A Simple Score That Predicts Paroxysmal Atrial Fibrillation on Outpatient Cardiac Monitoring after Embolic Stroke of Unknown Source

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Background: Occult paroxysmal atrial fibrillation (AF) is detected in 16%-30% of patients with embolic stroke of unknown source (ESUS). The identification of AF predictors on outpatient cardiac monitoring can help guide clinicians decide on a duration or method of cardiac monitoring after ESUS. *Methods:* We included all patients with ESUS who underwent an inpatient diagnostic evaluation and outpatient cardiac monitoring between January 1, 2013, and December 31, 2016. Patients were divided into 2 groups based on detection of AF or atrial flutter during monitoring. We compared demographic data, clinical risk factors, and cardiac biomarkers between the 2 groups. Multivariable logistic regression was used to determine predictors of AF. *Results:* We identified 296 consecutive patients during the study period; 38 (12.8%) patients had AF detected on outpatient cardiac monitoring. In a multivariable regression analysis, advanced age (ages 65-74: odds ratio [OR] 2.36, 95% confidence interval [CI] .85-6.52; ages 75 or older: OR 4.08, 95% CI 1.58-10.52) and moderate-to-severe left atrial enlargement (OR 4.66, 95% CI 1.79-12.12) were predictors of AF on outpatient monitoring. We developed the Brown ESUS-AF score: age (65-74 years: 1 point, 75 years or older: 2 points) and left atrial enlargement (moderate or severe: 2 points) with good prediction of AF (area under the curve .725) and was internally validated using bootstrapping. The percentage of patients with AF detected in each score category were as follows: 0: 4.2%; 1: 14.8%; 2: 20.8%; 3: 22.2%; 4: 55.6%. *Conclusions:* The Brown ESUS-AF score predicts AF on prolonged outpatient monitoring after ESUS. More studies are needed to externally validate our findings. **Key Words:** Atrial fibrillation—ischemic stroke—ESUS—cardioembolic stroke—cardiac monitoring.

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Introduction

Stroke is the fifth leading cause of death in the United States and can cause significant morbidity for patients who survive.[1] In approximately one third of ischemic strokes, a cause cannot be determined before discharge, despite extensive workup, and the stroke is classified as cryptogenic.[2,3] Up to 30% of cryptogenic strokes are found to be due to occult paroxysmal atrial fibrillation (AF), with a majority of these patients being over the age of 65.[4-6] Embolic stroke of unknown source (ESUS) is a subcategory of cryptogenic stroke that selects for patients specifically with nonlacunar infarcts in the absence of an apparent cause such as known atherosclerosis or major cardioembolic source.[7] Early identification of ESUS tailors clinical evaluations toward uncovering embolic sources of stroke such as AF.

In the absence of an AF diagnosis or known hypercoagulable state, patients with ischemic stroke are usually treated initially with antiplatelet agents for secondary stroke prevention.[8] Thus, monitoring for AF using outpatient cardiac monitoring after ESUS is of significant clinical importance. Although current guidelines from the American Heart Association require a minimum of 24 hours of continuous telemetry after cryptogenic stroke,[8] prolonged cardiac monitoring leads to higher detection rates of AF.[4-6]

Prior studies have investigated predictors of AF after cryptogenic stroke.[9-14] Clinical and radiographic variables that have been associated with increased risk of AF after cryptogenic stroke include older age and prior embolic infarct.[9-13] Measurements of left atrial volume index and left atrial diameter (LAD) by echocardiogram have both been found to be predictors of AF after stroke in patients without a history of prior AF; however, these patients were only monitored for 3 weeks.[9,12] Electrocardiographic evidence of premature atrial complex has also been suggested as a predictor of AF in patients with cryptogenic stroke.[12,14] However, none of these studies evaluated predictors of AF risk in a strictly ESUS population. For instance, the Cryptogenic Stroke and Underlying Atrial Fibrillation (CRYSTAL AF) trial excluded patients with left atrial appendage stasis who would otherwise be included in the ESUS category.[4] In this study, we aim to identify predictors of AF in a real-world ESUS registry.

Methods

Study Population

Institutional review board approval was obtained to analyze data from our prospective ischemic stroke inpatient database. We included patients 18 years or older admitted to our comprehensive stroke center and discharged with a diagnosis of ischemic stroke between January 1, 2013, and December 31, 2016. All patients admitted to our institution with a diagnosis of ischemic stroke underwent a standard inpatient diagnostic evaluation, including computed tomography (CT) and magnetic resonance imaging (MRI) of the brain, intracranial and extracranial vascular imaging, transthoracic echocardiography, 24-hour continuous telemetry monitoring, and, in some cases, a hypercoagulability panel and a transesophageal echocardiogram.

Stroke subtype was determined using the ESUS consensus criteria[7] by the treating vascular neurologist and adjudicated independently by another vascular neurologist, and, in case of disagreement, a discussion was held between the two and a consensus was achieved. We then limited the study sample to those with a discharge diagnosis of ESUS stroke subtype and excluded patients who did not receive prolonged outpatient cardiac monitoring 30-day cardiac monitor or implantable cardiac monitor (ICM).

Cardiac Monitoring Protocol

Cardiac monitoring is ordered on all patients with a discharge diagnosis of ESUS. Our protocol is to start with a 30-day cardiac monitor followed by an ICM if the 30-day monitor does not show AF, unless patients prefer to go with ICM first. All auto-triggered and patient-triggered events on cardiac monitoring were reviewed by a cardiologist specialized in electrophysiology for the presence of AF or atrial flutter. If AF or atrial flutter of 30 seconds or more duration is found, then patients are typically started on anticoagulation.

Study Variables

Demographic and Clinical Variables

We collected demographic data (age and sex), clinical risk factors (history of hypertension, history of diabetes mellitus, history of hyperlipidemia, history of coronary artery disease, history of stroke, current smoking status, history of prior superficial infarct), and National Institute of Health Stroke Scale (NIHSS) score on admission.

Cardiac Variables

We collected PR interval on admission electrocardiogram and LAD as determined by transthoracic echocardiography. We used LAD to further classify patients by degree of left atrial enlargement (LAE)—normal, mild, moderate, severe—using widely accepted clinical cutoffs.[15]

Outcome Variable

The outcome was detection of previously undiagnosed AF or atrial flutter of 30 seconds or more in duration on outpatient cardiac monitoring. Comprehensive chart review of each patient since discharge was performed to determine which method of prolonged cardiac monitoring was performed and to determine the outcome. Patients