A Score for Predicting Paroxysmal Atrial Fibrillation in Acute Stroke Patients: iPAB Score

Kotaro Yoshioka, MD,*† Kosuke Watanabe, MD,† Satoshi Zeniya, MD,‡
Yoko Ito, MD,‡ Masaki Hizume, MD, PhD,† Toshiro Kanazawa, MD, PhD,†
Makoto Tomita, PhD,§ Satoru Ishibashi, MD, PhD,* Hirotomo Miake, MD, PhD,‡
Hiroaki Tanaka, MD, PhD,† Takanori Yokota, MD, PhD,*
and Hidehiro Mizusawa, MD, PhD*

Background: Detection of paroxysmal atrial fibrillation (PAF) after a stroke is challenging. The purpose of this study was to develop a clinical score to predict PAF in a cohort of acute ischemic stroke patients prospectively and to validate it in an independent cohort. *Methods:* Consecutive acute ischemic stroke patients without permanent atrial fibrillation were enrolled in a derivation sample (n = 294) or a validation sample (n = 155). We developed a score for predicting PAF by independent risk factors derived from a logistic regression analysis of the derivation cohort and validated the score in the external cohort. *Results:* Multivariate analysis in the derivation cohort identified 3 variables independently associated with PAF. We calculated a score from these variables (history of arrhythmia or antiarrhythmic agent use [yes, 3 points], left atrial dilation [≥40 mm, 1 point], brain natriuretic peptide [BNP, ≥50 pg/mL, 1 point; ≥90 pg/mL, 2 points; ≥150 pg/ml, 3 points], total score, 0-7). The iPAB score (identified by past history of arrhythmia or antiarrhythmic agent use, atrial dilation, and BNP elevation) predicted PAF in the derivation (*c* statistic, .90) and validation (.94) cohorts at levels statistically superior to other biomarkers and clinical scores. For a total score 2 or more, the sensitivity and specificity were 93% and 71%, respectively. For a total score of 4 or more, the corresponding values were 60% and 95%. *Conclusions:* Our prospective study suggests that this simple risk score superior to other scores help clinicians predict PAF or identify good candidates for further evaluation to detect PAF. **Key Words:** Acute ischemic stroke—paroxysmal atrial fibrillation—cardioembolism—brain natriuretic peptide.
© 2015 by National Stroke Association

Introduction

Paroxysmal atrial fibrillation (PAF), an important risk factor for ischemic stroke, has risks similar to those of permanent atrial fibrillation (AF).[1-3] Because oral anticoagulation therapy can reduce the risk of ischemic stroke in patients with PAF,[2,4-6] diagnosing PAF at the acute phase of stroke has important management implications.

Although PAF is more prevalent than permanent AF in stroke survivors, detecting PAF is challenging.[7] Recent studies revealed that routine diagnostic techniques, such as Holter electrocardiography (ECG), have low

sensitivity for PAF.[8] Early-phase ECG monitoring, long-term Holter ECG monitoring,[9-13] cardiac event monitoring,[14] and implanted PAF monitoring device[15] have improved PAF detection. However, such methods are highly time consuming and early predicting the patients with PAF at the acute phase of stroke is critically important to reduce recurrent stroke by the appropriate secondary prevention therapy.

Several biomarkers that predict PAF in acute ischemic stroke patients, including brain natriuretic peptide (BNP)[16-19] and left atrial dilation,[20] have recently been reported. Identifying patients at particularly high risk of PAF by a score based on these biomarkers may represent a reasonable approach. Some studies have proposed new clinicoradiological scores, score for the targeting of AF (STAF)[21,22] and score by Fujii et al,[23] to screen for PAF or permanent AF in acute stroke patients. In patients with PAF, however, others have suggested that one of the scores had low sensitivity and was of limited use.[24] These studies were retrospective and single-center analysis, which cannot avoid selection and information bias.

The aim of the present study was to derive a simple score for determining the risk of PAF in acute stroke patients from prospective and multivariate analysis of clinical profiles and to externally validate the score.

Methods

Patient Selection

A prospective cohort study was performed on consecutive patients with acute ischemic strokes from September 2013 to September 2014 for the derivation cohort. Subsequently, an external validation cohort was recruited from September 2013 to September 2014 at another medical center. We excluded patients with permanent AF and diseases or conditions associated with elevated plasma BNP levels, such as acute heart failure on admission, dialysis-dependent chronic renal failure, and use of mechanical prosthetic valves. Patients with a known history of PAF and documented AF on initial ECG were also excluded. All patients underwent ECG monitoring from admission day to the situation when they walk without assistance or in case they could not keep monitoring, such as delirium or death. They also received 24-hour Holter ECG during hospitalization. Consistent with the 2006 guidelines for the management of AF patients,[25] AF was categorized as PAF if the ECG, ECG monitoring on the ward, and Holter ECG documented a sinus rhythm and at least 1 AF episode that terminated spontaneously during hospitalization. The patients without AF on the initial ECG were classified into a delayed PAF group if they developed AF during hospitalization. The study protocol received approval by the local institutional review board.

Clinical Data Collection

The following information were collected at the time of admission: demographic data, cardiovascular risk factors, and clinical data including a history of any arrhythmia (eg, PAF, supraventricular/ventricular tachycardia) and just arrhythmia unspecified or antiarrhythmic agent use. Because we excluded patients with a history of PAF from study cohort, we defined history of arrhythmia as history including any type of arrhythmia except PAF. Blood sampling and plasma BNP measurement were performed within 7 days of admission. The plasma BNP concentration was measured using a chemiluminesecence enzyme immunoassay for human BNP (Shionogi Co., Ltd., Osaka, Japan). A bedside continuous ECG monitoring during hospitalization was started from the admission day using DS-7680 (Fukuda Denshi, Tokyo, Japan). Whenever AF was suspected from the monitor trace by the staff, the monitor was reviewed by treating clinicians; 24-hour Holter monitoring was performed on the ward in the derivation cohort (RAC-3203; Nihon Kohden, Tokyo, Japan) and the validation cohort (FM-180; Fukuda Denshi). Holter data were analyzed by blinded cardiologists supported by an automatic measurement system in the derivation cohort (DSC-3200; MAC Science, Tokyo, Japan) and the validation cohort (SCM-6600; Fukuda Denshi). All patients underwent a cerebral scan (computed tomography or magnetic resonance imaging) and carotid ultrasound. For each patient, transthoracic echocardiography was performed using the Aplio SSA-700A (Toshiba Medical Systems, Tochigi, Japan). The left atrial diameter was measured at the parasternal level in motion mode. In accordance with the guidelines of the American Society of Echocardiology, left atrial dilation was defined as a diameter greater than 40 mm.[26] Mitral valvular disease included mitral valve stenosis and mitral regurgitation. Color Doppler echocardiography was used to detect mitral regurgitant jet and were rated none, trivial, mild, moderate, or severe; the latter 3 were combined into a single entity of mitral regurgitation. Mitral stenosis was based on the appearance of the mitral valve orifice on the 2-dimensional echocardiography and on the pulsed Doppler recording of the mitral flow velocity. Stroke etiology was assigned according to the Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria.[27] Initial National Institutes of Health Stroke Scale (NIHSS) score at admission and clinical scores of the studies by STAF[21] and Fujii et al[23] were calculated using data collected during hospitalization for the validation cohort.

Statistical Analyses

Univariate analysis was carried out using the following tests as appropriate: Student t, Mann–Whitney U, chi-square, and Fisher exact. The optimal cutoff points of