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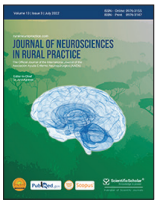

Original Article

Sequential carotid Doppler study in acute stroke and its clinical correlation: A prospective study

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ABSTRACT

Objectives: Resistive index (RI) and pulsatility index (PI) assessed on carotid Doppler assess the hemodynamic status of cranial vasculature. They are related to the severity of stroke and help determine the overall outcome. This study was done to compare the hospital stay and stroke severity with RI and PI of both internal carotid arteries.

Materials and Methods: Patients >18 years of age presenting within 48 h of anterior circulation stroke (either ischemic or hemorrhagic) were included. They were divided into two groups based on their length of stay (LOS). They were assessed clinically on days 1, 3, and 5, and underwent a carotid Doppler study on the same days. The Doppler parameters were correlated with the LOS and stroke severity for possible associations.

Results: One hundred and one patients were included. Forty-seven patients had a favorable outcome based on LOS. In this group, significant decrease in RI and PI scores was seen from days 1 to 3. In patients with unfavorable outcome, there was a significant increase in PI on days 1–3 and days 1–5. The National Institutes of Health Stroke Scale decreased significantly from days 1 to 5 in favorable group

Conclusion: For those with an unfavorable outcome and prolonged LOS, PI continues to increase suggesting a failure of autoregulation. Carotid Doppler can be a simple bedside tool to predict outcome in patients with acute stroke.

Keywords: Stroke, Carotid Doppler, Resistive index, Pulsatility index, National Institutes of Health Stroke Scale, Length of stay

INTRODUCTION

Cerebrovascular accidents (stroke) constitute a major health issue and are the second most common cause of morbidity and the leading cause of disability worldwide.[1] With increasing life expectancy in the developing world, there is an increase in age-related non-communicable diseases, making stroke as the fourth leading cause of death in our country.[2-4] Severity of stroke is objectively quantified by the National Institutes of Health Stroke Scale (NIHSS) and is a major predictor of length of stay (LOS).[5] LOS >7 days defined as a longer stay depends on the provision of acute stroke care, and preventing complications, which is generally achieved within the 1st week of the event.[6] The physiological mechanisms involved in maintaining a constant cerebral blood flow (CBF) and thus, preventing hypo- or hyper-perfusion with changes in cerebral perfusion pressure is disrupted after stroke.[7] This impaired cerebral autoregulation (CA) has been noted in patients with both ischemic and hemorrhagic strokes.[7] Dynamic cerebral CA (DCA), the active response of cerebral vessels to blood pressure fluctuations, is also impaired after acute stroke. This jeopardizes the CBF and renders the brain to further injury from edema and hemorrhagic conversion.[8] DCA can be assessed noninvasively by transcranial Doppler (TCD) sonography that studies spontaneous fluctuations in CBF and blood pressure.[9] DCA is known to worsen for the first few days after an ischemic stroke. It has been seen to be proportionate to the infarct volume and is associated with a poor outcome.[10]. Likewise, carotid Doppler is a non-invasive simple, accurate, and reproducible method to assess carotid arteries for evaluating blood flow.[11,12] It measures peak systolic velocity (PSV), end diastolic velocity (EDV), mean flow velocity (MFV), and peak diastolic velocity which measure the resistive index (RI) and pulsatility index (PI), the most practical parameters for assessing hemodynamic status of the common carotid artery, internal carotid artery (ICA), extracranial carotid artery, vertebral artery, and ophthalmic artery.[13] PI assesses vascular resistance and is considered a marker of small vessel disease and microangiopathic

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changes in the brain,[14,15] whereas RI relates to the vessel wall elasticity.[16] The normal values for PI and RI are typically <1.2 and <0.7, respectively.[17] Assessment of PSV, PI, and RI can provide important information for making therapeutic decisions and help as a prognostic tool in predicting functional outcomes in patients of ischemic stroke or after carotid interventions.[11,18-20] These parameters are related to the NIHSS in a direct relation and can predict the LOS in patients with acute ischemic stroke and hence predict the functional and prognostic outcome in such patients. The present study was done to compare NIHSS, RI, and PI of both ipsilateral and contralateral ICA with the type of stroke (ischemic or hemorrhagic) and duration of hospital stay.

MATERIALS AND METHODS

The present study was conducted at Dr. Ram Manohar Lohia Institute of Medical Sciences, Lucknow, a tertiary care referral teaching institute, from February 2020 to July 2021. Patients above 18 years of age who came to the hospital within 48 h of anterior circulation stroke (either ischemic or hemorrhagic) were included in the study. Those coming in the window period were taken up for stroke intervention and excluded. Furthermore, we excluded patients with renal or hepatic failure and those coming with severe cardiorespiratory distress and requiring mechanical ventilation soon after admission.

Patients fulfilling the selection criteria were assessed clinically with NIHSS on days 1, 3, and 5. Carotid Doppler done by an ultrasonologist, blinded to the study, measured ICA Doppler parameters (RI and PI) for both Ipsilateral and Contralateral ICAs on days 1, 3, and 5. Patients were divided into two groups based on their LOS. Patients with LOS <7 days were taken as favorable outcome and those with LOS ≥7 days were grouped as unfavorable outcome.

Duplex Doppler sonography was done using Mindray Ultrasonography machine with 7 megahertz array transducers. Both ipsilateral and contralateral ICAs were scanned following the standard carotid sonography protocol.[21] Patients were examined in the supine and semi-supine positions with the head slightly rotated to the opposite side. Spectral Doppler scanning was performed to measure the RI and PI of the ICA. The velocity of blood flow was measured in the proximal ICA with a Doppler angle of <60°. RI and PI were calculated from the difference in the systolic and diastolic velocities divided by the MFV and PSV, respectively.[11]

$$PI = (PSV–EDV)/MFV$$

$$RI = (PSV–EDV)/PSV$$

NIHSS was used as a measure of severity of stroke with higher scores indicating a poor neurological status and severe deficits.[22]

Statistical analysis

Data were analyzed using SPSS software. Mean and standard deviation were computed for all quantitative variables for all the 3 days for both the groups. An unpaired *t*-test was used to find the association between LOS and other variables. $P < 0.05$ was considered statistically significant.

RESULTS

One hundred and one patients were included in the study. There were 55 males and 46 females with 65 ischemic and 36 hemorrhagic strokes. Forty-seven patients had a LOS of <7 days (38 ischemic and 9 hemorrhagic stroke) whereas 54 patients had a prolonged LOS of >7 days (27 patients each with ischemic and hemorrhagic stroke). Four patients succumbed to the illness and 97 were discharged in a stable condition.

Comparison of Doppler parameters for ipsilateral ICA for the two groups

For patients having LOS <7 days ($n = 47$), we found that there was a significant decrease in RI score from days 1 to 3 and a non-significant decrease from days 1 to 5. However, PI score decreased from days 1 to day 3, it showed an increase from days 1 to 5, though the differences were not significant [Table 1]. For patients having LOS ≥7 days ($n = 54$), we found that PI scores significantly increased from days 1 to 3 and from days 1 to 5 [Table 1].

In patients with a favorable outcome, RI decreased significantly from days 1 to 3 in ischemic stroke patients whereas all other changes were non-significant. In both ischemic and hemorrhagic strokes, the PI increased non-significantly from days 1 to 5 [Table 2]. In patients with an unfavorable outcome, there was a significant increase in PI in days 1–3 and days 1–5 in ischemic and hemorrhagic stroke, respectively [Table 2]. In patients with hemorrhagic stroke, the RI score showed a significant increase from days 1 to 3 (mean change 0.188, $P = 0.046$) but decreased from days 1 to 5.

There was no statistically significant difference on the comparison of Doppler parameters for ipsilateral and contralateral ICA in the two groups of patients with ischemic stroke.

Comparison of NIHSS score in the two groups

NIHSS decreased in both favorable and unfavorable groups from days 1 to 3 and days 1 to 5, with a significant decrease in NIHSS in the favorable group ($P = 0.010$). The decrease in NIHSS on day 5 compared to day 1 was highly significant in patients with ischemic stroke (mean change −0.447, $P = 0.008$) as compared to hemorrhagic stroke (mean change −0.370, $P = 0.096$).

DISCUSSION

In this study, we evaluated the association of changes in physiological parameters of ICA and NIHSS score with LOS in hospital as a prognostic marker in patients presenting with acute stroke. We found that the markers of peripheral arterial resistance and blood vessel elasticity, PI and RI, decreased over the 5 days in patients with shorter stay compared to an increase in PI in those with prolonged LOS. Although, not all the parameters reached a statistical significance, our findings do indicate that patients with favorable outcomes had reduced peripheral resistance due to reperfusion which led to a decrease in RI. PI showed initial lowering, suggesting dysautoregulation that showed a gradual recovery by the 5th day of ictus. Likewise, in those with a shorter stay, the NIHSS decreased significantly over 5 days, a marker of clinical improvement.

Table 1 : Change in RI and PI for patients with favorable (LOS <7 days) and unfavorable outcome (LOS>7 days).

Index	Mean change	SD	*t*	*P*-value
Favorable outcome (LOC <7 days)				
RI change day 1–3	−0.040	0.102	−2.577	**0.010**
RI change day 1–5	−0.004	0.077	−0.396	0.694
PI change day 1–3	−0.044	0.325	−0.929	0.358
PI change day 1–5	0.022	0.271	0.555	0.582
Unfavorable outcome (LOC >7 days)				
RI change day 1–3	0.011	0.085	0.991	0.326
RI change day 1–5	0.001	0.089	0.076	0.940
PI change day 1–3	0.143	0.449	2.341	**0.023**
PI change day 1–5	0.116	0.396	2.145	**0.037**

LOS: Length of stay, LOC: Length of care, RI: Resistive index, PI: Pulsatility index, SD: Standard deviation. *P*<0.05

PI is a marker of increased vascular resistance caused by small vessel disease.[23] Higher PI is most likely associated with an increase in intracranial pressure and is an independent determinant of volume of infarct in acute stroke.[24,25] Increase in RI >0.70 and PI >1.35 in the middle cerebral artery (MCA) are prognostic indicators of unfavorable outcome in ischemic stroke.[1] Soon after stroke, pathophysiological abnormalities in cerebral microcirculation have been postulated to account for the high PI values in large strokes carrying a poor prognosis. Little *et al*. demonstrated that endothelium and astrocyte end feet get swollen in ischemic stroke.[26] In addition, despite attempts at reperfusion, the capillary beds narrow segmentally by contraction of pericytes, preventing passage of blood cells, as shown by Yemisci *et al*.[27] RI relates to elasticity or extensibility of the vessel and its related vascular resistance.[16] Tagelsir *et al*. found a significant increase in RI on carotid Doppler study in fifty Sudanese patients with acute stroke.[16] Similarly, Staub *et al*., in a prospective study of 146 patients with cardiovascular risk factors followed up for a median 36 months, showed a direct correlation between RI and intima–media thickness (IMT) of the CCA and ICA and cardiovascular and cerebrovascular events in these patients.[28] They concluded that like IMT, RI is an indicator of the vessel wall status and can be a predictive marker of stroke. Lin *et al*. studied 67 ischemic stroke patients, who underwent carotid stenting and found that contralateral

Table 2: Change in RI, PI for patients having favorable (LOS <7 days) and unfavorable outcome (LOC >7 days) in ischemic and hemorrhagic subgroups.

Index	Mean change	SD	*t*	*P*-value
Favorable outcome (LOC <7 days)				
Ischemic stroke RI change day 1–3	−0.045	0.018	−2.517	**0.016**
Ischemic stroke RI change day 1–5	−0.004	0.012	−0.337	0.738
Ischemic stroke PI change day 1–3	−0.043	0.056	−0.778	0.441
Ischemic stroke PI change day 1–5	0.020	0.042	0.483	0.632
Hemorrhagic stroke RI change day 1–3	−0.019	0.059	−0.953	0.369
Hemorrhagic stroke RI change day 1–5	−0.006	0.084	−0.199	0.847
Hemorrhagic stroke PI change day 1–3	−0.047	0.246	−0.570	0.584
Hemorrhagic stroke PI change day 1–5	0.029	0.336	0.258	0.803
Unfavorable outcome (LOC >7 days)				
Ischemic stroke RI change day 1–3	0.012	0.091	0.679	0.503
Ischemic stroke RI change day 1–5	0.007	0.111	0.346	0.732
Ischemic stroke PI change day 1–3	0.188	0.465	2.100	**0.046**
Ischemic stroke PI change day 1–5	0.084	0.447	0.982	0.335
Hemorrhagic stroke RI change day 1–3	0.011	0.081	0.713	0.482
Hemorrhagic stroke RI change day 1–5	−0.006	0.061	−0.471	0.642
Hemorrhagic stroke PI change day 1–3	0.098	0.436	1.169	0.253
Hemorrhagic stroke PI change day 1–5	0.147	0.343	2.220	**0.035**

LOS: Length of stay, LOC: Length of care, RI: Resistive index, PI: Pulsatility index, SD: Standard deviation. *P*<0.05

ICA RI was the most important indicator for differentiating between patients showing good improvement as against those with static symptoms as measured on modified Rankin score.[29] We found no statistically significant difference between ipsilateral and contralateral Doppler parameters in the two groups. El Khatib and El Ahwal, contrary to our findings, found a significant difference in the hemodynamic parameters in both ipsilateral and contralateral MCA on 100 patients of acute ischemic stroke.[19] Similarly, Reinhard *et al*. demonstrated that in large infarcts, deterioration in autoregulation is more on ipsilateral side.[30] They used TCD to look at the hemodynamic parameters of the MCA. Our findings were restricted to the neck vessels that probably account for the difference in our findings. NIHSS was seen to decrease in both our groups, but in those with a favorable outcome, the decrease was consistent and statistically significant. Similar findings were observed by Dawodu and Danesi, in their study on patients with ischemic stroke.[31] LOS is most closely and directly related to the severity of stroke as measured clinically by NIHSS. Koton *et al*. showed that in patients with a NIHSS of 16–20, the LOS was prolonged by 5 times than those with an NIHSS of 5 or less.[5]

In our study, patients with a favorable outcome showed a sequential decrease in RI values on days 3 and 5 in ipsilateral ICA whereas PI showed an initial lowering followed by recovery on day 5. For patients having an unfavorable outcome, PI continued to increase on days 3 and 5 probably suggesting a failure of autoregulation.

Our study has a few limitations. The sample size was small and hence an absolute cutoff value of PI and RI could not be determined in this small cohort. A larger study with both ischemic and hemorrhagic strokes with a good follow-up is worthwhile to come to definite standardized values for these predictive markers. Patients were assessed on NIHSS and LOS was determined based only on this clinical indicator. However, in acute stroke, metabolic and septic complications, especially in the acute period, are well-known and these could have been confounders in our study.

CONCLUSION

In patients with acute cerebrovascular events, measuring the hemodynamic parameters in the ICA using a carotid Doppler as a non-invasive, widely available, bedside reproducible tool can help prognosticating patients. For those with an unfavorable outcome and prolonged LOS, PI continues to increase on days 3 and 5, suggesting a failure of autoregulation. This study supports the notion that in addition to NIHSS, a simple objective bedside carotid Doppler study can be a predictor of outcome in patients with acute cerebrovascular episodes.

Ethical approval

The author(s) declare that they have taken the ethical approval from IRB/IEC.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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