Research Square

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Sex-related difference in outcomes of patients undergoing Aortic Valve Neocuspidization: A Propensity Score Matched Analysis of Immediate and Mid-Term Results

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Abstract

OBJECTIVES:

To evaluate the potential of Aortic Valve Neocuspidization (AVNeo) in reducing the gender-related gap in postoperative outcomes between female and male patients undergoing standard Surgical Aortic Valve Replacement (SAVR).

METHODS:

From December 2016 to December 2023, 155 patients received AVNeo at the Heart Institute. To assess the impact of gender on outcomes, the preoperative baseline characteristics of female and male patients were balanced using 1:1 Propensity Score Matching.

RESULTS:

Forty-seven female-male patient pairs with identical baseline characteristics were included in the analysis. The Aortic Annulus was smaller in the female group (19.59 ± 4.09 vs 21.70 ± 4.94 mm, ρ = 0.027). Aortic Valve pathology was similar (ρ = 0.404), with aortic stenosis being the main indication for surgery. There were no differences between the groups in the main perioperative characteristics, ICU, and postoperative course parameters. In-hospital mortality was 2 (4%) in the female group and 1 (2%) in the male group (ρ = 1.000). Echocardiographic data, including transvalvular gradients, the incidence of Postprocedural Aortic Stenosis, and Aortic Insufficiency, were similar. Follow-up durations were 68.84 ± 25.19 and 63.00 ± 23.67 months for the female and male subgroups, respectively. The freedom-from-reoperation (ρ = 1.000) was similar. Mortality during follow-up was numerically lower in the female group (2 (5%) vs 7 (15%)), though it did not reach statistical significance (ρ = 0.157).

CONCLUSIONS:

Immediate and midterm AVNeo outcomes showed similar perioperative, echocardiographic, and mid-term outcomes for both females and males. This suggests that neocuspidization reduces gender-related risks described for standard BioSAVR. AVNeo can be performed safely and effectively on both sexes.

INTRODUCTION

Surgical Aortic Valve Replacement (SAVR) is a reliable and straightforward option for treating significant aortic valve (AV) disease. It offers excellent immediate hemodynamic results and favorable long-term outcomes. Nonetheless, SAVR has known drawbacks, including side effects from long-term anticoagulation with mechanical valves and the structural deterioration of biological valves. Postoperative complications such as prosthesis-patient mismatch (PPM), paravalvular leak (PVL), prosthetic valve endocarditis (PVE), and serious arrhythmias requiring a permanent pacemaker implantation (PPI) can negatively impact patient

outcomes [1]. The significant incidence of these complications highlights the importance of developing new techniques and assessing their potential to address these ongoing challenges.

Sex-related differences in preoperative patient characteristics and postoperative outcomes after surgical treatment of AV pathology remain debated. Advanced age at the time of the operation, greater frailty, and a higher burden of comorbidities contribute to the elevated complexity of AV surgery in women [2, 3]. Specific anatomical characteristics of the female heart, such as the smaller size of the Left Ventricle Outflow Tract (LVOT), Aortic Annulus (AA), AV, and Aortic Root, make surgery technically more demanding [4]. This anatomical characteristic has been associated with higher postoperative transvalvular gradients, increased risk of prosthesis-patients mismatch (PPM), incomplete regression of left ventricular hypertrophy, persistent heart failure symptoms, and less favorable functional recovery [5, 6, 7, 8, 9]. There is evidence from the literature of a more complicated postoperative course in women than in men [2, 5, 6]. Several studies have documented that female patients often experience undertreatment or receive substandard care [5, 7, 8, 9].

Aortic Valve Neocuspidization (AVNeo) is a reconstructive technique in which the native valve is replaced with individually tailored autologous or xenopericardial leaflets without implantation of a prosthetic stented valve. By preserving the native aortic root geometry and avoiding a rigid prosthetic frame, AVNeo has the potential to maintain near-physiological valve hemodynamics while minimizing the risk of PPM. Previous studies have consistently demonstrated excellent early and mid-term clinical and echocardiographic outcomes following AVNeo [10–12]. However, evidence comparing outcomes between female and male patients undergoing AVNeo remains limited and the weight of sex on AVNeo outcomes is uncertain.

The objective of this research was to compare baseline characteristics, periprocedural outcomes, and mid-term follow-up results between female and male patients who underwent AVNeo. Our aim was to determine whether neocuspidization can help reduce the gender-related gap in postoperative outcomes described for standard BioSAVR.

PATIENTS AND METHODS

To comprehensively evaluate immediate and midterm AVNeo outcomes, our institution conducted a retrospective single-center study. The cohort included all adult patients who underwent AVNeo at our clinic between December 2016 and December 2023. Exclusion criteria were pediatric patients, emergency and redo cases, Infective Endocarditis (IE), and surgeries involving the ascending aorta and aortic root. The control group comprised patients who received SAVR with a biological valve (BioSAVR) during the same period [12].

As a sub-study of this research, we evaluated sex-related differences in outcomes between female and male AVNeo patients. The Clinical and Research Ethics Committee of the Heart Institute approved the Protocol of this clinical study (Protocol No.4/2: 21 October 2024). To improve cohort comparability and assess the impact of gender on AVNeo outcomes, preoperative/baseline characteristics were balanced using 1:1 Propensity Score Matching (PSM).

The primary outcomes included perioperative details, transvalvular hemodynamic parameters, all-cause mortality, and rates of major cardiac and other events during the 30-day in-hospital period. Secondary

outcomes comprised the incidence of aortic stenosis or regurgitation, valve-related adverse events, reoperations due to AVNeo failure, and mortality during follow-up.

SURGICAL TECHNIQUE

The standard AVNeo technique was used in most surgeries. Patients who underwent an operation using the CT-guided AVNeo method were also included in the study group. Technical details of these methods were previously documented [13, 14].

All patients were discharged on warfarin for a month, unless their pathology suggested otherwise. Then, they received low-dose aspirin for six months.

Patients underwent pre-discharge transthoracic echocardiography (TTE). Their clinical and instrumental follow-up, including TTE and ECG, was conducted at the outpatient Department of the Heart Institute or at a referral hospital at 6 and 12 months after discharge, and then annually. Most patients also participated in annual assessments by the Medical Sanitary Expert Commission to evaluate the need for government support. Furthermore, their clinical and psychoemotional conditions were monitored through phone interviews.

PROPENSITY-SCORE MATCHED ANALYSIS

Propensity score matching was performed to minimize differences in baseline clinical characteristics between female and male patients and to reduce potential confounding when comparing perioperative and mid-term outcomes after AVNeo. Anatomical characteristics were not included in the matching model to preserve inherent sex-related anatomical differences.

Propensity scores were estimated using logistic regression, with sex (female vs male) as the dependent variable. The matching model included age, hematocrit, creatinine clearance, left ventricular ejection fraction (LVEF), and concomitant procedures, including coronary artery bypass grafting (CABG), mitral valve surgery, and tricuspid valve surgery.

Patients were matched in a 1:1 ratio using nearest-neighbor matching without replacement and a caliper of 0.1. Patients for whom an appropriate match within the specified caliper could not be identified were excluded from the matched cohort.

Covariate balance before and after matching was evaluated using standardized mean differences (SMDs). An absolute SMD < 0.1 was considered indicative of adequate balance. The improvement in covariate balance after matching was additionally assessed graphically using a Love plot. All subsequent comparisons of perioperative and mid-term outcomes were performed in the propensity-score matched cohort.

STATISTICAL ANALYSIS

Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as absolute numbers and percentages. The distribution of continuous variables was assessed for

normality before statistical comparison. Normally distributed continuous variables were compared using Student's t-test, while non-normally distributed variables were analyzed using the Mann–Whitney U test. Categorical variables were compared using the Pearson chi-square test or Fisher's exact test, as appropriate.

For paired comparisons of echocardiographic parameters between the immediate postoperative period and mid-term follow-up, continuous variables were analyzed using the paired Student's t-test or Wilcoxon signed-rank test, depending on data distribution. McNemar's test was used for paired categorical variables.

Time-to-event outcomes, including overall survival, freedom from more than mild aortic regurgitation, freedom from more than mild postprocedural aortic stenosis, and freedom from reoperation, were analyzed using the Kaplan–Meier method. Differences between female and male groups were assessed using the log-rank test. Hazard ratios (HRs) with corresponding 95% confidence intervals (CIs) were estimated using Cox proportional hazards regression. Patients lost to follow-up were censored at the date of their last known clinical contact.

All statistical tests were two-sided, and a p-value < 0.05 was considered statistically significant. Statistical analyses were performed in R (R Foundation for Statistical Computing, Vienna, Austria) using the packages MatchIt, cobalt, dplyr, survival, and survminer.

IMMEDIATE RESULTS

During the study period, 155 consecutive patients underwent AVNeo at the Heart Institute. After 1:1 propensity-score matching, 47 female-male patient pairs were formed for analysis (Fig. 1). A Love-plot demonstrates the effectiveness of propensity-score matching (Fig. 2).

Both female and male groups were identical with respect to demographic and preoperative clinical characteristics, except that anthropometric indicators were, as expected, lower among women (Table 1). However, the groups did not differ in BMI ($\rho = 0.723$). The indications for surgery were similar ($\rho = 0.404$), with Aortic Stenosis (AS) being the main diagnosis (31 (66%) vs 26 (55%)), followed by Aortic Regurgitation (AR) (4 (9%) vs 8 (17%)) and combined AV pathology (12 (26%) vs 13 (28%)). Heart failure, NYHA Class III-IV, was diagnosed in 42 (89%) of women and 39 (83%) of men ($\rho = 0.671$).

Table 1
Baseline patients' characteristics

Variable	AVNeo Group f = 80	AVNeo Group m = 75	ρ-value	AVNeo Group f = 47	AVNeo Group m = 47	ρ-value
Age, y	65.41 ± 13.23	65.59 ± 13.25	0.932	64.32 ± 14.84	66.43 ± 13.64	0.476
Height, cm	163.77 ± 6.99	176.40 ± 7.77	0.000	163.43 ± 7.01	177.36 ± 7.43	0.000
Weight, kg	75.68 ± 15.58	85.97 ± 15.89	0.000	72.85 ± 14.00	87.15 ± 15.84	0.000
Body Mass Index (kg/m^2)	28.13 ± 5.20	27.49 ± 4.18	0.400	27.21 ± 4.77	27.53 ± 3.82	0.723
Body Surface Area (m^2)	1.85 ± 0.21	2.05 ± 0.23	0.000	1.81 ± 0.20	2.07 ± 0.23	0.000
Aortic valve stenosis, n(%)	56 (70%);	46 (61%);	0.066	31 (66%);	26 (55%)	0.404
Aortic valve regurgitation, n(%)	5 (6%);	14 (19%);		4 (9%)	8 (17%)	
Combined aortic valve pathology, n(%)	19 (24%)	15 (20%)		12 (26%)	13 (28%)	
Aortic annulus, mm	19.56 ± 3.94	21.88 ± 4.85	0.001	19.59 ± 4.09	21.70 ± 4.94	0.027
Aortic root, mm	29.82 ± 5.56	37.93 ± 40.92	0.093	30.36 ± 5.59	40.95 ± 51.11	0.165
Ascending aorta, mm	33.22 ± 6.78	34.07 ± 10.44	0.555	33.41 ± 6.91	33.18 ± 10.16	0.898
Aortic arch, mm	31.18 ± 3.64	33.88 ± 4.22	0.058	30.45 ± 3.96	33.09 ± 3.81	0.127
Peak preassure gradient, mmHG	92.58 ± 31.01	78.39 ± 32.96	0.007	87.74 ± 34.61	78.62 ± 37.00	0.220
Mean preassure gradient, mmHG	57.21 ± 20.21	51.12 ± 16.12	0.050	54.62 ± 23.10	52.62 ± 16.99	0.654
Velocity time integral, cm2	0.73 ± 0.18	0.71 ± 0.16	0.764	0.76 ± 0.18	0.76 ± 0.17	0.951
Pulmonary artery preassure, mmHG	39.01 ± 14.94	44.76 ± 19.86	0.059	38.20 ± 16.15	41.50 ± 21.37	0.434
End-systolic volume, ml	39.91 ± 19.05	71.21 ± 40.82	0.000	43.20 ± 22.82	59.31 ± 29.20	0.005

AVNeo – aortic valve neocuspidization, NYHA - New York Heart Association Functional Classification

Variable	AVNeo Group f = 80	AVNeo Group m = 75	ρ-value	AVNeo Group f = 47	AVNeo Group m = 47	ρ-value
End-diastolic volume, ml	100.03 ± 27.75	142.04 ± 49.94	0.000	102.66 ± 27.15	133.70 ± 47.13	0.000
End-diastolic index, ml/m2	53.25 ± 8.98	80.57 ± 29.53	0.002	58.33 ± 5.94	72.76 ± 27.41	0.102
Left Ventricle Ejection Fraction, %	60.48 ± 8.00	53.89 ± 13.07	0.000	58.91 ± 9.34	58.51 ± 9.80	0.838
NYHA III-IV class, n(%)	67 (84%)	63 (88%)	0.377	42 (89%)	39 (83%)	0.671
Arterial hypertension, n(%)	61 (76%)	53 (71%)	0.303	38 (81%)	33 (70%)	0.337
Diabetis, n(%)	19 (24%)	18 (24%)	1.000	13 (28%)	11 (23%)	0.813
Thyroid diseases, n(%)	6 (8%)	4 (5%)	0.746	2 (4%)	3 (6%)	1.000
Chronic kidney disease, n(%)	2 (3%)	3 (4%)	0.672	0 (0%)	1 (15%)	1.000
Hepatic disease, n(%)	0 (0%)	1 (1%)	0.493	0 (0%)	1 (2%)	1.000
Atrial fibrillation, n(%)	9 (11%)	15 (20%)	0.237	5 (11%)	10 (21%)	0.260
Lung disease, n(%)	2 (3%)	4 (5%)	0.439	1 (2%)	3 (6%)	0.617
Neurological events, n(%)	7 (9%)	9 (12%)	0.749	3 (6%)	5 (11%)	0.714
Peptic ulcer, n(%)	0 (0%)	1 (1%)	0.493	0	0	1.000
AVNeo – aortic valve neocuspidization, NYHA - New York Heart Association Functional Classification						

Preoperative transthoracic echocardiography (TTE) revealed that female patients had smaller Aortic Annuli (19.59 ± 4.09 vs 21.70 ± 4.94 mm, ρ = 0.027). Left ventricle (LV) end-systolic and end-diastolic volumes were also smaller, as expected, in the female group (ρ = 0.005 and ρ < 0.001, respectively). However, LV end-diastolic index was similar in both cohorts (ρ = 0.102) (Table 1).

AVNeo with a trileaflet valve was feasible in all cases. Glutaraldehyde-treated autologous pericardium (GTAP) was used for reconstruction in 92 (97.8%) cases. In two patients (one man and one woman), bovine xenopericardium was used for valve reconstruction because their autopericardium was either too thin (female patient) or was thickened and fibrotic due to prior pericarditis (male patient).

Intraoperative transesophageal echocardiography (TEE) demonstrated good neovalve function in all procedures. There was no need for repeat cross-clamping to correct neovalve dysfunction or to convert to valve replacement with a prosthesis.

Table 2 presents the perioperative course parameters. The incidence of combined operations was identical between cohorts: 17 (36%) in women and 19 (40%) in men (ρ = 0.832). Mean bypass and cross-clamp times

were similar (122.59 ± 30.95 vs. 133.84 ± 38.65 min, ρ = 0.128, and 94.74 ± 26.40 vs. 102.36 ± 31.63, ρ = 0.215, respectively).

Table 2
Perioperative data

Variable	AVNeo Group f = 47	AVNeo Group m = 47	ρ-value
Mean bypass time, hrs	122.59 ± 30.95	133.84 ± 38.65	0.128
Mean cross-clamp time, hrs	94.74 ± 26.40	102.36 ± 31.63	0.215
Mean ICU stay, days	4.39 ± 5.77	3.60 ± 3.20	0.415
Mean postoperative hospital stay, days	8.17 ± 1.90	8.17 ± 1.65	1.000
Concomitant procedures, n(%)	17 (36%)	19 (40%)	0.832
• CABG	13 (28%)	14 (30%)	1.000
• Mitral valve procedure	2 (4%)	0: 4 (9%)	0.677
• Tricuspid valve procedure	2 (4%)	1 (2%)	1.000
Postoperative complete AV blockage, n(%)	1 (2%)	0 (0%)	1.000
Postoperative AF, n(%)	2 (4%)	6 (13%)	0.267
Permanent pacemaker implantation, n(%)	0 (0%)	0 (0%)	1.000
Postoperative neurological events, n(%)	1 (2%)	2 (4%)	1.000
Renal failure, n(%)	2 (4%)	1 (2%)	1.000
Dyalisis, n(%)	1 (2%)	1 (2%)	1.000
Gastro-intestinal complications, n(%)	0(%)	0(%)	1.000
Pulmonary complications, n(%)	1 (2%)	0 (0%)	1.000
Rethoracotomy, n(%)	2 (4%)	0 (0%)	0.495
Prolonged ventilation time, n(%)	1 (2%)	1 (2%)	1.000
Tracheostomy, n(%)	0 (0%)	1 (2%)	1.000
Wound infection, n(%)	0(%)	0(%)	1.000
Myocardial infarction, n(%)	0(%)	0(%)	1.000
Heart failure, n(%)	0(%)	0(%)	1.000
30 day hospital readmission, n(%)	0(%)	0(%)	1.000
Infective endocarditis, n(%)	0 (0%)	1 (2%)	1.000

AVNeo – aortic valve neocuspidization, ICU – intensive care unit, CABG – coronary artery bypass grafting, AV – aortic valve, AF – atrial fibrillation

Variable	AVNeo Group f = 47	AVNeo Group m = 47	ρ-value
In-hospital mortality	2 (4%)	1 (2%)	1.000
Mean follow-up, month	68.84 ± 25.19	63.00 ± 23.67	0.266
Mortality during follow-up	2 (5%)	7 (15%)	0.157
Reoperations in follow-up	0 (0%)	1 (2%)	1.000
AVNeo – aortic valve neocuspidization, ICU – intensive care unit, CABG – coronary artery bypass grafting, AV – aortic valve, AF – atrial fibrillation			

In-hospital 30-day mortality was 4.0% (2 patients) in the female group and 2% (1 patient) in the male group (ρ = 1.000). Female patients died due to acute renal insufficiency and ischemic stroke. The male patient succumbed to COVID-19 pneumonia, complicated by sepsis.

There were no statistically significant differences between groups in any postoperative course parameter (Table 2). Mean ICU length of stay (ρ = 0.415) and postoperative hospital stay (ρ = 1.000) were similar.

Table 3 summarizes the echocardiography data obtained before discharge and during follow-up. In-hospital TTE did not reveal any differences in AVNeo valve function between female and male groups. Most patients in both cohorts left the hospital with no or trivial AR (40 (85%) females, 39 (85%) males; $\rho^1 = 1.000$). The incidence of mild AR was also similar (7 (15%) females, 8 (17%) males, $\rho^1 = 1.000$). No patients had moderate or severe AR. Predischarge TTE did not reveal any patient with postprocedural aortic stenosis (PPAS) or dehiscence of the neovalve suture line in any group. Average peak and mean pressure gradients were also comparable between women and men ($\rho^1 = 0.376$ and $\rho^1 = 0.186$, respectively).

Table 3
Echocardiographic findings at discharge and during follow-up

Characteristic	Immediate postoperative results		ρ-value[1]	Midterm follow-up		ρ-value[2]	ρ-value[3]	ρ-value[4]
	AVNeo f = 47	AVNeo m = 47		AVNeo f = 37	AVNeo m = 39			
AR none/ trivial	40 (85%)	39 (83%)	1.000	30 (81%)	28 (72%)	0.500	0.366	0.277
AR mild	7 (15%)	8 (17%)		5 (14%)	9 (23%)			
AR moderate	0	0		2 (5%)	1 (3%)			
AR severe	0	0		0 (0%)	1 (3%)			
PPAS none/ trivial	47(100%)	47(100%)	1.000	36 (97%)	38 (97%)	1.000	1.000	1.000
PPAS mild	0	0		0 (0%)	0(0%)			
PPAS moderate	0	0		1 (3%)	1 (3%)			
PPAS severe	0	0		0	0			
PVL none	47(100%)	47(100%)	-	37(100%)	39(100%)	1.000	1.000	1.000
PVL mild	0	0		0	0			
PVL mild-to-moderate	0	0		0	0			
PVL moderate	0	0		0	0			
PVL severe	0	0		0	0			
Average peak pressure gradient	15.81 ± 4.95	14.72 ± 6.72	0.376	14.89 ± 6.91	13.62 ± 11.82	0.565	0.489	0.608
Average mean pressure gradient	7.96 ± 3.23	7.07 ± 3.17	0.186	8.43 ± 3.71	7.77 ± 6.24	0.573	0.537	0.528

Characteristic	Immediate postoperative results		ρ-value[1]	Midterm follow-up		ρ-value[2]	ρ-value[3]	ρ-value[4]
	AVNeo f = 47	AVNeo m = 47		AVNeo f = 37	AVNeo m = 39			
ρ-value[1] – comparison between the AVNeo female and male groups in the immediate postoperative period.								
ρ-value[2] – comparison between the AVNeo female and male groups at follow-up								
ρ-value[3] – comparison within the AVNeo female group between the immediate postoperative and follow-up data								
ρ-value[4] – comparison within the AVNeo male group between the immediate postoperative and follow-up data								
AVNeo – aortic valve neocuspidization, AR – aortic regurgitation, PPAS – post procedural aortic stenosis, PVL – paravalvular leak								

FOLLOW-UP RESULTS

The mean follow-up duration was 68.84 ± 25.19 and 63.00 ± 23.67 months for the female and male groups, respectively (p = 0.266). Ten female and eight male patients were lost to follow-up due to emigration as war refugees. Overall, follow-up was 81% complete. There were two deaths (4.0%) in the female group: one cardiovascular (cardiac arrest) and one non-cardiovascular (cancer). In the male group, there were 7 deaths (15%), including one cardiovascular (cardiac arrest) and six non-cardiovascular (cancer 1, pneumonia 1, COVID-19 2, unknown 2). The difference in mortality did not reach statistical significance (p = 0.157). Survival probability was 95.7% in the female group and 85.1% in the male group (p = 0.103) (Fig. 3).

TTE showed stable diastolic valve function in the female and male groups ($\rho^2 = 0.500$). Most patients still had none/trivial or mild AR. Among female patients, 2 (5%) had moderate AR, and none had severe AR, compared with 1 (3%) and 1 (3%) in the male group, respectively ($\rho^2 = 0.500$). The freedom from more than mild AR was 95.7% in the female group and 95.7% in the Male group (ρ = 0.983) (Fig. 4).

There was one (3%) patient in each group who developed moderate postprocedural aortic stenosis (PPAS) ($\rho^2 = 1.000$). Freedom from more than mild PPAS was 97.9% in the female and male groups (ρ = 0.994) (Fig. 5).

The average peak and mean pressure gradients remained similar between groups ($\rho^2 = 0.565$ and $\rho^2 = 0.573$, respectively).

TTE showed that none of the patients developed suture-line dehiscence ($\rho^2 = 1.000$).

Among patients from both groups, only one male (2%) required reoperation during follow-up ($\rho^2 = 1.000$). The freedom from reoperations was 100% in the female group and 97.9% in the male group (ρ = 0.999) (Fig. 6).

All patients were in NYHA Class I or II. We obtained no data on thromboembolic events, major bleeding complications, or newly identified rhythm disturbances requiring PPI in any group.

DISCUSSION

The principal finding of the present study is that female patients achieved perioperative and mid-term outcomes comparable to those of male patients. In the female cohort, despite having a significantly smaller aortic annulus and more advanced aortic valve disease, no differences were observed in operative mortality, postoperative recovery, valve hemodynamics, or mid-term survival after propensity score matching. These findings suggest that AVNeo provides consistently favorable clinical and hemodynamic outcomes regardless of sex, while maintaining excellent valve performance even in patients with anatomically smaller LVOT.

The literature on AVNeo consistently reports excellent postoperative and follow-up results through mid-term [10, 11, 12]. Studies indicate that AVNeo's unique technical features, such as the absence of a rigid ring and preservation of the natural Left Ventricle Outflow Tract mobility, play an important role in achieving near-natural postoperative transvalvular hemodynamics. The number of meta-analyses indicates that AVNeo perioperative data, including morbidity and mortality rates, are within standard limits for SAVR [15, 16].

Sex differences in immediate and long-term outcomes after SAVR have been a central focus of recent studies [3, 6, 9]. However, the current body of knowledge lacks publications offering a comprehensive comparative analysis of outcomes between female and male patients undergoing AVNeo. We conducted such a study to evaluate the potential of neocuspidization to mitigate sex-related disparities in outcomes observed after standard SAVR. Propensity-score matching was performed to reduce bias, eliminate confounding by risk profile, and clarify the effect of sex on perioperative and follow-up outcomes.

Historically, female sex was associated with elevated operative mortality in AV surgery and was included as a risk factor in the STS-PROM and EuroSCORE II algorithms [2, 5, 8, 17, 18]. At the same time, emerging evidence suggests that the mortality gap may be narrowing with modern practice and the use of newer operative techniques [19, 20, 21].

Beyond in-hospital mortality, several postoperative complications show sex-related differences after SAVR. Female patients consistently experience higher rates of bleeding complications. Women often require more perioperative blood transfusions, reflecting lower baseline hemoglobin levels and smaller blood volume. Smaller female anatomy also poses technical challenges during surgery [5, 18]. At the same time, evidence suggests that acute kidney injury (AKI) is more common in men after SAVR [18, 20].

In the present study, neocuspidization with three leaflets was successfully completed in all patients regardless of sex. The difference in ischemic and bypass times between groups was not statistically significant, but these times were shorter in females. This indicates that the AVNeo can be performed on the smaller anatomical structures of the female heart without additional technical difficulty for the surgeon. Across all key parameters of the ICU course and in-hospital stay, the female and male groups showed identical outcomes. Our study demonstrated similar in-hospital mortality rates in the female and male groups (Table 2).

An important preoperative finding was that the aortic annulus size in the females was significantly smaller (ρ = 0.027). The mean diameter (19.59 ± 4.09 mm) was narrow, suggesting an increased risk of PPM if these patients underwent SAVR with a standard stented prosthesis. PPM is a notable sex-specific issue in SAVR. Several publications indicate a higher incidence of mismatch in females due to a greater likelihood of a narrow aortic annulus, leading to a higher rate of implantation of smaller prostheses [22]. A recent multicenter study from Quebec reported that PPM occurred in 31.9% of women compared with 19.7% of men undergoing SAVR, even with updated criteria, with severe mismatch in 2.4% of women versus 0.6% of men [23]. This elevated incidence of PPM in females contributes to higher postoperative gradients, incomplete relief of afterload, and myocardial damage. Ultimately, in follow-up, it may lead to the development of new-onset heart failure (HF). Evidence suggests that women, more than men, may be prone to HF symptoms or readmissions after SAVR, even if survival is similar [20]. Such studies emphasize the importance of measures to prevent PPM in women, including annular enlargement or AVNeo [12, 19, 20, 21].

Within our patient cohort, predischarge TTE showed that both groups were comparable across transvalvular hemodynamic parameters (Table 3). Mean and peak gradients were low in women and men. We did not obtain data indicating postprocedural aortic stenosis or impaired hemodynamics in any patient. Given the smaller aortic annulus size in the female group, we would expect a higher incidence of PPM among these patients if a standard bioprosthetic SAVR were used for treatment. These data demonstrate that AVNeo helps prevent PPM in this category of patients.

In the mid-term follow-up, the reoperation rate was similar between female and male cohorts. Echocardiographic parameters remained stable and were identical between groups. A moderate gradual increase in the incidence of more than mild AR was detected in both female and male patients. Our results align with those reported by other authors and warrant close monitoring of AVNeo patients for AR during follow-up. [11, 12].

Studies on follow-up survival after SAVR yield conflicting results. Some suggest that women had worse long-term survival [17]. Generally, this was associated with women's delayed referral, older age, and more comorbid conditions at operation. Recently, more data have emerged indicating that when matched for baseline factors, women and men have similar long-term survival. These data suggest that sex alone is not a decisive factor in long-term survival after SAVR, once initial surgical risk is managed [20, 24]. Meanwhile, some authors emphasize the “greater inherent longevity” of women: females generally live longer than males in the general population. Therefore, if surgical outcomes are equal, women may outlive men after valve replacement [21]. We hypothesize that it may occur due to restoration of natural LVOT mobility after neocuspidization, resulting in near-normal transvalvular hemodynamics across the AVNeo valve. This leads to faster reverse LV remodeling, improved diastolic function, and reduced myocardial fibrosis. Consequently, the negative effect of these factors on survival during follow-up is reduced. In our study, the difference in mortality during follow-up was not statistically significant, although it was numerically higher among men. The causes of death were typical for this age group and did not differ between the patient cohorts. This suggests that AVNeo has the potential to restore the natural relationship between women's and men's life expectancy, as observed in the overall population, which does not require SAVR. To confirm this hypothesis, larger, longer-term studies are warranted.

LIMITATIONS

The current study has several limitations that should be acknowledged. The single-center nature of this research cannot capture the effects of different protocols, practices, and techniques used in other clinical environments on outcomes. The retrospective design of the research has inherent limitations. The study period largely coincided with the COVID-19 pandemic and wartime, which significantly affected the clinical-epidemiological situation and the socioeconomic conditions under which patients were treated and followed up. The study's sample size is relatively small, and follow-up is limited to the mid-term period. Therefore, a large-scale, multicenter, long-term study is warranted to draw conclusions with sufficient power and to evaluate whether sex-related disparities emerge in long-term outcomes.

CONCLUSION

AVNeo was consistently reproducible, with perioperative, echocardiographic, and mid-term outcomes similar between females and males. Neocuspidization demonstrated the potential to mitigate the elevated risk of postprocedural aortic stenosis in women, resulting in excellent transvalvular hemodynamics comparable to those observed in men. Mid-term survival data support the assumption that AVNeo helps restore the natural relationship between women's and men's life expectancy in the overall population. However, larger and longer-term studies are needed to validate this hypothesis and define the long-term role of AVNeo in different patient populations.

Declarations

Conflict of interest

The authors have no conflicts of interest to declare.

Ethics approval

There is no ethical problem presented. The Clinical and Research Ethics Committee of the Heart Institute approved the clinical study of this procedure (Protocol No.4/2: 21 October 2024).

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None.

Author Contribution

I.M. and I.N. conceived and designed the study. I.N., S.M., and Y.K. collected and curated the clinical data. I.N. performed the statistical analysis and interpreted the results. I.M. and I.N. drafted the manuscript. S.M., Y.K., and B.T. critically revised the manuscript for important intellectual content. B.T. supervised the study. All authors reviewed and approved the final manuscript.

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Not applicable.

Data Availability

The datasets generated and analyzed during the current study are not publicly available due to patient privacy considerations, but are available from the corresponding author upon reasonable request.

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Figures

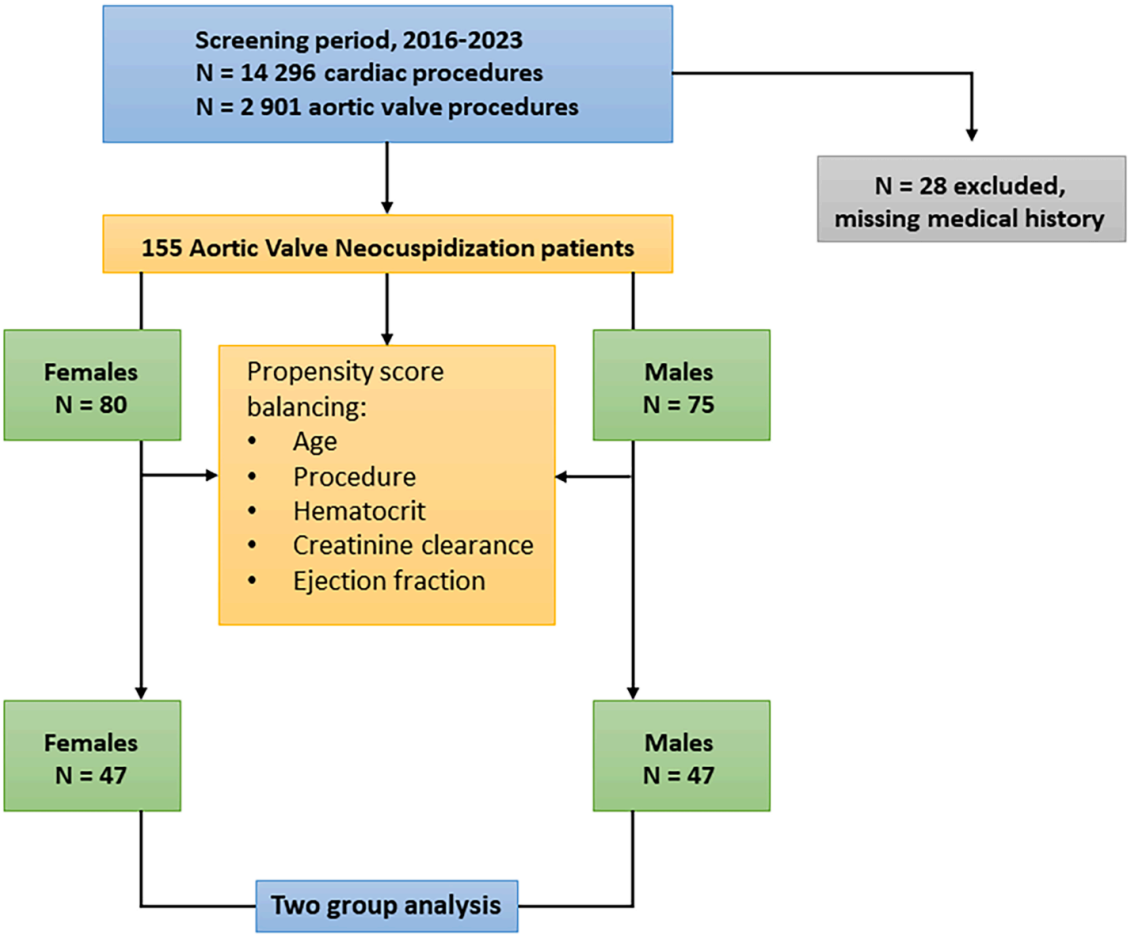


Figure 1

STrengthening the Reporting of OBservational studies in Epidemiology, or STROBE, diagram describing patient inclusion and propensitymatching. (AVNeo – aortic valve neocuspidization)

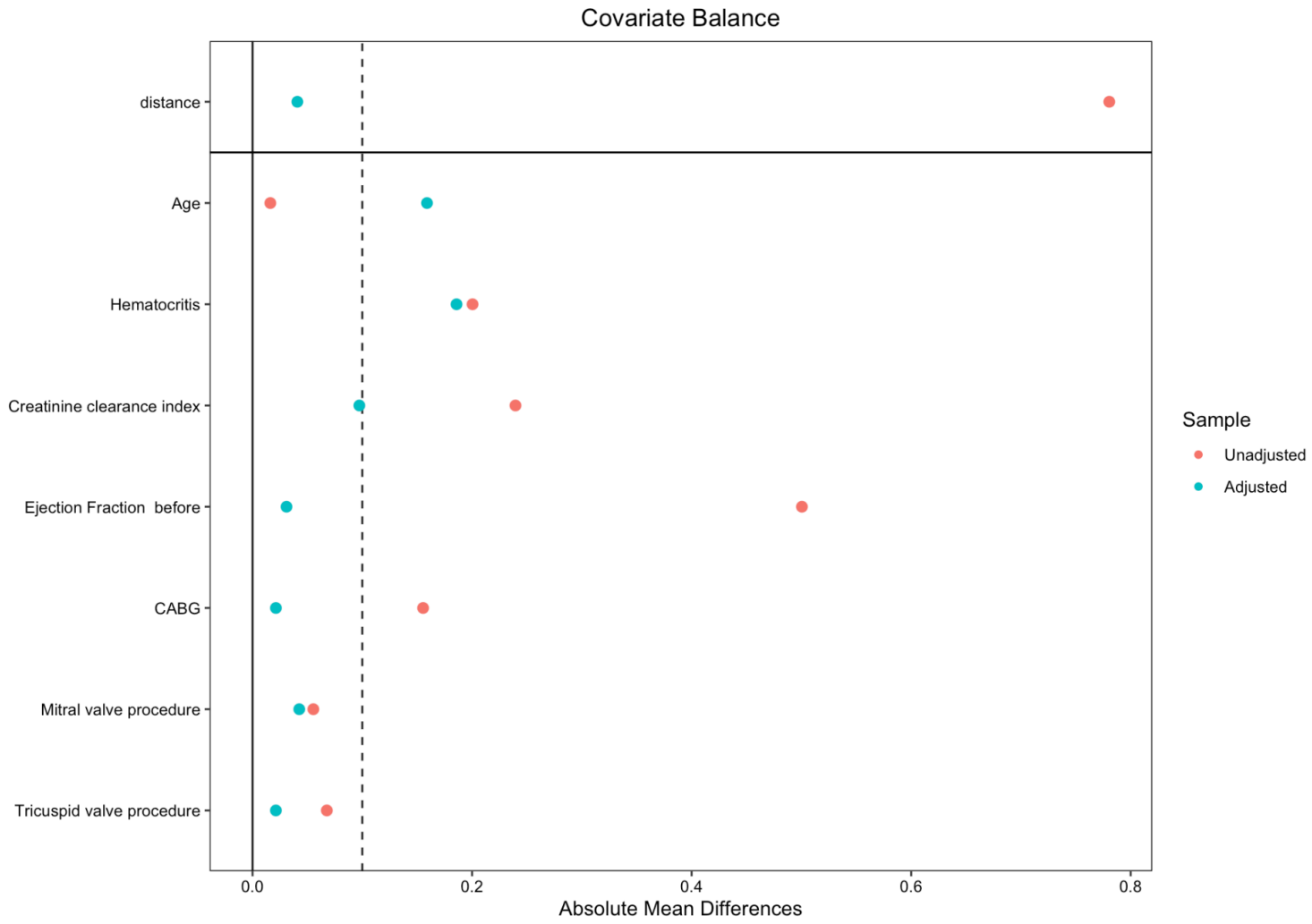


Figure 2

A Love-plot demonstrates the effectiveness of propensity-score matching. (LVEF – left ventricle ejection fraction, CABG – coronary artery bypass grafting)

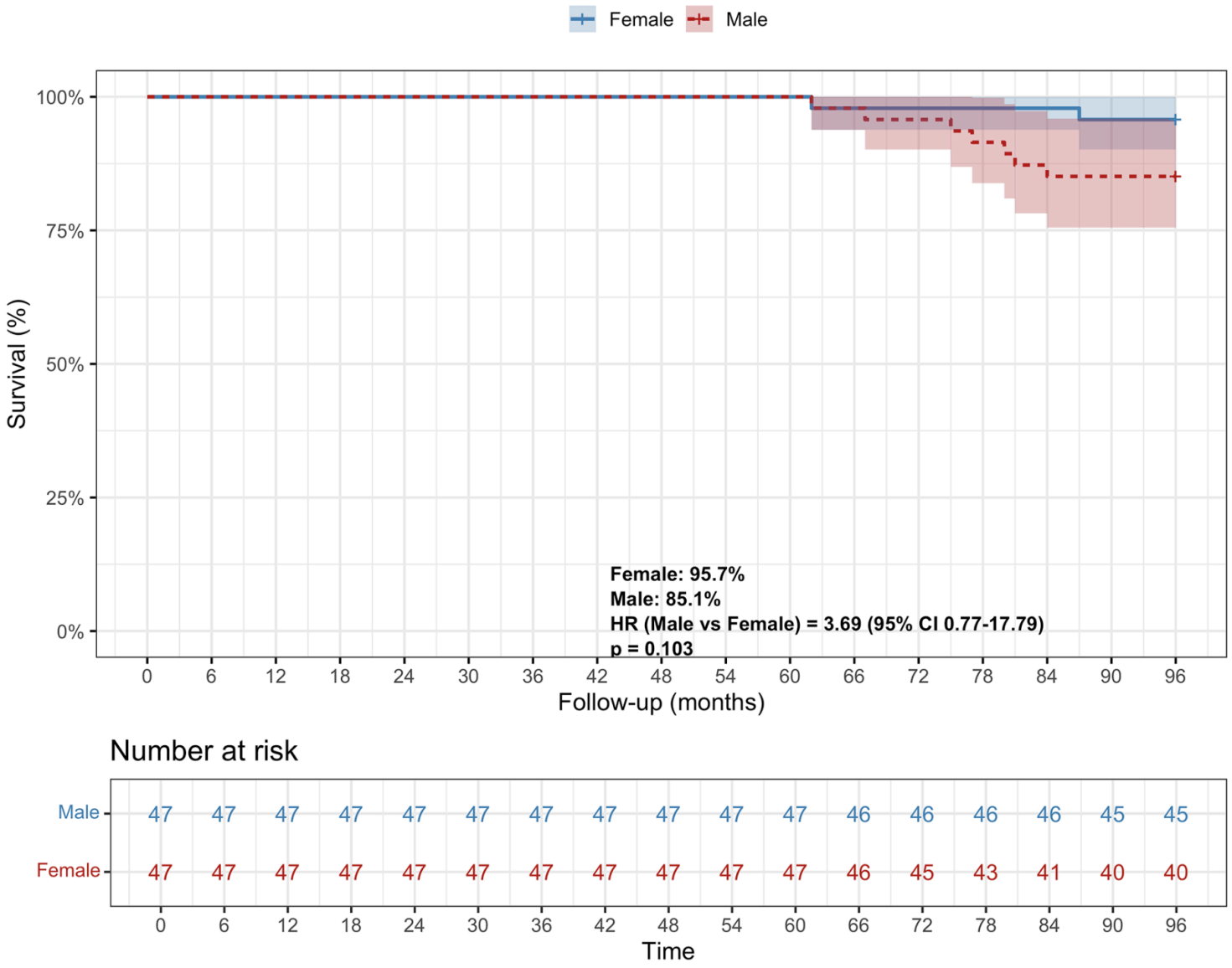


Figure 3

Kaplan–Meier chart showing survival analysis

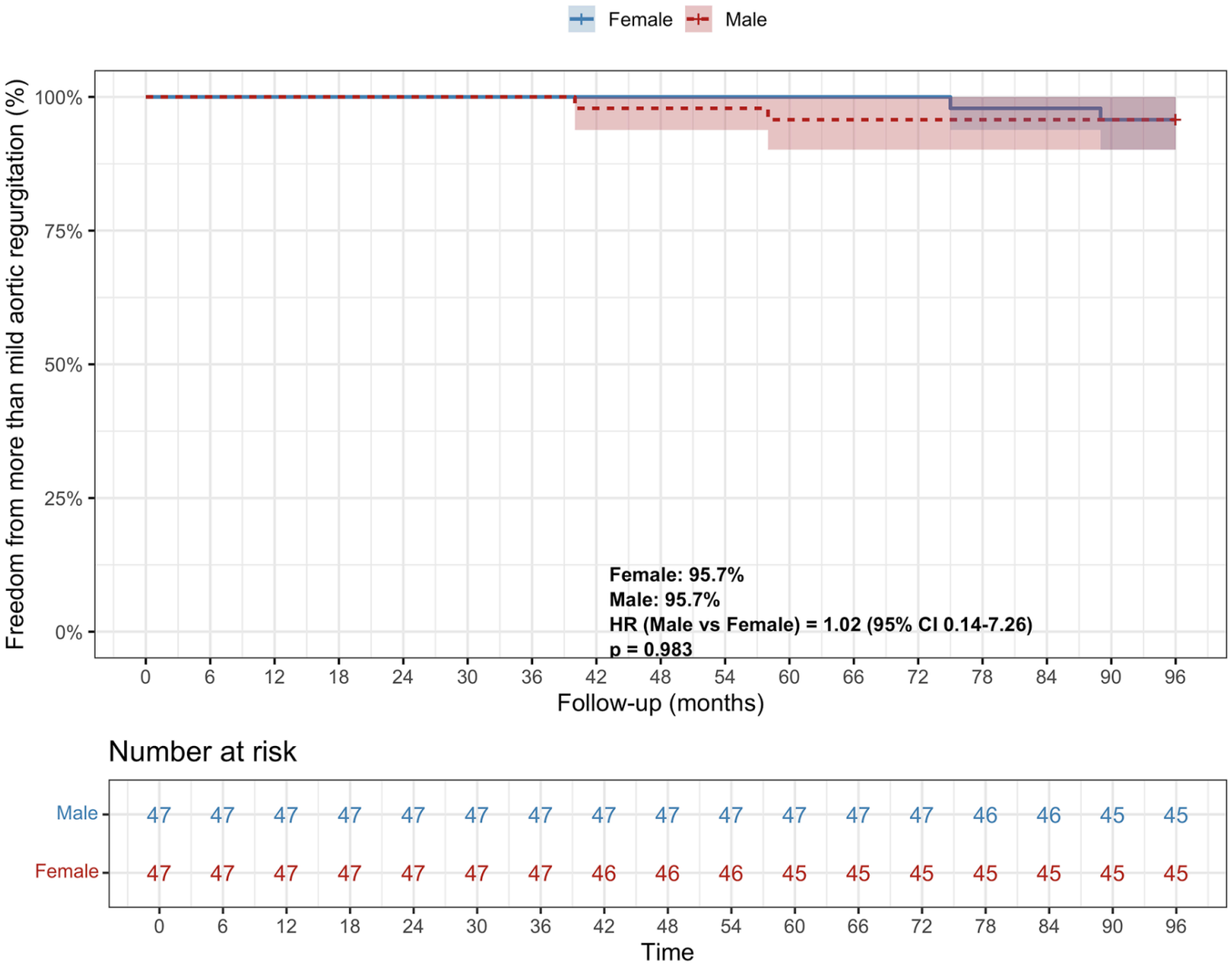


Figure 4

Kaplan–Meier chart showing freedom from more than mild aortic regurgitation

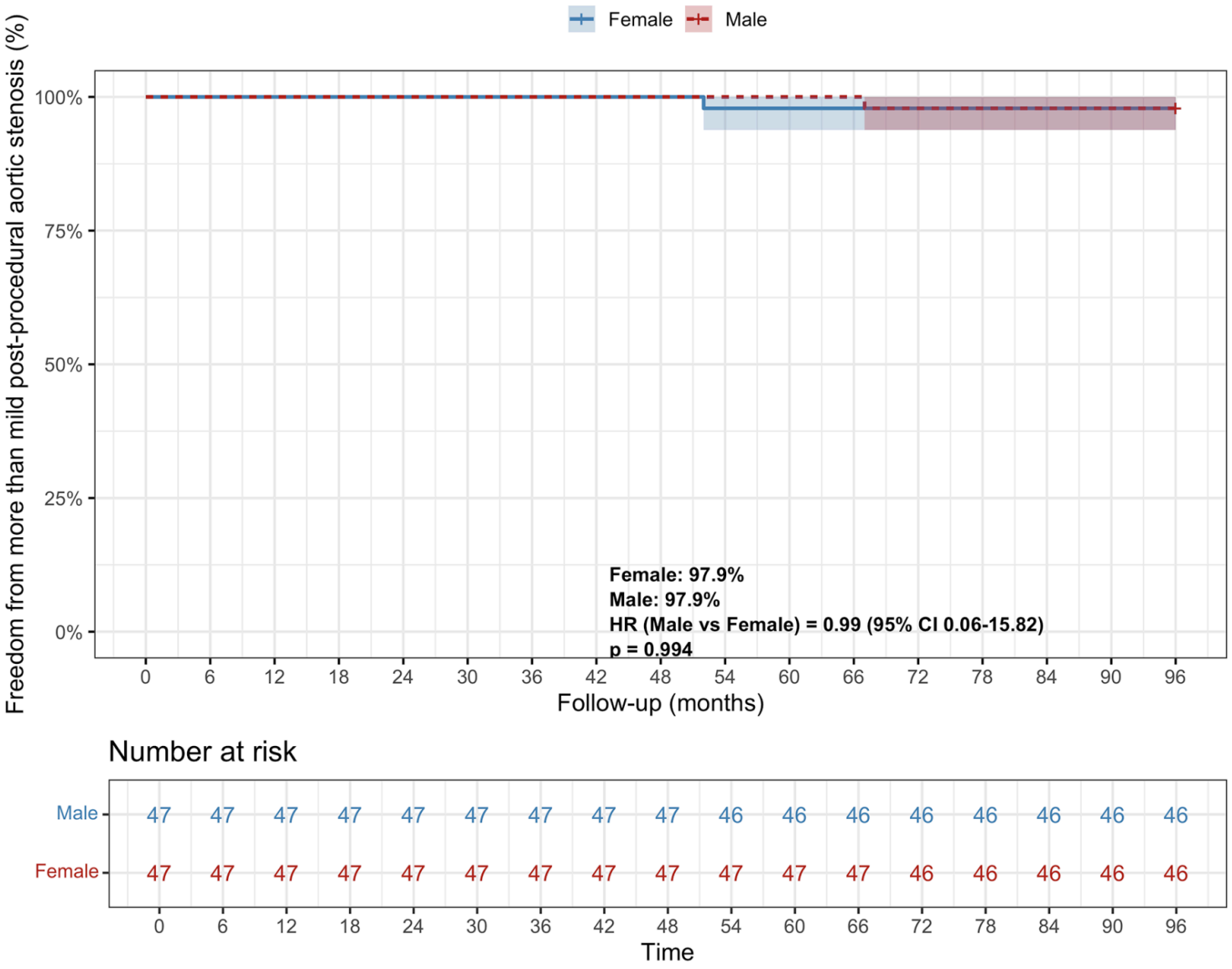


Figure 5

Kaplan–Meier chart showing freedom from more than mild post procedural aortic stenosis

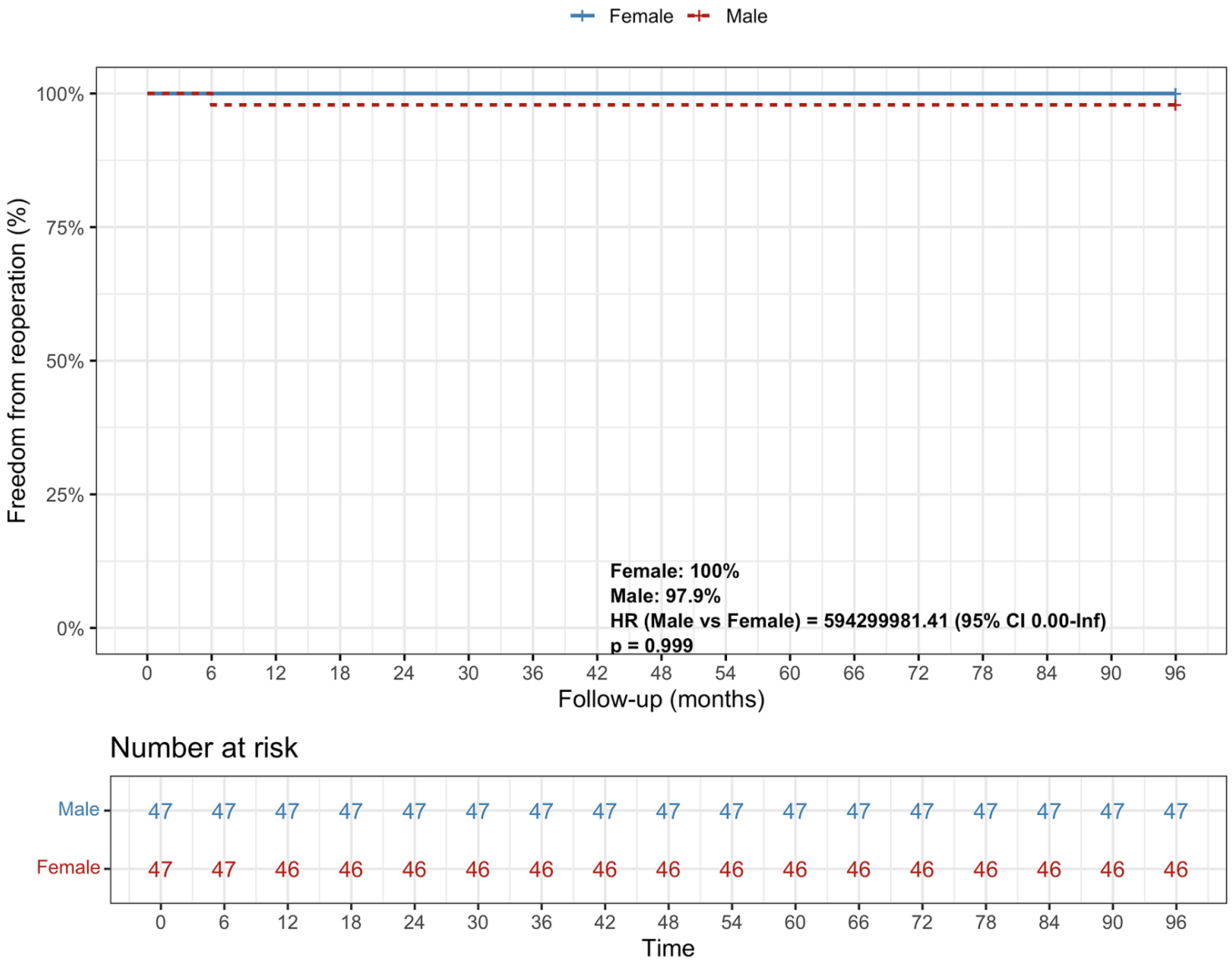


Figure 6

Kaplan–Meier chart showing freedom from reoperation