TAVR Device Selection – SMART

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Disclosure of relevant financial relationships

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below:

Financial Relationship	Company
Institutional grants/research support	Abbott Vascular, Edwards LifeSciences, Johnson and Johnson, Medtronic
Consulting fees/honoraria	Affluent Medical, Artedrone, Caranx, Johnson & Johnson, Medtronic, Microinterventional Devices, Prolifagen
Equity	Affluent Medical, Artedrone, Caranx, Microinterventional Devices
Editorial	Mass Medical Society

Discussion may include unapproved and off-label devices, procedures, and indications

SMART Trial Design

Prospective, randomized controlled, post-market trial conducted at 83 international sites

All-comer trial with all surgical risk categories including bicuspid patients

716 Patients Treated

Randomization

1:1 stratified by site & sex

(N=355)

Medtronic Evolut PRO/PRO+/FX

(N=361)

Edwards SAPIEN 3/SAPIEN 3 Ultra

Characteristic	Evolut (N=355)	SAPIEN (N=361)
Age – yr	80.1 ± 6.3	80.3 ± 6.1
Female sex	87.9%	85.6%
STS-PROM score – %	3.3 ± 1.9	3.2 ± 1.7

Key eligibility

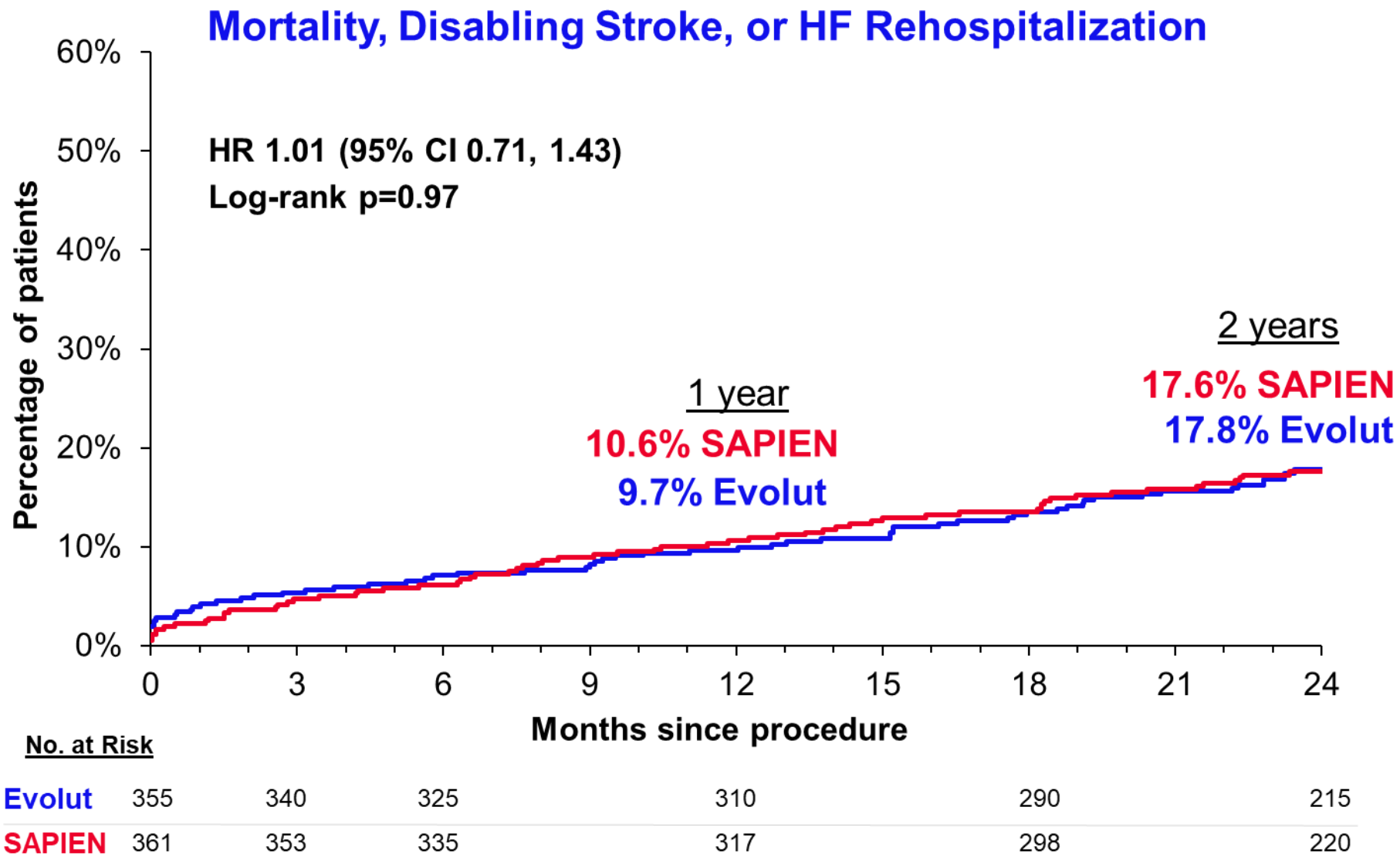
- Symptomatic severe AS*
- Small aortic annulus (≤430 mm^2 by MDCT)

Co-primary endpoints powered at 1 year

- **Co-Primary Endpoint 1:** Composite of mortality, disabling stroke, or heart failure rehospitalization through 12 months
- **Co-Primary Endpoint 2:** Bioprosthetic valve dysfunction through 12 months

*AVA ≤1.0 cm^2 (AVAi ≤0.6 cm^2/m^2) or mean gradient ≥40 mmHg or max velocity ≥4.0 m/s; 30-day predicted risk of surgical mortality <15% by heart team assessment.

Clinical outcome composite & components through 2 years



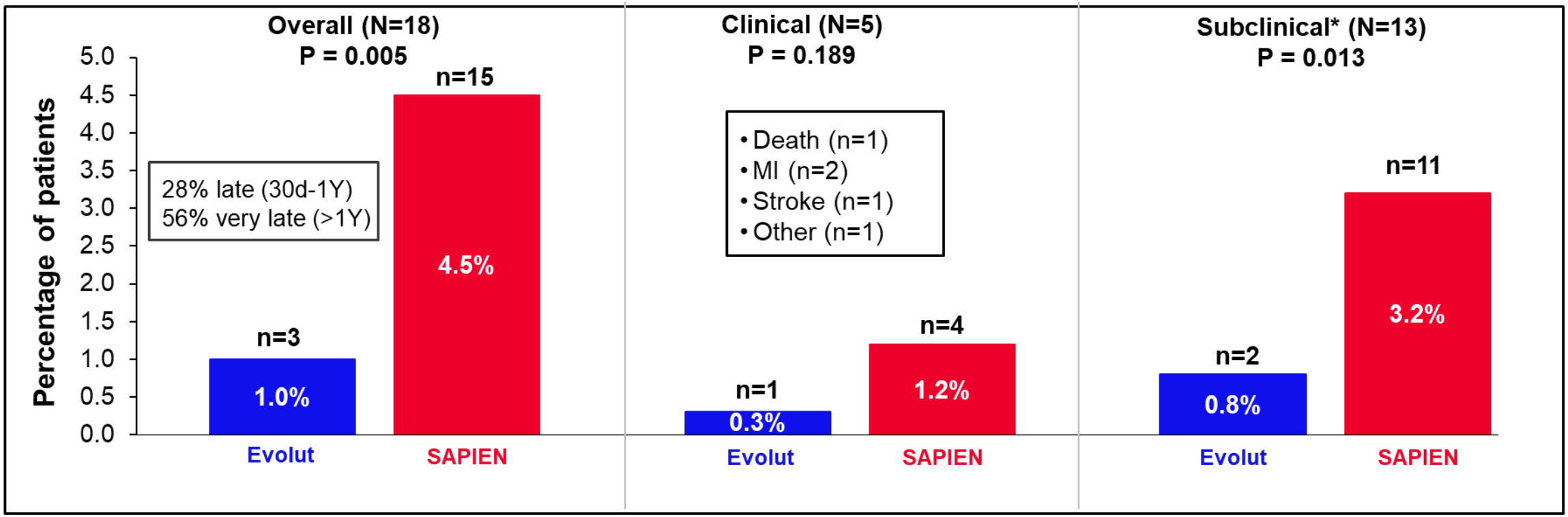
Safety events

KM%	1 Year			2 Years		
	Evolut (N=355)	SAPIEN (N=361)	Log-Rank P Value	Evolut (N=355)	SAPIEN (N=361)	Log-Rank P Value
All-cause mortality	5.1%	5.9%	0.676	12.7%	11.4%	0.657
Cardiovascular mortality	3.4%	3.7%	0.882	7.2%	6.4%	0.706
Heart failure rehospitalization	4.1%	3.5%	0.661	6.1%	6.0%	0.951
Aortic valve reintervention	0.9%	0.6%	0.637	0.9%	0.9%	0.978
New pacemaker implant[a]	14.0%	9.3%	0.052	15.4%	11.4%	0.097
Total pacemaker implant[b]	12.8%	8.7%	0.064	14.1%	10.6%	0.118
All stroke	5.4%	4.2%	0.439	7.3%	6.2%	0.487
Disabling stroke	3.1%	2.6%	0.616	4.7%	3.2%	0.302
Transient ischemic attack	0.9%	2.6%	0.087	1.2%	4.2%	0.020
Prosthetic valve thrombosis	0.3%	2.0%	0.035	1.0%	4.5%	0.005
Clinical valve thrombosis	0.3%	0.3%	0.990	0.3%	1.2%	0.189
Subclinical valve thrombosis	0.0%	1.7%	0.015	0.8%	3.2%	0.013

[a]Patients with pacemaker/ICD at baseline are excluded
[b]Patients with pacemaker/ICD at baseline are included

Values based on independent Clinical Events Committee adjudication.

Prosthetic Valve Thrombosis Through 2 Years (CEC adjudicated)



All thrombosis events, including subclinical ones, affected patient management (hospitalization or unscheduled visits, additional imaging, or medication augmentation)

*Protocol (modified VARC 2): thrombus causing ≥50% increase in mean gradient to ≥30 mmHg or a decrease in DVI ≥50% or increase in AR to ≥ moderate

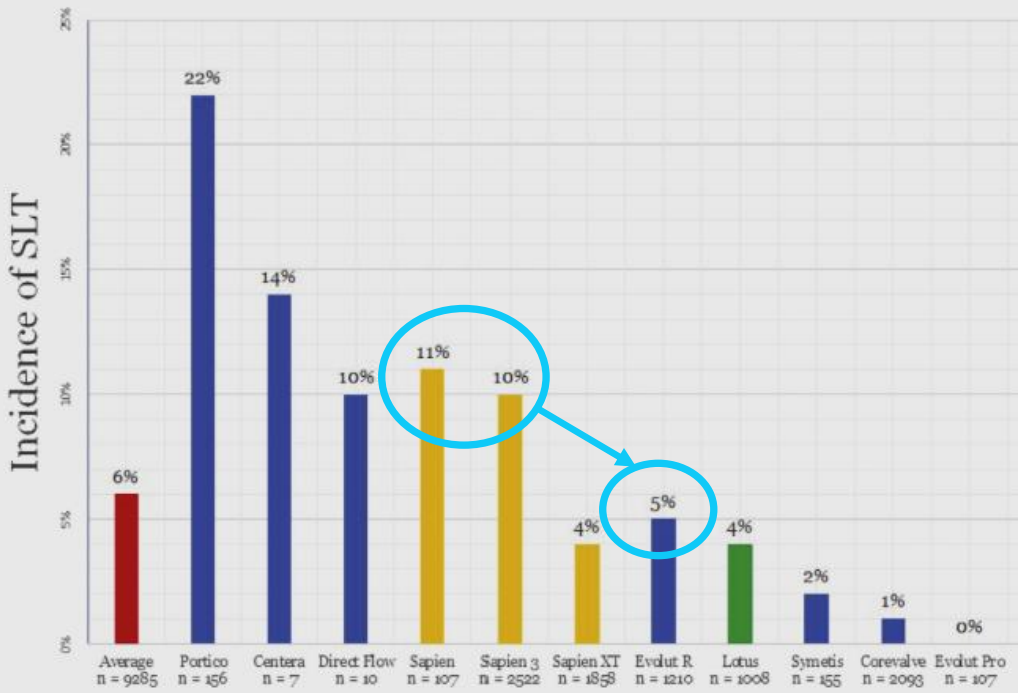
Intra-annular valves have greater frame deformation, larger regions of neo-sinus flow stagnation and longer washout times

Subclinical Leaflet Thrombosis After Transcatheter Aortic Valve Replacement

A Meta-Analysis

Matthias Bogyi, MD,[a] Rüdiger E. Schernthaner, MD, PhD,[b] Christian Loewe, MD,[b] Gloria M. Gager, MD,[a,c] Al Medina Dizdarevic, MD,[a] Christina Kronberger, MD,[a] Marek Postula, MD, PhD,[d] Jacek Legutko, MD, PhD,[e] Poonam Velagapudi, MD,[f] Christian Hengstenberg, MD,[a] Jolanta M. Siller-Matula, MD, PhD[a,d]

FIGURE 2 Incidence of SLT According to Valve Type



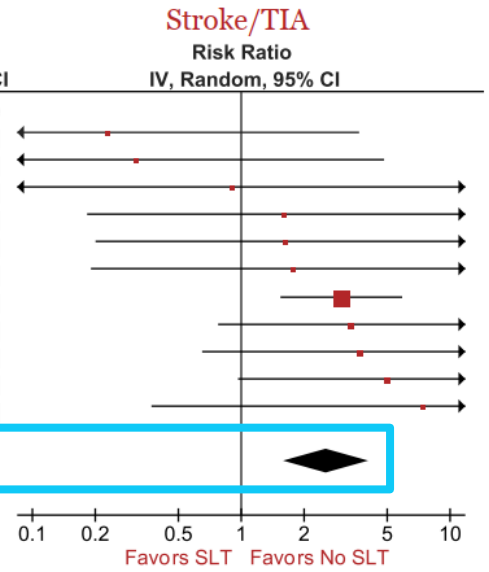
Meta-analysis of 25 studies demonstrates subclinical leaflet thrombosis is twice as frequent with Sapien compared with Evolut and the presences of SLT is associated with a 2.5-fold excess risk for stroke/TIA.

B

Stroke/TIA

Study or Subgroup	SLT Events	SLT Total	No SLT Events	No SLT Total	Weight	Risk Ratio IV, Random, 95% CI
Marwan et al. 2017	0	18	0	0		Not estimable
Vollema et al. 2017	0	16	14	112	2.9%	0.23 [0.01, 3.67]
Reardon et al. 2019	0	16	82	875	3.0%	0.31 [0.02, 4.83]
Blanke et al. 2020	0	35	2	162	2.4%	0.91 [0.04, 18.46]
Jimenez et al. 2019	1	12	3	58	4.7%	1.61 [0.18, 14.20]
Yanagisawa et al. 2019	1	45	6	440	5.1%	1.63 [0.20, 13.24]
Khan et al. 2020	1	27	3	143	4.5%	1.77 [0.19, 16.34]
Chakravarty et al. 2018	11	106	27	784	49.3%	3.01 [1.54, 5.90]
Hansson et al. 2016	2	17	8	229	10.3%	3.37 [0.78, 14.63]
Makkar et al. 2020	2	28	3	156	7.3%	3.71 [0.65, 21.23]
Tang et al. 2019	2	26	4	261	8.2%	5.02 [0.97, 26.10]
Makkar et al. 2017	2	22	0	33	2.5%	7.39 [0.37, 146.97]
Total (95% CI)		**368**		**3253**	**100.0%**	**2.56 [1.60, 4.09]**
Total events	22		152			

Heterogeneity: Tau² = 0.00; Chi² = 7.75, df = 10 (P = 0.65); I² = 0%
Test for overall effect: Z = 3.91 (P < 0.0001)

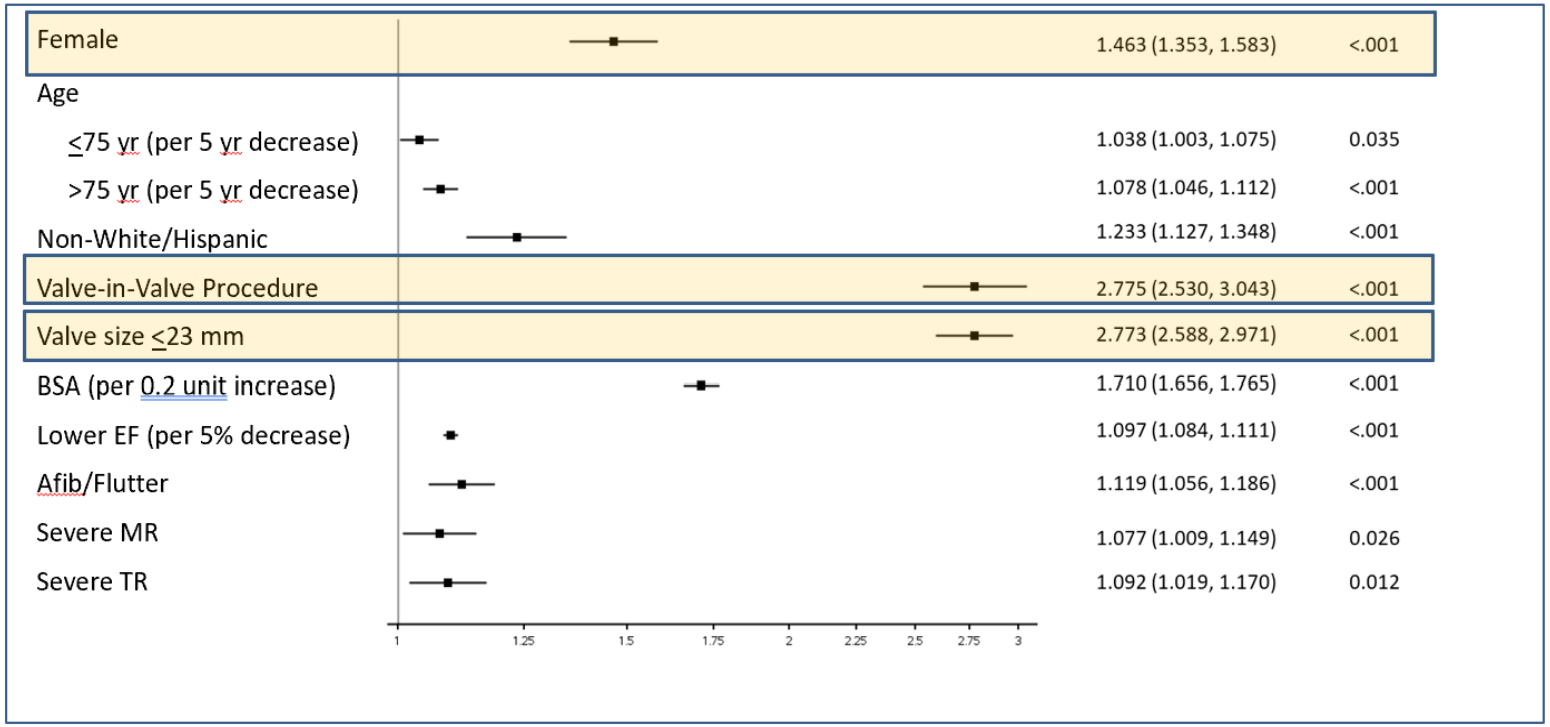


JACC Intv 2021;14:2643-2656

Penn Medicine

Predictors of Prosthesis-Patient Mismatch (PPM) After TAVR and in the SMART Trial

Odds Ratios (95% CI) for Multivariate Model Predictors of Severe PPM



STS National Database
Using data to drive quality

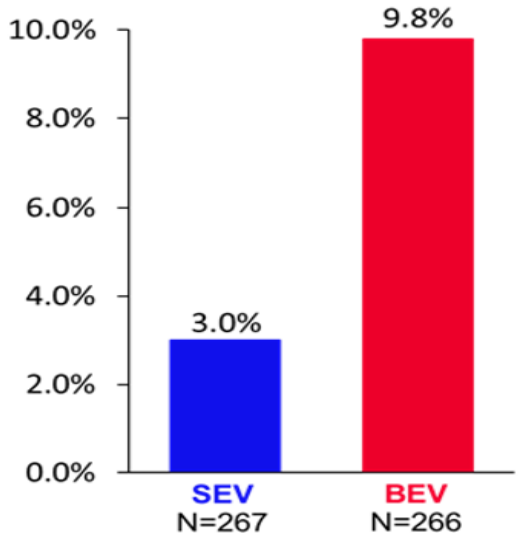
Herrmann et al, J Am Coll Cardiol 2018;72:2701–11

NCDR
NATIONAL CARDIOVASCULAR DATA REGISTRY

SMART Trial

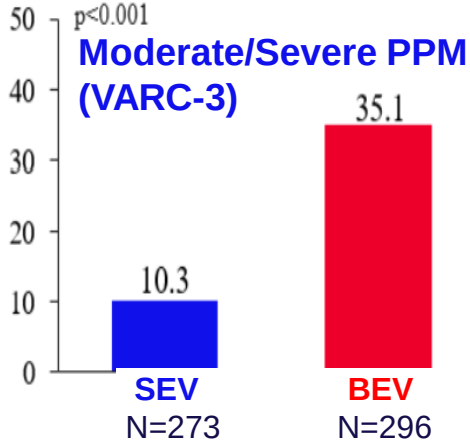
Severe Prosthesis-Patient Mismatch (VARC-3)

Difference, -6.8% (95% CI -10.9, -2.7)
p=0.001

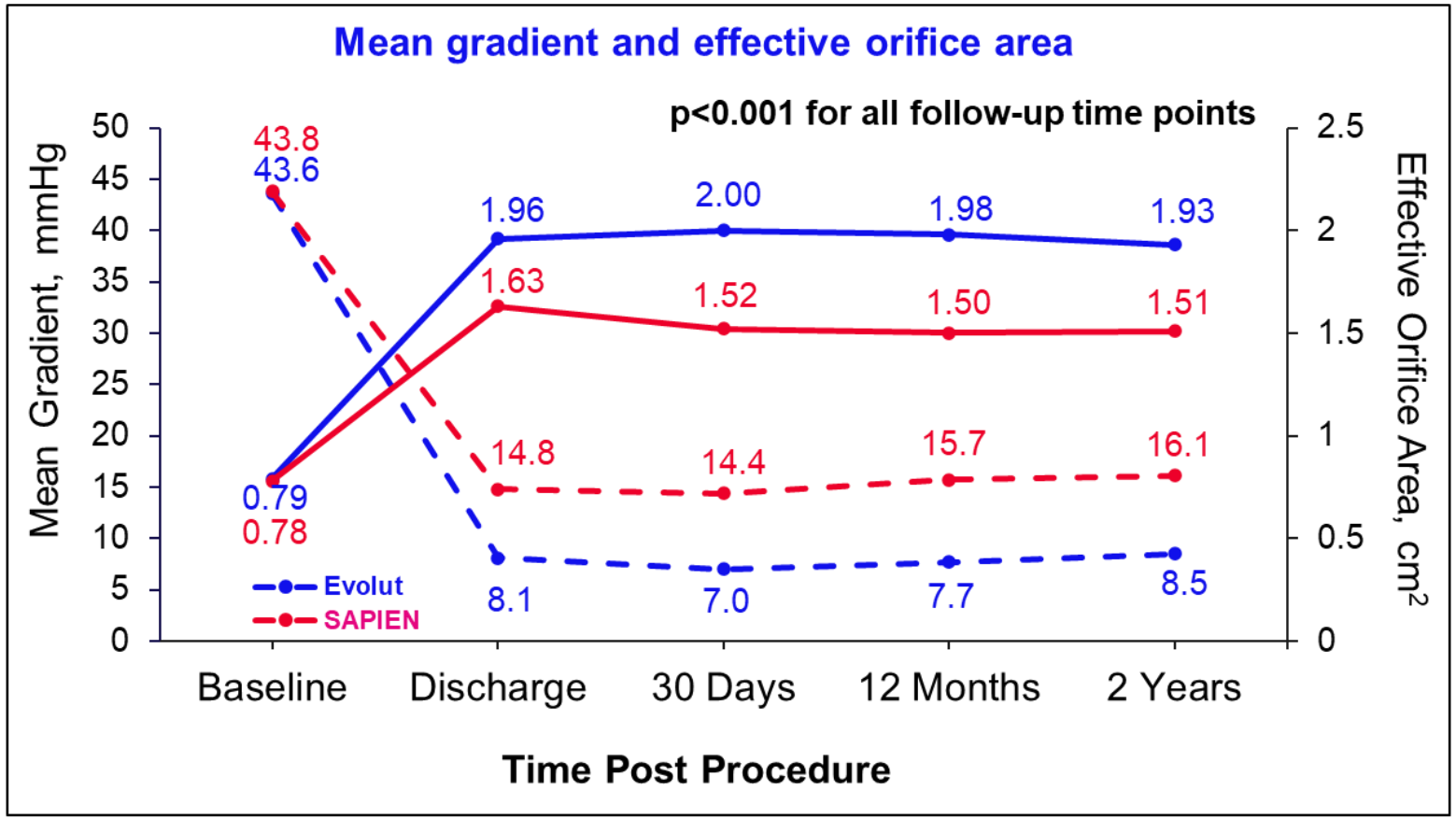


Difference, -24.9% (95% CI -31.4%, -18.4%)
p<0.001

Moderate/Severe PPM (VARC-3)

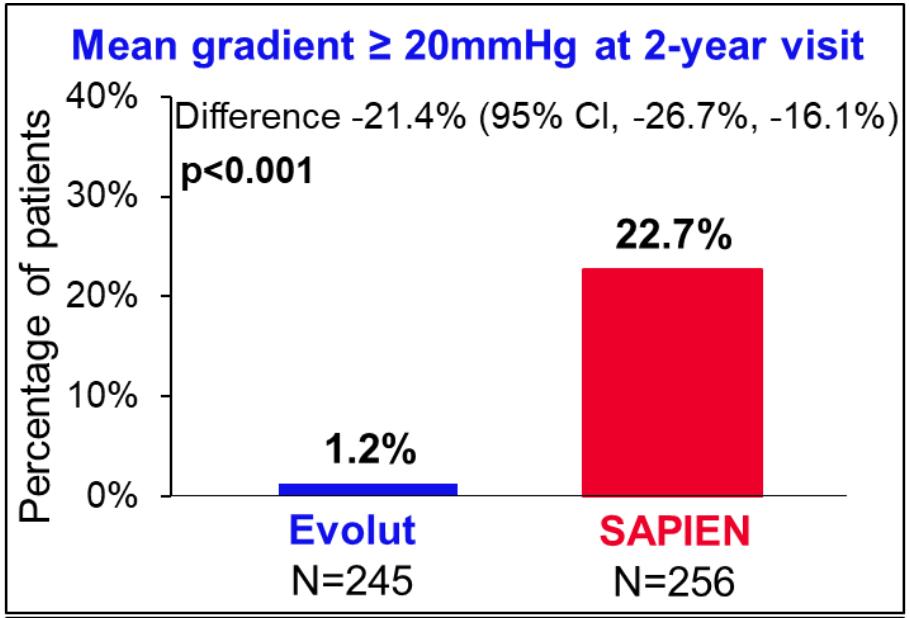


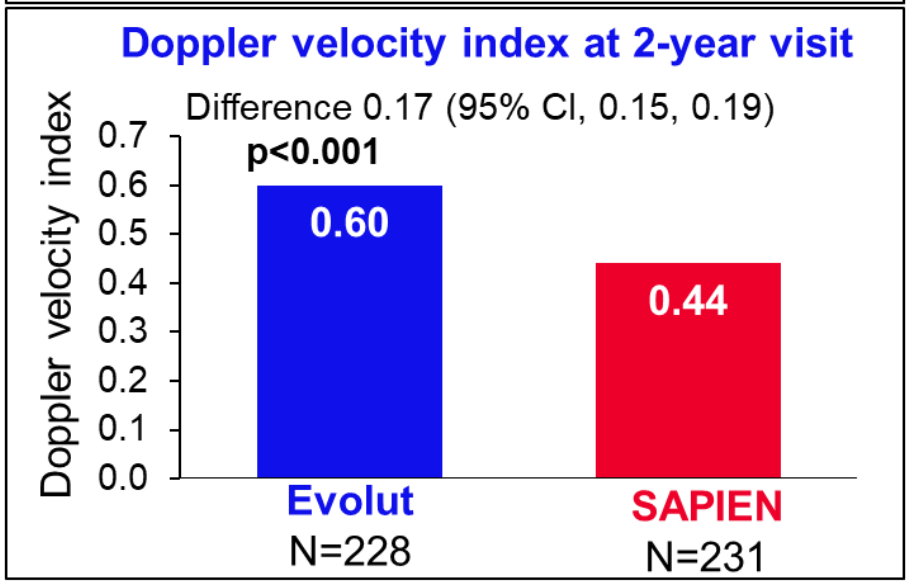
SMART Trial results at 2 years: Hemodynamics



Number of patients with echo data

Evolut MG	347	330	325	298	245
SAPIEN MG	359	348	331	301	256
Evolut EOA	264	250	273	267	215
SAPIEN EOA	281	304	296	266	223



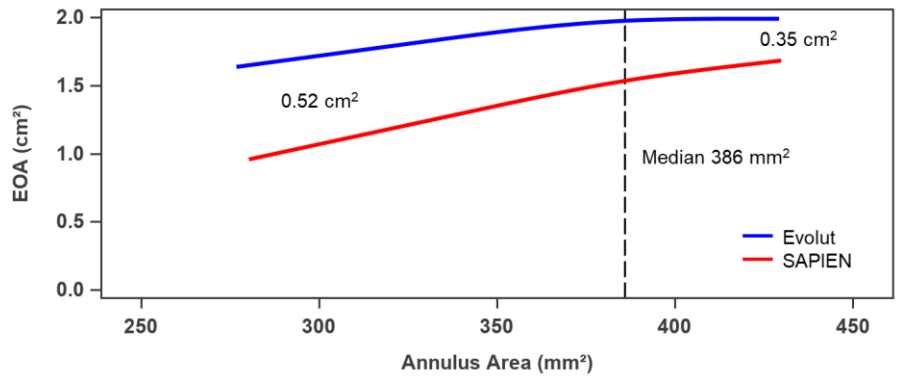


Values based on independent Echocardiography Core Laboratory (Mayo) assessment.

Use of SAPIEN valve was also a predictor of smaller EOA, lower Mean Gradient and DVI throughout the entire range of annulus area in the trial *at 2 years*

Effective Orifice Area at 2 Years

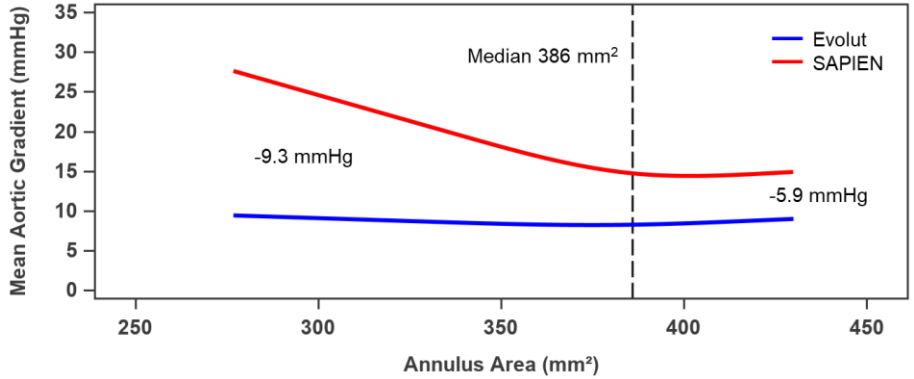
Restricted Cubic Spline Regression



EOA, cm²	Evolut		SAPIEN		Difference (95% CI)	P-value
Annulus area <386 mm²	N=116	1.90±0.49	N=108	1.38±0.33	0.52 (0.41, 0.63)	<.001
Annulus area ≥386 mm²	N=99	1.97±0.48	N=115	1.63±0.38	0.35 (0.23, 0.46)	<.001

Mean Gradient at 2 Years

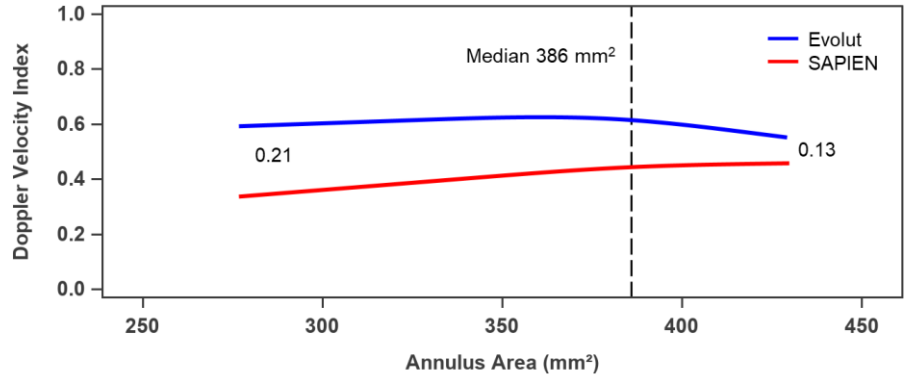
Restricted Cubic Spline Regression



Mean Gradient, mmHg	Evolut		SAPIEN		Difference (95% CI)	P-value
Annulus area <386 mm²	N=129	8.4±4.5	N=127	17.7±7.1	-9.3 (-10.8, -7.9)	<.001
Annulus area ≥386 mm²	N=116	8.7±3.8	N=129	14.6±5.8	-5.9 (-7.2, -4.7)	<.001

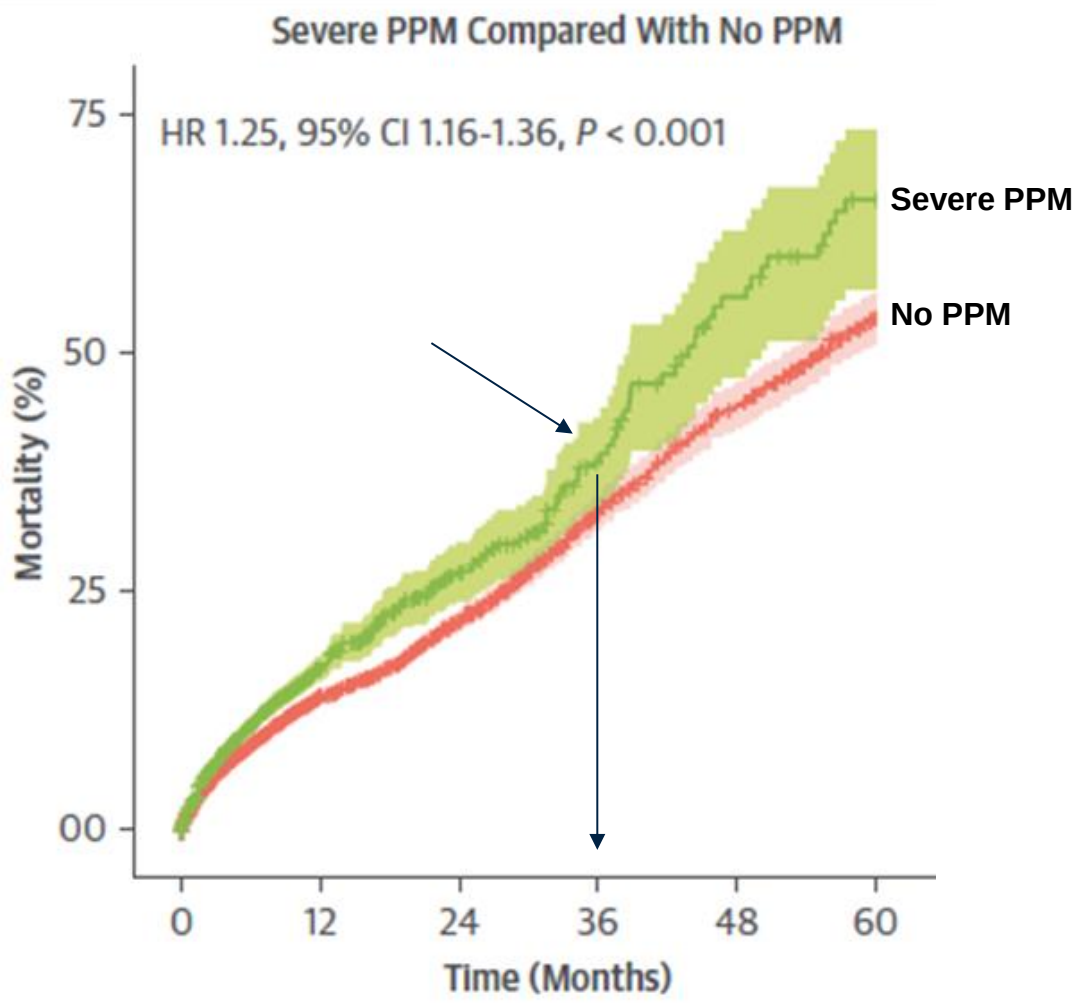
Doppler Velocity Index at 2 Years

Restricted Cubic Spline Regression

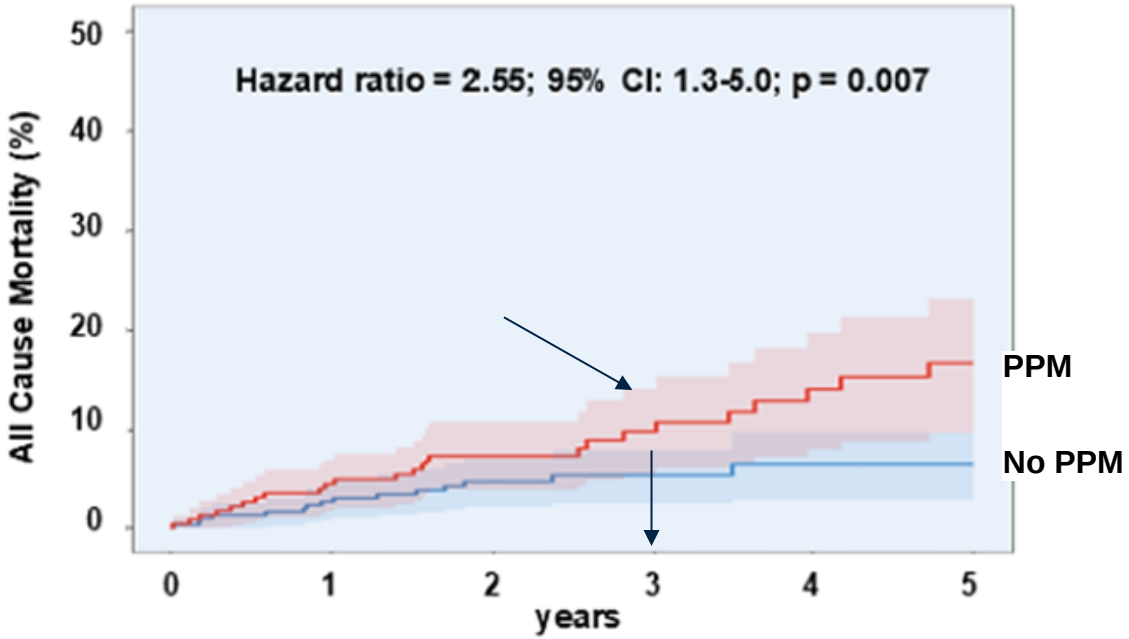


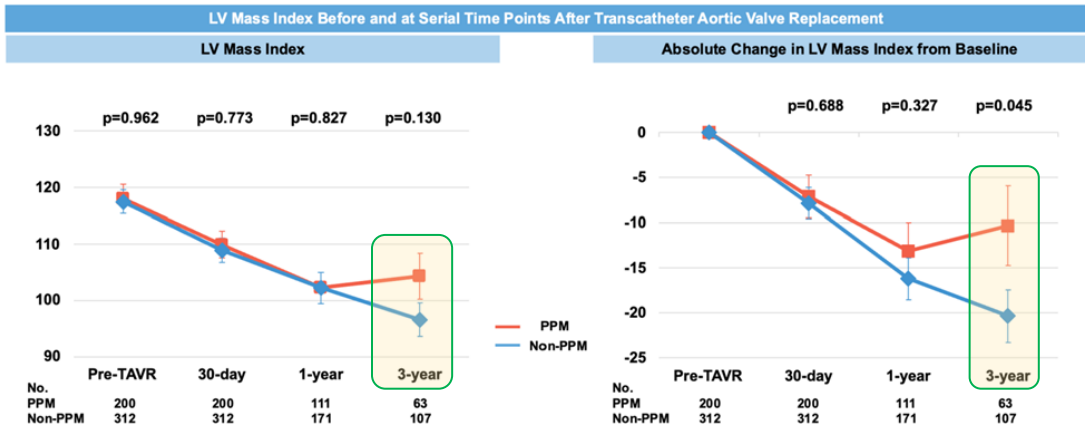
Doppler Velocity Index	Evolut		SAPIEN		Difference (95% CI)	P-value
Annulus area <386 mm²	N=123	0.62±0.14	N=113	0.41±0.09	0.21 (0.18, 0.24)	<.001
Annulus area ≥386 mm²	N=105	0.58±0.14	N=118	0.46±0.10	0.13 (0.09, 0.16)	<.001

Meta-analysis of patient data (23 TAVR studies and 81,969 patients) [1]



Prosthesis-Patient Mismatch in Young and Low-Risk Patients After Newer Generation Balloon-Expandable TAVR (2015-2022) [2]





[1] Sá MP, et al. JACC Cardiovasc Imaging. 2023 Mar;16(3):298-310.

[2] Suruga and Makkar et al, JACC Intv 2025;18:1512-1523

Conclusions

- In the randomized SMART trial, the Evolut supra-annular prosthesis had a lower risk of PPM and provided better hemodynamics at 2 years across the entire range of small aortic annulus areas compared with Sapien 3.
  - In addition, there were fewer patients with leaflet thrombosis and TIA in the Evolut arm.
- There was no difference in the co-primary clinical endpoint at 2 years, but the effect of hemodynamics on outcomes takes longer to become apparent.
  - SMART will follow patients for 5 years.
- In the meantime, Evolut remains an ideal choice for patients with a small aortic annulus, most of whom are women.