Rapid Identification of High-Risk Transient Ischemic Attacks
Prospective Validation of the ABCD Score

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Background and Purpose—A 6-point score, based on age, blood pressure, clinical features, and duration (ABCD), was shown to effectively stratify the short-term risk of stroke after a transient ischemic attack (TIA). Prospective validation in different populations of patients should precede its widespread use. Whether adding computed tomography (CT) scan findings to the score would improve its performance deserves exploring. We aimed to validate the ABCD score in a prospective cohort of patients accessing Emergency Departments within 24 hours of a TIA in an area of northern Italy and to acquire preliminary data on CT-based refinement.

Methods—During a 6-month period, all TIA patients accessing the Emergency Departments of 13 Piemonte and Valle d’Aosta hospitals were prospectively enrolled and stratified according to the 6-point ABCD score and to a 7-point score (ABCDI, where I¼imaging) incorporating CT findings.

Results—Of 274 patients, stroke occurred in 10 (3.6%) within 7 days and in 15 (5.5%) within 30 days. The ABCD score was predictive of stroke risk at both 7 and 30 days (odds ratio for every point of the score =2.55 at 7 days and 2.62 at 30 days; P for linear trend across the ABCD score levels =0.018 at 7 days and 0.0017 at 30 days). CT scan findings further increased prediction (odds ratio for every point of the score =2.68 at 7 days and 2.89 at 30 days; P for linear trend across the ABCDI score levels =0.0043 at 7 days and 0.0003 at 30 days).

Conclusions—The ABCD score confirmed its prognostic value in this prospective cohort. CT results could further improve prediction. (Stroke. 2008;39:297-302.)

Key Words: ABCD score ■ transient ischemic attack ■ prognosis ■ stroke

A number of studies have shown that transient ischemic attacks (TIAs) carry a significant short-term risk of stroke, especially in the first few days,1–4 but remarkable disagreement and wide variability in the urgent management of TIA patients still exist.5,6 Reliable and easily obtainable information on each patient’s risk profile should be promptly available in the emergency setting to help guide his/her individual management.

Recently, the ABCD score, a 6-point score based on clinical features (A¼age, B¼blood pressure, C¼clinical features [weakness/speech disturbance/other symptoms], and D¼duration of symptoms) was derived in the Oxfordshire Community Stroke Project and validated in both a population-based and a hospital-based TIA clinic-referred cohort.7 Subgroups of patients at higher risk of early stroke could be reliably identified, with scores of 5 or 6 being independently associated with an 8-fold greater risk of stroke at 1 month. Adding diabetes to the score (ABCD2) further enhanced predictability in a large group of TIA patients from different populations.8

When applied to cohorts of TIA patients, the predictive value of the ABCD score has been mostly9–10 but not universally11,12 confirmed, so that further prospective validation should precede its widespread adoption in the emergency setting. Whether the scoring system can be further improved by adding results from an urgent diagnostic work-up, provided that these reflect real-life Emergency Department (ED) practice, such as computed tomography (CT) scan, certainly deserves exploration.

We aimed to validate the ABCD score in a prospective cohort of patients accessing EDs within 24 hours of a TIA in an area of northern Italy and to explore whether the CT scan, an examination that is routinely performed in the vast majority of TIA patients in the emergency setting, can increase the predictive value of the score.

Subjects and Methods

Patients
The SINPAC Group (Societa` Inter-regionale Piemonte-Aosta Cerebrovascolarie) is a group of neurologists interested in cerebrovascular diseases who work at different Neurology Departments in both primary and secondary care hospitals throughout Piemonte and Valle d’Aosta in northwestern Italy.
From May 1 to October 31, 2006, all consecutive patients with a suspected TIA were prospectively evaluated in 13 EDs; only those presenting within 24 hours from the onset of symptoms and whose diagnosis was confirmed by the attending neurologist were enrolled. TIA was defined on the basis of the World Health Organization standards.13 Exclusion criteria were clinical evaluation beyond 24 hours from the end of the transient event and a final diagnosis of nonischemic causes of symptoms (such as seizure, migraine, anxiety, syncope, etc.).

Patients admitted for stroke and reporting a TIA in the previous 24 hours or longer were also excluded. Because the study was meant to prospectively validate (and not to derive) the predictive value of the ABCD score when applied to patients accessing the ED for a TIA, inclusion of patients who had already developed a stroke was avoided. All patients underwent routine clinical investigations while in the ED (in our country, these usually consist of blood tests, ECG, CT scan, and a neurology consultation). The decision to admit was left to the discretion of the attending neurologist.

The following items were recorded on a specific data collection form: date of the event, sex, age, blood pressure, clinical features, duration of symptoms, CT data, whether it was a first-ever event, and admission/discharge from hospital. These data, together with a copy of the ED report, were sent to the central trial office. Only data from the collection form were entered in a database. Written, informed consent was obtained from all subjects, and the protocol was approved by the institutional medical ethics review board of each participating center.

ABCD Score and ABCDI Score

Determination of the ABCD score was performed according to Rothwell et al.' The 6-point ABCD score incorporates A=age (≥60 years=1 point, <60 years=0 point), B=blood pressure (systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg=1 point), C=clinical features (unilateral weakness=2 points, speech disturbance without weakness=1 point, other symptoms=0 point), and D=duration of symptoms (≥60 minutes=2 points, 10 to 59 minutes=1 point, <10 minutes=0 point).

The 7-point ABCDI score was determined by adding to the ABCD score an additional item (I=imaging) from the CT scan performed in the ED (leukoaraiosis and/or old/new ischemic lesions=1 point, normal=0 point). Both the study neurologist and the radiology report had to agree on each finding. When in disagreement, consensus had to be reached by discussing discrepancies.

Patient Follow-Up and Outcome

Follow-up was performed at 1 month by a study neurologist, either by a centralized telephone interview or by consultation with the recruiting neurologist. Death, stroke, and further vascular events, as well as hospital admissions and ongoing medication, were recorded.

Stroke was defined as a cerebrovascular event of sudden onset, lasting for >24 hours, and clearly resulting in an increase of an existing or a new neurologic deficit. All strokes were assessed and investigated by a study neurologist. Brain imaging showing a new ischemic lesion in a vascular territory unaffected on the admission CT scan had to be present in all stroke cases. Strokes were then categorized on the basis of their ABCD and ABCDI scores. Strokes were also classified according to TOAST criteria:14 large-artery atherosclerosis, cardioembolic, small-artery disease, other determined, or undetermined cause.

Statistical Analysis

The Kaplan–Meier product-limit method was used to estimate the cumulative probability of stroke at 7 days and 1 month from the index TIA. Differences in stroke-free survival between groups stratified by the ABCD and the ABCDI scores were assessed for statistical significance with the log-rank test. Sensitivities and specificities of prediction were determined at each cut-off of both scores, and the receiver operating characteristic curves were plotted.

The predictive value of the CT scan as a risk factor for subsequent stroke was evaluated first in a univariate and then in a multivariate logistic-regression analysis (all items contributing to the ABCD score were included in the multivariate model). Associations were presented as odds ratio (OR) with corresponding 95% CIs. The statistical packages, Epi Info, version 3.3 for Windows, and Graph Pad Prism 4, were used for statistical analyses.

Results

During a 6-month period, 287 patients with a diagnosis of TIA were enrolled; 1 patient with an ABCD score of 6, who was lost to follow-up, and 12 patients, who did not undergo a CT scan while in the ED, were excluded from further evaluation. Demographic and clinical data of the remaining 274 patients are shown in Table 1. More than 60% of patients were male, the mean age of all patients was 71.5 years, and >88% of patients were >60 years of age. Blood pressure was >140/90 mm Hg in 65% of patients. Unilateral weakness was recorded in 58%, and symptoms persisted for longer than 1 hour in 40.5% of cases. The CT scan was abnormal in 44% of patients. Fifty-nine percent of TIA patients were admitted, their mean ABCD score tended to be higher than that of discharged patients (P=0.04).

During follow-up, 2 patients (both with an ABCD score of 6) died (1 of ischemic stroke and 1 of pulmonary embolism), 7 patients underwent carotid endarterectomy for symptomatic stenosis, 2 underwent intracranial stenting for symptomatic stenosis in the posterior circulation, and 2 patients were readmitted for de novo atrial fibrillation. All surviving patients (n=272) confirmed taking some kind of antiplatelet/anticoagulant agent at the time of follow-up.
Within 1 month of the index TIA, ischemic stroke had occurred in 15 patients; 10 strokes took place within 7 days (9 patients were already hospitalized, but none received recombinant tissue plasminogen activator) and 7 strokes occurred within 2 days. According to TOAST criteria, 11/15 (73.3%) strokes were due to large artery atherosclerosis, 1/15 (6.7%) was cardioembolic, and 3/15 (20%) were due to small vessel disease. No brain hemorrhages were recorded.

None of the patients with infarction attributed to large-artery disease had received surgery by the time of stroke, in 9 cases (stenoses of slightly ≥50%), endarterectomy had not been planned, whereas 2 patients, with higher degrees of stenosis, had a stroke within 2 days, before the intended surgery was performed. On the other hand, of the 7 patients who did undergo surgery, none went on to experience a stroke. The risk of stroke was 2.55% at 2 days (95% CI, 1.0 to 5.2), 3.6% at 7 days (95% CI, 1.8 to 6.6), and 5.5% at 1 month (95% CI, 3.1 to 8.9).

The distribution of the ABCD and ABCDI scores at the time of presentation to the ED is shown in Tables 2 and 3. The ABCD score was predictive of both the 7-day (odds ratio [OR]=2.55 for every point of the score; \(P\) for linear trend across the ABCD score levels \(0.018\)) and the 30-day (OR=2.62 for every point of the score; \(P\) for linear trend across the ABCD score levels=0.0017) risk of stroke, as shown in Table 2. The area under the receiver operating characteristic curve was 0.75 (95% CI, 0.63 to 0.88; \(P=0.0065\)) at 7 days (data not shown) and 0.76 (95% CI, 0.66 to 0.86; \(P<0.001\)) at 30 days (Figure 1a).

ABCDS scores of 4 to 6 were associated with a 4-fold increase in stroke risk at 7 days (hazard ratio [HR]=4.1; 95% CI, 1.02 to 16.35) and 1 month (HR=4.09; 95% CI, 1.32 to 12.61; data not shown), whereas the highest scores (5 or 6) led to a 6-fold increase in stroke risk at 7 days (HR=5.69; 95% CI, 1.42 to 17.88; Figure 1b) and 1 month (HR=5.80; 95% CI, 1.83 to 14.45; Figure 1c). CT analysis showed that 154 patients (56%) had a normal CT scan, 67 (24.5%) had leukoaraiosis, and 53 (19.5%) had old infarcts (no ischemic lesion was deemed to be "new") with or without white matter disease.

Because of the low number of strokes in our study, statistical power to detect the predictive value of the CT scan was limited. Nonetheless, a "positive" CT scan was associated with an almost 4-fold greater risk of stroke at 30 days in a univariate analysis (OR=3.78; 95% CI, 1.17 to 12.20; \(P=0.026\)), and, when added to a logistic-regression model

<table>
<thead>
<tr>
<th>ABCD Score</th>
<th>Patients, n (%)</th>
<th>Strokes, n (%)</th>
<th>Risk (%; 95% CI)</th>
<th>Patients, n (%)</th>
<th>Strokes, n (%)</th>
<th>Risk (%; 95% CI)</th>
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<tr>
<td>≤1</td>
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<td>2</td>
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<td>4</td>
<td>84 (30.7)</td>
<td>2 (20.0)</td>
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<td>3.6 (0.7–10.1)</td>
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<tr>
<td>5</td>
<td>74 (27.0)</td>
<td>4 (40.0)</td>
<td>5.4 (1.5–13.3)</td>
<td>6 (40.0)</td>
<td>8.1 (3.0–16.8)</td>
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<tr>
<td>6</td>
<td>40 (14.6)</td>
<td>4 (40.0)</td>
<td>10.0 (2.8–23.7)</td>
<td>6 (40.0)</td>
<td>15.0 (5.7–29.8)</td>
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<tr>
<td>Total</td>
<td>274 (100)</td>
<td>10 (100)</td>
<td>3.6 (1.8–6.6)</td>
<td>15 (100)</td>
<td>5.5 (3.1–8.9)</td>
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OR=2.55 (1.25 to 5.25); \(P\) for linear trend across the ABCD score levels=0.018

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<th>Strokes, n (%)</th>
<th>Risk (%; 95% CI)</th>
<th>Patients, n (%)</th>
<th>Strokes, n (%)</th>
<th>Risk (%; 95% CI)</th>
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<td>1 (10.0)</td>
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<td>74 (27.0)</td>
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<td>6.6 (1.8–15.9)</td>
<td>5 (33.3)</td>
<td>8.2 (2.7–18.1)</td>
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<td>17 (6.2)</td>
<td>3 (30.0)</td>
<td>17.6 (3.8–43.4)</td>
<td>5 (33.3)</td>
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<tr>
<td>Total</td>
<td>274 (100)</td>
<td>10 (100)</td>
<td>3.6 (1.8–6.6)</td>
<td>15 (100)</td>
<td>5.5 (3.1–8.9)</td>
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</tr>
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</table>

OR=2.68 (1.36 to 5.26); \(P\) for linear trend across the ABCDI score levels=0.0043

OR=2.89 (1.62 to 5.16); \(P\) for linear trend across the ABCDI score levels=0.0003

Table 2. Seven- and 30-Day Risk of Stroke, Stratified According to ABCD Score
Table 3. Seven- and 30-Day Risk of Stroke, Stratified According to ABCDI Score
containing the 4 components of the ABCD score, it remained an independent predictor of 30-day stroke (OR = 4.65; 95% CI, 1.25 to 17.21; P = 0.02). On the other hand, statistical significance was not reached at 7 days (univariate analysis OR = 3.12; 95% CI, 0.9 to 12.33; P = 0.105; multivariate analysis OR = 4.02; 95% CI, 0.83 to 19.39; P = 0.083). The ABCDI score performed slightly better than the ABCD score in predicting both the 7-day (OR = 2.68 for every point of the score; P for linear trend across the ABCDI score levels = 0.0043) and the 30-day (OR = 2.89 for every point of the score; P for linear trend across the ABCDI score levels = 0.0003) risk of stroke, as shown in Table 3.

The area under the receiver operating characteristic curve was 0.78 (95% CI, 0.65 to 0.91; P = 0.0026) at 7 days (data not shown) and 0.79 (95% CI, 0.69 to 0.89; P = 0.0015) at 30 days (Figure 2a). Furthermore, an ABCDI score of 5 to 7 at the ED was associated with a 7-fold increase in stroke risk at 7 days (HR = 7.32; 95% CI, 1.19 to 14.58; Figure 2b) and with an 11-fold increase at 1 month (HR = 11.59; 95% CI, 1.83 to 14.45; Figure 2c).

In the cohort of 197 patients with a first-ever cerebrovascular event, 6 patients (3%) experienced a stroke within 7 days and 10 (5.1%), within 30 days of the index TIA. In this group, the predictive value of the ABCD and ABCDI scores remained significant (supplemental Table I and supplemental Figure I, available online at http://stroke.ahajournals.org), with the ABCDI again performing slightly better (ABCD 7-day risk OR = 2.79 for every point of the score; P for linear trend across score levels = 0.0365; ABCD 30-day risk OR = 2.39 for every point of the score; P for linear trend across score levels = 0.0133; ABCDI 7-day risk OR = 2.44 for every point of the score; P for linear trend across score levels = 0.028; ABCDI 30-day risk OR = 2.43 for every point of the score; P for linear trend across score levels = 0.0053).

**Discussion**

In this observational multicenter study, TIA patients were prospectively enrolled with the aim of further evaluating the predictive value of the ABCD score for short-term stroke risk assessment. A well-defined target population was selected: all patients had to be seen within 24 hours by neurologists in the EDs of an area of northern Italy. We recruited patients in the ED because in Italy, this is the most widespread modality of seeking medical attention after a TIA. TIA clinics are few, and general practitioners tend to refer patients to the ED when confronted with an acute neurologic event. Once in the ED, a neurologic consultation is routinely requested if a TIA is suspected. So we believe that our cohort of patients is representative of a TIA population from our region.

In this setting, the ABCD score confirmed its reliability, with higher scores associated with mounting stroke risk. In fact, no strokes were documented in patients with ABCD scores < 4. A score of 4 carried a stroke risk of 2.4% at 7 days and of 3.6% at 1 month. Risk increased to 5.4% and 8.1% with a score of 5 and to 10% and 15% with a score of 6. Scores of 4 to 6 were associated with a 4-fold increase in
stroke risk, whereas scores of 5 to 6 were associated with a 6-fold increase in risk.

When taken together with other similar data derived from much larger cohorts, our results add to the increasing evidence that scores <4 carry a very low risk of subsequent stroke and could be advocated as a reason not to admit such patients. On the other hand, higher scores, especially in the range of 5 or 6, carry a significant risk, and these patients should be targeted in an effort to optimize their treatment. Indeed, the ability to effectively predict stroke risk for each patient should guide decisions regarding admission and antithrombotic treatment, but because no score will presumably ever reach an absolute predictive value, clinicians should be aware that some, albeit few, patients deemed to be at very low risk will still go on to have a stroke.

The ABCD score has the unquestionable appeal of being based on real-time clinical data, in that age, blood pressure, type, and duration of symptoms can all be obtained at presentation, without relying on previous medical history, which could introduce confusing biases. On the basis of the same practical approach, we chose CT as a possible tool for score refinement, as the vast majority of TIA patients receive a CT scan while in the ER. We are well aware that diffusion-weighted imaging looks much more promising to identify higher-risk patients, but we doubt that it will become universally available, at least not in the near future. Grouping together infarcts and white matter disease (imaging in ABCD: leukoaraiosis and/or old/new ischemic lesions = 1 point) was based on the belief that some prognostic significance could be attributed to any CT evidence of previous vascular disease versus none. Indeed, when scored in this way, the CT scan increased the predictive value of the ABCD score, especially in the high-risk group (ABCD > 4).

Only new ischemic lesions on CT have been shown by Douglas et al to be predictive of stroke risk, but in their study, CT findings were apparently abstracted from the radiology reports. In grading CT scans, we required agreement between the study neurologist and the radiology report. We wonder whether this might have contributed to a better performance of CT findings in terms of prognostic significance. Although our results should be taken with caution, based as they are on a small number of cases, they do call for further validation of CT as a tool to refine the ABCD score in much larger patient populations.

In our cohort, almost 60% of TIA patients were admitted; this proportion is definitely higher than that reported in other series. While admitting TIA patients is rather common in Italy, it is noteworthy that the mean ABCD scores of patients who were admitted were higher than those of patients who were not (4.23 vs 3.96, P = 0.04) and in the range of those scores (≥4) considered to suggest an increased short-term risk of stroke.

Although the study protocol did not make any suggestion regarding admission, we do not know whether the high rate of hospitalization was influenced by the scoring itself, with the attending neurologist being more prone to admit patients with higher scores, or whether it simply reflects the fact that the score expresses well-known risk factors that are already perceived as a reason for admission. In other terms, it is possible that a wider diffusion of the ABCD scores would result in a higher number of patients being admitted after a TIA, and this should be provided for in advance.

A higher risk of stroke in admitted patients is confirmed by the observation that 90% (9 of 10) of 7-day strokes occurred in these patients. Regrettably, none received thrombolysis, possibly not justifying the costs of hospitalization. In addition, most strokes in our cohort were classified as large-artery atherosclerosis; given that many such cases could be amenable to prophylactic treatment by endarterectomy, our results show that admission per se does not always guarantee effective prevention, unless it is coupled with expedited pathways to ensure proper therapies. On the other hand, 7 carotid endarterectomies and 2 intracranial stenting procedures for symptomatic stenoses performed in hospitalized patients may well have prevented additional cerebrovascular events in this group.

In this study, the short-term risks of stroke after a TIA were 2.55% at 2 days, 3.6% at 7 days, and 5.5% at 1 month. Although these rates confirm the high-risk nature of TIs, they are lower than recently reported by other authors. The easiest way to explain this finding would be a high number of TIA misdiagnoses, but this seems improbable for various reasons, as all patients were diagnosed by neurologists, who are supposedly more reliable than other physicians in identifying TIs. Recruitment was prospective, so as to avoid biases derived from misclassification. Patients had to access the hospital within 24 hours of their TIA to enhance precise recall of the type and duration of symptoms and to guarantee inclusion of very short-term strokes. The percentage of symptoms, such as motor weakness and speech disturbance, which have been shown to be rather specific predictors of TIA diagnosis, was comparable to that reported in TIA cohorts with higher stroke risks. Even age and the number of hypertensive patients did not significantly differ from those reported in similar studies.

Conversely, high rates of hospitalization, with its presumed protective effect, and adherence to antithrombotic medication, as reported at follow-up (100% of patients), could help explain the lower stroke rates. Finally, a higher incidence of stroke in some cohorts can in part be due to inclusion of patients actually referred for stroke after a previously unreported TIA, a type of patient we did not include in the present report.

Our study has a number of limitations. First, only patients evaluated by neurologists were enrolled, so whether our results can apply to TIs diagnosed by other “front-line” clinicians is debatable, but Rothwell et al demonstrated that the predictive value of the ABCD score remained highly consistent when applied to all referrals to OXVASC and TIA clinics by primary care sources. Second, the small size of our cohort leaves any conclusion regarding the value of the ABCDI score open to criticism. Indeed, we hope that the promising results of adding CT scan findings to the score will find further confirmation in studies with larger numbers of cases. Third, unlike other studies, we included both patients with first-ever and recurrent events. It is noteworthy that inclusion/exclusion of patients with recurrent events (online Table I) did not significantly change the predictive value of
the ABCD and ABCDI scores. In conclusion, the present study further validates the ability of the ABCD score to identify high-risk TIA patients and suggests the need to further evaluate the advantage of adding CT scan findings to refine its predictive value even more.

Appendix: SINPAC

We wish to thank the following members of the SINPAC group for enrolling TIA patients (numbers enrolled are in parentheses): E. Ursino, L. Ruiz, R. Bottaro–Alessandria (26); E. Bottacchi, G. Corso–Aosta (25); D. Papurrello, P. Gai, S. Gasverde–Cirì (10); E. Grasso, P.C. Gerbino–Cuneo (17); G. Ferrari, G. De Rosa, M. Maggio–Iverea (25); F. Monaco, M. Leone, M. Reggiani–Novara (5); C. Buffa, P. Filippi, L. Appendino, D. Cassano–Torino (Maria Vittoria Hospital, 21); M. Nobili, R. Bongioanni, F. Zurlò–Torino (Martini Hospital, 12); M. Gionco, C. Labate, M. Maniscalco–Torino (Mauriziano Hospital, 20); C. Doriguzzi, R. Bottero–Pinerolo (16); E. Luda, L. Vivalda, N. De Luca, S. Amaruì–S–Rivoli (47); L. Durelli, M. Iudicello, P. Barbeto–Orbassano (42); D. Seliak, L. Borsotti, A. Dutto–Savigliano (21).

Source of Funding

The research reported in this article was supported by an unrestricted grant from the Regione Piemonte, Public Health Department (Protocollo Ricerca Sanitaria Finalizzata bando 2006, prot. 3659/27.001).

Disclosures

None.

References

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Stroke. 2008;39:297-302; originally published online January 3, 2008;
doi: 10.1161/STROKEAHA.107.496612

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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