Cardiac Monitoring for Atrial Fibrillation in Cryptogenic Stroke

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KEYWORDS

• Stroke • Atrial fibrillation • Cardiac monitoring

KEY POINTS

- Despite an extensive initial evaluation, the cause of up to a third of ischemic strokes remains undetermined.
- New atrial fibrillation (AF) detection in patients with cryptogenic stroke is critical because it warrants anticoagulation for the secondary prevention of stroke.
- Observational studies and prospective randomized controlled trials illustrate that a substantial proportion of patients with cryptogenic stroke have AF detected by post-stroke cardiac monitoring.
- Monitoring for more extended periods of time increases the proportion of patients in whom AF is detected. Insertable cardiac monitors provide the highest yields of AF detection.
- Based on the current evidence, prolonged monitoring for AF in patients with cryptogenic stroke beyond the guideline-recommended 30 days may be beneficial.

BACKGROUND

Stroke is among the most feared adverse events in all of medicine. Annually, more than 600,000 cases of ischemic stroke are reported in the United States.[1] For people who experience ischemic stroke, morbidity and mortality have been estimated at 70% to 80%.[2,3] In fact, stroke is the leading cause of long-term disability and is responsible for $36.5 billion per year in health care costs.[4] Accurate determination of stroke cause has a substantial impact on secondary prevention therapies. Therefore, a comprehensive diagnostic evaluation is recommended, which includes but is not limited to brain imaging, vascular imaging, tests of hypercoagulability, and cardiac evaluation to assess for cardiac sources of emboli.[1,5]

Despite a complete diagnostic evaluation, a definitive cause cannot be identified for approximate one-third of ischemic strokes. These strokes are referred to as being cryptogenic in origin, and antiplatelet therapy is the recommended treatment. The most commonly used classification scheme for stroke cause is the TOAST (Trial of ORG 10172 in Acute Stroke Treatment) classification. TOAST defines cryptogenic stroke as brain infarction that is not attributable to a cardiac source of embolism, large artery atherosclerosis, or small artery disease despite extensive vascular, cardiac, and serologic evaluation. Cryptogenic stroke is, therefore, a diagnosis of exclusion.[6]

Thromboembolism due to atrial fibrillation (AF) is an established cause of both ischemic stroke and

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transient ischemic attack (TIA). Although first described in patients with mitral stenosis, the Framingham study conclusively demonstrated a 5-fold increased risk of stroke even in patients with nonvalvular AF.[7] Even though the association between AF and stroke is clear, the often paroxysmal and asymptomatic nature of AF has made the diagnosis challenging. Overall, about 40% of patients with AF are entirely asymptomatic; studies of patients with a known history of paroxysmal AF (PAF) demonstrate that 79% to 94% of AF episodes are asymptomatic.[8–11] Furthermore, the clustering and rarity of episodes over a short time frame has further complicated efforts at detection.[9–12] Despite these challenges, diagnosing AF in a survivor of ischemic stroke or TIA is of paramount importance as it potentially changes treatment from antiplatelet therapy to anticoagulation and by doing so may further reduce the risk of recurrent stroke.[13–15]

Anticoagulation following ischemic stroke is indicated only for those patients diagnosed with AF outside of some rare circumstances. Thus, an emerging component in managing patients after ischemic stroke has been the use of cardiac monitoring to assess for atrial arrhythmias after a comprehensive stroke workup has been negative and the event has been categorized as cryptogenic. Current guidelines recommend prolonged rhythm monitoring for approximately 30 days within 6 months of the index event in order to detect atrial fibrillation. This recommendation is a class IIA recommendation.[16] Importantly, data suggest that detection rates are likely to underestimate the total prevalence of AF with this strategy.[5] To date, the optimum duration of monitoring is unknown. This review discusses the various methods of monitoring for AF in patients with cryptogenic stroke with a focus on observational studies and prospective randomized controlled trials that have evaluated the use of external monitors and insertable cardiac monitors (ICMs) in this population.

OBSERVATIONAL STUDIES OF EXTERNAL MONITORS: INPATIENT MONITORING

Although the label of cryptogenic stroke is usually applied after a full workup of the stroke mechanism has been completed, observational studies that assessed cardiac monitoring in the inpatient setting laid the initial groundwork for continuous monitoring after discharge (**Table 1**).[17–35] Sulter and colleagues[17] evaluated the utility of stroke care monitoring units in the first 48 hours after a stroke. These units performed at least 48 hours of continuous inpatient heart rhythm monitoring as opposed to serial heart rate monitoring in the conventional monitoring group. The AF detection rate was 18.5% in the continuous monitoring group compared with 3.5% in the conventional monitoring group. Bansil and Karim[18] assessed 48 hours of cardiac monitoring in 150 consecutive patients who presented with stroke. The detection rate for new AF in the first 48 hours after stroke was 8%. More recently, Kallmünzer and colleagues[19] showed that among patients without AF on presenting electrocardiogram (ECG), new AF detection rates were 9.2% using telemetry monitoring. The median time to AF detection was 22 hours. Notably, in two-thirds of the 37 patients with a history of AF and no evidence of AF on presentation, AF was not detected during the inpatient monitoring period (median monitoring time of 75.5 hours). There is a concern that AF episodes on inpatient telemetry monitoring may go undetected or unnoticed. In a study of 133 consecutive patients admitted to a stroke unit for stroke or TIA, no AF episodes were detected on continuous telemetry over a mean observation time of 73.4 hours. However, simultaneous Holter monitors were placed on the same patients and demonstrated an actual AF incidence of 6% with a mean recording time of 29.8 hours.[36]

OBSERVATIONAL STUDIES OF EXTERNAL MONITORS: HOLTER MONITORING

In recognition that AF may go undetected or may not have occurred during continuous inpatient monitoring, observational studies have evaluated the utility of ambulatory monitoring after hospitalization for stroke. Holter monitoring for 24 hours after stroke has been shown to detect more AF compared with serial ECGs.[21] An observational study by Thakkar and Bagarhatta[25] reported an AF detection rate with 24-hour Holter monitoring of 5.8%. Studies on ambulatory monitoring have also suggested that AF detection rates were up to 6% after 72 hours of continuous ECG monitoring.[20] A multicenter trial was performed in 2013 and further supported the idea that 72-hour Holter monitoring was superior in detecting AF compared with 24-hour monitoring, with a 4.3% detection rate after 72 hours compared with a 2.6% with only 24 hours of monitoring.[24] The number needed to screen with 72 hours to make a new diagnoses of AF was 55 patients. Holter monitoring for a duration of 7 days was evaluated in 281 patients in the FIND-AF trial.[22] From the total cohort of patients, 224 patients had no history of AF on presentation and 12.5% of these patients had newly detected AF at 7 days. This detection rate was significantly higher than the 4.8%