# Stroke Subtypes and Topographic Locations Associated with Neurological Deterioration in Acute Isolated Pontine Infarction

Ruyue Huang, MD,\* Xia Zhang, MD,\* Weili Chen, MD,\* Jing Lin, MD,\* Zhenxiao Chai, MD,\* and Xingyang Yi, MD,†

> Objective: This study investigated predictors of neurological deterioration (ND) in acute isolated pontine infarction. Methods: Two hundred fifty-nine patients with acute isolated pontine infarctions identified using diffusion-weighted imaging were retrospectively analyzed. The patients were divided according to the presence/ absence of ND, defined as increased (≥2 units) National Institutes of Health Stroke Scale scores 5 days after onset. Pontine infarctions comprised 3 stroke subtypes: vertebrobasilar large-artery disease, basilar artery branch disease (BABD), and smallartery disease (SAD), according to basilar artery atherosclerosis severity and lesion extent of the transverse axial plane. Topographic locations of longitudinal pontine infarctions in the axial plane were divided into upper, middle, lower, and whole. *Results:* Of the 259 patients (male : female = 136:123,  $68.84 \pm 10.24$ ), only 27.4% exhibited ND. The prevalence was significantly increased in females, whereas smoking was significantly decreased in patients with ND. BABD and lower pontine infarctions were significantly more frequent in patients with ND (70.4% and 43.7%, respectively) than in patients without ND (51.6% and 30.3%, respectively). SAD and upper pontine infarctions were significantly less frequent in patients with ND (16.9% and 7.0%, respectively) than in patients without ND (30.3% and 23.4%, respectively). BABD and lower pontine infarctions were positively related to ND. Conclusions: This is the first study to demonstrate that BABD and lower pons lesions are predictors of ND in acute isolated pontine infarction. These findings indicate the potential importance of early identification of stroke subtypes and topographic locations in the prevention of ND in patients with suspected pontine infarction. Key Words: Infarction-pons-diffusion-weighted imaging-basilar artery branch disease-neurological deterioration.

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Address correspondence to Xingyang Yi, Department of Neurology, People's Hospital of Deyang City, No. 173 Taishan North Road, Deyang City, 618000 Sichuan Province, China. E-mail: 154379561 @qq.com. Introduction

Pontine infarctions account for approximately 7% of all ischemic strokes.<sup>1</sup> Isolated pontine infarctions, not part of larger vertebrobasilar infarctions, comprise approximately 15% of posterior circulation strokes.<sup>2</sup> Neurological deterioration (ND), which reflects worsening of neurological symptoms, is relatively common in acute pontine infarction cases and ranges from 14% to 35% according to different reports,<sup>2-5</sup> depending on the diagnostic criteria for ND and the time interval from onset of symptoms to evaluation. Furthermore, ND is associated with a worse short-term prognosis (modified Rankin Scale [mRS] score of 3 or higher at 1 month after ictus).<sup>6</sup> In a large retrospective analysis,<sup>7</sup> clinical deterioration was more frequent in large vessel disease and the vertebrobasilar circulation

From the \*Department of Neurology, Third Affiliated Hospital of Wenzhou Medical University, Ruian, Zhejiang Province, China; and †Department of Neurology, People's Hospital of Deyang City, Deyang, Sichuan Province, China.

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territory, which suggests that different mechanisms could be responsible for clinical deterioration in different etiological subtypes and lesion locations. However, studies have indicated that the severity of basilar artery atherosclerosis and transverse lesion extent were not related to deterioration in pontine infarctions.<sup>8,9</sup> These findings are inconsistent with previous studies that demonstrated that pontine infarcts that extended to the pontine base surface with mild atheromatous changes in the basilar artery were often correlated with deterioration.<sup>10</sup> Furthermore, findings regarding the relationship between the longitudinal topography of locations and deterioration have been inconsistent.9,11 In the current study, stroke subtypes determined via magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) were used to assess the basilar artery and topography of transverse lesions, whereas the topographic locations were used to assess longitudinal lesions in pontine infarctions. Therefore, the current study, which comprised a relatively larger sample, is the first study to simultaneously include the stroke subtype and topographic location to identify neuroimaging predictors of ND in pontine infarction.

### Subjects and Methods

#### Patient Selection

We retrospectively selected 259 patients with isolated pontine infarctions who sought treatment at the Department of Neurology, Third Affiliated Hospital of Wenzhou Medical University, within 24 hours after ictus from January 2010 to August 2013. Pontine infarctions were identified using diffusion-weighted imaging (DWI) within five days of arrival. The exclusion criteria included patients with pontine infarctions with anterior circulation infarcts or other vertebrobasilar infarcts; a potential cardiac source of embolism, such as atrial fibrillation, sick sinus syndrome, acute myocardial infarction, rheumatic heart disease, or dilated cardiomyopathy; infection; fever(temperature  $\geq$ 38.0°C);or serious diseases of the kidney, liver, or lung. This study was approved by the Ethics Committee at the Third Affiliated Hospital of Wenzhou Medical University, and patient consent was waived by the ethics committee. The following demographic features and conventional risk factors were investigated: sex, age, smoking ( $\geq$ 5 cigarettes per day), drinking ( $\geq$ 100 mL wine per day), prior infarction or transient ischemic attack, hypertension (antihypertensive medication or blood pressure  $\geq$ 140/90 mmHg at repeated measurements 2 weeks after stroke onset), and diabetes mellitus (diabetes medication or a spontaneous blood glucose level  $\geq$ 11.1 mmol/L).

#### Laboratory Tests

Glucose levels were assessed at the time of hospital admission. Other laboratory tests were conducted to assess glycated hemoglobin, triglyceride, total cholesterol, lowdensity lipoprotein, high-density lipoprotein, C-reactive protein, fibrinogen, blood urea nitrogen/serum creatinine ratio, albumin (ALB), and hemoglobin on the second day of hospital admission.

## MRI and MRA

All patients underwent MRI and MRA within 5 days of arrival. MRI was performed using 1.5-T superconducting magnets (Magnet Avanto 1.5; Siemens, Erlangen, Germany). DWI scans (time of repetition [TR]: 2900 ms/time of echo [TE]: 89 ms), T<sub>2</sub>-weighted scans (TR: 4000 ms/TE: 97 ms), and T<sub>1</sub>-weighted scans (TR: 410 ms/TE: 11 ms) were obtained at a 5-mm slice thickness. Three-dimensional time-of-flight MRA was acquired. Vertebrobasilar arteries were assessed via MRA.

#### Stroke Subtypes Detected by MRI and MRA

The potential causes of pontine infarction included 3 subtypes of artery-related diseases<sup>12</sup>: (1) vertebrobasilar large-artery disease was indicated by stenosis of at least 50% of the lumen diameter in the basilar artery, as determined via MRA (Fig 1); (2) basilar artery branch disease (BABD) was indicated by an infarct that reached the pontine surface in the absence of large artery disease and potential sources (Fig 2); and (3) small-artery disease (SAD) was indicated by a small (<15 mm) infarct that spared

**Figure 1.** VLAD. A 63-year-old male patient exhibited a substantial infarct that reached the pontine surface as detected by  $T_2WI$  (A) and DWI (B). Basilar artery occlusion was observed (C), and his neurological deficit deteriorated from an NIHSS score of 7 to 12, 36 hours after the onset of the first symptom. Abbreviations: DWI, diffusionweighted imaging; NIHSS, National Institutes of Health Stroke Scale;  $T_2WI$ ,  $T_2$ -weighted imaging; VLAD, vertebrobasilar large-artery disease.



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