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ORIGINAL ARTICLE

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Surgical aortic valve replacement with a stented pericardial bioprosthesis: 5-year outcomes

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Key question

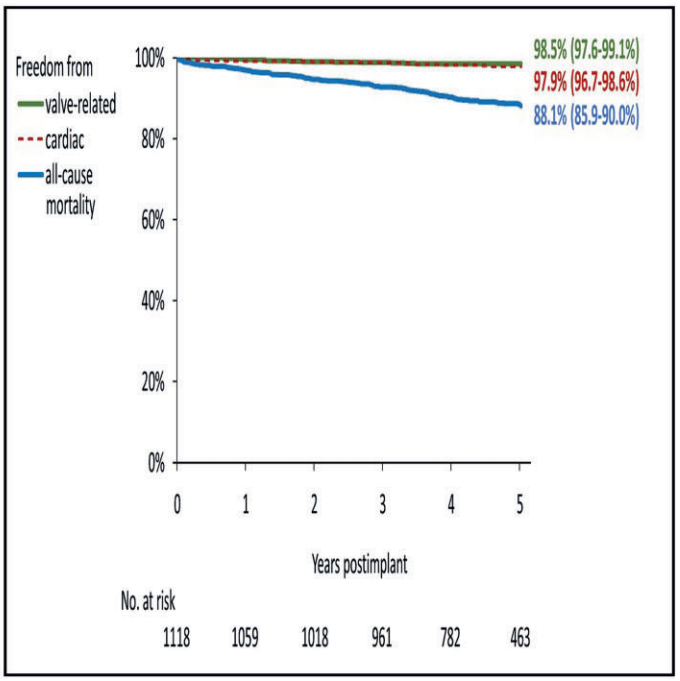
What outcomes were observed with the Avalus bioprosthesis at 5 years?

Key finding(s)

Overall survival at 5 years was 88% with no SVD, stable mean aortic gradients, and a low rate of reinterventions.

Take-home message

The Avalus valve has a favourable safety profile with good hemodynamic performance and durability through 5 years of follow-up.



[†]PERIcardial SurGical AOrtic Valve ReplacemeNt (PERIGON) Pivotal Trial of the Avalus valve.
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Abstract

OBJECTIVES: This analysis evaluated the safety, durability and haemodynamic performance of a stented bovine pericardial valve through 5 years of follow-up in patients with an indication for surgical aortic valve replacement.

METHODS: Kaplan–Meier analysis was used to estimate the incidence of survival and valve-related thromboembolism, major paravalvular leak, endocarditis, structural valve deterioration (SVD) and reintervention. The mean aortic gradient and New York Heart Association (NYHA) functional class were also evaluated.

RESULTS: A total of 1118 patients have received the Avalus valve; 564 have completed the 5-year follow-up. The median follow-up was 4.85 years (4810 patient-years total follow-up). At baseline, the mean age was 70.2 ± 9.0 years; 75.1% of patients were male. The Society of Thoracic Surgeons predicted risk of mortality was 2.0 ± 1.4%. Most patients were in NYHA functional class II (46.8%) or III (40.3%). At the 5-year follow-up, the overall Kaplan–Meier survival rate was 88.1% (85.9–90.0%). The Kaplan–Meier event rates were 5.6% (4.3–7.2%) for thromboembolism, 4.4% (3.2–6.0%) for endocarditis, 0.2% (0.0–0.7%) for a major paravalvular leak and 3.2% (2.3–4.6%) for reintervention. There were no cases of SVD. The mean gradient decreased from 42.1 ± 17.1 mmHg at baseline, to 13.1 ± 4.7 mmHg at discharge and remained stable at 12.5 ± 4.6 mmHg at 5 years. More than 95% of patients were in NYHA functional class I/II 5 years after surgery.

CONCLUSIONS: The findings of a high survival rate, excellent safety, no SVD and stable haemodynamic performance and functional status through 5 years of follow-up are encouraging. Additional follow-up is needed to assess the long-term durability of this contemporary surgical bioprosthesis.

Keywords: Cardiac surgery • Aortic valve disease • Surgical aortic valve replacement • Bovine pericardial aortic bioprosthesis

ABBREVIATIONS/ACRONYMS

EOA	Effective orifice area
NSVD	Nonstructural valve dysfunction
NYHA	New York Heart Association
OPC	Objective performance criteria
PPM	Prosthesis-patient mismatch
PVL	Paravalvular leak
SAVR	Surgical aortic valve replacement
SVD	Structural valve deterioration
TAVR	Transcatheter aortic valve replacement

INTRODUCTION

Surgical aortic valve replacement (SAVR) is one of the most frequently performed cardiac operations. For decades SAVR has been the standard of care for patients with aortic stenosis and/or regurgitation who require replacement of their native valve. Advances in transcatheter aortic valve replacement (TAVR) have led to the rapid adoption of this therapy worldwide, supported by data from various trials [1–4]. In the United States, the number of TAVR procedures performed in 2019 surpassed the number of SAVR procedures by 27% (72,991 vs 57,626) [5]. The wider availability of TAVR has changed the dynamics of valve selection, with surgeons and patients now having to weigh the trade-offs not only between mechanical and bioprosthetic valves but also between surgical and transcatheter valves. To make these decisions, it is important to have clinical data on the newest commercially available bioprosthetic valves in a "standard" low-risk patient population.

The PERIcardial SurGical AOrtic Valve ReplacemeNt (PERIGON) Pivotal Trial is evaluating the safety and efficacy of the Avalus bioprosthesis (Medtronic, Minneapolis, MN, USA). Early analyses demonstrated a favourable safety profile and good haemodynamic performance at 1 and 2 years postimplant [6–8]. This manuscript reports outcomes through 5 years of follow-up.

PATIENTS AND METHODS

Ethics statement

The protocol of the PERIGON Pivotal Trial (www.clinicaltrials.com, NCT02088554) was approved by the institutional review board/ethics committee at each study site (see Table S1). Written informed consent was obtained from all patients.

Study design

The PERIGON Pivotal Trial is a prospective, multicentre trial evaluating the Avalus bioprosthesis (Medtronic, Minneapolis, MN, USA) [6, 7]. The trial was designed and conducted in accordance with the Declaration of Helsinki and good clinical practice principles. Thirty-eight centres in Europe, Canada and the United States participated in the trial.

Patients with moderate or severe symptomatic aortic valve stenosis or chronic severe regurgitation and a clinical indication for SAVR were eligible for enrollment. Those who required concomitant procedures other than left atrial appendage ligation, coronary artery bypass grafting, patent foramen ovale closure, ascending aortic aneurysm/dissection repair not requiring circulatory arrest and subaortic membrane resection not requiring myectomy were ineligible. Patients found intraoperatively to require other procedures were treated with a commercial valve and were exited from the study. Patients with a pre-existing prosthetic valve or annuloplasty device in another position, need for repair of another heart valve, systemic infection, life expectancy <2 years or renal failure (i.e. dialysis therapy or glomerular filtration rate of <30 ml/min/1.73 m^2) were excluded. Patients with an anatomical abnormality that increased surgical risk (e.g. acute type A aortic dissection, ventricular aneurysm, porcelain aorta, hostile mediastinum) [6, 7], found before enrollment or intraoperatively, also were excluded.

Device description and implant technique

The bioprosthesis is a stented bovine pericardial valve with a low-profile height and interior-mounted leaflets. The leaflets are

treated with alpha-amino oleic acid for anti-calcification [9–11]. Supra-annular placement is recommended. Available sizes were 17, 19, 21, 23, 25, 27, and 29. The implant technique, cardioplegia and cardiopulmonary bypass strategies and postoperative anticoagulation were left to the discretion of the surgeon.

Follow-up and outcomes

Follow-up visits were scheduled for 3 to 6 months and 1 year postimplant. Afterwards, follow-up visits were conducted annually for 5 years with telephone contacts at 18 and 30 months.

Primary safety outcomes included the rate of survival (freedom from all-cause mortality) and valve-related adverse events [12]. Valve-related events included thromboembolism, thrombosis, major haemorrhage, major paravalvular leak (PVL) and endocarditis. We calculated linearized late event rates [13] to determine if the Avalus valve continues to perform within the objective performance criteria (OPC) of the International Standards Organization [13]. Secondary outcomes included haemolysis, structural valve deterioration (SVD), non-structural valve dysfunction (NSVD), reintervention and explant. The definitions of safety outcomes were published previously [8]. An additional outcome of severe haemodynamic dysfunction of indeterminate or evolving cause was used to categorize potential safety events with inconclusive information that did not meet the protocol-defined criteria for SVD or NSVD (see Supplemental Methods). Early (≤30 days) event rates and 5-year Kaplan–Meier event rates were calculated for safety outcomes. Independent event adjudication and data and safety monitoring were provided by the Baim Institute for Clinical Research (Boston, MA, USA). Explanted devices were evaluated by CV Path Institute (Gaithersburg, MD, USA).

Haemodynamic performance outcomes included the mean aortic gradient, peak aortic gradient, effective orifice area (EOA), indexed EOA and Doppler velocity index. Echocardiograms were assessed by MedStar Health Research Institute (Washington, DC, USA). New York Heart Association (NYHA) functional class was used to evaluate functional status.

Other analyses included comparison of outcomes in patients who underwent isolated SAVR and those who had a concomitant procedure, assessment of the risk of requiring a reintervention through 5 years of follow-up and the impact of prosthesis-patient mismatch (PPM) at 1 year on mortality and functional status at 5 years.

Statistical analyses

Categorical variables are reported as the frequency and continuous variables, as the mean±standard deviation (SD). The linearized rate of late events is calculated as the number of events >30 days post-implant divided by late patient-years. A Kaplan–Meier analysis of safety events was performed at 30 days, 1 year and annually for 5 years. A competing risk analysis was performed on the valve-related safety end points accounting for the competing risk of death. At each time point with data, the product-limit estimate of the event-free or event rate, the log-log transformed 95% confidence interval (CI) and the number of subjects with events are presented. Survival analyses using the LIFETEST procedure along with the Epanechnikov kernel smoothing method were used to estimate the instantaneous hazard rate of reintervention during 5 years of follow-up. The impact of 1-year PPM on survival (freedom from mortality) at 5 years was evaluated using Kaplan–Meier analysis and the log-rank test. PPM was calculated using the Valve Academic Research Consortium 3 criteria [14]; moderate and severe PPM were combined for this analysis. The temporal trend of the mean aortic gradient was analysed longitudinally, accounting for variability across subjects and with each subject's repeated measurements over time. A linear mixed-model was fit assuming a B-spline basis expansion with 5 basis functions and an unstructured covariance matrix; this model was used to predict the nonlinear mean response and 95% pointwise CIs in the follow-up mean aortic gradient over 5 years. Analyses were performed with SAS software, version 9.4 (SAS Institute, Cary, NC, USA).

Table 1: Baseline characteristics of the full cohort

Characteristic	Patients (N = 1118)
Age, years	70.2 ± 9.0
Male sex	840 (75.1%)
Body surface area (m^2)	2.0 ± 0.2
New York Heart Association functional class	
I	123 (11.0%)
II	523 (46.8%)
III	450 (40.3%)
IV	22 (2.0%)
Society of Thoracic Surgeons risk of mortality (%)	2.0 ± 1.4
Comorbidities	
Atrial fibrillation	117 (10.5%)
Congestive heart failure	222 (19.9%)
Coronary artery disease	487 (43.6%)
Diabetes	298 (26.7%)
Dyslipidaemia	690 (61.7%)
Endocarditis	4 (0.4%)
Hypertension	852 (76.2%)
Left ventricular hypertrophy	458 (41.0%)
Myocardial infarction	99 (8.9%)
Peripheral vascular disease	81 (7.2%)
Renal dysfunction/insufficiency	119 (10.6%)
Stroke/cerebrovascular accident	45 (4.0%)
Transient ischaemic attack	60 (5.4%)
Previous cardiovascular interventions	
Coronary artery bypass	25 (2.2%)
Stent implanted	119 (10.6%)
Arrhythmia surgery (e.g. ablation)	21 (1.9%)
Implanted cardiac device (e.g. pacemaker or defibrillator)	37 (3.3%)
Previous open-heart surgery	39 (3.5%)

RESULTS

In total, 1118 patients received the study device; 564 have completed the 5-year follow-up visit. The median follow-up for this analysis was 4.85 years with 4810 patient-years of total follow-up and 4719 years of late follow-up. Fig. S1 shows patient disposition over 5 years.

Patient characteristics and procedural outcomes

At baseline, the mean age was 70.2 ± 9.0 years; 75.1% of patients were male. The mean body surface area was 2.0 ± 0.2 m^2. Hypertension was the most common comorbidity (76.2%), followed by dyslipidaemia (61.7%), coronary artery disease (43.6%) and left ventricular hypertrophy (41.0%). The mean Society of

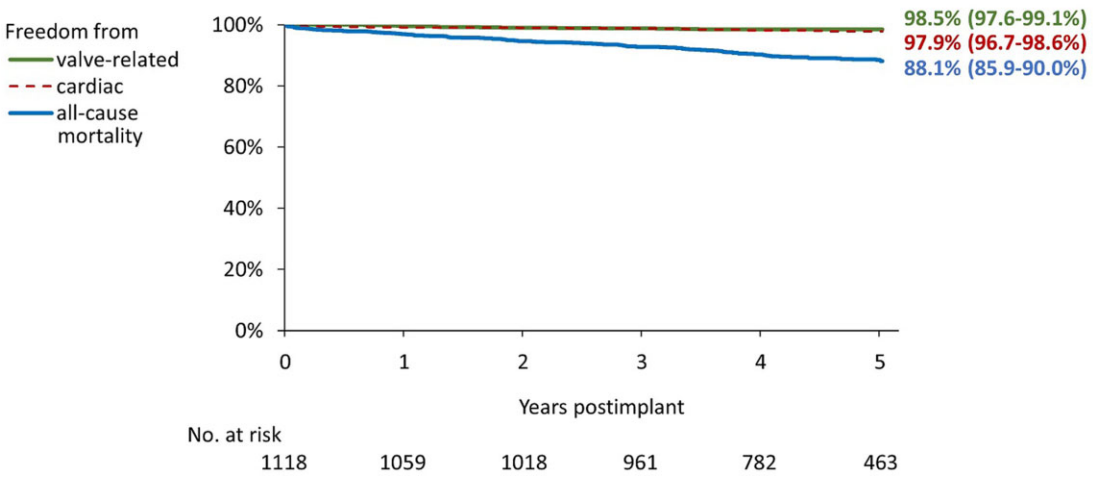

Figure 1: Survival over a 5-year period.

Thoracic Surgeons risk of mortality was 2.0 ± 1.4%. Most patients were in NYHA functional class II (46.8%) or III (40.3%) at baseline (Table 1). Patients who underwent isolated SAVR were younger, more frequently female and had better functional status, a lower risk of mortality and less comorbidity (Table S2).

Aortic stenosis was the primary indication for valve replacement in 84.3% of patients, followed by mixed stenosis/regurgitation (9.5%) and regurgitation (5.7%); 0.5% had a failed prosthesis. Aortic stenosis was also the most common indication in the subanalysis (isolated vs concomitant, 86.9% vs 81.7%, $P = 0.016$). Median sternotomy was performed in 79.6% of patients, and coronary artery bypass grafting, in 32.4%. Cardiopulmonary bypass time averaged 105.0 ± 41.1 min, with aortic cross-clamp time averaging 79.5 ± 31.6 min. Patients who had an isolated SAVR less frequently had a median sternotomy, more frequently had a hemisternotomy or right thoracotomy, and had shorter bypass and aortic cross-clamp times and less annular enlargement than those with a concomitant procedure (Table S3).

Safety end points

There were 118 deaths during the follow-up period; 10 deaths occurred within 30 days postimplant. Fifteen deaths were valve-related; all occurred >30 days postimplant. The causes were endocarditis ($n = 6$), major haemorrhage ($n = 4$), sepsis, cardiogenic shock, embolic stroke, congestive heart failure and acute cardiac death ($n = 1$ each). The survival rate was 88.1% (85.9–90.0%) in the full cohort (Fig. 1), 90.2% (87.0–92.6%) in the isolated SAVR cohort and 86.1% (82.7–88.9%) in the concomitant procedure cohort (Table S4).

There were no cases of SVD at 5 years (Table 2). NSVD occurred in 13 patients: 2 major PVL, 8 minor PVL, 2 entrapments (pannus or suture) and 1 "other" event (echocardiography showed a normally functioning valve with a high gradient, suggestive of PPM). Three patients had severe haemodynamic dysfunction of indeterminate/evolving cause. One appeared to be due to endocarditis, but the valve was not returned for examination. For 1 patient, who had chronic kidney disease, transoesophageal echocardiography and cardiac magnetic resonance imaging showed leaflet thickening but no calcifications. There also was a large discrepancy in the mean aortic gradients between the site and the core laboratory for the last (3-year) visit (40 vs 23 mmHg, respectively). For this patient, a transcatheter aortic valve-in-valve implant was performed. One patient had a valve thrombosis that was treated with Coumadin. Six months later, echocardiography indicated an increase in the mean aortic gradient from 24 to 34 mmHg (site reported). The CT scan done in preparation for a transcatheter aortic valve-in-valve implant showed a mural thrombus and mild aortic calcifications.

Figure 2 shows the linearized rates of late valve-related events compared with the OPC. At 5 years, all safety events remained below the OPC except major haemorrhage. The Kaplan–Meier rate of thromboembolism at 5 years was 5.6% (4.3–7.2%), and the rate of endocarditis was 4.4% (3.2–6.0%). The rates of both valve thrombosis and major PVL were <1%. Thirty-one patients underwent reintervention, yielding an event rate of 3.2% (2.3–4.6%) (Table 2). The reasons for reintervention were endocarditis ($n = 22$), severe haemodynamic dysfunction ($n = 3$), major PVL ($n = 3$), bleeding, valve thrombosis and septal myectomy ($n = 1$ each). Redo surgery with an explant was performed in 27 patients; 3 patients had transcatheter aortic valve-in-valve implants; and 1 patient received an aortic plug. Fig. 3 indicates an increased perioperative hazard of reintervention with a low and constant hazard for all 5 years. Valve-related events were not significantly different between patients who underwent isolated SAVR and those with a concomitant procedure (Table S4). The outcomes were similar when the valve-related events were analysed with death as a competing risk (Table S5, Figures S2 and S3).

Efficacy end points

The mean aortic gradient improved from 42.1 ± 17.1 mmHg at baseline to 13.1 ± 4.7 mmHg at discharge/up to 30 days (henceforth called discharge). During the following 5 years, the mean gradient remained stable (Figure 4). Mean gradients tended to be higher in the isolated SAVR group than in the full cohort and the concomitant procedure group (Table S6). The peak aortic gradient was 68.9 ± 26.6 mmHg at baseline, 24.0 ± 8.4 mmHg at discharge and 22.3 ± 7.9 mmHg at 5 years. The mean EOA increased from 0.90 ± 0.52 cm^2 to 1.59 ± 0.39 cm^2 at discharge and was 1.43 ± 0.35 cm^2 at 5 years. The indexed EOA was 0.45 ± 0.26 cm^2/m^2 at baseline, 0.81 ± 0.20 cm^2/m^2 at discharge and 0.73 ± 0.17 cm^2/m^2 at 5 years. The mean Doppler velocity index was 0.27 ± 0.13, 0.49 ± 0.10 and 0.42 ± 0.08 at those same time points, respectively.

Table 2: Early and 5-year clinical event rates

Event	30-Day event rate % (n)	5-Year Kaplan-Meier event rate % (95% CI) (n)
All-cause death	0.9 (10)	11.9 (10.0-14.1) (118)
Thromboembolism	1.4 (15)	5.6 (4.3-7.2) (57)
Valve thrombosis	0.0 (0)	0.3 (0.1-1.0) (3)
Major haemorrhage[a]	1.0 (11)	5.9 (4.7-7.6) (62)
Major paravalvular leak	0.1 (1)	0.2 (0.0-0.7) (2)
Endocarditis	0.2 (2)	4.4 (3.2-6.0) (42)
Haemolysis	0.0 (0)	1.4 (0.7-2.6) (10)
Non-structural valve dysfunction	0.2 (2)	1.5 (0.9-2.7) (13)
Structural valve deterioration	0.0 (0)	0.0 (0.0-0.0) (0)
Severe haemodynamic dysfunction, indeterminate/evolving cause	0.0 (0)	0.3 (0.1-1.0) (3)
Reintervention	0.4 (4)	3.2 (2.3-4.6) (31)
Explant	0.4 (4)	2.7 (1.9-4.0) (27)

[a]Anticoagulation-related.

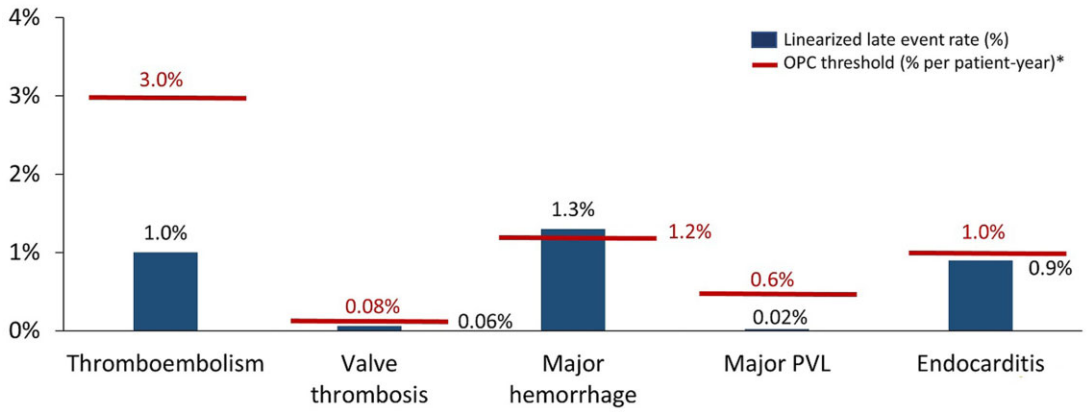

Figure 2: Comparison of valve-related safety end points with the objective performance criteria. OPC: objective performance criteria.

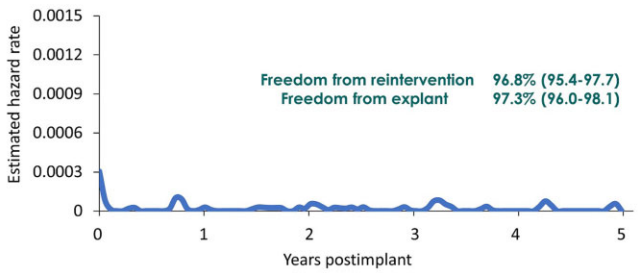

Figure 3: Estimated instantaneous hazard rate of all-cause reintervention over a 5- year period.

At 5 years, the rates of regurgitation were as follows: 87.4% none, 5.8% trace, 6.5% mild, 0.2% moderate and 0% severe. More than 97% of patients had no/trace PVL, and >95% had no/trace transvalvular regurgitation (Fig. S4).

At 5 years > 95% of subjects were in NYHA functional class I or II (Fig. 5). Compared with baseline, 1% of patients improved 3 classes, 25.2% improved 2 classes and 244 (46.6%) improved 1 class at 5 years. Twenty-four percent had no change from baseline. Three percent worsened by 1 class, but none worsened >1 class. PPM at 1 year had no impact on survival or functional status at 5 years (Table S7).

DISCUSSION

This study demonstrated excellent durability of the Avalus valve with no cases of SVD during the 5 years of follow-up. The reintervention hazard was low over time. Improvements in mean gradient, EOA and functional status were very good and, more importantly, stable over time. Survival at 5 years was high, performance against the OPC remained good, and PPM had no impact on survival or functional status at 5 years. Together these findings demonstrate "state-of-the-art" SAVR outcomes with a favourable safety profile and good haemodynamic performance and durability over 5 years. With an average age of 70 and a mean Society of Thoracic Surgeons score of 2.0, the patient population in this study likely reflects the "normal" population that nowadays presents for aortic valve surgery in most countries in the Western world. Only patients at high risk for premature death due to multiple valve procedures and severe comorbidities were excluded.

The 5-year outcomes in the PERIGON Pivotal Trial compare well with those reported for other contemporary bovine pericardial valves. In the PERIGON trial, there were no cases of SVD at 5 years, which corresponded to a freedom from SVD rate of 100%. Similarly, Bartus *et al.* [15] and Bavaria *et al.* [16] reported 100% freedom from SVD for the Perimount Magna Ease valve

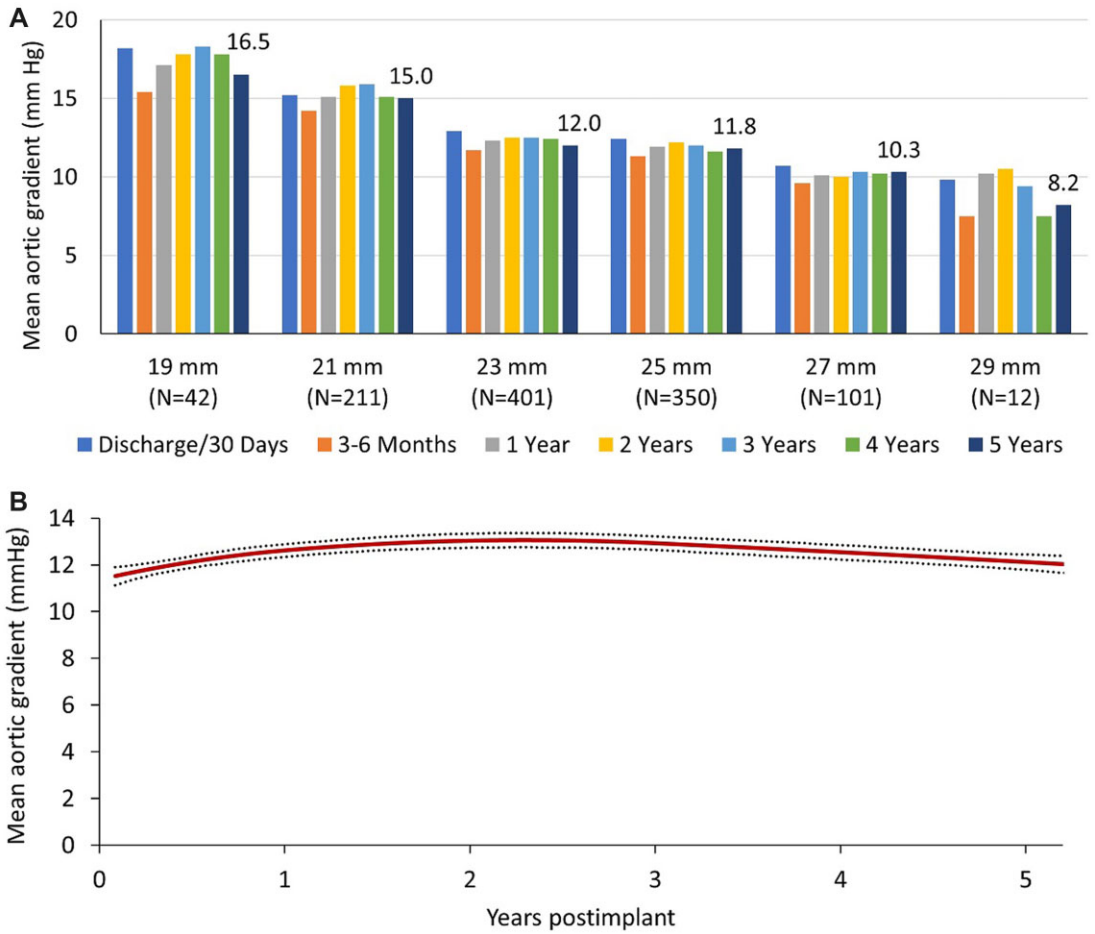

Figure 4: (**Top**) Mean aortic gradient by visit and valve size over a 5-year period. Values show gradients at 5 years. (**Bottom**) Temporal trend of mean aortic gradient analysed longitudinally.

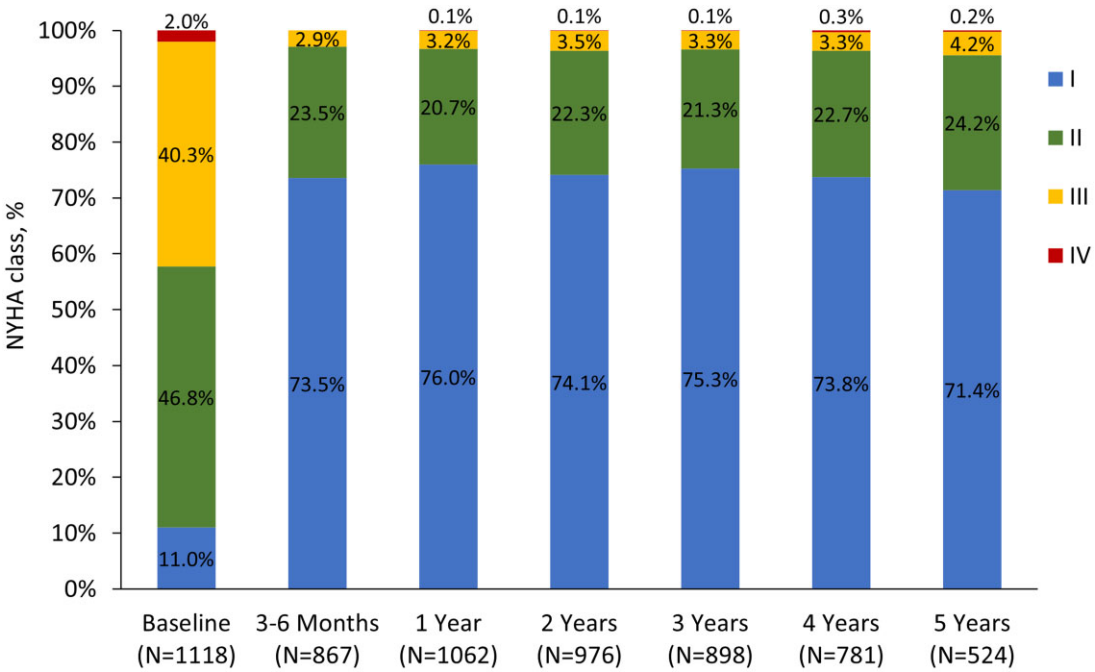

Figure 5: New York Heart Association (NYHA) functional class over a 5-year period.

with Resilia-treated leaflets (Edwards Lifesciences, Irvine, CA, USA). Kilic *et al.* [17] reported 99% freedom from SVD for the Trifecta valve (Abbott, Abbott Park, IL, USA), although some have raised concern about a higher rate of early failure with this valve [18, 19]. The rate of freedom from NSVD in PERIGON was 98.5% (97.3–99.1) at 5 years, compared with 99.1% (97.4–100.0) and 100.0% reported by others [15, 16]. Of note, the freedom from NSVD rate reported by Bavaria *et al.* [16] was defined as "NSVD (other than PVL)", whereas 10 of the 13 NSVD events in PERIGON were PVL (2 major, 8 minor). There were 3 cases of severe haemodynamic dysfunction in PERIGON. In these cases, the valve was not available for examination, and the investigators exited the patients from the study. Based on the reviews of available medical records by the independent clinical events committee, these 3 cases did not meet the protocol definitions of SVD or NSVD and were therefore adjudicated as severe haemodynamic dysfunction.

At 5 years, all valve-related safety events except major haemorrhage remained below the OPC thresholds. In the first report from PERIGON [6], the linearized late event rate of major bleeding was 2.7%/patient-year with a 95% upper bound of 4.3%, which exceeded the OPC (standard 5840:2009). That analysis, which included 1-year follow-up visits for 270 of 686 (39%) enrolled patients, showed that the inflated rate was likely related to patients taking periprocedural anticoagulation agents for concomitant diseases. Although linearization assumes a relatively constant rate of events over time, this is not true for bleeding, which is more frequent in the first months after an implant. Because the use of anticoagulation has decreased with longer follow-up, the linearized rate of late bleeding has also decreased [7, 8] and is currently 1.3%/patient-year. In addition, two-thirds of patients in our initial analysis were taking an antiplatelet, anticoagulant or both at baseline for comorbidities [6]. A subsequent in-depth analysis of antithrombotic therapy and bleeding after SAVR in the trial demonstrated that most bleeding events occurred >30 days post-implant and mostly in patients taking antiplatelet and/or anticoagulation for indications other than valve prophylaxis [20].

The linearized late event rates at 5 years observed for the Avalus valve also compare well with those reported by Bartus *et al.* [15]: thromboembolism: 1.0% versus 0.4%/patient-year, respectively; valve thrombosis: 0.06% versus 0.2%; major haemorrhage: 1.3% versus 0.4%; major PVL: 0.02% versus 0.0%; and endocarditis: 0.9% versus 0.2%. Bavaria *et al.* [16] did not report linearized late event rates, but the linearized late safety event rates reported for COMMENCE by Johnston *et al.* [21] (median follow-up, 4 years) seem in line with our data. Due to slightly different inclusion criteria, these numbers also may very well reflect the patient population.

Freedom from reintervention at 5 years was 96.8% (95.4–97.7%) in PERIGON, compared with 99.2% (97.7–100.0%), 98.7% (97.8–99.6%) and 96.0% reported by others [15–17]. Although reintervention was increased perioperatively in PERIGON, the hazard of reintervention over 5 years was low and constant (Fig. 3) and mainly linked to endocarditis. These data show the excellent performance of modern biological valve prostheses, but this time point is still too short to make definite conclusions about long-term durability.

The 5-year overall survival rate in PERIGON was 88.1% (85.9–90.0%) compared with 83.4% (76.8–89.9%) and 89.2% (86.7–91.6%) reported for the Magna Ease valve with Resilia tissue [15, 16]. Five-year survival in the study of Kilic *et al.* [17] was 70%, but their study population comprised all those at their centre who had Trifecta implants, including those who had urgent (36.6%), emergency (1.9%) and salvage (0.3%) procedures. Others have reported 6-year survival of 87.9% with the Trifecta valve [22]. These findings demonstrate the excellent survival that is attainable with contemporary surgical valves.

The mean aortic gradient across all valve sizes remained stable over time, not exceeding 20 mmHg at any time point for valve sizes 19 through 29 mm (Fig. 4). At 5 years the mean aortic gradient in PERIGON compared favourably with those reported by others [15, 16]. All these valves are designed to achieve low resistance to flow. The 5-year mean EOAs in these studies were also similar (1.43 ± 0.35 cm^2 in PERIGON vs 1.4 ± 0.5 cm^2 [15] and 1.6 ± 0.05 cm^2 [16]), although this value is less reliable due to echocardiographic estimations [23]. At 5 years, 97.4% of patients in PERIGON had none/trace PVL, and no patients had greater than mild regurgitation, similar to other contemporary trials [15, 16]. Rates of central regurgitation among these studies were also low and comparable.

Functional status was stable over time in PERIGON with more than 95% of patients in NYHA functional class I/II at 5 years. Our analysis comparing patients with moderate or severe PPM compared with no PPM at 1 year showed that PPM had no impact on survival or functional status at 5 years. This is unsurprising given the limitations of PPM categories to predict mortality or haemodynamic obstruction [24].

As the use of TAVR becomes more common, it will be critical for surgeons to focus on a lifetime management approach to treatment of aortic valvular heart disease. Transcatheter valves have an obvious appeal, and good results have been reported for lower-risk patients [1, 2, 4]. In addition, transcatheter aortic valve-in-valve procedures in high-risk patients seem promising [25]. However, long-term studies are limited, and TAVR may not be the optimal initial approach for some patients because explant is often necessary and complex in those who require reintervention [26, 27]. In light of this and the favourable 5-year results achieved with contemporary surgical tissue valves such as Avalus, it is likely that SAVR will remain the gold standard of treatment for younger, lower-risk patients.

Follow-up in the PERIGON Pivotal Trial will continue through 12 years in a subgroup of patients. There are currently 20 active long-term follow-up sites with 522 patients. This long-term study may serve as a comparison group for younger, low-risk TAVR patients in the future.

LIMITATIONS

The 5-year follow-up visit was not complete for the full study population. This single-arm observational study allowed only 8 concomitant procedures, which limits the generalizability of outcomes to real-world populations with different comorbidities and needs for concomitant procedures. The definition of SVD may underestimate this outcome compared with contemporary definitions. Longer follow-up is needed to fully understand valve safety and performance.

CONCLUSION

The findings of a high survival rate, no SVD, excellent safety and stable haemodynamic performance and functional status for 5 years in this large study of the Avalus valve are very good. Additional follow-up is needed to assess long-term durability.

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Conflicts of Interest: Robert J.M. Klautz reports research support and consultation fees from Medtronic. François Dagenais is a proctor and speaker for Medtronic and COOK Medical. Michael J. Reardon serves as a consultant to Medtronic, Abbott Medical, Boston Scientific, Gore Medical and Transverse Medical; the fees are paid to his department. Rüdiger Lange is a consultant and stockholder for and receives royalty fees from Medtronic; he also serves as a consultant to HighLife Medical. Michael G. Moront is a trainer and consultant for Medtronic; a trainer and speaker for Atricure; and a speaker and consultant for Haemonetics. Louis Labrousse has received meeting attendance fees from Medtronic. Neil J. Weissman receives grant support from Medtronic, Boston Scientific, Edwards and Abbott; the funds are paid to his institution. Vivek Rao is a consultant for Medtronic, W. L. Gore, and Abbott; he is a member of the Surgical Advisory Board for Medtronic. Himanshu J. Patel is a consultant for Medtronic. Fang Liu is an employee and stockholder of Medtronic. Joseph F. Sabik is the North American Principal Investigator for the PERIGON Pivotal Trial, which is sponsored by Medtronic Cardiac Surgery.

Data availability

The data, analytic methods and study materials are owned by the sponsor and will not be made available to other researchers for purposes of reproducing the results.

Author Contributions

Robert J.M. Klautz: Conceptualization; Investigation; Methodology; Visualization; Writing-original draft; Writing-review, editing. **François Dagenais:** Investigation, Writing–review, editing. **Michael J. Reardon**: Investigation; Writing–review, editing. **Rüdiger Lange:** Investigation, Writing–review, editing. **Michael G. Moront:** Investigation, Writing–review, editing. **Louis Labrousse:** Investigation, Writing–review, editing. **Neil J. Weissman**: Investigation, Writing–review, editing. **Vivek Rao:** Investigation, Writing–review, editing. **Himanshu J. Patel:** Investigation, Writing–review, editing. **Fang Liu:** Data curation, Formal analysis, Methodology, Software, Validation, Writing–original draft, Writing–review, editing. **Joseph F. Sabik, III**: Conceptualization, Investigation, Methodology, Writing–review, editing.

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Real-world experience with Thopaz+

The Oxford University Hospitals NHS Foundation Trust experience

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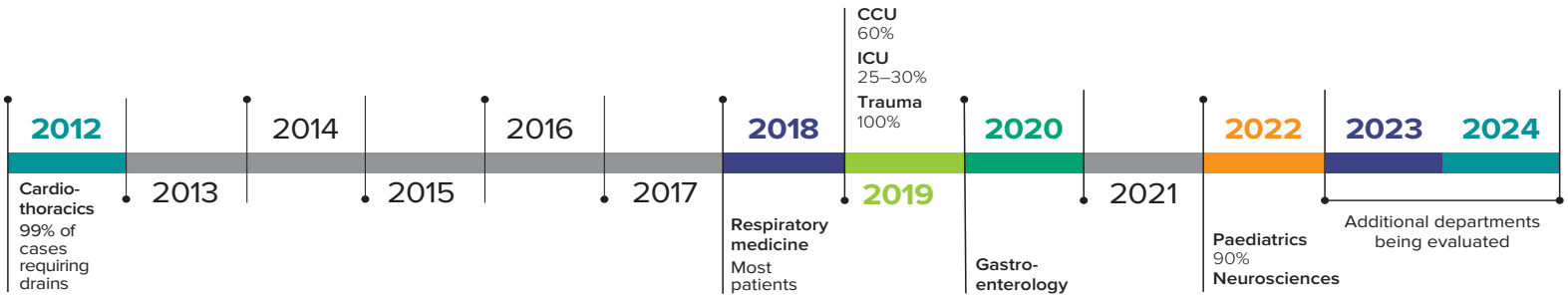
Thopaz+ is a portable digital chest drainage and monitoring system developed by Medela. It offers continuous objective monitoring of fluid loss and air leaks, which facilitates assessment of patients' progress, as well as standardisation of chest drainage management across different departments.[1] Clinical evidence has demonstrated that Thopaz+ is a useful tool in the management of patients that require chest drains and has clear clinical advantages compared with underwater seal drains.[1–3]

Thopaz+ and its predecessor, Thopaz, have been used within the Cardiothoracic Department at Oxford University Hospital NHS Trust since 2012. A report on this experience contributed to National Institute for Health and Care Excellence (NICE) Medical Technology Guidance 37.[1,4] Use of Thopaz+ in Oxford has since expanded to other departments within the trust. This document summarises the experience with Thopaz+ based on interviews with healthcare professionals (HCPs) at Oxford University Hospital NHS Trust in February/March 2024.

*Evolution of Thopaz+ use in Oxford: initial introduction by department and current usage**



*Percentage of cases using Thopaz+, where known from interviews.

CHEST DRAINAGE PROTOCOLS

Each department has a chest drain protocol based on their use of Thopaz+ or underwater seal drains, and whether active suction or physio mode is needed.

MOBILISATION

Improved and earlier mobilisation is a major advantage of Thopaz+ in relation to complications associated with immobility.

OBJECTIVE AND CONTINUOUS MONITORING LEADS TO IMPROVED DECISION-MAKING

Continuous monitoring improves chest drain decision-making by providing objective estimates/measurement of leakage. It helps determine when air leaks are resolving (allowing for earlier drain removal and discharge planning) or when further intervention is needed (such as referral to a surgeon).

LENGTH OF STAY

Digital drainage facilitates day-case procedures by giving HCPs confidence that their patients have no persistent air leaks or fluid loss.

RESPIRATORY

70% of patients following pleural intervention and 60% undergoing thoracoscopy return home the same day.

CORONARY CARE UNIT (CCU)

Length of stay of 7 days with Thopaz+ compared with 10 days with underwater seal drains.

THROUGHOUT THE PATIENT JOURNEY

Thopaz+ can be used throughout a patient's journey, which can reduce the possibility of issues and errors, because drains can become kinked or displaced whenever a device is changed. Suction can be added to a Thopaz+ device set up to provide straightforward drainage simply by pressing a button to initiate suction via the device itself.

COSTS AND EFFICIENCIES

The use of the device can lead to improved operational efficiencies and cost savings, which may justify the acquisition costs. From an evidence-based practice project in the USA, a digital air leak detection device after pulmonary lobectomy led to cost savings of $2,659 per hospital day.[5]

IMPROVED PATENT SAFETY

Thopaz+ is a closed system, reducing incidents, errors, mishaps, and infections. As a dry system, Thopaz+ prevents issues with water and device positioning. Non-medical staff can manage Thopaz+ if it is knocked over, with no patient impact. Thopaz+ has its own suction source, preventing complications with wall suction becoming displaced or unclipped.

STAFF EXPERIENCE

Precise fluid and air leak measurements including time trends, improve clinician confidence and decision-making and facilitate continuity of care. The user-friendly interface makes it easier to track air leaks and fluid output. Nursing time is saved with easy canister replacement, reduced manual monitoring, and visual and audible notifications alert HCPs of issues.

PATIENT EXPERIENCE

Patients can move around freely without nursing or healthcare assistant support. Earlier discharge reduces hospital stay. Patients can monitor their progress in terms of reducing volumes of fluid and air leaks on the display.

Summary of the real-world experience with Thopaz+

The experience of HCPs within Oxford University Hospitals NHS Foundation Trust over the past 12 years has shown that Thopaz+ has multiple benefits in the right circumstances and should be available for the vast majority of patients requiring a chest drain.

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Consultant Thoracic Surgeon Oxford University Hospitals NHS Foundation Trust

> Overall, our experience at Oxford University Hospitals NHS Foundation trust has shown that Thopaz+ is an indispensable asset for HCPs, redefining standards of care and operational efficiency across multiple medical departments. We encourage all units using chest drains to consider making the move from underwater seal drains to Thopaz+ in the vast majority of patients requiring chest drainage.

Quotes from interviews with a number of healthcare professionals at Oxford University Hospital NHS Trust:

> From the NHS perspective, I think it probably allows us to make earlier decisions about withdrawing chest drains and getting peopleout of hospital earlier.

> There are a number of ways to recoup the costs: efficiencies in the system, less litigation because things don't go wrong, staff sickness due to back injuries, and length of stay if you can get patients home quicker.

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Read the full report:

The summary report has been written by HSJ Advisory on behalf of Medela AG, reflecting the views expressed in interviews with healthcare professionals. Medela AG funded the project and had input into the development of this report.

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