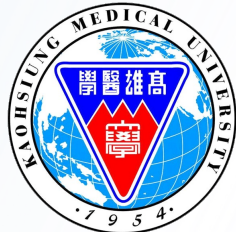


Female Showed Favorable Left Ventricle Hypertrophy Regression During Post-TAVR Follow-up



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Introduction

- Aortic stenosis (AS) is the most common acquired valvular heart disease in addition to degenerative mitral valve regurgitation in developed countries.
- Transcatheter aortic valve replacement (TAVR) is a well-established procedure for patients with severe aortic stenosis (AS).
- In Taiwan, TAVR was introduced in 2010 and has become a procedure included in the National Health Insurance reimbursement.
- Sex differences exist in procedural adverse events post-TAVR, with women more commonly having vascular complications; while thirty-day stroke and mortality rates are similar in both sexes.
- We hypothesized a sex difference in cardiac remodeling in patients who underwent TAVR.
- This study investigated sex-related differences in pre- and post-TAVR clinical and hemodynamic outcomes of the first 100 cases at Kaohsiung Medical University Chung-Ho Memorial Hospital (KMUH).

Methods

- Baseline characteristics, procedural outcomes and echocardiographic parameters were assessed between male and female patients.
- The cardio function parameters over time and temporal trends were demonstrated using scatter plots and non-linear fits.
- The generalized linear mixed model (GLMM) was adopted in the study for the assessment of the effect of sex on time-changeable cardiac function of the echocardiologic parameters throughout the pre- and post-TAVR periods, demonstrating in box plots.
- The Kaplan-Meier survival analysis was used to estimate the cumulative survival proportion during post-TAVR follow-up.

Results

- The baseline characteristics are summarized in **Table 1**. Men (n= 46) and women (n=54) had similar age (86.0 ± 6.4 years for men and 84.5 ± 5.8 years for women respectively).
- The devices used for TAVR and procedure-related parameters are listed in **Table 2**. Vascular complications were defined according to the VACR III criteria and occurred without disparity between sexes (men, 6.5% vs. women, 5.6%; $P=0.2165$).
- The hemodynamic parameters before and after TAVR are shown in **Figure 1**. The improvement in LV systolic function was significant for both men and women, and women showed better improvement than men (**Figure 1D**).
- A statistical method of mixed model analysis was conducted using women as the reference/control group (**Table 3**). Notably, the mean AV area and LVEDV were significantly larger in men ($+0.1548 \text{ cm}^2$ and $+39.77 \text{ mL}$ for men, respectively) (**Figure 2A,2E**). In contrast, women showed significantly better improvement in LVEF than men (**Figure 2F**).
- The cumulative 1-year, 2-year, and 5-year survival rates were higher in women (94.0, 88.8, and 65.4%, respectively) than in men (89.1, 83.9, and 46.8%, respectively) (**Figure 3A**). The largest disparity occurred in the fifth year, as the survival rate of men dropped below 50%, whereas that of women remained above 50% (**Figure 3B**).

Table 1. Clinical and echocardiographic parameters prior to TAVR

Parameters	All patients (n=100)	Men (n= 46)	Women (n= 54)	P value
Demographics, comorbidities, and clinical parameters				
Age†	85.2 ± 6.1	86.0 ± 6.4	84.5 ± 5.8	0.2367
Height (m) †	1.56 ± 0.08	1.62 ± 0.06	1.50 ± 0.06	0.3947
Weight (kg) †	58.8 ± 11.5	61.9 ± 11.6	56.1 ± 10.7	0.3947
Body mass index† (Kg/m2)	24.2 ± 4.3	23.5 ± 3.9	24.8 ± 4.5	0.4012
NYHA class, n (%)				0.6405
III	54 (54.0)	26 (56.5)	28 (51.9)	
IV	46 (46.0)	20 (48.1)	26 (48.1)	
Hypertension, n (%)	82 (82.0)	33 (71.7)	49 (90.7)	p<0.05*
Diabetes mellitus, n (%)	44 (44.0)	20 (43.5)	24 (44.4)	0.923
Atrial fibrillation, n (%)	23 (23.0)	11 (23.9)	12 (22.2)	0.8413
CKD stage 3–5, n (%)	41 (41.0)	22 (47.8)	19 (35.2)	0.2002
History of MI, n (%)	22 (22.0)	11 (23.9)	11 (20.4)	0.6700
Previous PCI, n (%)	33 (33.0)	16 (34.8)	17 (31.5)	0.7264
Previous CABG, n (%)	4 (4.0)	3 (6.5)	1 (1.9)	1.00‡
Previous Stroke/TIA, n (%)	11 (11.0)	6 (13.0)	5 (9.3)	0.5467
Pacemaker, n (%)	5 (5.0)	1 (2.2)	4 (7.4)	0.2314
Logistic EuroSCORE I † (%)	29.1 ± 12.8	29.2 ± 13.1	29.0 ± 12.7	0.9269
AR before				p < 0.05*
0	21 (21.0)	10 (22.2)	11 (21.6)	
1	38 (38.0)	11 (24.4)	27 (52.9)	
2	31 (31.0)	19 (42.2)	12 (23.5)	
3	6 (6.0)	5 (11.1)	1 (2.0)	
STS score† (%)	17.4 ± 13.7	18.5 ± 14.6	16.6 ± 12.9	0.4928
Echocardiographic parameters				
AV mean PG† [mmHg]	46.4 ± 17.8	47.5 ± 16.0	45.7 ± 19.2	0.0615
AV area† (Continuity Equation VTI) [cm2]	0.8 ± 0.3	0.8 ± 0.3	0.7 ± 0.2	p < 0.05*
AV area index (cm2/m2)	0.5 ± 0.2	0.5 ± 0.1	0.5 ± 0.2	0.8226
LVEF† (Simpson’s method) [%]	57.1 ± 16.0	54.7 ± 17.2	59.6 ± 14.0	p < 0.01**
LV mass (g)	305.3 ± 87.2	323.9 ± 89.1	278.3 ± 78.1	p < 0.001***
LV mass index† (g/m2)	180.5 ± 56.8	188.8 ± 60.0	175.2 ± 52.7	0.2432

AV, aortic valve; CABG, coronary artery bypass graft; CKD, chronic kidney disease; LVEF, left ventricle ejection fraction; MI, myocardial infarction; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; STS, Society of Thoracic Surgeons; PG, pressure gradient; TIA, transient ischemic attack. Statistical significance is presented as P< 0.05*, P< 0.01**, and P< 0.001***.

Table 2. The device and procedures-related parameters of TAVR

Parameters	All patients (n=100)	Men (n= 46)	Women (n= 54)	P value
Self-expanding valve, n (%)	75 (75.0)	36 (78.3)	39 (72.2)	0.3700
Balloon-expandable valve, n (%)	26 (26.0)	10 (21.7)	16 (29.6)	0.4870
Second valve, n (%)	11 (11.0)	6 (13.0)	5 (9.3)	0.5467
Prosthesis size [mm]	26.4 ± 2.7	28.0 ± 1.9	25.0 ± 2.4	p < 0.001***
AR or PVL after				0.6188
0	9 (9.0)	3 (6.8)	6 (11.3)	
1	71 (71.0)	33 (75.0)	38 (71.7)	
2	16 (16.0)	7 (15.9)	9 (17.0)	
3	1 (1.0)	1 (2.3)	0 (0.0)	
MR before				0.3470
0	14 (14.0)	4 (8.9)	10 (19.6)	
1	42 (42.0)	22 (48.9)	20 (39.2)	
2	36 (36.0)	18 (40.0)	18(35.3)	
3	4 (4.0)	1 (2.2)	3 (5.9)	
MR after				0.3578
0	2 (2.0)	0 (0.0)	2 (3.7)	
1	65 (65.0)	32 (72.7)	33 (61.1)	
2	30 (30.0)	12 (27.3)	18 (33.3)	
3	1 (1.0)	0 (0.0)	1 (1.9)	
Vascular complications, n (%)	6 (6.0)	3 (6.5)	3 (5.6)	0.2165
Major, n (%)	4 (4.0)	3 (6.5)	1(1.9)	
Minor, n (%)	2 (2.0)	0 (0.0)	2 (3.7)	
Pacemaker rates, n (%)	7 (7.0)	3 (6.5)	4 (7.4)	0.8626

AR, aortic regurgitation; PVL, paravalvular leak; MR: mitral regurgitation; Statistical significance is presented as P< 0.05*, P< 0.01**, and P< 0.001***.

Table 3. Estimated values of echocardiologic parameters by mixed model

		Estimate	95 % CI Lower	95 % CI Upper	P-value
AV area, cm ²	Women	0 [reference]			
	Men	0.15	0.02	0.29	p < 0.05*
AV area index, cm ² /m ²	Women	0 [reference]			
	Men	0.01	0.02	0.29	0.8478
AV mean PG, mmHg	Women	0 [reference]			
	Men	-2.3	-4.60	0.08	0.059
AV peak PG, mmHg	Women	0 [reference]			
	Men	-3.56	-7.27	0.15	0.061
E/E' (lat.)	Women	0 [reference]			
	Men	-3.56	-7.27	0.15	0.061
E/E' (med.)	Women	0 [reference]			
	Men	-3.56	-7.27	0.15	0.061
LV mass, g	Women	0 [reference]			
	Men	62.36	36.42	88.29	p < 0.001***
LV mass index, g/m ²	Women	0 [reference]			
	Men	25.79	41.61	9.98	p < 0.05*
LVEF, %	Women	0 [reference]			
	Men	-8.83	-12.72	-4.93	p < 0.001***
IVS, cm	Women	0 [reference]			
	Men	0.07	-0.02	0.15	0.137
LVPWd, cm	Women	0 [reference]			
	Men	0.03	-0.03	0.09	0.329
LVEDV, mL	Women	0 [reference]			
	Men	39.77 ± 6.08	27.85	51.69	p < 0.001***
LVEDD, cm	Women	0 [reference]			
	Men	0.60	0.37	0.83	p < 0.001***
LAD, cm	Women	0 [reference]			
	Men	-0.07	-0.31	0.17	0.588
TR peak PG, mmHg	Women	0 [reference]			
	Men	-0.97	-3.47	1.53	0.448

AV, aortic valve area; PG, pressure gradient; IVS, interventricular septum, LVPWd, left ventricular poster wall diameter, LVEDV, left ventricular end diastolic volume; LVEDD, left ventricular end diastolic diameter; LAD, left atrial dimension; TRPPG, tricuspid valve regurgitation pressure gradient; Statistical significance is presented as P< 0.05*, P< 0.01**, and P< 0.001***.

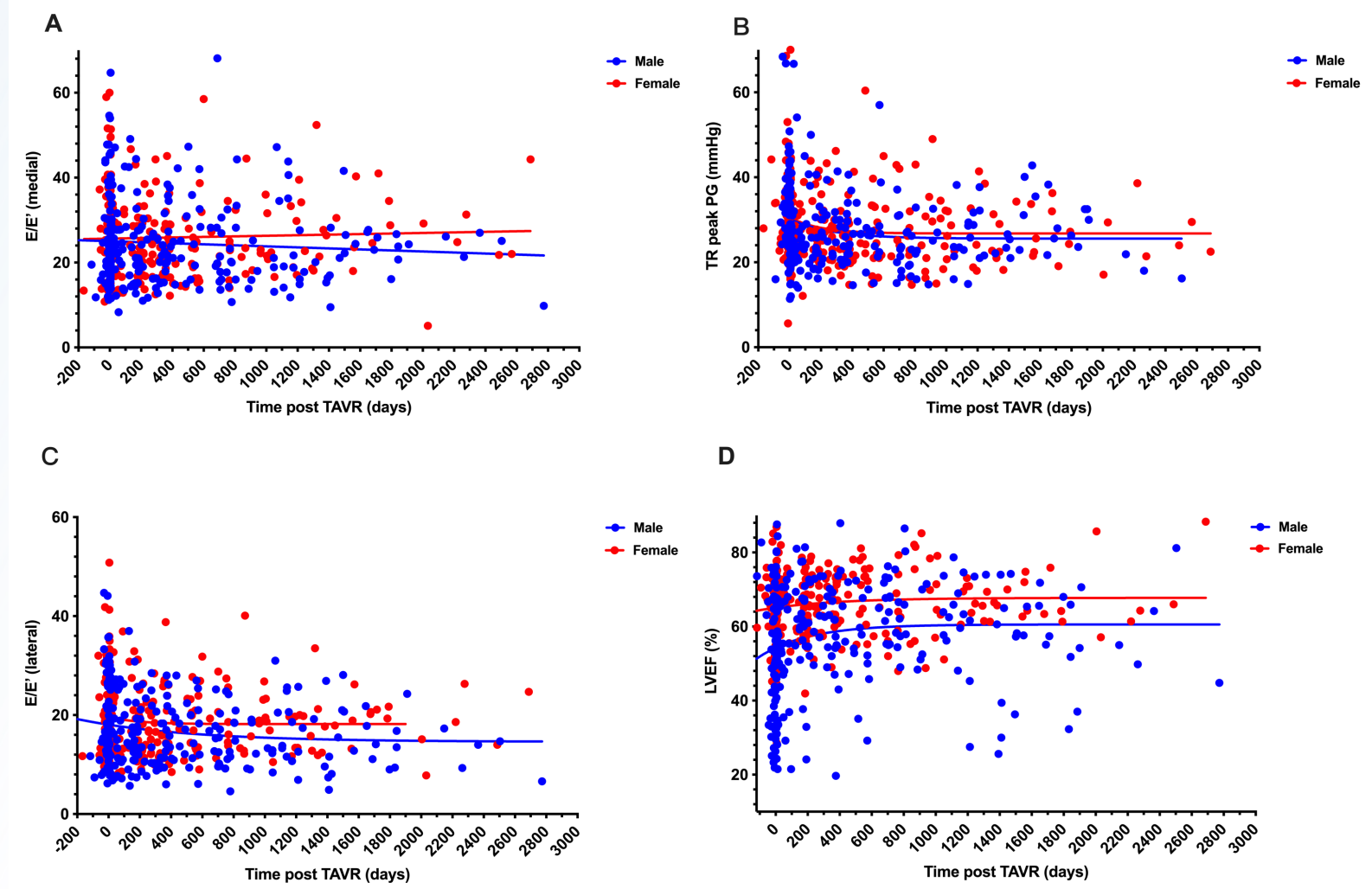


Figure 1. Changes in hemodynamic parameters after transcatheter aortic valve replacement. Blue points and line for the male; Red points and pink line for the female. LVEF, left ventricular ejection fraction; TR, tricuspid regurgitation; E/E', ratio of mitral E flow velocity to tissue Doppler mitral ring velocity.

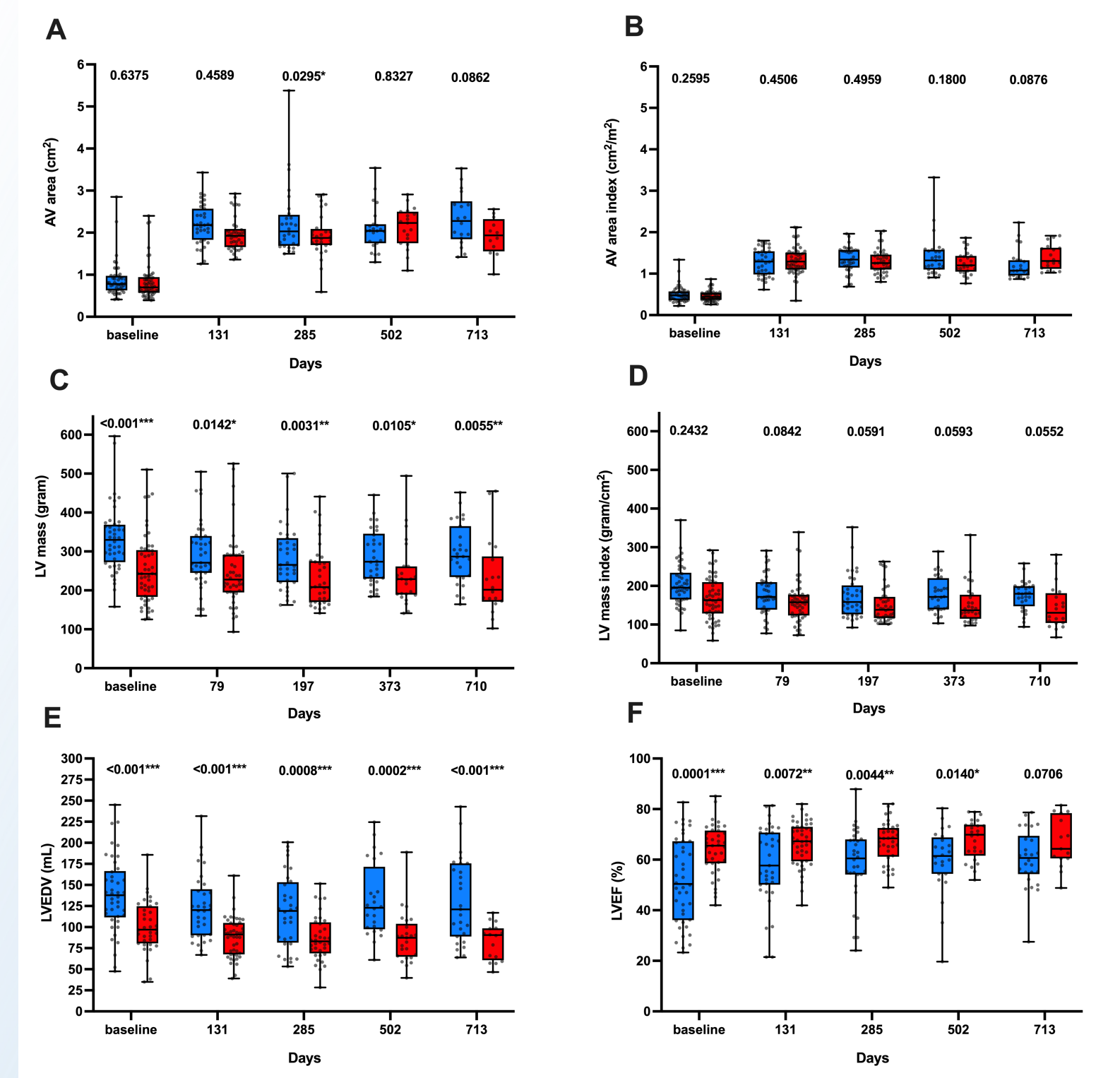


Figure 2. Changes in echocardiographic parameters from baseline to post-TAVR follow-up. Male in blue and female in red. The days indicate the post-TAVR medium follow-up time. The P values of each pair comparison are labeled at the top of all the histograms. AV, aortic valve; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction.

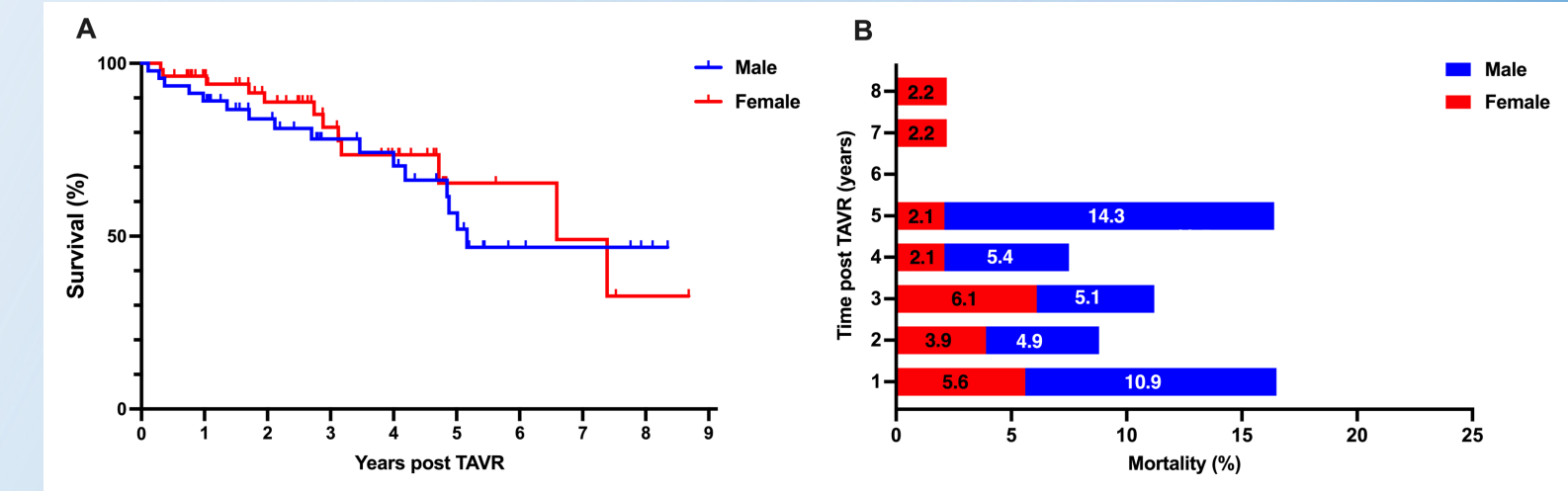


Figure 3. Clinical outcomes of 8.3 years in male and female TAVR patients. (A) Cumulative survival after TAVR. (B) Mortality in both sexes within each year. Male in blue and female in red.

Conclusions

- TAVR is a reliable procedure with exceptional outcomes for those with severe AS and have high risks for conventional SAVR.
- Sex-related differences exist after TAVR by measuring echocardiographic parameters, suggesting that women had better LVEF and LVMI than men.
- The clinical outcome demonstrated that there were no differences but a favorable influence on the overall survival of women.