39 ± 14 yrs). 1 had sustained ventricular fibrillation (VT), 3 had syncope, 2 had sustained ventricular tachycardia (VT) and a further 8 had non-sustained VT.

Methods: Electrode catheters were placed at 4 right ventricular sites: apex, septum, inferior wall and outflow tract. Electrogroms (EGM) were obtained by pacing at, in turn, one site with a 1 ms decremental extrastimulus after a two beat 480 ms drive chain and recording EGM from the other 3 sites. The transition in these EGM were used to construct a set of conduction curves. The longest interval at which latency increased and the greatest increase in EGM duration were extracted and plotted against each other.

Results: A range of abnormalities are shown with the patients with VT and syncope having the greatest increase in EGM duration and earliest increase in latency.

Conclusions: Quantification of intramyocardial conduction disturbance may form a basis for risk stratification in DCM.
INITIAL EXPERIENCE WITH MAPPING HUMAN ENDOCARDIAL ACTIVATION USING A NOVEL NON-CONTACT CATHETER MAPPING SYSTEM
RJ Schilling, WM Jackman, NS Peters, G Beatty, DW Davies, St Mary's Hospital, London and University of Oklahoma, Oklahoma, USA.

Ablation of ventricular tachycardia (VT) is limited by difficulty in identifying myocardial areas critical to sustaining the arrhythmia. To address the problems of the poor resolution and time consuming nature of conventional mapping techniques, a 9F catheter-mounted non-contact multielectrode array (MEA) consisting of a wire braid on the surface of the braid has been developed and was deployed in the left ventricle (LV) during electrophysiological study of 4 male patients (pts) with VT. Using inverse solution mathematicians (boundary element method) the system reconstructs 2,500 "virtual" electrograms, on a shell model of the endocardium with a theoretical limit for accuracy at a distance of 3 balloon radii (2.4cm) from its centre. From these data, isopotential maps of the virtual endocardium were made. The pts had haemodynamically stable VT. One had a normal heart and fascicular tachycardia (FT); 3 had severely impaired LV function, 1 from dilated cardiomyopathy and 2 from coronary heart disease with LV end-diastolic diameters ranging from 5.6 to 7.6cm. The MEA was safely deployed in all pts for a mean of 3h 56m without haemodynamic effect during either sinus rhythm (SR) or VT. Ablation was performed after conventional activation and entrainment mapping data being retrieved. In pt 1, this revealed a presystolic left bundle branch activity during both SR and, with an altered sequence, during FT. Sustained VT was induced in the other 3 pts from which MEA data later allowed ventricular activation patterns and diastolic reentrant activity to be traced. In 2, clinical VTs were found to share the same diastolic pathway. Extensive off-line analysis of the MEA data (even though parts of the circuit were further than 2.4cm from the MEA's centre) demonstrated that these were due to the same double-loop (figure-of-8) reentrant circuit in contra/torsation.

Initial experience with this novel mapping technique has been safe, even in patients with significantly impaired LV function and unique data have later been retrieved. Further development is required to explore its potential to facilitate complete, rapid and accurate arrhythmia mapping.

VENTRICULAR TACHYCARDIA OF ARRHYTHMOGENIC RIGHT VENTRICULAR DISEASE - EVIDENCE FOR LOCALISED REEMERGENT MAPPING
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Freeman Hospital, Newcastle upon Tyne, and Toronto General Hospital, Toronto, Canada

Ventricular tachycardia (VT) in patients with arrhythmogenic right ventricular disease (ARVD) may require a surgical approach for control of their arrhythmias. The mechanism of VT is thought to be reentry and diastolic potential mapping is useful in defining reentrant circuits. This report describes the intraoperative electrophysiological findings in ARVD-VT and highlights an unrecognised pattern of highly localised reentry. Four patients, mean age 37 years, with life-threatening ARVD-VT underwent map-guided surgical management of their arrhythmias. The two Toronto patients had simultaneous multipoint mapping of the epicardium and RV endocardium by means of multiple electrode arrays attached to a sock and RV balloon. Eight VTs were mapped. The two Newcastle patients underwent sequential single-point mapping of the epicardium and RV endocardium with a roving hand-held probe of the clinical, and only inducible, VT. Data, particularly of diastolic activity, were analysed offline and form the basis of this report. In every VT, the earliest activation point was located on the epicardial surface. Diastolic mapping demonstrated reentry circuits between adjacent points on the epicardial surface. These points were less than 1 cm apart. The example shows marked diastolic activity (R12E3) adjacent to the earliest activation (R13E3). All patients were treated by cryotherapy (three) and partial disarticulation (one). The VTs were successfully treated.

Intraoperative and diastolic mapping of ARVD-VT has not previously been described. Despite the often diffuse nature of the ARVD condition, a highly localised pattern of reentry on the epicardial surface is described. This information may modify the intraoperative strategy adopted in the management of ARVD-VT.

USE OF CHEST X-RAY (CXR) AFTER BIOPSY OF THE TRANSPLANTED HEART
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Transplant Unit, Wythenshawe Hospital, Manchester UK.

Background. Frequent biopsy of the transplanted heart is an essential part of monitoring graft rejection. By protocol a minimum of 14 biopsies are performed in the first year. Biopsies are followed by CXR in order to detect complications of the procedure as well as signs of infection and of malignancy.

Methods. The value of routine CXR following biopsy was prospectively evaluated in 90 consecutive cases. CXRs were reported by an experienced transplant surgeon and blindly by a Consultant Radiologist.

Results. Respiratory tract infection was diagnosed on 19 occasions. Clinically, 3 of these were evident on CXR. No episodes of infection were seen on CXR in which the diagnosis was not also made clinically. There were no episodes of malignancy on CXR; 5 patients were suffering from skin malignancies. There were 2 arterial punctures complicated by haematoma and 1 episode of transient atrial fibrillation. No complications were diagnosed on CXR. There were no silent pneumothoraces.

The annual cost of performing routine CXR after biopsy is £3,993.60 (25.12 per CXR). The patient is exposed to X-rays. The risk from each CXR is small but cumulative, and transplant patients receive many radiological examinations.

Since the inception of the transplant program in 1987 6480 biopsies have been performed. There have been 9 pneumothoraces (4 requiring chest drain) and one temporary paresis of the right phrenic nerve. There have been no episodes of cardiac tamponade and no deaths. All of the complications requiring treatment have been apparent clinically.

Conclusions. CXR need not be performed routinely after myocardial biopsy and should be used to confirm a clinical suspicion of complications or infection. Omitting the procedure saves time, resources and radiation exposure to the patient.

ROUTINE CORONARY ANGIOGRAPHY AFTER HEART TRANSPLANTATION: TIME TO STOP.
SCD Grant, A EElGamal, NH Brooks, RD Levy.
Transplant Unit, Wythenshawe Hospital, Manchester, UK.

Background. Accelerated graft atherosclerosis occurs in 40-70% of heart transplant recipients 5 years after transplantation. Following transplantation most units perform regular coronary angiograms.

Methods. A retrospective review of routine coronary angiography after heart transplantation.

Results. 278 angiograms were performed between August 1987 and September 1995: 196 at 2 years, 48 at 4 years, 23 at 6 years and 11 at 8 years post transplantation. Coronary artery disease was identified in 30 patients. Revascularisation by coronary angioplasty was performed in two patients with good results. Following angiography there was 1 myocardial infarction due to dissection of the right coronary artery and two patients required surgical repair of the right femoral artery: There were 3 episodes of symptomatic bacteriemia temporarily related to the procedure (all in patients who also underwent biopsy). The average radiation exposure (dose area product) per procedure was 3720 cGy.cm² (compared to 6 cGy.cm² for a chest X-ray). Based on the average cost of a coronary angiogram at 1995 prices the total cost of these procedures was £130,660.

Conclusions. The practice of surveillance coronary angiography following heart transplantation answers few clinical questions and leads to a low rate of revascularisation. It results in substantial cost and use of resources. There is also a risk, both from the well known complications of the procedure, and from repeated radiation exposure in an immunosuppressed group already at increased risk of malignancy. We believe that coronary angiography after heart transplantation should be confined to patients in whom a clinical question needs to be answered and those participating in trials specifically designed to address the problem of graft atherosclerosis Routine angiography for interest and unfocused data gathering is not justified.
(221) MODERATED POSTER

TESTING THE APPROPRIATENESS OF CORONARY REVASCULARISATION: APPLICATION OF THE UNIVERSITY OF MARYLAND REVERSAL POWERFUL APPEARANCES APPROPRIATENESS SCORING SYSTEM TO UK ANGIOPLASTY PRACTICE
H R Stable, L Denne. The Royal Brompton Hospital, London.

There has been much interest in the development of scoring systems to evaluate the appropriateness of coronary revascularisation by angioplasty (PTCA) and coronary bypass grafting (CABG). The University of Maryland RAS system has proven a practical tool for this purpose and, when compared to the most complete RAS system (MUS) in the USA, was the only index to predict clinical outcome. We have examined the allocation of patients with single vessel coronary disease (SVD) to PTCA or medical therapy and demonstrated that, in a cohort prospectively identified from a consecutive series of 2000 diagnostic catheter procedures, interventional cardiologists used a powerful and independent predictor of treatment allocation. The RAS methodology was applied to examine this variation in practice, with the RAS score, calculated for each case, determining if a PTCA intervention was indicated.

<table>
<thead>
<tr>
<th>Not Indicated and Not Performed</th>
<th>26%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indicated and Not Performed</td>
<td>24%</td>
</tr>
<tr>
<td>Indicated and Performed</td>
<td>10%</td>
</tr>
<tr>
<td>Not Indicated and Performed</td>
<td>2%</td>
</tr>
<tr>
<td>Total</td>
<td>64%</td>
</tr>
</tbody>
</table>

In the management of SVD, interventionists appear to practice in line with RAS recommendations and there is little evidence that they are performing significant numbers of inappropriate procedures. In contrast it appears that general cardiologists fail to recommend PTCA in a significant proportion (46%) of patients when the RAS suggests that revascularisation is indicated.

(222) MODERATED POSTER

FAVOURABLE ARTERIAL REMODELING DEFINED AS A NEGATIVE ABSOLUTE LOSS AFTER CORONARY ANGIOPLASTY. A QUANTITATIVE ANGIOGRAPHIC ANALYSIS
AG Viciari*, R Mellert, PW Serruya. The Thoraxcentre, Rotterdam, The Netherlands, and John Radcliffe Hospital, Oxford.

Intraoperator ultrasound studies suggest that unfavourable vascular remodelling (UR) may be important in restenosis post PTCA. We evaluated whether favourable remodelling (FR, defined as a negative absolute loss) may also occur after PTCA in a study population of 2,950 patients 1,578 with SVD, 419 with multivessel disease). FR was defined as a negative absolute loss of luminal diameter (MLD) and was evaluated for the left anterior descending (LAD), left circumflex (LCX), and right coronary artery (RCA). The primary endpoint was the presence of restenosis (MLD < 0.75 cm). The secondary endpoint was the degree of restenosis (MLD < 0.75 cm). The primary endpoint was met in 15% of patients with SVD, 27% of patients with multivessel disease, and 42% of patients with RCA. The secondary endpoint was met in 20% of patients with SVD, 31% of patients with multivessel disease, and 42% of patients with RCA.

(223) MODERATED POSTER

THE IMPORTANCE OF EARLY QUANTITATIVE EXERCISE THALLIUM-201 TOMOGRAPHY AFTER CORONARY ANGIOPLASTY FOR PREDICTING ANGINA RECURRENCE
HK Hamdan, PJ Jordan, RM Poyner, CM Boivin, WA Little. Departments of Cardiovascular and Nuclear Medicine, University Hospital Birmingham, Birmingham.

The value of quantitative exercise thallium-201 tomography (SPECT) in predicting angina recurrence after a primary successful coronary angioplasty (PTCA) was evaluated in 34 patients (24 males), mean age 57 (9) years with chronic stable angina and single vessel coronary artery disease. Exercise thallium-201 SPECT was performed before and 2 weeks after successful PTCA in all patients. The extent of myocardial ischaemia was calculated by comparing the polar map to a normal database. Coronary artery stenosis was determined by quantitative coronary angiography (QCA). The mean percent coronary artery diameter stenosis was 73 ± 4% vs 69 ± 3% before PTCA and 36 ± 4% vs 37 ± 2% after PTCA in the asymptomatic and recurrent angina groups respectively, p = NS in all. The patients were followed for 21.2 ± 8.3 months (mean ± SD). 20 patients (59%) remained asymptomatic and 14 (41%) developed recurrent angina, 13 within 12 months. After PTCA, the exercise stress test was positive in one patient (3%) in the asymptomatic group and in 7 patients (50%) in the angina group. The extent of myocardial ischaemia improved in the asymptomatic patients from 31.9 ± 4% to 9.9 ± 2.3%, p < 0.001, but did not change in patients with recurrent angina 26.5 ± 5% to 21.1 ± 5%, p = NS. The presence of substantial myocardial ischaemia (≥ 50% of pre-PTCA defect) identified patients at high risk of recurrent angina; it occurred in 12 patients (86%) in the recurrent angina group and in 5 (25%) in asymptomatic patients. Of the 14 symptomatic patients, 3 were controlled on medical therapy, 9 had angiography (7 had restenosis, one new lesion and one normal angiogram) and 2 declined investigations. In conclusion quantitative thallium-201 SPECT performed soon after successful PTCA strongly predicted angina recurrence.

(224) MODERATED POSTER

INTRAVASCULAR ULTRASOUND AND STENT IMPLANTATION: INTRA- AND INTER-OBSERVER VARIABILITY
E Blessing, D Haussmann, M Sturma, A Milege, I Amende Department of Cardiology, Medical School Hannover, Germany

Intravascular Ultrasound (IVUS) is increasingly used to optimize implantation of stents. However, the variability of the measurements remains unclear. 58 patients (48 males, 10 females) underwent implantation of Palmaz-Schatz stents (7.9, 15 or 20 mm length) in the LAD (n=35), the right coronary artery (n=11), the circumflex artery (n=6) or in bypass grafts (n=6). Indications for stent implantation were primary stenosis (n=45), restenosis (n=7) or bail-out (n=3). IVUS-registrations (3.5 F, 30 MHz) of the proximal and distal reference segment and of the area with the smallest lumen within the stents were performed and analyzed by 2 examiners to determine the intra- and interobserver variability. The intra- and interobserver correlations for the luminal area of the proximal reference were r=0.97 and r=0.94, for the distal reference r=0.94 and r=0.91, for the minimal luminal area within the stents r=0.97 and r=0.98, and for the stent expansion (area within the stent/mean of luminal areas of the proximal and distal reference) r=0.83 and r=0.79.

Conclusions: IVUS enables reproducible measurements of luminal areas within stents and of the reference areas, the degree of the stent expansion undergoes a higher observer variability. This can lead to a different clinical decision in the cath lab.
MYOCARDIAL PERFUSION IMAGING PERFORMED USING ECHO-PLANAR SINGLE SHOT MAGNETIC RESONANCE IMAGING WITH A MOBILE 0.5 TESLA SCANNER

Dj Pennell, PD Gatehouse, ED Burman, SR Underwood, DN Firmin

Myocardial perfusion imaging is an important technique for evaluating the physiological significance of coronary stenosis and the viability of dyscontractile myocardium. Current current nuclear perfusion techniques have disadvantages of X-ray exposure, need for isotope and relatively poor resolution. We used magnetic resonance imaging (MRI) to perform myocardial perfusion imaging in 7 patients with an abnormal thallium scan using echo-planar one shot imaging, with a 50ms acquisition time, and a mobile 0.5T scanner. A single short axis plane was defined in mid-ventricle and imaging started at one per cardiac cycle. Pixel size was approximately 3x3mm yielding several pixels across the myocardium with end-systolic gating. Fat suppression was used to reduce signal from surrounding structures and immediately before injection of 0.08mm/kg Gadolinium-DTPA, an inversion pulse was added in early systole to null out signal from myocardium. The gadolinium bolus was given using a right atrial catheter from the right antecubital fossa. Clear enhancement and subsequent wash-out of the myocardium was seen. Adenosine was then started at 140µg/kg/min and the procedure repeated after adjustment of the imaging parameters. Imaging lasted approximately 20 minutes. Images were acquired in cine loops of the contrast agent wash-in, and by placing regions of interest to generate signal time intensity curves. In one patient, poor gating hindered interpretation. In 6 patients, good visual agreement with the abnormal area of perfusion on the thallium scan was identified on the stress MRI study. Drawing of the signal curves demonstrated clearly slower wash-in, and a lower signal peak in the abnormal areas. This is the first clinical demonstration of echo-planar MRI perfusion imaging at 0.5T. This technique is very fast in comparison with nuclear imaging, and can be extended to multislice imaging with the same temporal resolution.

PREDICTIVE VALUE OF FDG IMAGING IN 502 PATIENTS WITH CHRONIC ISCHAEMIC LEFT VENTRICULAR DYSFUNCTION ENROLLED IN A PROSPECTIVE EUROPEAN MULTICENTRE VIABILITY STUDY

ECG Conduced Action on Positron (PET) Investigation of Cellular Regeneration and Degeneration. [London UK], Louvain (B.), Lyon (F) Groningen (NL), Liege (B), Turku (SF), Copenhagen (D), Aachen (G)]

Aim of this study was to ascertain the value of quantitative 18F-fluorodeoxyglucose (FDG) Positron Emission Tomography (PET) to identify those chronically dysfunctional (D) left ventricular (LV) segments (SEG) whose function improve after coronary revascularisation (R). A total of 502 patients (pts) with at least one D-SEG subtended by a stenotic coronary artery amenable to R were enrolled over 2 years. LV function was assessed before and 4-6 months after R by radionuclide ventriculography or echocardiography. To maximise myocardial FDG uptake and overcome insulin resistance, all studies were performed during Euglycaemic Hyperinsulinaemic Clamp (EHC). A total of 238 pts have undergone R by angioplasty (14%) or bypass. Complete follow up data on 105 pts (age 59±9) who had R were available: LV ejection Fraction was 37±13% before and 40±15% after R (p<0.01); the regional wall motion score (1=normal; 2=hypokinetic; 3=akinetik; 4=dyskinetik) was 2.0±0.6 before and 1.7±0.6 after R (p<0.001). A total of 708 LV SEG were analysed, 326 normal (N) and 382 D. After R 204 (53%) D-SEG improved (IMP), 149 (39%) were unchanged (UNC) and 29 (8%) worsened. The Metabolic Rate of Glucose (MRG; µmol/min/g; lamp constant =1) was 0.42±0.18 in N-SEG, 0.38±0.17 in IMP-SEG (p<0.01 vs N) and 0.31±0.17 in UNC-SEG (p<0.01 vs N and IMP).

In conclusion, these interim data from a prospective multicentre study indicate that FDG-PET during EHC can provide an accurate quantitative assessment of myocardial viability in the absence of perfusion measurement. This approach also allows for reliable comparisons of absolute values of MRG utilisation between different subjects and different trials.

POSITRON EMISSION TOMOGRAPHY DEMONSTRATES NORMAL MYOCARDIAL PERFUSION AFTER ARTERIAL SWITCH OPERATION IN THE NEONATAL PERIOD

Reid, M W, M. Yates, David R. Anderson, Michael J. Tynan, Michael N. Malsey, Edward J. Baker

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In 11 children aged 2.3±0.6 (1.3-3.7) years who had undergone a neonatal arterial switch operation, evaluation of myocardial perfusion and coronary flow reserve (CFR) was performed using positron emission tomography (PET) 1.8±0.4 (1.1-3.6) years after surgery. PET scans were performed at rest and after dipyridamole pharmacological stress (0.56mg/kg over 4 mins) using 113 labelled ammonia. Data from PET scans were correlated with ECG and echocardiographic data in all cases. Results: Myocardial perfusion at rest and after pharmacological stress assessed from static tomographic images was found to be normal in all but one patient who had a single clearly defined inferior perfusion defect which was enhanced with stress. This patient had developed intraoperative ECG changes and was considered post operative ECMO support. Absolute myocardial blood flow at rest obtained from dynamic imaging was 0.85±0.16 (0.7±1.1) ml/min/g and increased to 1.18±0.21 (0.5-1.3) ml/min/g with dipyridamole infusion. Calculated coronary flow reserve was 1.27±0.16 (1.1-1.4). All patients demonstrated a normal hypotensive response to dipyridamole and ECG monitoring during stress failed to demonstrate any significant ischaemic changes. Echocardiography confirmed normal left ventricular dimensions and function in all cases with no obvious dyskinetic segments. Conclusions: PET is a safe and practical technique for the evaluation of regional myocardial perfusion in small children. Normal myocardial perfusion after the arterial switch is further support for the efficacy of anatomical repair of complete transposition in the neonatal period. The decreased CFR in this group of children must be interpreted with caution as normal CFR data in small children are not available.

NEW TECHNOLOGIES FOR ECHOCARDIOGRAPHIC MYOCARDIAL PERFUSION IMAGING

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Intravenous myocardial contrast echocardiography has met with limited success in demonstrating myocardial perfusion. However, new ultrasound contrast agents and imaging technologies have recently become available which, in combination, may make this goal realistic. FS069 is a new transpulmonary ultrasound contrast agent consisting of Albunin shell microspheres (1-6um diameter) filled with perfluorooctane gas. FS069 has excellent ultrasound backscatter properties and long in-vivo persistence. Increased echocardiographic sensitivity and signal to tissue backscatter ratio may be obtained by analysis of the backscattered 2nd harmonic of the contrast agent resonant frequency. Thirty intravenous doses (0.1ml - 4.0ml) of FS069 were administered to 5 normal subjects and 7 patients with left ventricular dysfunction (EF<40%) during 2nd harmonic imaging using a proprietary ultrasound system transmitting at 1.8MHz and receiving at 3.6MHz. Real-time 2nd harmonic images were displayed in a conventional 2D echocardiographic format and recorded on SVHS video and on optical disc. Video densitometry and qualitative scoring (0 = no enhancement, 1 = faint, 2 = moderate, 3 = good, 4 = attenuation) was performed using a region of interest in myocardial segments before, during and after contrast injection. Mean 2nd harmonic myocardial video grey level increased from 43±8 units before to 93±4 units after intravenous injection (P<0.001) and qualitative evaluation by two observers demonstrated a mean enhancement score of 2.33.

In conclusion, recent advances in ultrasound contrast agent (FS069) and imaging (2nd harmonic) technologies appear to have made real-time echocardiographic evaluation of myocardial perfusion, following low volume intravenous administration, a reality.
(229) MODERATED POSTER

DO DE NOVO AND RESTENOSIS LESIONS REACT DIFFERENTLY TO CORONARY INTERVENTION? ANGIOGRAPHIC INSIGHTS FROM THE TRIAL OF ANGIPLASTY AND STENTS IN CANADA (TASC I)

Background: TASC I compared the strategies of coronary artery stenting to PTCA de novo (n = 149) and restenosis (n = 121) lesions with a primary endpoint of angiographic restenosis. The approach to the restenosis lesion is influenced by anecdotal characterisation as “easier” lesions, with a more benign procedural course but worse late outcome and increased restenosis rate. TASC I provides the opportunity to compare the baseline lesion characteristics, and procedural and late response to coronary intervention in the two lesion types.

Results: There was no difference in the baseline minimal lumen diameter (MLD), mean ± SD (0.73 ± 0.29 mm vs 0.75 ± 0.35 mm) or % stenosis (76 % ± 9% vs 74 ± 11%) between the de novo and restenosis groups. The reference vessel size was larger in the de novo as compared to the restenosis group (3.06 ± 0.45 mm vs 2.88 ± 0.47 mm, p = 0.001) and the lesion shorter (9.32 ± 2.9 mm vs 10.63 ± 3.6 mm, p = 0.002). DeNovo lesions were treated with slightly smaller balloons, Balloonee-airy Ratio (0.90 ± 0.02 vs 0.94 ± 0.01, p = 0.04), resulting in no difference in dissection (22% vs 29%, p = 0.15), immediate gain (14.6 ± 0.51 mm vs 13.5 ± 0.51 mm, p = 0.07), or late loss (0.61 ± 0.62 mm vs 0.55 ± 0.64 mm, p = 0.5). Despite increased lesion length, restenosis lesions had similar restenosis (> 50%) rates as de novo lesions, both after PTCA (45% vs 49%) and after stenting (34% vs 29%).

Conclusions: Restenosis lesions tend to be longer, in smaller vessels, and treated with larger balloons. The result is associated with no difference in dissection rates and other procedural complications or in long-term MLD as compared to de novo lesions. The benefit of stenting over PTCA in restenosis lesions is equivalent to that in the de novo lesions.

(230) MODERATED POSTER

EARLY RESULTS OF THE WEST EUROPEAN STENT TRIAL USING THE ACS MULTILINK STENT
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The WEST European stent trial was a multicentre trial undertaken in 7 centres in 5 countries to assess the efficacy and safety of the ACS Multilink® stent. This balloon expandable, tubular, stainless steel stent was inserted in 102 pts with stable angina undergoing elective stent placement in a de novo lesion in a single 3.0 - 3.5 mm diameter coronary artery. In the study group, mean age was 61 ± 8 yrs, 81% were male. Angina Class CCS 1 3.5%, II 39%, III 48%, IV 10%. Previous AMI 33%, CABG 2%, PTCA 4%. Stents were inserted into the LAD 56%, RCA 33% and LCX 11%. Patients were treated with "Classic" antiplatelet medication (pre-procedure: aspirin, dextran, heparin, post-procedure: aspirin, dipyridamole and warfarin).

By quantitative coronary arteriography (QCA) in the core lab, the reference diameter of the vessel segment was 3.02 ± 0.42 mm (pre-procedure), 3.25 ± 0.36 mm (post-procedure), MLD 1.08 ± 0.32 mm (pre), 2.67 ± 0.32 mm (post), diameter stenosis 64 ± 10% (pre), 17 ± 6% (post). At 30 day follow-up, there were no deaths, AMI 3% (Q-wave 2%, non-Q 1%), CABG 2%, re-PTCA 1%. Sub-acute stent thrombosis was documented in 2%. Thus 94% had an event free procedural success (using a ranking scale). Bleeding complications occurred in 5.9%. In hospital stay was 6 ± 4 days. Conclusion:

1. The ACS Multilink® stent is a safe and effective device.
2. The incidence of major adverse cardiac events was low and compared favourably with other stents analysed prospectively using the same protocol (REBEN). 3. Despite the use of "Classic" antiplatelet medication, the incidence of major bleeding complications was low.

(231) MODERATED POSTER

CORONARY STENTING WITHOUT ANTICOAGULATION OR INTRAVASCULAR ULTRASOUND: A RETROSPECTIVE ANALYSIS
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Objective: To assess the effect of ticlopidine and aspirin as compared with conventional anticoagulation following coronary stenting.

Background: Intense anticoagulation following coronary stent implantation is associated with a high incidence of bleeding complications. Stent deployment with high pressure balloon inflation may prevent sub-acute stent thrombosis and obviate the need for intense anticoagulation. Ticlopidine, when used in combination with aspirin, may be of benefit.

Patients and methods: June 1993 - May 1995, Group W: 97 patients with 123 stents treated with heparin, aspirin, and warfarin post stent insertion. From June 1995, Group T: 62 patients with 77 stents received ticlopidine (500 mg day) for 2 - 4 weeks and long term aspirin (150 mg day). All stents were at least 3.0 mm diameter. Stenting was performed electively in 45.5% W vs 44.4% T, for sub-optimal result in 43.0% W vs 45.4% T, and bailout in 10.6% W vs 5.24% T. Palmaz-Schatz stents were used in 88.64% W vs 80.8% T, Wiktor 1.51 W vs 29.88% T and AVE 2.48% W vs 18% T. Patients with residual thrombus also received low molecular weight heparin for two weeks. All patients were assessed clinically at 6 weeks.

Results: Subacute thrombosis rate was greater in W than with T: 4.17 vs 1.66 (p = 0.08). Higher rate of access site complications in W compared with T: 17.5 v 2.9% (p <0.001). In-patient stay (median (SD) was longer in W (3.87 ± 2.56) days vs 2.00 ± 0.001 days. Reasons and skin rashes were common in the Ticlopidine group.

Conclusion: These data suggest that coronary stenting can be performed safely with adjunctive aspirin and ticlopidine obviating the need for antiocoagulation or intravascular ultrasonography. Access site complications are minimal and in-patient stay is more than halved.

(232) MODERATED POSTER

EARLY EXPERIENCE WITH MINIMAL INVASIVE CORONARY ARTERY BY PASS GRADING
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Between 1st July and 1st November 1995, 14 patients underwent minimally invasive coronary artery bypass grafting (CABG) without the use of cardiopulmonary bypass and utilising either one or two internal mammary arteries. The technique involves making a small incision in the right thoracic wall, followed by direct access to the left mammary artery through the intercosal spaces to the mammary artery over at least three intercostal spaces with direct access to the coronary artery. The mobilised internal mammary artery is anastomosed to the coronary artery by direct open suture whilst the heart continues to beat at normal body temperature without extracorporeal support. The left internal mammary artery (LIMA) was anastomosed in the left anterior descending artery in 13 patients and the right internal mammary to the right coronary artery in 3 patients. All patients had bilateral grafts using bilateral anterior thoracoscies. In no patient was the sternum divided and no patient went on cardiopulmonary bypass, although 2 patients had femoral artery and vein cannulation electively, and 6 had elective access of these vessels. All patients survived. All had early angiography by DSA; one also had a femoral angigram. 17/18 grafts were patent with good run off. One (to an occluded right) was open but had no obvious run off, however angina was completely relieved. All 14 patients were asymptomatic on discharge. Complications included haemorrhage following peroperative heparin and aspirin (1) renal failure, of no apparent cause, and not requiring dialysis/infusion (1); superficial wound infection (1) and delayed discharge for social reasons (2). There were no cardiac arrhythmias during or after surgery, although greater than 3 mm elevation of ECG was not uncommon. Graft patency occurred in two patients (10.5 mm, and 4.0 mm- intermittently). Mobilisation following this operation appeared quicker than for standard sternotomy CABG, with patients doing the stairs in 3 days and ready for discharge at day four. Actual discharge day was prolonged by 1 to 4 days for need of elective post-operative angiography. Indications for this surgical approach were patients with symptomatic proximal one or two (LAD & RI) vessel disease, who had had previous angioplasty (PTCA) (1), or declined PTCA (4), or were unable for PTCA for because of occlusion or complexity of the lesion (2). BEN was used as an emergency following CABG. PTCA occlusion/diabetes/restenos (4) or as a phased procedure with potential corollaries PTCA (1) or with severe aortic disease unable to complicate standard CABG (1). Follow up of patients is continuing long term, the need for further studies comparing this technique to conventional IMA grafting and to PTCA is sought.
PROGRESSIVE RECOVERY OF TISSUE PERFUSION FOLLOWING CORONARY ARTERY BYPASS GRAFTING: EVIDENCE OF "MICROVASCULAR STUMMING" IN MAN

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Previous studies demonstrated a delay in the recovery of resistive vessel function following coronary angioplasty. This improvement occurred between seven days to three months. To investigate this phenomenon further, we studied 7 patients who had coronary artery bypass grafting (CABG) utilising the left internal mammary artery, gastroepiploic artery and saphenous vein grafts in all patients. The operations were carried out by the same surgeons. Regional myocardial blood flow (MBF, mL/min/g) at baseline and following iv diprydiamole infusion (Dip, 0.56 mg/kg over 4 minutes), was measured with H-15O and dynamic positron emission tomography before, 1 month and 6 months after CABG. Baseline MBF was corrected (c) for the rate pressure product (RPP) using the following formula: cMBF = MBF × RPP1/4.

<table>
<thead>
<tr>
<th>Test</th>
<th>Baseline</th>
<th>1 month post</th>
<th>6 months post</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-CABG</td>
<td>1.120.3</td>
<td>1.720.6</td>
<td>2.240.3**</td>
</tr>
<tr>
<td>MBF dip</td>
<td>1.420.3</td>
<td>2.020.5</td>
<td>2.330.6*</td>
</tr>
</tbody>
</table>

* = p<0.05 and ** = p<0.005 vs pre-CABG.

In conclusion: Our study shows that following CABG there is a progressive recovery of CVR over a six month period. Our data are in agreement with previous animal studies demonstrating a prolonged impairment of coronary vasodilator responsiveness following transient ischaemia and lend support to the concept of "microvascular stunning" in man.

COMBINED CAROTID AND CORONARY REVASCULARISATION

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From January 1st 1989 to October 31st 1995, 45 patients underwent coronary artery bypass grafting where carotid endarterectomy was performed immediately pre-stenotomy by surgeons from the local vascular service. All patients had clinical symptoms or signs of carotid disease and duplex scanning confirmed carotid stenosis >70%. Age and sex distribution of patients and post-operative morbidity (myocardial infarction and permanent stroke) and mortality were recorded. Results were compared with 350 patients undergoing carotid endarterectomy (CE) alone and 4335 patients undergoing coronary artery bypass grafting (CABG) alone during this same period. The data is shown in the following table:

<table>
<thead>
<tr>
<th>CABG + CE</th>
<th>CABG</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>47</td>
</tr>
<tr>
<td>male</td>
<td>63.8%</td>
</tr>
<tr>
<td>mean age (years)</td>
<td>63.4</td>
</tr>
<tr>
<td>mean age (female)</td>
<td>67.2</td>
</tr>
<tr>
<td>myocardial infarction</td>
<td>0%</td>
</tr>
<tr>
<td>post-op stroke</td>
<td>24.4%</td>
</tr>
<tr>
<td>death</td>
<td>12.2%</td>
</tr>
</tbody>
</table>

Combined carotid and coronary artery surgery does not result in a significantly greater morbidity and mortality in comparison with carotid or coronary revascularisation performed separately.

GRADIENT REDUCTION FOLLOWING NON-SURGICAL SEPTAL REDUCTION IN HYPERTROPHIC OBSTRUCTIVE CARDIOMYOPATHY IS MAINTAINED OVER THREE MONTH FOLLOW-UP

CJ Knight, M Gunning, M Henein, R Vecht, R Sutton, DG Gibson, J Somerville, U Sigwart. Royal Brompton Hospital, London.

Nine patients with symptomatic hypertrophic obstructive cardiomyopathy (HOCM) have now been treated by non-surgical septal reduction, which induces localized septal infarction by selective intra-coronary alcohol injection. We have compared the immediate haemodynamic effects with follow-up echocardiography to assess the medium term results of the procedure.

Immediate Results: The patients (age 14–79), (6 female, 3 male) with severe HOCM had a mean resting left ventricular outflow gradient of 53 (10–100) mm Hg on baseline echocardiography. At catheterisation, the mean resting gradient was 48 (10–101) mm Hg, rising to a mean maximal gradient of 127 (62–189) mm Hg on provocation (isotropes, pacing, PVC’s). Following the procedure the mean resting gradient was reduced to 5 mm Hg (0–35) and the mean gradient on provocation fell to 26 (0–90) mm Hg. On echocardiography the follow-up period showed sustained reduction in gradient.

Follow-up: There were no significant side-effects, all patients experienced transient chest discomfort, and one transient AV block. A patient developed ventricular fibrillation secondary to bradycardia on femoral sheath removal; this responded to DC cardioversion and there were no sequelae.

Conclusion: This early series, non-surgical septal reduction produced an immediate haemodynamic improvement, which is maintained over the medium term. The procedure may provide an alternative to surgery in symptomatic patients with HOCM.
OUTCOME AFTER TRANSCATHETER VALVOTOMY FOR PULMONARY VALVAR ATRESIA AND INSECTUM IN NEONATES

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Pulmonary valve atresia with intact ventricular septum (PA-IVS) remains a difficult problem in neonates. Transcatheter pulmonary valvotomy is a recent and promising development. Laser or radiofrequency valvotomy was attempted in 11 neonates with PA-IVS. The valve was successfully perforated in 9 patients allowing balloon dilation. Six of these 9 patients have survived. Tricuspid valve (TV) annulus dimensions were measured echocardiographically in these patients using the standard 4-chamber view. Z-scores were used to standardise TV dimensions with body surface area (BSA).

In the 9 patients in whom valvotomy was achieved, initial TV dimensions are expressed as mean (range):

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Alive (n=6)</th>
<th>Deceased (n=3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TV annulus (mm)</td>
<td>6.5 (8.0-12)</td>
<td>8.6 (8.0-10)</td>
</tr>
<tr>
<td>TV/BSA ratio</td>
<td>0.49 (0.41 to 0.57)</td>
<td>0.405 (0.37 to 0.44)</td>
</tr>
<tr>
<td>Z-score TV</td>
<td>-0.78 (-0.4 to -1.3)</td>
<td>-1.2 (-0.9 to -1.5)</td>
</tr>
</tbody>
</table>

In 5 of the survivors, follow-up ranges from 37 to 63 months. Their initial and latest measurements are expressed as mean (range):

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Before valvotomy</th>
<th>Latest follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td>TV annulus (mm)</td>
<td>9.8 (8.0-12)</td>
<td>20.6 (18.0-25)</td>
</tr>
<tr>
<td>Z-score TV</td>
<td>-0.68 (-0.4 to -1.0)</td>
<td>-1.86 (-0.8 to -3.0)</td>
</tr>
<tr>
<td>TV/MV ratio</td>
<td>0.63 (0.56 to 0.80)</td>
<td>0.88 (0.76 to 1.0)</td>
</tr>
</tbody>
</table>

The surviving patients tended to have larger initial TV dimensions than the deceased patients, even after correction for BSA. After successful valvotomy, the TV does grow, although slower than in normal hearts as shown by the Z-scores. The TV/MV ratio seems to improve also.

Transcatheter pulmonary valvotomy in neonates with PA-IVS allows growth of the RV as expressed by absolute TV annulus growth but RV growth does not occur at normal rate. It remains a good alternative to surgery.

UNIVENTRICULAR HEART WITH SYSTEMIC OUTFLOW OBSTRUCTION: THE PRIMARY DAMUS PROCEDURE AS AN ALTERNATIVE TO PULMONARY BANDING.

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In infants with a univentricular atrioventricular connection (UV) and systemic outflow obstruction (SOO), pulmonary artery banding (PAB) is suboptimal, as it exacerbates or accelerates SOO. 24 consecutive infants (18M, 6F) with UV+SOO who would have been candidates for PAB were entered into a protocol for a primary modified Damus operation (direct anastomosis of ascending aorta/ arch and descending aorta to proximal pulmonary trunk without patch augmentation, resection of ductal tissue and insertion of 3.5 mm arterial shunt). Median age at operation was 6.5 days, and weight 3.6 kg. There were 5 early deaths (<30 days after surgery), all among the first 7 patients undergoing surgery. Two of them (both >75 days old) had grade 3-4 pulmonary vascular disease at postmortem. Univariate analysis of morphologic, demographic, clinical and operative variables revealed chronicologic rank of the individual surgical procedure (the "learning curve") as the only significant risk factor for death. At serial echo- and angiography, no survivor has >grade 1 semilunar or atrioventricular valve regurgitation; left ventricular end-diastolic pressure was <10mm Hg in all pts. Three patients have had completion of Fontan, 12 a superior cavo-pulmonary shunt (median age of 4 months), 1 patient a biventricular repair, and 3 are awaiting a cavo-pulmonary shunt.

The modified Damus and early cavo-pulmonary shunt provide early relief of pressure and volume load of the systemic ventricle, and should provide a better long-term outcome. Early survival is comparable to a primary PAB protocol.
THE ROLE OF \(^{18}F\)-FDG SPET IN DETECTION OF HIBERNATING MYOCARDIUM: COMPARISON WITH REST-REDISTRIBUTION \(^{203}Tl\) SPET

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Several protocols have been described for the detection of hibernating myocardium when selecting patients for coronary revascularisation. Positron emission tomography (PET) with \(^{18}F\)-Fluorodeoxyglucose (FDG) is useful but this technique is restricted to a few centres only. It has recently become possible to modify the majority of dual headed gamma cameras to allow the use of high energy collimators and imaging of \(^{18}F\)-FDG using single photon emission tomography (SPET). The aim of this study was to evaluate the role of \(^{18}F\)-FDG SPET in the detection of viable hibernating myocardium. We studied 22 patients (20 male, 2 female, mean age 57, range 44 - 71 years) with dyspnoea from coronary artery disease (left ventricular ejection fraction < 40%, range 14% to 39%) and fixed perfusion defects under consideration for coronary revascularisation. All patients underwent rest (20 minutes after injection) - redistribution (3-4 hours after injection) \(^{203}Tl\) (TI) SPET and \(^{18}F\)-FDG SPET. \(^{18}F\)-FDG images were acquired one hour after injection using a General Electric Maxxus camera equipped with high energy collimators. Uptake of \(^{203}Tl\) and \(^{18}F\)-FDG was compared within nine myocardial segments per patient. All 22 patients had fixed perfusion defects \(^{203}Tl\) uptake 50% maximum). There were 2 - 6 myocardial segments per patient and a total of 50 myocardial segments with fixed perfusion defects. In six of 22 patients there was \(^{18}F\)-FDG uptake (> 50% maximum) within \(^{203}Tl\) perfusion defects: this was seen within a total of 15 myocardial segments and at least 2 myocardial segments per patient. Four of 6 patients with \(^{18}F\)-FDG uptake within fixed \(^{203}Tl\) perfusion defects have been successfully revascularised. 14/16 (88%) of patients without \(^{18}F\)-FDG uptake within fixed \(^{203}Tl\) defects have been managed medically. SPET imaging of \(^{18}F\)-FDG is feasible within many Nuclear Medicine Departments and can help in the detection of hibernating myocardium. It has the potential to assist in the appropriate selection of patients for coronary revascularisation.

IDENTIFICATION OF HIBERNATING MYOCARDIUM: A COMPARISON OF TI-201, TC-99m TETROFOSMIN, AND DOBUTAMINE CINE MAGNETIC RESONANCE IMAGING

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This study compared the use of TI-201 and TC-99m tetrofosmin SPECT and dobutamine cine magnetic resonance imaging (MRI) in identifying myocardial hibernation in patients with markedly impaired left ventricular (LV) function. Methods 17 patients underwent rest and dobutamine stress (5μg/kg/min) MRI, stress/redistribution and separate day early/late rest TI-201 SPECT, and stress/rest TC-99m tetrofosmin SPECT prior to coronary bypass surgery. Resting MRI was repeated post operatively. Analysis of tracer uptake and regional contractility was conducted using a 9 segment model of the LV. Tracer uptake was scored using a 5 (normal) point scale, motion using a point scale (0 = no motion) and thickening using a point scale (0 = nil). Segments with a wall motion score of ≤ 2, coupled with either tracer uptake of ≥ 2, rest-redistribution on TI-201 SPECT, or evidence of contractile reserve on stress MRI, were pre-operatively assigned as hibernating. Results 110 of a total 153 segments were scored ≤ 2 for wall motion; 59 improved function following surgery. The effects of coronary artery bypass grafting (CABG) on exercise capacity in patients with ischaemic cardiomyopathy and viable myocardium are not well characterised. In the present study we aimed to assess the effects of revascularisation on maximum oxygen consumption (peak VO₂) (modified Naughton protocol) and resting LVEF (MUGA) in 14 patients (12 male; mean age 54 years) with poor left ventricular ejection fraction (LVEF) (mean 24.9±7.9%) and viable dysfunctional myocardium, 4 to 6 months after CABG. All patients had predominant symptoms of heart failure and myocardial viability was assessed by quantitative regional \(^{123}I\) Fluorodeoxy-glucose (FDG) uptake during hyperpolarised euglycaemic clamp using positron emission tomography. NYHA functional class improved in all patients (IV to I in 2, II to I in 8, and III to II in 4). Although heart rate at maximal exercise remained unchanged (129±23 bpm versus 137±18 bpm; p = 0.2), peak VO₂, improved from 14.9±4.5 to 20.9±5.4 ml/kg/min (p < 0.01) and exercise time from 444±241 to 649±260 seconds (p = 0.01). Resting LVEF improved to 33.1±10% (p < 0.01 versus baseline). There was no correlation between LVEF values and absolute values of peak VO₂ before (r = 0.02; p = 0.9) and after surgery (r = 0.49; p = 0.07). No correlation was observed between the changes in absolute values of peak VO₂ and LVEF from the preoperative to the postoperative period (r = 0.33; p = 0.23). In patients with ischaemic cardiomyopathy and viable dysfunctional myocardium coronary artery revascularisation improves clinical status, exercise capacity and resting LVEF. These changes may constitute the basis for a possible improvement in prognosis.
PTCA IN ALLOGRAFT CORONARY DISEASE - IS IT WORTHWHILE?
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Allograft coronary artery disease is the most important threat to long term cardiac transplant survival. The prevalence increases with time, and treatment is difficult and unsatisfactory. At Harefield we consider PTCA for all severe discrete lesions (>80% stenosis) detected on surveillance angiography. Between 1987 and 1995, 45 transplant patients (40 orthotopic; 4 heterotopic; 1 heart-lung) have undergone 64 separate procedures to 100 lesions (53 LAD; 29 CX; 18 RCA), 84 de novo and 16 restenotic. The mean time from transplant to initial PTCA was 69±37 months (range 14-147). Standard techniques were used. Mean balloon size 2.7±0.4 mm; mean peak pressure 7.7±2.3 bar. 3 Palmar-Schatz stents have been deployed.

Procedural success was achieved in 93% (3 failures were in heterotopic hearts, due to difficulty with guide catheter support, and 3 were occluded vessels). 2 patients required DC shock for VF. There were no procedural deaths. Early follow-up angiography (mean 10±5 months) of successfully dilated lesions revealed 96% vessels were patent (48/53 lesions) with 37% showing restenosis. Late (≥1 year; mean 39±22 months) patency was 76% (35/46 lesions) and 39% lesions had a residual stenosis ≥50%.

33 (73.3%) patients are alive with a mean follow up of 35±28 months (range 0-100) after their first PTCA, whereas 12 died at a mean interval of 29±21 months (range 0-59). Actual survival was 89.7%, 84.8% and 77.8%, 1.2, and 3 years after the initial PTCA.

A subset of 19 patients had LV ejection fractions (EF) determined by MUGA scans before and within <1 year) after their initial PTCA. LVEF improved, at least initially, after PTCA (56±11 vs 66±11, pre and post respectively; p<0.01).

In conclusion 1) PTCA of allograft coronary arteries has similar initial success and restenosis rates to native vessels; 2) successful PTCA may improve allograft LV function; 3) the effect of PTCA on prognosis is unknown and requires further study.

IN-VITRO PREPARATION, CHARACTERISATION AND ANTITHROMBOGENICITY OF PLATELET-TARGETED UROKINASE IMMOBILISED TO POLYMER COATED STENT WIRE
RK Aggarwal, DC Ireland, DP de Bono, AH Gerachsh. Division of Cardiology, University of Leicester.

An appropriately targeted fibrinolytic agent eluting from intravascular stents may enhance thromboreversibility, obviating the need for systemic anticoagulation. We targeted 125I-labeled urokinase (UK) to platelets by chemically conjugating it, after reduction with dithiothreitol, to rabbit anti platelet glycoprotein (GP) IIb/IIIa antibody (AZI) (modified by reacting with N-Succinimidyl 3-[2-pyridyldithio]propionate). The resulting conjugate (AZI1-UK) was purified and characterised by polyacrylamide gel electrophoresis and autoradiography prior to immobilisation (by passive adsorption) to stainless steel wire coated with a hydrophobic cellulose polymer (Cook Inc.). Its antithrombotic activity was assessed by i) ex-vivo platelet aggregometry using ADP (20 μM) and collagen (4 μg/mL) and ii) perfusing wire segments (n=6 for each group) bound with no drugs (Gr A), AZI alone (Gr B), UK alone (Gr C), AZI1-UK (Gr D) and UK conjugated to antibody of irrelevant specificity (CMV-UK) (Gr E) with 1100μg labelled rabbit platelets.

Results: AZI1-UK had significantly enhanced platelet antiaggregatory effects compared with AZI alone.

PALM AZ SCHATZ STENT DEPLOYMENT WITHOUT INTRAVASCULAR ULTRASOUND GUIDANCE USING ANTIPILATEL ARTERY-LUGINGG GEL WITHOUT ASPIRIN ALONE
H C Lowe, P Roy, B W Walker, D W Baron, T P Gavaghan, J J Morgan, St Vincent's Hospital, Darlinghurst, Sydney, Australia

Two current areas of debate in stent deployment are the need for routine intravascular ultrasound, and the optimal antplatelet therapy required. 100 selected patients with 103 lesions were treated with 117 Palmaz Schatz intracoronary stents over 9 months. Intravascular ultrasound was not performed, and patients received aspirin 300mg bd alone. Post procedure, aspirin alone was used if there was absence of significant proximal or distal disease, thrombus, or coronary ectasia, and if the stented segment could be oversized in relation to the reference vessel, with complete apposition of the stent within the lumen. (Over this period 56 patients did not fulfill these criteria and were antiagregated.) The mean age of the study group was 60 (±11) years. 85 were male. Indications for stent deployment were: elective (44%), dissection (12), acute or threatened closure (4), and suboptimal result (43). Stented vessels were Left Anterior Descending=33, Circumflex=15, Right Coronary=34, Vein Grafts=21. Lesions were AHA/ACC type A=48, B1=22, B2=7, C=26. Reference vessel diameter=3.0 (±0.5) mm, largest balloon size=3.0±0.4 mm, maximum inflation pressure=14.0±3.7 atmpheres. Angiographic followup was in 94 patients with 97 lesions with 110 stents at 84 (±74) days. 6 asymptomatic patients declined angiography. There were 2 stent thromboses at 3 and 30 days. 3 stents were required for optimal results. The remaining stents were patent requiring no further intervention. Clinical followup was achieved in all patients at 140 (±81) days. 3 patients underwent hospitalisation because of lesion progression elsewhere, 1 procedure resulting in death. Of the remainder, 181 were asymptomatic, 18 had class I and 2 had class IIa angina. In those patients with simple lesions and low risk stent indications, there was good clinical and angiographic outcome and a low incidence of stent thrombosis. This was achieved without intravascular ultrasound, and using aspirin alone.

PROGNOSTIC SIGNIFICANCE OF CK-MB ELEVATION FOLLOWING ABILATIVE NEW-DEVICE ANGIOPLASTY IN NATIVE CORONARY ARTERIES
SR Redwood, JJ Popma, KM Kent, AD Pichard, LF Satler, GS Mintz, MK Hong, CE Clark, TA Bucher, AJ Lansky, DD Purkayastha, MB Leon. Washington Hospital Center, Washington, DC, USA.

To determine the impact of peri-procedural CK-MB elevations (minor: >1 and ≤5× NML [5-16ng/ml]; major: >4× NML [≥17ng/ml]) on in-hospital major complications (MC=death, Q-wave MI or CABG), procedural success (<50% residual stenosis without MC), and late clinical events, we examined the course of 2201 pts (follow-up time 153±46 days) undergoing new device angioplasty (NDA) of native coronaries treated by directional atherectomy (DCA, n=710), rotational atherectomy (RA, n=899) or excimer laser angioplasty (ELCA, n=592) between 1/90 and 2/94. Overall, 24% of pts had minor and 12% had major CK-MB elevations (p<0.05 vs Normal)

CK-MB Level
Nml (n=1408) Minor (n=526) Major (n=267)
Proc: Success (%) 94.2 93.5 69.3
In-Hospital MC 1.1 3.0* 25.8*
Late Death 1.3 3.9* 6.6*
Late QWMI 0.9 1.9 1.8
Late CABG 9.7 11.6 9.6
Late PTCA 18.2 19.0 16.8

Importantly, for each of the ablative angioplasty modalities, after minor CK-MB rises, late mortality was similarly increased (DCA 3.8%, RA 3.6%, ELCA 4.6%). By multivariate analysis, CK-MB elevation (both minor and major) and LVEF were independent predictors of late mortality. We conclude that: Minor CK-MB rises after all ablative (NDA) procedures in native coronaries (1) are frequently present (24% of pts), (2) are independently predictive of an increase in late cardiac mortality, and (3) do not predict other late clinical events (QWMI or PTCA/CABG). The mechanisms of late mortality after minor peri-procedural CK-MB rises remain obscure and warrant further study.
(249) THE PROGNOSTIC SIGNIFICANCE OF LIPOPROTEIN(a) CONCENTRATIONS FOLLOWING MYOCARDIAL INFARCTION. F. Stubbs, P. Collinson, F. Kendall, M. Noble, M. Seed, Academic Unit of Cardiovascular Medicine, Dept of Medicine, Charing Cross and Westminster Medical School, Dept of Chemical Pathology, Mayday University Hospital, London, UK.

Lipoprotein(a) (Lp(a)) concentrations above 30mg/dl are considered to be an independent risk factor for coronary disease. The prognostic significance of Lp(a) concentrations in patients admitted with myocardial infarction (MI) remains to be established. Methods. This was a single centre prospective blinded study. Patients with a final diagnosis of myocardial infarction according to WHO criteria were studied and followed for cardiac events. Full clinical details were recorded on all patients by proforma. Samples for Lp(a) concentrations were taken on admission and measured in batches, in duplicate, by Biopool ELISA (Porto). Within run CV 3.2%, between run CV 6% by a single operator blinded to the clinical data. Non parametric statistical tests were used for all analyses. Results. 266 patients (77% male, mean age 62 years, 27% hypertension, 17.5% previous MI, 15% diabetic) were studied and followed for a median of 965 days (lower quartile 813 days, upper quartile 1238 days), 21.4 (57/266) of the patients have died. Median admission Lp(a) was 12.6 mg/dl (103). 33.7% (77/266) of patients had admission Lp(a) concentrations >30mg/dl. And this group had a significantly higher cardiac mortality than patients with Lp(a) concentrations <30mg/dl (29.8%/20.6%) versus 18.6% (37/199) respectively p = 0.05. In a univariate analysis, four other variables were significant predictors of cardiac mortality; age, previous MI, infract size and hypertension. In a Cox multiple regression analysis of these five variables, Lp(a) concentrations >30mg/dl remained significant as an independent predictor of cardiac mortality. Chi-square 4.35, p=0.037. Relative Risk 2.16, 95% CI 1.05-4.46. Conclusion. We believe that this is the first study to demonstrate that Lp(a) concentrations are an independent risk factor for cardiac death on long term follow up in patients admitted with myocardial infarction.

(250) COST-EFFICACY OF CHOLESTEROL LOWERING: WEST OF SCOTLAND CORONARY PREVENTION STUDY VERSUS THE SCANDINAVIAN SIMVASTATIN SURVIVAL STUDY IG Mallik, MH Anderson Division of Cardiology, Hammersmith Hospital, London

To compare the cost-efficacy of primary versus secondary prevention of coronary artery disease using lipid-lowering drug therapy we compared the treatment strategies of the West of Scotland Coronary Prevention Study (WOSCOPS) and the Scandinavian Simvastatin Survival Study (4S). Both studies demonstrated improved total survival, a reduction in revascularisation procedures (RV) and reduced incidence of myocardial infarction (MI). The cost-efficacy of the two studies has been modelled to examine the net cost per year of life gained (£LY) for allowing for reduced MI and RV over the basic study period (6-years), and extrapolated over 10 years assuming continued divergence in survival with lipid-lowering therapy (10yr+) or parallel survival with lipid-lowering therapy (10yr-).

WOSCOPS 4S

<table>
<thead>
<tr>
<th></th>
<th>Primary prevention</th>
<th>Secondary Prevention</th>
</tr>
</thead>
<tbody>
<tr>
<td>£LY</td>
<td>£LY</td>
<td>£LY</td>
</tr>
<tr>
<td>6-years</td>
<td>119,600</td>
<td>30,600</td>
</tr>
<tr>
<td>10yr +</td>
<td>68,800</td>
<td>16,900</td>
</tr>
<tr>
<td>10yr -</td>
<td>85,500</td>
<td>21,500</td>
</tr>
</tbody>
</table>

The primary prevention strategy of WOSCOPS costs about four times as much per life-year gained when compared with the strategy of 4S, whatever assumptions are made about future survival. Whilst the cost-efficacy of secondary prevention of coronary disease with lipid-lowering agents lies well within the range of other accepted cardiovascular therapies primary prevention remains relatively expensive.

(251) MODERATED POSTER

MECHANISMS OF IMPAIRED VASCULAR REACTIVITY IN INSULIN DEPENDENT DIABETES MELLITUS AND HYPERCHOLESTEROLAEMIA

SA Thorne, P. Clarkson, R. Henry, AE Donald, H Thomson, AJ Powe, T Bull, JE Deafield

Vascular Physiology Unit. Hospital for Sick Children, Great Ormond Street, London WC1N 3JE

Endothelial dysfunction is an early event in atherogenesis, and we have previously shown impaired endothelium dependent (flow mediated) dilation (FMD) in healthy young adults with cardiovascular risk factors including hypercholesterolaemia (HC) and insulin dependent diabetes mellitus (IDDM). Aim. This study investigated the underlying mechanisms by intervention with intravenous L-arginine, the precursor to nitric oxide. Methods. We used high resolution vascular ultrasound to study vascular reactivity in 9 each of asymptomatic IDDM, HC and control subjects (mean age 30, range 23-40 years, mean LDL-cholesterol 2.97±0.6, 4.76±0.75, 2.52±0.62mmol/l). None were smokers, or had other vascular risk factors. A standard 7MHz linear array transducer and Acuson 128XP/10 system was used to study the brachial artery at rest, and in response to reactive hyperaemia (FMD) and to sublingual glyceryl trinitrate (GTN/endothelium independent dilation). Each assessment was made before and after infusion of L-arginine (0.1g/kg body weight) and the effect compared with 0.9% saline infusion. Results. Baseline FMD was impaired in both the IDDM and HC groups compared to the controls (p<0.001) and the response to GTN was impaired in the IDDM subjects (p<0.04). FMD improved significantly (from 100 91±1.3 to 103 94±1.7%; p=0.017) after L-arginine infusion in the HC group, but was unchanged in the IDDM and control subjects. Neither L-arginine or placebo induced any other effects in any of the groups. Conclusion. Impaired vascular function appears to be confined to the endothelium in HC, being reversed by L-arginine, but in young adults with IDDM, there is an additional component, reflected by the non-response to GTN and L-arginine. These findings suggest the pathophysiology of impaired vascular reactivity, which may underlie the development of atherosclerosis, is different in HC and in IDDM.

(252) MODERATED POSTER

ENDOTHELIAL FUNCTION OF THE BRACHIAL ARTERY IS NOT IMPAIRED IN PATIENTS WITH SYNDROME X

JB Ball, TN Bloomer, GJ Williams Non-invasive Heart Unit, Edinburgh Royal Infirmary, Edinburgh

Endothelium-dependent arterial vasomotor function in the coronary circulation is abnormal in patients with reversible myocardial ischaemia but angiographically normal coronary arteries. This condition is referred to as syndrome X. We studied the endothelium-dependent vasomotor function in the forearm circulation of patients with this condition. We studied 39 consecutive patients undergoing coronary angiography for investigation of chest pain. Twenty-two had angina, positive exercise tolerance test and/or Myoview SPECT exercise perfusion scan, and angiographically normal coronary arteries. Seventeen patients were controls having atypical chest pain, negative exercise tolerance test and/or Myoview SPECT exercise perfusion scan, and angiographically normal coronary arteries. Patients with hypertension or diabetes mellitus were excluded. High resolution ultrasound (4 MHz linear array transducer) was used to measure brachial artery diameter at baseline and during contralateral hand immersion in ice water (cold pressor test), following 4 minutes of ischaemic forearm vascular occlusion with a blood pressure cuff inflated to 250mmHg (flow-mediated vasodilatation) and 6 minutes after sublingual administration of 800mcg glyceryl trinitrate (GTN). The first and second are tests of endothelium-dependent function and the third of endothelium-independent function. Brachial artery diameter change (% ±SD) was calculated.

<table>
<thead>
<tr>
<th>Syndrome X (n=22)</th>
<th>Controls (n=17)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cold Pressor</td>
<td>1.7(1.5)</td>
<td>1.2(1.5)</td>
</tr>
<tr>
<td>Flow-mediated</td>
<td>4.0(5.5)</td>
<td>2.3(5.4)</td>
</tr>
<tr>
<td>GTN</td>
<td>15.9(16.6)</td>
<td>16.2(5.4)</td>
</tr>
</tbody>
</table>

No significant difference was shown providing evidence that patients with syndrome X do not have an abnormality of arterial endothelial function in the forearm circulation.
(253) MODERATED POSTER

LOCALISED ENDOTHELIAL DYSFUNCTION IN PATIENTS WITH CHEST PAIN AND NORMAL CORONARY ARTERIOGRAMS
D Tououlis, C Davie, D C Lefroy, S Rosen, AW Haider, T Crake
Cardiology Unit, Hammersmith Hospital and St Bartholomew's Hospital, London

It is known that acetylcholine (endothelium dependent vasodilator) causes dilatation of coronary arteries in patients with angiographically normal coronary arteries. Quantitative angiography was used to measure minimum lumen diameter of proximal and distal coronary artery segments at baseline, during intracoronary infusion of acetylcholine (10−7 to 10−3 M) and following a 2 mg intracoronary bolus of isosorbide dinitrate. In response to the low concentrations of acetylcholine (10−7 to 10−6 M) 20 (61%) distal and 11 (41%) proximal segments showed dilatation (group 1), whereas 13 (39%) distal segments (p=0.05) and 14 (52%) proximal segments showed constriction (group 2). In group 1, the maximum dilatation induced by acetylcholine in the proximal and distal segments was 7.8±1.1% and 11.6±2.2% respectively. In group 2, the maximum constriction at higher concentration was -16.5±3.9% and -33.1±1.6% in the proximal and distal segments respectively. The two different patterns of the vasomotor response coexisted in 8 (25%) of the 15 patients. In conclusion, in patients with chest pain and angiographically normal coronary arteries both constriction and dilatation may occur in response to a given dose of acetylcholine, in proximal and distal coronary artery segments, suggesting local areas of endothelial dysfunction. The magnitude of the vasomotor response to acetylcholine was greater in distal than in proximal segments.

(254) MODERATED POSTER

EXERCISE TRAINING ENHANCES ENDOTHELIAL FUNCTION IN YOUNG MEN
P Clarkson, H Montgomery, A Donald, A Powe, T Bull, A Dollery, JH Farington, A Donald, A Powe, T Bull, A Dollery, JH Farington
Great Ormond Street Hospital NHS Trust, †The Hatter Institute of Cardiovascular Studies, University College Hospital and the †Royal Army Medical College, London

Exercise has been shown to reduce cardiovascular morbidity and mortality but the mechanisms for this benefit are unclear. Endothelial dysfunction is an early event in atherogenesis and animal studies have shown that exercise training can enhance endothelial function. We have examined the effect of a standardised, 10 week, aerobic and anaerobic exercise training programme on arterial physiology in 23 male military recruits aged 17 to 24 (mean 20) years, with and without cardiovascular risk factors (10 moderate smokers, 5 pack years, and 15 lifelong non-smokers). Each subject was studied before starting, and after completing the exercise programme. At each visit, the diameter of the right brachial artery was measured at rest, during reactive hyperaemia (increased flow causing endothelium-dependent dilatation, EDD) and after sublingual glyceryl trinitrate (GTN, an endothelium-independent dilator), using high resolution external vascular ultrasound. Cholesterol and fibrinogen levels were also measured. After the exercise programme, endothelium-dependent dilatation improved from 2.3±2.4% to 3.9±2.5% (p<0.01), with no change in the GTN dilatation (13.4±6.3% vs 13.9±4.5% post exercise). At baseline, EDD was lower in the smokers (1.9±3.1% versus 2.5±1.1% in non-smokers, p=0.03) but there was no difference in improvement in EDD between the two groups. Changes in EDD were not related to LDL-cholesterol, HDL-cholesterol, Lp(a) or fibrinogen levels. Thus exercise training enhances endothelial function in young men of average fitness even in the presence of cardiovascular risk factors. This may contribute to the benefit of regular exercise in preventing cardiovascular disease.

(255) MODERATED POSTER

L-ARGININE REVERSES THE AGE ASSOCIATED ENDOTHELIAL DYSFUNCTION IN HUMANS
A Chauhan, RS More, PA Mullins, G Taylor, MC Petch, PM Schofield, *St Mary's Hospital, London, Papworth Hospital, Papworth Everard, Cambridge

Background: Age is a recognised risk factor for coronary disease and senescence is associated with both functional and morphological changes in the coronary vasculature. The aim of this study was to investigate the effect of age on vascular function of the human coronary circulation.

Methods and Results: We infused the endothelium-independent vasodilators papaverine and glycerol trinitrate and endothelium-dependent vasodilator acetylcholine (Ach, 1, 3, 10, and 30 μg/min) in to the left coronary artery of 34 patients (age 27-73 years) with asympatric chest pain, negative exercise test, and completely normal coronary angiograms who had no coronary risk factors. The changes in coronary blood flow (CBF) were measured with an intracoronary Doppler catheter and artery diameter was assessed using quantitative angiography. The papaverine and Ach infusions were repeated in 14 patients (27-73 years) after an intracoronary infusion of L-arginine (160 μmol/min for 20 minutes). There was a significant negative correlation between aging and the maximum diameter change evoked by Ach (r= -0.7, P<0.001), and the peak CBF response evoked by Ach (r= -0.73, P<0.001). The increase in peak CBF (%) evoked by Ach as compared to papaverine also decreased significantly with age (r= -0.7, P<0.001). However, there was no correlation between aging and the peak CBF response to papaverine (r= -0.04, P=0.82) and GTN (r= -0.24, P= 0.17). The peak CBF response evoked by Ach correlated significantly with aging before L-arginine infusion (r= -0.87, P<0.001) but this negative correlation was lost after L-arginine infusion (r= -0.37, P=0.19).

Conclusion: Aging selectively impairs endothelium-dependent coronary microvascular function and this impairment can be restored by the administration of L-arginine, a precursor of nitric oxide.

(256) MODERATED POSTER

THE HYPERTENSION AND PLATELET ACTIVATION OF PRE-ECLAMPSIA ARE REDUCED BY S-NITROSOGlutATHIONE
AJ de Belder, C Les, AS Brown, EJ Langford, S Campbell, JF Martin, Departments of Cardiology, Obstetrics and Medicine, King's College Hospital, London.

The hypertension and platelet activation of pre-eclampsia may be explained by a lack of endothelial nitric oxide (NO). To test this hypothesis, we investigated the effect on mean arterial pressure of an intravenous infusion of 50-250 micrograms of NO donor S-nitrosoglutathione (GSNO) in 10 women with severe pre-eclampsia and uteroplacental insufficiency. In addition, uterine artery resistance index and foetal blood flow were measured using Doppler. Systemic platelet activation (measured using flow cytometry to determine platelet P-selectin expression) was compared for 8 of these patients with 9 gestation-matched normal women.

Results:

<table>
<thead>
<tr>
<th>GSNO (μg/min)</th>
<th>0 (n=10)</th>
<th>50 (n=10)</th>
<th>100 (n=10)</th>
<th>250 (n=7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAP</td>
<td>87.9±2.3</td>
<td>84.6±2.5</td>
<td>81.4±2.5</td>
<td>80.6±2.7</td>
</tr>
<tr>
<td>RI</td>
<td>89.2±0.8</td>
<td>93.7±0.6</td>
<td>91.2±0.8</td>
<td>90.2±0.8</td>
</tr>
<tr>
<td>MAP: mean arterial pressure, RI: uterine artery resistance index (mean±SEM % of baseline): p&lt;0.01 for change in each vs. baseline</td>
<td></td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

There was a non-significant improvement in umbilical artery pressure index, with no deterioration in any of the foetal Doppler indices. Platelet P-selectin expression was 3.5±0.9% in pre-eclampsia compared to 1.1±0.1% in controls (p<0.001). In the pre-eclampsia patients, platelet P-selectin fell to 1.3±0.2% following infusion of 100μg/min GSNO (p<0.01). These data demonstrate effective reduction of maternal blood pressure, vascular resistance and platelet activation by doses of GSNO which have been found to cause no BP change in normal women. This fall was not accompanied by any compromise of foetal blood flow. Thus, the hypertension of pre-eclampsia is sensitive to low doses of NO donors such as GSNO, which may represent a novel treatment for this condition.
PLASMINOGEN ACTIVATOR INHIBITOR-1 (PAI-1) PROMOTER 4G/5G GENOTYPE AND LEVELS IN RELATION TO MYOCARDIAL INFARCTION IN PATIENTS UNDERGOING CORONARY ANGIOGRAPHY.

N. Osse-Geming, L. M. Mansfield, M. H. Stickland, L. W. Wilson, P. J. Grant.

Department of Cardiology, Pinderfields Hospital, Wakefield.

To investigate the relationship between an insertion/deletion (4G/5G) polymorphism in the promoter region of the plasminogen activator inhibitor-1 (PAI-1) gene and phenotypes of PAI-1 levels, the presence of coronary atheroma, and a past history of thrombosis, we studied 454 patients (320 male and 134 female) who presented for coronary angiography with chest pain. Patients were classified as having normal (n=132), single (n=93) or multi-vessel (n=233) disease on the basis of ≥50% stenosis. PAI-1 antigen levels were highest in patients with the 4G/4G genotype (22.5ng/ml), with a stepwise decrease in levels with a decrease in the number of 4G alleles (21.5ng/ml for 4G/5G and 15.8ng/ml for 5G/5G) (p=0.02, after adjusting for age, sex, triglyceride (TG) and body mass index (BMI)). The association between TG and PAI-1 was genotype specific at the 4G/4G genotype (p=0.004). In addition we found a similar gene-environment interaction between BMI, PAI-1 and genotype, with a steeper association in patients with the 5G/5G genotype (p=0.02).

The 4G/4G genotype was significantly associated with a history of myocardial infarction (p=0.03, odds ratio=1.96, 95% CI=1.1-3.7). This relationship was confined to men (p=0.007, OR=1.6, 95% CI=1.1-2.2) and was stronger in subjects with diseased vessels (p=0.004). There was no relationship between either genotype or PAI-1 levels and the extent of coronary atheroma. Our data suggest that this PAI-1 promoter polymorphism influences the development of myocardial infarction through its effect on thrombus formation in patients with pre-existing coronary atheroma.

PLASMA LEVELS OF ACTIVE TRANSFORMING GROWTH FACTOR-B ARE REDUCED IN PATIENTS WITH THREE VESSEL CORONARY ARTERY DISEASE.


Department of Cardiological Sciences, St. George's Hospital, London.

Recent evidence suggests that transforming growth factor-β (TGF-β) plays an important role in atherogenesis. Enzyme-linked immunosorbent assay was used to measure plasma levels of active (a) and acidically proteolysable latent (b) TGF-β in patients with chronic stable angina. 43 patients (age 55 ± 10 years) with normal coronaries (NC) were compared to 44 patients (age 64 ± 7 years) with three vessel disease (TVD). Active TGF-β was significantly lower in patients with TVD compared to NC (p < 0.0001).

MULTIPLE LOGISTIC REGRESSION ANALYSIS OF PLASMA ACTIVITY OF TGF-β 1 (Active TGF-β 1).

Multiple logistic regression analysis (including age, sex, previous myocardial infarction and aspirin therapy) shows that only TVD is predictive of active TGF-β (p = 0.0003 by Chi-square test). An active TGF-β < 1 ng/ml gives an estimated relative risk for TVD of 3.8 (95% CI: 2.3 - 6.3). Total (a+b) TGF-β increased with increasing dose of aspirin but did not reach significance (p = 0.097).

We conclude that in patients with chronic stable angina, plasma levels of active TGF-β are reduced in severe TVD, and that further investigations are warranted to elucidate the factors responsible for this.

CYCLICAL MECHANICAL STRAIN INDUCES PLASMINOGEN ACTIVATOR INHIBITOR-1 EXPRESSION IN HUMAN VASCULAR SMOOTH MUSCLE CELLS.


Department of Medicine (Division of Cardiology), University of Leeds School of Medicine, Leeds, UK.

Introduction: A possible cause of the increased thrombotic risk associated with hypertension is overproduction of plasminogen activator inhibitor-1 (PAI-1). Plasma PAI-1 levels are increased in hypertensive patients and we have shown that PAI-1 mRNA and protein is present in human vascular smooth muscle cells (hVSMC) in vivo. One explanation for the increase in PAI-1 levels is that the mechanical force of blood pressure augments PAI-1 production. We therefore examined the effect of cyclical mechanical strain on PAI-1 mRNA expression by hVSMC.

Methods: hVSMC were grown in 5% foetal calf serum to confluence in flexible culture plates before quiescence was achieved by culture in serum deprived media. To simulate blood pressures (BP) of 120/80, 160/100 and 200/120 mmHg, the cells were cycled stretched (60 cycles/min) to 24%, 28% and 30% of their length. The effect of frequency of stretch between 30 and 60 cycles/minute was also examined. After 3 hours of cyclical stretch, RNA was extracted and subjected to Northern blot analysis. Equilibrated cells were measured by cell counting. GAPDH mRNA and PAI-1 mRNA was identified by hybridisation against a specific anti-PARP cDNA probe.

Results: Varying the frequency of cyclical stretch between 30 and 60 cycles/minute had no effect on PAI-1 mRNA levels. However increasing the magnitude of cyclical stretch induced PAI-1 mRNA levels in a dose dependent manner as shown below:

<table>
<thead>
<tr>
<th>Simulated BP (mmHg)</th>
<th>PAI-1 mRNA Signal</th>
</tr>
</thead>
<tbody>
<tr>
<td>120/80</td>
<td>0.58</td>
</tr>
<tr>
<td>160/100</td>
<td>0.71</td>
</tr>
<tr>
<td>200/120</td>
<td>0.83</td>
</tr>
</tbody>
</table>

Conclusion: This study has identified an important effect of cyclical mechanical strain on hVSMC which could explain, at least in part, the increased plasma PAI-1 levels in hypertension with its resultant increased risk of thrombosis.

PLASMA ENDOTHELIN LEVELS CORRELATE WITH THE SEVERITY OF CORONARY ARTERIOSCLEROSIS IN PATIENTS WITH CHRONIC STABLE ANGINA PECTORIS.

M. A. Salame, P. M. Elliott, P. Zhang, R. Calvillo, D. Holt, J. C. Kaski.

Department of Cardiological Sciences, St. George’s Hospital, London.

Recent experimental and clinical studies suggest that plasma endothelin (ET) may play a role in the atherogenic process and in acute coronary syndromes. However, no previous study has demonstrated an association between ET and either the extent or severity of coronary artery disease in patients (pts). We studied 90 consecutive stable angina pts (70 men, aged 61±9 years), at the time of diagnostic coronary angiography. Pts with cardiac or renal failure were excluded. Quantitative angiography was used to assess extent and severity of coronary arteriosclerosis and lesion morphology. ET was measured by radioimmunoassay (Nichols Institute, Diagnostic B.V). Forty nine normal volunteers were used as controls. Eleven pts had normal coronary angiograms (group I), 65 had coronary artery stenoses ≥50% (group II), and 14 had coronary artery disease plus symptoms indicating atheroma in other vascular territories (group III). All pts had ejection fraction >50%. Mean ET concentration (pg/ml) was significantly higher in pts than in controls (7.29±4.07 vs. 3.48±1.29, p < 0.0001). ET levels were higher in pts of group III than in groups II and I (9.34±5.48, 7.20±3.72, and 4.94±2.89, respectively, p < 0.02). In pts of group II, ET correlated with the maximal degree of stenosis in each patient (r=0.25, p=0.04) and with the number of stenoses ≥70% narrowing diameter (r=0.36, p=0.002).

The highest ET levels were found in patients with total coronary occlusions (8.65±3.78 vs. 6.46±3.51 in pts without occlusions, p < 0.02).

We conclude that ET concentration is raised in patients with chronic stable angina. The highest levels occur in patients with severe coronary stenoses and total coronary occlusion.
HEART ATTACK ACTION!: A CAMPAIGN TO IMPROVE COMMUNITY KNOWLEDGE
Gaynor F Dixon, R M Norris, R Vincent. Cardiac Department, Royal Sussex County Hospital, Brighton.

Data from the United Kingdom Heart Attack Study show that approximately 75% of deaths from ischaemic heart disease occur outside hospital, and patients with acute myocardial infarction still delay in seeking help. Approximately two thirds of victims of sudden cardiac arrest are not hospitalised, and over 70% have attended their general practitioners within the previous six months. Accordingly, we enlisted the help of 80% of general practices within the Brighton Health District (population 280,000), to distribute carefully designed booklets to patients aged 40 to 75 years. The main message was "if you have chest pain lasting longer than 15 minutes dial 999 for an ambulance". This was supported by the help of posters, a video, and some media coverage. A simple 5 minute questionnaire is administered to randomly selected patients in GP waiting rooms before and after the six month campaign. Questionnaires before the campaign (n=315) showed that 44% of people had reasonable knowledge of the symptoms of a heart attack, 46% would call for an ambulance within 30 minutes of onset of symptoms, but only 20% could differentiate between heart attack and cardiac arrest. Six months after the start of the campaign, repeat questionnaires were given to 241 different people. These showed that 96.6% (p<0.01 vs before the campaign), 68% would call an ambulance promptly (p<0.001), and 31% could now differentiate between heart attack and cardiac arrest (p=0.05). Knowledge scores were unchanged in the 60% of people who had not heard of the campaign. We conclude that public education can be effective but additional strategies are needed. It is planned to extend the campaign by greater use of the video, extracts of which will be shown during this presentation.

THE PATHWAY THROUGH MYOCARDIAL INFARCTION - EFFECTS OF AGE, SEX AND SOCIO-ECONOMIC GROUP
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The Glasgow MONICA Coronary Event register has information on all male and female coronary events occurring in residents of North Glasgow since 1985. Aggregated data on events from 1985-1991 (5542 events) will be shown. The pathway through care embraces a total number of events, the arrival at hospital, the in-hospital case-fatality and the community (overall) case-fatality. There are more male (3991) events than female (1551). There is an increase in event rate with age and a decrease in the male/female ratio. The rate (male and female) increases with increasing deprivation; the increase is greater for women. In men the deprived/aﬄuent ratio decreases with increasing age and probably also in women. Around 63% arrive alive at hospital. This proportion decreases with age; more women than men arrive alive at hospital. Increasing deprivation lessens the chance of arriving alive at hospital for both sexes. In-hospital case-fatality is 21%. It increases with age; is greater for women than men. Male in-hospital case-fatality decreases with increasing deprivation but female rates increase. Community case-fatality varies by age, sex and socio-economic group. It is greater among the least aﬄuent; the crude rate is identical between the sexes (50%) but the age-standardised rate is slightly greater among women than men. Differences between first and recurrent events at these points along the pathway will also be discussed.

DIRECT ADMISSION TO THE CORONARY CARE UNIT BY THE AMBULANCE SERVICE IN PATIENTS WITH SUSPECTED MYOCARDIAL INFARCTION
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A direct admission policy to a coronary care unit (CCU) for patients with chest pain referred by General Practitioners (GP) has been shown to substantially reduce the time to thrombolysis in those patients with an acute myocardial infarction (AMI) fulfilling the criteria for this therapy. We have extended this fast-track admission policy to include referrals from ambulance personnel who respond to '999' calls in patients with chest pain. The time to admission and the final diagnosis of these cases referred to CCU by ambulance personnel are examined in this study to assess the effect on the overall time to thrombolysis and the appropriateness of the admissions. Method Ambulance personnel were instructed to take patients directly to CCU if an AMI was suspected in patients presenting with chest pain. This training was given to the ambulance personnel. The time from phone call from the ambulance personnel to admission noted and discharge diagnosis was confirmed from case records in 70 cases admitted directly to CCU by ambulance personnel. Results The median time from phone call to admission to CCU was 8 minutes (median time for GP referrals 43 minutes). The median diagnostic ECG to thrombolysis was similar to GP referred cases. The table shows the final diagnosis of these admissions, 40/70 (57.1%) exhibited symptoms of myocardial ischaemia and a further 10/70 (14.3%) required admission to CCU for other causes which are also similar to GP referred cases.

<table>
<thead>
<tr>
<th>Confirmed</th>
<th>Unstable</th>
<th>Other causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>MI</td>
<td>Angina</td>
<td>Angina</td>
</tr>
<tr>
<td>Total admissions (n=70)</td>
<td>18</td>
<td>14</td>
</tr>
<tr>
<td>Total admissions (n=70)</td>
<td>17</td>
<td>11</td>
</tr>
<tr>
<td>Transfer to ward (n=31)</td>
<td>3</td>
<td>2</td>
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</table>

Conclusion Extending fast-track admission policies to ambulance personnel results in a time saving of 35 minutes from GP referred cases which further reduces the overall time to thrombolysis in those with an AMI. The proportion of appropriate referrals by ambulance personnel is similar to GP referrals. Fast-track admission policies should include patients with suspected AMI referred via ambulance personnel.

A NATIONAL SURVEY OF SUDDEN UNEXPECTED CARDIAC OR UNEXPLAINED DEATH IN ADULTS (SADS)
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The objective of this national survey was to measure the frequency & causes of sudden unexpected adult death due to cardiac disease, and to determine whether there is a sudden adult death syndrome. A stratified random sample of 83 of the 132 HM Coroners' jurisdictions in England was drawn. For a 4 month period, each coroner identified consecutive deaths among caucasians, 16 to 64 years old, with no history of cardiac disease, last seen alive within 12 hours of death, & whose post mortem revealed either a cardiac or no identifiable cause of death. A transverse myocardial slice was obtained from each, examined histologically by three pathologists, & reported in a standard manner. If no cause of death was identified at post mortem, the whole heart was examined: 67 coroners (81%) participated in the survey and identified 665 deaths (81% male). In 562 (82%) death was ascribed to ischaemic heart disease. In 42% the ischaemia was acute, in 19% there was myocardial scarring but no acute ischaemia, and in 21% coronary atheroma only. Of the remaining 18% of cases, cardiac causes of death included 5.5% due to left ventricular hypertrophy (though in some there was minor coincident coronary disease), 1.9% to valve disease, 0.9% to idiopathic fibrosis syndrome, 0.8% to myocarditis, 0.8% to cardiomypathies, and other rarer cardiac causes. In 3% of cases no cause of death could be found despite a detailed histological examination and a toxicological screen. The frequency of sudden unexpected cardiac death in adults of employment age was 0.12 per 1000 per annum, which is about 3000 per year. Although the vast majority of these could be attributed to cardiac causes, mostly ischaemic heart disease, in 3% no cause could be found. For these cases, the term sudden adult death syndrome (SADS) is useful, and their aetiology needs to be determined.
WHAT DO WE DO WHEN THROMBOLYSIS FAILS? A UNITED KINGDOM SURVEY
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The benefits of thrombolytic therapy in acute myocardial infarction (AMI) are established. However, angiographic studies have demonstrated that reperfusion of the infarct-related artery is unsuccessful in 15-50% of patients and this is associated with a poor prognosis. We have undertaken a postal survey among British Cardiac Society members actively involved in the management of AMI to determine the current management of "failed" thrombolytic therapy. A reply was received from 290 (37%) (9% of the survey population). The survey data were submitted to the British Cardiac Society for publication.

There were 153 (57%) Cardiologists and 117 (43%) Physicians with a cardiac interest. 162 (60%) have an on-site cardiac catheterisation laboratory, 112 (69%) equipped and staffed for emergency angiography +/- PTCA. Streptokinase is the thrombolytic agent preferred for routine use by the majority (n=242, 90%). 149 (55%) routinely seek evidence of reperfusion of the infarct-related artery, although 55 (20%) confine their search to selected cases, usually young patients with anterior AMI. The most commonly used parameters of successful thrombolysis are the resolution of chest pain, the occurrence of reperfusion arrhythmias and improvement/resolution of electrocardiographic changes. Very few (n=14, 5%) seek proof of the achievement of a lytic state. In instances of "failed" initial thrombolysis, 128 (47%) continue conservative management of AMI, 50 (19%) proceed to urgent coronary angiography +/- PTCA, 49 (18%) employ an alternative thrombolytic agent, and 35 (13%) use a combination of these strategies. Urgent angiography is, not surprisingly, more commonly used by those with facilities available (74/162 vs. 11/106, p=0.0001). 131 (49%) respondents felt their approach would be modified if 24 hour access to this service was available. These data indicate that the most variable in the detection and management of failed thrombolysis. Randomised, controlled trials are required to elucidate optimal treatment for this group of patients.

DETERMINANTS OF GLOBAL LEFT VENTRICULAR SYSTOLIC DYSFUNCTION IN NORTH GLASGOW
TA McDonagh, *CE Morrison, JJ McMurry, I Ford,*H Tunstall-Pedoe, JI Dargie Cardiology Department, Western Infirmary, *Scottish Manisa Project, Glasgow,UK.

The prevalence of chronic heart failure (CHF) in major epidemiological studies has been determined using clinical criteria for its diagnosis, not by objective measurement of LV function. We have carried out an echocardiographic survey of 1954 men and women aged 40-89 years and randomly sampled from a general population, who had previously attended the Third Glasgow Monica Risk Factor Survey. LV systolic function was assessed by a biplane Simpson's Rule ejection fraction (LVEF). A LVEF ≤35% was defined as LV dysfunction (LVD) as it represented two standard deviations from the mean value for healthy individuals within this population. 1653 subjects finally attended (response rate 86%). The prevalence of LVD was 7.7% (n=113). This rose from 3.4% in females under 35 yrs to 17.7% in men over 66 yrs, males having a higher rate of LVD throughout the age groups. Of those with LVD, 47% (n=51) were breathless or on treatment for CHF, 53% (n=65) were asymptomatic. The prevalence rate for symptomatic LVD was 2.6% and that of asymptomatic LVD was 4.5%. In the LVD group 40.2% had evidence of a previous myocardial infarction (MI), ischaemia, left ventricular hypertrophy or left bundle branch block on their resting ECG compared to 18.9% of those with a normal LVEF (p<0.001). Similarly, 17.7% of those with LVD self reported a previous MI or had history of angina in contrast to 4% of those with a normal LVEF (p<0.001). Hypertension was more common in those with LVD (43.6% compared to 30.5% in those with a normal LVEF, p<0.005). Overall 71.5% of those with LVD had evidence of prior MI or angina, were hypertensive, had significant valvular heart disease or excessive alcohol intake. Only 39% of those with symptoms and 47% of those with a ACE inhibitor and/or a diuretic and or digoxin. LVD has a high prevalence in this population in keeping with its inflated rate of coronary heart disease and its common and fatal condition is underdiagnosed and undertreated.

(267) JUDGES' CHOICE II

ASSESSMENT OF STEADY STATE MYOFIBRIL CALCIUM RESPONSE IN INTACT ISOLATED CARDIAC MYOCYTES: MODULATION BY THE CARDIAC ENDOTHELIUM
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A number of endothelin-derived isotopics affect myocardial contraction in the absence of changes in the Ca2+ transient, suggesting that they act by altering the myofilament response to Ca2+ (Ca(2+)-transients, and (c) studied whether this factor was also produced by cardiac EC in situ. Myocytes rapidly stimulated (10Hz) in the presence of the irreversible SR Ca-ATPase inhibitor thapsigargin (0.2μM, 10-20 mins) developed a steady elevation of [Ca(2+)](i) (fura-2 fluorescence ratio, F) associated with reproducible tetanic shortening (video edge detection, S). The [Ca(2+)](i) length relationship was used as an index of MR. Both alkalosis (pH7.7) and EMD57033 (10μM), known to increase MR in skinned fibres increased S in the absence of similar changes in tetanic F. Similarly, 8-bromo-cGMP (50μM), which decreases MR, reduced S, F remaining unchanged. Butanedione monoxime (0.5-5mM) caused a marked reduction in tetanic S, associated with small dose-dependent reductions in tetanic F. A reduction in RCas was confirmed by a downward shift in the relationship between [Ca(2+)](i) and S after BDM, in the absence of similar changes in the Ca(2+)-transients. Cultured EC efficiently reduce [Ca(2+)](i) by multiple negative inotropic means, in association with small dose-dependent reductions in tetanic F without changing tetanic S, indicating a reduction in MR. The effects of coronary endothelial cells from isolated crystalloid-perfused rat hearts were tested on isolated myocytes. Coronary endothelial cells reduced tetanic S without changes in tetanic F, similar to responses seen with superfused myocytes from cultured endothelial cells. These data indicate that (a) tetranisation of SR-disabled myocytes allows assessment of changes in steady state myofilament response to Ca2+ in intact cells, (b) a novel negative inotropic EC-derived factor acts by reducing MR, and (c) this factor is released by cultured EC and is also present in the coronary effluent of intact hearts.

AQUAPORIN-L IS EXPRESSED IN RAT AND HUMAN ARTERIES AND MAY PLAY A ROLE IN VASCULAR FUNCTION IN HEALTH AND DISEASE
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Aquaporin-1 is a membrane water channel that is highly expressed in tissues required to transport water rapidly across cell membranes. We have recently shown that the gene for aquaporin-1 is highly expressed in differentiated rat vascular smooth muscle cells (VSMCs) derived from the aortic media. The present studies sought to determine its role and distribution in vascular cells both in health and disease. Immunochemistry and in situ hybridisation demonstrated high levels of aquaporin-1 protein and mRNA in human vascular endothelium and VSMCs in arteries, adventitial vessels and capillaries. AQP1 protein was also present in VSMCs in both the media and intima of atherosclerotic plaques but not in macrophages or fibroblasts in these lesions.

Cell volume analysis of isolated rat and human VSMCs and Human Umbilical Vein Endothelial Cells (HUVECs) using flow cytometry demonstrated that osmotically induced rapid transcellular water transport is inhibited by mercuric chloride at concentrations known to block water flux through aquaporin-1.

In the rat carotid artery balloon injury model of intimal proliferation, AQP1 mRNA and protein are markedly elevated in VSMCs during the proliferative stage of neointimal development. In vitro studies with rat VSMCs showed that its expression is induced by the vascular growth factors PDGF, bFGF, Angiotensin II and TGFβ1.

These data show that aquaporin-1 is highly expressed in vascular cells and that rapid water transport through these cells is mercury sensitive and therefore likely to be through aquaporin-1. Recently, aquaporins have been shown to be highly expressed in normal skeletal muscle and it has been proposed that they aid cellular contraction by allowing rapid changes in cell size via transmembrane water flux. Aquaporin-1 expression is also increased during vascular cell proliferation both in vitro and in vivo and this may also be to allow changes in cell shape associated with cell division. Further studies to elucidate these roles are in progress.
(269) JUDGES’ CHOICE II

ISCHEMIC PRECONDITIONING ATTENUATES MYOCARDIAL STUNNING FOLLOWING REPEITIVE EXERCISE

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Exercise-induced ischemia causes prolonged left ventricular (LV) dysfunction, which we have shown to be cumulative if exercise is repeated 1 hour later. To determine the effects of repeated exercise-induced ischemia on LV function at a shorter time interval, we studied 9 patients (mean age 58 ± 8 years) with angiographically-proven coronary artery disease, stable angina and normal LV function. Each underwent 2 consecutive symptom-limited treadmill tests, 30 minutes apart. Quantitative echocardiographic assessment of systolic and diastolic LV function (ECHO) was performed at baseline and at regular intervals after each exercise test.

Results: Heart rate, blood pressure and ST changes returned to baseline within 10 minutes of exercise in all cases. Exercise time, time to angina, workload, and maximum ST depression were all significantly improved with exercise 2 (p < 0.05).

Exercise duration (sec)

Time to Angina (sec)

Maximum ST Depression (mm)

Maximum Workload (METs)

ECHO data (mean ± SD) as follows: EF (shortening fraction), EF (% reduction in area), and end-diastolic volume (mL). N.S.

PRECONDITIONING ISCHAEMIC STUNNING IS ATTENUATED BY REPEITIVE EXERCISE

(271) JUDGES’ CHOICE II

THREE-DIMENSIONAL CONTRAST ECHOCARDIOGRAPHY IN ACUTE MYOCARDIAL INFARCTION: IN VIVO QUANTIFICATION OF INFARCT MASS

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We have previously reported the feasibility of three-dimensional reconstruction (3DE) of myocardial contrast echocardiographic (MCE) perfusion defects. To determine the accuracy of volume-rendered 3DE measurement of infarct mass, we studied 10 dogs in which acute myocardial infarction was created by 3 hour coronary ligation (LAD in 7, LCX in 3). MCE was performed using a scanner adapted for imaging of the second harmonic frequency (2.5 MHz emit / 5.0 MHz receive transducer) and intravenous injection of a new transpulmonary contrast agent (FS609). Rotational 3D acquisition was controlled by a TomTom computer. After 3DE reconstruction of the left ventricle (LV), the cross-sectional areas of (i) the LV and (ii) the contrast perfusion defect were measured by planimetry in 10 parallel short axis slices, from which the mass of the LV and of the perfusion defect were derived. After sacrifice, the true anatomic mass of the LV and of the infarct region (delineated by TTC staining) were measured. The infarct mass (IM) and fraction of the LV affected by infarction (%LVI) derived by anatomic inspection and by 3DE are shown in the table below:

<table>
<thead>
<tr>
<th>Fraction (%)</th>
<th>3DE (mL)</th>
<th>3DE (mL)</th>
<th>IM (mL)</th>
<th>3DE (%LVI)</th>
<th>3DE (%LVI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>15 ± 5</td>
<td>15 ± 5</td>
<td>15 ± 5</td>
<td>15 ± 5</td>
<td>15 ± 5</td>
<td>15 ± 5</td>
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<td>10 ± 5</td>
<td>10 ± 5</td>
<td>10 ± 5</td>
<td>10 ± 5</td>
<td>10 ± 5</td>
<td>10 ± 5</td>
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</tbody>
</table>

In conclusion, these data show that myocardial infarct mass can be quantified very accurately in vivo by 3DE reconstruction of MCE perfusion defects. This new non-invasive method may be of great value in clinical and experimental assessments of myocardial infarction.

(270) JUDGES’ CHOICE II

FOLLOWING MYOCARDIAL INFARCTION AND THROMBOLYSIS, STRESS AND NITROGLYCERINE ENHANCED REST TL-201 IMAGING HAS SUPERIOR PROGNOSTIC VALUE COMPARED TO REDISTRIBUTION IMAGING

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Thallium-201 (TI-201) imaging has been shown to have prognostic value following acute myocardial infarction (AMI). However, it is not clear whether post-discharge TI-201 studies have a prognostic value in patients (pts) with acute myocardial infarction (AMI) in the thrombolytic era. We have prospectively studied 100 such pts who underwent exercise, 4hr redistribution and separate day rest (post nitroglycerine) planar TI-201 studies. The scans were performed 5-7 weeks after AMI and the pts were followed-up for a mean of 19 (6-30) months and adverse cardiac events (death, reinfection, unstable angina and heart failure) were documented. The planar scans were converted to a polar image and read blindly by 2 investigators. Out of 100 pts, 68 had evidence of reversible perfusion defects by rest TI-201 imaging of whom 33 had events, while of 32 with no reversible perfusion defects only 4 had events (Hazard ratio 8.0, 95% CI 2.7-23.8, p < 0.001). However, by redistribution imaging only 29 pts demonstrated reversible perfusion defects, of whom 15 had events; while of 71 pts without reversible defects, 23 had events (Hazard ratio 1.5, 95% CI 0.8-3.0, p = 0.2). Multivariate analysis using clinical variables, exercise electrocardiography and imaging data showed that only past history of ischemic heart disease (Hazard ratio 3.1, 95% CI 1.3-7.3, p < 0.01) and reversible defects on stress and post-nitroglycerine rest TI-201 imaging predicted risk. Thus, these data suggest that presence of reversible ischemia, detected by a combination of stress and separate day post-nitroglycerine rest imaging, predicts adverse outcome compared to conventional TI-201 imaging.

(272) JUDGES’ CHOICE II

CONTINUOUS CONTINUOUS SINUS PH MONITORING DURING DIPYRIDAMOLE STRESS IN PATIENTS WITH ANGINA AND HYPERTROPIC CARDIOMYOPATHY

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The presence of angina and myocardial scarring in patients (pts) with hypertrophic cardiomyopathy (HCM) suggests that myocardial ischemia is important in the disease. Its detection in HCM is problematic as baseline ECG changes are common and serial thallium defects correlate poorly with symptoms. Continuous coronary sinus (CS) pH measurement is a validated technique for detecting myocardial ischemia. Eleven HCM pts with typical angina (8 M, 36 ± 11 yrs) and 6 controls (2 M, 49 ± 11 yrs) with atypical chest pain and normal coronary angiograms were studied. Eight HCM pts had 21 mm baseline ST depression and 4 had reversible thallium defects. A catheter mounted pH electrode was placed the CS and pH monitored continuously during LVPD (0.56 mg/kg). Maximal change in CS pH in the HCM group was 0.08 ± 0.03 vs 0.005 ± 0.006 in controls (p < 0.02). In 6 HCM pts there was a gradual fall in CS pH (0.12 ± 0.089), peaking at 44 ± 100 seconds:

- Dip: Chest pain

- Time (sec)

- pH

In HCM pts there was a correlation between maximum pH change and heart rate during dipyridamole (r = 0.70, p < 0.02) but no relation with LV dimensions or pain during dipyridamole infusion in HCM pts is associated with a fall in CS pH, indicating an ischemic origin. Continuous CS pH monitoring provides a unique method for evaluating symptoms suggestive of myocardial ischemia in HCM pts.
(273) MODERATED POSTER

CEREBRAL EVENTS AFTER CARDIAC SURGERY
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Introduction: Perioperative neurological injury (CVA) carries important implications for both patient and society. This study was performed to examine the incidence and aetiological factors for this condition in our own practice.

Methods: A daily computer record was maintained of all 3547 patients who passed through the cardiac intensive care unit (ITU) between January 1992 and April 1995. Case notes and radiological results were scrutinised for all patients recorded to have suffered a perioperative CVA.

Results: 67 patients (1.9%) were identified. 41 of these underwent a brain scan (CT). CVA was commoner amongst valve patients (22/780, 2.8%) compared to patients undergoing only coronary grafts (39/2481, 1.6%) (P<0.05, odds ratio 1.8, 95% confidence interval 1.06 - 3.06) and was commonest following repair of aortic dissection (5/40, 12.5%). Of the 41 patients undergoing CT, a new cerebral infarct was found in 28 (70%) and a cerebral bleed was found in 4 (10%). CVA patients spent longer on the ITU and 35 of them died. Parsonnet score, age, hypertension, valve surgery, re-exploration for bleeding and haemofiltration were all univariately associated with CVA. Multiple regression found age (P=0.001), hypertension (P=0.01), re-exploration (P=0.05) and haemofiltration (P=0.001) to be independently associated.

Conclusion: Perioperative CVA causes considerable morbidity and mortality. Surgeons should be sure to adequately inform their patients (especially older hypertensives) about the risk of stroke after cardiac surgery.

(274) MODERATED POSTER

A Randomised Study of the Effects of Cardiopulmonary Bypass Temperature on Neuropsychological Deficit After Coronary Artery Surgery
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Aim: To investigate the hypothesis that normothermic systemic perfusion may compromise neuropsychological outcome after coronary artery surgery.

Methods: Ninety six patients were randomised into three groups depending upon cardiopulmonary bypass temperature: hypothermia (28°C, n=31), moderate hypothermia (32°C, n=36) and normothermia (37°C, n=29). All patients were subjected to detailed clinical neurological examination, and neuropsychological evaluation using tests taken from the Revised Wechsler Adult Intelligence Scale and the Weschler Memory Scale. These were undertaken preoperatively, and six weeks postoperatively. Neuropsychological deficit was defined as a 20% reduction in the scores achieved preoperatively compared to post-operatively in at least 2 of the 7 tests used.

Results: Groups were matched with regard to age, sex, body surface area, and number of grafts performed. No episodes of gross neurological deficit were detected in any patient postoperatively. Although the scores in the various components of the neuropsychological assessment were similar between groups preoperatively, the incidence of neuropsychological deficit was higher after normothermic (17.2%) compared to moderately hypothermic (8.3%) and hypothermic perfusion (6.4%). Multiple response stepwise regression analysis identified an overall direct effect of higher perfusion temperature upon deficit with 93% confidence, and an effect of 37°C versus 32°C with 98% confidence. There were no added benefits of cooling to 28°C with regard to neuropsychological outcome.

Conclusion: Normothermic perfusion is associated with a higher incidence of neuropsychological deficit after coronary artery surgery.

(275) MODERATED POSTER

MODIFIED ULTRAFILTRATION IMPROVES CARDIAC SYSTOLIC AND DIASTOLIC FUNCTION IMMEDIATELY AFTER CARDIOPULMONARY BYPASS IN CHILDREN
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In children undergoing open heart surgery modified ultrafiltration(nuf) performed immediately after cardiopulmonary bypass reverses haemodilution and increases blood pressure and cardiac output. The impact of nuf on myocardial function was assessed by deriving indices of systolic (maximal rate of change of pressure rise, dp/dtm, end-systolic elastance, Ees) and diastolic function (time constant of isovolumic relaxation, tau; maximal rate of pressure decline, dp/dtm) from pressure-volume loops. Real-time pressure volume loops were measured in 17 children (mean weight 10.1kg:mean cross-clamp time 55min:AVSD1,ToF6,AVSD+ToF2, secundum ASD 1, RVOTO 1) using simultaneous micropip pressure (C.SF) and custom built (2 or 3F) conductance catheters inserted through the LV apex. (Ees measured by transient IVC snaring) and other indices were measured immediately before and after nuf. For the whole group haemococoncentration was achieved (haemoglobin increased 3.7±2.2g/dl(mean±sd) and there was a significant improvement in diastolic function: tau decreased (47±21±39±39mmHg/ml) and dp/dtm increased (706±224±340mmHg/p<0.05). Although dp/dtm increased (798±307 to 956±332mmHg/p<0.05) there was no increase in Ees. However for children<6kg (n=5) there was a significantly greater post nuf Ees as compared to children >6kg (p<0.05) although there was no difference between the two groups in cross-clamp time or haemococoncentration. In conclusion, pressure-volume loop analysis using a conductance catheter has demonstrated significant improvement in cardiac systolic and diastolic function after nuf.

(276) MODERATED POSTER

THE PULMONARY AUTOGRAPH TRANSPLANTATION: LONG TERM RESULTS OF THE PIONEER SERIES
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All 131 National Heart Hospital survivors of the pulmonary autograft operation from its invention in 1967 to 1984 were identified. 96% of patients were traced to 1994 (9-26 mean 21 years followup). Mean age at operation was 22 (range 11-52) years, 109 were male, 104 had mitral disease and none coronary disease. Autograft implantation was valve cusps only (107), mini-root replacement (20) or dacron mounted (4). Pulmonary position valves were: homograft (113) and other (18). At 10 and 20 years postoperative actuarial patient survival was 85% and 61%, survival of the autograft valve was 88% and 75%, survival of homografts in the pulmonary position was 85% and 79%, and freedom from any reoperation was 73% and 61% respectively. There were 53 deaths, of which 5 were early. Late deaths included chronic heart failure (21), sudden death (8), myocardial infarction (6), endocarditis (6) and non-cardiac (4). 46 patients were reoperated, 7 early indications were: autograft regurgitation (20), pulmonary stenosis (10), mitral valve disease (5), endocarditis (3), other (8). Autograft regurgitation was a leading cause of mortality and the most common indication for reoperation. It appeared primarily technical, usually dating from the time of operation and being the result of prolapsing or perforated cusps. Autograft cusps containing living cells at up to 24 years postoperative and rarely showed degeneration. There was no increase in valve failure in the young. Valve and mini-root replacement autografts performed equally well in the pulmonary position, homografts outperformed other prostheses. Endocarditis and thromboembolism were rare. Of the 72 survivors to 1994 75% were NYHA class i and 80% retained the autograft valve. By echocardiography 75% of late surviving autografts were functioning well without stenosis or regurgitation. We conclude from this pioneering series that the pulmonary autograft is an excellent aortic valve replacement, particularly in the young, offering durability with little degeneration and no need for anticoagulation.
**MODERATED POSTER**

**CHANGES IN LEFT VENTRICULAR DIMENSIONS AFTER AORTIC VALVE REPLACEMENT**

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**Introduction:** Improvement in left ventricular dimensions after surgical relief of aortic stenosis is probably indicative of satisfactory relief of obstruction. Recently such data have been presented in support of homograft and stentless tissue valves. The aim of this study was to see if similar changes can be demonstrated after mechanical valve replacement.

**Methods:** 42 patients (median age 62y, range 41-75) with predominant aortic stenosis underwent valve replacement with either a Starr Edwards (n=15) or St. Jude (n=27) mechanical prosthesis. All patients had clinical, radiographic and echocardiographic examinations before and 12 months after valve surgery.

**Results:** There were dramatic improvements in NYHA functional class. Cardiothoracic ratios were significantly reduced at one year (mean difference 5.4% SD 5.4, p<0.001). Of the 16 patients whose preoperative LV diastolic dimension exceeded the upper limit of normal, 13 showed a reduction at one year (p=0.001) and 7 now fell within the normal range. 16 of 20 patients with excessive systolic dimensions improved (p=0.001) and 8 of these now fell into the normal range. 7 of 8 patients with a hypertrophied interventricular septum had normal septal measurements at follow-up; 9 patients with a hypertrophied posterior LV wall now had normal measurements (p=0.003 & 0.001 respectively). 6 of 9 patients with reduced shortening fractions showed improvement (p=0.1).

**Conclusions:** Relief of aortic stenosis using a mechanical valve leads to regression of abnormal left ventricular dimensions at one year. We are unable to say from this small study whether there are discernable differences between the Starr Edwards and St. Jude valves in this regard.

**MODERATED POSTER**

**THE IMPORTANCE OF SUBVALVULAR PRESERVATION AND EARLY OPERATION IN MITRAL VALVE SURGERY**

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Mitral valve replacement has a high mortality and morbidity. It has been suggested that preservation of the subvalvular apparatus and optimization of the timing of surgery may improve the outcome from mitral valve surgery. We performed a retrospective study of 612 consecutive patients who underwent mitral valve repair or replacement. 226 patients had repair, 68 had replacement with subvalvular preservation (MVR+SVP) and 318 had replacement without subvalvular preservation (MVR-SVP). The mean age was 63±10.4 years and mean follow-up, 41.7±28.8 months. Baseline characteristics were most unfavourable in the repair group with respect to age (p=0.002), and in the repair and MVR+SVP groups with respect to NYHA class and left ventricular function (p=0.044). Thirty-day mortality was lower in the repair (1.8%, p=0.046) and MVR-SVP (1.5%, NS) groups than the MVR-SVP group (5.0%). Overall survival at 7 years was better in the repair (71.22±6.4%, p=0.022) and MVR+SVP (66.22±12.4%, p=0.017) groups than the MVR-SVP group (63.52±3.4%). Myocardial failure was the main cause of complications-related death. Multivariate analysis confirmed independent beneficial effects from repair on 30-day mortality (odds ratio 0.27, p=0.05) and from repair and MVR+SVP on overall mortality (hazard ratio 0.43, p<0.001 and 0.40, p=0.05 respectively) and complications-related death (hazard ratio 0.38, p<0.001 and 0.35, p<0.05 respectively).

Preoperative NYHA class III or IV symptoms and echocardiographic left ventricular impairment were independent risk factors for death and myocardial failure, and were already present in >70% patients at baseline. Therefore, mitral valve repair is superior to replacement. If repair is not feasible, the subvalvular apparatus should be preserved.

Early surgery prior to the development of severe symptoms and demonstrable left ventricular impairment is also needed to optimise outcome.

**MODERATED POSTER**

**EARLY RESPONSE GENE EXPRESSION AND VASCULAR CELL PROLIFERATION IN HUMAN SAPHENOUS VEIN PREPARED FOR CORONARY BYPASS GRAFTING**

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Early and late saphenous vein graft failure is a major complication of coronary artery bypass surgery. Early failure occurs as a result of thrombosis whereas late failure is due to the abnormal proliferation and migration of vascular smooth muscle cells into the vessel lumen. We hypothesized that surgical trauma induces the early response genes c-fos and c-jun. AP-1 (a heterodimer of c-fos and c-jun) and c-myc cause the transcription of cyclin D which is known to accelerate cell proliferation. We have therefore investigated the expression of the early response genes, c-fos, c-jun and c-myc in human saphenous vein before and after preparation for grafting. Freshly isolated saphenous vein was harvested using a no-touch technique immediately following the first incision. Surgically prepared vein consisted of distended (400mmHg for 2 minutes) or non-distended segments of vein maintained in serum free RPMI at 37°C and 5% CO2 for various time intervals. c-fos, c-jun and c-myc expression were detected by Northern analysis of RNA using 3P labelled cDNA probes. RNA expression was quantified by densitometry following correction for loading determined using β6 expression as a non-cell cycle-dependent gene transcript. Vascular cell proliferation was studied by 3H thymidine incorporation per μg DNA. Freshly isolated segments of saphenous vein showed no expression of c-fos, c-jun and c-myc. Surgically prepared vein showed expression of c-fos and c-jun at 20 minutes following harvesting and by 1 hour there was a significant increase in c-fos in the distended compared to the non-distended vein. Expression of c-fos and c-jun returned to basal levels 24 hours after isolation of saphenous vein. c-myc was not expressed until 3 hours after vein harvesting. There was a significant increase in vascular cell proliferation in the distended compared to the non-distended vein (110±32% 3P/μg DNA (SEM) vs 82±102% p<0.05. In conclusion, surgical preparation of human saphenous vein modulates early response gene expression and accelerates vascular cell proliferation and this may contribute to the failure of saphenous vein grafts.

**MODERATED POSTER**

**CAN THE TIMI-FLOW GRADE PREDICT THE PRESENCE OF HIBERNATING MYOCARDIUM?**

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**Introduction:** The importance of TIMI-flow grade (TIMI grd.) in determining prognosis following myocardial infarction is well documented. Positron emission tomography (PET) is well established in the detection of hibernating myocardium. However, is there any relationship between the TIMI grd. and the presence of "hibernation"? Patients and Methods: Nineteen patients with impaired left ventricular contraction underwent PET imaging. For PET, N-13-ammonia (13NH3) was used as the perfusion marker, and F-18-fluorodeoxyglucose (18FDG) uptake as a marker of metabolism. The 13NH3/18FDG distribution was displayed on polar maps. Each was divided into five segments: anterior, lateral, inferior, septal and apical. The relation between TIMI grd. 0,1,2&3 on the angiogram, and the presence of mismatch or "necrosis" was studied. Results: Ninety-five segments on the polar maps were available for analysis. 13NH3/18FDG mismatch indicates the likelihood of hibernation, whereas, necrotic areas are defined by the absence of 18FDG uptake. A total of 30 branches displayed TIMI grd. 0, 1, or 2. Of the segments supplied by them, 14 segments (47%) showed no uptake of FDG, and therefore were necrotic by definition, and 6 (20%) showed 13NH3-18FDG mismatch. Of the 9 segments supplied by arteries with TIMI grd. 3, 3 segments (33%) were necrotic and 3 segments (33%) showed mismatch. Conclusion: In patients with chronic stable ischaemic heart disease and impaired left ventricular contraction, TIMI-flow grades lower than 3 are more likely to supply areas of necrotic rather than "hibernating" myocardium.
(281) MODERATED POSTER

ADMISSION COAGULATION ACTIVATION IN PATIENTS WITH UNSTABLE ANGINA IN RELATION TO CARDIAC TROTONIN T CONCENTRATIONS.


The presence of cardiac Troponin T (cTnT) in the serum of patients with unstable angina identifies a subgroup at high risk of subsequent cardiac events. The need for newer antithrombotic therapies for this group has been recognised. Activation of coagulation on admission was studied using a new ELISA assay for prothrombin fragment 1+2 (F1+2) which defines in vivo thrombin activation and a standard fibrinogen assay in 96 patients admitted with unstable angina. There was a significant correlation between the admission F1+2 (mean 39.8 ng/ml, range 9.8-141) and fibrinogen (mean 1.99 g/l, range 1.1-4.1) values. Rank Spearman correlation (rS)=0.533 p=0.025 and the mean admission F1+2 values were significantly higher than the mean value for our healthy controls: 39.8 ng/ml v 22.0 ng/ml, p = <0.001 (Mann Whitney). The cTnT results for each patient were divided into admission values, the diagnostic values- the value at 12-24 hours from admission- and the peak values- the highest value recorded in the first 48 hours of admission. No significant correlations were obtained between F1+2 concentrations and admission cTnT values, f1+2= 0.017 p = 0.872, diagnostic cTnT values, f2 = 0.076 p = 0.472, or peak cTnT values, f3 = 0.050 p = 0.390 or between fibrinogen concentrations and the admission cTnT concentrations, f4= 0.181 p= 0.118, the diagnostic cTnT concentrations, f5=0.170 p= 0.151, or the peak cTnT concentrations, f6=0.206 p= 0.072. Conclusion. Whilst there is evidence of admission coagulation activation in unstable angina, the lack of difference and lack of correlations in the prothrombin fragment 1+2 and fibrinogen concentrations in relation to cTnT status in this study, would suggest that more specific inhibitors of platelet activation rather than thrombin inhibitors may be more appropriate for this high risk unstable angina subgroup.

(282) MODERATED POSTER

ANTICOAGULANT EFFECTS OF VITAMIN E TREATMENT IN PATIENTS WITH CORONARY DISEASE.

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Epidemiological studies have shown that high levels of factor VII and fibrinogen are major risk factors for atherosclerosis. In a clinical trial of α-tocopherol in 2000 patients with coronary artery disease (the Cambridge Heart Antioxidant Study - CHAOS), we have demonstrated a 75% reduction in non-fatal myocardial infarction (MI) and a halving in major cardiovascular events. In this present study we have tested the hypothesis that the reductions in the risk of MI in CHAOS were due in part to α-tocopherol-mediated inhibition of coagulation. We studied 178 patients taking 800IU α-tocopherol /day, 148 taking 400IU and 316 taking placebo over a followup period of 3 - 808 days (median 196).

None were taking anticoagulants. Prothrombin time (PTT), activated partial thromboplastin time (APTT) and fibrinogen were measured using standard techniques. Effects of treatment on these indices were examined by analysis of covariance. Covariates in the model were smoking, baseline α-tocopherol level, sex, age, treatment duration and compliance. Boxplots of adjusted plasma fibrinogen levels in the model are shown. α-Tocopherol 800IU/d, but not 400IU, reduced fibrinogen levels (P=0.009), increased PTT (from mean 12.7" to 13.1", P=0.001) and had no effect on APTT (P=0.44). We conclude that α-tocopherol inhibits blood clotting at a dose known to reduce risk of MI, although this reduction is not sufficient to explain the full treatment effect.