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Hemodynamics and durability: what have we learned from flow studies?

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EuroValve - Milano
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Disclosures

- Edwards Lifesciences: CT CoreLab RESILIENCE trials + research contract
- Medtronic: Reserach grant

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Importance of Hemodynamics Following TAVI

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- **Bioprosthetic valve dysfunction (BVD), structural or non-structural, may have an impact on:**
  - **LV Recovery**
  - **Symptoms and QoL**
  - **Valve durability**
  - **Re-hospitalization, mortality**

- **In low-risk population with long life expectancy, optimization of valve hemodynamics and durability is a key objective of TAVI**

Doppler-Echo: Evaluation of Prosthetic Aortic Valve

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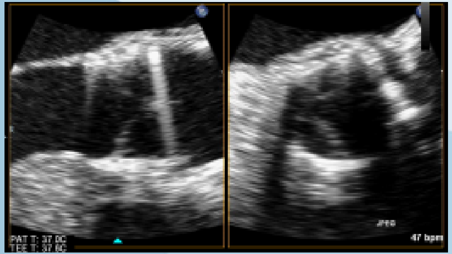
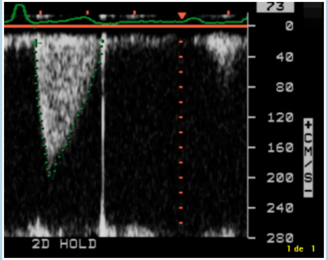
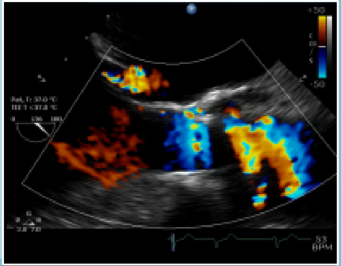
- Doppler-echocardiography is the primary imaging modality to evaluate THV function



- Structural evaluation (TTE and TEE)
  - Valve stent position and shape
  - Leaflet morphology and mobility
  - Paravalvular region



- Functional (Hemodynamic) evaluation
  - Transprosthetic gradients, EOA, and DVI
  - Localization (central vs. para) and degree of regurgitation



- LV/RV size and function, Pulmonary Arterial Pressure

Standardized Echo Measurements for Assessment of SVD

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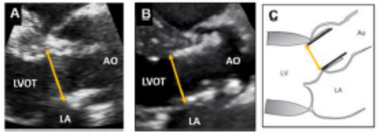
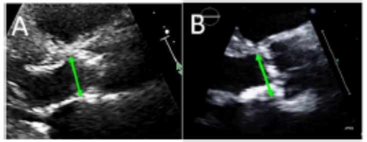
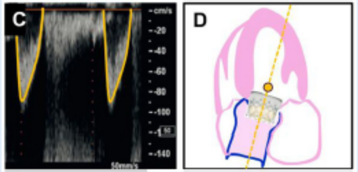
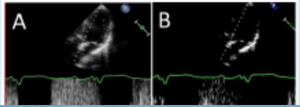
Echocardiographic Parameter	Measurement and Calculation	Caveats and Recommendations
Timing of TTE examinations	Aortic and mitral bioprostheses • Prehospital discharge • Baseline: between 1 and 3 mo • 1 y • Annually beyond 1 y	The assessment of the changes in structure and function of the bioprosthetic valves between the baseline and follow-up TTE is key to allow early detection of BVD. Such assessment requires a comprehensive baseline TTE between 1 and 3 mo postprocedure and routine annual TTE follow-up thereafter.
LVOT diameter by 2D echocardiography for calculation of left ventricular stroke volume: The LVOT diameter is measured from outer to outer edge of the stent or ring just below the sewing ring for surgical bioprostheses (A) or the stent for transcatheter bioprostheses (B and C).	Aortic bioprostheses  	Because the native aortic annulus and prosthetic aortic valve sewing ring remain relatively stable, to reduce interexamination variability in the measurement of AVA and MVA, it is recommended to use as standard whichever of the first FU visit or the baseline postprocedural echocardiogram gives the clearer LV outflow diameter
The LVOT diameter is measured from inner to inner edge of native structures at or just below the level of the native aortic annulus (A). In the setting of ectopic calcification in the LVOT, annulus, or anterior mitral leaflet, the diameter measurement should ignore this calcium and measure to the base of the anterior mitral valve leaflet (B).	Mitral bioprostheses (native aortic valve)  LVOT Area = 0.785 × (LVOT diameter)^2	
LVOT flow velocity by pulsed wave Doppler for calculation of left ventricular stroke volume: The LVOT velocity is measured by placing the pulsed-wave Doppler sample just apical (ie, proximal) to the ventricular aspect of the prosthesis sewing ring or stent (C and D) in systole.	Aortic bioprostheses  	The pulsed wave sample volume should remain apical (or proximal) to the sewing ring or stent frame in systole. Thus, depending on LV function, the diastolic position of the sample volume may appear as much as 1-1.5 cm apical to the systolic position. Unlike in the setting of a native aortic valve, a closure click is not typically seen because the sample volume remains apical to the bioprosthetic leaflets.
Pulsed wave Doppler of laminar flow just proximal to flow acceleration. The modal velocity should be traced to measure LVOT VTI and not the faint higher velocity profile. (A) (red line) An incorrectly traced Doppler signal. Reducing the gain or increasing the reject will result in a modal velocity profile (green tracing, B).	Aortic and mitral bioprostheses  	

Use same LVOTD throughout FU

Use same window for CWD of aortic valve flow throughout FU

Confirm findings by at least 2 imaging studies: Repeat Echo

TEE or CTA to visualized leaflet morphology / mobility

Pibarot et al. JACC 2022

Calculation of Prosthetic Valve EOA by Continuity Equation Method

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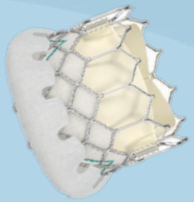
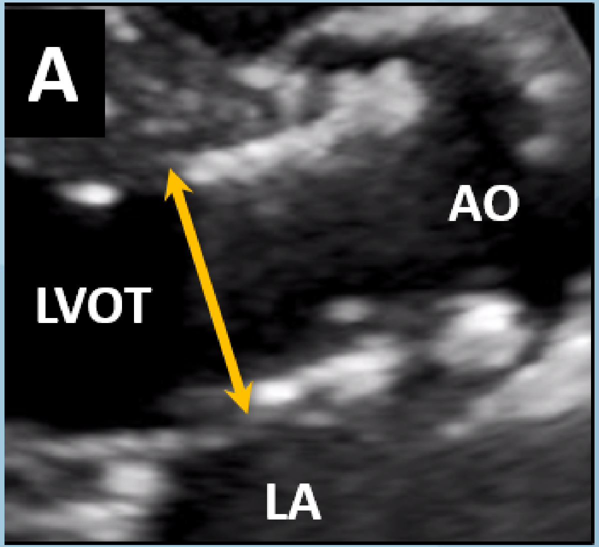
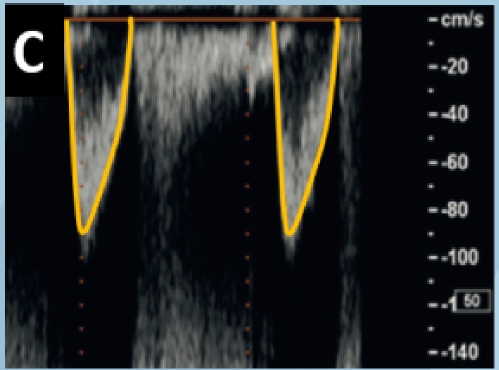


LVOT Diameter

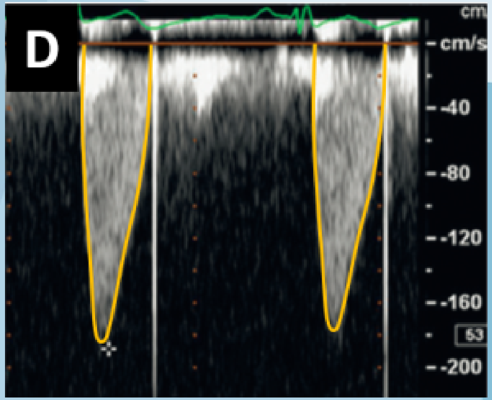
TAVR



LVOT PWD



AV CWD



$$AVA = \frac{(CSA_{LVOT} \times VTI_{LVOT})}{VTI_{Ao}}$$

$$DVI = \frac{VTI_{LVOT}}{VTI_{Ao}}$$

LVOT diameter should be measured just below the apical border of the stent from external border to external border

Velocity and Gradient

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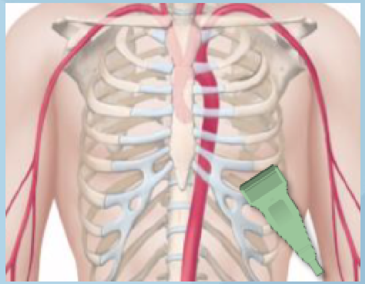
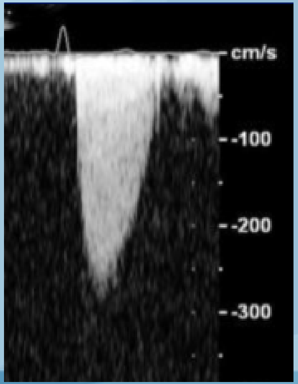
Try to use and compare the same window for CW Doppler interrogation of aortic valve flow

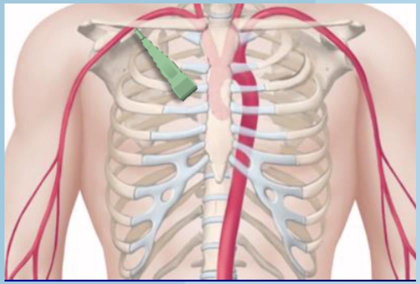
Apical

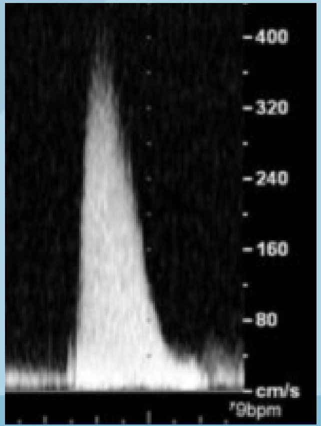


V_{Peak}: 2.9 m/s



RSB



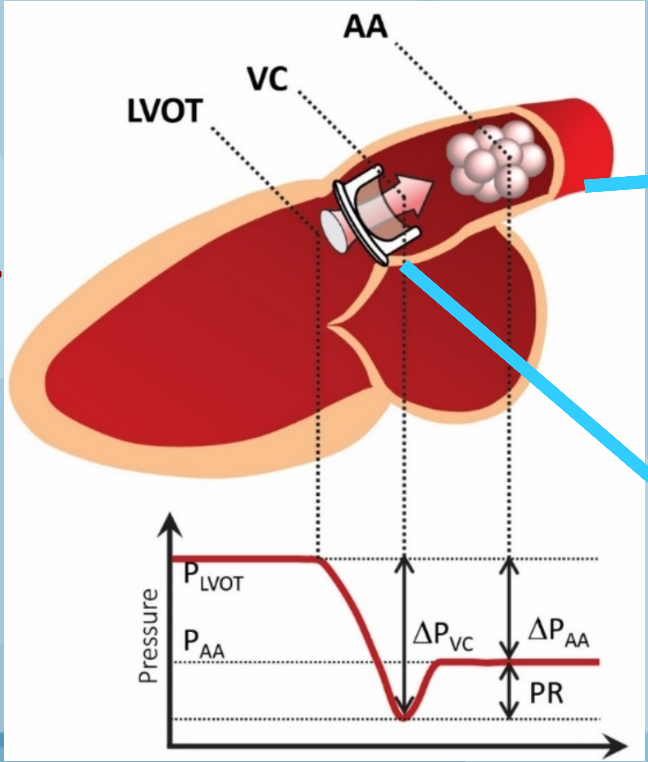


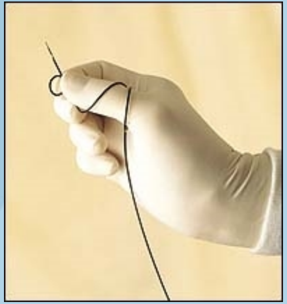
V_{Peak}: 4.0 m/s

Discordances Between Echo and Cath

A Manifestation of Pressure Recovery and (Over) Simplification of Bernoulli Formula

Echo measures higher gradients and smaller EOAs vs. cath.





Immediate Post-TAVI Echo vs. Cath Gradients in Balloon Expandable vs. Self-Expanding Valves

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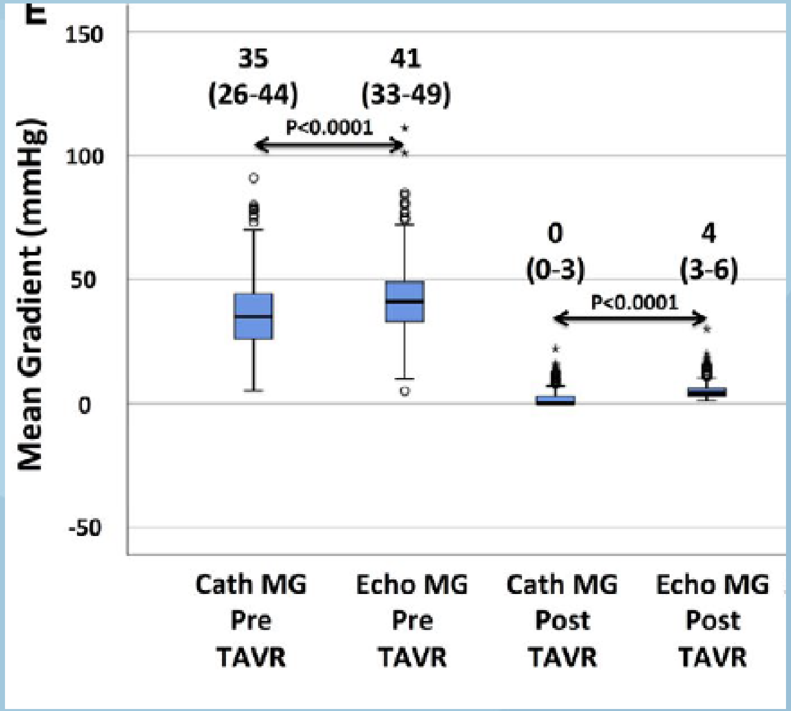

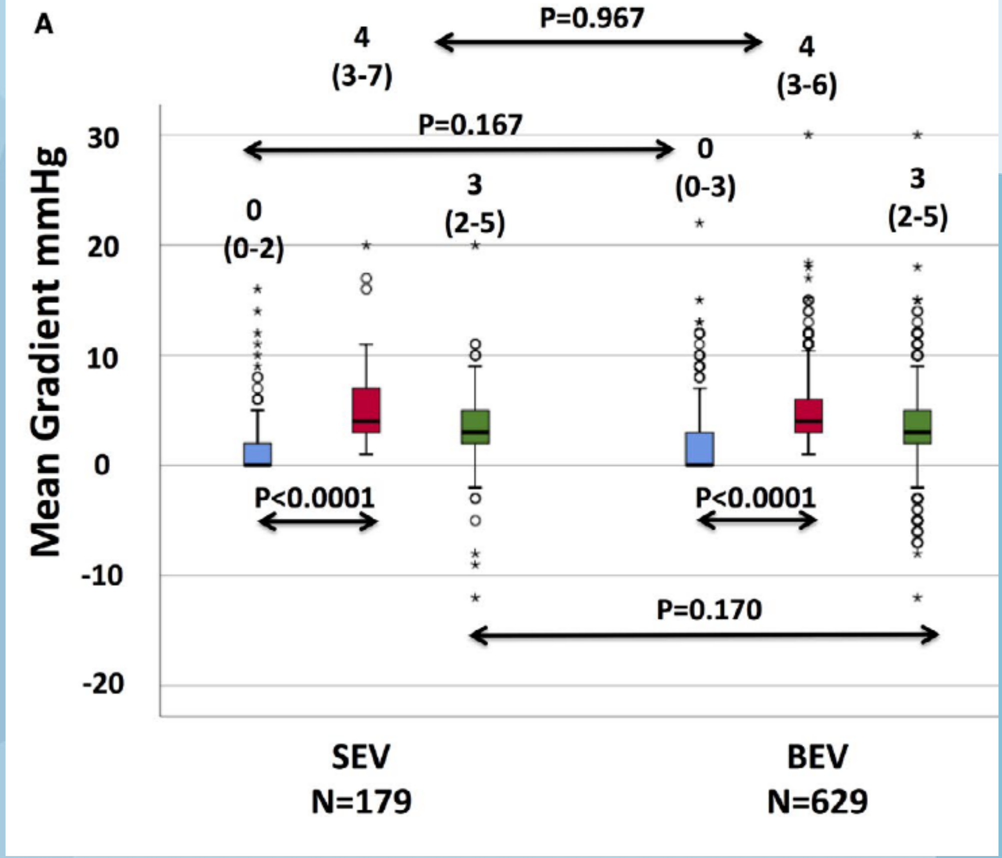

Invasive Mean Gradient
Echocardiography Mean Gradient
Echo Invasive MG Difference (Absolute Discordance)

Abbas et al. JAHA 2021

Association Between High Residual Gradients and Late Mortality after AVR

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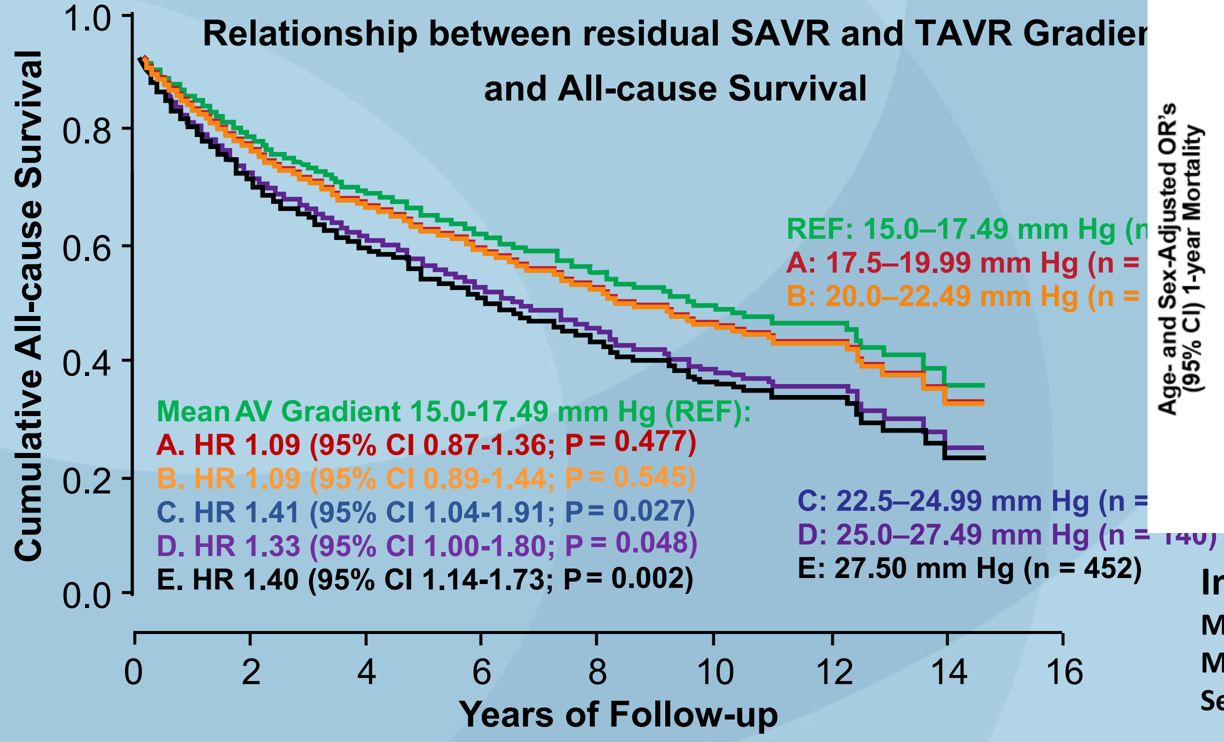

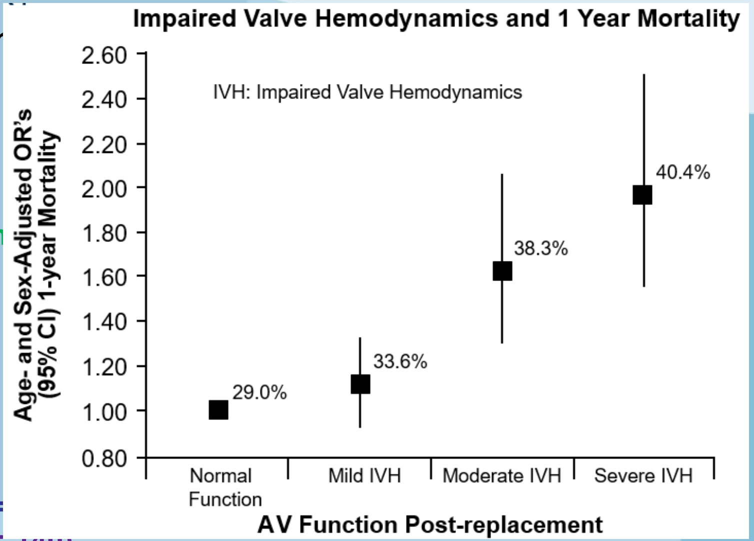

Impaired valve hemodynamics:
Mild: Mean gradient 10-19.9 mmHg
Moderate: Mean gradient 20-39.9 mmHg
Severe: mean gradient ≥ 40 mmHg or EOA <0.8 cm^2

Playford D, et al. J Am Soc Echocardiogr. 2020;33:1077-1086.e1.

Definition of Prosthesis-Patient Mismatch

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PPM definition: prosthesis functioning normally but too small for patient's BSA

Normal EOA but small indexed EOA

	None/Mild	Moderate	Severe
Valve structure and motion	Usually normal	Usually normal	Usually normal
Indexed EOA (cm^2/m^2)	>0.85	0.85-0.65	<0.65
Indexed EOA (cm^2/m^2) in obese patients (BMI ≥30 kg/m^2)	>0.70	0.70-0.55	<0.55

High residual gradient: > 20 mmHg (with DVI<0.25)

VARC-3
Lancellotti EHJ CV Img 2016

Reference EOA for BEV and SEV

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TABLE 2 Mean Gradient and EOA for Balloon-Expandable SAPIEN Valves

	Prosthetic Valve Size, mm					
Valve Iteration	20	23	26	29	All Sizes	p Value
SAPIEN						
EOA, cm^2	NA	1.56 ± 0.43 (1,212)	1.84 ± 0.52 (1,130)	NA	1.70 ± 0.49 (2,342)	<0.001
Mean gradient, mm Hg	NA	9.92 ± 4.27 (1,212)	8.76 ± 3.89 (1,130)	NA	9.36 ± 4.13 (2,342)	<0.001
DVI	NA	0.53 ± 0.13 (1,212)	0.53 ± 0.13 (1,130)	NA	0.53 ± 0.13 (2,342)	0.64
SAPIEN XT						
EOA, cm^2	NA	1.41 ± 0.30 (545)	1.74 ± 0.42 (675)	2.06 ± 0.52 (251)	1.67 ± 0.46 (1471)	<0.001
Mean gradient, mm Hg	NA	10.41 ± 3.74 (545)	9.24 ± 3.57 (675)	8.36 ± 3.14 (251)	9.52 ± 3.64 (1,471)	<0.001
DVI	NA	0.52 ± 0.10 (545)				
SAPIEN 3						
EOA, cm^2	1.22 ± 0.22 (47)	1.45 ± 0.26 (471)				
Mean gradient, mm Hg	16.23 ± 5.01 (47)	12.79 ± 4.65 (471)				
DVI	0.42 ± 0.07 (47)	0.43 ± 0.08 (471)				

Values are mean ± SD (n). This table shows the mean gradients and EOA for eac
were significantly different for each valve size for a given valve type (range p <
DVI = Doppler velocity index; EOA = effective orifice area; NA = not availabl

TABLE 4 Mean Gradient and EOA for CoreValve and Evolut R by Valve Size in Native Aortic Stenosis at 30 Days

	Prosthetic Valve Size, mm					
Valve Iteration	23	26	29	31	All Sizes	p Value
CoreValve						
EOA, cm^2	1.12 ± 0.36 (19)	1.74 ± 0.49 (289)	1.97 ± 0.53 (446)	2.15 ± 0.72 (81)	1.88 ± 0.56 (835)	<0.001
Mean gradient, mm Hg	14.43 ± 5.72 (22)	8.27 ± 3.82 (307)	8.85 ± 4.17 (478)	9.55 ± 3.44 (83)	8.85 ± 4.14 (890)	<0.001
DVI	0.44 ± 0.09 (20)	0.59 ± 0.15 (300)	0.54 ± 0.12 (463)	0.49 ± 0.12 (83)	0.55 ± 0.13 (866)	<0.001
	Prosthetic Valve Size, mm					
Valve Iteration	23	26	29	34	All Sizes	p Value
Evolut R						
EOA, cm^2	1.09 ± 0.26 (3)	1.69 ± 0.40 (71)	1.97 ± 0.54 (129)	2.60 ± 0.75 (52)	2.01 ± 0.65 (255)	<0.001
Mean gradient, mm Hg	14.97 ± 7.15 (3)	7.53 ± 2.65 (77)	7.85 ± 3.08 (141)	6.30 ± 3.23 (57)	7.52 ± 3.19 (278)	<0.001
DVI	0.42 ± 0.04 (3)	0.61 ± 0.13 (75)	0.59 ± 0.14 (135)	0.58 ± 0.15 (55)	0.59 ± 0.14 (268)	0.09

Values are mean ± SD (n). p values are from analysis of variance F-test.
Abbreviations as in Table 1.

Hahn et al. JACCi 2019

Incidence and Impact of PPM by Measured and Predicted EOAi Methods in PARTNER 2A Trial and S3i R

INCIDENCE OF SEVERE PPM

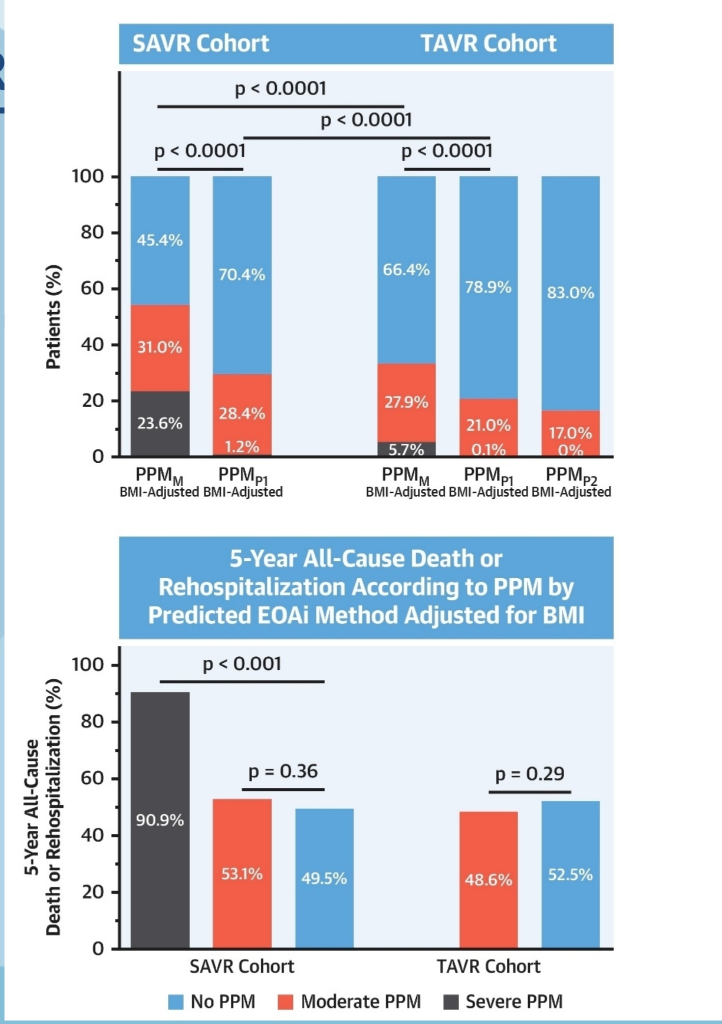
Much lower with predicted vs. measured EOAi

Lower in TAVR vs. SAVR, regardless of the EOAi method

IMPACT OF PPM ON OUTCOMES

In SAVR, severe predicted PPM is rare but independently associated with worse outcomes

In TAVR, severe predicted PPM method is absent



Impact of PPM on Structural Degeneration of Bioprosthetic Valves

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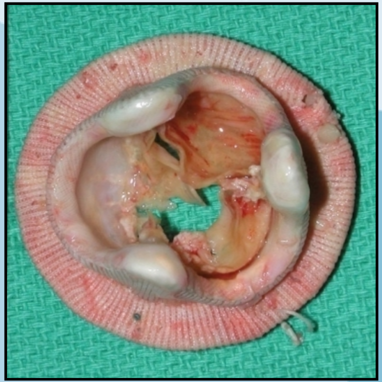

- **664 patients: AVR with a bioprosthesis**
- **Median FU time: 6.1 yr**
- **PPM is independently associated with 2.3-fold increase in the risk of SVD**

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

Doppler-Echo Criteria to Assess the Severity of Prosthetic Aortic Valve Stenosis

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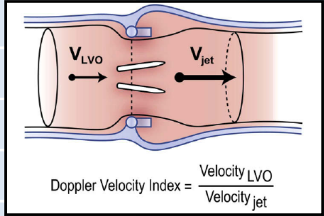
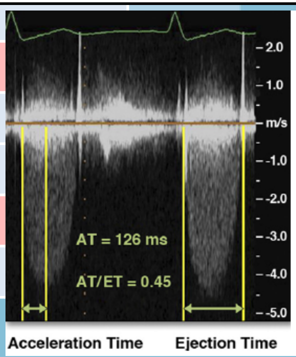
	Normal	Possible Stenosis	Significant Stenosis
2D/3D TTE/TEE / Cinefluoroscopy / CT			
Valve structure / leaflet mobility	Normal	Often abnormal	Abnormal
Doppler quantitative parameters			
Peak velocity (m/s)	<3	3-4	≥4
Mean gradient (mmHg)	<20	20-35	≥35
Doppler velocity index	≥0.35	0.25-0.35	<0.25
Effective orifice area (cm²)	>1.1	0.8-1.1	<0.8
Difference (Normal EOA - Measured EOA)	<0.30	0.30-0.59	>0.60
Doppler semi-quantitative parameters			
Acceleration time (ms)	<80	80-100	>100
Acceleration time / LV ejection time	<0.32	0.32-0.37	>0.37
Changes in echo parameters during FU			
Increase in mean gradient (mmHg)	<10	10-19	≥20

+ decrease in EOA (different from reference EOA <0.3)





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STEP 1: Red Flags of Aortic Bioprosthetic Valve Dysfunction (BVD)

Reduced or excessive leaflet mobility
Leaflet thickening
Color-flow Doppler systolic restriction
Mean gradient ≥20 mm Hg (≥30 mm Hg)*
Increase in mean gradient ≥10 mm Hg (≥20 mm Hg)* during follow-up
EOA <1.1 cm^2 (<0.8 cm^2)*
DVI <0.35 (<0.25)*
AT/LVET >0.32 (>0.37)*
New onset or worsening of intraprosthetic AR ≥mild
New onset or worsening of symptoms

STEP 2: Determination of Etiology and Category of BVD by TTE, TEE, CT

Nonstructural BVD
Any abnormality, not intrinsic to the prosthetic valve, resulting in valve dysfunction

Paravalvular Regurgitation

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 ≥30 kg/m^2

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

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

Structural BVD
Intrinsic permanent changes to the prosthetic valve, including:

- Wear and tear
- Leaflet disruption
- Flail leaflet
- Leaflet fibrosis and/or calcification
- Strut or stent fracture or deformation

Possible

Thrombosis
Subclinical leaflet thrombosis:
Imaging findings of HALT/RLM with absent or mild hemodynamic changes and no symptoms/sequelae

Clinically significant valve thrombosis:
1) Clinical sequelae of thromboembolic event or worsening AS/AR and BVD Stage 2-3 or confirmatory imaging (HALT/RLM)
2) In the absence of clinical sequelae, both BVD Stage 3 and confirmatory imaging (HALT/RLM)

Endocarditis
Meeting at least 1 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

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STEP 3: Determination of BVD Progression Stage by TTE

Stage 1
Morphologic Valve Deterioration:
Evidence of structural valve deterioration, nonstructural valve dysfunction (other than paravalvular regurgitation or prosthesis-patient mismatch) thrombosis, or endocarditis without significant hemodynamic changes.

Stage 2
Stage 1 AND Moderate Hemodynamic Valve Deterioration
Increase in mean transvalvular gradient ≥10 mm Hg resulting in mean gradient ≥20 mm Hg† with concomitant decrease in AVA ≥0.3 cm^2 or ≥25% and/or decrease in DVI ≥0.1 or ≥20% compared to echocardiographic assessment performed 1 to 3 months postprocedure,
OR
New occurrence or increase of ≥1 grade of intraprosthetic AR resulting in ≥ moderate AR.

Stage 3
Stage 1 AND Severe Hemodynamic Valve Deterioration:
Increase in mean transvalvular gradient ≥20 mm Hg resulting in mean gradient ≥30 mm Hg† with concomitant decrease in AVA ≥0.6 cm^2 or ≥50% and/or decrease in DVI ≥0.2 or ≥40% compared to echocardiographic assessment performed 1 to 3 months postprocedure,
OR
New occurrence, or increase of ≥2 grades, of intraprosthetic AR resulting in ≥ moderate-to-severe AR.

STEP 4: Clinical Consequences of BVD

Bioprosthetic Valve Failure (BVF)

Criteria 1: Any BVD with clinically expressive criteria (new-onset or worsening symptoms, LV dilation/hypertrophy/dysfunction, or pulmonary hypertension) OR irreversible Stage 3 BVD with confirmatory imaging of leaflet/stent abnormalities and/or confirmatory invasive assessment of BVD†
Criteria 2: Aortic valve reintervention or hemodynamic/symptomatic indication for reintervention
Criteria 3: Valve-related death

Thank you for your attention

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