

Satellite Symposium

Sapien 3 Higher Standard is Going to Make You An Offer You Can't Refuse  
Organized by CVRF and Supported by Educational Grant from Edwards Lifesciences Korea Co., Ltd.

# ***Small Annuli and Sapien 3: Clinical Outcome***

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Keiji Mitsube, Takeshi Kawamura, Ryuji Koshima, and Tsutomu Fujita***

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# COI Disclosure

***Daisuke Hachinohe**, Ryo Horita, Hidemasa Shitan, Umihiko Kaneko,  
Ken Kobayashi, Naohiro Wakabayashi, Makoto Hashimoto, Yosuke Kuroda,  
Keijiro Mitsube, Takeshi Kawamura, Ryuji Koshima, and Tsutomu Fujita*

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# *Small Annulus*

- There is No clear definition

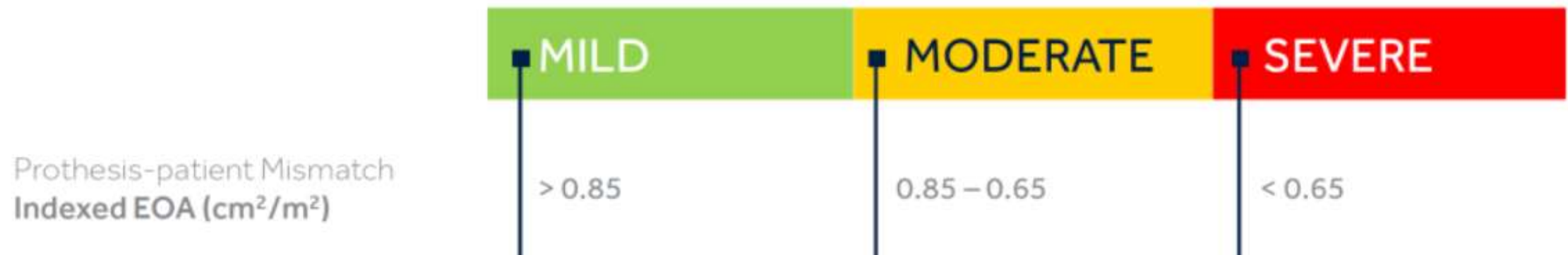
Annulus into which a surgical prosthesis  $> 21\text{mm}$  can't be accommodated

Annular diameter  $\leq 23\text{mm}$  ( $\leq 21\text{mm}$ )



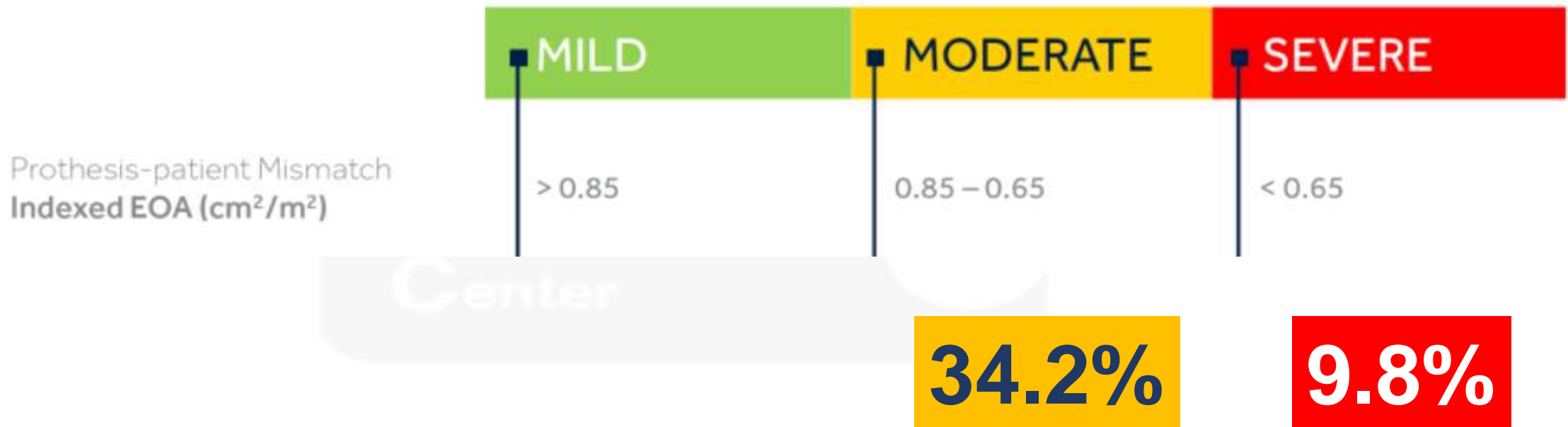
# Prosthesis-Patient Mismatch: PPM

PPM occurs when the effective orifice area (EOA) of the implanted prosthesis is too small in relation to the patient's body size, resulting in abnormally high postoperative gradients.



# PPM after SAVR

Systematic review and meta-analysis  
34 observational studies  
(n=27,186)



# PPM after SAVR

Systematic review and meta-analysis

34 observational studies

(n=27,186)

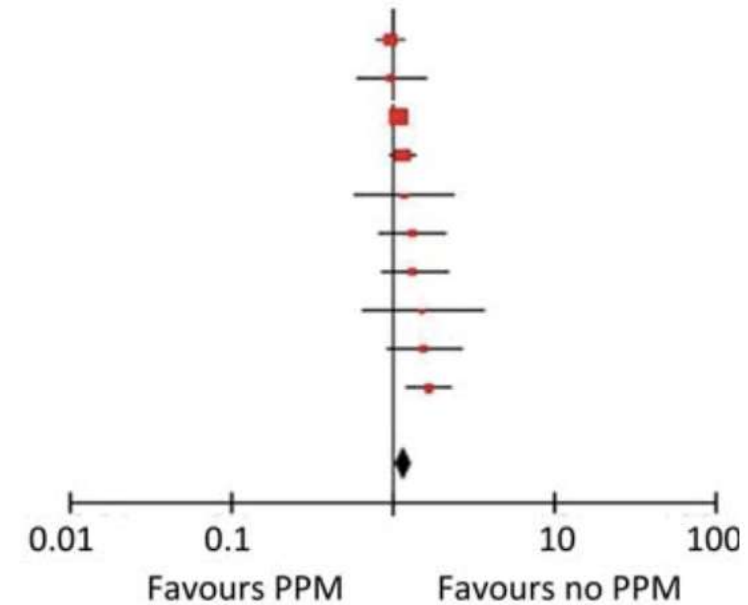
Follow-up ranged from **2.5 to 7.9 years**

PPM is associated with an increase in all-cause and cardiac-related mortality over long-term follow-up.

## Moderate PPM

Moon 2009	0.99 [0.81, 1.20]
Howell 2006	0.99 [0.61, 1.62]
Jamieson 2010	1.12 [0.99, 1.26]
Mohty 2009	1.19 [0.99, 1.41]
Vicchio 2008	1.21 [0.60, 2.45]
Mrowczynski 2009	1.34 [0.83, 2.14]
Mohty 2006	1.37 [0.86, 2.20]
Milano 2002	1.57 [0.68, 3.64]
Florath 2008	1.59 [0.95, 2.68]
Kohsaka 2008	1.72 [1.25, 2.35]

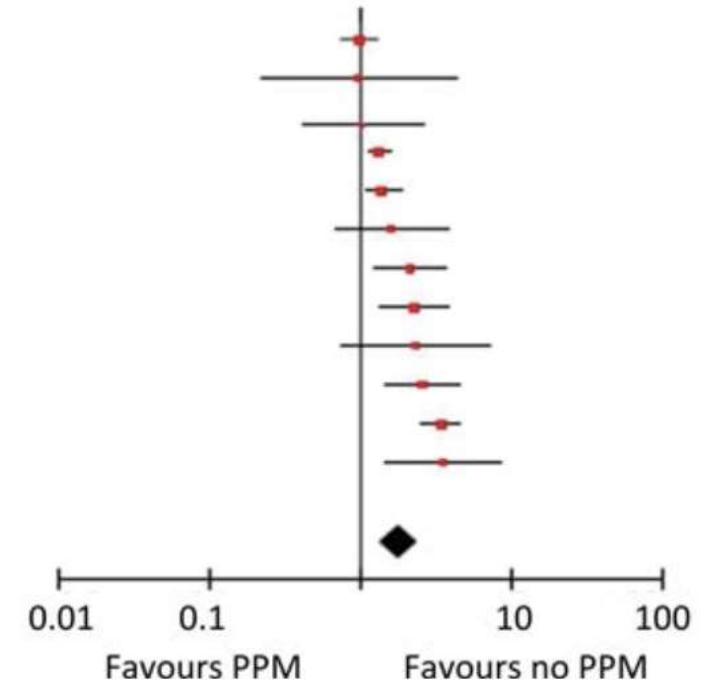
**Total [95% CI]** **1.19 [1.07, 1.33]**  
Heterogeneity:  $I^2 = 26\%$



## Severe PPM

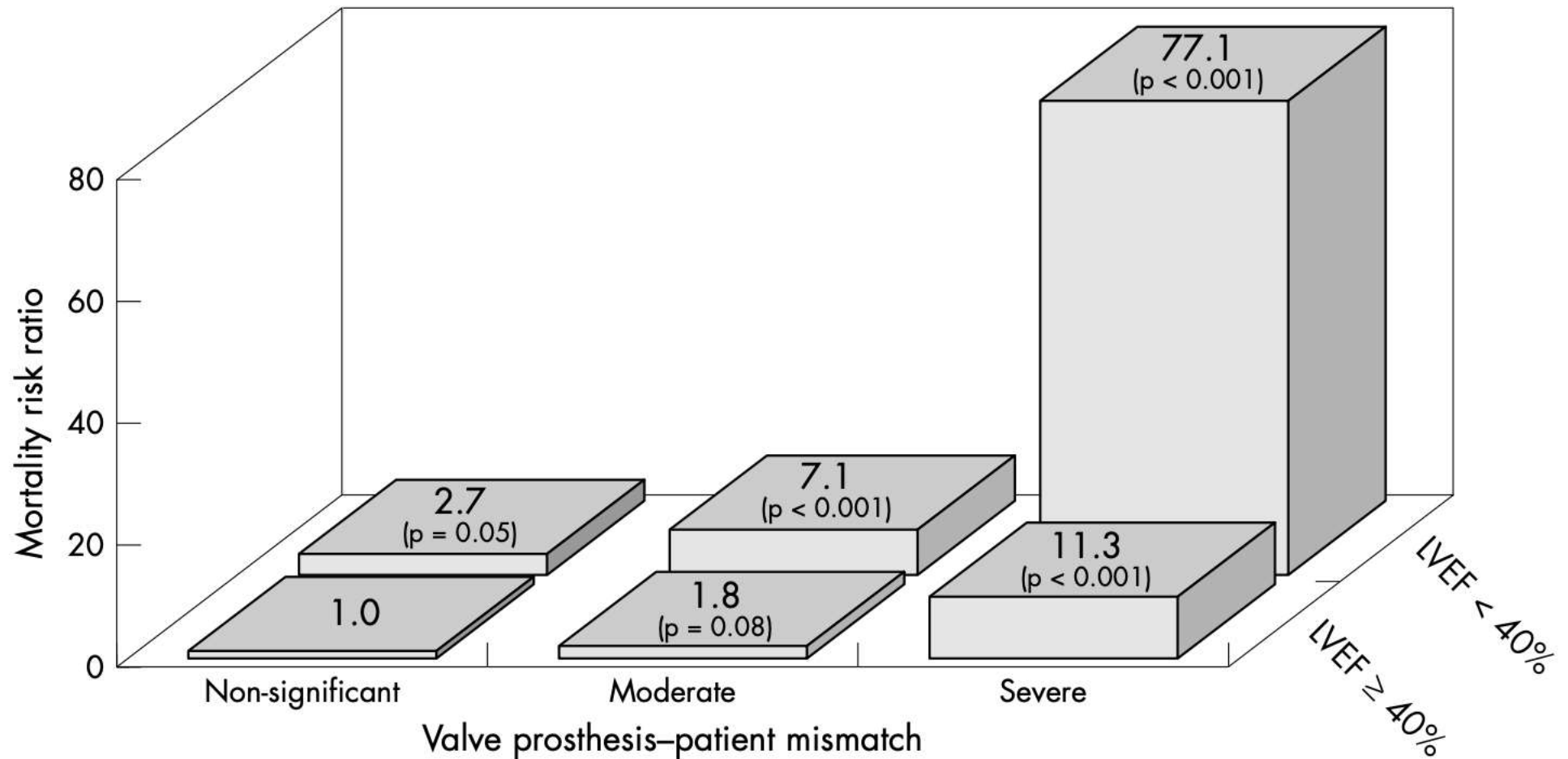
Moon 2009	0.99 [0.75, 1.30]
Milano 2002	1.00 [0.23, 4.35]
Hanayama 2002	1.03 [0.37, 2.86]
Walther 2006	1.38 [1.15, 1.64]
Jamieson 2010	1.43 [1.09, 1.89]
Mrowczynski 2009	1.63 [0.69, 3.87]
Florath 2008	2.18 [1.28, 3.72]
Mohty 2009	2.31 [1.38, 3.87]
Vicchio 2009	2.39 [0.77, 7.44]
Mohty 2006	2.64 [1.49, 4.66]
Howell 2006	3.49 [2.60, 4.68]
Kohsaka 2008	3.56 [1.47, 8.60]

**Total [95% CI]** **1.84 [1.38, 2.45]**  
Heterogeneity:  $I^2 = 79\%$



# In which patients PPM affects mortality after SAVR?

Retrospective  
Single-center  
(n=1,166)



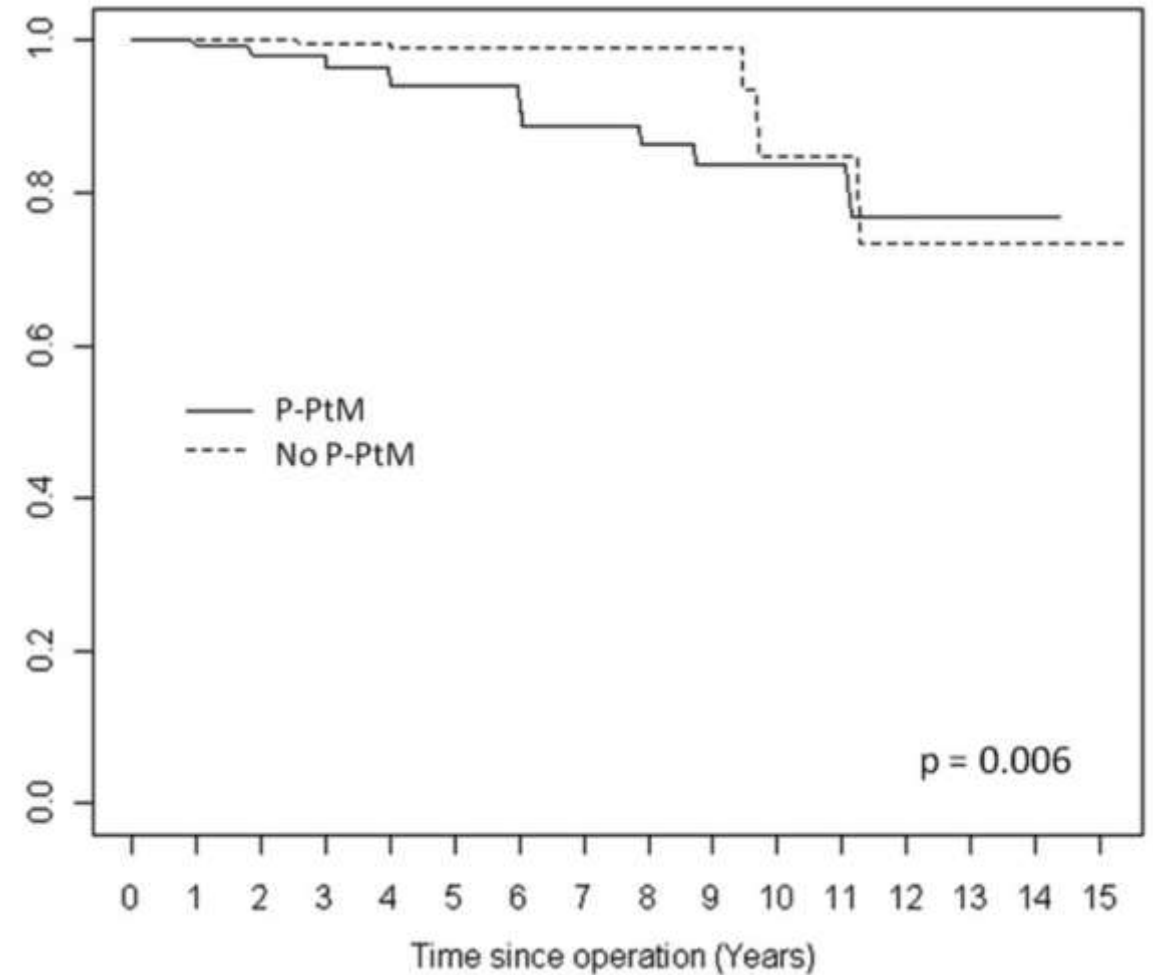
# PPM cause early structural valve deterioration (SVD)

Retrospective  
Single-center  
(n=564)

**Table 4. Multivariable Analysis of SVD (Cox With Multiple Imputation Method)**

	Hazard Ratio	95% CI	<i>P</i>
Size ≤21	2.35	1.14–4.85	0.02
Anticalcification treatment	0.34	0.17–0.66	0.002
P-PtM	2.29	1.03–5.06	0.04

CI indicates confidence interval.



In patients with PPM, SVD occurs 2 to 3 years earlier than in patients without PPM.  
Smaller valve may be independent predictor of SVD.



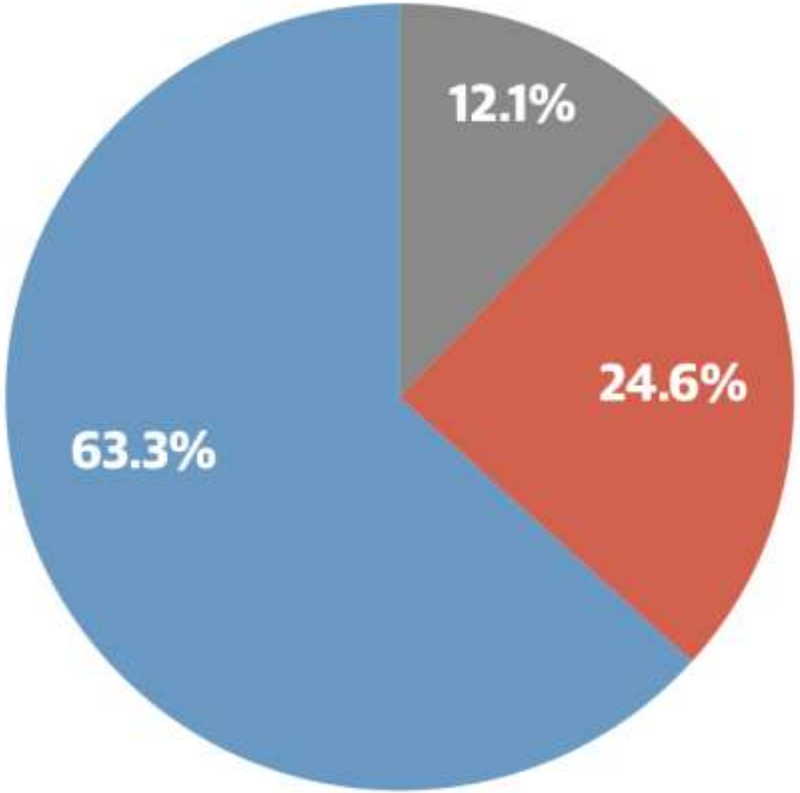
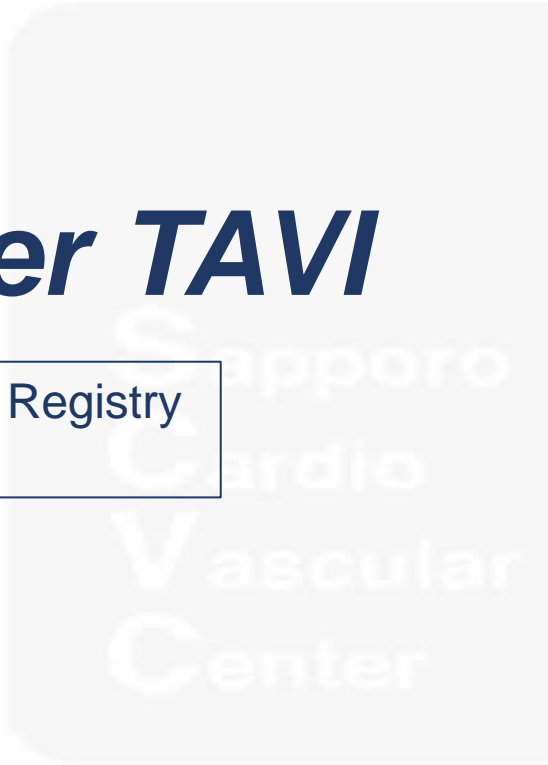
- ✓ *Severe PPM definitely affects mortality*
- ✓ *In patients with low EF, moderate PPM should be avoided*
- ✓ *PPM may cause early SVD*

***From SAVR data***

## Prosthesis-Patient Mismatch (PPM)

# PPM after TAVI

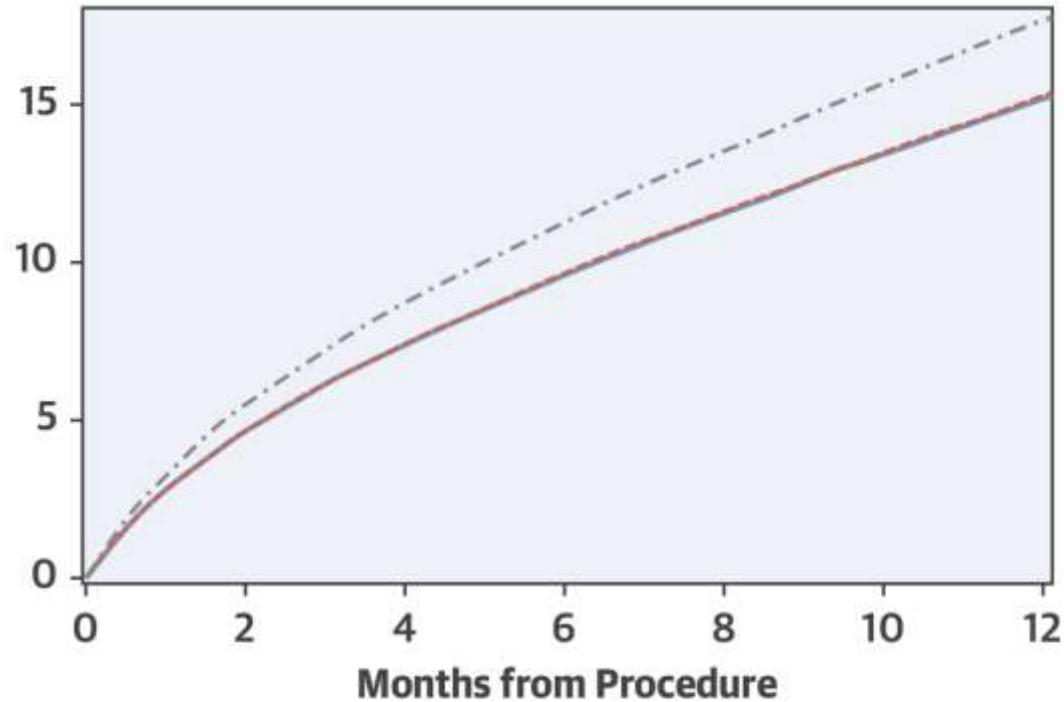
STS/ACC TVT Registry  
(n= 62,125)



- Severe (Sev)
- Moderate (Mod)
- None

# PPM after TAVI

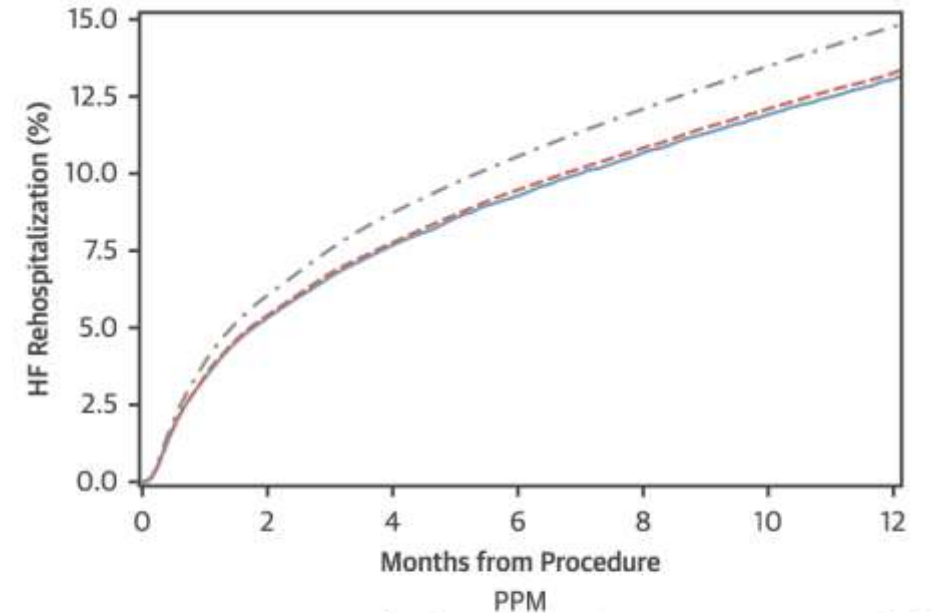
STS/ACC TVT Registry  
(n= 62,125)



PPM

--- Sev PPM (EOAi < 0.65 cm<sup>2</sup>/m<sup>2</sup>)    - - - Mod PPM (EOAi 0.65-0.85 cm<sup>2</sup>/m<sup>2</sup>)

— No PPM (EOAi > 0.85 cm<sup>2</sup>/m<sup>2</sup>)



PPM

— No PPM (EOAi > 0.85 cm<sup>2</sup>/m<sup>2</sup>)    - - - Mod PPM (EOAi 0.65-0.85 cm<sup>2</sup>/m<sup>2</sup>)

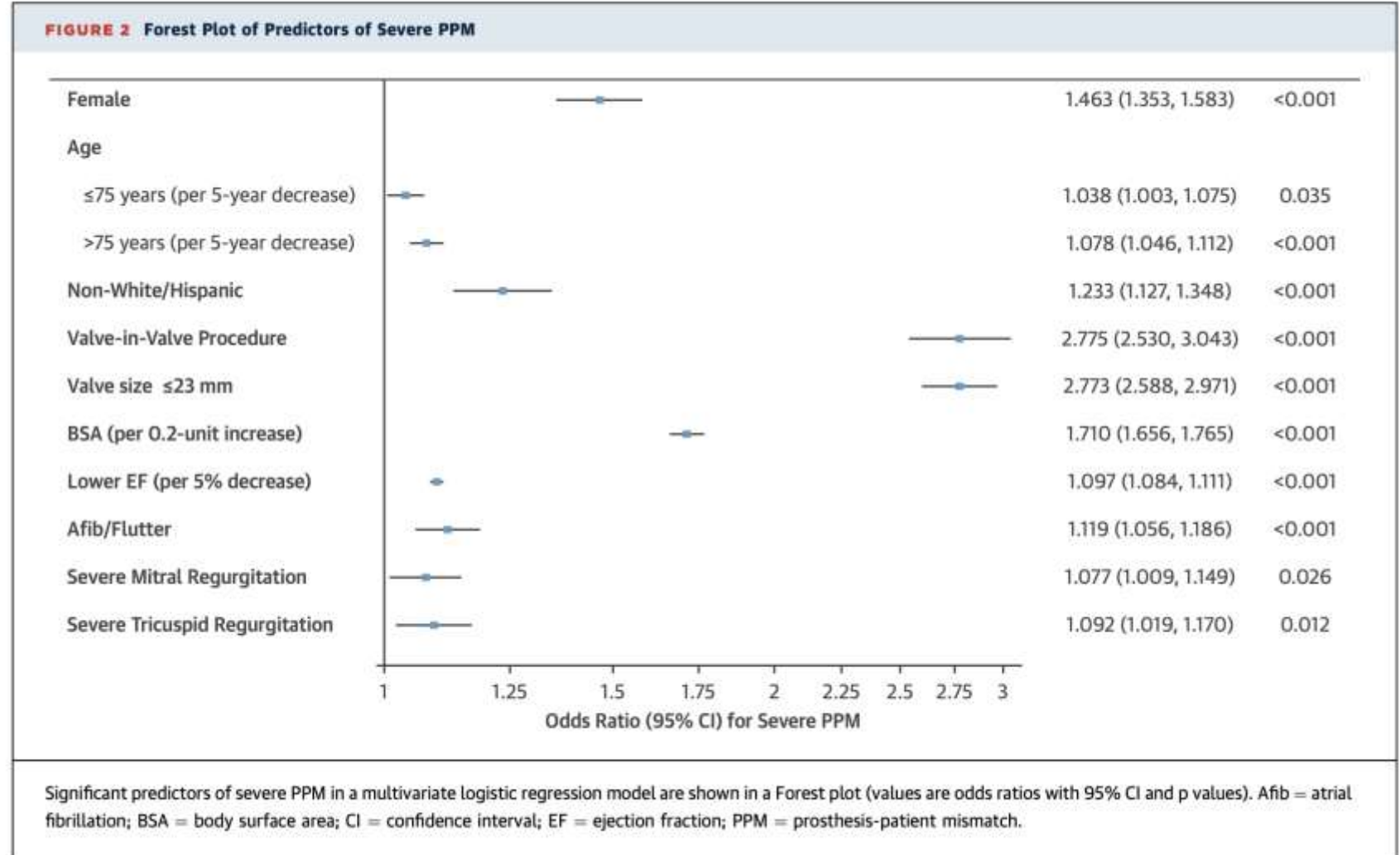
--- Sev PPM (EOAi < 0.65 cm<sup>2</sup>/m<sup>2</sup>)

Number at Risk Adjusting for baseline covariates:

	Day 0	Month 4	Month 8	Month 12
No PPM	23,642	19,561	15,086	11,502
Mod PPM	8,986	7,386	5,581	4,183
Sev PPM	4,153	3,328	2,475	1,819

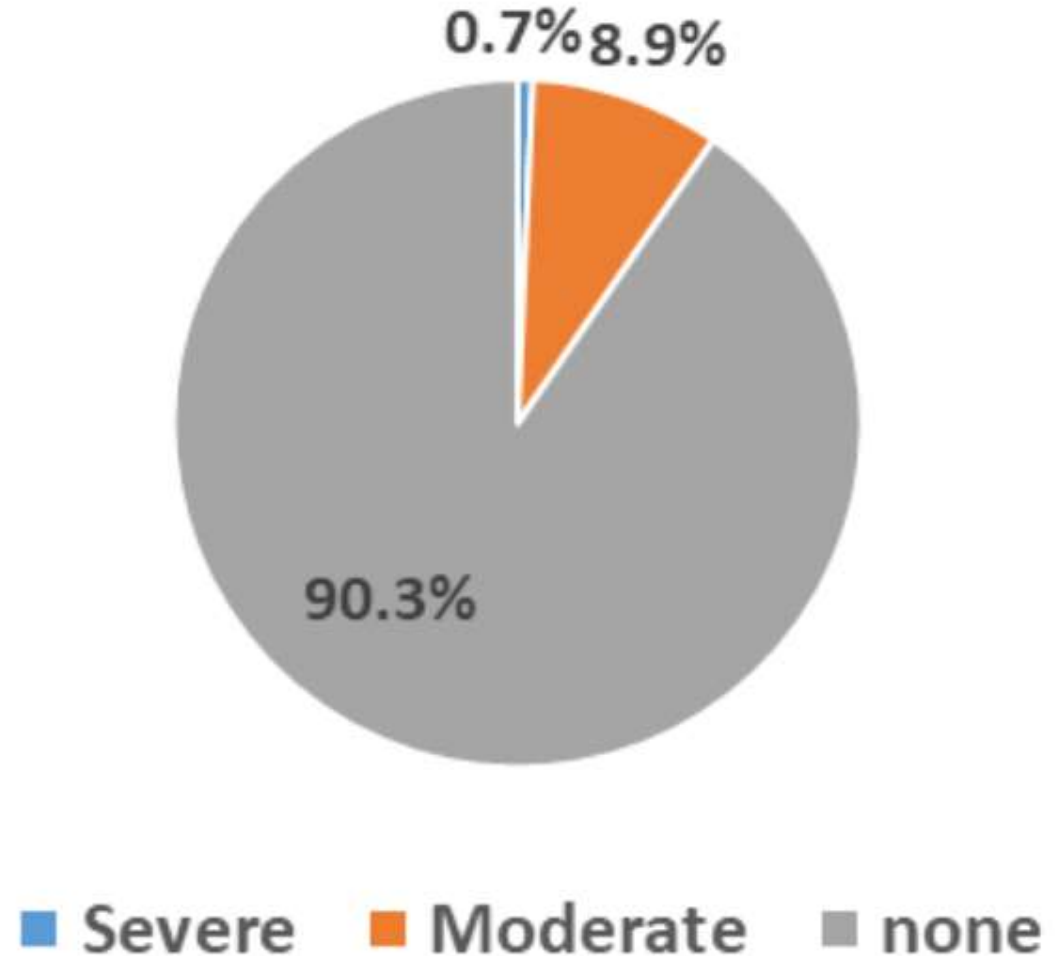
# PPM after TAVI

STS/ACC TVT Registry  
(n= 62,125)



# PPM after TAVI in Japanese patients

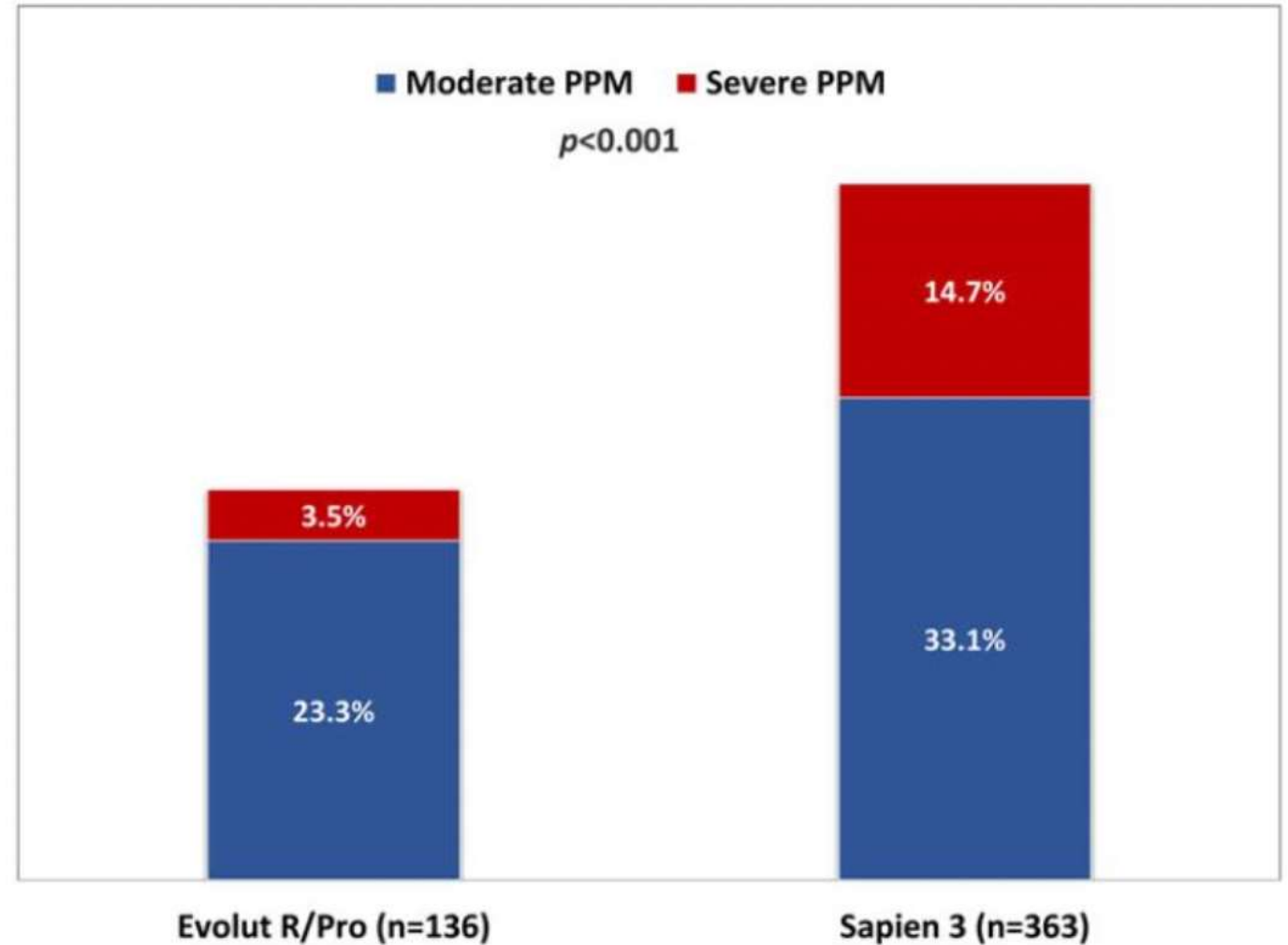
The OCEAN-TAVI Registry  
(n= 1,558)  
Female: 70%  
BSA: 1.41-1.46m<sup>2</sup>



# PPM after TAVI Evolut vs. Sapien 3

SE-THV vs. BE-THV

- The CHOICE trial  
Randomized control trial
- The CHOICE-Extend registry  
Prospective registry



# PPM after TAVI Evolut vs. Sapien 3

The OCEAN-TAVI Registry (n=1,558)

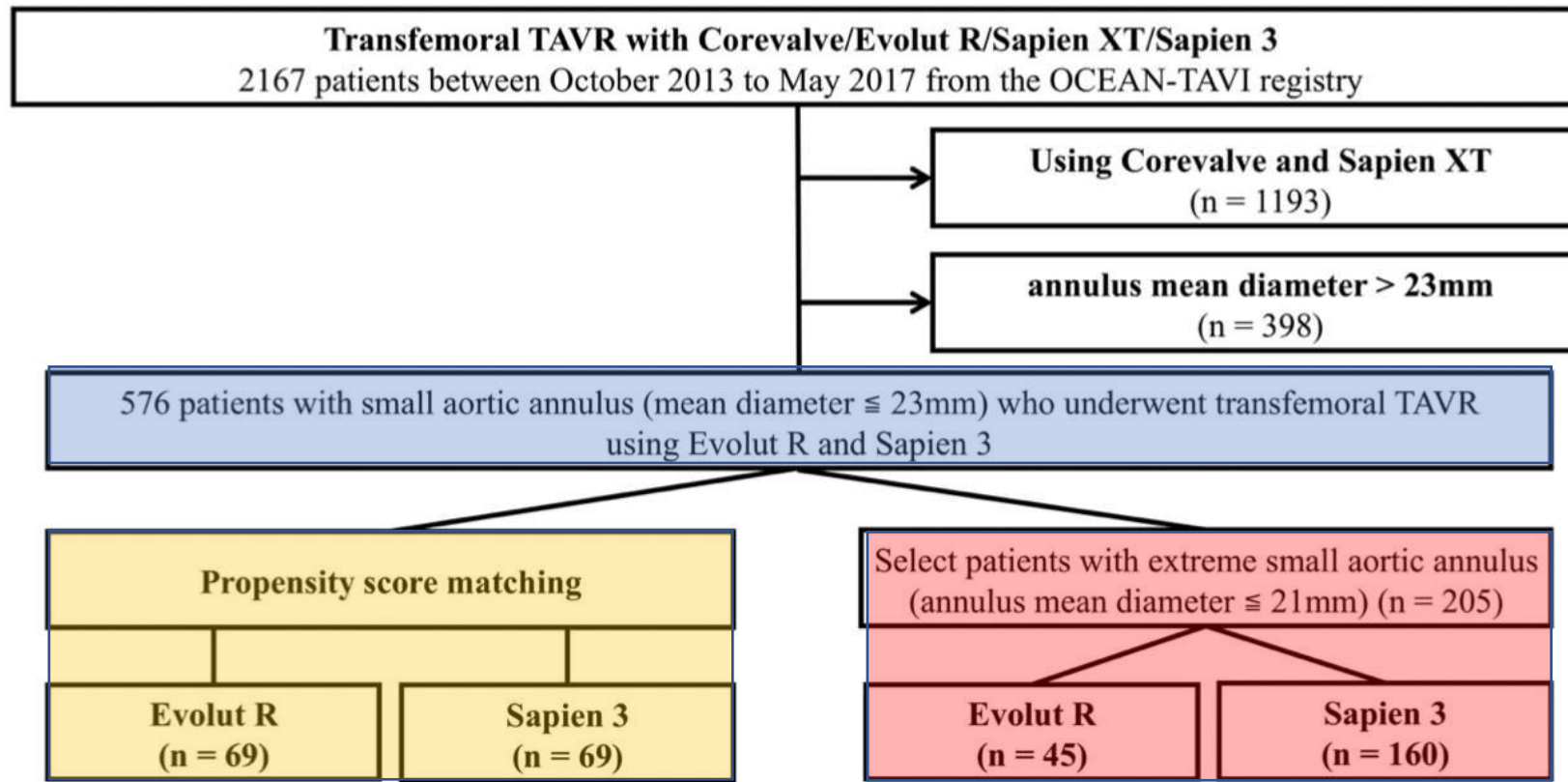
**TABLE 4** Multivariate Logistic Regression Analysis for the Predictive Factors of PPM

	Univariate		Multivariate (Model 1)		Multivariate (Model 2)	
	OR (95% CI)	p Value	OR (95% CI)	p Value	OR (95% CI)	p Value
Age, yrs	0.95 (0.92-0.99)	0.004	0.96 (0.93-0.99)	0.01	0.96 (0.93-0.99)	0.01
Body surface area (per 0.1 m <sup>2</sup> increase)	1.14 (1.04-1.26)	0.01	1.46 (1.29-1.66)	<0.0001	1.47 (1.29-1.67)	<0.0001
AVA (per 0.1 cm <sup>2</sup> increase)	0.83 (0.74-0.92)	0.0004	0.75 (0.67-0.85)	<0.0001	0.76 (0.67-0.85)	<0.0001
Annular area (per 10 cm <sup>2</sup> increase)	0.94 (0.91-0.97)	<0.0001	0.90 (0.87-0.93)	<0.0001	0.90 (0.87-0.93)	<0.0001
Balloon post-dilatation	0.47 (0.27-0.76)	0.0015	1.90 (1.16-3.31)	0.01	0.53 (0.30-0.87)	0.01
Device type						
Sapien 3 vs. non-Sapien 3	2.27 (1.39-3.58)	0.0014	2.73 (1.63-4.45)	0.0002	-	-
CoreValve vs. Sapien XT	1.40 (0.77-2.37)	0.25	-	-	1.58 (0.85-2.76)	0.14
Sapien 3 vs. Sapien XT	2.36 (1.44-3.74)	0.0009	-	-	2.88 (1.71-4.73)	0.0001

CI = confidence interval; OR = odds ratio; other abbreviations as in Table 1.

# PPM after TAVI Evolut vs. Sapien 3 in small annulus

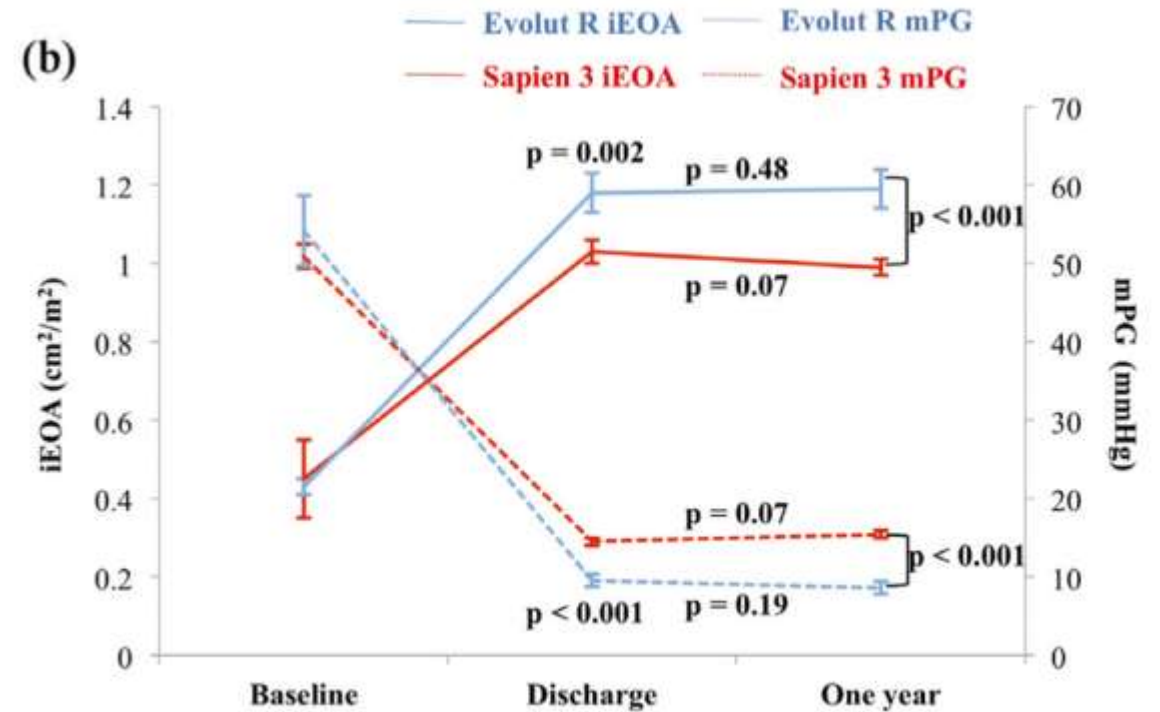
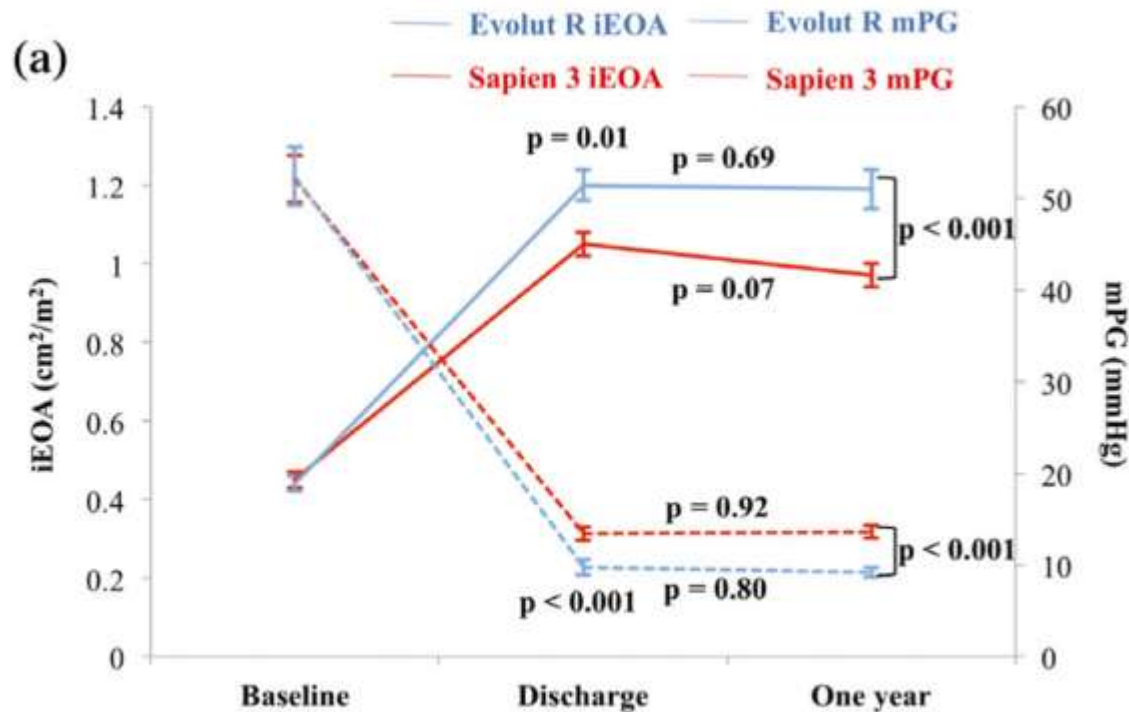
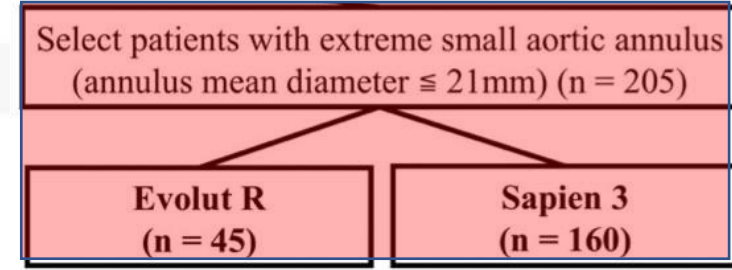
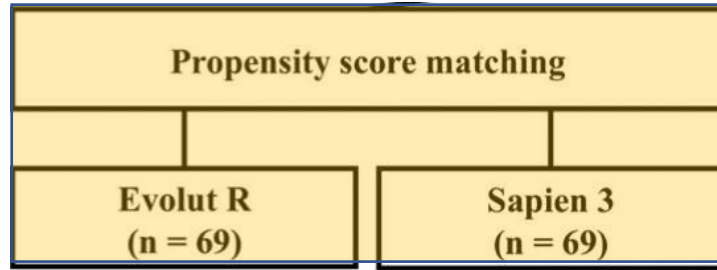
The OCEAN-TAVI Registry





# PPM after TAVI Evolut vs. Sapien 3 in small annulus

The OCEAN-TAVI Registry

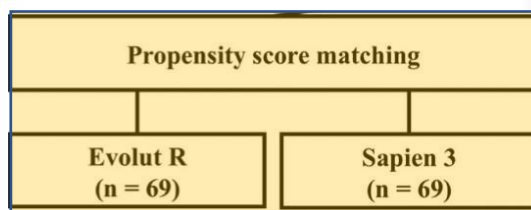


*In small annulus, Evolut may be better than Sapien 3 ??*



# PPM after TAVI Evolut vs. Sapien 3 in small annulus

OCEAN-TAVI Registry



**TABLE 5** Postprocedural echocardiographic data at discharge and at 1 year after TAVR in the matched cohort

	Discharge				One year			
	Overall (N = 138)	Evolut R (N = 69)	Sapien 3 (N = 69)	p-Value	Overall (N = 97)	Evolut R (N = 47)	Sapien 3 (N = 50)	p-Value
Indexed EOA, cm <sup>2</sup> /m <sup>2</sup>	1.12 (0.95–1.35)	1.20 (1.01–1.46)	1.08 (0.90–1.28)	.01	1.04 (0.87–1.26)	1.21 (0.92–1.35)	0.96 (0.83–1.12)	<.001
Moderate PPM (IEOA ≤0.85), n (%)	17 (12.9)	5 (7.7)	12 (17.9)	.08	21 (21.6)	7 (14.9)	14 (28.0)	.12
Severe PPM (IEOA ≤0.65), n (%)	3 (2.3)	1 (1.5)	2 (3.0)	1.00	2 (2.1)	0 (0.0)	2 (4.0)	.50
Mean PG, mmHg	11.0 (8.0–13.8)	9.0 (6.0–12.0)	12.0 (10.0–14.8)	<.001	10.0 (8.0–14.8)	9.0 (6.0–11.9)	12.0 (9.9–16.3)	<.001
AR				.05				.24
None, n (%)	25 (18.5)	15 (22.4)	10 (14.7)		20 (20.6)	11 (23.4)	9 (18.0)	
Trivial, n (%)	52 (38.5)	19 (28.4)	33 (48.5)		38 (39.2)	16 (34.0)	22 (44.0)	
Mild, n (%)	58 (43.0)	33 (49.3)	25 (36.8)		36 (37.1)	17 (36.2)	19 (38.0)	
≥Moderate, n (%)	0 (0.0)	0 (0.0)	0 (0.0)		3 (3.1)	3 (6.4)	0 (0.0)	

Note: Values are medians (25th–75th percentiles) or n (%).

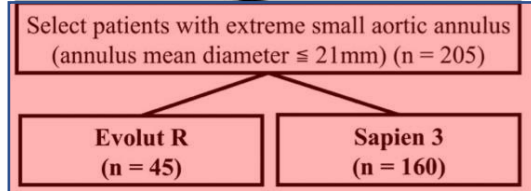
Abbreviations: AR, aortic regurgitation; EOA, effective orifice area; PG, pressure gradient; PPM, prosthesis-patient mismatch.

**TABLE 6** Postprocedural echocardiographic data at discharge and at 1 year after TAVR in the extreme small annulus cohort

	Discharge				One year			
	Overall (N = 205)	Evolut R (N = 45)	Sapien 3 (N = 160)	p-Value	Overall (N = 145)	Evolut R (N = 29)	Sapien 3 (N = 116)	p-Value
Indexed EOA, cm <sup>2</sup> /m <sup>2</sup>	1.07 (0.90–1.27)	1.17 (0.99–1.46)	1.04 (0.88–1.18)	.002	1.00 (0.86–1.19)	1.20 (1.01–1.37)	0.97 (0.82–1.14)	<.001
Moderate PPM (IEOA ≤0.85), n (%)	34 (17.0)	4 (9.1)	30 (19.2)	.11	35 (24.1)	2 (6.9)	33 (28.4)	.015
Severe PPM (IEOA ≤0.65), n (%)	4 (2.0)	1 (2.3)	3 (1.9)	1.00	5 (3.4)	0 (0.0)	5 (4.3)	.26
Mean PG, mmHg	12.5 (9.0–16.3)	9.0 (6.0–11.0)	13.6 (10.0–16.9)	<.001	13.1 (10.0–17.8)	8.0 (5.0–11.2)	15.0 (11.3–18.0)	<.001
AR				<.001				.31
None, n (%)	46 (22.5)	8 (17.8)	38 (23.9)		51 (35.2)	7 (24.1)	44 (37.9)	
Trivial, n (%)	93 (45.6)	13 (28.9)	80 (50.3)		42 (29.0)	9 (31.0)	33 (28.4)	
Mild, n (%)	61 (29.9)	20 (44.4)	41 (25.8)		38 (26.2)	11 (37.9)	27 (23.3)	
≥Moderate, n (%)	4 (2.0)	4 (8.9)	0 (0.0)		8 (5.5)	2 (6.9)	6 (5.2)	

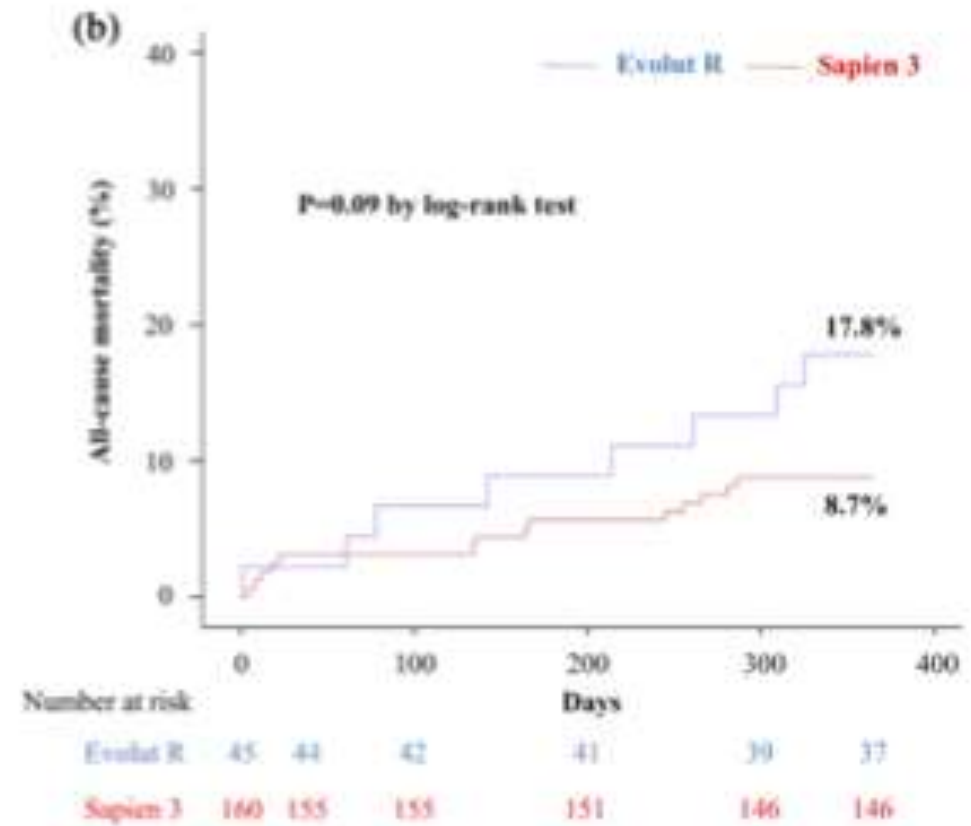
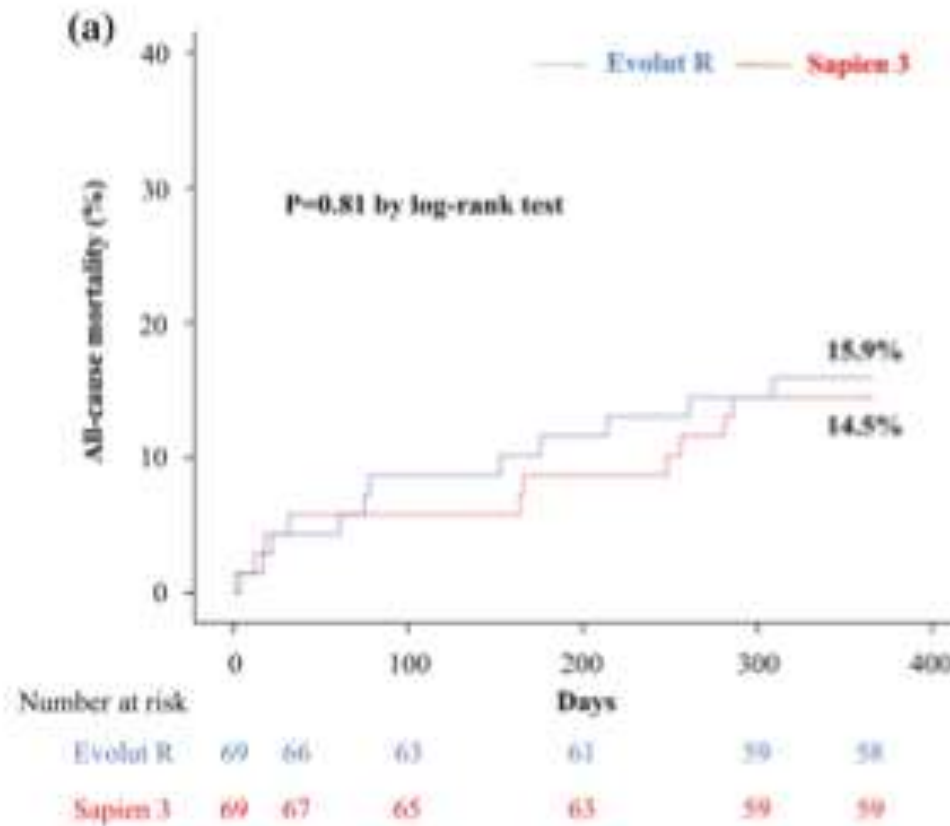
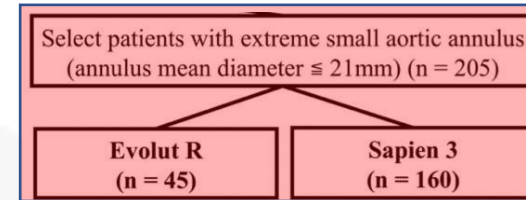
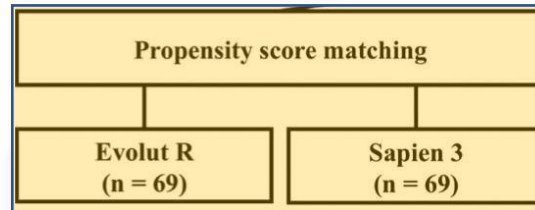
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Abbreviations: AR, aortic regurgitation; EOA, effective orifice area; PG, pressure gradient; PPM, prosthesis-patient mismatch.



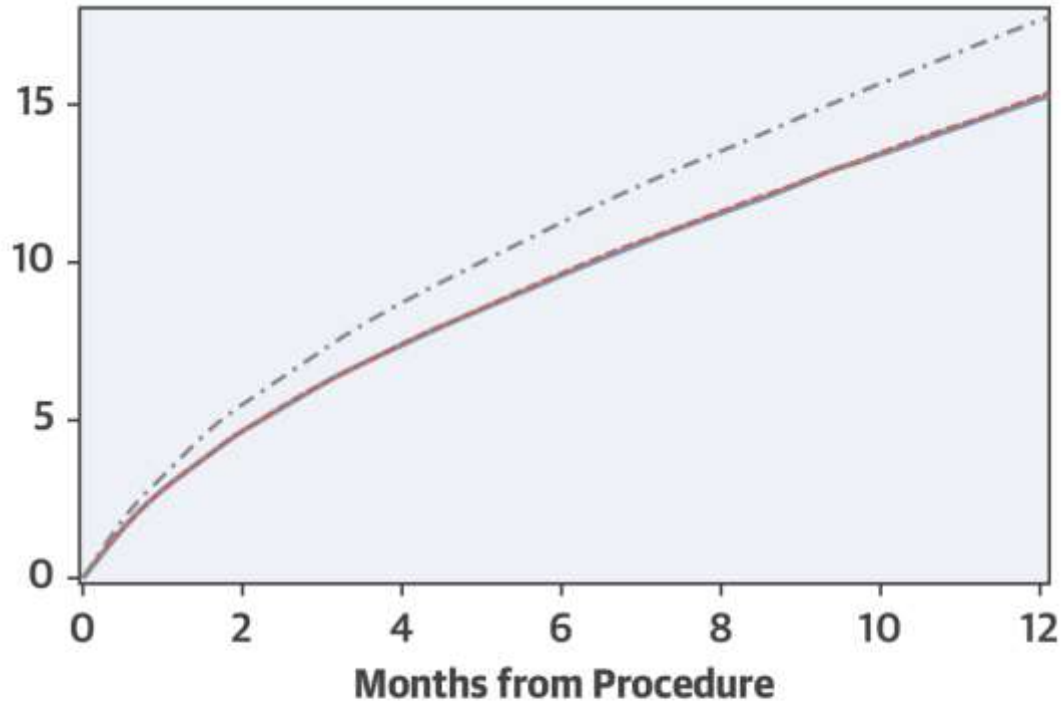
# PPM after TAVI Evolut vs. Sapien 3 in small annulus

OCEAN-TAVI  
Registry



# Moderate PPM after TAVI not affect clinical outcomes

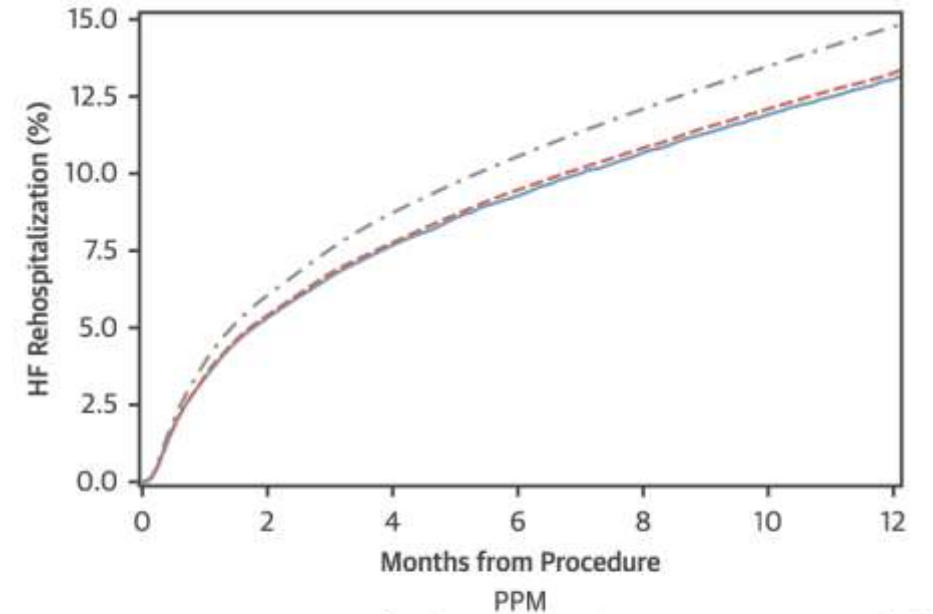
STS/ACC TVT Registry  
(n= 62,125)



PPM

--- Sev PPM (EOAi <0.65 cm<sup>2</sup>/m<sup>2</sup>)    - - - Mod PPM (EOAi 0.65-0.85 cm<sup>2</sup>/m<sup>2</sup>)

— No PPM (EOAi >0.85 cm<sup>2</sup>/m<sup>2</sup>)



PPM

— No PPM (EOAi >0.85 cm<sup>2</sup>/m<sup>2</sup>)    - - - Mod PPM (EOAi 0.65-0.85 cm<sup>2</sup>/m<sup>2</sup>)

--- Sev PPM (EOAi <0.65 cm<sup>2</sup>/m<sup>2</sup>)

Number at Risk Adjusting for baseline covariates:

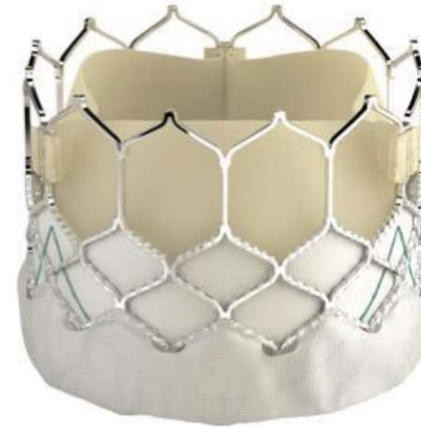
	Day 0	Month 4	Month 8	Month 12
No PPM	23,642	19,561	15,086	11,502
Mod PPM	8,986	7,386	5,581	4,183
Sev PPM	4,153	3,328	2,475	1,819

## 2.5-Year mortality of Evolut 23mm and Sapien3 20mm in SCVC



*Evolut R or PRO 23mm*

**1 death/ 15 cases**



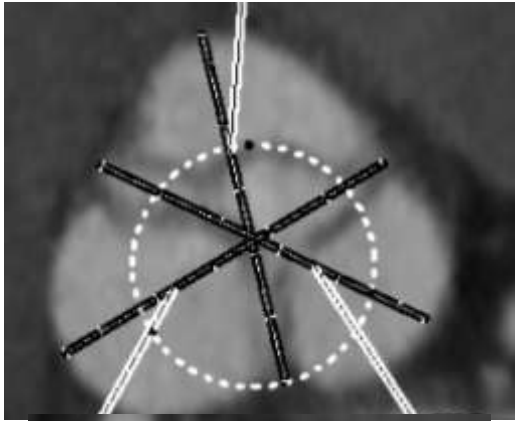
*Sapien3 20mm*

**No death/ 19 cases**

**/400 cases**



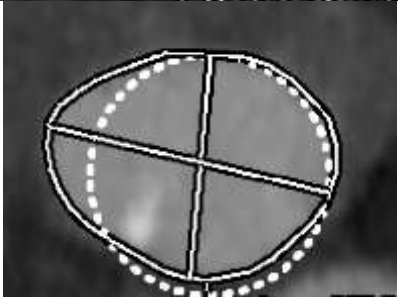
# 86 year-old female



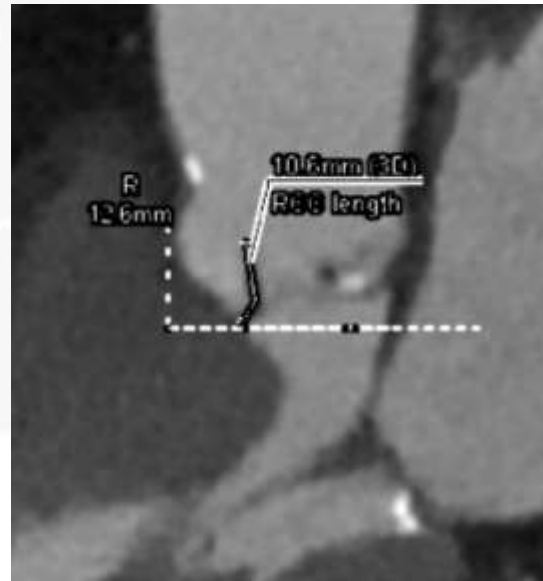
**SOV**  
27.2 (R)  
27.2 (L)  
28.0 (N)  
mm



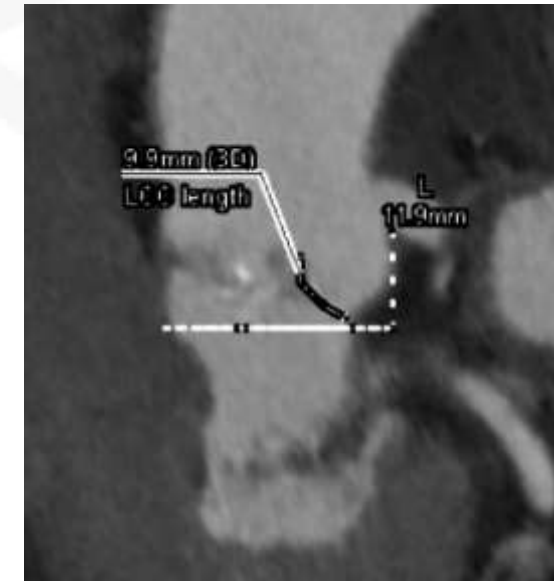
**STJ**  
24.6 x 25.8mm



**Annulus**  
295mm<sup>2</sup>  
perimeter : 62.2mm  
17.3 x 22.3mm

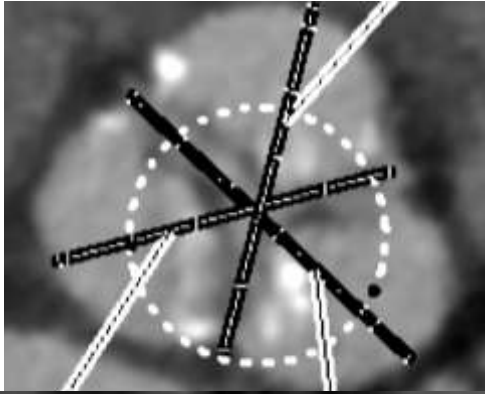


**RCA** 12.6mm

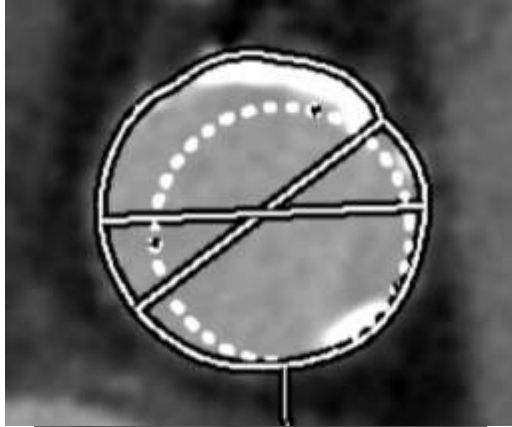
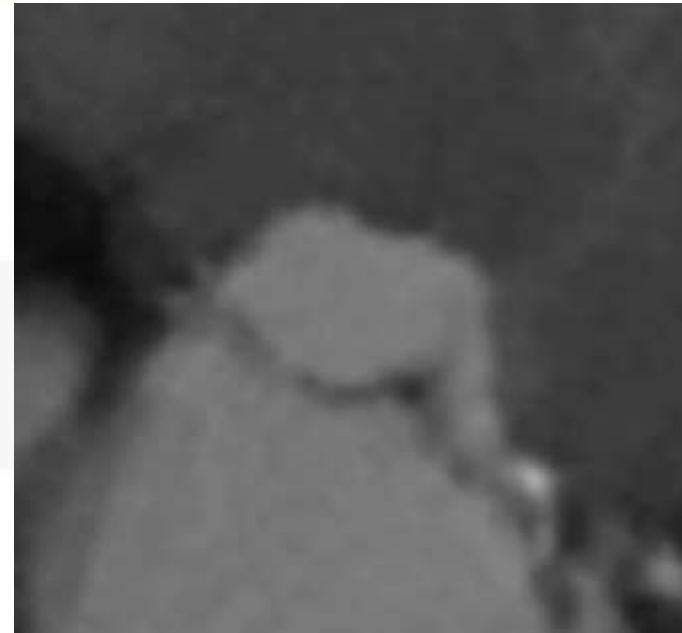


**LCA** 11.9mm

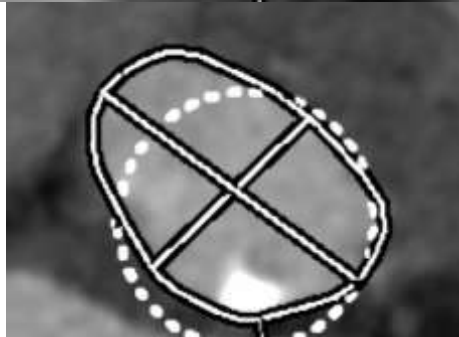
# 91 year-old female



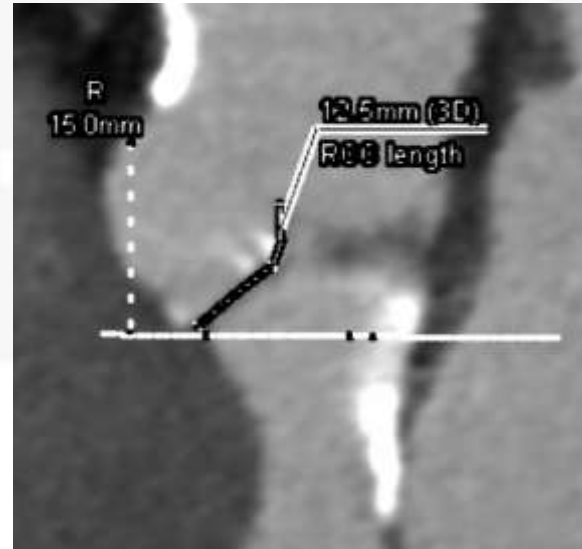
**SOV**  
26.5 (R)  
28.4 (L)  
25.7 (N)  
mm



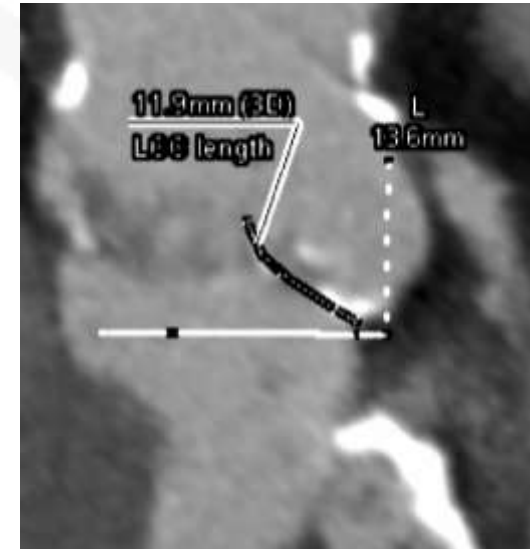
**STJ**  
23.3 × 24.4mm



**Annulus**  
303mm<sup>2</sup>  
perimeter : 64.22mm  
16.2 × 23.8mm



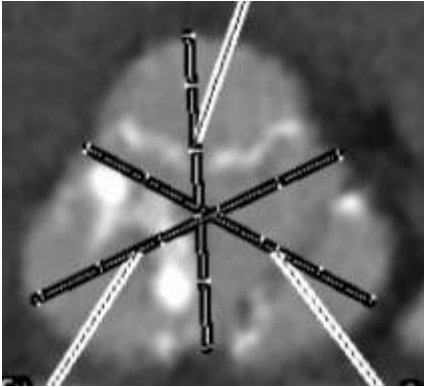
RCA 15.0mm



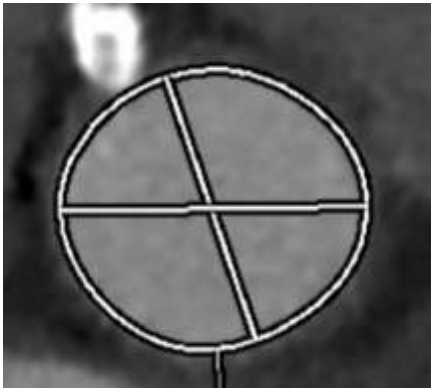
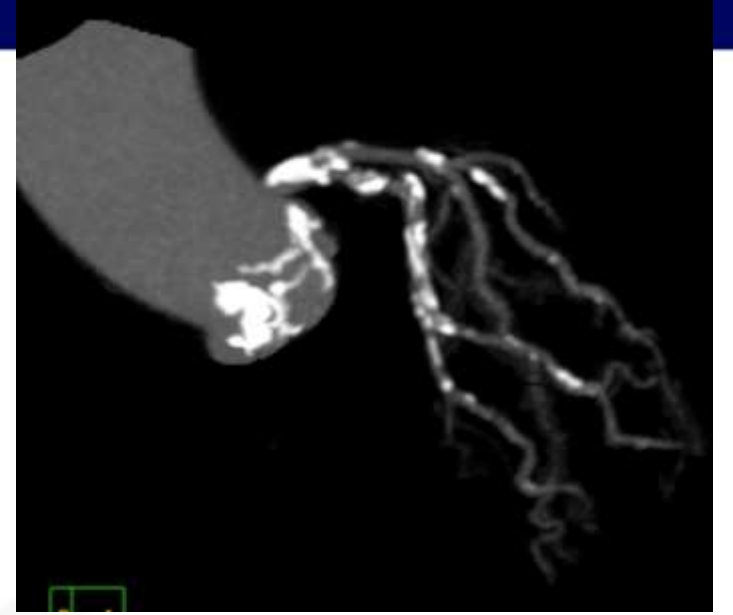
LCA 13.6mm



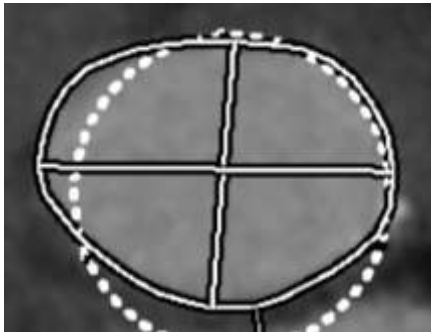
# 88 year-old female



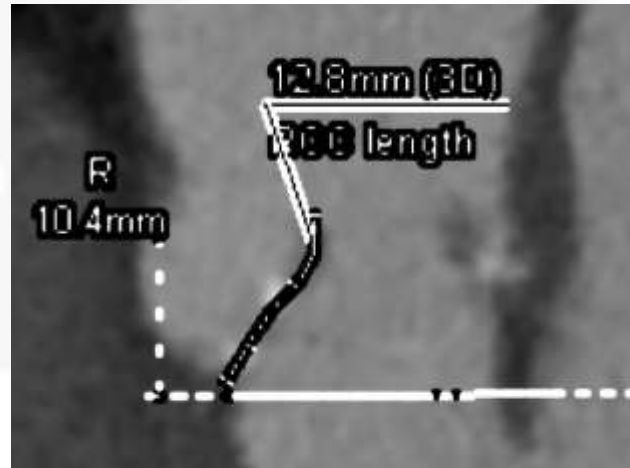
SOV  
23.7 (R)  
24.5 (L)  
25.5 (N)  
mm



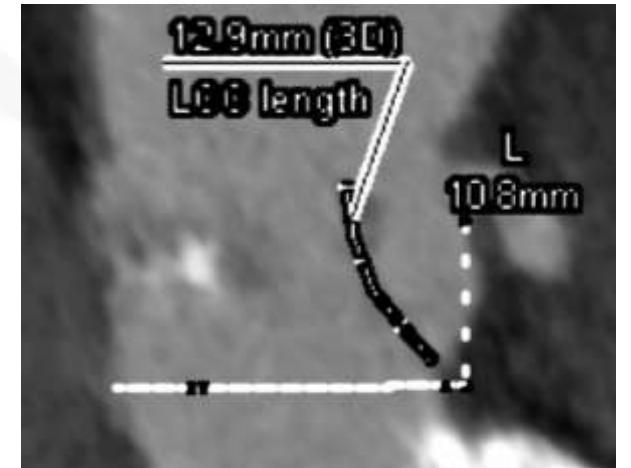
STJ  
21.0 × 23.3mm



Annulus  
333mm<sup>2</sup>  
perimeter : 66.2mm  
17.8 × 23.8mm



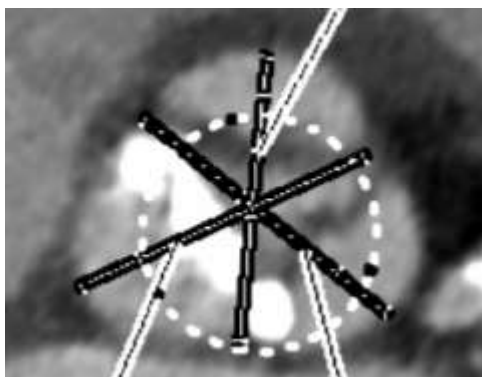
RCA 10.4mm



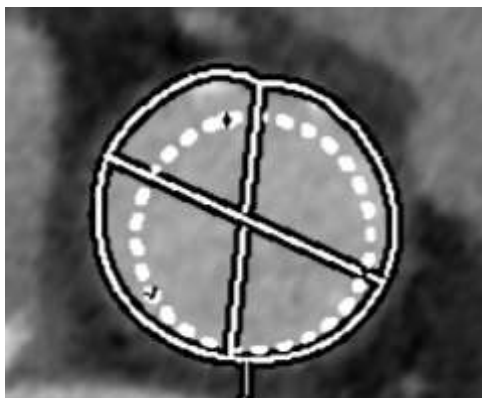
LCA 10.8mm



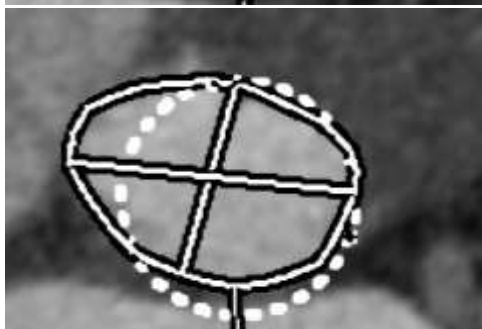
# 94 year-old female



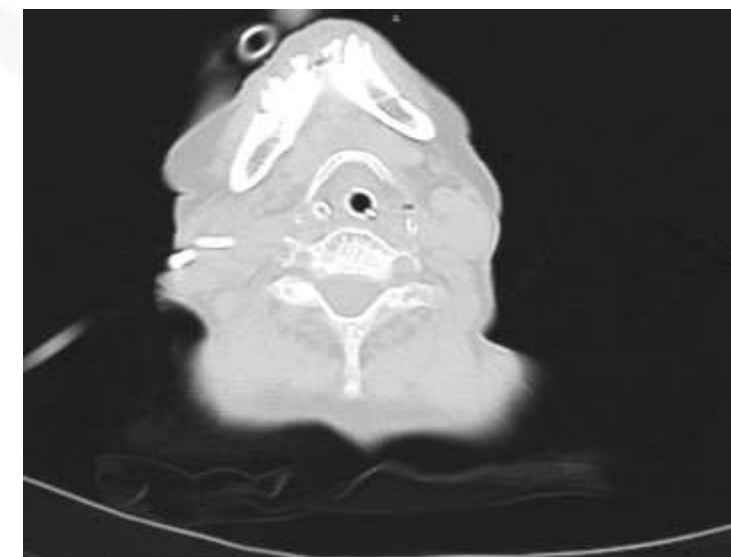
SOV  
23.0 (R)  
25.0 (L)  
25.2 (N)  
mm

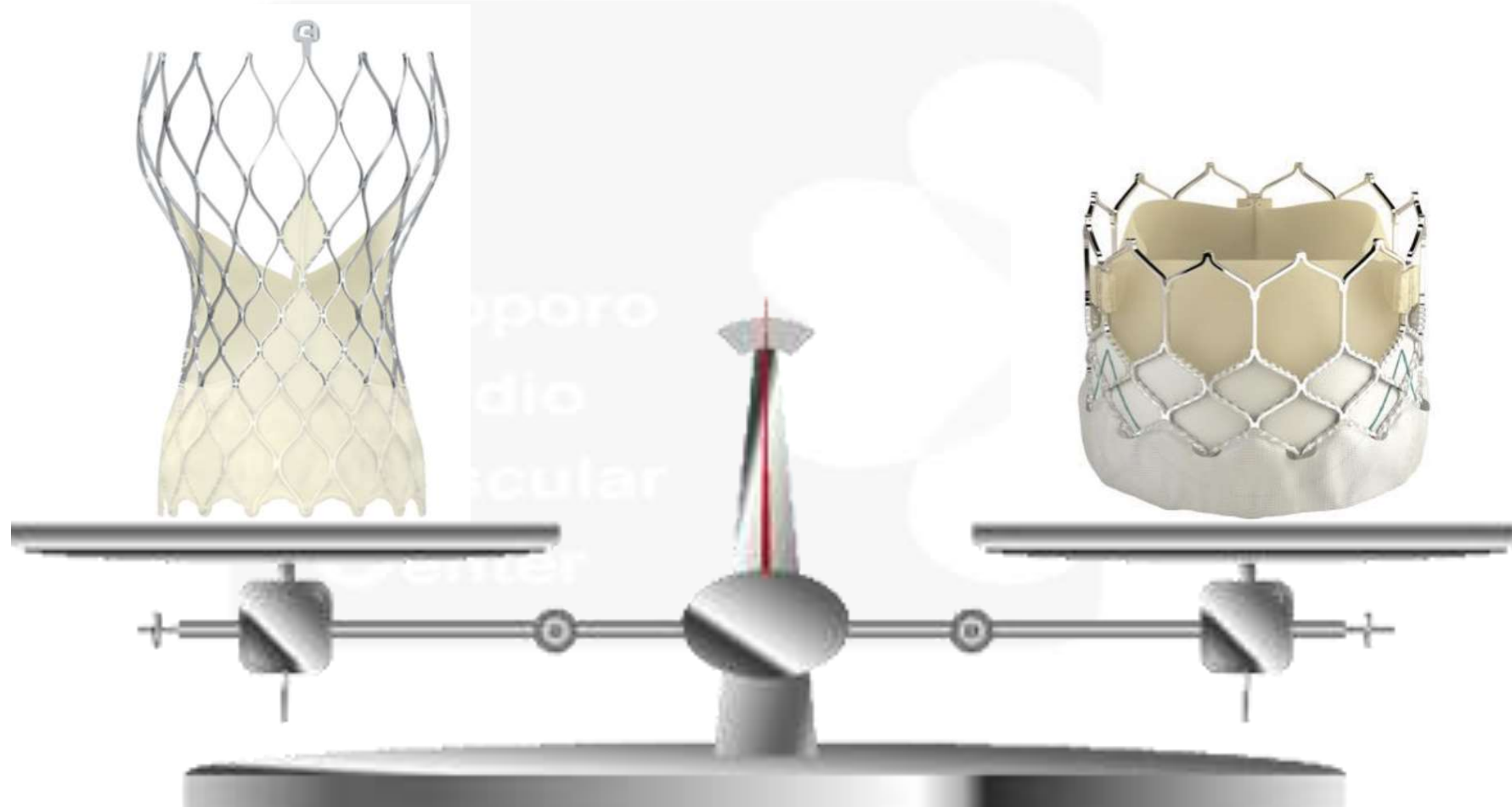


STJ  
22.3 × 24.5mm



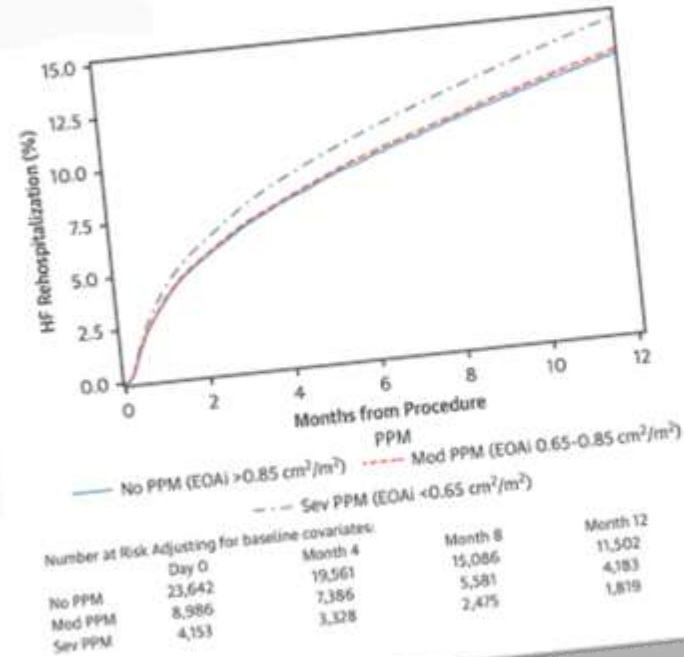
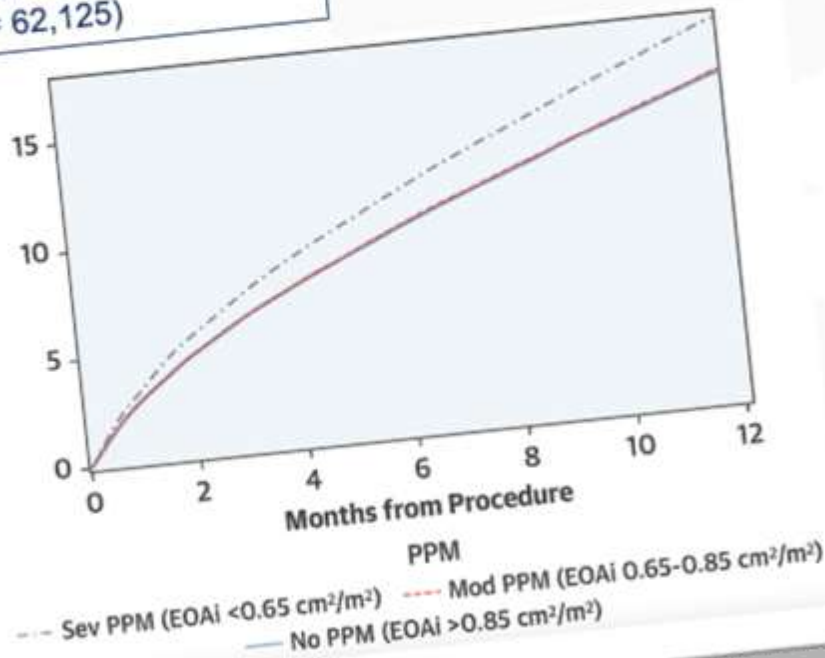
Annulus  
291mm<sup>2</sup>  
perimeter : 62.9mm  
15.9 × 23.3mm





# Moderate PPM after TAVI not affect clinical outcomes

STS/ACC TVT Registry  
(n= 62,125)



# PPM after TAVI Evolut vs. Sapien 3

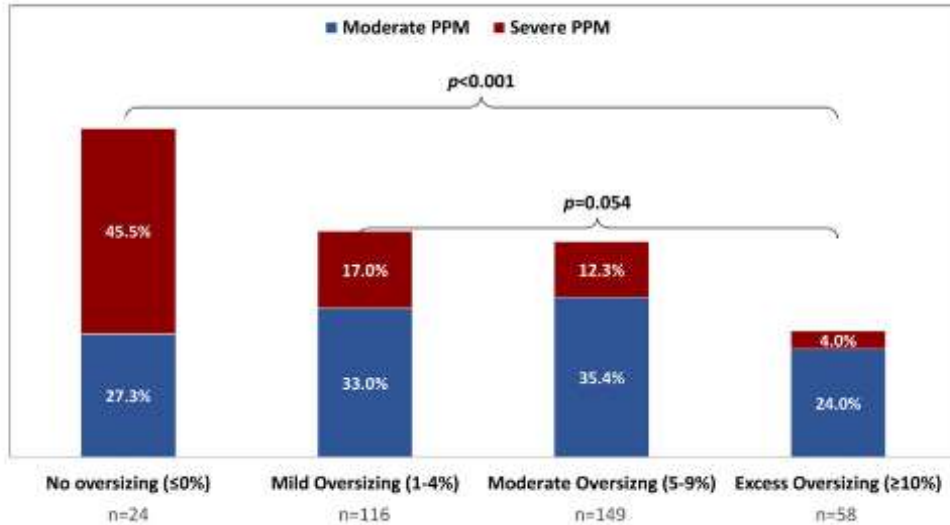
SE-THV vs. BE-THV

- The CHOICE trial  
Randomized control trial
- The CHOICE-Extend registry  
Prospective registry

**TABLE 2** Regression analysis of the predictors of prosthesis-patient mismatch<sup>a</sup>

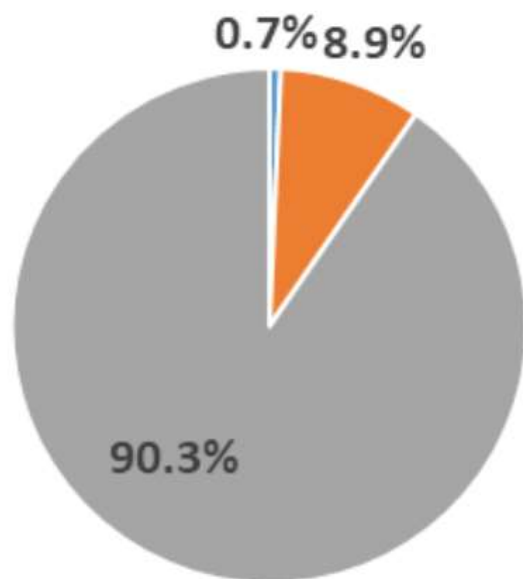
	Univariable analysis		Multivariable analysis	
	Odds ratio (95% confidence limits)	P value	Odds ratio (95% confidence limits)	P value
STS score	1.061 (1.007-1.119)	0.028	1.004 (0.938-1.074)	0.919
Previous myocardial infarction	1.817 (1.012-3.261)	0.046	2.086 (1.003-4.337)	0.049
Aortic valve area index at baseline (cm <sup>2</sup> /m <sup>2</sup> )	0.066 (0.012-0.362)	0.002	0.142 (0.020-1.022)	0.053
LV end-diastolic diameter at baseline (mm)	1.031 (1.006-1.057)	0.014	1.014 (0.984-1.046)	0.361
LV ejection fraction at baseline (%)	0.967 (0.951-0.984)	<0.001	0.969 (0.950-0.989)	0.002
Annulus Dmax	0.939 (0.876-1.007)	0.077	0.843 (0.773-0.920)	<0.001
Annulus eccentricity (%)	0.975 (0.948-1.002)	0.067	1.008 (0.552-1.068)	0.782
Sapien 3 THV (vs. Evolut R)	2.454 (1.509-3.991)	<0.001	0.738 (0.283-1.924)	0.534
THV nominal size	0.816 (0.755-0.881)	<0.001	0.914 (0.759-1.099)	0.338
THV area-derived diameter oversizing (%)	0.927 (0.900-0.955)	<0.001	0.902 (0.869-0.936)	<0.001

Abbreviations: Dmax, maximum diameter; LV, left ventricle; STS, Society of Thoracic Surgeons; THV, transcatheter heart valve.  
<sup>a</sup> Results from the CHOICE-Extend registry.



# BSA should be considered before TAVI

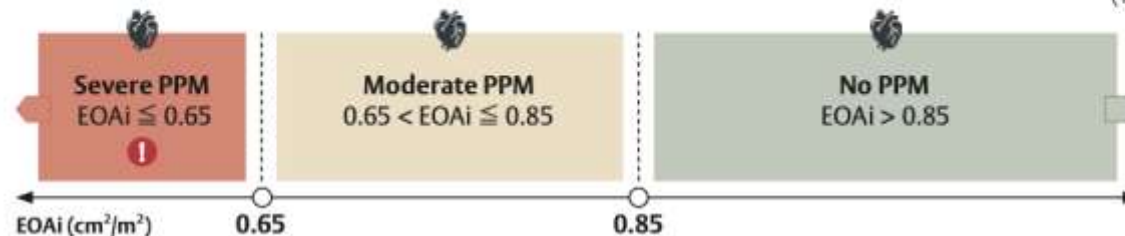
The OCEAN-TAVI Registry  
(n= 1,558)  
Female: 70%  
BSA: 1.41-1.46m<sup>2</sup>



■ Severe ■ Moderate ■ none

Valve Size \ BSA	20mm	23mm	26mm	29mm
1.0m <sup>2</sup>	1.22	1.45	1.74	1.89
1.1m <sup>2</sup>	1.11	1.32	1.58	1.72
1.2m <sup>2</sup>	1.02	1.21	1.45	1.58
1.3m <sup>2</sup>	0.94	1.12	1.34	1.45
1.4m <sup>2</sup>	0.87	1.04	1.24	1.35
1.5m <sup>2</sup>	0.81	0.97	1.16	1.26
1.6m <sup>2</sup>	0.76	0.91	1.09	1.18
1.7m <sup>2</sup>	0.72	0.85	1.02	1.11
1.8m <sup>2</sup>	0.68	0.81	0.97	1.05
1.9m <sup>2</sup>	0.64	0.76	0.92	0.99
2.0m <sup>2</sup>	0.61	0.73	0.87	0.95
2.1m <sup>2</sup>	0.58	0.69	0.83	0.90
2.2m <sup>2</sup>	0.55	0.66	0.79	0.86

(単位: cm<sup>2</sup>/m<sup>2</sup>)



## PPM cause early structural valve deterioration (SVD)

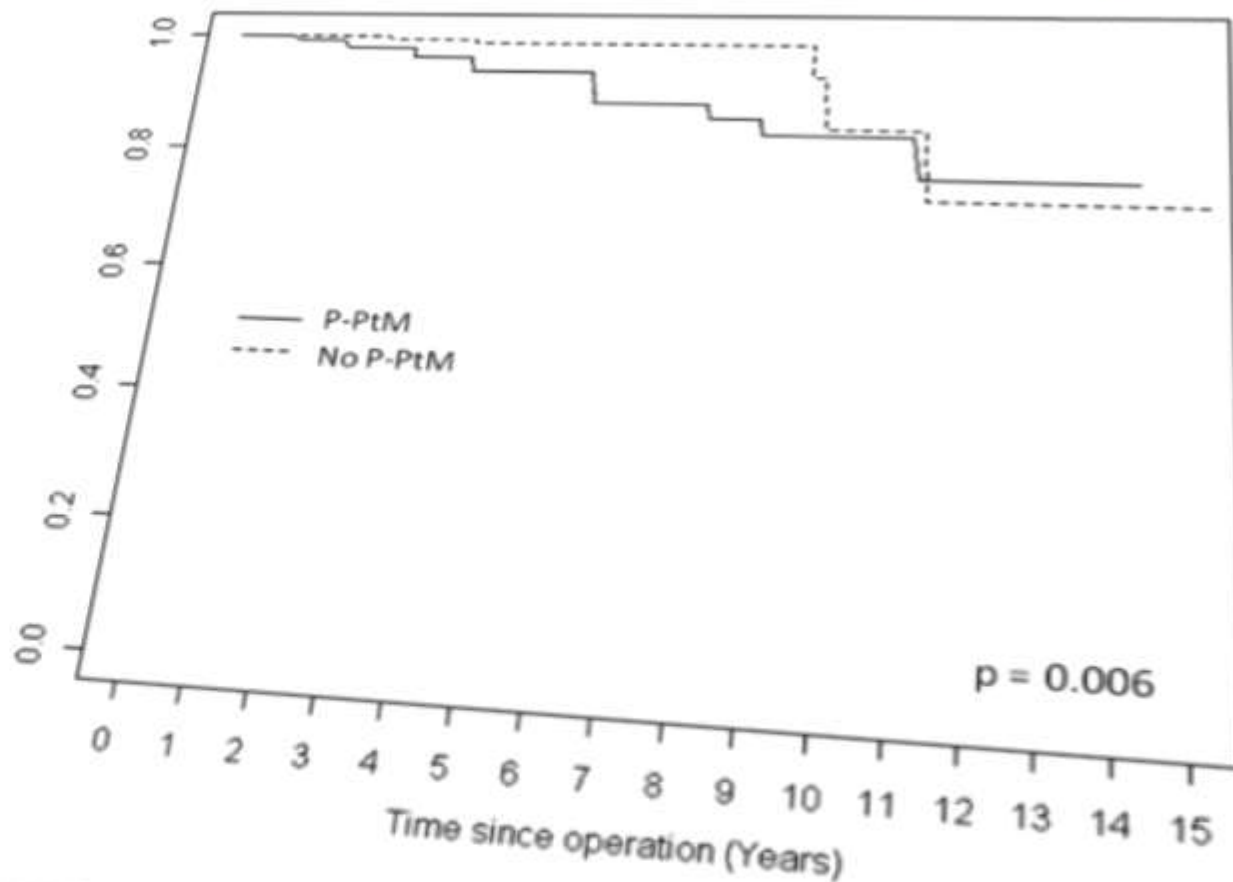
Retrospective  
Single-center  
(n=564)

Table 4. Multivariable Analysis of SVD (Cox With Multiple Imputation Method)

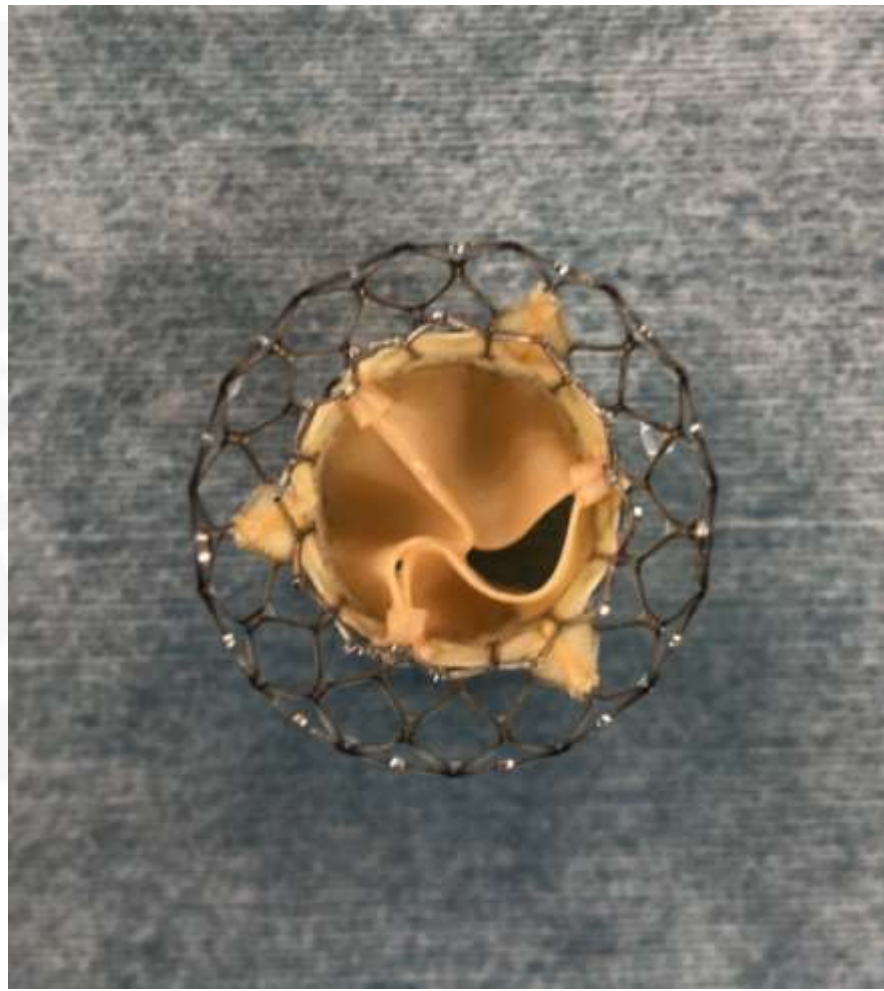
	Hazard Ratio	95% CI	P
Size $\leq 21$	2.35	1.14-4.85	0.02
Anticalcification treatment	0.34	0.17-0.66	0.002
P-PtM	2.29	1.03-5.06	0.04

CI indicates confidence interval.

In patients with PPM, SVD occurs 2 to 3 years earlier than in patients without PPM.  
Smaller valve may be independent predictor of SVD.



# ***SAPIEN3 26mm in Evolut 26mm***





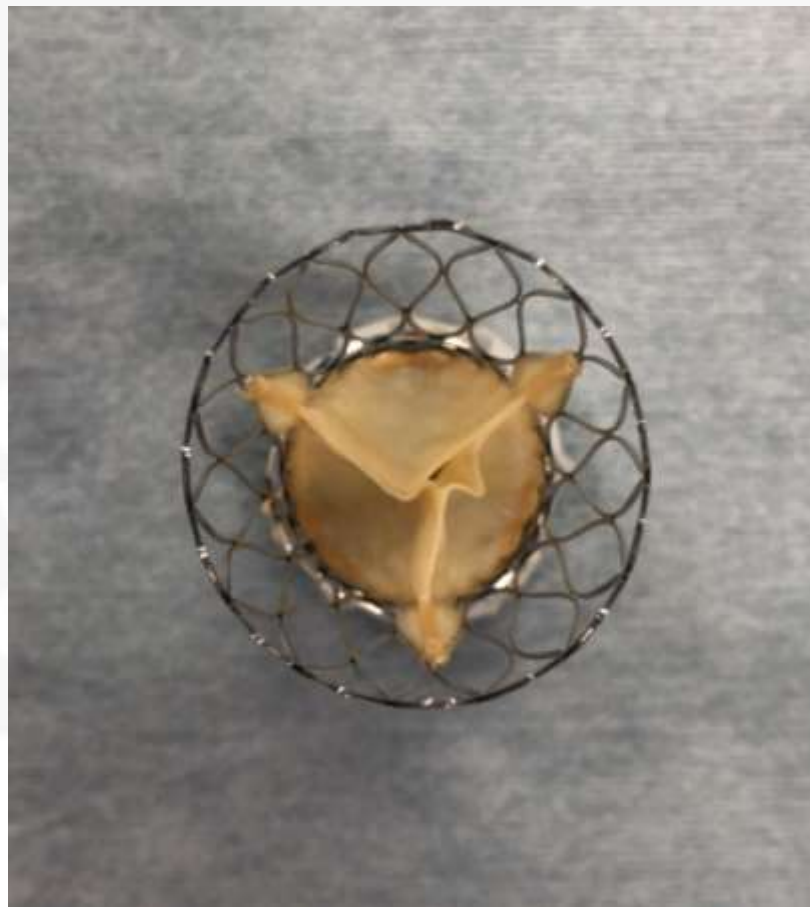
# ***SAPIEN3 26mm in Evolut 29mm***



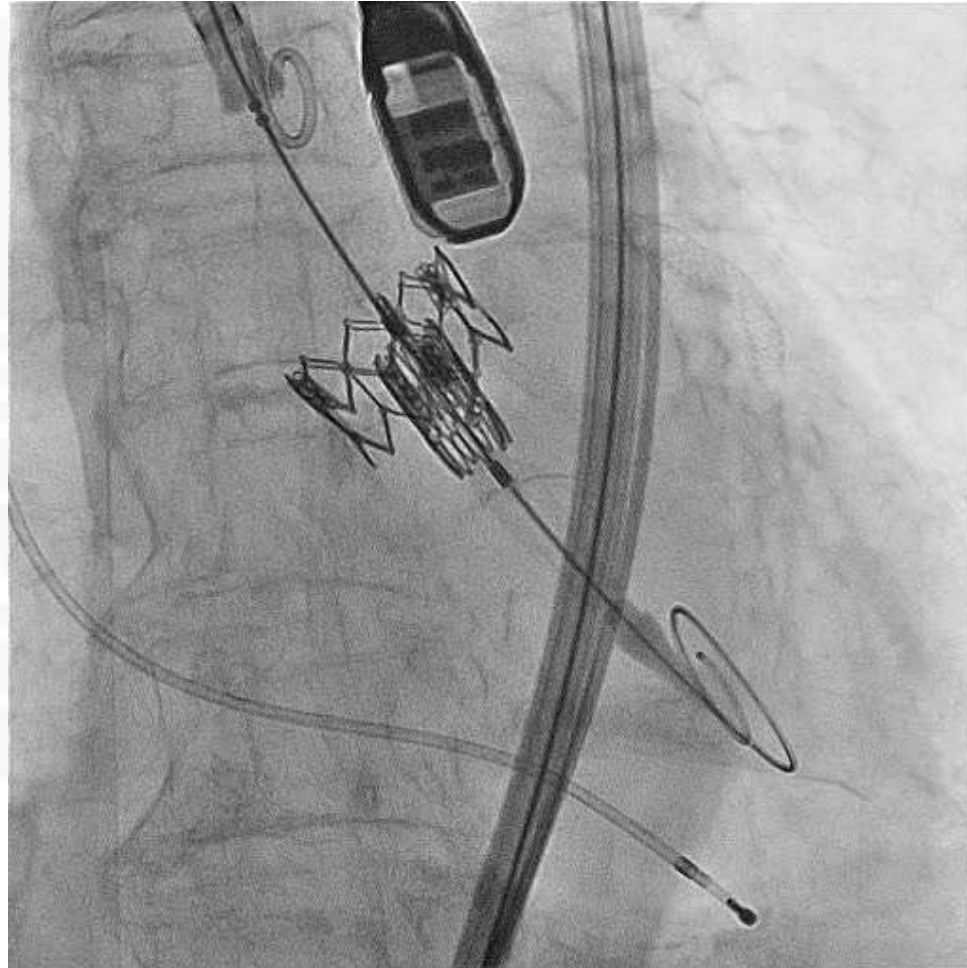
# Over dilatation of SAPIEN3 26mm in Evolut 29mm



# ***Evolut 26mm in SAPIEN 3 23mm***



# ***SAPIEN in SAPIEN***



# Summary

- Severe PPM after TAVI is associated with increased mortality.
- Moderate PPM after TAVI does not affect clinical outcomes.
- PPM after TAVI in Japanese patients is not often.
- Evolut is hemodynamically better than SAPIEN3 in small annulus, however, which does not affect short-term hard endpoint.
- High PG and low EOA might cause early SVD.
- Adequate sizing should be considered according to patients BSA.
- If SVD occur, TAV in TAVI may be good way to resolve it.
- In the case of SVD of TAVI valve, SAPIEN in SAPIEN or Evolut in SAPIEN might be good option.