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Minimally Invasive Aortic Valve Replacement with Sutureless Valves: Results From an International Prospective Registry

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Abstract

Objective: To report the early and mid-term results of patients who underwent minimally invasive aortic valve replacement (MI-AVR) with a sutureless prosthesis from an international prospective registry. **Methods:** Between March 2011 and September 2018, among 957 patients included in the prospective observational SURE-AVR (Sorin Universal REgistry on Aortic Valve Replacement) registry, 480 patients underwent MI-AVR with self-expandable Perceval aortic bioprosthesis (LivaNova PLC, London, UK) in 29 international institutions through either minithoracotomy (n = 266) or ministernotomy (n = 214). Postoperative, follow-up, and echocardiographic outcomes were analyzed for all patients. **Results:** Patient age was 76.1 ± 7.1 years; 64.4% were female. Median EuroSCORE I was 7.9% (interquartile range [IQR], 4.8 to 10.9). Median cardiopulmonary bypass and cross-clamp times were 81 minutes (IQR 64 to 100) and 51 minutes (IQR 40 to 63). First successful implantation was achieved in 97.9% of cases. Two in-hospital deaths occurred, 1 for noncardiovascular causes and 1 following a disabling stroke. In the early (≤30 days) period, stroke rate was 1.4%. Three early explants were reported: 2 due to nonstructural valve dysfunction (NSVD) and 1 for malpositioning. One mild and 1 moderate paravalvular leak were reported. In 16 patients (3.3%) pacemaker implantation was needed. Mean follow-up was 2.4 years (maximum = 7 years). During follow-up 5 explants were reported, 3 due to endocarditis and 2 due to NSVD. Follow-up stroke rate was 2.5%. Three structural valve deteriorations not requiring reintervention were reported. Five-year survival was 91.45%. **Conclusions:** In this large prospective international registry, MI-AVR with Perceval valve confirmed to be safe, reproducible, and effective in an intermediate-risk population, providing excellent clinical recovery both in early and mid-term follow-up.

Central Message

The data from SURE-AVR registry suggest that the combination of aortic sutureless valve technology and minimally invasive surgical approaches may represent, in the era of transcatheter valve, a viable option also in intermediate-risk patients, with reliable results in terms of postoperative recovery, morbidity, and mortality.

Keywords

MICS, sutureless, aortic stenosis

Introduction

In the past few years the incidence of degenerative aortic valve disease has increased as a consequence of increased life expectancy.[1,2] The majority of patients with severe aortic stenosis are elderly patients with several comorbidities leading to an increased operative risk profile and inherent higher morbidity and mortality risks.[3,4]

Emerging technologies as well as advanced techniques could allow to minimize the surgical risk in cardiac surgery.[5–7] The

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lesser invasiveness and the reduced surgical trauma of minimally invasive aortic valve replacement (MI-AVR) could lead to optimal outcomes even in increased-risk-profile patients.[8–10]

MI-AVR became popular in the 1990s and has gradually been recognized as a less traumatic approach when compared with median sternotomy.[11]

Currently, the upper ministernotomy (MS) and the right anterior minithoracotomy (RAT) are the most common approaches for MI-AVR. Although MI-AVR has shown multiple clinical benefits for the patients, such as reduced blood loss, decreased in-hospital length of stay and morbidities, it is still not widespread in the surgical community.[12–14]

This is likely due to the perceived increased surgical complexity of MI-AVR approaches that may lead to prolonged operative times when compared with conventional AVR. Although few studies have shown a lower mortality rate, no prospective randomized trial has been performed yet.[13,14]

Sutureless aortic valve prostheses have been developed in order to combine the best of 2 worlds, as they could facilitate the implantation, like transcatheter aortic valve implantation (TAVI), while maintaining the benefits of surgical AVR.[15–17]

The sutureless Perceval aortic valve is getting more attention, becoming widely used in many countries, since it has shown excellent hemodynamic performances, safety, and versatility of use.[15–18] However, concerns regarding permanent pacemaker implantation (PPI) rate, incidence of paravalvular leak (PVL) and durability are still present and require an answer.

The aim of this study was to investigate the outcomes of Perceval implanted through a minimally invasive approach, among the patients prospectively enrolled in the SURE-AVR registry.

Methods

Registry Design

LivaNova funded the SURE-AVR registry (NCT02679404), designed the study protocol, was responsible for site selection and trial management, and performed the statistical analysis.

The SURE-AVR registry is an all-comers prospective international, multicenter, observational registry conducted at 60 sites in 18 countries in Europe, USA, Canada, and Australia with the aim to collect safety and clinical performance data in a post-approval real-world environment on the AVR surgery; any of the commercially available LivaNova aortic products are eligible for enrollment. Ethics committee and/or institutional review board approval was obtained as required by local regulations. All LivaNova aortic valve devices that have obtained CE-mark or other local regulatory and/or commercial approvals may be included in the registry.

All patients were enrolled in a sequential and prospective manner and gave informed consent to participate. This analysis focuses on patients after Perceval valve implantation through a minimally invasive approach, either MS or RAT. No inclusion or exclusion criteria were established to enroll or select patients other than the technical manufacturer indications for Perceval valve implant. The choice of the surgical approach was based on surgeons' preference after assessment of the technical feasibility. Follow-up visits were performed at 1 year and annually thereafter up to 5 years.

Study Device

The Perceval valve is a self-anchoring, self-expanding, sutureless surgical aortic biological prosthesis, that can be used to replace calcified native aortic heart valves or degenerated biological prostheses.

This bioprosthesis features the functional component, made of bovine pericardium, stabilized in buffered gluteraldehyde solution, and the super-elastic metal alloy stent, which has the dual role of valve support and anchoring to the aortic root with no permanent sutures. Prior to implantation, the prosthesis diameter is reduced to a suitable size for loading it on a holder. The valve is then positioned and released in the aortic root and subsequently post-dilated using a dedicated balloon catheter. The device is available in 4 sizes (S—M—L—XL).

The implantation can be either achieved via traditional surgery or through minimally invasive cardiac surgery (MICS) procedures, both MS and RAT, for which the sutureless design is particularly suited. Indications for sutureless AVR were driven by recommendations of the International Consensus on Sutureless valves.[19]

Clinical Outcomes

Data on MICS procedure (MS and RAT) and hospital discharge variables were collected, including implant success, operative times, and intensive care unit (ICU) and hospital length of stay.

Site-reported echocardiographic and hemodynamic data were collected. Investigator-reported major adverse events were defined as death (all-cause, cardiovascular, non-cardiovascular), stroke/transient ischemic attack (TIA), and reintervention (surgery or any other cardiac invasive therapy). Serious valve-related adverse events included bleeding, thromboembolism, valve thrombosis, endocarditis, non-structural valve dysfunction (NSVD), and SVD.

Early outcomes were defined as those occurring up to 30 days after the procedure and late outcomes as those occurring >30 days after the procedure. Implant time was defined as the time from the first guiding suture position to the removal of the balloon catheter after dilatation.

Preoperative, periprocedural, and follow-up clinical and echocardiographic parameters, as well as clinical outcomes, were analysed for all available patients.

Statistical Analysis

Baseline, operative, and outcome data are presented as overall MICS population and by surgical approach. Patient characteristics are described as mean ± SD or median (quartile [Q1, Q3];

range) for continuous variables and as number (%) for categorical variables. Nonparametric Wilcoxon rank sum tests were performed to state if the distributions of 2 samples were significantly different and the resulting *P*-values are provided.

Outcomes are reported as descriptive statistics. The rates of adverse events were calculated as the total number of events and number of patients with at least 1 event divided by the total number of patients. Linearized complication rates (and 95% confidence intervals [CIs]) were calculated as the number of late events divided by the number of late patient-years. The statistical analyses were performed using SAS® (Release 9.4, by SAS Institute Inc., Cary, NC, USA).

Results

Study Population

Between March 2011 and September 2018, among the 957 patients included in the SURE-AVR registry, a total of 480 patients underwent MI-AVR with Perceval in 29 international institutions through either RAT (n = 266, 26 sites) or MS (n = 214, 8 sites). The preoperative baseline characteristics are reported in Table 1. The population included 64.4% female with an average age at surgery of 76.0 ± 6.8 years. Indication for Perceval implant was stenosis for 74.8% of the patients, combined stenosis/regurgitation and regurgitation for 22.3% and 2.3% of the patients. The main risk factors were left ventricular hypertrophy in 73.3%, dyslipidemia in 60.6% and diabetes in 29% of the cases.

The majority of patients were in NYHA class II to III (92.1%) and presented with sinus rhythm (82.5%), while 8.1% had atrial fibrillation and 5% were paced. The median EuroSCORE I was 7.9% (interquartile range [IQR], 4.8 to 10.9). Cardiac intervention prior the Perceval implant was reported in 14.2% of the patients; 9.8% of the patients had a bicuspid aortic valve.

Table 1. Preoperative Patient Characteristics.

	MICS (N = 480)	MS (n = 214)	RAT (n = 266)
Female gender	309 (64.4%)	133 (62.1%)	176 (66.2%)
Age (years)	76.0 (6.8)	76.1 (6.7)	75.9 (6.8)
Diagnosis			
Stenosis	359 (74.8%)	157 (73.4%)	202 (75.9%)
Regurgitation	11 (2.3%)	5 (2.3%)	6 (2.3%)
Steno-regurgitation	107 (22.3%)	51 (23.8%)	56 (21.1%)
Risk factors			
Left ventricular hypertrophy	352 (73.3%)	105 (49.1%)	247 (92.9%)
Dyslipidemia	291 (60.6%)	132 (61.7%)	159 (59.8%)
Diabetes	139 (29.0%)	62 (29.0%)	77 (28.9%)
Coronary artery disease	83 (17.3%)	38 (17.8%)	45 (16.9%)
Endocarditis	1 (0.2%)	-	1 (0.4%)
Renal insufficiency	40 (8.3%)	21 (9.8%)	19 (7.1%)
Cerebrovascular events	27 (5.6%)	14 (6.5%)	13 (4.9%)
Chronic lung disease	80 (16.7%)	35 (16.4%)	45 (16.9%)
NYHA class			
NYHA I	19 (4.0%)	8 (3.7%)	11 (4.1%)
NYHA II	284 (59.2%)	102 (47.7%)	182 (68.4%)
NYHA III	158 (32.9%)	91 (42.5%)	67 (25.2%)
NYHA IV	13 (2.7%)	12 (5.6%)	1 (0.4%)
Not accessible	6 (1.3%)	1 (0.5%)	5 (1.9%)
Cardiac rhythm			
Sinus rhythm	396 (82.5%)	170 (79.4%)	226 (85%)
Atrial fibrillation	39 (8.1%)	23 (10.7%)	16 (6.0%)
Paced	24 (5.0%)	5 (2.3%)	19 (7.1%)
EuroSCORE I (%)	7.9 [4.8; 10.9]	8.3 [6.2; 11.9]	7.9 [4.8; 10.7]
Previous cardiac procedures[a]	68 (14.2%)	15 (7.0%)	53 (19.9%)
CABG	5 (1.0%)	2 (0.9%)	3 (1.1%)
Pacemaker implantation	23 (4.8%)	4 (1.9%)	19 (7.1%)
Percutaneous coronary intervention	6 (1.3%)	4 (1.9%)	2 (0.8%)
Valve replacement	9 (1.9%)	4 (1.9%)	5 (1.9%)
Repair procedure	6 (1.3%)	1 (0.5%)	5 (1.9%)
Bicuspid aortic valve	47 (9.8%)	16 (7.5%)	31 (11.7%)

Abbreviations: CABG, coronary artery bypass graft; EuroSCORE, European System for Cardiac Operative Risk Evaluation; MICS, minimally invasive cardiac surgery; MS, ministernotomy; NYHA, New York Heart Association; RAT, right anterior minithoracotomy.
Data presented as n (%), mean (SD), or median [Q1; Q3]
[a]One patient may have more than 1 previous cardiac procedure.

Table 2. Procedural Details.

	MICS (*N* = 480)	MS (*n* = 214)	RAT (*n* = 266)
Valve size			
S	72 (15.0%)	35 (16.4%)	37 (13.9%)
M	151 (31.5%)	68 (31.8%)	83 (31.2%)
L	203 (42.3%)	73 (34.1%)	130 (48.9%)
XL	54 (11.3%)	38 (17.8%)	16 (6.0%)
Concomitant procedures[a]	23 (4.8%)	7 (3.3%)	16 (6.0%)
CABG	3 (0.6%)	3 (1.4%)	0 (0%)
AF ablation	0 (0%)	0 (0%)	0 (0%)
Mitral valve	10 (2.1%)	0 (0%)	10 (3.7%)
-Repair	9 (90.0%)	0 (0%)	9 (90%)
-Replacement	1 (10.0%)	0 (0%)	1 (10.0%)
First successful implant	470 (97.9%)	210 (98.1%)	260 (97.7%)
If no, a new Perceval was implanted	8 (100%)	2 (100%)	6 (100%)

Abbreviations: AF, atrial fibrillation; CABG, coronary artery bypass graft; MICS, minimally invasive cardiac surgery; MS, ministernotomy; RAT, right anterior minithoracotomy.
[a]One patient may have more than 1 concomitant procedure.

Surgical Procedures

The intraoperative characteristics and hospital stay values are reported in Tables 2–4. Perceval valve was successfully implanted in 97.9% at the first attempt. In all the 8 patients needing a second attempt, a new Perceval valve was successfully implanted. A concomitant procedure was reported in 4.8% of the patients, mainly for mitral valve repair/replacement. The most common sizes used were size M and L (31.5% and 42.3%).

Overall the median cardiopulmonary bypass and cross-clamp times were 81 minutes (IQR, 64 to 100) and 51 minutes (IQR, 40 to 63) (Table 3). In the MS group these values were 67 minutes (IQR, 49 to 88) and 43 minutes (IQR, 32 to 56), while in the RAT group they were 89 minutes (IQR, 75 to 112) and 55 minutes (IQR, 46 to 71). The median implantation time was 15 minutes (IQR, 12 to 18) with a faster procedure for the RAT group (MS: 15.5 minutes, RAT: 12 minutes; $P = 0.014$). The median total ventilation time was 6.0 hours (IQR, 5 to 10), the ICU stay was 1.0 day (IQR, 1 to 2), and the total length of hospital stay was 8.0 days (IQR, 7 to 11). All these last 3 parameters were shorter in the RAT group ($P < 0.05$; Table 4).

Early Outcomes

Mean pressure gradients decreased from 49.3 ± 14.6 mmHg preoperatively to 13.9 ± 4.7 mmHg at discharge from hospital. Mean effective orifice area increased from 0.7 ± 0.2 cm² before surgery to 1.7 ± 0.4 cm² at discharge (Table 5). The postoperative outcomes are reported in Table 6. Overall, in-hospital mortality was 0.4%: one patient died for non-cardiovascular death and another one for cardiovascular reasons, both in the MS group. Reintervention was needed in 13 patients (2.7%), in 6 for not valve-related reasons (2 bleeding, 2 tamponade, 1 right pleural effusion, 1 pericardial effusion), while in 7 patients for valve-related re-exploration: 1 case of malpositioning that was treated with a Perceval valve and 6 cases of NSVD, 5 treated surgically and 1 with the implant of a transcatheter valve. There were 6 NSVD cases: 5 treated surgically, through the same minimally invasive access and without conversion to sternotomy, and 1 treated with a TAVI due to a severe regurgitation detected on the fifth postoperative day. In the 5 surgical cases a significant leakage was detected: in 3 patients there was an intraoperative prostheses repositioning, while in the other 2 the valve explant was necessary. Regarding these 2 explants one patient was treated with a new Perceval (of the same size) on the first postoperative day, while the other one was implanted with a one-size bigger Perceval on the fifth postoperative day.

Four patients (0.8%) had TIA and 2 (0.4%) disabling strokes; 9 cases (1.9%) of bleeding occurred (2 of them requiring valve re-exploration). No cases of thrombosis or endocarditis were reported in the early phase.

Table 3. Operative Times (Median [Q1; Q3]).

	MICS (*N* = 480)	MS (*n* = 214)	RAT (*n* = 266)	Wilcoxon *P*-value
Total procedure time (minutes)	170.0 [132.5; 207.5]	165.0 [129.5; 198.5]	200.0 [150.0; 237.5]	0.057
Cross-clamp time (minutes)	51.0 [40.0; 63.0]	43.0 [32.0; 56.0]	55.0 [46.0; 71.0]	<0.001
Pump time (minutes)	81.0 [64.0; 100.0]	67.0 [49.0; 88.0]	89.0 [75.0; 112.0]	<0.001
Implantation time (minutes)	15.0 [12.0; 18.0]	15.5 [12.0; 20.0]	12.0 [10.0; 12.0]	0.014

Abbreviations: MICS, minimally invasive cardiac surgery; MS, ministernotomy; RAT, right anterior minithoracotomy.

Table 4. ICU and Length of Stay (Median [Q1; Q3]).

	MICS (*N* = 480)	MS (*n* = 214)	RAT (*n* = 266)	Wilcoxon *P*-value
Total ventilator (hours)	6.0 [5.0; 10.0]	8.0 [6.0; 14.0]	6.0 [4.0; 8.0]	<0.001
ICU stay (days)	1.0 [1.0; 2.0]	1.5 [1.0; 3.0]	1.0 [1.0; 1.0]	<0.001
Total length of stay (days)	8.0 [7.0; 11.0]	9.0 [7.0; 13.0]	8.0 [7.0; 10.0]	<0.001

Abbreviations: ICU, intensive care unit; MICS, minimally invasive cardiac surgery; MS, ministernotomy; RAT, right anterior minithoracotomy.

Moderate central leak was reported in 0.6% of the patients and moderate-to-severe PVL was reported in 0.4% of patients. PPI was required in 16 patients (3.3%), mainly due to atrioventricular block (AVB) grade III.

Late Outcomes

Mean follow-up was 2.4 years (maximum follow-up 7 years), while the median study follow-up duration was 27.8 months (quartiles Q1;Q3: 0.5; 51.0) with a cumulative follow-up of 1132.5 late patient-years.

At 5 years of follow-up the mean gradient was 13.6 ± 8.6 mmHg and the effective orifice area was 1.5 ± 0.5 cm^2 (Table 5). A significant improvement in the NYHA classes was reported; patients in NYHA class I moved from 4.0% preoperative to 46.5% at 5-year follow-up, while patients in NYHA III decreased from 32.9% to 12.1%. Six cardiovascular deaths (0.5%) and 13 noncardiovascular deaths (1.1%) were reported (Table 7). Six (0.5%) valve-related reintervention occurred: 4 cases of endocarditis (in 3 cases the valves were explanted) and 2 cases of NSVD: in one case an annular rupture with a pseudoaneurysm and intraprosthetic regurgitation were reported requiring valve explant, annular repair, and implantation of a new Perceval; in the other patient a significant intraprosthetic valve regurgitation occurred requiring valve explant and replacement with a new Perceval valve.

Moderate intraprosthetic regurgitation was reported in 0.7% of the patients, while only 1.2% of patients had mild PVL. Bleeding occurred in 10 patients (1.0%), all in the RAT group. Three cases (0.3%) of SVD were reported. One patient had an early SVD with a valve cusp tear resulting in a severe aortic regurgitation treated with TAVI. Another patient, monitored through annual echocardiography, had a worsening central regurgitation within the sixth year of follow-up due to a calcified stiffened cusp. This patient was treated with TAVI as well. In the last case, the patients had a medically treated endocarditis 3 years after surgery that progressed in a valve calcification with a severe aortic stenosis requiring surgical AVR with a new Perceval valve implant.

Six patients (0.5%) had TIA and 8 (0.7%) strokes; PPI was required in 11 patients (1.0%) due to AVB III in 4 cases, AVB II in 2 cases, and other non specified conduction disorders in 3 patients.

Survival analysis reports a freedom from death at 24 and 60 months of 96.7% (95% CI: 94.7% to 98.6%) and 91.5% (95%

Table 5. Echocardiography Data at Discharge and Follow-Up.

	MICS (*N* = 480)	MS (*n* = 214)	RAT (*n* = 266)
Preoperative			
Effective orifice area (cm^2)	0.7 (0.2)	0.7 (0.2)	0.7 (0.2)
Mean gradient (mmHg)	49.3 (14.6)	47.5 (15.2)	50.7 (14.0)
1-year follow-up			
Effective orifice area (cm^2)	1.7 (0.5)	1.6 (0.5)	1.7 (0.5)
Mean gradient (mmHg)	11.6 (5.1)	11.9 (5.5)	11.5 (5.0)
2-year follow-up			
Effective orifice area (cm^2)	1.6 (0.4)	1.6 (0.4)	1.6 (0.4)
Mean gradient (mmHg)	11.3 (5.4)	12.8 (7.3)	10.9 (4.9)
3-year follow-up			
Effective orifice area (cm^2)	1.4 (0.4)	1.4 (0.4)	1.4 (0.4)
Mean gradient (mmHg)	11.3 (5.4)	11.8 (4.8)	11.2 (5.5)
4-year follow-up			
Effective orifice area (cm^2)	1.5 (0.4)	1.7 (0.4)	1.5 (0.4)
Mean gradient (mmHg)	12.6 (6.2)	10.9 (2.8)	12.7 (6.5)
5-year follow-up			
Effective orifice area (cm^2)	1.5 (0.5)	1.5 (0.5)	1.5 (0.5)
Mean gradient (mmHg)	13.6 (8.6)	10.8 (1.0)	13.8 (8.9)

Abbreviations: MICS, minimally invasive cardiac surgery; MS, ministernotomy; RAT, right anterior minithoracotomy.
Data presented as mean (SD)

Table 6. Early Outcomes (≤30 days).

	MICS (*N* = 480)		MS (*n* = 214)		RAT (*n* = 266)	
	Number of patients (number of AE)	% of patients	Number of patients (number of AE)	% of patients	Number of patients (number of AE)	% of patients
Any death	2 (2)	0.4%	2 (2)	0.9%	-	-
Noncardiovascular mortality	1 (1)	0.2%	1 (1)	0.5%	-	-
Cardiovascular mortality	1 (1)	0.2%	1 (1)	0.5%	-	-
Non-valve-related reintervention	6 (7)	1.3%	4 (4)	2.9%	2 (3)	0.8%
Re-exploration for bleeding	2 (2)	0.4%	2 (2)	0.9%	-	-
Tamponade	2 (2)	0.4%	1 (1)	0.5%	1 (1)	0.4%
Right pleural effusion	1 (1)	0.2%	-	-	1 (1)	0.4%
Pericardial effusion	1 (1)	0.2%	1 (1)	0.5%	-	-
Valve-related reintervention	7 (7)	1.5%	1 (1)	0.5%	6 (6)	2.3%
NSVD	6 (6)	1.3%	1 (1)	0.5%	5 (5)	1.9%
-Open surgical procedure	5 (5)	1.0%	-	-	5 (5)	1.9%
--Without device explant	3 (3)	0.6%	-	-	3 (3)	1.1%
--With device explant	2 (2)	0.4%	-	-	2 (2)	0.8%
-Transcatheter valve replacement	1 (1)	0.2%	1 (1)	0.5%	-	-
Malpositioning	1 (1)	0.2%	-	-	1 (1)	0.4%
-With device explant	1 (1)	0.2%	-	-	1 (1)	0.4%
Nondisabling stroke	5 (6)	1.0%	3 (4)	1.4%	2 (2)	0.8%
Disabling stroke	2 (2)	0.4%	2 (2)	0.9%	-	-
TIA	4 (4)	0.8%	1 (1)	0.5%	3 (3)	1.1%
Pulmonary thromboembolism	1 (1)	0.2%	1 (1)	0.5%	-	-
Bleeding	9 (9)	1.9%	3 (3)	1.4%	6 (6)	2.3%
Myocardial infarction	2 (2)	0.4%	-	-	2 (2)	0.8%
NSVD	56 (56)	11.7%	10 (10)	4.7%	46 (46)	17.3%
Central leak	32 (32)	6.7%	6 (6)	2.8%	26 (26)	9.8%
1+	29 (29)	6.0%	6 (6)	2.8%	23 (23)	8.6%
2+	3 (3)	0.6%	-	-	3 (3)	1.1%
PVL	15 (15)	3.1%	2 (2)	0.9%	13 (13)	4.9%
1+	13 (13)	2.7%	1 (1)	0.5%	12 (12)	4.5%
2+	1 (1)	0.2%	-	-	1 (1)	0.4%
3+	1 (1)	0.2%	1 (1)	0.5%	-	-
PVL + central leak	9 (9)	1.9%	2 (2)	0.9%	7 (7)	2.6%
1+/1+	5 (5)	1.0%	-	-	5 (5)	1.9%
2+/1+	3 (3)	0.6%	2 (2)	0.9%	1 (1)	0.4%
2+/2+	1 (1)	0.2%	-	-	1 (1)	0.4%
PPI	16 (16)	3.3%	5 (5)	2.3%	11 (11)	4.1%

Abbreviations: AE, adverse event; MICS, minimally invasive cardiac surgery; MS, ministernotomy; NSVD, nonstructural valve dysfunction; PPI, permanent pacemaker implantation; PVL, paravalvular leak; RAT, right anterior minithoracotomy; TIA, transient ischemic attack.

CI: 87.4% to 95.5%; Fig. 1). Freedom from valve-related reoperation at 24 and 60 months were 97.3% (95% CI: 95.7% to 98.9%) and 96.2% (95% CI: 94.0% to 98.4%) (Fig. 2), while freedom from SVD was 100% at 24 months and 99.5% at 60 months (95% CI: 98.4% to 100%; Fig. 3).

Discussion

The treatment of aortic stenosis has extremely evolved over the past decades.[20] The adoption of transcatheter technologies significantly impacted on the management of patients affected by severe aortic stenosis.[6,7] As a consequence, transcatheter approaches have gained a primary role in the treatment of this disease, particularly in intermediate to high risk patients.[21,22]

These profound changes led the surgical community to move toward minimally invasive surgical accesses, introducing new tools in order to improve patients' outcomes, as well as to give a new impulse to surgery.

In the present study, we investigated the clinical outcomes of patients enrolled in the SURE-AVR registry, after Perceval sutureless implantation for both isolated and combined aortic valve replacement. The analysis included 480 patients treated by either MS or RAT approaches, which remain the most commonly adopted techniques in MI-AVR.

In this series, 30-day mortality rate was low (0.4%), although a low to intermediate preoperative risk. These outcomes confirm the safety and the reliability of Perceval sutureless valve,[18–23] showing improved outcomes when compared with

Table 7. Late Outcomes (>30 days).

	MICS		MS		RAT	
	Number of patients (number of AE)	% over 1132.5 patient-years	Number of patients (number of AE)	% over 260.3 patient-years	Number of patients (number of AE)	% over 872.2 patient-years
Any death	19 (19)	1.7%	6 (6)	2.3%	13 (13)	1.5%
Noncardiovascular mortality	13 (13)	1.1%	4 (4)	1.5%	9 (9)	1.0%
Cardiovascular mortality	6 (6)	0.5%	2 (2)	0.8%	4 (4)	0.5%
Valve-related re-exploration	6 (6)	0.5%	2 (2)	0.8%	4 (4)	0.5%
Endocarditis	4 (4)	0.4%	2 (2)	0.8%	2 (2)	0.2%
-With device explant	3 (3)	0.3%	1 (1)	0.4%	2 (2)	0.2%
-Without device explant	1 (1)	0.1%	1 (1)	0.4%	-	-
NSVD	2 (2)	0.2%	-	-	2 (2)	0.2%
-With device explant	2 (2)	0.2%	-	-	2 (2)	0.2%
Nondisabling stroke	5 (5)	0.4%	2 (2)	0.8%	3 (3)	0.3%
Disabling stroke	3 (3)	0.3%	1 (1)	0.4%	2 (2)	0.2%
TIA	6 (6)	0.5%	2 (2)	0.8%	4 (4)	0.5%
Pulmonary thromboembolism	1 (1)	0.1%	-	-	1 (1)	0.1%
Bleeding	10 (11)	1.0%	-	-	10 (11)	1.3%
Myocardial infarction	5 (5)	0.4%	1 (1)	0.4%	4 (4)	0.5%
SVD	3 (3)	0.3%	-	-	3 (3)	0.3%
Endocarditis	3 (3)	0.3%	3 (3)	1.2%	-	-
Central leak	57 (60)	5.3%	3 (3)	1.2%	54 (57)	6.5%
1+	51 (51)	4.5%	2 (2)	0.8%	49 (49)	5.6%
2+	1 (1)	0.1%	-	-	1 (1)	0.1%
3+	7 (7)	0.6%	1(1)	0.4%	6 (6)	0.7%
4+	1 (1)	0.1%	-	-	1 (1)	0.1%
PVL	14 (14)	1.2%	2 (2)	0.8%	12 (12)	1.4%
1+	14 (14)	1.2%	2 (2)	0.8%	12 (12)	1.4%
PVL + central leak	7 (7)	0.6%	1 (1)	0.4%	6 (6)	0.7%
1+/1+	6 (6)	0.5%	-	-	6 (6)	0.7%
3+/1+	1 (1)	0.1%	1 (1)	0.4%	-	-
PPI	11 (11)	1.0%	4 (4)	1.5%	7 (7)	0.8%

Abbreviations: AE, adverse event; MICS, minimally invasive cardiac surgery; MS, ministernotomy; NSVD, nonstructural valve dysfunction; PPI, permanent pacemaker implantation; PVL, paravalvular leak; RAT, right anterior minithoracotomy; SVD, structural valve dysfunction; TIA, transient ischemic attack.

the reported results of GARY registry on conventional AVR.[24] These results positively compare with another registry reporting results on sutureless and rapid deployment valve, the SURD-IR registry.[15,17]

The reported mortality also favorably compares with TAVI in the same subset of patients. Notably, the PARTNER II trial reported a 30-day mortality of 3.9%, while the SURTAVI trial a 2.8% mortality rate.[25,26] These results are consistent with the data recently published in the PARNTER III trial, where the mortality rate was 0.4% in low risk patients after TAVI.[27]

Since MI-AVR could represent a technical challenge for the surgeon, the use of Perceval sutureless valve radically simplifies the surgical procedure overcoming annular exposure problems during suture positioning and knotting, with inherent benefits for the patients.[15–17] As reported from our previous experiences, the learning curve of minimally invasive AVR and MI-AVR with sutureless valves did not reveal any significant learning effect, showing that proficiency can be obtained and maintained after few procedures.[28,29] Troubles in starting a minimally invasive program may be overcome introducing new surgeons to these techniques through an expert surgeon tutoring. Moreover, in order to reduce variability, in particular in RAT technique, preparation, sizing and implantation have to follow a strictly standardized approach.[28,29]

The use of sutureless valve in MICS reduces cardiopulmonary bypass and cross-clamp times if compared with conventional valves implanted in sternotomy and MICS, as reported by other previous experience and data reported from STS registry.[30,31] Of note, longer CPB and cross-clamp times were reported in RAT group, probably due to the higher rate of REDO cases in this group (7.0% in MS vs 19.9% in RAT), where mediastinal tissue and adherence dissection can be completed once CPB is started, and the higher rate of concomitant procedures (3.3% in MS, 6.0% in RAT), mostly mitral repair/replacements.

In this surgical cohort treated via MI-AVR using a Perceval valve, a low rate of postoperative complications was reported. In particular, re-exploration for bleeding rate was 0.4%, lower than that previously reported via full-sternotomy and minimally invasive AVR for both sutureless and conventional valves, reporting an average rate of 3.0%.[15,27–30]

The incidence of neurological adverse events was 2.2%, with disabling stroke incidence of 0.4%, which is comparable with

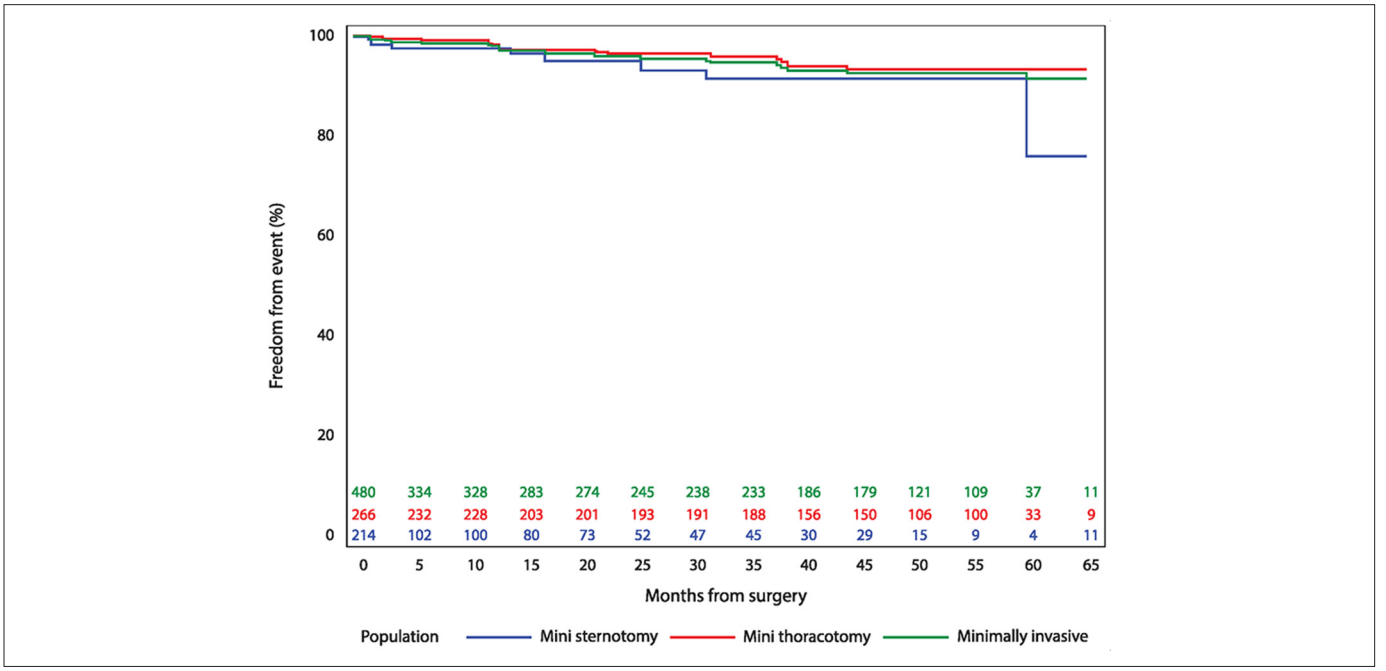

Fig. 1. Kaplan–Meier curve for freedom from death for any cause.

other international experiences.[15,17,20] Moreover, the incidence of stroke in the surgical arm of the Partner III trial was 3.2%.[27]

The presence of a significant PVL at discharge is a well-established negative predictive factor for survival and in the PARTNER II trial moderate-to-severe PVLs are demonstrated to negatively affect the survival.[26] The Perceval valve is designed to expand itself to an outer diameter larger than the patient's measured annular diameter. The expansion of the frame provides the proper interference fit to secure the Perceval device in place with high stability at physiologic pressure, flow, and movement. A recent study compared the accuracy of the annulus measurement of contrast-enhanced multidetector row computerized tomography (MDCT) and echocardiography, demonstrating a higher precision in annulus measurement of MDCT and establishing that CT scan investigation is preferable than echocardiography.[32]

CT-scan annuls measurement is a fundamental prerequisite before TAVI procedure. The TAVI prosthesis is usually

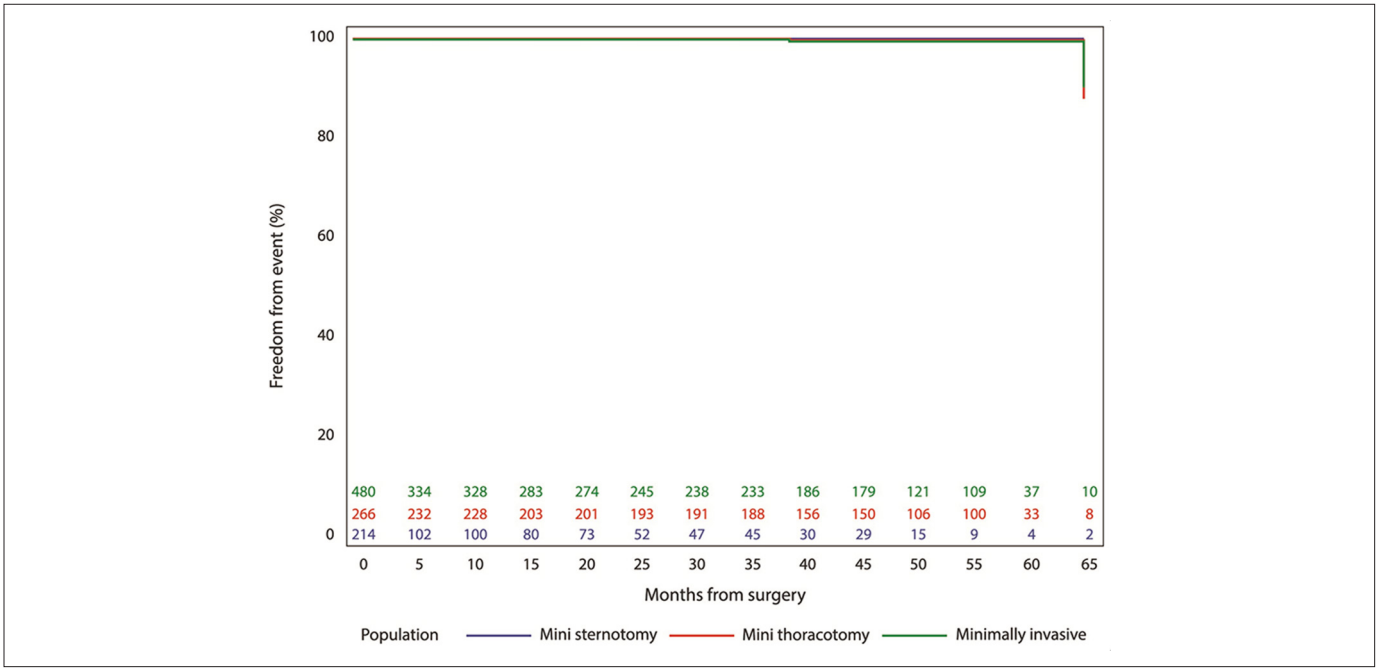

Fig. 2. Kaplan–Meier curve for freedom from valve-related reintervention.

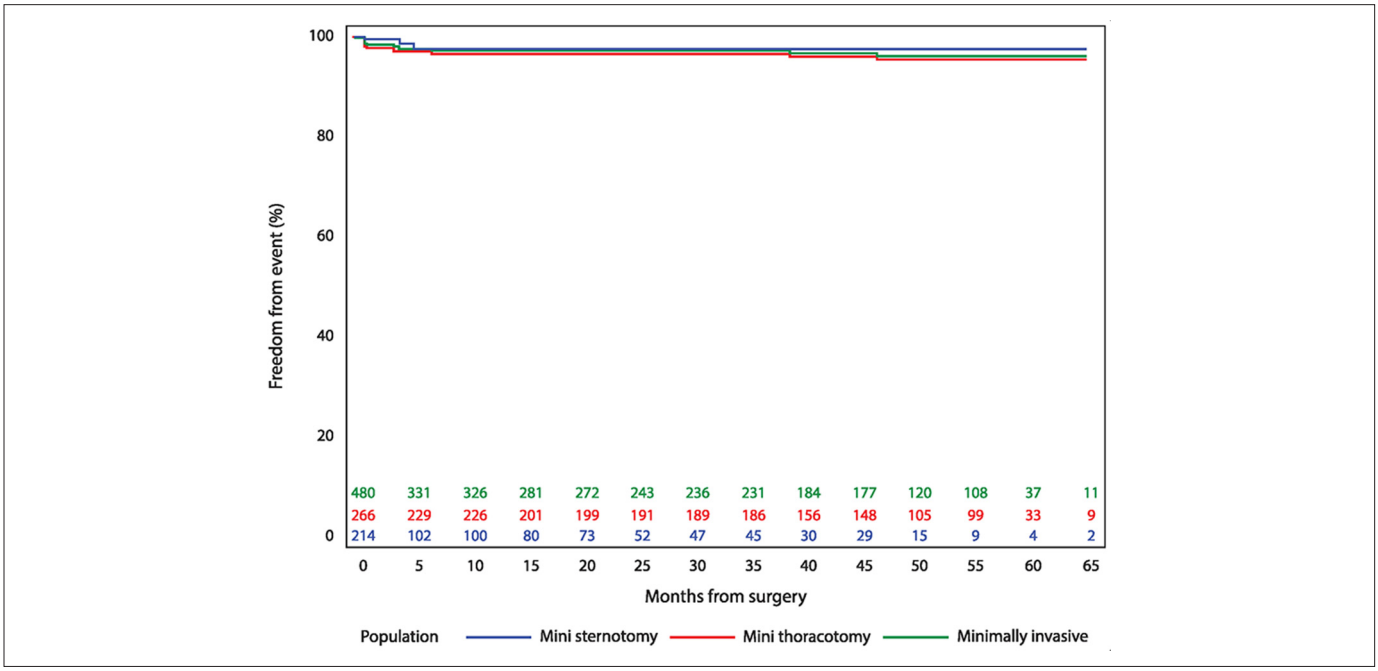

Fig. 3. Kaplan–Meier curve for freedom from structural valve dysfunction.

oversized compared to the annulus dimension, in order to assure the best anchorage of the valve, avoiding PVL (controlled oversizing). On the other hand, excessive oversizing may lead to serious procedural complications such as annular rupture or atrioventricular conduction disorders.

In the SURE-AVR registry the use of Perceval was associated with a very low incidence of PVL. Early aortic regurgitation equal or superior to grade II was reported in 0.6% of patients. D'Onofrio et al.[16] reported in 2016 a postprocedural significant PVL (AR ≥II) of 5.1% in TAVI patients, while different studies reported a moderate-to-severe PVL worse for TAVI than sutureless implantation: in PARTNER II trial[26] the incidence is 3.7% and increased up to 10% at 2-year follow-up; Biancari et al.[33] reported a 13.3% of incidence while Santarpino et al.[34] 13.5% and the German registry[35] for aortic valve 5.8%. These data indicate that the incidence of PVL after TAVI is significantly higher when compared with sutureless aortic valve, as confirmed in the CAVALIER trial,[18] where major PVL for Perceval valve was 0.5%. This difference may be clinically relevant, since significant PVL has been showed to affect negatively the survival.[26]

Data from trial on surgery and TAVI also suggest that rhythm disturbances requiring a permanent pacemaker impact negatively upon survival, but this finding did not find a statistical support.[36] PPI due to complete AV block still represents an issue for sutureless valves, with reported incidence up to 10%.[10,34] Reduction of the incidence was observed with the adoption of "watchful waiting" strategy instead of an early pacemaker implantation, with the surgical procedural "learning curve" effect and with an appropriate valve sizing.

Moreover, increasing experience in sutureless valve implantation and more deep comprehension of the technical aspects of this technology may have played a determining role in reducing this risk. Positioning the 3 guiding sutures of the Perceval at the nadir of each cusp, instead of a few millimeters below, led to a dramatic decrease in the incidence of PPI.[37] In addition, the importance of maintaining coaxiality of the prosthesis with the aortic annulus during deployment is an additional tip that must be taken into account.[38] Moreover, decalcification of the aortic annulus, as well as adequate sizing, are 2 additional key factors to reduce postoperative conduction disorders onset. Oversizing should be avoided, since this may lead to stent infolding or incomplete expansion with central leak and prostheses dysfunction, as well as excessive compression near the bundle of His with consequent PPI.[39] Some authors considered post-implant balloon dilation as an additional risk factor for PPI. Nevertheless, no difference was found between patients with or without balloon post-dilation.[40]

We reported a 3.3% early rate of complete AV block requiring pacemaker implantation, comparable with the recent published data of a large single-center series from Concistrè et al.[23] (5.0%) and with the PARTNER III surgical cohort. (4.1%).[27]

TAVI registries and the GARY registry report a PPI rate after TAVI procedure of 17%, while higher rates are described in SURTAVI trial (25.9%).[18,25,34]

Finally, we would like to highlight that in this study we had a considerable proportion of women, as the study represents a real-world experience, similar to other international registries.[15,17] This can be explained by the fact that Perceval sutureless valves are particularly suitable for small aortic annuli,

which are more common in females, giving to this patient subset a valuable alternative to TAVI.

Limitations

This study has limitations like any observational registry involving no adjudication of patient inclusion and outcomes and lack of a comparative arm. Since the surgical approach was not randomized, the presence of any statistically significant difference in outcomes between the 2 groups (MS and RAT) cannot be considered conclusive as some confounding factors could be present. There is no core laboratory to review images so the investigators were responsible for echo data reporting from their own institutions. Since this prospective registry is still ongoing, some missing data are present, due to data not yet entered in the database. Moreover, the follow-up data were collected up to September 2018; therefore, no complete data were available for all patients at the time of the analysis. We are expecting more complete data and longer follow-up in the near future.

Conclusions

The present experience with Perceval valve in MI-AVR showed remarkable results in terms of operative time, mortality, and postoperative complications both with MS and RAT, in intermediate surgical risk patients. This sutureless prosthesis provides a real advantage in MI-AVR, facilitating a surgical procedure that is otherwise technically demanding, with a good reliability in terms of duration and survival freedom from SVD at mid-term follow-up.

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: Max Baghai, Theodor Fischlein, Mattia Glauber, Marco Solinas and Giovanni Troise are Proctors for LivaNova PLC. Daniela Zakova also reports a financial relationship with LivaNova PLC. Jose Cuenca, Roberto Di Bartolomeo, and Giorgio Vigano declare that there is no conflict of interest.

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