Original Article

Early results of the Sorin® Perceval S sutureless valve: systematic review and meta-analysis

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Background: Minimally invasive aortic valve replacement (MAVR) has demonstrated a benefit with respect to increased patient satisfaction due to minimised pain and earlier recovery. Sutureless valves may benefit MAVR and conventional aortic valve replacement (AVR) by reducing operative times and blood transfusion requirements. The Perceval valve (Sorin, Salluggia, Italy) is a self-expanding prosthesis made from bovine pericardium mounted in a nitinol stent, designed to simplify the implantation of an aortic valve. This meta-analysis evaluates the clinical, haemodynamic, and survival outcomes of the Perceval sutureless valve.

Methods: An electronic search of 4 databases was performed from January 2000 to December 2016. Primary outcomes included mortality and stroke. Secondary outcomes included minimally invasive access, paravalvular leak, overall long-term survival, postoperative echocardiographic findings, and functional class improvement.

Results: After the application of inclusion and exclusion criteria, 14 of 66 relevant articles were selected for assessment. Of these 14 studies, a total number of 2,505 patients were included. The current evidence on the Perceval valve for aortic valve disease is limited to observational studies only. Minimally invasive surgery was performed in 976 patients, of which 336 were via the right anterior thoracotomy approach. The Perceval M and L sutureless valves were the most frequently used, 782 and 770 respectively. The incidence of major adverse events included 30-day mortality (0 to 4.9%), cerebrovascular accident (0 to 3%), permanent pacemaker insertion (0 to 17%), moderate to severe paravalvular leak (0 to 8.6%), and re-operation (0 to 4.8%). Post-operative mean aortic valve gradient ranged from 9 to 15.9 mmHg and post-operative New York Heart Association (NYHA) Class I or II ranged from 82% to 96%. The 1-year survival ranged from 86% to 100%; and 5-year survival was 71.3% to 85.5% in two studies.

Conclusions: The Perceval valve is associated with excellent post-operative results in MAVR and in conventional AVR. Larger randomised controlled studies are required to evaluate the long-term efficacy of the prosthesis.

Keywords: Perceval; sutureless; minimally invasive; meta-analysis; aortic valve replacement

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Introduction

Aortic stenosis (AS) is the most common valvular disorder, resulting in decreased life expectancy in symptomatic individuals (1,2).

Surgical aortic valve replacement (AVR) has long been the definitive therapy in treating symptomatic AS. Transcatheter aortic valve implantation (TAVI) has become an accepted alternative to surgery in treating high-risk or non-operative individuals with severe AS (3). The emergence of TAVI has led to renewed interest in developing artificial valves not requiring sutures to secure the valve in position. Rapid deployment employing a radial force to secure the valve within the annulus has significantly reduced implantation time.

In the 1960s, Magovern pioneered a sutureless heart valve made from titanium using a ball-in-cage design; and achieved a reduction in cardiopulmonary bypass time (CPB) (4). Implantation of this novel valve continued into the 1980s. However, the potential for paravalvular leak and embolisation limited it's further development (4,5). The TAVI technology has been adopted in sutureless valves, which can be deployed under direct vision via conventional or minimally invasive approaches without the need of a catheter. Minimally invasive AVR (MAVR) has demonstrated similar results to conventional AVR in regards to clinical outcomes, with the added benefit of improved patient satisfaction (6).

Currently, MAVR is limited to select cardiac centers. They can require specialised equipment and surgeons may experience a steep learning curve (7). MAVR is attributed to longer aortic cross-clamp (ACC) and CPB time, which inherently links to a higher risk of adverse events, especially amongst a high-risk surgical group (8). Therefore, the use of sutureless valves may be advantageous in the setting of MAVR by potentially reducing the operating time.

At present the Perceval (Sorin, Saluggia, Italy, CE approved 2011, FDA approved 2016) is the only true sutureless valve available for the implantation. It's direct competitor, the Intuity Elite (Edwards Lifesciences, Irvine, US, CE approved 2014, FDA approved 2016) is a rapid deployment aortic valve prosthesis requires 3 sutures to secure the valve to the annulus. Both valves are bioprosthetic and are anchored to the aortic annulus with an expandable metal stent frame.

The Perceval features an inflow ring designed to sit at the level of the annulus and an outflow ring, which sits at the level of the sinotubular junction. The outward flexion of the winged struts, connects the two rings and occupies the sinuses of Valsalva (*Figure 1*). Perceval aortic valve prosthesis is currently available in four sizes: S (19–21 mm), M (22–23 mm), L (24–25 mm), and XL (27 mm).

Figure 1 Sorin Perceval S sutureless valve (Sorin, Saluggia, Italy).

As the worldwide use of the Perceval valve continues to rise, there are no comprehensive reviews, assessing the efficacy and safety of the Perceval valve. Therefore we have performed this meta-analysis to assess the safety, clinical, and survival benefits of Perceval valve.

Methods

Search strategy

An electronic database search of four databases (MEDLINE, EMBASE, PubMed, Cochrane) was performed starting from January 2000 to December 2016. To attain the maximal search yield, we used the following free text "Perceval" or "sutureless" and "aortic valve replacement". We identified further relevant studies after reviewing the reference lists of all retrieved articles and the Sorin Perceval website (http://www.livanova.sorin.com/products/cardiac-surgery/aortic/perceval).

Outcomes

The primary end points included procedural success rate, 30-day mortality, cerebrovascular accident, permanent pacemaker insertion, paravalvular leak (mild, moderate and severe), re-operation, and the length of hospital and intensive care stay. The secondary end points included

echocardiographic findings including mean post-operative gradients (mmHg), mean long-term gradients, effective orifice area (EOA), New York Heart Association (NYHA) functional class improvement from baseline, and survival at 1-, 2-year, and longer. Additional outcomes included the procedural approach (minimally invasive *vs.* conventional sternotomy), valve sizes used, and ACC and CPB times.

Selection criteria

All patients undergoing implantation of the Perceval valve were eligible for this meta-analysis. The patient selection criteria for Perceval valve implantation varied with each institution. Only observational studies were included in this review. Case reports, case series with less than thirty patients, recent abstracts, expert opinions and editorial reports were excluded.

Data analysis and critical appraisal

Two reviewers (KS, SL) separately appraised the selected studies using a standardised data table. The relevant data extracted from the articles' text, tables, and figures was tabulated. Any discrepancies were resolved by discussion. The quality of scoring of observational studies used in meta-analyses can be controversial; therefore each article was analysed in accordance with the critical review checklist from the Dutch Cochrane Centre, as suggested by the MOOSE group (9).

Quality appraisal included: (I) a clear definition of study population; (II) a clear definition of outcomes and outcome assessment; (III) independent assessment of outcome parameters; (IV) sufficient duration period for follow-up; (V) no selective loss during follow-up; and (VI) identification of important confounders and prognostic factors.

Intervention

Despite some variation, similar steps were performed at different centers. The surgical approach was via a right anterior thoracotomy, mini-sternotomy or full sternotomy. In general, a transverse aortotomy was made 1.5 to 2 cm above the sinotubular junction. The aortic valve leaflets were excised and the annulus was either semi-debrided or fully debrided. Three guiding sutures, commonly 4-0 monofilament, were passed at the nadir of the aortic annulus. An appropriately sized prosthesis was collapsed onto the dual holder. Each guiding thread is passed through eyelets on the prosthesis inflow ring, to allow for accurate seating of the prosthetic valve onto the debrided annulus. A deflated post-dilation catheter was placed across the prosthesis and the balloon was inflated at 4 atmospheres for 30 s, as per the manufacturer's recommendations. Warm sterile saline at 37 degree Celsius was poured within the aortic root to allow for fixing of the nitinol stent and ensure optimal valve sealing. Following closure of the aortotomy, a transesophageal echocardiography was performed to assess the correct implantation of the prosthesis and exclude the presence of a paravalvular leak.

Results

Quality of the studies

After removal of duplicated studies, the titles and abstracts of 66 publications were identified as described in the search strategy. An initial review of these abstracts identified 24 potentially relevant articles. After applying the inclusion and exclusion criteria, 14 articles were reviewed (10-23) (See *Figure 2* PRISMA diagram). A total of 2,505 patients were represented in this study, of which 2,205 patients had undergone AVR using the Perceval valve. Quality assessment using the MOOSE criteria (9) checklist is summarised in *Table S1*.

Quality of evidence

All 14 studies were observational, which included 7 prospective (11,14,16,19-22) and 7 retrospective studies (10,12,13,15,17,18,23). There were no randomized controlled trials. The mean follow-up time was 6 to 8 months for 3 studies (15,18,19), 10 to 16 months for 5 studies (10,11,13,21,22), and 18 to 24 months for 3 studies (12,20,23), as seen in *Table 1*.

One study compared conventional AVR, sutureless valve implantation and TAVI (14). Shrestha *et al.* (22) compared patients receiving conventional aortic valves to patients receiving the Perceval valve. The study by Villa (12) chose to stratify patient groups to the size of the valve implanted. Patients with a "S" size valve were compared to patients implanted with a "L" sized valve. Three studies (13,15,19) compared the minimally invasive to full sternotomy surgical approach. All studies originated from specialised tertiary referral centers. Eleven centers reported results in greater than 100 patients (range, 120–314) (11-23). Seven studies presented multi-center data (12,13,15-17,19,23).

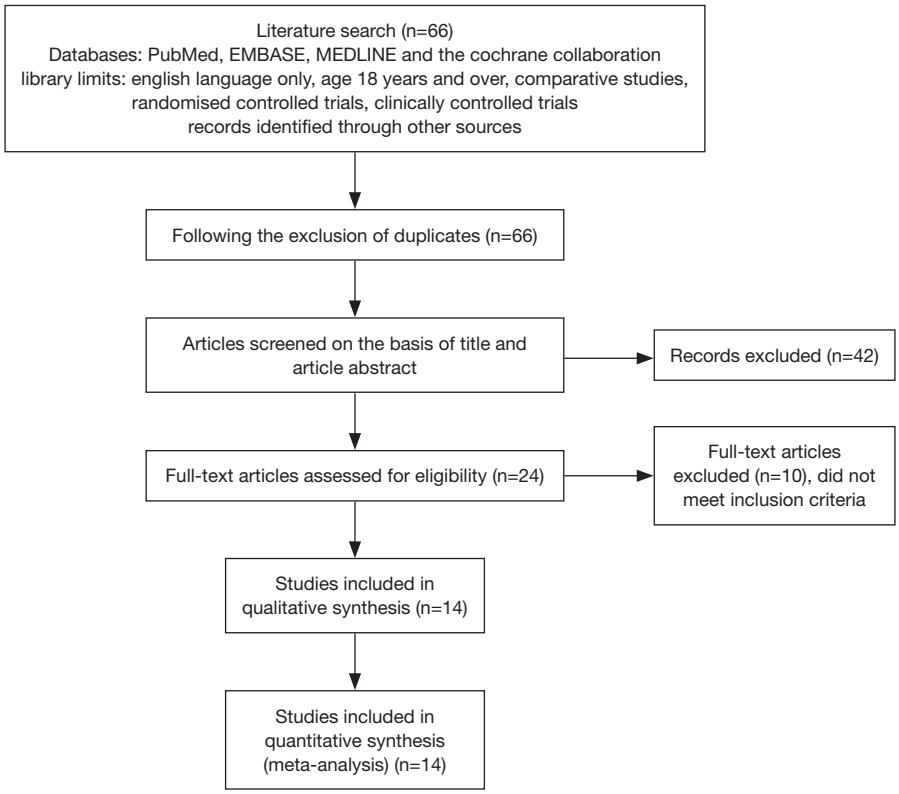

Figure 2 PRISMA diagram.

Seven studies published explicit inclusion criteria (13,15,16,18,19,21,22). The definition of patients not suitable for the Perceval valve varied between institutions. For example, Flameng *et al.* (21) chose to include only those patients with an aortic annulus between 19 to 23 mm; whereas Meuris *et al.* (16) excluded patients with intraoperative annulus diameters greater than 23 mm. The operative technique was defined in ten studies (10,12-16,18).

Overall, 61.5% of patients were female. The mean age was 78.7 years old (range, 76.6–80.4 years old). The mean body surface area was 1.78 m^2 (range, 1.6–1.85 m^2). The mean of patients with AS was 57.9% (range, 56.1–76.7%). The reported mean left ventricular ejection fraction was 56.9%. Hypertension and hyperlipidemia were reported in the majority of patients, 77.6 and 63.4% respectively. Additional comorbidities included chronic lung disease (18.7%), diabetes (28.1%), coronary artery disease (22.6%), peripheral vascular disease (18.7%), atrial fibrillation (15.9%) and chronic renal impairment (12.8%). The mean NYHA Class III or IV reported was 70.9% (range, 47.7–100%). European System for Cardiac Operative Risk Evaluation (EuroSCORE) was inconsistently reported; logistic versus additive, hence a mean could not be calculated (see *Table S2*).

Median sternotomy approach was used most frequently for valve implantation (weighted mean 75.2%; range, 15.3–100%). The Perceval valve size "M" was used in 46.4% of patients (range, 32–78.1%). The weighted mean ACC and CPB times for an isolated AVR were 39.7 minutes (range, 17–59.3 minutes) and 64.2 minutes (range, 35–92.3 minutes) respectively. Additional cardiac procedures were performed in 42.6% of patients (range, 9.7–100%) (see *Table 2*).

Assessment of safety

The 30-day mortality rate was 2.3% (pooled weighted mean, 95% CI, 1.44–3.25%) (*Figure 3A*). The pooled rate of pacemaker implantation 6.76% (95% CI, 4.68–8.86%) (*Figure 3B*) and the pooled rate of cerebrovascular accidents was 1.73% (95% CI, 1.23–2.22%) (*Figure 3C*). *Table 3* provides a summary of additional perioperative outcomes including atrial fibrillation, pericardial tamponade, myocardial infarction, reoperation, explantation of the sutureless valve, exploration for bleeding, infection, length

Table 1 Study characteristics

Study	Year	Institution	Country	Study Period	Study type	Sample size	Mean follow-up time (months)
Santarpino	2013	Klinikum Nürnberg, Nuremberg	Germany	2010–2012	OS, R	78	13.5±2.4
Zannis	2014	L'Institut Mutualiste Montsouris, Paris	France	2007–2011	OS, P	143	13.4±11.6
Villa	2015	Fondazione Poliambulanza, Brescia	Italy	2007–2013	OS, R	276	18.0±15.6
		L'Institut Mutualiste Montsouris, Paris	France				
		Medizinische Hochschule, Hannover	Germany				
		Centre Hospitalier Universitaire de Nancy, Universite de Lorraine, Vandœuvre-les-Nancy	France				
Rubino	2014	A.O.U. Policlinico-Vittorio Emanuele, University of Catania, Catania	Italy	2007–2013	OS, R	314	10.7
		Klinikum Nürnberg	Germany				
		University Hospital Gasthuisberg, Leuven	Belgium				
		Karolinska Institute, Karolinska University Hospital, Stockholm	Sweden				
		Oulu University Hospital, Oulu	Finland				
Muneretto	2014	University of Brescia Medical School, Brescia	Italy	2010–2013	OS, P	163	NR
Miceli	2014	Fondazione Toscana G. Monasterio, Massa	Italy	2010–2013	OS, R	281	8.0
		Klinikum Nürnberg, Nuremberg	Germany		OS, P	30	NR
Meuris	2015	Hannover Medical School, Hannover	Germany	2007–2008	OS, R	215	NR
		Universitaire Ziekenhuizen Gasthuisberg, Leuven	Belgium				
		L'Institut Mutualiste Montsouris, Paris	France				
Mazine	2015	Montreal Heart Institute, Universite de Montreal, Montreal, Quebec	Canada	2011–2015			
		Southlake Regional Health Center, McMaster University, Newmarket, Ontario					
		Hamilton Health Sciences, McMaster University, Hamilton, Ontario					
		Trillium Health Center, Mississauga, Ontario					
		New Brunswick Heart Center, Saint John, New Brunswick					
		Institut Universitaire de Cardiologie de Qu ebec/Hôpital Laval, Quebec					
Gilmanov	2013	G. Pasquinucci Heart Hospital, Massa	Italy	2011–2013	OS, R	137	6.0 (3.0–12.0)

Table 1 (*continued*)

Table 1 (*continued*)

Study	Year	Institution	Country	Study Period	Study type	Sample size	Mean follow-up time (months)
Folliguet	2012	Medizinsche Hochschule Hannover, Hannover	Germany	2007–2011	OS, P	211	6.0 (1.0-18.0)
		L'Institut Mutualiste Montsouris, Paris	Italy		OS, P	262	23.5±14.4
Fischlein	2015	Klinikum Nürnberg, Paracelsus Medical University Nuremberg	Germany	2010–2015	OS, P	32	15.8
Fleming	2011	Katholieke Universiteit Leuven, Leuven	Belgium	2007–2009	OS, R	243	14.5
Shrestha	2014	Hannover Medical School, Hannover	Germany	2007–2013			
		L'Institut Mutualiste Montsouris, Paris	France				
		Klinikum Nuremberg	Germany				
		U.Z. Gasthuisberg, Leuven	Belgium				
		Inselspital, Bern	Switzerland				
		Ruhr University of Bochum, Bochum	Germany				
Shrestha	2013	Hannover Medical School, Hannover	Germany	2007–2012	OS, P	120	22.7±17.5

OS, observational study; P, prospective; R, retrospective; NR, not recorded.

of intensive care unit stay and hospital stay.

Haemodynamic outcomes

Prior to MAVR, the pooled baseline mean gradient was 32.9 mmHg (95% CI, 24.4–41.5 mmHg) and the post-operative pooled mean gradient improved to 8.02 mmHg (95% CI, 5.12–8.00 mmHg). The weight mean pre-operative EOA was 0.75 cm^2 (range, 0.7–0.8 cm^2), which improved to 1.51 cm^2 (range, 1.4–1.6 cm^2). The pooled post-operative indexed EOA was 0.85 cm^2/m^2 (range, 0.80–0.90 cm^2/m^2). Patient prosthesis mismatch (PPM) was defined and reported in only one study (12). The pooled mean of moderate to severe paravalvular leak was 1.9% (95% CI, 0.97–3.7%). *Table 4* shows a summary of haemodynamic measurements including follow-up gradients.

Long-term outcomes

Post-operative NYHA Class improvement of one or two classes occurred in 87.8% of patients (95% CI, 81.0–92.5%). Survival at 1-year was a pooled weighted mean of 90.4% (95% CI, 87.2–93.7%). Loss to follow-up, reoperation, and endocarditis were inconsistently reported. Survival beyond 1-year was reported variably in the included studies, with the longest period of survival, 5-year reported in two studies (11,16) for a weighted mean of 83% (range, 71.3–85.5%) (see *Table 5*).

Discussion

As life expectancy improves, the prevalence of severe AS increases. Subsequently, patients are of higher risk due to their age and other comorbidities. In the past several years, TAVI has emerged as an established alternative to conventional AVR, particularly in the high-risk surgical cohort. TAVI has shown that rapid deployment and anchoring of the aortic valve without sutures, is feasible and safe. The advantage of the Perceval valve is that rapid deployment is achieved under direct visualisation in a semi-debrided annulus. The procedure can be performed using a minimally invasive approach, potentially reducing morbidity and mortality. This meta-analysis of the Perceval valve has demonstrated excellent initial results, which are comparable to conventional AVR.

In a cohort consisting of near octogenarians (mean age 78.5 years old), we found that the early postoperative outcomes are promising, as the 30-day mortality rate was 2.34% and the cerebrovascular event rate of 1.37%. This is in the context of a concomitant procedure rate of 42.5%.

Table 2 Operative characteristics

Study	Incision					Aortic crossclamp (min)		Cardiopulmonary bypass time (min)		Valve by size			
	RT	Mini	Stern	Redo	Add Pro	AVR	Combined	AVR	Combined	S	M	L	XL
Santarpino	3.8	80.7	15.3	15.3	NR	38.3±12.6	NR	68.2±19.4	NR	7.7	42.3	47.4	2.6
Zannis	NR	NR	100.0	NR	33.5	NR	32.0±14.9	NR	44.7±18.6	100.0	NR	NR	NR
Villa[a]	NR	12.8	87.2	NR	31.9	NR	40.0±17.1	NR	61.6±25.5	100.0	NR	NR	NR
Villa[b]	NR	20.5	79.5	NR	34.5	NR	38.6±17.4	NR	60.9±27.2	NR	66.3	33.6	NR
Rubino	2.8	41.7	55.4	7.6	29.9	39.0±15.0	43.0±20.0	66.0±23.0	73.0±28.0	11.8	43.0	40.0	5.0
Muneretto	NR	18.8	81.1	NR	NR	30.9±13.6	NR	47.0±18.5	NR	16.9	62.3	26.4	NR
Miceli	58.3	41.6[&]	NR	NR	NR	55.0 (47.0–65.0); 37.0 (30.0–46.0)[&]	48.0 (37.0–60.0)	74.0 (87.0–107.0); 72.0 (58.0–89.0)[&]	81.0 (68.0–98.0)	7.5/4.8[&]	20.3; 14.2[&]	30.6; 19.6[&]	3.2[&]
Meuris	NR	NR	100.0	10.0	46.7	29.3±8.0 (23.0-55.0)	45.4±15.4 (21.0–79.0)	46.4±6.7 (34.0–60.0)	73.4±21.8 (41.0–130.0)	36.7	63.3	NR	NR
Mazine	10.7	8.8	80.4	8.8	52.5	40.5±11.6	69.6±28.8	56.6±16.6	88.7±38.4	21.4	32.0	42.3	4.2
Gilmanov	100.0	NR	NR	NR	NR	59.3±19.5	NR	92.3±27.4	NR	13.9	32.8	53.2	–
Folliguet**	NR	21.6	78.3[#]	NR	23.1	33.6±9.5; 33.5±14.9[#]	44.2±13.4	65.7±21.4; 51.1±24.0[#]	67.6±23.9	15.4	53.8	30.7	NR
Fischlein	NR	100.0	NR	1.4	9.7	35.0±11.0	38.0±12.0	NR	NR	8.3	33.8	46.2	11.7
Fleming	NR	3.3	96.8	NR	50.0	17.0 (12.0–34.0)	22.0 (17.0–51.0)	35.0 (24.0–54.0)	62.0 (40.0–120.0)	21.9	78.1	NR	NR
Shrestha	NR	5.8	94.2	NR	100.0	NR	50.7±22.8	NR	78.9±32.3	14.0	53.0	33.0	NR
Shrestha*	NR	72.0	28.0	NR	NR	30.1±9.0	NR	58.7±20.9	NR	24.0	76.0	NR	NR
Weighted mean	32.4	36.6	75.2	7.2	42.6	39.7	45.6	64.2	66.5	22.7	46.4	40.3	6.1
Max	100.0	100.0	100.0	15.3	100.0	59.3	69.6	92.3	88.7	100.0	78.1	53.2	11.7
Mean	2.8	3.3	15.3	0	9.7	17.0	22.0	35.0	44.7	7.7	32.0	26.4	2.6

Values are % unless indicated. Study by Villa is represented by "a" and "b" as Villa chose to compare cohorts by valve type (S *vs.* M, L, XL). The study by Miceli chose to compare cohorts by incision hence those values with [&] represent cohort approached via ministernotomy. Folliguet** chose to compare cohorts aortic cross clamp and cardiopulmonary bypass times for isolated AVR hence [#] values represent patients undergoing surgery via sternotomy. *, represents the study by Shrestha 2013. RT, right anterior thoracotomy; Mini, ministernotomy; Stern, sternotomy; Redo, redosternotomy; Add pro, additional cardiac procedure; AVR, aortic valve replacement; S, M, L, XL, Perceval S valve types; NR, not reported.

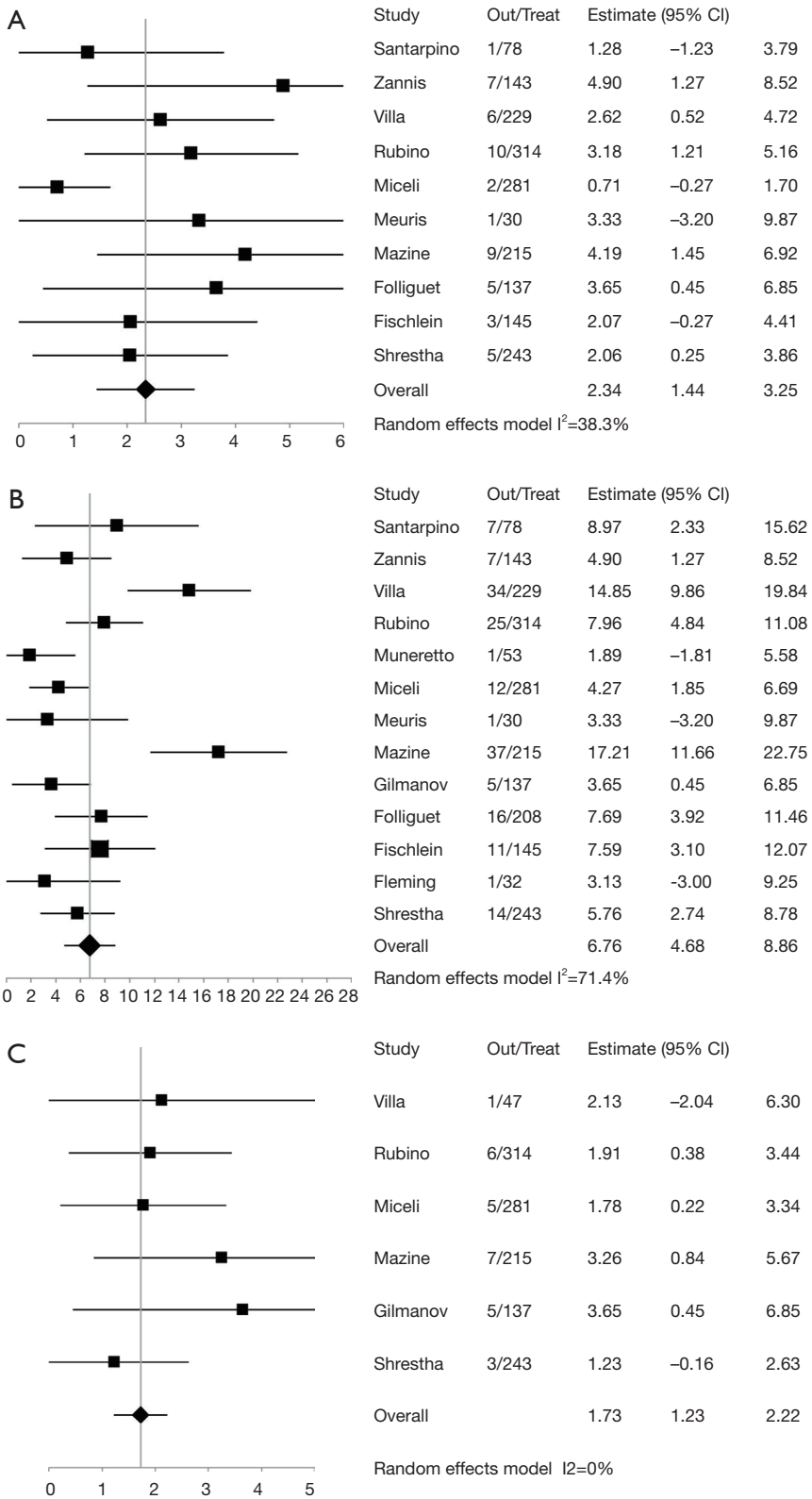

Figure 3 Patients undergoing perceval sutureless valve insertion, forest plots indicate: (A) 30-day mortality; (B) pacemaker insertion; (C) cerebrovascular accidents. Out, outcomes; Treat; treatment.

Table 3 Procedural outcomes

Study	30-d mortality	PPM	CVA	AF	Tamp	MI	Re-op	Explant	Re-exp	Infection	Con	ICU stay (d)	Hospital stay (d)
Santarpino	1.2	8.9	0	NR	NR	0	NR	NR	NR	NR	NR	NR	12.3±4.5
Zannis	4.9	4.9	NR	NR	NR	NR	4.1	NR	NR	NR	NR	NR	NR
Villa[a]	0	0	2.1	13.6	NR	NR	NR	NR	NR	NR	NR	NR	7.48±2.7
Villa[b]	2.6	15.0	0	2.3	NR	NR	NR	NR	NR	NR	NR	NR	12±29.9
Rubino	3.2	8.0	1.9	NR	NR	NR	1.0	NR	2.5	NR	0.6	3.2±3.4	13.4±6.5
Muneretto	0	2.0	0	58.5	5.4	NR	NR	NR	7.5	NR	NR	1.07±0.4	NR
Miceli	0.7	4.2	1.8	NR	NR	NR	0.3	NR	2.8	NR	1.4	1.0 (1.0–2.0)	8.0 (6.0–10.0)
Meuris	3.3	3.3	NR	NR	3.3	NR	0	NR	10.0	6.7	NR	NR	NR
Mazine	4.0	17.0	3.0	41.0	NR	NR	0	NR	5.0	0	NR	3.7±3.9	11.4±7.6
Gilmanov	0	3.6	2.2	27.0	NR	0.7	0.7	NR	5.1	NR	NR	1.6±1.8	7.1±3.1
Folliguet	2.4	7.0	NR	NR	NR	NR	3.2	NR	NR	NR	NR	NR	NR
Fischlein	2.1	7.6	NR	NR	NR	NR	NR	NR	NR	NR	2.0	NR	11.6±4.9
Fleming	0	3.1	0	NR	NR	NR	NR	NR	3.1	NR	NR	2.0	15.0 (4.0–30.0)
Shrestha	2.1	5.9	1.3	NR	NR	0.8	2.1	2.1	3.8	0.4	NR	NR	NR
Shrestha*	0	NR	NR	NR	NR	NR	NR	NR	4.0	NR	NR	1.8±1.8	14.1±7.5
Weighted mean	2.21	7.9	1.5	24.6	4.6	0.6	1.4	NA	3.9	0.6	1.2	2.3	11.0
Max	4.9	17.0	3.0	58.5	5.4	0.8	4.1	NA	10.0	6.7	1.4	3.2	13.4
Min	0	0	0	2.3	3.3	0	0	NA	2.5	0	0.6	1.0	7.1

Values are %, unless otherwise indicated. Study by Villa is represented by "a" and "b" as Villa chose to compare cohorts by valve (S *vs.* M, L, XL). *, represents the study by Shrestha 2013. PPM, permanent pacemaker insertion; CVA, cerebrovascular accident; AF, new onset atrial fibrillation; Tamp, cardiac tamponade; MI, myocardial infarction; Re-op, reoperation; Explant, explantation; Conv, conversion to sternotomy; ICU, intensive care unit; NR, not reported; NA, not applicable.

Table 4 Echocardiography measurements and clinical data following Perceval S implantation

Study	Preop Echo (mean gradient)	Pre op EOA (cm^2)	Post op Echo (mean gradient)	Mean gradient			Post op EOA (cm^2)	EOAi (cm^2/m^2)	Mild PVL (%)	Mod to Sev PVL (%)
				6 months	1 year	2 years				
Santarpino	49.5±15.8	NR	11.6±5.1	NR	NR	NR	NR	NR	NR	0
Zannis	38.8±17.0	0.8±0.2	9.0±3.4	NR	NR	NR	1.6±0.3	NR	NR	2.1
Villa[a]	43.1±20.0	NR	11.3±3.6	NR	NR	NR	NR	0.8±0.2	4.3	NR
Villa[b]	40.2±15.1	NR	10.3±4.4	NR	NR	NR	NR	0.8±0.2	4.3	NR
Rubino	51.9±18.3	NR	14.6±6.0	NR	NR	NR	NR	NR	11.9	0.6
Muneretto	50.5±15.3	0.7±0.3	10.8±6.8	NR	NR	NR	NR	NR	NR	NR
Miceli	NR	NR	13.0±4.0	NR	NR	NR	NR	NR	1.4	NR
Meuris	NR	NR	NR	NR	9.9±4.6	8.0±4.1	1.6±0.4	0.9±0.2	0	NR
Mazine	47.3±18.9	NR	13.3±6.4	NR	NR	NR	1.6±0.4	0.9±0.2	9.3	NR
Gilmanov	NR	NR	11.0	11	10	NR	NR	NR	1.5	NR
Folliguet	48.6±18.6	0.7±0.2	10.4±4.3	8.9±3.2	NR	NR	1.4 ±0.4	0.85±0.23	2.4	8.7
Fischlein	NR	NR	NR	12.8±4.9	12.5±4.5	11.8±4.7	NR	NR	0	0
Flameng	NR	NR	11.0 (5.0–28.0)	10.0 (6.0–28.0)	9.0 (3.0–21.0)	NR	1.5 (0.8–2.2)	NR	15.6	NR
Shrestha	40.6 ±16.6	0.8±0.2	10.1±4.7	8.9±4.2	8.9±50.4.6	9.0±3.4	1.5±0.4	0.8±0.2	0.4	NR
Shrestha*	NR	0.7±0.2	13.6±5.4	NR	NR	NR	1.5±0.3	NR	8.0	NR
Weighted mean	45.6	0.75	12.1	10.1	10.1	9.9	1.5	0.8	4.7	5.4
Max	51.9	0.8	14.6	12.8	12.5	11.8	1.6	0.9	15.6	8.7
Min	38.8	0.7	9	8.9	8.9	8	1.4	0.8	0	0

Values are mmHg unless indicated. Study by Villa is represented by "a" and "b" as Villa chose to compare cohorts solely by valve type (S *vs.* M, L, XL). *, represents the study by Shrestha 2013. Echo, echocardiography; EOA, effective orifice area; EOAi, indexed effective orifice area; NR, not reported.

Table 5 NYHA functional class and survival data in patients post Perceval S insertion

Study	Post-op NYHA class I II, (1 year)	Loss to follow-up 1 year	Re-operation	Endocarditis	1-year survival	2-year survival	3-year survival	4-year survival	5-year survival
Santarpino	NR	0	NR	NR	NR	NR	NR	NR	NR
Zannis	94.0	0	0.7	0.7	100	NR	NR	NR	85.5
Villa[a]	NR	NR	NR	NR	NR	NR	84.0	NR	NR
Villa[b]	NR	NR	NR	NR	NR	NR	77.0	NR	NR
Rubino	NR	NR	NR	NR	90.5	87.0	NR	NR	NR
Muneretto	NR	NR	NR	NR	90.6	NR	NR	NR	NR
Miceli	NR	0	0.4	0.4	90.0	NR	NR	NR	NR
Meuris	95.6	NR	NR	6.7	NR	NR	NR	NR	71.3
Mazine	NR	NR	NR	NR	NR	NR	NR	NR	NR
Gilmanov	92.0	NR	0.7	0.7	NR	NR	NR	NR	NR
Folliguet	82.0	NR	0.9	0.5	87.1	82.4	82.0	69.4	NR
Fischlein	NR	NR	NR	NR	NR	NR	NR	NR	NR
Fleming	96.0	NR	3.1	3.1	90.6	NR	NR	NR	NR
Shrestha	91.9	13.4	NR	NR	NR	86.4	NR	NR	NR
Shrestha*	NR	6.1	4.0	6.0	86.8	NR	60.9	NR	NR
Weighted mean	90.0	4.1	0.7	0.8	86.8	85.6	72.4	NA	83.0
Max	96.0	13.4	4.0	6.7	100.0	86.4	84.0	NA	85.5
Min	82.0	0	0.7	0.5	87.1	82.4	60.9	NA	71.3

Values are % unless indicated. Study by Villa is represented by "a" and "b" as Villa chose to compare cohorts solely by valve type (S *vs.* M, L, XL). *, represents the study by Shrestha 2013. NR, not reported.

This result is similar to another recently published meta-analysis which demonstrated an acceptable early mortality rate of 2.1% and stroke rate of 1.4%, when compared to conventional AVR (24).

Interestingly, the pacemaker rate was 6.76% and is higher than in conventional AVR (3.6%) (25). One theory is that the radial force applied during deployment of the sutureless valve may be a precipitant for a higher pacemaker implantation rate (26) Pacemaker rates following after TAVI have ranged between 9% to 42% (27,28) and have been associated with the continued expansion of the valve following implantation. This has resulted in conduction blocks occurring days after TAVI (29). However recently, there is evidence to suggest that the depth of placement of the Perceval has a correlation with a higher pacemaker implantation rate (30). Yanagawa *et al.* have shown a reduction in pacemaker implantation from 28% to 0% by the placement of guiding sutures millimeters higher than the manufacturer recommendation resulting in a slightly shallower valve position with respect to the aortic annulus (31).

Additional adverse events related to valve implantation are very low. There was one reported case of endocarditis in the perioperative phase after the sutureless valve was explanted (23). Overall rates of reoperation (1.43%) and early infection (<1%) rates are low, further supporting the safe early outcomes.

Long ACC and CPB times are associated with increased perioperative mortality (8). Our analysis has shown that the Perceval valve has significantly reduced the ACC and CPB times when compared to conventional AVR. The weighted mean ACC and CPB times for isolated AVR was 39.7 and 64.2 minutes respectively, which were less than the established conventional AVR times of 76 and 106 minutes

respectively (15).

Overall, there were 1,022 patients that underwent Perceval valve implantation via median sternotomy, representing a weighted mean of 75.2%. Several studies undertook a primarily minimally invasive approach (15,18) with no concomitant cardiac surgical procedure. Currently, minimally invasive approaches have been associated with longer ACC and CPB time, with no concise evidence to suggest reduced mortality and improved survival rates (32,33).

Even with the use of a rapid deployment valve, studies using the right thoracotomy approach were found to have longer ACC and CPB times, compared to the median sternotomy approach (see *Table 2*). This could be explained by difficult access, inability in debriding the aortic annulus effectively, patient selection and operator experience in minimally invasive surgery.

Early haemodynamic values have been promising with weighted mean valve gradient of 12.1 mmHg and post-operative EOA of 1.51 cm^2. Several studies have shown further improvement at 1 and 2 years with weighted mean gradients of 10.1 and 9.9 mmHg respectively (see *Table 5*). Moderate to severe paravalvular leak was noted to be a pooled mean of 1.9%. Several authors advocate the need for proper annular decalcification or potential replacement with a conventional aortic valve at the time of implantation if there is significant paravalvular leak (19,20). In one study, severe paravalvular leak was not corrected at the time of surgery, and in those patients the leak remained stable with no further intervention at a later date (13). Though the early results with the Perceval valve suggest excellent haemodynamic results, demonstrating stable mean gradients up to at least 2 years, the long-term follow-up data was limited in most instances and not statistically comparable to other sutureless valves such as the Intuity (Edwards LifeSciences, Irvine, Calif, USA) or conventional valves such as the Mosaic (Medtronic, Inc., Minneapolis, Minn, USA).

This study is limited by several factors. The majority of the studies reviewed in this meta-analysis have only reported early survival and haemodynamics outcomes. The available long-term data is limited to a very small cohort of patients. Although the early haemodynamic data was encouraging, the data cannot be stratified to a particular valve type or size. The studies presented were observational and in many instances, they involve the same specialised centers; thereby causing a sample selection and publication bias. Additional limiting factors to consider were the proportion of isolated AVRs to concomitant procedures, bias introduced by surgical approach and the experience of the surgeon. Further randomised controlled trials at specialised centers with extensive experience in implanting Perceval valves are required to validate the data in this meta-analysis (34). The Perceval Sutureless Implant *vs.* Standard Aortic Valve Replacement (PERSIST-AVR) trial (http:livanova.sorin.com), will be the first such large international multicenter trial to adequately compare the efficacy and performance of the Perceval valve to conventional AVR.

Conclusions

This systematic review and meta-analysis has demonstrated that early clinical and haemodynamic performance of the Perceval valve is satisfactory and comparable to that of conventional AVR. However, the long-term durability and haemodynamic data for the Perceval valve is somewhat limited. Large-scale randomised studies are recommended to accurately assess long-term durability and complications associated with the Perceval valve.

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Footnote

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References

1. Iung B, Baron G, Butchart EG, et al. A prospective survey of patients with valvular heart disease in Europe: The Euro Heart Survey on Valvular Heart Disease. Eur Heart J 2003;24:1231-43.
2. Carabello BA, Paulus WJ. Aortic stenosis. Lancet 2009;373:956-66.
3. Zahn R, Gerckens U, Grube E, et al. Transcatheter aortic valve implantation: first results from a multi-centre real-world registry. Eur Heart J 2011;32:198-204.
4. Magovern GJ, Cromie HW. Sutureless prosthetic heart valves. J Thorac Cardiovasc Surg 1963;46:726-36.
5. Gott VL, Alejo DE, Cameron DE. Mechanical heart valves: 50 years of evolution. Ann Thorac Surg 2003;76:S2230-9.
6. Brown ML, McKellar SH, Sundt TM, et al. Ministernotomy versus conventional sternotomy for aortic valve replacement: a systematic review and meta-analysis. J

Thorac Cardiovasc Surg 2009;137:670-679.e5.
7. Di Eusanio M, Phan K. Sutureless aortic valve replacement. Ann Cardiothorac Surg 2015;4:123-130.
8. Ranucci M, Frigiola A, Menicanti L, et al. Aortic cross-clamp time, new prostheses, and outcome in aortic valve replacement. J Heart Valve Dis 2012;21:732-9.
9. Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. JAMA 2000;283:2008-12.
10. Santarpino G, Pfeiffer S, Pollari F, et al. Left ventricular mass regression after sutureless implantation of the Perceval S aortic valve bioprosthesis: preliminary results. Interact Cardiovasc Thorac Surg 2014;18:38-42.
11. Zannis K, Joffre J, Czitrom D, et al. Aortic valve replacement with the perceval S bioprosthesis: single-center experience in 143 patients. J Heart Valve Dis 2014;23:795-802.
12. Villa E, Messina A, Laborde F, et al. Challenge for perceval: aortic valve replacement with small sutureless valves--a multicenter study. Ann Thorac Surg 2015;99:1248-54.
13. Rubino AS, Santarpino G, De Praetere H, et al. Early and intermediate outcome after aortic valve replacement with a sutureless bioprosthesis: Results of a multicenter study. J Thorac Cardiovasc Surg 2014;148:865-71; discussion 871.
14. Muneretto C, Bisleri G, Moggi A, et al. Treating the patients in the 'grey-zone' with aortic valve disease: a comparison among conventional surgery, sutureless valves and transcatheter aortic valve replacement. Interact Cardiovasc Thorac Surg 2015;20:90-5.
15. Miceli A, Santarpino G, Pfeiffer S, et al. Minimally invasive aortic valve replacement with Perceval S sutureless valve: early outcomes and one-year survival from two European centers. J Thorac Cardiovasc Surg 2014;148:2838-43.
16. Meuris B, Flameng WJ, Laborde F, et al. Five-year results of the pilot trial of a sutureless valve. J Thorac Cardiovasc Surg. 2015;150:84-8.
17. Mazine A, Teoh K, Bouhout I, et al. Sutureless aortic valve replacement: a Canadian multicentre study. Can J Cardiol 2015;31:63-8.
18. Gilmanov D, Miceli A, Bevilacqua S, et al. Sutureless implantation of the perceval s aortic valve prosthesis through right anterior minithoracotomy. Ann Thorac Surg 2013;96:2101-8.
19. Folliguet TA, Laborde F, Zannis K, et al. Sutureless perceval aortic valve replacement: results of two European centers. Ann Thorac Surg 2012;93:1483-8.
20. Fischlein T, Pfeiffer S, Pollari F, et al. Sutureless Valve Implantation via Mini J-Sternotomy: A Single Center Experience with 2 Years Mean Follow-up. Thorac Cardiovasc Surg 2015;63:467-71.
21. Flameng W, Herregods MC, Hermans H, et al. Effect of sutureless implantation of the Perceval S aortic valve bioprosthesis on intraoperative and early postoperative outcomes. J Thorac Cardiovasc Surg 2011;142:1453-7.
22. Shrestha M, Maeding I, Höffler K, et al. Aortic valve replacement in geriatric patients with small aortic roots: are sutureless valves the future? Interact Cardiovasc Thorac Surg 2013;17:778-82; discussion 782.
23. Shrestha M, Folliguet TA, Pfeiffer S, et al. Aortic valve replacement and concomitant procedures with the Perceval valve: results of European trials. Ann Thorac Surg 2014;98:1294-300.
24. Phan K, Tsai YC, Niranjan N, et al. Sutureless aortic valve replacement: a systematic review and meta-analysis. Ann Cardiothorac Surg 2015;4:100-111.
25. Smith CR, Leon MB, Mack MJ, et al. Transcatheter versus surgical aortic-valve replacement in high-risk patients. N Engl J Med 2011;364:2187-98.
26. Bouhout I, Mazine A, Rivard L, et al. Conduction Disorders After Sutureless Aortic Valve Replacement. Ann Thorac Surg 2016. [Epub ahead of print].
27. Roten L, Wenaweser P, Delacrétaz E, et al. Incidence and predictors of atrioventricular conduction impairment after transcatheter aortic valve implantation. Am J Cardiol 2010;106:1473-80.
28. Khawaja MZ, Rajani R, Cook A, et al. Permanent pacemaker insertion after CoreValve transcatheter aortic valve implantation: incidence and contributing factors (the UK CoreValve Collaborative). Circulation 2011;123:951-60.
29. Bagur R, Rodés-Cabau J, Gurvitch R, et al. Need for permanent pacemaker as a complication of transcatheter aortic valve implantation and surgical aortic valve replacement in elderly patients with severe aortic stenosis and similar baseline electrocardiographic findings. JACC Cardiovasc Interv 2012;5:540-51.
30. Miceli A, Lio A, Glauber M. Size, position, and timing: A mixture of success. J Thorac Cardiovasc Surg 2016;152:633-4.
31. Yanagawa B, Cruz J, Boisvert L, et al. A simple modification to lower incidence of heart block with sutureless valve implantation. J Thorac Cardiovasc Surg 2016;152:630-2.
32. Murtuza B, Pepper JR, Stanbridge RD, et al. Minimal access aortic valve replacement: is it worth it? Ann Thorac

Surg 2008;85:1121-31.
33. Brown ML, McKellar SH, Sundt TM, et al. Ministernotomy versus conventional sternotomy for aortic valve replacement: a systematic review and meta-analysis. J Thorac Cardiovasc Surg 2009;137:670-679.e5.
34. Leon MB, Smith CR, Mack MJ, et al. Transcatheter or Surgical Aortic-Valve Replacement in Intermediate-Risk Patients. N Engl J Med 2016;374:1609-20.

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