Short cuts

What's new in the other general journals

Sharp rise in stress related cardiomyopathy after Japanese earthquakes

In October 2004 three powerful earthquakes hit the centre of Niigata in Japan, and the aftershocks, which eventually numbered about 90, went on for weeks. A retrospective look at cardiac admissions to the eight hospitals in the area found 52 people who had an acute cardiovascular event in the week after the earthquakes. This was a significant increase on the four weeks before the earthquakes and on the corresponding four weeks in 2002 and 2003.

The cardiovascular events included an increase in sudden cardiac death, but the most noticeable feature was a sharp rise in the number of people admitted with "takotsubo" cardiomyopathy, a reversible ventricular dysfunction thought to be caused by stress. There were 25 cases in the four weeks after the earthquakes, compared with only one case in the previous four weeks and none or one in the same four weeks in 2002 and 2003 ($P < 0.001$).

This is the first study to show a link between a natural disaster and stress related cardiomyopathy. The authors suggest that, as there were no extra admissions for acute coronary syndrome after these quakes, the increase in sudden deaths was at least partly due to stress related cardiomyopathy. It's impossible to say for certain because people who died suddenly did not have postmortem examinations.

JAMA 2005;294:305-7

Diagnostic aid for deep vein thrombosis score can't replace clinical judgment

Accurate diagnosis of deep vein thrombosis has always been a challenge, and various clinical scoring systems are available to help doctors get it right. The nine point version of the Wells score is one of the most popular, although it seems to be more accurate in hospitals than in primary care settings, according to two recent papers.

In the first paper, a meta-analysis of 54 studies, the Wells score seemed to be good for categorising patients in clinics or emergency departments as at high or low risk of deep vein thrombosis: a low score had a negative likelihood ratio of 0.25 (good for ruling out thrombosis) and a high score had a positive likelihood ratio of 5.2 (good for ruling in thrombosis and referring for more definitive tests such as venography). In the second paper, a cross sectional study of 1295 primary care patients from the Netherlands, the Wells score looked less promising; 12% of patients with a low score had a deep vein thrombosis, which translates as a negative likelihood ratio of 0.48, nearly double the ratio reported by the meta-analysis. A low Wells score plus a negative D-dimer test was more accurate—3% of these patients had a deep vein thrombosis—but not accurate enough to safely defer definitive testing, say the authors.

An accompanying editorial (pp 140-2) concludes that the Wells score probably performs differently in different clinical settings and should be evaluated accordingly. In the meantime, doctors should also use their own clinical judgment—as they always have.

Annals of Internal Medicine 2005;143:100-7, 129-39

More than a third of US adults take the discredited supplement vitamin E

It now seems clear that the antioxidant vitamin E does not help anyone live longer or avoid heart disease, cancer, or dementia. Doses above 400 IU a day may even increase mortality, a message that has so far failed to reach the 37% of US adults who supplement their diet with vitamin E.

Data from the latest nation health and nutrition examination survey—a representative sample of 4609 American adults—shows that 11% take ≥ 400 IU of vitamin E a day, and a further 26% take smaller doses. In this survey, vitamin E was

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most popular among older people and those with diabetes, stroke, or heart disease. Men and women were equally likely to take supplements containing vitamin E, a habit that was reflected in their serum concentrations of α -tocopherol. Most of the respondents who took vitamin E also took vitamin C, and between a half and two thirds took β -carotene.

The message is clear, says one commentator (pp 143-5): people should not be using vitamin E to prevent heart disease, cancer, or dementia, and the 24 million US adults taking ≥ 400 IU a day should be warned that it could endanger their health.

Annals of Internal Medicine 2005;143:116-20

Elderly Australian men have more reproductive health problems but fewer worries

We already know that men's reproductive and sexual health deteriorates with age. To help quantify the problem in developed countries with rapidly ageing populations, researchers surveyed 5990 randomly selected middle-aged and older men from across Australia (achieving a response rate of 78%).

As expected, the percentage of men reporting erectile dysfunction, lower urinary tract symptoms, or prostate disease increased rapidly with age—from 12% of men aged 40-49 to 80% of those aged over 70. Severe erectile dysfunction was extremely common (40%) among men over 70, and nocturia was the commonest (41%) urinary symptom. Despite these problems, 37% of men over 70 said they were still sexually active and enjoyed sex as much as younger men, rating it 2.1 on a scale of 1 (delightful) to 6 (very unsatisfactory). In this ethnically diverse survey, respondents of Italian origin were most likely to report

erectile problems to the researchers and among the least likely to report them to doctors. Overall, only a third of men with erectile dysfunction sought medical advice.

Older men reported substantially more problems than younger men, but seemed to worry less about them. Only a fifth of the men over 70 with erectile dysfunction said they were concerned about it, while over four fifths of men between 40 and 60 with perfectly good erectile function worried about losing it.

Lancet 2005;366:218-24

Buccal midazolam is better than rectal diazepam at stopping seizures in children

As an emergency treatment for children with seizures, buccal midazolam works better, faster, and for longer than rectal diazepam, according to a large randomised trial. The trial, which was conducted in four emergency departments in the United Kingdom, included 177 children with a median age of 3 years who had had 219 separate episodes of seizure. Treatment with about 0.5 mg/kg of buccal midazolam was more likely to be successful than the same dose of rectal diazepam, where success was defined as stopping the seizures within 10 minutes without respiratory depression and with no recurrence within an hour (61/109 (56%) *v* 30/110 (27%); adjusted odds ratio 4.1 (confidence interval 2.2 to 7.6)). Seizures treated with buccal midazolam stopped faster (median 8 minutes *v* 15 minutes, $P=0.01$) than those treated with diazepam and were less likely to recur within an hour (10/71 (14%) *v* 15/45 (33%); $P=0.02$).

This was a pragmatic trial with no blinding, no concealed allocation of treatments, and no prior informed consent from parents. About half the children were already taking antiepileptic drugs and about a third had had emergency treatments on the way to hospital—usually rectal diazepam. Even so, the authors and a linked editorial (pp 182-3) think the findings are robust and important. Buccal midazolam is easy to give and more

acceptable to some parents than rectal diazepam. It also seems to be safe. In this trial, only about 1 in 20 children in each group had clinically significant respiratory depression.

Lancet 2005;366:205-10

Insulin resistance linked to heart failure in Swedish men

Researchers from Sweden have found a new risk factor for congestive heart failure. In a large cohort study, insulin resistance predicted the development of heart failure among 1187 older Swedish men. The researchers measured insulin resistance using the euglycaemic insulin clamp technique and found that a 1 standard deviation decrease in insulin resistance reduced the risk of heart failure by about a third (hazard ratio 0.66 (95% confidence interval 0.51 to 0.86)). The men were all free of heart failure and valve disease when the study began, and the analyses were adjusted for other risk factors for heart failure including diabetes. The men were followed up for a mean of 8.9 years, during which time 104 developed congestive heart failure.

As expected, obese men also had a higher risk of heart failure (hazard ratio for 1 standard deviation increase in body mass index 1.35 (1.11 to 1.65)), although the link disappeared when adjusted for insulin resistance. The authors think that this is because obesity does not cause heart failure directly, but via its well known effects on glucose metabolism.

JAMA 2005;294:334-41

Carboplatin works as well as adjuvant radiotherapy for stage I seminoma

Men with stage I seminoma have been treated with orchidectomy and adjuvant radiotherapy for over 50 years. It works, but the radiation causes well documented side effects, including further cancers. Reserving the radiotherapy for patients who relapse is one established alternative. Replacing radiation with carboplatin is the third and newest option, and it looked as effective as routine radiotherapy in a recent head to head trial.

The trial included 1477 men with stage I seminoma. They had an orchidectomy followed by either one dose of carboplatin or a course of radiotherapy. Three years later, relapse-free survival was 95.9% in the radiotherapy group and 94.8% in the carboplatin group (hazard ratio 1.28, 95% confidence interval 0.85 to 1.93). Since the trial was big enough to detect any difference greater than 3%, the authors conclude that carboplatin is at least as effective as radiotherapy. It was also less toxic in the short term: patients who had carboplatin were less lethargic and were able to return to work faster than the patients given radiotherapy. It's too early to say for certain whether carboplatin reduces the risk of second cancers, although 10 of the 885 patients given radiotherapy developed a second germ cell primary, compared with only two of the 560 patients given carboplatin (five year rate 1.96% *v* 0.54%, $P=0.04$). The authors plan a 10 year follow up to find out more about the comparative safety of these two effective treatments.

Lancet 2005;366:293-300

Statins do not prolong survival in patients with diabetes and end stage renal failure

Since statins help prevent cardiovascular events in people with type 2 diabetes, you might expect they would do the same or better for the high risk subgroup having long term haemodialysis for renal failure. But in one large trial, patients who took atorvastatin for a median of four years were no less likely to have a heart attack or a stroke or to die from cardiac causes than patients who took a placebo (relative risk 0.92, 95% confidence interval 0.77 to 1.1; $P=0.37$). Atorvastatin (20 mg daily) did reduce the risk of all cardiac events combined, but not by much (relative risk 0.82, 0.68 to 0.99), and it had no impact on cerebral events combined or on mortality from all causes.

The trial, which was carefully double blinded, included 1255 patients with type 2 diabetes and end stage renal failure who had been having haemodialysis for less than two years. Serum concentrations of low density lipoprotein cholesterol fell by 42% (from 3.13 mmol/l to 1.86 mmol/l) in the patients given atorvastatin, and the authors say this should have reduced their risk of cardiovascular events by about 30%.

They are not sure why it didn't, but speculate that end stage renal failure changes the pathogenesis of cardiovascular disease in ways we don't yet understand.

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