



## MIXED BAG

### WHAT ARE THE RISKS AFTER A TIA?

Transient ischaemic attacks (TIAs) are relatively common. They are generally seen as a warning of future, and possibly imminent, vascular events. But, as Van Wijk and colleagues point out in a recent paper in *The Lancet*, determinants of survival and risk of vascular events after TIA or minor ischaemic stroke are not well defined in the long term. Worldwide, fatality rates from cerebrovascular disease have fallen, but stroke remains a serious neurological problem, leaving most patients with chronic disability. Secondary stroke prevention, according to these authors, is standard practice after TIA or minor ischaemic stroke, but many of these people carry on to a recurrent stroke or other vascular complications. Clinical studies of further stroke, myocardial infarction and death from vascular causes have so far not lasted longer than 3 - 5 years. Findings to date are that the 5-year cumulative risk of recurrent stroke is 22.5% and that major determinants of recurrence are advanced age, haemorrhagic index, stroke and diabetes. In cohorts from clinical trials, the annual risk of vascular events ranged from 4% to 11% if the presumed cause of cerebral ischaemia was arterial disease. The corresponding estimate for population-based surveys is 9% per year. This team provide one of the few long-term studies of the long-term risk of death and vascular events in patients with TIA or minor stroke of arterial origin. They also studied changes in risk over time and identified any independent predictors of mortality and vascular events.

The team assessed the survival status and occurrence of vascular events in 2 473 participants in the Dutch TIA Trial. The patients were recruited between 1986 and 1989 and had an arterial cause of cerebral ischaemia. Researchers measured all-cause mortality, the composite event of death from all vascular causes, non-fatal stroke and non-fatal myocardial infarction.

Follow-up was complete in 2 447 patients. After an average of 10.1 years, 1 489 patients (60%) had died and 1 336 (54%) had suffered at least 1 vascular event. The 10-year risk of death was 42.6%. The 10-year risk of a vascular event was 44.1%. Independent risk factors were age over 65 years, diabetes, history of claudication, previous peripheral vascular surgery and pathological Q waves on baseline ECG. Event-free survival over 10 years was 48%. The risk of a vascular event was highest immediately after the ischaemic event, reached its lowest point at about 3 years and gradually rose thereafter. The same pattern was seen for the risk of stroke during the first 3 years. But, the risk of mortality gradually rose throughout the study. These changes in the risk of ischaemic events and stroke over time have not been seen in other studies. The authors suggest that one explanation for the raised risk after 3 years may be that people's drug compliance is reduced and that they may not pay as much attention to lifestyle factors. A

physiological reason could be that the unstable plaque causing the initial event might become stable, and additional attention to lifestyle factors could slow the ongoing process of atherosclerosis. This explanation is supported by evidence that risk-factor modification does lead to reduced formation of new lesions, reduced progression of lesions and, in some cases, actual regression.

The authors concluded that their hospital-based study of long-term prognosis after TIA or minor ischaemic stroke shows that the risk of death remains high, and the risk of a vascular event increases even after 3 years. These findings imply that further improvements can be made in long-term secondary prevention of vascular disease in these patients.

Van Wijk I, *et al. Lancet* 2005; **365**: 2098-2104.

### ANEURYSM REPAIR

Those with abdominal aortic aneurysm are, not infrequently, in poor health and unfit for the major surgery that repair of this lesion entails. This early online paper in *The Lancet* asks whether endovascular aneurysm repair (EVAR) to exclude abdominal aortic aneurysm (AAA), which was introduced for patients of poor health status considered unfit for major surgery, improves survival. They carried out a randomised controlled trial of 338 patients aged 60 years or older who had aneurysms of at least 5.5 cm in diameter and who had been referred to one of 31 hospitals in the UK. Patients received either EVAR or no intervention. The team investigated all-cause mortality, aneurysm-related mortality, health-related quality of life (HRQL), postoperative complications, and hospital costs.

A total of 197 patients underwent aneurysm repair (47 were assigned no intervention). The 30-day operative mortality in the EVAR group was 9% and the no-intervention group had a rupture rate of 9.0 per 100 person years. By the end of follow-up 142 patients had died, 42 from aneurysm-related factors, and overall mortality after 4 years was 64%. All-cause mortality was not significantly different between the EVAR group and the no-intervention group. There was no difference in aneurysm-related mortality. The mean hospital costs per patient over 4 years were £13 632 in the EVAR group and £4 983 in the no-intervention group, with no difference in HRQL scores.

The group concluded that EVAR had a considerable 30-day operative mortality in patients already unfit for open repair of their aneurysm. It did not improve survival over no intervention, and was associated with a need for continued surveillance and reinterventions, at substantially increased cost. Ongoing follow-up and improved fitness of these patients is a priority.

EVAR trial participants. *Lancet* 2005; early online publication, 17 June 2005.



## HEART FAILURE, COXIBS AND NSAIDS

This recent paper in the *British Medical Journal* picks up on the controversial subject of the cardiovascular effects of non-steroidal anti-inflammatory drugs (NSAIDs) and cyclo-oxygenase-2 inhibitors. The study compared the risk of death and recurrent congestive heart failure in elderly patients prescribed celecoxib, rofecoxib, or NSAIDs. It also looked at class differences between celecoxib and rofecoxib.

The authors point out that studies of NSAIDs, naproxen in particular, have been equivocal, showing decreases, increases and no effects on the risk of ischaemic heart disease. However, rofecoxib has been consistently associated with an increased risk of myocardial infarction (MI) and was recently withdrawn when a trial on benign sporadic colonic adenomas showed a significant increase in the incidence of cardiovascular events compared with placebo. Currently, there is no established association between celecoxib and an increased risk of MI, but recent meta-studies have cast doubt on this assumption. Selective cyclo-oxygenase-2 inhibitors can be cardioprotective at the level of the failing myocardium. However, both NSAIDs and the coxibs have various renovascular effects, including increased volume retention, leading to oedema and raised

blood pressure, all of which can exacerbate heart failure. Clinically, NSAIDs have been associated with the onset and exacerbation of congestive heart failure, but clinical data on the association between coxibs and congestive heart failure are scarce. A recent population study showed that people using rofecoxib and NSAIDs, but not celecoxib, had a higher risk of admission for congestive cardiac failure than controls not taking NSAIDs.

The team used databases of hospital discharge summaries and prescription drug claims in Quebec. Participants were 2 256 patients aged 66 or more, who had been prescribed celecoxib, rofecoxib, or an NSAID after admission for congestive heart failure between April 2000 and March 2002. They found that the risk of death and recurrent congestive heart failure combined was higher in patients prescribed NSAIDs or rofecoxib than in those prescribed celecoxib. So it does seem that celecoxib is safer than rofecoxib and NSAIDs in elderly patients with congestive heart failure.

Hudson M, *et al.* *BMJ* 2005; **330**: 1370.

**Bridget Farham**