Original Article

Application of the Intracranial Arterial Pulsatility Index for Determination of Prognosis after Lacunar Infarct

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Abstract

Background: We aimed to investigate the usefulness of intracranial arterial pulsatility index to assess the prognosis of lacunar infarcts.

Materials and Methods: Forty-nine patients with confirmed acute lacunar infarct were enrolled in the study. A transcranial color-coded sonography was performed to assess the pulsatility index of bilateral middle cerebral, posterior cerebral, vertebral, and proximal internal carotid arteries. Patients' clinical status was assessed using a modified Rankin scale. Spearman correlation was used for reporting the relation between quantitative data. Statistical significance was defined as a two-tail *p*-value of less than 0.05.

Results: The mean age ± standard deviation was 64.1 ± 9.07 years old, and 57.1% of the patients were male. Upon discharge, only 8.2% of the patients were ranked as 0 on the modified Rankin scale; however, after a 6-month follow-up period, this number increased to 49%. There were no significant differences between the left and right pulsatility index measurements in any of the assessed arteries. Patients with vertebral artery pulsatility indexes >1 on their primary assessment had significantly worse outcomes during the first, third, and sixth months follow-up (all $r > 0.3$, p-values < 0.01). Pulsatility indexes from other arteries did not predict the prognosis.

Conclusion: Sonography-assisted assessment of the vertebral artery blood flow during the early stage of lacunar infarct provides a reliable reference for prognosis estimation.

Keywords: Arterial blood flow velocity, lacunar infarct, pulsatility index, transcranial color-coded sonography

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Introduction

Lacunar infarct, also known as small vessel stroke, is a subset of ischemic cerebrovascular accident that originates from a blockage of flow in the perforating branches of large brain arteries, resulting in specific clinical and radiological outcomes.[1,2] Diagnosis of lacunar infarct is based on the Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria: a clinical syndrome suggestive of lacunar obstruction, without any cortical pathologies, no cardiac source for embolic accidents, and no stenosis of more than 50% in the large extracranial vessels.[3] Lacunar infarct is shown to be less aggressive than other ischemic accidents of the brain; however, follow-up studies suggest undesirable outcomes in the long-term and call for proper treatments to minimize the effects of this disease on cognitive and other neurological dimensions.[4]

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Cerebrovascular accidents with suspected obstructive etiology can be studied using transcranial color-coded sonography (TCCS). This noninvasive method allows the assessment of arterial resistance and the quality of blood flow.[5] Pulsatility index (PI) is a measure of variable blood velocity and could serve as a proxy for arterial resistance.[6] PI increases with aging, as well as in pathologic conditions such as diabetes mellitus, hypertension, high intracranial blood pressure, vascular dementia, and small vessel disease.[7,8] The link between arterial blood flow and prognosis of lacunar infarct has already been investigated, as well as the role of PI in pathology involving small vessels.[9,10]

Finding a reliable method to measure arterial PI could help establish tailored management of patients depending on their suspected outcomes. In this study, we aim to investigate the usefulness of intracranial arterial PI to assess the prognosis of lacunar infarcts.

Material and Methods

Study design

This is a prospective, observational study conducted from January 2016 to June 2016 at the Alzahra Hospital in Isfahan, Iran. We included patients with a diagnosis of lacunar infarct, based on the TOAST classification (with ischemic lesions smaller than 1.5 cm in diameter), who were referred to the neurology ward of our institution.[3] We excluded patients in whom there were clinical deficits associated with cortical functions, such as agnosia or aphasia, presence of cortical lesions on imaging, and/or presence of previous cardiac conditions that increased the risk of embolic strokes (i.e., atrial fibrillation, congestive heart failure, previous myocardial infarctions, and extracranial arterial stenosis of more than 50%). An authorized study member obtained verbal and written informed consent from all participants, or their medical proxy, in a private setting. The study was approved by the Committee on Research Ethics of the Isfahan University of Medical Sciences, and was conducted according to the World Medical Association Declaration of Helsinki.

Data collection

Detailed demographic and baseline data including age, sex, medical and pharmacological history, and history of smoking were retrieved from the patient's electronic charts. Data regarding neurological symptoms at presentation, imaging, and pharmacological treatments after discharge were also collected from all patients.

TCCS exams were performed by a skilled neurologist using a MEDISON Doppler sonography unit with a 2 MHz probe, 1 day after the infarction onset. The following vascular structures were evaluated based on the institutional sonographic protocols: middle cerebral artery, posterior cerebral artery, vertebral artery, and proximal internal carotid arteries on both sides. In each case, PI was defined as the difference between the maximum systolic velocity and end-diastolic velocity (EDV) of blood in each artery over the average blood flow velocity in that artery. After PI measurements, each patient was categorized into two groups based on the PI score (<1 or ≥1) for each of the above-mentioned arteries. The threshold of 1 was established because PI less than 1 is considered to be in the reference range for normality.[11,12] The mean PI of both sides was considered as the indicator of PI for analysis.

Upon discharge, each patient was evaluated and categorized based on clinical symptoms. The modified Rankin scale (mRS) [Table 1] was used to rate the patients' status, and it was also used for the follow-up visits. During each visit, patients were assessed for the improvement of clinical symptoms and disability. Patients with mRS ≥3 were categorized as dependents while patients with mRS <3 were considered independent for basic daily activities.

Data analysis

Data were analyzed using the SPSS software (version 18.0, Chicago, IL, USA). The relation between PI categories (<1 or ≥1) and mRS categories (≥3 or <3) was investigated using the Chi-square test and the calculation of odds ratios (ORs) with 95% confidence intervals (95% CIs). Quantitative data were reported as mean ± standard deviation (SD). Spearman correlation was used for reporting the relation between quantitative data. Statistical significance was defined as a two-tail *P* value of less than 0.05.

Results

A total of 49 patients were enrolled in the study, of which 57.1% were male. The mean age ± SD was 64.1 ± 9.07 years old. More than one-fifth of our patients were smokers, while hypertension was the most frequent comorbidity, followed by dyslipidemia and diabetes mellitus. Half of the patients were undergoing antihypertensive treatment while 30% had antiaggregant therapy. At admission, most patients presented with typical symptoms of cerebral anterior circulation impairment, including hemiparesis, dysarthria, and loss of consciousness, among others. Brain image on computed tomography demonstrated predominant compromise of the internal capsule, followed by small vessel changes. and

Table 1: The modified Rankin scale

Score	Definition
0	No symptoms at all
1	No significant disability despite symptoms; able to carry out all usual duties and activities
2	Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance
3	Moderate disability; requiring some help, but able to walk without assistance
4	Moderately severe disability; unable to walk and attend to bodily needs without assistance
5	Severe disability; bedridden, incontinent and requiring constant nursing care and attention
6	Dead

basal ganglia loss of attenuation [Table 2]. Upon discharge only 8.2% of the patients were ranked as 0 on the mRS; however, after a 6-month follow-up period, this percentage increased to 49% [Table 3]. Two patients died during the follow-up period. Deaths were due to complications of urinary tract infection (2 months after discharge) and pulmonary thromboembolism (4 months after discharge).

There were no significant differences between the left and right PI measurements in any of the assessed arteries. Table 4 presents the correlation of the mean PI ± SD in the middle cerebral arteries, the posterior cerebral arteries, the vertebral arteries, and the proximal internal carotid arteries with mRS at the time of discharge, and 1, 3, and 6 months after discharge. Our results showed that all of the mRS measurements after discharge significantly correlated with PI in proximal internal carotid arteries (r >0.2, p-value < 0.05) and vertebral arteries (r >0.3, p-value < 0.01). In other arteries, we did not find any significant correlation between mRS and PI.

The relation between PI categories (<1 or ≥1) and mRS categories (≥3 as dependent or <3 as independent) showed that a higher PI in the vertebral arteries significantly increases the odds of higher levels of disability in all four measured mRS: at time of discharge (OR: 3.15, 95% CI: 1.6–11.5), 1 month (OR: 4.5, 95% CI: 1.2–16.8), 3 months (OR: 5.6, 95% CI: 1.2–26.1) and 6 months after discharge (OR: 10.6, 95% CI: 1.3–84.7). Higher PI in other arteries showed no significant increase in levels of mRS.

Table 2: Demographic and patient characteristics

Characteristics	Mean±SD/Frequency (%)	
Age	64.1±9.07 years	
Sex	Male	57.1%
	Female	42.9%
History of smoking	Yes	22.4%
	No	77.6%
Past medical history	Diabetes	28%
	Hypertension	70%
	Dyslipidemia	30%
	Ischemic heart disease	4%
	Previous stroke/TIA	14%
Pharmacological history	Aspirin	30%
	Warfarin	4%
	Insulin	4%
	Antihypertensive drugs	50%
	Statins	10%
	Oral hypoglycemic agents	12%
	Oral contraceptives	2%
Affected cerebral circulation	Anterior	70%
	Posterior	30%
Symptoms at presentation	Hemiparesis	70%
	Dysarthria	54%
	Visual loss/diplopia	8%
	Loss of consciousness	12%
	Dizziness/vertigo	8%
	Nausea/vomiting	4%
	Headache	2%
	Hemisensory loss	4%
Affected cerebral area in CT imaging	Basal ganglia	16%
	Thalamus	4%
	Internal capsule	52%
	Subcortical white matter	6%
	Small vessel changes	34%
	Periventricular white matter	16%
Medications at discharge	Aspirin	80%
	Warfarin	2%
	Clopidogrel	16%
	Antihypertensive drugs	40%
	Statins	16%
	Oral hypoglycemic agents	12%
	Insulin	2%

Data were reported as mean±SD or percentage. TIA: transient ischemic attack; CT: computarized tomography

Discussion

We used TCCS to measure the PI in four major intracranial arteries in a group of patients with lacunar infarct, and followed up their clinical outcome over 6 months. Our investigation showed that blood flow velocity in the vertebral arteries and its estimated resistance using PI could significantly predict prognoses among patients with lacunar stroke; PI higher than one was directly correlated with worse prognosis during the 6-month follow-up period when evaluated with the mRS.

The use of TCCS has been suggested previously as a noninvasive test for screening of patients with higher risks for intracranial diseases, although lack of accuracy for grading arterial stenosis has been claimed.[13,14] Notwithstanding, this modality could be a safe method for monitoring patients with significant ICA obstruction at the bedside, when hemodynamic instability may occur.[15]

Intracranial arterial PI, measurable by the TCCS, has been frequently proposed as an index for the assessment of arterial resistance and cerebral circulation status. Several studies have shown that hazardous structural and functional alteration in the wall of the central arteries results in high PI.[16] Consistently, both central systolic blood pressure and carotid blood flow jointly could predict the probability of stroke in at-risk individuals.[17] Also, similar observations have been made on

Table 3: Percentage of each mRS score at follow-ups

Modified rank	At discharge (%)	1 month F/U (%)	3 month F/U (%)	6 month F/U (%)
0	8.2	30.6	44.9	49
1	22.4	28.6	26.5	28.6
2	26.5	16.3	8.2	4.1
3	10.2	6.1	12.2	10.2
4	22.4	16.3	4.1	2
5	10.2	2	2	2
6	0	0	2	4.1

mRS: modified Rankin scale; F/U: Follow-up

Table 4: Correlation of PI in each vessel with mRS at follow-ups

	mRS at discharge		mRS at 1 month F/U		mRS at 3 month F/U		mRS at 6 month F/U	
	r	*P*	*r*	*P*	*r*	*P*	*r*	*P*
MCA	0.03	0.40	0.1	0.44	0.06	0.29	0.07	0.27
Proximal ICA	0.16	0.08	0.23	0.05*	0.27	0.01**	0.28	0.01**
VA	0.28	0.01**	0.36	0.01**	0.34	0.01**	0.34	0.01**
PCA	0.13	0.20	0.02	0.50	0.14	0.17	0.15	0.16

*Significant at 0.05. **Significant at 0.01. PI: pulsatility index; mRS: modified Rankin Scale; F/U: follow-up; r: Spearman correlation coefficient; MCA: middle cerebral artery; ICA: internal carotid artery; VA: vertebral artery; PCA: posterior cerebral artery

EDV. Dilic *et al*.[18] reported that lower EDVs are associated with higher chances for ischemic strokes and recurrence of the episodes. PI in intracranial arteries corresponds to the systemic circulation[19]; it is not surprising that, as reported by Mitchell *et al*.,[20] a marked stiffness of the aorta leads to excessive pulsatility of intracranial arteries and damage of the cerebral microvasculature accompanied by cognitive impairment.

On the other hand, a variety of other factors play important roles that contribute to cerebral arterial PI. In a study by An *et al*.,[21] elevated total homocysteine serum levels were associated with increased PI in the distal cranial arteries among patients with lacunar infarct. Chronic hypertension also affects PI as it decreases the mean blood flow velocity and hence increases the PI.[22] Intracranial arteries such as the middle cerebral artery are also affected by structural changes caused by chronic hypertension.[23] Diabetes mellitus, male gender, aging, smoking, renal dysfunction, and the thickness of intima-media in carotid arteries have also been suggested as contributors to higher PI in distal cerebral arteries.[24–27] In our study, most of our subjects were relatively old-aged males and frequently positive for a history of a chronic disease such as hypertension, diabetes mellitus, or dyslipidemia.

In a study by Heyer *et al*.,[28] PI levels lower than 0.8 were associated with more favorable outcomes and better cerebral blood flow after carotid endarterectomy. Furthermore, as illustrated by Kim *et al*.,[29] PI measurement in patients with lacunar infarct strongly correlated with the infarct size and the severity of ischemia in the brain. Interhemispheric differences of PI in cerebral arteries showed that an imbalance of blood flow in at-risk patients predicted their neuropsychological wellbeing and their cognitive ability.[30]

It has also been reported that higher arterial PI in the brain correlates with progressive lacunar infarction.[31] Lien *et al*.[32] showed that elevated blood flow velocity in the middle cerebral artery is related to intracranial evidence of stenosis, assessed by magnetic imaging. Similar reports also suggest a positive correlation between elevated arterial PI in the brain and intracranial arterial calcification.[33] In the study by Watanabe *et al*.,[34] plaque score and PI were reported to be better predictors of atheroembolic infarct in an elderly sample than the intima-media thickness of arteries.

The prognostic value of the PI of particular brain arteries such as the middle cerebral artery was emphasized in previous studies.[35] The combination of variables provided by TCCS such as minimum velocity and PI was also reported to differentiate various types of stroke, comparable to the TOAST categorization.[36] Similar to our study, some evidence mentioned that the PI of the middle cerebral artery alone could not predict the probability of stroke.[37]

Throughout the follow-up process in our study, all of the enrolled patients showed improvement of clinical status, except for two patients who died due to secondary complications of their disease. The arterial PI of all four major intracranial arteries was used as a reference for the assessment of prognoses. The average mRS ratings of patients had a constant decreasing trend based on data from all four evaluated arteries; however, statistical significance was achieved only when the vertebral artery was used as the comparison reference. This could be found because of the small sample size, and the fact that many of the demographic and disease characteristics among our sample were homogeneously distributed, meaning that significant differences were harder to reveal.

Conclusion

We conclude that using sonography-assisted assessment of blood flow of the vertebral arteries during the early stage of lacunar infarct provides a reliable reference for the estimation of prognosis. Nevertheless, validation of our results with larger studies is needed.

Declarations

Ethics approval and consent to participate

This retrospective study was approved by our Institutional Review Board and is HIPPA compliant; a waiver for consent was granted.

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Conflicts of interest

There are no conflicts of interest.

References

1. Fisher CM. The arterial lesions underlying lacunes. Acta Neuropathol 1968;12:1–15.

2. Moroni F, Ammirati E, Hainsworth AH, Camici PG. Association of white matter hyperintensities and cardiovascular disease: The importance of microcirculatory disease. Circ Cardiovasc Imaging 2020;13:e010460.
3. Adams HP, Bendixen BH, Kappelle LJ, Biller J, Love BB, Gordon DL, *et al*. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of Org 10172 in acute stroke treatment. Stroke 1993;24:35–41.
4. Fu S, Zhang J, Zhang H, Zhang S. Predictive value of transcranial doppler ultrasound for cerebral small vessel disease in elderly patients. Arq Neuropsiquiatr 2019;77:310–4.
5. Ghorbani A, Ahmadi MJ, Shemshaki H. The value of transcranial Doppler derived pulsatility index for diagnosing cerebral small-vessel disease. Adv Biomed Res 2015;4:54.
6. Purroy F, Sánchez E, Lecube A, Arqué G, Vicente-Pascual M, Mauri-Capdevila G, *et al*. Prevalence and predictors of cerebral microangiopathy determined by pulsatility index in an asymptomatic population from the ILERVAS project. Front Neurol 2021;12:785640.
7. Kozera GM, Neubauer-Geryk J, Wolnik B, Szczyrba S, Wojczal J, Nyka WM, *et al*. Cerebral and skin microcirculatory dysfunction in type 1 diabetes. Postepy Dermatol Alergol 2019;36:44–50.
8. Bonow RH, Young CC, Bass DI, Moore A, Levitt MR. Transcranial Doppler ultrasonography in neurological surgery and neurocritical care. Neurosurg Focus 2019;47:E2.
9. Nam K-W, Kwon H-M, Lee Y-S. Distinct association between cerebral arterial pulsatility and subtypes of cerebral small vessel disease. PLoS One 2020;15:e0236049.
10. Regenhardt RW, Das AS, Lo EH, Caplan LR. Advances in understanding the pathophysiology of lacunar stroke: A review. JAMA Neurol 2018;75:1273–81.
11. Figaji AA, Zwane E, Fieggen AG, Siesjo P, Peter JC. Transcranial Doppler pulsatility index is not a reliable indicator of intracranial pressure in children with severe traumatic brain injury. Surg Neurol 2009;72:389–94.
12. Bellner J, Romner B, Reinstrup P, Kristiansson K-A, Ryding E, Brandt L. Transcranial doppler sonography pulsatility index (PI) reflects intracranial pressure (ICP). Surg Neurol 2004;62:45–51; discussion 51.
13. Sharma VK, Tsivgoulis G, Lao AY, Malkoff MD, Alexandrov AV. Noninvasive detection of diffuse intracranial disease. Stroke 2007;38:3175–81.
14. Ghorbani A, Ashtari F, Fatehi F. The assessment value of transcranial Doppler sonography versus magnetic resonance angiography in vertebrobasilar stroke. J Res Med Sci 2010;15:133–9.
15. Christou I, Felberg RA, Demchuk AM, Grotta JC, Burgin WS, Malkoff M, *et al*. A broad diagnostic battery for bedside transcranial Doppler to detect flow changes with internal carotid artery stenosis or occlusion. J Neuroimaging 2001;11:236–42.
16. Brar I, Robertson AD, Hughson RL. Increased central arterial stiffness and altered cerebrovascular haemodynamic properties in South Asian older adults. J Hum Hypertens 2016;30:309–14.
17. Chuang S-Y, Cheng H-M, Bai C-H, Yeh W-T, Chen J-R, Pan W-H. Blood pressure, carotid flow pulsatility, and the risk of stroke: A community-based study. Stroke 2016;47:2262–8.
18. Dilic M, Hadziomerovic M, Fazlibegovic E, Mlaco A, Terzic O, Kazic S, *et al*. Risk factors for cerebrovascular events: End-diastolic flow velocity. Med Arh 2007;61 (2 Suppl 1):11–4.
19. Kim JY, Bushnell CD, Park JH, Han SM, Im JH, Han SW, *et al*. Central aortic pressure and pulsatility index in acute ischemic stroke. J Neuroimaging 2015;25:438–42.
20. Mitchell GF, van Buchem MA, Sigurdsson S, Gotal JD, Jonsdottir MK, Kjartansson Ó, *et al*. Arterial stiffness, pressure and flow pulsatility and brain structure and function: The age, gene/environment susceptibility--Reykjavik study. Brain 2011;134:3398–407.
21. An S-A, Lee H-B, Kim Y, Kim J, Kim H-S, Kim W-C, *et al*. Plasma total homocysteine level is associated with the pulsatility index of cerebral arteries in lacunar infarction. Yonsei Med J 2013;54:819–24.
22. Cho SJ, Sohn YH, Kim GW, Kim JS. Blood flow velocity changes in the middle cerebral artery as an index of the chronicity of hypertension. J Neurol Sci 1997;150:77–80.
23. Heliopoulos I, Artemis D, Vadikolias K, Tripsianis G, Piperidou C, Tsivgoulis G. Association of ultrasonographic parameters with subclinical white-matter hyperintensities in hypertensive patients. Cardiovasc Psychiatry Neurol 2012;2012:616572.
24. Karakurt F, Carlioglu A, Koktener A, Ozbek M, Kaya A, Uyar ME, *et al*. Relationship between cerebral arterial pulsatility and carotid intima media thickness in diabetic and non-diabetic patients with non-alcoholic fatty liver disease. J Endocrinol Invest 2009;32:63–8.
25. Kochanowicz J, Lewko J, Rutkowski R, Turek G, Sieskiewicz A, Lyson T, *et al*. Influence of smoking cigarettes on cerebral blood flow parameters. Biol Res Nurs 2015;17:8–12.
26. Lee K-O, Lee K-Y, Lee S-Y, Ahn C-W, Park JS. Lacunar infarction in type 2 diabetes is associated with an elevated intracranial arterial pulsatility index. Yonsei Med J 2007;48:802–6.
27. Lee E-J, Jeong H-B, Bae J, Guk HS, Jeong H-Y, Lee EJ, *et al*. Renal dysfunction is associated with middle cerebral artery pulsatility index and total burden of cerebral small vessel disease. Cerebrovasc Dis 2021;50:722–8.
28. Heyer EJ, Mergeche JL, Connolly ES. Middle cerebral artery pulsatility index and cognitive improvement after carotid endarterectomy for symptomatic stenosis. J Neurosurg 2014;120:126–31.
29. Kim Y, Lee H, An SA, Yim B, Kim J, Kim OJ, *et al*. The effect of pulsatility index on infarct volume in acute lacunar stroke. Yonsei Med J 2016;57:950–5.
30. Krejza J, Arkuszewski M, Radcliffe J, Flynn TB, Chen R, Kwiatkowski JL, *et al*. Association of pulsatility index in the middle cerebral artery with intelligence quotient in children with sickle cell disease. Neuroradiol J 2012;25:351–9.
31. Lee K-J, Jung K-H, Park C-Y, Kim J-M, Lee S-T, Chu K, *et al*. Increased arterial pulsatility and progression of single subcortical infarction. Eur Radiol 2017;27:899–906.
32. Lien LM, Chen WH, Chen JR, Chiu HC, Tsai YF, Choi WM, *et al*. Comparison of transcranial color-coded sonography and magnetic resonance angiography in acute ischemic stroke. J Neuroimaging 2001;11:363–8.
33. Park K-Y, Chung P-W, Kim YB, Moon H-S, Suh B-C, Yoon WT. Increased pulsatility index is associated with intracranial arterial calcification. Eur Neurol 2013;69:83–8.
34. Watanabe K, Suzuki T, Nakano H, Oba K. [Carotid parameters measured by ultrasonography as a marker of atherothrombotic infarction and lacunar infarction in high risk elderly people]. Nippon Ronen Igakkai Zasshi 2005;42:684–90.
35. Wijnhoud AD, Koudstaal PJ, Dippel DW. The prognostic value of pulsatility index, flow velocity, and their ratio, measured with TCD ultrasound, in patients with a recent TIA or ischemic stroke. Acta Neurol Scand 2011;124:238–44.
36. Nishiyama Y, Katsumata T, Otori T, Katayama Y. Carotid hemodynamic parameters are useful for discriminating between atherothrombotic infarction and lacunar infarction. J Stroke Cerebrovasc Dis 2010;19:441–9.
37. Markus H, Cullinane M. Severely impaired cerebrovascular reactivity predicts stroke and TIA risk in patients with carotid artery stenosis and occlusion. Brain 2001;124:457–67.