



# Il "continuum cardiovascolare" nel genere femminile: tappe di vita, malattia e cura

## Donna e malattia degenerativa valvola aortica

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Eur Heart J. 2003 Jul;24(13):1231-43.

## **A prospective survey of patients with valvular heart disease in Europe: The Euro Heart Survey on Valvular Heart Disease.**

Iung B<sup>1</sup>, Baron G, Butchart EG, Delahaye F, Gohlke-Bärwolf C, Levang OW, Tornos P, Vanoverschelde JL, Vermeer F, Boersma E, Ravaud P, Vahanian A.

Severe aortic stenosis is the commonest form of valvular abnormality in the developed world and accounts for 40% of patients with native valvular disease with an approximately **equal prevalence in males and females**

# Trends of Hospitalizations in the United States from 2000 to 2012 of Patients >60 Years With Aortic Valve Disease



Table 1  
Hospitalization for aortic valve disorders in US from 2000-2012 (ICD-9 code 424.1)

Demographic Variables	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	Total	P-value for Trend
<b>Total No. of Observations (&gt;60 yrs age) with AV Disorders</b>	7,213	7,905	7,830	7,881	7,696	7,546	8,267	7,931	8,950	10,539	8,895	11,663	11,531	113,847	<0.001
<b>Age (years)</b>															
60-69	23.4%	22.1%	23.1%	24.3%	24.0%	24.4%	24.0%	24.4%	24.1%	25.0%	24.9%	24.2%	23.4%	24.0%	<0.001
70-79	44.3%	44.5%	43.8%	41.1%	40.9%	40.6%	41.7%	39.0%	37.2%	38.0%	35.9%	35.1%	34.6%	39.3%	<0.001
>80	32.3%	33.4%	33.1%	34.6%	35.1%	35.1%	34.3%	36.6%	38.7%	37.0%	39.2%	40.8%	42.1%	36.7%	<0.001
<b>Sex</b>															
Male	53.6%	52.8%	53.6%	53.9%	54.7%	55.4%	54.6%	56.4%	55.5%	56.7%	56.3%	55.4%	56.0%	55.1%	<0.001
Female	46.4%	47.2%	46.4%	46.1%	45.3%	44.6%	45.4%	43.6%	44.5%	43.3%	43.7%	44.6%	44.0%	44.9%	<0.001
<b>Race</b>															
Non-hispanic Whites	69.0%	65.5%	60.6%	62.3%	64.9%	64.1%	65.3%	66.6%	69.7%	68.6%	74.7%	77.6%	79.1%	69.0%	<0.001
Others	9.0%	10.1%	10.0%	10.7%	9.4%	9.7%	10.4%	12.0%	11.8%	12.3%	12.8%	14.2%	14.9%	11.6%	<0.001
Missing	22.1%	24.4%	29.4%	27.0%	25.7%	26.3%	24.2%	21.4%	18.5%	19.1%	12.5%	8.2%	6.0%	19.4%	<0.001

**Among 113 847 patients admitted with an aortic valve disorder diagnosis in the United States, 44,9% were female**



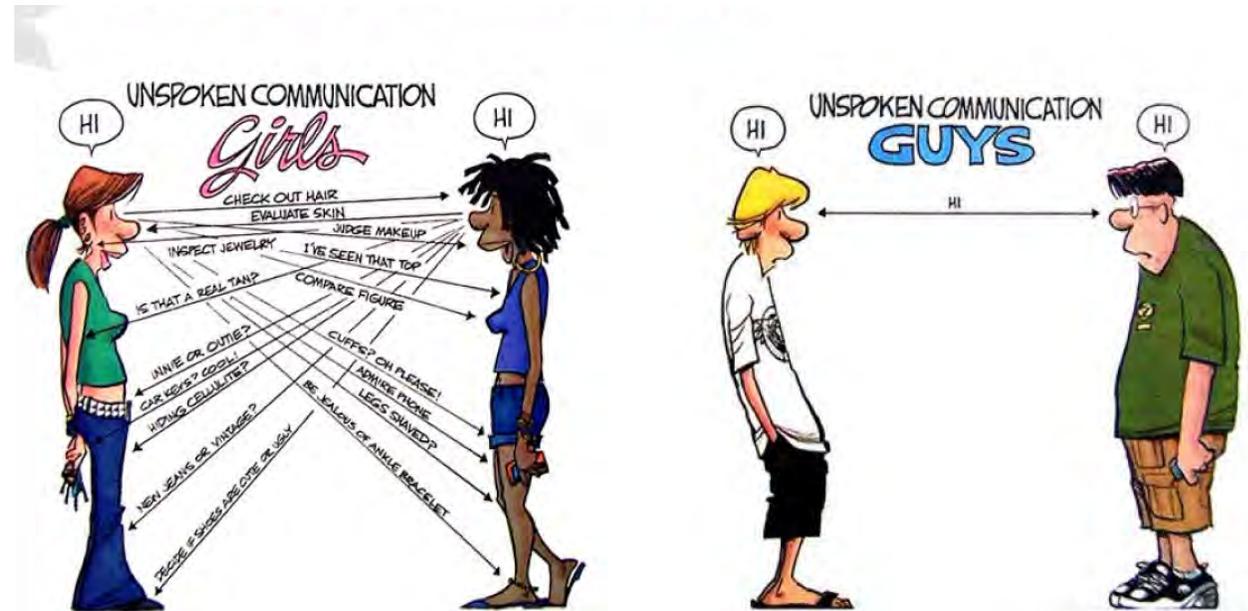
WE HAVE STUDIES OF FRUIT FLIES, MICE,  
HAMSTERS, FROGS, MONKEYS AND MEN  
WITH THIS CONDITION - BUT MEDICAL  
RESEARCH USING WOMEN AS SUBJECTS  
JUST NEVER OCCURRED TO ANYBODY.

# Gender differences

le malattie delle donne sono diagnosticate e trattate sulla base di modelli clinici studiati sugli uomini??????



diverso modo di vedersi



diverso modo di comunicare

# Prevalence, Referral Patterns, Testing, and Surgery in Aortic Valve Disease: Leaving Women and Elderly Patients Behind?

Treatment	Female gender	Male gender	p-value
Diagnosed patients (age ≥65)	73,674	54,550	
Specialist visit (%)	85.4	88.0	<0.001
Echocardiogram (%)	84.3	84.8	0.01
Stress test (%)	25.1	33.0	<0.001
AVR	1.4	2.7	<0.001

**Female gender is associated with lower rates of specialist visits, diagnostic testing, and AVR**

AVR: Aortic valve replacement.

Treatment	Female gender			Male gender		
	Age 65-79 years	Age ≥80 years	p-value	Age 65-79 years	Age ≥80 years	p-value
Diagnosed patients (age ≥65)	42,316	31,358		37,300	17,250	
Specialist visit (%)	85.9	84.8	<0.001	88.0	87.7	0.32
Echocardiogram (%)	85.2	83.0	<0.001	84.7	84.9	0.62
Stress test (%)	31.3	16.9	<0.001	37.3	23.6	<0.001
AVR (%)	1.9	0.8	<0.001	3.2	1.6	<0.001

AVR: Aortic valve replacement.

# Prevalence, Referral Patterns, Testing, and Surgery in Aortic Valve Disease: Leaving Women and Elderly Patients Behind?

Table VI: Multivariate logistic models for the association of gender and age group with treatment of aortic valve disease.

Variable	Specialist visit		Echocardiogram		Stress test		AVR	
	OR (95% CI)	p-value						
Female	0.74 (0.72-0.76)	<0.001	0.93 (0.9-0.96)	<0.001	0.68 (0.66-0.7)	<0.001	0.5 (0.46-0.54)	<0.001
Age ≥80 years	0.83 (0.81-0.86)	<0.001	0.82 (0.8-0.85)	<0.001	0.48 (0.47-0.49)	<0.001	0.39 (0.36-0.43)	<0.001
Angina	2.37 (2.3-2.44)	<0.001	1.45 (1.4-1.49)	<0.001	3.57 (3.46-3.67)	<0.001	1.86 (1.69-2.04)	<0.001
Heart failure	1.77 (1.72-1.83)	<0.001	1.55 (1.49-1.61)	<0.001	0.7 (0.68-0.72)	<0.001	3.3 (3.02-3.62)	<0.001
Syncope	1.4 (1.36-1.45)	<0.001	1.37 (1.32-1.42)	<0.001	1.02 (0.99-1.05)	0.21	0.95 (0.87-1.04)	0.28
Dyspnea	1.56 (1.52-1.61)	<0.001	1.58 (1.52-1.63)	<0.001	1.31 (1.28-1.35)	<0.001	2.17 (1.98-2.39)	<0.001
CCI	1.04 (1.03-1.04)	<0.001	0.97 (0.96-0.97)	<0.001	0.97 (0.96-0.97)	<0.001	0.71 (0.7-0.73)	<0.001

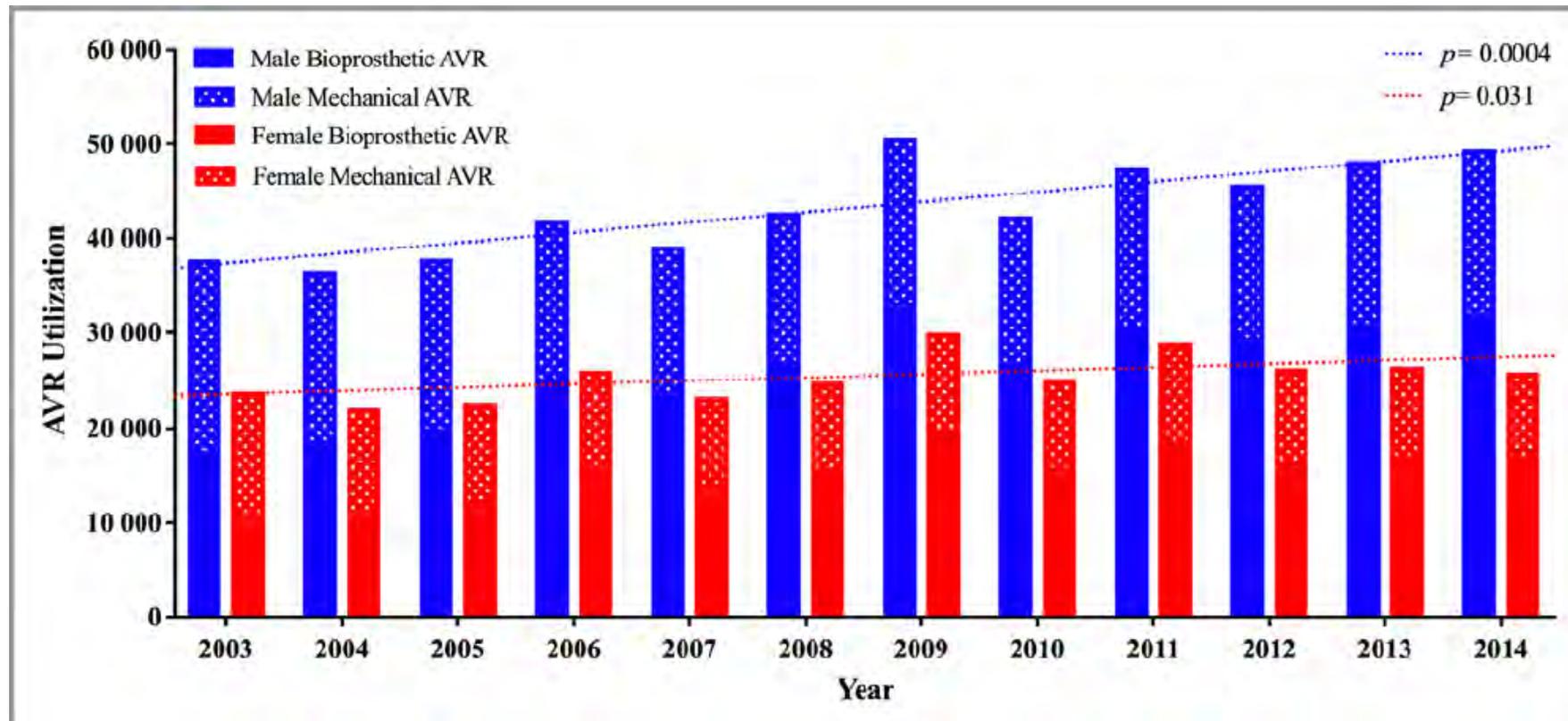
AVR: Aortic valve replacement; CCI: Charlson Comorbidity Index; CI: Confidence interval; OR: Odds ratio.

## Sex Differences in the Utilization and Outcomes of Surgical Aortic Valve Replacement for Severe Aortic Stenosis

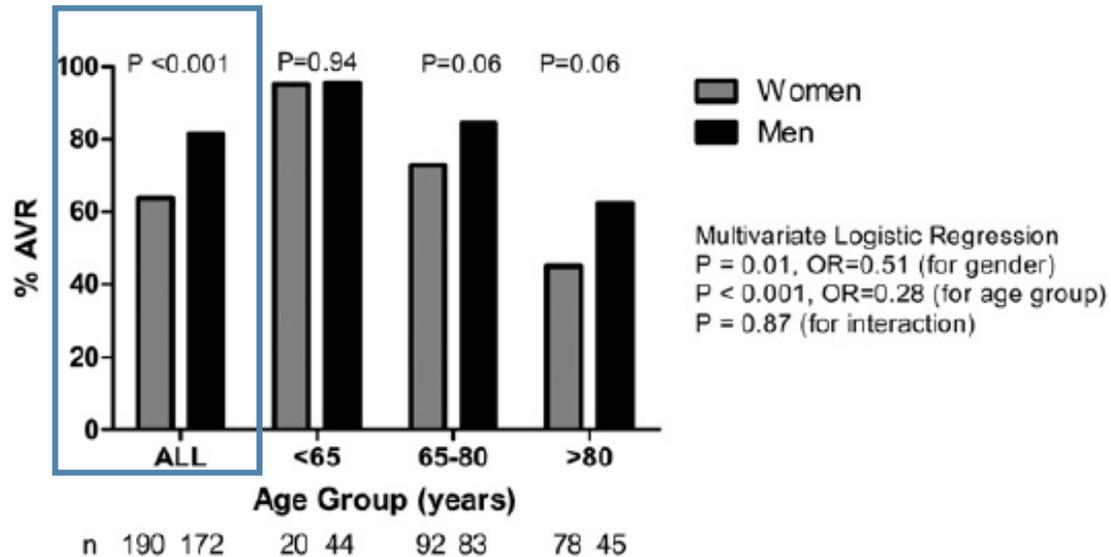
Zakeih Chaker, MD; Vinay Badhwar, MD; Fahad Alqahtani, MD; Sami Aljohani, MD; Chad J. Zack, MD; David R. Holmes, MD; Charanjit S. Rihal, MD; Mohamad Alkhouli, MD

166.890 pts  
underwent AVR

higher utilization of AVR in men compared with women



# Effect of Gender on Treatment and Outcomes in Severe Aortic Stenosis



## Independent predictors of undergoing aortic valve replacement

Variable	Odds Ratio (95% confidence interval)	p Value
Age	0.87 (0.83–0.91)	<0.001
Chest pain	2.34 (1.11–4.94)	0.03
New York Heart Association class (every class decrease)	1.66 (1.21–2.28)	0.002
Absence of previous myocardial infarction	2.85 (1.31–6.19)	0.008
Absence of chronic renal insufficiency	2.48 (1.25–4.90)	0.010
Absence of cancer	7.88 (2.35–26.5)	0.001
Aortic valve mean gradient (every 10-mm Hg increase)	1.34 (1.05–1.71)	0.018
Male gender	2.08 (1.13–3.81)	0.018

# Gender differences in clinical presentation

## AVR patients

**Table 1** Baseline clinical characteristics

	All patients n = 408	Women n = 215, 53%	Men n = 193, 47%	p Value
<b>Demographic data</b>				
Age, years	70.3 ± 10.7	73.7 ± 9.3	66.5 ± 11.0	<0.001
Age >75 years	152 (37.3)	104 (48.4)	48 (24.9)	<0.001†
Body mass index, kg/m <sup>2</sup>	27.3 ± 4.5	27.3 ± 5.1	27.3 ± 3.8	0.926
Body surface area, m <sup>2</sup>	1.87 ± 0.21	1.77 ± 0.20	1.99 ± 0.17	<0.001
<b>Clinical data</b>				
NYHA functional class, mean ± SD	2.1 ± 0.7	2.3 ± 0.7	2.0 ± 0.7	<0.001‡
Class I	74 (18.2)	30 (14.0)	44 (23.0)	
Class II	208 (51.2)	97 (45.1)	111 (58.1)	
Class III	123 (30.3)	87 (40.5)	36 (18.9)	
Class IV	1 (0.3)	1 (0.5)	0 (0.0)	
CCS class, mean ± SD	1.5 ± 0.7	1.6 ± 0.7	1.5 ± 0.6	0.043†
CCS ≥ III	40 (9.9)	27 (12.6)	13 (6.8)	
Presyncope	12 (2.9)	9 (4.2)	3 (1.6)	0.116†
Syncope	60 (14.7)	35 (16.3)	25 (13.0)	0.344†
Dizziness during exercise	57 (14.0)	39 (18.4)	18 (9.3)	0.010†
EuroSCORE	6.5 ± 2.6	7.3 ± 2.3	5.5 ± 2.6	<0.001
Creatinine, mmol/l	1.11 ± 0.47	1.09 ± 0.57	1.13 ± 0.31	0.035*

# Gender differences in clinical presentation

## TAVI patients

Table 1  
Characteristics of the study population

	Women (n = 423)	Men (n = 487)	p
<b>Baseline characteristics</b>			
Age (years)	82.0 ± 7.6	80.9 ± 8.4	0.051
Body Mass Index (Kg/m <sup>2</sup> )	28.7 ± 16.2	27.5 ± 5.8	0.115
Body Surface Area (m <sup>2</sup> )	1.75 ± 0.22	2.02 ± 0.21	<0.0001
Society of Thoracic Surgery Risk Score (%)	7.9 ± 3.7	7.1 ± 4.0	0.007
Hypertension	367 (88.0%)	401 (82.9%)	0.030
Hyperlipidemia	301 (72.7%)	359 (74.8%)	0.479
Diabetes mellitus	151 (37.7%)	194 (42.0%)	0.195
Chronic kidney disease	188 (45.0%)	229 (47.6%)	0.430
End stage renal disease	10 (2.6%)	16 (3.6%)	0.376
↓ Coronary artery disease	263 (63.1%)	360 (74.7%)	<0.0001
Peripheral artery disease	118 (29.4%)	163 (35.3%)	0.067
Chronic obstructive pulmonary disease	85 (21.9%)	98 (21.9%)	0.993
↓ Atrial fibrillation	115 (27.2%)	155 (31.8%)	0.259
↓ Previous coronary bypass/percutaneous coronary intervention	147 (36.8%)	265 (56.9%)	<0.0001
Previous cerebrovascular accident	81 (20.7%)	88 (19.8%)	0.749
Permanent pacemaker	69 (16.4%)	103 (21.6%)	0.050

# Acute and 30-Day Outcomes in Women After TAVR

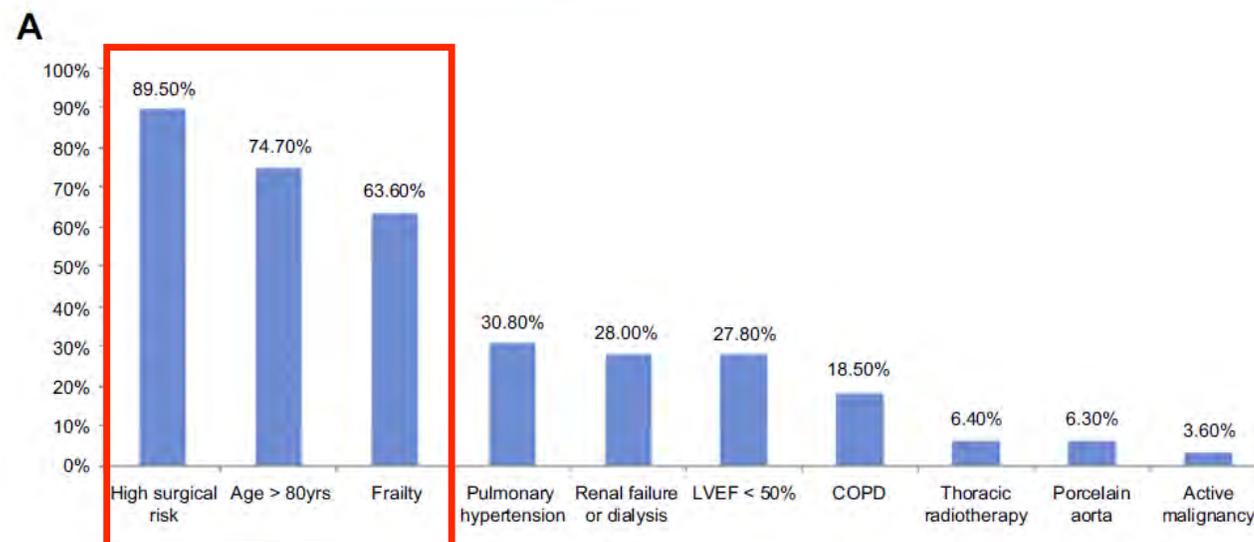


## Results From the WIN-TAVI (Women's International Transcatheter Aortic Valve Implantation) Real-World Registry

**TABLE 1** Baseline Characteristics (N = 1,019)

Age, yrs	82.5 ± 6.3
Caucasian	976 (95.8)
Body mass index, kg/m <sup>2</sup>	26.0 ± 5.5
Hypertension	819 (81.7)
Diabetes mellitus	264 (26.1)
Current smoker	33 (3.3)
Prior myocardial infarction	98 (9.6)
Prior PCI	233 (22.9)
PCI within 30 days of TAVR	58 (24.9)
Prior CABG	63 (6.2)
Prior other cardiac surgery	117 (11.6)
Prior aortic valve procedure	68 (6.8)
Prior TAVR	4 (5.9)
Atrial fibrillation on baseline electrocardiography	200 (19.6)
Prior stroke	76 (7.5)
Chronic kidney disease	306 (30.8)
EuroSCORE I	14.4 (10.1-21.8)
	17.8 ± 11.7
Society of Thoracic Surgeons score	6.0 (4.1-9.7)
	8.3 ± 7.4

**FIGURE 1** Key Reasons for Transcatheter Aortic Valve Replacement



# Gender differences in echocardiographic characteristics

## AVR patients

Table 2  
Baseline echocardiographic characteristics

	Women (n = 190)	Men (n = 172)	p Value
Ejection fraction (%)	69 (60–75)	62 (54–70)	<0.001
Ejection fraction <50%	11% (21)	17% (30)	0.08
Ejection fraction ≤35%	4% (7)	6% (11)	0.24
Left ventricular outflow tract (cm)	1.9 ± 0.2	2.1 ± 0.2	<0.001
End-diastolic dimension (mm)	42 ± 5	49 ± 7	<0.001
Posterior wall thickness (mm)	11.9 ± 2.0	12.4 ± 2.0	0.02
Septal wall thickness (mm)	12.7 ± 2.0	13.1 ± 1.9	0.09
Relative wall thickness	0.58 ± 0.13	0.52 ± 0.11	<0.001
Aortic valve area (cm <sup>2</sup> )	0.62 ± 0.15	0.70 ± 0.15	<0.001
Aortic valve area index	0.36 ± 0.09	0.35 ± 0.08	0.26
Aortic valve peak gradient (mm Hg)	91 ± 24	88 ± 22	0.28
Aortic valve mean gradient (mm Hg)	56 ± 15	54 ± 13	0.22
Mitral regurgitation grade 3 or 4	15% (29)	10% (18)	0.18
Aortic insufficiency grade 3 or 4	6% (11)	6% (11)	0.81
Bicuspid aortic valve	8% (15)	16% (28)	0.01
Pulmonary artery systolic pressure (mmHg)	47 ± 14	45 ± 14	0.31

Measurements are presented as mean ± SD, median (interquartile range), or percentage of patients (number).

*Hartzell M et al, AM J Cardiol 2011*

## TAVI patients

Table 1  
Characteristics of the study population

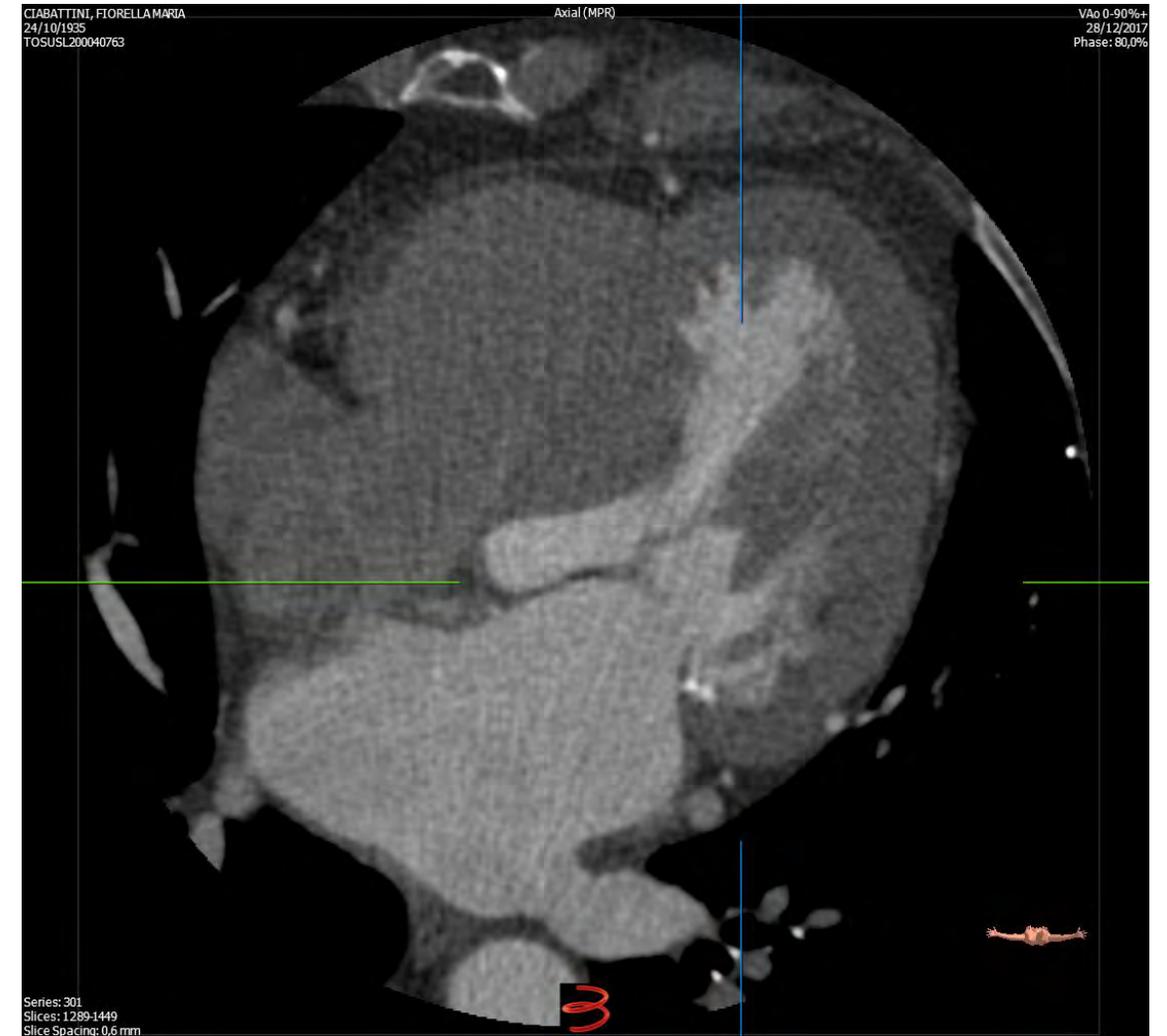
	Women (n = 423)	Men (n = 487)	p
<b>Echocardiographic findings</b>			
Left ventricle ejection fraction <40%	56 (13.3%)	96 (20.0%)	0.008
Left ventricle ejection fraction (%)	57.1 ± 12.8	52.3 ± 13.1	<0.0001
Stroke Volume Indexed (ml/beat/m <sup>2</sup> )	39.5 ± 11.3	36.2 ± 12.3	<0.0001
Aortic valve mean gradient (mmHg)	46.4 ± 14.4	43.2 ± 13.2	0.001
Aortic valve area (cm <sup>2</sup> )	0.65 ± 0.18	0.71 ± 0.19	<0.0001
Aortic peak velocity (m/sec)	4.4 ± 0.62	4.3 ± 0.62	0.001
Bicuspid aortic valve	44 (10.5%)	61 (12.6%)	0.325
Mitral valve mean gradient (mmHg)	4.0 ± 2.5	2.9 ± 1.8	<0.0001
Mitral annular calcium	394 (93.1%)	407 (83.6%)	<0.0001
Aortic regurgitation ≥moderate	54 (12.9%)	41 (8.5%)	0.051
Mitral regurgitation ≥moderate	74 (17.5%)	88 (18.1%)	0.810
Pulmonary Hypertension	240 (74.8%)	269 (75.6%)	0.811
Left atrial volume (ml)	81.8 ± 33.7	85.3 ± 29.3	0.164

*Sannino et al; Am J Cardiol 2018*

# Gender differences in echocardiographic characteristics

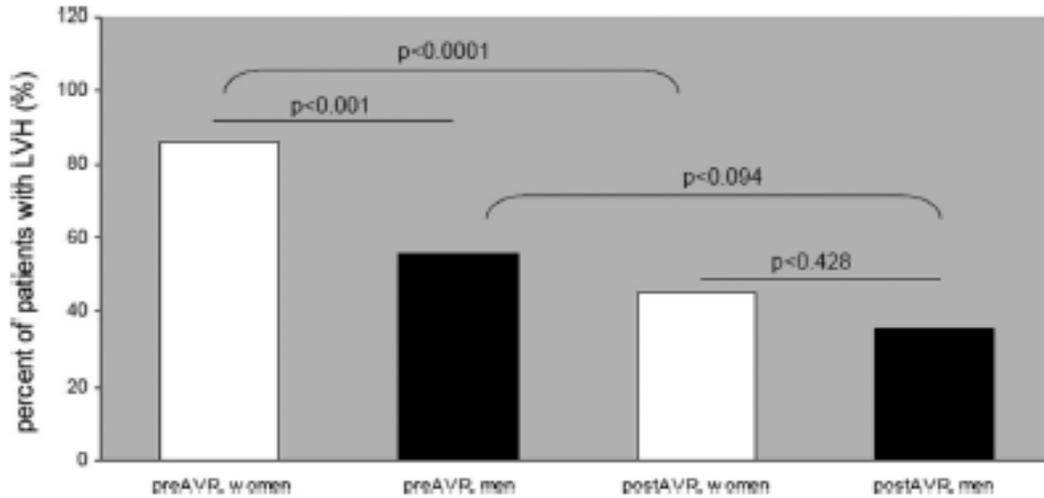


# Gender differences in MSCT characteristics

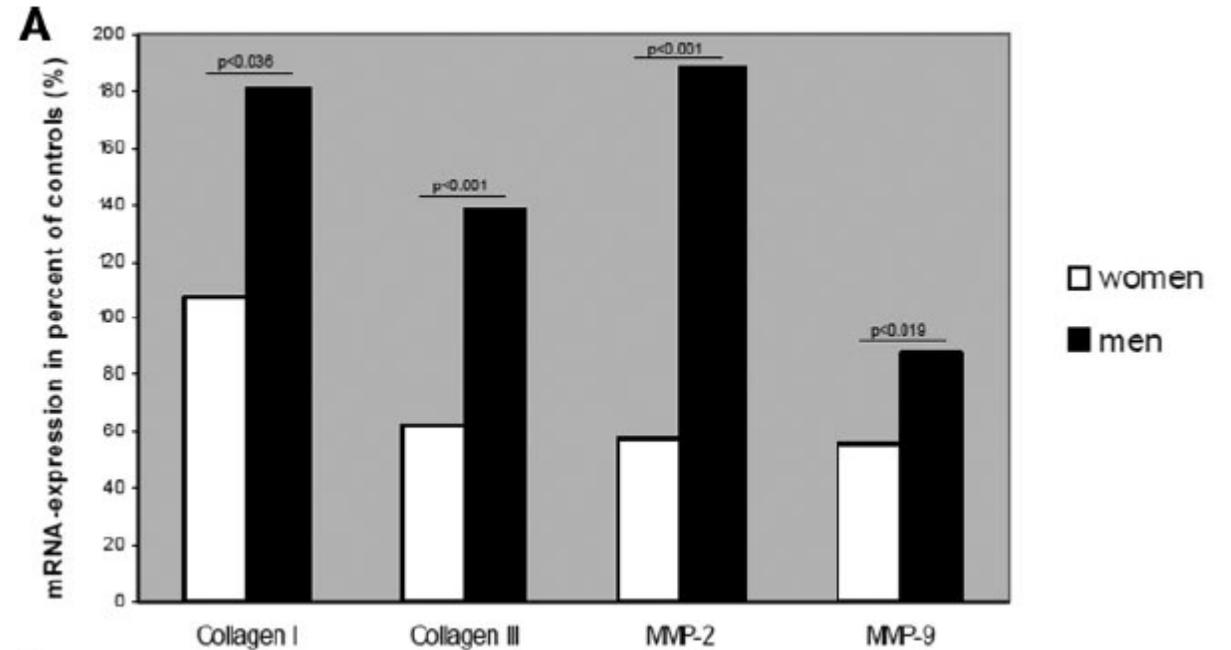


## Regression of Myocardial Hypertrophy After Aortic Valve Replacement Faster in Women?

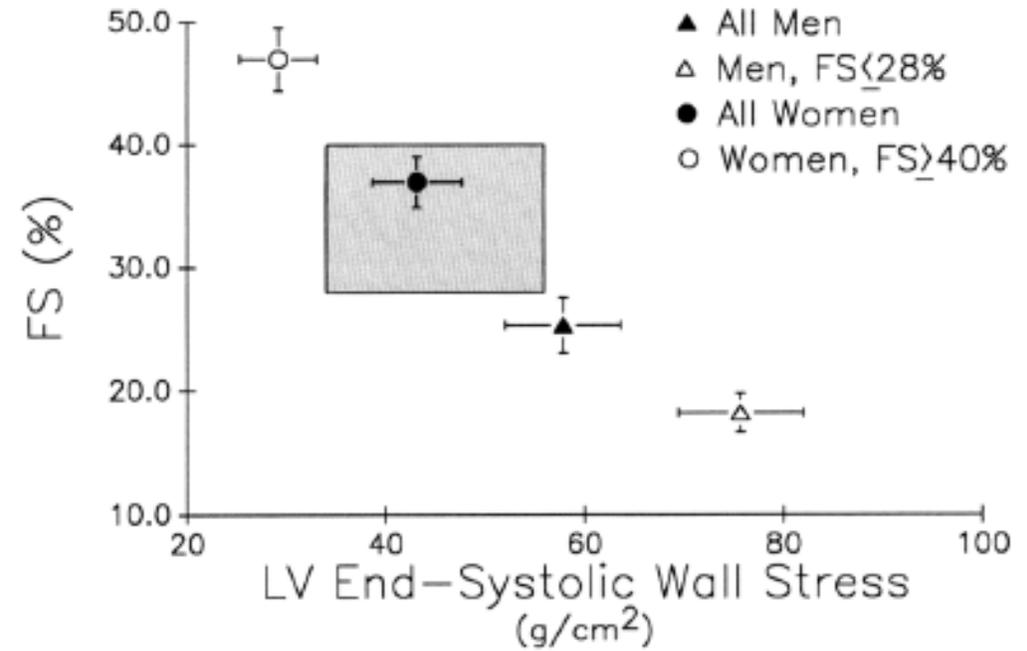
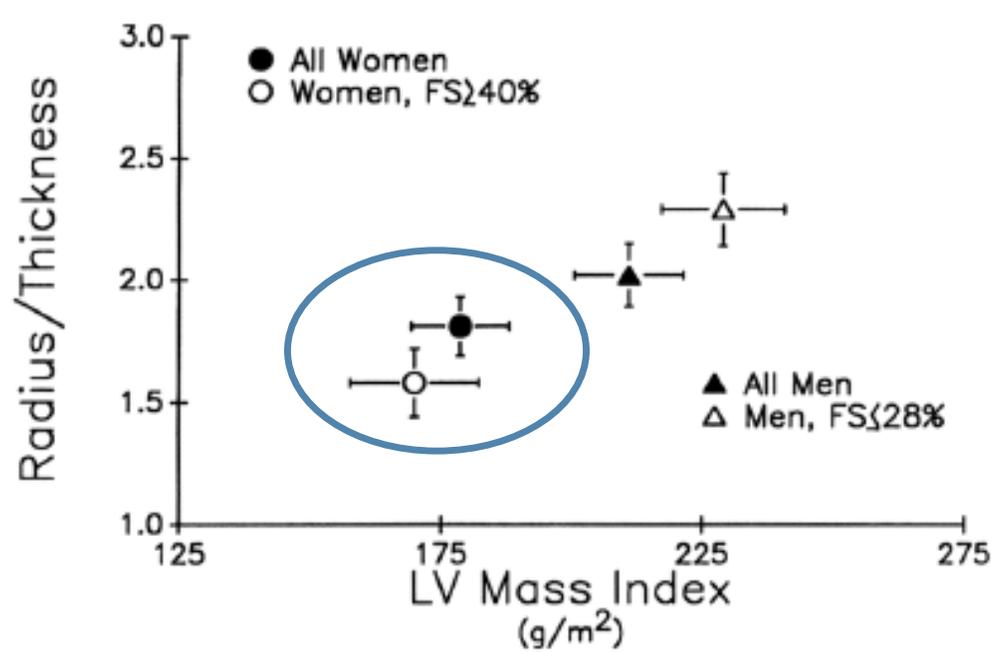
women exhibit faster regression of LVH in the early postoperative course after AVR compared with men



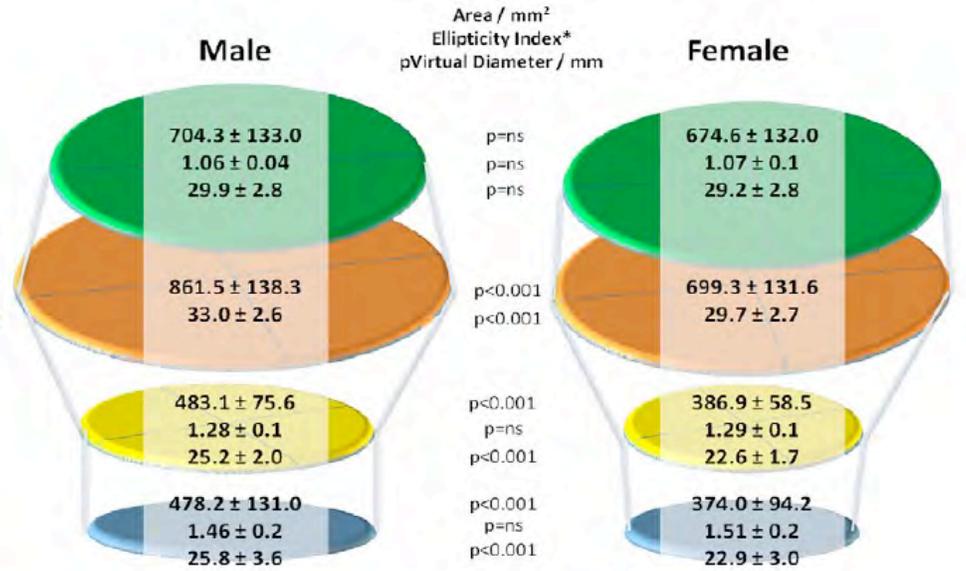
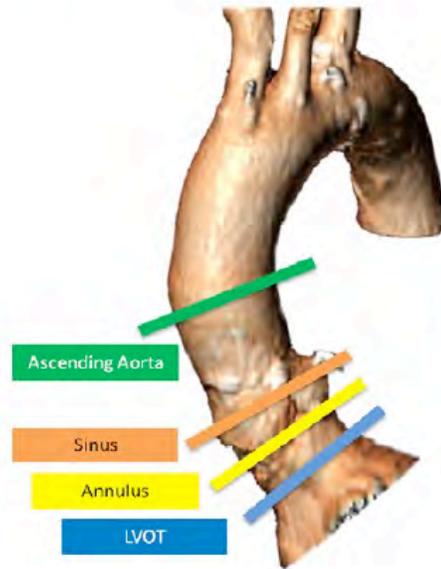
dysregulation of extracellular matrix turnover



## Sex-associated differences in left ventricular function in aortic stenosis of the elderly



# Aortic Root Dimensions Among Patients With Severe Aortic Stenosis Undergoing Transcatheter Aortic Valve Replacement



computed tomography

**Table 2. Sex-Specific Anatomic Dimensions of the Aortic Root**

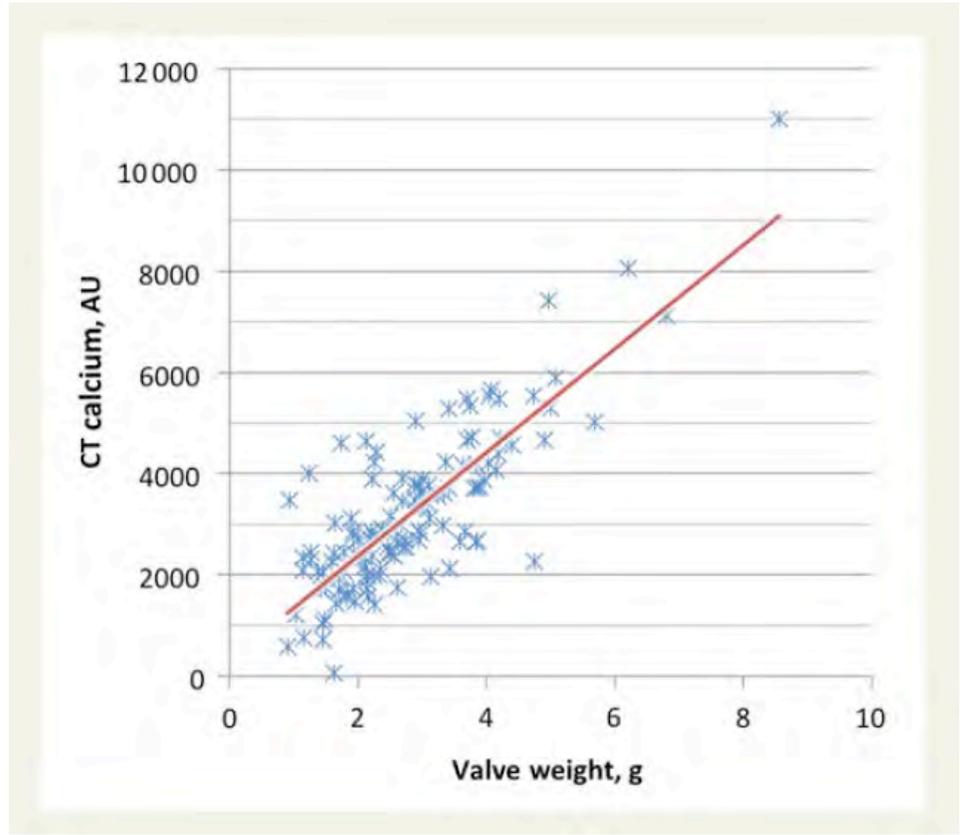
	All (n = 177)	Male (n = 80) (45.2%)	Female (n = 97) (54.8%)	p Value
<b>Annulus</b>				
Perimeter	74.7 (7.1)	79.1 (6.1)	71.0 (5.5)	<0.0001
Area (mm <sup>2</sup> )	430.4 (82.1)	483.1 (75.6)	386.9 (58.5)	<0.0001
Diameter max.	26.2 (2.6)	27.7 (2.4)	25.0 (2.2)	<0.0001
Diameter min.	20.5 (2.3)	21.8 (2.1)	19.4 (1.9)	<0.0001
<b>Left ventricular outflow tract</b>				
Perimeter	76.0 (11.4)	81.1 (11.4)	71.8 (9.5)	<0.0001
Area (mm <sup>2</sup> )	421.1 (123)	478.2 (131)	374.0 (94.2)	<0.0001
Diameter max.	27.9 (4.4)	29.6 (4.5)	26.5 (3.8)	<0.0001
Diameter min.	19.0 (3.1)	20.5 (2.9)	17.8 (2.7)	<0.0001
<b>Coronary ostia</b>				
Height left coronary ostium	14.4 (3.6)	15.1 (3.7)	13.7 (3.4)	0.011
Height right coronary ostium	16.7 (3.6)	17.7 (3.9)	15.9 (3.1)	0.001

Female sex is associated with smaller **annular and LVOT** but not aortic dimensions.

## Sex-related differences in calcific aortic stenosis: correlating clinical and echocardiographic characteristics and computed tomography aortic valve calcium score to excised aortic valve weight

**Table 3** Sex differences in valve weight after stratification by valve morphology and correcting for body surface area and left ventricular outflow tract area

	Male	Female	P-value
All patients			
Valve morphology			0.08
Bicuspid (%)	165 (30)	79 (24)	
Tricuspid (%)	394 (70)	250 (76)	
Valve weight (g)	3.08 ± 1.32	1.94 ± 0.88	<0.0001
Valve weight indexed to BSA (g/m <sup>2</sup> )	1.48 ± 0.62	1.09 ± 0.48	<0.0001
Valve weight indexed to LVOT area (g/cm <sup>2</sup> )	0.71 ± 0.29	0.54 ± 0.23	<0.0001



# Impact of Aortic Valve Calcification, as Measured by MDCT, on Survival in Patients With Aortic Stenosis

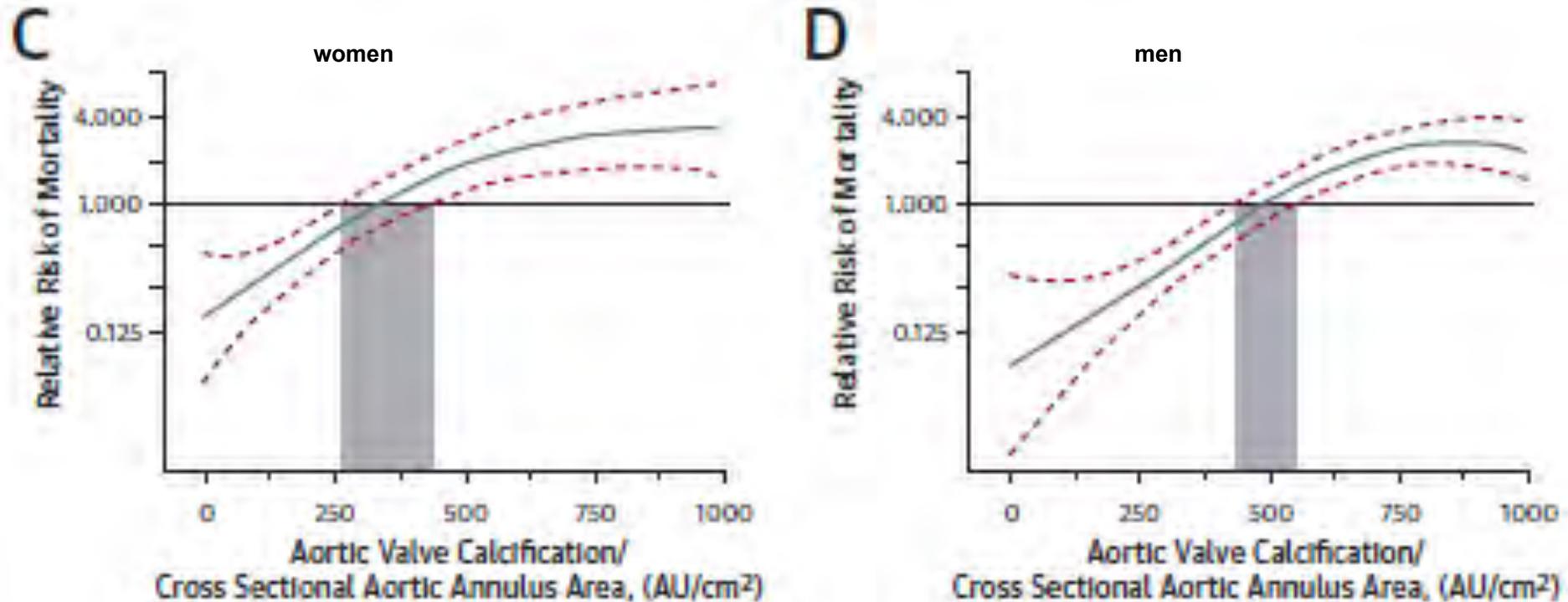
Results of an International Registry Study

**TABLE 1** Baseline Clinical, Echocardiographic, and MDCT Characteristics

	Study Groups		p Value	All Patients (N = 794)
	Nonsevere AVC <sub>density</sub> * (n = 384)	Severe AVC <sub>density</sub> † (n = 410)		
<b>Echocardiographic data</b>				
Peak aortic jet velocity, m/s	3.0 ± 0.7	4.4 ± 0.8	<0.0001	3.7 ± 1.0
Mean gradient, mm Hg	22 ± 11	47 ± 17	<0.0001	35 ± 19
Aortic valve area, cm <sup>2</sup>	1.34 ± 0.39	0.87 ± 0.21	<0.0001	1.10 ± 0.39
AVA <sub>i</sub> , cm <sup>2</sup> /m <sup>2</sup>	0.71 ± 0.20	0.46 ± 0.11	<0.0001	0.58 ± 0.20
LV outflow tract diameter, cm	2.25 ± 0.20	2.22 ± 0.22	0.10	2.23 ± 0.21
LV ejection fraction, %	62 ± 10	58 ± 14	<0.0001	60 ± 12
LV mass index, g/m <sup>2</sup>	108 ± 26	127 ± 37	<0.0001	118 ± 33
<b>MDCT data</b>				
Aortic valve calcification, AU				
Men	1,070 (575-1,531)	3,403 (2,662-4,458)	<0.0001	2,022 (1,042-3,397)
Women	436 (211-782)	1,879 (1,355-2,774)	<0.0001	1,103 (495-2,028)
AVC <sub>density</sub> , AU/cm <sup>2</sup>				
Men	257 (136-364)	790 (630-1,011)	<0.0001	473 (256-789)
Women	127 (58-215)	553 (401-819)	<0.0001	318 (142-593)
Coronary artery calcium load,‡ AU	362 (39-1,199)	920 (235-2,322)	<0.0001	719 (107-1,916)

# Impact of Aortic Valve Calcification, as Measured by MDCT, on Survival in Patients With Aortic Stenosis

Results of an International Registry Study



impact on mortality occurs at lower scores in women compared with men

# EuroIntervention

## The gender paradox



**WORST BASIC CONDITIONS  
BETTER LONG TERM RESULTS**

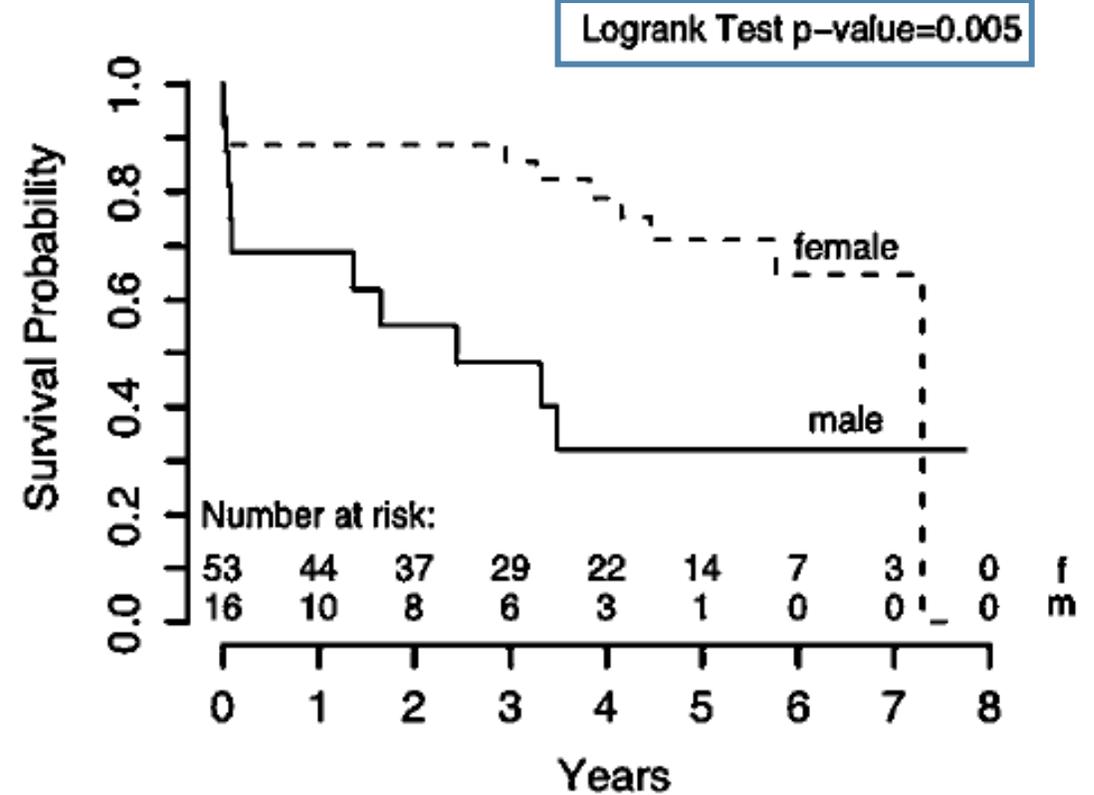
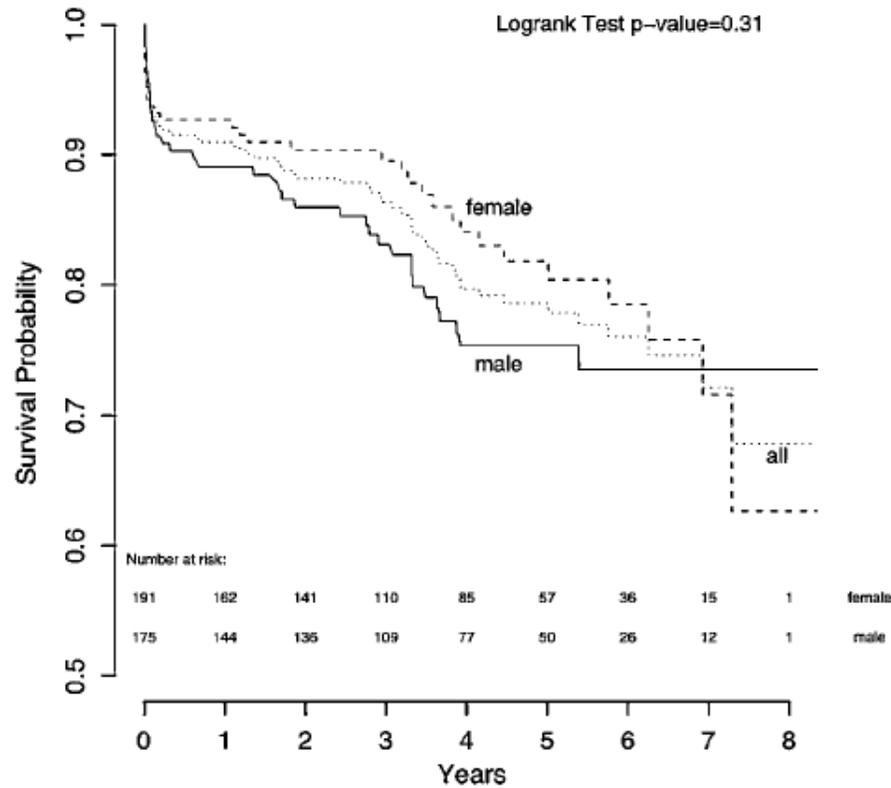
# Summary of the Literature on Gender Disparity Following Surgical Aortic Valve Replacement

Combined Surgical AVR* and CABG†				
Author, Year	# Patients (F)	Settings	Results	Conclusions
Arank'i et al. 1993	717 (326)	Single Center, Retrospective	30-day mortality: M‡: 5.6% AVR vs 7.4% AVR+CABG (p=0.31) F§: 2.9% AVR vs 10.3% AVR+CABG (p=0.006)	Short term Mortality better in females after isolated AVR but worse after AVR/CABG
Morris <sup>2</sup> et al. 1994	1012 (329)	Single Center, Retrospective	Combined AVR+ CABG: 30-day mortality: 6% F, 2% M (p<0.02). 5-year mortality: 23% F, 17% M (p<0.02).	Short and long term mortality worse in females.
Ibrahim <sup>3</sup> et al. 2003	1570 (497)	Single Center, Retrospective	In-hospital mortality: Isolated AVR: 2.3% F vs. 1.7% M (p=NS) Combined AVR/CABG 7% F vs. 4% M (p=0.02).	Short-term mortality similar for isolated AVR but worse in females after combined AVR+CABG.
Doenst <sup>4</sup> et al. 2006	1567 (496)	Single Center, Retrospective	Combined AVR+ CABG: 30-day mortality: 7% in F vs. 4% in M (p=0.026). 5-yr survival rate: 77% F vs 78% M (p= 0.062). 10-yr survival rate: 50% F vs 56% M (p= 0.062).	Short-term mortality worse in females in combined AVR+CABG but long term mortality similar
Isolated Surgical AVR				
Author, Year	# Patients (F)	Settings	Results	Conclusions
Hanssen <sup>5</sup> et al. 1999	195 (99)	Single Center, Prospective	30-day mortality: 5.6% F vs. 3.1% M (p=0.229).	Similar short term mortality (underpowered)
Duncan <sup>6</sup> et al. 2006	2212 (782)	Single Center, Retrospective	In-hospital mortality: Unadjusted 3.5% F vs. 1.6% M (p=0.005) Adjusted 3.9% F vs. 3.9% M (p=0.99)	Similar short term mortality
Caballero-Borrego <sup>7</sup> et al. 2009	577 (254)	Single Center, Retrospective	In-hospital mortality: Unadjusted 13% F vs. 7.4% M (p=0.019) Adjusted HR in F 2.5 (CI 0.79-7.26, P=0.12)	Similar short term mortality
Hamed <sup>8</sup> et al. 2009	406 (183)	Single Center, Retrospective	30-day mortality: 3.4% overall with no difference between F and M	Similar short term mortality
Kulik <sup>9</sup> et al. 2009	3118 (1261)	Single Center, Retrospective	10-yr actuarial survival rate: Bioprosthetic AVR: 70% F vs. 55.9% M (p<0.001). Mechanical AVR: 79.1% F vs. 73.3% (p=0.74).	Long term mortality better in females only in bioprosthetic AVRs
Fuchs <sup>10</sup> et al. 2010	408 (215)	Single Center, Retrospective	1,2,5 years actuarial survival rates: 92.8%, 89.8%, 81.4% F vs. 89.1%, 86.6%, 76.3% M (p=0.31)	Similar short term mortality
Elhmidi <sup>11</sup> et al. 2014	2197 (907)	Single Center, Retrospective	30-day mortality: 4.4% F vs. 1.6% M (p<0.001) 1-yr mortality: 13% F vs. 9.6% M (p=0.04)	Short and long term mortality worse in females

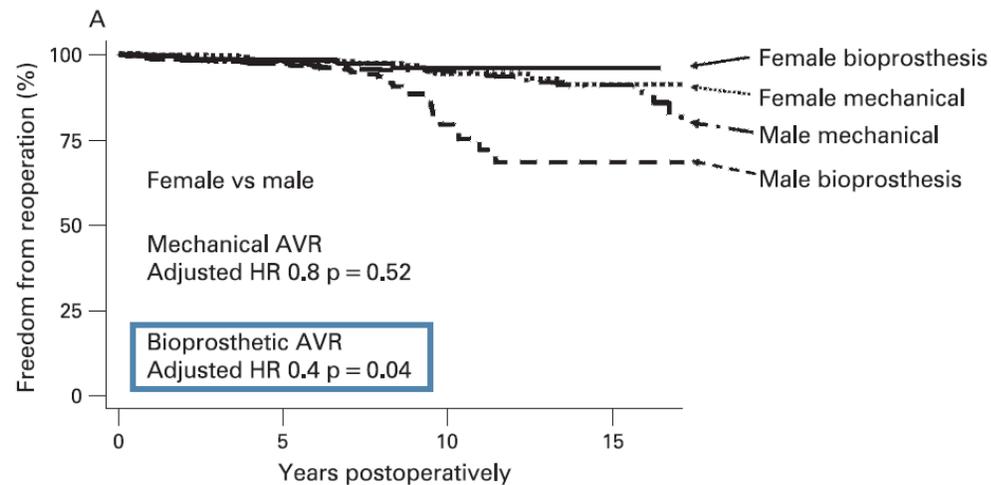
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# Gender differences in the long term outcomes after valve replacement

79 years and older



# Gender differences in the long term outcomes after valve replacement



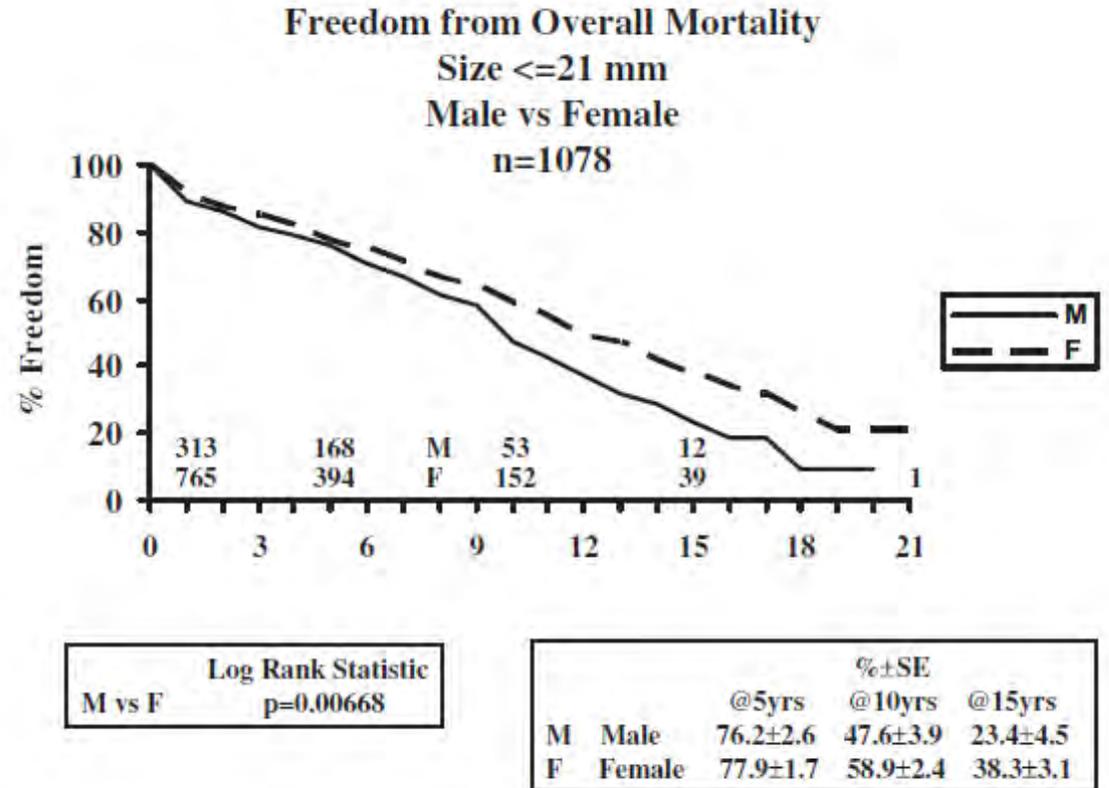
Patients at risk:	0	5	10	15
Female	766	386	150	32
Male	1489	812	260	57

	AVR (n = 2255)		p Value
	Female (n = 766)	Male (n = 1489)	
<b>Preoperative characteristics</b>			
Age	68.3 (12.3)	64.3 (14.1)	<0.0001
BMI	27.7 (6.2)	28.0 (5.6)	0.46
Preoperative NYHA III/IV	269 (35.1%)	497 (33.4%)	0.42
Non-elective surgery	147 (19.2%)	331 (22.2%)	0.1
LVEF < 50%	84 (11.0%)	202 (13.6%)	0.08
Preoperative hypertension	447 (58.4%)	758 (50.9%)	0.16
Smoker	95 (12.4%)	280 (18.8%)	<0.0001
Diabetes	42 (5.5%)	65 (4.4%)	0.25
Atrial fibrillation	30 (3.9%)	49 (3.3%)	0.47
Cerebrovascular disease	3 (0.4%)	5 (0.3%)	1.0
<b>Operative characteristics</b>			
Reoperation	5 (0.6%)	11 (0.7%)	1.0
Bioprosthesis	486 (63.6%)	815 (54.7%)	<0.0001
Mechanical valve	278 (36.4%)	674 (45.3%)	<0.0001
CABG	238 (31.2%)	651 (44.0%)	<0.0001
CPB time	117.1 (39.6)	127.0 (44.8)	<0.0001
Cross-clamp time	78.1 (24.9)	84.9 (27.4)	<0.0001

# Influence of patient gender on mortality after aortic valve replacement for aortic stenosis

TABLE 4. Multivariate predictors of late mortality

	Late (overall)	
	HR (95% CI)	P value
Male gender	1.25 (1.07-1.45)	0.006
Age 61-70 y	2.15 (1.75-2.65)	<0.0001
Age > 70 y	3.87 (3.13-4.79)	<0.0001
LVEF < 35%	1.41 (1.05-1.89)	0.022
NYHA III/IV	1.23 (1.04-1.46)	0.014
Diabetes mellitus	1.51 (1.18-1.93)	0.001
Renal failure	1.47 (1.17-1.85)	0.001
COPD	1.35 (1.06-1.72)	0.015
CHF	1.37 (1.18-1.60)	<0.0001
Bioprosthetic valve	1.26 (1.06-1.49)	0.009
Concomitant CABG	1.24 (1.09-1.41)	0.001



Male gender increased the risk of late mortality

Transcatheter aortic valve implantation for severe aortic stenosis is the first area of interventional cardiology where women are treated as often as men



# TAVI Registries: Female Rate

## Pilot European registry

Variable (nb observations)	Total, n (%) 4,571	<80, n (%) 1,721 (37.5%)	>80, n (%) 2,850 (62.4)	p-value
Male/Female (4,571 patients)	2,291 (50.1)/2,280 (49.9)	(58.6)/(41.4)	(45.0)/(55.0)	<0.01
Diabetes mellitus (4,547 patients)	1,259 (27.7)	618 (36.1)	641 (22.6)	<0.01

EuroIntervention 2013

## French Registry

**Table 1. Characteristics of the Patients at Baseline.\***

Characteristic	All Patients (N=3195)	Edwards SAPIEN (N=2107)	Medtronic CoreValve (N=1043)
Age — yr	82.7±7.2	82.9±7.2	82.3±7.2
Male sex — no. (%)	1630 (51.0)	981 (46.6)	626 (60.0)
Society of Thoracic Surgeons score — %†	14.4±11.9	15.6±12.4	14.2±11.2
Logistic EuroSCORE — %‡	21.9±14.3	22.2±14.3	21.3±14.3

N ENGL J MED 366;18 NEJM.ORG MAY 3, 2012

## STS/ACC TVT Registry

**TABLE 1 Patient Demographics (N = 2,952)**

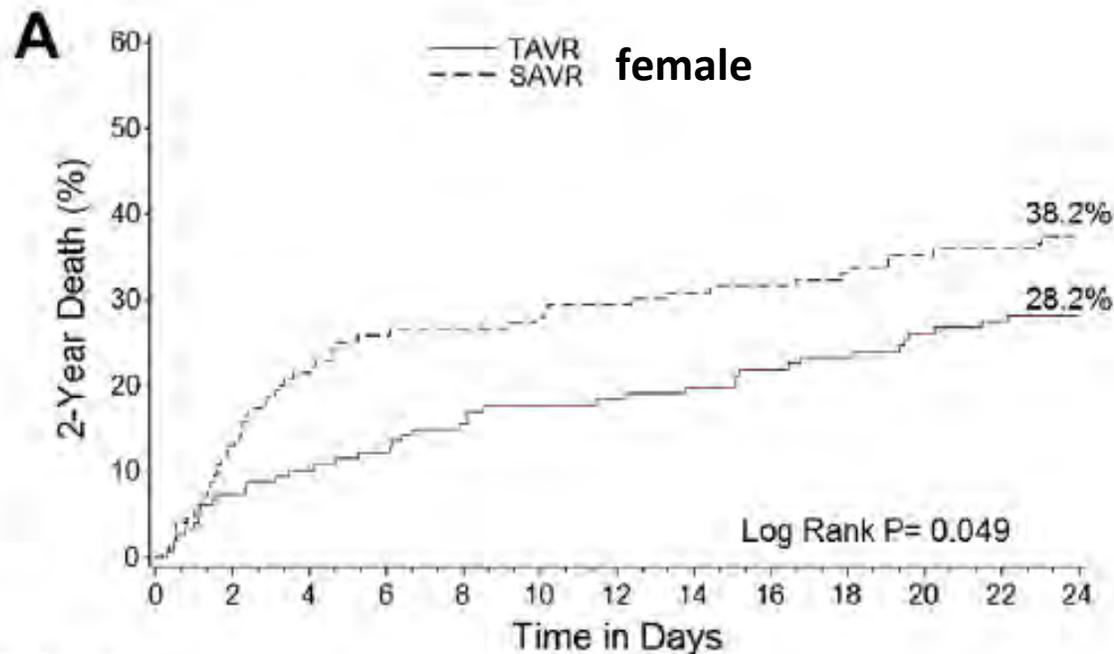
Age, yrs	82 (74-86)
Male	55.8
Ethnicity	
White	90.2
Black or African American	5.8
Hispanic or Latino	4.7
Asian	2.6

Sorajja et al. 2016

Transcatheter Mitral Valve Repair in the United States

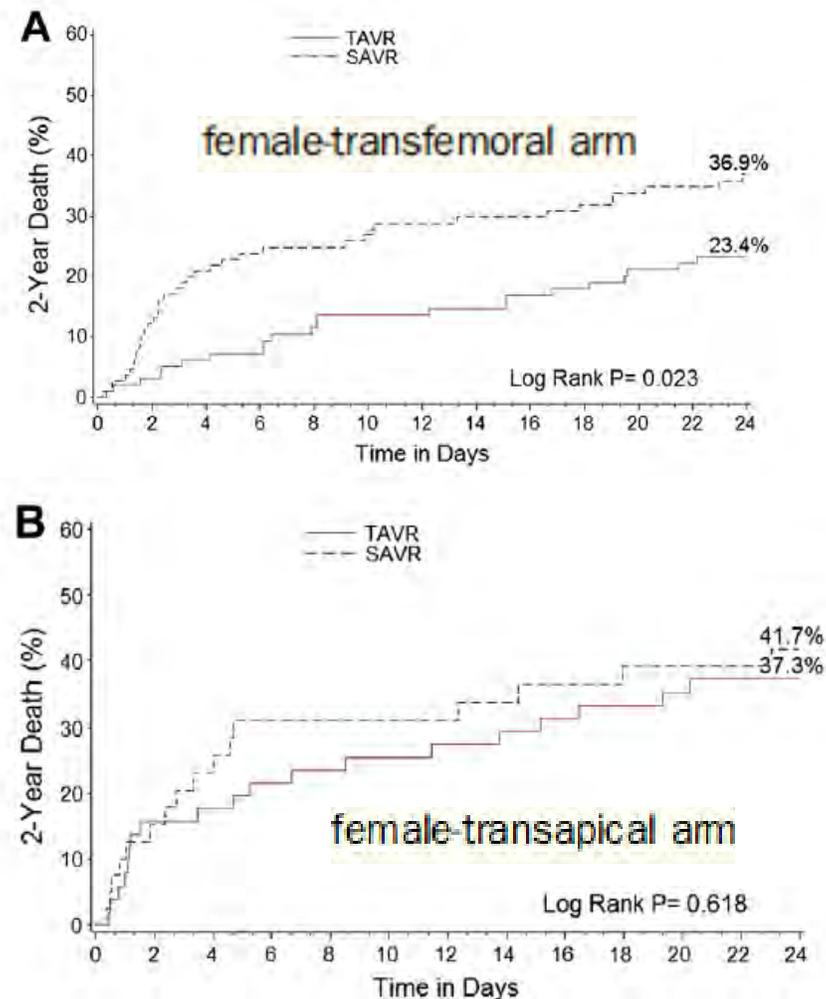
# Sex-Related Differences in Outcomes After Transcatheter or Surgical Aortic Valve Replacement in Patients With Severe Aortic Stenosis

Insights From the PARTNER Trial  
(Placement of Aortic Transcatheter Valve)

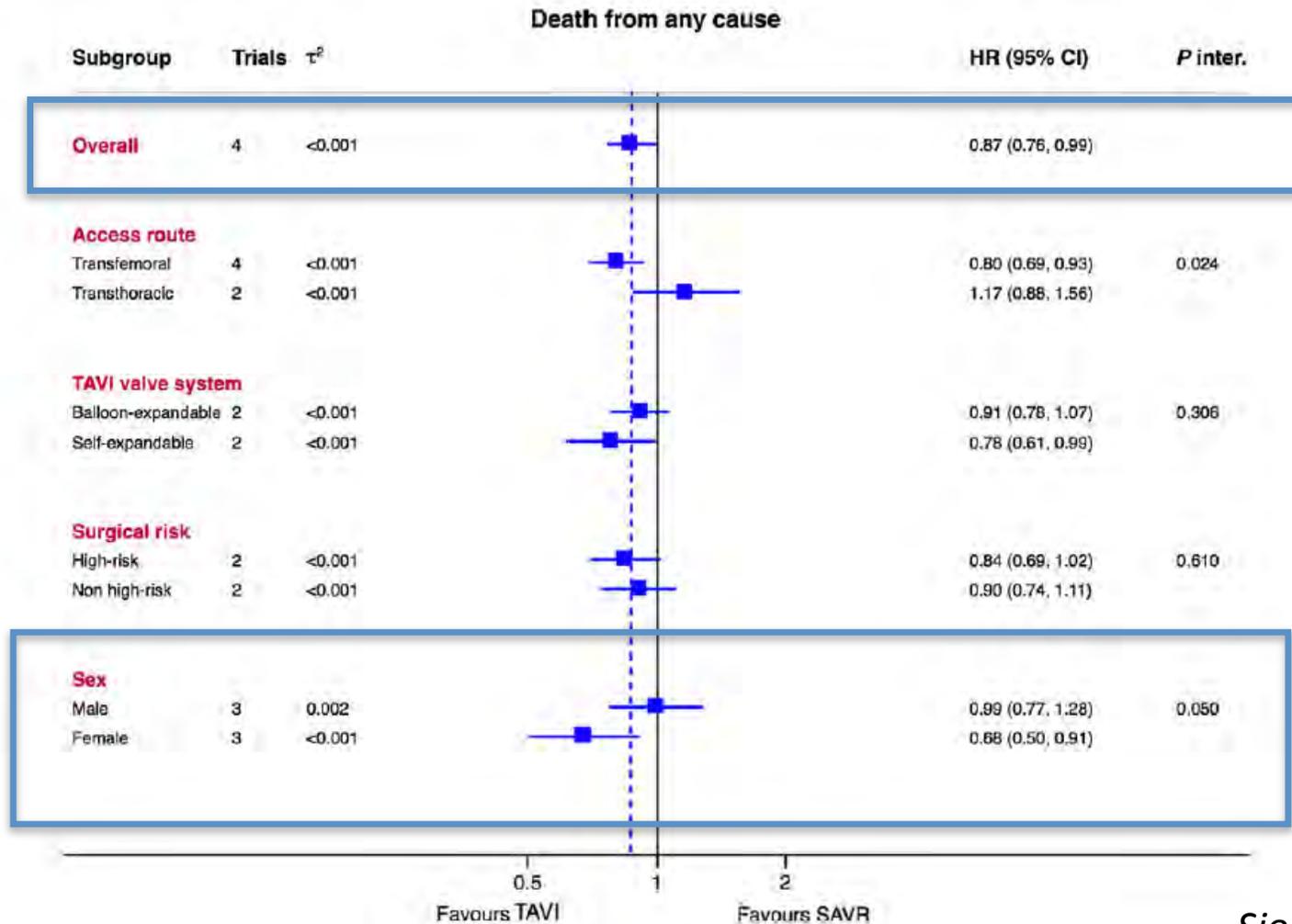


Number At Risk		0	2	4	6	8	10	12	14	16	18	20	22	24
TAVR		147	136	128	118	110	101							
SAVR		153	124	103	97	91	80							

TAVR may be preferred over surgery for high-risk female patients

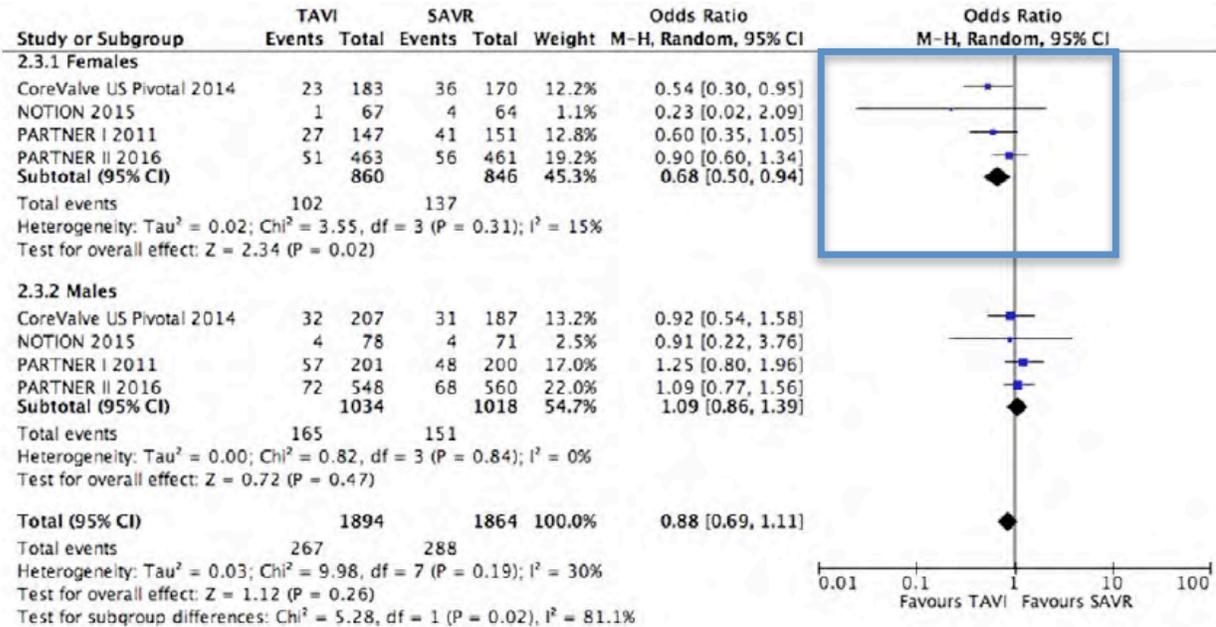


# Transcatheter aortic valve implantation vs. surgical aortic valve replacement for treatment of severe aortic stenosis: a meta-analysis of randomized trials



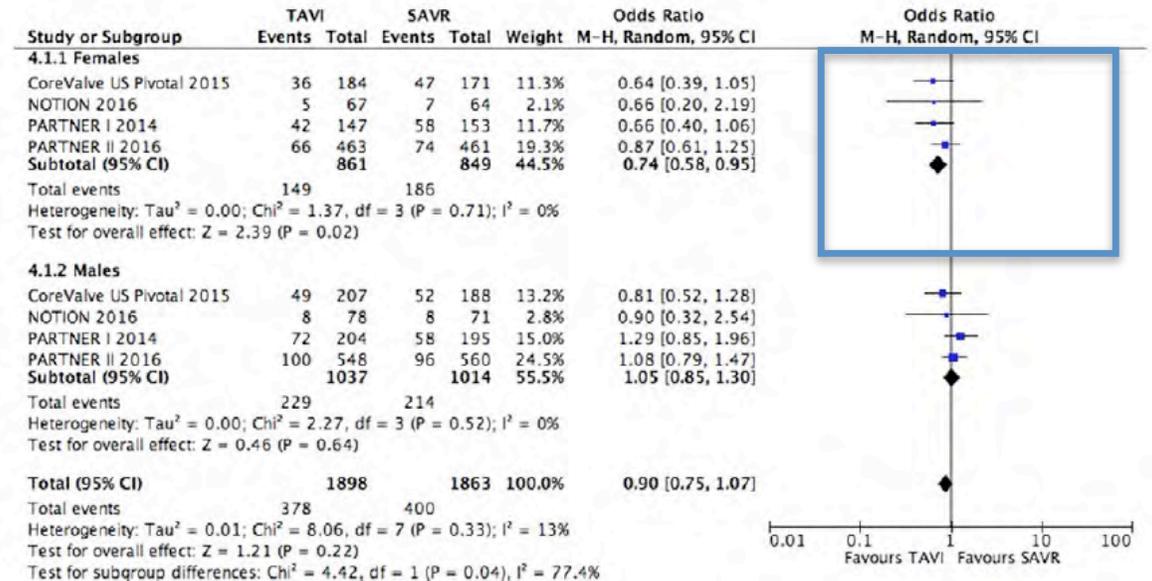
# Female-specific survival advantage from transcatheter aortic valve implantation over surgical aortic valve replacement: Meta-analysis of the gender subgroups of randomised controlled trials including 3758 patients

1 year



In women TAVI has a 26 to 31% lower mortality odds than SAVR

2 year



TAVR may be preferred over surgery for high-risk female patients

# Summary of the Literature on Gender Disparity Following Surgical and Transcatheter Aortic Valve Replacement

Transcatheter AVR				
Author, Year	# Patients (F)	Settings	Results	Conclusions
Buchanan <sup>12</sup> et al. 2011	305 (146)	Single Center, Retrospective	30-day mortality following TAVR: 4.7% F vs. 4.7% M (p=0.99)	Similar short term mortality
Humphries <sup>13</sup> et al. 2012	641 (329)	Multicenter, Retrospective	30-day mortality: 6.5% F, 11.2% M (p=0.05).	Better short term mortality in females
Hayashida <sup>14</sup> et al. 2012	260 (131)	Single Center, Prospective	30-day mortality: 12.2% F, 17.8% M (p=0.207) 1-yr mortality: (HR 1.62, CI 1.03-2.53, p=0.037)	Similar short term but better 1-yr mortality in females
Zhao <sup>15</sup> et al. 2013	9118 (4942)	Meta analysis (through April 2013)	30-day mortality: Higher in males (HR 1.37, 95% CI 1.07-1.76). 1-yr mortality: Higher in males (HR 1.30, 95% CI 1.14-1.49).	Short and long term mortality better in females
Conrotto <sup>16</sup> et al. 2014	836 (464)	Multicenter, Retrospective	30-day mortality: 6.5% F, 5.6% M (p=0.62) 1-yr mortality: 18.1% F, 22.6% M (p=0.11)	Similar short and long term mortality
Stangl <sup>17</sup> et al. 2014	7973 (4242)	Meta analysis (through June 2014)	30-day mortality: Lower in F (HR 0.78, CI 0.64-0.96) Long-term mortality: Lower in F (HR 0.70, CI 0.59, 0.82)	Short and long term mortality better in females
Erez <sup>18</sup> et al. 2014	224 (127)	Single Center, Retrospective	30-day mortality: 4% F, 5% M (p=0.45).	Similar short term mortality
Williams <sup>19</sup> et al. 2014	699 (300)	Multicenter, Prospective	2-yr mortality: In F, 28.2% TAVR vs. 38.2% SAVR (p=0.049) In M, 37.7% TAVR vs. 32.3% SAVR (p=0.42)	Long term survival benefit for female but not for males with TAVR

# Sex-Based Differences in Outcomes With Transcatheter Aortic Valve Therapy



TVT Registry From 2011 to 2014

Old generation device

**TABLE 1** Baseline Characteristics

	Female Patients (n = 11,808)	Male Patients (n = 11,844)	p Value
Age, yrs	82.28 ± 8.52	81.67 ± 8.63	<0.0001
Race			<0.0001
White	10,972 (92.92)	11,273 (95.18)	
African American	566 (4.79)	300 (2.53)	
Asian	124 (1.05)	159 (1.34)	
Other	45 (0.38)	50 (0.42)	
Body surface area, m <sup>2</sup>	1.7 (1.6-1.9)	1.9 (1.8-2.1)	<0.0001
BMI, kg/m <sup>2</sup>	28.38 ± 7.48	27.51 ± 5.68	<0.0001
STS risk score, %	9 ± 6	8 ± 6	<0.0001
Diabetes	4,133 (35.00)	4,679 (39.51)	<0.0001
Current smoker	508 (4.30)	709 (5.99)	<0.0001
Prior PCI	3,485 (29.51)	4,965 (41.92)	<0.0001
Prior PCI <360 days	1,906 (16.18)	2,561 (21.68)	<0.0001
Prior CABG	1,941 (16.44)	5,460 (46.10)	<0.0001
Prior aortic valve procedure	1,737 (14.71)	1,823 (15.39)	<0.0001

**TABLE 4** In-Hospital Clinical Outcomes

	Females (n = 11,808)	Males (n = 11,844)	Unadjusted OR*	Adjusted OR* (95% CI)	p Value
NACE	2,239 (18.96)	1,630 (13.76)	1.48	1.14 (0.99-1.30)	0.0662
Death, MI, or stroke	961 (8.14)	726 (6.13)	1.35	0.94 (0.77-1.15)	0.5350
Death or MI	710 (6.01)	538 (4.54)	1.34	0.90 (0.73-1.13)	0.3711
Death or stroke	914 (7.74)	699 (5.90)	1.33	0.93 (0.76-1.13)	0.4631
Death	661 (5.6)	507 (4.28)	1.32	0.89 (0.71-1.11)	0.2936
MI	74 (0.63)	52 (0.44)	1.45	-	-
Stroke	305 (2.58)	220 (1.86)	1.41	-	-
VARC-2 major bleeding	946 (8.01)	706 (5.96)	1.40	1.19 (0.99-1.44)	0.0680
Major vascular complication	976 (8.27)	520 (4.39)	2.01	1.70 (1.34-2.14)	<0.0001
New requirement for dialysis	203 (1.7)	211 (1.8)	0.97	0.62 (0.44-0.87)	0.008
Conduction/native pacer disturbance	1,057 (8.9)	1,014 (8.5)	1.04	1.08 (0.88-1.32)	0.45
Atrial fibrillation	933 (7.9)	607 (5.1)	1.59	1.16 (0.95-1.42)	0.11

# Sex-Based Differences in Outcomes With Transcatheter Aortic Valve Therapy



TVT Registry From 2011 to 2014

**TABLE 2** Continued

	Overall (N = 23,652)	Female Patients (n = 11,808)	Male Patients (n = 11,844)	p Value
Device success	21,531 (92.56)	10,725 (92.45)	10,806 (92.68)	0.5096
Conversion to open surgery	319 (1.35)	205 (1.74)	114 (0.96)	<0.0001
Reasons for conversion				<0.0001
Ventricular rupture	60 (18.93)	45 (22.17)	15 (13.16)	
Annulus rupture	40 (12.62)	28 (13.79)	12 (10.53)	
Aortic dissection	27 (8.52)	22 (10.84)	5 (4.39)	
Coronary occlusion	21 (6.62)	19 (9.36)	2 (1.75)	
Valve dislodged in aorta	8 (2.52)	6 (2.96)	2 (1.75)	
Valve dislodged in the left ventricle	69 (21.77)	24 (11.82)	45 (39.47)	
Other	92 (29.0)	59 (29.1)	33 (29.0)	
Urgent valve-in-valve implantation	600 (2.54)	250 (2.1)	350 (3.0)	0.0001

**TABLE 3** In-Hospital Device-related Complications

	Females (n = 11,808)	Males (n = 11,844)	Unadjusted OR*	p Value
Device embolization in the aorta	35 (0.30)	29 (0.24)	1.20	0.5234
Device migration	36 (0.30)	45 (0.38)	0.80	0.3807
Device recapture	39 (0.33)	59 (0.50)	0.67	0.0561
Aortic valve re-intervention	35 (0.30)	50 (0.42)	0.71	0.1318
Coronary obstruction or compression	83 (0.70)	17 (0.14)	4.92	0.0001
Unplanned other cardiac surgery	288 (2.4)	189 (1.6)	1.53	0.0001
Post-procedure severe AI	367 (3.1)	399 (3.4)	0.92	0.2731

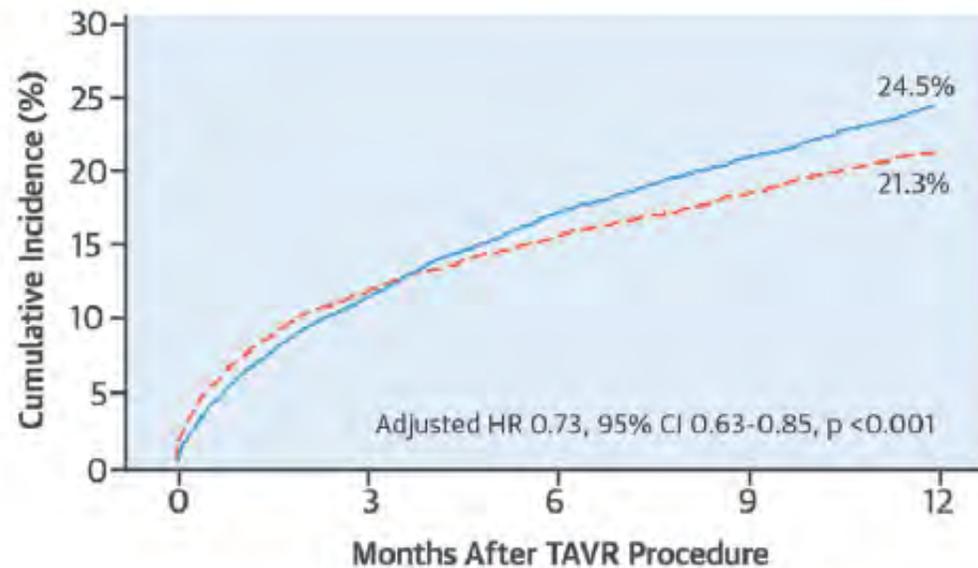
# Sex-Based Differences in Outcomes With Transcatheter Aortic Valve Therapy



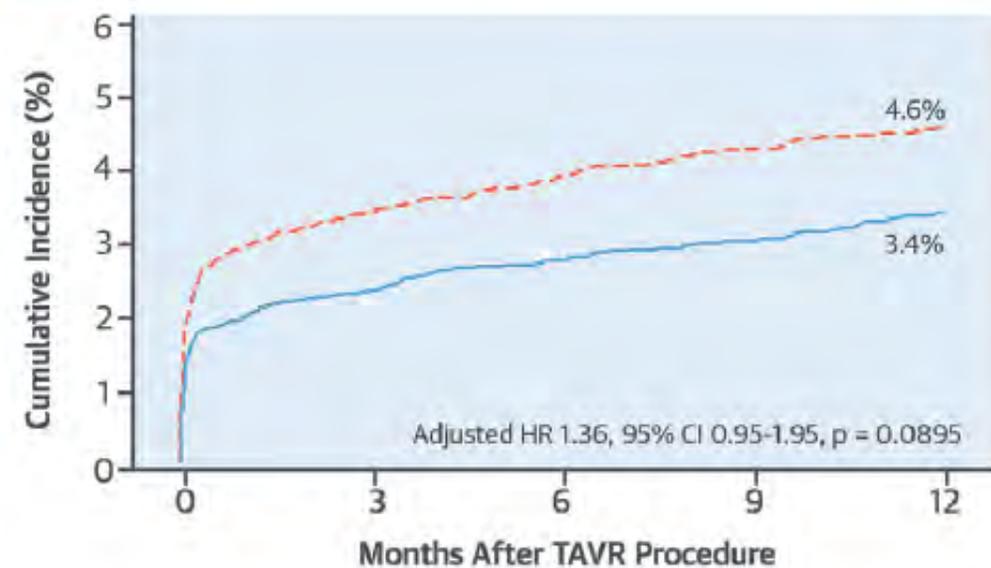
TVT Registry From 2011 to 2014

## CENTRAL ILLUSTRATION Sex-Based Differences in TAVR: Crude and Adjusted 1-Year Outcomes

### Death



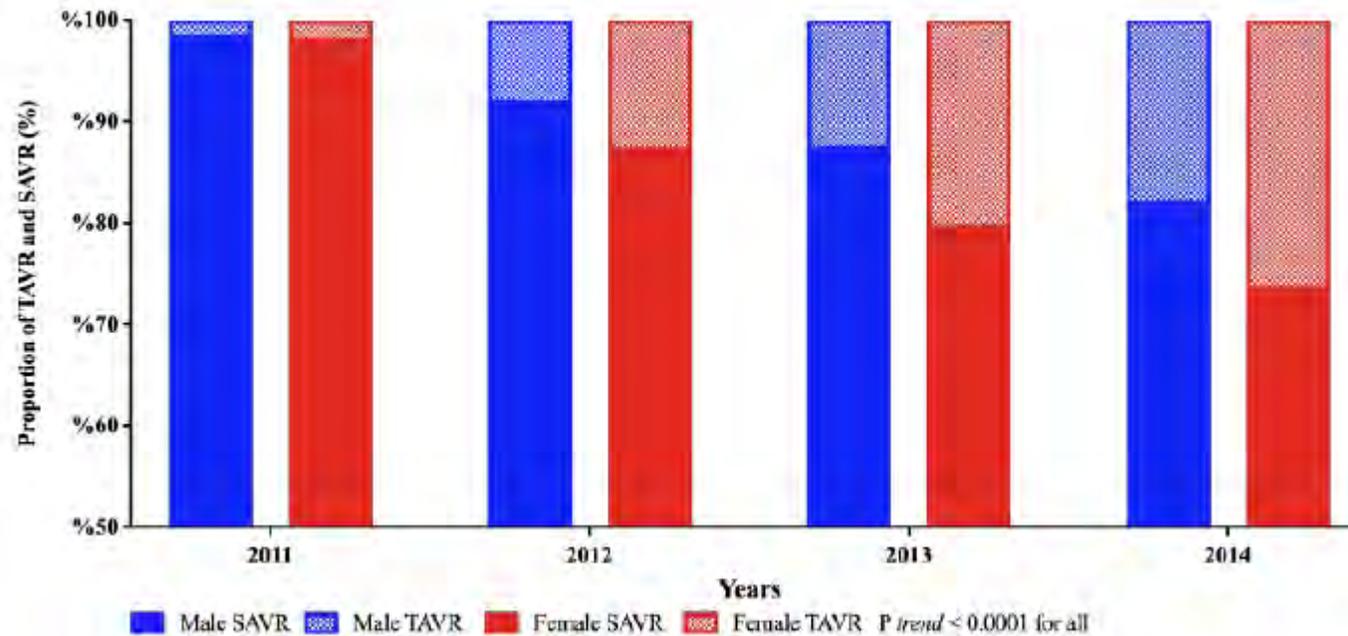
### Stroke



## Sex Differences in the Utilization and Outcomes of Surgical Aortic Valve Replacement for Severe Aortic Stenosis

Zakeih Chaker, MD; Vinay Badhwar, MD; Fahad Alqahtani, MD; Sami Aljohani, MD; Chad J. Zack, MD; David R. Holmes, MD; Charanjit S. Rihal, MD; Mohamad Alkhoul, MD

Proportion of TAVR and SAVR among Males and Females who underwent aortic valve replacement since commercial approval of TAVR

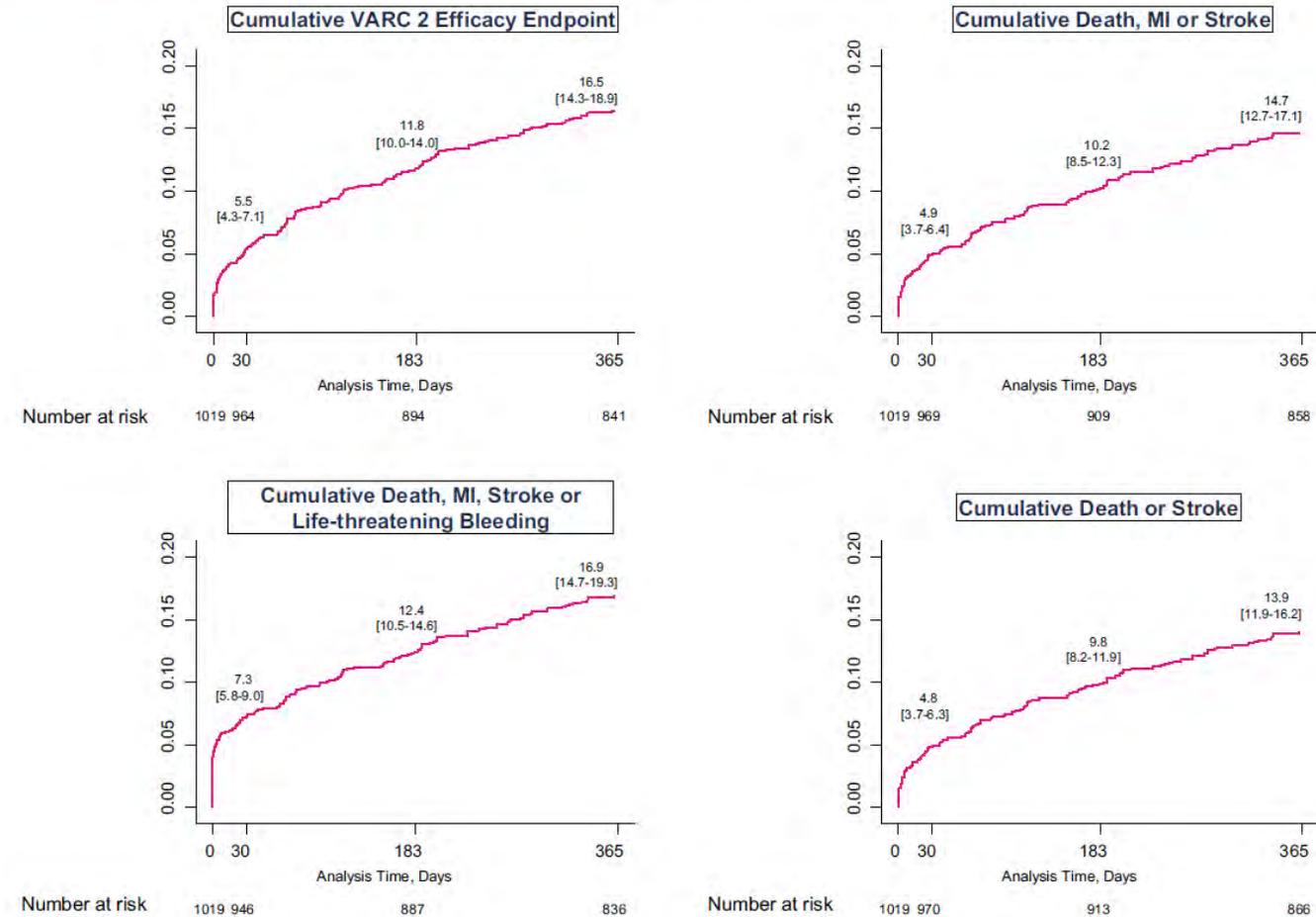


# 1-Year Clinical Outcomes in Women After Transcatheter Aortic Valve Replacement



## Results From the First WIN-TAVI Registry

**FIGURE 2** Cumulative Incidence of 1-Year Clinical Outcomes in Women Undergoing TAVR



# Acute and 30-Day Outcomes in Women After TAVR

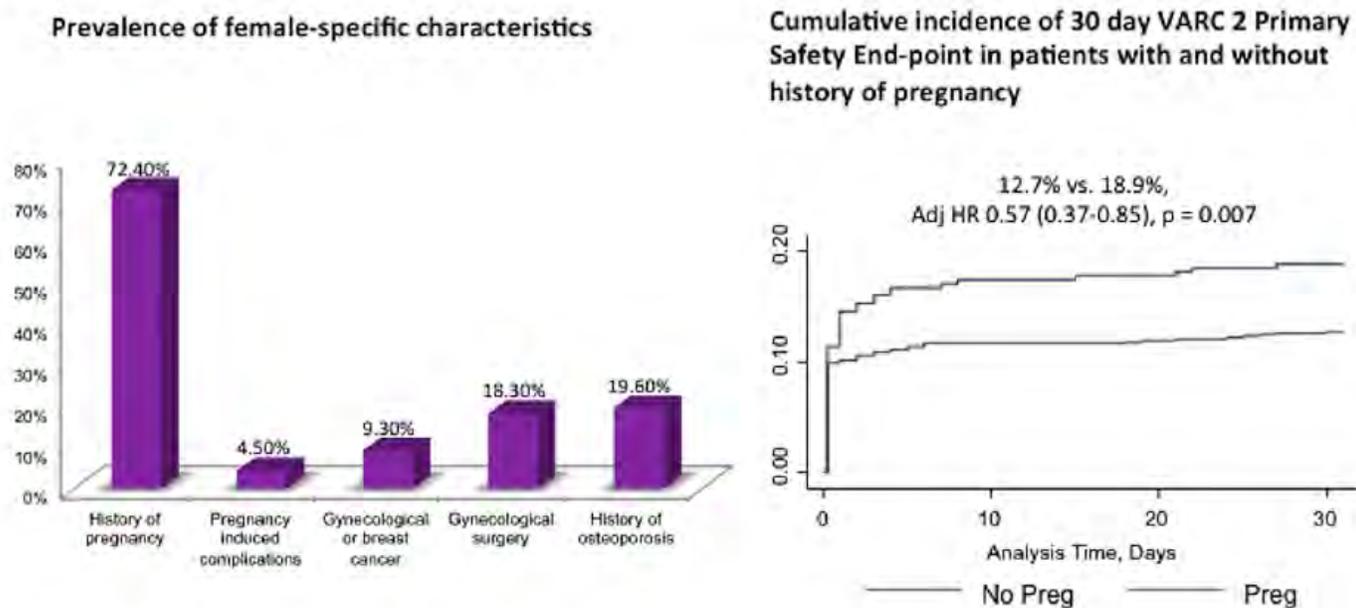
Results From the WIN-TAVI (Women's International Transcatheter Aortic Valve Implantation) Real-World Registry

# 1-Year Clinical Outcomes in Women After Transcatheter Aortic Valve Replacement

Results From the First WIN-TAVI Registry



**FIGURE 3** Prevalence of Female-Specific Characteristics and Effect of Pregnancy History on Primary VARC-2 Safety Endpoint



**TABLE 2** Predictors of VARC-2 Efficacy Endpoint\*

	Univariate Associations		Multivariate Associations	
	HR (95% CI)	p Value	HR (95% CI)	p Value
Age, yrs	1.02 (0.99-1.05)	0.14		
BMI, kgm <sup>2</sup>	0.98 (0.95-1.00)	0.10		
Prior stroke	1.59 (0.97-2.59)	0.064		
Prior PCI or CABG	1.29 (0.93-1.79)	0.13	1.72 (1.17-2.52)	0.006
Prior MI	1.38 (0.87-2.18)	0.17		
Baseline PAD	1.35 (0.85-2.16)	0.21		
Baseline atrial fibrillation	1.37 (0.96-1.96)	0.079		
LVEF <30%	0.84 (0.35-2.05)	0.71		
EuroSCORE I	1.02 (1.01-1.04)	0.004	1.02 (1.00-1.04)	0.027
Baseline renal dysfunction	1.27 (0.92-1.74)	0.14		
Diabetes	0.98 (0.69-1.38)	0.89		
Frailty	0.90 (0.66-1.24)	0.53		
Discharge DAPT	0.76 (0.54-1.07)	0.12	0.70 (0.49-1.01)	0.059
Discharge anti-coagulant agent	1.45 (1.01-2.08)	0.043		
<b>Procedure-related variables</b>				
TAVR device generation (new vs. old)	0.87 (0.63-1.20)	0.39		
Access (transfemoral vs. nontransfemoral)	1.01 (0.60-1.69)	0.96		
Device size (>26 mm vs. ≤26 mm)	1.24 (0.86-1.81)	0.25		
Moderate or severe aortic regurgitation	1.16 (0.76-1.78)	0.50		
<b>Female-specific characteristics</b>				
History of pregnancy	0.83 (0.60-1.16)	0.28		
Age of menopause	1.01 (0.98-1.05)	0.50		
History of osteoporosis	0.93 (0.62-1.40)	0.73		

## Sex-Related Differences in Outcomes After Transcatheter or Surgical Aortic Valve Replacement in Patients With Severe Aortic Stenosis

men had a more than 3-fold higher incidence of moderate-to-severe **paravalvular leak** compared with women (10.3% vs. 3%)

**Table 4** Echocardiographic Findings at Discharge

	Female			Male			p Value (a) vs. (d)	p Value (b) vs. (e)
	(a) TAVR (n = 146)	(b) Surgery (n = 134)	p Value	(d) TAVR (n = 201)	(e) Surgery (n = 198)	p Value		
Peak gradient	22.72 ± 8.55	25.00 ± 9.91	0.06	19.60 ± 8.18	22.04 ± 10.19	0.08	0.001	0.008
Mean gradient	11.86 ± 4.84	12.91 ± 5.45	0.08	10.13 ± 4.30	11.13 ± 5.13	0.17	0.002	0.004
AVA, cm <sup>2</sup>	1.49 ± 0.42	1.36 ± 0.42	0.01	1.71 ± 0.55	1.56 ± 0.48	0.009	<0.001	0.001
AVA <sub>i</sub> , cm <sup>2</sup> /m <sup>2</sup>	0.89 ± 0.27	0.81 ± 0.26	0.03	0.90 ± 0.30	0.81 ± 0.27	0.009	0.97	0.98
PVL								
None	28.0	83.9	<0.0001	23.9	80.7	<0.0001	0.41	0.50
Trace	27.3	12.5	0.004	23.9	13.8	0.02	0.50	0.76
Mild	41.7	3.6	<0.0001	41.8	4.8	<0.0001	0.97	0.76
Moderate	3.0	0.0	0.13	9.2	0.7	0.0007	0.03	1.0
Severe	0.0	0.0	NA	1.1	0.0	0.51	0.51	NA
Ejection fraction	57.8 ± 11.4	54.4 ± 12.40	0.20	53.6 ± 12.0	52.0 ± 12.0	0.39	0.07	0.35

# Sex-Based Differences in Outcomes With Transcatheter Aortic Valve Therapy



TVT Registry From 2011 to 2014

**TABLE 2** Procedural Characteristics

	Overall (N = 23,652)	Female Patients (n = 11,808)	Male Patients (n = 11,844)	p Value
Cover index				<0.0001
Median	10.34 (4.35-15.38)	11.54 (4.35-17.24)	10.34 (3.85-15.38)	
<8%	8,435 (40.21)	3,600 (34.30)	4,835 (46.13)	
≥8%	12,541 (59.79)	6,895 (65.70)	5,646 (53.87)	

Female have a higher cover index after TAVI

# Conclusion

Severe aortic stenosis has an equal prevalence in males and female

Higher utilization of AVR in men compared with women

Disparity in referral to valve replacement is not seen with the current TAVI practice

TAVR may be preferred over surgery for high-risk female patients



Tank for Your attention