

Clinical Article

Is Transcranial Doppler Ultrasonography Old-fashioned?: One Institutional Validity Study

Pan Yeal Han, M.D., Jae Hoon Kim, M.D., Hee In Kang, M.D., Byung Gwan Moon, M.D., Seung Jin Lee, M.D., Joo Seung Kim, M.D.

Department of Neurosurgery, School of Medicine, Eulji University, Nowon Eulji Hospital, Seoul, Korea

Objective : The purpose of this study is to investigate the correlation between various transcranial Doppler (TCD) ultrasonography parameters and clinical vasospasm after aneurysmal subarachnoid hemorrhage (SAH).

Methods : This study enrolled 40 patients presented with aneurysmal SAH between September 2006 and August 2007. We measured differences of mean blood flow velocity (BFVm), highest systolic blood flow velocity (BFVh), and Lindegaard ratio (LR) in the middle cerebral artery on TCD examination. These parameters were evaluated for correlation with clinical vasospasm by univariate analysis and the receiver operating characteristic analysis.

Results : Twelve patients (30%) developed clinical vasospasm. The best TCD parameters for the detection of clinical vasospasm were revealed to be differences of BFM, BFVh, and LR values between 1st TCD test and 3rd TCD (7 cm/s, 11.5 cm/s, 0.45 respectively). The positive predictive value of any one of three parameters was 60% and the negative predictive value was 100%.

Conclusion : TCD is still considered a useful tool for screening clinical vasospasm. To confirm the predictive value of the above parameters, further prospective study will be needed.

KEY WORDS : Receiver operating characteristic analysis · Subarachnoid hemorrhage · Transcranial doppler ultrasonography · Vasospasm.

INTRODUCTION

Despite the advance in treatment of vasospasm after aneurysmal subarachnoid hemorrhage (SAH), delayed symptomatic vasospasm occurs in patients with aneurysmal SAH, ranging from 20 to 30%¹⁴. Transcranial Doppler (TCD) ultrasonography was introduced by Aaslid et al.²⁾ in the clinical field after SAH to detect vasospasm as manifested by elevated flow velocities.

However, there have been many criticisms about the ability to detect impending vasospasm of TCD. In particular, classic TCD parameters were considered to be oversimplified to detect symptomatic vasospasm with difficulty in detecting the range of cerebral perfusion patterns and were unable to correlate with symptomatic vasospasm^{9,14,18,21}.

Therefore, we investigated the correlation between various TCD parameters and clinical vasospasm after aneurysmal

SAH to obtain institutional validity of TCD monitoring as a screening tool.

MATERIALS AND METHODS

Study population

The study population included 40 patients presented with aneurysmal SAH in the anterior circulation, all treated by surgical clipping within 48 hours after SAH at our hospital between September 2006 and August 2007. All patients underwent initial computed tomographic angiography for diagnosis of aneurysmal SAH.

TCD parameters

A 2-MHz, hand-held ultrasonic transducer (trans-scan 3-Dimensional Multifrequency Transcranial Doppler Scanner and Pioneer TCD system; EME Medizinische, Berlin, Germany) was used to measure blood flow velocities in the middle cerebral artery (MCA) through the transtemporal window. The flow velocity in the extracranial internal carotid artery (ICA) was measured through the submandibular window. The time-averaged mean flow velocities in the MCA were obtained at three depths usually 5, 5.5, and 6

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• Address for reprints : Jae Hoon Kim, M.D.

Department of Neurosurgery, School of Medicine, Eulji University, Nowon Eulji Hospital, 280-1 Hagye 1-dong, Nowon-gu, Seoul 139-711, Korea

Tel : +82-2-970-8267, Fax : +82-2-979-8268

E-mail : grimi2@hanmail.net

cm. The following parameters were recorded for both right and left MCAs : difference of mean blood flow velocity (BFVm), highest systolic blood flow velocity (BFVh), and Lindegaard ratio (LR) (MCA BFVm/extracranial ICA BFVm) values between 1st (base line) and 2nd, 3rd, 4th, 5th TCD test, respectively. TCD monitoring was performed initially within the first 48 hours after onset of SAH in all patients every other day. TCD examinations were performed by an experienced technologist not involved in the patient's care who regularly performed TCD examinations for period of two years before the beginning of the study.

Symptomatic vasospasm

The symptomatic vasospasm was defined as a clinical deterioration in the patient's neurological condition (i.e., insidious onset of confusion, disorientation, or decline in level of consciousness, and focal deficits) later than day 3 after SAH with no evidence of hydrocephalus, hemorrhage, surgical complications, metabolic disturbances, or infection. Two independent investigators directly assessed the patient's neurological status and agreed on symptomatic vasospasm. The angiography was not reliably performed in the presence of clinical vasospasm. Therefore, angiographic criteria were not used for the determination of vasospasm.

Statistical analyses

We performed univariate analysis separately between the measured parameters (difference values of BFVm, BFVh, and LR) and clinical symptomatic vasospasm. Receiver operating characteristic (ROC) curve is a plot of trade-off

Table 1. Demographic and clinical data of 40 patients studied

Variables	Vasospasm (+)	Vasospasm (-)	p value
Sex (M/F) (n)	5 / 7	12 / 16	0.94
Age (years, mean ± SD)	48.25 ± 11.16	58.39 ± 10.94	0.01
Hunt Hess grade			0.66
I	1	0	
II	6	16	
III	2	6	
IV	3	5	
V	0	1	
Fisher grade			0.92
I	0	1	
II	5	8	
III	5	14	
IV	2	5	
Location of ruptured aneurysm			0.82
ACA	6	12	
MCA	2	8	
ICA	4	8	

ACA : anterior cerebral artery, MCA : middle cerebral artery, ICA : internal cerebral artery

between sensitivity and 1-specificity at each point originally developed in electronics^{3,5,22}. Moreover, it allows the diagnostic performance of different tests to be easily compared. An ideal diagnostic test is one that reaches the upper left corner of the graph produce an area 1, whereas worthless test to discriminate between two states would be equal to a value of 0.5^{4,5,22}. We divided study population by two groups (no vasospasm group vs. vasospasm group), and calculated critical cut-off point of TCD parameters (BFVm, BFVh, and LR) to predict symptomatic vasospasm using ROC curve analysis. Analysis was performed using the SPSS 13.0 statistical software program (SPSS Inc., Chicago, IL).

RESULTS

A total of 40 patients were included for evaluation of correlation between symptomatic vasospasm and TCD parameters in aneurysmal SAH. There were 23 (57.5%) women and 17 (42.5%) men. Mean age at time of presentation was 55.35 ± 11.84 years. Demographic characteristics of all patients studied divided into symptomatic and nonsymptomatic vasospasm groups (Table 1). Twenty eight patients had no sign of vasospasm and 12 became symptomatic during the second week after SAH. Symptomatic

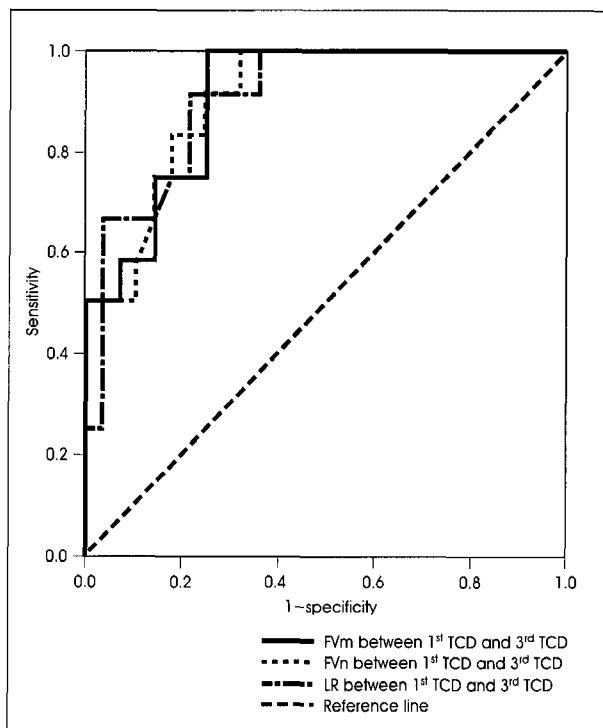


Fig. 1. Graph showing receiver operating characteristic (ROC) curves for mean, highest systolic blood flow velocities (BFVm, BFVh) and Lindegaard ratio (LR) at different levels between 1st and 3rd transcranial Doppler (TCD) test. The area under the ROC curve was equal to 0.908 for BFVm between 1st TCD and 3rd TCD. The ROC area for BFVh between 1st and 3rd TCD was equal to 0.906. The ROC area for LR between 1st and 3rd TCD was equal to 0.906.

vasospasm occurrence ratio was 30%.

The differences of BFVm between 1st TCD and 2nd TCD, 1st TCD and 3rd TCD, and 1st TCD and 4th TCD were statistically significant ($p=0.003$, 0.000, 0.001 respectively). The differences of BFVh between 1st TCD and 2nd TCD, 1st TCD and 3rd TCD, 1st TCD and 4th TCD, and 1st TCD and 5th TCD were statistically significant ($p=0.002$, 0.000, 0.001, 0.002 respectively). The differences of LR between 1st TCD and 3rd TCD, 1st TCD and 4th TCD, and 1st TCD and 5th TCD were statistically significant ($p=0.009$, 0.012, 0.023 respectively) (Table 2).

The area under the ROC curve was equal to 0.908 for BFVm between 1st TCD and 3rd TCD. The ROC area for BFVs between 1st and 3rd TCD was equal to 0.906. The ROC area for LR between 1st and 3rd TCD was equal to 0.906 (Fig. 1). The best efficient cut off point for detecting symptomatic vasospasm were 7 cm/s of BFVm, 11.5 cm/s of BFVs, and 0.45 of LR. The positive predictive value of any one among 3 parameters was 60% and the negative predictive value was 100% (Table 3).

DISCUSSION

Since Aaslid²⁾ and Lindegaard⁸⁾ have suggested that severe vasospasm was diagnosed by using criteria as mean flow velocity >200 cm/s and hemispheric index >6, many investigators have studied about cut-off values for TCD parameter to discriminate between patients with and without vasospasm. However, the optimal threshold of BFV for the diagnosis of vasospasm has not been clearly determined.

Vora et al.²¹⁾ investigated various TCD parameters including highest velocity, greatest one day increase in velocity before angiography, greatest velocity difference, consecutive number of days of velocity increase, largest right-left velocity difference. They concluded that TCD monitoring was not found to be useful for diagnosing symptomatic vasospasm. In their meta-analysis including twenty-six studies, Lysakowski et al.⁹⁾ suggested that there was no evidence for any usefulness of TCD as a diagnostic tool for vasospasm and TCD could not be recommended as a screening method in patient with

possible vasospasm after aneurysmal SAH. Also, there was a report that TCD-defined vasospasm did not independently influence the clinical decision-making after SAH¹³⁾. On the contrary, several studies have shown good correlation between elevated BFV and symptomatic vasospasm^{6,17,19)}. Recently, color TCD study performed by Mariak et al.¹¹⁾ has shown that the color TCD in the diagnosis of advanced MCA narrowing was very good, and the best-performing parameter was peak systolic velocity of 182 cm/s. Also, Mascia et al.¹²⁾ reported that a TCD mean velocity threshold of 160 cm/s, calculated by ROC curve analysis, accurately detects clinical vasospasm.

In this study, we investigated our TCD data to validate institutionally with modification. The main distinction between our study and others is that we used the differences of TCD parameters between base line study and successive study. One knotty problem in interpreting TCD results was diagnostic ability of absolute BFV. Some patients had BFV of 200 cm/s without symptomatic vasospasm, while others had values below 100 cm/s with symptomatic vasospasm. This explains that BFV may be influenced by various clinical parameters i.e intracranial pressure, blood pressure, blood volume, triple H therapy, and technical problems^{1,7,10,15,18,20)}. Considering for this discrepancy of absolute flow velocity

Table 2. Time course of the differences of mean blood flow velocity, highest systolic blood velocity, and Lindegaard ratio of 40 patients studied

TCD parameters	Vasospasm (+)*	Vasospasm (-)*	p value
Δ BFVm (1 st -2 nd) (cm/s)	22.65 ± 22.53	-4.55 ± 24.87	0.002
Δ BFVm (1 st -3 rd) (cm/s)	38.00 ± 26.27	-3.95 ± 27.59	0.000
Δ BFVm (1 st -4 th) (cm/s)	35.95 ± 23.49	-1.50 ± 31.58	0.000
Δ BFVm (1 st -5 th) (cm/s)	31.65 ± 18.70	29.27 ± 154.73	0.958
Δ BFVh (1 st -2 nd) (cm/s)	35.79 ± 31.74	-6.83 ± 36.39	0.001
Δ BFVh (1 st -3 rd) (cm/s)	58.45 ± 38.00	-4.91 ± 39.57	0.000
Δ BFVh (1 st -4 th) (cm/s)	51.87 ± 27.87	-2.50 ± 45.95	0.001
Δ BFVh (1 st -5 th) (cm/s)	49.45 ± 30.87	0.00 ± 46.49	0.002
Δ LR (1 st -2 nd)	0.70 ± 0.67	-0.04 ± 1.29	0.068
Δ LR (1 st -3 rd)	1.12 ± 0.70	-0.00 ± 1.31	0.008
Δ LR (1 st -4 th)	1.26 ± 0.91	0.11 ± 1.37	0.011
Δ LR (1 st -5 th)	1.10 ± 0.60	0.09 ± 1.40	0.023

*mean ± standard deviation. BFVm : mean blood flow velocity, BFVh : highest systolic blood flow velocity, LR : Lindegaard ratio, TCD : transcranial Doppler

Table 3. Measures of predictive values for the differences of mean blood flow velocity, highest systolic blood flow velocity, and Lindegaard ratio between 1st and 3rd transcranial Doppler ultrasonography test

Sufficient condition of TCD parameters (Δ BFVm, Δ BFVh, Δ LR between 1 st TCD and 3 rd TCD test)	Positive predictive value (%)	Negative predictive value (%)
All three parameters	66.7	92
Any two among 3 parameters	63.15	100
Any one among 3 parameters	60	100

BFVm : mean blood flow velocity, BFVh : highest systolic blood flow velocity, LR : Lindegaard ratio, TCD : transcranial Doppler

from person to person in the various clinical settings, the differences of parameters in a serial test still be useful to generalize individual TCD data. Naval et al.¹⁶⁾ reported that relative changes in flow velocity in patient with aneurysmal SAH correlated better with clinically significant vasospasm than absolute flow velocity indices. To the best of our knowledge, there were no domestic clinical studies in which the differences of various TCD parameters were measured in successive days. Also, we performed ROC curve analysis for various parameters to assess TCD's ability to discriminate symptomatic vasospasm.

This study has some limitations. First, we were not able to correlate clinical vasospasm with angiographic vasospasm and combine TCD data with other noninvasive methods, such as Xe computed tomography (CT), perfusion CT, single photon emission computed tomography, and perfusion magnetic resonance imaging which help to identify vasospasm in patients with aneurysmal SAH. Second, we did not investigate intraobserver's reproducibility in measuring TCD parameters. Finally, current data should be validated prospectively in another series of patients.

CONCLUSION

TCD is still a useful tool for screening symptomatic vasospasm. To confirm the predictive value of the above parameters, it will be necessary to validate the TCD findings prospectively in the symptomatic vasospasm patients.

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