Short cuts

What's new in the other general journals

Angioplasty is beneficial if thrombolysis fails

What is the best treatment for patients with acute myocardial infarction when thrombolysis fails? It's an important question because intravenous thrombolysis restores good blood flow in the infarct related artery in only about 60% of cases. Some doctors, especially in hospitals without interventional facilities, treat such patients conservatively. Another option is to try a second dose of a thrombolytic agent. Small trials have suggested that percutaneous coronary intervention is justified, but current guidelines recommend it only for high risk patients.

The results of a multicentre trial in Britain now indicate that angioplasty is probably best for everyone. In the trial 427 patients in whom thrombolytic treatment had failed (judged by lack of ST segment resolution) were randomly assigned to repeated thrombolysis, conservative therapy, or emergency percutaneous coronary intervention. The primary end point was a composite of death, reinfarction, stroke, or severe heart failure within six months. Event-free survival was significantly better among patients assigned to rescue angioplasty, even though a substantial proportion of the patients treated in this way had to be transferred from hospitals without interventional facilities. In comparison with the group receiving repeated thrombolysis, their treatment was delayed by a median time of 84 minutes. There were no differences in rates of major bleeding complications between groups, although minor bleeding episodes, mostly at the access site, occurred in more than 20% of those treated percutaneously.

N Engl J Med 2005;353:2758-68

Dietary antioxidants may help prevent age related macular degeneration

Age related macular degeneration is the commonest cause of irreversible blindness in elderly people. We know little about its causation, but—because the retina may be particularly susceptible to oxidative stress owing to its high concentrations of oxygen, polyunsaturated fatty acids, and photosensitisers—it's thought that levels of antioxidant vitamins may be important. A randomised controlled trial found that high doses of β carotene, vitamins C and E, and zinc tended to slow progression in people with established disease, but epidemiological studies that have investigated whether these antioxidants influence risk of developing macular degeneration have reported inconsistent findings.

Analysis of longitudinal data from a cohort of middle aged and elderly people living in the Netherlands now lends support to the idea. The study involved nearly 6000 people who, when examined by an ophthalmologist at the time of recruitment, were free of features of macular disease. During a mean follow up of eight years, 560 participants developed signs of macular degeneration—mainly those of the early stages of the disease. High dietary intake of β carotene, vitamins C and E, and zinc, estimated by a food frequency questionnaire at baseline, was associated with a reduced risk of developing macular degeneration. In people whose intake of all four nutrients had been above the median values for the cohort as a whole, risk was reduced by 35%. Excluding users of vitamin supplements from the analysis did not affect the results.

JAMA 2005;294:3101-7

Perioperative amiodarone prevents atrial tachyarrhythmias

Atrial fibrillation is by far the commonest postoperative complication of cardiac surgery, with an incidence of 30-40%. It often leads to neurological, renal, and infectious complications, especially when the arrhythmia is recurrent. Risk increases steeply with age, and, as the number of elderly people presenting for cardiac surgery increases, it is likely to become an even commoner problem.

Results of a randomised trial indicate that amiodarone given perioperatively is an

effective prophylactic measure. The study recruited 600 patients receiving non-emergency cardiac surgery. Treatment with amiodarone (or placebo) started six days before surgery and continued for six days afterwards. Overall, atrial tachyarrhythmias occurred substantially less often in patients receiving amiodarone than in patients given placebo (16.1% v 29.5%). The beneficial effect was present in all age groups and was seen regardless of the type of operation performed. There were no differences in serious postoperative complications, in-hospital mortality, readmission to hospital within six months of discharge, or mortality within one year. No major adverse events occurred as a result of amiodarone, although the dose had to be reduced in 11% of patients, largely because of bradycardia or QT prolongation.

Whether reducing the postoperative incidence of atrial arrhythmias will translate into shorter hospital stays for patients isn't yet clear. There were no significant differences in time spent in intensive care or in hospital between the two treatment groups.

JAMA 2005;294:3093-100

Intensive control of type 1 diabetes reduces cardiovascular risk

Achieving normoglycaemia, or something close to it, is well established as an effective way of reducing the risk of microvascular and neurological complications of type 1 diabetes. But whether long term glycaemic control can also reduce the risk of cardiovascular disease is another matter. Data from a group of diabetic patients who took part in a randomised controlled trial of intensive therapy 17 years earlier now make it clear that it can.

Between 1983 and 1993, 1441 patients with type 1 diabetes, aged 13-40 years, were

recruited to the diabetes control and complications trial and randomly assigned to intensive or conventional therapy and treated for a mean of 6.5 years. When the trial closed all participants were offered help in initiating intensive insulin therapy and encouraged to join a follow-up observational study: 93% agreed to do so and were followed until 2005.

During the mean 17 years of follow-up, 46 cardiovascular disease events occurred in patients who had received intensive treatment from the start, compared with 98 events in patients who had received conventional treatment. Intensive treatment reduced the risk of any cardiovascular disease event by 42% and the risk of non-fatal myocardial infarction, stroke, or death from cardiovascular disease by 57%. The results strongly suggest that the intensive diabetes control during the original trial had a sustained effect on the risk of cardiovascular disease.

The author of an accompanying editorial is worried by how long it takes for findings like these to influence clinical practice. A first step, he suggests, would be to consider whether current glycaemic targets for diabetic patients are pitched at the right level, bearing in mind that they were set to prevent microvascular complications not cardiovascular disease.

N Engl J Med 2005;353:2643-53

Confirmation that aromatase inhibitors are superior to tamoxifen in the adjuvant treatment of breast cancer

Unlike tamoxifen, which inhibits the activity of oestrogen by competitively binding to oestrogen receptors, aromatase inhibitors block the conversion of androgens to oestrogens and reduce oestrogen concentrations in tissue and plasma. The latest in a series of randomised comparisons of third generation aromatase inhibitors, in this case letrozole, with tamoxifen as adjuvant therapy for breast cancer in postmenopausal women confirms that these drugs are superior to tamoxifen.

More than 8000 women with hormone receptor positive cancer were randomised to postoperative treatment with either tamoxifen or letrozole. The five year survival rates were 84.0% in the letrozole group

compared with 81.4% in the tamoxifen group ($P = 0.003$). A new finding is that letrozole reduced the incidence of both distant recurrence and contralateral breast cancers. The benefit was greatest in patients who had also received chemotherapy, who did not receive radiotherapy, and who had positive nodes. Longer follow-up is required to determine whether letrozole continues to reduce the risk of relapse for several years after the end of treatment, as has been shown for tamoxifen.

As an accompanying editorial points out, important questions remain. What is the optimal duration of treatment with an aromatase inhibitor? Which aromatase inhibitor is best? Is sequential treatment better than monotherapy, and, if so, should tamoxifen or an aromatase inhibitor be given first? Ongoing trials should provide answers.

N Engl J Med 2005;353:2747-57

Having a sibling with cardiovascular disease increases individual risk

Diseases often run in families and, despite the obvious fact that family members share many things other than their DNA, it's usually assumed that the reason is genetic. Cardiovascular disease is no exception. Having an affected parent more or less doubles an individual's risk, but how strongly disease in a sibling influences risk has been less clear. Data from the Framingham offspring study now show that cardiovascular disease in a sibling is associated with around a 50% increase in risk of cardiovascular events.

The strengths of this study are its prospective design, the validation of cardiovascular events from medical records, direct measurement of other risk factors among participants, and the availability of information about parents. The investigators were able to show that the increase in risk conferred by the presence of disease in a sibling was independent of whether either parent had cardiovascular disease and that it could only partly be explained by traditional risk factors. Among the possible explanations for the increased risk are shared environmental exposures in early life as well as a shared genetic background.

A weakness of the study is that the Framingham cohorts are predominantly white, which may limit the generalisability of the findings to other ethnic groups. Even so, the investigators suggest that it might be worth incorporating a history of sibling cardiovascular disease into existing risk prediction and prevention algorithms.

JAMA 2005;294:3117-23

Walking slows functional decline in peripheral arterial disease

"Stop smoking and keep walking" is an invariable prescription for patients with intermittent claudication, so you could be

forgiven for assuming that this advice is soundly based. But, while it's true that supervised walking on treadmills is well established as effective, there's no direct evidence that the unsupervised sort of walking that we ask our patients to take is as useful.

The results of a study from Chicago, in which 400 men and women with peripheral arterial disease were followed for three years, are reassuring. Participants who reported walking for exercise three or more times a week at baseline and at subsequent annual visits showed a considerably smaller average annual decline in how far and how fast they could walk compared with those who exercised less frequently. Adjustment for smoking habit, ethnicity, sex, body mass index, and comorbid conditions did not affect the findings. Neither did taking account of treatment with aspirin, statins, or angiotensin converting enzyme inhibitors.

The editors' notes accompanying the paper say that observational studies such as this one cannot prove a causal relation between walking frequency and functional decline. Strictly speaking, of course, this is true; on the other hand, it's hard to see the point of publishing the paper if no inferences about cause and effect should be drawn.

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