Monitoring for arrhythmia in transthyretin cardiac amyloidosis with noninvasive ambulatory patch devices

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BACKGROUND Transthyretin cardiac amyloidosis (ATTR-CA) is associated with an increased incidence of arrhythmias. We hypothesized that 2-week noninvasive ambulatory cardiac rhythm monitoring of patients with ATTR-CA would detect high rates of atrial fibrillation/atrial flutter (AF/AFL) and nonsustained ventricular tachycardia (NSVT).

OBJECTIVE The study sought to characterize arrhythmia in patients with ATTR-CA on 2-week, noninvasive cardiac rhythm monitors.

METHODS A total of 38 patients with ATTR-CA who underwent 2-week remote external patch monitoring were included in this single-center retrospective study. An age-matched control group included 38 patients who underwent the same cardiac rhythm monitoring as part of neurological workup.

RESULTS Of the ATTR-CA cohort, 26.3% had AF/AFL and 81.6% had NSVT. ATTR-CA was associated with higher rates of AF/AFL and NSVT compared with the control group. At a median follow-up of 45 weeks, there was no association between the presence of AF/AFL or NSVT on remote monitor in the ATTR-CA group and a composite of adverse clinical outcome.

CONCLUSION ATTR-CA was associated with an elevated rate of AF/AFL and an even higher rate of NSVT on noninvasive ambulatory monitors. While evidence regarding the management of arrhythmias, particularly NSVT/ventricular tachycardia, in ATTR-CA remains limited, 2-week noninvasive cardiac monitoring can be considered to aid in risk stratification for both atrial and ventricular arrhythmias.

KEYWORDS Ambulatory arrhythmia monitoring; Arrhythmia; Atrial fibrillation; Nonsustained ventricular tachycardia; Transthyretin cardiac amyloidosis

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Introduction

Systemic amyloidosis is characterized by extracellular protein deposition throughout organ systems.[1] Cardiac amyloidosis (CA) is a historically underdiagnosed cause of nonischemic cardiomyopathy, and is most commonly caused by misfolded transthyretin (ATTR) or immunoglobulin light-chain (AL) protein.[2] Arrhythmias, including atrial, conduction disturbances, and ventricular are common in all forms of CA. Atrial fibrillation (AF) is particularly prevalent and is associated with thromboembolism regardless of CHA_2DS_2-VASc (congestive heart failure, hypertension, age $\geq$75 years, diabetes mellitus, prior stroke or transient ischemic attack or thromboembolism, vascular disease, age 65–74 years, sex category) score.[3] Conduction disease is also common with high rates of implanted pacemakers.[2] Ventricular arrhythmia, particularly nonsustained ventricular tachycardia (NSVT), is also common, with an unclear association with sudden cardiac death.[4–8] While data are still lacking on the clinical utility of outpatient rhythm monitors in this population, expert consensus recommends Holter monitoring every 6 months in transthyretin cardiac amyloidosis (ATTR-CA).[9]

Most prior studies of arrhythmia monitoring in CA are either a mixture of AL and ATTR amyloidosis or only include patients with AL amyloidosis. In addition, prior studies have characterized arrhythmia in CA mainly via telemetry, 24-hour Holter monitor, and/or implanted device interrogation, often mixing modalities in published reports. However, weeks-long noninvasive monitors have emerged

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KEY FINDINGS

- In this transthyretin cardiac amyloidosis (ATTR-CA) population, 26.3% had atrial fibrillation and 81.6% had nonsustained ventricular tachycardia detected on remote patch monitors.
- ATTR-CA was associated with markedly higher rates of both atrial fibrillation and nonsustained ventricular tachycardia compared with an age-matched control group.
- Two-week noninvasive cardiac monitoring may be considered to aid in risk stratification for both atrial and ventricular arrhythmias in ATTR-CA.

as a viable option for ambulatory rhythm monitoring and, intuitively, have shown increased yield in the detection of arrhythmias vs 24-hour monitors in other clinical contexts.[10] This study aims to characterize the results of such remote, 2-week noninvasive cardiac rhythm monitoring in a cohort of patients with ATTR-CA alone. We hypothesized that patients with ATTR-CA would have a high burden of arrhythmias detected by these 2-week ambulatory monitors.

Methods

Study design

This is a single-center retrospective observational study of patients with previously diagnosed ATTR-CA who underwent 2-week term remote patch monitoring for cardiac arrhythmias between June 2018 and August 2021 at Columbia Irving University Medical Center. The control group included patients referred by the neurology department for long-term remote patch monitoring for cardiac arrhythmia between August 2020 and June 2021, most commonly as part of the workup for stroke. All included patients had remote monitoring with the Zio patch (iRhythm Technologies). The study was approved by the Columbia Irving University Medical Center Institutional Review Board. The research reported in this study adhered to Helsinki Declaration guidelines. The study qualified for a waiver of consent as the research involved a chart review that utilized confidential methods to ensure that collected, stored, and reported information cannot be linked to patients.

Clinical data

Demographics, clinical data, and adverse clinical outcomes were collected from the electronic medical record (EMR). Disease stage was assessed using the UK National Amyloidosis Center (NAC) score (Gillmore stage) and Columbia score. The UK NAC score assigns 1 point for each of N-terminal pro–B-type natriuretic peptide >3000 pg/mL and estimated glomerular filtration rate <45 mL/min/1.73 m^2, which corresponds to disease stages 1 to 3 for 0 to 2 points, respectively.[11] The Columbia score builds on the UK NAC score by adding diuretic dose (0 points = no diuretics, 1 point = ≤0.5 mg/kg, 2 points = >0.5 to 1 mg/kg, 3 points = >1 mg/kg of oral furosemide equivalent per day) and New York Heart Association functional class 1 to IV.[12] This corresponds to low risk (1–3 points), intermediate risk (4–6 points), and high risk (7–9 points) groups. As available, results of transthoracic echocardiograms were collected with parameters recorded directly from the clinical reports in the EMR. Adverse clinical outcomes were collected at the most recent available time point in the EMR at the time of data collection including all-cause mortality, hospitalizations for heart failure (defined as primary reason for hospitalization being heart failure), cardiovascular events (combined outcome including myocardial infarction, cerebrovascular accident, sustained ventricular tachycardia (VT), ventricular fibrillation, or other cardiac arrest), and new device implantation (permanent pacemaker [PPM], cardiac resynchronization therapy [CRT], and/or implantable cardioverter-defibrillator [ICD]). A composite of these adverse clinical outcomes was used for analysis.

Remote arrhythmia monitor data

Arrhythmia data were gathered directly from the remote monitor reports, previously confirmed by an electrophysiologist. We followed the device report's definitions: supraventricular tachycardia >3 beats, VT >3 beats, pause ≥3 seconds, AF/atrial flutter (AFL) ≥30 seconds, and advanced atrioventricular block as Mobitz II or complete heart block. We recorded the reported computation of supraventricular ectopic burden and ventricular ectopic burden each as a percentage of total QRS complexes with values reported as < 1% to be zero. We further classified VT as (1) NSVT <30 seconds or (2) sustained VT ≥30 seconds. For each patient with VT, we recorded the number of runs, the maximum peak rate of a run, the maximum average rate of a run, and the longest run (in beats and seconds) as recorded in the remote monitor report. For each patient with at least 1 pause, we noted the total number of pauses, the length of the longest pause, and confirmed clinical significance of the pause (defined as night ≥5 seconds or day ≥3 seconds).

Statistics

Statistics were performed in SAS 9.4 (SAS Institute) and data visualization in R (R Version 2023.09.1+494 Foundation for Statistical Computing). Control individuals were frequency matched for age (within 3 years). Continuous data were summarized with descriptive statistics (means, medians, standard deviations, minimums, and maximums). Categorial data were summarized with patient counts and percentages. Fisher's exact test was used to compare binary variables. For variables that have 3 or more ordered responses, the Mantel-Haenszel chi-square test was used. The rank sum test was used for non-normally distributed continuous variables. Normally distributed continuous variables were compared with the Student's *t* test. Multivariable analysis of binary outcome was performed with logistic regression. A survival analysis using Cox proportional hazards models

was used to analyze the association of arrhythmia with outcomes. A P value $<.05$ was considered significant.

Results

Patient characteristics

Seventy-six patients who underwent long-term remote monitoring for cardiac arrhythmias were included in our study: 38 patients with ATTR-CA and 38 age-matched control individuals. The ATTR-CA group had a mean age 76.9 ± 10.0 years and was 89.5% male. There were 26 with wild-type ATTR and 12 had variant disease. The age-matched control group had a mean age 73.9 ± 12.3 years and was 76.3% male. Table 1 outlines demographics, past medical history, baseline medications, and echocardiographic data for each group. Among those with an available transthoracic echocardiograms prior to the remote monitor (37 in the ATTR-CA group, 24 in the control group), the ATTR-CA group had a lower estimated left ventricular ejection fraction (mean 48.9 ± 11.3% vs mean 60.4 ± 4.8%) and a thicker intraventricular septum (mean 1.56 ± 0.27 cm vs mean 1.09 ± 0.19 cm).

Table 1 also outlines biomarkers (cardiac and renal) and amyloid disease staging for the ATTR-CA group. Prior to remote monitoring, 63.2% of the ATTR-CA group were prescribed ATTR-specific therapy and by the time of follow-up this had grown to 37 of 38 (97%). Of note, 26.3% of amyloid patients were taking beta-blockers at baseline and 34.2% were taking angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, or angiotensin receptor-neprilysin inhibitors. Of the ATTR-CA group, 37 of 38 patients had sufficient biomarkers available to calculate UK NAC and Columbia Scores used to stage amyloid disease severity. Of these patients by the UK NAC, 48.6% were stage 1, 43.2% were stage 2, and 8.1% were stage 3 (with higher stage denoting further progression of amyloid disease). By the Columbia score, 27.0% were categorized as low risk, 54.1% as intermediate risk, and 18.9% as high risk. There was no association between amyloid disease severity (by either score) and the presence of AF/AFL or NSVT on remote monitors.

Remote monitor data

Results from remote rhythm monitoring are summarized, by group, in Table 2. Both groups wore the remote monitor for a similar period, with the average monitoring period being 13.3 (range 2–14) days and 13.5 (range 7–14) days for the ATTR-CA and control groups, respectively. The ATTR-CA group was associated with higher incidence of AF/AFL: 26.3% vs 5.3% in the control group ($P = .025$). The ATTR-CA group was also associated with a higher rate of NSVT: 81.6% vs 28.9% of patients in the control group ($P < .001$). The ATTR-CA group also had a nonsignificant trend for faster rate of NSVT vs the control group (180 ± 28 beats/min vs 164 ± 36 beats/min, $P = .07$). There was no sustained VT detected in either group. ATTR-CA was associated with a nonsignificant trend for more frequent pauses compared with the control group (18.4% vs 5.3%, $P = .15$) and advanced atrioventricular block (7.9% vs 2.6%, $P = .61$). The ATTR-CA group had higher burden of ventricular ectopy vs the control group ($P = .009$). There was no difference in supraventricular ectopy between the groups. Notably, as seen in Figure 1, there were only 3 ATTR-CA patients without AF/AFL, NSVT, advanced atrioventricular block, or a significant pause detected on remote monitor.

Adverse clinical outcomes

A total of 7 patients in the ATTR-CA group had at least 1 adverse clinical outcome at a follow-up of a median of 45 weeks. As seen in Table 3, there were no deaths, 4 heart failure hospitalizations, 2 cardiovascular events (1 episode of sustained VT and 1 stroke [patient had AF/AFL on remote monitor]), 6 PPMs placed, and 3 ICDs placed. Indications for the 6 PPMs implanted included symptomatic bradycardia (n = 2), complete heart block (n = 2), sick sinus syndrome (n = 1), and CRT as indicated (n = 1). Of the 3 ICDs implanted, 2 were initially placed CRT defibrillator devices and 1 was an upgrade after a previously placed PPM picked up an episode of sustained VT (approximately 180 beats/min for about 1 hour). By a Cox proportional hazards model, neither AF/AFL nor NSVT was associated with a composite of adverse clinical outcomes.

Discussion

In this study, we present the results of 2-week remote external patch arrhythmia monitoring in patients with ATTR-CA. While prior studies have characterized arrhythmia in CA via telemetry, 24-hour Holter monitor, and implanted devices, to our knowledge this is the first study to characterize arrhythmia in patients with ATTR-CA alone, using solely 2-week remote external patch monitor. The present study found that in an ATTR-CA population, the burden of NSVT detected on remote patch monitors was very high (81.6%). Additionally, as would be expected, ATTR-CA was associated with markedly higher rates of both AF/AFL and NSVT compared with an age-matched control group. In sum, 2-week noninvasive cardiac monitoring may be a useful modality to aid in the detection and risk stratification for arrhythmias in ATTR-CA.

A priori, we hypothesized that amyloid patients would have high rates of AF on 2-week remote rhythm monitors. Indeed, a clinical motivation of this remote monitoring was to increase early detection of AF with the goal of mitigating the increased risk of thromboembolic events for those with AF/AFL in CA. While ATTR-CA was associated with significantly higher rates of AF/AFL compared with control individuals, we discovered that the rates of NSVT in the ATTR-CA group was even higher. These findings are directionally similar to a prior study of 24 hospitalized light-chain cardiac amyloidosis (AL-CA) patients monitored on continuous telemetry for an average of 24 days, which found 36% of record arrhythmia events to be supraventricular and 64% to be ventricular (most commonly NSVT).[4] However, our observation is different from a recently published cohort of 130 predominantly hereditary ATTR-CA patients, with 61%

Table 1 Patient characteristics

	ATTR-CA (n = 38)	Control (n = 38)	*P* value
Demographics			
Age, y	76.9 ± 10.0 (38)	73.9 ± 12.3 (38)	
Sex			.22
Male	34 (89.5)	29 (76.3)	
Female	4 (10.5)	9 (23.7)	
Race			
Asian	1 (2.6)	1 (2.6)	
Black or African American	6 (15.8)	4 (10.5)	
Declined	5 (13.2)	9 (23.7)	
Other	1 (2.6)	6 (15.8)	
White	25 (65.8)	18 (47.4)	
Ethnicity			
Hispanic or Latino or Spanish origin	5 (13.2)	5 (13.2)	
Not Hispanic or Latino or Spanish origin	21 (55.3)	22 (57.9)	
Declined or unknown	12 (31.6)	11 (29.0)	
Comorbidities			
Hypertension	18 (47.4)	30 (78.9)	.008*
Stroke or transient ischemic attack	1 (2.6)	29 (76.3)	<.0001*
Coronary artery disease	10 (26.3)	10 (26.3)	1
Peripheral arterial disease	2 (5.3)	2 (5.3)	1
Diabetes mellitus	3 (7.9)	14 (36.8)	.005*
Prior arrhythmia†	13 (34.2)	8 (21.1)	.3
AF/AFL	11 (28.9)	8 (21.1)	
AVNRT	1 (2.6)	—	
AT	1 (2.6)	—	
CHB	1 (2.6)	1 (2.6)	
Baseline medications			
Anticoagulation	11 (28.9)	6 (15.8)	.27
Beta-blocker	10 (26.3)	13 (34.2)	.62
ACE inhibitor or ARB or ARNI	13 (34.2)	16 (42.1)	.64
Mineralocorticoid receptor antagonist	9 (23.7)	—	.002*
Aspirin	16 (42.1)	29 (76.3)	.005*
Clopidogrel	3 (7.9)	9 (23.7)	.11
Statin	26 (68.4)	32 (84.2)	.18
Loop diuretic	24 (63.2)	3 (7.9)	<.0001*
Echocardiography			
Left ventricular end-diastolic diameter, cm	4.46 ± 0.614 (30)	4.75 ± 0.628 (22)	.09
Intraventricular septal thickness, cm	1.56 ± 0.271 (32)	1.09 ± 0.187 (21)	<.0001*
Left atrial diameter, cm	4.23 ± 0.670 (21)	3.84 ± 0.758 (17)	.09
LVEF, %	48.9 ± 11.3 (37)	60.4 ± 4.78 (24)	<.0001*
ATTR-CA biomarkers/severity/treatment			
NT-proBNP, pg/mL	2687.2 ± 2531.6 (37)	—	
Troponin T, ng/mL	64.4 ± 58.7 (31)	—	
NYHA functional class			
I	6 (15.8)	—	
II	21 (55.3)	—	
III	10 (26.3)	—	
IV	1 (2.6)	—	
eGFR			
<30 mL/min/1.73 m^2	4 (10.5)	—	
30–60 mL/min/1.73 m^2	16 (42.1)	—	
>60 mL/min/1.73 m^2	18 (47.4)	—	
UK NAC			
Stage 1	18 (48.6)	—	
Stage 2	16 (43.2)	—	
Stage 3	3 (8.1)	—	
Columbia score category			
Low risk	10 (27.0)	—	
Intermediate risk	20 (54.1)	—	
High risk	7 (18.9)	—	

Table 1 (*Continued*)

	ATTR-CA (n = 38)	Control (n = 38)	*P* value
ATTR-directed treatment			
Baseline	24 (63.2)	—	
At follow-up	37 (97.4)	—	

Values are n (%) or mean ± SD (n). *P* values are reported for the statistical tests as described in the Methods.

ACE = angiotensin-converting enzyme; AF = atrial fibrillation; AFL = atrial flutter; ARB = angiotensin receptor blocker; ARNI = angiotensin receptor-neprilysin inhibitor; ATTR = transthyretin; ATTR-CA = transthyretin cardiac amyloidosis; AVNRT = atrioventricular nodal re-entrant tachycardia; AT = atrial tachycardia; CHB = complete heart block; eGFR = estimated glomerular filtration rate; LVEF = left ventricular ejection fraction; NAC = National Amyloidosis Center; NT-proBNP = N-terminal pro–B-type natriuretic peptide; NYHA = New York Heart Association; SVT = supraventricular tachycardia.

*$P < .05$.

†Defined as documented history of arrhythmia in the chart prior to remote monitoring including supraventricular tachycardia, AF/AFL, atrioventricular block, or ventricular tachycardia.

having AF/AFL and 53% having NSVT on a review of a mixture of rhythm monitoring modalities (electrocardiogram, telemetry, outpatient monitors, and device interrogation where available).[8] Further investigation is warranted to ascertain the impact of the choice of rhythm monitoring modality on the variable yield of arrhythmia detection, in particular to help develop optimal strategies for early AF/AFL detection to prevent thromboembolic events.

Despite such high rates of NSVT in the ATTR-CA group, there was no sustained VT on the initial remote monitors, and only 1 patient developed sustained VT during the follow-up period. This event was detected on remote PPM monitoring in an asymptomatic patient, and subsequently resulted in an upgrade to an ICD. Detection of sustained VT was limited by length and modality of follow-up, as most patients did not undergo further

Table 2 Remote monitor data of the ATTR-CA group vs control group

	ATTR-CA (n = 38)	Control (n = 38)	*P* value
Time on remote monitor			.89
1–6 d	2 (5.3)	—	
7–13 d	5 (13.2)	9 (23.7)	
14 d (complete)	31 (81.6)	29 (76.3)	
SVT (<30 s)	27 (71.1)	30 (78.9)	.6
Sustained SVT	3 (7.9)	1 (2.6)	.61
AF (≥30 s)	10 (26.3)	2 (5.3)	.02*
NSVT	31 (81.6)	11 (28.9)	<.0001*
Advanced AV Block	3 (7.9)	1 (2.6)	.61
Pauses	7 (18.4)	2 (5.3)	.15
Pause by duration			
3–5 s	6 (15.8)	1 (2.6)	
>5 s	1 (2.6)	1 (2.6)	
Pause by time of day			
Day: 6 AM to 10 PM	4 (10.5)	—	
Night: 10 PM to 6 AM	3 (7.9)	2 (5.3)	
PVC burden, %			
Mean ± SD	1.25 ± 2.52	0.450 ± 1.67	.009*
Median (range) (n)	0 (0–11.0) (38)	0 (0–7.50) (38)	
SV ectopy burden, %			
Mean ± SD	0.463 ± 1.76	0.461 ± 2.41	.3
Median (range) (n)	0 (0–10.6) (38)	0 (0–14.8) (38)	
NSVT runs per day			
Mean ± SD	1.26 ± 3.34	1.81 ± 4.63	.046*
Median (range) (n)	0.357 (0.0714–17.4) (28)	0.143 (0.0714–14.9) (10)	
Longest NSVT run, s			
Mean ± SD	7.10 ± 4.53	5.82 ± 3.42	.62
Median (range) (n)	5.90 (1.70–19.3) (31)	4.80 (1.80–13.4) (11)	
NSVT fastest rate, beats/min			
Mean ± SD	180 ± 27.5	164 ± 36.5	.07
Median (range) (n)	179 (128–250) (31)	158 (108–245) (11)	

Values are n (%), unless otherwise indicated. *P* values are reported for the statistical tests as described in the Methods.

AF = atrial fibrillation or atrial flutter; ATTR-CA = transthyretin cardiac amyloidosis; AV = atrioventricular; NSVT = nonsustained ventricular tachycardia; PVC = premature ventricular contraction; SV = supraventricular; SVT = supraventricular tachycardia.

*$P < .05$.

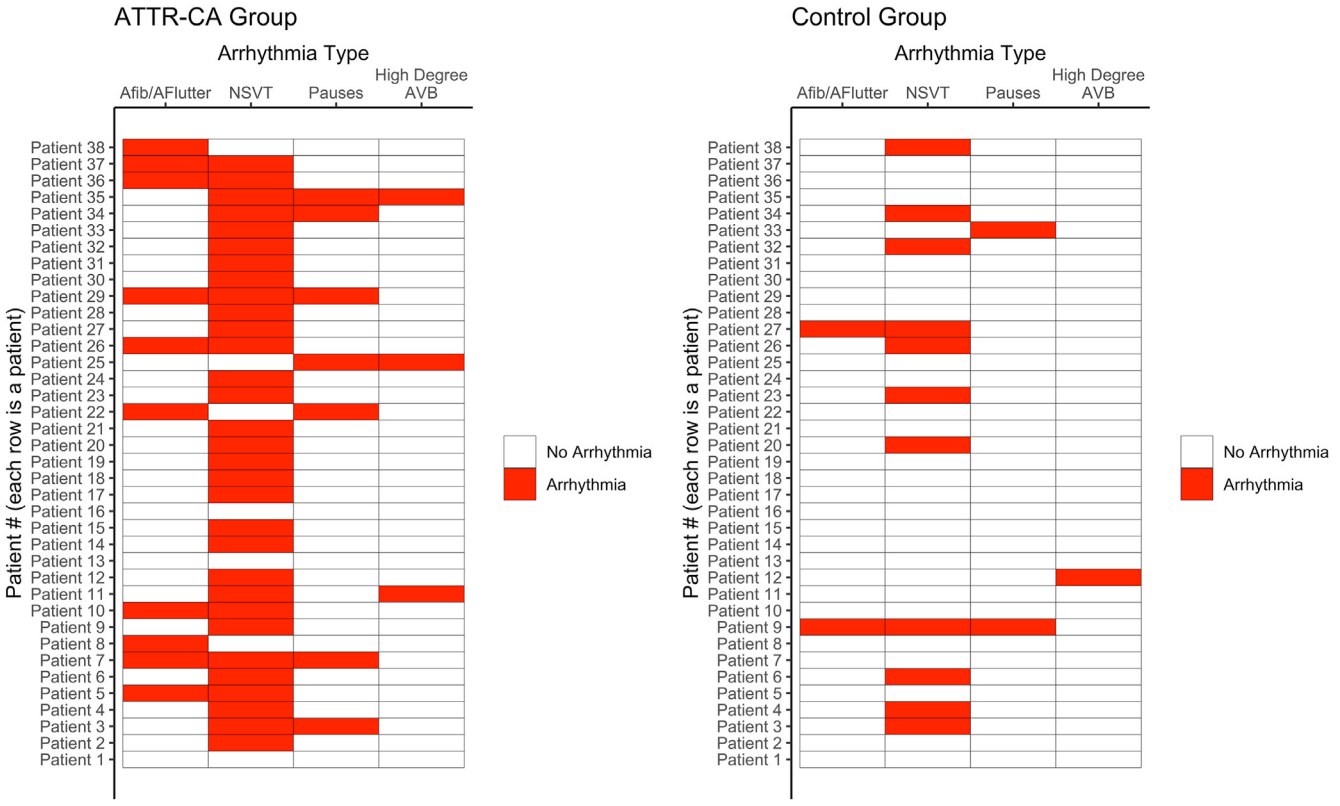

Figure 1 Remote monitor arrhythmia heatmap for transthyretin cardiac amyloidosis (ATTR-CA) and control groups. Each row represents an individual patient, and each column represents an arrhythmia subtype. AVB = atrioventricular block; NSVT = nonsustained ventricular tachycardia.

arrhythmia monitoring after the initial 2-week period. As such, prior literature shows mixed rates of sustained VT in amyloidosis. In a study of 95 patients with familial amyloid polyneuropathy with permanent pacemakers placed, no episodes of sustained VT were detected at follow-up.[13] Similarly, Garan and colleagues[14] found no episodes of sustained VT on 24-hour Holter monitor despite 58% rate of NSVT. Furthermore, the previously mentioned study of 130 ATTR-CA patients found sustained VT in 5% and VF in 2%.[8] Varr and colleagues[5] described a series of 31 patients of which 6 (5 AL-CA, 1 ATTR-CA) developed sustained VT. While the 5 AL-CA patients required antitachycardia pacing, defibrillation, or both to terminate the rhythm, the 1 patient who had ATTR-CA self-terminated prior to ICD therapy.[5] There remain open questions related to possible heterogeneity in the risks associated with ventricular arrhythmias between subtypes of amyloidosis.

As such, further study is warranted to investigate the differences in pathophysiology of ventricular arrhythmias within CA generally, and more specifically between AL-CA vs ATTR-CA. While ATTR-CA, as compared with AL-CA, has been associated with a greater volume of amyloid fibril infiltration in the left ventricle, AL-CA has been associated with higher rates of sudden cardiac death.[15–17] A comparative study of ATTR-CA and AL-CA found higher spatial conduction and repolarization abnormalities in AL-CA despite a lower volume of amyloid infiltration, with the authors hypothesizing that a mechanism beyond amyloid fibril deposition alone, such as direct AL toxicity, might contribute to increased electrophysiological abnormalities in AL amyloidosis.[15] These differences raise caution in generalizing studies of electrophysiology abnormalities in AL-CA to ATTR-CA.

In particular, the clinical significance of NSVT as a prognostic factor for adverse clinical outcomes, including sudden cardiac death, in ATTR-CA, specifically, remains

Table 3 Adverse clinical outcomes at last known follow-up of ATTR

Outcome	ATTR-CA (n = 38)
Time from remote monitor to last known follow-up, wk	45 (1–172)
Death	0 (0)
Heart failure hospitalization	4 (10.5)
Cardiovascular events*	2 (5.3)
Pacemaker implanted	6 (15.8)
ICD implanted	3 (10.3)

Values are median (range) or n (%).

ATTR = transthyretin; ATTR-CA = transthyretin cardiac amyloidosis; ICD = implantable cardioverter-defibrillator.

*Composite of myocardial infarction, cerebrovascular accident, sustained ventricular tachycardia, ventricular fibrillation, or other cardiac arrest.

unclear. While prior studies of AL-CA patients have found NSVT and ventricular couplets to be predictors of worsened outcomes,[6,7] the previously mentioned study of ATTR-CA patients on 24-hour Holter monitor found no difference in long-term survival in those with or without NSVT.[14] In our study, NSVT was similarly not associated with a composite of adverse clinical outcomes. However, it should be noted that a similar lack of association of AF/AFL with adverse clinical outcomes suggests caution in generalizing this result, as this study's power is limited by both small sample size and short follow-up period. Additional investigation involving more patients and longer follow-up periods are required to assess the relationship between NSVT and clinical outcomes in ATTR-CA including the development of sustained VT and sudden cardiac death.

The high rate of NSVT in the ATTR-CA group is an important finding that warrants further study into its possible mechanisms as well as clinical implications/treatment options. While sudden cardiac death is a relatively common cause of death in CA, it is postulated to be predominantly driven by electromechanical dissociation, rather than by primary arrhythmia.[17,18] Both recommendations and evidence for ICD placement for both primary and secondary prevention in CA remain mixed.[2,19] While observational studies have demonstrated appropriate ICD shocks,[5,8] a recent meta-analysis showed no survival benefit for ICD placement.[20] In contrast, there is evidence for improved clinical outcomes with CRT implantation when appropriately indicated.[21] Further study is warranted to address questions related to the association of NSVT with amyloid disease progression, along with the role of risk stratification of such patients for additional therapies including antiarrhythmics and ICD.

Study limitations

Our study is limited by the small sample size of ATTR-CA patients at our single center who underwent 2-week remote cardiac monitoring. As a retrospective observational study, any conclusions are limited to hypothesis-generating associations, rather than to causative inference. Additionally, the relatively short duration of follow-up limits conclusions that can be drawn regarding outcomes analysis. Finally, the control group was matched by age only. Furthermore, patients in the control group did not necessarily have cardiac disease and had relatively normal left ventricular systolic function compared with the ATTR-CA group. Overall, one would expect them to have lower rates of arrhythmias than a group with known structural heart disease. While this limits the utility of the comparison between groups, the study's observed association of higher rates of arrhythmia among the ATTR-CA group matches expectations and gives confidence to the remote monitoring as a useful modality for arrhythmia detection in ATTR-CA. Future studies should compare 2-week remote patch monitors with standard 24-hour monitors in ATTR-CA to assess its impact on arrhythmia detection, management, and outcomes.

Conclusion

Remote 2-week cardiac rhythm monitoring of ATTR-CA patients identified high rates of clinically relevant arrhythmias, in particular very high rates of NSVT. While evidence regarding the management of arrhythmias, particularly NSVT/VT, in ATTR-CA remains limited, 2-week noninvasive cardiac monitoring can be considered to aid in risk stratification for both atrial and ventricular arrhythmias in ATTR-CA.

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Authorship: All authors attest they meet the current ICMJE criteria for authorship.

Patient Consent: The study qualified for a waiver of consent.

Ethics Statement: The study was approved by the Columbia Irving University Medical Center Institutional Review Board. The research reported in this study adhered to Helsinki Declaration guidelines.

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