

The Importance of Hemodynamic Performance in TAVI Technology Selection

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TAVI

A Shift in Focus

Now that TAVI has been proven safe and complications have been greatly mitigated with new generation devices, focus is shifting more towards valve performance

Safety & Outcomes

Mortality

Morbidity

Quality of Life

Focus



Valve Performance & Function

Hemodynamics

Durability

PVL

Hemodynamic Performance

History

The concept of **patient prosthesis mismatch (PPM)** was introduced by Dr. Rahimtoola in the 1970s and has remained an area of focus for surgical aortic valve replacement for decades.

Current Topics

The Problem of Valve Prosthesis-Patient Mismatch

SHAHBUDIN H. RAHIMTOOLA, M.D.

SUMMARY Valve prostheses have played an important part in the past two decades in the management of patients with valvular heart disease. However, many of the devices used in valve replacement have introduced new clinical problems. This paper deals with some of the problems associated with valve replacement, including one not previously emphasized — valve prosthesis-patient mismatch, which may cause obstruction to ventricular outflow and/or inflow.

clinical medicine, so that in effect, the patient is exchanging one disease process for another. Many com-

broadened.³⁷ Mismatch can be considered to be present when the effective prosthetic valve area, after insertion into the patient, is less than that of a normal human valve. The reduced prosthetic valve area is

CIRCULATION

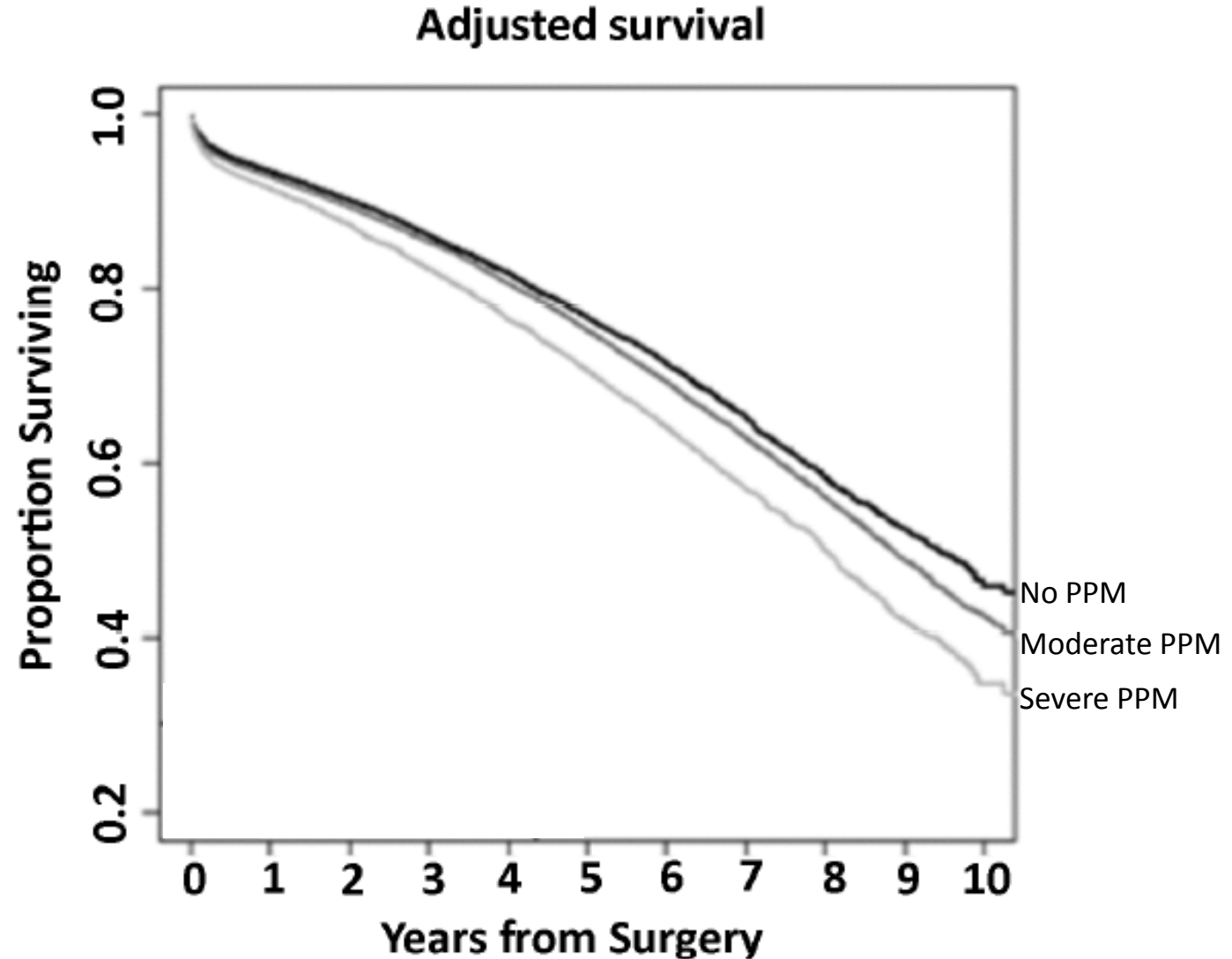
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Hemodynamic Performance

Clinical Impact | SAVR

A recent study from the multi-institutional Society of Thoracic Surgeons evaluated nearly 60,000 patients undergoing SAVR in the United States and showed

- Patients with moderate or severe PPM had increased risk of readmission for heart failure and redo AVR
- Survival was significantly worse for any degree of PPM



Hemodynamic Performance

History | TAVI

With the advent of TAVI, the importance of hemodynamic performance was not forgotten. Early trials comparing TAVI and SAVR included hemodynamic performance as a critical measure of TAVI valve effectiveness.

PARTNER US IDE Study Protocol

6.2 Echocardiography

The pre-procedure transthoracic or transesophageal echocardiograms (TTE or TEE) will be performed to assess risk factors and eligibility. Post procedure TTE will be performed at the intervals specified in Table 6. If post procedure TTE is not adequate, TEE will also be performed. All echocardiograms will be independently analyzed by the Echocardiographic Core Lab (see Appendix D). The aortic valve effective orifice area (EOA) that will be used to assess the AVA effectiveness endpoint will be the aortic valve EOA after valvuloplasty, after final valve deployment, and at follow-up time-points calculated from echocardiographic data using the continuity equation, and the AVA calculated from cardiac catheterization data using the Gorlin formula will be used only to calculate an estimated AVA at baseline, after valvuloplasty and after final valve deployment at the time of the study valve implant.

Hemodynamic Performance

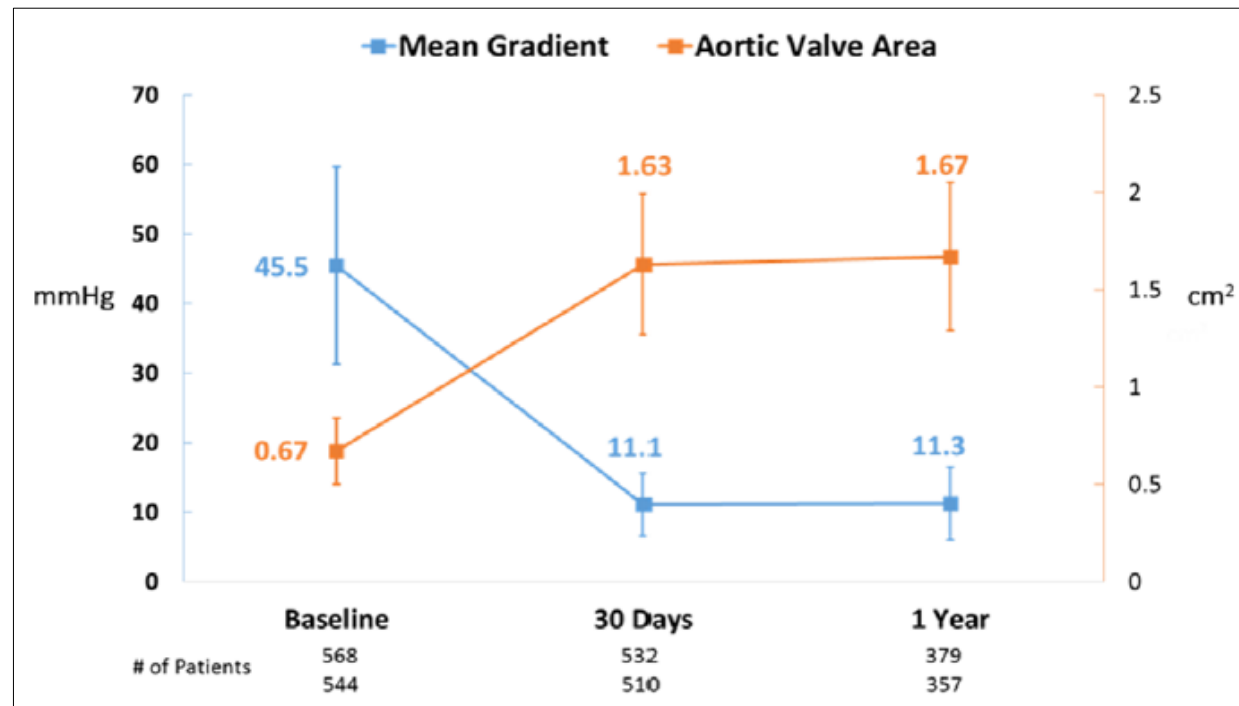
Outcomes | TAVI vs SAVR

TAVI trials have consistently shown hemodynamic outcomes are as good or better than SAVR.

Evolut R/CoreValve SURTAVI



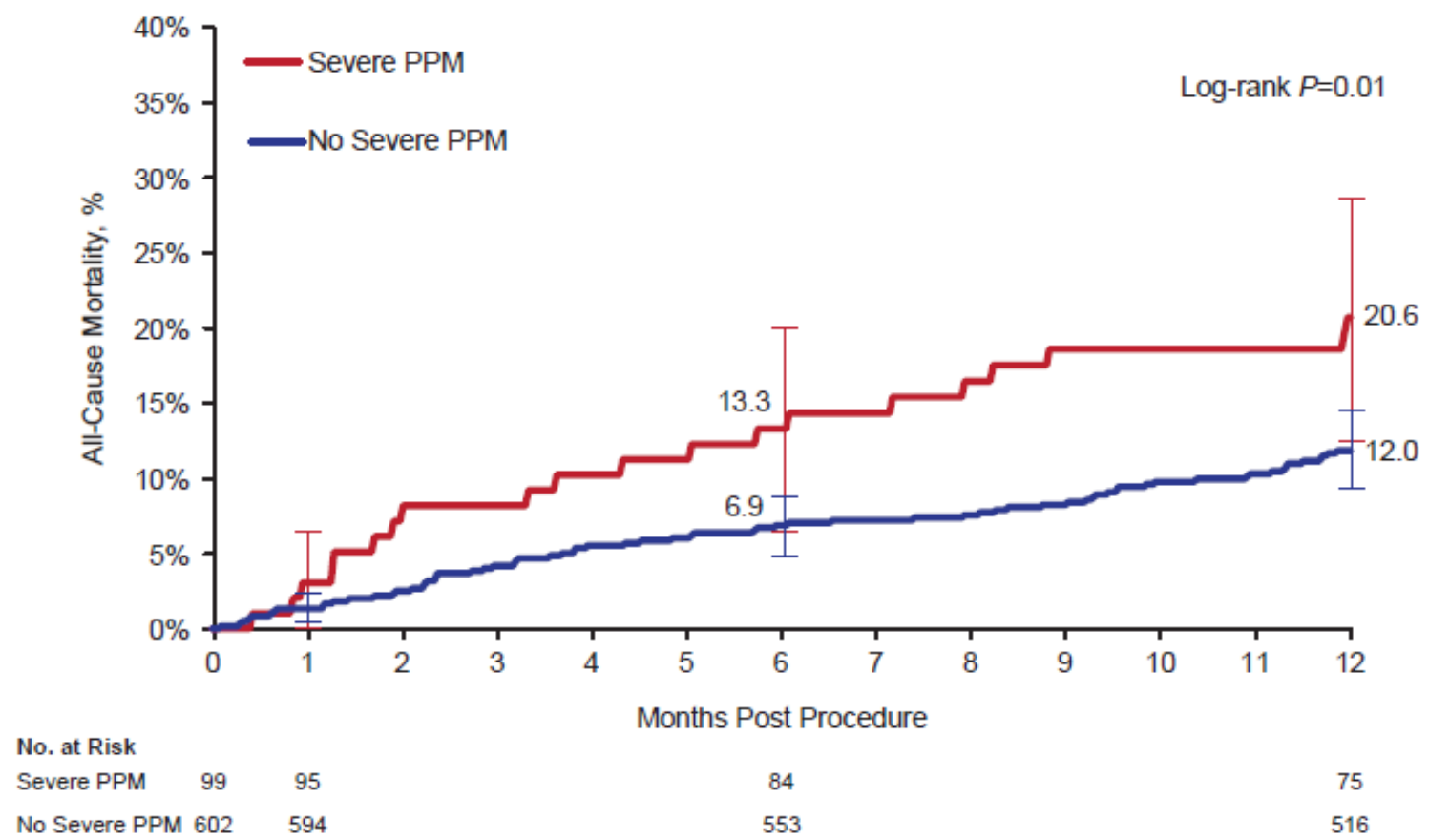
SAPIEN 3 PARTNER S3I



Hemodynamic Performance

Clinical Impact | TAVI

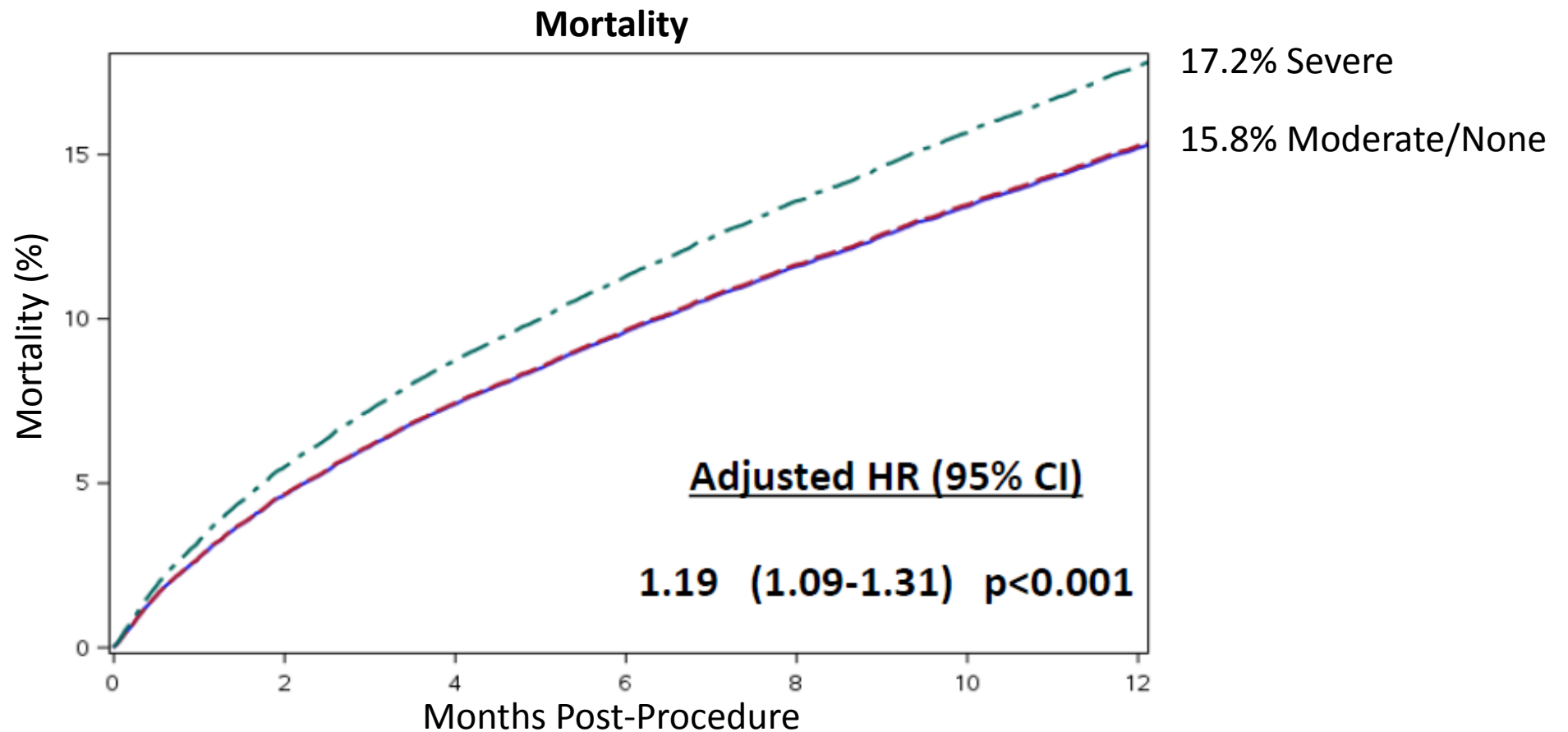
The CoreValve High-Risk trial was one of the first TAVI studies to demonstrate severe PPM had an impact on early mortality. Results showed significantly higher 1-year mortality rates when combining TAVI and SAVR patients with severe PPM.



Hemodynamic Performance

Clinical Impact | TAVI

Recent data from the STS/ACC TVT registry analyzed the impact of PPM in over 62,000 TAVI patients in the United States. Severe PPM was associated with increased mortality and heart failure rehospitalization at 1-year.



Hemodynamic Performance

Clinical Impact | TAV-in-SAV (Valve-in-Valve)

Elevated gradients have also been associated with increased mortality in TAV-in-SAV patients.

- A recent multicenter study demonstrated a near-significant increase in mortality risk with only 1 mm Hg increase in mean discharge gradient.
- Identifying patients at risk for PPM and selecting technology that will achieve optimal hemodynamics in these populations is critical.

Univariable Model for Factors Associated with Late Mortality

| | Univariable Model | |
|---|-----------------------|---------|
| | Hazard Ratio (95% CI) | P Value |
| Age, y | 1.05* (1.02–1.08) | 0.002 |
| eGFR <60 mL/min per 1.73 m ² | 2.58 (1.52–4.39) | <0.001 |
| LVEF <50% | 3.19 (1.86–5.47) | <0.001 |
| Stented surgical valve | 0.67 (0.25–1.77) | 0.417 |
| Surgical valve size | 1.02 (0.88–1.17) | 0.833 |
| Nontransfemoral approach | 2.12 (1.24–3.61) | 0.006 |
| Balloon-expandable valve | 3.11 (1.17–8.30) | 0.023 |
| Transcatheter valve size | 0.80 (0.60–1.07) | 0.136 |
| Mean gradient at discharge | 1.02† (0.99–1.05) | 0.089 |
| Severe PPM | 1.74 (0.48–6.26) | 0.396 |

eGFR indicates estimated glomerular filtration rate; LVEF, left ventricular ejection fraction; and PPM, patient-prosthesis mismatch.

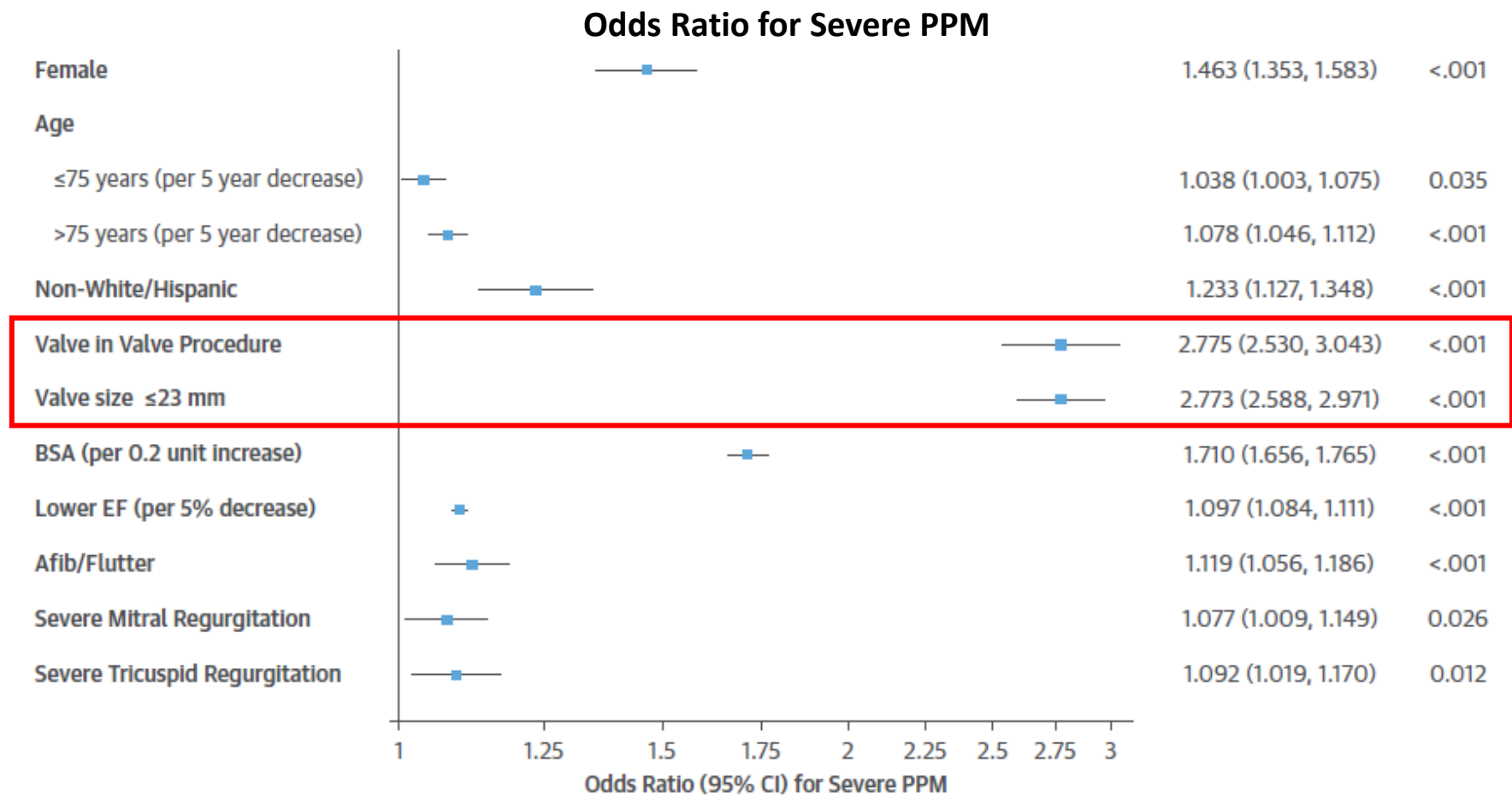
*For each increase of 1 y.

†For each increase of 1 mm Hg.

Challenging Patients

Small Annuli and TAV-in-SAV

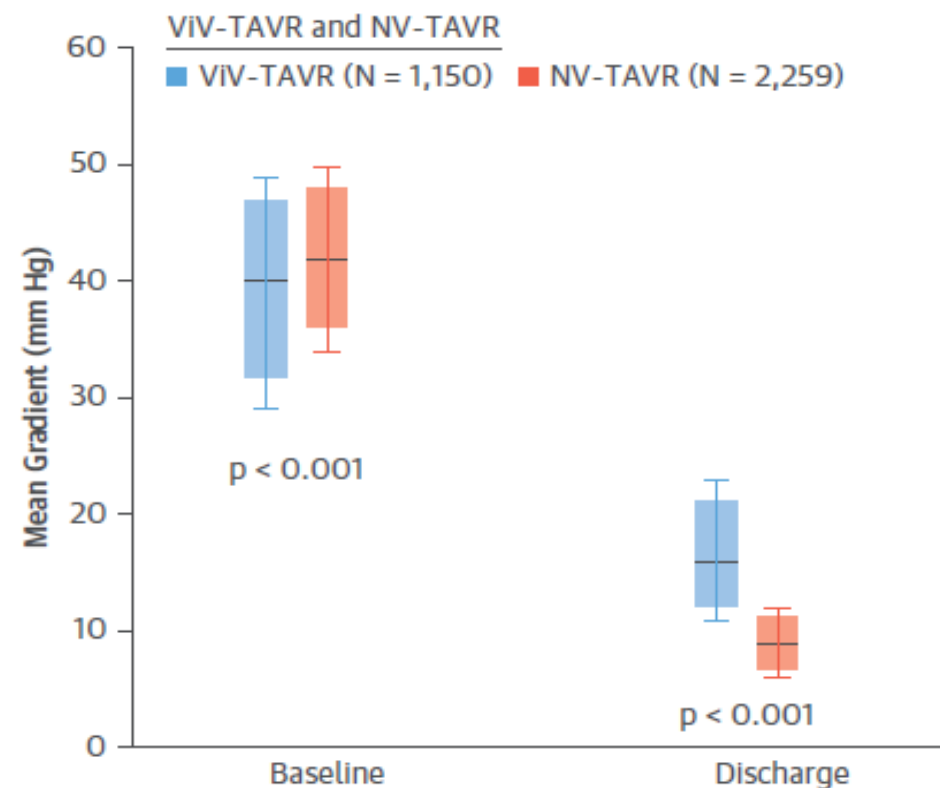
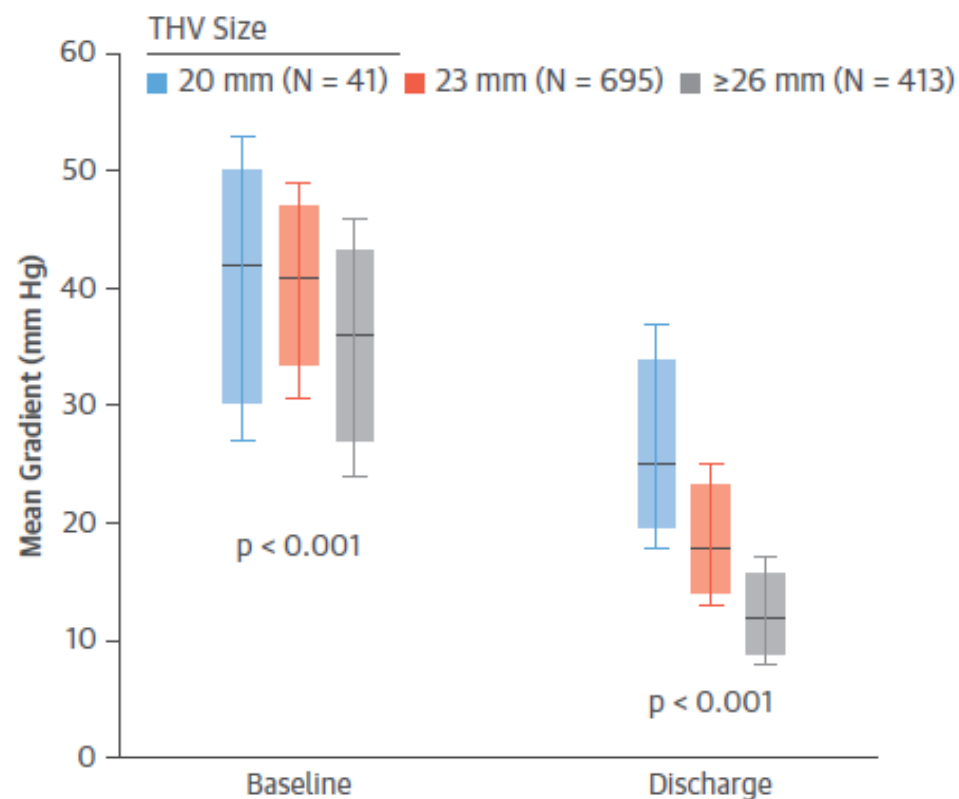
With the clinical impact of hemodynamic performance in mind, extensive research was initiated. While overall hemodynamic performance was as good or better with TAVI than SAVR, it quickly became apparent that achieving optimal hemodynamics may be challenging in patients with small aortic annuli and those undergoing TAV-in-SAV procedures.



Challenging Patients

Small Annuli and TAV-in-SAV

Data from the TVT registry showed that in addition to a greater risk of PPM, patients with small annuli and TAV-in-SAV procedures had elevated gradients at discharge compared to patients undergoing TAVI in native aortic valves.



Technology Selection

Contemporary Devices

With many TAVI devices on the market, or undergoing clinical trials, proper device selection is critical in achieving optimal hemodynamic performance.

Supra-Annular



Evolut R



Evolut PRO



SAPIEN 3



Lotus



CENTERA



Portico



ACURATE neo

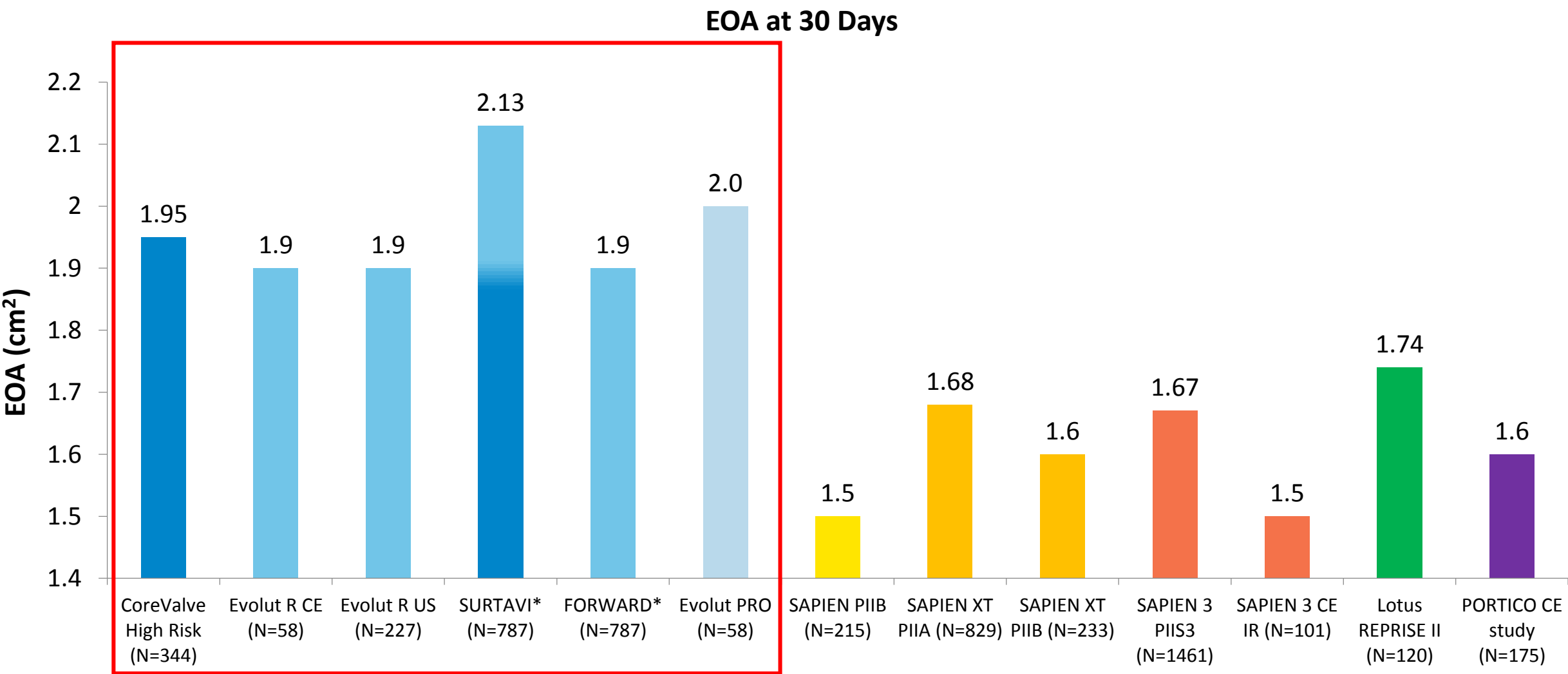
Intra-Annular

Supra-Annular

Technology Selection

Small Annuli | Supra-Annular vs Intra-Annular TAVI

Data from clinical trials show the largest EOAs have been achieved with supra-annular valves.



¹Adams, et al., *N Engl J Med* 2014; 370: 1790-8; ²Manoharan, et al., *J Am Coll Cardiol Interv* 2015; 8: 1359-67; ³Williams, et al., presented at ACC 2016; ⁴Van Mieghem et al. Presented at TCT 2017; ⁵Grube et al., presented at EuroPCR 2018; ⁶Forrest et al., *JACC: Cardiovascular Interventions* Jan 2018, 11 (2) 160-168; ⁷Meredith, et al., presented at PCR London Valves 2014; ⁸Leon, et al., *N Engl J Med* 2016 Apr 2; ⁹Kodali, et al., *Eur Heart J* 2016; doi:10. 1093/eurheartj/ehw112; ¹⁰Webb, et al., *J Am Coll Cardiol Interv* 2015; 8: 1797-806; ¹¹Manoharan, et al., et al. presented at TCT 2014; ¹²Vahanian, et al. presented at EuroPCR 2015; ¹³Webb, et al., *J Am Coll Cardiol Interv* 2015; 8: 1797-806

Technology Selection

Small Annuli | Supra-Annular vs Intra-Annular TAVI

A recent study characterized expected TAVI EOAs and hemodynamic performance for 3 generations of balloon- and self-expandable valves to facilitate pre-implantation decision making.

- The study focused on patient specific anatomy, analyzing valve performance by aortic annuli size. In the smallest valve sizes, supra-annular valves were predicted to have the largest EOAs and smallest gradients.

Normal Reference Values Table for Evolut R

| Quintiles | ≤22.3 mm | >22.3 to ≤23.2 mm | >23.2 to ≤24.7 mm | >24.7 to ≤26.2 mm | >26.2 to ≤30.2 mm | p Value for Trend |
|---------------------------------------|------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Evolut R | | | | | | |
| EOA, cm ² | 1.66 ± 0.42 (53) | 1.82 ± 0.43 (38) | 1.98 ± 0.56 (62) | 1.98 ± 0.59 (49) | 2.56 ± 0.77 (53) | < 0.001 |
| EOAi, cm ² /m ² | 0.99 ± 0.27 (53) | 1.09 ± 0.26 (38) | 1.10 ± 0.32 (62) | 1.06 ± 0.34 (49) | 1.29 ± 0.37 (53) | < 0.001 |
| Mean gradient, mm Hg | 7.94 ± 3.10 (58) | 6.91 ± 2.58 (43) | 7.66 ± 2.94 (63) | 8.53 ± 3.49 (56) | 6.40 ± 3.34 (57) | 0.21 |
| DVI | 0.61 ± 0.11 (57) | 0.61 ± 0.14 (41) | 0.61 ± 0.15 (63) | 0.56 ± 0.14 (51) | 0.58 ± 0.15 (55) | 0.07 |

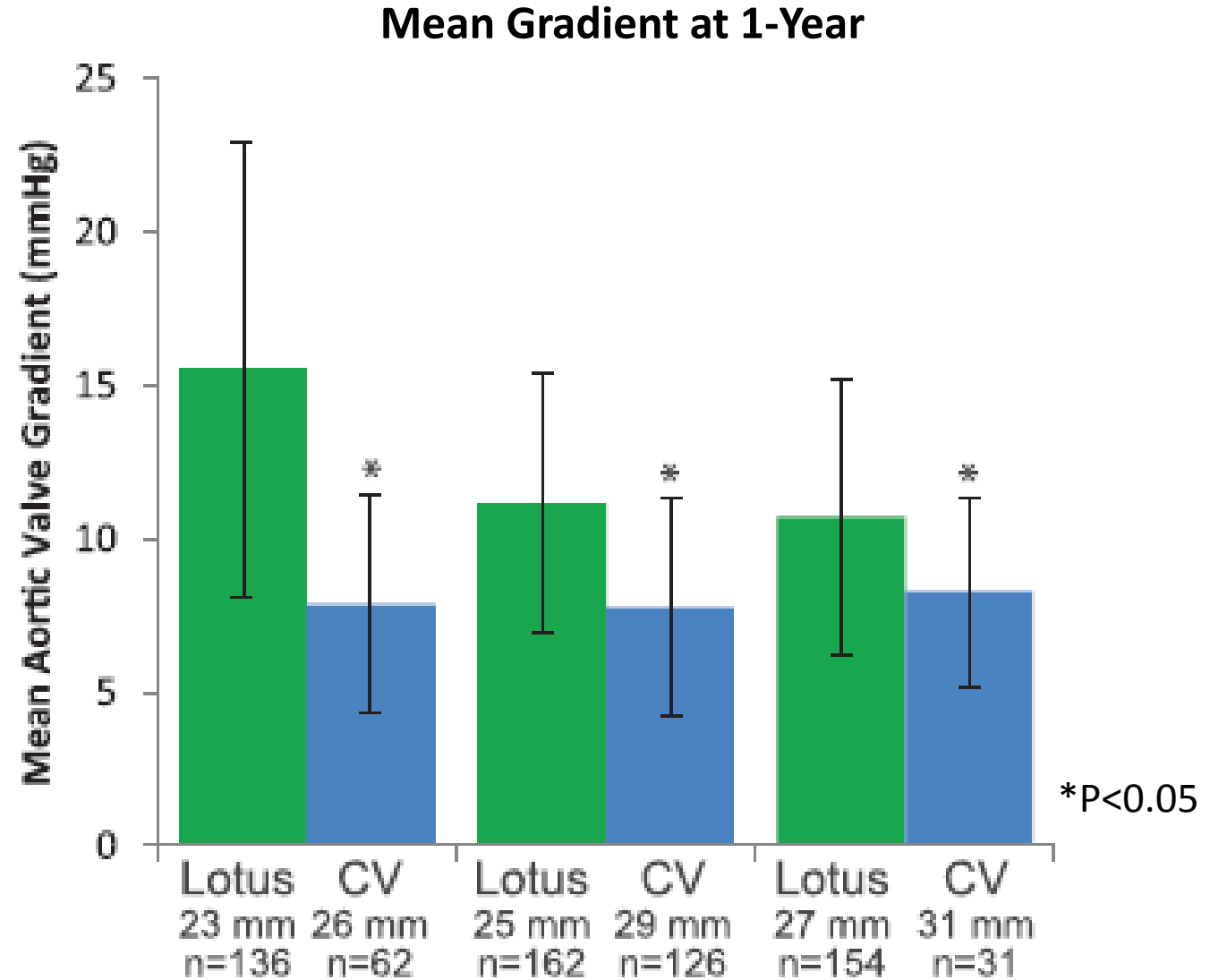
Normal Reference Values Table for Sapien 3

| | 248 to 384 mm ² (n = 189) | 385 to 439 mm ² (n = 191) | 440 to 488 mm ² (n = 192) | 489 to 537 mm ² (n = 191) | 538 to 678 mm ² (n = 188) | p Values for Trend |
|---------------------------------------|---|---|---|---|---|--------------------|
| EOA, cm ² | 1.41 ± 0.27 | 1.58 ± 0.33 | 1.73 ± 0.36 | 1.79 ± 0.35 | 1.91 ± 0.42 | <0.0001 |
| EOAi, cm ² /m ² | 0.80 ± 0.16 | 0.86 ± 0.19 | 0.92 ± 0.21 | 0.90 ± 0.20 | 0.93 ± 0.21 | <0.0001 |
| Mean gradient, mm Hg | 13.96 ± 5.28 | 11.94 ± 4.82 | 10.93 ± 5.04 | 10.56 ± 4.16 | 9.17 ± 3.35 | <0.0001 |
| DVI | 0.43 ± 0.1 | 0.44 ± 0.1 | 0.42 ± 0.09 | 0.43 ± 0.09 | 0.42 ± 0.09 | 0.13 |

Technology Selection

Small Annuli | Supra-Annular vs Intra-Annular TAVI

The REPRISE III clinical trial directly compared the intra-annular Lotus valve to the supra-annular CoreValve. While both valves had acceptable gradients, the supra-annular CoreValve had significantly lower gradients across all valve sizes at 1-year with the biggest difference seen in patients implanted with the smallest valves.



Technology Selection

Small Annuli | Supra-Annular vs Supra-Annular TAVI

A recent propensity matched comparison of two supra-annular valves, Acurate Neo and Evolut PRO, found excellent hemodynamic performance by both valves. Of these 2 supra-annular valves, Evolut PRO valve had significantly lower mean gradients post-procedure.

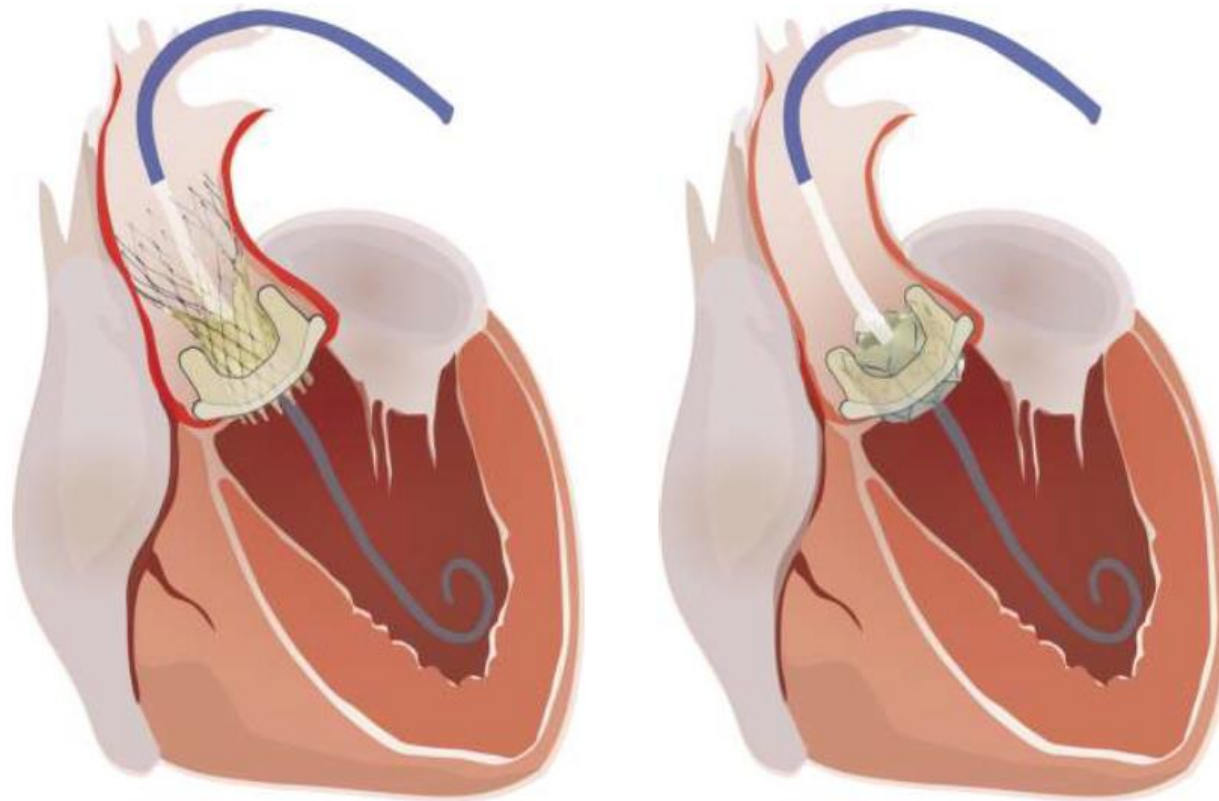
| | Acurate neo (n=1263) | Evolut PRO (n=288) | p-value |
|-------------------------|-------------------------|-----------------------|---------|
| Conscious sedation | 96.4% | 92.8% | 0.112 |
| Valve size | | | - |
| S or 23 mm | 23.9% | 2.0% | |
| M or 26 mm | 41.8% | 38.3% | |
| L or 29 mm | 34.3% | 59.8% | |
| Predilatation | 86.5% | 37.9% | <0.001 |
| Postdilatation | 41.4% | 25.0% | <0.001 |
| Valve repositioning | - | 8.6% | - |
| Second THV implanted | 0.8% | 1.2% | 1.000 |
| Valve embolization | 0.4% | 0.8% | 1.000 |
| Annular rupture | 0.0% | 0.0% | - |
| Pericardial tamponade | 2.0% | 0.0% | 0.061 |
| Conversion to surgery | 0.8% | 0.0% | 0.499 |
| Mean AV gradient (mmHg) | 8.3 ± 4.0 | 7.3 ± 3.6 | 0.003 |

Technology Selection

TAV-in-SAV | Hemodynamic Challenges

Although TAV-in-SAV has proven to be a promising less invasive approach for failed bioprosthesis, residual stenosis is the Achilles heel of TAV-in-SAV.

- With the surgical valve in the native aortic annuli, there is a lack of space in the aortic root for the TAVI valve, which makes achieving optimal hemodynamic performance a challenge.



Technology Selection

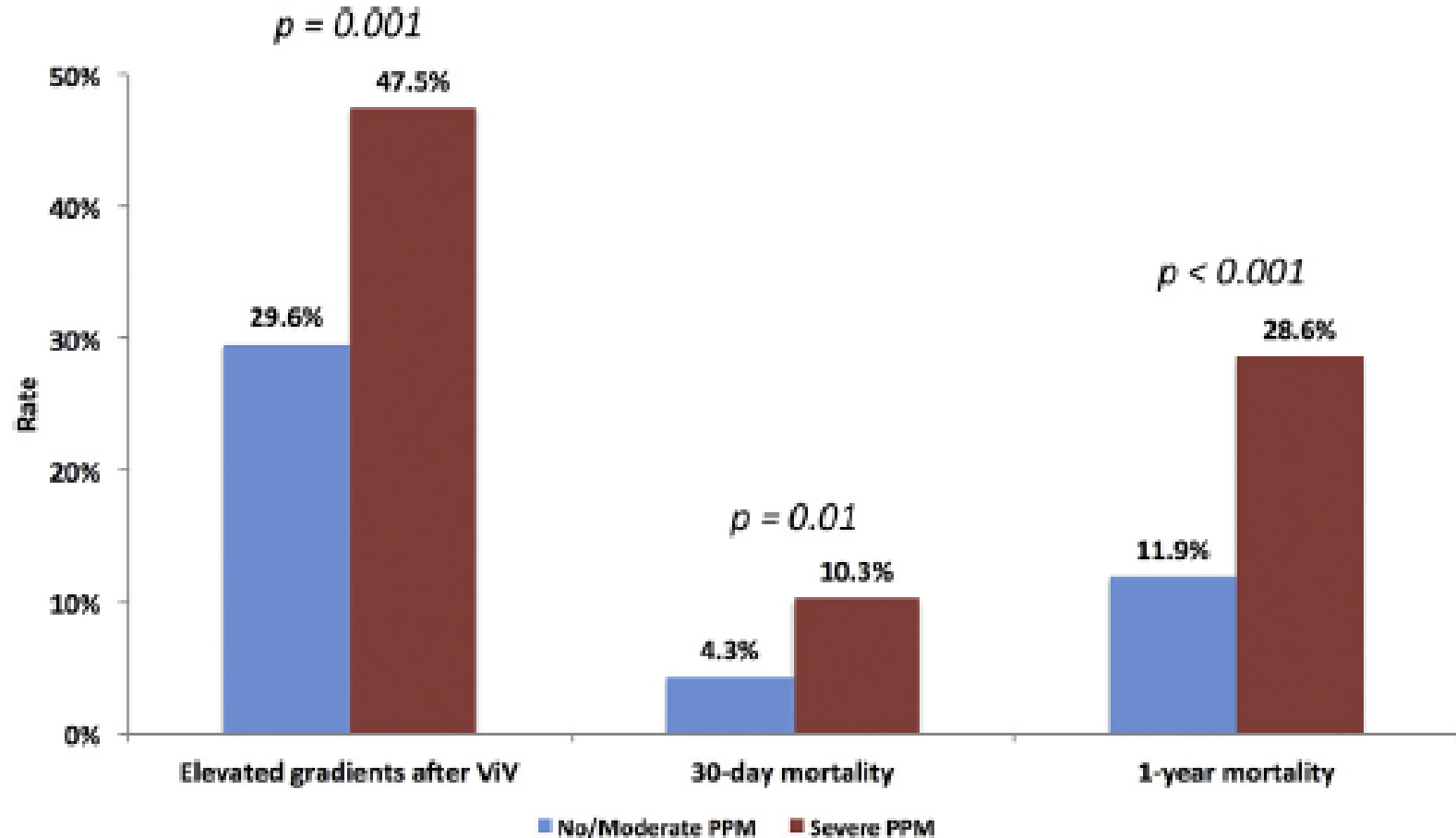
TAV-in-SAV | Hemodynamic Challenges

Additionally, surgical bioprosthesis often have a small internal orifice diameter and a nonelastic stent which can constrain the TAVI valve.

Registries have demonstrated that up to 75% of surgical valves implanted have a small internal diameter (<23mm)

Results from the valve-in-valve international data (VIVID) registry demonstrated that pre-existing PPM of the failed surgical valve is strongly and independently associated with an increased risk for mortality following TAV-in-SAV implantation.

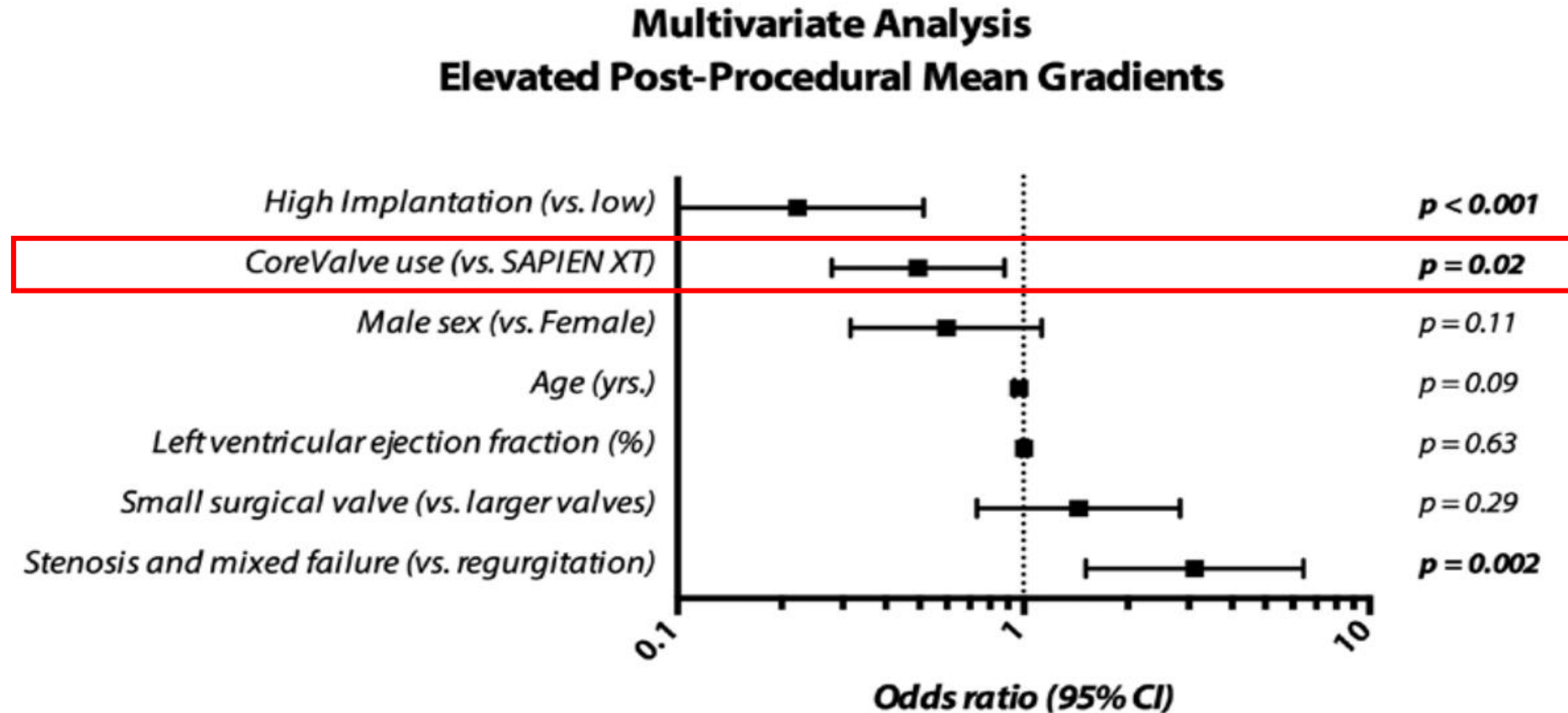
Rates of Elevated Post-Procedural Gradients and 30-Day and 1-Year Mortality According to Pre-Existing PPM



Technology Selection

TAV-in-SAV | Supra-Annular vs Intra-Annular TAVI

A separate analysis from the VIVID registry found that the use of intra-annular SAPIEN XT vs. supra-annular CoreValve devices resulted in significantly elevated gradients post-TAV-in-SAV procedure.



Hemodynamic Performance

Impact on Valve Durability

Mortality and rehospitalization are important complications associated with PPM. However, long-term consequences of PPM have also been reported. Elevated gradients may impact valve durability over time, which is increasingly important in younger, healthier patients.

Procedural Safety

Mortality

Morbidity

Quality of Life

Focus



Valve Performance

Hemodynamics

Durability

PVL

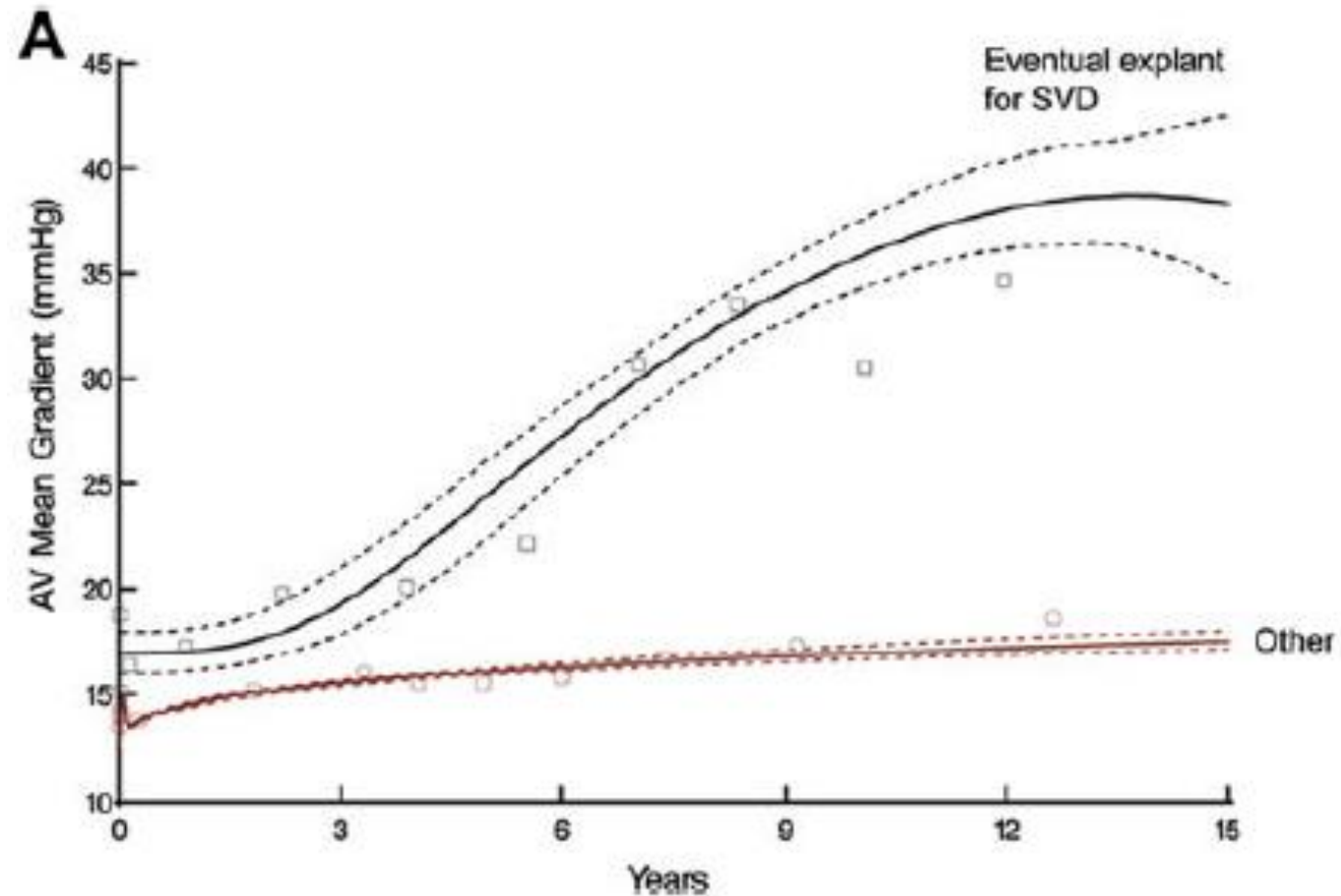
Hemodynamic Performance

Impact on Durability | SAVR

Association of PPM and structural valve deterioration (SVD) has been documented in the SAVR literature.

A recent study on valve durability in nearly 13,000 SAVR patients demonstrated that patients with PPM and higher postoperative peak and mean gradients were at greatest risk of explant for SVD.

Trend of Mean Gradient in Patients With and Without Explant for SVD



Solid lines represent parametric estimates enclosed within 68% bootstrap percentile confidence intervals. Symbols represent data grouped without regard to repeated measurements within time frame to provide crude verification of model fit.

Hemodynamic Performance

Impact on Durability | TAVI

The impact of hemodynamic performance is essential for evaluating TAVI valve durability. Both the EAPCI/ESC/EACTS and VARC definitions of structural valve deterioration (SVD) include hemodynamic performance.

EAPCI/ESC/EACTS Standardized Definition of SVD

| Type | Definition |
|-------------|--|
| Morphologic | <ul style="list-style-type: none">▶ Leaflet integrity abnormality (i.e. torn or flail causing intra-frame regurgitation)▶ Leaflet structure abnormality (i.e. pathological thickening and/or calcification causing valvular stenosis or central regurgitation)▶ Leaflet function abnormality (impaired mobility resulting in stenosis and/or central regurgitation)▶ Strut/frame abnormality (i.e. fracture) |
| Hemodynamic | <p>Moderate</p> <ul style="list-style-type: none">▶ Mean transprosthetic gradient ≥ 20 mmHg and < 40 mmHg▶ Mean transprosthetic gradient ≥ 10 and < 20 mmHg change from baseline▶ Moderate intra-prosthetic AR, new or worsening ($> 1+/4+$) from baseline <p>Severe</p> <ul style="list-style-type: none">▶ Mean transprosthetic gradient ≥ 40 mmHg▶ Mean transprosthetic gradient ≥ 20 mmHg change from baseline▶ Severe intra-prosthetic AR, new or worsening ($> 2+/4+$) from baseline |

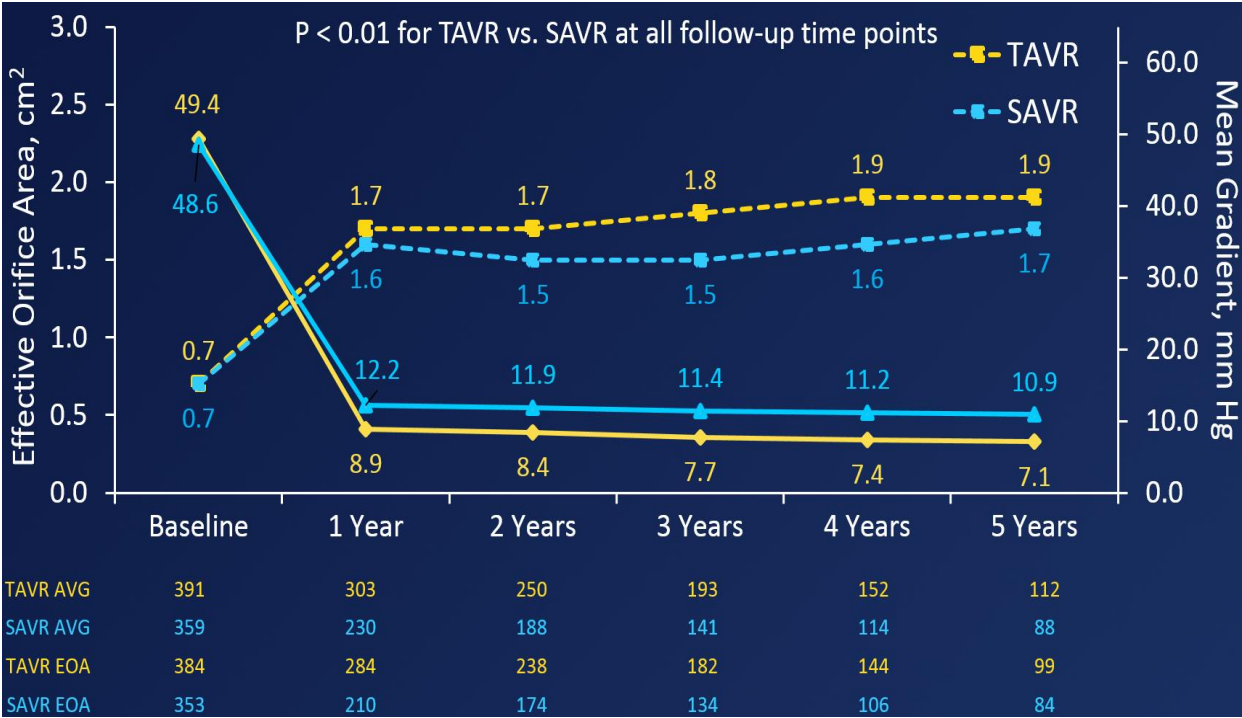
¹Capodanno et al., Eur Heart J. 2017 Dec 1;38(45):3382-3390; ²Kappetein et al., J Thorac Cardiovasc Surg. 2013 Jan;145(1):6-23

Hemodynamic Performance

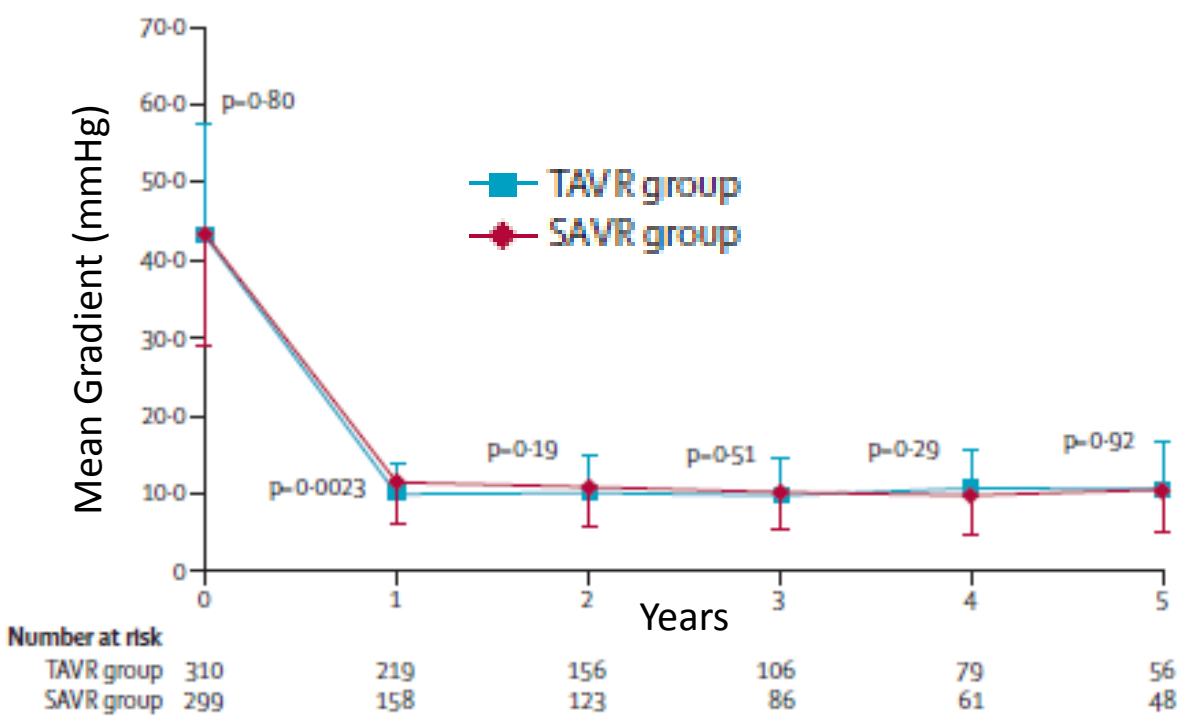
Impact on Durability | TAVI

Due to the limited availability of long-term data on TAVI, the impact of PPM on TAVI durability is not well-known. Overall, the long-term hemodynamic performance outcomes are promising and demonstrate similar or better hemodynamic performance than SAVR 5 years and beyond.

CoreValve High-Risk 5-Year EOAs and Mean Gradients



PARTNER 1B 5-Year Mean Gradients



¹Gleason et al., J Am Coll Cardiol. 2018 Sep 18; ²Mack et al., Lancet. 2015 Jun 20;385(9986):2477-84

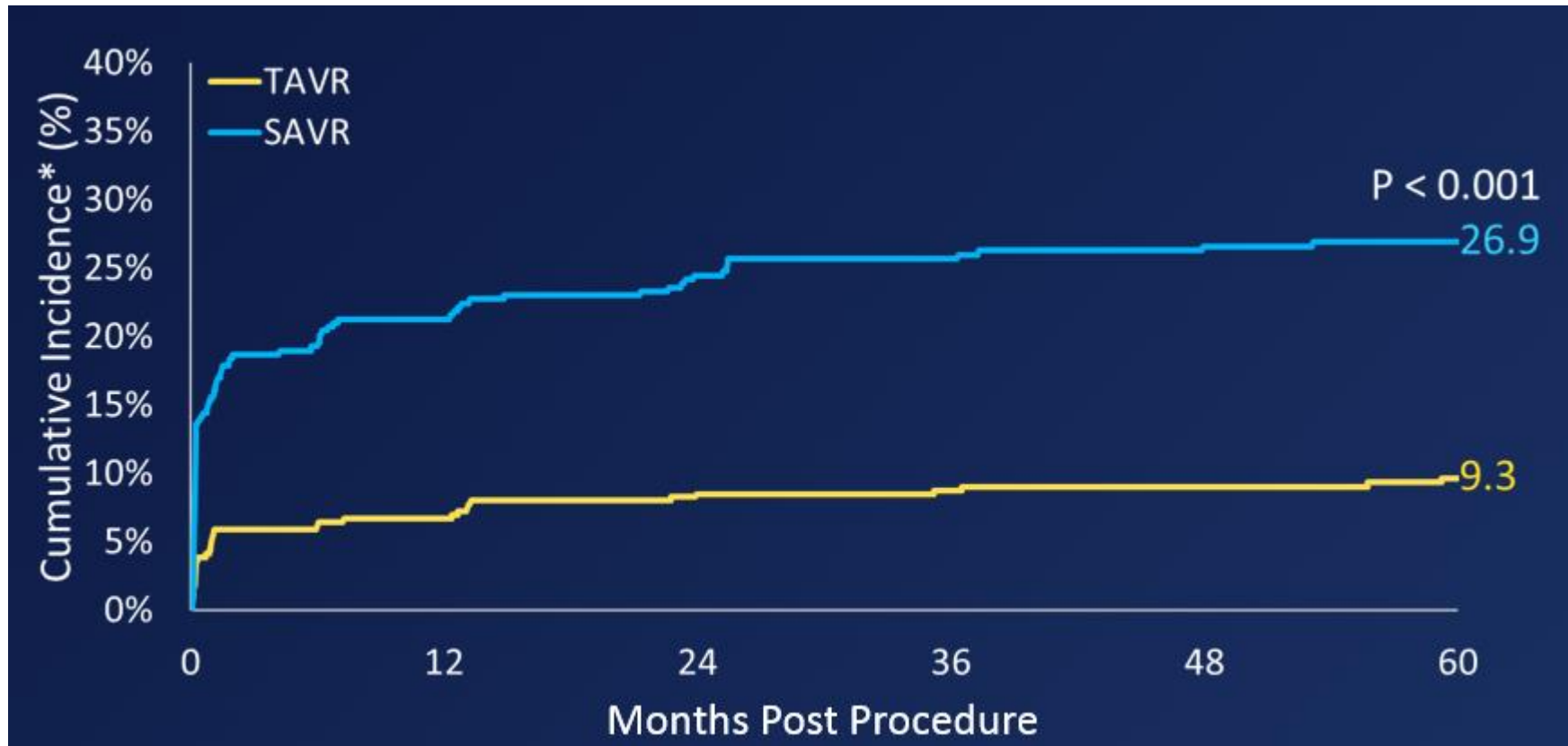
Hemodynamic Performance

Impact on Durability | TAVI

Promising hemodynamic performance has been translated to SVD and durability in TAVI patients.

- Long-term data from the supra-annular CoreValve High-Risk and NOTION trials demonstrated significantly less SVD in TAVI compared to SAVR.

Moderate SVD (%) from CoreValve High-Risk Trial



Summary

- Optimal hemodynamic performance has been shown to affect clinical outcomes and has been used as a benchmark for SAVR and TAVI success for decades.
- Clinical trials consistently show TAVI has as good or better EOAs and hemodynamic outcomes compared to SAVR. However, patients with small annuli and TAV-in-SAV are at increased risk of elevated gradients and PPM.
- Supra-annular valves achieve larger EOAs and lower mean gradients, especially in patients with small annuli and undergoing TAV-in-SAV.
- PPM may affect valve durability, which becomes increasingly important as TAVI moves down the risk spectrum.