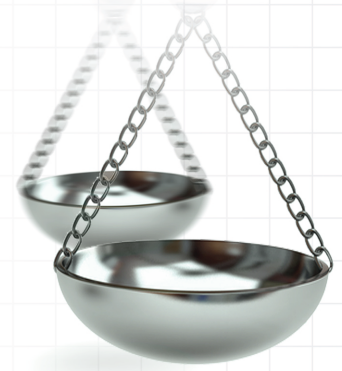




Structural hemodynamic valve deterioration durability of RESILIA-tissue versus contemporary aortic bioprostheses

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Aim: Durability of aortic valve replacement is becoming increasingly important. Aortic bioprostheses with RESILIA tissue have demonstrated outstanding outcomes thus far, but only in single-arm studies. **Methods:** We compared structural valve deterioration (SVD)-related hemodynamic valve deterioration (HVD) of grade ≥ 2 of RESILIA tissue valves from the COMMENCE trial ($n = 689$) to those from the PARTNER 2A contemporary AVR arm ($n = 936$) based upon annual core laboratory echocardiograms through 5 years of follow-up. **Results:** SVD-related HVD in the COMMENCE and PARTNER 2A cohorts were 1.8 versus 3.5%, respectively (one-sided 95% lower-bound hazard ratio of 0.92; $p = 0.07$). In propensity-matched cohorts ($n = 239$), these outcomes were 1.0 versus 4.8%, respectively (one-sided 95% lower-bound hazard ratio of 1.15; $p = 0.03$). **Conclusion:** RESILIA tissue-based AVR exhibited reduced SVD-related HVD compared with a contemporary AVR cohort devoid of RESILIA tissue.

Plain language summary

What is this article about? Artificial heart valves with leaflets made of tissue are becoming preferred more commonly compared with mechanical valves due to the requirement of lifetime anticoagulation and various restrictions associated with mechanical valves. Tissue valves, however, are limited by their durability and typically last 8–15 years depending on various factors; thus valve tissue technology is an active area of research. RESILIA tissue is a new heart valve tissue that has demonstrated encouraging results in animals and in single-arm human studies; but the durability of RESILIA tissue valves has never been compared with contemporary valves. In this study, we compared the structural hemodynamic valve deterioration of RESILIA tissue valves from a recent large US FDA pivotal trial to that of non-RESILIA contemporary valves from a separate randomized controlled trial.

What were the results? There were 689 patients with RESILIA tissue valves compared with 936 patients with valves with other, contemporary tissue valves. Over 5 years following valve implantation, the RESILIA-tissue valves exhibited significantly reduced levels of structural hemodynamic valve deterioration compared with the contemporary valves.

What do the results of the study mean? These results are encouraging for the durability of RESILIA-tissue heart valves. Still, broader and longer-term data are required to confer durability superiority of RESILIA tissue compared with contemporary tissue valves.

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Surgical aortic valve replacement (SAVR) has been indicated for patients with symptomatic severe aortic stenosis and regurgitation for 60 years and has improved quality of life and life expectancy for these patients. Upon determining



SAVR is the appropriate treatment, two primary options are available—mechanical valves and tissue valves [1]. While mechanical valves generally provide superior longevity, they require life-long anticoagulation, which imposes dietary restrictions, limits activity and increases the risk of bleeding and thromboembolic events. Tissue valves do not require long-term anticoagulation, and are potentially amenable to transcatheter valve-in-valve procedures in the future. However, tissue valves historically have poorer durability (~10–20 years depending on patient age and risk factors), mostly due to calcification of the tissue leaflets over time [2,3].

With patients living longer and with the age of bioprosthetic SAVR patients trending lower over time due significantly to the expanded indications of transcatheter aortic valve replacement (TAVR), durability is becoming increasingly important [4]. Bioprosthesis durability may be evaluated in a myriad of ways. Historically, durability was largely based upon intrinsic structural valve deterioration (SVD) of the valve ultimately requiring reintervention. More recently, acknowledging that some patients are unable to undergo reintervention, definitions of valve durability include bioprosthesis hemodynamic compromise.

We sought to compare the structural hemodynamic valve deterioration (HVD) of a bioprosthesis with the novel RESILIA tissue to that of contemporary bioprostheses without RESILIA tissue. RESILIA tissue is a bovine pericardial tissue incorporating a novel integrity preservation technology that includes stable capping of free aldehydes, preventing calcium binding, and glycerolization, which further prevents exposure to aldehydes and calcification [5,6]. In a randomized study in a chronic juvenile sheep model, RESILIA tissue calcified on average 72% less than a contemporary bovine pericardial valve [7]. More recently, RESILIA tissue has been investigated in the COMMENCE Aortic trial, an Investigational Device Exemption (IDE) trial evaluating SAVR with RESILIA tissue in a contemporary SAVR population. Recently published 5-year outcomes of this trial included low and clinically stable echocardiographic mean gradients, very low levels of transvalvular regurgitation, and no events of SVD per the trial's pre-specified definition of Akins *et al.* [8,9]. In the present report, we re-evaluate the structural hemodynamic valve deterioration of the RESILIA tissue valves from the COMMENCE trial cohort and compare this outcome to that from a modern contemporary non-RESILIA tissue cohort, the SAVR arm of the Placement of Aortic Transcatheter Valves (PARTNER) 2 cohort A (P2A) trial.

Patients & methods

Study design & patients

The COMMENCE study was a prospective, multicenter, single arm, observational IDE study designed to evaluate the safety and hemodynamic performance of the model 11000A aortic bioprosthesis (clinical trial no.: NCT01757665). This tri-leaflet bioprosthesis is essentially the same as the Carpentier–Edwards PERIMOUNT Magna Ease aortic valve (Model 3300TFX, Edwards Lifesciences, CA, USA) except the valve includes RESILIA tissue leaflets. A total of 689 patients were implanted with this study valve between January 2013 and March 2016. Details regarding patient inclusion and exclusion criteria and primary outcomes through 5 years post-operatively have been previously reported [9,10]. The P2A trial randomized patients of intermediate operative risk (Society of Thoracic Surgeons [STS] Predicted Risk or Operative Mortality [PROM] 4–8%) to receive TAVR or SAVR (NCT01314313). The P2A SAVR arm was deemed appropriate as a comparator for a variety of reasons namely: sample size, patient annual follow-up through 5 years, accessibility to patient-level data, clinical events committee adjudication, and echo core-lab adjudication. In the P2A trial, 936 patients were assigned to SAVR and received a bioprosthesis at the surgeon's discretion between December 2011 and November 2013. Details regarding patient inclusion and exclusion criteria and primary outcomes through 5 years post-operatively have been reported [11]; also the durability of the trial's two arms through 5 years have been compared based upon a modern definition of SVD incorporating hemodynamic compromise [12]. The analysis of the present report is based upon the same COMMENCE trial data extract as its primary 5-year outcomes report [9] and the same P2A trial data extract as its primary 5-year outcomes report and durability analysis [11,12].

End points

Patients in the COMMENCE and P2A trials underwent clinical and hemodynamic evaluations pre-operatively (both trials), at discharge (both trials), at 1 month (P2A), at 3–6 months (COMMENCE), and at 1, 2, 3, 4 and 5 years (both trials). Each trial utilized independent Clinical Events Committees (CECs) to adjudicate serious clinical adverse events. Hemodynamic end points in both trials were assessed by Doppler-echocardiography and included mean transvalvular pressure gradients, valve effective orifice area (EOA), and Doppler velocity index; these were evaluated by independent echocardiography core laboratories.

In this analysis, study valve durability data from the COMMENCE and P2A trials were evaluated based upon the Valve Research Academic Consortium (VARC)-3 guidelines [13]. The primary end point in this analysis was the incidence of SVD-related HVD stage ≥ 2 during echocardiographic follow-up at 5 years. Potential HVD for each patient was identified based on the objective changes in echocardiographic parameters of hemodynamic valve function from the 1 month (P2A) or 3–6 month (COMMENCE) echocardiogram and follow-up annual echocardiograms through 5 years. The stages of HVD were defined according to the VARC-3: stage 2 (or moderate) HVD: increase in mean gradient ≥ 10 and < 20 mm Hg with final mean gradient ≥ 20 mm Hg and any of: 1) decrease in EOA ≥ 0.3 cm² or $\geq 25\%$; or 2) decrease in Doppler velocity index ≥ 0.1 or $\geq 20\%$, and/or ≥ 1 grade new-onset or worsening transvalvular aortic regurgitation with a moderate final grade. Stage 3 (or severe) HVD: increase in mean gradient ≥ 20 mm Hg with final mean gradient ≥ 30 mm Hg and any of: 1) decrease in EOA ≥ 0.6 cm² or $\geq 50\%$; or 2) decrease in Doppler velocity index ≥ 0.2 or $\geq 40\%$, and/or ≥ 2 grades new-onset or worsening transvalvular aortic regurgitation with a severe final grade. The etiology of HVD was categorized as: SVD, thrombosis or endocarditis [13].

Statistical analyses

The 5-year cumulative rates of SVD-related HVD are reported as Kaplan–Meier curves, with rates at 5 years including 95% confidence intervals. The rates of events of the COMMENCE trial were tested for superiority compared with those of the P2A SAVR arm using a one-sided Cox Regression Analysis, with $p < 0.05$ considered significant.

Since the test and comparator data came from different studies, it was important to address any potential disparity of the two patient populations. As such, a propensity score method was implemented to achieve balance between the two patient populations' underlying characteristics. Accordingly, a propensity score matched analysis was utilized to compare the rates of SVD-related HVD from similar patients within the COMMENCE and P2A SAVR arm cohorts. First, a logistic regression model was performed on 8 patient baseline characteristic variables reported to be associated with SVD (age, body mass index, baseline native annular diameter, hypertension, hyperlipidemia, diabetes mellitus, renal insufficiency and previous or current smoker) [14] to calculate a propensity score for each patient. Missing baseline values were imputed using the Markov-chain Monte Carlo method prior to modeling. Patients of the COMMENCE cohort were matched 1:1 to patients of the P2A SAVR cohort according to the propensity score using the greedy nearest neighbor matching algorithm according to a caliper width of 0.2 SD of logit of propensity score. SAS version 9.4 (SAS Institute Inc., NC, USA) was used for all statistical analyses.

Results

Patient baseline characteristics

The 689 patients of the COMMENCE trial undergoing SAVR with a bioprosthesis with RESILIA tissue had an average age at implant of 66.9 ± 11.6 years, and STS PROM score was $2.0 \pm 1.8\%$; various additional patient baseline characteristics have been reported previously [10]. In the P2A trial, the average age at implant and STS PROM score of the 936 patients undergoing SAVR was 81.7 ± 6.7 years and $5.8 \pm 1.9\%$, respectively; additional baseline characteristics have been previously reported [15]. The composition of bioprostheses comprising the P2A SAVR arm did not include RESILIA tissue and included 40.6% Carpentier–Edwards PERIMOUNT Magna Ease (Edwards Lifesciences, Irvine, CA, USA), 24.1% Carpentier–Edwards PERIMOUNT Magna (Edwards Lifesciences), 16.9% specified as either Carpentier–Edwards PERIMOUNT (Edwards Lifesciences), Carpentier–Edwards PERIMOUNT Theon (Edwards Lifesciences), or unspecified but within the Carpentier–Edwards PERIMOUNT family of bioprostheses (Edwards Lifesciences), 7.8% Mitroflow (Sorin Group USA Inc., CO, USA), 6.2% Trifecta/Trifecta GT (Abbott Laboratories, IL, USA), 1.9% Mosaic (Medtronic, MN, USA), and 2.5% other or unknown.

A total of 620 COMMENCE patients and 664 P2A SAVR patients underwent a post-operative baseline echocardiogram and ≥ 1 annual follow-up echocardiogram and were eligible for this evaluation. Table 1 shows principal baseline characteristics of the complete COMMENCE and P2A SAVR arm cohorts. Mean age of the complete COMMENCE and P2A SAVR arm cohorts were 66.5 ± 11.7 and 81.4 ± 6.7 years, respectively.

Propensity matching

Figure 1 shows the LOVE plot specifying the absolute standardized differences between the cohorts before and after propensity matching among the adjusted covariates. After propensity score matching, there were 239 matched patient pairs whose absolute standardized difference was $< 10\%$ for each of these patient baseline variables. Mean

Table 1. Baseline characteristics of the full and matched cohorts.

Baseline characteristic	Full cohorts			Matched cohorts		
	COMMENCE	P2A SAVR	p-value	COMMENCE	P2A SAVR	p-value
Age, years	66.5 ± 11.78 (620)	81.4 ± 6.68 (664)	<0.0001	75.2 ± 6.47 (239)	75.6 ± 3.64 (239)	0.51
Male	445/620 (71.8%)	360/664 (54.2%)	<0.0001	170/239 (71.1%)	141/239 (59.0%)	0.005
BMI (kg/m ²)	29.8 ± 5.55 (620)	28.5 ± 5.97 (664)	<0.0001	29.5 ± 5.15 (239)	29.8 ± 7.03 (239)	0.56
Baseline native annular diameter (mm)	22.5 ± 4.24 (582)	21.6 ± 2.03 (662)	<0.0001	21.8 ± 4.12 (239)	21.9 ± 2.02 (239)	0.82
STS PROM score, %	1.9 ± 1.67 (486)	5.7 ± 1.78 (63)	<0.0001	2.6 ± 2.00 (186)	5.0 ± 1.55 (239)	<0.0001
NYHA class I	146/620 (23.6%)	0/663 (0.0%)	<0.0001	42/239 (17.6%)	0/239 (0.00%)	<0.0001
NYHA class II	312/620 (50.3%)	172/663 (25.9%)	<0.0001	111/239 (46.4%)	55/239 (23.0%)	<0.0001
NYHA class III	151/620 (24.4%)	369/663 (55.7%)	<0.0001	80/239 (33.5%)	129/239 (54.0%)	<0.0001
NYHA class IV	11/620 (1.8%)	122/663 (18.4%)	<0.0001	6/239 (2.5%)	55/239 (23.0%)	<0.0001
Angina class None	352/620 (56.8%)	502/663 (75.7%)	<0.0001	134/239 (56.07%)	168/239 (70.3%)	0.001
Angina class I	121/620 (19.5%)	56/663 (8.4%)	<0.0001	47/239 (19.7%)	24/239 (10.0%)	0.003
Angina class II	98/620 (15.8%)	65/663 (9.8%)	0.001	32/239 (13.4%)	27/239 (11.3%)	0.49
Angina class III	31/620 (5.0%)	37/663 (5.6%)	0.64	15/239 (6.3%)	18/239 (7.5%)	0.59
Angina class IV	2/620 (0.3%)	3/663 (0.5%)	1	2/239 (0.8%)	2/239 (0.8%)	1
Hypertension	488/620 (78.7%)	625/664 (94.1%)	<0.0001	219/239 (91.6%)	223/239 (93.3%)	0.49
Hyperlipidemia	466/620 (75.2%)	440/664 (66.3%)	0.0005	193/239 (80.8%)	187/239 (78.2%)	0.5
Coronary artery disease	338/620 (54.5%)	441/664 (66.4%)	<0.0001	153/239 (64.0%)	166/239 (69.5%)	0.21
Previous MI	43/620 (6.9%)	114/664 (17.2%)	<0.0001	23/239 (9.6%)	54/239 (22.6%)	0.0001
Previous CABG	21/620 (3.4%)	182/664 (27.4%)	<0.0001	8/239 (3.3%)	81/239 (33.9%)	<0.0001
Previous PCI	86/620 (13.9%)	182/664 (27.4%)	<0.0001	44/239 (18.4%)	72/239 (30.1%)	0.003
Prior aortic valvuloplasty	5/619 (0.8%)	30/664 (4.5%)	<0.0001	1/239 (0.4%)	12/239 (5.0%)	0.002
Prior stroke	25/620 (4.0%)	66/664 (9.9%)	<0.0001	17/239 (7.1%)	31/239 (13.0%)	0.03
Peripheral vascular disease	84/620 (13.6%)	209/664 (31.5%)	<0.0001	27/239 (11.3%)	86/239 (36.0%)	<0.0001
Diabetes mellitus	168/620 (27.1%)	240/664 (36.1%)	0.0005	82/239 (34.3%)	92/239 (38.5%)	0.34
COPD	88/620 (14.2%)	190/660 (28.8%)	<0.0001	50/239 (20.9%)	89/238 (37.4%)	<0.0001
Renal insufficiency	52/620 (8.4%)	27/664 (4.1%)	0.001	20/239 (8.4%)	22/239 (9.2%)	0.75
Permanent pacemaker	18/620 (2.9%)	76/664 (11.4%)	<0.0001	12/239 (5.0%)	28/239 (11.7%)	0.008
Cardiomyopathy	21/620 (3.4%)	63/664 (9.5%)	<0.0001	12/239 (5.0%)	32/239 (13.4%)	0.002
Carotid disease	178/620 (28.7%)	124/664 (18.7%)	<0.0001	94/239 (39.3%)	48/239 (20.1%)	<0.0001
Previous/current smoker	303/620 (48.9%)	321/664 (48.3%)	0.85	116/239 (48.5%)	123/239 (51.5%)	0.52
Baseline LVEF (%)	62.1 ± 9.76 (480)	56.1 ± 11.46 (463)	<0.0001	62.5 ± 9.85 (188)	54.2 ± 12.20 (152)	<0.0001
Moderate/severe MR	13/620 (2.1%)	106/600 (17.7%)	<0.0001	9/239 (3.8%)	28/218 (12.8%)	0.0004

CABG: Coronary artery bypass grafting; COPD: Chronic obstructive pulmonary disease; LVEF: Left ventricular ejection fraction; MI: Myocardial infarction; MR: Mitral regurgitation; NYHA: New York Heart Association; PCI: Percutaneous coronary intervention; STS PROM: Society of Thoracic Surgeons predicted risk of mortality.

age of the matched COMMENCE and P2A SAVR arm cohorts were 75.2 ± 6.5 and 75.6 ± 6.3 years, respectively ($p = 0.51$). Table 1 also shows the principal baseline characteristics of the propensity-matched sub-cohorts.

SVD-related hemodynamic valve deterioration

All patients underwent objective evaluation for stage 2 or 3 HVD at any timepoint through 5 years based upon their post-operative baseline echocardiogram and their annual follow-up echocardiograms. Individual patients that met such condition were evaluated for etiology of the condition as being either SVD-related or not. Figure 2 shows the Kaplan–Meier cumulative incidence curves of SVD-related HVD for the full COMMENCE trial and P2A SAVR arm cohorts. Through 5 years, the event rate of the COMMENCE trial was 1.8% (95% CI: 1.0–3.4%), and that of the P2A SAVR arm was 3.5% (95% CI: 2.1–5.8%). There was a trend to improved COMMENCE SVD-related HVD rate compared with the P2A SAVR arm, as the one-sided 95% lower-bound hazard ratio was 0.92 ($p = 0.07$).

Since any analysis results on the unmatched cohort may be attributable to disparity between the two populations, we repeated the analysis on the better comparable cohort (propensity score matched cohort) that adjusted for the

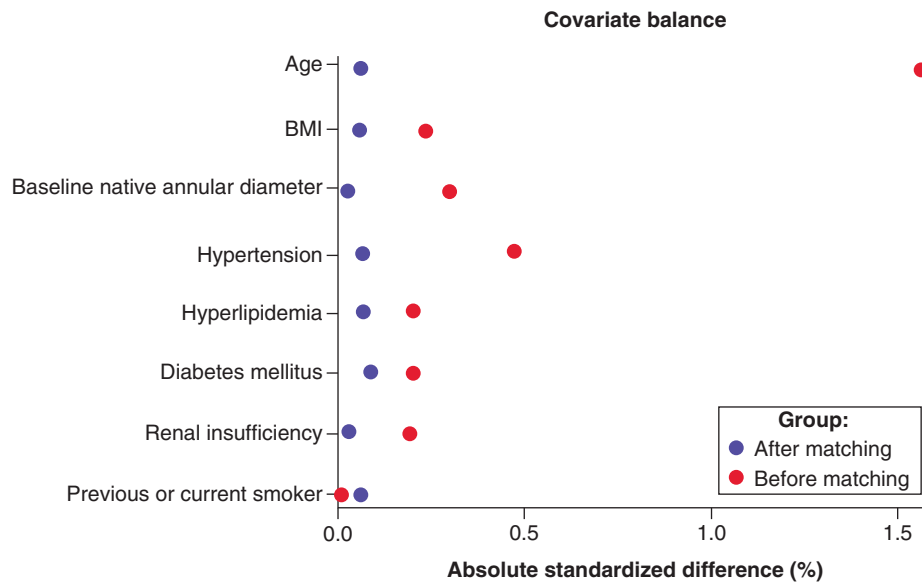


Figure 1. LOVE plot showing the absolute standardized differences between the cohorts before and after propensity matching among the adjusted covariates.

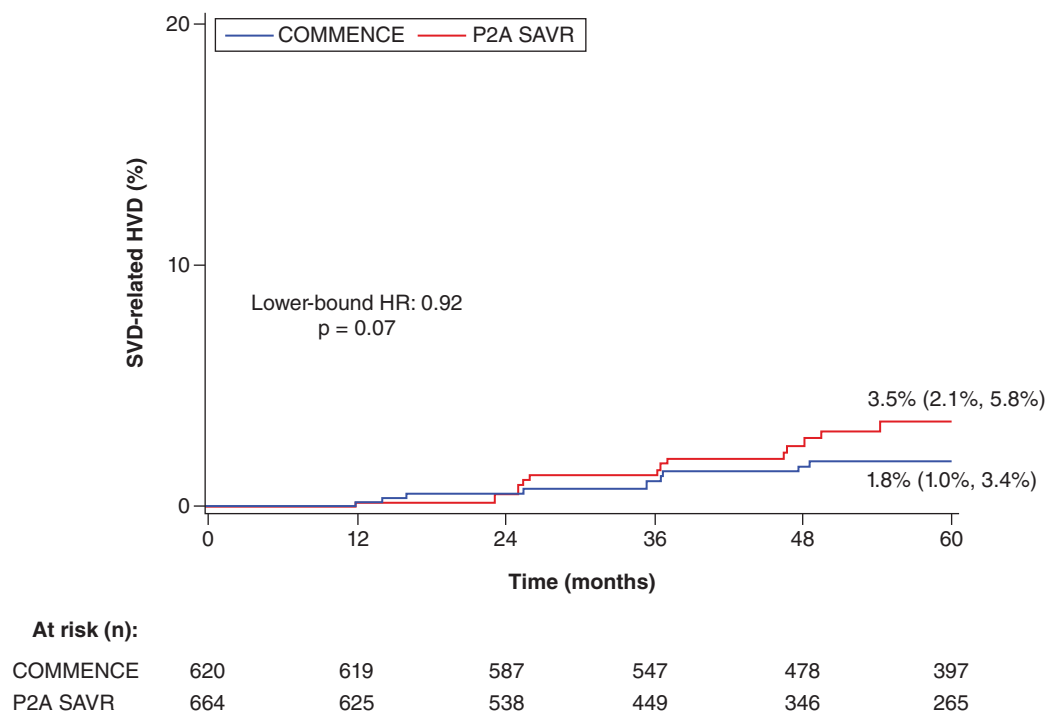


Figure 2. Kaplan-Meier incidence curves of SVD-related hemodynamic valve deterioration in the full COMMENCE and PARTNER 2A SAVR arm cohorts.

HR: Hazard ratio; SVD: Structural valve deterioration HVD: Hemodynamic valve deterioration.

possible disparity. Figure 3 shows these results for the propensity-matched cohorts. Based upon the 239 matched patient pairs, the SVD-related HVD event rate was significantly lower in the COMMENCE cohort (1.0%; 95% CI: 0.2–4.0%) compared with the P2A SAVR cohort (4.8%; 95% CI: 2.3–10.0%). The one-sided 95% lower-bound hazard ratio was 1.15 ($p = 0.03$).

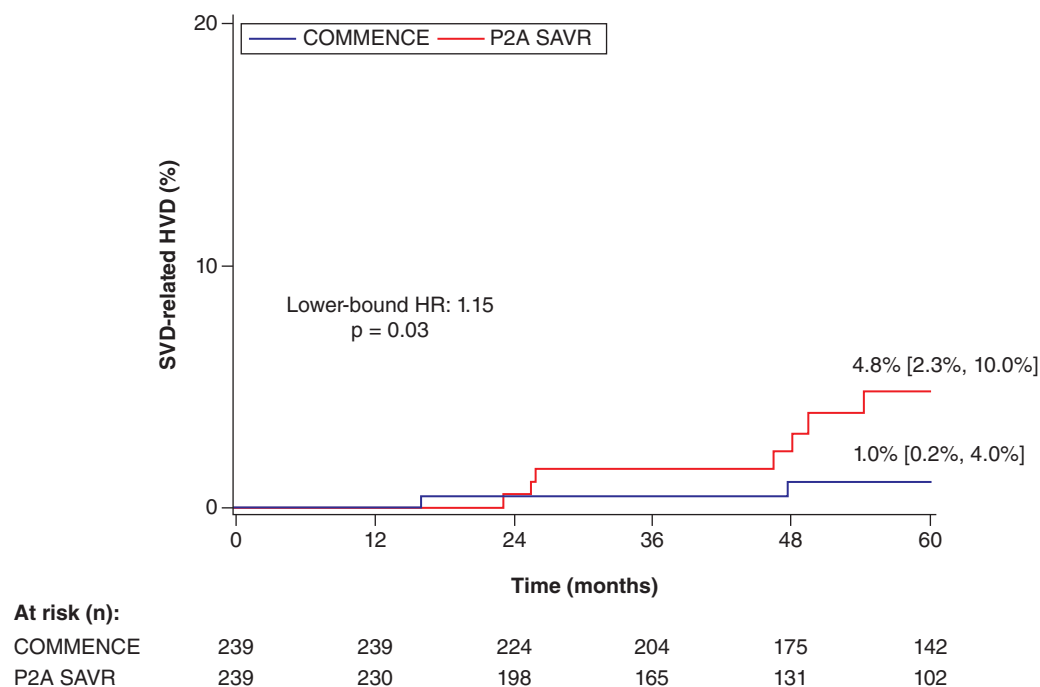


Figure 3. Kaplan–Meier incidence curves of SVD-related hemodynamic valve deterioration in the matched sub-cohorts from the COMMENCE trial and the PARTNER 2A SAVR arm.

HR: Hazard ratio; SVD: Structural valve deterioration HVD: Hemodynamic valve deterioration.

Discussion

This analysis is the first to compare any measure of durability of the novel RESILIA tissue during SAVR to a non-RESILIA SAVR cohort. Since these cohorts came from different studies, it was important to address any potential disparity of the two patient populations. As such, a propensity score method was implemented to achieve balance between two patient populations' underlying characteristics. Using the P2A randomized trial SAVR arm as a comparator, RESILIA tissue in the COMMENCE trial demonstrated a lower incidence of SVD-related HVD compared with the P2A SAVR arm among propensity-matched sub-cohorts.

RESILIA tissue's ultimate durability will need to await longer-term data, but these results are especially encouraging at this time for multiple reasons. One, these results were obtained using the sensitive indicator of HVD based upon the recent VARC-3 updated end point definitions for aortic valve clinical research. Second, the comparative SAVR arm of the P2A trial is a modern cohort of SAVR patients whose valve composition represents a strong set of bioprostheses. The Carpentier–Edwards PERIMOUNT, Magna, and Magna Ease aortic valve models comprise approximately 82% of this comparator arm, and these valve models represent the gold standard surgical aortic valves over the past 20 years, with demonstrated outstanding durability [2,3,16,17]. For the RESILIA tissue valves in COMMENCE to be demonstrably superior to this comparative SAVR cohort is meaningful.

In the comparison of SVD-related HVD between the full COMMENCE and P2A SAVR cohorts, the COMMENCE cohort exhibited a numerically lower rate than that of the P2A SAVR arm. This is impactful since patients in the COMMENCE trial were on average 14 years younger than the P2A SAVR arm, and it is well known that bioprostheses in younger patients calcify more frequently. Given this, it is not surprising that the matched cohorts demonstrated a greater difference. Tissue calcification of the valve leaflet cusps leading to incomplete opening during systole is the likely pathophysiologic phenomenon resulting in increased mean gradients and HVD, and is also the leading precursor to calcific deterioration that is known to be the predominant form of deterioration with bovine pericardial bioprostheses. It is tissue calcification that RESILIA tissue was designed to mitigate, and pre-clinical animal models have demonstrated effectiveness of RESILIA tissue compared with contemporary bioprosthetic tissue anti-calcification treatments [5–7].

The COMMENCE study and an earlier precursor feasibility study of 133 patients demonstrated encouraging outcomes for RESILIA tissue, based largely on outcomes through 5 years of low and clinically stable gradients,

very low levels of transvalvular regurgitation, and zero events of SVD [9,18–20]. However, the outcome of zero SVD events in these studies in a total of 822 patients through 5 years of follow-up were limited in two important ways. One, the definition of SVD that was employed in these studies was a conservative one that did not incorporate hemodynamic compromise as a criterion. Therefore, the prospect on the ultimate long-term durability of RESILIA tissue that these studies hold, with their zero events of SVD through 5 years, is limited. Secondly, as these were single-arm studies, the results were not comparative in nature. Our present analysis utilizes a more sensitive marker of structural compromise – hemodynamic valve deterioration – even if not yet potentially requiring reintervention, and provides a stronger assay with which to evaluate valve durability, especially under the lens of a comparative analysis against a gold standard contemporary cohort.

Establishing a single optimal definition of SVD for surgical bioprostheses in a patient-specific manner is very challenging. Older, traditional, more conservative measures based much upon reoperation or more recently valve-in-valve TAVR, tend to underestimate the incidence of true structural valve breakdown, as some patients may simply be incapable of undergoing such interventions. On the other hand, use of more modern liberal measures of SVD that include hemodynamic compromise, such as the VARC-3-based criteria, may overestimate structural valve breakdown depending on the patient's physiologic condition, and would ideally require the exclusion of other conditions that might cause hemodynamic compromise such as valve thrombosis before the patient becomes symptomatic. In this analysis, we took the approach to compare study valves from the COMMENCE trial with RESILIA tissue to a contemporary SAVR cohort in a manner as objectively as possible; hence we are using the VARC-3-based criteria of HVD. The association of HVD to patient symptoms, with native or prosthetic valves, is largely unknown, and so the extent to which these cases of HVD represent events that are symptomatic is unknown.

The potential implications of a more durable surgical aortic tissue valve are far-reaching [19]. Recently updated guidelines for the management of valvular disease in USA suggest it is reasonable to choose a mechanical aortic prosthesis in patients <50 years of age who do not have a contraindication to anticoagulation, and that it is reasonable to individualize the choice of either a mechanical or tissue valve in patients 50–65 years of age [1]. Given the patient lifestyle modifications and restrictions associated with anticoagulation, and the lack of future transcatheter valve-in-valve options for mechanical valves, the last 20 years has seen a significant increase in the proportion of aortic valves that are tissue bioprostheses. A more durable tissue valve option would likely further tip the scales toward these bioprostheses, and potentially impact the age cut-offs recommended in the guidelines. A more durable bioprosthesis could also impact the guidance balance between SAVR with such a durable bioprosthesis versus TAVR.

Limitations

This analysis does include some meaningful limitations. First and foremost, these two cohorts compared were not designed to be compared, and the two patient groups are quite different. As such, these results should be viewed as hypothesis-generating. Fortunately, the cohorts are large and broad enough that propensity-score-based patient matching allows for a still-meaningful number of patients matched to multiple patient baseline characteristics reported to impact bioprosthetic valve structural deterioration such that a difference in an outcome metric such as HVD was able to be resolved. Additionally, per the VARC-3 criteria, SVD-related HVD is but one, albeit important, component of overall bioprosthetic valve failure [13]. Lastly, this analysis of 5 years is too small and too short in duration to confidently conclude that any cohort is more durable than another when it is anticipated that SVD is more likely to occur in contemporary bioprostheses in years 5–20 post-operatively. As additional follow-up data becomes available beyond 5 years, it will be prudent to conduct a follow-up observational study to determine if the present study's findings are maintained at later timepoints. Further, an economic analysis between these two cohorts would be of interest since it would shed light on potential healthcare cost-savings associated with RESILIA tissue valve implantation.

Conclusion

RESILIA tissue-based AVR exhibited significantly reduced SVD-related HVD compared with contemporary AVR cohort devoid of RESILIA tissue. Longer-term investigation is necessary.

Future perspective

RESILIA tissue is presently <10 years old, and therefore its long-term performance as a heart valve tissue is still being evaluated. However, this tissue is utilized in four heart valve products by a leading heart valve manufacturer,

Edwards Lifesciences. Over the coming 10 years, in addition to the reports of the company-sponsored studies, there will be hundreds of independent publications that will begin to define RESILIA tissue's durability.

Summary points

- With the footprint of aortic valve replacement (AVR) with tissue bioprostheses expanding to younger populations and longer patient life expectancies, the durability of AVR with tissue valves is becoming ever more important.
- RESILIA tissue has recently demonstrated encouraging safety and effectiveness outcomes in the n = 689 patient single-arm COMMENCE AVR study.
- Here, we compare RESILIA tissue's durability from COMMENCE to that of the recently published (n = 936) patient contemporary AVR arm of the PARTNER 2 randomized control trial through 5 years post-operatively using the recent Valve Academic Research Consortium-3's structural hemodynamic valve deterioration outcome measure.
- Structural valve deterioration-based hemodynamic valve deterioration through 5 years was 1.8% for COMMENCE versus 3.5% for PARTNER 2 contemporary AVR arm (one-sided 95% lower-bound hazard ratio = 0.92; p = 0.07).
- In propensity-matched cohorts of (n = 239) each from these two cohorts, the structural valve deterioration-based hemodynamic valve deterioration were 1.0 versus 4.8%, respectively (one-sided 95% lower-bound hazard ratio = 1.15; p = 0.03).
- These results are encouraging for the long-term durability of RESILIA tissue, but broader and longer-term investigation is still necessary.

Financial & competing interests disclosure

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No writing assistance was utilized in the production of this manuscript.

Ethical conduct of research

This research is a comparative analysis from two human trials. The primary and 5-year outcomes of each of these trials have been reported previously. Appropriate IRB approvals were attained in each of the two trials, and all patients in both trials signed informed consent forms to participate in these trials.

Data sharing statement

In the two trials from which this research is based, all relevant site-specific data are maintained at the participating centers, and the relevant aggregated data and analyses are maintained at the sponsors of the trials, Edwards Lifesciences (CA, USA). The data and analyses undertaken in this research will not be made available to other researchers or organizations.

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Papers of special note have been highlighted as: • of interest; •• of considerable interest

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