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Embolic stroke and after-admission atrial fibrillation

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ABSTRACT

Background: Although atrial fibrillation (AF) is a leading cause of recurrent embolic stroke, secondary AF after stroke has been reported frequently. Because of the different treatment each uses, it is important to detect the exact stroke-etiology.
Objectives: The aim of this study was to compare the embolic stroke in patients with known AF and after-admission AF (AAAF).
Methods: Between October 2002 and July 2009, those who were diagnosed with AF (n = 354) were enrolled in our study out of a total of 2026 acute ischemic stroke (IS) patients. The embolic lesion patterns were assessed by two stroke specialists who were blinded to the clinical information.
Results: Among 354 IS patients with AF, the number of patients with embolic stroke was 314. Patients with embolic stroke were younger and more likely to have larger left atrial (LA)/Aortic diameter ratio. Approximately 90.4% of those with known AF had embolic stroke, while <60% of patients with AAAF had embolic stroke. Nevertheless, anticoagulants were prescribed similarly in both groups at discharge. The LA/Aortic diameter ratio < 1.5 was significantly related to AAAF. After adjusting for multiple co-variables, compared to the patients with known AF, patients with AAAF had reduced risk of embolic stroke (Odds ratio 0.11, 95% Confidence interval 0.03–0.36, *p*-value < 0.001).
Conclusions: Compared to AAAF after stroke, known AF was associated with embolic stroke. Therefore, we suggest that stroke etiology and some novel echocardiographic indicators such as LA enlargement might be contemplated before routine using of anticoagulants in IS patients with AF.

1. Introduction

Because of increased lifespan and public awareness, stroke characteristics have changed to a Westernized pattern in Korea [1,2]. Approximately 20% of ischemic strokes (IS) are caused by cardioembolic (CE) etiology [3]. Among the IS subtypes, cardioembolic stroke (CS) was associated with the poor functional outcomes and the fatal prognosis [4].

Although atrial fibrillation (AF) is a well-known risk factor for CS, it is not always directly responsible for the embolism [5]. About one third of IS patients with AF were not categorized as CE etiology and frequently had additional potential sources of CS [5–7]. Because the cardiac arrhythmia including AF has been reported after IS frequently, AF may be the consequence instead of the cause of the stroke [8]. Multiple regions of the brain have been implicated in neural control of cardiac rhythm [9].

However, quite a proportion of patients with CS have unknown or paroxysmal AF [10,11]. Anticoagulation might not be recommended unless AF has been documented as the source of CS. Because oral anticoagulants can reduce risk of stroke recurrence by up to two-thirds, it is crucial to evaluate the exact thromboembolic mechanisms in patients with CS [12]. The aim of this study was to compare the patients with the known AF and those with after-admission AF (AAAF) and to evaluate the predictive value for embolic stroke.

2. Methods

2.1. Study population

Between October 2002 and July 2009, patients with acute (<7 days from stroke onset) IS were consecutively enrolled in our prospective stroke registry. Initially, a total of 2026 patients were included in this study. Among them, those who were diagnosed with AF (n = 354) were enrolled in our study. The number of patients with AAAF was 19 (Fig. 1). AAAF was defined as AF discovered at or after admission in patients without any previous history of AF [13].

We performed extensive work-ups to evaluate stroke pathophysiology in almost all patients: head/neck angiography, Transthoracic echocardiography (TTE), 24-h Holter monitoring, and magnetic resonance (MR) imaging including diffusion-weighted imaging (DWI), Fluid-attenuated inversion recover (FLAIR), susceptibility weighted imaging (SWI), T2 weighted imaging, MR angiography, and aortography. Furthermore, we sequentially applied Transesophageal echocardiography (TEE) to a selected population at higher suspicion of cardioembolism in cases of unknown etiology.

2.2. Clinical information

We assessed demographic information such as age, gender, history of previous stroke, and smoking. Diabetes, hypertension, and dyslipidemia were assessed as previously

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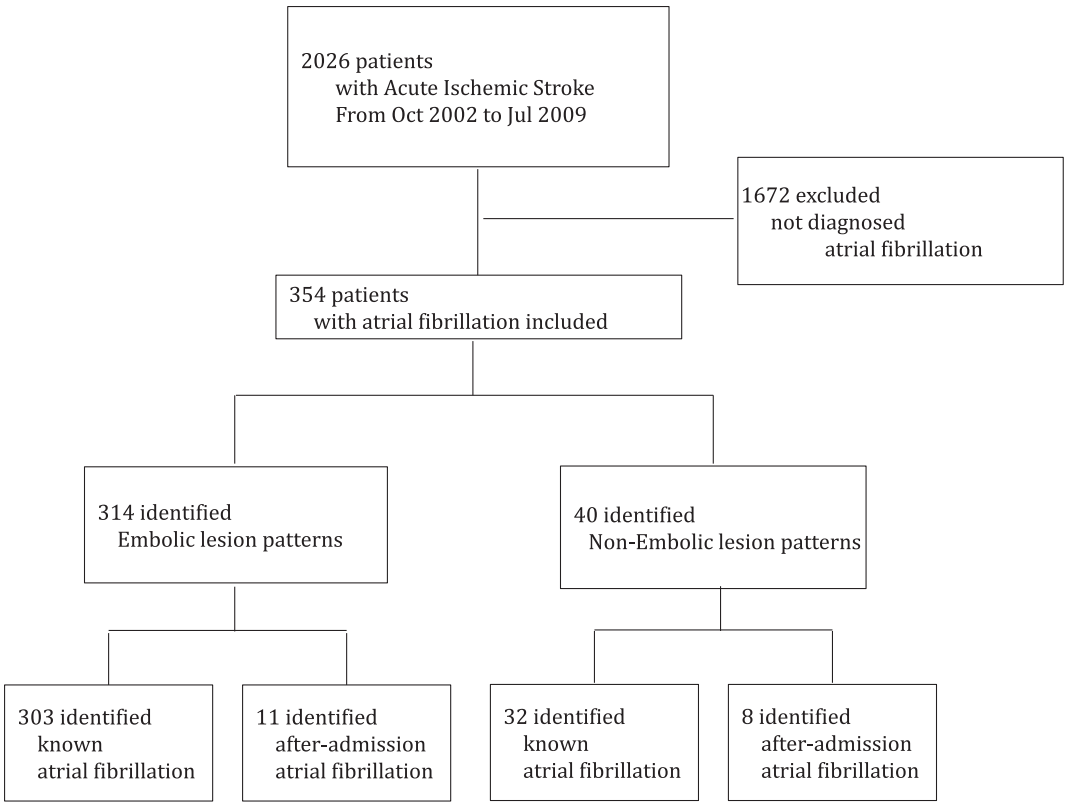

Fig. 1. Flow chart of acute ischemic patients with atrial fibrillation according to the embolic lesion patterns.

described [14,15]. We classified the stroke subtypes based on the modified Trial of Org 10,172 in Acute Stroke Treatment (TOAST). Based on previous reports, large artery atherosclerosis was defined as clinical and brain imaging of either significant stenosis (>50%) or occlusion of a major relevant artery, probably due to atherosclerosis. Cardiembolism includes arterial occlusions presumably due to at least one cardiac source for an embolus [16].

MR imaging was performed by using a 1.5-T or a 3.0-T system. The patterns of embolic lesion were defined as follows: (1) cortico-subcortical territorial lesion without relevant large artery diseases or (2) multiple non-contiguous lesions in bilateral hemispheres or both anterior and posterior circulations [17]. The patterns of embolic lesion were assessed by two stroke specialists (Y.K. and S-H. L; inter-rater kappa = 0.86), who were blinded to the clinical information. The institutional review board of Seoul National University Hospital approved the study protocol, and written informed consent was obtained from all subjects or from their next of kin when the consent from the patient was impossible.

The GE E9 (GE Healthcare, Wauwatosa, WI) or the Philips iE33 (Philips Medical Systems, Bothwell, WA) was used for M-mode and Doppler TTE in all patients. We measured the LV ejection fraction (LVEF), left atrial (LA) diameter, and LA/Aortic diameter ratio. The LA/Aortic diameter ratio was obtained from the 2-D short axis view. Based on the previous reports, LVEF < 55% [18] and LA/Aortic diameter ratio < 1.5 [19,20] were used as reference values.

2.3. Statistical analysis

Categorical variables are reported as frequencies (%), and continuous variables are reported as the mean ± standard deviation (SD). The Student's t-test and chi-square test were used between the two groups. In multivariate logistic regression, the odds ratios (ORs) and 95% confidence intervals (CIs) were used to calculate the probability values. A probability value of ≤.05 was considered statistically significant. Analyses were performed using SPSS version 21.0 (SPSS Inc., Chicago, IL, USA).

3. Results

Among 354 patients with AF in acute ischemic stroke, the number of patients with embolic stroke was 314. The number of patients with AAAF was 5.37% (n = 19). Patients with embolic stroke were younger (70 ± 11 years versus 74 ± 9 years) and more likely to have larger LA/Aortic diameter ratio (1.61 ± 0.40 versus 1.48 ± 0.26) (Table 1). In initial stroke subtypes, CE etiology was prevalent in patients with known AF (81.5%). On the other hand, undetermined etiology was more prevalent in patients with AAAF (89.5%). In two patients with atherosclerotic etiology, they had internal borderzone infarction between the deep and superficial perforating arterial territories of the MCA. There were no differences in lesion side between the two groups. Compared to the patients with AAAF, patients with known AF were more likely to have embolic lesion-patterns in MRI and larger LA/Aortic diameter ratio (see the Supplementary table). Approximately 90.4% of patients with known AF had embolic strokes, while <60% of patients with AAAF had embolic strokes (Fig. 2). At discharge, anticoagulations were prescribed similarly in both IS patients with AF (embolic stroke group; 84.3% versus non-embolic stroke group; 85.0%, *p*-value = 0.91) (Table 1).

After adjusting for age, gender, history of previous stroke, hypertension, diabetes, smoking, dyslipidemia, LVEF, and LA/Aortic diameter ratio, we conducted the binary logistic regression analysis for AAAF compared to known AF. The LA/Aortic diameter ratio < 1.5 had 4-fold risks of AAAF (Odds ratio 4.27, 95% Confidence interval 1.28–13.55, *p*-value 0.02) (Table 2).

We performed the binary logistic regression analysis after adjusting for age, gender, history of previous stroke, hypertension, diabetes, smoking, dyslipidemia, type of atrial fibrillation, LVEF, and LA/Aortic diameter ratio. Compared to the patients with known AF, patients with AAAF were associated with reduced risks of embolic strokes (Odds ratio 0.11, 95% Confidence interval 0.03–0.36, *p*-value <0.001) (Table 3).

4. Discussion

We demonstrated that embolic lesion-patterns were less common in patients with AAAF, compared to those with known AF. In addition, IS patients with known AF had larger LA/Aortic diameter ratio. The LA/Aortic diameter ratio < 1.5 was significantly related with AAAF. In binary logistic regression, compared to the known AF, AAAF had an 89% reduced risk of embolic stroke. Unlike our expectations, LVEF was not related to embolic strokes. Based on our results, anticoagulants were