JournalScan

Iqbal Malik, Editor

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ISCHAEMIC HEART DISEASE

The Mediterranean diet may save lives ► A total of 74 607 men and women, aged 60 years or more, without coronary heart disease, stroke, or cancer at enrolment and with complete information about dietary intake and potentially confounding variables, were assessed in the EPIC-elderly study. An increase in the modified Mediterranean diet score (a composite score which includes nine components of a Mediterranean diet such as legumes, fruit, cereal, alcohol intake, etc) was associated with lower overall mortality, a two unit increment corresponding to a significant reduction of 8% (95% confidence interval (CI) 3% to 12%). No significant evidence of heterogeneity was found among countries in the association of the score with overall mortality even though the association was stronger in Greece and Spain.

▲ Trichopoulou A, Orfanos P, Norat T, *et al*. Modified Mediterranean diet and survival: EPIC-elderly prospective cohort study. *BMJ* 2005;**330**:991.

No end in site for CHD just yet ► The incidence of ST elevation myocardial infarction (MI) is decreasing as is coronary heart disease (CHD) mortality over the course of time. This population based study looked at trends in less severe brands of CHD, namely angina. The age adjusted annual relative changes were −3.6% (95% CI −4.8% to −2.4%; $p < 0.001$) for all major coronary events, +2.6% (95% CI 1.1% to 4.0%; $p < 0.001$) for first diagnosed angina, and −0.8% (95% CI −1.8% to 0.3%; $p = 0.18$) for first diagnosed coronary heart disease. The fall in major coronary events occurred across all categories of event (fatal and non-fatal, first and recurrent). The increase in angina may well reflect earlier and better diagnosis rather than a genuine increase over time.

▲ Lampe FC, Morris RW, Walker M, *et al*. Trends in rates of different forms of diagnosed coronary heart disease, 1978 to 2000: prospective, population based study of British men. *BMJ* 2005;**330**:1046.

Antibiotics do not reduce the risk of CHD events ► Both the ACES (azithromycin and coronary events study) trial by Grayson *et al* and the PROVE IT–TIMI (pravastatin or atorvastatin evaluation and infection therapy–thrombolysis in myocardial infarction) study by Cannon *et al* confirm the same thing: in large scale randomised controlled trials in stable angina and in acute coronary syndromes, antibiotic treatment against *Chlamydia pneumoniae* does not reduce CHD risk. Although the infection leading to atherosclerosis hypothesis is not totally discounted, it has become harder to confirm. Acute and chronic infections, by increasing the inflammatory milieu, can plausibly accelerate atherosclerosis.

▲ Grayston JT, Kronmal RA, Jackson LA, *et al*. Azithromycin for the secondary prevention of coronary events. *N Engl J Med* 2005;**352**:1637–45.

▲ Cannon CP, Braunwald E, McCabe CH, *et al*. Antibiotic treatment of Chlamydia pneumoniae after acute coronary syndrome. *N Engl J Med* 2005;**352**:1646–54.

HYPERTENSION

Thiazide diuretics first line in all patients ► ALLHAT is the first large scale trial looking at the effect of dihydropyridine calcium channel blockers (CCBs) and angiotensin converting enzyme (ACE) inhibitors on cardiovascular outcomes that includes a significant number of black participants; approximately a third of all participants were black. A subgroup analysis of the blood pressure effects of these drugs in black patients confirmed that, as was the case in the cohort as a whole, neither ACE inhibition nor CCBs were more effective than a thiazide-type diuretic (chlorthalidone) in preventing the primary outcome of fatal CHD or non-fatal MI, or any other major cardiovascular or renal outcome. Furthermore, diuretic based treatment was found to be superior to ACE inhibitors in reducing the incidence of heart failure. Therefore in black patients with hypertension, but without renal disease or heart failure, the authors suggest the use of a thiazide diuretic as an initial line of treatment. If this is not possible, a CCB is proposed as the next best alternative, based on data from the study showing a greater risk of stroke, combined CHD, combined cardiovascular disease, and angio-oedema with ACE inhibition.

▲ Wright JT, Dunn JK, Cutler JA, *et al*. Outcomes in hypertensive black and non-black patients treated with chlorthalidone, amlodipine, and lisinopril. *JAMA* 2005;**293**:1595–608.

GENERAL CARDIOLOGY

Multi-slice CT scanning as the new ''gold standard'' to diagnose PE ► The days of V/Q scanners are ended, and the modern investigation of possible pulmonary embolism (PE) is to do a D-dimer test. If negative, then the diagnosis is excluded, but if positive, a multislice computed tomographic (CT) scan excludes significant PE, without the need for ultrasonography. The Geneve study by Perrier *et al* validates this strategy. The three month risk of PE would have been 1.5% if D-dimers and CT scanning were used alone without ultrasonography, similar to in studies with negative pulmonary angiography. CT scanning to include the pelvic veins would have picked up the few cases of venous thrombosis with negative CT chest scan. The authors suggest a larger outcome study is needed, but the approach already looks convincing.

▲ Perrier A, Roy P-M, Sanchez O, *et al*. Multidetector-row computed tomography in suspected pulmonary embolism. *N Engl J Med* 2005;**352**:1760–8.

Amiodarone is superior to sotalol to maintain sinus rhythm after atrial fibrillation ► In this double blind, placebo controlled trial, 665 patients who were receiving anticoagulants and had persistent atrial fibrillation were randomly assigned to receive amiodarone (267 patients), sotalol (261 patients), or placebo (137 patients) and monitored for 1–4.5 years. The primary end point was the time to recurrence of atrial fibrillation beginning on day 28, determined by means of weekly transtelephonic monitoring. Spontaneous conversion occurred in 27.1% of the amiodarone group, 24.2% of the sotalol group, and 0.8% of the placebo group, and direct current cardioversion failed in 27.7%, 26.5%, and 32.1%, respectively. The median times to a recurrence of atrial fibrillation were 487 days in the amiodarone group, 74 days in the sotalol group, and six days in the placebo group according to intention to treat. Amiodarone was superior to sotalol ($p < 0.001$) and to placebo ($p < 0.001$), and sotalol was superior to placebo ($p < 0.001$). However, in patients with ischaemic heart disease, the median time to a recurrence of atrial fibrillation was 569 days with amiodarone treatment and 428 days with sotalol treatment ($p < 0.53$). Restoration and maintenance of sinus rhythm significantly improved the quality of life and exercise capacity. The study was not powered to assess mortality.

▲ Singh BN, Singh SN, Reda DJ, *et al*, for the Sotalol Amiodarone Atrial Fibrillation Efficacy Trial (SAFE-T) Investigators. Amiodarone versus sotalol for atrial fibrillation. *N Engl J Med* 2005;**352**:1861–72.

CRT is coming of age ► The comparison of medical therapy, pacing, and defibrillation in heart failure (COMPANION) trial evaluated the effect of cardiac resynchronisation therapy (CRT), with or without an implantable cardioverter-defibrillator (ICD), on survival. Mortality from all causes was significantly reduced by the combination of CRT and use of an ICD (hazard ratio (HR) 0.64; $p = 0.003$); the reduction in mortality from all causes with CRT alone was slightly less pronounced and not significant (HR 0.76; $p = 0.059$). The cardiac resynchronization–heart failure (CARE-HF) trial, reported by Cleland *et al*, demonstrated that CRT alone prolongs survival in patients with advanced congestive heart failure. Study participants were patients with New York Heart Association (NYHA) functional class III or IV congestive heart failure and a left

ventricular ejection fraction of 35% or less who were randomly assigned to either standard medical treatment alone or standard medical treatment plus CRT. Resynchronisation therapy significantly reduced the incidence of the primary end point (the time to death or an unplanned hospitalisation for a major cardiovascular event). In addition, however, mortality from all causes was significantly reduced, from 30% in the medical treatment group to 20% in the CRT group (HR 0.64; $p < 0.002$). As compared with the control group, the CRT group also had significant improvements in indexes of left ventricular function, symptoms, and quality of life.

▲ Bristow MR, Saxon LA, Boehmer J, *et al*. Cardiac-resynchronization therapy with or without an implantable defibrillator in advanced chronic heart failure. The COMPANION study. *N Engl J Med* 2004;**350**:2140–50.

▲ Cleland JGF, Daubert J-C, Erdmann E, *et al*, for the Heart Failure (CARE-HF) Study Investigators. The effect of cardiac resynchronization on morbidity and mortality in heart failure. *N Engl J Med* 2005;**352**:1539–49.

Population screening with BNP? ► The prognostic value of B-type natriuretic peptide (BNP) has already been established in patients with heart failure and acute coronary syndromes, and it can predict cardiovascular disease in apparently healthy individuals. Kistorp and colleagues looked at 626 patients aged 50–89 years over the course of five years, during which 94 participants died and 65 developed a first major cardiovascular event. After adjusting for the traditional cardiovascular risk factors, values above the 80th centile of BNP were associated with mortality (HR 1.96, compared to 1.46 for BNP and 1.88 for urinary albumin/creatinine ratio). Adjustment for poor left ventricular function did not notably change the predictive value (HR 1.82). Furthermore, raised BNP concentrations were associated with first major cardiovascular events with an adjusted HR of 3.24, compared to 1.02 for C reactive protein (CRP) and 2.32 for urinary albumin/creatinine ratio, when comparing participants with values above the 80th centile with those with values equal to or below the 80th centile. The finding that CRP does not contribute to risk stratification in older non-hospitalised individuals is at odds with data from younger individuals in which it seems to be a stronger risk marker. The authors suggest their findings should be confirmed in a larger scale study in other populations.

▲ Kistorp C, Raymond I, Pedersen F, *et al*. N-terminal pro-brain natriuretic peptide, C-reactive protein, and urinary albumin levels as predictors of mortality and cardiovascular events in older adults. *JAMA* 2005;**293**:1609–16.

Over or under dosing placebo is associated with adverse risk in trials ► Incorrect dosing of alteplase has been associated with worse clinical outcomes in patients. However, those at high risk of adverse events are also more prone to dosing errors, thus making the relation difficult to interpret. Mehta and colleagues examined data from the ASSENT-2 (assessment of the safety and efficacy of a new thrombolytic) to find out whether this adverse relation is in fact due to cause and effect or to confounding. Looking at 16 949 patients, 4.9% of those who received alteplase and 4.6% of those who received alteplase placebo received incorrect doses. Patients receiving incorrect doses were more likely to be older, female, black, shorter, have lower body weight and systolic blood pressure, and have a higher Killip class at presentation. Thirty day mortality was higher in patients who received an overdose (9.8%) or underdose (19.5%) of alteplase compared to those who received a correct dose (5.4%). The same pattern was present in patients who received an alteplase placebo (10.0% for overdose, 23.5% for underdose, and 5.4% for correct dose). However, the excess risk of death, intracranial haemorrhage, and bleeding associated with incorrect dosing of alteplase was noted in both the active and placebo groups, thus suggesting that most, if not all, of the association between incorrect dosing of alteplase and adverse outcome was due to confounding factors (that is, the patient characteristics listed above), rather than resulting directly from incorrect dosing.

▲ Mehta RH, Alexander JH, Van de Werf F, *et al*. Relationship of incorrect dosing of fibrinolytic therapy and clinical outcomes. *JAMA* 2005;**293**:1746–50.

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