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FOCUS ON ARRHYTHMIA AFTER TRANSCATHETER AORTIC VALVE REPLACEMENT

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

Josep Rodés-Cabau, MD,[a] Marina Urena, MD, PhD,[b] Luis Nombela-Franco, MD, PhD,[c] Ignacio Amat-Santos, MD, PhD,[d] Neal Kleiman, MD,[e] Antonio Munoz-Garcia, MD, PhD,[f] Felipe Atienza, MD, PhD,[g] Vicenç Serra, MD,[h] Marc W. Deyell, MD,[i] Gabriela Veiga-Fernandez, MD,[j] Jean-Bernard Masson, MD,[k] Victoria Canadas-Godoy, MD,[c] Dominique Himbert, MD,[b] Javier Castrodeza, MD,[d] Jaime Elizaga, MD,[g] Jaume Francisco Pascual, MD,[h] John G. Webb, MD,[i] Jose Maria de la Torre, MD,[j] Lluis Asmarats, MD,[a] Emilie Pelletier-Beaumont, MSc,[a] François Philippon, MD[a]

ABSTRACT

OBJECTIVES The authors sought to determine: 1) the global arrhythmic burden; 2) the rate of arrhythmias leading to a treatment change; and 3) the incidence of high-degree atrioventricular block (HAVB) at 12-month follow-up in patients with new-onset persistent left bundle branch block (LBBB) following transcatheter aortic valve replacement (TAVR).

BACKGROUND Controversial data exist on the occurrence of significant arrhythmias in patients with LBBB post-TAVR.

METHODS This was a multicenter prospective study including 103 consecutive patients with new-onset persistent LBBB post-TAVR with the balloon-expandable SAPIEN XT/3 valve (n = 53), or the self-expanding CoreValve/Evolut R system (n = 50). An implantable cardiac monitor (Reveal XT, Reveal Linq) was implanted at 4 (3 to 6) days post-TAVR, and patients had continuous electrocardiogram monitoring for 12 months. All arrhythmic events were adjudicated in a central electrocardiography core lab. Primary endpoints were the incidence of arrhythmias leading to a treatment change, and the incidence of HAVB at 12-month follow-up.

RESULTS A total of 1,553 new arrhythmic events were detected in 44 patients (1,443 episodes of tachyarrhythmia in 26 patients [atrial fibrillation/flutter/atrial tachycardia: 1,427, ventricular tachycardia 16]; 110 episodes of bradyarrhythmia in 21 patients [HAVB 54, severe bradycardia 56]). All arrhythmic events were silent in 34 patients (77%), the arrhythmic event led to a treatment change in 19 patients (18%), and 11 patients (11%) required pacemaker or implantable cardioverter-defibrillator implantation (due to HAVB, severe bradycardia, or ventricular tachycardia episodes in 9, 1, and 1 patient, respectively). A total of 12 patients died at 1-year follow-up, 1 from sudden death.

CONCLUSIONS A high incidence of arrhythmic events was observed at 1-year follow-up in close to one-half of the patients with LBBB post-TAVR. Significant bradyarrhythmias occurred in one-fifth of the patients, and PPM was required in nearly one-half of them. These data support the use of a cardiac monitoring device for close follow-up and expediting the initiation of treatment in this challenging group of patients. (Ambulatory Electrocardiographic Monitoring for the Detection of High-Degree Atrio-Ventricular Block in Patients With New-onset PeRsistent LEft Bundle Branch Block After Transcatheter Aortic Valve Implantation [MARE study]: NCT02153307)
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ABBREVIATIONS AND ACRONYMS

ACC/AHA/HRS = American College of Cardiology/American Heart Association/Heart Rhythm Society

AF = atrial fibrillation

AFL = atrial flutter

ECG = electrocardiogram

HAVB = high-degree atrioventricular block

ICD = implantable cardioverter-defibrillator

ILR = implantable loop recorders

IQR = interquartile range

LBBB = left bundle branch block

PPM = permanent pacemaker implantation

TAVR = transcatheter aortic valve replacement

Transcatheter aortic valve replacement (TAVR) has become a well-accepted option for treating patients with aortic stenosis at intermediate-to-high surgical risk. However, conduction disturbances, particularly new-onset left bundle branch block (LBBB), remain the most frequent complication of TAVR (1). New-onset LBBB has been reported in about one-fourth of TAVR procedures, with a varying incidence across different studies and valve types (1). Although the impact of LBBB post-TAVR on clinical outcomes remains controversial, some studies have suggested an increased risk of cardiovascular death and sudden death in patients with new-onset LBBB (2–4). Also, conflicting results have been reported regarding the risk of high-degree atrioventricular block (HAVB) and the need for permanent pacemaker implantation (PPM) at midterm follow-up in those patients leaving the hospital with a new LBBB after the TAVR procedure (1,5–7). In fact, the real incidence of late HAVB (silent, symptomatic) in these patients remains largely unknown.

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Implantable loop recorders (ILR) with prolonged electrocardiogram (ECG) monitoring have recently emerged as valuable tools for the diagnosis of transient arrhythmic events with recognized advantages compared with traditional methods of external ECG monitoring (8,9). The use of ILR have also been demonstrated in patients with syncope and bundle branch block (10). However, the usefulness of ILR devices in the setting of TAVR, and particularly among patients with conduction disturbances following the procedure, has not been evaluated yet. The objectives of this study were to determine, with the use of ILR in patients with new-onset persistent LBBB post-TAVR: 1) the global arrhythmic burden; 2) the incidence of significant arrhythmias leading to a treatment change; and 3) the incidence of HAVB at 12-month follow-up.

METHODS

STUDY DESIGN AND PATIENTS. This was a prospective multicenter study including patients undergoing TAVR with either self- or balloon-expandable valves (CoreValve or Evolut R [Medtronic, Minneapolis, Minnesota]; Edwards SAPIEN XT or SAPIEN 3 [Edwards Lifesciences, Irvine, California]). Patients receiving other transcatheter valve types were excluded. Following the procedure, patients were on continuous ECG monitoring during the hospitalization period (or at least during 72 h), and a 12-lead ECG was performed daily until hospital discharge in all patients. Patients with new-onset LBBB that persisted ≥3 days post-TAVR received a Reveal ICM XT or LINQ device as ILR before hospital discharge. LBBB was defined according to the American College of Cardiology/American Heart Association/Heart Rhythm Society (ACC/AHA/HRS) recommendations (11). The device was implanted subcutaneously in the most appropriate position to record adequate QRS and P complexes. Details on the Reveal XT and LINQ devices have been provided elsewhere (12,13). Patients with PPM or LBBB before TAVR and those who had PPM or died in the periprocedural period post-TAVR were excluded.

Patients were followed during 12 months, and in-office visits and 12-lead ECG were performed at 1- and 12-month follow-up. Automatic wireless transmission of data (daily reports, alerts, monthly complete reports) was obtained in those patients with

From the [a]Department of Cardiology, Quebec Heart & Lung Institute, Laval University, Quebec City, Quebec, Canada; [b]Department of Cardiology, Assistance Publique-Hôpitaux de Paris, Höpital Bichat-Claude Bernard, Paris, France; [c]Instituto Cardiovascular, Hospital Clinico San Carlos, IdISSC, Madrid, Spain; [d]Department of Cardiology, Hospital Universitario de Valladolid, Valladolid, Spain; [e]Department of Cardiology, Hospital Virgen de la Victoria, Málaga, Spain; [f]Department of Cardiology, Houston Methodist DeBakey Heart and Vascular Center, Houston, Texas; [g]Department of Cardiology, Hospital General Universitario Gregorio Marañón, Madrid, Spain; [h]Department of Cardiology, Hospital Universitari Vall d'Hebron, Barcelona, Spain; [i]Department of Cardiology, St Paul's Hospital, Vancouver, British Columbia, Canada; [j]Department of Cardiology, Hospital Marques de Valdecilla, Santander, Spain; and the [k]Department of Cardiology, Centre Hospitalier Universitaire de Montreal, Montreal, Quebec, Canada.
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the Reveal LINQ device. Device interrogation at 1-, 3-, 6-, 9-, and 12-month follow-up was performed in those patients who received the Reveal XT device. Clinical events were also recorded and classified according to VARC-2 (Valve Academic Research Consortium-2) recommendations (14).

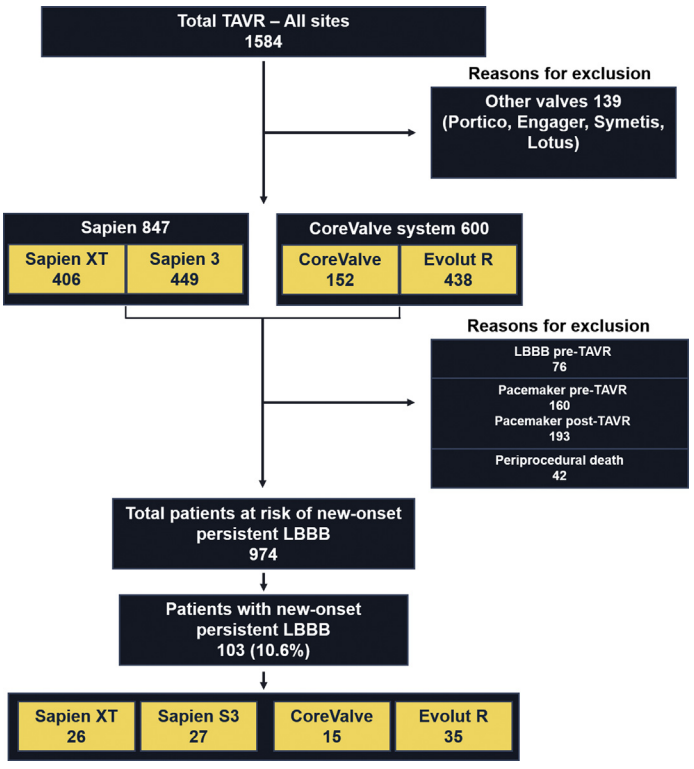
The study was conducted in 11 centers in Canada, Europe, and the United States, from June 2014 to July 2016. The study was approved by the institutional ethics committee of each participating center, and all patients provided signed informed consent before participation in the study.

OUTCOMES. The primary outcomes were incidence of adjudicated arrhythmic events leading to a treatment change at 12-month follow-up, and incidence of adjudicated HAVB at 12-month follow-up. Secondary endpoints were the incidence of significant arrhythmic episodes (irrespective of symptoms or treatment changes), significant tachyarrhythmias, significant bradyarrhythmias, and atrial fibrillation (AF)/atrial flutter (AFL) episodes. The occurrence of arrhythmic episodes was also analyzed according to valve type (CoreValve/Evolut R system or SAPIEN XT/3 valve). The records of all arrhythmic episodes and 12-lead ECGs (baseline, 1-month, 12-month follow-up) were analyzed in a central ECG laboratory, and all episodes/ECGs were adjudicated by an experienced electrophysiologist (F.P.).

Significant arrhythmias were defined according to the ACC/AHA/HRS guidelines (15) and classified as: 1) significant bradyarrhythmia (HAVB, severe bradycardia due to sinus node dysfunction); 2) AF/AFL/atrial tachycardia/supraventricular tachycardia episodes lasting >30 s; 3) ventricular tachycardia (non-sustained: lasting between 6 and 30 s; sustained: lasting ≥30 s); and 4) ventricular fibrillation. The initial diagnosis and management of arrhythmic events was a responsibility of the investigators of each participating center. It was strongly recommended that investigators follow the ACC/AHA/HRS guidelines regarding the indications for PPM and implantable cardioverter-defibrillator (ICD) implantation (15).

STATISTICAL ANALYSIS. There were no prior studies of continuous ECG post-TAVR at the time of study design. The sample size was therefore empirically estimated at 80 patients. It was considered that this sample size would permit an appropriate description of the arrhythmic events occurring in these patients. The sample size was increased to 100 patients to allow a minimum patient enrollment in those centers that were activated late in the study period. It was specified per protocol to include one-half of the patients following TAVR with the self-expanding CoreValve/Evolut R system, and one-half following TAVR with the balloon-expandable SAPIEN XT/SAPIEN 3 valve.

FIGURE 1 Flowchart of the Study Population



LBBB = left bundle branch block; TAVR = transcatheter aortic valve replacement.

Qualitative variables were expressed as percentages and numerical variables as mean ± SD or median (interquartile range [IQR]) according to variable distribution. Categorical variables were compared using the chi-square or Fisher exact test as appropriate. Numerical variables were compared using the *t*-test or Wilcoxon test as appropriate. Event rates over time were summarized using Kaplan-Meier estimates, and log-rank tests were used to perform comparisons between groups. A p value ≤0.05 was considered statistically significant. Statistical analyses were conducted using SAS version 9.4 (SAS Institute, Cary, North Carolina).

RESULTS

The flowchart of the study population is shown in Figure 1. Of 1,584 consecutive TAVR recipients, 610 patients were excluded because of the following reasons: use of other transcatheter valve types (n = 139), LBBB pre-TAVR (n = 76), pacemaker pre-TAVR

TABLE 1 Clinical and Procedural Characteristics of the Study Population

	Overall (N = 103)	Sapien XT/3 (n = 53)	CoreValve/EvolutR (n = 50)	p Value
Age, yrs	80 ± 7	79 ± 8	82 ± 7	0.13
Female	59 (57)	24 (45)	35 (70)	0.01
Hypertension	88 (85)	47 (89)	41 (84)	0.46
Diabetes mellitus	44 (43)	27 (51)	17 (35)	0.10
Coronary artery disease	46 (45)	28 (53)	18 (37)	0.10
Atrial fibrillation (paroxysmal or chronic)	27 (26)	17 (32)	10 (20)	0.20
STS-PROM score, %	5.0 (3.3-7.7)	5.0 (3.1-9.2)	4.7 (3.6-7.1)	0.26
CHADS-VASc score, %	4.7 ± 1.4	4.6 ± 1.5	4.9 ± 1.2	0.39
Baseline treatment				
Beta-blockers	49 (48)	29 (55)	20 (40)	0.14
Calcium channel blockers	30 (29)	17 (32)	13 (27)	0.54
Amiodarone	5 (5)	2 (4)	3 (6)	0.60
Anticoagulation	24 (23)	13 (25)	11 (22)	0.80
ECG				
PR interval, ms	183 ± 36	181 ± 35	186 ± 38	0.51
QRS duration, ms	102 ± 24	103 ± 21	103 ± 27	0.90
Echocardiography				
LVEF, %	56 ± 11	55 ± 11	56 ± 11	0.67
Mean gradient, mm Hg	41 ± 14	41 ± 14	41 ± 15	0.87
Aortic valve area, cm^2	0.70 (0.52-0.82)	0.72 (0.62-0.87)	0.60 (0.50-0.80)	0.19
Valve type				
CoreValve or Evolut R	50 (49)	–	50 (100)	–
CoreValve/Evolut R	15/35	–	15/35	–
Sapien XT or Sapien 3	53 (51)	53 (100)	–	–
Sapien XT/Sapien 3	26/27	26/27	–	–
Approach				
Transfemoral	89 (86)	44 (83)	45 (90)	0.92
Transapical/transaortic	10 (10)	9 (17)	1 (2)	0.01
Subclavian/transcarotid	4 (4)	0 (0)	4 (8)	0.05
New-onset persistent LBBB				
PR interval, ms	197 ± 42	188 ± 32	207 ± 50	0.07
QRS duration, ms	142 ± 20	144 ± 18	141 ± 22	0.40
Time to reveal device, days post-TAVR	4 (3-6)	5 (3-7)	4 (2-6)	0.22
Type of device, XT/LINQ	8/95	5/47	3/45	0.53
Hospitalization length, days	7 (5-8)	7 (6-8)	6 (4-8)	0.71

Values are mean ± SD, n (%), or median (interquartile range).

ECG = electrocardiogram; LBBB = left bundle branch block; LVEF = left ventricular ejection fraction; STS-PROM = Society of Thoracic Surgeons Predicted Risk of Mortality; TAVR = transcatheter aortic valve replacement.

(n = 160), pacemaker post-TAVR (n = 193), or periprocedural death (n = 42). Of the 974 patients at risk, 103 patients (10.6%) presented new-onset persistent LBBB post-TAVR and received either the Reveal XT (8 patients) or Reveal LINQ (95 patients) device at a median of 4 (IQR: 3 to 6) days post-TAVR. The device was implanted with no complications in all cases. The main baseline and procedural characteristics of the study population are shown in **Table 1**. The mean age of the patients was 80 ± 7 years, 57% of them were women, and the median STS-PROM (Society of Thoracic Surgeons Predicted Risk of Mortality) score was 5.0% (IQR: 3.3% to 7.7%). A total of 27 patients (26%) had a history of AF (paroxysmal or chronic). Most procedures (86%) were performed through a transfemoral approach and 50 patients received the CoreValve (n = 15) or Evolut R (n = 35) valves, and 53 patients, the SAPIEN XT (n = 26) or SAPIEN 3 (n = 27) valves. There were no differences in the main characteristics between valve types, except for a higher prevalence of women (p = 0.01) and a lower and higher rate of transapical-transaortic approach (p = 0.01) and subclavian-transcarotid approach (p = 0.05), respectively, in those patients who received a CoreValve/Evolut R valve.

ARRHYTHMIC BURDEN AT 12-MONTH FOLLOW-UP. The main arrhythmic events detected within 12 months are shown in **Table 2**. A total of 1,553 significant arrhythmic events occurred in 44 patients (43%), with a median number of 3 events (1 to 9) per patient. In 19 patients (18%), the arrhythmic episode(s) led to a treatment change within the 12-month period (coprimary endpoint). In 34 patients (77%), all arrhythmic events were silent (not associated with symptoms). There were no significant differences in the global incidence of arrhythmias between valve types (**Table 2**). Kaplan-Meier curves showing the time to first arrhythmic event throughout the study period for all patients and according to valve type are shown in **Figures 2A and 3A**, respectively. The first arrhythmic event occurred within the 30 days following the implantation of the Reveal device in 57% of patients, and in the subsequent months in 43% of patients. No differences were observed between valve types in the global burden or timing of arrhythmic events. The percentage of patients with arrhythmic events at different time periods (overall and according to valve type) up to 12-month follow-up are shown in **Figure 4**. Similar results were obtained when the analyses were restricted to those patients who had transfemoral TAVR (Online Figure 1). The main baseline and procedural characteristics of patients grouped according to the occurrence of at least one arrhythmic event at follow-up are shown in Online Table 1.

A summary of the bradyarrhythmic burden is shown in **Table 2**. A total of 110 episodes of significant bradyarrhythmia (HAVB 54, severe bradycardia 56) occurred in 21 patients (20%) at 12-month follow-up. Ten patients (10%) had at least 1 episode of severe bradycardia, and 15 patients (15%) had at least 1 episode of HAVB (coprimary endpoint). The bradyarrhythmic episode led to a treatment change in 11 patients (11%), with PPM in 10 patients (10%) and change in medical treatment (beta-blocker decrease or withdrawal) in 4 patients (4%). In 16 patients (76% of patients with bradyarrhythmias), all

bradyarrhythmic events were silent. There were no differences between valve types in the rate of bradyarrhythmic events. The time to first bradyarrhythmic episode overall and according to valve type is shown in **Figures 2B and 3B**, respectively. The first bradyarrhythmic episode occurred within the 30 days following the implantation of the Reveal device in 48% of patients. No differences were observed between valve types, and similar results were obtained when only transfemoral-TAVR patients were included (Online Figure 1). The percentage of patients with at least 1 bradyarrhythmic episode at different time points, overall and according to valve type, is shown in **Figure 4**. The main baseline and procedural characteristics of the patients grouped according to the occurrence of a bradyarrhythmic event during the follow-up period are shown in Online Table 2.

Individual data of the 11 patients who received a PPM or a ICD during the study period are detailed in **Table 3**. The mean age of patients requiring PPM at follow-up was 80 ± 7 years, and 7 of them (64%) were men. The mean time to PPM-ICD was 42 (6 to 217) days post-TAVR. A total of 5 and 6 patients had received a CoreValve/Evolut R system and a SAPIEN XT/3 valve, respectively, and HAVB was the reason for PPM in 9 patients. In 6 patients, the bradyarrhythmic episode leading to PPM was not accompanied by symptoms, whereas pre-syncope or syncope occurred in 4 patients.

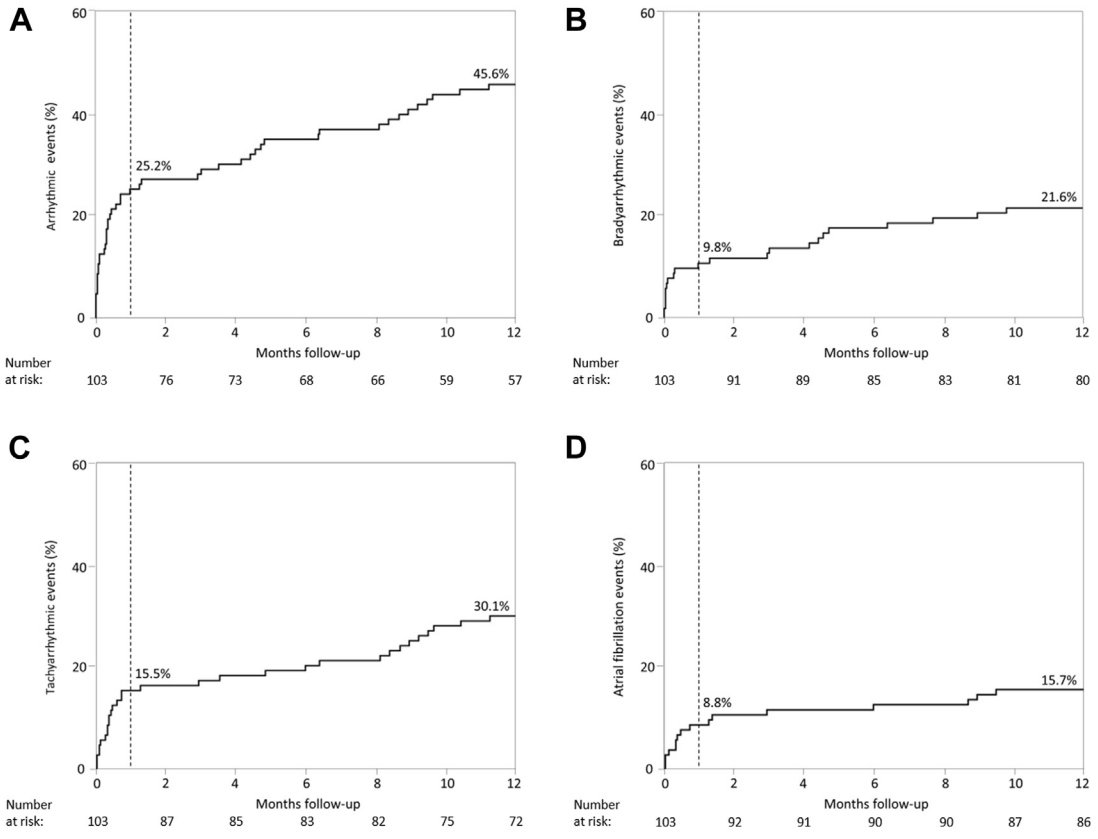
A summary of the tachyarrhythmic burden is shown in **Table 2**. A total of 1,443 tachyarrhythmic events occurred at 12-month follow-up, mainly AF/AFL episodes (n = 1,350). A total of 13 patients had new AF/AFL episodes (17% among those patients with no prior history of AF), with a mean number of 10 episodes (2 to 24) per patient, and a median duration of 54 min (IQR: 39 to 270 min) per patient. The AF/AFL episodes led to a treatment change in 5 patients (7%), as follows: anticoagulation therapy (n = 3), antiarrhythmic therapy (n = 3). A total of 16 episodes of ventricular tachycardia occurred in 13 patients (13%), most of them (94%) nonsustained ventricular tachycardia. Ventricular tachycardia led to a treatment change in 5 patients (ICD, n = 2; antiarrhythmic therapy, n = 4; cardioversion, n = 1). In 21 patients (81% of patients with tachyarrhythmias), all tachyarrhythmic events were silent. A higher rate (p = 0.050) of AF/AFL episodes was observed in those patients who received a SAPIEN XT/3 valve. The time to first tachyarrhythmic event and first AF/AFL episode, overall and according to valve type, are shown in **Figures 2C, 2D, 3C, and 3D**, respectively. The first episode of tachyarrhythmia

TABLE 2 Arrhythmic Events at 12-Month Follow-Up

	Overall (N = 103)	Sapien XT/3 (n = 53)	CoreValve/ Evolut R (n = 50)	p Value
Global arrhythmic burden				
Total number of new arrhythmic events	1,553	1,418	135	–
Patients with new arrhythmic events	44 (43)	26 (49)	18 (36)	0.18
Arrhythmic events per patient	3 (1–9)	4 (1–14)	2 (1–5)	0.20
Patients with arrhythmic events requiring treatment	19 (18)	11 (21)	8 (16)	0.53
Bradyarrhythmias				
Total number of events	110	60	50	–
High-degree atrioventricular block	54	23	31	–
Severe bradycardia	56	37	19	–
Patients with bradyarrhythmic events	21 (20)	10 (19)	11 (22)	0.69
Patients with high-degree atrioventricular block	15 (15)	8 (15)	7 (14)	0.88
Patients with severe bradycardia	10 (10)	4 (8)	6 (12)	0.45
Patients with bradyarrhythmias requiring treatment	11 (11)	6 (11)	5 (10)	0.83
Pacemaker implantation	10 (10)	6 (11)	4 (8)	0.74
Change in medical treatment	4 (4)	1 (2)	3 (6)	0.35
Tachyarrhythmias				
Total number of events	1,443	1,358	85	–
Atrial arrhythmias	1,427	1,346	81	–
Atrial fibrillation/atrial flutter	1,350	1,335	15	–
Atrial tachycardia	74	9	65	–
Supraventricular tachycardia	3	2	1	–
Ventricular arrhythmias	16	12	4	–
Sustained ventricular tachycardia	1	1	0	–
Nonsustained ventricular tachycardia	15	11	4	–
Atrial fibrillation/atrial flutter				
Patients with new episodes of atrial fibrillation/atrial flutter*	13/76 (17)	10/36 (28)	3/40 (8)	0.05
Atrial fibrillation episodes per patient	10 (2-24)	20 (2-38)	4 (1-10)	0.30
Duration of atrial fibrillation episodes per patient, min	54 (39-270)	48 (36-309)	120 (54-270)	0.48
Patients with atrial fibrillation/atrial flutter episodes				
≥6 min	13 (100)	10 (100)	3 (100)	0.05
≥30 min	11 (85)	8 (80)	3 (100)	0.14
>6 h	4 (31)	4 (40)	0 (0)	0.07
Patients with new episodes of atrial fibrillation/atrial flutter leading to a treatment modification	5/76 (7)	4/36 (11)	1/40 (3)	0.36
Anticoagulation therapy	3/76 (4)	3/36 (8)	0	0.24
Antiarrhythmic therapy	3/76 (4)	2/36 (6)	1/40 (3)	0.60
Ventricular tachycardia				
Patients with episodes of ventricular tachycardia	13 (13)	9 (17)	4 (8)	0.15
Ventricular tachycardia episodes per patient	1 (1-1)	1 (1-2)	1 (1-1)	0.48
Duration of ventricular tachycardia episodes per patient, s	7 (6-9)	7 (6-8)	7 (6-11)	0.96
Patients with ventricular tachycardia episodes who had a treatment modification	5 (4)	3	2	0.70
Implantable cardioverter defibrillator	2 (2)	1 (2)	1 (2)	1.0
Antiarrhythmic therapy	4 (4)	2 (4)	2 (4)	1.0
Cardioversion	1 (1)	1 (2)	0 (0)	1.0

Values are n, n (%), median (interquartile range), or n/N (%). *Only patients without prior atrial fibrillation in the denominator for the %.

FIGURE 2 Time to First Arrhythmic Event Post-TAVR for the Entire Study Population



(A) Time to first arrhythmic (brady- or tachyarrhythmia) event. **(B)** Time to first episode of bradyarrhythmia. **(C)** Time to first episode of tachyarrhythmia. **(D)** Time to first episode of atrial fibrillation/atrial flutter. TAVR = transcatheter aortic valve replacement.

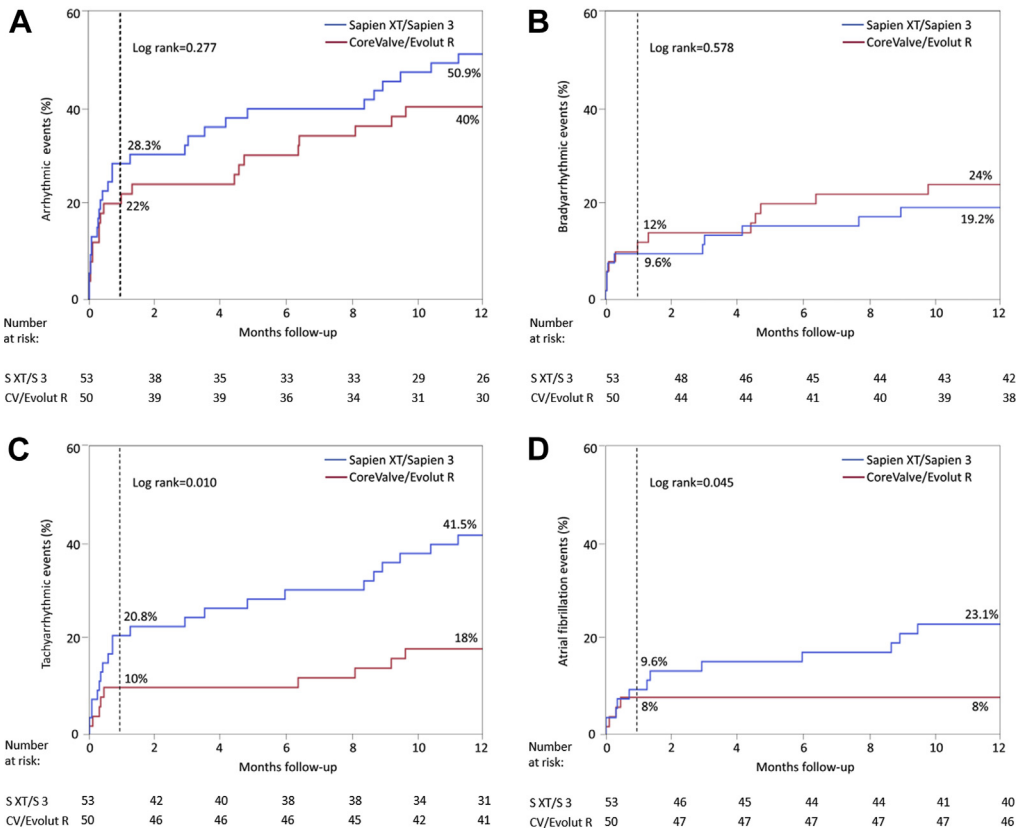
and AF/AFL occurred within the first 30 days post-Reveal implantation in 65% and 62% of the patients, respectively. The results remained similar after excluding all approaches other than transfemoral (Online Figure 1). The baseline and procedural characteristics of the patients grouped according to the occurrence of atrial arrhythmias or ventricular arrhythmias at follow-up are shown in Online Tables 3 and 4, respectively.

ECG CHANGES OVER TIME. The changes of ECG over time, overall and according to valve type, are shown in **Figure 5**. The LBBB persisted in 64% and 62% of patients at 1- and 12-month follow-up, respectively, with no significant differences between valve types (CoreValve/Evolut R 59% and 53%; SAPIEN XT/3 68% and 70%; $p = 0.37$ and $p = 0.13$ for LBBB persistence at 1 and 12 months, respectively, according to valve type). A complete recovery of the conduction disturbance was observed in 20% and 22% of patients at 1- and 12-month follow-up, respectively.

OTHER CLINICAL EVENTS. Clinical events (non-arrhythmic), overall and according to valve type, at 1-year follow-up are shown in **Table 4**. Global and cardiac mortality rates were 12% and 4%, respectively. Global and cardiac mortality events occurred at a median of 4 (IQR: 2 to 8) months and 4 (IQR: 2 to 6) months post-TAVR, respectively. One patient had a sudden death 10 months after TAVR. The patient had a history of coronary artery disease and normal ventricular function, and no arrhythmias were detected with the Reveal device preceding the sudden death. The patient collapsed and was in asystole on arrival at a medical center. The Reveal device was not interrogated, precluding determination of the potential arrhythmic cause of the death.

A total of 8 cerebrovascular events occurred at 1-year follow-up (6 strokes), 3 during the periprocedural period. Among the 5 late (median 5 [3 to 6] months) cerebrovascular events months post-TAVR),

FIGURE 3 Time to First Arrhythmic Event Post-TAVR, According to Valve Type



(A) Time to first arrhythmic (brady- or tachyarrhythmia) event. **(B)** Time to first episode of bradyarrhythmia. **(C)** Time to first episode of tachyarrhythmia. **(D)** Time to first episode of atrial fibrillation/flutter. TAVR = transcatheter aortic valve replacement.

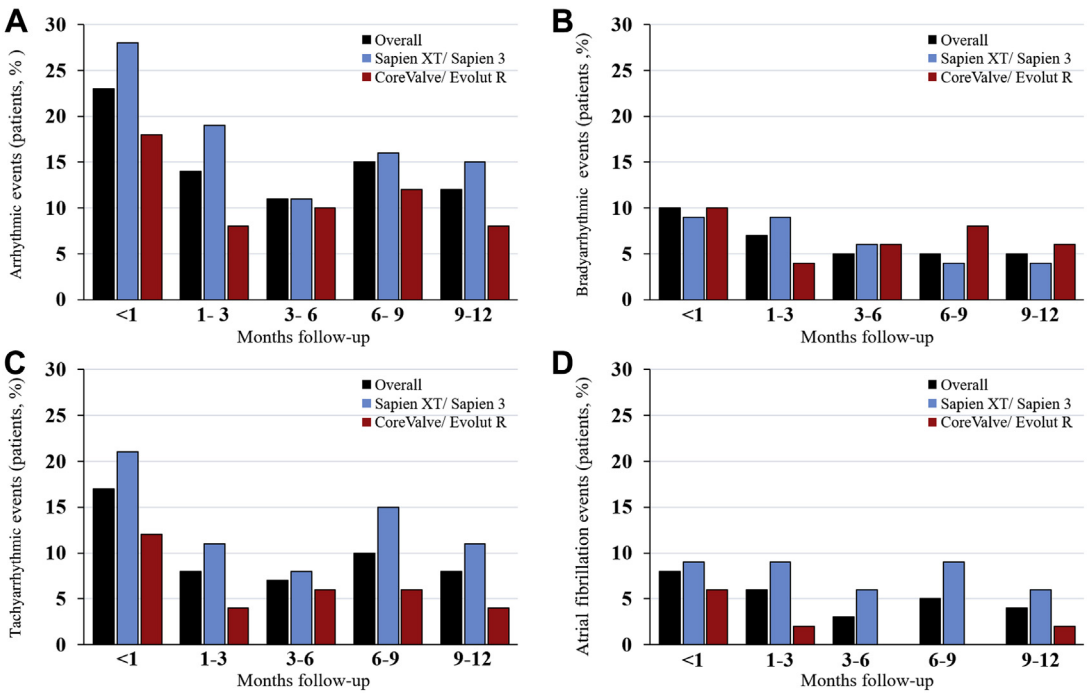
1 occurred in a patient with a prior history of AF, and 1 in a patient with new episodes of AF.

DISCUSSION

This first study using continuous cardiac monitoring in patients with LBBB post-TAVR showed a high burden of arrhythmic events at 1-year follow-up in nearly one-half of patients, leading to a treatment change in more than one-third of them. Significant bradyarrhythmias were detected in 20% of the patients (HAVB in more than one-half), with PPM required in nearly one-half of them. Episodes of new-onset AF/AFL occurred in close to one-fifth of the patients, leading to a therapy change in approximately one-half of them. Finally, in about 77% of the patients with new arrhythmias, all arrhythmic events were silent (not associated with symptoms).

PPM rates of 5% to 14% have been reported at follow-up among patients with new-onset LBBB post-TAVR, with progression toward HAVB being the most frequent indication for PPM across studies (5,6,16–18). The use of continuous cardiac monitoring allowed the detection of episodes of HAVB in 15% of patients with new-onset LBBB post-TAVR, a slightly higher rate compared with previous studies. However, the PPM rate at 1-year follow-up was 10%, which is similar to prior studies. There may be multiple reasons for this discordance, including some differences in the diagnosis of adjudicated versus site-reported events, and the decision of some centers not to recommend PPM in some of these cases. Of note, HAVB episodes, frequently asymptomatic, were the reason for PPM in 90% of cases. It is unknown whether PPM following the detection of silent episodes of significant bradyarrhythmias could have prevented the occurrence of either more severe symptomatic episodes or sudden death. Urena et al. (3) reported a 2.5% rate of sudden death at 1-year follow-up in a large cohort of patients with LBBB

FIGURE 4 Rate of Arrhythmic Events Post-TAVR, According to Different Time Periods



(A) Rate of arrhythmic events over time. **(B)** Rate of bradyarrhythmias over time. **(C)** Rate of tachyarrhythmias over time. **(D)** Rate of atrial fibrillation/atrial flutter episodes over time. TAVR = transcatheter aortic valve replacement.

post-TAVR, which is higher than the 1% rate observed in the present study. In fact, the 1% rate is similar to the sudden death rate at follow-up reported in patients with no prior LBBB in previous studies (3).

TABLE 3 Individual Characteristics of the Patients Requiring Permanent Pacemaker or Implantable Cardioverter Defibrillator

Age, yrs (Sex)	Valve Type	Timing of PPM or ICD (Days)	PPM or ICD	Reasons for PPM or ICD
65 (male)	SAPIEN 3	5	ICD-CRT	HAVB (A), low LVEF
73 (male)	Evolut R	6	PPM	HAVB (S), syncope
75 (female)	SAPIEN 3	108	PPM	HAVB (S), pre-syncope
75 (female)	CoreValve	217	ICD	Polymorphic NSVT (A)
81 (male)	SAPIEN 3	12	ICD	HAVB (A)/VT (S), chest pain
83 (male)	SAPIEN 3	281	PPM	Severe bradycardia (A)
84 (female)	SAPIEN 3	42	PPM	HAVB (A)
85 (female)	Evolut R	280	PPM	HAVB (A)
85 (male)	CoreValve	18	PPM	HAVB (S), pre-syncope
86 (male)	SAPIEN XT	127	PPM	HAVB (A)
90 (male)	Evolut R	5	PPM	HAVB (S), syncope

A = asymptomatic; HAVB = high-degree atrioventricular block; ICD = implantable cardioverter-defibrillator; LVEF = left ventricular ejection fraction; NSVT = nonsustained ventricular tachycardia; PPM = permanent pacemaker implantation; S = symptomatic; VT = ventricular tachycardia.

Importantly, about one-half of the episodes of bradyarrhythmia occurred within the first weeks following TAVR, whereas the other half were equally distributed within the subsequent months. These findings suggest a period of increased risk of progression towards HAVB early on following TAVR, and highlight the importance of closer follow-up during the early weeks after hospital discharge in patients with LBBB post-TAVR. Of note, the rate and timing of significant bradyarrhythmias (including HAVB) were similar between valve types despite design differences, suggesting that a similar level of monitoring and follow-up should be applied for all patients who develop new-onset persistent LBBB following TAVR.

Whereas some studies have evaluated the occurrence of new-onset AF episodes in the periprocedural TAVR period (19–21), data are scarce on the presence of silent or symptomatic episodes of AF during the follow-up period post-TAVR. Newly detected AF after hospital discharge occurred in close to one-fifth of the patients with no prior history of AF in our study, leading to a treatment change (including the initiation of anticoagulation therapy) in about one-half of them. It has been shown that TAVR approaches requiring thoracotomy, and particularly the

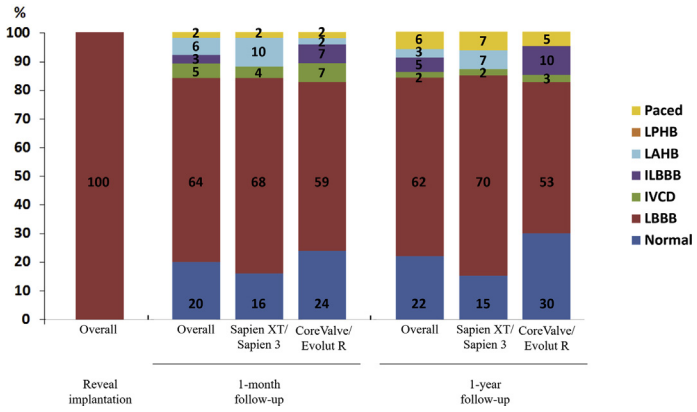
transapical approach, are the main factors determining an increased risk of AF post-TAVR (19). This may partially explain the higher risk of AF episodes among those patients receiving a SAPIEN valve (close to 20% of them had had transapical TAVR). However, no clear explanation exists for the tendency towards a higher rate of AF following transfemoral TAVR with the SAPIEN valve system compared with CoreValve/Evolut R system. Although no major differences in baseline characteristics were observed between groups (except for sex), other factors involved in the higher risk of AF post-TAVR such as larger atrial size were not available, and their possible influence on these results cannot be excluded. Also, a study using 24-h ECG recording pre-TAVR, suggested that a significant percentage of those patients with AF post-TAVR had had silent episodes of AF or atrial tachycardia before TAVR (22). Other ongoing studies using more prolonged (weeks) ECG monitoring pre-TAVR will shed more light on the arrhythmic burden of elderly patients with aortic stenosis (Assessment of Arrhythmias in Patients Undergoing Transcatheter Aortic Valve Implantation Using a Small Insertable Cardiac Monitoring Device-Reveal [REVEAL]; NCT02559011).

Previous studies in populations outside the aortic stenosis/TAVR field have shown the usefulness of ILR devices for detecting silent episodes of AF (23,24). Although most AF episodes in the present study had a limited duration (<1 h), a significant number lasted several hours, which probably increases the risk of cardioembolic events, particularly in a high-risk population like that of elderly TAVR candidates (mean CHADsVasc score >4). In fact, the occurrence of periprocedural new-onset AF post-TAVR has already been identified as an important risk factor for cerebrovascular events (25). Whether the implementation of anticoagulation therapy following these findings will translate into a reduction of stroke events needs to be demonstrated in future studies.

Scarce data exists on the occurrence of ventricular arrhythmias in TAVR recipients (26). The occurrence of ventricular tachycardia in 14% of the patients is a novel finding that introduces a new element into the risk stratification of these patients. Whereas therapeutic measures (including ICD) were implemented in a minority of patients with ventricular arrhythmias, their potential for preventing life-threatening events may have a significant influence on the improvement of the late outcomes in such patients. Further studies with a larger number of patients and a longer follow-up are warranted.

Previous studies have shown that LBBB persists at 1-year follow-up in about 60% of patients with new-onset LBBB post-TAVR, with a lower rate of conduction abnormality recovery among those patients who received a CoreValve (vs. Sapien) system (6,16,27). Similar global results were observed in our study, with a rate of 62% of LBBB persistence at 1-year follow-up as adjudicated in a central ECG core lab. However, no significant differences were detected between self-expanding and balloon-expandable systems regarding the recovery rate of conduction disturbances. This may be in part secondary to the use of newer-generation valve systems such as Evolut R and Sapien 3, for which no prior data existed on the occurrence and persistence of conduction disturbances over time. Future studies including larger number of patients with these latest-generation transcatheter valves are needed to further evaluate the rates of LBBB recovery at follow-up.

FIGURE 5 ECG Changes Over Time, Overall, and According to Valve Type (CoreValve/Evolut R or SAPIEN XT/SAPIEN 3)



ECG = electrocardiogram; ILBBB = incomplete left bundle branch block; IVCD = nonspecific intraventricular conduction delay; LAHB = left anterior hemiblock; LBBB = left bundle branch block; LPHB = left posterior hemiblock.

TABLE 4 Clinical Events at 12-Month Follow-Up

	Overall (N = 103)	Sapien XT/3 (n = 53)	CoreValve/ Evolut R (n = 50)	p Value
Overall death	12 (12)	8 (15)	4 (8)	0.26
Cardiovascular death	4 (4)	2 (4)	2 (4)	1.0
Sudden death	1 (1)	1 (2)	0 (0)	1.0
Stroke/TIA	8 (8)	4 (8)	4 (8)	1.0
Myocardial infarction	4 (5)	2 (4)	2 (4)	1.0
Rehospitalization*	19 (18)	12 (23)	7 (14)	0.26
Rehospitalization because of cardiac causes*	12 (12)	8 (15)	4 (8)	0.26

Values are n (%). *Number of patients.
TIA = transient ischemic attack.

STUDY LIMITATIONS. The limited sample size of the study precluded the evaluation of the predictive factors of arrhythmic (bradyarrhythmias or tachyarrhythmias) events through an appropriate multivariable analysis. Also, no control group was included in this study. Finally, although all arrhythmic events were adjudicated, the initial diagnosis and management of such events was the responsibility of the investigators in each participating center. We cannot rule out some variability in the interpretation and management of events between centers.

CONCLUSIONS

Patients with new-onset persistent LBBB post-TAVR exhibited a high burden of arrhythmic events at 1-year follow-up, particularly within the early weeks following hospital discharge. The detection of significant bradyarrhythmias or tachyarrhythmias (frequently asymptomatic) leading to a treatment change (PPM, ICD, anticoagulation, antiarrhythmic therapy) in about one-fifth of the patients reflects the high risk of this population and supports the use of a cardiac monitoring device for close follow-up and expediting the initiation of treatment if required. Future studies will need to evaluate the factors determining a higher risk of significant arrhythmic events in such patients. This would help to establish a strategy of tailored therapy according to arrhythmic risk in this challenging group.

ADDRESS FOR CORRESPONDENCE: Dr. Josep Rodés-Cabau, Quebec Heart & Lung Institute, Laval University, 2725 chemin Ste-Foy, G1V4G5 Quebec City, Quebec, Canada. E-mail: josep.rodes@criucpq.ulaval.ca.

PERSPECTIVES

WHAT IS KNOWN? Some studies have suggested an increased risk of cardiovascular and sudden death in patients with new-onset LBBB post-TAVR.

WHAT IS NEW? The use of an implantable cardiac monitor in LBBB post-TAVR recipients showed a high burden of arrhythmic events at 1-year follow-up in close to one-half of the patients, leading to a treatment change in more than one-third of them. Significant bradyarrhythmias were detected in one-fifth of patients, with PPM required in nearly one-half of them. Significant tachyarrhythmias were detected in another one-fifth of patients.

WHAT IS NEXT? Future studies will need to evaluate the factors determining a higher risk of significant arrhythmic events in LBBB post-TAVR patients.

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KEY WORDS atrial fibrillation, bradyarrhythmias, left bundle branch block, pacemaker implantation, transcatheter aortic valve replacement

APPENDIX For a supplemental figure and tables, please see the online version of this paper.