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ORIGINAL ARTICLE

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Final 5-year outcomes following aortic valve replacement with a RESILIA™ tissue bioprosthesis

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Key question

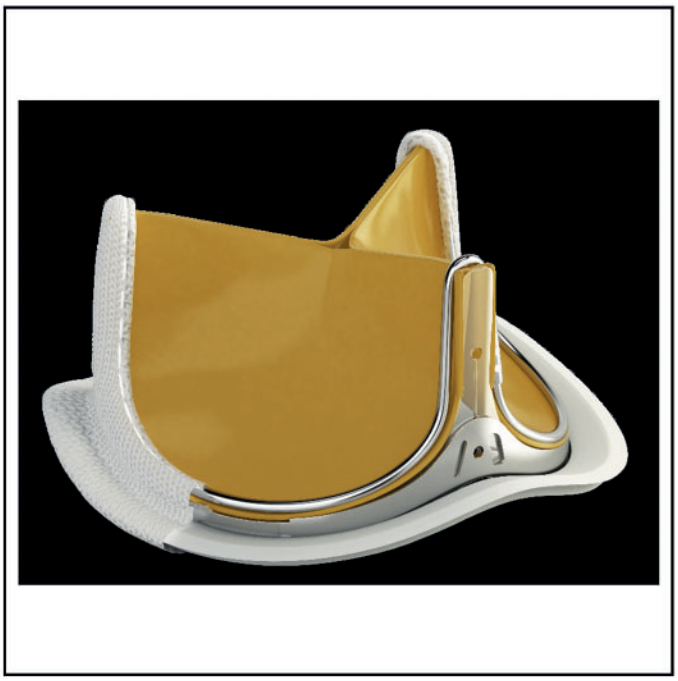
What are the 5-year outcomes of aortic valve replacement with an aortic valve with RESILIA tissue?

Key finding(s)

In 133 patients, an aortic valve with RESILIA tissue was safe and effective through 5 years of follow-up.

Take-home message

Through 5 years of follow-up, an aortic valve with RESILIA tissue exhibited good haemodynamics and zero structural valve deterioration events.



Abstract

OBJECTIVES: Long-term durability of bioprosthetic valves is predominantly limited by structural valve deterioration. RESILIA™ tissue has exhibited reduced calcification in pre-clinical and early clinical studies. This study evaluated the 5-year clinical and haemodynamic outcomes of an aortic valve with this tissue.

METHODS: This was a prospective, non-randomized, single-arm study of 133 patients implanted with a RESILIA aortic bioprosthesis between July 2011 and February 2013 at 2 sites in Poland. Clinical outcomes and haemodynamic performance were assessed annually for 5 years post-implant. Safety events were adjudicated by a Clinical Events Committee and echocardiographic data were assessed by an independent core laboratory.

Presented at Heart Valve Society Annual Meeting, Sitges, Spain, 11–13 April 2019.

RESULTS: Mean patient age was 65.3 ± 13.5 years, with 34 patients (25.6%) ≤60. The mean follow-up was 4.2 ± 1.5 years. Early (≤30 days) and late (>30 days) all-cause mortality were 2.3% (*N* = 3) and 3.2%/late patients-years (*N* = 18) respectively. Early events included thromboembolism in 3 patients (2.3%). Late valve-related events included endocarditis in 1 patient, which led to explant, and valve thrombosis in another patient. There were no events of structural valve deterioration throughout the study. At 5 years, mean gradient was 14.8 ± 7.6 mmHg and effective orifice area was 1.4 ± 0.5 cm^2, a marked improvement over baseline values. All New York Heart Association class III patients and most class II patients at baseline had improved classifications at 5 years.

CONCLUSIONS: The bioprosthesis with RESILIA tissue demonstrated a good safety profile with excellent haemodynamic performance over 5 years of follow-up. These encouraging outcomes warrant additional investigation of this novel tissue.

Clinical trial registration number: NCT01651052

Keywords: Aortic valve replacement • RESILIA • Bioprosthesis

ABBREVIATIONS

AVR	Aortic valve replacement
EOA	Effective orifice area
NYHA	New York Heart Association
PVL	Paravalvular leak
SVD	Structural valve deterioration

INTRODUCTION

Aortic valve replacement (AVR) in patients with severe aortic stenosis relieves symptoms and increases survival [1–4]. Although bioprosthetic valves are recommended for surgical AVR in patients >60–65 years old, the optimal type of prosthesis in younger patients is less clear [1–3]. The excellent durability of mechanical valves may be offset by the need for lifetime anticoagulation. Bioprosthetic valves, on the other hand, are associated with an increased risk of structural valve deterioration (SVD), particularly in younger patients [5].

Through mid-term follow-up, contemporary bioprostheses for AVR are not expected to deteriorate structurally, and have been reported to exhibit freedom from either SVD or reoperation due to SVD of between 97% and 100%. Over 5 years of follow-up, the Carpentier-Edwards PERIMOUNT™ Magna valve series (Edwards Lifesciences, Irvine, CA, USA) has exhibited freedom from SVD or reoperation due to SVD of 99% [6–8]. The Trifecta bioprosthesis (Abbott Laboratories, Santa Clara, CA, USA) over 5 years has demonstrated similar durability, between 97% and 99% [9–12]. However, long-term durability >10 years is key, and such data with contemporary bioprostheses are still lacking.

In an attempt to reduce SVD and improve bioprosthetic durability, a new bioprosthesis tissue platform has been developed. RESILIA™ tissue is made of bovine pericardium that undergoes integrity preservation technology [13]. This technology consists of stable capping that permanently blocks calcium (Ca^{2+}) binding sites, and glycerolization that allows dry storage of the bioprosthesis prior to implant. The RESILIA tissue was incorporated within a standard bioprosthesis design and implanted in a cohort of 133 patients who underwent surgical AVR at 2 centres in Poland. An earlier report of this study through 1 year of follow-up found this bioprosthesis to be safe and associated with improved haemodynamic performance compared with baseline [14]. This report specifies upon the final outcomes of this study over a follow-up period of 5 years.

PATIENTS AND METHODS

Study design and patient population

This study was prospective, multicentre, single arm, and observational, designed to evaluate the safety and haemodynamic performance of a novel aortic valve incorporating RESILIA tissue (Clinical Trial Number NCT01651052). Patients who were 18 years of age or older and were candidate for AVR with or without concomitant procedures were included. Details regarding patient inclusion and exclusion criteria have been reported previously [14]. The study protocol was reviewed and approved by the local Ethics Committee (Jagiellonian University Bio-Ethics Committee no. KBET/163/l/2010 of 7 October 2010) and Polish Ministry of Health (CEBK). All study participants provided written informed consent prior to enrolment. This report is based upon the study's final data extraction of 20 April 2018.

Study device and surgical procedures

The study device consisted of the model 11000 aortic bioprosthesis (Edwards Lifesciences, Irvine, CA, USA). This tri-leaflet bioprosthesis is similar to the Carpentier-Edwards PERIMOUNT Magna Ease aortic valve (Model 3300TFX, Edwards Lifesciences), except for the RESILIA tissue leaflets. All cases were performed at the 2 largest cardiac surgery centres in Poland. Details about the surgical procedure have been previously reported [14]. The decision to implant the study device was based on an indication for surgical AVR, an appropriate risk profile and a surgeon confirmation that the bioprosthesis could be implanted in the consenting patient. Per protocol, it was suggested that patients be maintained on oral anticoagulant therapy for ∼2–3 months based on American College of Cardiology/American Heart Association 2008 guidelines [15]; however, this was left to the discretion of the investigator.

Study end points and follow-up

Safety end points were evaluated during the early (≤30 days) and late (>30 days) postoperative periods and were based on objective performance criteria described previously [16]. All safety events were defined according to established guidelines [17] and were adjudicated by an independent Clinical Events Committee and included all-cause mortality, valve-related mortality, thromboembolism, all bleeding, major bleeding that required transfusion, major paravalvular leak (PVL), haemolysis, valve thrombosis, endocarditis, valve explant, non-structural valve

dysfunction and SVD. Major PVL was defined as a PVL of any grade resulting in intervention or considered a serious adverse event. The definition of SVD included dysfunction or deterioration involving the operated valve (exclusive of infection or thrombosis), as determined by reoperation, autopsy or clinical investigation [17].

Haemodynamic end points were assessed by echocardiography and included the mean systolic transvalvular pressure gradients and the effective orifice area (EOA). All echocardiography data were analysed by an independent core laboratory (BioTelemetry Research, Rockville, MD, USA). Patients were assessed preoperatively, at discharge, at 3–6 months and at 1, 2, 3, 4 and 5 years of follow-up. The preoperative assessments included valve haemodynamic performance and New York Heart Association (NYHA) functional class. These same parameters as well as the safety end points were assessed postoperatively, except that haemodynamic measures were not required at the 2- or 4-year follow-up unless murmur was heard on auscultation.

Data management and statistical analysis

The 2 investigational sites collected and recorded the clinical data. Edwards Lifesciences, the study sponsor, monitored and aggregated the clinical data, and analysed them per the protocol and the statistical analysis plan. The investigators were responsible for an accurate accounting of these data as represented in this report. Summary statistics for categorical variables include the number and percentage of subjects with a recorded value for the variable of interest and mean ± standard deviation for continuous measures. Early safety events were defined as those occurring ≤30 days of the index procedure, and were reported as the number of events divided by the number of enrolled subjects. Linearized rates were used to summarize safety events for the late (>30 day) postoperative period. Late event rates were calculated as the number of late events divided by the total number of late patient-years. In addition, Kaplan–Meier analyses were undertaken on each of the safety end points and the freedom from many of these events is reported at 5 years. SAS version 9.3 was used for all statistical analyses.

RESULTS

Baseline characteristics

A total of 133 patients requiring surgical AVR were implanted with the study valve between July 2011 and February 2013. The average age of the patients at implant was 65.3 ± 13.5 years, and 26% were ≤60 years old. The proportion of patients with NYHA class I, II, III and IV symptoms at baseline was 21.1%, 45.9%, 32.3% and 0.8%, respectively. Patients underwent AVR for one or more of the following reasons: degenerative valve disease in 93 (69.9%), dystrophic calcification in 24 (18.0%), rheumatic heart disease in 9 (6.8%), endocarditis in 2 (1.5%) and other aetiologies in 18 (13.5%). The baseline characteristics of the patients implanted with the study valve are summarized in Table 1. Among key comorbidities and risk factors at baseline, 82% had mitral insufficiency, 79% systemic hypertension, 72% aortic insufficiency, 69% hyperlipidaemia/hypercholesterolaemia, 68% tricuspid insufficiency, 48% coronary artery disease, 25% cardiac rhythm/conduction disturbance and 20% were smokers.

Procedural outcomes

All 133 patients were successfully implanted with the study valve during the first attempt (100% technical success). Twelve patients (9%) were implanted with a valve of 19 mm, 46 patients (35%) with a valve of 21 mm, 41 patients (31%) with a valve of 23 mm, 24 patients (18%) with a valve of 25 mm and 10 patients (8%) with a valve of 27 mm. Figures 1 and 2 display the surgical approach as well as aortic cross-clamp and cardiopulmonary bypass times. Out of 133 patients successfully implanted, 114 patients (85.7%) underwent isolated surgical AVR. The surgical approaches consisted of a full sternotomy in 117 patients (88.0%) and an upper mini sternotomy in 16 (12.0%). Mean aortic cross-clamp and cardiopulmonary bypass times in all 133 patients who underwent study device implant were 61.7 ± 14.4 and 96.2 ± 25.6 min, respectively. In the 114 patients who underwent isolated AVR, the mean aortic cross-clamp and cardiopulmonary bypass times were 59.6 ± 13.1 and 94.5 ± 25.2 min, respectively. The length of hospital stay for all 133 patients was 9.7 ± 5.0 days, with 2.2 ± 2.4 days in the intensive care unit and 7.6 ± 5.4 days in the general ward.

Table 1: Demographics and baseline characteristics

All subjects	
Variables	Implanted (*N* = 133)
Age (years)	
Mean ± SD	65.3 ± 13.5
Range (min–max)	22.0–88.0
Gender/sex, *n* (%)	
Female	68 (51.1)
Male	65 (48.9)
LVEF	
Mean ± SD	61.2 ± 13.7
Range (min–max)	22.4–85.6
EuroSCORE II (%)	
Mean ± SD	1.4 ± 1.0
Range (min–max)	0.5–6.0
STS risk of mortality (%)	
Mean ± SD	1.4 ± 0.9
Range (min–max)	0.4–4.0
BMI (kg/m^2)	
Mean ± SD	29.2 ± 6.7
Range (min–max)	15.8–62.1
Underweight, *n* (%)	2 (1.5)
Normal weight, *n* (%)	31 (23.3)
Overweight, *n* (%)	51 (38.3)
Obese, *n* (%)	49 (36.8)
Aortic valve pathology, *n* (%)	
Aortic stenosis	108 (96)
Aortic insufficiency	81 (72)
NYHA, *n* (%)	
Class I	28 (21.1)
Class II	61 (45.9)
Class III	43 (32.3)
Class IV	1 (0.8)

Percentages are based on the total number of implanted subjects. Baseline LVEF data were not available for 20 subjects. EuroSCORE II was not available for 20 subjects. STS risk of mortality score was not available for 23 subjects.

BMI: body mass index; EuroSCORE: European System for Cardiac Operative Risk Evaluation; LVEF: left ventricular ejection fraction; NYHS: New York Heart Association; SD: standard deviation; STS: Society of Thoracic Surgeons.

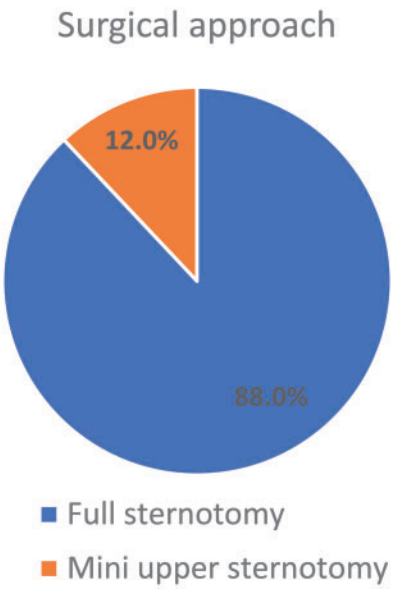


Figure 1: Surgical approach undertaken for the study cohort.

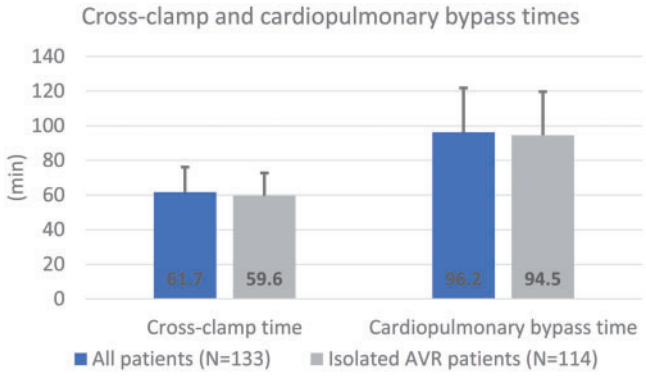


Figure 2: Intraoperative outcomes for the study cohort. The error bars represent ± standard deviation. AVR: aortic valve replacement.

Safety outcomes

Patients were followed up for a mean of 4.2 ± 1.5 years. Early and late safety event rates, including valve-relatedness, are summarized in Table 2. In the early period, there were 3 all-cause deaths (2.3%), of which 1 (0.8%) was valve-related. In the late period, there were 18 all-cause deaths (3.2%/late patient-years), of which 4 (0.7%/late patient-years) were valve-related. Nine patients (6.8%) and 2 patients (0.4%/late patient-years) had major bleeding in the early and late period, respectively. There was 1 case of endocarditis in the late period, which led to explant of the valve and 1 other case of valve thrombosis which was discovered postmortem. There were no events of SVD or of major PVL in either the early or late period. Table 3 shows the Kaplan–Meier freedom from various safety end points over 5 years, and Fig. 3 shows a Kaplan–Meier curve of 2 event types: all-cause mortality and SVD.

Haemodynamic outcomes

The mean transvalvular gradients and EOAs over 5 years by valve size are shown in Fig. 4. The gradients over 5 years represent a sustained improvement compared to the values at baseline. Across all valve sizes, the mean gradients were 13.9 ± 6.1, 13.8 ± 6.4, 14.3 ± 6.1, 15.0 ± 7.2 and 14.8 ± 7.6 mmHg at years 1–5, respectively. Similarly, the overall EOAs at years 1–5 were 1.8 ± 0.6, 1.6 ± 0.5, 1.5 ± 0.5, 1.5 ± 0.4 and 1.4 ± 0.5 cm^2 and represented a marked improvement over that observed at baseline (1.0 ± 0.8 cm^2).

Transvalvular/central, paravalvular and total regurgitation are shown in Fig. 5. The severity of transvalvular/central leak was mild in no >5% of patients each year over the 5-year observational period, with no measurements of moderate or severe, and with all other patients exhibiting none/trivial such leak. One patient exhibited moderate PVL at discharge, but over the annual follow-ups, there were no observations of moderate or severe PVL, and only a few per cent of patients exhibited even mild PVL.

New York Heart Association functional status

Ninety-one patients had their NYHA classification assessed at baseline and 5 years (Table 4). Of the 18 class I patients at baseline,

Table 2: Safety outcomes

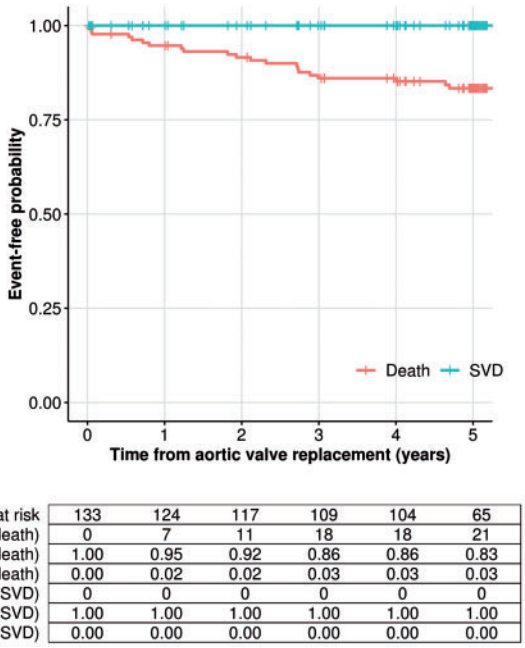
	Early (≤30 days) events *N* = 133 *n*, (*n*/*N*)	Early valve-related events *N* = 133 *n*, (*n*/*N*)	Late events (>30 days) Late pt yrs = 554.4 *n*, *m* (*m*/late pt yrs)	Late valve-related events Late pt yrs = 554.4 *n*, *m* (*m*/late pt yrs)
Mortality	3 (2.3%)	1 (0.8%)	18, 18 (3.2%)	4, 4 (0.7%)
Reoperation on study valve	0 (0%)	0 (0%)	1, 1 (0.2%)	1, 1 (0.2%)
Explant	0 (0%)	0 (0%)	1, 1 (0.2%)	1, 1 (0.2%)
Thromboembolism	3 (2.3%)	3 (2.3%)	2, 2 (0.4%)	2, 2 (0.4%)
Valve thrombosis	0 (0%)	0 (0%)	1, 1 (0.2%)	1, 1 (0.2%)
Bleeding	11 (8.3%)	0 (0%)	2, 2 (0.4%)	0, 0 (0%)
Major bleeding	9 (6.8%)	0 (0%)	2, 2 (0.4%)	0, 0 (0%)
Major paravalvular leak	0 (0%)	0 (0%)	0, 0 (0%)	0, 0 (0%)
Endocarditis	0 (0%)	0 (0%)	1, 1 (0.2%)	1, 1 (0.2%)
Haemolysis	0 (0%)	0 (0%)	0, 0 (0%)	0, 0 (0%)
Non-structural valve dysfunction	0 (0%)	0 (0%)	1, 1 (0.2%)	1, 1 (0.2%)
Structural valve deterioration	0 (0%)	0 (0%)	0, 0 (0%)	0, 0 (0%)

'*n*' is the number of subjects who experienced the specific type of adverse event. '*m*' is the number of specific adverse events observed.

Table 3: Kaplan–Meier survival rates at 5 years of various safety events

	Patients at risk at 5 years	Cumulative events	Probability event free	Standard error	95% CI
Mortality	65	21	0.834	0.033	0.768–0.899
Reoperation on study valve	65	1	0.992	0.008	0.977–1.000
Explant	65	1	0.992	0.008	0.977–1.000
Thromboembolism	65	5	0.959	0.018	0.923–0.995
Valve thrombosis	65	1	0.992	0.008	0.976–1.000
All bleeding	60	13	0.898	0.027	0.845–0.951
Major bleeding	60	11	0.913	0.025	0.864–0.963
Major paravalvular leak	65	0	1.000	0.000	1.000–1.000
Endocarditis	65	1	0.992	0.008	0.977–1.000
Haemolysis	65	0	1.000	0.000	1.000–1.000
Non-structural valve dysfunction	64	1	0.991	0.009	0.974–1.000
Structural valve deterioration	65	0	1.000	0.000	1.000–1.000

CI: confidence interval.



Patients at risk	133	124	117	109	104	65
Cum. Events (death)	0	7	11	18	18	21
Prob. (death)	1.00	0.95	0.92	0.86	0.86	0.83
SE (death)	0.00	0.02	0.02	0.03	0.03	0.03
Cum. Events (SVD)	0	0	0	0	0	0
Prob. (SVD)	1.00	1.00	1.00	1.00	1.00	1.00
SE (SVD)	0.00	0.00	0.00	0.00	0.00	0.00

Figure 3: Kaplan–Meier curve showing freedom from all-cause mortality and structural valve deterioration. SE: standard error; SVD: structural valve degeneration.

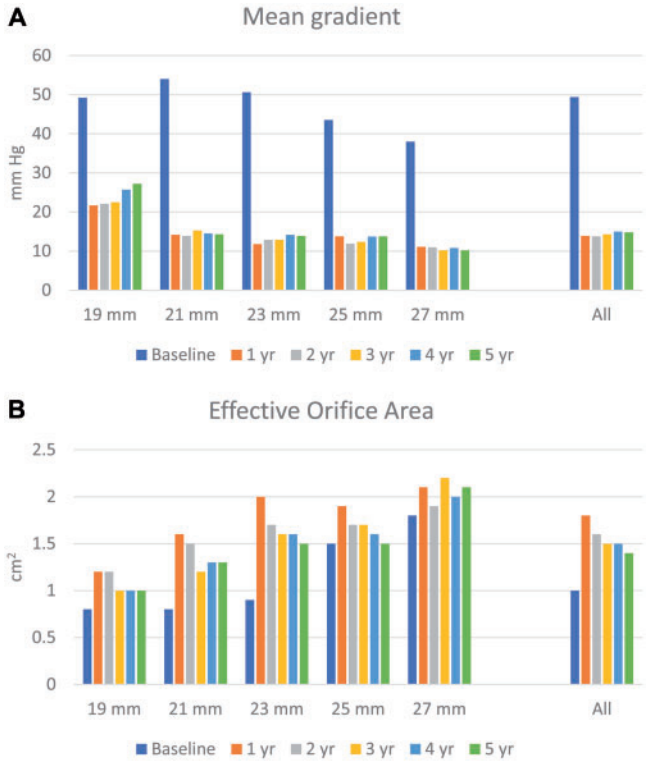


Figure 4: (**A**) Mean gradients in the patient cohort by valve size over the 5 year observational period. (**B**) Mean effective orifice areas in the patient cohort by valve size and over the 5 year observational period.

72% of them remained class I after 5 years and 28% worsened. Of the 47 class II patients at baseline, 51% improved after 5 years, 43% remained class II and 6% worsened. Of the 25 class III patients at baseline, all of them were either class I or class II after 5 years. The 1 class IV patient at baseline improved to class I at 5 years.

DISCUSSION

This trial evaluated the clinical outcomes and haemodynamic performance of an aortic bioprosthesis with RESILIA tissue in 133 patients monitored over 5 years of follow-up. Valve haemodynamics and safety outcomes were good. Furthermore, there were no events of SVD over the follow-up period. A larger recent multicentre observational study of 689 patients investigating AVR outcomes with the same aortic valve with RESILIA tissue also exhibited good haemodynamics and safety outcomes and zero events of SVD through 4 years of follow-up [18, 19]. In their totality, these data are encouraging for RESILIA tissue; but, of course, longer-term data are mandatory.

Although mechanical valves are often recommended for younger patients because they provide superior long-term durability compared to bioprostheses, patients with mechanical valves require lifetime anticoagulation, which increases the risk of major bleeding [2, 3]. The On-X mechanical valve, however, does offer the advantage of requiring a lower international normalized

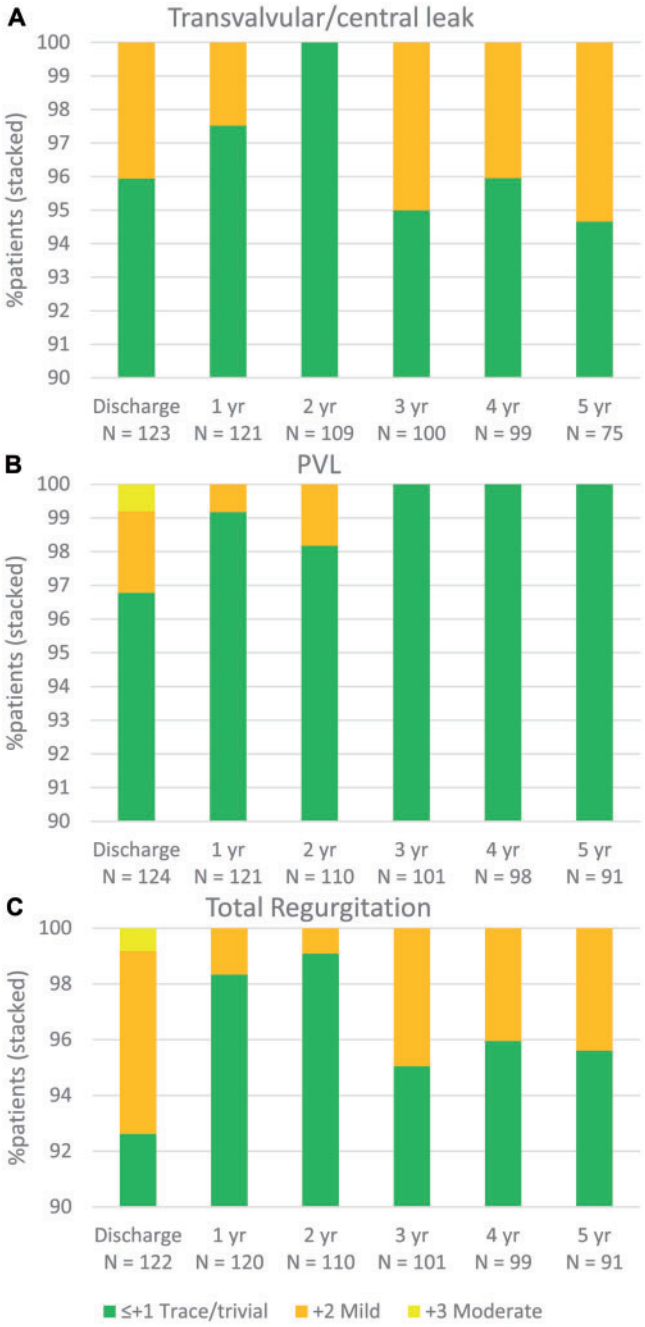


Figure 5: Central/transvalvular (**A**), paravalvular (**B**) and total regurgitation (**C**) in the study cohort over the 5 year observational study period.

ratio of 1.5–2.0, which should reduce the risk of bleeding. Bioprosthetic valves are a reasonable option for patients who wish to avoid long-term anticoagulation; however, these valves are susceptible to SVD, especially in younger patients. Patient-related risk factors for SVD include younger age, increased body mass index, hypertension, diabetes, smoking, dyslipidaemia and chronic renal failure; valve-related risk factors for SVD include glutaraldehyde fixation of the leaflets, persistent left ventricular hypertrophy, smaller prosthesis size and prosthesis–patient mismatch [20, 21]. One of the prominent mechanisms by which SVD occurs with tissue valves is believed to be due to calcification over time, resulting in leaflet stiffening and/or tearing [22].

Several methods of processing leaflet tissue have been developed in order to try to reduce tissue calcification [13, 23–26]. The RESILIA pericardial tissue undergoes an aldehyde capping process that permanently reduces Ca^{2+} binding [25]. This is followed by glycerolization to replace water, allowing dry storage. In an elegant randomized chronic study in juvenile sheep, RESILIA tissue exhibited significantly less Ca^{2+} content and improved haemodynamics compared with PERIMOUNT tissue [26].

The haemodynamics of the study valve reported here over 5 years are encouraging. Mean gradients were between 10 and 15 mmHg for all valve sizes except 19 mm, which were in the 20 s mmHg; these are qualitatively very similar to those reported over 5 years for the Carpentier-Edwards PERIMOUNT Magna valve by Chang *et al.*, [27] which were 11–13 mmHg. The breakdown of haemodynamics by valve size reported here highlight the need for consideration of aortic annular/root enlargement in AVR patients with small annuli, especially those requiring a 19 mm valve. Smaller valves exhibit greater increased gradients, and should serve a reminder to all surgeons to implement as safe as possible means to provide increased EOAs and reduced gradients [28, 29]. Smaller valves also limit the viable options that are available to patients in the future in the event that they require reintervention.

An important finding in the present study is that the prostheses with RESILIA tissue showed no evidence of SVD over 5 years of follow-up. Although these mid-term results are promising, it must be recognized that SVD is infrequent in the first few years following AVR. Based upon 12 569 patients who underwent AVR using a Carpentier-Edwards PERIMOUNT valve, the actuarial estimates of explant for SVD at 10, 15 and 20 years in patients 60–80 years old were 1.5%, 5.1% and 8.1%, respectively [29]. In patients <60 years old, the actuarial estimate of explant for SVD at 10, 5 and 20 years was 5.6%, 20% and 45%, respectively.

Our observation of no SVD over 5 years compares well with recent observations of contemporary bioprostheses. Investigating Carpentier-Edwards PERIMOUNT Magna valves over 5 years,

Table 4: NYHA heart failure functional class improvement from baseline to 5 years in the study cohort

Follow-up NYHA class at 5 years	Class I (*N* = 28)	Class II (*N* = 61)	Class III (*N* = 43)	Class IV (*N* = 1)	Total (*N* = 133)
N	18	47	25	1	91
Improved, *n* (%)	0 (0)	24 (51)	25 (100)	1 (100)	50 (55)
Same, *n* (%)	13 (72)	20 (43)	0 (0)	0 (0)	33 (36)
Worse, *n* (%)	5 (28)	3 (6)	0 (0)	0 (0)	8 (9)
Unknown, not done, or censored, *n*	10	14	18	0	42

The top row header represents patients' NYHA class status at baseline.
NYHA: New York Heart Association.

Anselmi *et al*. [6] and Blasco-Lucas *et al*. [8] reported 99.1% and 99.2% freedom from SVD, respectively; Axtell *et al*. [7] reported 99% freedom from reoperation due to SVD. One other contemporary bioprosthesis, the Trifecta valve, has demonstrated similar durability over 5 years of follow-up. Lehmann *et al*. [12] and Fukuhara *et al*. [10] reported 98.7% and 97.9% freedom from SVD, respectively. Anselmi *et al*. [9] and Kilic *et al*. [11] reported 98.9% and 98.7% freedom from reoperation due to SVD. Additionally, it should be noted that all of these published studies report upon AVR populations with a mean age of between 70 and 75, while our cohort investigating the RESILIA tissue had a mean age of only 65. Regardless, however, in the end, testing with RESILIA tissue will require follow-up much beyond 5 years in order to determine its true long-term durability [30].

Limitations

As the study was not designed with a comparator group, comparison of various performance measures from this study to similar measures from other studies is intrinsically compromised. Also, because the study's enrolment was non-consecutive, selection bias cannot be excluded. Further, a longer follow-up is required to establish durability of this new tissue.

CONCLUSIONS

One-hundred and thirty-three patients undergoing AVR with a RESILIA tissue valve exhibited good safety and haemodynamic outcomes over 5 years of follow-up. Most importantly in the elucidation of this tissue's durability, zero events of SVD were observed. Still, additional longer-term data will be necessary to draw conclusions about the durability of this tissue compared to that of contemporary tissue.

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Author contributions

Krzysztof Bartus: Conceptualization; Data curation; Methodology; Writing–original draft; Writing–review & editing. **Radoslaw Litwinowicz:** Project administration; Writing–review & editing. **Agata Bilewska:** Data curation; Investigation; Writing–review & editing. **Maciej Stapor:** Data curation; Investigation; Writing–review & editing. **Maciej Bochenek:** Data curation; Investigation; Writing–review & editing. **Jacek Rozanski**: Data curation; Project administration; Validation; Writing–review & editing. **Jerzy Sadowski:** Project administration; Supervision; Visualization; Writing–review & editing. **Grzegorz Filip:** Formal analysis; Visualization; Writing–review & editing. **Mariusz Kusmierczyk:** Formal analysis; Visualization; Writing–review & editing. **Boguslaw Kapelak:** Formal analysis; Visualization; Writing–review & editing.

Reviewer information

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