Original Article

Transcranial Doppler and Hematoma Expansion in Acute Spontaneous Primary Intracerebral Hemorrhage

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Abstract

Context: The data on the role of Transcranial Doppler (TCD) in the management of acute primary intracerebral hemorrhage (ICH) is meager. **Aims:** To study TCD variables associated with hematoma expansion in acute primary ICH. **Settings and Design:** The study was carried out in the neurosciences department of Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh from July 2010 to September 2011 employing a prospective, double blinded non randomized study design. **Materials and Methods:** Acute ICH patients within 24 h of symptom onset were recruited. Baseline neuroimaging study (Computerized tomography, CT scan of brain) was performed to assess the pure hematoma volume by AXBXC/2 method. Baseline TCD parameters were obtained from both the middle cerebral arteries (MCAs; affected and unaffected hemisphere): Peak Systolic velocity, End Diastolic velocity, Mean Flow velocity, Resistance Index, and Pulsatility Index. Follow up (24 h) assessment of hematoma volume and TCD were carried out. Each of the TCD variables were compared in hematoma expansion (>33% increase in hematoma volume on the follow-up CT) and non-expansion group. **Statistical analysis:** On univariate analysis, the Student's t-test and contingency tables with the X^2 test were used. A forward stepwise multivariate logistic regression analysis with hematoma expansion at 24 h as the dependent variable and ROC analysis was carried out, using SPSS software version 16 (Chicago, IL). *P* value < 0.05 was considered significant. **Results:** Twenty-five patients completed the study. Ten patients (40%) had hematoma expansion. Multivariate analysis revealed unaffected hemisphere MCA Pulsatility Index ratio [unaffected hemisphere MCA Follow up Pulsatility Index/baseline Pulsatility Index] of > 1.055 as the lone correlate of hematoma expansion (sensitivity of 90% and specificity of 60%). **Conclusion:** Frequent assessment with TCD could aid in prediction of hematoma expansion by measuring unaffected hemisphere Pulsatility Index ratios.

Keywords: Hematoma expansion, intracerebral hemorrhage, transcranial doppler

Introduction

Intra cerebral hemorrhage (ICH) constitutes 10-15% of all strokes and has mortality rates approaching 50%, with little effective treatment available at hand.[1] Hematoma expansion is proven to be a determinant of mortality and poor outcome after ICH.[1] Major part of hematoma expansion occurs within first 6-8 h of occurrence of hemorrhage.[2] The presence of contrast extravasation on computerised tomographic angiography (CTA),[2,3] "CT SPOT SIGN",[4] CT swirl sign,[5] infratentorial ICH,[6] and presence of intraventricular hemorrhage[3] are predictors of poor functional outcomes in acute primary ICH. The presence of a spot sign may predict hematoma expansion.[4] Transcranial Doppler (TCD) is a reliable, easy to use, low-cost, portable (bedside) diagnostic tool devoid of radiation hazards. The signal changes noted on performing serial TCD evaluations (especially, the mean flow velocity, MFV, and Pulsatility Index, PI) during the acute phase of ICH reflects the effect of raised intracranial pressure (ICP) on intracranial hemodynamics.[7] Data regarding correlation of hematoma expansion with one or more specific TCD variables is lacking. We attempted to evaluate the TCD variables during the acute stage of spontaneous non traumatic supratentorial primary ICH and their correlation with hematoma expansion.

Materials and Methods

Patients >18 years with first-ever supratentorial non-traumatic primary ICH on Non-Contrast Computerized Tomograph scan (NCCT) of head were prospectively recruited within 24 h of symptom onset. Patients were excluded if any one of the following were present: 1) Onset of symptoms beyond 24 h at the time of presentation or if time of symptom onset unknown, 2) Patients with ICH secondary to trauma, 3) Poor temporal acoustic window, 4) Past ischemic stroke, 5) Those requiring emergency surgical procedures such as hemicraniectomy/hematoma evacuation over the next 24 h of study period as a part of life-saving procedures, 6) Presence of intraventricular hemorrhage (IVH) or infratentorial

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DOI: 10.4103/0972-2327.144277

hemorrhage. The study was approved by the Institute ethics committee, and all patients or their legal representatives gave informed written consent to participate. All patients underwent detailed neurological examination, Glasgow coma scale (GCS) assessment, and National Institute of Health stoke scale (NIHSS) score; both at baseline and at 24-h follow up.

Neuroimaging protocol

Baseline neuroimaging studies of head (NCCT scan: slice thickness of 4.0 mm with reconstruction of 0.75 mm and CT angiography) were carried out using a 16-slice multidetector CT scanner (Siemens Sensation, Germany). CTA was carried out using 100 ml of non-ionic contrast injected at the rate of 3.5 ml/s using the bolus chase technique with the following protocol: 120 KV, 200 MA, table feed/rotation 13.5 mm, gantry speed 0.5 s, slice collimation 4 mm (16 mm × 0.75 mm), section width 10 mm, reconstruction interval 1.0 mm, image order caudocranial, Matrix 1024 × 1024, Field or view 120 mm × 120 mm, CTD/vol 21.1 mGy. Hematoma volume was assessed by ABC/2 method.[8] A follow-up (24 h) assessment of hematoma volume was assessed by repeating NCCT scan of the head and utilizing the same parameters as mentioned. Hematoma expansion was defined as >33% increase in the hematoma volume on follow-up NCCT.[5]

TCD protocol

Baseline TCD assessment of bilateral middle cerebral arteries (MCA) was carried out simultaneously immediately after the baseline imaging studies using a 2 MHz probe (SONORA Viasys TCD Machine, Healthcare solutions, Cardinal Health, Madison, WI 53711). Both MCAs were insonated from the transtemporal window at depths of 45-55 mm with the prime focus on the M1 segment of MCA. The following variables were recorded: Peak Systolic Velocity (*PSV*), End Diastolic Velocity (*EDV*), Mean Velocities (*MFV*), Pulsatility Index (PI), and Resistance Index (RI) from the affected (a) and unaffected (u) hemispheres. A follow-up (24 h) TCD assessment was carried out utilizing the same protocol. All patients were managed in a stroke unit during the study period with standard practice parameters applied for patient care.[9,10]

Statistics

We compared the above mentioned TCD variables between patients with and without hematoma expansion. On univariate analysis, the Student's *t*-test was applied to continuous variables and contingency tables with the X^2 test applied to dichotomous variables. A forward stepwise multivariate logistic regression analysis with hematoma expansion at 24 h as the dependent variable was carried out. ROC analysis was carried out to determine the TCD variable cut offs with highest sensitivity and specificity. *P* value < 0.05 was considered significant. All statistical analysis was performed with SPSS software version 16 (Chicago, IL).

Results

In this study, 102 consecutive patients with primary spontaneous supratentorial ICH were screened, out of which 25 were recruited. The reasons for exclusion were intraventricular hemorrhage (*n* = 31); presentation beyond 24 h of symptom onset (*n* = 20); infratentorial ICH (*n* = 10); prior history of CVA (*n* = 4); coagulopathy (*n* = 2); vascular anomalies (*n* = 2), death before TCD examination (*n* = 3), and poor temporal acoustic window (*n* = 5). The study population had a mean age of 52.44 ± 11.35 years with 18 (72%) males. The mean time of presentation from symptom onset was 499 ± 210.8 minutes (Range: 180-990). Fourteen patients (56%) had left hemiplegia; 18 (72%) were hypertensive with mean duration of hypertension being 4.78 ± 3.06 years. Seventeen patients (68%) had basal ganglionic bleed, seven patients (28%) had lobar bleed, with the remaining one patient having basal ganglionic bleed extending into the lobar area. The baseline and 24-h (follow up) characteristics and investigational parameters are outlined in Table 1. Hematoma expansion was noted in 10 patients (40%) at 24-h follow up. Patients with hematoma expansion were younger (45.50 ± 10.4 years) compared to non-expanders (57.07 ± 9.69 years; *P* value: 0.009), had lower mean baseline GCS score (10.0 ± 2.36) versus the non-expander group (11.33 ± 2.26; *P* value: 0.168), higher mean baseline NIHSS score (20.0 ± 7.73) versus the non-expander group (19.6 ± 5.83; *P* value: 0.884). At the 24-h follow up, TCD MCA parameters in the hematoma

Table 1: Baseline and 24-h follow up clinical and investigational data

Parameters	Baseline [Mean ± SD; range]	24-h follow up [Mean ± SD; Range]	*P* value
Number of study subjects	25	25	NA
GCS	10.8±2.4 (7-15)	10.96±2.63 (8-15)	0.07
NIHSS	19.76±6.5 (6-33)	18.9±6.5 (6-31)	0.45
Systolic Blood Pressure (mm of hg)	186.4±29.7 (140-220)	150.8±20.5 (130-210)	0.54
Diastolic Blood Pressure (mm of hg)	108.7±14.9 (80-138)	91.6±10.6 (74-136)	0.66
Mean Arterial Pressure (mm of hg)	134.3±18.9 (113.3-133.3)	111.4±12.8 (100-130)	0.59
Heart Rate (beats per minute)	88.18±11.8 (60-118)	76.32±13.76 (54-120)	0.62
NCCT head, from symptom onset (minutes)	658.4±261.9 (210-1200)	2031.2±314.7 (1500-2640)	NA
Pure hematoma volume	17.62±14.16 ml	23.06±20.2 ml	0.002
TCD from symptom onset (minutes)	733±275.55 (270-1380)	2120±444.7 (1530-3780)	NA

GCS = Glasgow coma scale, NIHSS = National institute of health stoke scale, NCCT head = Non-contrast computerised tomograph scan, TCD = Transcranial doppler

expanders were not significantly altered as compared to those in the non-expanders [Table 2]. Unaffected MCA PI Ratio (u PI ratio = follow up (24 h) u PI/ baseline u PI) was higher in the expanders (1.33 ± 0.35) versus in the non-expanders (1.03 ± 0.6; *P* value: 0.021). Receiver Operating Characteristic (ROC) curve of unaffected hemisphere MCA PI ratio revealed a value of ≥1.055 to be associated with hematoma expansion (sensitivity 90%, specificity 60% ; AUC: 0.740; *P* value: 0.04; 95% CI 0.54-0.94) [Figure 1]. On multivariate logistic regression analysis, unaffected hemisphere MCA PI ratio was significantly associated with hematoma expansion (*P* value: 0.04; Cox and Snell $r^2 = 0.210$; Nagel Kerke $r^2 = 0.284$; 95% CI 1.02–2.02) [Figure 2].

Discussion

Our study demonstrates that the unaffected hemisphere MCA PI ratio ≥ 1.055 is associated with hematoma expansion. The mean increase in unaffected hemisphere MCA PI ratio from baseline in the hematoma expansion group was 48% (*P* = 0.032). The mean age and gender distribution of our study population was comparable to that in the previous epidemiological studies.[11-14] In the present study, the mean duration of performance of baseline CTA/NCCT head and TCD from the point of symptom onset were longer when compared to a previous study on ICH prognostication with TCD[15] [658.4 ± 261.9 minutes and 733 ± 275.55 minutes respectively as against 186 ± 167 minutes and 335 ± 216 minutes, respectively]. This discrepancy could be probably attributed to the fact that only patients presenting within 12 h of symptom onset were recruited in the previous study,[15] without any follow up assessment of TCD or NCCT head to determine hematoma expansion. The baseline stroke severity was moderate to severe (GCS and NIHSS score: 10.8 ± 2.36 and 20 ± 7.73, respectively), and majority (68%) had basal ganglionic bleeds, both of which were comparable to previous studies.[13-15] The baseline and follow-up (24 h) TCD MCA study revealed all parameters (mean PSV, EDV, MFV, PI, and RI) of MCA at 55 mm to be higher on the affected side when compared to the unaffected side, which was consistent with the previous study,[15] with higher overall mean values in the follow-up study without significant difference being observed. Prevalence

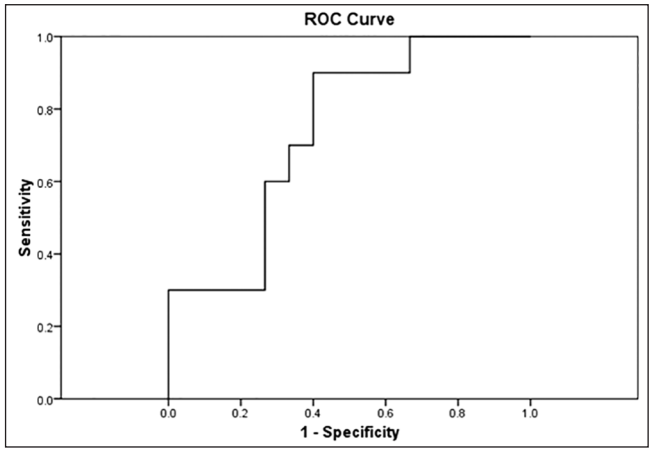

Figure 1: R.O.C curve of u PI ratio and hematoma expansion

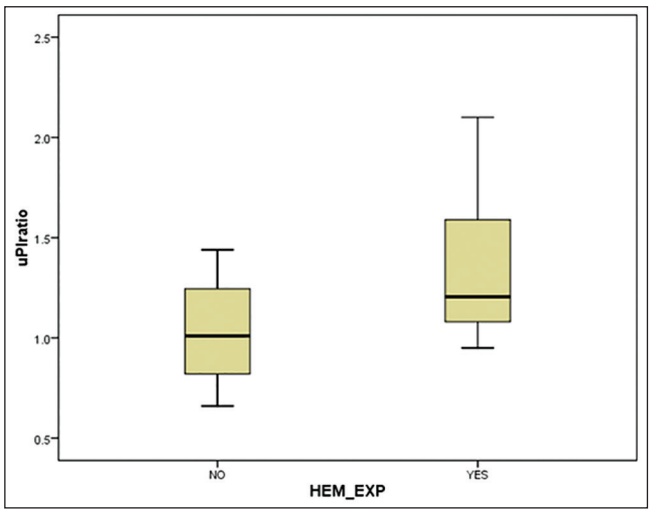

Figure 2: Box plot depicting correlation of u.PI ratio with hematoma expansion

Table 2: Correlation of TCD MCA variables with hematoma expansion

Parameter	Baseline MCA (affected)		*P* value	24-h MCA (affected)		*P* value
	Hem Exp⁺	Hem Exp⁻		Hem Exp⁺	Hem Exp⁻	
PSV (cm/s)	88.8±35.0	77.6±19.9	0.32	89.2±33.1	81.6±31	0.56
EDV (cm/s)	26.4±20.8	23.2±10.1	0.61	28.8±19.9	25.3±14	0.61
MFV (cm/s)	46.5±27.6	40.8±11.9	0.48	48.2±26.6	43.9±19	0.64
PI	1.62±0.55	1.37±0.42	0.22	1.62±0.29	1.38±0.6	0.28
RI	0.73+0.09	0.69+0.09	0.32	0.76+0.05	0.6+0.1	0.02
	Baseline MCA (unaffected)			24 h MCA (unaffected)		
PSV (cm/s)	82.1±32.7	67.88±17	0.17	82.96±26	72.9±16.0	0.25
EDV (cm/s)	27.64±11	21.67±11	0.19	27.38±12	23.1±11.2	0.39
MFV (cm/s)	46.32±14	37.9±12	0.13	45.34±17	40.2±12.0	0.38
PI	1.16±0.3	1.28±0.5	0.48	1.48±0.28	1.32±0.57	0.44
RI	0.65±0.08	0.67±0.1	0.46	0.68±0.05	0.68±0.12	0.93

TCD = Transcranial doppler, MCA = Middle cerebral artery, PSV = Peak systolic velocity, EDV = End diastolic velocity, MFV = Mean systolic velocity, PI = Pulsatility index, RI = Resistance index, Hem Exp⁺ = Those with hematoma expansion, Hem Exp = Those without hematoma expansion. Significant *P* value: < 0.05

of hematoma expansion (40%) was comparable to previous studies (28.4-35%), despite patients being evaluated beyond 6-8 h of stroke.[1,16] Both PI and RI are reliable indicators of ICP. A PI value of more than 1.2 and/or a RI value of more than 0.6 are faithful indicators for raised ICP, indirectly indicating ICP of at least 20 mm of Hg.[17] A persistently elevated ICP may be responsible for the higher unaffected hemisphere MCA PI ratio.[15,17,18] Raised ICP is also expected to result in similar changes in intracranial hemodynamics on both affected and unaffected hemispheres.[19] The distortion of the intracranial vascular anatomy on the affected hemisphere could potentially interfere with the assessment of intracranial hemodynamics by TCD at a fixed depth of insonation, e.g., 55 mm for MCA. The change in PI of the contralateral MCA might also be due to the relative change in the arterial carbon dioxide (CO_2) levels. Such changes may not be evident in the ipsilateral artery due to multiple factors like ischemia-induced vasodilatation, release of various necrotic products, or other chemical mediators of inflammation/oxidative stress/necrosis.[15] This may contribute to the unaffected hemisphere parameter (PI ratio) being the significant variable associated with hematoma expansion. In a previous study, unaffected hemisphere PI value of > 1.75 was found to be an independent predictor of 30-day mortality[15] (sensitivity 80%; specificity 94%); however, TCD variables associated with hematoma expansion were not studied. Based upon our finding of PI correlates to hematoma expansion, we propose that PI may be utilized as a therapeutic target in addition to blood pressure targets currently being used in trials,[20] which have been shown to be associated with limiting hematoma expansion and improving outcomes. A non-invasive technique like TCD does not entail complications of invasive monitoring (e.g., ICP monitoring). The utility of serial TCD measurements to monitor the longitudinal changes in ICP has been well-established.[21,22] The findings of our study need to be further validated on ICH patients recruited at shorter time from symptom onset (<6 h). The limitations of our study are smaller number of patients, longer time window of recruitment and lack of availability of arterial/end tidal CO_2 levels during TCD monitoring as they might be potential confounders in assessment of TCD variables. TCD may thus prove to be useful adjunct to cranial NCCT in prediction of hematoma expansion in the setting of acute spontaneous non traumatic supratentorial primary ICH.

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