ORIGINAL ARTICLE

Atrial fibrillation in elderly patients with implantable loop recorders for unexplained syncope

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Abstract

Background: An implantable loop recorder (ILR) assists in the diagnosis of unexplained syncope and atrial fibrillation (AF). Both become prevalent with age. Limited data exist describing the incidence of AF as the diagnostic rhythm underlying syncope in the elderly. This study aims to report the incidence of AF in older adults with ILRs for unexplained syncope and identify clinical characteristics associated with AF in this population.

Methods: Retrospective observational study on patients with unexplained syncope seen in syncope clinics from two Canadian centers. Participants were ≥ 65 years old, without a history of AF, and received an ILR for unexplained syncope. Data were collected from patient's clinic charts. Arrhythmia diagnosis was based on ILR electrocardiogram reading during syncope (symptom–rhythm correlation). Fisher's exact test and the Student's *t* test were used to compare participants with and without AF.

Results: In our cohort of 222 patients, 124 were females and 98 were males. Mean age at implant was 80 ± 8 years. Arrhythmia was diagnosed in 98 patients (44.1%). Median time to diagnosis was 18 months. AF was diagnosed in 17 (7.7%) participants. There were fewer males in the AF group than the no AF group (11.8%, 46.8%, $p = 0.01$). Age, baseline EKG, and prevalence of hypertension, diabetes, stroke, or ischemic heart disease were not statistically different between patients with AF and without AF.

Conclusions: Atrial fibrillation was a common diagnostic rhythm in this cohort of adults, aged 65 and older, with ILRs for unexplained syncope. It was observed more frequently in females.

1 | INTRODUCTION

Syncope and atrial fibrillation (AF) are common clinical entities (Brignole, 2018; Burkowitz, Merzenich, Grassme, & Brüggengjürgen, 2016; Chen, Shen, Mahoney, Jacobsen, & Rodeheffer, 2006; Krahn, Klein, Yee, & Skanes, 2001). Syncope is a transient loss of consciousness caused by decreased cerebral blood flow (Brignole, 2018). AF is an irregularly irregular heart rhythm and is a risk factor for stroke, cardiovascular diseases, renal disease, and death (Odutayo et al., 2016). Syncope, particularly unexplained syncope (undiagnosed after thorough clinical evaluation

and diagnostic testing (Brignole, 2018)), and AF both become increasingly prevalent with age (Benjamin, 1994; Chen et al., 2006; Jansen et al., 2015; Roberto, Ronaldo, & Silvio, 2012). Thus, some elderly patients presenting with syncope may have concurrent AF.

Implantable loop recorders (ILRs) are small subcutaneous devices capable of long-term electrocardiogram monitoring of up to 3 years. They have emerged as important diagnostic tools for unexplained syncope as they can detect infrequent and intermittent arrhythmias such as AF (Brignole et al., 2009; Burkowitz et al., 2016; Krahn et al., 2001).

TABLE 1 Symptom-ILR rhythm diagnoses in unexplained syncope

Diagnoses	Number of patients	% (of total)
Atrial fibrillation	17	7.7
With a rapid ventricular rate ^a	10	
With a normal heart rate ^b	4	
With a conversion pause ^c	3	
Atrial flutter	3	1.4
No events identified	124	55.9
Asystole	8	3.6
AVNRT	3	1.4
Type 2 AV block, Mobitz II	3	1.4
Junctional bradycardia	2	0.9
Other bradyarrhythmia	2	0.9
Ventricular tachycardia	2	0.9
Ectopic pacemaker	1	0.5
Sinus bradycardia	1	0.5
Sinus tachycardia	1	0.5
Supraventricular tachycardia	1	0.5
Type 2 AV block, Mobitz I	1	0.5
Total number of patients	222	

Notes. AV: atrioventricular; AVNRT: atrioventricular nodal re-entry tachycardia; ILR: implantable loop recorder.

^aRapid ventricular rate defined as heart rate of >100 beats/min. ^bNormal heart rate defined as 60–100 beats/min. ^cConversion pause defined as a sinus pause for 3 s or greater following atrial fibrillation.

Atrial fibrillation is an uncommon cause of syncope (Jansen et al., 2015). However, multiple large cohort studies have shown an association between atrial fibrillation and syncope among the general and elderly population (Jansen et al., 2015; Ruwald et al., 2013). Several proposed pathways provide a pathophysiologic link between AF and syncope (Benjamin, 1994; Brignole et al., 1993; Jansen et al., 2015; Leitch, Klein, & Tee, 1991). AF is associated with an abnormal neural response, including carotid sinus hypersensitivity, increased vagal tone at the onset of tachycardia, and increased rates of orthostatic hypotension, all of which can lead to syncope (Brignole et al., 1993; Leitch et al., 1991; McNicholas, Tobin, O'Callaghan, & Kenny, 2017; Wong et al., 2011). This can be exacerbated by polypharmacy, as commonly encountered in older people (Ruwald et al., 2013).

To date, only three clinical studies have shown a link between AF and syncope in older patients (Jansen et al., (2015); McIntyre, Liebrecht, Daba, & Seifer, 2016; Ibrahim et al., 2017). As of yet, there has been no study dedicated to describing the rates of AF among older patients with ILRs for unexplained syncope. An ILR may establish a temporal relationship between AF and syncope. If AF is shown to be a common diagnostic rhythm in this population, then this may help promote further studies, particularly on the implications of

ILR-detected AF in stroke and anticoagulation for patients with unexplained syncope.

The primary aim of this study was to estimate the prevalence of AF as the diagnostic rhythm concurrent with syncope (symptom-rhythm correlation) among patients ≥65 years old who received ILRs for unexplained syncope. Our secondary aim was to identify characteristics that are associated with AF in this population.

2 | METHODS

This was a two-center, retrospective chart review of patients ≥65 years old from syncope clinics at two tertiary academic acute care facilities in Canada. Patients underwent ILR implantation for unexplained syncope between April 2005 and December 2016. All participants received comprehensive guideline-directed assessments and were deemed to have unexplained syncope prior to implantation (Brignole, 2018; Brignole et al., 2009). Patients with a prior history of AF and who had other indications for ILR implantation (e.g., palpitations, cryptogenic stroke) were excluded. Participant demographics and baseline clinical characteristics (including hypertension, ischemic heart disease, stroke, and diabetes) were obtained from clinic charts. The diagnosis of syncope was made based on symptom-rhythm correlation, defined as the ILR rhythm reading at the time of syncope or symptoms of pre-syncope (lightheadedness, dizziness, or feeling of fainting). All ILRs used (Medtronic™ Reveal LINQ, Plus, XT, DX, and St. Jude Medical™ DM2100) had manual patient activation capabilities and proprietary automatic AF detection algorithms. Symptom-rhythm diagnosis was made after a physician read the ILR ECG recordings and correlated these with the patient's symptom diary, patient device triggering during symptoms, and/or self-reported timing of symptoms at clinic visit. AF is defined as the primary arrhythmia diagnosis only when it is the rhythm recorded immediately before or during syncope or pre-syncope. AF is further subclassified as with rapid ventricular response (heart rate >100 beats/min), with normal ventricular response (heart rate at or between 60 and 100 beats/min) or with conversion pauses (sinus pause of greater than or equal to 3 s following atrial fibrillation). Data were collected at baseline and at follow-up appointments. We followed participants for up to 3 years or until the date of their ILR explant. We compared patients with and without AF using Fisher's exact test for categorical variables and the Student's *t* test for continuous variables.

3 | RESULTS

A total of 222 patients (124 females, 98 males) were included, with an average age of 80 ± 8 years. A diagnosis of cardiac arrhythmia was made in 98 patients (44.1%), based on symptom-rhythm correlation (i.e., cardiac arrhythmia during pre-syncope or syncope). The time from implantation to diagnosis of a cardiac arrhythmia based on symptom-rhythm correlation ranged from <1 month to over 3 years (median of 18 months). A diagnosis of AF through symptom-rhythm correlation was made in 17 (7.7%) patients. Atrial flutter was

TABLE 2 Characteristics of individuals found to have atrial fibrillation using symptom-ILR rhythm correlation

Age	Baseline ECG	ILR activation	Rhythm	Treatment
67	RBBB	Patient	AF RVR ^a	BB, dabigatran
70	NSR, LVH	Patient	AF with normal HR ^b	N/A
71	1° AVB	Automatic	AF with conversion pause ^c	PPM
75	NSR	Patient	AF RVR	BB, warfarin, PPM
75	1° AVB	Automatic	AF RVR	Warfarin, CCB
81	NSR	Patient	AF RVR	CCB
82	LBBB	Patient	AF RVR	None
82	LBBB	Automatic	AF with conversion pause	PPM
83	Sinus bradycardia	Automatic	AF RVR	BB
85	NSR	Automatic	AF RVR	Digoxin, warfarin
86	1° AVB	Patient	AF RVR	BB, warfarin
87	Sinus bradycardia	Patient	AF RVR	PPM
87	NSR	Patient	AF with normal HR	Warfarin
87	NSR	Patient	AF with conversion pause	BB, apixaban, PPM
88	1° AVB	Patient	AF	N/A
90	NSR	Automatic	AF RVR	Warfarin, BB
94	NSR	Patient	AF	N/A

Notes. 1°: first degree; AF: atrial fibrillation; AVB: atrioventricular block; AVNRT: atrioventricular nodal re-entry tachycardia; BB: beta blocker; CCB: calcium channel blocker; ILR: implantable loop recorder; LVH: left ventricular hypertrophy; N/A: not available; NSR: normal sinus rhythm; PPM: pacemaker.

^aRVR: rapid ventricular rate defined as a heart rate of >100 beats/min. ^bNormal HR: normal heart rate defined as a heart rate of 60–100 beats/min. ^cConversion pause: defined as a sinus pause for 3 s or greater following atrial fibrillation.

found in three (1.4%) patients (Table 1). Other arrhythmic diagnoses identified by symptom–rhythm correlation are identified in Table 1. When age was stratified, the incidence of AF increased with age (65–<75 years old: 1.4%, 75–<85 years old: 2.7%, ≥85 years old: 3.6%). AF was documented in three asymptomatic patients.

Of the participants with AF and symptom–rhythm correlation, 10 (58.8%) had rapid ventricular rates, while three (17%) had conversion pauses (Table 2). Eight were placed on anticoagulation, eight were started on rate-controlling medications, and four had pacemaker implantation (Table 2).

There were significantly fewer males (11.8%) in the AF group when compared to the no AF group (46.8%; Table 3). Age and the prevalence of hypertension, diabetes, stroke, and ischemic heart disease were not statistically different between the AF and the no AF group (Table 3).

4 | DISCUSSION

This retrospective, two-center observational study found AF to be a common diagnostic rhythm (7.7%) for syncope among patients

65 years and older who were implanted with ILRs for unexplained syncope. AF was the third most common arrhythmia associated with syncope in this cohort, following sinus pauses and complete heart block. Atrial flutter accounted for a further 1.4% of symptom–rhythm diagnoses for syncope in these elderly patients (Table 1). AF as a diagnosis for syncope was also shown to increase in incidence in this population when age was stratified.

Comparison of patients who had AF versus those with no AF revealed a significant difference in sex, with predominantly more females in the AF group. Other characteristics, which included baseline (preimplantation) EKGs, hypertension, diabetes, ischemic heart disease, and stroke, were not significantly different between patients with and without AF.

To the best of our knowledge, this is the first cohort study to examine the incidence of AF as the diagnosed arrhythmia for unexplained syncope in ILR patients 65 years and older. Although AF, in the absence of pauses, is not classically considered a common cause of syncope, it has received attention as of late, with results from the Irish Longitudinal Study on Ageing showing that adults aged 65–74 years old with self-reported syncope have twice-fold

TABLE 3 Baseline characteristics of syncope patients found to have atrial fibrillation compared to those in whom no atrial fibrillation was found

Characteristics	AF (n = 17 participants)	No AF (n = 205 participants)	p-value
Age (year $\pm$ SD)	82 $\pm$ 8	80 $\pm$ 8	0.24*
Male	2	96	<0.01**
Hypertension	14	153	0.57*
Diabetes	2	46	0.54*
IHD	6	70	1*
Stroke	2	31	1*
Baseline EKG			
NSR	11	81	0.07*
LVH	1	22	1*
Sinus bradycardia	2	34	0.75*
1° AVB	4	57	1*
LBBB	2	22	1*
RBBB	1	36	0.32*

Notes. 1°: first degree; AF: atrial fibrillation; AVB: atrioventricular block; IHD: ischemic heart disease; NSR: normal sinus rhythm; LVH: left ventricular hypertrophy; LBBB: left bundle branch block; RBBB: right bundle branch block; SD: standard deviation.

*Calculated using Student's t test for continuous variables. **Calculated using Fisher's exact test for categorical variables.

likelihood of having AF (Jansen et al., 2015). The results of this study support this finding.

This study is limited by its small sample size and retrospective design. Another limitation of this study is the different models of ILR used (i.e., different AF detection algorithms) as well as non-standardized device programming. It is also likely that we underestimated the incidence of AF in this population given that some patients might not have been able to activate their ILR during pre-syncope/syncope and/or recall symptoms for comparison with their ILR recordings. Given the known increased prevalence of cardiac and non-cardiac causes of syncope in older patients (Chen et al., 2006), it is also possible that some of the AF diagnosed in this study may be a bystander diagnosis (Wong et al., 2011), although establishing symptom-rhythm correlation for all our arrhythmia diagnoses and the ILRs' retrograde memory have protected against this effect. Previous decision analysis has shown that the benefits of stroke prevention generally outweigh the risk of anticoagulation in older AF patients with predisposition to falls and syncope (Man-Son-Hing & Laupaci, 2003). Thus, whether treatment of ILR-detected AF associated with syncope confers benefit, such as stroke reduction through anticoagulation, is an interesting avenue to be explored.

5 | CONCLUSION

In conclusion, this study shows that atrial fibrillation and atrial flutter were common diagnostic rhythms in our cohort of older patients

65 years and older with ILRs for unexplained syncope. Atrial fibrillation was observed more frequently in females. Further studies are needed to define the need for AF treatment and assessment of stroke risk in this population.

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