Clinical Outcomes of Persistent and Paroxysmal Atrial Fibrillation in Patients with Stroke

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Background: We compared the clinical outcomes of persistent atrial fibrillation (PeAF) and paroxysmal atrial fibrillation (PAF) in patients with cardioembolic stroke caused by nonvalvular atrial fibrillation (NVAF) because the nature of the fibrillation can cause persistent cerebral infarction. *Methods:* We classified 619 of 964 patients hospitalized with cardioembolic stroke between April 2007 and December 2013 within 24 hours of onset as having PeAF (n = 447) and PAF (n = 172) according to a retrospective analysis of their clinical records, including National Institutes of Health Stroke Scale (NIHSS) scores on admission, clinical outcomes (modified Rankin Scale [mRS] scores) at 90 days after admission, and major cerebral artery occlusion. *Results:* The PeAF group was significantly older ($P < .001$) and had a higher prevalence of hypertension ($P = .007$), diabetes ($P = .039$), heart failure ($P = .004$), previous coronary artery disease ($P = .002$) and cerebral infarction ($P < .001$), medication with anticoagulants ($P < .001$), and elevated blood glucose on admission ($P = .002$). Neurologic severity assessed by NIHSS scores on admission was significantly worse in the PeAF than in the PAF group ($P < .001$). Significantly more patients in the PAF group had favorable outcomes (mRS, 0-2) after 90 days ($P < .001$). The incidence of major cerebral artery occlusion was significantly higher in the PeAF group ($P < .001$). *Conclusions:* Patients with PeAF and cardioembolic stroke due to NVAF had more severe neurologic deficits on admission, more frequent major arterial occlusion, and poorer outcomes than those with PAF. **Key Words:** Atrial fibrillation—cardioembolic stroke—arterial occlusion—clinical outcome.

Introduction

Atrial fibrillation (AF), particularly nonvalvular atrial fibrillation (NVAF), is a risk factor for cerebral infarction, and preventing the onset of both paroxysmal and persistent cerebral infarction is extremely important. The American College of Cardiology/American Heart Association/European Society of Cardiology guidelines recommend anticoagulant therapy based on congestive heart failure, hypertension, age greater than or equal to 75 years, diabetes mellitus, and stroke/transient ischemic attack ($CHADS_2$) and CHA_2DS_2-VASc (vascular disease, age group 65–74 years, and female sex category) scores.[1,2] We also previously associated higher $CHADS_2$ and CHA_2DS_2-VASc scores with more severe neurologic deficits on admission and less favorable clinical outcomes among patients with cardioembolic stroke due to NVAF,[3,4] as well as a higher incidence of major cerebral artery occlusion.[5] Although paroxysmal atrial fibrillation (PAF) and persistent atrial fibrillation (PeAF)

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are considered to similarly contribute to the onset of cerebral infarction,[6] to our knowledge, disease severity and clinical outcomes have not been compared among patients with cardioembolic stroke and PAF or PeAF.

We investigated associations between disease severity on hospital admission and clinical outcomes of PeAF and PAF in patients with cardioembolic stroke due to NVAF.

Patients and Methods

We selected 619 (male, n = 360; female, n = 259; mean age ± standard deviation, 75 ± 10 years) of 964 patients who had been hospitalized within 24 hours of cardioembolic stroke onset between April 2007 and December 2013 and who had previously been independent (modified Rankin Scale [mRS] ≤1). All patients were examined by brain computed tomography and magnetic resonance imaging using a 1.5-T Achieva Nova Dual (Philips, Best, The Netherlands) and a 1.5-T Magnetom Avanto (Siemens, Erlangen, Germany) on admission and were diagnosed with cardioembolic stroke according to the classification applied in the Trial of Org 10172 in Acute Stroke Treatment.[7] Valvular disease was assessed by cardiac ultrasound. We defined NVAF as AF without a history of rheumatic mitral valve disease, a prosthetic heart valve or mitral valve reconstruction.[8] We defined PeAF as AF persisting for 7 days or more and PAF as AF characterized by a return to sinus rhythm within 7 days. The type of AF was classified based on the findings a retrospective analysis of data including electrocardiographic findings on admission, electrocardiographic monitoring (bedside monitor) findings after admission, 24-hour Holter monitoring, and medical history, based on the patients' charts.

We then retrospectively compared the clinical background factors of age, sex, hypertension (HT), diabetes mellitus (DM), coronary heart disease, congestive heart failure, blood pressure and blood glucose level, National Institutes of Health Stroke Scale (NIHSS) score on admission, recanalization therapy, under antithrombotic therapy and $CHADS_2$ score at the time of stroke onset, clinical outcomes and occlusion of the internal carotid artery, middle cerebral artery (M1 segment and M2 proximal segment), and basilar artery between the PeAF and PAF groups. HT was defined as blood pressure greater than or equal to 140/90 mm Hg or under medication with oral antihypertensive drugs before stroke onset. DM was defined as casual blood glucose of greater than or equal to 200 mg/dL and hemoglobin A1c (National Glycohemoglobin Standardization Program) of greater than or equal to 6.5% or medication with antidiabetic drugs. We defined congestive heart failure as New York Heart Association class II or more or a history of heart failure. The $CHADS_2$ scores were categorized as low (0-1), moderate (2 or 3), or high (≥4). Clinical outcomes evaluated based on mRS scores at 90 days after admission were defined as either favorable (0-2) or poor (3-6). Two neurologists and 1 neuroradiologist who were blinded to the backgrounds of the patients defined vessel occlusion as signal loss.

The Ethics Committee at Saitama Medical University International Medical Center approved the study protocol.

Statistical Analysis

Data were statistically analyzed using SPSS Statistics 20 (IBM Corporation, Armonk, NY). Age, blood pressure, and blood glucose were compared among groups using the Student *t* test; NIHSS scores were compared using the Wilcoxon rank sum test, and ratios were compared using the Fisher exact test (2-sided). Multivariate analysis of factors related to clinical outcomes was assessed using a logistic regression model. Values of P less than .05 were considered significant.

Results

Table 1 lists the clinical backgrounds of the 447 patients (72%) with PeAF and 172 patients (28%) with PAF. The patients with PeAF were significantly older (76 ± 9 vs. 72 ± 12 years, $P < .001$), had a higher prevalence of HT (71% vs. 59%, $P = .007$), DM (24% vs. 16%, $P = .039$), heart failure (21% vs. 11%, $P = .004$), previous coronary artery disease (13% vs. 6%, $P = .002$), previous cerebral infarction (17% vs. 6%, $P < .001$), elevated blood glucose on admission (137 ± 45 vs. 126 ± 37 mg/dL, $P = .002$), and medication with anticoagulants (24% vs. 10%, $P < .001$). A significantly higher proportion of patients with PAF had low $CHADS_2$ scores (0 or 1), whereas significantly higher proportions of those with PeAF had moderate (2 or 3) and high (≥4) $CHADS_2$ scores (low, high, and moderate scores: 35% vs. 58%, $P < .001$; 52% vs. 39%, $P = .003$; and 13% vs. 3%, $P < .001$, respectively). The incidence of occluded major cerebral arteries was significantly higher in the PeAF group (internal carotid artery, 22% vs. 9%, $P < .001$; M1, 26% vs. 9%, $P < .001$; M2 proximal, 10% vs. 2%, $P = .001$). Figure 1, A shows the NIHSS scores of the PeAF and PAF groups on admission. The degree of neurologic severity as assessed by median NIHSS scores on admission was significantly higher in the PeAF than in the PAF group (11; interquartile range: 4-17 vs. 6; interquartile range; 3-12). A comparison between the 2 groups stratified by $CHADS_2$ scores revealed significantly worse neurologic severity for those with low (7 [4-14] vs. 5 [2-12], $P = .042$) and moderate (12 [6-18] vs. 7 [3-14], $P < .001$) scores but not for those with high scores (12 [5-17] vs. 11 [7-16]) in the PeAF group. Figure 1, B shows the clinical outcomes of the PeAF and PAF groups. The proportion of patients who achieved favorable outcomes (mRS, 0-2) after 90 days was significantly higher in the PAF than in the PeAF group (n = 116, 67% vs. n = 176, 39%; $P < .001$). A comparison between the PeAF and PAF groups stratified by $CHADS_2$ scores revealed