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Letters

RESEARCH LETTER

Long-Term, Implantable Event Monitoring of Patients With Wild-Type Transthyretin Cardiac Amyloidosis

A Pilot Study

Syncope is a challenging management dilemma in cardiac amyloidosis (CA). Although it may result from bradycardia or tachyarrhythmias leading to sudden cardiac death (SCD),[1] syncope can also reflect hypotension or autonomic neuropathy. A further challenge is that although ventricular arrhythmias (VAs) are prevalent in CA, their role in SCD in CA is controversial.[2] A previous study of implantable loop recorders (ILRs) in a small number of patients with amyloid light chain amyloidosis suggested that bradycardia leading to asystole is a more likely culprit than VA, at least in advanced CA.[3] Whether the mechanism of syncope and SCD differs in wild-type transthyretin (ATTR-wt) amyloidosis and amyloid light chain CA is unknown. Data on the prevalence of atrial fibrillation (AF), sinus node dysfunction or high-grade atrioventricular block in ATTR-wt CA, are also limited.[4]

ILRs have been used to determine arrhythmia burden in patients with unexplained syncope in other cardiovascular diseases.[5] Therefore, we proposed a pilot study to assess the utility of ILR in patients with ATTR-wt CA. Our aim was to monitor the occurrence of clinically actionable conduction system disease and arrhythmia burden.

The Mayo Clinic Institutional Review Board approved the study, and research written consent was obtained from all participants. A total of 24 patients with ATTR-wt CA (mean age 75 ± 5 years, 100% White men, and 83% receiving tafamidis therapy) were prospectively recruited and underwent monitoring with the Biotronik Biomonitor 3 ILR for 6 months. The diagnosis of ATTR-wt CA was confirmed by endomyocardial biopsy, fat aspirate with cardiac imaging consistent with CA, or a positive nuclear technetium pyrophosphate study in the absence of a plasma cell dyscrasia graded with the Mayo Clinic staging system. Patients with clinically significant coronary artery disease, congenital heart disease, greater than moderate valvular heart disease, existing permanent pacemaker or implantable cardioverter-defibrillator, or previous cardiac transplant and pregnant patients were excluded. After 6 months, patients were given the option of device explantation or continued long-term monitoring with the ILR.

The mean monitoring duration was 10.3 ± 6.6 months; 6 patients retained the ILR for long-term monitoring. At baseline, 18 patients had a history of AF (4 with associated conduction disease), and 2 had VA. During follow-up, 10 patients experienced arrhythmic events (**Table 1**). AF occurred in 9 patients (7 symptomatic and 2 new onset and asymptomatic), and VA (presenting as exertional syncope) occurred in 1. Of these, 3 patients complained of fatigue, lightheadedness, or syncope that corresponded to concurrent conduction system disease (2 AF with slow ventricular response and 1 with Mobitz II second-degree block presenting as syncope) during ILR monitoring. These patients underwent dual-chamber permanent pacemaker implantation. Complete heart block was observed in another patient with AF who denied symptoms when questioned after the event was recorded. Because of reduced ejection fraction, this patient underwent implantation of a cardiac resynchronization therapy pacemaker. The patient who experienced symptomatic VA underwent implantable cardioverter-defibrillator implantation.

Both patients with new onset asymptomatic AF (patients 9 and 10, **Table 1**) had a history of stroke; anticoagulation was initiated in both cases. Anticoagulation was also initiated in a patient with a remote history of AF who was not previously anticoagulated and who later developed Mobitz II second-degree heart block (patient 8, **Table 1**) during extended monitoring, 11 months after ILR implantation. Two patients died; neither death was related to arrhythmias.

Although arrhythmias and conduction system disease occur frequently in ATTR-wt CA,[5] symptoms vary widely, and long-term monitoring with ILR can provide additional clinical information that affects treatment decisions. Among asymptomatic patients,

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TABLE 1 Patients Who Experienced Arrhythmic or Actionable Events

Patient	Event	Time Frame	Symptoms	Arrhythmia History	Outcome
1	pAF with RVR	6 months	SOB, palpitations, and fatigue	AF	AF ablation
2	pAF with RVR	5 months	Palpitations	AF	DCCV, amiodarone, AF ablation
3	pAF with SVR	12 months	Fatigue	AF	PPM
4	pAF with RVR	7 months	Palpitations	AF	DCCV, sotalol
5	pAF with SVR and high-degree AVB	2 months	Lightheadedness and syncope	AF	PPM
6	Sustained VT	1 month	Syncope	AF	Single-chamber ICD
7	pAF with RVR	1 month	Palpitations	AF	DCCV, amiodarone
8	AF and Mobitz type II	AC: 3 months PPM: 11 months	Fatigue correlated to Mobitz type II AVB	Remote history of AF not on AC	AC initiated, PPM
9	pAF and complete heart block	4 months	None	None	AC initiated, DCCV and CRT-P
10	pAF	2 months	None	None	AC initiated

AVB = atrioventricular block; AC = anticoagulation; CRT-P = cardiac resynchronization therapy pacemaker; DCCV = direct cardioversion; ICD = implantable cardioverter-defibrillator; pAF = paroxysmal atrial fibrillation; PPM = permanent pacemaker; RVR = rapid ventricular response; SVR = slow ventricular response.

ILR monitoring may identify AF or heart block events that would otherwise remain undetected. In highly symptomatic patients, ILR monitoring can correlate symptoms (eg, syncope) to ventricular tachycardia or conduction system disease. Although external telemetry monitoring is an alternative to ILR, capturing the heart rhythm during syncope is challenging because the timing of occurrences is often unpredictable. Finally, symptom correlation with AF occurrences on ILR can inform decisions to proceed with a rhythm control strategy, either with antiarrhythmic drugs or catheter ablation.

Our results suggest that prospective ILR monitoring in ATTR-wt may be clinically useful. However, our study was limited by a small sample size, the lack of a control group, and referral bias. Whether ILR monitoring is routinely indicated in all ATTR-wt CA patients to prospectively screen for arrhythmias and heart block needs to be investigated in larger, prospective, randomized longitudinal studies.

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