JACC: CARDIOVASCULAR INTERVENTIONS VOL. 13, NO. 15, 2020

PUBLISHED BY ELSEVIER

Prolonged Continuous Electrocardiographic Monitoring Prior to Transcatheter Aortic Valve Replacement

The PARE Study

Lluis Asmarats, MD, Isabelle Nault, MD, Alfredo Nunes Ferreira-Neto, MD, Guillem Muntané-Carol, MD, David del Val, MD, Lucia Junquera, MD, Jean-Michel Paradis, MD, Robert Delarochellière, MD, Siamak Mohammadi, MD, Dimitri Kalavrouziotis, MD, Eric Dumont, MD, Emilie Pelletier-Beaumont, MSc, François Philippon, MD, Josep Rodés-Cabau, MD

ABSTRACT

OBJECTIVES This study sought to determine, using continuous electrocardiographic monitoring (CEM) pre-transcatheter aortic valve replacement (TAVR), the incidence and type of unknown pre-existing arrhythmic events (AEs) in TAVR candidates, and to evaluate the occurrence and impact of therapeutic changes secondary to the detection of AEs pre-TAVR.

BACKGROUND Scarce data exist on the arrhythmic burden of TAVR candidates (pre-procedure).

METHODS This was a prospective study including 106 patients with severe aortic stenosis and no prior permanent pacemaker screened for TAVR. A prolonged (1 week) CEM was implanted within the 3 months pre-TAVR. Following heart team evaluation, 90 patients underwent elective TAVR.

RESULTS New AEs were detected by CEM in 51 (48.1%) patients, leading to a treatment change in 14 of 51 (27.5%) patients. Atrial fibrillation or tachycardia was detected in 8 of 79 (10.1%) patients without known atrial fibrillation or tachycardia, and nonsustained ventricular arrhythmias were detected in 31 (29.2%) patients. Significant bradyarrhythmias were observed in 22 (20.8%) patients, leading to treatment change and permanent pacemaker in 8 of 22 (36.4%) and 4 of 22 (18.2%) patients, respectively. The detection of bradyarrhythmias increased up to 30% and 47% among those patients with pre-existing first-degree atrioventricular block and right bundle branch block, respectively. Chronic renal failure, higher valve calcification, and left ventricular dysfunction determined (or tended to determine) an increased risk of AEs pre-TAVR ($p = 0.028$, 0.052, and 0.069, respectively). New onset AEs post-TAVR occurred in 22.1% of patients, and CEM pre-TAVR allowed early arrhythmia diagnosis in one-third of them.

CONCLUSIONS Prolonged CEM in TAVR candidates allowed identification of previously unknown AEs in nearly one-half of the patients, leading to prompt therapeutic measures (pre-TAVR) in about one-fourth of them. Pre-existing conduction disturbances (particularly right bundle branch block) and chronic renal failure were associated with a higher burden of AEs. (J Am Coll Cardiol Intv 2020;13:1763–73) © 2020 by the American College of Cardiology Foundation.

From the Quebec Heart and Lung Institute, Laval University, Quebec City, Canada. Drs. Asmarats, Muntané-Carol, Del Val, and Junquera were supported by a grant from the Fundación Alfonso Martin Escudero (Madrid, Spain). Dr. Rodés-Cabau holds the Research Chair "Fondation Famille Jacques Larivière" for the Development of Structural Heart Disease Interventions; and has received research institutional grants from Medtronic, Edwards Lifesciences, and Boston Scientific. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the *JACC: Cardiovascular Interventions* author instructions page.

Manuscript received January 22, 2020; revised manuscript received March 16, 2020, accepted March 24, 2020.

ISSN 1936-8798/$36.00 https://doi.org/10.1016/j.jcin.2020.03.031

ABBREVIATIONS AND ACRONYMS

AF = atrial fibrillation

AT = atrial tachycardia

AVB = atrioventricular block

CEM = continuous electrocardiographic monitoring

CI = confidence interval

ECG = electrocardiographic

ESVEA = excessive supraventricular ectopic activity

HAVB = high-degree atrioventricular block

LBBB = left bundle branch block

NSVT = nonsustained ventricular tachycardia

OR = odds ratio

PPM = permanent pacemaker

RBBB = right bundle branch block

TAVR = transcatheter aortic valve replacement

Transcatheter aortic valve replacement (TAVR) has emerged as a viable alternative for the treatment of elderly patients with severe aortic stenosis (1–3). However, the occurrence of arrhythmic events (either bradyarrhythmia or tachyarrhythmia) remains the most frequent complication of TAVR (4,5). Whereas most arrhythmic events post-TAVR are directly related to the procedure or valve prosthesis, few data exist on the occurrence of pre-existing arrhythmias in TAVR candidates. A study using 24-h continuous electrocardiographic monitoring (CEM) within the days before the TAVR procedure showed that a significant proportion of silent arrhythmias were already present before the procedure (6). However, it is well known that 24-h continuous monitoring has a low sensitivity, and electrocardiographic (ECG) monitoring >24 h has shown a much higher sensitivity for detecting arrhythmias (7). In addition to determining the real impact of the TAVR procedure on arrhythmic events, the detection of arrhythmias pre-procedure may help to implement specific treatment measures (e.g., pacemaker implantation, anticoagulation therapy) that can improve the global care of TAVR candidates, reduce hospitalization length, and improve clinical outcomes post-TAVR. The objectives of this study were to: 1) determine the incidence and type of arrhythmic events in TAVR candidates as assessed by prolonged CEM pre-TAVR; and 2) evaluate the occurrence and impact of therapeutic changes secondary to the detection of arrhythmic events pre-TAVR.

SEE PAGE 1774

METHODS

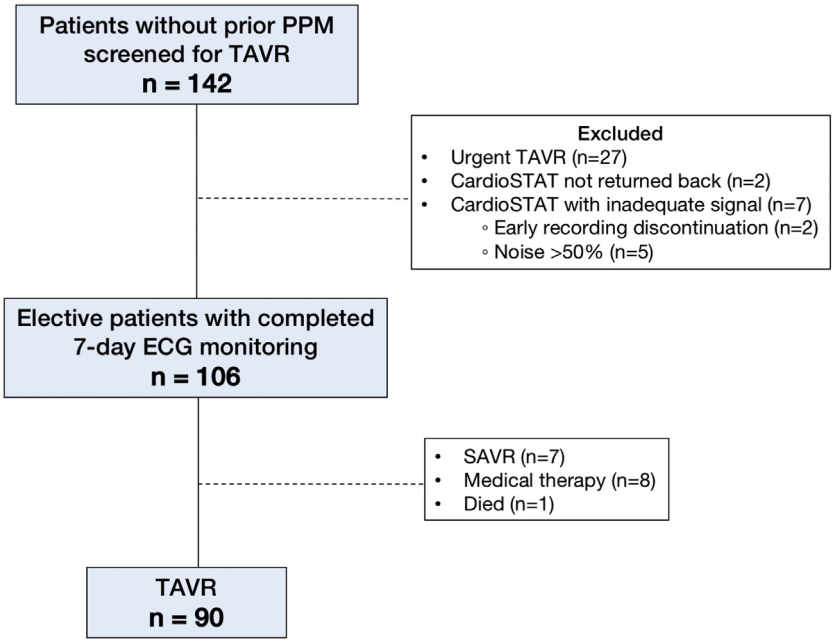
STUDY DESIGN AND PATIENTS. The PARE (Prolonged Continuous ECG Monitoring Prior to Transcatheter Aortic Valve Implantation) study (NCT03561805) was a prospective, single-center study, approved by the institutional ethics committee, and all patients provided signed informed consent to participate. Patients with severe symptomatic aortic stenosis referred for TAVR who did not have a pre-existing permanent pacemaker (PPM) were included. There was no restriction regarding the type of valve and approach used for the TAVR procedure. Patients underwent a prolonged (1 week) CEM using the CardioSTAT device (Icentia, Quebec City, Canada) within the 3 months before the TAVR procedure. Patients requiring urgent TAVR precluding 1 week ECG monitoring within the 3 months pre-TAVR were excluded. All types of arrhythmic events were recorded, as well as the specific therapeutic measures implemented upon the occurrence of the arrhythmic event. Following the TAVR procedure, the patients were monitored (telemetry) until hospital discharge. All arrhythmic events during the hospitalization period were recorded. Clinical follow-up was also performed at 30 days.

CardioSTAT DEVICE. The CardioSTAT is a single-use, wire-free, wearable heart monitoring patch that provides continuous ECG recording of a single-lead tracing up to 14 days. CardioSTAT comes in the form of a thin flexible strip designed to be worn on the upper part of the torso and features conventional gel electrodes allowing a low impedance between the skin and the electrode in order to obtain an optimal signal. The device has been clinically validated, showing excellent correlation with the standard Holter ECG monitoring (8). The monitoring period in the present study was of 7 days. Patients were asked to report any symptom potentially related to arrhythmic events (e.g., palpitations, dizziness, dyspnea, exercise intolerance) by pressing a symptom trigger button located on the front of the device. Once the registration was complete, the patient returned the device personally or by mail. The data were analyzed at the service center by a certified technologist and a report was sent electronically to the cardiac electrophysiologist (I.N.) for validation and final reporting. The time delay between the end of the monitoring and data interpretation was no longer than 7 days.

OUTCOMES. The primary outcomes were: 1) the incidence and type of arrhythmic events; and 2) the therapeutic changes related to the diagnosis of arrhythmic events before the TAVR procedure. Secondary outcomes were incidence and duration of atrial fibrillation (AF), incidence of high-degree atrioventricular block (HAVB), incidence of severe bradycardia, percentage of patients with an indication of PPM, and percentage of patients with an indication for anticoagulation therapy.

Significant arrhythmias were defined according to current guidelines. Excessive supraventricular ectopic activity (ESVEA) was defined as ≥30 premature supraventricular contractions/hour (≥729 per 24 h) or an episode of premature supraventricular contractions runs ≥20 beats (9). Paroxysmal AF was defined as irregular RR intervals with absent P waves lasting at least 30 s, and atrial tachycardia (AT) as sudden rapid regular atrial rhythm with identifiable P waves (10). Nonsustained ventricular tachycardia

FIGURE 1 Patient Flowchart



The overall population included 142 patients who did not have a prior pacemaker, screened for transcatheter aortic valve replacement (TAVR). Patients requiring an urgent procedure and those in whom electrocardiographic (ECG) recording was insufficient or not returned back (n = 36) were excluded. Among the 106 TAVR candidates with complete 7-day ECG monitoring, 90 patients ultimately underwent elective TAVR. PPM = permanent pacemaker implantation; SAVR = surgical aortic valve replacement.

(NSVT) was defined as ≥3 consecutive complexes originating in the ventricles at a rate >100 beats/min (11). Severe bradycardia was defined as heart rate <40 beats/min (12). HAVB was defined as any of the following: second-degree atrioventricular block (AVB) type 2 (Mobitz II), 2:1 AVB, or ≥2 consecutive P waves that do not conduct to the ventricle. Complete heart block was defined as P waves with a constant rate with dissociated ventricular rhythm (no association between P waves and R waves) or fixed slow ventricular rhythm in the presence of AF (5,13). PPM implantation was indicated in the presence of HAVB or complete heart block (13). Clinical events were defined according to the Valve Academic Research Consortium-2 criteria (14).

STATISTICAL ANALYSIS. Data on CEM before TAVR was limited to a single study with ECG monitoring duration limited to 24 h, which identified newly diagnosed arrhythmias in about 16% of patients (6). Assuming that extending the duration of CEM to 7 days would significantly increase the detection of arrhythmic events (to ≥25% of patients), the sample size of this observational study was estimated at 100 patients. Qualitative variables were reported as counts and percentages and continuous variables as mean ± SD or median (interquartile range), depending on variable distribution. Categorical variables were compared using the chi-square or Fisher exact test as appropriate, and the Student's *t*-test or Wilcoxon rank sum test for continuous variables. The factors associated with newly diagnosed arrhythmic events were determined using a multivariable logistic regression analysis. Parameters with a p value < 0.15 in the univariable analysis were modeled in a multivariable analysis using a stepwise procedure in a logistic regression model. After stepwise elimination, 3 variables were retained in the model: chronic renal failure, left ventricular systolic dysfunction (ejection fraction <50%), and valvular calcification (Agatston score). A p value < 0.05 was considered significant for all statistical tests. All data were analyzed using the statistical package STATA version 14.0 (StataCorp LP, College Station, Texas).

RESULTS

Of 142 patients with severe symptomatic aortic stenosis and no prior PPM screened for TAVR in our institution, 27 patients were excluded due to the need

TABLE 1 Clinical Characteristics According to the Occurrence of AEs During 7-Day Continuous Electrocardiographic Monitoring

	Overall (N = 106)	New AEs (n = 51)	No AEs (n = 55)	p Value
Baseline variables				
Age, yrs	80 ± 8	81 ± 6	80 ± 9	0.206
Male	62 (58.5)	31 (60.8)	31 (56.4)	0.644
Hypertension	91 (85.8)	45 (88.2)	46 (83.6)	0.497
Previous coronary disease	58 (54.7)	30 (58.8)	28 (50.9)	0.413
Atrial fibrillation/flutter	27 (25.5)	18 (35.3)	9 (16.4)	0.025
COPD	29 (27.4)	14 (27.5)	15 (27.3)	0.984
eGFR <60 ml/min	51 (48.1)	30 (58.8)	21 (38.2)	0.034
CHA_2DS_2-VASc	4.3 ± 1.3	4.4 ± 1.2	4.2 ± 1.3	0.357
STS-PROM, %	4.8 ± 2.7	4.5 ± 2.4	5.0 ± 2.9	0.301
Electrocardiographic variables				
PR interval, ms	180 ± 41	183 ± 54	179 ± 27	0.626
QRS duration, ms	105 ± 28	109 ± 29	101 ± 25	0.125
First-degree atrioventricular block*	20 (22.5)	11 (29.0)	9 (17.7)	0.206
Right bundle branch block	15 (14.2)	10 (19.6)	5 (9.1)	0.121
Left bundle branch block	9 (8.5)	4 (7.8)	5 (9.1)	1.000
Intraventricular conduction delay	4 (3.8)	3 (5.9)	1 (1.8)	0.350
Echocardiographic variables				
LVEF <50%	27 (25.5)	17 (33.3)	10 (18.2)	0.074
Mean AV gradient, mm Hg	42 ± 16	43 ± 17	40 ± 15	0.306
AV area, cm^2	0.72 ± 0.22	0.69 ± 0.19	0.74 ± 0.23	0.232
Computed tomography variables				
Aortic annular area, mm^2	429 ± 119	441 ± 119	419 ± 119	0.414
Aortic annular perimeter, mm	75 ± 10	74 ± 12	75 ± 8	0.709
Agatston calcium score, AU	2,164 ± 1,376	2,394 ± 1,612	1,947 ± 1,081	0.107
Baseline treatment				
Anticoagulation	22 (20.8)	14 (27.5)	8 (14.6)	0.102
Beta-blockers	53 (50.0)	25 (49.0)	28 (50.9)	0.846
Calcium-channel blockers	30 (28.3)	17 (33.3)	13 (23.6)	0.268
Digoxin	2 (1.9)	2 (3.9)	0 (0.0)	0.229
Amiodarone	3 (2.8)	1 (2.0)	2 (3.6)	1.000

Values are mean ± SD, n (%), or median (interquartile range). *Patients in sinus rhythm (n = 89).

AE = arrhythmic event; AU = Agatston units AV = aortic valve; CHA_2DS_2-VASc = congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, prior stroke or transient ischemic attack or thromboembolism, vascular disease, age 65–74 years, sex category; COPD = chronic obstructive pulmonary disease; eGFR = estimated glomerular filtration rate; LVEF = left ventricular ejection fraction; STS-PROM = Society of Thoracic Surgeons Predicted Risk of Mortality.

for urgent TAVR, and 9 patients were excluded due to inadequate ECG recording (n = 7) or monitor not returned appropriately (n = 2), leading to a study cohort of 106 patients with completed 7-day CEM (Figure 1). The main baseline characteristics of the study population are summarized in Table 1. Mean age of the patients was 80 ± 8 years, and 58.5% were men, with a mean Society of Thoracic Surgeons Predicted Risk of Mortality of 4.8 ± 2.7%. Twenty-seven (25.5%) patients had a history of prior AF (either paroxysmal or permanent), and pre-existing first-degree AVB and any intraventricular conduction disturbances were present in 20 (22.5%) and 28 (26.4%) patients, respectively.

INCIDENCE AND TYPE OF ARRHYTHMIC EVENTS DURING 7-DAY CEM. The main ambulatory CEM findings are displayed in Table 2. Arrhythmic events were diagnosed in 51 (48.1%) patients, with a median number of 2 (interquartile range: 1 to 6) episodes per patient. In 14 patients (13.2% of the overall population; 27.5% of the 51 patients with newly diagnosed arrhythmias), the arrhythmic events led to therapeutic changes.

Newly diagnosed tachyarrhythmic events were found in 37 (34.9%) patients, most of them (97.3%) asymptomatic. Among the 79 patients without a prior history of AF, paroxysmal AF or AT was identified in 8 (10.1%) patients, leading to a treatment change in 5 of them (oral anticoagulation in 4, antiarrhythmic agent in 1). Of the patients with newly diagnosed paroxysmal AF, the median AF burden was 0.2% (interquartile range: 0.1% to 0.3%), with a median duration of AF episodes of 2.1 (interquartile range: 1.3 to 10.7) min. NSVT occurred in 31 (29.2%) patients, with no episodes of sustained ventricular tachycardia.

Twenty-two (20.8%) patients experienced significant bradyarrhythmias, most of them asymptomatic (90.9%): severe bradycardia in 16, HAVB and severe bradycardia in 4, and HAVB in 2 patients. Bradyarrhythmic events led to a treatment change in 10 patients (9.4% of the cohort study, 45.5% of the patients with bradyarrhythmias): change in medical therapy in 6 and PPM in 4 patients with HAVB while awake (2 of them with concomitant medical therapy modification). Among those patients treated with PPM, 2 presented symptoms associated with HAVB (shortness of breath), with none of them experiencing dizziness or syncope (Central Illustration).

FACTORS ASSOCIATED WITH ARRHYTHMIC EVENTS. Clinical characteristics of the study population according to the occurrence of arrhythmic events as assessed by 7-day CEM are presented in Table 1. Patients with arrhythmic events more frequently had a history of chronic kidney disease (58.8% vs. 38.2%; p = 0.034), a trend toward a higher prevalence of left ventricular dysfunction (33.3% vs. 18.2%; p = 0.074), and increased aortic valve calcification (Agatston score: 2,394 ± 1,612 vs. 1,947 ± 1,081 Agatston units; p = 0.107). By multivariable logistic regression analysis, the factors determining an increased risk of arrhythmic events were chronic renal failure (odds ratio [OR]: 2.67; 95% confidence interval [CI]: 1.11 to 6.41; p = 0.028), and a higher Agatston calcium score (OR: 1.04; 95% CI: 1.00 to 1.08; p = 0.052 for each increase of 100 Agatston units) and left ventricular dysfunction (OR: 2.50; 95% CI: 0.93 to 6.69; p = 0.069) exhibited a tendency toward an increased risk of arrhythmic events as assessed by 7-day CEM.

The occurrence of significant bradyarrhythmic events during 7-day CEM according to the presence of pre-existing conduction disturbances at baseline ECG

are shown in Figure 2. The presence of first-degree AVB (p = 0.047) and right bundle branch block (RBBB) (p = 0.008), but not left bundle branch block (LBBB) or nonspecific intraventricular conduction disturbances (p = 0.910 and p = 0.831, respectively) were associated with a higher incidence of bradyarrhythmic events at CEM.

ARRHYTHMIC EVENTS POST-TAVR. Among the 106 TAVR candidates that underwent 7-day CEM, 7 and 8 patients were finally referred to surgical valve replacement and conservative management (frailty condition or excessive comorbidity burden) after heart team evaluation, respectively (Figure 1). One additional patient, with pre-existing first-degree AVB and a nonspecific intraventricular conduction disturbance, died before the TAVR procedure from sudden death. This led to a total of 90 patients who finally underwent elective TAVR. The main procedural and 30-day outcomes of TAVR are outlined in Table 3. At 30 days, there was 1 (1.1%) noncardiac death and 1 (1.1%) stroke in another patient with history of AF and no relevant arrhythmic events detected on pre-procedural 7-day CEM. Nineteen (21.1%) patients developed new onset persistent LBBB post-TAVR, and new onset AF post-TAVR occurred in 3 (3.3%) patients. Significant bradyarrhythmias requiring PPM after TAVR occurred in 17 (18.9%) patients. Fifteen (16.7%) patients presented HAVB or complete heart block post-TAVR, 1 patient had alternant RBBB and LBBB, and another patient had sinus node dysfunction.

In one-third of the patients with new onset arrhythmic events post-TAVR (AF, bradyarrhythmic events requiring PPM), significant arrhythmic events had already been diagnosed during pre-procedural 7-day CEM (Figure 3). Frequent episodes of silent ESVEA (not meeting the criteria for AF) were identified during CEM pre-TAVR in 1 of the 3 patients with new onset AF post-TAVR. Similarly, significant bradyarrhythmias had been previously detected with CEM pre-TAVR in 5 of 17 (29.4%) patients requiring a PPM within 30 days post-TAVR and in 9 of 21 (42.9%) patients receiving a PPM because of severe bradyarrhythmias either before or after the procedure. Among those patients with pre-existing first-degree AVB or RBBB, and concomitant severe bradyarrhythmias during CEM pre-TAVR, 66.7% and 50.0% required PPM implantation before or after TAVR, respectively.

TABLE 2 New Onset AEs Observed During 1-Week Continuous Electrocardiographic Monitoring With CardioSTAT Before TAVR (N = 106)

Duration of CardioSTAT, days	7 (6–7)
Global arrhythmic burden	
Patients with new AEs	51 (48.1)
Patients with new AEs requiring therapeutic changes	14 (13.2)
AEs recorded per patient	2 (1–6)
Noise, %	9.8 (5.2–19.3)
HR, beats/min	68 ± 10
Tachyarrhythmias	
Time in tachycardia (HR >100 beats/min), %	1.6 (0.4–6.1)
Patients with tachyarrhythmic events	37 (34.9)
Symptomatic tachyarrhythmias	1/37 (2.7)
Atrial arrhythmias*	8/79 (10.1)
Atrial tachycardia (>30 s)	2/79 (2.5)
AF (>30 s)	6/79 (7.6)
Duration of AF episodes	
≥30 s	6 (100)
≥6 min	2 (33.3)
≥30 min	1 (16.7)
Ventricular arrhythmias	31 (29.2)
Nonsustained VT (≥3 beats, >100 beats/min)	31 (29.2)
≥3 beats	28 (26.4)
>6 s	3 (2.8)
Sustained VT (>30 s)	0 (0)
Tachyarrhythmias requiring therapeutic changes	5 (4.7)
Anticoagulation therapy	4 (3.8)
Antiarrhythmic therapy	1 (0.9)
Bradyarrhythmias	
Time in bradycardia (HR <60 beats/min), %	16.4 (2.6–49.2)
Patients with bradyarrhythmic events	22 (20.8)
Symptomatic bradyarrhythmias	2/22 (9.1)
HAVB	2 (1.9)
HAVB + severe bradycardia	4 (3.8)
Severe bradycardia	16 (15.1)
Bradyarrhythmias requiring therapeutic changes	10 (9.4)
Change in medical therapy	6 (5.7)
Change in medical therapy + PPM pre-TAVR	2 (1.9)
PPM pre-TAVR	2 (1.9)

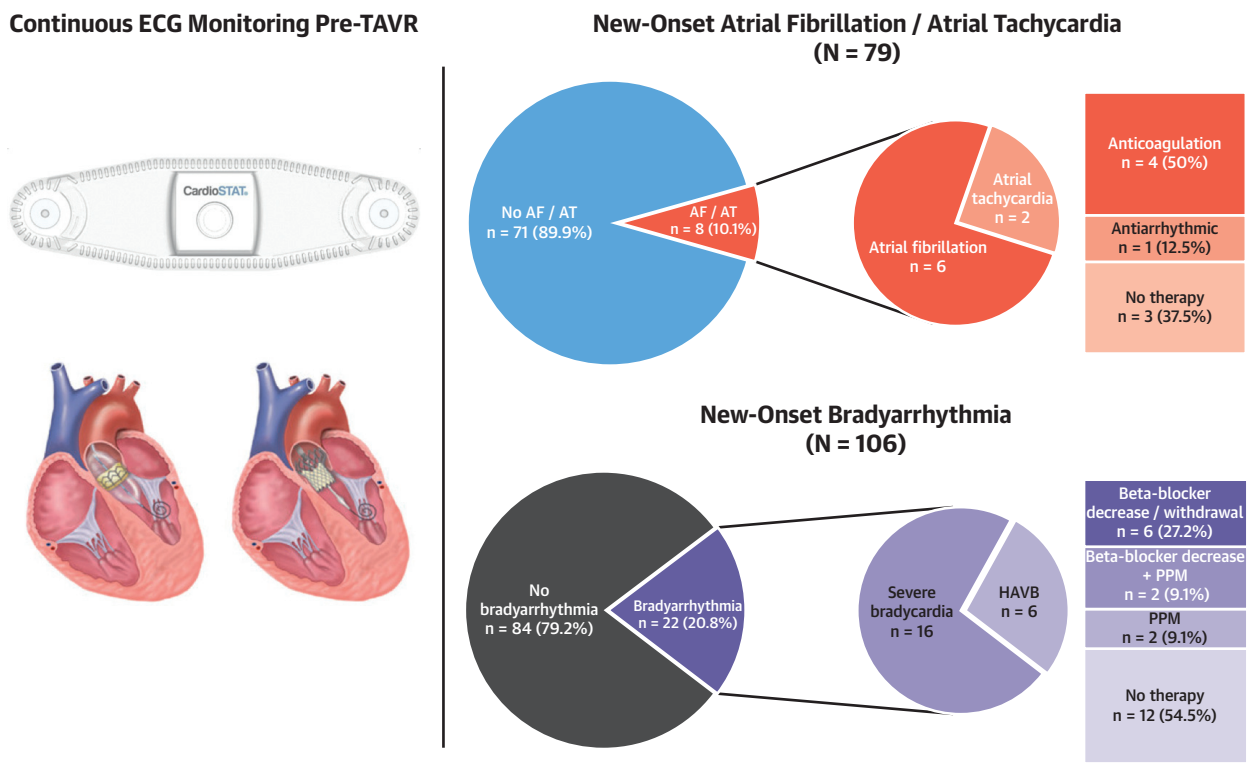
Values are median (interquartile range), n (%), mean ± SD, or n/N (%). *Only patients without prior AF or atrial tachycardia in the denominator.

AE = arrhythmic event; AF = atrial fibrillation; HR = heart rate; PPM = permanent pacemaker; TAVR = transcatheter aortic valve replacement; VT = ventricular tachycardia.

DISCUSSION

The results of this first study evaluating the usefulness of pre-procedural prolonged CEM in patients with severe aortic stenosis screened for TAVR can be summarized as follows: 1) 1 of 10 patients exhibited subclinical episodes of AF or AT, and a therapeutic change (anticoagulation or antiarrhythmic therapy) was implemented in close to two-thirds of such patients; 2) significant bradyarrhythmias were detected in ~20% of patients (HAVB in about one-fourth of the cases), with treatment changes and PPM required in approximately one-half and one-fifth of them, respectively; and 3) pre-TAVR CEM allowed early

CENTRAL ILLUSTRATION **New-Onset Arrhythmic Events Pre-TAVR and Associated Therapeutic Changes**



Asmarats, L. et al. J Am Coll Cardiol Intv. 2020;13(15):1763–73.

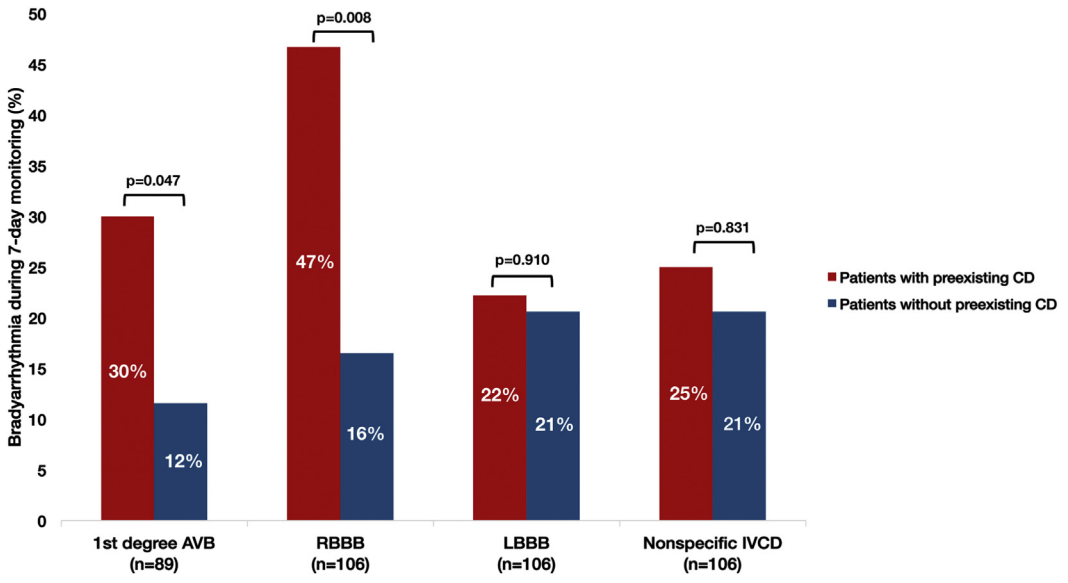
Patients with newly diagnosed atrial fibrillation (AF) or atrial tachycardia (AT) (79 patients with no prior history of AF or AT) **(top right)** using the CardioSTAT device within the 3 months before the transcatheter aortic valve replacement (TAVR) procedure. Patients with newly diagnosed significant bradyarrhythmia **(bottom right)**. ECG = electrocardiographic; PPM = permanent pacemaker.

arrhythmia diagnosis in about one-third of the patients with new onset arrhythmic events post-TAVR.

A high arrhythmic burden has been shown in elderly patients with calcific aortic valve stenosis (6,15). Progressive pathophysiological changes such as calcium deposit on the conduction system, along with increased left ventricular overload resulting in left ventricular hypertrophy or fibrosis and left atrium overload, have been suggested to play a role in the pathogenesis of dysrhythmias in this population (16,17). Urena et al. (6) identified previously unknown arrhythmias in 16% of TAVR candidates who had 24-h ECG monitoring the day before the procedure (paroxysmal AF or AT in 10.5% of patients without known AF or AT, NSVT in 6.0%, significant bradyarrhythmias in 6.4% patients without prior PPM), resulting in therapeutic changes in 43% of such patients. Nevertheless, the efficacy of arrhythmic detection by monitoring devices depends on the duration and method of ECG monitoring, and 24-h ECG Holter exhibits moderate sensitivity (44% to 66%) compared with longer event recorders (>90%) (7,9). Notably, the use of 7-day CEM in the present study translated into a higher diagnostic yield for the detection of previously unknown arrhythmias (overall 48.1%; paroxysmal AF or AT in 10.1%, NSVT in 29.2%, significant bradyarrhythmias in 20.8%).

The prevalence of silent AF in the elderly has ranged between 1.5% and 14%, depending on type and duration of ECG monitoring (9). Of note, asymptomatic AF detection increases in higher-risk populations (e.g., history of stroke, patients with structural heart disease) and extended duration of ECG monitoring (≥7 days), and it has been associated with a worse prognosis, given the potential delay in anticoagulation prescription in the absence of symptoms (18). Importantly, the occurrence of ESVEA has been strongly associated with an increased risk of incident AF, stroke, and mortality (9). In the present study, the prevalence of newly diagnosed ESVEA and

FIGURE 2 Incidence of Bradyarrhythmic Events During 7-Day Ambulatory Cardiac Monitoring Pre-TAVR According to Pre-Existing CDs at Baseline Electrocardiogram



Occurrence of relevant bradyarrhytmic events during 7-day ECG monitoring pre-TAVR according to baseline ECG. Pre-existing 1st-degree atrioventricular block (AVB) and right bundle branch block (RBBB), but not left bundle branch block (LBBB)/intraventricular conduction disturbance (IVCD), associated with a higher incidence of arrhythmic events. CD = conduction disturbance; other abbreviations as in Figure 1.

paroxysmal AF were 32.9% and 7.6%, respectively, but was not associated with an increased risk for stroke (occurring in 1 single patient with prior history of AF). Interestingly, new onset AF post-TAVR occurred in 3 patients, of whom 1 had ESVEA during preprocedural 7-day CEM. Whereas ESVEA has been considered a surrogate marker for paroxysmal AF, future studies are needed to evaluate whether intensive risk factor or therapeutic modification in these patients could improve outcomes or mitigate the progression from supraventricular ectopy to AF.

Whether to initiate anticoagulation in patients with device-detected AF remains controversial. In the present study, anticoagulation treatment was initiated in 4 patients with newly diagnosed episodes of AF and high stroke risk (mean CHA_2DS_2-VASc [congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, prior stroke or transient ischemic attack or thromboembolism, vascular disease, age 65 to 74 years, sex category] score: 5.5). Although a device-detected threshold of >5.5 h has been suggested for anticoagulation initiation for patients with long-term CEM (i.e., cardiac implantable electronic devices) (9), it seems prudent to offer a much lower threshold for patients undergoing CEM of shorter duration, and current guidelines recommend that patients with AF should be given oral anticoagulants, irrespective of paroxysmal (≥30 s) or persisting AF (10). Of note, integration of AF burden and CHA_2DS_2-VASc score is crucial in the decision to prescribe anticoagulation, with recent studies suggesting an increased risk of thromboembolic events in patients with CHA_2DS_2-VASc score ≥5, regardless of device-detected AF duration (19). Further trials are needed to determine the minimal duration of AF needed to warrant anticoagulation initiation.

A high prevalence of ventricular arrhythmias has been classically described in patients with severe aortic stenosis (17). The prevalence of pre-existing NSVT in TAVR recipients, defined according to current guidelines, has been established between 6.0% and 9.6% in previous studies using short 24-h ECG monitoring before the procedure (6,20), and up to 13% (episodes >6 s) within the year post-TAVR by implantable CEM (15). A higher rate of NSVT was observed in the present study (29.2%), mainly attributable to extended ECG recording, although most episodes (90%) lasted <6 s (none sustained), and did not lead to pre-TAVR therapeutic measures. One patient with mild left ventricular dysfunction,

TABLE 3 Procedural and 30-Day Outcomes in Patients Undergoing TAVR, Overall and According to the Occurrence of AEs During 7-Day Continuous Electrocardiographic Monitoring Pre-TAVR

	Overall (N = 90)	New AEs (n = 41)	No AEs (n = 49)	p Value
Procedural findings				
Valve type				
Balloon-expandable valve	58 (64.4)	29 (70.7)	29 (59.2)	0.254
Self-expandable valve	32 (35.6)	12 (29.3)	20 (40.8)	
Approach				
Transfemoral	55 (61.1)	22 (53.7)	33 (67.4)	0.185
Non-transfemoral	35 (38.9)	19 (46.3)	16 (32.7)	
Valve size, mm	26.6 ± 2.7	26.5 ± 2.7	26.7 ± 2.7	0.663
Valve-in-valve	5 (5.6)	2 (4.9)	3 (6.1)	1.000
Pre-dilatation	9 (10.0)	6 (14.6)	3 (6.1)	0.180
Post-dilatation	17 (18.9)	8 (19.5)	9 (18.4)	0.890
Procedural success	88 (97.8)	40 (97.6)	48 (98.0)	0.898
30-day outcomes				
All-cause death	1 (1.1)	0 (0.0)	1 (2.0)	1.000
Cardiovascular death	0 (0)	0 (0)	0 (0)	–
Stroke	1 (1.1)	0 (0.0)	1 (2.0)	1.000
Myocardial infarction	2 (2.2)	1 (2.4)	1 (2.0)	1.000
Major or life-threatening bleeding	6 (6.7)	2 (4.9)	4 (8.2)	0.685
AEs				
New onset AF*	3 (4.5)	2 (7.7)	1 (2.4)	0.555
Severe bradyarrhythmias requiring PPM	17 (18.9)	8 (19.5)	9 (18.4)	0.890
HAVB/CHB	15 (16.7)	7 (17.1)	8 (16.3)	0.925
Alternant RBBB + LBBB	1 (1.1)	1 (2.4)	0 (0.0)	0.456
Sick sinus syndrome	1 (1.1)	0 (0.0)	1 (2.0)	1.000

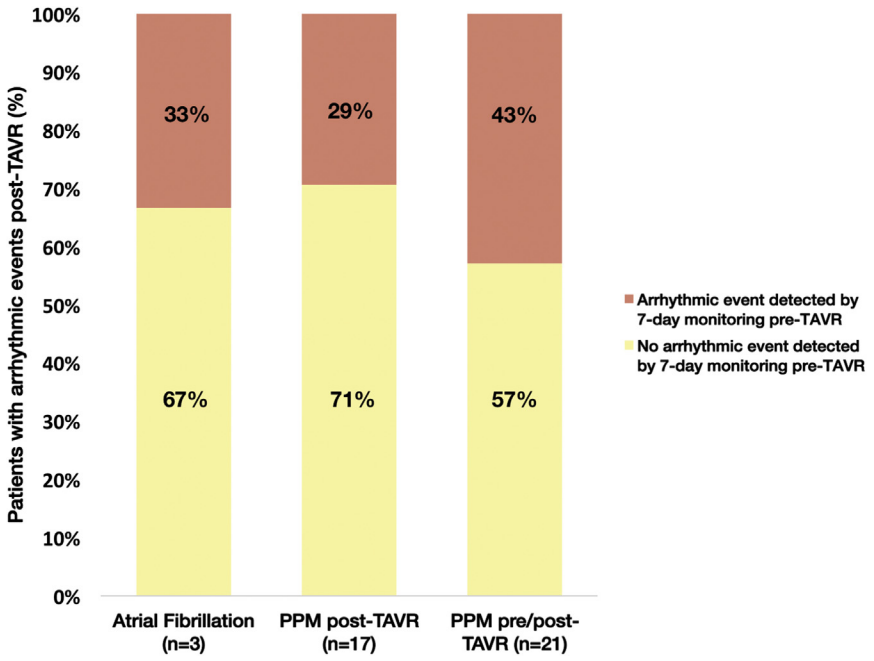
Values are n (%) or mean ± SD. No patient was lost to follow-up. *Patients with no history of AF (n = 67).
CHB = complete heart block; HAVB = high-degree atrioventricular block; LBBB = left bundle branch block; RBBB = right bundle branch block; other abbreviations as in Table 2.

newly diagnosed AF and NSVT during pre-TAVR CEM, died before the procedure, although no definite arrhythmic cause could be confirmed at the time of sudden death. Larger studies are needed to assess the potential association between pre-existing ventricular arrhythmias and sudden cardiac death in patients undergoing TAVR.

The prevalence of pre-existing significant bradyarrhythmias—severe bradycardia or HAVB—in TAVR candidates was higher (20.8%) than previously reported (5.5% in overall patients and 6.4% in patients without prior PPM) (6). This translates into a number needed to screen of 5 TAVR candidates to diagnose 1 previously unknown significant bradyarrhythmia (18 patients to diagnose 1 HAVB before TAVR). Of note, therapeutic intervention was required in one-half of the patients with bradyarrhythmias during 7-day CEM before the procedure. Additionally, and in accordance with previous studies (6), CEM pre-TAVR allowed prompt identification of previously unknown bradyarrhythmias in approximately one-third of patients requiring PPM post-TAVR (possibly not related to the procedure but already pre-existent in this high-risk population), although CEM seemed to fail reducing the global rate of PPM post-TAVR. Indeed, the rate of significant bradyarrhythmias requiring PPM after TAVR in the present study was high (18.9%), which may be explained by several factors. First, unlike our study, most studies to date have not excluded patients with prior PPM when reporting post-TAVR PPM rates (denominator including patients with an intracardiac device at baseline), leading to a systematic underestimation of the real incidence of PPM post-TAVR (21). Second, the SAPIEN 3 valve (Edwards Lifesciences, Irvine, California)—for which higher rates of PPM have been reported compared with SAPIEN XT valves—was used in 58% of the TAVR procedures, which may have influenced the rate of PPM in the present study (22). Indeed, the reported PPM rates with the SAPIEN 3 valve have been higher than 10%, almost double than the rates generally observed with previous-generation balloon-expandable valves (4). This phenomenon may be due to either its design (bulkier skirt aimed to reduce paravalvular regurgitation, longer stent frame) or a potential learning curve effect with the new-generation valve likely related to valve positioning issues (too low ventricular positioning in the initial experience with this valve type) (22). Of note, a trend toward a reduction in the need for PPM was observed throughout the study period, from 23.1% to 7.7% when comparing the first with the second half of SAPIEN 3 valve implantations ($p = 0.124$).

Chronic kidney disease was the strongest predictor of new onset arrhythmic events during preprocedural ambulatory CEM. It is well known that patients with chronic renal disease are predisposed to heart rhythm disorders, including AF (16% to 21% in patients not dependent on dialysis, 15% to 40% in patients on dialysis), ventricular arrhythmias, and sudden cardiac death, with annual rates of sudden death in nondialysis patients comparable to that of post-infarction patients (23). Several mechanisms have been proposed to explain this relationship: common risk factors, long-standing abnormalities predisposing to arrhythmogenic conditions, myocardial ischemia, volume shifts, or left ventricular hypertrophy and dysfunction. Also, there was a trend toward increased pre-TAVR arrhythmic burden in patients with left ventricular dysfunction, as previously shown by Urena et al. (6), and in several previous studies evaluating patients with aortic stenosis (24,25). Likewise, calcium deposition at the level of the conduction system in patients with calcific aortic stenosis could translate into prolonged His-ventricular intervals and HAVB (26), partially

FIGURE 3 New Onset Atrial Fibrillation and Need for Pacemaker According to the Occurrence of Previously Unknown Arrhythmic Events During 7-Day Cardiac Monitoring Pre-TAVR



Continuous ECG monitoring pre-TAVR identified early arrhythmic events in 33% of the patients with new-onset atrial fibrillation post-TAVR, and in 29% and 43% of the patients requiring a pacemaker post-TAVR or pre-/post-TAVR, respectively. Abbreviations as in Figure 1.

explaining the observed trend toward increased pre-existing unknown arrhythmias in patients with severe valve calcification.

Patients with pre-existing first-degree AVB or RBBB exhibited higher rates of new onset bradyarrhythmic events during the 7-day CEM pre-TAVR, although the relatively small sample size and number of bradyarrhythmic events observed precluded the assessment of independent predictive factors. Of note, the presence of first-degree AVB and RBBB have been associated with increased risk of PPM (4- to 11-fold, and 3- to 47-fold, respectively), the latter being the strongest and most consistent predictor of PPM post-TAVR in the literature (5). This raises the question whether this subset of patients may particularly benefit from pre-TAVR screening strategy with long-term CEM to improve detection of severe subclinical bradyarrhythmias before TAVR, although larger studies are warranted to further evaluate these findings.

STUDY LIMITATIONS. This was a single-center study, and potential variations in the arrhythmic burden related to geographic patterns cannot be ruled out and may limit generalizability of our findings. Second, a significant portion (one-fourth) of the study patients had previously documented AF, although none of those patients had a prior PPM. Third, the single-lead design of the ambulatory CEM used in the present study did not allow the assessment of the incidence of new-onset LBBB before the TAVR procedure. Last, the relatively limited sample size of the study precluded the evaluation of the predictive factors associated with newly diagnosed tachyarrhythmic and bradyarrhythmic events (analyzed separately).

CONCLUSIONS

Nearly one-half of elderly patients with severe symptomatic aortic stenosis presented newly diagnosed arrhythmic events during 7-day CEM pre-TAVR. Paroxysmal AF or AT and significant bradyarrhythmias were observed in one-tenth and one-fifth of patients, respectively, with pharmacological or

invasive intervention required in about half of them. These findings support the usefulness of CEM for the early diagnosis and treatment of arrhythmic events in TAVR candidates. Also, they open the door to further studies evaluating the possibility of tailored CEM pre-TAVR in selected populations with certain baseline clinical features (e.g., chronic renal failure, left ventricular dysfunction, higher valve calcification) or pre-existing conduction disturbances (first-degree AVB, RBBB).

ADDRESS FOR CORRESPONDENCE: Dr. Josep Rodés-Cabau, Quebec Heart and Lung Institute, Laval University, 2725 Chemin Ste-Foy, Quebec City, Quebec G1V 4GS, Canada. E-mail: josep.rodes@criucpq.ulaval.ca. Twitter: @IUCPQ.

PERSPECTIVES

WHAT IS KNOWN? TAVR candidates are at risk of developing cardiac arrhythmias.

WHAT IS NEW? Pre-TAVR prolonged CEM detects previously unknown arrhythmic events in nearly 50% of the patients and allows prompt therapy implementation in nearly one-fourth of them.

WHAT IS NEXT? Further studies are needed to evaluate the role of tailored CEM in selected high-risk populations (pre-existing conduction disturbances [RBBB], chronic renal failure, or increased valve calcification).

REFERENCES

1. Puri R, Chamandi C, Rodriguez-Gabella T, Rodes-Cabau J. Future of transcatheter aortic valve implantation - evolving clinical indications. Nat Rev Cardiol 2018;15:57–65.

2. Mack MJ, Leon MB, Thourani VH, et al. Transcatheter aortic-valve replacement with a balloon-expandable valve in low-risk patients. N Engl J Med 2019;380:1695–705.

3. Popma JJ, Deeb GM, Yakubov SJ, et al. Transcatheter aortic-valve replacement with a self-expanding valve in low-risk patients. N Engl J Med 2019;380:1706–15.

4. Auffret V, Puri R, Urena M, et al. Conduction disturbances after transcatheter aortic valve replacement: current status and future perspectives. Circulation 2017;136:1049–69.

5. Rodes-Cabau J, Ellenbogen KA, Krahn AD, et al. Management of conduction disturbances associated with transcatheter aortic valve replacement: JACC Scientific Expert Panel. J Am Coll Cardiol 2019;74:1086–106.

6. Urena M, Hayek S, Cheema AN, et al. Arrhythmia burden in elderly patients with severe aortic stenosis as determined by continuous electrocardiographic recording: toward a better understanding of arrhythmic events after transcatheter aortic valve replacement. Circulation 2015;131:469–77.

7. Rosero SZ, Kutyifa V, Olshansky B, Zareba W. Ambulatory ECG monitoring in atrial fibrillation management. Prog Cardiovasc Dis 2013;56:143–52.

8. Nault I, Andre P, Plourde B, et al. Validation of a novel single lead ambulatory ECG monitor - Cardiostat - compared with a standard ECG Holter monitoring. J Electrocardiol 2019;53:57–63.

9. Gorenek BC, Bax J, Boriani G, et al. Device-detected subclinical atrial tachyarrhythmias: definition, implications and management-an European Heart Rhythm Association (EHRA) consensus document, endorsed by Heart Rhythm Society (HRS), Asia Pacific Heart Rhythm Society (APHRS) and Sociedad Latinoamericana de Estimulacion Cardiaca y Electrofisiologia (SOLEACE). Europace 2017;19:1556–78.

10. Kirchhof P, Benussi S, Kotecha D, et al. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Eur Heart J 2016;37. 2893–62.

11. Al-Khatib SM, Stevenson WG, Ackerman MJ, et al. 2017 AHA/ACC/HRS Guideline for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death. J Am Coll Cardiol 2018;72:e91–220.

12. Epstein AE, DiMarco JP, Ellenbogen KA, et al. 2012 ACCF/AHA/HRS focused update incorporated into the ACCF/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol 2013;61:e6–75.

13. Kusumoto FM, Schoenfeld MH, Barrett C, et al. 2018 ACC/AHA/HRS Guideline on the Evaluation and Management of Patients With Bradycardia and Cardiac Conduction Delay: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol 2019;74:e51–156.

14. Kappetein AP, Head SJ, Genereux P, et al. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document. Eur Heart J 2012;33:2403–18.

15. Rodes-Cabau J, Urena M, Nombela-Franco L, et al. Arrhythmic burden as determined by ambulatory continuous cardiac monitoring in patients with new-onset persistent left bundle branch block following transcatheter aortic valve replacement: the MARE study. J Am Coll Cardiol Intv 2018;11:1495–505.

16. Wolfe RR, Driscoll DJ, Gersony WM, et al. Arrhythmias in patients with valvar aortic stenosis, valvar pulmonary stenosis, and ventricular septal defect. Results of 24-hour ECG monitoring. Circulation 1993;87:189–101.

17. Sorgato A, Faggiano P, Aurigemma GP, Rusconi C, Gaasch WH. Ventricular arrhythmias in adult aortic stenosis: prevalence, mechanisms, and clinical relevance. Chest 1998;113:482–91.

18. Potpara TS, Polovina MM, Marinkovic JM, Lip GY. A comparison of clinical characteristics and long-term prognosis in asymptomatic and symptomatic patients with first-diagnosed atrial fibrillation: the Belgrade Atrial Fibrillation Study. Int J Cardiol 2013;168:4744–9.

19. Kaplan RM, Koehler J, Ziegler PD, Sarkar S, Zweibel S, Passman RS. Stroke risk as a function of atrial fibrillation duration and CHA2DS2-VASc score. Circulation 2019;140:1639–46.

20. Tempio D, Pruiti GP, Conti S, et al. Ventricular arrhythmias in aortic valve stenosis before and after transcatheter aortic valve implantation. Europace 2015;17:1136–40.

21. Chamandi C, Regueiro A, Auffret V, et al. Reported versus "real" incidence of new pacemaker implantation post-transcatheter aortic valve replacement. J Am Coll Cardiol 2016;68:2387–9.

22. De Torres-Alba F, Kaleschke G, Diller GP, et al. Changes in the pacemaker rate after transition

from Edwards SAPIEN XT to SAPIEN 3 transcatheter aortic valve implantation: the critical role of valve implantation height. J Am Coll Cardiol Intv 2016;9:805–13.

23. Turakhia MP, Blankestijn PJ, Carrero JJ, et al. Chronic kidney disease and arrhythmias: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference. Eur Heart J 2018;39:2314–25.

24. MacMillan RM, Demorizi NM, Gessman LJ, Maranhao V. Correlates of prolonged HV conduction in aortic stenosis. Am Heart J 1985;110:56–60.

25. Widgren V, Dencker M, Juhlin T, Platonov P, Willenheimer R. Aortic stenosis and mitral regurgitation as predictors of atrial fibrillation during 11 years of follow-up. BMC Cardiovasc Disord 2012;12:92.

26. Yater WM, Cornell VH. Heart block due to calcareous lesions of the bundle of His: review and report of a case with detailed histopathologic study. Ann Intern Med 1935;8:777–89.

KEY WORDS ambulatory electrocardiographic, aortic valve stenosis, arrhythmia, monitoring, pacemaker, transcatheter aortic valve replacement