Transient Ischemic Attack: New Studies, New Questions

The risk of stroke is high, even for those with “vague” symptoms. Here’s a look at recent research that suggests changes to our approach may be needed.

Recently, there has been a flurry of publications on TIA management. In the next few issues of this column, we will examine the results of some of these studies, which could have a substantial practical impact on the management of patients with TIAs.

What’s the Risk of Stroke Following TIA?
Not surprisingly, it is fairly well established that patients experiencing TIAs are at increased risk for future vascular events. Recently, a meta-analysis of all studies regarding this issue has been published. In this analysis, 11 natural history studies encompassing 7238 patients were reviewed. Only 2/11 of the studies had been performed before the year 2000, reducing bias related to differences in management in different time epochs.

In nearly all cases, the TIAs were well defined. The studies consistently report a significant increase in the risk of stroke. The pooled risk of stroke was 3.5 percent (95% confidence interval [CI], 2.1%-5.0%), 8.0 percent (95% CI, 5.7%-10.2%), and 9.2 percent (6.8%-11.5%) at two, 30 and 90 days, respectively. However, in those studies in which patients were directly interviewed by the investigators (n=3) the rate of stroke was two to three times higher (Table 1).

What About Transient Neurological Attacks?
Moreover, a recent population-based study from the Netherlands analyzed the risk of stroke and other vascular events associated with not only clear cut TIAs, but also other “transient neurological attacks” or TNAs. In this study, TNAs were defined as “attacks of sudden neurological symptoms that completely resolved within 24 hours, with no clear evidence for the diagnosis of migraine, epilepsy, Ménière disease, hyperventilation, cardiac syncope, hypoglycaemia or orthostatic hypotension.” In short, these are vague episodes of neurological symptoms lasting less than 24 hours without an obvious etiology. Using this definition, TIAs would be considered a subset of TNA, with focal features.

The authors also define a third group of patients called TNA with mixed features, i.e., both localizing and non-localizing features. The two newly-defined groups, TNA without focal features and TNA with mixed features, comprise a substantially larger group of patients than classic TIA, and previously had been thought to have a relatively
benign prognosis. However, in this study they were associated with a significant vascular event rate.

The Rotterdam Study, a cohort study that began in 1990, enrolled 7983 individuals (6062 included in this substudy). Patients received serial follow-up over the next 15 years, and any episodes of recurrent symptoms were identified. They reported that patients with focal or mixed symptoms had a significant greater incidence of ischemic stroke than those without symptoms (Table 2). Patients with mixed symptoms also had a great risk of cardiovascular disease (HR 2.28), and vascular dementia (HR 3.46).

However, there are significant limitations to this study. First, there was a lack of complete case ascertainment and many events (n=129) had to be excluded due to a lack of sufficient information regarding them. Also, since the clinical characteristics were based upon chart review, it is likely that there was missing information on many of the patients. Since this was an observational trial, many confounders are likely to be present, including variations in medication and evaluation between different subjects. This may be reflected in the relatively low 90-day stroke rate in patients with focal symptoms. In this group, the stroke rate was only 3.5 percent, far lower than in other cohort studies.

Despite these limitations, taken together these studies support the high risk of recurrent neurological events in patients with both focal and focal/mixed transient neurological symptoms. Given these results, it is imperative that such patients be considered at high risk, and appropriate measures be taken to evaluate and treat these patients.

However, two major questions remain: First, what treatments should be instituted, and will they affect outcome? Second, how quickly must this evaluation occur, and in what setting (hospital or clinic)? Are there any data to help answer these questions? Stay tuned until next month to see if there may be some potential answers. PN


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