Atrial Fibrillation Predictors on Mobile Cardiac Telemetry in Cryptogenic Ischemic Stroke

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Abstract

Background and Purpose: The objective of our study was to evaluate magnetic resonance imaging (MRI) and echocardiographic characteristics that would identify patients with cryptogenic ischemic stroke (IS) and transient ischemic attack (TIA) who subsequently developed paroxysmal atrial fibrillation (PAF) on mobile cardiac outpatient telemetry (MCOT). **Methods:** All patients with cryptogenic IS or TIA seen at the Emory University Hospital and Emory University Hospital Midtown from January 1, 2009, to June 30, 2013, who underwent MCOT were included in this analysis. Location (cortical, high subcortical, or neither) of current and prior strokes on MRI and left atrial (LA) functional and anatomical echocardiographic parameters were evaluated to determine their association with subsequent detection of PAF. **Results:** Of 132 patients, 17 (13%) had evidence of newly diagnosed PAF on MCOT (mean duration of monitoring = 25 days). The presence (vs absence) of ≥ 1 cortical infarct on baseline MRI was a significant predictor of identifying PAF (odds ratio: 5.2, 95% confidence interval: 1.3-19; $P = .01$). On baseline echocardiography, patients who had PAF (vs non-PAF) had significantly higher mean LA diameters (4.2 vs 3.7 cm, $P = .03$) and lower tissue Doppler velocity (a' ; 5.5 vs 13.5 cm/s, $P = .03$). In receiver operating characteristic analysis, the ratio of LA volume index to the septal Doppler velocity ($LAVI/a'$) of >4.6 was associated with a higher likelihood of PAF. Combining MRI with echocardiographic variables did not improve the predictive ability beyond echocardiography alone. **Conclusion:** Although the presence of cortical-based infarcts on MRI in patients with cryptogenic IS or TIA increases the likelihood of detecting PAF on MCOT, LA functional and anatomic parameters alone best predicted which patients subsequently had PAF.

Keywords

atrial fibrillation, magnetic resonance imaging, echocardiography, atrial function, stroke

Background

Paroxysmal atrial fibrillation (PAF) is associated with a 5-fold increased risk of stroke and embolism.¹ In 25% to 30% of ischemic stroke (IS), the mechanism cannot be determined despite extensive evaluation; however, previous studies have suggested that some patients with cryptogenic stroke or TIA may have clinically undetected asymptomatic PAF. Published data using 21- or 30-day cardiac monitoring (event recorders or mobile telemetry) have shown previously undetected asymptomatic PAF in 5% to 20% of patients with cryptogenic stroke.²⁻⁵ The objective of our study was to evaluate MRI and echocardiographic characteristics that would identify patients with cryptogenic IS and TIA who subsequently developed PAF on mobile cardiac outpatient telemetry (MCOT).

Methods

We retrospectively performed a chart review of all patients with cryptogenic stroke or TIA who underwent MCOT and brain MRI at The Emory University Hospital and Emory University Hospital Midtown from January 1, 2009, through June 30, 2013. We defined cryptogenic stroke according to trial of ORG 10172 in acute stroke treatment (TOAST) criteria as a

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Figure 1. Cortical lesion (A) and high subcortical lesions (B) on MRI. MRI indicates magnetic resonance imaging.

nonlacunar brain infarction on neuroimaging with no cause identified despite extensive workup (noninvasive angiography, echocardiography, electrocardiography, inpatient telemetry, hematologic, and inflammatory tests).^{6,7} Transient ischemic attack was defined as a transient episode of neurological dysfunction caused by focal brain, spinal cord, or retinal ischemia, without acute infarction and with no cause identified.⁸ Baseline patient and clinical characteristics were obtained through chart review. A waiver of the informed consent was granted by the institutional review board that approved this study.

Brain MRIs were evaluated by a neuroradiologist and a vascular neurologist for evidence of recent or chronic infarcts as seen on diffusion-weighted imaging (DWI) and T2-weighted imaging sequences. These infarcts were classified as cortical lesions (CLs) if ≥ 1 was present, high subcortical (HS) lesions, defined as lesions less than 5 mm beneath the cortex without any cortical involvement, or none if the MRI did not show either of these lesions (Figure 1).

We evaluated the following left atrial (LA) echocardiographic parameters obtained by transthoracic echocardiography (TTE): left atrial diameter (LAD), late diastolic Doppler velocity (A), tissue Doppler velocity (a'), left atrial volume index (LAVI), Interventricular Septal thickness in Late diastole (IVSD), and the ratios LAVI/A and LAVI/a'.⁹

All MCOTs were reviewed by a cardiologist to determine whether PAF was present. Atrial fibrillation was defined as an episode of irregular heart rhythm, without detectable P waves, lasting more than 30 seconds.

Statistical Analysis

The χ^2 test was used to compare proportions of patients with PAF in the different MRI subgroups. We used unpaired 2-tailed *t* test to compare the differences in the means of the echocardiographic data between the PAF and non-PAF subgroups. Logistic regression was used to obtain the corresponding adjusted odds ratios with the outcome variable of PAF. Areas under the curve (AUCs), sensitivity, and

Table 1. Baseline Characteristics of the Cohort.

Variable	PAF (n = 17)	Non-PAF (n = 115)	P Value ^a
Age, mean (SD)	74 (14.7)	69 (10.9)	.15
Female, n (%)	11 (64.7)	55 (47.8)	.21
Caucasian, n (%)	13 (76.5)	76 (66)	.16
Diabetes mellitus, n (%)	28 (25.5)	15 (17.7)	.49
Hypertension, n(%)	15 (88.24)	85 (73.9)	.12
Dyslipidemia, n (%)	12 (70.6)	73 (63.5)	.57
Cryptogenic stroke, n (%)	13 (76.5)	82 (71.3)	.78

Abbreviations: PAF, paroxysmal atrial fibrillation; SD, standard deviation.

^aTwo-sample *t* test was used to compare continuous variables. χ^2 was used to compare proportions between 2 groups. *P* < .05 was considered statistically significant.

Table 2. Absolute Numbers and Percentages of PAF Found by Stroke Location.^a

MRI Findings	Atrial Fibrillation	
	No, n (%)	Yes, n (%)
Cortical	52 (78.79)	14 (21.21)
High subcortical	47 (95.92)	2 (4.08)
None	16 (94.12)	1 (5.88)

Abbreviation: MRI, magnetic resonance imaging.

^aA total of 28 patients were lost to follow-up.

specificity were produced for each of the echocardiographic variables to evaluate their sensitivity and specificity for detecting PAF.

Results

During the study period, 132 patients met our inclusion criteria. Mean age was 70 years $\pm$ 14.4, 50% were female, and 72% had a cryptogenic IS (Table 1).

A total of 17 (13%) patients had newly diagnosed PAF detected on MCOT (mean duration of monitoring was 25 days). Baseline demographic and clinical characteristics of patients found to have PAF versus those who did not have PAF were similar, including mean age, sex, race, history of diabetes, hypertension, dyslipidemia, history of cryptogenic stroke (vs TIA), and duration of monitoring (Table 1).

Patients with CL present on their MRI were significantly more likely to have PAF detected on MCOT than those patients with HS lesions or no lesions after adjusting for age, sex, race, history of diabetes, hypertension, and dyslipidemia (odds ratio: 5.5; 95% confidence interval: 1.4-20.9). Of the patients with cortical MRI findings, 21.21% had PAF on MCOT. Of those with HS lesions, only 4.08% were found to have PAF. Similarly, 5.88% of patients with no MRI lesions had PAF (Table 2; Figure 2).

Figure 2. Distribution of patients with and without paroxysmal atrial fibrillation among the different subclasses of MRI findings. C indicates cortical; HS, high subcortical; MRI, magnetic resonance imaging.

Table 3. Echocardiographic Variables Compared Between Patients With and Without Paroxysmal Atrial Fibrillation Detected on Cardiac Outpatient Telemetry.

Variable	n	PAF	Non-PAF	P Value
LA diameter cm, mean	76	4.2	3.7	.03
a' (septal, cm/s), mean	29	5.5	13.5	.03
a' (lateral, cm/s), mean	82	11.3	12.5	.6
A (cm/s), mean	83	78.2	83.5	.6
LAVI (mL/m ²), mean	68	37.5	29.2	.07
LAVI/A, mean	66	0.67	0.37	.006
LAVI/a' (lateral), mean	65	4.6	2.8	.06
LAVI/a' (Septal), mean	26	8.7	2.2	.0001
IVSD, mean	104	1.3	1.1	0.03

Abbreviations: a', Tissue Doppler velocity; A, late diastolic Doppler velocity; IVSD, Interventricular Septal thickness in Late diastole; LA, left atrium; LAVI, left atrial volume index.

The mean values of the LAD, a' (septal), LAVI/A, IVSD, and LAVI/a' significantly differed between the PAF and non-PAF groups (Table 3). Table 3 demonstrates the AUC for the echocardiographic variables in identifying patients with MCOT-detected PAF. Left atrial volume index to the septal Doppler velocity (septal) and a' septal velocities were found to have the highest AUC among the echocardiographic variables (0.98 and 0.93, respectively; Figure 3 and Table 4). The AUC, sensitivity, and specificity cutoffs did not change significantly when performed for the subgroup of patients with CL on MRI.

In our sample, 17.5% of the data were not available for interpretations due to artifact and loss to follow-up. The range of total days of monitoring was 4 to 30 days with a median of 29 days and with the vast majority of the patient being monitored for more than 25 days. The range of days to initiate monitoring from discharge was 3 to 557 days, with a median of 30 days; however, this information was only available in 43% of the time. Although the age was not statistically different between the patients with atrial fibrillation and the nonatrial fibrillation patients, there was a tendency of increase in Paroxysmal atrial fibrillation (PAFIB) by age, with the highest incidence for decade 71 to 80 years old (7 patients), followed by 81 to 90 years old (4 patients).

Discussion

We found that baseline factors on MRI and echocardiography could predict which patients with cryptogenic stroke or TIA undergoing outpatient cardiac telemetry were found to have PAF. Based on MRI DWI and T2 sequences, the presence of a cortical-based infarct increased the likelihood of finding PAF more than 5-fold. About 21% of patients with CLs were found

Figure 3. A, a' (septal) ROC curve. B, LAVI/a' (septal) ROC curve. a' indicates tissue Doppler velocity; LAVI, left atrial volume index; ROC, receiver operating characteristic.

Table 4. Receiver Operator Curve Analysis of Echocardiographic Variables.

Variable	AUC	Value	Sensitivity (%)	Specificity (%)
LA diameter	0.67 (0.48-0.87)	3.75	83	52
A	0.49 (0.25-0.74)	82.5	67	49
a' septal	0.93 (0.80-0.99)	8.5	99	85
a' lateral	0.52 (0.29-0.76)	13.5	71	32
LAVI	0.7 (0.52-0.88)	31.5	83	68
LAVI/A	0.61 (0.37-0.86)	0.33	83	45
LAVI/a' (lateral)	0.67 (0.45-0.9)	0.67	83	2.3
83	59			
LAVI/a' (septal)	0.98 (0.92-0.99)	4.6	99	96
IVSD	0.71 (0.56-0.86)	1.1	89%	48%

Abbreviations: a', tissue Doppler velocity; A, late diastolic Doppler velocity; AUC, area under curve; IVSD, Interventricular Septal thickness in Late diastole; LA, left atrium; LAVI, left atrial volume index.

to have PAF on MCOT. This is probably related to the embolic nature of IS in patients with PAF.

Among echocardiographic parameters, we found that the ratio of LAVI to the tissue Doppler velocity during diastole of the LA using a cutoff of 4.6 (LAVI/a') had a tendency to be associated with a higher likelihood of PAF ($P = .06$). This finding is limited by the small number of patients who met this cutoff. Larger sample size study is required to better study this value.

Our study was limited by its retrospective design which inherently carries the possibility of selection bias as data collection started with patients who underwent MCOT and MRI of the brain. Further, we had to exclude patients who only underwent transesophageal echocardiography (TEE) and not TTE, given that TEE is unable to measure all of the LA parameters we evaluated in this analysis. Since our echocardiographic data were obtained retrospectively, not all patients had both septal and lateral a' measurements available for analysis, so we did not calculate an average a' value, as was done in prior research.⁹ Our outcomes are similar to the Find-AF cohort, which identified the LAVI/a' ratio as a predictor for patients with cryptogenic stroke who would be most likely to have atrial fibrillation identified on 7-day Holter monitoring.⁹ Our study used extended MCOT monitoring with a mean of 25 days to diagnose incidence PAF, although the percentage of patients diagnosed with PAF was similar in both studies (13%). Longer periods of monitoring could have potentially identified PAF in additional patients that the study yielded.

The LAVI/a' ratio has thus been proposed as a useful parameter to identify both PAF and advanced diastolic dysfunction.^{9,10} The pathophysiology behind the association between this ratio and atrial fibrillation is probably related to the fact that it reflects both structural remodeling and functional deterioration of the LA. Parameters of functional and structural remodeling, including increased atrial size, have

been associated with atrial fibrillation.¹¹ This may explain the value of the LAVI/a' ratio since it reflects both the anatomic predisposition to atrial fibrillation, as indicated by an increased LA size, and a functional predisposition, as indicated by a decrease in LA contractility. A larger LAVI/a' ratio suggests a larger LA size, decreased LA contractility, or some combination of the two and thus may be a more robust predictor of the development of atrial fibrillation than either variable alone.

Further studies are needed to determine whether this combination of findings is robust enough to affect the yield of MCOT and potentially the need for it to be done.

In conclusion, cortical-based infarcts seen on MRI DWI and Fluid Attenuation Inversion Recovery (FLAIR) sequences and baseline echocardiographic variables may help to predict patients with cryptogenic IS or TIA who are found to have PAF on cardiac outpatient telemetry. A prospective validation study is needed to evaluate our optimal cutoff values for echocardiographic data.

Declaration of Conflicting Interests

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