You Refuse to Compromise: We Couldn't Agree More

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Focus on the Patient Outcomes that Truly Matter: Clinical Perspective Update

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Rebecca T. Hahn Disclosures

- No direct compensation for:
  - Core Lab Director for multiple Tricuspid Valve Device Trials
- Speaker:
  - Abbott Vascular, Edwards Lifescience, Philips Healthcare,
- Consultant:
  - 3Mensio, Abbott Vascular, Edwards Lifescience Medtronic, Gore & Associates, Navigate, Philips Healthcare

Parameters to Consider for Valve Choice

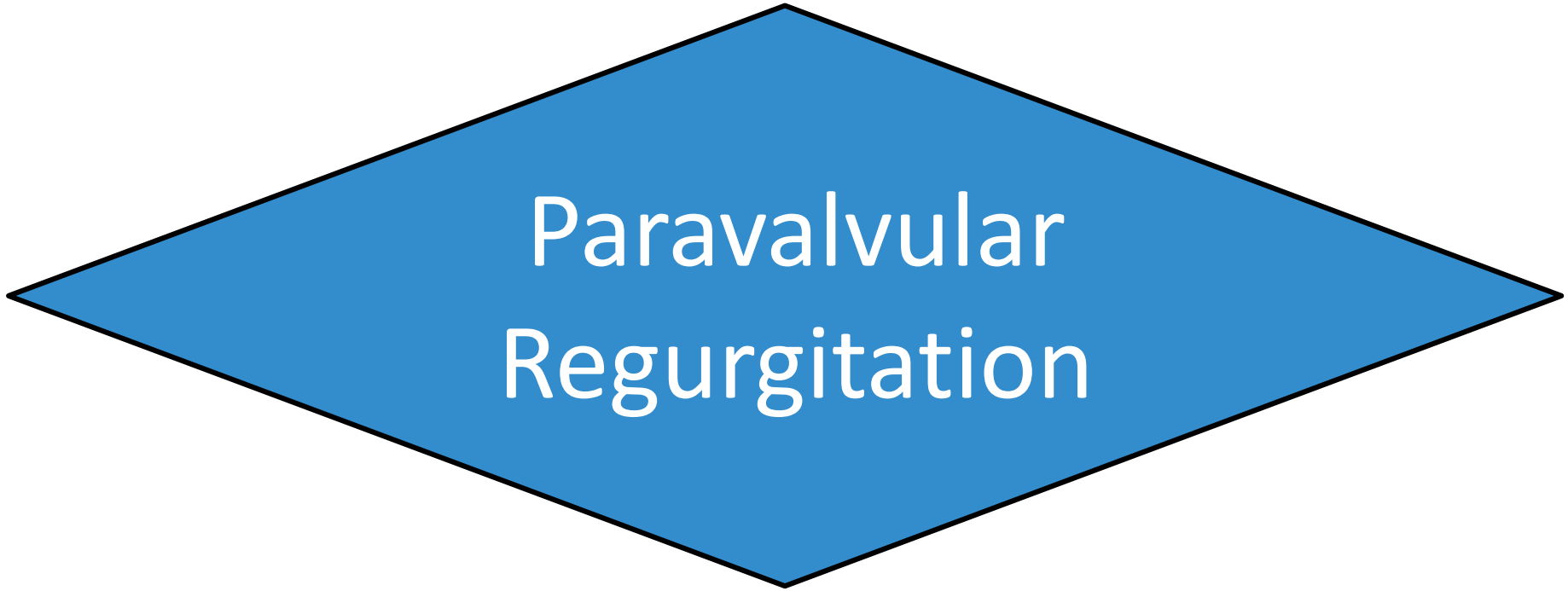
- Access Size
- Anatomic Restrictions
  - Bicuspid aortic Valve
  - Distorted/Horizontal Ao
- Annular Rupture Risk
- High Risk Coronary
  - Implantation risks
  - Re-access to coronaries risk
  - Delayed Coronary Obstruction (DCO)
- Deployment technique
  - Post-dilatation rates
  - Repositioning
- Pacemaker Rate
- Risk for Structural Valve Deterioration
- Paravalvular regurgitation Rate
- Prosthesis-patient Mismatch
- Outcomes

Valve Choice Considerations

+ = Favors Use
- = Disfavors Use

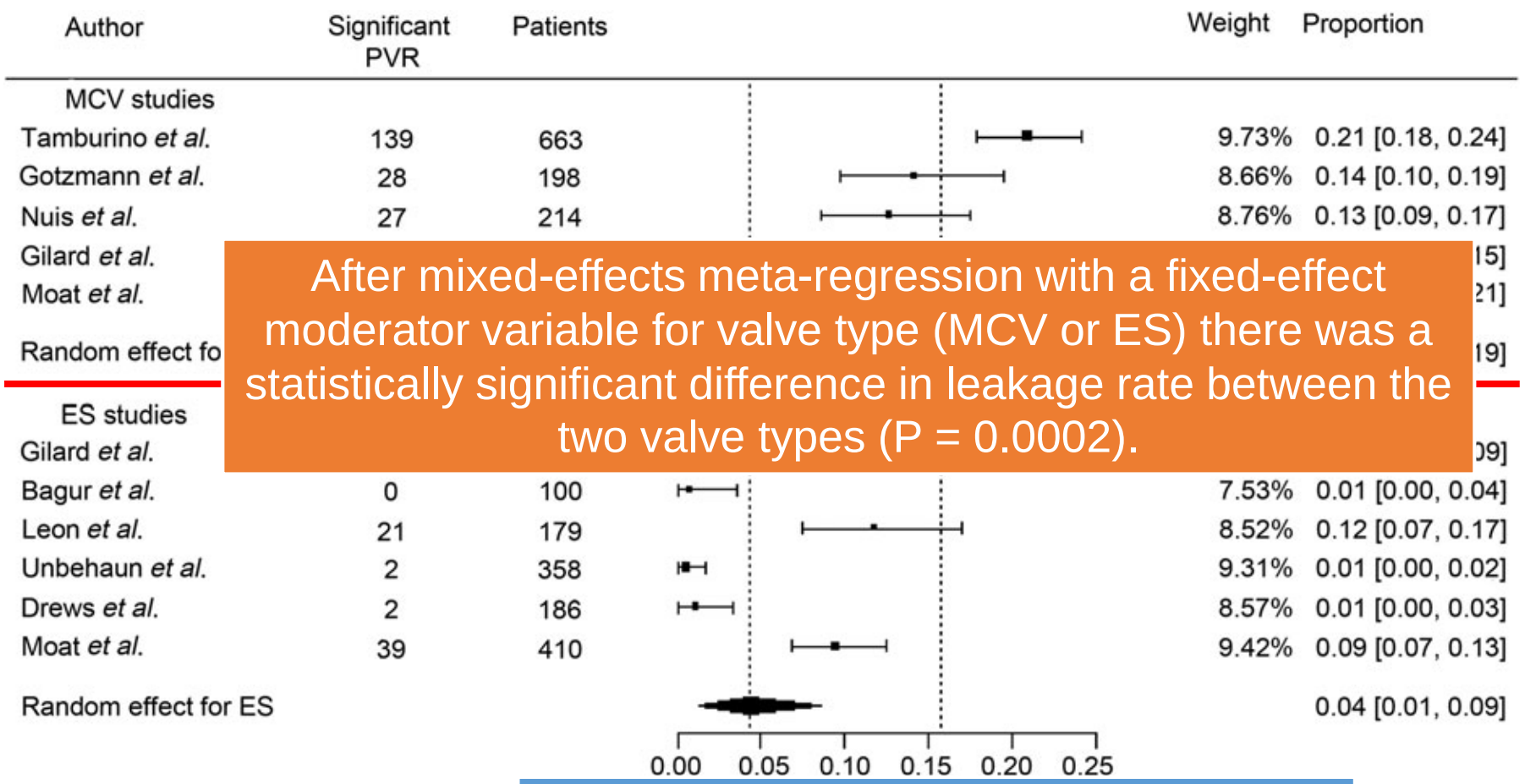
	Balloon-expandable	Self-expanding
Extensive annular/aortic root calcification	+	++
Excessive Aortic Root Angulation	+	-
Low Coronary Height/Anticipated Need for Coronary re-access	+	-
Risk For Permanent Pacemaker	+	-
Risk for Paravalvular Regurgitation	+	-
Risk for Prosthesis-Patient Mismatch	+	-
Cerebro-embolic Protection Device Not Feasible*	+	±
Treatment of Bicuspid Aortic Valve	+	+
Treatment of Pure Aortic Regurgitation	-	+
Treatment of Degenerated Surgical Bioprosthesis	+	+
All-Cause Mortality	+	±

After Esposito, G, Franzone A. JACC CV Inter; 2020;13(9)1083-1085



Meta-analysis: Moderate or Severe Paravalvular AR

MCV PVR rate of 15.75% [95% CI 12.48–19.32]



After mixed-effects meta-regression with a fixed-effect moderator variable for valve type (MCV or ES) there was a statistically significant difference in leakage rate between the two valve types (P = 0.0002).

ES PVR rate of 3.93% [95% CI 1.05–8.38].

Original Investigation

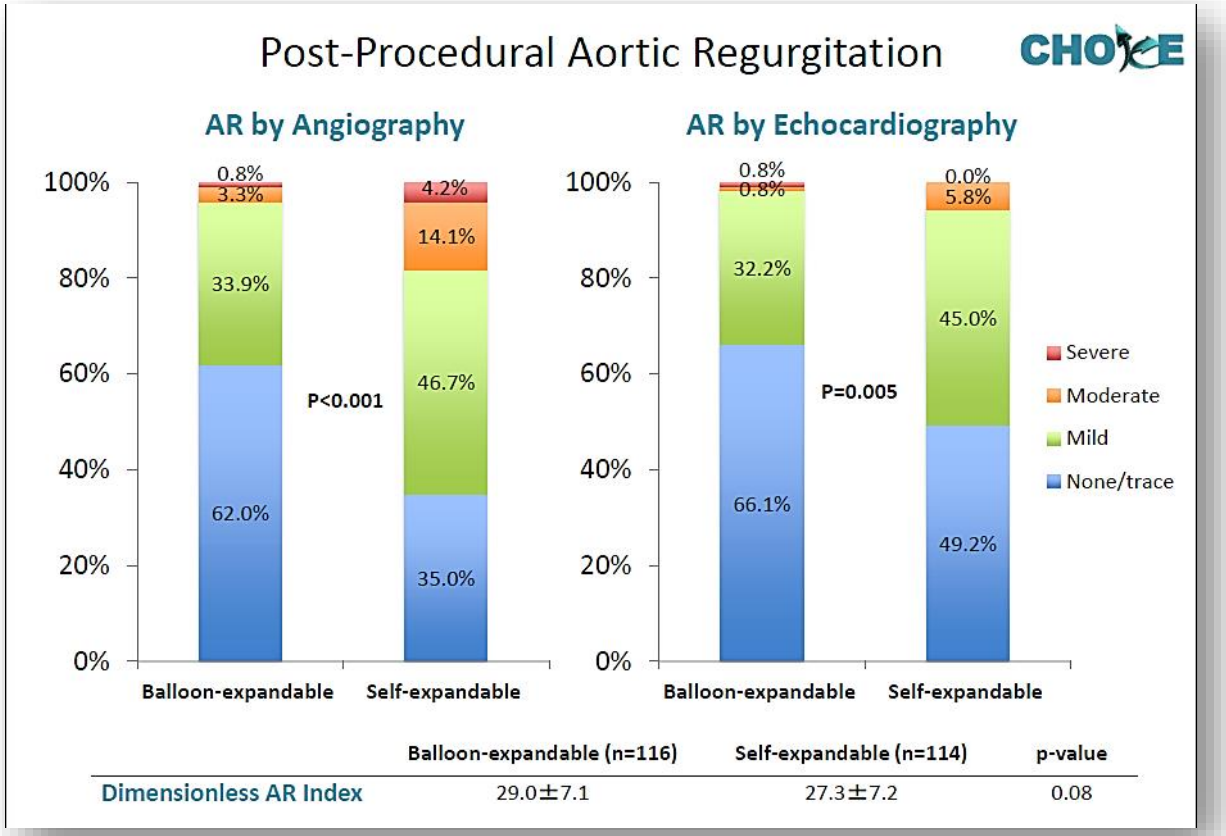
Comparison of Balloon-Expandable vs Self-expandable Valves in Patients Undergoing Transcatheter Aortic Valve Replacement
The CHOICE Randomized Clinical Trial

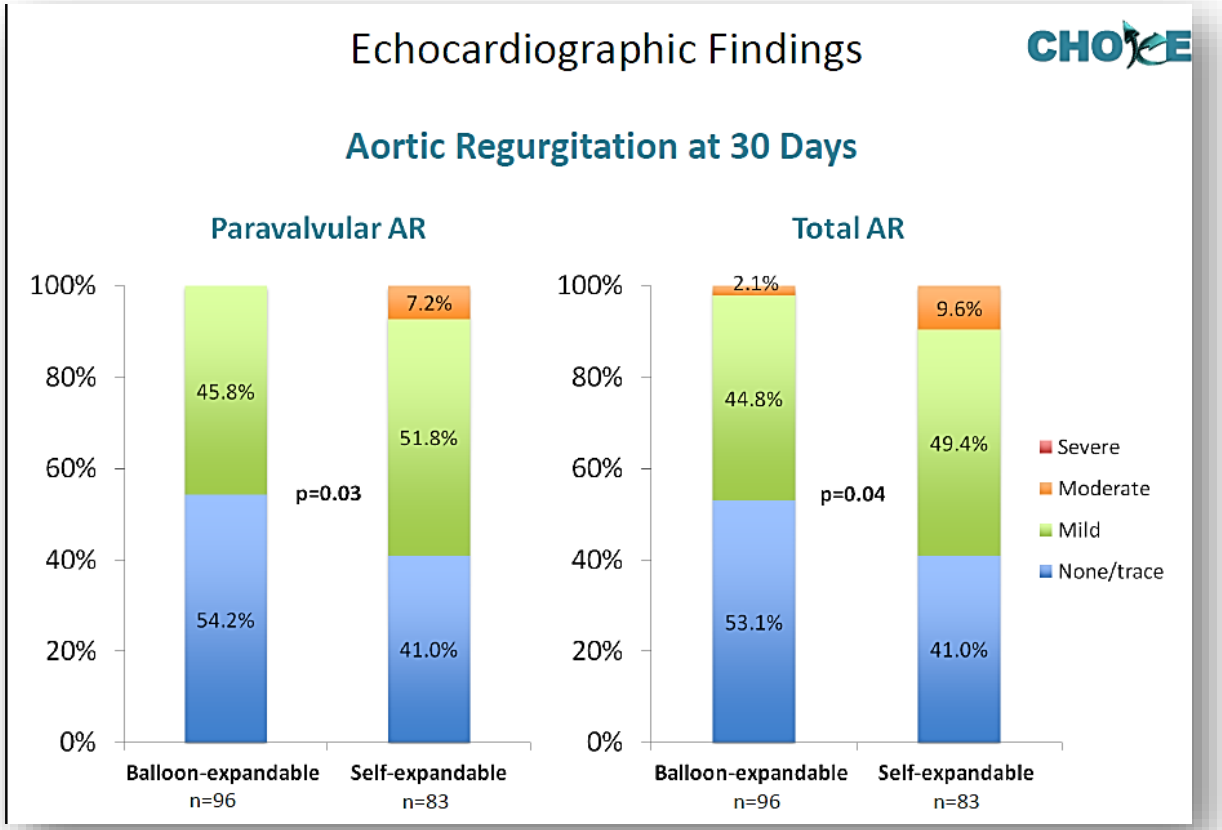
Mohamed Abdel-Wahab, MD; Julinda Mehilli, MD; Christian Frerker, MD; Franz-Josef Neumann, MD; Thomas Kurz, MD; Ralph Tölg, MD; Dirk Zachow, MD; Elena Guerra, MD; Steffen Massberg, MD; Ulrich Schäfer, MD; Mohamed El-Mawardy, MD; Gert Richardt, MD; for the CHOICE Investigators

121 patients were randomly assigned to receive a balloon-expandable valve (Edwards Sapien XT) and 120 were assigned to receive a self-expandable valve (Medtronic CoreValve).

- No difference in:
  1. Cardiovascular mortality at 30 days
  2. Bleeding and vascular complications were not significantly different,
  3. Combined safety end point
- Placement of a new permanent pacemaker was less frequent in the balloon-expandable valve group (17.3%vs 37.6%, P = .001).

Abdel-Wahab, M et al. *JAMA* 2014;311:1503-1514. doi:10.1001/jama.2014.3316

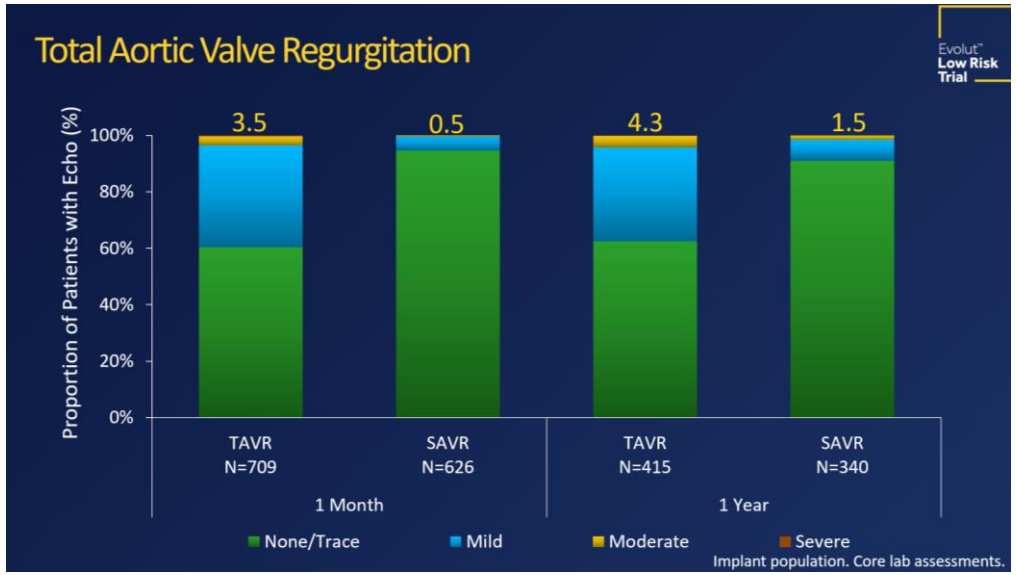




Conclusions and relevance: Among patients with high-risk aortic stenosis undergoing TAVR, the use of a balloon-expandable valve resulted in a greater rate of device success than use of a self-expandable valve.

Paravalvular Regurgitation: Low Risk Trials

Self-expanding THV

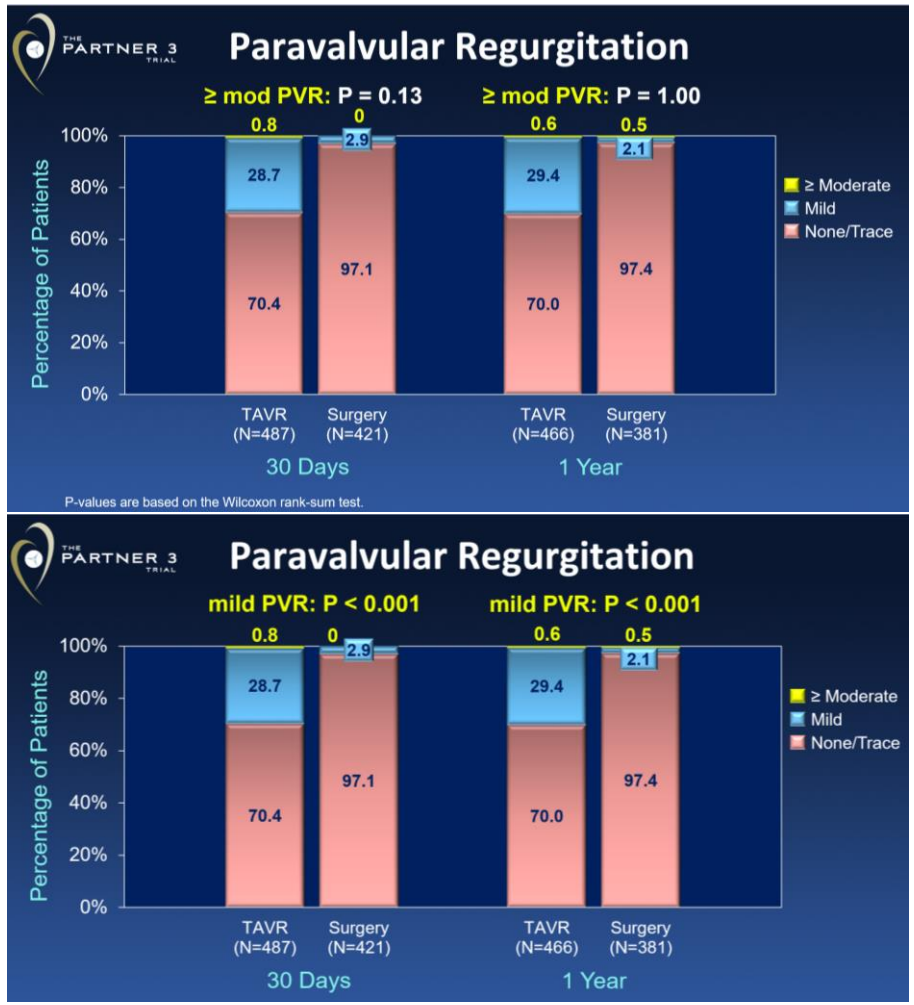


≥ Moderate PVL:

30 d: 3.5% inTAVR vs 0.5% in SAVR

1 yr: 4.3% in TAVR vs 2.5% in SAVR

Balloon-expandable THV



≥ Moderate PVL: Not statistically different

1 yr: 0.8% in TAVR vs 0% in SAVR

Comparison of outcomes using balloon-expandable versus self-expanding transcatheter prostheses according to the extent of aortic valve calcification

- Balloon-expandable valve (the highest radial force) demonstrated very low rates of PVR ≥2° across all AVC_{dens} strata
- Independent Predictors of PVR ≥2°
  - Presence of malpositioning [<0.001; OR 6.32 (95% CI3.67-10.88)],
  - Use of SE devices [p<0.001; OR 7.68 (95% CI 3.04-19.43)],
  - AVC_{dens} [<0.001; per 1 AU/cm^2 increase, OR 1.002 (95% CI 1.001-1.003)]

1232 patients undergoing transfemoral TAVI

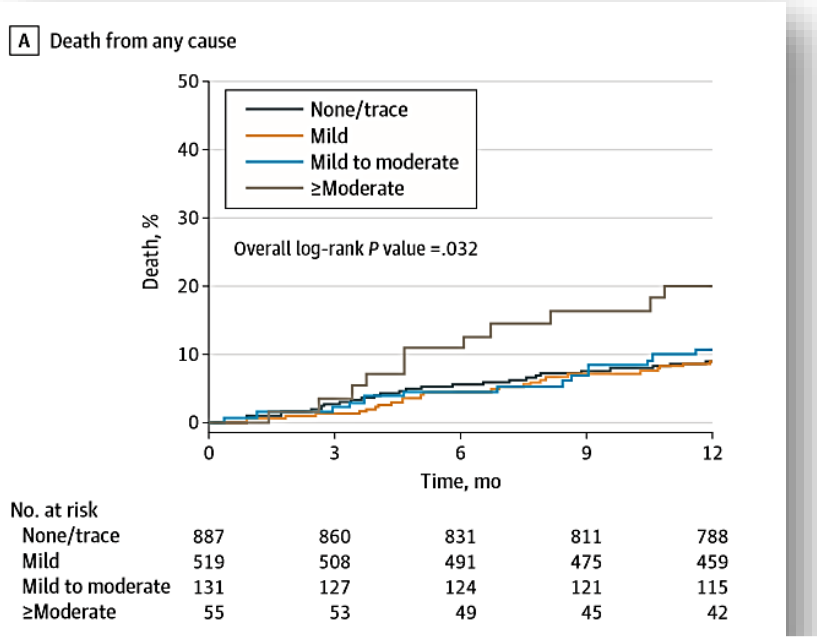
Table 2 Comparison between SE and BE THV

	Total cohort ($n = 1232$)	BE THV ($n = 488$)	SE THV ($n = 744$)	p
Complications				
In-hospital mortality	42 (3.4%)	19 (3.9%)	23 (3.1%)	0.45
30-day mortality	52/1210 (4.3%)	21/488 (4.3%)	31/722 (4.3%)	0.99
1-year mortality	148/860 (17.2%)	57/338 (16.9%)	91/522 (17.4%)	0.83
PVR ≥2° (angio)	78/1228 (6.4%)	13/485 (2.7%)	65/743 (8.7%)	**<0.001**
PVR ≥2° (echo)	69/1228 (5.6%)	10/485 (2.1%)	59/743 (7.9%)	**<0.001**
Malpositioning	138 (11.2%)	41 (8.4%)	97 (13.0%)	**0.01**
Device embolization	21 (1.7%)	2 (0.4%)	19 (2.6%)	**0.004**
Need for second valve	33 (2.7%)	6 (1.2%)	27 (3.6%)	**0.01**
Aortic root injury	19 (1.5%)	13 (2.7%)	6 (0.8%)	**0.01**
Conversion to surgery	31 (2.5%)	9 (1.8%)	22 (3.0%)	0.22
Major stroke	33 (2.7%)	10 (2.0%)	23 (3.1%)	0.27
Major bleeding	72 (5.8%)	28 (5.7%)	44 (5.9%)	0.89
Major vascular complication	118 (9.6%)	45 (9.2%)	73 (9.8%)	0.73
Pacemaker implantation	194 (15.7%)	80 (16.4%)	114 (15.3%)	0.61
Acute kidney injury St 2 and 3	47 (3.8%)	20 (4.1%)	27 (3.6%)	0.68

JAMA Cardiology | Original Investigation

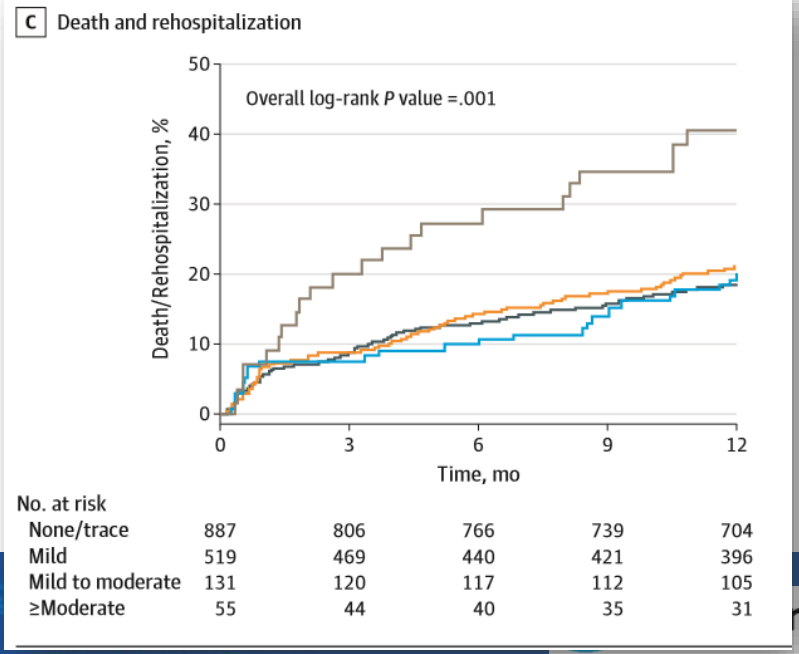
Association of Paravalvular Regurgitation With 1-Year Outcomes After Transcatheter Aortic Valve Replacement With the SAPIEN 3 Valve

Philippe Pibarot, DVM, PhD; Rebecca T. Hahn, MD; Neil J. Weissman, MD; Marie Arsenault, MD; Jonathan Beaudoin, MD; Mathieu Bernier, MD; Abdellaziz Dahou, MD, MS; Omar K. Khalique, MD; Federico M. Asch, MD; Oumhani Toubal, MD; Jonathon Leipsic, MD; Philipp Blanke, MD; Feifan Zhang, PhD; Rupa Parvataneni, MS; Maria Alu; Howard Herrmann, MD; Raj Makkar, MD; Michael Mack, MD; Richard Smalling, MD; Martin Leon, MD; Vinod H. Thourani, MD; Susheel Kodali, MD



- **≥ Moderate PVR was rare but associated with increased risk of death and heart failure rehospitalization at 1 year.**
  - **HR for All-cause Mortality 2.59 (1.39-4.85) .003**

High and Intermediate Risk



- Even the upper range of the mild class in the 3-class grading scheme (ie, mild to moderate in the 5-class scheme) had no significant effect on short-term mortality or rehospitalization.

- Most patients with ≥moderate PVR at 30 days showed a decrease of PVR severity grade at 1 year.

Pibarot P et al. JAMACardiol.2017;2(11):1208-1216

Circulation

HR Mild vs None/Trace = 0.85 [0.39, 1.89]

ORIGINAL RESEARCH ARTICLE

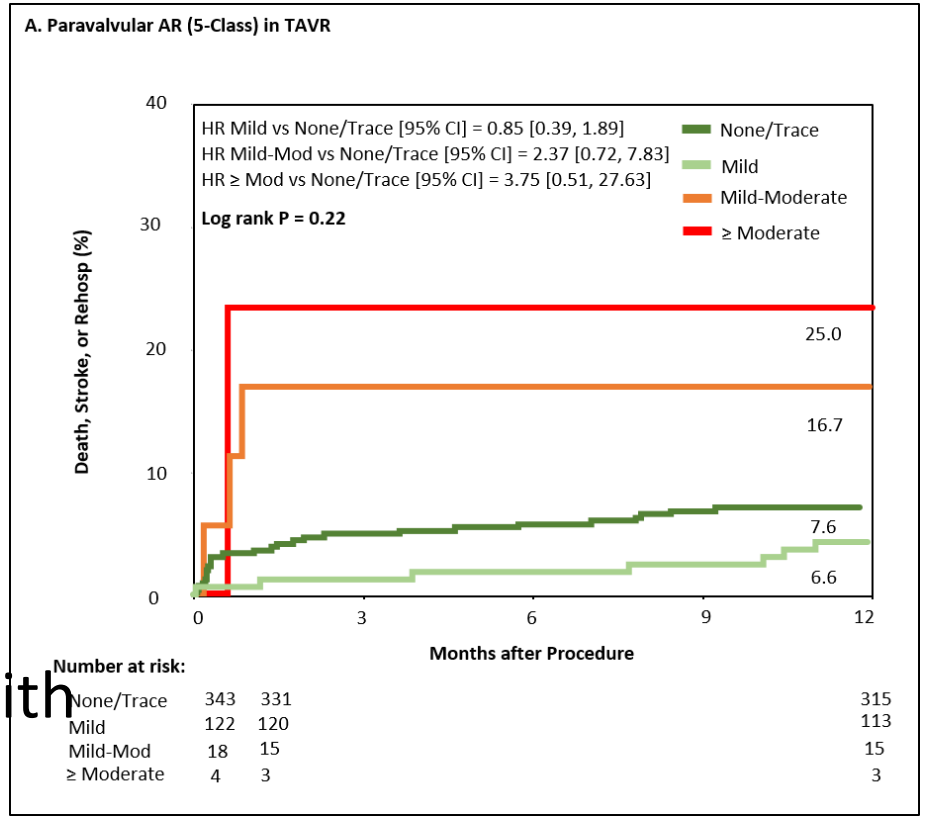
Echocardiographic Results of Transcatheter Versus Surgical Aortic Valve Replacement in Low-Risk Patients

The PARTNER 3 Trial

Editorial, see p 1538

Philippe Pibarot, DVM, PhD
⋮
Rebecca T. Hahn, MD
For the PARTNER 3

BACKGROUND: This study aimed to compare echocardiographic findings in low-risk patients with severe aortic stenosis after surgical aortic valve replacement (SAVR) or transcatheter aortic valve replacement (TAVR).



- In PARTNER 3
  - Moderate AR in only 5 patients (no association with mortality, stroke or rehospitalization)
  - Mild AR at 30 days was not associated with 1-year outcomes.

Low Risk

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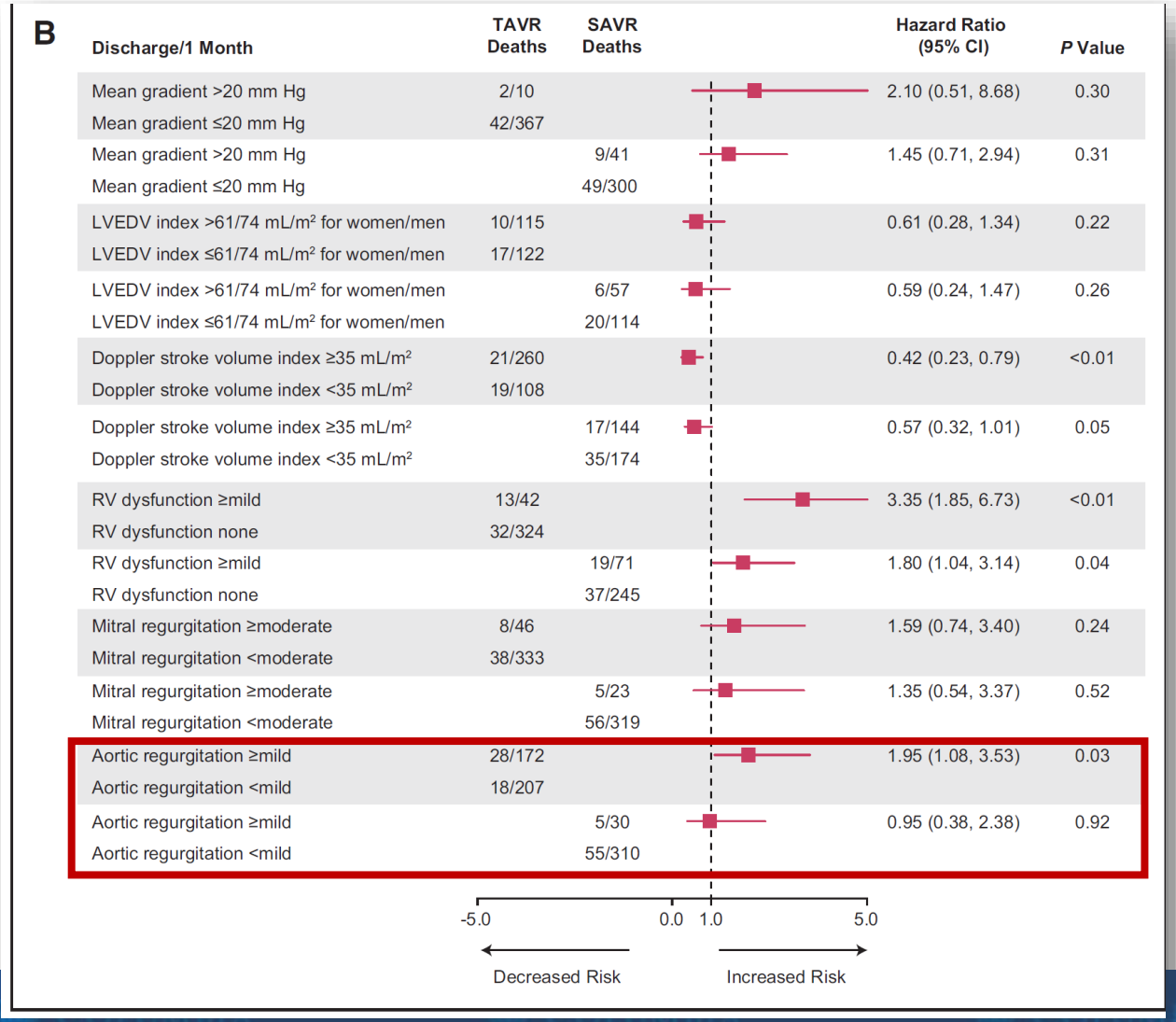
Self-Expanding Transcatheter Aortic Valve Replacement Versus Surgical Valve Replacement in Patients at High Risk for Surgery



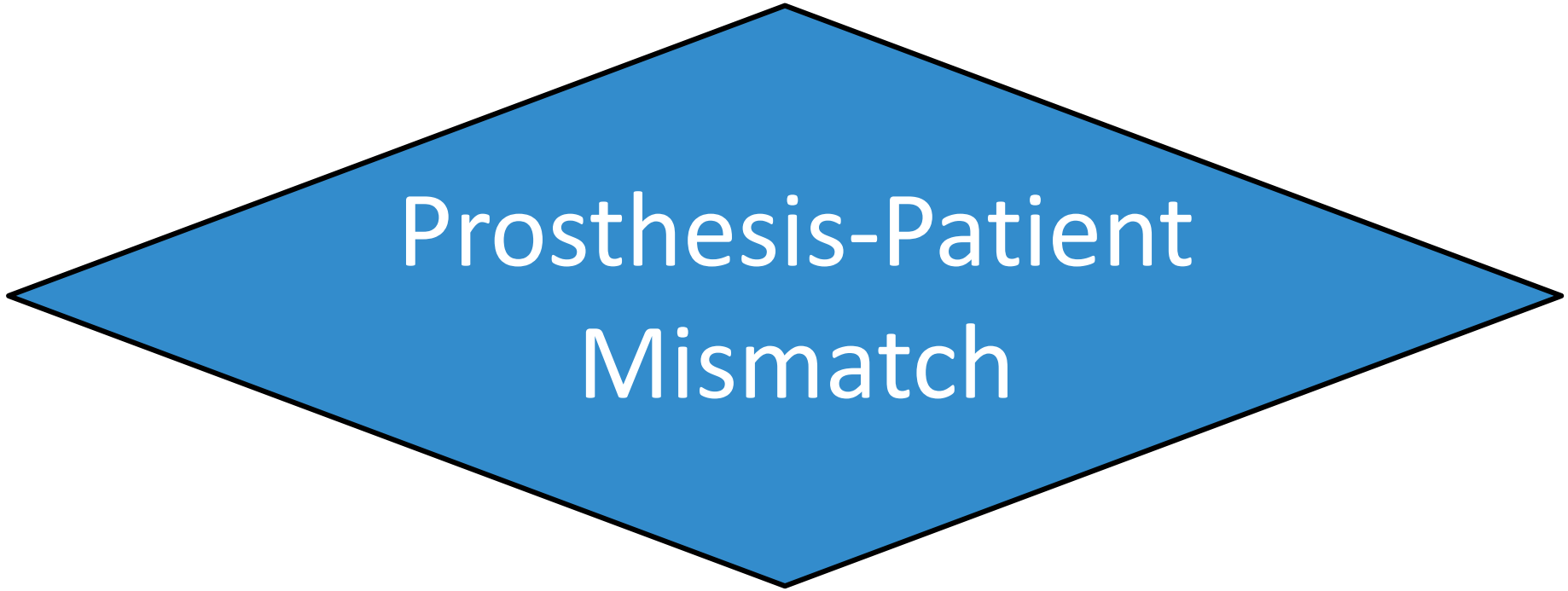
B

Discharge/1 Month	TAVR Deaths	SAVR Deaths	Hazard Ratio (95% CI)	*P* Value
Mean gradient >20 mm Hg	2/10		2.10 (0.51, 8.68)	0.30
Mean gradient ≤20 mm Hg	42/367			
Mean gradient >20 mm Hg		9/41	1.45 (0.71, 2.94)	0.31
Mean gradient ≤20 mm Hg		49/300		
LVEDV index >61/74 mL/m² for women/men	10/115		0.61 (0.28, 1.34)	0.22
LVEDV index ≤61/74 mL/m² for women/men	17/122			
LVEDV index >61/74 mL/m² for women/men		6/57	0.59 (0.24, 1.47)	0.26
LVEDV index ≤61/74 mL/m² for women/men		20/114		
Doppler stroke volume index ≥35 mL/m²	21/260		0.42 (0.23, 0.79)	<0.01
Doppler stroke volume index <35 mL/m²	19/108			
Doppler stroke volume index ≥35 mL/m²		17/144	0.57 (0.32, 1.01)	0.05
Doppler stroke volume index <35 mL/m²		35/174		
RV dysfunction ≥mild	13/42		3.35 (1.85, 6.73)	<0.01
RV dysfunction none	32/324			
RV dysfunction ≥mild		19/71	1.80 (1.04, 3.14)	0.04
RV dysfunction none		37/245		
Mitral regurgitation ≥moderate	8/46		1.59 (0.74, 3.40)	0.24
Mitral regurgitation <moderate	38/333			
Mitral regurgitation ≥moderate		5/23	1.35 (0.54, 3.37)	0.52
Mitral regurgitation <moderate		56/319		
Aortic regurgitation ≥mild	28/172		1.95 (1.08, 3.53)	0.03
Aortic regurgitation <mild	18/207			
Aortic regurgitation ≥mild		5/30	0.95 (0.38, 2.38)	0.92
Aortic regurgitation <mild		55/310		

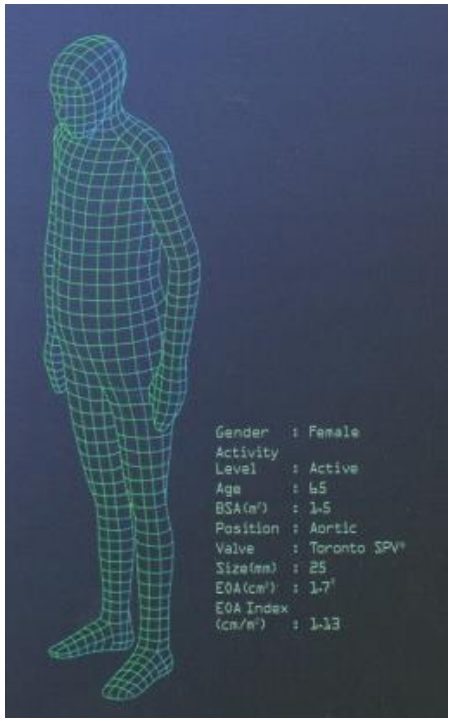
Predictors of All-Cause Mortality in TAVR:

1. **RV dysfunction ≥ mild**
   a. **HR 1.80 [CI 1.04, 3.14]**
2. **AR ≥ mild**
   a. **HR 1.95 [CI 1.08 3.53], p = 0.03**

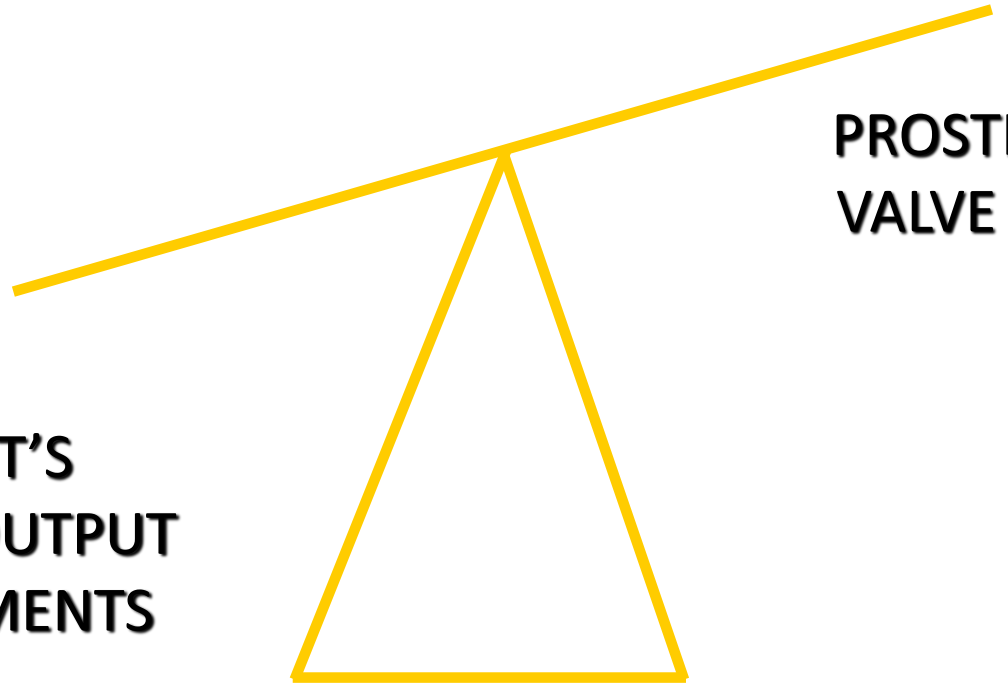
***Little S.et al. Circ Cardiovasc Interv*. 2016;9:e003426.**



BSA



PROSTHESIS-PATIENT MISMATCH



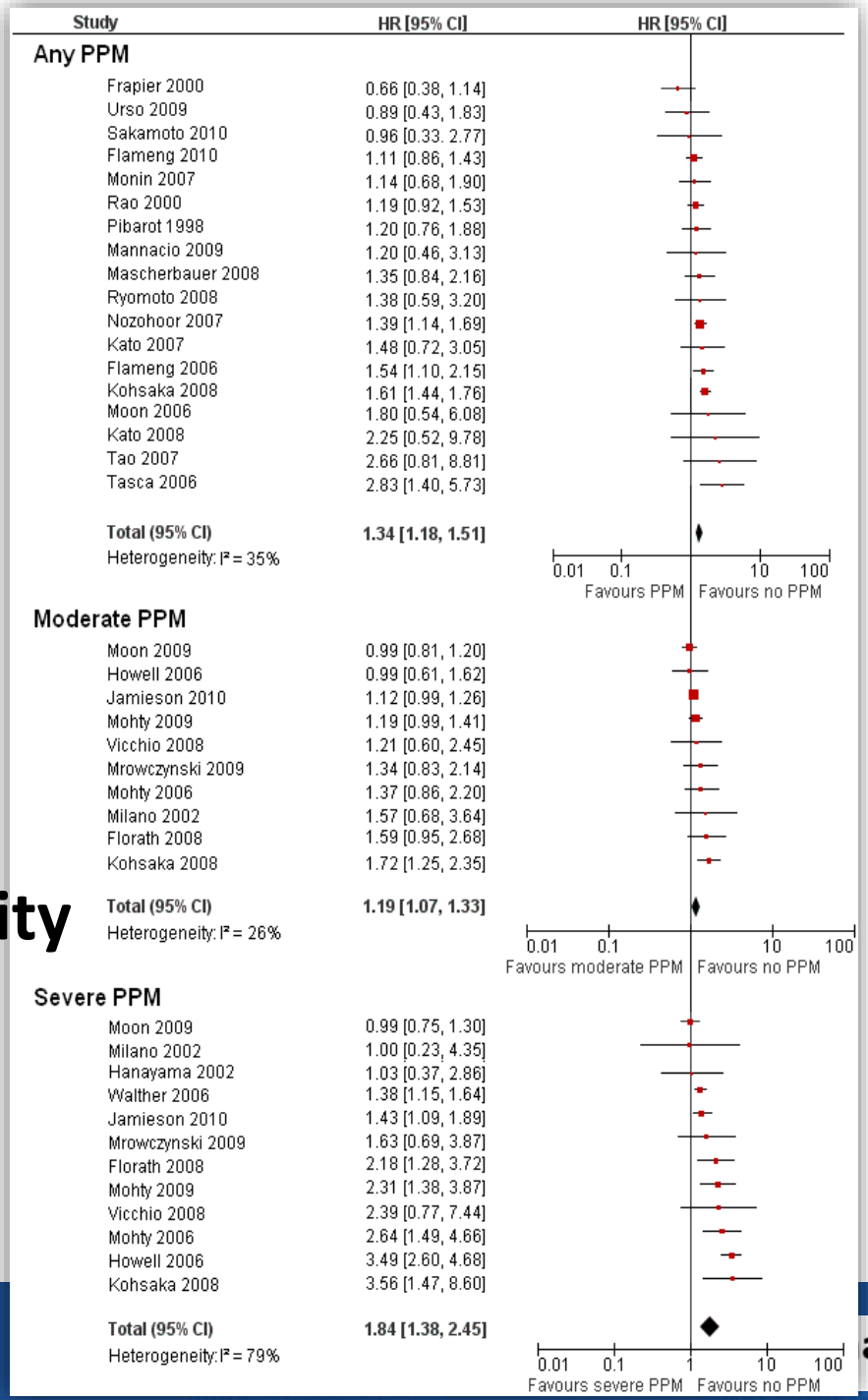
PPM occurs when the EOA of the prosthesis is too small in relation to patient's body size / cardiac output requirements

Courtesy of Philippe Pibarot

Impact of SAVR PPM on All-Cause Mortality

Systematic Review and Meta-analysis of
34 observational studies, 27,186 patients
and 133,141 patient-years

- **Moderate PPM: 1.2-fold increase in mortality**
- **Severe PPM: 1.8-fold increase in mortality**

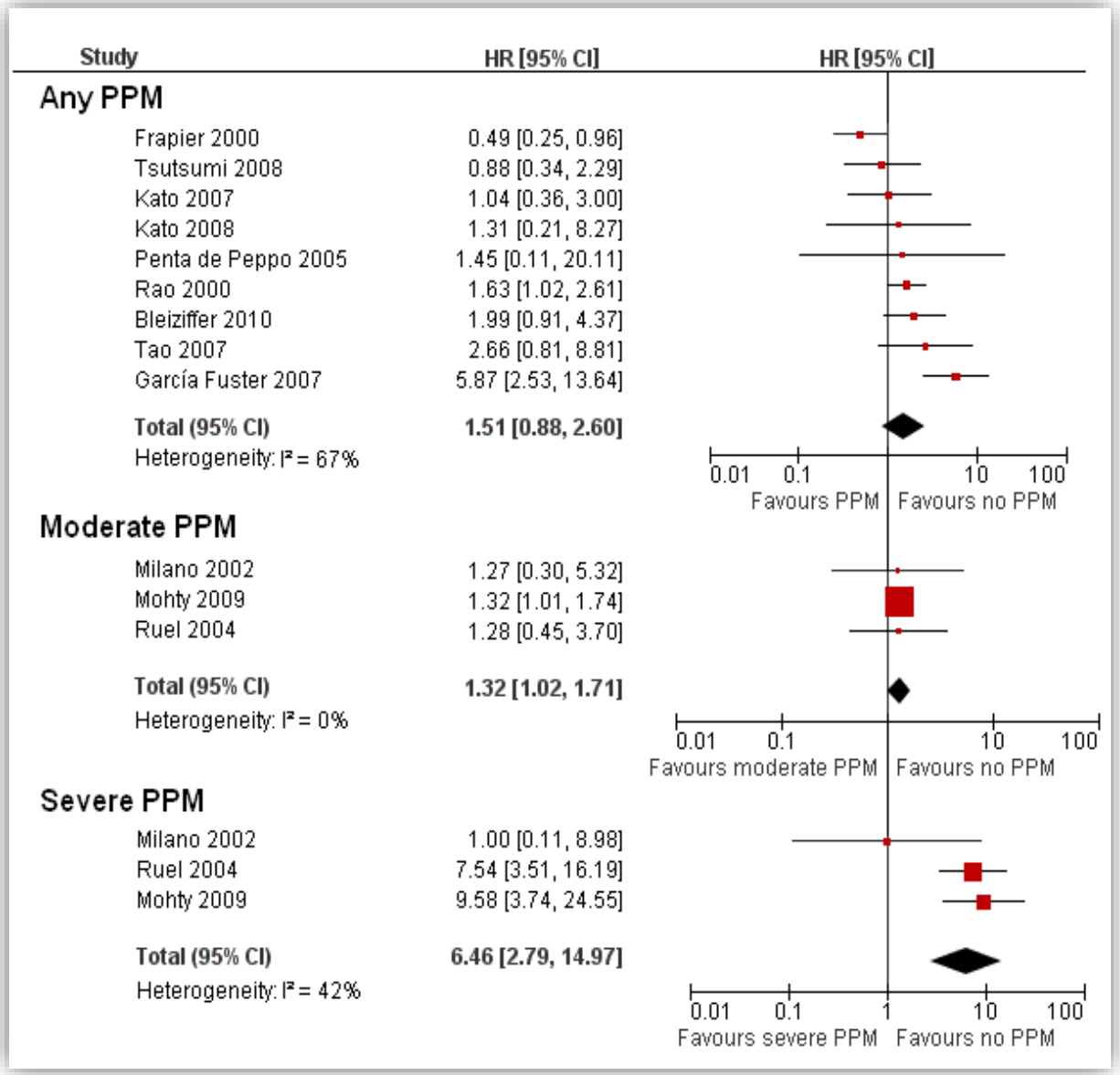


Head et al Eur Heart J. 2012;33:1518-29

Impact of SAVR PPM on Cardiac Mortality

Systematic Review and Meta-analysis of
34 observational studies, 27,186 patients
and 133,141 patient-years

- **Moderate PPM: 1.3-fold increase in cardiac mortality**
- **Severe PPM: 6.5-fold increase in cardiac mortality**



Head et al Eur Heart J. 2012;33:1518-29

@hahn_rt

Impact of PPM on Outcomes of SAVR

FIGURE 3 Summary Effect for Impact of PPM on Outcomes

A Any PPM

Outcomes	Studies	Patients	Odds/HR/MD	No PPM	PPM	P
Perioperative Mortality	33	25956	1.54 [1.25, 1.91]			<0.0001
Overall Mortality	38	29560	1.26 [1.16, 1.36]			<0.0001
PNC	9	7690	1.59 [1.05, 2.44]			0.003
ΔLVEF	6	1174	-1.02 [0.24, -2.28]			0.067
ΔLVMI	14	2927	18.38 [24.99, 12.06]		Truncated due to size	<0.0001

OR/HR 0.01 0.1 1 10 100
+/- MD 10 5 0 5 10

B Moderate PPM vs No PPM

Outcomes	Studies	Patients	Odds/HR/MD	No PPM	Mod PPM	P
Perioperative Mortality	12	12042	1.57 [1.17, 2.11]			0.003
Overall Mortality	13	12566	1.01 [0.95, 1.08]			0.68
PNC	4	1234	1.50 [0.66, 3.44]			0.34
ΔLVEF	2	180	-0.07 [2.98, -3.12]			0.97
ΔLVMI	4	843	13.57 [27.94, -0.81]		Truncated due to size	<0.0001

OR/HR 0.01 0.1 1 10 100
+/- MD 10 5 0 5 10

C Severe PPM vs No PPM

Outcomes	Studies	Patients	Odds/HR/MD	No PPM	Severe PPM	P
Perioperative Mortality	12	7906	2.57 [1.12, 5.88]			0.03
Overall Mortality	12	8500	1.43 [1.14, 1.80]			0.002
PNC	4	976	1.24 [0.49, 3.12]			0.65
ΔLVEF	1	50	-0.30 [5.91, -6.51]			0.92
ΔLVMI	3	801	17.86 [36.36, -0.55]		Truncated due to size	0.06

OR/HR 0.01 0.1 1 10 100
+/- MD 10 5 0 5 10

D Severe PPM vs Moderate PPM

Outcomes	Studies	Patients	Odds/HR/MD	Mod PPM	Severe PPM	P
Perioperative Mortality	12	6084	1.68 [0.89, 3.14]			0.11
Overall Mortality	12	7688	1.33 [1.18, 1.51]			<0.0001
PNC	4	1007	1.79 [0.62, 5.16]			0.28
ΔLVEF	1	79	-1.30 [-6.88, 4.28]			0.65
ΔLVMI	3	506	4.34 [15.17, -6.48]		Truncated due to size	0.45

OR/HR 0.01 0.1 1 10 100
+/- MD 10 5 0 5 10

This figure shows the summary effect of PPM on outcomes including perioperative mortality, overall mortality, PNC, and post-operative change in LVEF and LVMi. The panels show the risk of these outcomes with the following: **(A)** any degree of PPM versus no PPM; **(B)** moderate PPM versus no PPM; **(C)** severe PPM versus no PPM; and **(D)** moderate PPM versus severe PPM. HR = hazard ratio; LVMi = left ventricular mass index (g/m^2); PNC = post-operative neurologic complications; other abbreviations as in Figures 1 and 2.

Table 12 Imaging criteria or the identification and quantitation of prosthesis-patient mismatch

	Mild or not clinically significant	Moderate	Severe
Aortic prosthetic valves			
Indexed EOA (projected or measured)			
BMI <30 kg/m^2	>0.85	0.85–0.66	≤ 0.65
BMI ≥ 30 kg/m^2	>0.70	0.70–0.56	≤ 0.55
Measured EOA vs. normal reference value[a]	Reference $\pm$ 1SD	Reference $\pm$ 1SD	Reference $\pm$ 1SD
Difference (reference EOA − measured EOA) (cm^2)[a]	<0.25	<0.25	<0.25
Valve structure and motion	Usually normal	Usually normal	Usually normal
Mitral prosthetic valves			
Indexed EOA (projected or measured)			
BMI <30 kg/m^2	>1.2	1.2–0.91	≤ 0.90
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See *Tab*
EOA, e
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- **In overweight and obese patients, the cardiac output requirement does not increase in proportion to the increase in BSA that results from the larger body weight.**
- **EOA indexed to BSA may overestimate the degree of PPM in patients with larger BMI.**

Bioprosthetic Valve Dysfunction

Is the dysfunction related to intrinsic permanent changes to the prosthetic valve?

YES

Structural Valve Deterioration
Intrinsic permanent changes to the prosthetic valve, including wear and tear, leaflet disruption, flail leaflet, leaflet fibrosis and/or calcification, strut fracture

Are there hemodynamic changes?

NO

Stage 1
Morphological Valve Deterioration:
Intrinsic permanent changes to the prosthetic valve, including leaflet tear, disruption, flail leaflet, leaflet fibrosis and/or calcification, strut fracture without significant hemodynamic changes.

YES

Stage 2
Moderate hemodynamic valve deterioration (HVD):
Increase in mean transvalvular gradient ≥10 mmHg resulting in mean gradient ≥20 mmHg† with concomitant decrease in EOA ≥0.3 cm^2 or ≥25% and/or decrease in Doppler velocity index ≥0.1 or ≥20% compared to echocardiographic assessment performed 1 to 3 months post-procedure,
OR
New occurrence or increase of ≥1 grade of intraprosthetic AR resulting in ≥ moderate AR.

Stage 3
Severe HVD:
Increase in mean transvalvular gradient ≥20 mmHg resulting in mean gradient ≥30 mmHg† with concomitant decrease in EOA ≥0.6 cm^2 or ≥50% and/or decrease in Doppler velocity index ≥0.2 or ≥40% compared to echocardiographic assessment performed 1 to 3 months post-procedure,
OR
New occurrence, or increase of ≥2 grades, of intraprosthetic AR resulting in ≥ severe AR.

NO

Non-Structural Valve Dysfunction
Any abnormality, **not** intrinsic to the prosthetic valve, resulting in valve dysfunction.

Paravalvular Regurgitation
see Table 15

Prosthesis-Patient Mismatch

If BMI < 30 kg/m^2

Severity	Indexed EOA (cm^2/m^2)
Insignificant	>0.85
Moderate	0.85-0.66
Severe	≤0.65

If BMI ≥ 30kg/m^2

Severity	Indexed EOA (cm^2/m^2)
Insignificant	>0.70
Moderate	0.70-0.56
Severe	≤0.55

Other
May include: leaflet entrapment by pannus, tissue, or suture; inappropriate positioning or sizing; dilatation of the aortic root after stentless bioprostheses or aortic valve sparing operations; and embolization

Thrombosis
(1) Hypo-attenuated leaflet thickening (HALT) (2) Reduced leaflet motion (RELM) (3)Leaflet thrombosis or hypo-attenuation affecting leaflet motion (HAM)

See Table 14

Endocarditis
Meeting at least one of the following criteria: (1) Fulfillment of the Duke endocarditis criteria (2) Evidence of abscess, pus, or vegetation confirmed as secondary to infection by histological or microbiological studies during re-operation; (3) Evidence of abscess, pus, or vegetation confirmed on autopsy.

Bioprosthetic Valve Failure (BVF)

Stage 1: Clinically expressive criteria (new-onset or worsening symptoms, LV dilation/hypertrophy/dysfunction, or pulmonary hypertension), or Stage 3 HVD

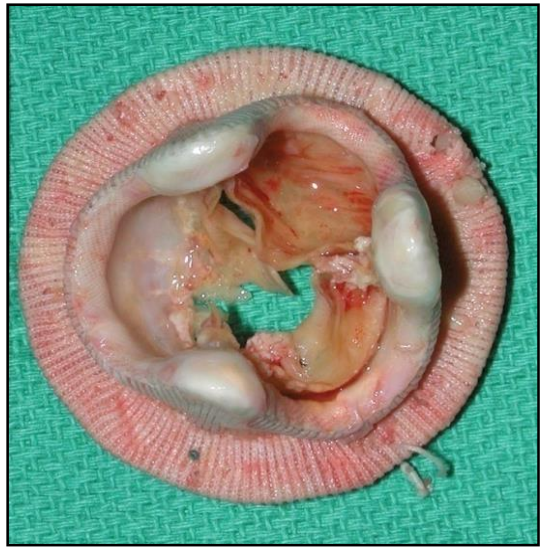
Stage 2: Aortic valve reintervention

Stage 3: Valve-related death

VARC-3…in press

†This criteria for hemodynamic dysfunction assumes normal flow.

Impact of PPM on SVD of Bioprosthetic Valves



- 664 patients: AVR with a bioprosthesis
- Median FU time: 6.1 yr
- PPM is independently associated with **2.3-fold increase in the risk of SVD**

Predictors of Bioprosthetic Valve Calcification

Prospective study: 204 patients with aortic BPs evaluated by MDCT: 24% had cusp calcification

	OR	95% CI	P value
Age (per 1 year increment)	0.96	0.92-1.01	0.1
Time since implant (per 1 year increment)	1.16	1.05-1.29	0.003
Ca Ph product (per 0.1 increment)	1.11	1.01-1.23	0.02
Prosthesis-Patient Mismatch	3.67	1.25-10.6	0.01

Courtesy of Philippe Pibarot

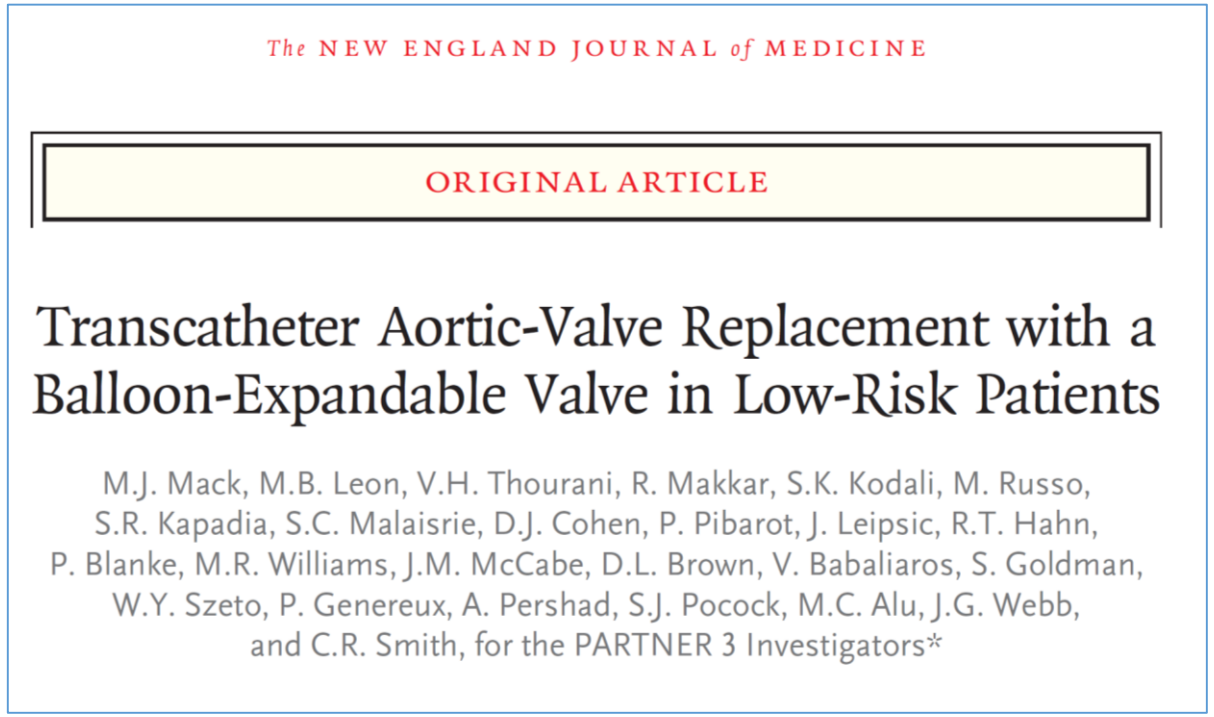
Flameng et al., Circulation, 18;121:2123-9, 2010

Mahjoub et al. Heart 2015;101:472–477

Recommendations for the Prevention of PPM in **Surgical Bioprosthetic Valves**

- Avoid severe PPM (EOAI<0.65) in every patient undergoing AVR
  - This may not be true for obese patients
- Avoid moderate PPM (EOAI<0.85) in:
  - Patients with LV dysfunction
  - Patients with concomitant MR
  - Young (< 65-70 yr) patients
  - Athlete patients

Presented at the American College of Cardiology, Sunday, March 17, 2019



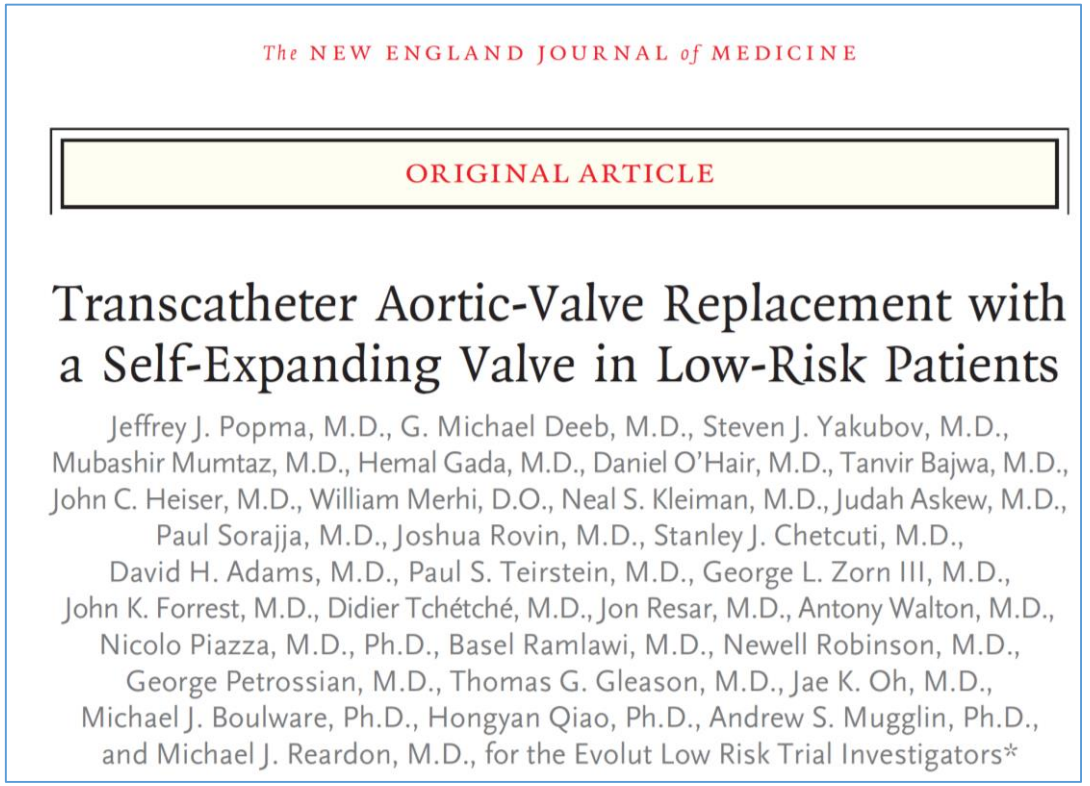
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Transcatheter Aortic-Valve Replacement with a Balloon-Expandable Valve in Low-Risk Patients

M.J. Mack, M.B. Leon, V.H. Thourani, R. Makkar, S.K. Kodali, M. Russo, S.R. Kapadia, S.C. Malaisrie, D.J. Cohen, P. Pibarot, J. Leipsic, R.T. Hahn, P. Blanke, M.R. Williams, J.M. McCabe, D.L. Brown, V. Babaliaros, S. Goldman, W.Y. Szeto, P. Genereux, A. Pershad, S.J. Pocock, M.C. Alu, J.G. Webb, and C.R. Smith, for the PARTNER 3 Investigators*

Mack MJ, Leon MB, Thourani VH, et al. Transcatheter Aortic-Valve Replacement with a Balloon-Expandable Valve in Low-Risk Patients. March 16, 2019,DOI: 10.1056/NEJMoa1814052



The NEW ENGLAND JOURNAL of MEDICINE

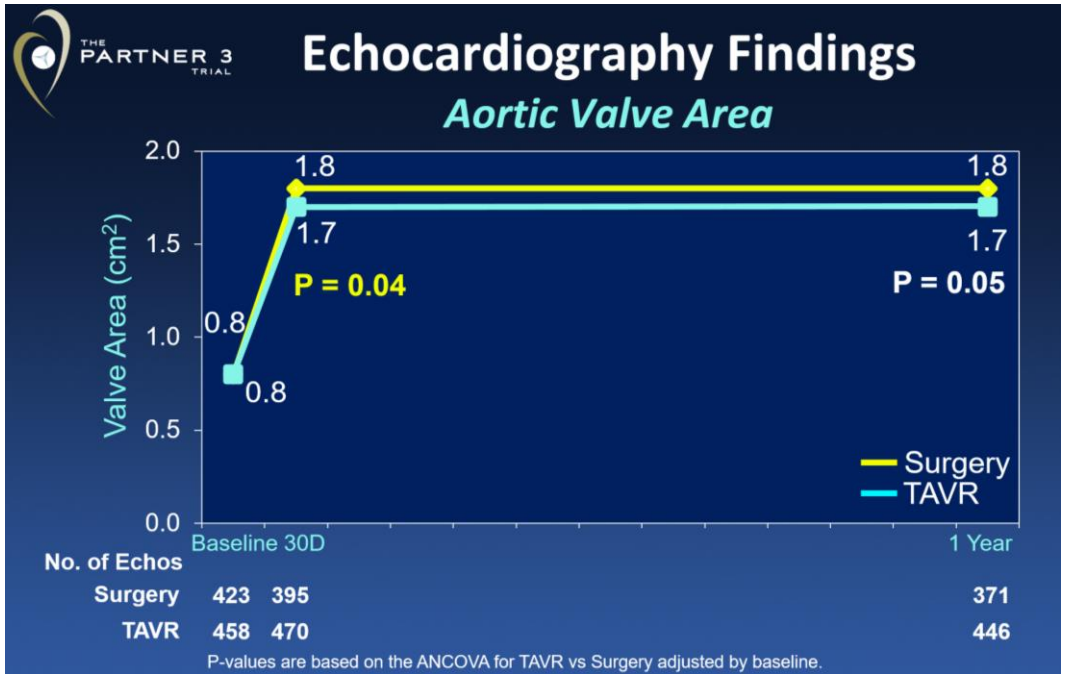
ORIGINAL ARTICLE

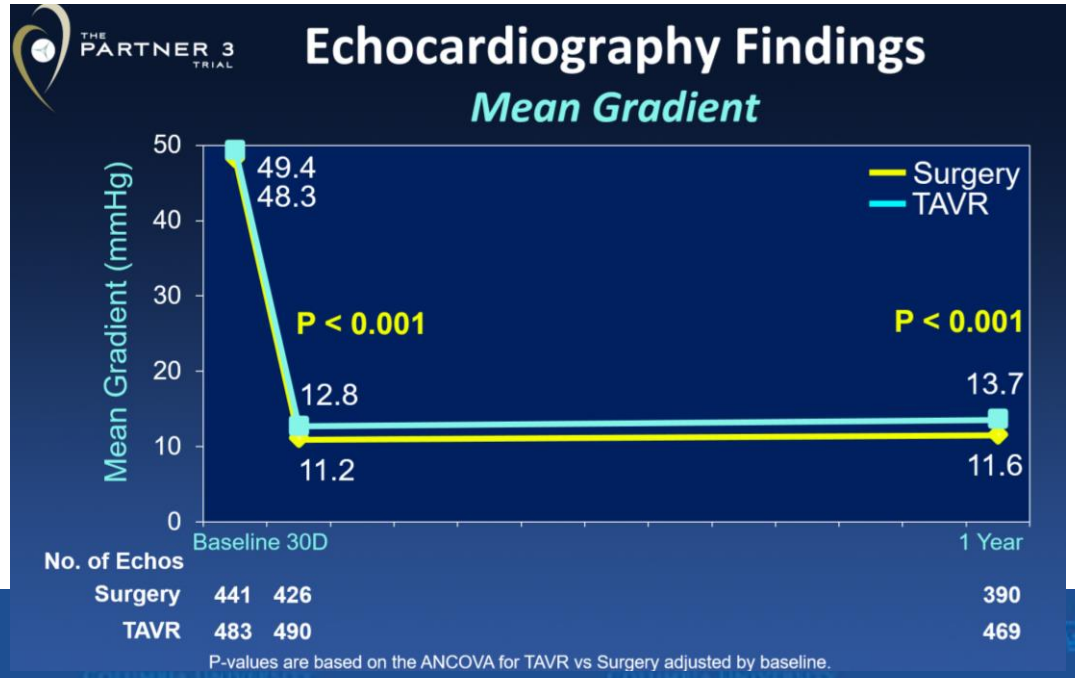
Transcatheter Aortic-Valve Replacement with a Self-Expanding Valve in Low-Risk Patients

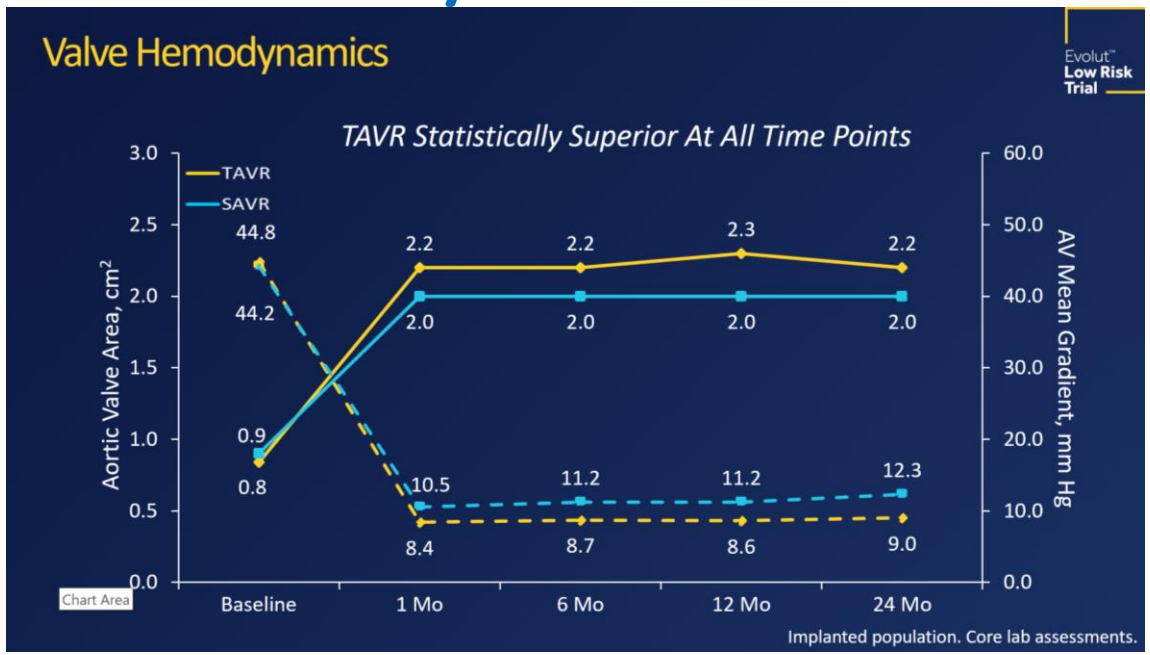
Jeffrey J. Popma, M.D., G. Michael Deeb, M.D., Steven J. Yakubov, M.D., Mubashir Mumtaz, M.D., Hemal Gada, M.D., Daniel O'Hair, M.D., Tanvir Bajwa, M.D., John C. Heiser, M.D., William Merhi, D.O., Neal S. Kleiman, M.D., Judah Askew, M.D., Paul Sorajja, M.D., Joshua Rovin, M.D., Stanley J. Chetcuti, M.D., David H. Adams, M.D., Paul S. Teirstein, M.D., George L. Zorn III, M.D., John K. Forrest, M.D., Didier Tchétché, M.D., Jon Resar, M.D., Antony Walton, M.D., Nicolo Piazza, M.D., Ph.D., Basel Ramlawi, M.D., Newell Robinson, M.D., George Petrossian, M.D., Thomas G. Gleason, M.D., Jae K. Oh, M.D., Michael J. Boulware, Ph.D., Hongyan Qiao, Ph.D., Andrew S. Mugglin, Ph.D., and Michael J. Reardon, M.D., for the Evolut Low Risk Trial Investigators*

Popma JJ, Deeb GM, Yakubov SJ, et al. Transcatheter Aortic-Valve Replacement with a Self-Expanding Valve in Low-Risk Patients. March 16, 2019 DOI: 10.1056/NEJMoa1816885

Possible Overestimation of EOA by CoreValve







1 yr	Mean Gradient	EOA
SAVR PARTNER	11.6	1.8
SAVR EVOLUT	11.2	2.0*
TAVR PARTNER	13.7	1.7
TAVR EVOLUT	8.7	2.2*

Likely a systematic over-estimation of ~0.2 cm²

@hahn_rt

CoreValve High Risk Trial: PPM and Mortality

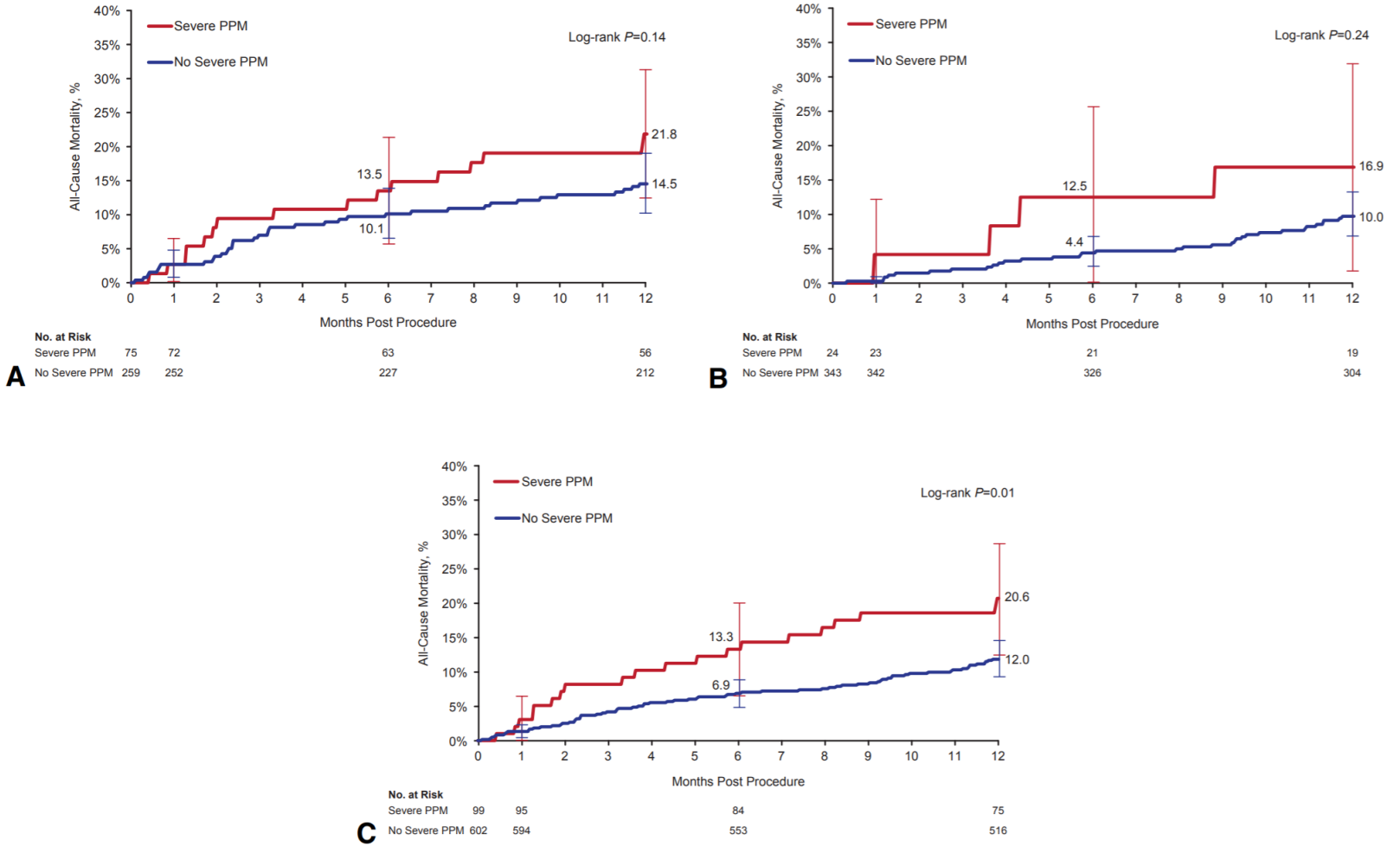


FIGURE 2. Cumulative incidence of all-cause mortality at 1 year for A, surgical aortic valve replacement, B, transcatheter aortic valve replacement, and C, patients undergoing combined transcatheter aortic valve replacement plus surgical aortic valve replacement. *PPM*, Prosthesis–patient mismatch.

When adjusted for treatment differences between TAVR and SAVR overall, the P value was .0666 for the difference in all-cause mortality between severe and no severe PPM

In the combined group the patients with severe PPM had a higher rate of all-cause mortality (20.6% vs 12.0%; P ¼ .0145)

Zorn et al. J Thorac Cardiovasc Surg 2016;151:1014-23.

PARTNER High Risk: PPM and Mortality

SAPIEN Valve Cohort A

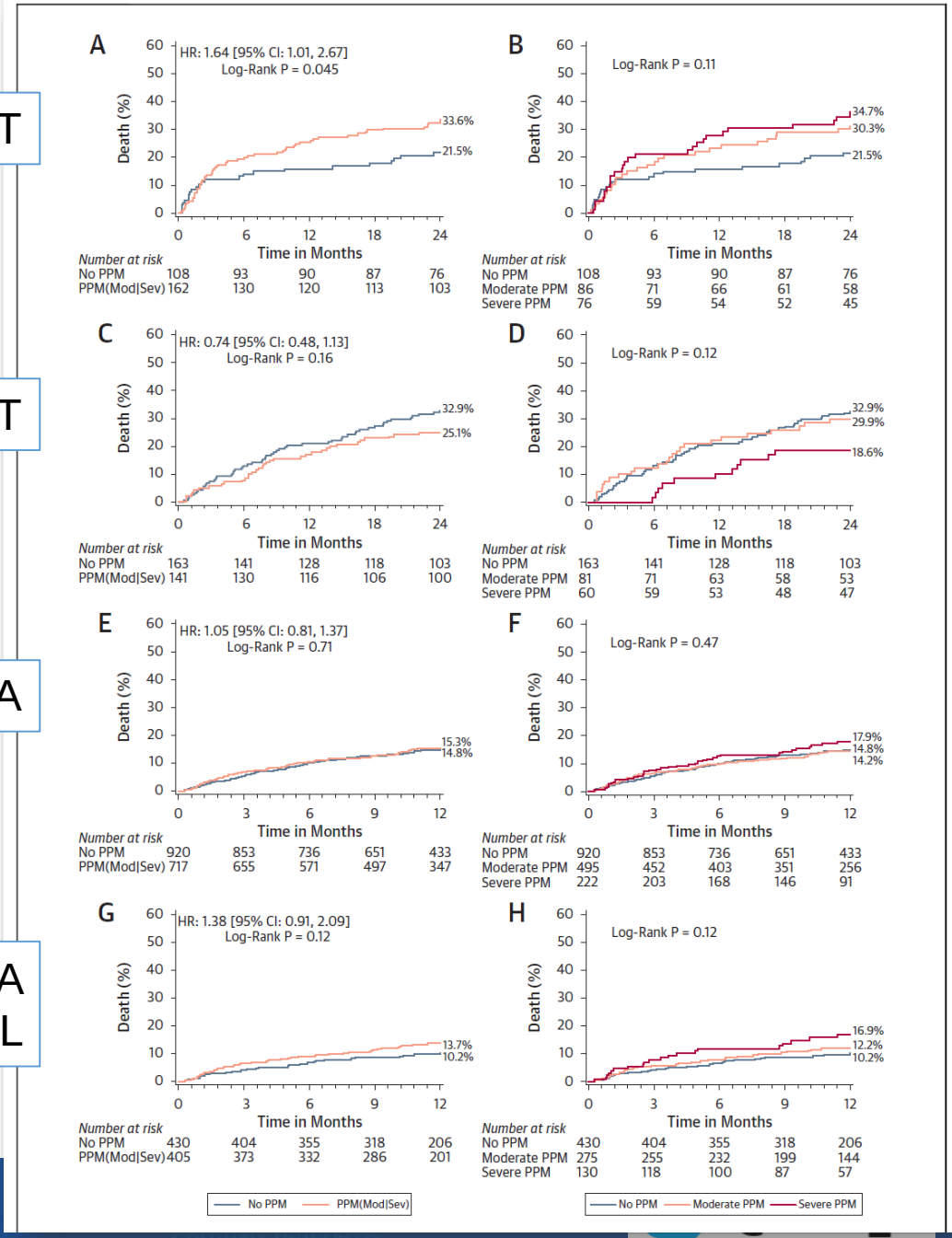
- **PPM was an independent predictor of 2-year mortality in the SAVR-RCT cohort** (hazard ratio [HR]: 1.78; p = 0.041). This finding is similar to other surgical AVR studies which supports the validity of findings in this study.
- PPM **was NOT associated with mortality** in the **TAVR-RCT** cohort (HR: 0.58; p = 0.11).
- PPM **was not a predictor of 1-year mortality** in **all TAVR patients** (HR: 1.05; p = 0.60).
- In the **subset of non-randomized, continued access (NRCA) patients with no PVL**, PPM was an independent predictor of mortality (HR: 1.88; p = 0.02).

SAVR-RCT

TAVR-RCT

TAVR-NRCA

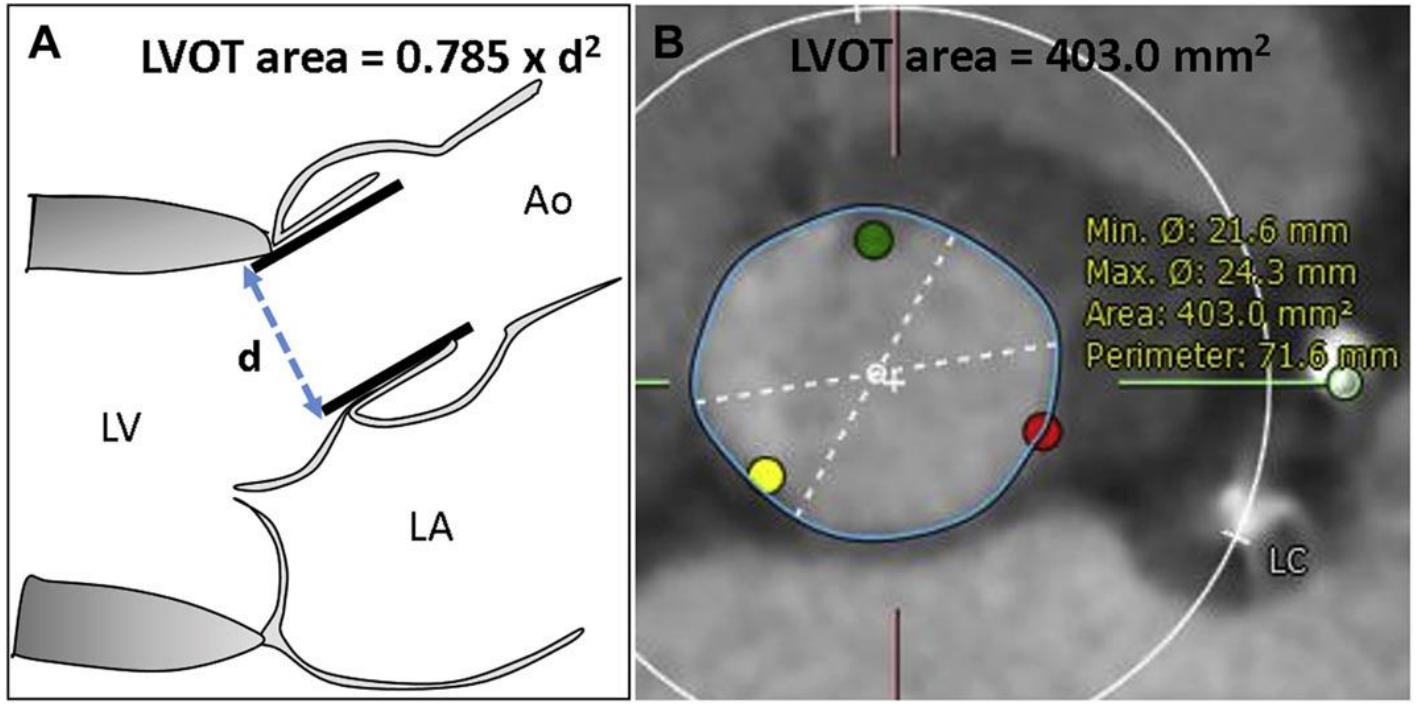
TAVR-NRCA with no PVL



Pibarot P et al. J Am Coll Cardiol 2014;64:1323–34

PARTNER Intermediate Risk: PPM by TTE and CT

- 765 TAVR patients from the PARTNER II (Placement of Aortic Transcatheter Valves II) trial S3i cohort
- EOAi was calculated using the continuity equation, and the left ventricular outflow tract area was derived from baseline computed tomography.
- Traditional TTE categories defined PPM: absent (>0.85 cm^2/m^2), moderate (≥0.65 and ≤0.85 cm^2/m^2), or severe (≤0.65 cm^2/m^2)

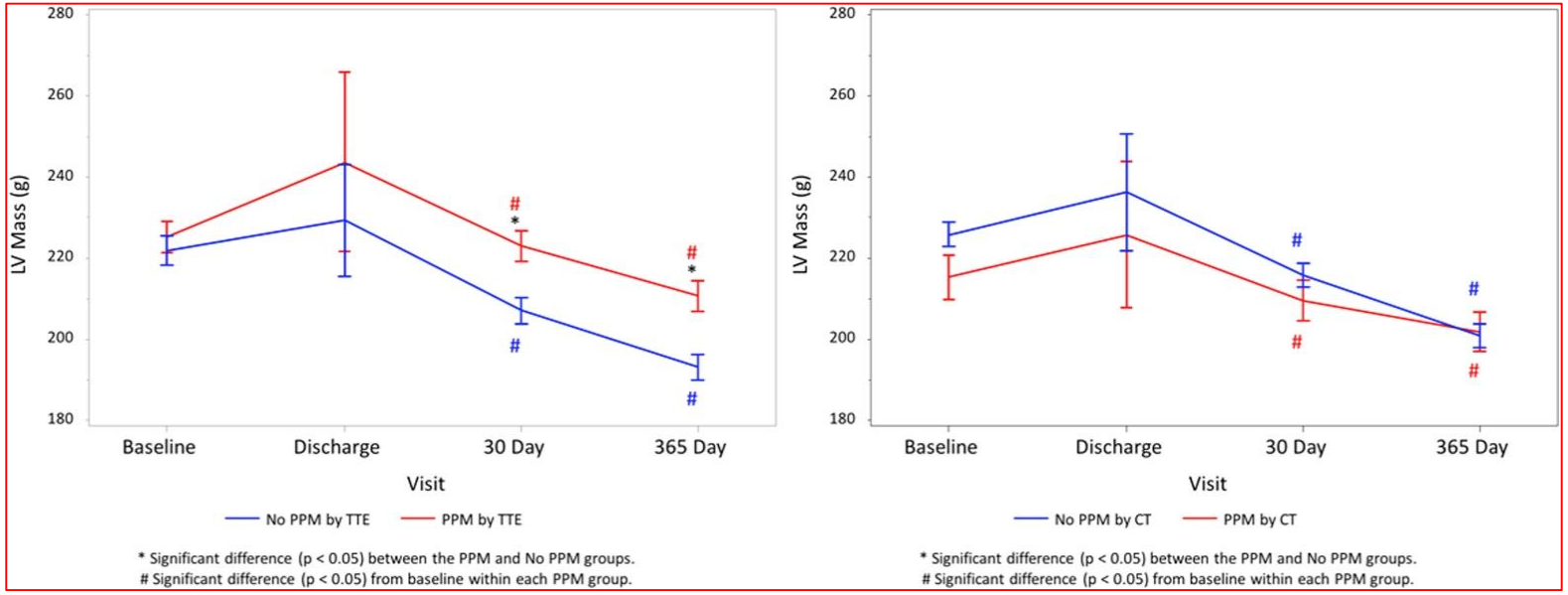


- The incidence of any PPM was 24% with EOA_{CT} compared with 45% with $EOAi_{TTE}$.
- Only 6% of PPM was graded severe by $EOAi_{CT}$ compared with 9% by $EOAi_{TTE}$.

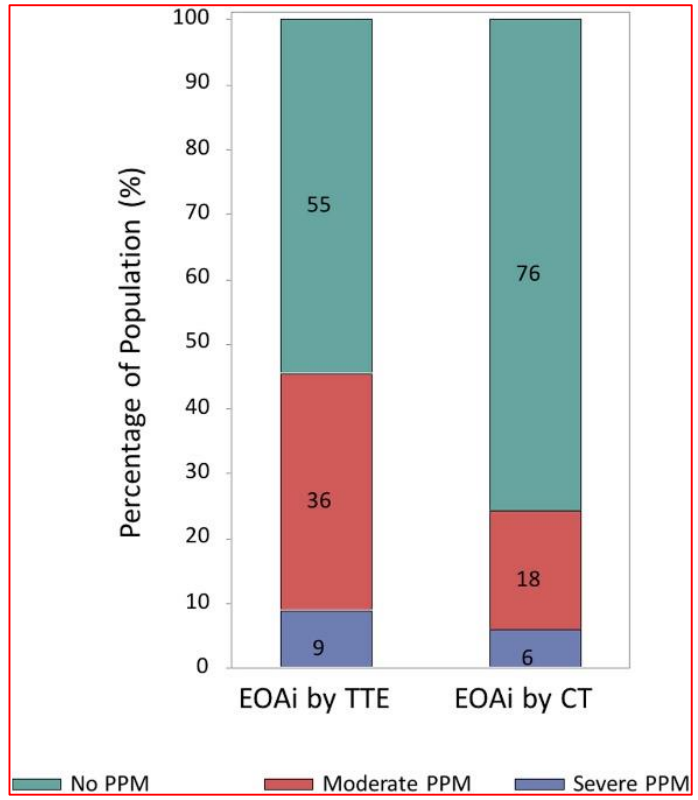
Mooney Jet al *JACC Cardiovasc Interv*. 2017;10(15):1578-1587.

Intermediate Risk PARTNER: PPM Incidence and Impact

- The incidence of PPM was 24% with EOA_{CT} compared with 45% with $EOAi_{TTE}$. Only 6% of PPM was graded severe by $EOAi_{CT}$ compared with 9% by $EOAi_{TTE}$.



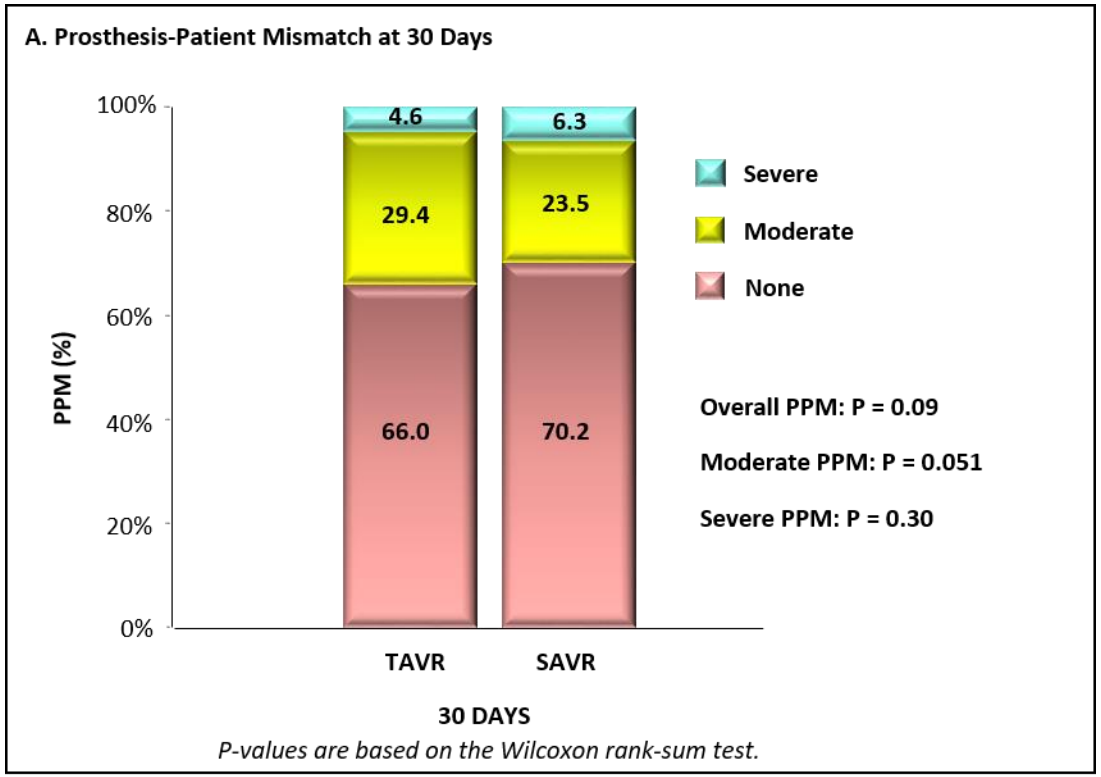
There was no association between PPM and death or rehospitalization at 1 year with either modality.

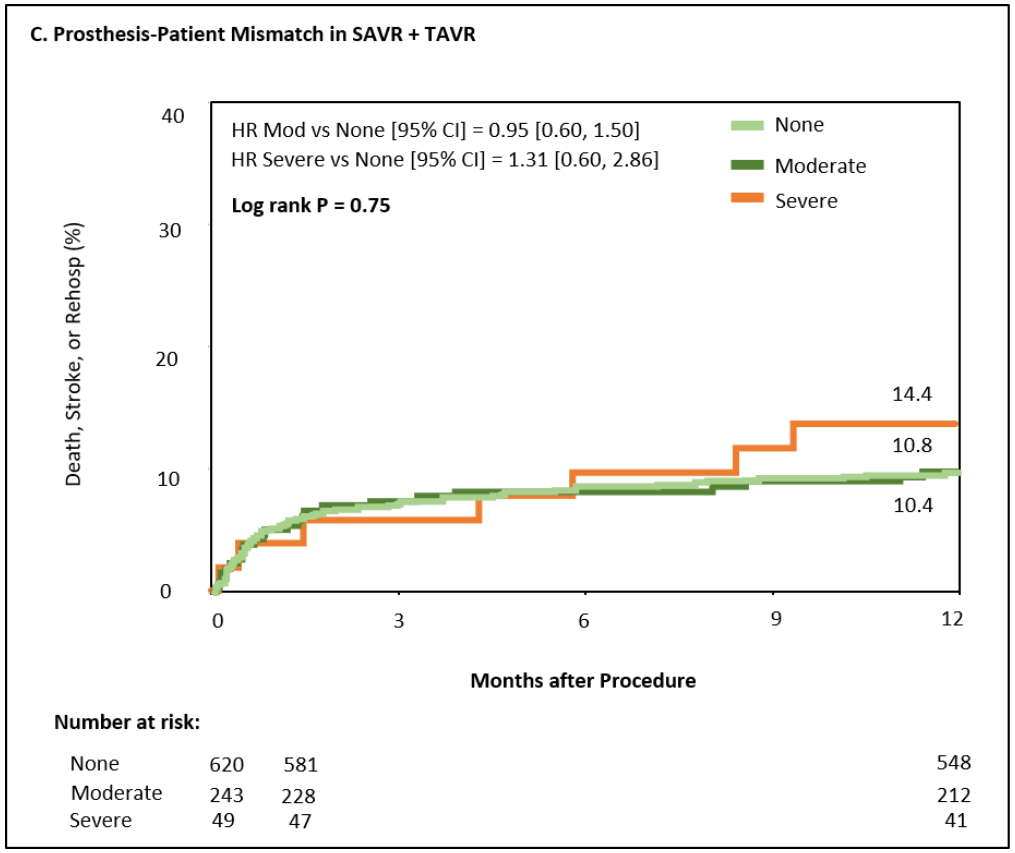


$EOAi_{TTE}$, but not $EOAi_{CT}$, defined PPM showed association with reduced left ventricular mass regression (p = 0.03 vs. p = 0.52).

Mooney Jet al *JACC Cardiovasc Interv*. 2017;10(15):1578-15

PARTNER Low Risk: PPM and Outcomes





- **Lack of association between severe PPM or high residual gradient at 30 days and 1-year outcomes**

Pibarot P et al. Circulation. 2020;141:1527–1537

CRT-600.06

Clinical Outcomes and Valve Hemodynamics Following Transcatheter and Surgical Aortic Valve Replacement

Nicolas Van Mieghem,[1] Jeffrey Popma,[2] Lars Søndergaard,[3] Jae Oh,[4] Yanping Chang,[5] Michael Reardon[6]
[1]Erasmus Medical Center, Rotterdam, Netherlands; [2]Beth Israel Deaconess Medical Center, Boston, MA; [3]The Heart Center, Rigshospitalet University of Copenhagen, Copenhagen, Denmark; [4]Mayo Clinic, Rochester, MN; [5]Medtronic, Minneapolis, MN; [6]Houston Methodist DeBakey Heart and Vascular Institute, Houston, TX

BACKGROUND Transcatheter aortic valve replacement (TAVR) is now approved for treatment of severe, symptomatic aortic stenosis across

One explanation for association of an "normal" DVI with Mortality is a systematic overestimation of DVI!!

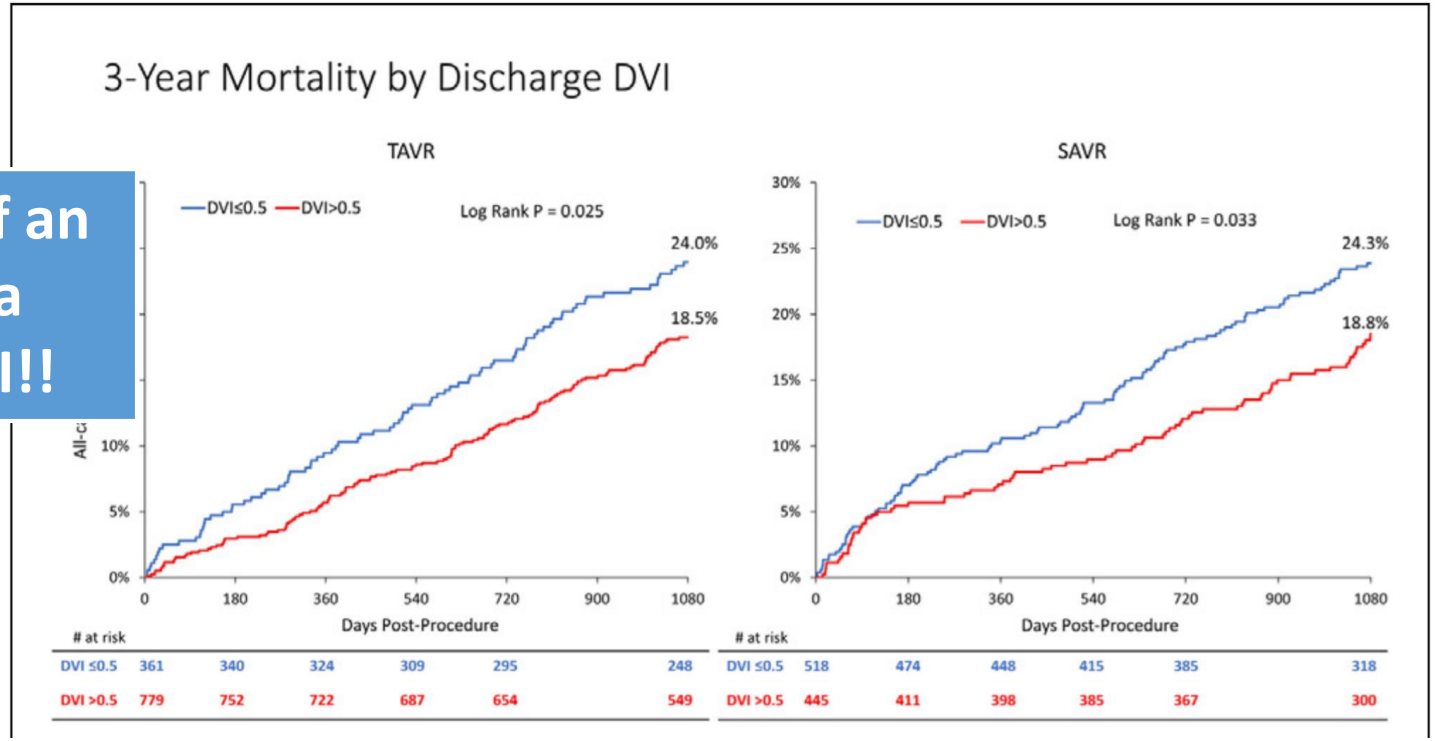
(n=1140) or surgical valve (n=963) were pooled. Echocardiographies were adjudicated by an independent core lab. A restricted cubic spline technique was used to examine the relationship between discharge DVI and mortality. Patients were stratified by treatment modality (SAVR or TAVR) and discharge DVI of ≤0.5 and >0.5. Kaplan-Meier estimates of 3-year all-cause mortality and mortality or rehospitalization were compared between low vs high DVI within each treatment group.

RESULTS DVI <0.5 was present in 32% of TAVR and 54% of SAVR patients. At baseline there were more females than males with DVI >0.5 in the TAVR group but not the SAVR group. Discharge DVI ≤0.5 was associated with higher 3-year mortality after TAVR (24.0% vs. 18.5%, p=0.025) and SAVR (24.3% vs. 18.8%, p=0.033) (Figure). Discharge DVI <0.5 was also associated with 3-year mortality or rehospitalization for TAVR (37.1% vs. 29.6%, p=0.007), but this association was not significant in the SAVR group (33.1% vs. 28.1%, p=0.087).

CONCLUSION Improved forward-flow hemodynamics as measured by discharge DVI >0.5 are associated with a significant clinical benefit to patients with severe aortic stenosis undergoing aortic valve replacement and is more frequent after TAVR.

JACC: CARDIOVASCULAR INTERVENTIONS, VOL. 13, NO. 4, SUPPL S, 2020

DVI > 0.5 predicted MORTALITY in BOTH SAVR and TAVR (self-expanding valve)



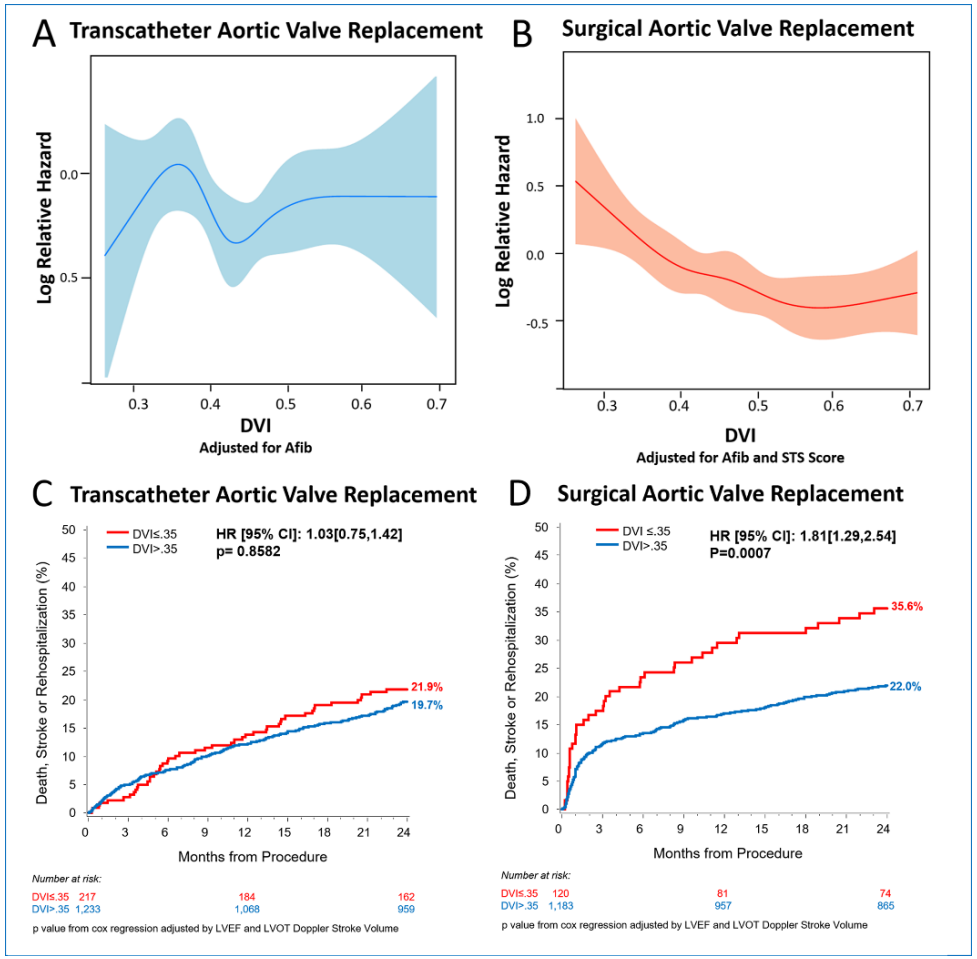
Van Mieghem N, Popma J, Søndergaard L, Oh J, Chang Y, Reardon M. CRT-600.06 Clinical Outcomes and Valve Hemodynamics Following Transcatheter and Surgical Aortic Valve Replacement. JACC Int 2020;13:S48.

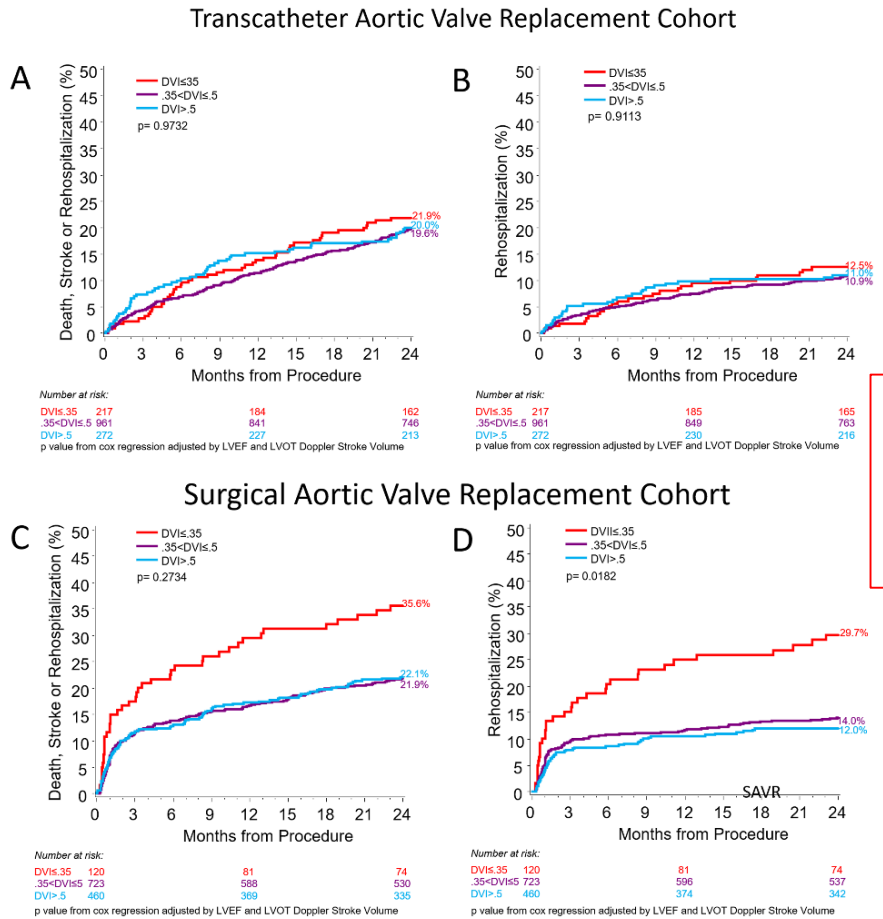
Doppler Parameters of Prosthetic Aortic Valve Function in Mechanical and Stented Biological Valves*

	Normal	Possible Stenosis	Suggests Significant Stenosis
Peak velocity$^{\psi}$	< 3 m/s	3-4 m/s	> 4 m/s
Mean gradient$^{\psi}$	< 20 mmHg	20-35 mmHg	>35 mmHg
Doppler velocity index	≥ 0.30	0.29- 0.25	< 0.25
Effective orifice area	> 1.2 cm^2	1.2- 0.8 cm^2	< 0.8 cm^2
Contour of the jet velocity through the PrAV	Triangular, Early peaking	Triangular to Intermediate	Rounded, symmetrical contour
Acceleration time	< 80 ms	80-100 ms	> 100 ms

* In conditions of normal or near normal stroke volume (50-70 ml) through the aortic valve.
ψ These parameters are more affected by flow, including concomitant aortic regurgitation.

PARTNER Intermediate and Low Risk: Doppler Velocity Index and Outcomes



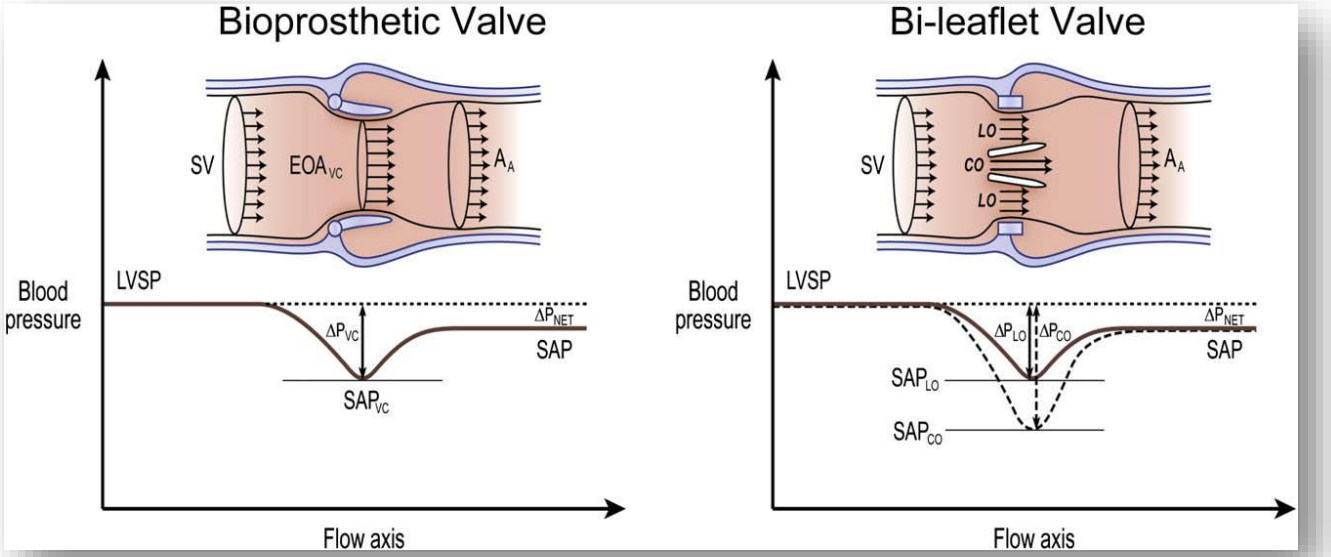


DVI_{LOW} ≤0.35
$DVI_{INTERMED}$ >0.35, ≤0.5
DVI_{HIGH} >0.50

Hahn RT et al. Sumbitted for publication JACC Interventions

@hahn_rt

Why might PPM or DVI in the SAPIEN Valve not predict outcomes?



Pressure Recovery

- Most of the kinetic energy is dissipated in heat as a result of turbulence—this results in less pressure recovery
- With small aortas there is more pressure recovery

•Pressure Recover: velocities are lower and systolic arterial pressure (SAP) is higher at the distal aorta than at the level of the vena contracta(VC)

•Doppler gradients are estimated from maximal velocity at the level of the vena contracta and represent the maximal pressure drop.

•Invasive estimation of gradients usually reflect net pressure difference (DP) between LV systolic pressure (LVSP) and ascending aorta.

Annals of Biomedical Engineering, Vol. 48, No. 2, February 2020 *(© 2019)* pp. 860–867
https://doi.org/10.1007/s10439-019-02425-8

BMES BIOMEDICAL ENGINEERING SOCIETY

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Original Article

Differences in Pressure Recovery Between Balloon Expandable and Self-expandable Transcatheter Aortic Valves

HODA HATOUM,[1] REBECCA T. HAHN,[2] SCOTT LILLY,[3] and LAKSHMI PRASAD DASI[1]

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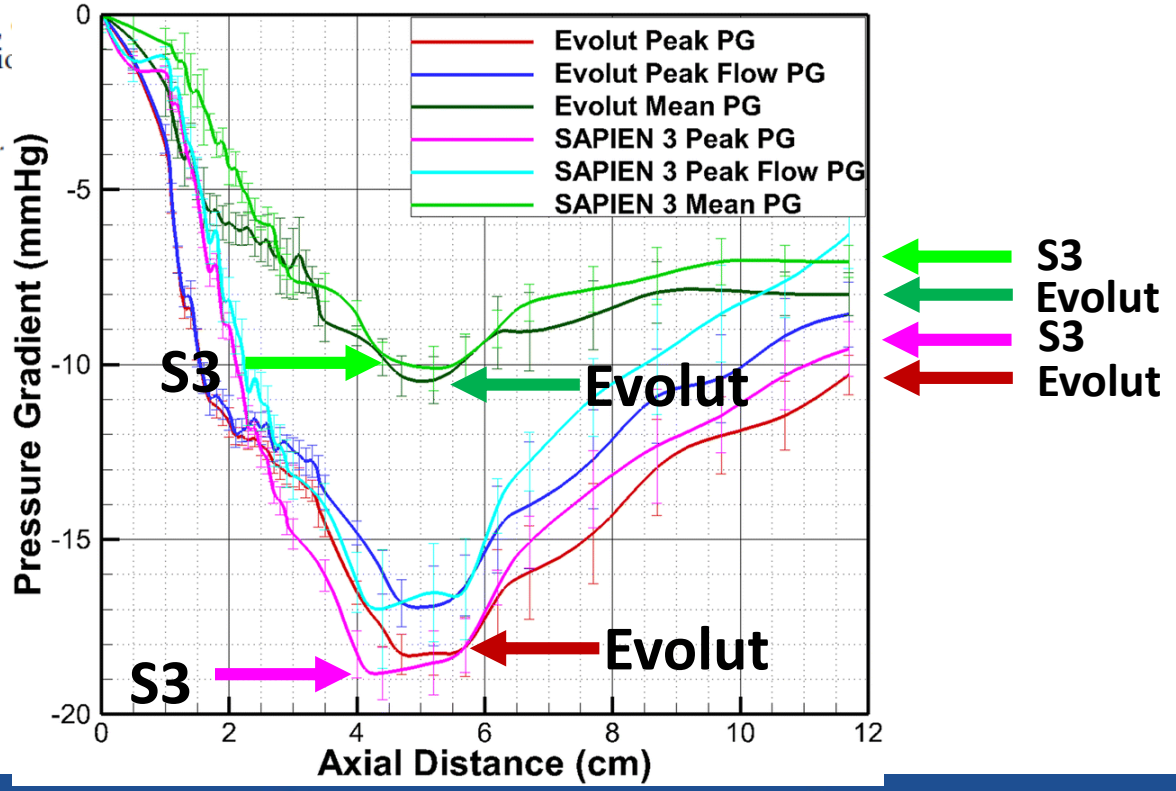
(Received 14 July 2019; accepted 24 November 2019; published online 2 December

Associate Editor Joel Stitzel oversaw the review of this article.

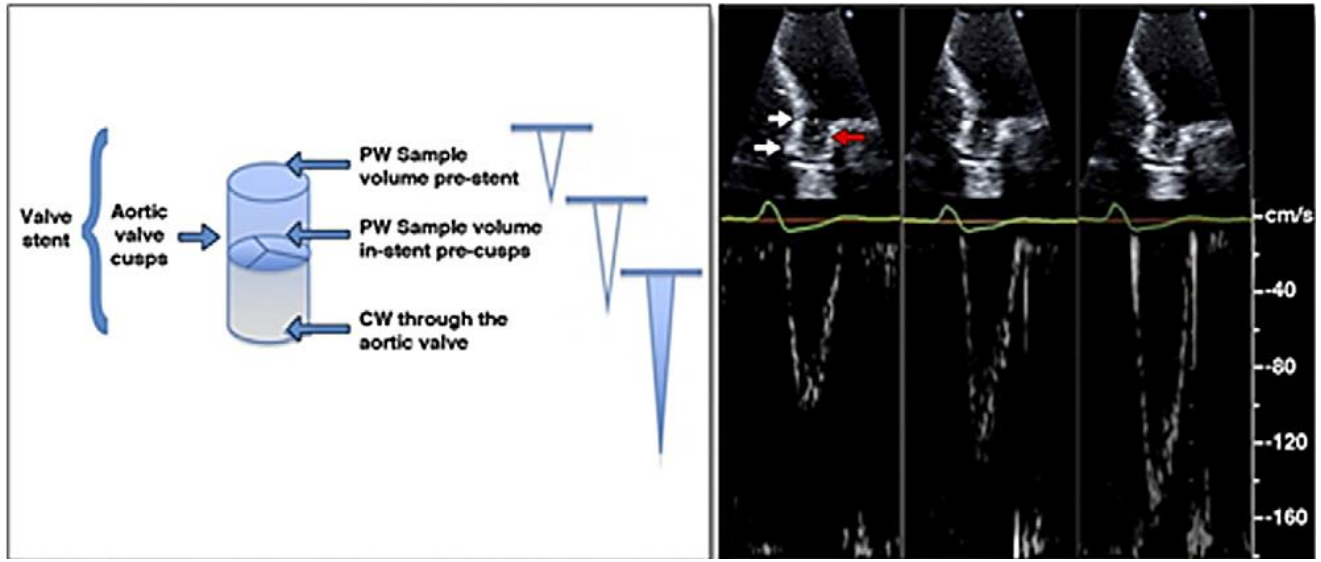
SAPIEN 3 and Evolut valves were implanted in a pulse duplicator designed to mimic the LVOT/aortic root and ascending aorta. A Millar catheter was used to record 50 cycles of pressure data along the centerline of the valve chamber upstream and downstream of the valve



Why might PPM in the SAPIEN Valve not predict outcomes?

Flow acceleration within the stent

1. SAPIEN® TAVR (Edwards Lifesciences) has a unique hemodynamic profile characterized by in-stent flow acceleration.
2. This in-stent, pre-cusp flow acceleration is not accounted for with traditional methods of assessing prosthetic valve function.

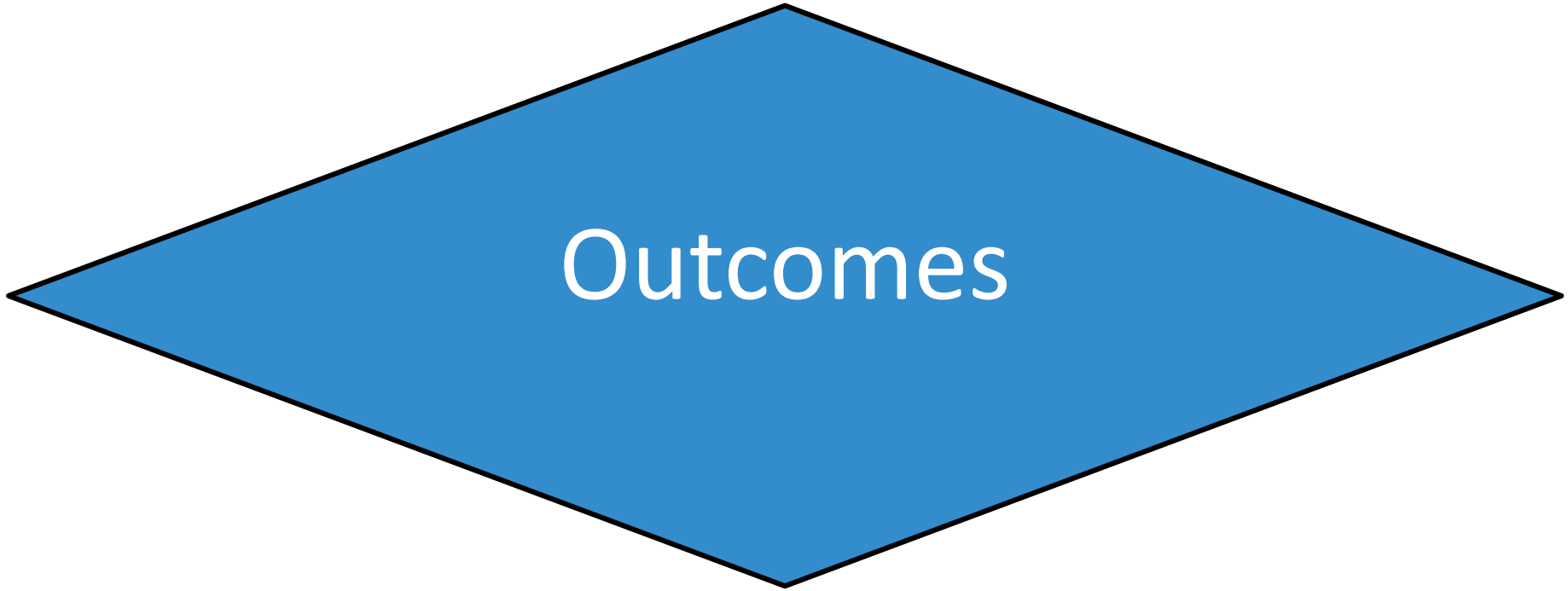


Peak velocity across the SAPIEN valve represents the SUM of the pre-valve acceleration and the flow across the valve leaflets.

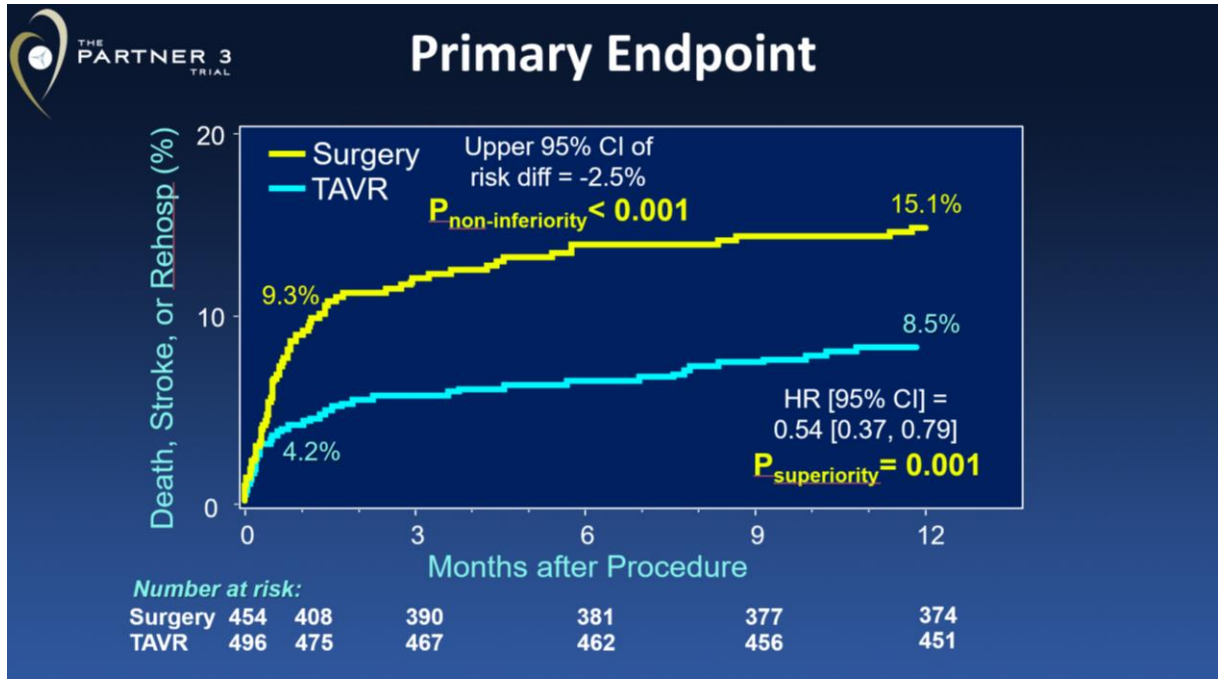
Gradients may be systematically overestimated and thus EOA may be underestimated.

Explanations for Discordant results

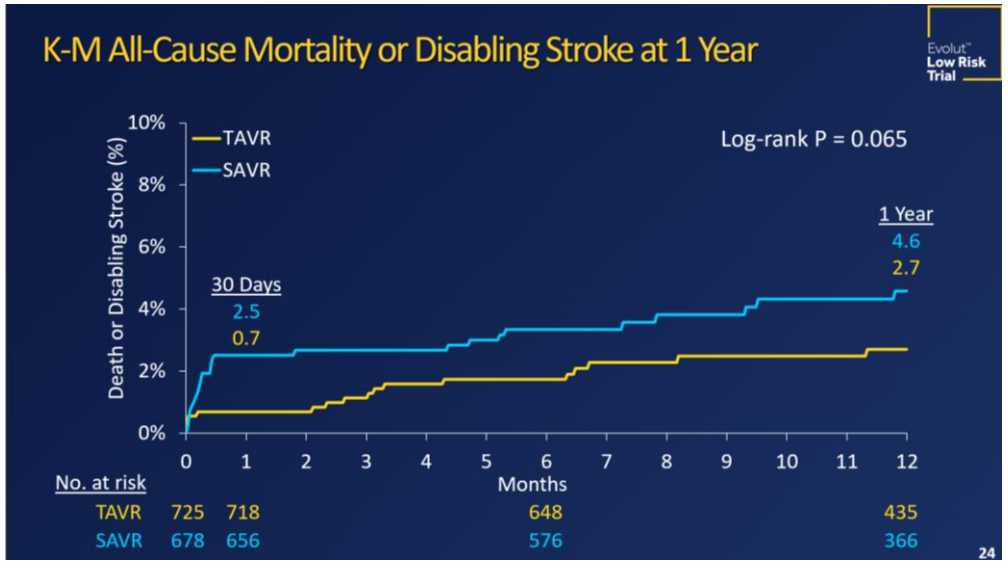
1. **Intrinsic difference between Self-expanding valve and Balloon-expandable valve with BE valve "efficiency" (pressure recovery) much greater**
   - **Intrinsic differences seem likely because both SAVR and Self-expanding valve outcomes are DVI dependent whereas in the PARTNER study only SAVR DVI predictive**
2. **Measurement Inaccuracies**
   - **DVI and EOA for the Core Valve trials has been consistently OVERESTIMATED (by perhaps >30%) thus both the surgical and transcatheter valve results are overestimated**
     - **This is supported by the trials reporting very similar gradients and +0.2 cm^2 larger EOA for both SAVR and TAVR in the Core Valve trials. Given the similar baseline characteristics of the patients (age, BSA, distribution of men vs. men) measurement error seems likely.**
   - **DVI and EOA for the SAPIEN valve is consistently UNDERESTIMATED**
     - **In-stent DVI and EOA are currently being investigated**

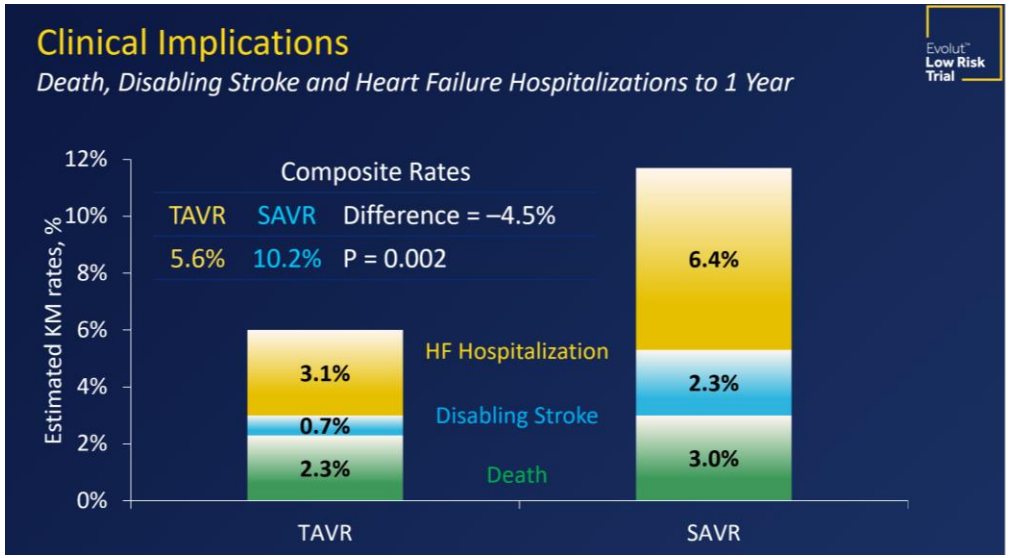

Outcomes

Primary Endpoint



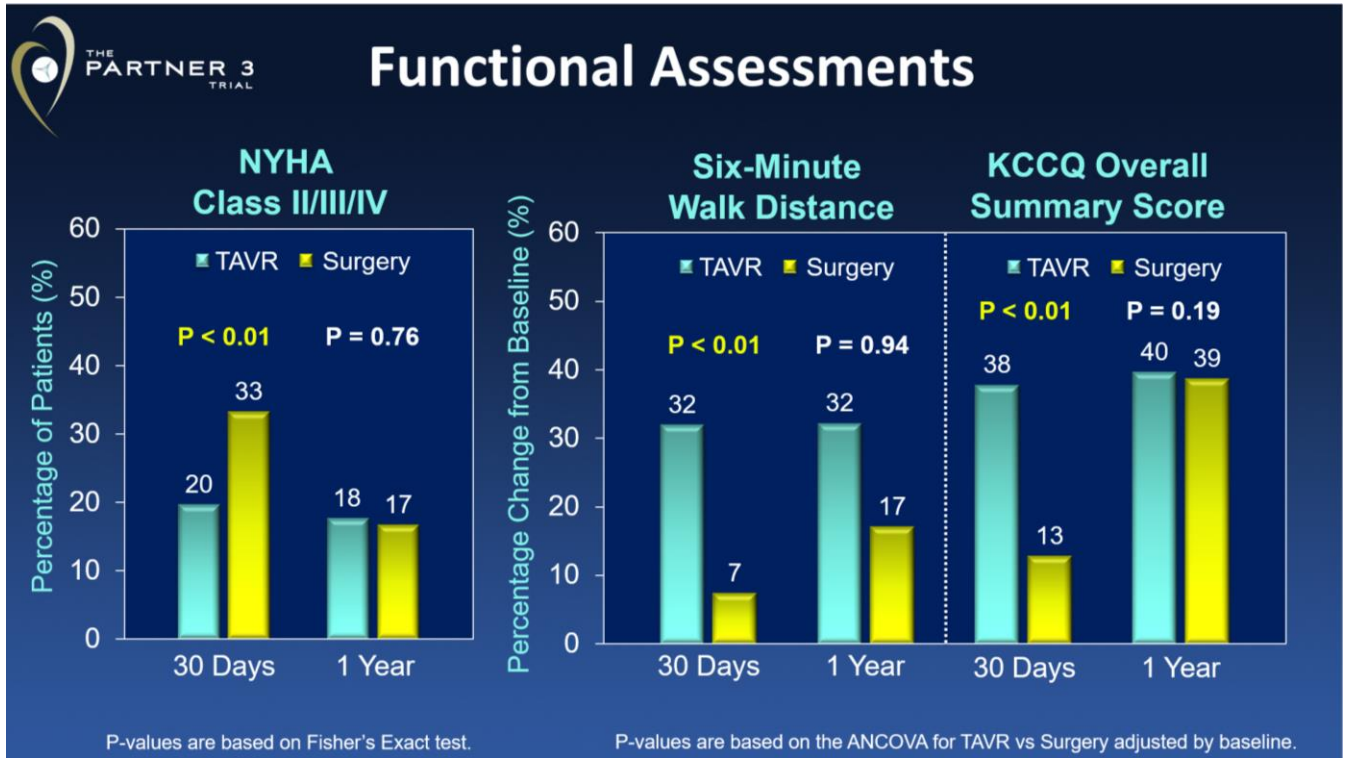
Mack MJ, Leon MB, Thourani VH, et al. Transcatheter Aortic-Valve Replacement with a Balloon-Expandable Valve in Low-Risk Patients. March 16, 2019,DOI: 10.1056/NEJMoa1814052





Popma JJ, Deeb GM, Yakubov SJ, et al. Transcatheter Aortic-Valve Replacement with a Self-Expanding Valve in Low-Risk Patients. March 16, 2019 DOI: 10.1056/NEJMoa1816885

Functional Improvement



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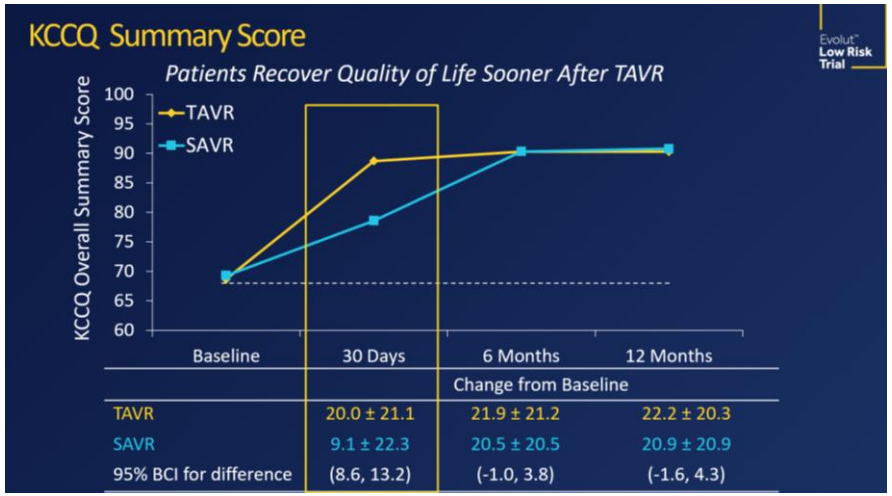


Popma JJ, Deeb GM, Yakubov SJ, et al. Transcatheter Aortic-Valve Replacement with a Self-Expanding Valve in Low-Risk Patients. March 16, 2019 DOI: 10.1056/NEJMoa1816885

Circulation

ORIGINAL RESEARCH ARTICLE

Balloon-Expandable Versus Self-Expanding Transcatheter Aortic Valve Replacement

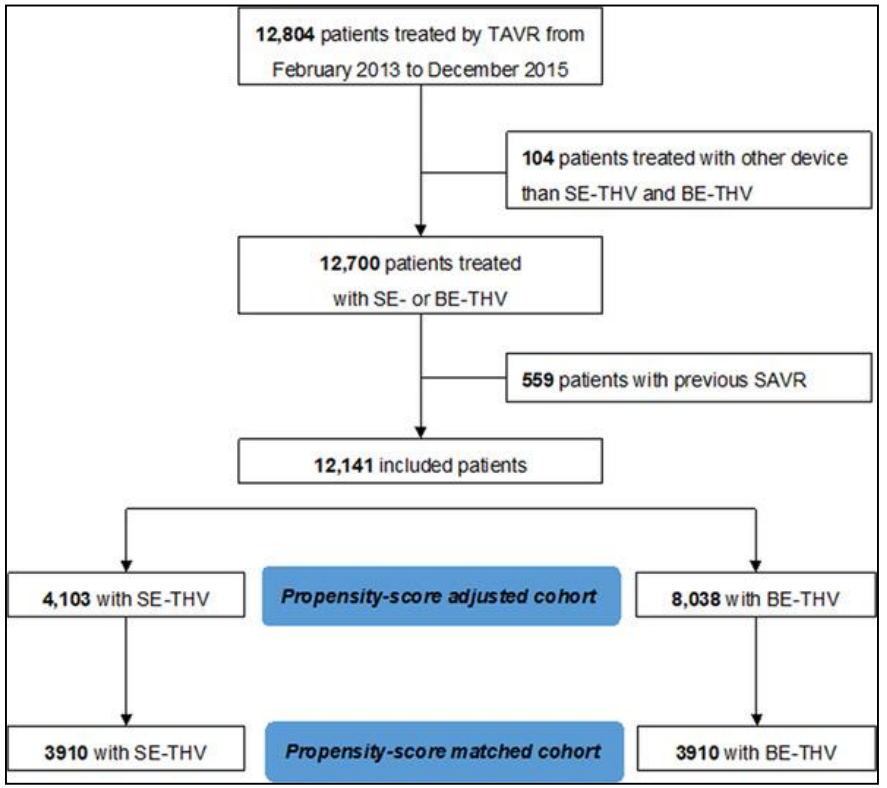
A Propensity-Matched Comparison From the FRANCE-TAVI Registry

Editorial, see p 269

Eric Van Belle, MD*
Flavien Vincent, MD*
Julien Labreuche, BST*
et al

BACKGROUND: No randomized study powered to compare balloon-expandable (BE) with selfexpanding (SE) transcatheter heart valves (THVs) on individual end points after transcatheter aortic valve replacement has been conducted to date.

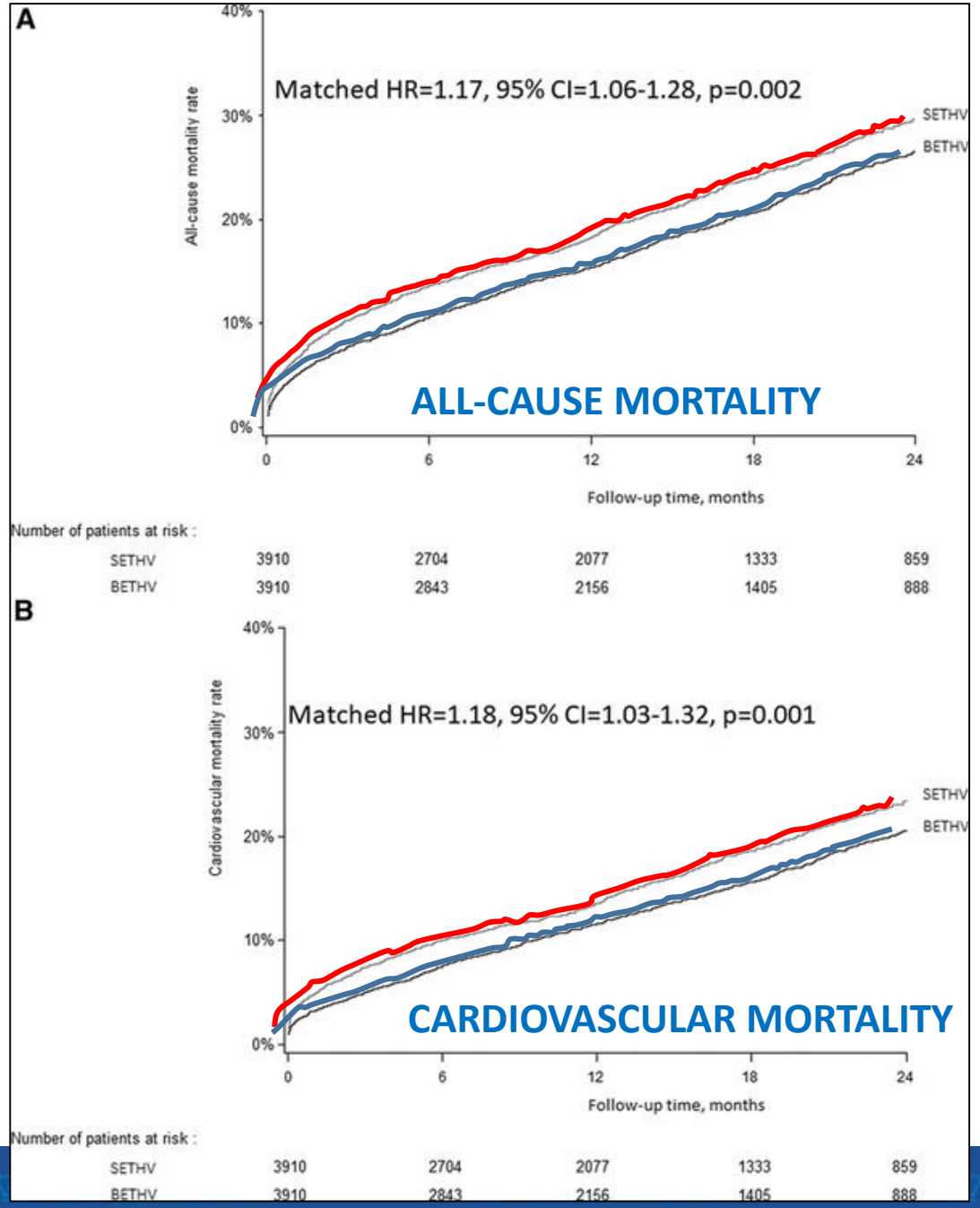
- 12 141 patients undergoing BE-THV (Edwards, n=8038) or SE-THV (Medtronic, n=4103) for treatment of native aortic stenosis
- 3910 patients matched 1:1 by using propensity score (25 clinical, anatomical, and procedural variables)



➢ **The first co-primary outcome was ≥ moderate PVR or in-hospital mortality, or both.**

➢ **The second co-primary outcome was 2-year all-cause mortality.**

FRANCE-TAVI



- In the propensity score– matched analyses, the incidence of the first co-primary outcome:
  - Higher with SE-THV (19.8%) compared with BE-THV (11.9%; relative risk, 1.68 [95% CI, 1.46–1.91]; *P*<0.0001).
  - Each component of the outcome was also higher in patients receiving SE-THV: ≥ **moderate paravalvular regurgitation** (15.5% versus 8.3%; relative risk, 1.90 [95% CI, 1.63–2.22]; *P*<0.0001) **and in hospital mortality** (5.6% versus 4.2%; relative risk, 1.34 [95% CI, 1.07–1.66]; *P*=0.01).
  - All-cause mortality
    - **Matched hazard ratio for SE-THV = 1.17 (95% CI, 1.06–1.28)**

Van Belle, E et al. Circulation. 2020;141:4

Circulation

ORIGINAL RESEARCH ARTICLE

Impact of Sapien 3 Balloon-Expandable Versus Evolut R Self-Expandable Transcatheter Aortic Valve Implantation in Patients With Aortic Stenosis

Data From a Nationwide Analysis

Editorial, see p 269

BACKGROUND: Two competing transcatheter aortic valve replacement (TAVR) technologies are currently available. Head-to-head comparisons of the relative performances of these 2 devices have been published. However, long-term clinical outcome evaluation remains limited by the number of patients analyzed, in particular, for recent-generation devices.

METHODS: Based on the French administrative hospital-discharge database, the study collected information for all consecutive patients treated with a TAVR device commercialized in France between 2014 and 2018. Propensity score matching was used for the analysis of outcomes during follow-up. The objective of this study was to analyze the outcomes of TAVR according to Sapien 3 balloon-expandable (BE) versus Evolut R

Pierre Deharo, MD, PhD
Arnaud Bisson, MD
Julien Herbert, MD
Thibaud Lacour, MD
Christophe Saint Etienne, MD
Leslie Grammatico-Guillon, MD, PhD
Alizée Porto, MD
Frederic Collart, MD, PhD
Thierry Bourguignon, MD, PhD
Thomas Cuisset, MD, PhD
Laurent Fauchier, MD, PhD

France Nationwide Analysis: Real-world Experience

- Based on the **French administrative hospital-discharge database**, the study collected information for all consecutive patients treated with a TAVR device commercialized in France between 2014 and 2018. Propensity score matching was used for the analysis of outcomes during follow-up.
- A total of 31 113 patients treated with either Sapien 3 BE or Evolut R self-expanding TAVR were found in the database.
- After matching on baseline characteristics, 20 918 patients were analyzed (10 459 in each group with BE or self-expanding valves).

Deharo P et al. Circulation. 2020;141:260–268.

France Nationwide Analysis

Table 3. Clinical Outcomes in the Matched Cohort

Clinical Outcomes	BE TAVR (n=10459)	SE TAVR (n=10459)	RR (95% CI) for BE TAVR vs SE TAVR	*P* (Uncorrected)	*P* (Bonferroni Correction)
All-cause death	1270 (14.4)	1352 (16.4)	0.88 (0.82–0.95)	0.001	0.005
Cardiovascular death	567 (6.4)	652 (7.9)	0.82 (0.73–0.92)	0.0004	0.002
All-cause stroke	429 (5.0)	429 (5.3)	0.94 (0.82–1.08)	0.39	1.0
Rehospitalization for HF	1529 (19.5)	1685 (23.2)	0.84 (0.78–0.90)	<0.0001	<0.0001
Combined end point*	2072 (26.9)	2302 (32.2)	0.84 (0.79–0.89)	<0.0001	<0.0001
Negative control analysis					
Noncardiovascular death	703 (8.0)	700 (8.5)	0.94 (0.85–1.05)	0.28	1.0
Cancer	535 (6.3)	495 (6.2)	1.02 (0.90-1.15)	0.76	1.0
Urinary tract infection	554 (6.5)	544 (6.8)	0.96 (0.85–1.08)	0.46	1.0

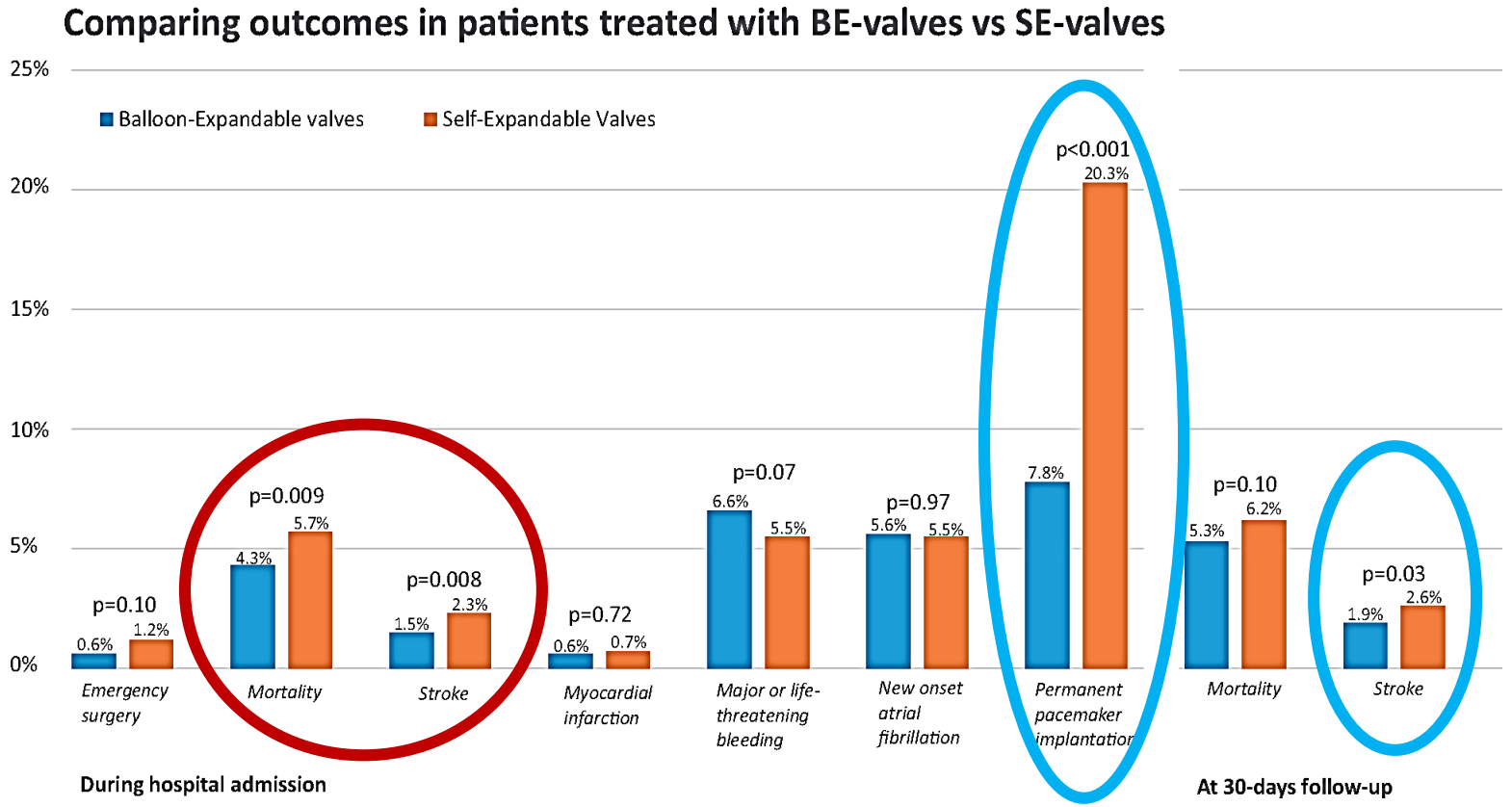
Values are n (incidence rate, %/y). BE indicates balloon-expandable; HF, heart failure; RR, incidence rate ratio; SE, self-expandable; and TAVR, transcatheter aortic valve replacement.

*Cardiovascular death, all-cause stroke, rehospitalization for HF.

- All-cause death was lower with BE TAVR
- Cardiovascular death was lower with BE TAVR
- Rehospitalization for heart failure was lower with BE TAVR
- Combined end point was lower with BE TAVR

CENTER-trial: International collaboration, including patients with severe aortic valve stenosis undergoing transfemoral TAVI

In-hospital mortality was lower among patients treated with a BE-valves compared with SE-valves (BE: 4.3% vs. SE: 5.7%, RR 0.8; 95% CI 0.6–0.9, *P* = 0.009)

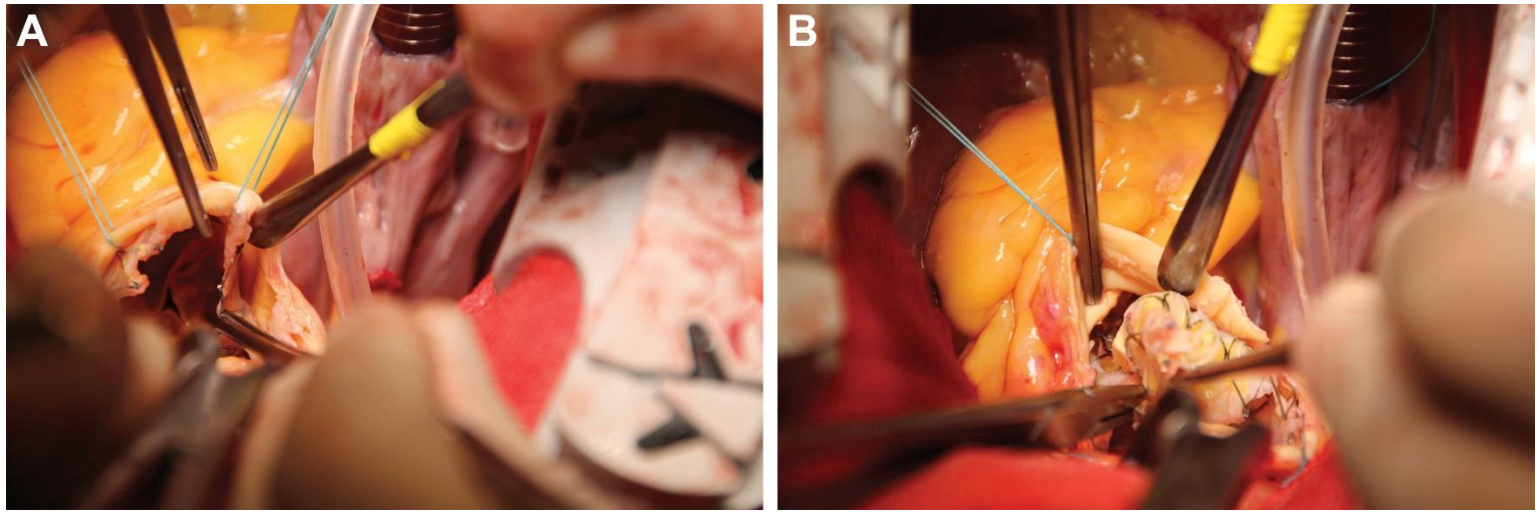


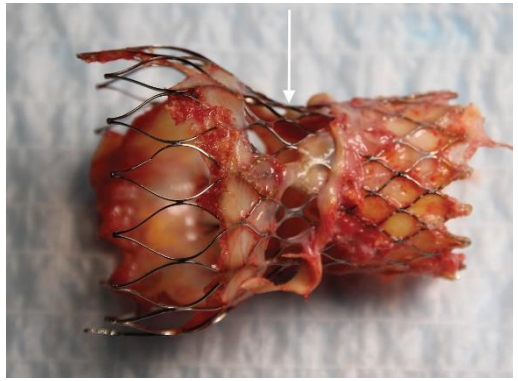
- Data from 10 registries or clinical trials, selected through a systematic search, were pooled and analysed.
- Propensity score methodology was used to reduce treatment selection bias and potential confounding.
- The primary endpoints were mortality and stroke at 30 days follow-up in patients treated with BE-valves compared with SE-valves.
- Overall patient population (N = 12 381) included 6239 patients undergoing TAVI with BE-valves and 6142 patients with SE-valves. The propensity matched population had a mean age of 81 ± 7 years and a median STS-PROM score or 6.5% [interquartile range (IQR) 4.0-13.0%].

Vlastra W et al. Eur Heart J. 2019 Feb 1;40(5):456-465.

Unknowns

- Risk of valve thrombosis
- Risk of Structural Valve Dysfunction
  - Although multiple reports of more difficult surgical removal of the self-expanding valve





Traction of the stent frame of the CoreValve prosthesis allows the endarterectomy with a spatula (shown from different angles).

https://doi.org/10.1016/j.athoracsur.2017.01.058

Valve Choice Considerations

+ = Favors Use
- = Disfavors Use

	Balloon-expandable	Self-expanding
Extensive annular/aortic root calcification	+	+
Excessive Aortic Root Angulation	+	-
Low Coronary Height/Anticipated Need for Coronary re-access	+	-
Risk For Permanent Pacemaker	+	-
Risk for Paravalvular Regurgitation	+	-
Risk for Prosthesis-Patient Mismatch	+	-
Cerebro-embolic Protection Device Not Feasible*	+	±
Treatment of Bicuspid Aortic Valve	+	+
Treatment of Pure Aortic Regurgitation	-	+
Treatment of Degenerated Surgical Bioprosthesis	+	+
All-Cause Mortality	+	±

After Esposito, G, Franzone A. JACC CV Inter; 2020;13(9)1083-1085

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Thank You

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