Impact of Gender on Transcatheter Aortic Valve Implantation Outcomes

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Previous studies indicate that women who underwentwho underwent transcatheter aortic valve implantation (TAVI) have poorer 30-day outcomes compared with men. However, the effect of gender as a prognostic factor for long-term outcomes following TAVI remains unclear. Between 2008 and 2018, all patients (n = 683) who underwent TAVI in 2 centres in Melbourne, Australia were prospectively included in a registry. The primary end-point was long-term mortality. The secondary end points were Valve Academic Research Consortium-2 (VARC-2) in-hospital complications and mortality at 30-days and 1-year. Of 683 patients, 328 (48%) were women. Women had a higher mean STS-PROM score (5.2 ± 3.1 vs 4.6 ± 3.5, p < 0.001) but less co-morbidities than men. Women had a significantly higher in-hospital bleeding rates (3.3% vs 1.0%, Odds Ratio 4.21, 95% confidence interval [CI] 1.16 to15.25, p = 0.027) and higher 30-day mortality (2.4% vs 0.3%, hazard ratio [HR] 8.75, 95% CI 1.09 to 69.6, p = 0.040) than men. Other VARC-2 outcomes were similar between genders. Overall mortality rate was 36% (246) over a median follow up of 2.7 (interquartile rang [IQR] 1.7 to 4.2) years. Median time to death was 5.3 (95% CI 4.7 to 5.7) years. One-year mortality was similar between genders (8.3% vs 7.8%), as was long-term mortality (HR = 0.91, 95% CI 0.71 to 1.17, p = 0.38). On multivariable analysis, female gender was an independent predictor for 1-year mortality (HR = 2.33, 95% CI 1.11 to 4.92, p = 0.026), but not long-term mortality (HR = 0.78, 95% CI 0.54 to 1.14, p = 0.20). In the women only cohort, STS-PROM was the only independent predictor of long-term mortality (HR 1.88, 95% CI 1.42 to 2.48, p < 0.001). In conclusion, women had higher rates of peri-procedural major bleeding and 30-day mortality following TAVI. However, long-term outcomes were similar between genders. **(Am J Cardiol 2020;133:98−104)**

The prevalence of aortic stenosis (AS) increases with age and is estimated to be almost 10% in patients above the age of 80.[1] Despite being more frequent in men in younger patients, amongst those over 75 years of age the prevalence is higher in women.[2] Notably, women accounted for only 30% of patients in the recently published low risk trials.[3,4] Female gender has been associated with increased perioperative mortality following surgical aortic valve replacement (SAVR).[5] However, a recent meta-analysis of randomized trials found that women have a significant mortality benefit with transcatheter aortic valve implantation (TAVI) compared with SAVR.[6] Several analyses of TAVI registries including a large meta-analysis investigating gender-specific outcomes have published similar findings: Women are older, but have less co-morbidities[7−10] and at 30 days, they have more bleeding events, vascular complications and strokes.[7-10] Some analyses demonstrated better long-term survival for female patients (7,8,11) whereas others showed no difference in mortality between genders.[8,9,12] Nevertheless, data about gender differences in long-term follow up over 1-year are scarce.[8] TAVI has excellent evidence for improved short-term and mid-term clinical outcomes across the risk spectrum; equally so for women and men.[4,13] With the increased use of TAVI it is important that we gain a better understanding of the long-term contributors to morbidity and mortality to confine

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TAVI to those most likely to benefit. Our multicentre study is the first to examine gender differences in long-term outcomes after TAVI.

Methods

Between August 2008 and July 2018, all patients who underwent TAVI in 2 experienced centres in Melbourne, Australia (The Alfred Hospital and the Epworth Hospital, Richmond Campus) with the CoreValve, Evolut R, and Evolut Pro (Medtronic Inc., MN, USA), Edwards Sapien XT, Sapien 3, and Centera (Edwards Lifesciences, CA, USA) or Portico (Abbott, IL, USA) bioprostheses were included in a registry. Ethics approval for this study was gained from the Alfred and Epworth hospital research and ethics committees with an opt-out consent (local ethics project number: 200/17). Further details regarding local TAVI programs have been reported previously.[14] Severe AS was defined as aortic valve area (AVA) <1.0 cm^2 and/or an aortic valve mean pressure gradient (MPG) ≥40 mm Hg. Patients were deemed suitable for TAVI on consensus by the local heart team. All patients underwent pre-procedural work-up with coronary and peripheral angiograms, and transthoracic echocardiogram (TTE). From 2012 onwards, this also included a computed tomography angiography (CTA) of the chest. Baseline TTE was obtained after TAVI before hospital discharge. Follow-up appointments were scheduled at 30 days, and thereafter according to the treating physician with the aim of performing annual clinical assessment and TTE.

The primary end point was long-term mortality. The secondary outcomes were in-hospital complications according to the Valve Academic Research Consortium-2 (VARC-2) (15) including myocardial infarction, stroke, and transient ischaemic attack, major bleeding, access site complications, and acute kidney injury; as well as device success and mortality at 30 days. Device success was defined as absence of procedural mortality, correct positioning of a single prosthetic heart valve and adequate performance of the prosthetic heart valve.[15] One-year outcomes included valve failure requiring re-intervention, conduction disturbances requiring permanent pacemaker (PPM), cerebrovascular events, heart failure requiring rehospitalisation, and mortality. Additionally, for a measurement of functional ability and frailty, the clinical frailty score, according to Rockwood,[16] and their 'living support status' (LSS) was determined yearly. The latter was defined as reliance on daily life assistance and stratified to 'independent in activities of daily living' (ADL-i), 'dependent on another person in the same household in activities of daily living' (ADL-d) or 'living in an aged care facility' (ACF).

The distribution of baseline characteristics and postprocedure outcomes were compared between men and women. Categorical variables are expressed as number (%) and compared using the Pearson chi-squared test or Fisher exact test when there were cells with fewer than 5 cases. Continuous variables are expressed as mean ± standard deviation (SD) or median (interquartile range, [IQR]) depending on distribution of the data and were compared using Student's *t* test for normally distributed variables or Wilcoxon rank sum test for non-normally distributed variables. Crude relations between gender and 1-year and long-term mortality were first assessed by plotting Kaplan-Meier survival curves by gender and comparing them using the log-rank test. The relation between gender and mortality after adjusting for potential confounders was assessed using univariable and multivariable Cox proportional hazards models. Variables were included in the multivariable model if found to be significant at 0.10 level in a univariable model. Proportional hazards assumption was assessed by z-test based on Schoenfeld residuals (at 0.10 significance level) and by visually inspecting log-log plots and standardised Schoenfeld residuals plots. In case of violation of proportional hazards assumption for a predictor, a term for its interaction with time was added to the model and assessed at 0.10 significance level. The final multivariable model included all predictors and their interactions with time significant at 0.10 level. Predictors of 30-day mortality were examined by logistic regression models due to virtually no censoring by 1 month. A 2-sided p-value of <0.05 was considered statistically significant. All statistical analyses were performed using SAS software version 9.4, SAS/STAT version 13.1 (SAS Institute, Cary NC, USA).

Results

From a total of 683 patients who underwent TAVI over the study period from 2008 to 2018, 328 (48%) were women. Baseline characteristics are detailed in Table 1. Mean age of the overall cohort was 83.2 ± 6.9 years and women were on average 1 year older than men. Women had a higher mean STS-PROM score (5.2 ± 3.1 vs 4.6 ± 3.5, $p < 0.001$) and lower estimated glomerular filtration rate (eGFR). However, they were more independent with activities of daily living (68% vs 53%, $p < 0.001$) and had fewer co-morbidities. Peri-procedural characteristics are detailed in Table 2. The transfemoral approach was utilised significantly less often in female patients (92% vs 95%, $p < 0.001$) and women were more likely to receive a self-expanding valve (90% vs 79%, $p < 0.001$).

Table 3 details in-hospital, 30-day and 1-year outcomes. Postprocedure, women had 4.2 times higher odds of major bleeding compared with men (3.3% vs 1.0%, OR 4.21, $p = 0.03$ for the entire cohort and the cohort with transfemoral access). Other VARC-2 outcomes were similar across genders, including the need for PPM. More men required a second valve as bailout (TAVI valve-in-valve procedure) compared with women (2.7% vs 5.9%, $p = 0.04$). Mortality at 30-days was significantly higher for women compared with men (2.4% vs 0.3%, HR 8.75, 95% CI 1.09 to 69.6, $p = 0.02$). This did not persist at 1-year, with no gender difference in 1-year mortality on univariable analysis (8.3% vs 7.8%, HR 1.08, 95% CI 0.61 to 1.85, $p = 0.8$). However, multivariate analysis found female gender to be an independent predictor of 1-year mortality (HR 2.33, 95% CI 1.11 to 4.92, $p = 0.026$, not shown in table). Looking at the female cohort separately, multivariate analysis demonstrated that larger pre-procedural AVA was associated with reduced mortality at 30-days (HR 0.58 per 0.1 cm^2 increase in AVA, 95% CI 0.36 to 0.92, $p = 0.02$, not shown in table).

Table 1
Baseline characteristics

	Women (n = 328, 48%)	Men (n = 355, 52%)	pValue
Age (years)	84.2 ± 5.2 5.20 5.20	83.2 ± 6.9	0.15
Estimated glomerular filtration rate (ml/min)	56.9 ± 18.5	60.3 ± 20.2	0.02
Coronary artery disease	112 (34.4%)	192 (55.2%)	<0.001
Triple vessel disease	25 (7.7%)	72 (20.7%)	<0.001
Previous percutaneous coronary intervention	56 (17.2%)	85 (24.4%)	0.02
Previous cardiac surgery	39 (12.0%)	108 (30.9%)	<0.001
Atrial fibrillation	96 (29.4%)	112 (32.0%)	0.47
Cerebrovascular disease	47 (14.4%)	50 (14.3%)	0.96
Hypertension	240 (73.8%)	236 (67.8%)	0.09
Diabetes mellitus	83 (25.5%)	90 (25.6%)	0.98
Peripheral arterial disease	42 (13.6%)	67 (19.9%)	0.03
Chronic obstructive pulmonary disease	41 (13.7%)	64 (19.2%)	0.07
Existing permanent pacemaker	28 (8.5%)	58 (16.3%)	0.002
NYHA classification III/IV	203 (61.9%)	219 (61.7%)	0.92
Frailty score	4.1 ± 0.8	3.9 ± 0.8	0.02
Living support status			
Activities of daily living- independent	183 (67.5%)	149 (52.3%)	<0.001
Activities of daily living- dependent	77 (28.4%)	128 (44.9%)	
Aged care facility	11 (4.1%)	8 (2.8%)	
STS-PROM score	5.2 ± 3.1	4.6 ± 3.5	<0.001
< 4%	125 (38.2%)	207 (58.5%)	<0.001
4 - <8%	164 (50.2%)	108 (30.5%)	
≥ 8 %	38 (11.6%)	39 (11.0%)	
EuroSCORE II	5.2 ± 4.4	5.1±4.5	0.08
Mean pressure gradient, mm Hg	50.9 ± 15.2	46.2 ± 13.4	<0.001
Aortic valve area (cm^2)	0.7 ± 0.1	0.8 ± 0.2	<0.001
Left ventricular ejection fraction (%)	60.9 ± 9.6	55.7 ± 12.2	<0.001
Left ventricle ejection fraction <35 %	2 (0.7%)	23 (7.0%)	<0.001
Moderate or severe mitral regurgitation	49 (15.0%)	49 (14.0%)	0.72
Pulmonary artery pressure > 55mm Hg	37 (13.7%)	37 (14.0%)	0.92
Moderate or severe aortic regurgitation	26 (8.1%)	31 (9.1%)	0.64

Data presented as mean ± SD or number (%)

Other 1-year outcomes were similar between women and men: A similar number of women changed from ADL-i and ADL-d to living in an ACF at 1 year compared with men. There were no differences in valve parameters at post procedure; however, at 1 year of follow up, rates of ≧moderate paravalvular AR were higher amongst men compared with women (9.5% vs 5.1%, p = 0.05) and average MPG was lower in women (9.6 mm Hg vs 10.5 mm Hg, p = 0.007). Overall mortality rate was 36% (246) over a median follow up of 2.7 (IQR 1.7 to 4.2) years. Median time to death was 5.3 (95% CI 4.7 to 5.7) years. Long-term mortality was similar between genders (HR 0.91, 95% CI 0.71 to 1.17, p = 0.38; Kaplan-Meier survival analysis, Figure 1). Multivariable analysis, adjusting for age and co-morbidities, demonstrated that female gender was not an independent predictor for long-term mortality (HR 0.78, 95% CI 0.65 to 1.14, p = 0.2). On multivariable subgroup analysis of women only, STS-PROM score (HR 1.88, 95% CI 1.42 to 2.48, p < 0.001) was associated with increased long-term mortality (Table 4).

Analysis over time demonstrated a stable proportion of women who underwent TAVI during the study period. Total complication rates in women decreased from 46% in 2008 to 2013 to 34% in 2014 to 2018, however this did not reach statistical significance (OR 0.53, 95% CI 0.24 to 1.2, p = 0.12). The reason was predominantly a decrease in post-procedure PPM requirement over time (OR 0.54, 95% CI 0.29 to 0.99, p = 0.04). Mortality rates of women remained stable at 30 days (OR 0.85, 95% CI 0.17 to 4.29, p = 0.9) and 1 year (OR 0.79, 95% CI 0.32 to 1.96, p = 0.6) in the period of 2008 to 2013 compared with 2014 to 2018.

Discussion

To our knowledge, this is the first multi-centre registry to look at long-term outcomes extended to 10 years for women who underwent TAVI. Our major findings are: Peri-procedural major bleeding and 30-day mortality were higher in women compared with men, and female gender was an independent predictor of 1-year mortality. However, long-term mortality was similar in women and men (Figure 2).

Similar to previous studies, our findings identified that women were more likely to be frail and have fewer co-morbidities compared with men.[11,17] Despite less co-morbidities, women had higher STS-PROM scores, which likely reflects that this score includes female sex as a risk factor.

Table 2
Peri-procedural characteristics

	Women (n = 328)	Men (n = 355)	pValue
Access*			
Trans-femoral	300 (92.%)	337 (95%)	<0.001
Subclavian	7 (2.1%)	10 (2.8%)	
Direct-aortic	16 (4.9%)	4 (1.1%)	
Trans-apical	1 (0.3%)	1 (0.3%)	
Femoral cutdown	2 (0.6%)	3 (0.8%)	
Type of valve			
CoreValve	154 (47%)	165 (47%)	<0.001
Evolut R/Pro	123 (38%)	99 (28%)	
Sapien XT	19 (5.8%)	18 (5.1%)	
Sapien 3	15 (4.6%)	58 (16%)	
Other	17 (5.2%)	15 (4.2%)	
Valve size (mm)			
20−27	185 (57%)	59 (17%)	<0.001
29−34	142 (43%)	295 (83%)	
Valve in surgical valve	5 (1.5%)	15 (4.2%)	0.036
Intraprocedural valve failure requiring second valve	9 (2.7%)	21 (5.9%)	0.043
Intensive care unit admission	19 (6.1%)	13 (3.8%)	0.17
Length of stay (days)	5 [4−7]	5 [4−6]	0.75
Year of procedure			
2008−2012	72 (22%)	77 (22%)	0.93
2013−2018	256 (78%)	278 (78%)	
Pre-procedural CTA	280 (85%)	300 (85%)	0.99

CTA, Computed tomography angiography.
Data presented as number (%) or median [IQR].
* Subclavian, direct-aortic, trans-apical and femoral cutdown were combined for analysis and compared with trans-femoral.

Women in our cohort had higher rates of peri-procedural major bleeding. Previous reports have demonstrated conflicting results, with some studies demonstrating similar rates of bleeding between men and women[18] and other reports agrees with ours.[11,17,19] In our cohort, bleeding was due to access site vascular complications in 46% in women and in 50% in men. This is interesting, given the fact that the higher bleeding rates in women were often interpreted as a consequence of smaller femoral artery sizes in women,[20] leading to more vascular complications. Recently, multiple mechanisms have been proposed to be responsible for bleeding after TAVI, including intrinsic bleeding abnormalities that extend beyond just the platelet system.[21] They are therefore different from the ones seen in patients with coronary artery disease who underwent PCI, where bleeding complications are also higher in women.[22] It may be that sub analyses of data from the GALILEO study will give further insight into the question of which patients are at increased risk of bleeding post TAVI.[23] Major bleeding events have previously been associated with increased risk of mortality following TAVI.[7,18] In our cohort, women indeed had a higher 30-day mortality, which may partly be explained by the increased frequency of bleeding events. A further explanation could be that non trans-femoral, particularly a trans-aortic approach was utilised significantly more often in women, which is associated with higher short-term mortality.[24] Further, women not only have smaller femoral artery diameters, but are also known to have smaller mean aortic annulus diameters and lower coronary ostial heights.[20] This leaves women at increased risk of peri-procedural complications such as annular rupture, aortic dissection, and coronary occlusion.[7]

Women less often had ≧ moderate paravalvular aortic regurgitation compared with men at 1 year. This is likely

Table 3
In-hospital, 30-day, 1-year, and long-term outcomes

	Women n = 328	Men n = 355	OR	95% CI	p Value
In-hospital complications					
Myocardial Infarction	5 (1.5%)	4 (1.1%)	1.38	0.37−5.19	0.74
Cerebrovascular event	7 (2.1%)	4 (1.1%)	1.91	0.55−6.60	0.37
Major bleeding (3a, 3b, and 5)	11 (3.3%)	3 (1.0%)	4.21	1.16−15.2	0.03
Femoral access cohort only	9 (3.6%)	2 (0.7%)	5.25	1.12−24.5	0.03
Access site complications	27 (8.2%)	20 (5.6%)	1.49	0.82−2.73	0.19
Acute kidney injury stage 2 and 3	2 (0.6%)	4 (1.1%)	0.54	0.1−2.98	0.69
Need for permanent pacemaker	64 (19.5%)	86 (24.2%)	0.75	0.52−1.09	0.13
Mortality	6 (1.8%)	1 (0.2%)	6.53	0.78−54.4	0.061
30-day mortality (HR)*	8 (2.4%)	1 (0.3%)	8.75	1.09−69.6	0.02
30-day device success	289 (88.1%)	300 (84.5%)	1.38	0.89−2.15	0.15
	1-year outcomes†				
Mortality (HR)*	27/326 (8.3%)	27/344 (7.8%)	1.06	0.61−1.85	0.8
New aged care facility	13/194 (6.7%)	13/209 (6.2%)	1.08	0.49−2.40	0.84
Cerebrovascular event	8/191 (4.2%)	7/214 (3.3%)	1.29	0.46−3.63	0.67
Hospitalizations for valve-related symptoms or heart failure	27/194 (13.9%)	34/212 (16.0%)	0.85	0.49−1.46	0.55
Left ventricle ejection fraction, %	60.5±8.4	56.1±10.6			<0.001
≥ Moderate paravalvular aortic regurgitation	14 (5.1%)	27 (9.5%)	0.52	0.26−1.01	0.049
Mean pressure gradient, mm Hg	9.6 ± 4.14	10.5 ± 4.61			0.007
Long-term mortality (HR)*			0.91		0.38

HR, Hazard ratio; OR, Odds ratio.
Data displayed as number (%) or mean±SD.
* Mortality is displayed as hazard ratio, proportional hazard assumption tested and met.
† For 1-year outcomes, numbers are displayed as ratios with number of patients having complete follow up in the denominator.

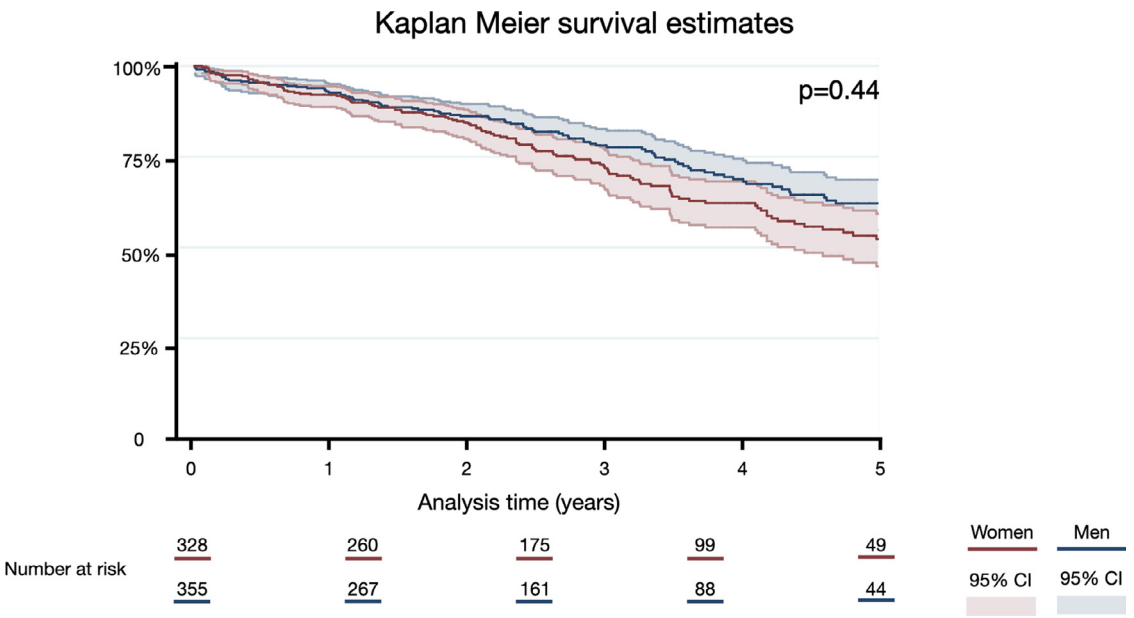

Figure 1. Kaplan-Meier survival analysis showing similar long-term mortality between genders out to 10-year follow up (HR 0.91, 95% CI 0.71 to 1.17, p = 0.38).

Table 4
Predictors of long-term mortality

	Univariate Cox regression						Final multivariate Cox regression					
	Entire cohort			Female cohort			Entire cohort			Female cohort		
	HR	95% CI	p-Value	HR	95% CI	p-Value	HR	95% CI	p-Value	HR	95% CI	p-Value
Female gender	0.91	0.71−1.17	0.48	NA	NA	NA	0.78	0.54−1.14	0.20	NA	NA	NA
Frailty score	1.32	1.08−1.60	0.006	1.21	0.92−1.58	0.17	1.74	1.21−2.51	0.003			
Pre-procedural eGFR, per 10 ml/min/1.73m2 increase	0.88	0.82−0.95	<0.001	0.88	0.79−0.98	0.016	0.98	0.88−1.10	0.73	0.95	0.80−1.12	0.54
Atrial fibrillation	1.66	1.28−2.15	<0.001	1.54	1.04−2.27	0.030	3.49	1.81−6.72	<0.001	1.55	0.80−2.99	0.19
STS-PROM score, per 1 level increase (<4%, 4%−8%, >8%)	1.69	1.41−2.02	<0.001	1.74	1.32−2.30	<0.001	1.44	1.12−1.85	0.004	1.88	1.42−2.48	<0.001
LV-EF (per 10% increase)	0.82	0.74−0.92	<0.001	0.82	0.68−1.00	0.05	0.84	0.74−0.92	0.026			

eGFR, estimated glomerular filtration rate; LV-EF, left ventricular ejection fraction.

Variables included in the univariable and multivariable models were gender, frailty score, preprocedural estimated glomerular filtration rate, atrial fibrillation, STS-Score, left ventricular ejection fraction, previous coronary artery bypass grafting and percutaneous coronary intervention, previous cerebrovascular and peripheral vascular disease, coronary artery disease, diabetes mellitus, chronic obstructive pulmonary artery disease, aortic valve area and mean pressure gradient, ≥ moderate mitral regurgitation, systolic pulmonary artery pressure (per 10mm Hg increase), year of procedure, access type (not femoral transcutaneous), transcatheter aortic valve size, balloon-expandable valves (versus self-expandable valve)

reflective of the smaller aortic annulus sizes in women in which valve oversizing is more common.[11] Conduction disturbances requiring PPM occurred at a similar rate in both groups. This was despite significantly more men having undergone previous PPM and women more often receiving self-expanding valves, which has previously been associated with increased risk for PPM insertion.[25] An explanation for this finding could be the lower rate of co-morbidities in the female cohort.

Female gender was an independent predictor of 1-year mortality in the multivariate analysis. However, there was no gender difference in long-mortality out to 10-year follow up. Earlier studies identified higher survival rates for women compared with men[7,26] and more recent studies demonstrated no gender difference in mortality rates during follow up ≧1 year.[9,11] The comparison of these show that earlier studies[7] included predominantly high risk patients (STS-score ≧8) whereas contemporary studies[9] included more low and intermediate risk patients. A further difference is that more contemporary studies included pre-procedural assessment by CTA and introduction of the 29mm Edwards Sapien S3 valve, which seem to have benefitted men more than women.[7,9] The lack of worse outcome in women ≧1 year of follow up is likely due to the lower rates of co-morbidities, which ameliorate the higher complication rate at the time of valve implantation. In comparison to the entire cohort, the only predictor for higher long-term mortality in the female cohort after multivariate adjustment was an increase in STS-PROM score.

Our analysis over time showed that complication rates in women decreased numerically over time. This was predominantly driven by a reduction in PPM. Overall increasing

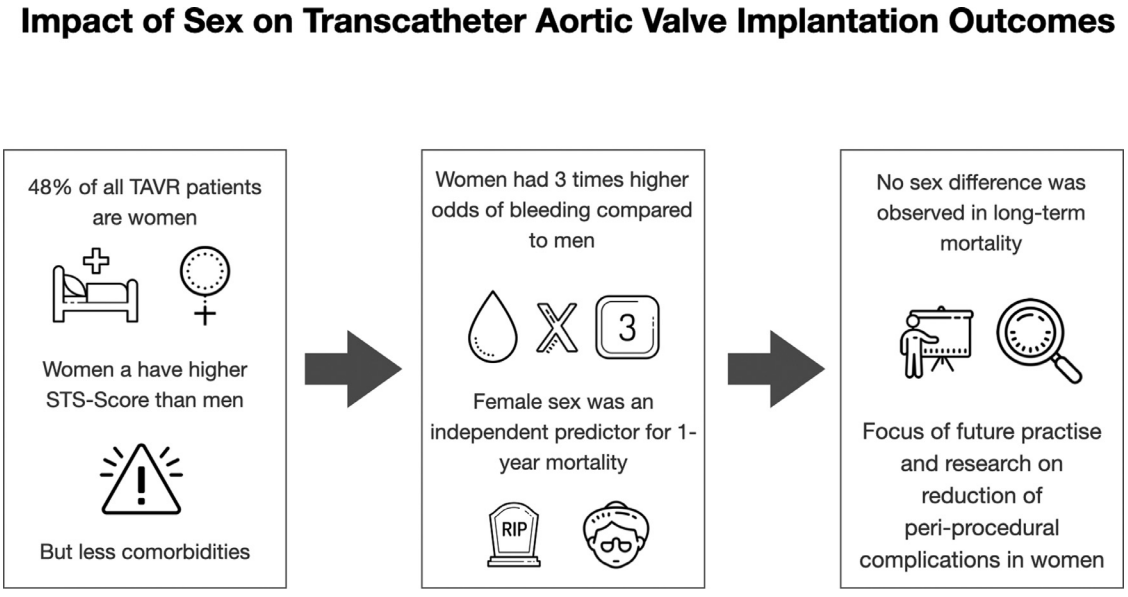

Figure 2. Central illustration summarizing the main findings of the study.

centre and operator experience and advancement in valvular and sheath technology are likely all contributors to these findings.

The major strength of our study is the long-term follow up out to 10 years. Important limitations are those inherent to the observational design, including the possibility of unmeasured confounders. Data presented in this study spans 10 years of TAVI experience, and includes both early and more contemporary practice. Therefore, results include a combination of both new and older technology and evolving degree of operator experience, which may impact outcomes, however the relatively small sample size does not allow for meaningful subgroup analyses. Lastly, despite the follow-up out to 10 years, the median follow-up is only 2.7 years, which is due to the larger numbers of patients who underwent TAVI in most recent years and therefore shorter follow-up compared with patients who underwent TAVI at the beginning of our program.

Although women had higher rates of peri-procedural major bleeding and 30-day mortality, other adverse outcomes were similar between women and men. The mortality difference seen at 30 days did not persist at follow up $\geqq$1 year, with similar rates of mortality out to 10 years. The increased rate of major bleeding and higher STS score at time of valve implantation is likely ameliorated by the lower rates of other co-morbidities amongst women that are not measured in the STS-PROM score, which potentially evens out the mortality risk between genders. As valvular technology improves and patient cohorts become more diverse, the role of gender on outcomes will continue to be dynamic. Reduction of peri-procedural complications, including major bleeding for women, should be a focus of future developments.

Author contributions

JS, MD, SD: Conceptualization. EQ, CC and MD: Data curation. NG and MD: Formal analysis. JQSK: Investigation. JS and SN: Methodology. NH and RD: Project administration. AW and RD: Resources. SD and SZ: Supervision. JS and MD: Writing - original draft. JS, MD, SD, DS and AW: Writing - review & editing.

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Disclosures

The authors have nothing to disclose.

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