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# Transient neurological attack before vertebrobasilar stroke

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ABSTRACT

*Background:* Patients with vertebrobasilar (VB) circulation ischemia can present with nonspecific symptoms, which complicate the distinction of transient ischemic attack (TIA) from other benign disorders. According to previously accepted classifications, typical TIA does not occur with VB symptom such as vertigo, diplopia, or dysarthria in isolation. However, there is a lack of evidence to support this hypothesis.
*Methods:* This hospital-based study included 214 consecutive patients with acute ischemic VB stroke. We defined transient neurological attacks (TNAs) as temporary (<24 h) episodes with neurological symptoms, and further divided them into TIA, nonspecific TNA, or other specific disorder groups. We investigated the incidence and clinical symptoms of TNAs within 3 months prior to the stroke episode, and comparisons were made between patients with and without previous TNA history with respect to their background and stroke profiles.
*Results:* Among 214 patients with VB stroke, 56 (26.2%) had previous TNAs. Six of them were diagnosed with other specific disorders and excluded from the analysis. The remaining 33 and 17 were diagnosed with TIA and nonspecific TNA, respectively. Twenty-one (42.0%) had attacks with a nonfocal symptom in isolation, and acute infarction in neuroimaging was confirmed in 4 of these patients. Vertigo was the most frequent nonspecific TNA symptom. Patients with prior TNA had a significantly higher rate of atherothrombotic stroke than those without TNA (40.0% vs. 21.5%, $P=0.009$).
*Conclusions:* A considerable fraction of TIAs due to VB circulation ischemia may be overlooked among clinically nonfocal TNAs.



## 1. Introduction

It is important to accurately diagnose transient ischemic attacks (TIAs) because they increase patients' risk of stroke [1,2]. Immediate evaluation and treatment can significantly reduce subsequent stroke risk [3]. However, because the symptoms usually disappear in a short time, even without treatment, it can be difficult to diagnose TIA. In addition, TIAs often present with symptoms that are common to several different diagnoses, making it difficult to distinguish TIAs from other transient neurological symptoms, or nonspecific "transient neurological attacks" (TNAs). It may be impossible to differentiate symptoms including peripheral vestibulopathy, migraine, syncope, seizure, hypoglycemia, and psychiatric disorders from TIA [4]. Previous studies have found that neurologist interobserver agreement for diagnosing TIA is far from excellent [5,6]. Magnetic resonance (MR) diffusion-weighted imaging shows lesions in some patients [7] and can support the diagnosis of ischemic event, but these radiological observations are not regarded as TIA according to the proposed new definition [7]. Therefore, the diagnosis of TIA is mostly clinical.

The National Institute of Neurological Disorders and Stroke (NINDS) defined TIA as a brief episode of focal brain function loss, presumably due to ischemia, that can usually be localized to a brain region supplied by a single vascular system: left or right carotid or vertebrobasilar (VB) system [8]. However, it may be difficult to distinguish VB system TIAs from other nonspecific TNAs because VB symptoms sometimes manifest in patients with nonspecific TNAs. VB system TIA symptoms are itemized in the NINDS III classification as follows: loss of balance, vertigo, unsteadiness or disequilibrium, diplopia, and dysphasia/dysarthria. That publication also noted that none of these symptoms would occur alone in true TIA [8]. However, to our knowledge, no study has published reliable data to verify this statement. We hypothesize that at least some TIA patients would report one of these VB symptoms in isolation. Moreover, Bos et al. reported that nonfocal TNAs could be a risk factor for major vascular diseases in the general population [9]. However, there have been no descriptions of antecedent TNAs followed by a stroke episode. Thus, our aim was to investigate the incidence and clinical characteristics of TNAs prior to VB stroke.

## 2. Methods

### 2.1. Study population

The ethic committee of our institution approved the protocol of this study. We conducted a hospital-based study of 235 consecutive

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patients with acute ischemic VB stroke who were hospitalized in the Department of Neurology at the Tokyo Women's Medical University Hospital between April 2005 and July 2011. We enrolled patients who had symptomatic ischemic stroke within 1 week from onset and were independent in activities of daily living before the stroke. Of 235 patients, 214 met the inclusion criteria.

We maintain a prospective registry of all consecutive patients admitted to our institution with suspected stroke or TIA. We used a standardized case report form and gathered a number of demographic and clinical variables, including date of the event, past medical history, risk factors for stroke, prior medications, physiological examination findings, and neurological symptoms. We also documented diagnostic test results and details of treatments performed during hospitalization. The persons computing data were blinded to the purpose of this study.

### 2.2. Event assessment

TNA was defined as a sudden attack of neurological symptoms that completely resolved within 24 h. During the hospitalization, a trained neurologist asked all the participants whether they had had brief (<24 h) motor disturbances in their face, arms, or legs within 3 months prior to the stroke episode. Similar questions were asked for sensory disturbances, speech, vision, consciousness, vertigo, and dizziness. If they answered affirmatively, they were asked additional questions regarding the time of onset, detailed symptom description, duration and number of attacks, and whether they consulted a doctor. All information obtained from the patient and their relatives, as well as medical records and radiological findings of our hospital, other hospitals, and general practitioners were evaluated, and a board-certified stroke neurologist verified a final classification of TNA. Fifty-six patients had TNAs within 3 months before stroke, but 6 were excluded from the analysis because they had clear evidence of orthostatic hypotension ($n=2$), epilepsy ($n=1$), Ménierè's disease ($n=1$), psychiatric disorders ($n=1$), or cardiac syncope ($n=1$). We classified the remaining TNAs into 2 groups: TIA and nonspecific TNA.

TIA was defined as an acute loss of focal brain function lasting <24 h with or without corresponding imaging evidence of an ischemic lesion. In accordance with the NINDS III classification [8], focal brain symptoms included: hemilateral motor dysfunction (weakness, paralysis, or clumsiness), hemilateral sensory symptoms (loss of feeling, numbness, or paresthesia), aphasia, amaurosis fugax, hemianopia, or hemiataxia. If 2 or more VB symptoms, including loss of balance, vertigo, dysarthria/dysphasia or diplopia, were reported, they were also regarded as focal signs. Attack with one of these VB symptoms in isolation was regarded as nonspecific. Other symptoms of nonspecific TNA included nonrotatory dizziness, unconsciousness, or bilateral motor dysfunction. In cases of an isolated nonfocal symptom with acute infarction confirmed with brain imaging (MR imaging or computed tomography [CT]), or with any of abovementioned focal symptoms, patients were classified as TIA. Eight patients who did not undergo brain imaging during or shortly after TNA were judged on the basis of a detailed interview performed during the hospitalization (self-reported TNAs).

$ABCD^2$ score [10] was calculated as follows: age ≥60 years, 1; systolic blood pressure ≥140 mm Hg and/or diastolic blood pressure ≥90 mm Hg, 1; unilateral weakness, 2; speech disturbance, 1; duration of symptoms (≥60 min, 2; 10–59 min, 1; <10 min, 0); and diabetes, 1. In cases of multiple TNAs, the most recent attack was used for the analyses. When patients had not sought medical attention shortly after the prior TNA, their $ABCD^2$ score was calculated using the first blood pressure recorded after the attack.

Ischemic stroke was defined as an episode of focal neurological deficits with acute onset lasting >24 h with imaging evidence of cerebral infarction corresponding to the current symptoms. All strokes were diagnosed by stroke neurologists based on clinical observations and MR imaging or CT findings. Assessments were made for event severity according to the National Institutes of Health Stroke Scale (NIHSS); scores range from 0 to 42, with higher values reflecting more severe neurologic deficits. Subtypes classified by etiology were large artery atherosclerosis (LAA), cardioembolism, small vessel occlusion, other cause, or undetermined cause, in conformity with the Trial of Org 10172 in Acute Stroke Treatment criteria [11].

### 2.3. Baseline risk factors

The estimated glomerular filtration rate (eGFR) was calculated from the Modification of Diet in Renal Disease formula and the Japanese coefficient; chronic kidney disease (CKD) was defined as eGFR<60 mL/min/1.73 $m^2$. Intracranial arterial stenosis >50% on MR angiography, 3D CT angiography, or digital subtraction angiography was considered significant. Carotid artery ultrasounds were read by appropriately trained neurologists, and stenosis >50% was defined as significant extracranial arterial stenosis. Histories of ischemic heart disease (IHD) (myocardial infarction or angina pectoris) and peripheral arterial disease (PAD) were recorded, and any kind of past medical condition was considered as a prior condition. Atrial fibrillation (AF) was judged based on 2 or more electrocardiograms recorded before or during hospitalization.

### 2.4. Statistical analysis

Analyses were performed with SPSS software (version 11.0; SPSS, Inc, Chicago, IL). Statistical significance for intergroup differences was assessed by the $\chi^2$ test or Fisher's exact test for categorical variables, and the Student's *t*-test or the Mann–Whitney *U*-test for continuous variables. In all analyses, $P<0.05$ was considered significant (two-sided test).

## 3. Results

As shown in Fig. 1, of 214 patients with VB stroke, 56 (26.2%) had history of any TNAs. Six patients had definite diagnoses of orthostatic hypotension ($n=2$), epilepsy ($n=1$), Ménierè's disease ($n=1$), psychiatric disorders ($n=1$), or cardiac syncope ($n=1$), and were excluded from the analysis. The remaining 33/208 (15.9%) and 17/208 (8.2%) patients were diagnosed with TIA and nonspecific TNA, respectively. Four patients had nonfocal symptom (vertigo, 2; nonrotatory dizziness, 1; dysarthria, 1) in isolation, but were classified as TIA according to the corresponding lesion on brain imaging. The clinical symptoms of the TNA patients with isolated nonfocal symptoms are listed in Table 1. Vertigo was the most frequent symptom. Comparisons were made between patients with TIA and nonspecific TNA with regard to the clinical findings of prior attacks and subsequent stroke (Table 2). Approximately a quarter of both TIA and nonspecific TNA groups (24.2% vs. 29.4%, $P=0.69$)

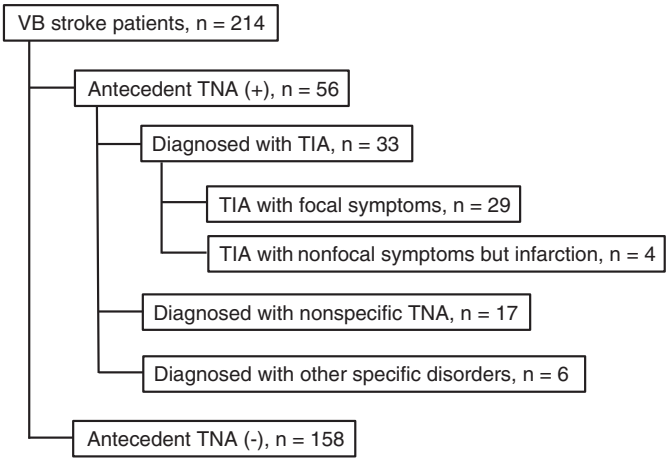


**Fig. 1.** Patient distribution of the present study.