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Clinical Significance of Intraplaque Hemorrhage in Low- and High-grade Basilar Artery Stenosis on High-resolution MRI

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Abstract

Background and Purpose—Intraplaque haemorrhage (IPH) within intracranial atherosclerotic plaques identified by high resolution MRI (hrMRI) has been studied as a potential marker of stroke risk. However, previous studies only examined intracranial arteries with significant stenosis (degree of stenosis >50%). This study aimed to ascertain the clinical relevance of IPH in patients with low and high grade stenotic basilar artery plaques.

Methods—Patients with basilar artery stenosis (n= 126; mean age 62±10; 66 symptomatic and 60 asymptomatic) underwent hrMRI. The relationship between imaging findings (IPH, contrast enhancement, degree of stenosis, minimal lumen area [MLA] and plaque burden [PB]) and symptoms were analysed.

Results—IPH was identified in 22 patients (22%), including 21 (31.8%) symptomatic patients, and 1 (1.7%) asymptomatic patient. Multivariate analysis showed IPH was the strongest independent marker of symptomatic status (odds ratio [95% confidence interval]: 27.5 [3.4, 221.5]; p=0.002). Contrast enhancement was also independently associated with symptomatic status (odds ratio: 9.9 [1.5, 23.6]; p=0.016). Stenosis, MLA and PB were not correlated with symptoms (p>0.05). IPH was present in both low and high grade stenotic basilar arteries (11.3% vs. 16.3%, p=0.63). Diagnostic performance values of IPH for acute/subacute symptomatic stroke patients were: specificity 98.3%, sensitivity 31.8%, positive predictive value 95.5% and negative predictive value 56.7%.

Conclusions—IPH is present in both low and high grade stenotic basilar artery plaque and independently associated with symptomatic stroke status. IPH may identify high-risk plaque and provide new insight into the management of stroke patients without significant stenosis.

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Introduction

Intracranial atherosclerotic disease (ICAD) is a major cause of stroke that has likely been underappreciated, in part due to challenges in detecting intracranial atherosclerotic plaque [1]. ICAD may produce ischemia through multiple mechanisms including: thrombotic occlusion; occlusion of small perforating arteries; plaque rupture leading to artery-to-artery embolization; and vessel luminal narrowing leading to hypoperfusion [2]. Current practice guidelines rely solely on the degree of stenosis (often ≥ 50%) of major intracranial arteries in determining management strategies. However, many authors have questioned this practice, especially given the high prevalence at autopsy of mild and moderate intracranial arterial stenosis in fatal stroke [2–6]. Branch occlusive disease, in particular, has been underestimated and appears to constitute a more common cause of stroke [5]. Other factors including plaque composition, arterial hemodynamic features, and collateral status have been proposed as alternative variables to better predict recurrent stroke risk [4].

ICAD with ischemia caused by artery-to-artery embolization from plaque rupture may require more aggressive antiplatelet therapy to mitigate clot progression whereas stenotic disease resulting in hypoperfusion might benefit more from angioplasty [2]. Given these important distinctions in treatment selection for patients with ICAD based on stroke mechanism, the assessment of culprit plaque location and morphology is clinically relevant [2]. In the past decade, many advances have been made in visualizing large vessel intracranial plaque morphology and composition using high-resolution MRI (hrMRI) [7, 8]. Expanded use of hrMRI could result in the reclassification of many strokes previously termed cryptogenic and could improve clinical decision-making. A few studies have examined atherosclerotic plaque of the posterior circulation using hrMRI with improved characterization of basilar ICAD [9–13].

Intraplaque hemorrhage (IPH) occurs in atherosclerotic plaque and is attributed to fragile neovascularity with endothelial disruption that increases plaque wall stress, making plaque more vulnerable [14]. IPH was first identified as T_1-weighted hyperintense signal in extracranial carotid plaque imaging [15], and subsequent papers have supported carotid IPH as a risk factor for recurrent stroke independent of stenosis [16, 17]. Preliminary work using intracranial hrMRI showed similar appearance of IPH within intracranial arteries in symptomatic ICAD [18]. Xu *et al.* observed T_1-weighted hyperintense signal more often in symptomatic middle cerebral artery plaque than in asymptomatic plaques [19]. More recently, in patients with basilar artery stenosis, hrMRI has found IPH to be more frequent in symptomatic patients than in asymptomatic patients (42.3% versus 21.4%), suggesting a risk for IPH with a relative risk of 1.64 [12].

These prior basilar artery hrMRI studies have only imaged basilar artery plaque with high grade stenosis. The primary aim of this study is to ascertain the presentation and clinical relevance of basilar artery IPH in both low and high grade stenotic basilar artery plaques. Given the frequency of non-stenotic ICAD in stroke and preliminary evidence supporting IPH as a risk factor, we hypothesize that IPH status might be useful in distinguishing acute/subacute symptomatic from chronic/asymptomatic basilar artery plaque regardless of degree of stenosis.

Methods

The authors declare that all supporting data are available within the article.

Study Population

This study was approved by the local Institutional Review Board with all patients providing written informed consent.

This is a prospective study. Patients with basilar artery atherosclerotic disease were recruited to this study between September 2013 and October 2016. The inclusion criteria were: 1) ischemic stroke or transient ischemic attacks (TIA) in the basilar artery territory, and/or basilar artery stenosis >30% on DSA, CTA or MRA; and 2) more than one atherosclerotic risk factors, including hypercholesterolemia, hypertension, smoking, and diabetes mellitus. Exclusion criteria included: 1) coexistent unilateral or bilateral vertebral artery stenosis >50% on MRA; 2) complete basilar artery occlusion; 3) dissection; 4) intracranial dolichoectasia; 5) non-atherosclerotic intracranial arterial disease, e.g. inflammatory arteritis and congenital agenesis; 6) presence of atrial fibrillation on 24-hour monitoring; (7) clinical contraindications to MRI.

Symptomatic plaque was defined if conventional neuroimaging (FLAIR and DWI images) demonstrated infarct within the basilar artery territory. Patients were classified into two groups based on their symptom presentation: 1) symptomatic ischemic stroke/TIA symptoms presented less than 12 weeks before imaging; and 2) patients with asymptomatic basilar plaque without neuroimaging evidence of infarct.

Patients' clinical information including age, sex, diabetes, hypertension, smoking, hyperlipidemia, pre-admission statin and aspirin use, ischemic coronary heart disease and National Institute of Health Stroke Scale (NIHSS) score were collected.

MRI protocol

MRI was performed on a 3 Tesla whole body MRI scanner (Skyra; Siemens Healthcare, Erlangen, Germany) with a 20-channel phased array head and neck coil. Three-dimensional time-of-flight images were acquired in the axial plane (TR/TE = 21/3.43ms, FOV = 181×200mm, thickness = 0.7mm, and matrix = 331×384). 3D TOF images were reformatted using multi-planar reconstruction. HrMRI scanning was then performed in planes perpendicular to the basilar artery. The hrMRI protocol included three sequences with one sequence repeated post-contrast (12 slices with 2mm slice thickness; in-plane resolution of 0.4mm × 0.3mm; FOV 100mm100mm; matrix 256× 320): pre-contrast T1-weighted fast-spin-echo (TR/TE=581/18ms; echo train length (ETL)=4; number of excitations (NEX)=4), T2-weighted FSE (TR/TE = 2890ms/46ms; ETL=20; NEX=3), and post-contrast T1-weighted FSE. In-flow saturation bands was placed below the imaging slab for blood suppression. In addition, 12 coronal slices were scanned with similar scan parameters, to help exclude the potential IPH-mimicking flow artefacts. Clinical DWI and FLAIR imaging were used for the identification of infarct.

Image Analysis

Stenosis value was measured independently on hrMRI images by two experienced radiologists (XT and QL, 7 and 15 years' experience in neuroradiology), who were blinded to the patients' clinical information [20]. The stenosis value was calculated as $(1-D_{Stenosis}/D_{Normal}) \times 100\%$, while $D_{Stenosis}$ is the minimal lumen diameter at the site of at the site maximal stenosis, and D_{Normal} is the lumen diameter at the site of normal basilar artery (either distal or proximal to the stenosis site). Presence of fresh IPH was identified as >150% signal relative to nearby medial pterygoid muscles on pre-contrast T1-weighted images by the two radiologists independently, blinded to the patient's clinical information [12]. Because intraluminal thrombus/hematoma in intracranial dolichoectasia or dissection also exhibits hyperintense signal on pre-contrast T1-weighted images, we carefully excluded these conditions based on their imaging features [2122]. Basilar dolichoectasia was identified if the basilar diameter was enlarged greater than 4 mm and demonstrated a tortuous appearance on MRA [21]. Dissection might appear with a dissection flap, double lumen or as a tapering vessel; intraluminal thrombus in dissection also usually involves a long segment [22]. Acute or subacute thrombus demonstrates different morphology compared with IPH. Thrombus is long and close to the lumen, while IPH is focal within plaque and is often eccentric to the lumen.

Lumen and outer wall boundary was manually segmented using CMRTools software (Cardiovascular Imaging Solutions Ltd, UK) on T2-weighted images. Reproducibility of this area measurement method was previously reported (measurement error for plaque area: 7.5%) [23].

The contrast enhancement percentage was measured at the slice of greatest enhancement, using adjacent gray matter (in a region of ~15 mm^2) to normalize signal intensity. The contrast enhancement percentage was calculated as ((signal of plaque [post-contrast]/signal of gray matter [post-contrast])/(signal of plaque [pre-contrast]/signal of gray matter[pre-contrast]) − 1) × 100%. Plaque burden was measured on the maximal stenosis site, and was defined as (1 − Lumen Area/Outer Area) × 100%.

Statistical Analysis

Normality assumptions were formally assessed using a Shapiro–Wilk's test. Distributions were summarized using the mean ± standard deviation or median [inter-quartile range]. Categorical data were expressed as counts or percentages. Continuous data were compared using either a Mann-Whitney U test or Student's t-test. Categorical variables were analyzed using Fisher's exact test. Multivariate logistic regression analysis was used to determine the independent factors associated with acute/sub-acute symptom. Intraclass correlation coefficient (ICC) and Cohen's kappa coefficient were used to evaluate the agreement between two reviewers for the measurement of degree of stenosis and the identification of IPH. A p-value of less than 0.05 was considered statistically significant. All p-values were two-sided. GraphPad prism 5 (GraphPad Software Inc., CA, USA) and R Statistics (version 3.1.3, www.r-project.org) were used for data analysis.

Results

Patients demographics and imaging findings

A total of 175 patients met the inclusion criteria. 49 patients were excluded due to intracranial aneurysm (n=28), moyamoya disease (n=3), vasculitis (n=1), dissection (n=6), coexistent vertebral artery stenosis >50% (n=8) and bad image quality (n=3). As a result, 126 patients were included in the final analysis (age 61.2±10.4, 71 male, mean degree of stenosis of 51.6±15.5%). A total of 66 patients were symptomatic and 60 were asymptomatic. 46 patients had a degree of stenosis ≤50% (low grade stenosis, range 13.4% to 48.7%), while 80 patients had a degree of stenosis >50% (high grade stenosis, range 50.1% to 80.3%). Demographic information and imaging findings are summarized in Table 1 and Table 2 based on patients' degree of stenosis and symptom status.

IPH was identified in 22 patients (17.5%), including 21 symptomatic patients (31.8%), and 1 (1.7%) asymptomatic patient (Table 2). IPH appeared over a range of stenosis values (Table 1), and there was no difference in the presentation rate in low and high grade stenosis basilar arteries (19.6% vs. 16.3%, p=0.63). The IPH to muscle signal ratio was 2.10±0.54 (range 1.50 to 3.19). In these 21 stroke patients with IPH, 15 were paramedian pontine infarct stroke, and 6 were lacunar infarction stroke. Univariate and multivariate analysis of the parameters associated with symptoms is shown in Table 3. IPH was the strongest independent indicator of symptomatic status (odds ratio [95% confidence interval]: 27.5 [3.4, 221.5]; p=0.002). Contrast enhancement was also independently associated with symptomatic status (odds ratio: 9.9 [1.5, 23.6]; p=0.016). Degree of stenosis, minimal lumen area and plaque burden were not significantly associated with symptoms (p>0.05). Presence of IPH was not associate with stenosis (r = 0.16, p=0.10) or plaque burden (r = 0.16, p=0.11). Representative basilar artery plaque images with and without IPH were shown in Figure 1 to 3.

Diagnostic performance of IPH for acute/sub-acute symptomatic stroke patients is summarized in Table 4. IPH had a high specificity of 98.3% and a high positive predictive value of 95.5%, however the sensitivity (31.8%) and negative predictive value (56.7%) were lower.

MRI measurements reproducibility

There was excellent inter-reader agreement for measuring degree of stenosis (ICC = 0.97, 95% CI: [0.94, 0.98]) and for identification of IPH (96% agreement, kappa = 0.88, 95% CI: [0.76,1.00]).

Discussion

This study adds to the growing literature that emphasizes the importance of intracranial plaque properties compared to degree of luminal narrowing [2]. In this study, IPH was the only finding associated with stroke symptom status whereas contrast enhancement, degree of stenosis, minimal lumen area and plaque burden were not associated with symptom status. As IPH was present in both low and high grade stenotic basilar artery plaque with a high positive predictive value (95.5%) for symptomatic stroke, it is evident that symptomatic

ischemia may be explained by factors other than stenosis resulting in hypoperfusion. The presence of IPH likely indicates a high risk for artery-to-artery embolic occlusion following plaque rupture. In this conceptualization, future stroke risk for a smaller plaque with IPH is possibly greater than for a larger plaque with a stable fibrous cap.

A study of basilar artery ICAD in patients with at least 30% stenosis found T_1-weighted hyperintense intraplaque signal in 8 of 38 cases (21%) that could indicate IPH, although the authors did not specifically term this finding IPH [9]. The prevalence of basilar artery T_1-weighted hyperintense signal reported by Huang *et al.* (21%) was similar to that reported in the current study (19.6%). On the other hand, a study of 74 patients with greater than 50% stenosis documented IPH in 42.3% of patients with an increased frequency in symptomatic patients [12]. The reason for this higher incidence of IPH may be related to the larger plaque size in these patients with a mean stenosis of 72.9%, although we did not observe a significant difference between IPH frequency in stenotic versus non-stenotic plaque in our study [12]. Alternatively, patients in our study were younger than those of Yu *et al.* with a difference in mean age of approximately ten years between the populations in the two studies. IPH may occur more frequently with age, although this hypothesis is untested. The diagnostic performance of IPH in the aforementioned study was similar to the current study with relatively high specificity (79%) but low sensitivity (53%) [12]. Studies of IPH in other intracranial arteries have observed similar findings. IPH was significantly more frequent in symptomatic middle cerebral artery plaque than in asymptomatic plaque (19.6% versus 3.2%) [19].

While current management guidelines focus on stenosis, our work and that of others supports the use of identification of plaque properties to better indicate future stroke risk. Our study emphasizes the highly specific (98.3%) nature of IPH as an indicator of symptomatic stroke, implying that this represents unstable basilar artery atherosclerotic plaque. Unfortunately, IPH is not particularly sensitive (31.8%) in indicating the presence of a symptomatic basilar artery. These observations likely reflect the multiple stroke mechanisms encountered in ICAD, where IPH could predispose to artery-to-artery embolization with small vessel occlusion and could cause branch occlusive disease affecting perforating arteries. On the other hand, some symptomatic strokes in this study could also be caused by stenotic basilar artery plaque leading to hypoperfusion. IPH was the best overall marker of symptomatic plaque with an odds ratio of 27.5. This study's findings support the use of IPH in basilar artery atherosclerotic plaque as a better indicator of symptomatic plaque rather than stenosis or plaque burden alone.

Other intracranial plaque characteristics including contrast enhancement and minimal lumen area have been associated with symptoms [2425]. We observed a similar relationship between contrast enhancement and symptom status in our study. A smaller study examining the basilar artery with contrast-enhanced hrMRI observed wall enhancement in patients with recent infarction and also those who would go on to have ischemic events [26]. Another study of intracranial atherosclerotic disease also concluded that contrast enhancement was associated with culprit plaques with a substantial odds ratio of approximately 35 [25]. Research suggests that the vasa vasorum evolve with age and demonstrate different distributions with less vasa vasorum in the intracranial vasculature and differing distributions

within cerebral vascular territories [27]. Theoretically, enhancement of the basilar artery wall could reflect physiologic enhancement of the vasa vasorum rather than pathological plaque enhancement, which could reduce the specificity of vessel wall enhancement. An improved understanding of the vasa vasorum may enhance the specificity of basilar artery enhancement.

Further work is needed to histologically validate hrMRI assessment of IPH with only one case of histologically verified intracranial IPH demonstrated as T1-weighted hyperintense intraplaque signal on post-mortem hrMRI [28]. Due to the reliance on post-mortem assessment of plaque, histological validation of intracranial plaque imaging characteristics is more challenging than in the extracranial carotid artery plaque, which may be ascertained following endarterectomy. While a study of intracranial plaque characterization using *ex vivo* 3T hrMRI in 53 post-mortem specimens determined relaxation times for many plaque components, no IPH was encountered in these plaque specimens [29]. Therefore, IPH detection on hrMRI largely infers plaque characteristics from existing extracranial atherosclerosis imaging literature.

Our results cannot directly confer causality of IPH in the setting of symptomatic stroke and this cross-sectional study design cannot provide an assessment of future stroke risk. Prospective assessment of IPH and subsequent stroke risk would extend the clinical relevance of this study's findings and such data could be utilized in risk assessment calculations. HrMRI can also determine IPH timing and duration. Potentially, signal characteristics of IPH could provide information on the onset of hemorrhage, and serial examination of patients with ICAD exhibiting IPH could provide insight into its natural history. Moreover, serial assessment of intracranial IPH evolution while on different pharmacologic therapies might potentially provide objective information regarding treatment efficacy.

In addition, there are technical limitations of our study to consider. Our study used a standard 2D T_1-weighted black blood fast-spin-echo sequence. The use of 3D sequences with higher resolution [30], better T_1-weighted contrast [31], and advanced blood suppression techniques (such as diffusion preparation [32] or variable flip angle train [30]) can potentially improve the identification of IPH. However, the 3D high resolution sequences can increase scan time, and the use of diffusion preparation can reduce the signal to noise ratio and induce T2 contrast [32], and variable flip angle train can induce blurring with a wider point spread function [30]. All of these limitations will need to be accounted for in future clinical studies.

Conclusion

In conclusion, evidence from this study suggests that IPH in the basilar artery found on hrMRI identifies atherosclerotic lesions that are more likely to be symptomatic regardless of the degree of stenosis. This plaque property appears to be substantially associated with symptom status whereas many other factors including plaque size, contrast enhancement and degree of stenosis do not. In the future, the use of hrMRI for the early detection of basilar

artery IPH may allow clinicians to select individuals at greater risk of imminent stroke and help provide optimal therapeutic intervention.

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Abbreviations

IPH	intraplaque haemorrhage
MLA	minimal lumen area
ICAD	Intracranial atherosclerotic disease

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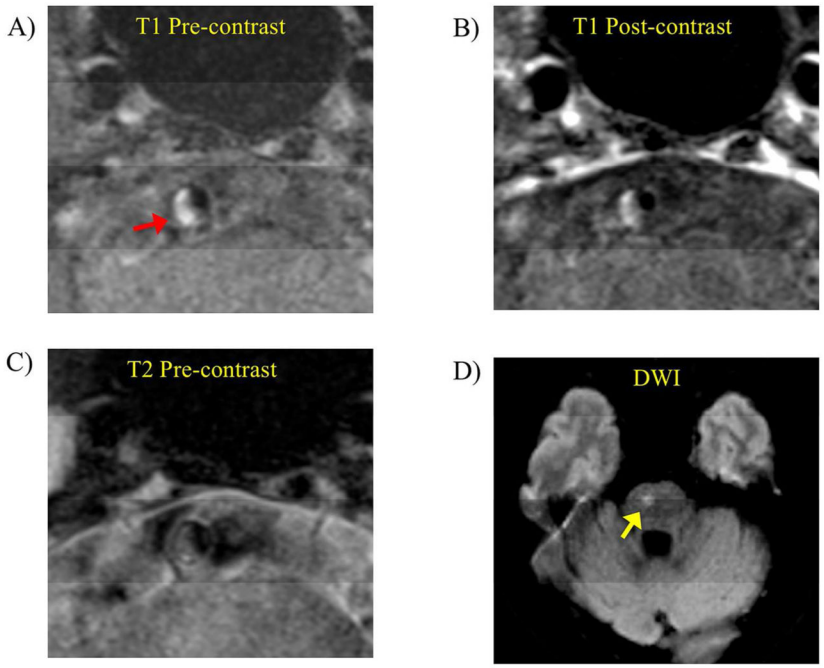

Figure 1.

Intraplaque hemorrhage presented in a low grade stenotic basilar artery plaque (43% degree of stenosis) in an acute symptomatic patient (age 65, female). A) T1 weighted black blood MRI showed high signal (fresh IPH, red arrow) in the plaque. B) Post contrast T1 weighted images showed slight enhancement of the plaque. C) T2 weighted images showed iso-intense signal of the plaque. D) DWI showed infarct in the brain stem (yellow arrow).

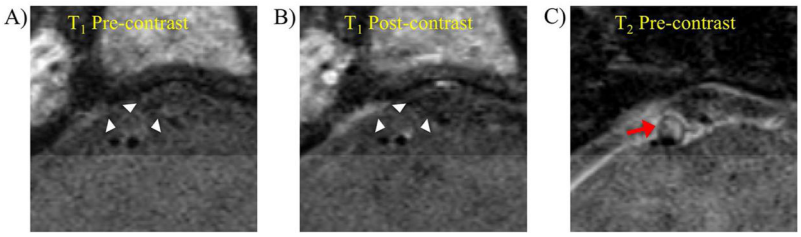

Figure 2.

A high grade stenotic basilar artery plaque (degree of stenosis 73%) without intraplaque hemorrhage in an asymptomatic patient (age 56, female). A) T_1-weighted black blood MRI showed isointense signal in the plaque. B) Post-contrast T_1-weighted images showed enhancement of the plaque surface. C) T_2-weighted images showed high signal of the plaque.

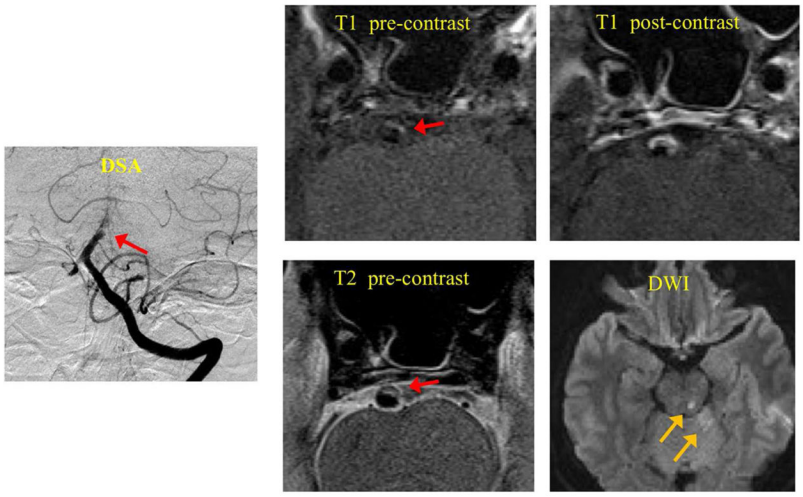

Figure 3.

A symptomatic patient with infarctions distal to the location of basilar artery plaque. Red arrows show the location of the plaque. Yellow arrows show the location of infarctions on DWI. T1 weighted black blood MRI showed high signal in the plaque (IPH). Post contrast T1 weighted images showed strong enhancement of the plaque.

Table 1

Clinical Characteristics and Imaging Findings of Patients with low and high grade stenotic basilar artery plaque.

	ALL (n=126)	Low grade stenosis (<50%, n=46)	High grade stenosis (≥50%, n=80)	p value
Age	61.5±10.0	63.70±9.4	60.3±10.1	0.07
Sex (male)	82 (65.1%)	33(71.7%)	49(61.3%)	0.23
Diabetes	42 (33.3%)	15 (32.6%)	27 (33.8%)	0.90
Smoking	35 (27.8%)	13 (28.3%)	22 (27.5%)	0.93
Hypertension	101(80.2%)	37 (80.4%)	64 (80.0%)	0.96
Hyperlipidemia	65 (51.6%)	18 (39.1%)	47 (58.8%)	0.03*
Coronary Artery Disease	5 (4.0%)	3 (6.5%)	2 (2.5%)	0.27
Pre-admission Aspirin use	31 (24.6%)	9 (19.6%)	22 (27.5%)	0.32
Pre-admission Statin use	17 (13.5%)	4 (8.7%)	13 (16.3%)	0.23
NIHSS score (median and range)	1 (0,11)	2 (0,11)	0(0,6)	<0.001*
Degree of Stenosis (%)	52.6±15.8	35.2±9.7	62.6±7.9	<0.001*
Enhancement Percentage (%)	17.4±28.4	21.1 ±33.1	15.3 ±25.3	0.27
Intraplaque Haemorrhage	22 (17.5%)	9 (19.6%)	13(16.3%)	0.63
Minimum Lumen Area	3.2±2.97	5.1±3.4	2.1±1.3	<0.001*
Plaque Burden (%)	84.0±9.1	75.9±8.2	88.6±5.7	<0.001*
Symptomatic	66 (52.4%)	28(60.9%)	38 (47.5%)	0.15

NIHSS: National Institute of Health Stroke Scale

*Statistically significant

Table 2

Clinical characteristics and imaging findings of patients with different symptom stages.

	ALL (n=126)	Symptomatic (n=66)	Asymptomatic (n=60)	p value
Age	61.5±10.0	61.7±10.5	61.4±9.4	0.86
Sex (male)	82 (65.1%)	50 (75.8%)	32 (53.3%)	<0.001*
Diabetes	42 (33.3%)	23 (34.8%)	19 (31.7%)	0.71
Smoking	35 (27.8%)	25 (37.9%)	10 (16.7%)	<0.001*
Hypertension	101(80.2%)	52 (78.8%)	49 (81.7%)	0.69
Hyperlipidemia	65 (51.6%)	38 (57.6%)	27 (45.0%)	0.16
Coronary Artery Disease	5 (4.0%)	3 (4.5%)	2 (3.3%)	0.73
Pre-admission Aspirin use	31 (24.6%)	21 (31.8%)	10 (16.7%)	0.06
Pre-admission Statin use	17 (13.5%)	10 (15.2%)	7 (11.7%)	0.57
NIHSS score (median and range)	1 (0,11)	2 (0,11)	0 (0,4)	<0.001*
Degree of Stenosis (%)	52.6±15.8	52.4±15.5	52.8±16.1	0.88
Enhancement Percentage (%)	17.4± 28.4	25.5±26.1	8.5±28.5	<0.001*
Intraplaque Haemorrhage	22 (17.5%)	21 (31.8%)	1 (1.7%)	<0.001*
Minimum Lumen Area (mm^2)	3.2±2.7	3.7±2.8	2.7±2.6	0.04*
Plaque Burden (%)	84.0±9.1	83.6±9.8	84.4±8.2	0.62

NIHSS: National Institute of Health Stroke Scale

*Statistically significant

Table 3

Univariate and multivariate analysis of the parameters associated with symptomatic status.

	Univariate Analysis		Multivariate Analysis	
Variable	**Odds Ratio (95% CI)**	**p**	**Odds Ratio (95% CI)**	**p**
Sex (male)	2.7 (1.2,5.8)	<0.001		
Smoking	3.0 (1.3, 7.1)	<0.001		
Enhancement Percentage (%)	13.0 (2.6, 25.0)	<0.001	9.9 (1.5, 23.6)	0.016
Intraplaque Haemorrhage	27.5 (3.6, 212.4)	0.002	27.5 (3.4, 221.5)	0.002
Minimum Lumen Area	1.2 (1.0, 1.4)	0.04		

Table 4

Diagnostic performance of intraplaque hemorrhage in identifying symptomatic/asymptomatic basilar artery plaque.

	IPH-positive (n=22)	IPH-Negative (n=104)
Symptomatic	21	45
Asymptomatic	1	59
Diagnostic Performance		
Specificity (%, 95% CI)	98.3 (91.1,100.0)	
Sensitivity (%)	31.8 (20.9, 44.4)	
PPV (%)	95.5 (74.4, 99.3)	
NPV (%)	56.7 (52.6, 60.8)	

IPH: Intraplaque haemorrhage

PPV: Positive predict value

NPV: Negative predict value