

Intermittent Atrial Fibrillation May Account for a Large Proportion of Otherwise Cryptogenic Stroke: A Study of 30-Day Cardiac Event Monitors

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Introduction: Despite extensive inpatient workup including telemetry monitoring, a significant proportion of stroke is classified as cryptogenic at hospital discharge. It is possible that a significant proportion of cryptogenic stroke is a result of intermittent atrial fibrillation (AF). Thirty-day cardiac event monitors (30-DEM) may increase the rate of AF detection compared with standard investigations that include a combination of electrocardiography, cardiac telemetry, and short-term Holter monitoring. *Methods:* Charts were reviewed of patients who were admitted to a university stroke center or who were evaluated in the outpatient clinic during a 9-month period to determine whether the cause of stroke was cryptogenic. As a matter of protocol, such patients typically underwent 30-DEM and the results of such monitoring were documented along with the duration of inpatient cardiac monitoring if relevant. *Results:* In all, 218 patients with a diagnosis of ischemic stroke or transient ischemic attack were identified. Of the strokes, 36 (16.5%) were classified as cryptogenic. Twenty patients with cryptogenic stroke or transient ischemic attack were evaluated with 30-DEM. Four (20%) were found to have AF, and all 4 patients were treated with warfarin. *Conclusion:* The 30-DEM changed the medical treatment of 20% of patients with otherwise cryptogenic stroke because of the detection of intermittent AF despite no detection of AF on electrocardiography and inpatient telemetry monitoring in the majority of patients. Further prospective studies of extended cardiac event monitors in the setting of cryptogenic stroke are warranted. **Key Words:** Stroke—cryptogenic—atrial fibrillation—cardiac event monitors.

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Cryptogenic stroke is defined by the TOAST classification as cases where the origin is unclear after extensive investigation or where multiple causes are possible and a definitive cause can not be determined.¹ This accounts for up to 30% of all ischemic strokes in most large series.²

Atrial fibrillation (AF) is often suspected in cases of cryptogenic stroke, and identification of AF is important because it necessitates a change in therapy from antiplatelet agents to a more effective prophylaxis with oral anticoagulation in almost all patients.³ Standard stroke investigations, including electrocardiography (ECG), cardiac telemetry monitoring, and echocardiograms have a low yield for identifying AF.⁴ Strategies that monitor patients with cryptogenic stroke and Holter monitors or ambulatory ECGs for up to 72 hours to identify AF have reported rates of approximately 1% to 6% and, therefore, the standard use of ambulatory ECG in patients with unexplained stroke is not recommended.⁵

Given the well-proven benefits of oral anticoagulation in both primary and secondary stroke prevention in patients with AF, the development of strategies that would

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increase the sensitivity of detecting paroxysmal AF would be useful. In this report we describe our preliminary experience with the use of ambulatory 30-day cardiac event monitors (30-DEM) in patients with cryptogenic stroke or transient ischemic attack (TIA).

Methods

We conducted a retrospective chart review of all patients admitted to a university stroke center or evaluated in the outpatient stroke clinic, from June 2006 to March 2007, who were diagnosed with a cryptogenic stroke or TIA. The study protocol was approved by our committee for human research.

Patient Identification

The administrative database was queried for a diagnosis of ischemic stroke or TIA and the results were cross-referenced with referrals for 30-DEM to ensure capture of all patients. Charts were reviewed and clinical information was abstracted for patient baseline characteristics and details of the medical evaluation. Cryptogenic stroke or TIA was defined by the attending neurologist if a thorough workup did not identify a cause for the stroke. One investigator (L. E.) reviewed the cause of all strokes and TIAs, and two additional investigators (S. A. J. and W. S. S.) independent of each other confirmed all cryptogenic strokes. In cases where the diagnosis of cryptogenic stroke was not agreed on, cases were adjudicated by group consensus. All patients underwent investigation for stroke origin with a standard set of investigations. The chart was reviewed to confirm that a complete workup had been completed to exclude other causes of stroke including: (1) verifying absence of a history of AF; (2) normal inpatient cardiac telemetry monitoring result; (3) echocardiogram demonstrated a cause of stroke/TIA that would require anticoagulation such as intracardiac thrombus or severe mitral regurgitation; (4) vascular imaging of the cervical and intracranial circulation to rule out large-vessel stenosis responsible for the ischemic event; and (5) normal hypercoagulability profile when clinically indicated.

Echocardiogram findings were defined as normal when all of the following criteria were met: (1) normal ejection fraction; (2) absence of severe atrial enlargement; (3) no intracardiac masses, vegetations, or thrombi; (4) normal valvular function; (5) no prosthetic valve requiring anticoagulation; (6) no right-to-left shunt demonstrated on agitated saline injection; and (7) absence of patent foramen ovale and/or atrial septal defect.

Event Monitors

Two models of 30-day event monitors were used: the AFIB Dual Alert (PDS Heart, West Palm Beach, FL) and LifeStar AF Express 3X (LifeWatch, Buffalo Grove, IL).

These systems are worn around the neck or on the belt at all times for 30 days except while bathing, with 4 leads positioned on the precordium. These devices are both programmed to automatically detect R-R interval irregularities that may represent malignant arrhythmias and transmit these two-channel recordings to a central monitoring site indicating the rhythm and the time of the event. These alerts are subsequently forwarded in real time to the ordering physician. Patients can also activate the device to record and transmit an event if they have any symptoms. The ordering physician and a cardiologist reviewed any event transmission within 24 hours and a cardiologist reviewed the entire record on completion of the 30-day study period.

Statistical Analysis

Baseline characteristics of patients with cryptogenic stroke who received a full workup and 30-DEM were compared with patients with cryptogenic stroke not referred for 30-DEM with the Fisher exact test for dichotomous variables and the Wilcoxon rank sum test for continuous variables.

Results

A total of 218 patients were included in the study. In all, 37 (17.0%) patients had TIA and 182 (83.0%) patients had an ischemic stroke. A total of 36 (16.5%) patients were classified as having a cryptogenic stroke or TIA, 173 (79.4%) had a defined cause after a complete workup, and 9 (4.1%) had an incomplete evaluation thus a determination of origin was not possible (Fig 1). Reasons for incomplete workup included change of goals of care to comfort measures only (3 patients), two patients were deemed not suitable for anticoagulation, one patient was transferred to another acute care hospital, and 3 patients in whom it was unclear why the workup was incomplete. New AF as the cause of stroke was diagnosed in 12 (5.5%) patients, 9 (4.1%) at the time of admission in the emergency department and 3 (1.4%) within 48 hours of admission using standard telemetry.

Of the 36 patients with cryptogenic stroke, 21 were referred and completed the 30-DEM (one of these patients did not have an echocardiogram). The baseline characteristics of the remaining 20 patients with cryptogenic stroke are shown in Table 1. There were no significant differences in the baseline characteristics of patients with cryptogenic stroke when comparing those with a complete workup and 30-DEM versus those with either an incomplete evaluation or those not referred for 30-DEM.

In the 20 patients who completed the 30-DEM and had a complete evaluation, 17 had no identifiable cause of stroke or TIA whereas 3 had possible cardioembolic sources with an additional separate cause identified (the first with a severely enlarged left atrium with suggestion of cardiac embolic source and >60% common carotid stenosis, another

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