Relative Changes in Transcranial Doppler Velocities Are Inferior to Absolute Thresholds in Prediction of Symptomatic Vasospasm after Subarachnoid Hemorrhage

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The absolute transcranial Doppler (TCD) velocity threshold has been validated as a screening tool for vasospasm after subarchnoid hemorrhage (SAH). We assessed whether relative changes in velocity were superior to absolute TCD thresholds in the detection of symptomatic vasospasm. We reviewed consecutive patients with aneurysmal SAH who underwent serial TCD monitoring and survived at least 7 days. We recorded initial flow velocity (IFV) and maximal flow velocity (MFV) of the middle cerebral artery (MCA) serially up to 14 days from admission. We calculated relative flow velocity changes (MFV/IFV) and maximum change in mean flow velocity (FV_{mean}) over any consecutive 2 days in addition to standard absolute measures of Lindegaard ratio (LR) and FV_{mean}. We calculated receiver operating characteristic curve and area under curve (AUC) values, sensitivity, specificity, and positive predictive and negative predictive values for these parameters, optimal cutpoints, and various combinations. Forty-eight of 211 patients (23%) developed symptomatic MCA vasospasm. AUC values for various TCD parameters were 0.80 for MCA MFV >175 cm/s, 0.71 for LR >6, 0.64 for MFV/IFV >2, and 0.64 for >70% change in MFV over 2 days. The best characteristics were observed for the combination of MFV >175 cm/s and/or maximal LR >6 (AUC 0.81). Our data suggest that absolute thresholds of TCD FV_{mean} provide the most accurate prediction of symptomatic MCA vasospasm after SAH. Other thresholds, including relative change from baseline and day-to-day changes, are inferior to established absolute thresholds. **Key Words:** Delayed cerebral ischemia—cerebral blood flow—hemorrhagic stroke—aneurysm.
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Subarachnoid hemorrhage (SAH) accounts for approximately 5% of all strokes and affects as many as 30,000 Americans each year.[1] Outcomes in patients sustaining SAH remain poor, with mortality as high as 45% and significant morbidity in survivors.[2,3] Symptomatic vasospasm is a particularly common complication after SAH, occurring in one-third of patients. Vasospasm leads to delayed cerebral ischemia (DCI) and is a major contributor to long-term disability. Although the causes of DCI may be multifactorial, angiographic vasospasm and DCI remain strongly correlated.[4]

Conventional angiography is the most accurate and reliable method for detecting vasospasm, but is invasive and carries risks with serial examinations.[5] Transcranial Doppler (TCD), a noninvasive method that uses pulsed-wave Doppler ultrasonography to measure blood flow velocity in the major branches of the circle of Willis, has proven particularly valuable in screening for middle cerebral artery (MCA) vasospasm.[6] Although numerous

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studies have validated absolute TCD velocity as a predictor of MCA vasospasm,[7-16] a common bedside approach uses changes in velocity over time to predict vasospasm. Few previous studies have assessed change in velocity, or a rapid rise in velocity, as a predictor of vasospasm.[12,17] In the present study, we sought to evaluate relative changes in TCD velocities compared with absolute thresholds for predicting symptomatic MCA vasospasm after SAH.

Patients and Methods

Patients

A total of 350 consecutive patients with nontraumatic SAH were admitted to our institution between August 2006 and June 2010. The study cohort included patients with an aneurysmal source who underwent serial TCD monitoring initiated within 48 hours of SAH, survived to least 7 days, and had adequate transtemporal TCD windows.

Demographic and Clinical Data

Age, sex, race, medical history (ie, diabetes mellitus, hypertension, smoking, hyperlipidemia, coronary artery disease, previous stroke), and Hunt and Hess grade on admission were recorded. Radiographic features included Fisher grade, presence of intraventricular hemorrhage, and presence of angiographic vasospasm in the MCA.

Definition of Symptomatic Vasospasm

The diagnostic criteria for symptomatic MCA vasospasm included (1) development of new focal neurologic signs or deterioration in level of consciousness while excluding other causes of neurologic deterioration, such as hydrocephalus, hemorrhage, surgical complications, metabolic abnormalities, or infection; (2) detection of MCA vasospasm (>50% narrowing) on catheter angiography; and (3) endovascular treatment with pharmacotherapy or angioplasty. The day of angiographic treatment was recorded as the date of vasospasm, and the day of the onset of SAH symptoms was defined as day 0. All patients were admitted to a neurosciences intensive care unit and cared for by a team of neurointensivists, neurosurgeons, and stroke neurologists. Standard protocols were followed for patient observation and management; all patients were treated with nimodipine and underwent early aneurysm treatment by clipping or coiling. Hemodynamic augmentation ("triple H" therapy) was provided if patients were symptomatic but not for prophylaxis. Angiographic evaluation and treatment is routine at our center and is instituted whenever symptomatic vasospasm is suspected.

TCD Evaluation

All TCD measurements were obtained through transtemporal windows using a standard 2-MHz pulsed-wave multigated transducer with power M-mode Doppler (100M; Spencer Technologies, Seattle, WA). The Lindegaard ratio (LR) was calculated bilaterally as the ratio of MCA velocity to ipsilateral extracranial internal carotid artery velocity.[18] We used the following TCD criteria, validated annually against conventional angiography, for vasospasm in the MCA: mild, >120 cm/s; moderate, >150 cm/s; severe, >200 cm/s. We recorded initial flow velocity (IFV) in the middle cerebral artery within 48 hours of admission. Daily flow velocities were measured serially up to 14 days along with the maximal flow velocity (MFV). Along with the LR and MCA-MFV, we also assessed relative flow changes (MFV/IFV) and maximum increase in mean flow velocity (FV_{mean}) over any consecutive 2 days. Various operators participated in our study, but data on each individual patient were obtained by the same operator.

Statistical Analysis

Optimal cutpoints were selected using the common point of maximum sensitivity and specificity for detection of symptomatic vasospasm for any particular continuous TCD parameter. Receiver operating characteristic (ROC) curves, sensitivity, specificity, positive predictive value, and negative predictive value were calculated for these parameters, optimal cutpoints, and their combinations. All analyses were performed using SPSS 16.0 (SPSS, Chicago, IL).

Results

Of 350 patients with SAH admitted during the study period, 211 (mean age, 55 years; 69% female) met our inclusion criteria. The median time to initial TCD was 2 days (interquartile range [IQR], 1-2 days), and the median number of TCDs performed was 11 (IQR, 8-13). Forty-eight patients (23%) developed symptomatic MCA vasospasm. Other clinical, radiographic, and TCD characteristics are presented in Table 1.

ROC curves of various TCD parameters for detection of symptomatic vasospasm are shown in Figure 1. Absolute parameters performed better than relative parameters. C-statistic (area under the curve [AUC]) values were 0.86 for MFV, 0.81 for LR, 0.78 for maximum absolute increase in FV_{mean} over 2 days, 0.68 for MFV/IFV ratio, and 0.66 for maximum percent increase in FV_{mean} over 2 days. AUC values for absolute thresholds (MFV and LR) were not statistically different from each other but were significantly superior to relative (MFV/IFV ratio and percent increase over 2 days) thresholds ($P < .001$); however, the maximum increase over any 2 consecutive days performed equally as well as a single absolute maximal FV_{mean} and maximal LR.

Optimal cutpoints for each parameter that best discriminated symptomatic MCA vasospasm were MFV >175 cm/s, LR >5, maximal absolute increase over