High Rate of Magnetic Resonance Imaging Stroke Recurrence in Cryptogenic Transient Ischemic Attack and Minor Stroke Patients

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Background and Purpose—Cryptogenic stroke is common in patients with transient ischemic attack (TIA) and minor stroke. It is likely that the imaging recurrence risk is higher than the clinical recurrence rate. We sought to determine the rate of clinical and radiographic stroke recurrence in a population of cryptogenic TIA and minor stroke.

Methods—Patients with TIA/minor stroke (National Institutes of Health Stroke Scale score ≤3) were prospectively enrolled and imaged within 24 hours of symptom onset as part of 2 cohorts. Patients were assessed at 3 months to document any clinical recurrence and underwent repeat magnetic resonance imaging (MRI) at either 30 or 90 days. Stroke mechanism was categorized as cryptogenic after standard etiologic work-up was completed and was negative. Follow-up MRI was assessed for any new lesions in comparison with baseline imaging.

Results—Three hundred thirty-three of 693 (48%) patients had cryptogenic stroke. Of these cryptogenic patients, 207 (62%) had follow-up imaging. At 30-day MRI follow-up, 6.6% (5/76) had new lesions (3 in a remote arterial territory). At 90-day MRI follow-up, 14.5% (19/131) had new lesions (9 in a remote arterial territory). Clinical recurrent stroke was seen in 1.2% (4/333) of patients within 90 days.

Conclusions—Cryptogenic etiology is common in a TIA/minor stroke population. This population shows a high rate of silent radiographic recurrence, suggesting active disease. Use of MRI as a surrogate marker of disease activity is 1 potential way of assessing efficacy of new treatments in this population with reduced sample size. (Stroke. 2012;43:3387-3388.)

Key Words: magnetic resonance imaging ■ minor stroke ■ recurrent event ■ transient ischemic attack

Patients with transient ischemic attacks (TIA) and minor stroke are at high risk for recurrent cerebral ischemia. New treatment approaches are needed to reduce this early stroke recurrence. Few studies, however, have examined the recurrence risk in minor stroke or TIA patients when no definitive cause can be identified (cryptogenic stroke). This group is currently treated with antiplatelet therapies despite a lack of clear pathophyslogic understanding of what causes recurrence in this group. In the only study that explored clinical and radiological event rates in cryptogenic stroke, a relatively low clinical event rate (2%) but a much higher silent radiological event rate (21%; 4/19) was seen. If this high radiological event rate is true, then it may allow for secondary stroke prevention treatment trials in this population to occur with smaller sample size.

We therefore sought to determine the recurrent clinical and radiological event rates in cryptogenic TIA and minor stroke population.

Subjects and Methods

Patients with high-risk TIA (transient focal neurological symptoms including motor or speech symptomatology lasting ≥5 minutes) or minor stroke (National Institutes of Health Stroke Scale score ≤3) were prospectively enrolled and imaged within 24 hours of symptom onset as part of 2 prospective imaging cohorts (VISION1 and CATCH). Details for each study have been previously described. Only patients with minor stroke or TIA as defined were included from the VISION study. Most patients underwent magnetic resonance imaging (MRI) of the brain, including diffusion-weighted imaging within 24 hours of symptom onset. All imaging was interpreted blind to clinical information other than symptom side. Stroke mechanism was categorized as per TOAST criteria after parenchymal, vascular imaging and cardiac investigations. Standard etiologic work-up for ischemic stroke in our institution would routinely include blood work, intracranial and extracranial vascular imaging, electrocardiogram, transthoracic echocardiogram, and 24-hour cardiac (Holter) monitoring. Most investigations were completed in hospital before discharge. Any amount of definite atrial fibrillation was considered a cardioembolic source. The treating physician labeled patients as cryptogenic at the time of the 90-day follow-up if all the investigations did not find another cause. Patients were followed for 90 days to document any clinical recurrent stroke and underwent repeat MRI either at day 30 (VISION) or at day 90 (CATCH). Only patients with a distinct recurrent stroke (not symptom progression) were included for the outcome of clinical recurrent stroke. Follow-up diffusion-weighted imaging and
sequences were directly by guest on April 13, 2017

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these patients are not severely disabled, with only small vol-

large artery disease who are at the highest early recurrence

relatively late, and this may be attributable to patients with

than 1 month from onset. All the recurrent clinical events were

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source such as the heart or aortic arch in these cryptogenic

patients. If this population is actively embolizing, then the

remote arterial distribution point to an unidentified proximal

surveillance. Furthermore, high rates of recurrent infarcts in

estimates disease activity as compared with

identifiable cause found. The cumulative clinical stroke recur-

patients show evidence of a high rate of silent radiological

accumulation of disease on follow-up imaging despite no

identifiable cause found. The cumulative clinical stroke recur-

rate in cryptogenic TIA and minor stroke patients under-

estimates disease activity as compared with follow-up MRI

surveillance. Furthermore, high rates of recurrent infarcts in

remote arterial distribution point to an unidentified proximal

such as the heart or aortic arch in these cryptogenic patients.

If this population is actively embolizing, then the best choice of antithrombotic treatment in this population is unclear. There is intriguing data suggesting a potential role for anticoagulant therapy rather than antiplatelet agents in crypto-

genic stroke. The cryptogenic TIA/minor stroke population is an ideal target group for the new oral anticoagulants because these patients are not severely disabled, with only small volumes of infarction at presentation, and thus have much to gain from stroke prevention.

Although the confidence intervals overlap because of small sample size, we found a trend that there were more new lesions when a patient was scanned at 90 days as compared with 30 days. All of the clinical events we saw were also later than 1 month from onset. All the recurrent clinical events were relatively late, and this may be attributable to patients with large artery disease who are at the highest early recurrence risk being excluded from this study.

A limitation of this study is that we did not prospectively collect details on how comprehensive the stroke etiologic work-up was. However, we are a tertiary stroke center where patients routinely have a cardiac work-up that includes at least an echocardiogram and 24-hour Holter monitoring. More recent studies have used extended cardiac monitoring to iden-

tify paroxysmal atrial fibrillation. This was not available to

us and its lack of use is a potential limitation. The proportion

of patients with cryptogenic etiology is high in this study, but

it is similar to that seen in a recent large cohort study of TIA and minor stroke.

This study highlights that follow-up brain imaging may be a useful surrogate marker for disease activity and may allow reduced sample sizes in randomized controlled trials of stroke prevention in this cryptogenic minor stroke and TIA population.

Sources of Funding

The CATCH study was supported by a grant-in-aid from the Canadian Institute of Health Research (CIHR) and a Pfizer Cardiovascular research award. The VISION study was supported by grant fund-

ing from CIHR and Heart and Stroke Foundation (HSF) of Alberta, NWT, and Nunavut.

Disclosures

Dr Coutts received salary support from the Alberta-Innovates-Health solutions and the Heart and Stroke Foundation of Canada’s Distinguished Clinician Scientist award, and is supported in partnership with the Canadian Institute of Health Research (CIHR), Institute of Circulatory and Respiratory Health, and AstraZeneca Canada Inc. Dr Demchuk receives salary support from Alberta Innovates-Health Solutions. Dr Coutts and Dr Demchuk have been advisory board members for Bristol Myer Squibb. Dr Demchuk has been an advisory board member for Boehringer Ingelheim and Bayer. All other authors report no conflicts of interest.

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Stroke. 2012;43:3387-3388; originally published online October 2, 2012;
doi: 10.1161/STROKEAHA.112.671172
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2012 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/43/12/3387

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