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ORIGINAL ARTICLE

Retrospective Cohort Study

Sutureless aortic valve and post-operative atrial fibrillation: Five-year outcomes from a propensity matched cohort study

Thomas French, Sanjeet Singh Avtaar Singh, Vincenzo Giordano, Charilaos-Panagiotis Koutsogiannidis, Kelvin Hao Han Lim, Renzo Pessotto, Vipin Zamvar

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Thomas French, Sanjeet Singh Avtaar Singh, Vincenzo Giordano, Charilaos-Panagiotis Koutsogiannidis, Kelvin Hao Han Lim, Renzo Pessotto, Vipin Zamvar, Department of Cardiothoracic Surgery, Royal Infirmary of Edinburgh, Edinburgh EH16 4SA, United Kingdom

Sanjeet Singh Avtaar Singh, Institute of Cardiovascular and Medical Sciences, University of Glasgow, Glasgow G12 8TA, United Kingdom

Co-corresponding authors: Thomas French and Sanjeet Singh Avtaar Singh.

Corresponding author: Thomas French, MD, Research Fellow, Department of Cardiothoracic Surgery, Royal Infirmary of Edinburgh, Little France Crescent, Edinburgh EH16 4SA, United Kingdom. thomfren12@gmail.com

Abstract

BACKGROUND

The Perceval Sorin S (perceval valve) is a sutureless bioprosthetic designed for use in a high-risk cohort who may not be suitable for transcatheter aortic valve implantation or a conventional surgical aortic valve replacement (AVR).

AIM

To compare five-year post-operative outcomes in a cohort undergoing isolated AVR with the perceval valve to a contemporary cohort undergoing surgical AVR with a sutured bioprosthesis.

METHODS

This study was a retrospective, cohort study at a single tertiary unit. Between 2017 and 2023, 982 suitable patients were identified. 174 Perceval valve replacements were matched to 174 sutured valve replacements. Cohort characteristics, intra-operative details, and post-operative outcomes were compared between the two groups.

RESULTS

Time under the aortic cross-clamp ($P < 0.001$), time on the cardiopulmonary bypass ($P < 0.001$) and total operative time ($P < 0.001$) were significantly reduced in the Perceval group. Patients in the Perceval valve group were at a lower risk of postoperative pneumonia [odds ratio (OR) = 0.53 (0.29-0.94)] and atrial fibrillation [OR = 0.58 (0.36-0.93)]. After propensity-matching, all-cause mortality did not

significantly differ between the two groups in the five-year follow-up period. Larger valve sizes conferred an increased risk of mortality (P = 0.020).

CONCLUSION

Sutureless surgical AVR (SAVR) is a safe and efficient alternative to SAVR with a sutured bioprosthesis, and may confer a reduced risk of post-operative atrial fibrillation. Clinician tendency towards 'oversizing' sutureless aortic valves translates into adverse clinical outcomes. Less time on the cardiopulmonary bypass circuit allows for the treatment of otherwise high-risk patients.

Key Words: Sutureless valves; Aortic valve replacements; Survival; Atrial fibrillation

Core Tip: The use of sutureless aortic valves has been well established in the past decade. However, its midterm outcomes are not fully established in comparison to standard surgical aortic valve replacements (AVR). With the advent of Transcatheter aortic valve insertions, the use of sutureless valves may play a major role especially post transcatheter aortic valve implantation explants. We look at the midterm outcomes compared to standard surgical AVR.

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INTRODUCTION

The prevalence of aortic valve disease is notable, particularly in patients aged over 65, in which calcific aortic valve degeneration over time results in the development of aortic stenosis – the second most common cause of valvular heart disease worldwide[1]. Developing an effective, definitive treatment for aortic valve pathologies, remains a priority in both developing and developed nations, and will only become increasingly important in a rapidly aging and increasingly wealthy global population.

One alternative to the traditional surgical method of aortic valve replacement (AVR) is the transcatheter aortic valve implantation (TAVI)[2]. Valves implanted in this manner are secured to the aortic annulus through radial force on surrounding tissues, and a TAVI approach to AVR negates the requirement for sutures and invasive thoracotomy or sternotomy[3]. Consequently, TAVI represents an appealing alternative to surgical AVR in the elderly, comorbid population[4].

There exists a population of high-risk patients with aortic valve pathology who might not be suitable for TAVI replacement, due to reasons such as tortuous coronary artery anatomy, difficult femoral or radial artery access, active endocarditis, or those requiring several concomitant cardiac surgical procedures[5].

In this select high-surgical risk group of patients for whom surgical valve replacement remains the preferred option, and the use of surgically implanted sutureless aortic valves may be a suitable option. These constitute a group of valves requiring few or no securing sutures between the aortic annulus and the valve frame. This allows for faster implantation of the prosthetic valve, and the associated benefits – reduced time on the cardiac bypass machine, reduced time spent under general anaesthetic – whilst retaining the benefits of the traditional surgical approach, including debridement of the calcified aortic annulus, and concomitant heart surgery, such as coronary artery bypass grafting (CABG)[6]. The practical benefit of this valve type, then, is that it allows for surgical valve replacement in a higher risk population, who might not have been suitable for TAVI due to tortuous coronary artery anatomy, or difficult femoral or radial artery access[5].

Unfortunately, due to the relatively recent introduction of the sutureless surgically implanted valve to commercial markets, there exists only a small body of literature investigating the medium term and long-term outcomes of sutureless valve replacement compared to sutured bioprostheses[7]. Recent multicentre randomised control trials include the CAVALIER trial[8], the PERCEVAL trial[9] and, more recently, the PERSIST-AVR trial[10], the pooled results of which suggest non-inferiority of sutureless AVR, but indicate a tendency towards postoperative thrombocytopaenia.

The objective of this study was to address this paucity of evidence by investigating immediate and mid-term outcomes in a large cohort of patients undergoing AVR with a sutureless aortic valve over a period of up to five years, and comparing these to outcomes of patients undergoing AVR with a sutured bioprosthesis.

We hypothesised that all-cause mortality would be higher in the group of patients undergoing AVR with a sutureless bioprosthesis than patients undergoing AVR with a traditional sutured bioprosthesis, due to higher rates of paravalvular leak and structural valve degeneration. The primary aim of this study was to test this hypothesis.

Secondary aims of the study were to compare the frequency of early mortality and common post-operative complications between the two groups. Post-operative complications were judged to be of interest due either to high post-operative frequency (*e.g.* atrial fibrillation) or perceived negative effect on patient outcomes (*e.g.* cardiac arrest).

MATERIALS AND METHODS

The need for local NHS Research and Ethics Committee approval was evaluated with the NHS Health Research Authority toolkit, which deemed the study would be exempt from local committee review given the anonymized, retrospective nature of the study. Written consent was not sought from study participants.

Study design

A retrospective case-control design was used to compare patients who had undergone AVR with a perceval valve to who had undergone valve replacement with one of several subtypes of traditional sutured bioprosthesis over a period of five years.

Demographic details, operational details and data on post-operative patient course is routinely logged before, during and after operation for all patients undergoing AVR at the hospital site for use in the Central Cardiac Audit Database. The hospital database was searched for patients undergoing tissue AVR at the Edinburgh Royal Infirmary during the period March 1, 2017 to April 3, 2022. Participant records were prospectively updated with the study endpoint fixed at March 3, 2023.

A minimum sample size of 115 participants per arm was considered sufficient to prove non-inferiority of the sutureless valve based on a statistical power of 0.8, a presumed hazard ratio of 2.5, and an estimated two-year survival of 80%.

Demographic, inter-operative and post-operative data were compared both before and after propensity score matching, which enabled evaluation of the matching process, and some insight into the patient characteristics that might determine valve-type recommendations.

The study was reported according to the STROBE guidelines for case-control studies[11,12].

Participants

Inclusion criteria included consecutive patients from fifty to eighty-five years of age undergoing tissue AVR (tAVR)at the Edinburgh Royal Infirmary between the specified dates. Exclusion criteria included concomitant CABG and concomitant mitral valve repair (MVR). Numbers of individuals at each stage are summarized under Figure 1. Valve selection was determined by surgeon's preference and familiarity.

Variables

The primary outcome in this study was all-cause mortality. In-hospital mortality was considered to mean patients who died before discharge home from any ward. Thirty-day mortality was defined as patients who died within thirty days of the operation, regardless of discharge status.

Secondary outcomes of interest were post-operative atrial fibrillation, cardiac arrest, pneumonia, complete heart block, delirium, myocardial infarction, permanent pace-maker (PPM) insertion, ventricular fibrillation, ventricular tachycardia, pneumothorax, stroke, time spent ventilated, time spent in the cardiac intensive care unit, total length of hospital stay, total time in theatre, total time spent ventilated, and time spent on cardiopulmonary bypass, and time spent under aortic cross-clamping. Total time in theatre was calculated from induction of anaesthesia to recorded surgery finish time. Total length of stay was calculated in hours, from the time and date of admission to the time and date of discharge to either home or bridging care.

Baseline characteristics of interest for patients undergoing elective surgery were reported in a pre-operative clinic, and included age, sex, gender, BMI, smoking status, diabetic status, pre-operative heart rhythm, angina status grouped according to the Canadian Cardiovascular Society guidelines[12], breathlessness status (defined by New York Heart Association of Heart Failure classification), hypertension status, left ventricular ejection fraction (LVEF) [measured through pre-operative echocardiography and classified into either good (LVEF > 50%), moderate (LVEF 31%-50%), poor (LVEF 21%-30%) or very poor (LVEF < 21%)], previous myocardial infarction, re-operative status, and Additive Euroscore, as calculated from the variables described by Nashef *et al*[13].

Bias

It was predicted that patients undergoing Perceval valve replacement would be older and more co-morbid than their tissue valve counterparts, and in order to address this treatment bias, propensity score matching was conducted on the cohort.

Statistical analysis

Continuous variables were assessed for normality visually by means of histograms. Normally distributed continuous variables between the two groups were represented as the group mean and 95%CI, and were compared with two-tailed, unpaired *t*-tests. Non-normally distributed continuous variables were represented as the group median and accompanying interquartile ranges, and were compared using the Wilcoxon rank-sum test. Categorical variables were reported as absolute frequencies, along with percentage frequency, and were compared with the χ^2 test.

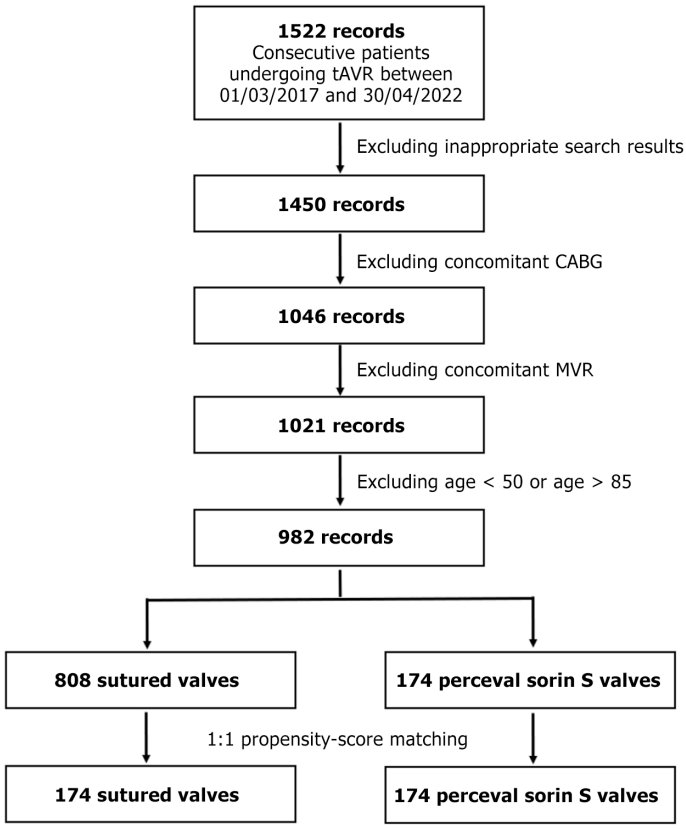

Figure 1 Patient selection process. MVR: Mitral valve repair; CABG: Coronary artery bypass grafting; tAVR: Tissue aortic valve replacement.

Univariable logistic regression was used to identify seven patient characteristics (age, gender, additive Euroscore, NYHA status, diabetic status, hypertension and smoking status) potentially confounding valve choice (alpha value ≤ 0.25) [14]. These characteristics were included as confounders in the multivariable logistic regression equation used to generate propensity scores. Participants were matched using nearest neighbour-matching with calipers of width 0.2 of the standard deviation of the logit of the propensity score[15]. Participants were matched with 1:1 matching based on propensity score, resulting in 174 patients in the perceval valve being matched to 174 patients in the sutured group. Acceptable standardised mean difference between the two groups for all measured characteristics was considered to be < 0.1 following matching.

Propensity score matching was chosen to simulate randomisation of participants over alternative methods of adjusting for treatment bias such as propensity score stratification, inverse probability weighting, or traditional statistical controlling. Propensity score matching is frequently shown to achieve more accurate estimations of covariate balance than the aforementioned methods, and has been recommended for matching covariates in observational studies with a high proportion of 'untreated' participants[16,17].

A summary of demographic details prior to matching is visible in Supplementary Table 1, immediate post-operative outcomes (adjusted and unadjusted odds ratios) in Supplementary Table 2, and a summary of standardized mean differences and density plots for continuous variables are available in Supplementary Table 3, Supplementary Figures 1 and 2. Propensity score distributions before and after matching are visible in Supplementary Figure 3.

Unadjusted odds ratios for the rates of complication in the two groups were obtained using univariate logistic regression.

Survival analysis was performed, examining all-cause mortality in both patient groups. Records were considered censored in the event of either patient death or loss to follow-up. The results of time-to-event analysis were plotted in Kaplan-Meier survival charts, and the Log-rank test was used to compare all-cause mortality between the two groups. For all statistical tests except the specific example given above, an alpha value of 0.05 or less was considered statistically significant. All statistical testing was carried out using R Statistical Software (v4.3.2; R Core team 2023). The package 'MatchIt' was used for propensity score matching.

Missing data

Missing data was treated as missing completely at random. Mode imputation for categorical variables and median imputation for continuous variables was used in propensity score generation. A sensitivity analysis was conducted, comparing results to those obtained after analysis on a 'complete case' basis. The detailed analysis can be seen in Supplementary Tables 4 and 5.

RESULTS

Participants

A search for patients undergoing tAVR for the specified dates yielded 1522 records. Excluding inappropriate valve types, concomitant CABG, concomitant MVR and individuals outside of the specified range resulted in 982 suitable records, of which 174 were in the Perceval group, and 808 were in the sutured group. 1:1 propensity score matching resulted in 174 records in both groups, resulting in a matched cohort of 348 patients. Patient selection is summarised in the flow diagram below (Figure 1).

Pre-operative characteristics

The pre-operative characteristics of both treatment groups are presented in Table 1. Patients undergoing Perceval valve replacement were on average older than their sutured tissue valve counterparts [77 (74-80) *vs* 70 (64-76), $P < 0.001$] and had a higher median Additive Euroscore [5.00 (1.88-7.00) *vs* 6.00 (2.22-7.00), $P = 0.003$] suggestive of an increased pre-operative risk. A higher proportion of patients in the perceval group were hypertensive [126 (72.4) *vs* 511 (63.2), $P = 0.022$] and a higher proportion in the Perceval group were diabetic ($P = 0.002$). No significant difference in angina status, LVEF status or NYHA grade was measured between the two groups.

Intra-operative details

Intra-operative details are presented in Table 2. After propensity score matching, patients in the Perceval group spent, on average, less time on the cardiopulmonary bypass circuit [60 (49-78) minutes *vs* 82 (69-110) minutes, $P < 0.001$], less time under aortic cross-clamping [46 (36-57) minutes *vs* 71 (56-91) minutes, $P < 0.001$], less time ventilated [9.9 (7.3-18) hours *vs* 14 hours (9.4-21), $P = 0.005$], and less total time in theatre [140 (120-170) minutes *vs* 170 (140-200) minutes, $P < 0.001$] (Supplementary Figures 4 and 5).

Early post-operative outcomes

Immediate post-operative outcomes before and after matching are present in Table 3 and Supplementary Figure 6. There were no cases of intra-operative mortality in either treatment group. Rate of in-hospital mortality [1 (0.6) *vs* 2 (1.1), $P = 0.562$] and thirty-day mortality [4 (2.3) *vs* 3 (1.7), $P = 0.703$] did not significantly differ across the two groups, both before and after matching.

After propensity score matching, rates of atrial fibrillation [39 (22.4) *vs* 58 (33.3), $P = 0.023$] and pneumonia [21 (12.1) *vs* 36 (20.7), $P = 0.030$] were significantly lower in the Perceval group compared to the sutured tissue valve group.

Long-term survival

Survival curves in relation to all-cause mortality are shown in Figure 2. Survival curves with event tables are visible in Supplementary Figures 7 and 8.

Median follow-up time for the entire cohort was 3.05 years. Cohort survival at 1 year was 91.6% (95%CI: 88.7-94.5), 2 years was 88% (95%CI: 84.6-91.5) and 4 years was 73.8% (95%CI: 68.2-79.8).

Perceval group survival at 1 year was 90.8% (95%CI: 86.6-95.2). This dropped to 87.9% (95%CI: 83.1-93.1) at 2 years, and 72.3% (95%CI: 63.4-82.5) at four years.

After propensity matching, in the sutured valve group, 1-year, 2-year and 4-year survival rates were 95.4% (95%CI: 92.3-98.6), 91.6% (95%CI: 87.4-95.9) and 77.4% (95%CI: 69.6-86.2) respectively.

Prior to propensity score matching, post-operative survival rates were significantly lower in the Perceval valve group ($P = 0.030$). However, following matching, survival rates did not significantly differ between the two groups across the duration of the study ($P = 0.400$).

The most common valve size implanted was medium [59 (34.1%)], followed by extra-large [48 (27.7%)], small [45 (26.0%)], and large [21 (12.1%)]. All-cause mortality was higher across the follow-up period in patients treated with large or extra-large valves compared to those treated with medium or small valves (log-rank $P = 0.020$) (Supplementary Figures 9 and 10).

DISCUSSION

Atrial fibrillation

Patients in the cohort treated with a sutureless aortic valve were significantly less likely to suffer from new onset post-operative atrial fibrillation. This is a new finding: Similar literature on this topic has shown comparable rates of atrial fibrillation on both perceval and stented groups[18,19], but not significantly reduced rates of atrial fibrillation in cohorts treated with a sutureless valve. Post-operative atrial fibrillation is associated with higher rates of rehospitalisation, mortality stroke, prolonged hospital stays and higher per-patient costs[20].

One potential explanation for this finding is the observed difference in times under cardiopulmonary bypass. Increased time on the cardiopulmonary bypass circuit confers a higher likelihood of increased oxidative stress, bypass-triggered inflammation and electrolyte imbalances – all factors conferring a higher likelihood of post-operative atrial fibrillation [21]. Use of a minimally invasive approach in implanting a sutureless aortic valve may result in reduced levels of key pro-inflammatory cytokines such as tumor necrosis factor alpha, interleukin (IL) -6 and IL-2 compared to a traditional surgical approach[20]. Plasma concentration of inflammatory cytokines has been suggested as a potential mediator of atrial fibril-

Table 1 Cohort characteristics, median (25th-75th percentiles)

	Sutured (*n* = 808)	Perceval (*n* = 174)	*P* value
Demographics			
Age (*n* = 982)	70 (64-76)	77 (74-80)	< 0.001
Gender (*n* = 982)			< 0.001
Male	520 (64.4)	70 (40.2)	
Female	288 (35.6)	104 (59.8)	
BMI (*n* = 982)	28.4 (25.0-32.4)	29.0 (25.6-32.8)	0.165
Smoking status (*n* = 848)			0.024
Non-smoker	334 (41.3)	65 (37.4)	
Ex-smoker	279 (34.5)	76 (43.7)	
Current smoker	86 (10.6)	8 (4.6)	
Diabetes (*n* = 982)			0.002
No	659 (81.6)	124 (71.3)	
Diet	38 (4.7)	7 (4.0)	
Oral therapy	79 (9.8)	27 (15.5)	
Insulin	32 (4.0)	16 (9.2)	
NYHA grade (*n* = 879)			0.148
Grade I	144 (17.8)	21 (12.1)	
Grade II	208 (25.7)	37 (21.3)	
Grade III	282 (34.9)	69 (39.7)	
Grade IV	93 (11.5)	25 (14.4)	
Cardiovascular risk factors			
Heart rhythm (*n* = 914)			0.54
Sinus rhythm	607 (80.8)	129 (79.1)	
Atrial fibrillation/flutter	123 (16.4)	32 (19.6)	
Complete heart block/pacing	11 (1.5)	2 (1.2)	
Other dysrhythmia	9 (1.2)	0 (0.0)	
Hypertension (*n* = 882)	511 (63.2)	126 (72.4)	0.022
CCS angina status (*n* = 858)			0.863
CCS0	422 (59.1)	79 (54.9)	
CCS1	83 (11.6)	19 (13.2)	
CCS2	95 (13.3)	23 (16.0)	
CCS3	82 (11.5)	16 (11.1)	
CCS4	32 (4.5)	7 (4.9)	
LVEF (*n* = 681)			0.578
Good (> 50%)	424 (75.7)	92 (76.0)	
Moderate (21%-30%)	109 (19.5)	22 (18.2)	
Poor (31%-50%)	22 (3.9)	7 (5.8)	
Very poor (< 25%)	5 (0.9)	0 (0.0)	
Previous MI (*n* = 918)	62 (8.2)	12 (7.5)	0.794
Reoperation procedure (*n* = 982)	42 (5.2)	7 (4.0)	0.518
Risk scores			

Additive Euroscore (n = 980)	5.00 (1.88-7.00)	6.00 (2.22-7.00)	0.003
Logistic Euroscore (n = 600)	5.28 (3.29-8.56)	7.01 (5.48-10.27)	< 0.001

BMI: Body-mass index; NYHA: New York Heart Association; CCS: Canadian Cardiovascular Society; LVEF: Left Ventricular Ejection Fraction; MI: Myocardial infarction.

Table 2 Intra-operative details before and after propensity matching, median (25th-75th percentiles)

	Before propensity score matching			After propensity score matching		
	Sutured	Perceval	*P* value	Sutured	Perceval	*P* value
Bypass time (minutes) (n = 925)	93.0 (72.0-123)	60.0 (49.0-78.0)	< 0.001	87.0 (69.0-112)	60.0 (49.0-78.0)	< 0.001
Cross-clamp time (minutes) (n = 924)	75.0 (58.0-99.0)	45.5 (36.0-57.0)	< 0.001	71.0 (56.0-90.6)	45.5 (36.0-57.0)	< 0.001
Time Ventilated (hours) (n = 873)	11.5 (7.6-19.0)	9.9 (7.3-17.9)	0.383	13.6 (9.35-20.5)	9.88 (7.33-17.9)	0.005
Time in theatre (minutes) (n = 981)	180 (153-215)	139 (119-165)	< 0.001	171 (143-201)	139 (119-165)	< 0.001

Table 3 Immediate post-operative outcomes before and after propensity score matching, median (25th-75th percentiles)

	Before propensity score matching			After propensity score matching			Odds ratio[1]
	Sutured valves	Perceval valves	*P* value	Sutured valves	Perceval valves	*P* value	
Intra-operative mortality	0 (0.0)	0 (0.0)	NA	0 (0.0)	0 (0.0)	NA	NA
In-hospital mortality	16 (2.0)	1 (0.6)	0.197	2 (1.1)	1 (0.6)	0.562	0.50 (0.04-5.55)
< 30 days mortality	23 (2.8)	3 (1.7)	0.403	4 (2.3)	3 (1.7)	0.703	0.73 (0.16-3.35)
Length of CICU stay (days) (n = 917)	1.14 (0.97-2.11)	1.13 (0.98-1.91)	0.543	1.25 (1.00-2.50)	1.13 (0.96-2.00)	0.132	NA
Total length of stay (days) (n = 917)	6.90 (5.31-9.99)	7.08 (5.93-9.90)	0.248	8 (6.00-11.0)	7 (6.00-10.00)	0.315	NA
Post-operative complications							
Atrial fibrillation	229 (28.3)	39 (22.4)	0.111	58 (33.3)	39 (22.4)	0.023	0.57 (0.35-0.91)
Pneumonia	152 (18.8)	21 (12.1)	0.030	36 (20.7)	21 (12.1)	0.030	0.49 (0.27-0.90)
Delirium	100 (12.4)	28 (16.1)	0.187	27 (15.5)	28 (16.1)	0.883	1.03 (0.58-1.83)
MI	1 (0.1)	0 (0.0)	0.642	0 (0.0)	0 (0.0)	NA	NA
PPM	19 (2.4)	6 (3.4)	0.405	4 (3.10)	6 (3.4)	0.521	1.50 (0.42-5.44)
VT/VF	9 (1.1)	0 (0.0)	0.162	0 (0.0)	0 (0.0)	NA	0.94 (0.06-15.9)
Pneumothorax	8 (1.0)	1 (0.6)	0.602	1 (0.6)	1 (0.60)	1.000	0.95 (0.06-15.89)
Stroke	25 (3.1)	6 (3.4)	0.808	4 (2.3)	6 (3.4)	0.521	1.51 (0.42-5.47)

[1]After matching, adjusted for additive Euroscore. *P* values for adjusted odds ratios available in Supplementary Table 2.
CICU: Cardiothoracic intensive care unit; MI: Myocardial infarction; PPM: Permanent pace-maker; VT/VF: Ventricular tachycardia/ventricular fibrillation.

lation through direct action on the cardiac myocardium[22]. The incidence and effect on outcomes of postoperative atrial fibrillation is also dependent to some degree on treatment strategy – rapid correction with amiodarone and prophylactic postoperative beta-blockers may result in a lessened impact on outcomes.

The same mechanisms might account for the differences observed in rates of post-operative pneumonia between the two cohorts[23]. Prolonged time on cardiopulmonary bypass confers an increased risk of pulmonary compromise as a result of alveocapillary membrane injury, surfactant impairment, and mucociliary dysfunction[24,25]. Additionally, a thoracotomy or mini-sternotomy might minimise changes to the topology of the chest wall compared to a sternotomy, thus reducing the impact on ventilation of chest wall trauma from surgical incision[25].

The observed lower rates of post-operative atrial fibrillation, however, did not translate into reduced post-operative mortality or a significantly reduced hospital stay across the post-operative period in this study.

All-cause mortality

No significant difference in early mortality (in-hospital, intra-operative and less-than-thirty-day mortality) was elicited

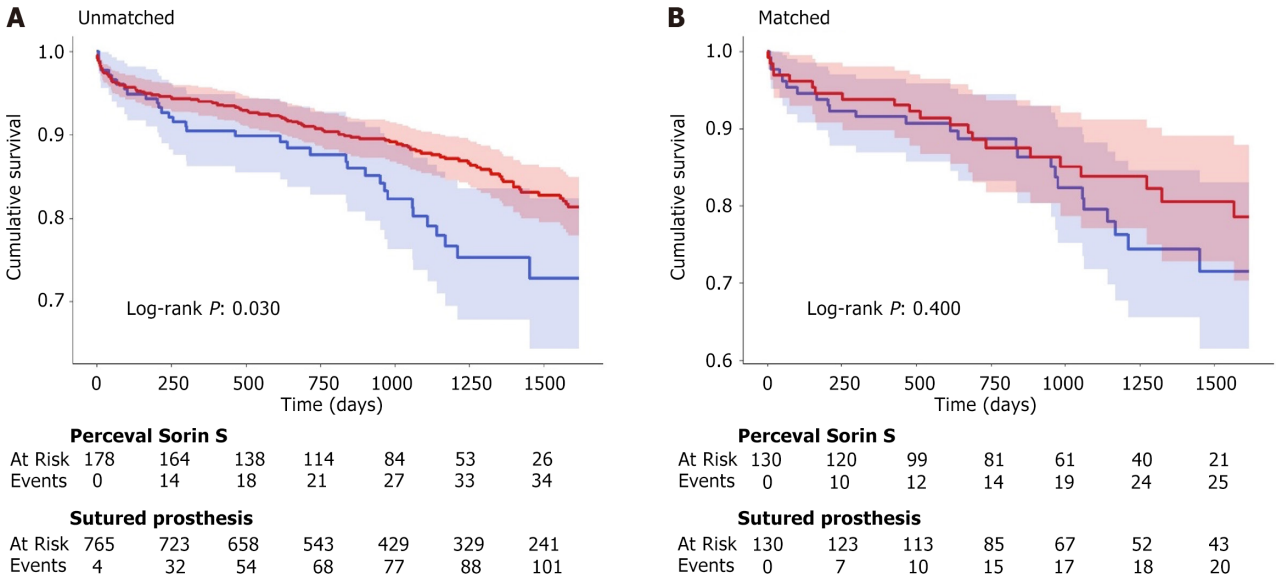

Figure 2 Kaplan-Meier survival curves comparing cumulative mortality in the two treatment groups before and after propensity score matching. A: Unmatched; B: Matched.

between the two groups both before and after matching, in-keeping with a 2023 meta-analysis by Colarossi *et al*[23] comparing sutureless and sutured valve replacement across 20 retrospective case-control studies, finding no significant difference in the aforementioned outcomes between the two groups.

As expected, the average patient undergoing Perceval valve replacement was older and had a higher surgical risk-score compared to their counterparts undergoing sutured valve replacement. This could account for the higher observed death rates in the Perceval group prior to matching.

Mortality rates in this study were comparable to the current literature on the topic. A 2023 meta-analysis by Jolliffe *et al* [24] examining mid to long-term outcomes across seven studies investigating long term outcomes for the Perceval valve alone showed comparable average 1 year (93.4%), 2 year (89.4%) and 4 year (82%) mortality rates[26,27].

Shorter cardiopulmonary bypass and aortic cross clamp times

Patients in the Perceval group spent a lower average time both on the cardiac bypass circuit and under aortic cross-clamping without a corresponding increased risk of mortality both in the immediate and long term. This is important from a patient safety perspective, as both cardiopulmonary bypass and aortic cross-clamping time are independent predictors of short-term and long-term mortality[28,29].

The reduction in time operational time and time on the bypass in particular, then, in patients treated with rapid deployment valves, is of particular benefit to older, more co-morbid patients that might not have been otherwise suitable for surgery, a fact of particular relevance to the United Kingdom population where the absolute numbers of people aged 65 years or older in England will increase by 48.6% between 2015-2035[30].

Reduced time spent on the bypass without a corresponding increase in mortality or side-effect profile is beneficial also from a cost-benefit perspective. AVR is an expensive and time-consuming operation[31]. Median operation times in both groups were well above three hours, but patients in the Perceval group spent significantly less time in theatre [210, interquartile range (IQR): 190-235] *vs* 248 (IQR: 220-290), $P < 0.001$]. Faster operations may help to reduce costs associated with performing the procedure, enable more operations in a given time period and reduce patient waiting lists for elective operations.

Valve sizes

The observed difference in mortality rates by valve size is likely indicative of the tendency for clinicians to insert the largest possible valve that fits in the aortic annulus, as a means of avoiding patient-prosthesis mismatch. Currently, the Perceval valve is available in four sizes: Small (referring to an aortic annulus diameter of 19-21 mm), medium (21-23 mm), large (23-25 mm) and extra-large (aortic annulus diameter 25-27 mm). In contrast to TAVI–in which valve size is determined by non-invasive imaging such as transthoracic echocardiogram or ECG-gated multidetector computerized tomographic imaging, valve sizing in surgical AVR with a sutureless prosthetic is somewhat subjective, with a surgeon measuring the aortic annulus with a sizing device. Patient's with a particularly small aortic annulus (*i.e.* less than or equal to 19mm), or a particular large aortic annulus (greater than 27 mm) may benefit from a sutured bioprosthesis instead of a sutureless device.

The expandable nature of the Perceval valve introduces the potential to 'oversize' a valve. A nitinol frame implanted into small an annulus may fail to expand suitably, resulting in recoil, crimped leaflets and a lower effective orifice area. Oversizing of the perceval valve results in higher post-operative transvalvular gradients and earlier structural degeneration of the valve[32]. Resulting pressure on the atrio-ventricular node may disrupt normal conductive function,

and lead to higher rates of AV-block in patients treated with poorly sized sutureless aortic valve[33].

Clinician education as to the appropriate use of sizing obturators may mitigate this risk and result in further improved post-operative outcomes in patients treated with a sutureless valve. Further analysis investigating the immediate and long-term outcomes of patients treated with different sizes of valve stratified by patient body surface area and estimated aortic annulus size may suggest an optimal treatment strategy for those treated with this particular valve type – for example, the avoidance of sutureless AVR in patients with a particularly small body surface area.

No difference in rates of PPM insertion and stroke between two groups

Higher rates of heart block requiring PPM implantation and higher rates of stroke have been observed in patients undergoing SAVR with a perceval valve compared to a sutured valve, along with a propensity for thrombocytopaenia in the Perceval valve group[34].

However, no significant difference in the rate of PPM insertion or stroke was elicited between the two groups observed in this study.

The self-expanding design of surgically implanted sutureless valves such as the perceval valve has been suggested as a cause for the high observed rate of post-operative PPM. Notably, high rates of PPM implantation are observed in TAVI-treated patients. High calcium load on the left coronary cusps may shift a sutureless prosthetic towards the right coronary cusp (and therefore the bundle of His), predisposing to post-procedural complete heart block[33]. Implantation of a sutureless valve through a surgical technique allows for debridement of the aortic annulus, and this study results suggest that high grade AV block may not be an inevitable outcome of the expanding prosthesis model, but rather the implantation technique used.

With regards to stroke, it is important to mention the potential link between post-operative thrombocytopaenia and haemorrhagic stroke in perceval valve treated patients. Thrombocytopaenia is commonly observed in patients treated with the perceval valve[32], which may go someway towards explaining previously observed high rates of stroke.

Examining this relationship was felt to be outside the bounds of this study, as post-operative platelet count was not recorded routinely for the study population, but the link between the two post-operative complications is still poorly understood, and merits further exploration.

This study was limited by the fact that it was a retrospective study, and thus whilst able to identify correlations, was not able to conclusively identify causative links between variables. The propensity score matching method used to account for bias is in itself prone to bias – selecting inappropriate confounders or simply omitting important confounders can result in a poorly matched patient cohort. Although a systematic approach to choosing confounders for propensity score matching has been applied here, the loss of a significant difference in long-term survival between the two groups after propensity score matching could be an artefact of the matching process, and this result will need confirmation from a prospective trial involving true randomisation of participants. One example would be the choice of anticoagulation and antiplatelet agent was primarily driven by the presence of post-operative atrial fibrillation lasting for more than 48 hours. However, the patients who may have been on an anticoagulant pre-operatively would be resumed on this rather than be commenced on an antiplatelet agent.

Due to a lack of routinely recorded echocardiographic data, the authors were not able to comment on the estimated effective orifice area for individual patients, nor rates of post-operative paravalvular leak or valve embolism. We were also unable to control for echocardiographic data in the propensity-matching process. Reoperation was not considered as a competing risk for mortality.

Finally, this was a single-center study, and the findings observed here may not be generalisable to a wider population. Future prospective studies with a multi-centre design will be necessary to confirm the generalisability of the findings observed in this study.

CONCLUSION

This retrospective, single-center cohort study investigated all-cause mortality across five years following isolated AVR with either a surgically implanted sutureless valve or a sutured stented bioprosthesis. We note higher rates of all-cause mortality in those treated with larger valve sizes, highlighting the risk of over-sizing this particular valve design. We note also, in contrast to previously published literature on the topic, that use of a sutureless valve was associated with a lower rate of post-operative atrial fibrillation and post-operative pneumonia, without a correspondingly increased risk of PPM implantation or stroke.

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FOOTNOTES

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Institutional review board statement: The need for local NHS Research and Ethics Committee approval was evaluated with the NHS Health Research Authority toolkit, which deemed the study would be exempt from local committee review given the anonymised, retrospective nature of the study. Written consent was not sought from study participants.

Informed consent statement: Informed consent was obtained at the time of surgery for use of data for study purposes. A copy of the consent form can be made available at request.

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Country of origin: United Kingdom

ORCID number: Thomas French 0009-0009-9987-8588; Sanjeet Singh Avtaar Singh 0000-0003-4320-0734; Vipin Zamvar 0000-0003-2447-828X.

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