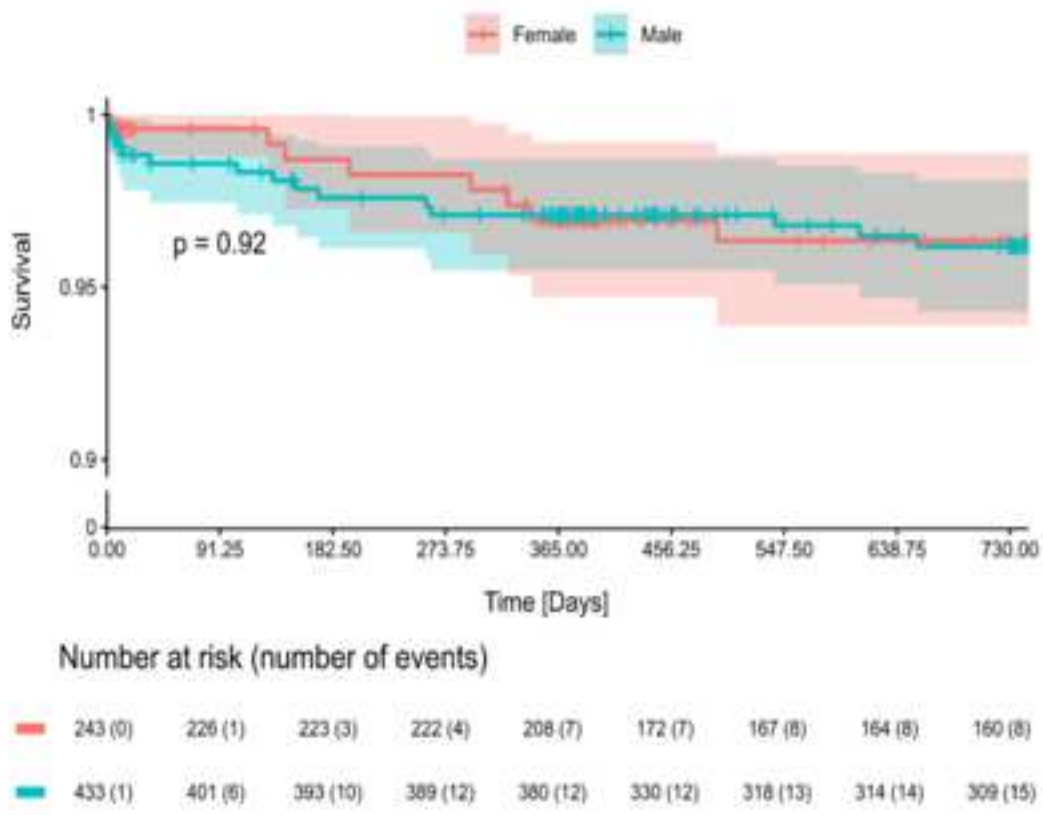
Sex-related Differences in Patient Outcomes after SAVR

Summary

In the propensity-score matched cohort of 433 males and 243 females undergoing first-time SAVR ± root replacement/CABG using a bioprosthetic valve, there were no sex-related differences at 2 years post surgery, indicating safety of SAVR and good valve performance in both sexes.



Legend: CABG, coronary artery bypass graft; SAVR, surgical aortic valve replacement

Sex-related Differences among Patients Undergoing Surgical Aortic Valve Replacement - A Propensity Score Matched Study

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Graphical abstract

Caption: Sex-related Differences in Patient Outcomes at 2 years after SAVR

Legend: CABG, Coronary artery bypass graft; SAVR, surgical aortic valve replacement.

Trial registration ClinicalTrials.gov NCT04053088 / - NCT03666741

Highlights:

Key question

What is the role of sex in clinical presentation and clinical outcomes after SAVR?

Key findings

Despite a worse baseline profile of females, there were no differences in 2-year outcomes after SAVR between males and females.

Take-home message

SAVR appears similarly effective and safe for males and females as no sex-specific differences were observed.

ABSTRACT

Objectives: We investigated the sex-related difference in characteristics and 2-year outcomes after surgical aortic valve replacement (SAVR) by propensity-score matching (PSM).

Methods: Data from two prospective registries, INDURE and IMPACT, were merged, resulting in a total of 933 patients: 735 males and 253 females undergoing first-time SAVR. PSM was performed to assess the impact of sex on the SAVR outcomes, yielding 433 males and 243 females with comparable baseline characteristics.

Results: Females had a lower body mass index (BMI; median 27.1 vs 28.0 kg/m^2; p=0.008), fewer bicuspid valves (52% vs 59%; p=0.036), higher EuroSCORE II (mean 2.3 vs 1.8 %; p<0.001) and STS score (mean 1.6 vs 0.9 %; p<0.001), were more often in NYHA class III/IV (47% vs 30%; p<0.001) and angina CCS III/IV (8.2% vs 4.4%; p<0.001), but had a lower rate of myocardial infarction (1.9% vs 5.2%; p=0.028) compared to males. These differences vanished after PSM, except for EuroSCORE II and STS scores, which were still significantly higher in females. Furthermore, females required smaller valves (median diameter 23.0 vs 25.0 mm, p<0.001). There were no differences in the length of hospital stay (median 8 days) or ICU stay (median 24 vs 25 hours) between both sexes. At two years, post-SAVR outcomes were comparable between males and females, even after PSM.

Conclusions: Despite females presenting with a significantly higher surgical risk profile, 2-year outcomes following SAVR were comparable between males and females.

Keywords: Aortic stenosis; Surgical aortic valve replacement; sex disparities

LIST OF ABBREVIATIONS

AS – aortic stenosis

BMI – body mass index

CABG – coronary artery bypass surgery

CCS – Canadian Cardiovascular Society

MI – myocardial infarction

NYHA – New York Heart Association

PSM – propensity score matching

SAVR – surgical aortic valve replacement

STS – Society of Thoracic Surgeons

TIA – transient ischaemic attack

INTRODUCTION

Surgical aortic valve replacement (SAVR) has been the gold standard treatment for aortic stenosis (AS) for decades [1]. However, a precise understanding of specific sex-related differences in baseline characteristics and post-SAVR long-term outcomes and safety remains debated [2, 3]. Although women and men share a similar prevalence of AS, SAVR is less often performed in female patients. Specific anatomical characteristics peculiar to women's hearts, such as smaller valvular size, aortic annulus/root, and left ventricular outflow tract dimensions, make it technically more complicated and challenging for SAVR in women [4]. Besides, factors such as advanced age, greater frailty, lower body size, and the presence of more non-atherosclerotic comorbidities place females in a high-risk category for SAVR [3, 5, 6].

Several studies indicated that women undergoing SAVR experience worse short-term outcomes, including higher in-hospital and 30-day mortality, vascular complications, blood transfusion and increased length of hospital stay [2, 7] compared to men [2, 3, 6, 8]. Although a comparable long-term survival after SAVR was observed among both sexes [8, 9], extensive research is imperative to elucidate the male-female differences in the baseline characteristics and clinical outcomes to optimize the treatment for aortic valve diseases.

PATIENTS AND METHODS

In the present analysis, we combined data from two prospective, observational, multicentre registries - INDURE and IMPACT [10, 11], to study the sex-related difference in SAVR outcomes. We aimed to report 2-year follow-up data of male and female patients undergoing SAVR by propensity score matching (PSM).

Ethics statement

The study was approved by the institutional review board/ethics committee at each participating centre (**Supplementary Tabe 1).** A written informed consent was obtained from every patient before enrolment.

Patient population

Adult patients over 18 years of age undergoing SAVR and receiving Edwards INSPIRIS RESILIA bioprosthesis were enrolled in the registries. In addition, patients undergoing a planned native valve replacement with or without combined aortic root replacement and/or coronary artery bypass surgery (CABG) based on the pre-procedural evaluation were included. Exclusion criteria included prior myocarditis within three months before SAVR and a double valve procedure (replacement and repair). Additionally, when valve implantation was not possible as per device instruction for use, individuals with a life expectancy <12 months and pregnant patients at the time of the surgery were excluded.

Objectives

The primary objective of the analysis was to compare baseline and procedural characteristics of male and female patients undergoing SAVR.

The secondary objective was to compare the sex-related difference in post-SAVR clinical outcomes defined by Valve Academic Research Consortium-2 [12] at 2-year follow-up, which includes incidence of all-cause mortality, prosthetic endocarditis, thromboembolic events (stroke /transient ischaemic attack [TIA]), life-threatening valve-related bleeding, repeated procedure requirement and permanent pacemaker implantation (PPI).

Statistical analysis

Data were analyzed using descriptive statistics, with categorical variables presented as absolute values and frequencies (%) and the continuous variables presented as means (standard deviation [SD]) and/or median (interquartile range [IQR]). The percentages were calculated based on the number of patients with valid data per parameter, i.e. excluding patients with missing information. Comparisons were performed using a t-test or Mann-Whitney U-test for continuous variables, depending on distribution, and a Fisher's exact or Chi-square test for categorical variables. Propensity scores (PS) were calculated using a Generalized Linear Model to assess the sex-specific effects (male

vs. female). The following covariates were selected to calculate the PS: body mass index (BMI), valve morphology, New York Heart Association (NYHA) III/IV, Canadian Cardiovascular Society (CCS) angina III/IV, diabetes mellitus, hypertension, left ventricular ejection fraction (LVEF), mean transvalvular pressure gradient, previous percutaneous intervention, pacemaker, chronic obstructive pulmonary disease (COPD), dialysis, aortic valve regurgitation (moderate/severe), myocardial infarction (MI), TIA/stroke, peripheral arterial disease, and coronary artery disease. The 1:2 ratio matching was performed using nearest neighbour matching with a caliper width equal to 0.2 times the standard deviation of the PS logit. Post-matching, standardized mean differences were analyzed for all covariates included in the PS calculation. The mean differences for all covariates post-matching were within a desirable threshold (±0.1), indicating adequate balance. Statistical analyses were performed using R version 4.3 (https://www.R-project.org/).

RESULTS

A total of 993 patients, 735 males and 253 females, who underwent SAVR using INSPIRIS RESILIA between 2019 and 2021 were included in the entire cohort. To assess the impact of sex on SAVR outcomes, a PSM cohort was created, resulting in a total of 676 matched pairs of 433 males and 243 females (**Figure 1**).

Patient characteristics

In the entire cohort, female patients had a lower BMI (median 27.1 [IQR 23.4-31.0] vs 28.0 kg/m^2 [IQR 25.2-31.0]; p=0.008) and were less likely to have bicuspid valves (52% vs 59%; p=0.036) compared to male patients (**Table 1**). Additionally, females exhibited a higher prevalence of advanced NYHA class III/IV symptoms (47% vs 30%; p<0.001) and angina CCS class III/IV symptoms (8.2% vs 4.4%; p=0.019), indicating a higher symptomatic burden at baseline. However, after PSM, the differences were not significant in any cases.

Compared to males, female patients in both cohorts exhibited significantly higher surgical risk with higher EuroSCORE II (2.3±3.1% vs 1.8±2.0%; p<0.001) and Society of Thoracic Surgeons (STS) score (1.6±2.2% vs 0.90±2.5%; p<0.001). Notably, these differences persisted after PSM (EuroSCORE II: 2.4±3.0% vs 1.6±1.7% in; p<0.001 and STS score: 1.7±2.0% vs 1.0±2.3%; p<0.001). In the entire cohort, females had a lower history of MI (1.9% vs 5.2%; p=0.028) than males.

In baseline echocardiography, females exhibited a lower prevalence of moderate to severe aortic valve regurgitation (27% vs 35%; p=0.015), along with better LVEF (60±10% vs 58±10%; p<0.001) and slightly higher mean transvalvular pressure gradient (46±21 vs 43±20 mmHg; p=0.249) compared to males. This trend did not persist after PSM.

Procedural characteristics

In our study, both females and males had distinct AS aetiology (p=0.047), primarily showing congenital AS (51.6% in females vs 59.8% in males) followed by degenerative AS (44.6% vs 37.1%) (**Supplementary Table 2**).

In the total cohort, minimally invasive surgery (MIS) was more frequent in females (46.5% vs 38.6%; p=0.027) with less concomitant CABG (10.9% vs 16.3%; p=0.034) (**Supplementary Table 2**). Notably, these differences disappeared after PSM (**Table 2**). Females required smaller valves (median 23.0 mm [IQR 21.0-23.0]) compared to males (median 25.0 mm [IQR 23.0-27.0]), which was significant in both total and PSM cohorts (p<0.001). The majority of female patients received either 23 (44.4%) or 21 (39.9%) mm valves, while male patients received either 25 (37.2%) or 23 (30.7%) mm valves. There were no differences in the the overall procedural time (skin-to-skin) between males and females in the matched cohort (p=0.170). The first implantation attempt was successful in both sexes (>99.0%), with no intraprocedural mortality.

Discharge characteristics

The overall hospital stay during SAVR was similar between female and male patients in the matched cohort (median 8.0 [IQR 6.0-10.0] vs 8.0 [IQR 7.0-11.5] days, p=0.144; **Table 3**). There was no

difference in the LoS in intensive care unit (ICU) and duration of mechanical ventilation in both groups. A similar proportion of patients were discharged alive (females 99.6% and males 99.3%; **Supplementary Table 3**). The majority of patients were discharged to home after surgery, followed by discharge to a rehabilitation unit or another hospital.

Clinical outcomes

Both in the entire and PS-matched cohorts, no significant differences were observed in the incidence of clinical outcomes at 2 years, including endocarditis, thromboembolic events, valve-related dysfunction, repeated procedure, permanent pacemaker implantation, and valve-related bleeding between males and females undergoing SAVR ± CABG/root replacement (**Supplementary Table 4**; **Table 4**) as well as in patients undergoing isolated AVR (**Supplementary Table 5**) . The 2-year survival rate in the PS-matched cohort was 96.2% (95% CI: 94.3–98.1%) in males and 96.3% (95% Confidence Interval [CI]: 93.9–98.9%) in females (p=0.920); no differences were observed in the total cohort either (**Figure 2, Supplementary Figure 1**). Athough the rate of valve thrombosis at 2 years seemed to be higher in females (1.3% vs. 0.4% in the PS-matched cohort), the difference did not reach statistical significance (p=0.093).

The majority of patients requiring a repeated procedure at the 2-year follow-up in our study did so due the presence of the endocarditis; in 1 patient repeated procedure was due to valve thrombosis while another one had a moderate paravalvular leakage. One patient underwent valve-in-valve procedure due to AS. Furthermore, all patients reporting a prosthetic valve thrombosis at 2 years in our study either initiated or changed anticoagulation therapy and had a regression and good prosthesis function as showed by the decreased mean pressure gradient at the follow-up echocardiography. For 1 patient, the valve thrombosis was reverted despite the absence of anticoagulant therapy. Therefore, the presence of the valve thrombosis was mostly sublinical and did not lead to detrimental clinical consquences after SAVR using a biosprosthetic valve.

DISCUSSION

Key findings of this propensity-score matched study on 2-year data from INDURE and IMPACT registries were: 1) Females exhibited higher surgical risk (EuroSCORE II and STS score), had higher symptomatic burden (NYHA class III/IV and angina CCS III/IV) than males with similar comorbidity prevalence; 2) Females received smaller valves than males with a median diameter of 23 mm compared to 25 mm in males; 3) Both male and female patients experienced similar hospital LoS and ICU stay after SAVR; 4) Patients demonstrated comparable outcomes at 2 years after SAVR, suggesting that sex-related differences observed at baseline did not impact clinical outcomes.

In the overall population (n=993), the proportion of female patients undergoing SAVR from 2019 to 2021 was lower compared to male patients (258 [26.0%] vs 735 [74.0%]). This disparity suggests a lower incidence of SAVR in females than males, consistent with findings reported in prior literature [2, 3, 7]. Despite a similar AS prevalence in AS [13], the specific factors contributing to the lower rate of SAVR in women remain unclear. Several studies have proposed potential explanations, such as the insidious onset of the disease in females, delayed diagnosis, conservative management, less frequent referrals to specialists, and fewer diagnostic tests conducted among women [2, 14, 15]. However, it is important to note that our study did not focus on the male-female disparity in the incidence of SAVR, the time that elapsed between diagnosis and intervention or the urgency of SAVR, which represents a limitation of our findings.

Several previously published studies [2, 9, 16-18] have investigated sex-related differences in patients undergoing SAVR. These studies consistently report that females undergoing SAVR tend to be older, exhibit advanced NYHA symptoms and angina symptoms, and have higher surgical risks compared to males. Our study aligns with these findings, as females exhibited significantly higher EuroSCORE II and STS scores in both cohorts ($p<0.001$), indicating a greater surgical risk profile in females. Nevertheless, there was no significant difference in age between males and females in our study, and

they were younger (both sexes) than the population studied earlier [15, 17, 18]. Furthermore, in our cohort, females showed advanced NYHA class III/IV and angina CCS III/IV symptoms than males ($p<0.001$), indicating a heightened cardiac risk and symptomatic burden than male patients and this trend was consistent with the observations of previous studies [9, 17, 18]. Contrary to the lower comorbidity prevalence observed among female patients undergoing SAVR in the PARTNER trial [15] and the study by Triboulloy et al. [17], our study did not reveal significant differences between males and females. Nonetheless, our study did note a higher prevalence of previous MI among males, aligning with the findings of Hernandez-Vaquero et al. [16] and Tribouilloy et al. [17].

Notably, a significant difference was observed in implanted valve size between the sexes, with females being implanted with smaller valves than males (median diameter 23 vs 25 mm; $p<0.001$). This is attributed to anatomical differences, with women typically having smaller hearts and aortic annuli [19] than men. Consequently, the need for smaller aortic bioprosthesis in women has been recognized in previous research and is associated with increased risk in SAVR [20]. Therefore, it underscores the importance of selecting valve size based on precise in vivo measurements of the patient's specific annular dimensions.

Despite significant differences in baseline characteristics, indicating a high surgical risk among females in our study, the 2-year outcomes after SAVR revealed comparable outcomes in both sexes. However, existing literature shows varied findings. For instance, a study by Kulik et al. comparing long-term outcomes of SAVR over 5.6 years reported a significantly lower reoperation rate in women (comorbidity-adjusted hazard ratio (HR) 0.4; 95% CI: 0.2 to 0.9) and a higher incidence of late stroke (HR 1.7; 95% CI: 1.1 to 2.7) compared to men, indicating sex-related differences in long-term SAVR outcomes exists [21]. Despite these discrepancies, women exhibited better overall long-term survival than men in their study. Similarly, findings from the Simvastatin Ezetimibe in Aortic Stenosis (SEAS) study, with a median follow-up of 4 years, revealed that females exhibited lower total mortality and a reduced rate of ischemic cardiovascular events compared to men, independent of confounding factors, despite similar AS progression and more severity in females based on echocardiographic

indices [22]. On the other hand, another baseline-matched retrospective study reported comparable long-term survival benefits in females at a 5-year follow-up. However, men faced a higher risk of bleeding, endocarditis, and early reoperation after SAVR [9]. Thus, collectively, these studies suggest that female sex does not significantly impact the long-term survival of SAVR when preoperative characteristics are adjusted between both sexes.

Limitations

Our study did not capture data on matching-based postoperative ventricular remodelling and prosthetic valve performance following surgery, which could elucidate casual factors impacting the outcome for males and females. Additionally, we did not gather information on the timing of intervention and the urgency of SAVR. Furthermore, our study lacks data on prosthetic-patient mismatch, a common complication of cardiac surgery [23].

CONCLUSION

Women undergo SAVR less frequently and exhibit a higher risk profile, posing unique challenges for cardiac surgery. Nevertheless, our analysis reveals that the 2-year clinical outcomes of SAVR are similar between sexes when baseline characteristics are matched. These findings highlight the importance of considering sex-related factors in evaluating surgical risk and treatment strategies for SAVR patients.

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COMPETING INTERESTS

AZ, RdP, FB, TB, NB, MB, JS, PBr, and BM have received lecture fees and/or research support from Edwards Lifesciences. RF, AL and AV have received lecture fees/proctoring fees from Edwards Lifesciences. BB received research support from Edwards Lifesciences for their institution. The institutions of all authors representing study centers have received patient inclusion-based funding and have no conflict of interest to disclose.

AUTHOR'S CONTRIBUTIONS

AZ, RdP, FB, TB, AESA, MB, BB, PBr and BM were involved in the conception, design, data acquisition and interpretation of the study. PB and BB drafted the manuscript and all other authors revised the article for important intellectual content. All authors gave approval of the final version and submission of the manuscript.

AVAILABILITY OF DATA AND MATERIALS

The datasets generated and analyzed during the current study may be available from the corresponding author upon reasonable request.

ETHICAL APPROVAL/PATIENT CONSENT

The study was approved by the institutional review board/ethics committee at each participating centre and a written informed consent was obtained from every patient before enrolment.

Figure Titles/Legends:

Figure 1: Study flowchart

Legends: CABG, coronary artery bypass graft; PS, propensity score; SAVR, surgical aortic valve replacement

*Reasons: Not meeting inclusion/exclusion criteria (n=9); Not receiving INSPIRIS Resilia valve (n=10); Double valve procedure (replacement or repair; n=10), Withdrew from the study (n=2)

Figure 2: Kaplan-Meier survival curve at 2-year all-cause mortality stratified by sex – PS-matched cohort

Legend: PS, propensity score

Table 1: Patient characteristics

	Full cohort					**PS matched cohort**				
Mean±SD or median (IQR) or n (%)	Male, N=735	Female, N=258	SMD	95% CI	p-value	Male, N=433	Female, N=243	SMD	95% CI	p-value
Age, years	58.8±9.2	59.8±9.5	-0.11	-0.25, 0.03	0.159	59.0±9.7	59.8±9.5	-0.09	-0.24, 0.07	0.430
Body mass index, kg/m^2	28.0 (25.2-31.0)	27.1 (23.4-31.0)	0.11	-0.03, 0.25	0.008	27.1 (24.7-30.2)	27.3 (23.5-31.3)	-0.05	-0.20, 0.11	0.601
Valve morphology			0.15	0.01, 0.29	0.036			0.04	-0.12, 0.19	0.647
Bicuspid	434 (59)	133 (52)				236 (55)	128 (53)			
Tricuspid	301 (41)	125 (48)				197 (45)	115 (47)			
NYHA class III/IV	220 (30)	121 (47)	0.36	0.22, 0.50	<0.001	169 (39)	110 (45)	0.13	-0.03, 0.28	0.114
Angina CCS III/IV	32 (4.4)	21 (8.2)	0.16	0.02, 0.30	0.019	22 (5.1)	17 (7.0)	0.08	-0.08, 0.24	0.306
EuroSCORE II, %	1.8±2.0	2.3±3.1	-0.18	-0.32, -0.04	<0.001	1.6±1.7	2.4±3.0	-0.18	-0.32, -0.04	<0.001
STS score, %	0.9±2.5	1.6±2.2	-0.31	-0.46, -0.17	<0.001	1.0±2.3	1.7±2.0	-0.33	-0.48, -0.17	<0.001
Medical history										
Diabetes mellitus	115 (16)	45 (17)	0.05	-0.09, 0.19	0.500	73 (17)	42 (17)	0.01	-0.15, 0.17	0.888
Systemic hypertension	438 (60)	148 (57)	0.05	-0.10, 0.19	0.531	243 (56)	138 (57)	0.01	-0.14, 0.17	0.866
Coronary artery disease	504 (69)	192 (75)	0.14	-0.01, 0.28	0.068	313 (72)	180 (74)	0.04	-0.12, 0.20	0.616
Myocardial infarction	38 (5.2)	5 (1.9)	0.18	0.03, 0.32	0.028	11 (2.5)	5 (2.1)	0.03	-0.12, 0.19	0.692
Peripheral vascular disease	43 (5.9)	11 (4.3)	0.07	-0.07, 0.21	0.334	21 (4.8)	11 (4.5)	0.02	-0.14, 0.17	0.849
TIA/stroke	36 (4.9)	13 (5.0)	0.01	-0.14, 0.15	0.928	19 (4.4)	11 (4.5)	0.01	-0.15, 0.16	0.933
COPD	52 (7.1)	27 (10)	0.12	-0.02, 0.26	0.083	35 (8.1)	22 (9.1)	0.03	-0.12, 0.19	0.663
PPI	13 (1.8)	4 (1.6)	0.02	-0.12, 0.16	1.000	8 (1.8)	4 (1.6)	0.02	-0.14, 0.17	1.000
Previous PCI	78 (11)	19 (7.4)	0.11	-0.03, 0.26	0.131	35 (8.1)	19 (7.8)	0.01	-0.15, 0.17	0.903
Dialysis	8 (1.1)	2 (0.8)	0.03	-0.11, 0.17	1.000	5 (1.2)	2 (0.8)	0.03	-0.12, 0.19	1.000

Echocardiography										
AV regurgitation (moderate/severe)	255 (35)	68 (27)	0.18	0.04, 0.32	0.015	128 (30)	66 (27)	0.05	-0.10, 0.21	0.508
LVEF, %	58±10	60±10	-0.28	-0.43, -0.14	<0.001	60±9	60±10	-0.04	-0.20, 0.12	0.464
Mean transvalvular pressure gradient, mmHg	43±20	46±21	-0.16	-0.30, -0.01	0.249	45±18	46±21	-0.05	-0.21, 0.12	0.690

Legend: AV, aortic valve; CCS, Canadian Cardiovascular Society; EuroSCORE, European System for Cardiac Operative Risk Evaluation; CI; confidence interval;COPD, chronic obstructive pulmonary disease; IQR, interquartile range; LVEF, left ventricular ejection fraction; PCI, percutaneous intervention; PPI, permanent pacemaker implantation; PS, propensity score; SMD, standard mean difference; STS, Society of Thoracic Surgeons; TIA, transient ischaemic attack

Table 2: Procedural details – PS-matched cohort

Mean±SD or median (IQR) or n (%)	Male, N=433	Female, N=243	p-value
Etiology of valve pathology			0.769
Congenital	239 (55.3)	128 (52.7)	
Degenerative	183 (42.4)	106 (43.6)	
Endocarditic	1 (0.2)	1 (0.4)	
Rheumatic	2 (0.5)	2 (0.8)	
None (no aortic stenosis)	7 (1.6)	6 (2.5)	
Isolated AVR	259 (59.8)	149 (61.3)	0.702
MIS	178 (41.1)	114 (46.9)	0.144
Concomitant procedures			
CABG	67 (15.5)	27 (11.1)	0.116
Root replacement	31 (7.2)	11 (4.5)	0.174
Supracoronary tube graft	58 (13.4)	31 (12.8)	0.814
Total operation time (skin-to-skin),	198.3±62.9	191.1±59.0	0.170
min	190.0 (155.0, 233.5)	184.5 (148.0, 224.0)	
Cross-clamp time, min	75.0±26.8	71.7±26.3	0.111
	70.0 (56.0, 92.0)	68.0 (54.0, 88.0)	
Cardiopulmonary bypass time, min	103.9±39.3	102.1±38.1	0.542
	98.0 (76.0, 126.0)	94.0 (77.0, 121.0)	
Final valve size, mm	25.0 (23.0, 25.0)	23.0 (21.0, 23.0)	<0.001
	24.7±2.1	22.3±1.5	
19	0 (0.0)	8 (3.3)	
21	32 (7.4)	97 (39.9)	
23	133 (30.7)	108 (44.4)	
25	161 (37.2)	27 (11.1)	
27	75 (17.3)	3 (1.2)	
29	32 (7.4)	0 (0.0)	
Implantation details			
1st implantation success	432 (99.8)	242 (99.6)	1.000
2nd implantation with INSPIRIS	1 (0.2)	1 (0.4)	1.000
Resilia			
Paravalvular leak (final)	5 (1.2)	1 (0.4)	0.427
Intraprocedural mortality	0 (0.0)	0 (0.0)	1.000

Legend: CABG; coronary artery bypass graft; IQR, interquartile range; MIS, minimally invasive surgery; PS, propensity score; SD, standard deviation

Table 3: Discharge details – PS-matched cohort

Mean±SD or Median (IQR) or n (%)	Male, N=433[1]	Female, N=243	p-value
Hospital stay, days	9.0±4.5 8.0 (6.0, 10.0)	9.9±6.5 8.0 (7.0, 11.5)	0.144
Discharged alive	428 (99.3)	242 (99.6)	1.000
Discharge to			0.428
Home	257 (59.6)	151 (62.1)	
Other hospital	33 (7.7)	25 (10.3)	
Rehabilitation unit	135 (31.3)	66 (27.2)	
Other	3 (0.7)	0 (0.0)	
Death	3 (0.7)	1 (0.4)	
ICU stay, hours	46.4±54.7 24.0 (21.0, 48.0)	52.0±59.0 25.0 (22.0, 62.0)	0.449
Mechanical ventilation, hours	11.9±39.5 7.0 (4.0, 10.0)	10.1±15.0 7.0 (5.0, 10.0)	0.609

Legends: ICU; intensive care unit; IQR, interquartile range; LoS, length of stay; PS, propensity score; SD, standard deviation

Table 4: Two-year clinical outcomes – PS-matched cohort

n (%)	Early (≤30 days)		Late (>30 days to 2 year)		Freedom from events at 2 years %(95%CI)		
	Male, N=433	Female, N=243	Male, 732 vy	Female, 400 vy	Male	Female	p-value
All-cause mortality	5 (1.2)	1 (0.4)	10 (1.4)	7 (1.8)	96.2 (94.3, 98.1)	96.3 (93.9, 98.9)	0.920
Cardiovascular-related	5 (1.2)	1 (0.4)	7 (1.0)	3 (0.8)	97.0 (95.4, 98.7)	98.1 (96.3, 100.0)	0.365
Valve-related	2 (0.5)	0 (0)	5 (0.7)	2 (0.5)	98.3 (97.0, 99.6)	98.9 (97.5, 100.0)	0.394
Valve-related - Unknown	1 (0.2)	0 (0)	2 (0.3)	4 (1.0)	99.1 (98.2, 100.0)	98.1 (96.2, 100.0)	0.233
Prosthesis endocarditis	0 (0)	0 (0)	4 (0.5)	2 (0.5)	99.0 (98.0, 100.0)	99.0 (97.5, 100.0)	0.909
Thromboembolic events	11 (2.5)	4 (1.6)	4 (0.5)	4 (1.0)	95.9 (93.8, 97.9)	95.8 (93.0, 98.7)	0.967
Stroke	7 (1.6)	4 (1.6)	0 (0)	1 (0.3)	98.1 (96.7, 99.5)	97.4 (95.2, 99.7)	0.594
Valve thrombosis	0 (0)	0 (0)	3 (0.4)	5 (1.3)	99.7 (99.1, 100.0)	98.0 (96.0, 100.0)	0.093
Valve-related dysfunction	1 (0.2)	0 (0)	3 (0.4)	5 (1.3)	99.5 (98.8, 100.0)	98.6 (97.1, 100.0)	0.196
Repeated procedure	1 (0.2)	0 (0)	0 (0)	3 (0.8)	99.8 (99.3, 100.0)	99.0 (97.5, 100.0)	0.096
Permanent pacemaker	18 (4.2)	9 (3.7)	2 (0.3)	2 (0.5)	95.2 (93.2, 97.3)	95.4 (92.7, 98.1)	0.944
Valve-related bleeding	43 (9.9)	29 (11.9)	2 (0.3)	3 (0.8)	89.5 (86.7, 92.5)	86.6 (82.4, 91.1)	0.282

Legends: CI, confidence interval; vy, valve years

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