Early hemodynamic performance of the third generation St Jude Trifecta aortic prosthesis: A systematic review and meta-analysis

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ABSTRACT

Objective: The Trifecta aortic prosthesis is a latest-generation trileaflet stented pericardial valve designed for supra-annular placement in the aortic position. Robust clinical evidence and long-term follow-up data for this new prosthesis are lacking; a systematic review was conducted to assess current evidence.

Methods: A comprehensive search from 6 electronic databases was performed, with time period parameters dating from database inception to January 2014. Results utilizing Trifecta prosthesis for aortic valve replacement (AVR) were identified.

Results: A total of 13 studies with 2549 patients undergoing AVR with this prosthesis were included in this review. The mean proportion of patients with aortic stenosis was 82.4%, with a mean gradient of 47.4 mm Hg, and a pooled effective orifice area (EOA) of 0.74 cm². Valve sizes of 21 mm and 23 mm were implanted in 71.3% of patients. The pooled rates of 30-day mortality, cerebrovascular accidents, and acute kidney injuries were 2.7%, 1.9%, and 2.6%, respectively. After implantation, the pooled mean gradient decreased to 9.2 mm Hg, whereas discharge EOA increased to 1.8 cm², compared with preoperative parameters. Among included studies with significant heterogeneity detected, most patients had satisfactory patient-prosthesis mismatch, with 2.7% having severe mismatch.

Conclusions: The present systematic review demonstrated that short-term AVR with this prosthesis provided excellent early safety and hemodynamic outcomes with acceptable mean gradients and EOA. Long-term follow-up and randomized controlled trials are warranted to confirm the early results. (*J Thorac Cardiovasc Surg* 2015;149:1567-75)

Significant improvement in all echocardiographic outcomes postoperatively.

Central Message

The present systematic review demonstrated that short-term Trifecta aortic valve replacement provided excellent results of early safety and haemodynamic outcomes with acceptable mean gradients and effective orifice area. Future long-term follow-up and randomized controlled trials are warranted to conform the early promising results of the Trifecta prosthesis.

Perspective

The Trifecta aortic prosthesis is a latest-generation trileaflet stented pericardial valve designed for supra-annular placement in the aortic position. There is still a lack of robust clinical evidence and long-term follow-up data for this new prosthesis, thus a systematic review was conducted to assess the current evidence available. Pooled results from 13 studies and 2549 Trifecta prosthesis patients demonstrated excellent safety and haemodynamic outcomes in the short-term, with acceptable mean gradients and effective orifice area. Future long-term follow-up and randomized control trials are warranted to conform the early promising results.

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Abbreviations and Acronyms

AVR	= aortic valve replacement
CI	= confidence interval
EOA	= effective orifice area
EOAi	= effective orifice area index
EuroSCORE	= European System for Cardiac Operative Risk Evaluation
PPM	= patient-prosthesis mismatch

Supplemental material is available online.

Although surgical aortic valve replacement (AVR) remains the gold standard as a treatment approach for patients with severe aortic stenosis, the design and efficacy of aortic valves have progressed and evolved with time. The latest generation of aortic valves has been manufactured with

the aim of improving hemodynamic parameters and minimizing leaflet stress, while maintaining or improving the durability of previous valves.

The Trifecta (St Jude Medical Inc, St Paul, Minn) prosthesis is a third-generation, trileaflet, stented, pericardial valve designed for supra-annular placement in the aortic position.^{1,2} This prosthesis consists of bovine pericardial tissue mounted on a titanium stent, the purpose of which is to optimize direct tissue-to-tissue contact and reduce mechanical wear. The valve was approved by the US Food and Drug Administration in 2010, and some studies since have advocated its potential benefits, including claims of increased effective orifice area (EOA), reduced risk of abrasion and structural valve deterioration, as well as improved resistance to cardiac stress on leaflets.^{1,3-5} However, these potential benefits have yet to be verified by robust clinical evidence; randomized controlled studies and long-term follow-up data for this new prosthesis are still lacking.

Few single-center and multi-institutional studies have been conducted to investigate the efficacy and hemodynamic profile of this valve. To evaluate the current evidence

FIGURE 1. PRISMA flowchart of search strategy for studies investigating the aortic valve prosthesis.

TABLE 1. Study characteristics

First author	Year	Institution	Country	Study period	Study type	Sample size (n)	Follow-up (months)*
Yadlapati ⁸	2014	David Geffen School of Medicine, University of California Los Angeles	United States	2010-2012	OS, P	75	21.2 ± 7.9
Wendt ²	2014	West German Heart Centre Essen, University Hospital Essen	Germany	2003-2011	OS, R	121	6
Ugur ⁹	2014	Mayo Clinic	United States	2007-2009	OS, P	346	12
Seo ¹⁰	2014	Fukui Cardiovascular Centre	Japan	2012	OS, P	23	None
Remadi ¹¹	2014	Amiens Hospital	France	2011-2012	OS, P	100	12
Modi ¹²	2014	Wessex Cardiothoracic Centre, Southampton	United Kingdom	2011-2013	OS, P	400	12 ± 7.44
Maruyama ¹⁴	2014	Juntedo University School of Medicine	Japan	2012-2013	OS, R	33	NR
Levy ¹³	2014	Amiens Hospital, Rennes Hospital, Angers Hospital	France	2011-2012	OS, P	85	6
Bavaria ¹	2014	Hospital for the University of Pennsylvania, St Paul's Hospital, Vanderbilt Medical Centre, Mission Health and Hospital, Herzzentrum Leipzig GmbH, Mayo Clinic	United States, Canada, Germany	2007-2009	OS, P	1014	10.8 ± 5.4
Permanyer ⁴	2013	Hospiten Rambla	Spain	2010-2012	OS, P	200	None
Minardi ¹⁵	2013	S. Camillo-Forlanini	Italy	2011-2012	OS, R	50	6
Hanke ¹⁶	2013	University Clinic of Schleswig-Holstein	Germany	2010-2012	OS, R	32	5 ± 2
Dell'Aquila ⁵	2013	Universitätsklinikum Munster	Germany	2010-2011	OS, R	70	None

OS, Observational study; P, prospective; R, retrospective; NR, not reported. *Follow-up expressed as mean ± standard deviation.

for early outcomes and hemodynamic profile with this prosthesis, the present systematic review was performed.

METHODS

Literature Search Strategy

Electronic searches were performed using Ovid MEDLINE, PubMed, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, ACP (American College of Physicians) Journal Club, and the Database of Abstracts of Review of Effectiveness (DARE), encompassing the time period from the dates of inception to January 2014. To achieve maximum sensitivity with the search strategy, we combined the following terms, as either key words or MeSH (medical

subject headings) terms: “Trifecta” AND “aortic valve” OR “surgery OR operation OR replacement.” An example of the precise search strategy is provided in [Appendix E1](#).

The reference lists of all retrieved articles were reviewed for further identification of potentially relevant studies, assessed using the inclusion and exclusion criteria. Additionally, we considered whether we knew of any unpublished data. The study selection process and reporting process was performed according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement.⁶

Selection Criteria

Eligible studies for the present systematic review and meta-analysis included those in which patient cohorts underwent AVR with a

TABLE 2. Operative characteristics

First author	Aortic crossclamp time (min)		Cardiopulmonary bypass time (min)		Isolated AVR (%)	Concomitant (%)		Aortic root enlargement (%)	Septal myomectomy (%)	Valve size in mm (%)					
	All	AVR only	All	AVR only		Valve	CABG			19	21	23	25	27	29
Yadlapati ⁸	NR	NR	NR	NR	NR	10	17.1	0	NR	NR	NR	NR	NR	NR	NR
Wendt ²	85 ± 30	NR	127 ± 52	NR	NR	32.2	53.7	9.1	19.8	4.9	21.5	33.9	28.1	8.3	3.3
Ugur ⁹	81.4 ± 36.5	64.0 ± 25.0	106.9 ± 47.8	84.7 ± 34.8	45.4	NR	35.5	NR	NR	28	72	0	0	0	0
Seo ¹⁰	97 ± 19	NR	148 ± 36	NR	26	17.4	39.1	13.1	NR	17.4	52.2	30.4	0	0	0
Remadi ¹¹	42.9 ± 18.1	31 ± 20.2	63.72 ± 29	45.5 ± 20.7	59	3	36	2	NR	4	43	37	12	4	0
Modi ¹²	76 ± 30.3	62 ± 18.9	104.4 ± 43.6	83.7 ± 25.8	48	6	39	0.5	1	7	40	34	15	3.5	0.5
Maruyama ¹⁴	85 (40)	NR	95 (46)	NR	NR	27.3	18.2	24.2	18.2	27.3	45.5	21.2	6.1	0	0
Levy ¹³	40 ± 12	NR	61 ± 22	NR	NR	NR	29.4	NR	NR	5.9	42.4	36.5	12.9	2.4	0
Bavaria ¹	83.2 ± 37.3	64.3 ± 25.5	111.5 ± 51.0	86.6 ± 35.8	42.2	6	36.7	1.7	NR	NR	NR	NR	NR	NR	NR
Permanyer ⁴	NR	NR	NR	NR	56.5	10.5	27.5	5.5	0	16.5	40.5	29.5	11.5	2	0
Minardi ¹⁵	62 ± 22	NR	78 ± 22	NR	64	6	24	0	6	18	46	30	6	0	0
Hanke ¹⁶	150.22 ± 54.77	NR	NR	NR	28.1	21.9	46.9	NR	NR	9.4	25	46.9	18.8	NR	NR
Dell'Aquila ⁵	74.95 ± 22.18	65.42 ± 13.93	113.31 ± 32.45	102.04 ± 23.30	60	1.4	35.7	0	1.4	11.4	30	25.7	27.1	5.7	0
Minimum	40	31	61	45.5	26	1.4	17.1	0	0	4	21.5	0	0	0	0
Maximum	150	65.4	148	102	64	32.2	53.7	24.2	19.8	28	72	46.9	28.1	8.3	3.3
Pooled weighted average	78.7	62.1	105.8	84.1	46.4	8.5	35.8	2.6	4.3	14.1	46.2	25.1	11.6	2.7	0.4

AVR, Aortic valve replacement; CABG, coronary artery bypass graft surgery; NR, not reported.

FIGURE 2. Pooled proportions of patients who received prostheses of the following sizes (mm): 19, 21, 23, 25, 27, and 29. Each individual point denotes the mean % reported by an included study. The 3 horizontal bars for each valve size represent median and interquartile range. The percentage above the bars is the overall proportion.

third-generation Trifecta prosthesis (St Jude Medical Inc, St Paul, Minn). Studies that did not include mortality or complications as endpoints were excluded. When institutions published duplicate studies with accumulating numbers of patients or longer follow-up periods, only the most complete reports were included for quantitative assessment at each time interval. In addition, reference lists were hand-searched for further relevant studies. All publications were limited to those that involve human subjects and are written in English. Abstracts, case reports, conference presentations, editorials, reviews, and expert opinions were excluded.

Data Extraction and Critical Appraisal

Data extraction was conducted with a standardized data collection form. All data were extracted from article texts, tables, and figures. Two investigators independently reviewed each retrieved article, and selection of relevant articles for the meta-analysis was done by discussion and consensus according to inclusion and exclusion criteria. Two investigators independently performed the extraction of data. Discrepancies were resolved by discussion and consensus.

Because quality scoring is controversial in the meta-analysis of observational studies, 2 investigators independently appraised each article included in the meta-analysis according to a critical review checklist from the Dutch Cochrane Center, as proposed by the Meta-analysis of Observational Studies in Epidemiology (MOOSE) group.⁷ The key points on this checklist include: (1) a clear definition of the study population; (2) a clear definition of outcomes and outcome assessment; (3) an independent assessment of outcome parameters; (4) a sufficient follow-up duration; (5) no selective loss during follow-up; and (6) identification of important confounders and prognostic factors. The final results were reviewed by the investigators.

Statistical Analysis

A meta-analysis of proportions was conducted for the available main preoperative and postoperative variables. First, to establish variance of raw proportions, a Freeman-Tukey transformation was applied. To incorporate heterogeneity (anticipated among the included studies), transformed proportions were combined using DerSimonian-Laird random effects models. Heterogeneity between trials was studied using χ^2 analysis. The I^2 statistic was used to estimate the percentage of total variation across studies that was due to heterogeneity rather than chance. This statistic

can be calculated as: $I^2 = 100\% \times (Q - df) / Q$, with Q defined as Cochran's heterogeneity statistic, and df defined as degrees of freedom. An I^2 value of $>50\%$ was considered to represent substantial heterogeneity. All these analyses were performed using Open Meta-Analyst and the metafor package for R, version 3.01.

RESULTS

From the systematic search of 6 databases and other sources, 146 studies were identified and screened. After exclusion of duplicates and irrelevant articles, 27 studies remained for detailed assessment. Finally, 13 studies were included for systematic review and meta-analysis of proportions, including 2549 patients who underwent AVR with this prosthesis, for assessment (Figure 1). Quality assessment using the MOOSE checklist criteria is summarized in Table E1.

All 13 included articles were observational studies, including 8 prospective^{1,4,8-13} and 5 retrospective studies.^{2,5,14-16} Seven studies reported <100 patients,^{5,8,10,13-16} and 1 study reported >1000 patients.¹ Four included studies^{4,5,15,16} were published in 2013, and 9 studies^{1,2,8-14} were published in 2014. The mean follow-up time was up to 6 months for 4 studies,^{2,13,15,16} up to 12 months for 4 studies,^{1,9,11,12} and >20 months for 1 study⁸ (Table 1).

For procedural parameters, aortic crossclamp durations were reported in 11 studies; cardiopulmonary bypass duration was reported in 10 studies. Discharge peak gradient, mean gradient, EOA and EOA index (EOAi) were reported in 7, 12, 8, and 8 studies, respectively. The 30-day mortality was reported in 9 studies.

Baseline Patient Characteristics

The 13 included studies had, overall, 54.7% male patients, with a mean age of 73.7 years (range: 71-76). The mean body surface area was 1.9 m^2 (range: 1.49-1.95). The mean proportion of patients with aortic stenosis was 82.4%. The mean left ventricular ejection fraction of included patients was 57.7% (range: 50.5%-63.3%). Most patients had coronary artery disease, hypertension, and hyperlipidemia (weighted mean: 53.1%, 77.1%, and 61.5%, respectively). Other comorbidities included diabetes (24.8%), chronic lung disease (13.6%), pulmonary hypertension (16%), atrial fibrillation (6.7%), chronic kidney disease (8.0%) and peripheral vascular disease (12.4%). Prior surgery was performed in 18.6% of included patients. Risk assessment using logistic versus additive EuroSCORE (European System for Cardiac Operative Risk Evaluation) was inconsistent among included studies, and thus a mean EuroSCORE could not be validly calculated (Table E2).

The weighted mean crossclamp duration was 78.7 minutes (range: 40-150) and 62.1 minutes (range: 31-65.4) for isolated AVR. For cardiopulmonary bypass, the weighted mean was 105.8 minutes (range: 61-148) for

FIGURE 3. In patients undergoing aortic valve replacement using the prosthesis, the forest plot shows: (A) 30-day mortality; (B) cerebrovascular accidents; (C) acute kidney injury; (D) moderate patient-prosthesis mismatch; and (E) severe patient-prosthesis mismatch. *C.I.*, Confidence interval; *Ev*, events number; *Trt*, treatment number.

TABLE 3. Perioperative outcomes

	30-d				AV		Blood		New	Low		ICU	Hospital	Rehosp			
	mortality	CVA	MI	Infection	AKI	block	transfusion	Re-op	AF	CO	PVL	stay (days)	stay (days)	valve issues	Moderate PPM	Severe PPM	
Yadlapati ⁸	8.6	4.3	0	NR	5.7	NR	2.9	NR	NR	NR	NR	NR	NR	1.43	15.7	5.7	
Wendt ²	8.3	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	21	0	
Ugur ⁹	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	54.9	14.7	
Seo ¹⁰	0	4	0	0	0	0	0	0	0	0	0	NR	NR	0	NR	NR	
Remadi ¹¹	2	0	0	0	13	8	0	0	1	42	0	3	3.38 ± 2.44	11 ± 4.7	NR	0	0
Modi ¹²	2.8	2	NR	NR	2.5	NR	NR	NR	NR	NR	NR	0	NR	10 (5-62)	NR	NR	NR
Maruyama ¹⁴	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	0	NR	NR	3	0	
Levy ¹³	NR	0	0	0	0	0	0	0	0	NR	NR	6	NR	NR	21.2	2.3	
Bavaria ¹	1.8	2.5	NR	NR	NR	NR	8.1	NR	0.1	NR	NR	0.1	NR	NR	22.8	5.5	
Permyer ⁴	2.5	1.5	NR	1	3.5	2	NR	NR	0.5	18	NR	NR	1.5	8.5	3	0	
Minardi ¹⁵	NR	NR	0	NR	0	NR	NR	NR	2	8	NR	NR	NR	NR	28	0	
Hanke ¹⁶	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	
Dell'Aquila ⁵	2.9	2.9	1.4	1.4	1.4	4.2	0	0	10	NR	NR	1.4	NR	NR	NR	NR	
Minimum	0	0	0	0	0	0	0	0	0	0	NA	0	NA	NA	0	0	
Maximum	8.6	4.3	1.4	1.4	13	8	8.1	0	10	42	NA	6	NA	NA	54.9	14.7	
Pooled weighted average	2.7	1.9	0.2	0.6	2.6	3.1	6.2	0	0.7	22.0	NA	0.6	NA	NA	18.4	2.7	

Values are %, unless otherwise indicated. Moderate PPM is defined as EOAi <0.8. Severe PPM is defined as EOAi <0.65. CVA, Cerebrovascular accident; MI, myocardial infarction; AKI, acute kidney injury; AV, atrioventricular; Re-op, reoperation; AF, atrial fibrillation; CO, cardiac output; PVL, paravalvular leak; ICU, intensive care unit; Rehosp, rehospitalization; PPM, patient-prosthesis mismatch; NR, not reported; NA, not available.

all Trifecta cases, and 84.1 minutes (range: 45.5-102) for isolated procedures. Concomitant valve procedures were performed in 8.5% of patients; concomitant coronary artery bypass grafting was performed in 35.8% of patients. The proportions of patients with valve sizes of 19, 21, 23, 25, 27, and 29 mm, respectively, are shown in Table 2 and Figure 2.

Before AVR, the mean baseline peak gradient was 73.9 mm Hg (95% confidence interval [CI], 68.3-79.6), whereas the mean gradient was 47.4 mm Hg (95% CI, 45.1-49.7). The pooled EOA was 0.74 cm² (95% CI, 68.8-79.8), and the pooled EOAi was 0.475 cm²/m² (95% CI, 0.30-0.65).

Assessment of Safety

The pooled weighted mean of the 30-day mortality rate was 2.7% (95% CI, 1.6%-3.8%) (Figure 3, A). From 1877 patients, the pooled rate of cerebrovascular accidents was 1.9% (95% CI, 1.1%-2.6%) (Figure 3, B), whereas the pooled rate of acute kidney injuries was 2.6% (95% CI, 1.0%-4.2%) (Figure 3, C). Other perioperative outcomes, including myocardial infarctions, bleeding rates, blood transfusion requirements, reoperations, new atrial fibrillation, paravalvular leakage, intensive care unit stay, hospital stay, and rehospitalizations are summarized in Table 3.

Assessment of Hemodynamic Outcomes

All included studies reported echocardiographic hemodynamic outcomes. The pooled peak gradient was 17.7 mm Hg (95% CI, 16.3-19.2); the pooled mean gradient was 9.2 mm Hg (95% CI, 8.7-9.6). The pooled discharge EOA was 1.8 cm² (95% CI, 1.6-2.0); the EOAi was 1.0

cm²/m² (95% CI, 0.9-1.1). Summary of peak gradient, mean gradient, EOA, and EOAi, stratified according to valve size, is provided in Figure 4 and Table 4.

Among the studies that defined moderate patient-prosthesis mismatch (PPM), the cutoff of EOAi of <0.8 was uniformly reported. Nine studies defined severe PPM as an EOAi of <0.65; and 5 studies did not report definitions for severe PPM. Accordingly, there was moderate PPM in 18.4% (95% CI, 8.5%-28.3%) (Figure 3, D); severe PPM was evident in 2.7% (95% CI, 0.9%-4.4%) of included patients (Figure 3, E). Significant heterogeneity among included studies was detected for PPM outcomes.

COMMENT

The prosthesis was CE (Conformité Européenne) approved and introduced into clinical practice in 2011, with the aim of providing better hemodynamic profiles, while maintaining the durability and efficacy of previous bioprostheses. Given its recent introduction, few studies have reported on the valve's long-term durability, efficacy, and safety outcomes. The present systematic review assessed the early safety and hemodynamic outcomes of this aortic prosthesis from available evidence.

Although long-term durability and hemodynamic data for the prosthesis are currently unavailable, a few short-term studies demonstrate promising performance, but these require further validation. This valve consists of a sewing ring and supra-annular design, which has been previously suggested to reduce flow obstruction⁵ by better matching the internal diameter to the tissue annulus diameter. As with other third-generation aortic valves, this

FIGURE 4. A-H, Summary of discharge echocardiographic findings of the present systematic review, stratified by valve size. Pooled weighted mean valves represented as mean (95% confidence interval). *Preop*, Preoperative; *Postop*, postoperative; *EOA*, effective orifice area; *EOAI*, effective orifice area index.

ACD

TABLE 4. Pooled weighted mean estimates of hemodynamic function

Hemodynamic outcome by valve size	n	N	Weighted pooled proportion or estimate (95% CI)
19 mm			
Peak gradient (mm Hg)	182	7	22.0 (18.7, 25.4)
Mean gradient (mm Hg)	182	7	10.7 (10.0, 11.5)
EOA	154	7	1.44 (1.3, 1.56)
EOAi	154	7	0.89 (0.78, 1.01)
21 mm			
Peak gradient (mm Hg)	575	7	18.5 (17.0, 20.1)
Mean gradient (mm Hg)	575	7	10.0 (9.1, 10.9)
EOA	472	7	1.72 (1.61, 1.83)
EOAi	472	7	1.00 (0.90, 1.10)
23 mm			
Peak gradient (mm Hg)	253	7	16.7 (14.0, 19.4)
Mean gradient (mm Hg)	284	7	8.7 (7.6, 9.7)
EOA	168	6	2.00 (1.85, 2.15)
EOAi	168	6	1.07 (0.97, 1.16)
25 mm			
Peak gradient (mm Hg)	118	5	14.8 (13.2, 16.4)
Mean gradient (mm Hg)	118	5	7.6 (7.1, 8.1)
EOA	63	5	2.27 (2.11, 2.42)
EOAi	168	6	1.10 (1.01, 1.18)
27 mm			
Peak gradient (mm Hg)	28	4	11.3 (8.9, 13.8)
Mean gradient (mm Hg)	30	5	6.0 (4.9, 7.0)
EOA	16	4	2.50 (2.40, 2.59)
EOAi	16	4	1.15 (1.12, 1.18)

n, Number of patients analyzed; *N*, number of studies included in analysis; *CI*, confidence interval; *EOA*, effective orifice area; *EOAi*, effective orifice area index.

prosthesis includes an anticalcification agent, either glutaraldehyde or ethanol.¹ The valve design, with the pericardial leaflets mounted externally to the stent frame, is meant to increase EOA and hemodynamic performance. In addition, the valve has been claimed to have inherent distensibility,⁸ to promote optimal function and durability in periods of duress and high load, such as during exercise.

From early postoperative outcomes, the prosthesis seems to be safe, with a low 30-day mortality rate of 2.7%. This rate occurred despite 8.5% of patients undergoing concomitant valve surgery, and 35.8% undergoing concomitant bypass grafting. Given that all included studies were published between 2013 and 2014, the low mortality rate supports improved and excellent outcomes after conventional AVR in the modern era. Other complications, including infection (0.6%), reoperations (0.7%), and paravalvular leaks (0.6%), were also low, suggesting that early outcomes with the valve are safe. The multicenter study of 1014 patients who received the valve reported a single case of early explantation that was needed because of structural valve degeneration.¹ In another recent case report by Saxena and colleagues,¹⁷ structural valve degeneration with prosthesis thickening and calcification was evident after 4-year follow-up of 1 patient.

The present systematic review demonstrates promising short-term valve hemodynamics, with a pooled mean gradient of 9.2 mm Hg, and a pooled discharge EOA of 1.8 cm². Although these short-term results suggest that the valve has the potential to provide excellent hemodynamic outcomes, the available evidence is not propensity-matched or randomized, and long-term follow-up evidence is very limited. Furthermore, the direct comparative data between this and other prostheses, such as the Mitroflow (Sorin Group, Saluggio, Italy), the Mosaic (Medtronic, Inc, Minneapolis, Minn), and the Magna (Edwards LifeSciences, Irvine, Calif), are insufficient to yield valid statistical comparisons.

As shown in Figure 4, EOA and EOAi show an increasing trend as size of the prosthesis increases, which coincides with decreasing trends of peak and mean gradients. Additionally, >60% of the Trifecta prostheses were sized at 19 mm or 21 mm and implanted in patients with a small annulus, in contrast with the valve-size distribution reported^{18,19} with other valves, such as the Perimount Magna (Edwards LifeSciences, Irvine, Calif). Although no concrete comparative conclusions can be drawn, these trends do suggest that the valve may provide good hemodynamic performance. These early outcomes require further validation and confirmation in clinically robust, well-designed, and well-organized multicenter studies.

The influence of PPM on patient prognosis is controversial, with some studies showing increased all-cause and cardiac mortality in this setting.^{20,21} Given that finding, PPM prevention and minimization is becoming increasingly important when choosing which valve prosthesis to implant. Previously, low PPM could be achieved by using only stentless prostheses²²; however, their implantation is technically difficult and is associated with a steep learning curve. Furthermore, stentless prostheses are associated with extended crossclamp and cardiopulmonary bypass durations,²³ and they do not favor minimally invasive approaches. In addition, reoperations with stentless valves are more extensive and demanding, often requiring aortic root replacement.²⁴

For these reasons, stented valves are still used by most surgeons, despite the less favorable hemodynamic properties and a revived interest in stentless valves in the early 1990s. Although data reported on PPM may vary, our review suggests that the prosthesis is associated with excellent early EOA and mean gradients, and a low incidence of severe PPM of 2.7%, which is considerably lower than the 9.8% incidence in the general population undergoing AVR.²¹

Another known limitation of the prosthesis is that structural deviations occur during implantation that may result in suboptimal hemodynamics. This prosthesis has a very high profile, with pericardial leaflets mounted on a titanium stent. During implantation, if the stent posts are indented, the structural deformation may be permanent

and can cause altered hemodynamics with low gradients and reduced PPM. Therefore, the prosthesis must be implanted with extreme caution, to avoid any deviation of the titanium stent. Lower PPM values, and severe PPM, may be partially attributed to permanent titanium stent deviation during implantation.

Limitations

The present study is limited by several factors. First, most studies have reported only early hemodynamic and safety outcomes, limiting the data available for analysis. Results from early outcomes are promising, with the valve demonstrating excellent early EOA and acceptable mean gradients. However, longer-term follow-up definitely is warranted to balance the risks and benefits of this new, third-generation prosthesis.

Second, the available evidence included in this review is limited to observational studies, which are susceptible to selection bias and publication bias. Ideally, randomized controlled trials would provide the best evidence base for an assessment of the valve. Several included studies consisted of small sample sizes with populations of <100 patients, which prevented further meta-regression analysis to determine potential risk factors. Other limiting factors include the varied proportion of concomitant valvular and bypass procedures performed during AVR with the prosthesis, which may undermine the validity of the presented results. Future directions may include studies that compare the valve directly with stentless aortic prostheses, as well as current-generation bioprostheses, on long-term safety and hemodynamic outcomes.

CONCLUSIONS

Early safety and hemodynamic outcomes are excellent, providing acceptable mean gradients. Future long-term follow-up and randomized trials are warranted to confirm the early results with use of this prosthesis.

Conflict of Interest Statement

M.M. has received lecture funding from St Jude Medical. The other authors have nothing to disclose with regard to commercial support.

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Key Words: Aortic valve, replacement, outcomes

**APPENDIX E1. MEDLINE (OVID) SEARCH
STRATEGY**

1. aortic adj3 (implant\$ or valv\$ or insert\$ or replac\$ or approach\$ or surgery or operation).mp.
2. Trifecta.mp.
3. Heart Valve Prosthesis/
4. or/1-3
5. Aortic Valve Stenosis/
6. aortic valve stenosis.mp.
7. valvular aortic stenosis.mp.
8. exp Heart Valve Diseases/
9. aortic valv\$ disease\$.mp.
10. heart valve disease\$.mp.
11. or/5-10
12. 4 and 11

TABLE E1. Assessment of quality of included studies

First author	Clear definition of study population	Clear definition of outcomes and outcome assessment	Independent assessment of outcome parameters	Sufficient duration of follow-up?	Sufficient sample size?	No selective loss during follow-up?	Important confounders and prognostic factors identified?
Yadlapati ⁸	Yes	Yes	Yes	Yes	No	Yes	Yes
Wendt ²	Yes	Yes	Yes	No	Yes	Yes	Yes
Ugur ⁹	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Seo ¹⁰	Yes	Yes	Yes	No	No	Yes	Yes
Remadi ¹¹	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Modi ¹²	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Maruyama ¹⁴	Yes	Yes	Yes	No	No	Yes	Yes
Levy ¹³	Yes	Yes	Yes	No	No	Yes	Yes
Bavaria ¹	Yes	Yes	Yes	No	Yes	Yes	Yes
Permanyer ⁴	Yes	Yes	Yes	No	Yes	Yes	Yes
Minardi ¹⁵	Yes	Yes	Yes	No	No	Yes	Yes
Hanke ¹⁶	Yes	Yes	Yes	No	No	Yes	Yes
Dell'Aquila ⁵	Yes	Yes	Yes	No	No	Yes	Yes

TABLE E2. Baseline characteristics

																			NYHA
First author	Age (y)	Male	BSA (m ²)	AS ^d	AR	LVEF	CAD	HTN	lipidemia	DM	COPD	HTN	CVA	AF	CKD	PVD	Prior surgery	Euro-SCORE	class III/IV
Yadlapati ⁸	71.9 (11.1)	68	1.92 (0.23)	NR	NR	60 ± 14	36	92	80	NR	6.7	NR	18.7	42.7	4	NR	NR	NR	NR
Wendt ²	72.2 ± 6.7	70.2	1.9 ± 0.3	NR	NR	50.5 ± 13.4	64.5	76	NR	28.9	18.2	14	NR	17.4	9.1	20.7	5.8	15.8 ± 13.4 [*]	NR
Ugur ⁹	75.5 ± 8.1	29.5	NR	NR	NR	NR	57.5	83.8	NR	24.9	NR	NR	NR	NR	NR	NR	22.3	NR	55.5
Seo ¹⁰	75 ± 9	39.1	1.49 ± 0.18	87	8.7	NR	39.1	70	61	0	NR	NR	26	22	0	NR	4	NR	52.2
Remadi ¹¹	75.2 ± 7.5	57	NR	91	17	60.4 ± 10.8	49	75	NR	8	16	5.4	NR	5	17	13	5	9.28 ± 4.19	37.0
Modi ¹²	75.9 ± 8.5	49	1.88 ± 0.2	91	6.5	NR	44	65	51	22	NR	NR	NR	NR	NR	NR	7.5	NR	NR
Maruyama ¹⁴	75.8 ± 6.0	27.3	1.50 ± 0.16	69.7	24.2	63.3 ± 12.8	24.2	78.8	48.5	27.3	NR	NR	15.2	15.2	6.1	NR	NR	3.5 ± 5.1	18.2
Levy ¹³	76 ± 8	58	1.84 ± 0.18	NR	NR	60 ± 12	34	76	NR	27	NR	NR	NR	NR	NR	NR	NR	NR	NR
Bavaria ¹	72.5 ± 9.0	64.1	NR	NR	NR	NR	58.2	81.9	71.2	24.8	NR	17.3	13		7	10.9	28	NR	49.3
Permanyer ⁴	71.18 ± 7.7	57.5	1.86 ± 0.2	64.5	13.5	NR	NR	72	37	40	10	NR	NR	17	11	NR	6.5	3.98	75.0
Minardi ¹⁵	75.5 ± 5	36	1.78 ± 0.16	NR	NR	58 ± 11	NR	12	24	18	22	NR	4	4	NR	26	6	NR	50.0
Hanke ¹⁶	71 ± 7	59.4	1.9 ± 0.21	50	21.9	59.00 ± 13.08	59.4	90.6	NR	28.1	NR	NR	NR	NR	NR	NR	NR	NR	NR
Dell'Aquila ⁵	74.65 ± 7.63	47.1	1.95 ± 0.2	91.4	1.6	NR	NR	91.4	64.3	22.9	14.3	NR	NR	12.9	NR	10	NR	8.36 ± 2.64	NR
Minimum	71	27.3	1.49	50	1.6	50.5	24.2	12	24	0	6.7	5.4	4	4	0	10	4	NA	18.2
Maximum	76	70.2	1.95	91.4	24.2	63.3	64.5	92	80	40	22	17.3	26	42.7	17	26	28	NA	75.0
Weighted mean	73.7	54.7	1.9	82.4	10.3	57.7	53.1	77.1	61.5	24.8	13.6	16.0	13.3	6.7	8.0	12.4	18.6	NA	52.2

Values are %, unless otherwise indicated. Wendt, Remadi, and Modi used logistic EuroSCORE. Dell'Aquila used additive Euroscore. Permanyer did not report type of Euroscore used. BSA, Body surface area; AS, (predominant) aortic stenosis; AR, aortic regurgitation; LVEF, left ventricular ejection fraction; CAD, coronary artery disease; HTN, hypertension; DM, diabetes mellitus; COPD, chronic obstructive pulmonary disease; Pulm, pulmonary; CVA, cerebral vascular accident; CKD, chronic kidney disease; PVD, peripheral vascular disease; EuroSCORE, European System for Cardiac Operative Risk Evaluation; NYHA, New York Heart Association; NR, not reported; NA, not available; AF, atrial fibrillation. *Non-logistic EuroSCORE.