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ISCHAEMIC HEART DISEASE

Late presentation with acute MI: do nothing or do a primary angioplasty? ► No studies to date have specifically addressed whether primary PCI is the most beneficial strategy in the patient presenting more than 12 hours from the onset of an ST elevation myocardial infarction (STEMI). In the BRAVE-2 trial, 365 patients presenting between 12–48 hours after the start of symptoms were randomised to immediate invasive treatment (stenting with abciximab) or a conventional conservative treatment strategy. The primary end point of left ventricular infarct size (as measured by a single photon emission computed tomography (SPECT) study with technetium sestamibi) was found to be significantly smaller in patients assigned to the invasive group (median 8% v 13%). The mean difference in final left ventricular infarct size was –6.8% smaller in the invasive group. No significant differences between the two treatment groups were found on comparing the secondary end point, a composite of death, recurrent myocardial infarction (MI), or stroke at 30 days.

▲ Schomig A, Mehilli J, Antoniucci D, *et al.* Mechanical reperfusion in patients with acute myocardial infarction presenting more than 12 hours from symptom onset. *JAMA* 2005;293:2865–72.

Routine invasive treatment for ACS is better than selective use of catheterisation ► A meta-analysis of seven trials examining a routine invasive versus a selective invasive strategy following non-STEMI (NSTEMI) looked at the rates of death or MI in the 9212 patients studied. Overall, death or MI was reduced from 14.4% of patients in the selective invasive group to 12.2% of patients in the routine invasive group. Higher risk patients with elevated cardiac biomarker values at baseline benefited more from routine intervention, with no significant benefit observed in patients with negative baseline marker values. However, during initial hospitalisation, a routine invasive strategy was associated with a significantly higher early mortality (1.1% v 1.8%), and the composite of death or MI. But after discharge, a routine invasive strategy led to fewer subsequent deaths and MIs (11.0% v 7.4%). At the end of follow up, a routine invasive strategy led to a 33% reduction in severe angina, and a 34% reduction in rehospitalisation.

▲ Mehta SR, Cannon CP, Fox KAA, *et al.* Routine vs selective invasive strategies in patients with acute coronary syndromes. *JAMA* 2005;293:2908–17.

Oxidised phospholipids may be a marker for coronary disease ► Concentrations of oxidised low density lipoprotein (LDL) and Lp(a) lipoprotein were measured in a total of 504 patients immediately before coronary angiography. Concentrations of oxidised LDL are reported as the oxidised phospholipid content per particle of apolipoprotein B-100 (oxidised phospholipid:apo B-100 ratio). Measurements of the oxidised phospholipid:apo B-100 ratio and Lp(a) lipoprotein concentrations were skewed toward lower values, and the values for the oxidised phospholipid:apo B-100 ratio correlated strongly with those for Lp(a) lipoprotein ($r = 0.83$, $p < 0.001$). In the entire cohort, the oxidised phospholipid:apo B-100 ratio and Lp(a) lipoprotein concentrations showed a strong and graded association with the presence and extent of coronary artery disease (that is, the number of vessels with a stenosis of more than 50% of the luminal diameter) ($p < 0.001$). Among patients 60 years of age or younger, those in the highest quartiles for the oxidised phospholipid:apo B-100 ratio and Lp(a) lipoprotein concentrations had odds ratios (ORs) for coronary artery disease of 3.12 ($p < 0.001$) and 3.64 ($p < 0.001$), respectively, as compared with patients in the lowest quartile. The combined effect of hypercholesterolaemia and being in the highest quartiles of the

oxidised phospholipid:apo B-100 ratio (OR 16.8; $p < 0.001$) and Lp(a) lipoprotein concentrations (OR 14.2; $p < 0.001$) significantly increased the probability of coronary artery disease among patients 60 years of age or younger.

▲ Tsimikas S, Brilakis ES, Emmanouil S, *et al.* Oxidized phospholipids, Lp(a) lipoprotein, and coronary artery disease. *N Engl J Med* 2005;353:46–57.

Highest risk of sudden death post-MI is in the first 30 days ► In VALIANT (valsartan in acute myocardial infarction trial), 14 609 patients with left ventricular dysfunction, heart failure, or both after MI were assessed for the incidence and timing of sudden unexpected death or cardiac arrest with resuscitation in relation to the left ventricular ejection fraction. Of 14 609 patients, 1067 (7%) had an event a median of 180 days after MI: 903 died suddenly, and 164 were resuscitated after cardiac arrest. Patients with a left ventricular ejection fraction of 30% or less were at highest risk in this early period (rate of events in first six months, 2.3% per month, 95% confidence interval (CI) 1.8% to 2.8%). Nineteen per cent of all sudden deaths or episodes of cardiac arrest with resuscitation occurred within the first 30 days after MI, and 83% of all patients who died suddenly did so in the first 30 days after hospital discharge. Each decrease of 5 percentage points in the left ventricular ejection fraction was associated with a 21% adjusted increase in the risk of sudden death or cardiac arrest with resuscitation in the first 30 days. However, left ventricular function on its own was not a very discriminatory way of assessing risk, and would have missed many events. An accompanying editorial suggests defibrillators in these acute patients are also not proven.

▲ Solomon SD, Zelenkofske S, McMurray JJV, *et al.* for the Valsartan in Acute Myocardial Infarction Trial (VALIANT) Investigators. Sudden death in patients with myocardial infarction and left ventricular dysfunction, heart failure, or both. *N Engl J Med* 2005;352:2581–8.

Confirmation that fat people do not get as much care

► More than 100 000 patients with acute MI in US Medicare hospitals were surveyed. Participants had a mean age of 75.8 years; 53% were men and 90% were white. Individuals with a body mass index (BMI, kg/m²) of 25.0 to 35.0 had the highest rates of coronary procedure utilisation. Compared with patients with a BMI of 25.0 to 29.9, those with a BMI of 35.0 to 39.9 had a reduced adjusted odds ratio of receiving coronary artery bypass grafting (OR 0.88, 95% CI 0.79 to 0.98), whereas patients with a BMI of 40.0 or greater had the lowest odds of receiving cardiac catheterisation (OR 0.82, 95% CI 0.73 to 0.92), percutaneous coronary intervention (OR 0.89, 95% CI 0.77 to 1.03), and coronary artery bypass grafting (OR 0.68, 95% CI 0.57 to 0.82). Patients who did not receive coronary revascularisation had higher mortality rates than those who did. The reason for the reduction in care was not concern about damaging the cardiac catheterisation table, since all participants were < 160 kg to be in the survey.

▲ Yancy WS, Olsen MK, Curtis LH, *et al.* Variations in coronary procedure utilization depending on body mass index. *Arch Intern Med* 2005;165:1381–7.

HYPERTENSION

Routine ocular funduscopy in hypertension is not warranted ► To be beneficial, a test must predict something useful or change practice. Studies were included that assessed hypertensive retinopathy with blinding for blood pressure and cardiovascular risk factors. Studies on observer agreement had to be assessed by two or more observers and expressed as a κ statistic. Studies on the association between hypertensive retinopathy and hypertensive organ damage were carried out in patients with hypertension. The association between hypertensive retinopathy and cardiovascular risk was carried out in unselected normotensive and hypertensive people without diabetes mellitus. The assessment of microvascular changes in the retina is limited by large variation between observers. The positive and negative predictive values for the association between hypertensive retinopathy and blood pressure were low (47–72% and 32–67%, respectively).

Associations between retinal microvascular changes and cardiovascular risk were inconsistent, except for retinopathy and stroke. The increased risk of stroke, however, was also present in normotensive people with retinopathy. These studies did not adjust for other indicators of hypertensive organ damage.

▲ van den Born B-J H, Hulsman CAA, Hoekstra JBL, *et al.* Value of routine fundoscopy in patients with hypertension: systematic review. *BMJ* 2005;331:73.

ALLHAT suggests thiazides are as good as any other treatment in hypertension ► ALLHAT (antihypertensive and lipid-lowering treatment to prevent heart attack trial) was an active controlled trial in 31 512 adults, 55 years or older, with hypertension and at least one other risk factor for coronary heart disease, stratified into diabetes ($n = 13\,101$), impaired glucose tolerance ($n = 1399$), and normal ($n = 17\,012$) groups on the basis of national guidelines. Participants were randomly assigned to double blind, first step treatment with chlorthalidone 12.5–25 mg/day, amlodipine besylate 2.5–10 mg/day, or lisinopril 10–40 mg/day. In an intention-to-treat analysis of fatal coronary heart disease or non-fatal MI (primary outcome), total mortality, and other clinical complications, angiotensin converting enzyme inhibitors and calcium channel blockers showed no beneficial effects over other treatment in any group.

▲ Whelton PK, Barzilay J, Cushman WC, *et al.* for the ALLHAT Collaborative Research Group. Clinical outcomes in antihypertensive treatment of type 2 diabetes, impaired fasting glucose concentration, and normoglycemia: antihypertensive and lipid-lowering treatment to prevent heart attack trial (ALLHAT). *Arch Intern Med* 2005;165:1401–9.

Blood pressure targets in diabetic and non-diabetic patients ► Twenty seven randomised trials ($n = 158\,709$ participants) that included 33 395 individuals with diabetes and 125 314 without diabetes contributed to the analyses. For each outcome and each comparison summary, estimates of effect and 95% confidence intervals were calculated for patients with and without diabetes using a random effects model. Total major cardiovascular events were reduced to a comparable extent in individuals with and without diabetes by regimens based on angiotensin converting enzyme inhibitors, calcium antagonists, angiotensin receptor blockers, and diuretics/ β blockers ($p > 0.19$ for all by χ^2 test of homogeneity). There was limited evidence that lower blood pressure goals produced larger reductions in total major cardiovascular events in individuals with versus without diabetes ($p = 0.03$ by χ^2 test of homogeneity). This does not exclude such effects and UK guidelines still suggest harsher blood pressure targets in patients with diabetes.

▲ Blood Pressure Lowering Treatment Trialists' Collaboration. Effects of different blood pressure-lowering regimens on major cardiovascular events in individuals with and without diabetes mellitus: results of prospectively designed overviews of randomized trials. *Arch Intern Med* 2005;165:1410–19.

Sustained weight loss lowers risk of hypertension

► Weight loss was assessed among 623 overweight (BMI ≥ 25) middle aged (aged 30–49 years) and 605 overweight older (aged 50–65 years) adults in Framingham. Subjects were classified first according to the amount of weight lost over four years: (1) weight changed by less than 1.8 kg (stable weight); (2) lost 1.8 kg to less than 3.6 kg; (3) lost 3.6 kg to less than 6.8 kg; and (4) lost 6.8 kg or more. We also classified weight loss according to whether it was sustained during the next four years. After adjusting for age, sex, education, baseline body mass index, height, activity, smoking, and alcohol intake, weight loss of 6.8 kg or more led to a 21–29% reduction in long term hypertension risk. After adjusting for cancer or cardiovascular disease occurring during follow up, weight loss of 6.8 kg or more led to a 28% reduction in risk (relative risk (RR) 0.72, 95% CI 0.49 to 1.05) for middle aged adults and a 37% reduction (RR 0.63, 95% CI 0.42 to 0.95) for older adults. Sustained weight loss led to a 22% reduction in hypertension risk (RR 0.78, 95% CI 0.60 to 1.03) among middle aged and a 26% reduction (RR 0.74, 95% CI 0.56 to 0.97) in older adults. This risk reduction was strengthened by adjustment for prevalent cancer or cardiovascular disease during follow up.

▲ Moore LL, VISION AJ, Qureshi MM, *et al.* Weight loss in overweight adults and the long-term risk of hypertension: the Framingham study. *Arch Intern Med* 2005;165:1298–303.

GENERAL CARDIOLOGY

AF ablation reduces AF recurrence, but what about the need for warfarin? ► A randomised study of pulmonary vein isolation (PVI) with radiofrequency ablation ($n = 33$) compared to antiarrhythmic drug treatment ($n = 37$) has demonstrated the feasibility of PVI as a first line approach for treating patients with symptomatic atrial fibrillation (AF). At the end of one year follow up, 63% of the patients receiving drugs suffered at least one recurrence of symptomatic AF, compared to 13% of the patients treated with PVI ($p < 0.001$). The number of hospitalisations (54% v 9%) also decreased in the PVI group, and there was an improvement in quality of life as assessed by a short health survey. Moderate pulmonary vein stenosis was found in two patients in the PVI group. The authors stress the need for a multicentre randomised trial to investigate whether the benefits of AF ablation outweigh the inherent risks of an invasive procedure. In addition, it is certainly not clear if warfarin treatment can then be stopped or not.

▲ Wazni OM, Marrouche NF, Martin DO, *et al.* Radiofrequency ablation vs antiarrhythmic drugs as first-line treatment of symptomatic atrial fibrillation. *JAMA* 2005;293:2634–40.

Infective endocarditis: still rare but is *S aureus* increasing? ► Data from the International Collaboration on Endocarditis (ICE), a prospective observational cohort study set in 39 medical centres in 16 countries, has revealed the perhaps surprising discovery that *Staphylococcus aureus* was the most common pathogen among the 1779 cases studied. Although *S aureus* infective endocarditis (IE) is relatively infrequent at any individual institution, it appears that recent changes in health care delivery and in antimicrobial resistance patterns have changed the epidemiology of *S aureus* infections. Rates of both *S aureus* and methicillin resistant *S aureus* (MRSA) infection, especially as a cause of bacteraemia in those in contact with health services either as an inpatient or outpatient, have increased substantially, and those with implanted medical devices are naturally at high risk. However, a second study from the Mayo Clinic published in the same issue of *JAMA* found viridans group streptococci to be the most common cause of IE in Minnesota over the last three decades. Furthermore, no substantial change in the incidence of IE was noted. In an accompanying editorial, Vincent Quagliarello from Yale University highlights that in populations where injection drug abuse is uncommon, viridans streptococci remain a common underlying cause of IE. However, because of the increasingly invasive nature of modern medicine, an increase in the complications from *S aureus* endocarditis can be expected.

▲ Fowler VG, Miro JM, Hoen B, *et al.* *Staphylococcus aureus* endocarditis – a consequence of medical progress. *JAMA* 2005;293:3012–21.

▲ Tleyjeh IM, Steckelberg JM, Murad HS, *et al.* Temporal trends in infective endocarditis. *JAMA* 2005;293:3022–8.

Fish oils are not a panacea for arrhythmias ► Based on clinical studies showing a reduction in rates of sudden cardiac death in patients taking $\omega 3$ polyunsaturated fatty acids (PUFAs), Raitt and colleagues assigned 200 patients with implantable cardioverter-defibrillators (ICDs) and a recent episode of ventricular tachycardia (VT) or ventricular fibrillation (VF) to receive either a fish oil supplement or placebo and followed them up for a median of 718 days. By 24 months, 65% of patients randomised to receive fish oil had needed ICD therapy for VT/VF, compared with 59% of patients randomised to receive placebo ($p = 0.19$). Recurrent VT/VF events were overall more common in patients randomised to receive fish oil ($p < 0.001$). The authors therefore conclude that in high risk patients such as these, fish oil supplementation does not reduce the risk of VT/VF, and may even be proarrhythmic in some patients.

▲ Raitt MH, Connor WE, Morris C, *et al.* Fish oil supplementation and risk of ventricular tachycardia and ventricular fibrillation in patients with implantable defibrillators. *JAMA* 2005;293:2884–91.

The emergency medical team: expensive scare? ► The medical emergency team (MET) has been suggested as a method of spotting sick patients and preventing their deterioration and demise. Of 23 hospitals in Australia, some were randomised to continue functioning as usual ($n = 11$) and others to introduce a MET system ($n = 12$). The primary outcome was the composite of cardiac arrest, unexpected death, or unplanned intensive care unit (ICU) admission during the six month study period after MET activation. Analysis was by intention to treat. Introduction of the MET increased

the overall calling incidence for an emergency team ($3.1 \text{ v } 8.7$ per 1000 admissions, $p = 0.0001$). The MET was called to 30% of patients who fulfilled the calling criteria and who were subsequently admitted to the ICU. During the study, similar incidence of the composite primary outcome occurred in the control and MET hospitals ($5.86 \text{ v } 5.31$ per 1000 admissions, $p = 0.640$), as well as of the individual secondary outcomes (cardiac arrests, $1.64 \text{ v } 1.31$, $p = 0.736$; unplanned ICU admissions, $4.68 \text{ v } 4.19$, $p = 0.599$; and unexpected deaths, $1.18 \text{ v } 1.06$, $p = 0.752$). A reduction in the rate of cardiac arrests ($p = 0.003$) and unexpected deaths ($p = 0.01$) was seen from baseline to the study period for both groups combined. Thus the MET system does not seem to work as effectively as was expected.

▲ MERIT Study Investigators. Introduction of the medical emergency team (MET) system: a cluster-randomised controlled trial. *Lancet* 2005;365:2091–7.

Detecting loss of biventricular pacing from the surface ECG ► Loss of left ventricular capture in patients with cardiac resynchronisation devices may account for worsening heart failure and can be difficult to diagnose without a programmer. After analysis of the R–S spike ratio in the 12 lead ECG during right ventricular and biventricular pacing in 10 patients, an algorithm to detect loss of left ventricular capture was developed. Fifty four patients with a cardiac resynchronisation device and underlying left bundle branch block were then assessed. Leads V1 and I of a 12 lead ECG were assessed after biventricular pacing was confirmed and after the device was programmed to right ventricular pacing only (simulating loss of left ventricular capture). The sensitivity of the algorithm to correctly identify loss of left ventricular capture was 94% (95% CI 88.2% to 97.7%), and the specificity was 93% (95% CI 86.3% to 95.8%). The likelihood ratio of a positive test result was 12.8 (95% CI 6.443 to 23.310), and the likelihood ratio of a negative test result was 0.06 (95% CI 0.024 to 0.137).

▲ Ammann P, Sticherling C, Kalusche D, et al. An electrocardiogram-based algorithm to detect loss of left ventricular capture during cardiac resynchronization therapy. *Ann Intern Med* 2005;142:968–73.

Moderate aortic stenosis and CABG needed: do the valve as well? ► From 1985 to 1995 all patients at one institution who underwent coronary artery bypass graft surgery (CABG) and who had the echocardiographic diagnosis of mild (mean gradient < 0 mm Hg and/or valve area $> 1.5 \text{ cm}^2$) or moderate (mean gradient ≥ 30 and ≤ 40 mm Hg and/or valve area > 1.0 and $\leq 1.5 \text{ cm}^2$) aortic stenosis were assessed. Using propensity analysis, survival was compared between 129 patients who underwent CABG alone and 78 patients who underwent concomitant CABG and aortic valve replacement. Admittedly, this was not a randomised comparison. Perioperative mortality was similar among patients who underwent CABG alone compared with patients who underwent concomitant CABG and aortic valve replacement. By Kaplan-Meier analysis, one year and eight year survival were better at 90% and 55% for patients who underwent concomitant CABG and aortic valve replacement compared with 85% and 39% for patients who underwent CABG alone ($p < 0.001$). This benefit was limited to patients with moderate aortic stenosis (propensity adjusted RR 0.43, 95% CI 0.20 to 0.96; $p = 0.04$).

▲ Pereira JJ, Balaban K, Lauer MS, et al. Aortic valve replacement in patients with mild or moderate aortic stenosis and coronary bypass surgery. *Am J Med* 2005;118:735–42.

Journals scanned

American Journal of Medicine; American Journal of Physiology: Heart and Circulatory Physiology; Annals of Emergency Medicine; Annals of Thoracic Surgery; Archives of Internal Medicine; BMJ; Chest; European Journal of Cardiothoracic Surgery; Lancet; JAMA; Journal of Clinical Investigation; Journal of Diabetes and its Complications; Journal of Immunology; Journal of Thoracic and Cardiovascular Surgery; Nature Medicine; New England Journal of Medicine; Pharmacoeconomics; Thorax

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IMAGES IN CARDIOLOGY

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Multiple ventricular thrombus in HIV cardiomyopathy

A 46 year old woman with a history of dilated cardiomyopathy, an ejection fraction of 10% and a left ventricular thrombus, HIV, hypertension, and a history of hepatitis B, was admitted with increasing shortness of breath, paroxysmal nocturnal dyspnoea (PND), orthopnoea, and pedal oedema over a three week period. On admission, the patient was in respiratory distress and hypertensive. Her cardiovascular examination showed tachycardia and an S3, and her respiratory examination revealed crackles throughout; she also had pedal oedema. The patient was admitted and treated for pulmonary oedema with aggressive diuresis. On the second day after admission the patient had a cardiac arrest and was resuscitated, requiring endotracheal intubation. Subsequent to this episode the patient became hypotensive; she also had fevers and a chest x ray showed a left lower lobe infiltrate. She was treated for sepsis and started on fluids and noradrenaline (norepinephrine). A two dimensional echocardiogram showed a dilated left and right ventricle with an ejection fraction of 10%, and two thrombi—one measuring 4.1×3.2 cm and the other 1.2×1.6 cm (panel). Both thrombi were freely mobile, with the large one almost obliterating the left ventricular cavity; there was also a hint of a right ventricular thrombus. The patient was started on dobutamine and weaned off noradrenaline. Her blood pressure stabilised over the next few days and her fluid boluses were stopped; she was also placed on anticoagulation with enoxaparin. However, on day 5 after admission, the patient had an embolic stroke in the right gangliocapsular

region. A repeat echocardiogram no longer revealed any thrombus. The patient was eventually discharged with minimal signs of the stroke. She was clinically stable at six months follow up.

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