The Utility of Extended Electrocardiographic Monitoring for Detecting Atrial Fibrillation in Cryptogenic Stroke in the African-American population

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Abstract

Introduction: Cryptogenic stroke comprises about 25% of all ischemic strokes. Depending on modality and duration of ECG monitoring, subclinical atrial fibrillation (AF) is detectable in 2.7-30% of cryptogenic stroke patients. Hypothesis: Extended ECG monitoring after cryptogenic stroke has not been studied in the African American (AA) population. This retrospective study aims to study the incidence and risk factors of subclinical AF in African Americans. Methods: We retrospectively reviewed 96 patients who received implantable loop recorders (ILR) for detecting subclinical atrial fibrillation after cryptogenic stroke. In the vast majority of patients, the ILR was implanted during index hospitalization. Binary univariate and multivariate analyses were performed to determine predictors for AF detection. Results: AF was detected in 29% of patients (28/96) at 1000 days. All AF that was detected was exquisitely paroxysmal and ranged in duration between 0.05-103 minutes (mean 8.4 minutes with SD= 22.1 minutes). Binary univariate analysis revealed the use of non-dihydropyridine calcium-channel blockers to be associated with decreased odds of AF detection. Multivariate analysis found coronary artery disease diagnosis to be associated with increased odds of AF detection. Fifty percent of the events in the AF group were detected within the first 36 days of loop recorder implantation. Conclusions: AF detection in our population occurs very early after index stroke and at significantly higher rates that reported before. Baseline characteristics have a poor predictive ability for the detection of AF. These findings emphasize the need for pre-discharge ILR implantation to improve AF detection in all patients with cryptogenic stroke.

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Introduction

Determining the presence of AF in patients with cryptogenic stroke (CIS) significantly impacts prognosis as anticoagulation in. these patients is superior to aspirin for the secondary prevention of stroke .[3] Multiples studies have evaluated if baseline clinical and epidemiological characteristics can predict the detection of AF on prolonged cardiac monitoring and allow to risk stratify patients. These have resulted in the development of new scores (HAVOC, Brown ESUS AF, etc.,) and the use of previous scores (CHADS, $CHADS_2$-VASc, etc.) as means of evaluation of patients after CIS, yet none of these methods have demonstrated enough discriminating capacity to be used reliably to differentiate in which patients AF will be detected.

Two trials (CRYSTAL AF and EMBRACE) have established the effectiveness of continued cardiac monitoring for the detection of AF, and laid foundation for extended cardiac monitoring to became standard of care for patients with cryptogenic stroke.[1,2]

Both of these studies have mainly enrolled patients of Caucasian descent (less than 4% Blacks). Two other studies included Chinese population.[4,5] As of now very little is known about effectiveness of monitoring and frequency as well as pattern of AF in AA patients with CIS.

Methods

This was a retrospective data analysis at SUNY Downstate Medical Center, an academic, tertiary care center that serves a largely African American and Afro-Caribbean population in Brooklyn, NY. Data was analyzed in patients that were admitted with an acute ischemic stroke that after standard evaluation by a stroke neurologist where not found to have a clear etiology for stroke and were denominated as cryptogenic stroke.

All patients received at least 24-hours of continuous telemetry monitoring that did not reveal the presence of AF and subsequently underwent implantable loop recorder (ILR) placement in standard left chest location. [6] Both Abbott and Medtronic ILR were implanted and programmed to AF duration detection of >30 sec and tachycardia detection > 130 bpm and manufactured specific setting allowing for "balanced" detection of AF. Patients were followed-up in the outpatient device clinic by in-person interrogations of ILR or remotely. Each event identified as AF was initially reviewed by experienced mid-level practitioner and verified by a senior electrophysiologist.

Descriptive statistics were collected for all variables. All continuous variables are provided with mean, standard deviations, and proportions as percentages. Means were compared using independent sample t-tests; and proportions were compared using Chi square analysis. Binary univariate and multivariate regression were performed to determine predictors for A-fib detection. All analysis was done using SPSS (IBM SPSS Statistics for Macintosh, Version 24.0. Armonk, NY) using a P-value of <0.05 for statistical significance. Kaplan Meier curve was created using Prism (Prism 8 for macOS, Version 8.4.2, San Diego, CA). Study design was approved by SUNY Downstate IRB.

Results

A total of 96 patients were analyzed who underwent cardiac loop recorder implantation during the period between 2014 and 2019 for an indication of cryptogenic stroke. Most of the patients were female 60.4%, mean age was 66.8±12.9 years and the group where atrial fibrillation was detected was slightly older (70.7±12.8 vs 65.2±12.7 years) although the difference was not statistically significant. Atrial fibrillation was detected in 28 of 96 patients (29%). Forty-eight percent of the events in the AF group were detected within the first 36 days of loop recorder implantation (Figure 1). All detected AF episodes were exquisitely paroxysmal in nature and ranged in duration between 0.05-103 minutes (mean 8.4±22.1 minutes). The mean time from implantation of the loop recorder to analysis was 20 ± 15.8 months. Baseline characteristics are illustrated in Table (1).

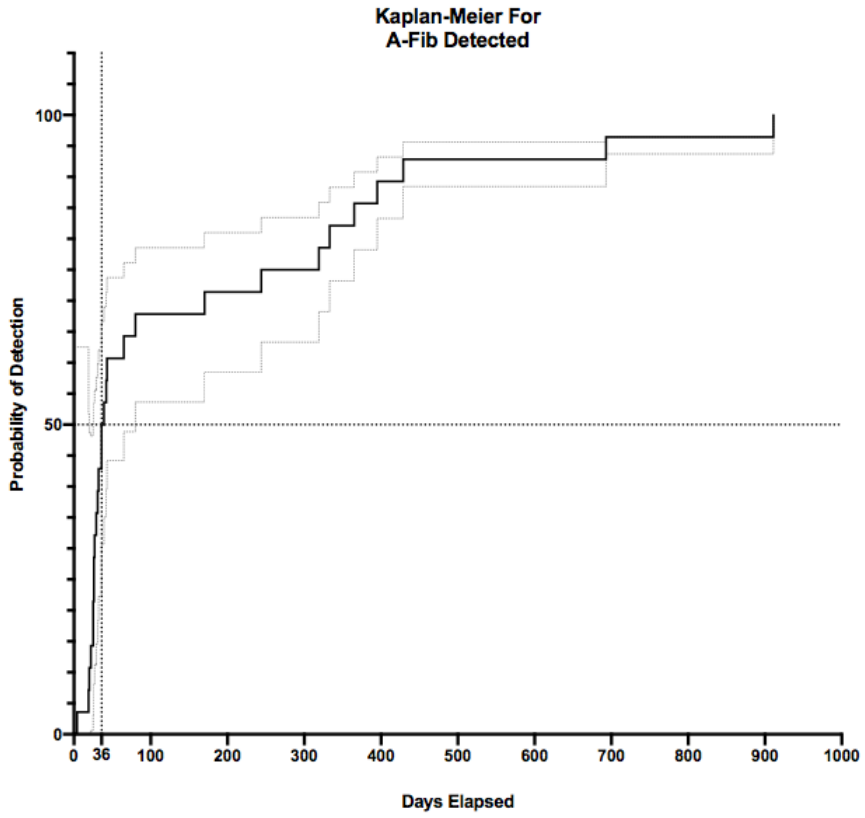

Figure 1. Time to detection of Atrial Fibrillation after implantable loop recorder.

Table 1: Baseline Characteristics of Patients

Sex	
BMI	
Stroke Location	
CVA Laterality	
Medical History	

Smoking

Risk Scores

Labs

Medications

Cardiac Findings

* p-values are not reported given small sample. P-values: continuous variables are compared using independent sample t-tes

The most frequent location of stroke was the right sided circulation, and the most commonly affected vessel was the middle cerebral artery (MCA), comprising 47.8% and 47.3% respectively of all strokes. Multiple acute ischemic lesions tended to be more frequent in those with AF detected vs without AF (16.0% vs 9.1% NS). Forty percent of the patients had a prior stroke, and there was a trend towards higher prevalence of AF (50% vs 38.2%, p=0.288). A history of coronary artery disease (CAD) was present in 29.6% of those with detected AF vs 14.7% in those without detected AF (p=0.094). There was no significant difference in CHA2DS2VASc and ASCVD 10-year risk between the two groups.

On univariate analysis (Table 2) age, cholesterol, not-being on a dihydropyridine calcium-channel blocker, and coronary artery disease were the only variables with a p value [?] 0.1, but none of the variables achieved a p value <0.05. A multivariate model including these variables demonstrated that being on CCB decreased the odds of having AF (OR 0.086, 95% CI: 0.016-0.464, p 0.004) and a history of coronary artery disease (OR 4.7, 95% CI: 1.266-17.659, p=0.021) and higher cholesterol levels (OR 1.013, 95% CI: 1.001-1.025, p=0.033) increased the odds of having AF in this population. Advancing age slightly increased the odds of detection but this result was not statistically significant (p=0.078).

Table 2. Univariate Predictors of AF Detection

	Predictors	OR	95%CI Lower	95%CI Upper	P Value
	Age	1.036	0.999	1.074	0.059
	Sex (reference Males)	1.570	0.621	3.968	0.341
	BMI	1.003	0.931	1.08	0.941
PMH	PMH				
	Prior Stroke	1.615	0.665	3.925	0.290
	HTN	0.581	0.151	2.24	0.430
	DM	0.644	0.266	1.561	0.330
	HLD	1.120	0.446	2.809	0.810
	CAD	2.442	0.842	7.079	0.100
	CHF	2.442	0.842	7.079	0.872
Medications	Medications				
	Aspirin	1.528	0.539	4.334	0.426
	Statin	0.475	0.180	1.257	0.134
	Beta Blockers	0.906	0.354	2.319	0.837
	ACE/ARB/ARNI	0.798	0.325	1.96	0.623
	Non-DHP CCB	0.28	0.087	0.901	**0.033**
Risk Scores	Risk Scores				
	CHA2DS2VASc	1.019	0.782	1.329	0.887
	ASCVD	1.019	0.992	1.046	0.174
Labs					
	LDL	1.008	0.997	1.018	0.142
	Cholesterol	1.008	0.999	1.017	0.099
	HDL	1.008	0.973	1.044	0.652
	HbA1c	0.965	0.768	1.211	0.757
	Troponin	0.004	0	197.713	0.316
	BNP	0.999	0.996	1.002	0.508
	eGFR	1.017	0.976	1.059	0.427
EKG/ ECHO Findings	EKG/ ECHO Findings				
	Ejection Fraction	0.978	0.932	1.027	0.372
	LA Size (mm)	1.022	0.942	1.108	0.606
	P wave duration (ms)	0.994	0.964	1.024	0.677
	P wave area (mV*ms)	0.589	0.278	1.25	0.168
	P wave terminal force (μV*ms)	1	1	1	0.399

Table 3. Multivariate Predictors of AF Detection on Loop Record

Predictors	Beta	95%CI Lower	95%CI Upper	P Value
Age	1.037	0.996	1.08	0.078
CCB (ref not on CCB)	0.086	0.016	0.464	0.004
Cholesterol	1.013	1.001	1.025	0.033
CAD (ref No CAD)	4.728	1.266	17.659	0.021

Discussion

Our findings indicate that in African American patients with cryptogenic stroke detection of AF occurs earlier and yet at similar rate that in other populations[1,7-9]. Brachmann et al, specifically found near identical detection rates in the ILR monitoring arm at 36 months (30% vs 29%), but detection occurred

later after implantation compared to our population (median time to detection = 8.4 months vs 37.5 days. Furthermore, the detection rate after 1 month was 3.7% in this study compared to around 14% in our population.[9] In the CRYSTAL-AF trial at 1 month out from implantation the detection rate was also lower that in our population with only about 4%. [1]

Given the retrospective nature and lack of control group we are not able to conclude with certainty that the detection of AF would occur earlier after implantation that in other ethnic groups. Our patients had more comorbidities as indicated by a higher $CHADS_2VASc$ than those in the CRYSTAL-AF trial (4.4 vs 3.0) and Brachmann et al. yet similar rates of AF detection suggesting a "protective effect".[1,9] African Americans appear to have an increased risk of developing stroke in the setting of AF independent of the relative higher prevalence of comorbidities in this population.[10]

Those with detected AF had a numerical older age, greater prevalence of prior stroke, and incidence of CAD but none of these results were statistically significant. This is likely related to insufficient power to detect a difference as multiple other studies have demonstrated a correlation between these variables and an increased detection rate of AF. [8,11] No electrocardiographic or echocardiographic parameters were associated with an increased detection rate in this group despite some parameters like PR interval prolongation, LA size and frequent premature atrial beats have been reported as predictors of AF detection in other studies. [8, 11, 12]

When a multivariate regression analysis was performed including variables that approached significance the presence of CAD, hyperlipidemia, age, and nonuse of calcium channel blockers demonstrated predictive capacity. It is uncertain though what mechanism may be involved but CCB are known to decrease aldosterone synthesis and that in turn might decrease the odds of developing AF. [13] The combination of these factors demonstrating significance might have been driven mainly by the combination of age and CAD which are well documented predictors of development of atrial fibrillation.[14]

In conclusion, it appears that extended electrocardiographic monitoring with an implantable loop recorder it as effective for the detection of AF in African Americans as in the general population, time to detection is shorter and baseline characteristics were unable to predict the detection of AF.

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