Characteristics of basilar artery atherosclerotic plaques in pontine infarctions: A high-resolution magnetic resonance imaging study

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ABSTRACT

Objective: This study used a 3.0T high-resolution magnetic resonance imaging approach to explore basilar artery plaque characteristics in patients suffering from acute isolated pontine infarction.

Materials and methods: 30 consecutive patients suffering from acute isolated pontine infarction were enrolled in this study and underwent examinations including high-resolution MRI assessment of the basilar artery within 7 days following infarction.

Results: The basilar artery plaque burden of 16 patients with paramedian pontine infarction was 0.26±0.085, while the reconstruction index and enhancement rate index values in these patients were 1.097±0.133 and 1.750±0.447, respectively. In the 14 patients suffering from deep pontine infarction, these three values were 0.21±0.055, 0.896±0.223, and 1.285±0.611, respectively.These values differed significantly when comparing patients suffering from paramedian pontine infarction to those suffering from deep pontine infarction.

Conclusion: This study suggests that the characteristics of basilar artery plaques differ between the two subtypes of pontine infarctions, which may account for the differences in prognosis associated with these two infarct subtypes.

Acute isolated pontine infarction (AIPI) events account for about 15% of total posterior circulation infarction events [1], which can be clinically separated into paramedian pontine infarction (PPI) and lacunar pontine infarction (LPI) subtypes [2]. In PPI, the infarct affects the basal surface of the pons, whereas this is not the case for LPI [3]. PPI events generally present with more severe clinical symptoms than LPI events. Consistent with this, Erro et al. determined that the average modified Rankin Scale (mRS) score of PPI patients on admission was 3.1 ± 0.9, whereas for LPI patients it was 1.6 ± 1.04 [4]. Kunz et al. further determined that PPI was associated with worse acute phase progression, with mRS scores reaching as high as 5 [5]. Although the clinical symptoms of the two types of pontine infarction are similar, the underlying pathogenesis and associated treatments differ between the two.

In recent years, high-resolution MRI(HR-MRI) has been increasingly used in clinical studies.HR-MRI yields high spatial resolution images that can more effectively display vessel walls, thereby improving the power of MRI scans as a means of understanding the pathogenesis of cerebral vascular disease [6,7]. High-resolution magnetic resonance

plaque imaging can differentiate the pathological characteristics of the two types of pontine infarctions and provide a basis for their differential treatment [7,8].Therefore, the present study used high-resolution magnetic resonance plaque analysis software to calculate the properties of the plaques and to fully analyze and compare the differences between them.

Materials and methods

Patients

The study was conducted in accordance with the Ethical Principles for Medical Research Involving Human Subjects outlined in the Declaration of Helsinki. The Institutional Ethics Committees of Zhujiang Hospital, Southern Medical University approved the present study, and all patients provided written informed consent prior to HRMRI scans. Patients were enrolled from Zhujiang Hospital from May 2018 to January 2020. Patients eligible for enrollment in this study were those that met the following criteria: 1) patients experiencing their first-ever symptomatic

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stroke; 2) patients that had suffered an acute isolated pontine infarction identified via diffusion-weighted imaging (DWI); 3) HRMRI, DWI, ECG, magnetic resonance angiography (MRA), and blood lipid analyses were conducted within 7 days of infarct onset; 4) MRA or CTA scans had confirmed basilar artery stenosis. Patients were excluded from this study if they exhibited the following conditions: 1)non-atherosclerotic vasculopathy, such as dissection, arteritis, or Moyamoya disease; 2) atrial fibrillation, rheumatic heart disease, or a metallic heart valve; 3) an infarction not confined to the pontine region; 4) ultrasound-confirmed severe stenosis of the vertebral artery; 5) poor image quality.

HR-MRI scanning

Patients were scanned with a 3.0 T MR scanner (Siemens 3.0T Magnetom Verio, Erlangen, Germany). The whole brain was scanned with a slice thickness of 5.5 mm in the axial plane with a protocol consisting of T1- and T2-weighted imaging, FLAIR, and DWI. Black-blood HR-MRI sequences including proton-density TSE (TR/TE = 3290/ 16, FOV = 150 *150 mm, matrix = 272×320, number of excitations = 2) and T2-dark-fluid-SPAIR sequences (TR/ TE = 3000/26, FOV = 150×150 mm, matrix = 251×256, number of excitations = 1) were obtained in the axial plane with a slice thickness of 2 mm.

Assessment of basilar arterial plaques

Image analyses were performed using a workstation (Advantage Workstation AW4.3_08) in the Department of Radiology.Two neuroradiologists blinded to patient clinical data independently assessed and provided descriptive analyses of patient HRMRI and MRA images. Any discrepancies were resolved through discussion and consensus. Basilar artery stenosis was detected by MRA, and the degree of vascular stenosis (%) was defined as [(1 - (D stenosis /D normal)] × 100, where 'D stenosis' and 'D normal' corresponded to the arterial diameter at the region with the most severe stenosis and the proximal normal arterial diameter, respectively [8]. Plaques were defined as eccentric wall thickening of the basilar artery in HRMRI scan results [9]. Annular plaques were those growing in a circle on the wall of the basilar artery, whereas arc plaques were those exhibiting eccentric growth [10]. The basilar arterial lumen was separated into four quadrants on axial images: dorsal, ventral, left, and right [11]. An experienced neuroradiologist selected the narrowest vascular layer, after which the vascular boundary, lumen boundary, and plaque boundary were manually traced. Wall area was defined by subtracting the lumen area from the vessel area. Before measurement, three specific sites (the maximal-lumen-narrowing site where the stenosis of basilar artery was most severe and two reference sites where the vessel walls of the basilar artery were normal or had minimal atherosclerosis proximal and distal to the maximal-lumen-narrowing site, respectively) were selected after visual comparison. All measurements were carried out on these three sites.Plaque burden was calculated as follows: (plaque area/vessel area at the site of maximal lumen narrowing) *100%. The lumen stenosis rate was calculated as follows: plaque area/(plaque area + lumen area) at the site of maximal lumen narrowing *100%.The remodeling index was defined as follows: (vessel area at the site of maximal lumen narrowing/reference vessel area) *100%. A remodeling index > 1.05 was indicative of positive remodeling, whereas a remodeling index < 0.95 was indicative of negative remodeling.When remodeling index values were between 0.95 and 1.05, this was considered to be consistent with intermediate remodeling of the basilar artery [12,13]. Intraplaque hemorrhage (IPH) measurements were made at multiple locations. Three levels of plaque enhancement were measured. When no significant T1W1 changes were detected before enhancement, no enhancement was considered to be present (grade 0). Weaker than pituitary parenchymal enhancement was considered to be mild enhancement (grade 1), while enhancement similar to the pituitary parenchyma was considered to be indicative of significant enhancement (grade 2) [14]. Intraplaque hemorrhage was defined as a
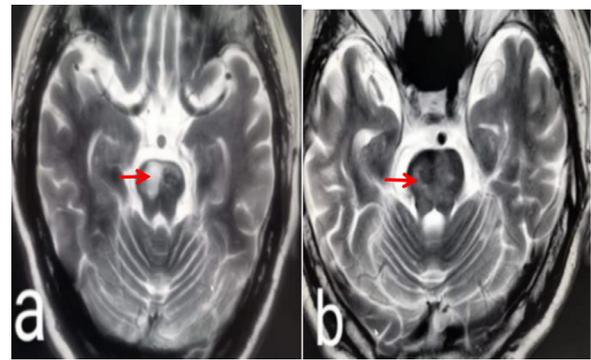

Fig. 1. (a) Paramedian pontine infarction. b) Deep pontine infarction.The red arrow points to the pontine infarction lesion.
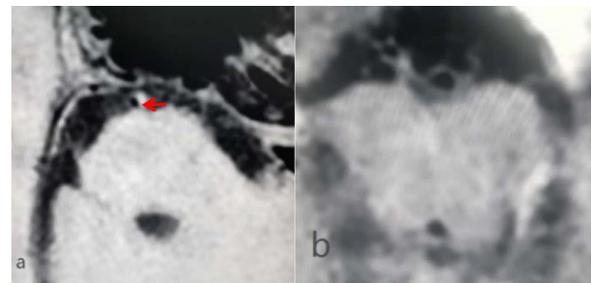

Fig. 2. High-resolution images of the basilar artery in a patient with LPI. a) The right eccentric plaque at its narrowest point; b) the proximal normal lumen. This plaque exhibited negative remodeling. The red arrow points to the eccentric plaque.
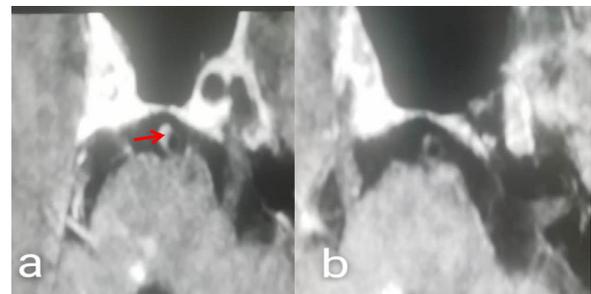

Fig. 3. High-resolution images of the basilar artery in a patient with PPI. a) The left eccentric plaque at its narrowest point, b) the proximal normal lumen. This plaque exhibits positive remodeling. The red arrow points to the eccentric plaque.

plaque enhancement signal strength greater than 150% of that of adjacent muscles after T1WI sequence enhancement [15] Figs. 1–4.

Data analysis

SPSS v24.0 was used for all data analyses. Continuous data were given as means ± standard deviation, and were compared via Student's t-tests. Categorical data were given as percentages and were compared via chi-squared tests. $P < 0.05$ was the significance threshold for this study.

Results

Clinical data

Among 30 enrolled patients (23 male, 7 female; male-female ratio: 3.29: 1), 16 and 14 were affected by PPI and LPI, respectively. A total
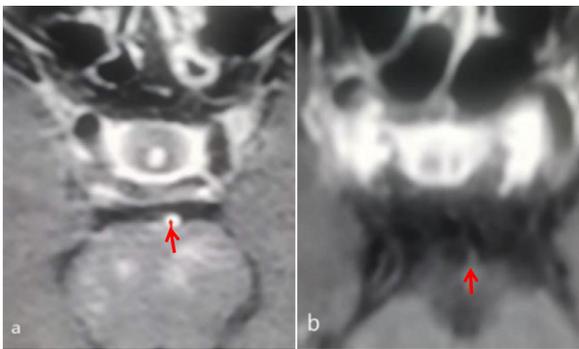
Fig. 4. (a) A plaque showing obvious enhancement; b) a plaque showing mild enhancement. The red arrow points to the plaque.

Table 1
Basic clinical information in LPI and PPI patients.

	PPI (16)	LPI (14)	P
Gender (male)	15	8	0.017
age	65.31±7.02	64.71±7.13	0.842
diabetes	8	5	0.448
coronary heart disease	1	2	0.481
smoking	8	5	0.448
hypertension	14	10	0.288
total cholesterol	4.36±1.70	5.13±1.37	0.200
triglyceride	1.39±0.58	1.85±1.21	0.200
HDL	3.41±9.29	1.277±0.33	0.398
LDL	2.74±1.38	2.98±1.17	0.627

Table 2
Characteristics of basilar artery plaques in PPI and LPI patients.

	PPI(16)	LPI(14)	P
eccentricity	0.47±0.098	0.52±0.117	0.60
Plaque scale	5.13±2.25mm^2	3.36±8.42mm^2	0.01
Plaque burden	0.26±0.085	0.21±0.055	0.039
Remodeling index	1.097±0.133	0.896±0.223	0.005
Intraplaque hemorrhage	0.313±0.478	0.071±0.267	0.106
Enhancement index	1.750±0.447	1.285±0.611	0.024

of 24, 13, 13, and 3 patients exhibited hypertension, diabetes, a history of smoking, and coronary heart disease, respectively (Table 1). Other than gender, clinical characteristics were similar between these groups. There were significantly more female patients in the LPI group relative to the PPI group.

The eccentricity in the PPI and LPI cohorts was 0.47±0.098 and 0.52±0.117, respectively, with no significant differences between these two groups ($P = 0.60$). The average plaque scale in the LPI group was significantly lower than that in the PPI group ($P = 0.01$), while plaque burden, remodeling index, and enhancement index values in the LPI cohort were significantly lower than those in the PPI cohort ($P<0.05$). In the PPI cohort, the remodeling index was 1.097±0.133, with positive and negative remodeling being evident in 12 and 4 cases, respectively. In contrast, the remodeling index in the LPI cohort was 0.896±0.223, with 5 and 9 cases exhibiting positive and negative remodeling, respectively. These results differed significantly between these two groups ($P = 0.005$). The incidence of intraplaque hemorrhage in the PPI and LPI cohorts was 0.313±0.478 and 0.071±0.267, respectively, with no significant differences between these two groups ($P = 0.106$). Obvious and mild enhancement were evident in 12 and 4 PPI patients, respectively, and in 5 and 8 LPI patients, respectively, with a significant difference between these two groups ($P = 0.024$) (Table 2).

Discussion

Previous studies in patients with isolated pontine infarctions have demonstrated that PPI is associated with a worse prognosis relative to LPI. As a large number of patients with acute pontine infarction experience neurological deterioration, many studies have investigated predictors of early neurologic deterioration, with lower pontine lesions, larger lesion volume, and longer basilar artery diameter all having been found to be associated with a worse prognosis. However, these studies evaluated the basilar artery by MRA.The present study used HRMRI plaque analysis software to calculate the properties of the plaques in PPI and LPI patients. The common causes of pontine infarction include (1) the hyaline degeneration of the perforating artery itself, particularly in the context of lacunar cerebral infarction; (2) stenosis or occlusion of the main artery that gives rise to the perforator artery, resulting in decreased perfusion in the area supplied by the perforator artery; (3) cardiogenic embolism; (4) stenosis or occlusion caused by atherosclerosis at the entrance of the perforating artery in what has been termed branch atheromatous disease (BAD). Basilar arterial plaques in PPI patients primarily exhibited an arc-like conformation, and were distributed at the opening of the ipsilateral perforator artery, potentially confirming the diagnosis of PPI as a perforator vascular disease. The mechanistic basis for perforator artery stenosis is uncertain, but it is speculated to be related to atherosclerotic plaques forming at the opening of the perforator artery [16], main artery atherosclerotic plaques which cause the occlusion of the perforator artery [3], and/or atherosclerotic plaques extending from the main artery to the perforator arterial junction [17].

HRMRI revealed that basilar artery plaques in PPI patients were primarily located on the right, whereas in LPI patients they were primarily located on the left. However, according to Wanqian et al., symptomatic basilar artery plaques are primarily distributed in the ventral region (39.3%) or in more than two regions, whereas asymptomatic basilar artery plaques are primarily observed in the left (33.3%) and right (25.0%) regions [18]. However, post-mortem histological analyses conducted by Ravensbergen et al. have yielded contrasting results, suggesting that basilar artery plaques were more common in the right or left regions [19]. These inconsistencies may be attributable to the small sample size in our study.

We found that in PPI patients, the basilar artery was dominated by positive remodeling, whereas in LPI patients it was instead dominated by negative remodeling. Such vascular remodeling reflects the atherosclerosis-related structural changes involved in the adaptation to vascular injury [20]. Prior research regarding plaques in the carotid and coronary arteries studies has shown that positive remodeling is associated with plaque instability and a tendency for bleeding to occur [21], whereas negative remodeling is linked to plaque sclerosis and calcification, resulting in vessel constriction [22,23]. There is recent evidence suggesting that the same may also be true for the basilar artery. For example, Ma et al. found that the remodeling ratio of the symptomatic basilar artery was 1.2 ± 0.4, including 19 cases of positive remodeling and 11 cases of negative remodeling [13]. They also determined that LDL and homocysteine levels were typically higher in patients exhibiting positive remodeling than in those exhibiting negative remodeling. Additional evidence indicated that remodeling is closely associated with interventional surgery complications [24], suggesting that basilar artery HRMRI scans should be conducted prior to interventional surgery [25].

We observed intraplaque hemorrhage rates associated with PPI and LPI of 0.313±0.478 and 0.071±0.267, respectively. Intraplaque hemorrhage is a major signal of plaque instability and elevated ischemic stroke risk [26]. Previous studies have shown that intraplaque hemorrhage indicates plaque instability, and basilar artery plaques with PPI are more unstable [15]. However, the results of this study are different from previous reports, which may be related to the insufficient sample size of this study.

We further determined that the degree of plaque enhancement was better for PPI patients than for LPI patients, which may be attributable

to the greater instability of basilar artery plaques in the context of PPI. Indeed, plaque enhancement is a known indicator of plaque instability [14,27]. Qiao et al. also found plaque enhancement to be positively correlated with ischemic stroke incidence [28], while Vakil et al. found that the degree of plaque enhancement within 24 h was significantly greater for symptomatic plaques relative to non-symptomatic plaques [29]. However, the exact causes of intracranial atherosclerotic plaque enhancement have remained uncertain [30].

This study has multiple limitations. First, as this was a single-center study with a small sample size, there is a risk of selection bias. Second, no additional follow-up of patients was conducted to compare PPI and LPI patient outcomes.Third, a pathology-wall imaging control study of coronary and carotid artery plaques confirmed that the plaque components included necrotic cores, intraplaque hemorrhage, fibrous caps, and calcification, preliminarily confirming that vulnerable plaques exhibited thin fibrous caps, large necrotic cores, and intraplaque hemorrhage. However, due to the small diameter of the basilar artery, the limited resolution of the current approach was insufficient to accurately identify the intracranial plaque components such as necrotic cores or calcification.Finally, our HRMRI findings were limited by our inability to conduct histologic verification, as collecting intracranial vessel samples is difficult.

Conclusion

In patients suffering from PPI, the basilar artery was dominated by positive remodeling, whereas in individuals that suffered from LPI, it was instead dominated by negative remodeling. The basilar artery plaque area, plaque burden, and plaque enhancement ratio values associated with PPI were greater than those associated with LPI, which may account for the different prognosis associated with these two stroke subtypes.

Declaration of Competing Interest

The authors report no conflicts of interest.

Acknowledgment

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