Detection and Predictors of Paroxysmal Atrial Fibrillation in Acute Ischemic Stroke and Transient Ischemic Attack Patients in Singapore

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Background: Detection of paroxysmal atrial fibrillation (pAF) is important for optimal secondary stroke prevention. Data are limited from Asia regarding inpatient occurrence and predictors of pAF to optimize electrocardiographic (ECG) monitoring despite it having nearly two thirds of the world's population and different subtypes of stroke from the West. *Methods:* We analyzed a prospective dataset comprising 370 acute ischemic stroke (AIS) and 25 transient ischemic attack (TIA) patients without known atrial fibrillation who underwent continuous ECG monitoring (CEM) in an acute stroke unit from July 2012 to February 2013. The median duration of monitoring was 61 hours. *Results:* There were 31 cases of pAF. The detection rate was 8% for both AIS and TIA patients. It occurred less often in lacunar infarcts (3%) compared to nonlacunar infarcts (10%) ($P = .047$). The detection rates in cryptogenic infarcts (10%) and infarcts of known causes (7%) were not significantly different ($P = .224$). The predictors of pAF according to logistic regression were hemorrhagic conversion ($P = .006$), scattered infarcts ($P = .007$), radiological cardiomegaly ($P = .007$), occlusion of symptomatic artery ($P = .023$), and older age ($P < .001$). *Conclusions:* pAF occurred in 8% of AIS and TIA in a hospitalized cohort of Asian patients. All patients without known atrial fibrillation should undergo CEM for at least 3 days during hospitalization and priority given to patients with predictors of pAF in centers with resource constraints. **Key Words:** Stroke— transient ischemic attack—ECG—atrial fibrillation—Asian.
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Systematic reviews and meta-analysis of studies from the West have shown that paroxysmal atrial fibrillation (pAF) occurs in 3.8% to 14% of acute ischemic stroke (AIS) patients.[1,2] pAF-related strokes are usually larger and associated with higher mortality.[3-6] The risk of stroke is similar for pAF and sustained AF.[7] Therefore, it is important to detect AF and pAF because anticoagulation is effective in preventing recurrent stroke.[8,9] However, there are scanty data on pAF from Asia despite it having nearly two-thirds of the world's population and different subtypes of stroke from the West.[10] Furthermore, the optimum duration of continuous electrocardiographic (ECG) monitoring (CEM) during hospitalization for AIS is unknown.[11] The American Heart Association/American Stroke Association recommends CEM for at least the first 24 hours after stroke.[12] Knowledge of occurrence of pAF among different subtypes of infarct and predictors of pAF will help optimize and

prioritize CEM as well as improve cost-effectiveness. Detection of pAF is challenging because of its transient occurrence and silent nature. It has been shown that inpatient CEM using telemetry equipped with automatic AF detection software is as good as ECG Holter in detecting pAF.[13] We analyzed a prospectively collected audit dataset on CEM in hospitalized patients in Singapore with AIS and transient ischemic attack (TIA) without known AF to determine the detection rate and predictors of pAF.

Methods

A prospective audit was conducted from July 2012 to February 2013 on patients with AIS and TIA who underwent CEM in the acute stroke unit (ASU) of a large tertiary hospital. All the patients were managed according to the ASU protocol, and the data were collected prospectively. Patients who did not have AF based on history and admission ECG, who had no contraindications to long-term anticoagulation, and who did not require anticoagulation for other reasons underwent CEM. The ASU protocol specifies CEM for at least 3 days, unless the patient is for early transfer or discharge. Some ASU teams, which are rotated monthly, monitored the patients for a longer duration. CEM was performed using GE Medical Systems Information Technologies (GE) ApexPro telemetry system with central monitoring station equipped with automatic AF detection software (Marquette EK-Pro arrhythmia analysis algorithm). CEM was stopped once AF greater than 30 seconds in duration was detected and confirmed by ASU medical staff who were all certified in advanced cardiac life support. All patients underwent magnetic resonance imaging (MRI)/magnetic resonance angiography (MRA) brain (stroke protocol) except for 1 TIA patient who had computed tomography brain. Lacunar infarct was defined as a small infarct less than 15 mm in diameter at the subcortical or brainstem region.[14] Cryptogenic infarct was diagnosed if the cause of the stroke was unclear after MRI/MRA brain (stroke protocol), duplex Doppler carotid ultrasound, transthoracic echocardiography, ECG, chest X-ray, hemogram, erythrocyte sedimentation rate, as well as screening tests for common immune disorders, thrombophilic states, homocysteine, and syphilis. The analysis of the prospectively collected audit dataset was approved by the Institutional Review Board (IRB) of National Healthcare Group in Singapore with waiver of informed consent.

Univariate tests were applied for comparing characteristics and clinical parameters of patients between pAF-positive and pAF-negative groups. Nominal data were compared using chi-square or Fisher's exact tests. Numerical data were compared using t test or Mann–Whitney U test. Multiple logistic regression was applied for identifying significant predictors for pAF positive. Only significant variables ($P \le .2$) in univariate tests with at least 10 outcome events were included in the logistic regression. Kaplan–Meier analysis was applied to estimate the cumulative detection rate of pAF among all the patients. All statistical analyses were performed using PASW Statistics (version 18).

Results

The demographic, clinical, and imaging characteristics of the audit cohort are summarized in Table 1. There were a total of 395 patients, of whom 370 (94%) had AIS. The median age was 66 years (IQR, 56-76), and 38% of patients were women. Chinese comprised 79%, Malay 10%, Indian 7%, and others 4%.

There were 31 cases of pAF. The median duration of CEM was 61 hours (IQR, 35-98). The detection rate of pAF was 8% for both AIS and TIA patients. The cumulative detection rate of pAF was about 9.1% (SE = 1.7%) at day 7 and 15.0% (SE = 6.1%) at day 28 of monitoring by Kaplan–Meier analysis (Fig 1). The cumulative detection rate at day 7 is a useful reference point for comparison as most ASU discharged their patients usually within 7 days.[15] Time interval from admission to starting CEM (median, 16 hours; IQR, 7-35) did not affect the rate of detection of pAF ($P = .215$). Among all the pAF detected, 60% were detected by the first day of monitoring, 80% by the second day, and 94% by the third day.

pAF occurred less often in lacunar infarcts (3%) compared to nonlacunar infarcts (10%) (odds ratio [OR], .3; 95% confidence interval [CI], .1-1.0; $P = .047$). The detection rate of pAF in cryptogenic infarcts (10%) was not significantly higher than that in infarcts of known causes (7%) (OR, 1.6; 95% CI, .8-3.3; $P = .224$).

After adjusting for confounding factors by multiple logistic regression, the significant predictors of pAF were hemorrhagic conversion (OR, 3.8; 95% CI, 1.5-10; $P = .006$), scattered infarcts (OR, 3.6; 95% CI, 1.4-9; $P = .007$), radiological cardiomegaly (OR, 3.5; 95% CI, 1.4-8.4; $P = .007$), occlusion of symptomatic artery (OR, 3.0; 95% CI, 1.2-7.6; $P = .023$), and older age (OR, 1.1; 95% CI, 1.1-1.2; $P < .001$) (Table 2). Among the scattered infarcts in 12 patients with pAF, 5 (42%) were located in 1 anterior circulation territory, 3 (25%) in bilateral anterior circulation, 2 (17%) in unilateral anterior and posterior circulation, and 2 (17%) in bilateral posterior cerebral artery territory. Among 15 patients with pAF and radiological cardiomegaly, 12 (80%) had hypertension and none of them had heart failure. The symptomatic artery associated with pAF showed occlusion on MRA in 11 (38%) patients and greater than 50% stenosis associated with atherosclerosis in 5 (17%) patients. Many of the occlusions showed an abrupt cutoff pattern in an otherwise normal-appearing artery (Fig 2). Patients with pAF were older (median, 78 years; IQR, 71-84) compared to those without pAF (median, 65 years; IQR, 56-76) ($P < .001$).