Recurrent Risk of Ischemic Stroke due to Vertebrobasilar Dolichoectasia

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Abstract

Background

Patients with vertebrobasilar dolichoectasia usually have persistent hemodynamic abnormalities, and therefore, may bear an increased risk of stroke. This study aimed to evaluate ischemic stroke recurrence in patients with vertebrobasilar dolichoectasia.

Methods

Patients with acute ischemic stroke were screened and evaluated for eligibility. Enrolled patients were followed via scheduled clinical visits or telephone interviews. Ischemic stroke recurrence was proposed with clinical symptoms and confirmed with cranial Magnetic Resonance Imaging or Computerized Tomography scans. Baseline characteristics and vascular geometry were compared between patients with and without stroke recurrence. Significant parameters were introduced into COX proportional hazard model to detect possible predictors of stroke recurrence.

Results

A total of 115 stroke patients with vertebrobasilar dolichoectasia were enrolled, of which 22 (19.1%) had recurrence during 22 ± 6 months follow-up. Basilar artery diameter ≥ 5.3 mm (HR = 4.744; 95% CI, 1.718-13.097; P = 0.003), diffuse intracranial dolichoectasia (HR = 3.603; 95% CI, 1.367-9.496; P = 0.010) and ischemic heart disease history (HR = 4.095; 95% CI, 1.221-13.740; P = 0.022) had increased risk of recurrence.

Conclusions

Stroke patients with vertebrobasilar dolichoectasia may have a high risk of recurrence. Larger basilar artery diameter or diffuse intracranial dolichoectasia may increase the risk of recurrence.

Background
Vertebrobasilar dolichoectasia (VBD) has been associated with stroke and all-cause mortality [1]. Subsequent stroke risk is higher in non-selective VBD patients [2] or VBD patients with stroke [3]. Of even greater concern is that the most common recurrence form is an ischemic stroke (IS) or transient ischemic attack (TIA) [2]. In addition to common vascular risk factors such as hypertension, obesity, diabetes mellitus, smoking [4], and ethnicity [5], geometrical changes of the dolichoectasia arteries, which subsequently leads to intraluminal thrombus formation, or perforator vessel occlusion through stretching or squeezing, may also increase the risk of stroke recurrence [2].

Previous studies on stroke recurrence of VBD patients might have relatively small sample sizes [3, 6], did not include patients with VBD of anterior circulation [2] or lack the evaluation of total arterial geometry abnormalities. Also, the study of VBD in Chinese Han population was absent. Hence, we included the baseline characters and arterial geometry such as dolichoectasia features and arterial stenosis, to identify the predictors for IS recurrence in VBD patients.

**Methods**

For this stroke-registry based retrospective cohort study, we retrieved data from Nanjing Stroke Registry Program [7] and The Affiliated Hospital of Nanjing University of Chinese Medicine. The study was approved by the local research ethics committees of Jinling Hospital and Jiangsu Province Hospital of Chinese Medicine and conducted in accordance with the Declaration of Helsinki. All participants or their guardians gave written informed consent.

**Participants**

Consecutive patients with first acute ischemic stroke within seven days of stroke onset
from September 1, 2015 to August 31, 2016 were included in this study. All ischemic stroke events were confirmed by magnetic resonance imaging (MRI) or computerized tomography (CT). We excluded patients with a brain hemorrhage, subarachnoid hemorrhage, traumatic brain injury, venous stroke, cardioembolic stroke, or treated with percutaneous transluminal angioplasty and stent; patients who died within seven days were also excluded because their diagnosis of stroke recurrence was mostly undetermined. Besides, patients were excluded if they had no brain MRI/MRA or CT/CTA or digital subtraction angiography (DSA) source images which would be used for the measurement of intracranial arterial diameter and subsequently the determination of absence or presence of intracranial dolichoectasia (IADE) or intracranial atherosclerosis (ICAS). Flowchart of patient enrollment in this study is shown in Fig. 1.

**Diagnosis of VBD and ICAS**

The diameter of main seven intracranial arteries, include the basilar artery (BA) at midpons, the intracranial vertebral arteries (VA) (R and L) at the V4 segment, the internal carotid arteries (ICA) (R and L) at the intracavernous segment and the middle cerebral artery (MCA) (R and L) at the M1 segment, were measured. We focused on the basilar artery in this study because it is the most commonly affected dolichoectasia artery [8]. VBD is defined according to widely accepted criteria [9, 10]. Ectasia was diagnosed if the BA diameter ≥ 4.6 mm and elongated or enlarged over its entire course; not including segmental saccular enlargement or giant aneurysms (diameter > 25mm) which were described as translational type [11]. A semi-quantitative four-point scale was used to determine the elongation of BA: the height of BA bifurcation was scored as 0 (at or below the dorsum sellae), 1 (within the suprasellar cistern), 2 (at the third ventricle floor) and 3 (indentation and elevation of the third ventricle floor). The laterality of BA was scored as 0
(midline throughout), 1 (R or L, the medial-to-lateral margin of clivus or dorsum sellae), 2 (R or L, the lateral-to-lateral margin of clivus or dorsum sellae) and 3 (R or L, at cerebellopontine angle cistern). Dolichos was diagnosed if the height of BA bifurcation or laterality of BA ≥ 2 scale. Diagnosed criteria for anterior circulation dolichoectasia is limited; we defined this condition if ICA or MCA was circuitous or enlargement on visual impression and an ICA diameter ≥ 7 mm or an MCA diameter ≥ 4 mm according to a previous study [1]. Diffuse intracranial dolichoectasia was defined with dilation of at least two intracranial arterial supply system (for example, vertebrobasilar system, left or right anterior circulation) [12]. Intra-rater and inter-rater reliability for determinate the existing of VBD or not were 0.821 and 0.796, respectively.

Intracranial arterial stenoses on ICA distal to the ophthalmic artery, anterior cerebral artery (ACA) A1/A2, MCA M1/M2, posterior cerebral artery (PCA) P1/P2, BA, and intracranial VA were measured on 3D-TOF MRA, CTA, or DSA. Stenoses were group as < 50%, 50% to 69%, 70% to 99%, and occlusion according to previous criteria [13]. Extracranial arterial stenosis was examined by CTA, contrast-enhanced MRA, or DSA [14]. If a patient experienced with more than one radiological spectrum, the degree of cerebral artery stenosis calculated on DSA image was finally adopted. We defined the presence of intracranial atherosclerosis (ICAS) or extracranial atherosclerosis (ECAS) once a cerebral artery has ≥ 50% stenosis or occlusion.

**Baseline Assessments**

Baseline demographics, vascular risk factors, in hospital treatment, and medical records were retrieved. Vascular risk factors include hypertension, diabetes mellitus, hyperlipidemia, history of ischemic heart disease and smoking was recorded. All patients
underwent brain MRI (sequences included axial T1-weighted, axial T2-weighted, axial diffusion-weighted imaging, fluid-attenuated inversion recovery, and in most cases, 3D time-of-flight MRA) in either 3.0-T (MAGENTOM Trio, Siemens, Erlangen, Germany) or 1.5-T (GE Medical Systems, Milwaukee, WI) system. The image data was stored as Digital Imaging Communications in Medicine (DICOM) format for further analysis in Centricity Enterprise Web 3.0 Client (GE Medical Systems, Milwaukee, WI). All MRI source and maximum intensity projection (MIP) images were evaluated by two neurologists who were blinded to clinical information.

Follow-up Assessments
Patients were invited to have a face-to-face interview or a telephone interview every three months by trained research doctors. The guardians were contacted if patients were died or can’t help themselves with the inquiry. The follow-up interval was defined as the time between the stroke onset and contact or decease. Data collection began when all dolichoectasia cases had been documented. The primary outcome was the IS recurrence. All IS recurrence was verified using the medical records that indicated a new focal neurological deficit of vascular origin lasting > 24 hours, confirmed by CT or MRI images, and could not be attributed to stroke mimics, hemorrhage, mass effect or hemorrhagic transformation [15]. An experienced stroke specialist reviewed the medical documents to make sure the diagnosis of stroke recurrence is reliable.

Statistical Analysis
Continuous variables were recorded as mean ± SD or as median [IQR]. Categorical variables were presented as proportions. Between-group comparisons of the distribution of continuous variables were performed using the Independent samples t-test or Mann-
Whitney U test. Comparisons of categorical variables were performed using the $\chi^2$ test or Fisher-exact test. Risk factors with a $P$ value of $<0.1$ in the univariate analysis were included in multivariate Cox proportional hazards regression forward: LR model, to analyze levels of hazard ratio (HR) of recurrence. All statistical testing was two-tailed, $P < 0.05$ was considered statistically significant. All analyses were performed in PASW Statistics 18.0 (SPSS Inc., Chicago, IL).

Results

115 VBD patients were consecutively included with a mean age of $63.1 \pm 10.7$ years (ranged from 41 to 83 years). 88 (76.5%) patients were men and 27 (23.5%) patients were women. Baseline demographic and clinical characteristics of VBD patients are delineated in Table 1, 85 (73.9%) patients had hypertension, 38 (33.0%) patients had diabetes mellitus, and 10 (8.7%) patients had a history of ischemic heart disease (IHD). Besides, 34 (29.6%) had hyperlipidemia, 37 (32.2%) had a smoke history. The median National Institute of Health stroke scale (NIHSS) score at admission was 3 (IQR 1-6). The general treatment during hospitalization included in this study referred to antiplatelet (85.5%) or anticoagulant (20.0%) therapy; also, 101 (87.8%) patients received statins treatment.

The mean diameter of the major intracranial arteries was measured as follows, BA $4.3 \pm 1.1$ mm, RVA $3.0 \pm 1.0$ mm, LVA $3.2 \pm 1.0$ mm, RICA $5.2 \pm 1.0$ mm, LICA $5.2 \pm 0.9$ mm, RMCA $2.7 \pm 0.5$ mm, LMCA $2.7 \pm 0.5$ mm. The median of BA diameter was $4.1$ mm (IQR 3.6 mm - 4.8 mm ), and the 90th percentile was 5.3 mm. 46 (40.0%) patients had basilar artery ectasia (BA diameter $\geq$ 4.6 mm), BA bifurcations of 73 (63.5%) patients were at the third ventricle floor ($\geq$ grade 2), of these, seven (6.1%) were indented over the third ventricle floor, and BA laterality reached the lateral-to-lateral margin of clivus or dorsum
sellae (grade 2) was seen in 19 (16.7%) patients. 15 (13.0%) patients had diffuse intracranial dolichoectasia (DID). Arterial stenosis was common in VBD patients, in this study, 35 (30.4%) patients had ICAS, among them, nine (7.8%) patients with basilar artery atherosclerosis, also, 15 (13.0%) patients had extracranial arterial stenosis ≥ 50%.

During a 22 ± 6 months (ranged from two to 30 months) follow-up, 22 patients (19.1%) suffered IS recurrence, of these, 12 patients had recurrent IS involving posterior circulation and ten patients involving anterior circulation. Four patients (3.5%) died, in detail, two died due to ischemic stroke recurrence, one for abdominal aneurysm rupture and one for lung cancer. Only one patient suffered non-fatal hemorrhage stroke.

Univariate analysis (Table 1) found that risk factors such as hypertension (90.9% vs 69.9%, \( P = 0.044 \)), diabetic mellitus (54.5% vs 28.0%, \( P = 0.017 \)), and ischemic heart disease history (22.7% vs 5.4%, \( P = 0.030 \)) were separately associated with IS recurrence.

Patients with BA diameter ≥5.3 mm (the 90th percentile ) had more IS recurrence than patients with BA diameter < 5.3 mm (Table 1), the percentage was 36.4% vs 4.3% (HR = 12.741; 95% CI, 3.376 - 47.878; \( P < 0.001 \)). Other intracranial arterial geometry such as height of BA bifurcation (score = 3) (18.2% vs 3.2%; HR = 6.667; 95% CI, 1.373-32.372; \( P = 0.024 \)), diffuse intracranial dolichoectasia (36.4% vs 7.5%; HR = 7.020; 95% CI, 2.199-22.418; \( P = 0.001 \)), ICAS (50.0% vs 25.8%; HR = 2.875; 95% CI, 1.015-7.480; \( P = 0.027 \)) was either associated with IS recurrence.

We introduced BA diameters into COX proportional-hazards model as a continuous variable, and found a significant relationship between BA diameter and IS recurrence, the crude HR per 1mm-increase of BA diameter is 1.902 (95% CI, 1.439-2.514; \( P < 0.001 \)).
After adjusting for hypertension, ischemic heart disease, diabetes mellitus, Height of BA bifurcation (score = 3), diffuse intracranial dolichoectasia, and ICAS, increasing BA diameter remain significantly associated with IS recurrence (HR = 1.756; 95% CI, 1.244-2.478; \( P = 0.001 \)).

In multivariate analysis (Table 2), BA diameter \( \geq 5.3 \) mm (HR = 4.744; 95% CI, 1.718-13.097; \( P = 0.003 \)) was an independent predictor of IS recurrence. Diffuse intracranial dolichoectasia (HR = 3.603; 95% CI, 1.367-9.496; \( P = 0.010 \)) and ischemic heart disease history (HR = 4.095; 95% CI, 1.221-13.740; \( P = 0.022 \)) were also independent predictors for IS recurrence.

**Discussion**

Ischemic stroke is the primary clinical manifestation of VBD; others included hemorrhage, SAH, compression of a cranial nerve, hydrocephalus et al. [16]. In this stroke registry-based study, 19.1% of VBD patients suffered a IS recurrence during a maximum 30-month follow-up. It seemed that stroke patients with VBD might have a higher recurrence risk than the general population, for example, Flemming et al. selected 159 VBD cases from the radiological database which included not only stroke patients, after an average of 3.8-years follow-up, 44 patients occurred cerebral infarction or TIA. The 1, 5, and 10-year risk of an ischemic stroke was 6.1%, 17.3%, and 25.4% [2]. Passero et al. performed a clinical and imaging follow-up study and found that 75 (48%) of the 156 VBD patients had a stroke after an average of 11.7 years follow-up [1]. Besides, it seemed that the mortality (3.5%) in our study is lower than the previous study [17], this may be due to the relatively short follow-up time and exclusion of patients who died within seven days because their diagnoses of stroke recurrence were mostly undetermined. Also, patients with none MRI were excluded; many of them were under unstable condition. These may lead to the
underestimate of mortality. However, our report seemed similar with a previous study, which performed an average of 3.4 years follow-up of first ischemic stroke patients with IADE and found a high stroke recurrence (58%) but low mortality (17%) [3].

Although VBD patients have a high stroke-recurrence rate, studies about the predictive factors of recurrence were limited. This study evaluated variables potentially associated with stroke recurrence in VBD patients and found that extremely dolichoectasia such as basilar artery diameter ≥ 5.3 mm (90th percentile) was independently associated with IS recurrence. The higher IS recurrence among patients with extremely enlarged or kinking elongated arteries may be related to the multiple mechanisms that could lead to stroke occurrence [3], including local thrombosis, embolism, penetrating artery occlusion induced by compression or stretching of deep branches (Fig. 2) of the basilar artery.

Interestingly, Pico et al. found that the BA diameter was also associated with a 5-year risk of death in stroke patients, the adjusted hazard ratio of stroke mortality was 1.23 (95% CI, 1.07-1.41) with per 1-mm increase in BA diameter [8].

In another hand, we found another intracranial arterial geometry abnormality, the diffuse intracranial dolichoectasia, was correlated with IS recurrence. Patients with anterior circulation dolichoectasia have been reported in previous studies [1, 12]; however, the IS recurrence of patients with diffuse intracranial dolichoectasia was seldom mentioned [12]. Diffuse intracranial dolichoectasia patients suffered more IS recurrence mainly because it may be the severe form of arterial dolichoectasia. Brinjikji, W. et al. suggested that diffuse intracranial dolichoectasia is a systemic arteriopathy affecting multiple vascular beds, which may be different from a single intracranial artery dolichoectasia [12]. However, in this study, we could not uniquely say patients with diffuse dolichoectasia are
different with the rest of patients with VBD alone, as we did not screen if any patients in this study have diseases that may often coexist with systemic vascular expansion, such as connective tissue disease, autosomal dominant polycystic kidney disease, or infection in this study.

This study found that previous ischemic heart disease was the independent predictors for IS recurrence in VBD patients. Interestingly, a previous study suggested that IADE patients were eligible to have a previous myocardial infarction [18], and the coronary artery ectasia was also correlated with ischemic heart disease [19]. Concomitant coronary and basilar artery ectasia in stroke patients may suggest common pathogenesis [20]. However, in multivariable analysis, we did not find the statistical difference of vascular risk factors such as age, hypertension, diabetes mellitus, hyperlipidemia, smoking between the recurrence and none-recurrence group. It may vary due to the small number of recurrent patients in our study. Also, the negative findings of between-group differences refers to vascular risk factors might suggest the different pathogenesis between IADE and ICAS, as the characters above were widely accepted as risk factors for atherosclerosis vascular disease.

In China, ICAS is the most common vascular lesions in patients suffered cerebral vascular disease, and the stroke recurrence is higher in patients with serve stenosis [21]. However, the relationship between large arterial atherosclerosis and dolichoectasia has always been debated. This study found that VBD patients had a frequent incidence of ICAS, and this proportion was higher in recurrent cases; however, we did not find its association with IS recurrence in multivariate analysis. IADE may differ with ICAS; autopsy study found that IADE is associated with rarefaction of elastic tissue of the tunica media with the
degeneration of the internal elastic laminin [20, 22], while atherosclerosis always has a pathological change of plaque with a lipid core and the fibrous cap [23]. Also, hemodynamic abnormalities such as the wall shear stress, noticeable eddy currents in dolichoectasia vertebrobasilar artery were reported, and notably, without apparent arterial stenosis [24]. Interestingly, the ischemic lesions in the BA branches-supplied territories often exit at the contralateral side of the laterality of the BA [25], as is shown in Fig. 2. These findings suggested that the hemodynamic abnormality may promote the development of ischemic vascular events without atherosclerosis but due to stretching of the small branch vessels.

IADE and ICAS often coexisted in the large cranial arteries [1]. It implies that these two large artery abnormalities may share some common pathogenic factors. For example, Matrix metalloproteinases (MMPs) was related to IADE as it could degrade various extracellular proteins including collagen, elastin, or proteoglycans that located in the tunica media [26]. Also, MMPs degrade the extracellular matrix and then causes vascular remodeling, finally leads to atherosclerosis [27]. And the high turbulent shear stresses and the region of flow separation and stagnation (especially in patients under long term hemodynamic changes such as hypertension) all give rise to the risk of thrombosis, and then caused the occlusion of the perforating artery [23] or the distal embolism. However, it is also possible that IADE is merely a hint for severe atherosclerosis.

The widely accepted consensus of the second prevention for IS recurrence in VBD patients is absent. The safety and effectiveness of antiplatelet or anticoagulant therapy in VBD patients has not yet been assessed [23]. Our study did not find the differences in treatment between groups referring to the IS recurrence, such as antiplatelet,
anticoagulant, or statin. However, previous small sample (13 patients) study suggested anticoagulant therapy because they observed a more favorable outcome in this group than that using antiplatelet treatment [28], but other study cautioned that using antiplatelet or anticoagulant agents may increase the incidence of intracranial bleeding in VBD patients [29]. It seemed reasonable to give antithrombotic therapy conservatively in patients with a basilar artery diameter larger than 10 mm, in consideration of the high risk of rupture [23]. A favorable outcome was reported in patients with subarachnoid hemorrhage caused by posterior circulation fusiform aneurysms by using surgery or endovascular procedure [30]. However, randomized clinical trials are needed to access the safety and efficacy of these approaches.

Our research has some limitations. First, this is a retrospective and hospital-based study, it was limited with case selection or referral bias, so the predictors of stroke recurrence in our study may not be an accurate reflection of the general population. Second, we did not include susceptible TIA patients or patients with negative CT/MRI findings as the recurrent cases, because it is difficult giving the definite diagnosis based on the retrospective medical records, as the mimic neurological deficits might be caused by epilepsy, peripheral vertigo, or syncope. Therefore, this may underestimate the true IS recurrence. Third, we did not use the high-resolution MRI analyzing the vascular wall or the plaque stability as previous studies [31], as the negative arterial remolding may underestimate arterial diameter [32]. However, this is a stroke registry-based study; patients were included prospectively and consecutively. Also, this is relatively a large cohort; it provided some assistance in predicting IS recurrence in VBD patients and had a likely warning effect on some unique VBD patients such as combined with diffuse intracranial dolichoectasia. This study may be helpful to guide medical therapy and may improve the
counseling of patients with VBD. The large sample of prospective studies, use high-resolution MRI or fluid dynamics, or randomized clinical trials aimed to access the effective treatment of VBD, needs further developed.

Conclusions

Ischemic stroke patients with VBD may suffer a high risk of recurrence. Larger basilar artery diameter or diffuse intracranial dolichoectasia may increase the risk of recurrence.

Abbreviations

ACA: anterior cerebral artery; BA: basilar artery; CI: confidence interval; CT: computerized tomography; DID: diffuse intracranial dolichoectasia; DSA: digital subtraction angiography; ECAS: extracranial atherosclerosis; HR: hazard ratio; ICA: internal carotid artery; ICAS: intracranial atherosclerosis; IHD: ischemic heart disease; IS: ischemic stroke; MCA: middle cerebral artery; MMPs: matrix metalloproteinases; MRI: magnetic resonance imaging; NIHSS: National Institute of Health Stroke Scale; TIA: transient ischemic attack; VA: vertebral artery; VBD: vertebrobasilar Dolichoectasia.

Declarations

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Availability of data and material

All data are available without restriction from the corresponding author on reasonable request.

Authors’ contributions

ZC, XL, and GX designed and prepared the study; ZC, SZ, and ZD acquired data; XC and MW analyzed the data; ZC and GX drafted the manuscript; QD and GX advised on the method of data analysis, presentation of results and critical revision of the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The study was approved by the local research ethics committees of Jinling Hospital and Jiangsu Province Hospital of Chinese Medicine and conducted in accordance with the Declaration of Helsinki. All participants or their guardians gave written informed consent.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

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Tables

Table 1. Baseline Characteristics of the VBD patients
### Characteristics

| Characteristics                          | Total (n = 115) | With IS Recurrence (n = 22) | Without IS Recurrence (n = 93) | P value |
|-----------------------------------------|----------------|-----------------------------|-------------------------------|---------|
| Age, y; mean ± SD                        | 63.1 ± 10.7    | 64.9 ± 10.0                 | 62.7 ± 10.8                   | 0.389   |
| Male (%)                                 | 88 (76.5)      | 16 (72.7)                   | 72 (77.4)                     | 0.641   |
| Hypertension, n (%)                      | 85 (73.9)      | 20 (90.9)                   | 65 (69.9)                     | 0.044   |
| Diabetes mellitus, n (%)                 | 38 (33.0)      | 12 (54.5)                   | 26 (28.0)                     | 0.017   |
| IHD, n (%)                               | 10 (8.7)       | 5 (22.7)                    | 5 (5.4)                       | 0.030   |
| Hyperlipemia, n (%)                      | 34 (29.6)      | 5 (22.7)                    | 29 (31.2)                     | 0.434   |
| Smoke, n (%)                             | 37 (32.2)      | 5 (22.7)                    | 32 (34.4)                     | 0.292   |
| NIHSS, median (IQR)                      | 3 (1-6)        | 4 (1-9)                     | 3 (1-6)                       | 0.194   |

### Basilar artery geometry

|                  | Total (n = 115) | With IS Recurrence (n = 22) | Without IS Recurrence (n = 93) | P value |
|------------------|----------------|-----------------------------|-------------------------------|---------|
| \( \geq 5.3 \text{ mm, 90}^{\text{th}} \text{ percentile} \) | 12 (10.4)      | 8 (36.4)                    | 4 (4.3)                        | <0.001  |
| BA bifurcation, score = 3               | 7 (6.1)        | 4 (18.2)                    | 3 (3.2)                        | 0.032   |
| BA laterality, score \( \geq 2^* \)     | 19 (16.7)      | 4 (18.2)                    | 15 (16.3)                      | 1.000   |
| DID                          | 15 (13.0)      | 8 (36.4)                    | 7 (7.5)                        | 0.001   |
| ICAS                         | 35 (30.4)      | 11 (50.0)                   | 24 (25.8)                      | 0.027   |
| ECAS                         | 15 (13.0)      | 3 (13.6)                    | 12 (12.9)                      | 1.000   |

### In-hospital treatment

|                  | Total (n = 115) | With IS Recurrence (n = 22) | Without IS Recurrence (n = 93) | P value |
|------------------|----------------|-----------------------------|-------------------------------|---------|
| Antiplatelet     | 98 (85.2)      | 18 (81.8)                   | 80 (86.0)                     | 0.869   |
| Anticoagulant    | 23 (20.0)      | 2 (9.1)                     | 21 (22.6)                     | 0.236   |
| Statins          | 101 (87.8)     | 20 (90.9)                   | 81 (87.1)                     | 0.897   |

*One case of BA laterality could not be measured. Continuous variables are expressed as mean ± SD or median (IQR); other values are shown as n (%).

### Table 2. Multivariate Analysis of Predictors for Recurrence

| Independent predictors                  | HR (95% CI)            | P value |
|----------------------------------------|------------------------|---------|
| Ischemic heart disease history         | 4.095 (1.221-13.740)   | 0.022   |
| Basilar artery diameter \( \geq 5.3 \text{ mm} \) | 4.744 (1.718-13.097)   | 0.003   |
| Diffuse intracranial dolichoectasia    | 3.603 (1.367-9.496)    | 0.010   |

Cox proportional hazards regression Forward LR method was used to examine the predictors of IS recurrence. The included covariates were conventional risk factors with a P value < 0.1 in the univariate analysis and MRI parameters such as basilar artery diameter \( \geq 5.3 \text{ mm} \), the height of basilar artery bifurcation (score = 3), diffuse intracranial dolichoectasia, and intracranial atherosclerosis. All tests were 2-tailed, and P < 0.05 was considered significant.
Figures

Flow-Chart of Patient Enrollment in This Study.

N = 1140

- First acute ischemic stroke patients within 7 days of stroke onset
- Cardioembolic stroke (n = 150)
- Died within 7 days after admission (n = 12)
- Without MRI during hospitalization (n = 85)
- Inappropriate MRI sequences (n = 6)
- Without any intra or extra cranial vascular examination (n = 20)
- Treated with percutaneous transluminal angioplasty or Stent (n = 91)

N = 776

Exclude

N = 776

Screen for Vertebrobasilar Dolichoectasia

Enrollment N = 115

Follow-up

N = 22
- With recurrence

N = 93
- Without recurrence

Followed-up by March, 2018
Brain ischemia Due to Vertebrobasilar Dolichoectasia. A 76-year-old man admitted to the hospital with dizziness and slightly slurred speech. The 3D-TOF MRA showed extremely distorted basilar artery (A). The left vertebral artery (B) crossed the midline (white arrowhead) and merged the contralateral vertebral artery at the right cerebellopontine foot (C). In the contralateral side of the
lateral displacement of the basilar artery tortuosity, a hyperintensity of lacuna lesions (C) can be seen in the center of the pons (white arrow), which may be caused by perforating artery occlusion due to the buckling or stretching of the circuitous basilar artery.