The impact of sex on in-hospital and long-term mortality rates in patients undergoing surgical aortic valve replacement: The SAVR and SEX study

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ABSTRACT

Background: Surgical aortic valve replacement (SAVR) is among the most commonly performed valvular surgeries. Despite many previous studies conducted in this setting, the impact of sex on outcomes in patients undergoing SAVR is still unclear.

Aims: This study aimed to define sex differences in short- and long-term mortality in patients undergoing SAVR.

Methods: We analyzed retrospectively all the patients undergoing isolated SAVR from January 2006 to March 2020 in the Department of Cardiovascular Surgery and Transplantology in John Paul II Hospital in Kraków. The primary endpoint was in-hospital and long-term mortality. Secondary endpoints included the duration of hospital stay and perioperative complications. Groups of men and women were compared with regard to the prosthesis type. Propensity score matching was performed to adjust for differences in baseline characteristics.

Results: A total number of 4 510 patients undergoing isolated surgical SAVR were analyzed. A follow-up median (interquartile range [IQR]) was 2120 (1000–3452) days. Females made up 41.55% of the cohort and were older, displayed more non-cardiac comorbidities, and faced a higher operative risk. In both sexes, bioprostheses were more often applied (55.5% vs. 44.5%; P <0.0001). In univariable analysis, sex was not linked to in-hospital mortality (3.7% vs. 3%; P = 0.15) and late mortality rates (23.37% vs. 23.52 %; P = 0.9). Upon adjustment for baseline characteristics (propensity score matching analysis) and considering 5-year survival, a long-term prognosis turned out to be better in women (86.8%) compared to men (82.7%, P = 0.03).

Conclusions: A key finding from this study suggests that female sex was not associated with higher in-hospital and late mortality rates compared to men. Further studies are needed to confirm long-term benefits in women undergoing SAVR.

Key words: mortality, SAVR, sex, TAVI

WHAT'S NEW?

Traditionally, female sex is considered a factor that worsens prognosis after heart surgeries. In this analysis, based on 4 510 patients undergoing isolated aortic valve replacement, in-hospital and late mortality did not differ significantly between men and women. In propensity score matching analysis, 5-year survival in women increased in comparison to men.

INTRODUCTION

Surgical aortic valve replacement (SAVR) is among the most commonly performed heart surgeries and most frequently conducted valvular interventions in Western countries [1]. The obvious indication for SAVR is aortic stenosis (AS), which has equal prevalence in elderly women and men [2]. With the onset of AS symptoms, the prognosis dramatically deteriorates as the disorder is resistant to pharmacological treatment [3]. On the other hand, surgery for AS reduces mortality and symptoms and increases the quality of life in both sexes [4, 5]. Nonetheless, sex differences in outcomes after SAVR are not unequivocally defined because of mixed results of previous studies, with greater evidence of worse prognosis for women [2, 6–11]. Unfavorable outcomes observed in women were explained by smaller anatomical structures rendering the procedure more technically demanding, more frequent frailty syndrome, and more comorbidities increasing the operative risk.

Recently, promising results of transcatheter aortic valve implantation (TAVI) in women were achieved [12, 13]. Nonetheless, the availability of this technique is not yet sufficient to include AS patients; therefore, improving results after the SAVR procedure is still of the utmost importance as surgery remains the gold standard of AS and aortic regurgitation (AR) treatment. This study aimed to assess sex differences in SAVR outcomes.

METHODS

We analyzed all patients undergoing SAVR in a single department of cardiac surgery from January 2006 to March 2020. To rule out the impact of other procedures on subjects undergoing TAVI, patients after annuloplasty and concomitant surgery were excluded. The baseline, clinical, and follow-up data were recorded, including demographic characteristics, concomitant diseases, course of hospitalization with procedural details, and possible complications. Late mortality was assessed with the Polish National PESEL database for the highest accuracy. A decision about the type and model of the prosthesis was made with patients. The primary study endpoints were in-hospital and late mortality. Secondary endpoints included length of hospital stay (LoHS) and periprocedural complications. Propensity score matching was applied for adjustment of baseline differences. All included characteristics are listed in Table 1. The study was conducted in accordance with the Declaration of Helsinki. Due to the retrospective nature of the collected data, patient consent was not required, and the bioethics committee approval was waived.

Study database

Data for this study were collected retrospectively based on the standardized form of the Polish National Database of Cardiac Surgery Procedures ("KROK" registry; www.krok.csioz.gov.pl). The registry is an ongoing, nationwide, multi-institutional record of cardiac surgery procedures in Poland, which was established on the initiative of the Club of Polish Cardiac Surgeons and compiled in cooperation with the Polish Ministry of Health. Centers enrolling patients in the KROK registry are required to transfer the data regarding every cardiac surgery to the central database in the National Center for Healthcare Information Systems at the Ministry of Health.

The data gathered included age, sex, body mass index (BMI), ejection fraction (EF), previous percutaneous coronary intervention (PCI), Canadian Cardiovascular Society (CCS) class, New York Heart Association (NYHA) class, smoking status, diabetes mellitus (DM), arterial hypertension, hypercholesterolemia, asthma, and chronic obstructive pulmonary disease (COPD). The follow-up time was defined as the period to the last observation or death. Data on late mortality were collected from the Polish National PESEL database to achieve the highest possible accuracy.

Based on the KROK registry form, a computer database was built for further statistical analysis.

Missing data in the database

We decided to exclude patients if records of outcomes (i.e., mortality/survivors) were missing. The completeness of each patient record was assessed: records were only analyzed if the percentage of complete data entered was higher than 90%. Records that were lower than 90% were excluded from this analysis. To handle missing data in propensity score matching (PSM), an additional level for the missing values was created for categorical data. In other words, the arbitrary value imputation technique was applied to those parameters. Cases with missing data in continuous parameters were excluded from PSM.

Statistical analysis

Categorical variables were presented as counts and percentages. Continuous variables were expressed as the mean with standard deviation (SD) or the median with the lower and upper quartile (interquartile range [IQR]). Normality was assessed by the Shapiro-Wilk test. Equality of variances was assessed using Levene's test. Differences between groups were compared using the Student's or Welch's t-test depending on the equality of variances for

Table 1. Baseline characteristics after propensity score matching (PSM)

		Men, n = 763	Women, n = 763	*P*-value
Age, years, median (IQR)		67 (58–74)	67 (60–73)	0.73
Body mass index, kg/m^2, median (IQR)		28.2 (25.1–31.5)	28.3 (25.1–32.4)	0.08
Overweight (BMI ≥25 kg/m^2), n (%)		574 (75.2)	577 (75.6)	0.86
Obesity (BMI ≥30 kg/m^2), n (%)		282 (37)	284 (37.2)	0.91
Body surface area, kg/m^2, mean (SD)		2 (0.2)	1.8 (0.2)	<0.001
LVEF, %, median (IQR)		60 (50–65)	60 (50–63)	0.22
AV gradient, mm Hg, median (IQR)		81 (66–96)	86.5 (73–104)	0.56
AR	None, n (%)	94 (12.3)	91 (11.9)	0.98
	Trivial, n (%)	281 (36.8)	279 (36.6)	
	Mild, n (%)	255 (33.4)	256 (33.6)	
	Moderate, n (%)	113 (14.8)	115 (15.1)	
	Severe, n (%)	20 (2.6%)	22 (2.9%)	
Smoking	None, n (%)	605 (79.3)	606 (79.4)	0.82
	Former, n (%)	107 (14)	101 (13.2)	
	Current, n (%)	51 (6.7)	56 (7.3)	
Last creatinine level, mg/dl, median (IQR)		0.9 (0.8–1.03)	0.8 (0.7–1)	<0.001[a]
CCS	N/A, n (%)	62 (8.1)	54 (7.1)	0.86
	I, n (%)	289 (37.9)	294 (38.5)	
	II, n (%)	344 (45.1)	341 (44.7)	
	III, n (%)	63 (8.3)	69 (9)	
	IV, n (%)	5 (0.7)	5 (0.7)	
NYHA	N/A, n (%)	62 (8.1)	54 (7.1)	0.96
	I, n (%)	142 (18.6)	138 (18.1)	
	II, n (%)	374 (49)	370 (48.5)	
	III, n (%)	208 (27.2)	212 (27.8)	
	IV, n (%)	30 (3.9)	34 (4.5)	
Prior MI, n (%)		57 (7.5)	62 (8.13)	0.63
Prior PCI, n (%)		26 (7.8)	32 (9.5)	0.82
Diabetes mellitus, n (%)		171 (22.4)	166 (21.8)	0.76
IDDM, n (%)		72 (9.4)	74 (9.7)	0.86
COPD	None, n (%)	611 (80.1)	615 (80.6)	0.56
	Treated, n (%)	150 (19.7)	148 (19.4)	
	Non-treated/untreated, n (%)	2 (0.3)	0 (0)	
Hypertension, n (%)		645(84.5)	637 (83.5)	0.57
Dyslipidemia, n (%)		290 (38)	280 (36.7)	0.61
EuroSCORE II, median (IQR)		0.9 (0.7–1.4)	1.1 (0.9–1.5)	<0.001[a]

Abbreviations: see Table 4

normally distributed variables. The Mann-Whitney U test was used for non-normally distributed continuous variables or ordinal variables. Categorical variables were compared by Pearson's χ^2 test or by Fisher's exact test if 20% of the cells had an expected count of less than 5. To evaluate the influence of sex on mortality (overall death), the Cox proportional-hazards model was created and adjusted for baseline covariates (age, prior myocardial infarction, current or former smoking status, DM, sinus rhythm before procedure, planned or emergency/urgent procedure, EuroSCORE II, hyperlipidemia and NYHA class). The multivariable model was fitted in backward stepwise regression with a *P*-value threshold of 0.05 stopping rule. Survival probabilities were presented using the Kaplan-Meier curves and compared with the log-rank test.

To avoid the potential influence of the non-randomized design and reduce bias, a propensity score was calculated using a multivariable logistic regression model with sex considered a dependent variable. The propensity score was calculated based on baseline variables (see Table 1 for details). Covariate balance was assessed using standardized mean differences (SMD) that were less than 5. Pairs of male and female patients were formed using 1:1 caliper matching. A caliper width of 0.07 was used. Unpaired patients were rejected from the analysis. Clinical outcomes (including mortality) for matched samples were compared using McNemar's test (Tables 2 and 3). Additionally, a matched pairs design of the win ratio method was applied for lifetime data [14]. The results of this method are presented on the forest plot (Figure 1).

The level of statistical significance was set at $P < 0.05$. Statistical analyses were performed with JMP®, version 16.2.0 (SAS Institute Inc, Cary, NC, US) and using R, Version 4.1.0 (R Core Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing. Vienna, Austria, 2017, www.r-project.org/).

Table 2. Procedural and clinical outcomes after propensity score matching (PSM)

		Women, n = 763	Men, n = 763	*P*-value
Duration of hospitalization, days, median (IQR)		10 (8–14)	10 (8–14)	0.45
Valve type	Bioprosthesis, n (%)	457 (59.9)	453 (59.4)	0.83
	Mechanical, n (%)	306 (40.1)	310 (40.6)	
Valve diameter, mm, median (IQR)		23 (21–23)	23 (21–23)	0.14
Cardioplegia	Crystalloid, n (%)	469 (61.6)	497 (65.5)	0.11
	Blood, n (%)	293 (38.5)	262 (34.5)	
Re-operation	Re-sternotomy, n (%)	44 (9.4)	36 (7.8)	0.8
	Secondary sternal repair, n (%)	10 (2.2)	6 (1.3)	
Death in operating room, n (%)		1 (0.1)	2 (0.3)	0.56

Continuous variables were expressed as the median with the lower and upper quartile (IQR, interquartile range)

Table 3. In-hospital and late mortality after propensity score matching (McNemar's test)

	Female, n = 763	Male, n = 763	*P*-value
Procedural complications, n (%)	72 (9.5)	82 (10.8)	0.40
In-hospital mortality, n (%)	26 (3.4)	27 (3.5)	0.89
Death (within 1 year), n (%)	48 (6.3)	66 (8.7)	0.08
Death (within 2 years), n (%)	61 (8)	84 (11)	0.046
Death (within 3 years), n (%)	72 (9.4)	97 (12.7)	0.04
Death (within 4 years), n (%)	86 (11.3)	117 (15.3)	0.02
Death (within 5 years), n (%)	101 (13.2)	132 (17.3)	0.03
Overall death, n (%)	161 (21.1)	186 (24.4)	0.12

RESULTS

General characteristics

A total of 5035 consecutive patients undergoing invasive replacement of the aortic valve (AV) were included. Following exclusion, 4510 patients treated with isolated SAVR were analyzed (Supplementary material, *Figure S1*). Men formed 58.5 % of the cohort. Women were older (mean age 67.3 years vs. 61.6 years; P <0.001) and more often overweight or obese (mean body mass index [BMI], 29.2 kg/m^2 vs. 28 kg/m^2; P <0.001) with more non-cardiovascular concomitant diseases. Men were more often smokers (10.6% vs. 4.6%; P <0.001), and they more often suffered from prior MI (11.2% vs. 5.4%; P <0.001). The majority of patients were affected by aortic stenosis (85%). The maximal transvalvular (pressure) gradient was higher in women (89.2 vs. 79.4 mm Hg; P <0.001). Men had more often moderate or severe aortic regurgitation. Symptoms assessed by the NYHA functional classification differed significantly in both groups, with female predominance in class III. The baseline patient characteristics are shown in Table 4.

Procedural outcomes

Except for 4 cases, all procedures were performed with the cardioplegic solution. The procedure was longer in men (214 vs. 208 min; P = 0.002), and they received bigger prostheses (23.7 vs. 21.3 mm; P <0.001). Also, the average time of extracorporeal circulation was longer in men (113.2 vs. 108.7 min; P <0.001). Bioprostheses were chosen more often in both sexes, especially in women (61.6% vs. 51.2%; P <0.001).

Clinical outcomes

A follow-up median (IQR) was 2120 (1000–3452) days, for men 2186 (1000–3568) days, and for women 2042 (1006–3270; P = 0.01) days. The frequency of complications did not differ between sexes (10.75% vs. 11.2%; P = 0.67). Univariate analysis did not show differences between women and men in terms of in-hospital mortality (3.7% vs. 3%; P = 0.15) and late mortality (23.37% vs. 23.52%; P = 0.9) (Table 5). Nonetheless, the propensity score analysis disclosed that after 1-year follow-up, the mortality rate in men was higher and remained so until the last observation period when we used McNemar's test for matched pairs (Table 3). The Kaplan-Meier estimate did not show significant differences between men and women in long-term follow-up (Figure 1). In the win ratio approach, a statistically significant mortality rate difference was observed only at 5 years; however, all analyses show similar win ratio results (Figure 2). At 5-year follow-up, women had 33% more wins over death (win ratio [WR], 1.33; 95% CI, 1.00–1.79; P = 0.048). Additionally, the multivariable Cox regression indicated that male sex was associated with higher risk of death (hazard ratio [HR], 1.22; 95% CI, 1.07–1.39; P = 0.003).

DISCUSSION

The key findings of this study led to the conclusion that women do not have higher in-hospital and long-term mortality than men. Traditionally, female sex was associated

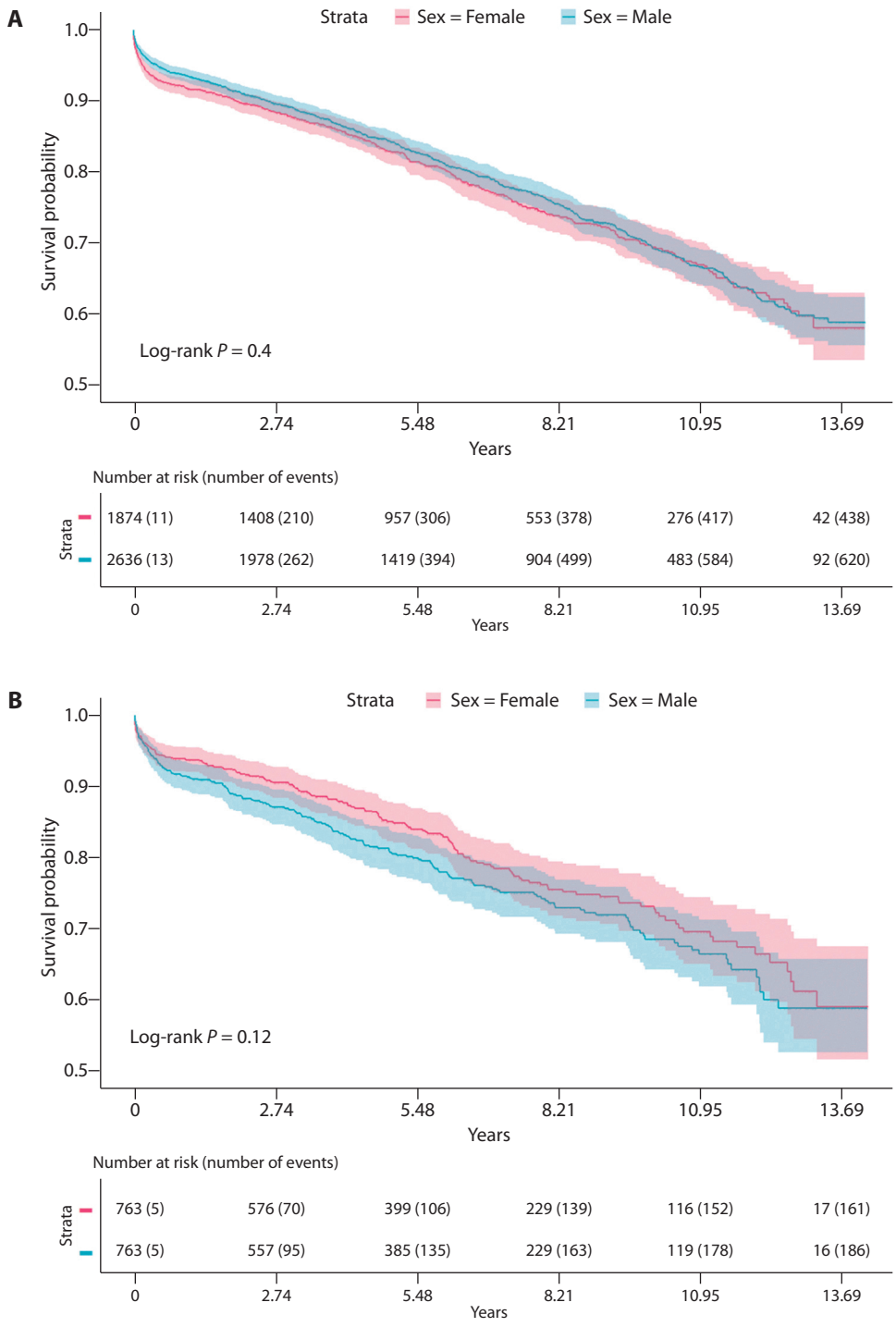

Figure 1. A. Kaplan-Meier curves before propensity score matching (PSM). **B.** Kaplan-Meier curves after PSM
Abbreviations: see Table 3

with worse clinical outcomes after heart surgeries. Female sex is embedded in the Society of Thoracic Surgeons (STS) and EuroSCORE II risk models as a factor worsening prognosis [15]. Nevertheless, it should be pointed out that these scales were designed based on data from coronary artery bypass grafting (CABG) procedures and might not accurately define an operative risk for SAVR.

In previous studies, despite more symptoms, females were treated conservatively for a longer time and were referred for SAVR more rarely; as a consequence, at the time of operation, they presented with worse baseline characteristics [2]. Similarly, in our study, women were older, more often with diabetes, hypertension, and higher operative risk.

Table 4. Baseline characteristics before propensity score matching (PSM)

		Women, n = 1874	Men, n = 2636	Total, n = 4510	*P*-value
Age, years, median (IQR)		69 (62–75)	63 (55–71)	66 (57–73)	<0.001
Body mass index, kg/m^2, median (IQR)		28.8 (25.4–32.5)	27.7 (24.8–30.9)	28.1 (25–31)	<0.001
Overweight (BMI ≥25 kg/m^2), n (%)		1442 (77.2)	1904 (72.7)	3346 (74.6)	0.006
Obesity (BMI ≥30 kg/m^2), n (%)		785 (42.1)	806 (30.8)	1591 (35.5)	<0.001
Body surface area, m^2, median (IQR)		1.8 (1.7–1.9)	2 (1.8–2.1)	1.9 (1.8–2)	<0.001
LVEF, %, median (IQR)		60 (50–65)	55 (45–60)	60 (50–63)	<0.001
AV mean gradient, mm Hg, median (IQR)		86.5 (73–104)	81 (66–96)	84 (70–100)	<0.001
AR	None, n (%)	205 (11)	240 (9.1)	445 (9.9)	<0.001
	Trivial, n (%)	692 (37)	793 (30.2)	1485 (33)	
	Mild, n (%)	649 (34.7)	762 (29)	1411 (31.4)	
	Moderate, n (%)	245 (13.1)	543 (20.7)	788 (17.5)	
	Severe, n (%)	79 (4.2)	287 (10.9)	366 (8.1)	
Smoking	None, n (%)	1604 (85.8)	1878 (71.6)	3482 (77.5)	<0.001
	Former, n (%)	179 (9.6)	469 (17.9)	648 (14.4)	
	Current, n (%)	86 (4.6)	277 (10.6)	363 (8.1)	
Last creatinine level, mg/dl, median (IQR)		0.85 (0.7–1)	0.95 (0.8–1)	0.9 (0.7–1)	<0.001
CCS	N/A, n (%)	144 (7.7)	209 (8)	353 (7.9)	0.77
	I, n (%)	690 (36.9)	962 (36.7)	1652 (36.8)	
	II, n (%)	852 (45.6)	1212 (46.2)	2064 (46)	
	III, n (%)	162 (8.7)	205 (7.8)	367 (8.2)	
	IV, n (%)	21 (1.1)	35 (1.3)	56 (1.3)	
NYHA	N/A, n (%)	21 (1.1)	25 (1)	46 (1)	0.03
	I, n (%)	311 (16.6)	497 (18.9)	808 (18)	
	II, n (%)	856 (45.8)	1255 (47.8)	2111 (47)	
	III, n (%)	606 (32.4)	719 (27.4)	1325 (29.5)	
	IV, n (%)	76 (4.1)	128 (4.9)	204 (4.5)	
Prior MI, n (%)		101 (5.4)	294 (11.2)	395 (8.8)	<0.001
Prior PCI, n (%)		56 (6.9)	122 (11.6)	178 (9.5)	0.001
Diabetes mellitus, n (%)		438 (23.4)	478 (18.2)	916 (20.4)	<0.001
IDDM, n (%)		183 (9.8)	200 (7.6)	383 (8.5)	0.01
COPD	None, n (%)	1548 (82.8)	2095 (79.9)	3643 (81.1)	0.04
	Treated, n (%)	320 (17.1)	526 (20.1)	846 (18.8)	
	Non-treated/untreated, n (%)	1 (0.1)	2 (0.1)	3 (0.1)	
Hypertension, n (%)		1585 (84.8)	2118 (80.7)	3703 (82.4)	0.001
Dyslipidemia, n (%)		676 (36.2)	966 (36.8)	1642 (36.6)	0.66
EuroSCORE II, median (IQR)		1.2 (0.9–1.6)	0.8 (0.7–1.2)	1 (0.7–1.4)	<0.001

Abbreviations: AV, aortic valve; AR, aortic regurgitation; COPD chronic obstructive pulmonary disease; IDDM, insulin-dependent diabetes mellitus; IQR, interquartile range; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NYHA, New York Heart Association; PCI, percutaneous coronary intervention

Table 5. Procedural and clinical outcomes before propensity score matching (PSM)

		Women, n = 1 874	Men, n = 2 636	Total, n = 4 510	*P*-value
Duration of hospitalization, days, median (IQR)		10 (8–14)	10 (8–14)	10 (8–14)	0.14
Valve type	Bioprosthesis	1155 (61.6)	1349 (51.2)	2504 (55.5)	<0.001
	Mechanical	719 (38.4)	1287 (48.8)	2006 (44.5)	
Valve diameter, mm, median (IQR)		21 (21–23)	23 (23–25)	23 (21–25)	<0.001
Cardioplegia	Crystalloid, n (%)	717 (38.5)	930 (35.5)	1647 (36.8)	0.04
	Blood, n (%)	1145 (61.5)	1689 (64.5)	2834 (63.2)	
Complications, n (%)		200 (10.8)	291 (11.1)	491 (11)	0.67
Re-operation	Re-sternotomy, n (%)	98 (8.5)	161 (9.9)	259 (9.3)	0.21
	Secondary sternal repair, n (%)	19 (1.7)	38 (2.3)	57 (2)	
In-hospital mortality, n (%)		70 (3.7)	78 (3)	148 (3.3)	0.15
Death in operating room, n (%)		6 (0.3)	7 (0.3)	13 (0.3)	0.74

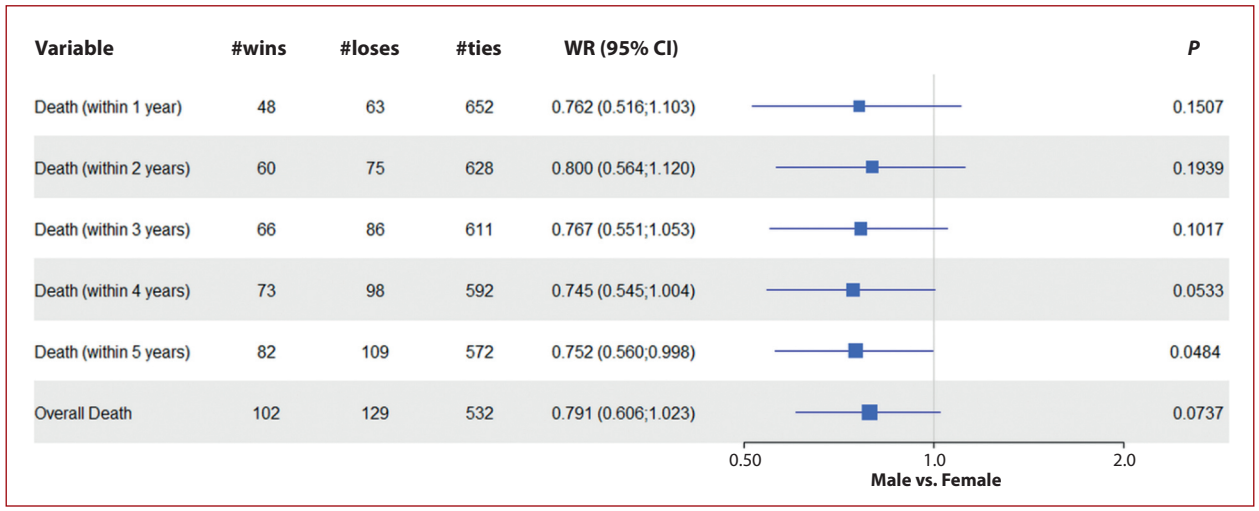

Figure 2. Differences in long-term mortality after surgical aortic valve replacement by sex shown on the forest plot of the win ratio method after propensity score matching

It was postulated that the later presentation of women for SAVR might be related to delayed development of AS in women. Older studies based on echocardiographic data showed that men are twice as likely to be diagnosed with AS [16]. Nonetheless, data from a large national registry from Sweden showed that the frequency of AS is nearly equivalent in elderly women and men [17]. As argued earlier [16], sex discrepancies among patients undergoing SAVR are probably caused by referral bias.

Sex-dependent pathophysiological development of AS was described previously [18]. Women face a greater risk of developing left ventricular concentric geometry in response to AS, decrease in ejection fraction, and fibrosis. As far as calcifications are concerned, women have a lower aortic valve calcium burden than men. Nonetheless, in women, calcifications have a more profound impact on AS severity. Therefore, sex is not associated with AS progression [19, 20].

The histogram representing the average 365-day survival for each year of the study period shows the mortality peak in 2015 with a subsequent tendency to decrease (Figure 3). This finding might be attributed to 240 patients who were qualified for TAVI mostly after 2015 (Supplementary material, *Figure S1*). Their risk profile based on EuroSCORE II was 2.55, higher than that of patients undergoing isolated SAVR. Therefore, we might assume that the transfer of the sickest patients to TAVI procedures has impacted SAVR outcomes. There are many studies supporting TAVI utilization in high- and medium-risk patients, given its favorable outcomes, especially in women. Nonetheless, the majority of TAVI studies were based on octogenarians, which raises doubts as longer life expectancy in women might influence these outcomes [21–26]. Moreover, the studies assessing sex differences in SAVR patients who were at least 80 years old also revealed better outcomes in the women's group [10, 17]. For all patients at that age, the newer generation bioprostheses might offer excellent outcomes [27–30]. In a post-hoc analysis of the SURTAVI study, van Mieghem et al. did not show significant sex differences between SAVR and TAVI groups in 2-year follow-up [9]. Similarly, in a recent analysis, Marzec et al. did not find a statistically significant difference in the 24-month mortality rate between the two methods [31]. Available meta-analyses comparing TAVI and SAVR show distinct benefits of each technique. TAVI seems to reduce the incidence of bleeding, new-onset atrial fibrillation, and acute kidney injury but has a higher rate of vascular complications, prosthesis-patient mismatch, and reinterventions. In terms of all-cause mortality, no significant differences between both methods were found [32, 33]. Noteworthy is the emergence of new surgical techniques that reduce the rate of cerebrovascular events and make SAVR more accessible for patients with COPD, which is a common contraindication for SAVR [34]. Comparable results of TAVI and SAVR in the mentioned studies suggest that both methods should be considered in patients suffering from aortic valve disease. Our study has demonstrated that SAVR is a reasonable option for women with outcomes comparable to men in short- and long-term follow-ups. There was a trend towards better results in women shown in PSM, but this needs to be confirmed in further studies. Also, in the presence of a growing body of evidence suggesting comparable outcomes in men and women after SAVR, female sex as a risk factor for SAVR should be reconsidered [35].

Limitations

This was a single-center retrospective study. Not all determinants of the outcomes could be recorded. The lack of comprehensive echocardiographic data prevented assessment of patient-prosthesis mismatch (PPM). In the case of

late mortality, it was not possible to distinguish between cardiac and non-cardiac causes of death.

CONCLUSIONS

In the present study, crude analysis demonstrated that female sex was not associated with higher in-hospital and late mortality rates after SAVR compared to men. Further studies are needed to confirm long-term benefits in women undergoing SAVR.

Supplementary material

Supplementary material is available at https://journals.viamedica.pl/kardiologia_polska.

Article information

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