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Heart Institute
Foundation
GRAND ROUNDS

Modern Definitions of Aortic Stenosis
The Frontier

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Disclosures

I, Nadira Hamid DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation

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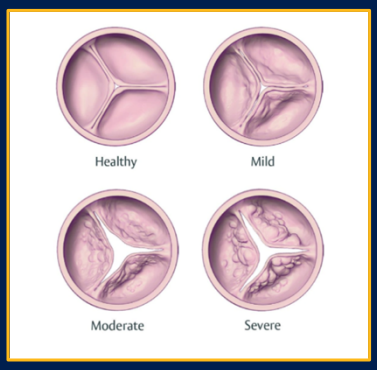
Definitions for Severity of AS

Conventional Criteria



AVA <1 cm^2

PV ≥4 m/s

Mean grad >40 mmHg

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Discordant Grading – Low Gradient AS

AVA≤1.0 cm^2 MG<40 mmHg

LVEF

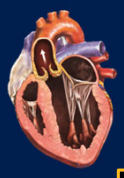
<50%

>50%

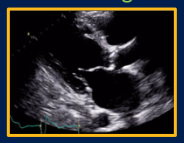
SVi

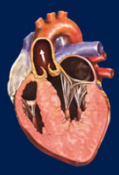
<35 mL/m^2

>35 mL/m^2

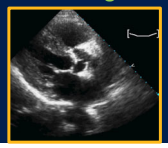


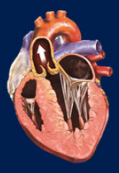
«CLASSICAL» LOW-FLOW LOW-GRADIENT (HFrEF) D2 Stage



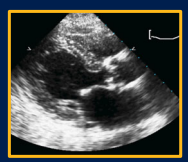


«PARADOXICAL» LOW-FLOW LOW-GRADIENT (HFpEF) D3 Stage





NORMAL-FLOW LOW-GRADIENT D1 Stage



Courtesy of Philippe Pibarot

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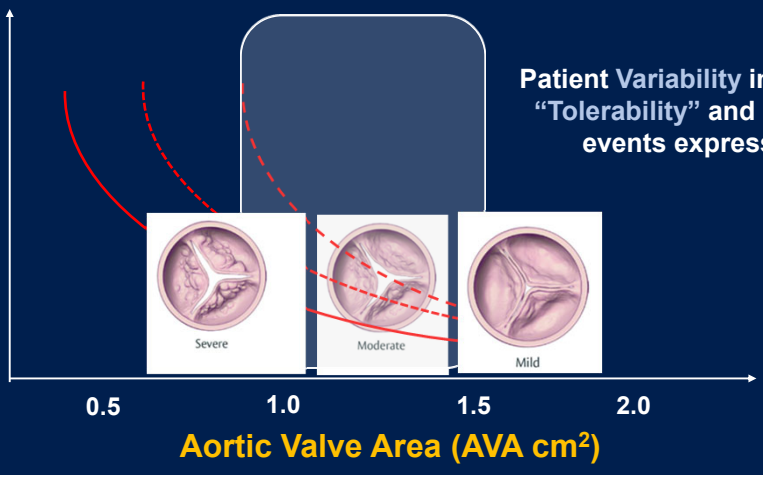
What is the Threshold For Adverse Events?

Adverse Events
Mortality
Valve-related symptoms
Cardiac damage



Patient Variability in AS load "Tolerability" and adverse events expression

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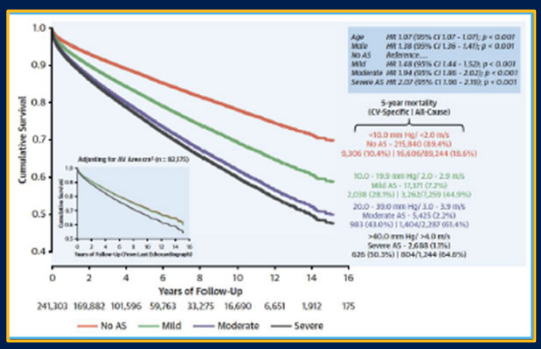
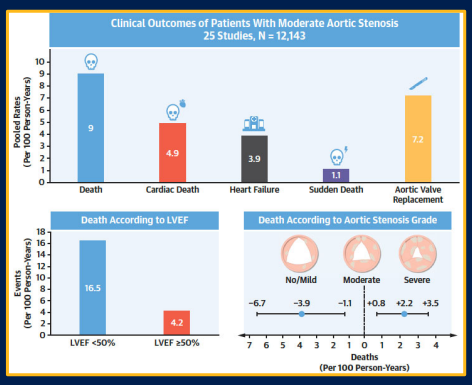
Is Moderate AS Bad?





Strange et al. J Am Coll Cardiol. 2019 Oct 15, 74(15):1851-1863

Coisne et al. J Am Coll Cardiol. Inter 2022;15(16): 1664-74

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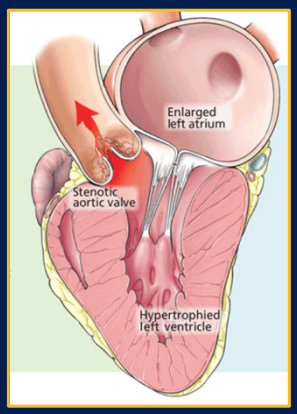
Why Moderate AS is Bad

Cardiac Consequences

- ECHO diagnostic challenges
- Rapid undetected progression
- Subclinical cardiac damage
- Late presentation
- Failure to intervene timely



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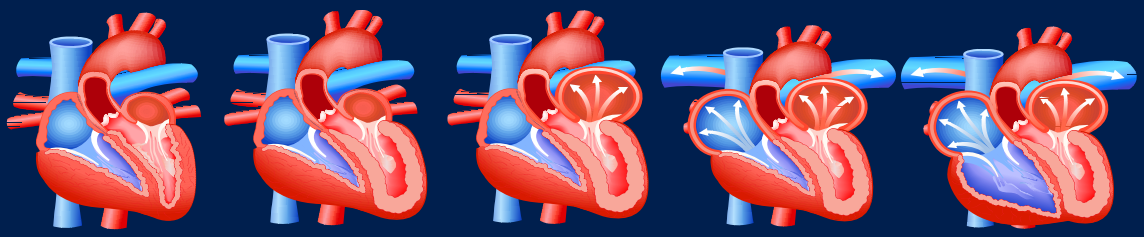
Cardiac Damage in AS Impairs Survival

Often Silent



Stage 0	Stage 1	Stage 2	Stage 3	Stage 4
No damage	LV damage	LA/Mitral damage	PA/Tricuspid damage	RV damage
	Increased LV Mass Index >115 g/m² Male >95 g/m² Female	Indexed left atrial volume >34mL/m²	PAS ≥60mmhg	Moderate-Severe RV dysfunction
	E/e' >14	Moderate-Severe MR	Moderate-Severe TR	
	EF <50%	Atrial Fibrillation		

Généreux et al. Eur Heart J 2017 Jul 21

Patients hierarchically classified based on the presence of at least one variable in the highest stage (independent, not additive)

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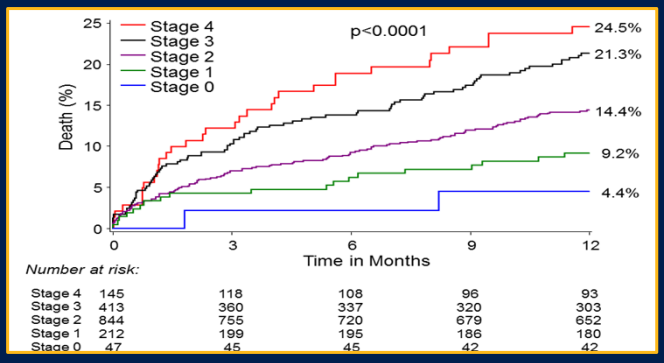
Extent of Cardiac Damage

Severe AS with Symptoms



1 Year Death After AVR
N = 1661 patients

Généreux et al. Eur Heart J 2017 Jul 21

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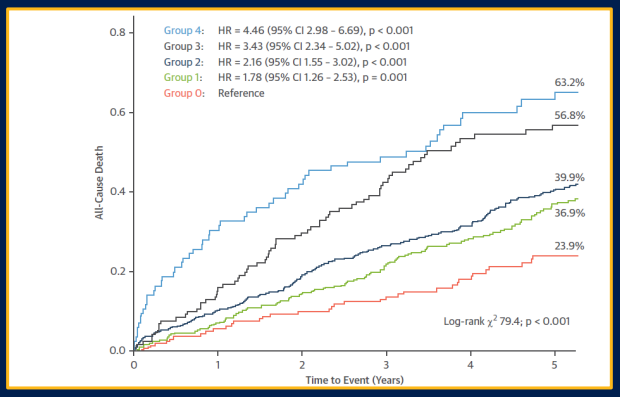
Extent of Cardiac Damage

Moderate AS



5 Year Death
N = 1245 patients

Amanullah et al. JACC Imaging 2021

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How do we improve detection of AS patients at risk?

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Follow-up in Patients With Aortic Stenosis

Aortic Severity	Follow-up Recommendation
Mild (Vmax 2.0–2.9 m/s)	Every 3-5 years
Moderate (Vmax 3.0–3.9 m/s)	**Every 1-2 years**
Severe Asymptomatic (Vmax ≥4 m/s)	Every 6-12 months

Vmax = peak aortic velocity. Adapted from Otto et al.

Otto, Nishimura, Bonow et al. J Am Coll Cardiol. 2021 Feb, 77 (4) e25–e197

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Predictors of Mortality in Moderate AS

- Low EF (<60%)
- Atrial Fibrillation
- Diastolic Dysfunction
- Fast Progression of AS (>0.3 m/s/year)
- Low stroke volume index (<35 cc/m^2)
- Elevated BNP
- Elevated AV Calcium Score by CT

Lancelotti et al. JAMA Cardiol. 2018; 3 (11);1060-8
Strange et al. J Am Coll Cardiol 2019;74:1851–63
Delesalle et al. JAHA 2019;8

Murphy et al. Am J Cardiol.2019;124:1924–1931
Benfari et al. JASE; 2019:34 ;3:237-244
Ito et al. JASE 2021; 34(3):248-256

Samad et al. EHJ; 2016: 37, 2276–2286
Van Gils et al. JACC 2017;69:2383–92
Moon et al. KCJ; 2020 50(9):791-800

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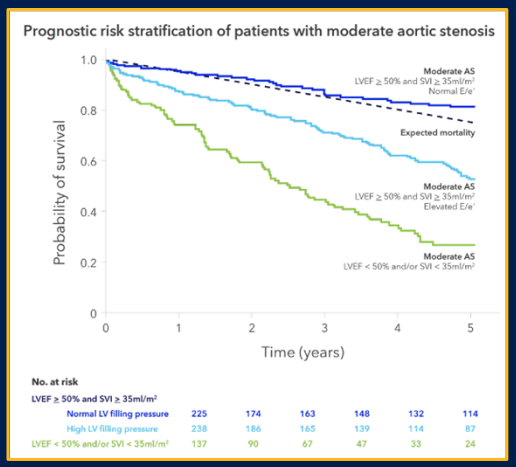
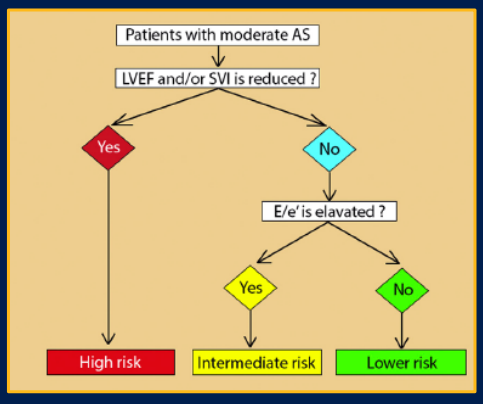
Beyond LVEF …





Ito S et al. JASE 2020

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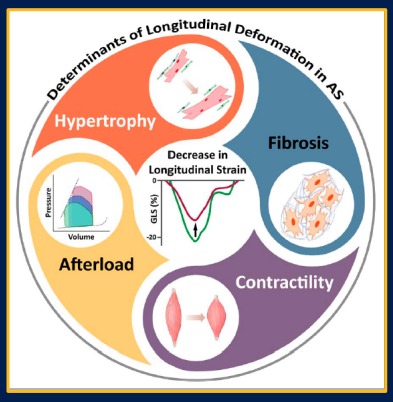
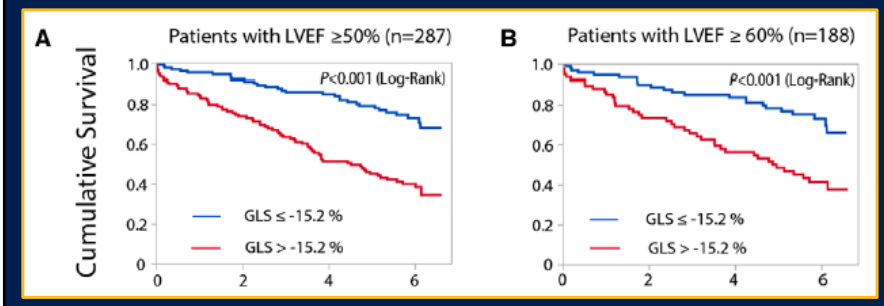
Global Longitudinal Strain



Speckle Tracking Echocardiography
Gatekeeper for AS
Prognostic value
Early Intervention

Lakatos et al. Circ Cardiovascular Imaging 2020;13:e010711

Global Longitudinal Strain
Moderate AS

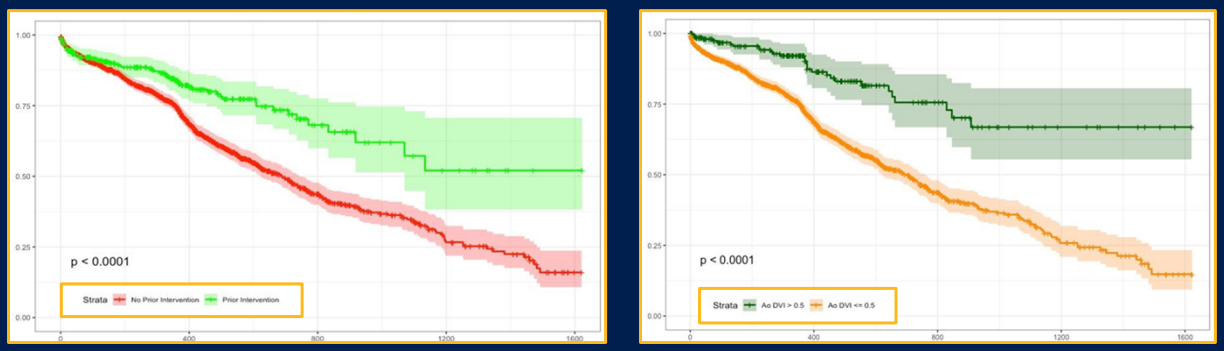


Higher Mortality
GLS > -15.2%
Including AVR pts

Zhu et al. Circ Cardiovascular Imaging 2020;13:e009958

Artificial Intelligence for Disease Monitoring

Personalized Timely Surveillance For Evaluation and Treatment



Courtesy of Mpirik

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Redefining Aortic Stenosis

Key Points

- Accurate diagnosis and follow-up
- Key echocardiographic parameters
- New clinical pathways being established
- More timely intervention
- Artificial intelligence

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The Rationale for TAVR in Moderate Aortic Stenosis

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Roger L. and Lynn C. Headrick Family Chair
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Abbott Northwestern Hospital

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Disclosures

- Consulting or Advisory Board: Abbott Structural, Anteris, Boston Scientific, Edwards Lifesciences, Foldax, Medtronic, Shifamed, VDyne, WL Gore
- Institutional Research: Abbott Structural, Boston Scientific, Edwards Lifesciences, Medtronic
- National P.I.: EXPAND II, HighLife (US), SOAR EFS, SUMMIT MAC, TRILUMINATE II, VDyne

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Why TAVR for "moderate" AS?

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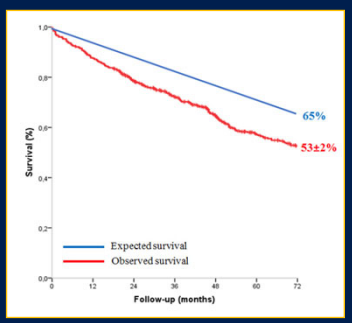
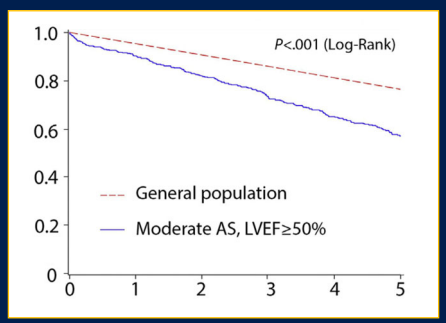
Moderate Aortic Stenosis and Survival

AMIENS UNIVERSITY



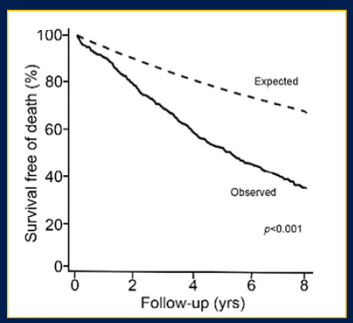
All Comers

MAYO CLINIC



Preserved EF

MINNEAPOLIS HEART INSTITUTE



Normal EF, no morbidities

7 to 8% annual mortality

Ito S et al. JASE 2020; Delesalle G., et al. JAHA 2019; Du Y et al. BMC Cardiovasc Dis 2021

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Prevalence of Moderate Aortic Stenosis

Allina Health System

10x more than severe

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Moderate Aortic Stenosis and HF

2020 Valve Guidelines for AVR

COR	LOE	RECOMMENDATIONS
1	A	1. In adults with severe high-gradient AS (Stage D1) and symptoms of exertional dyspnea, HF, angina, syncope, or presyncope by history or on exercise testing, AVR is indicated (1-7).
1	B-NR	2. In asymptomatic patients with severe AS and an LVEF <50% (Stage C2), AVR is indicated (8-11).
1	B-NR	3. In asymptomatic patients with severe AS (Stage C1) who are undergoing cardiac surgery for other indications, AVR is indicated (12-16).
1	B-NR	4. In symptomatic patients with low-flow, low-gradient severe AS with reduced LVEF (Stage D2), AVR is recommended (17-24).
1	B-NR	5. In symptomatic patients with low-flow, low-gradient severe AS with normal LVEF (Stage D3), AVR is recommended if AS is the most likely cause of symptoms (25-27).
2a	B-NR	6. In apparently asymptomatic patients with severe AS (Stage C1) and low surgical risk, AVR is reasonable when an exercise test demonstrates decreased exercise tolerance (normalized for age and sex) or a fall in systolic blood pressure of ≥10 mm Hg from baseline to peak exercise (13,28-30).
2a	B-R	7. In asymptomatic patients with very severe AS (defined as an aortic velocity of ≥5 m/s) and low surgical risk, AVR is reasonable (15,31-35).
2a	B-NR	8. In apparently asymptomatic patients with severe AS (Stage C1) and low surgical risk, AVR is reasonable when the serum B-type natriuretic peptide (BNP) level is >3 times normal (32,36-38).
2a	B-NR	9. In asymptomatic patients with high-gradient severe AS (Stage C1) and low surgical risk, AVR is reasonable when serial testing shows an increase in aortic velocity ≥0.3 m/s per year (39,40).
2b	B-NR	10. In asymptomatic patients with severe high-gradient AS (Stage C1) and a progressive decrease in LVEF on at least 3 serial imaging studies to <60%, AVR may be considered (8-11,33).
2b	C-EO	11. In patients with moderate AS (Stage B) who are undergoing cardiac surgery for other indications, AVR may be considered.

None for isolated moderate AS

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Moderate Aortic Stenosis

Many patients + Poor survival + No guidelines

Rationale for Therapeutic Trials

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Transcatheter AVR

Clinical Trials of TAVR vs. Surveillance for "moderate" AS

PROGRESS (n=750)
P.I.'s: Philipp Généreux, Raj Makkar, Jeroen Bax

EXPAND II (n=650)
P.I.'s: Josep Rodes-Cabau, Paul Sorajja, Stephan Windecker

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TAVR Trials in Moderate AS

Enrollment Criteria for EXPAND II

Moderate AS	Symptomatic	At Risk
Vmax, ≥3.0 to <4.0 m/s Grad, ≥20 to <40 mmHg AVA, >1.0 to 1.5 cm^2	Dyspnea Angina Fatigue Syncope	HF hosp. past 1 yr NT proBNP ≥600 GLS ≤ -15% E/e' ≥14.0

Notable exclusions: Sievers 0 or 2, CAD, amyloidosis

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TAVR Trials in Moderate AS

Treatment Plan

Moderate AS
Symptomatic
At Risk

→ *1:1 Randomization* →

TAVR vs. GDMT

→ Clinical endpoints for 10 years

Not natural AV progession

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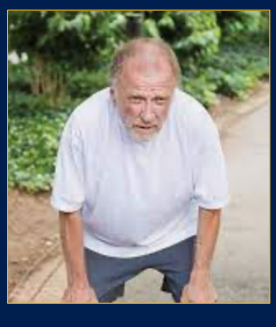
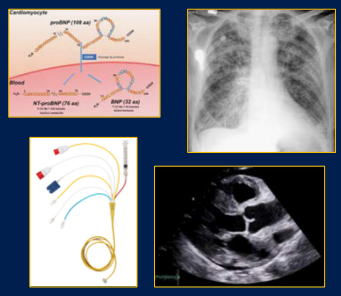
Medical Instability Requiring Treatment

Part of the Clinical Effectiveness Endpoint for EXPAND II

Worse symptoms



Laboratory decompensation



Intervention

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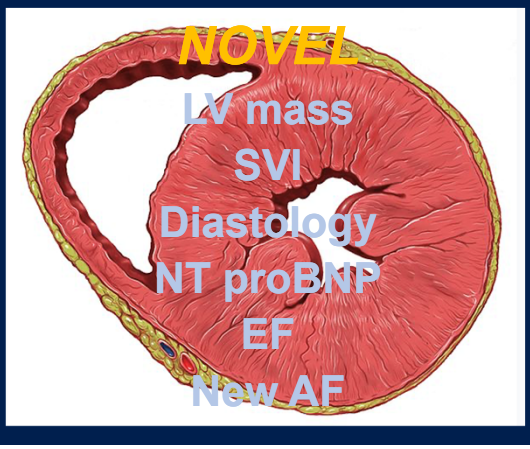
TAVR Trials in Moderate AS

What We Will Learn From Scientific Study

USUAL

Safety
KCCQ QOL
Survival
HF events
Unplanned CV hosp.



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MHIF Leadership in EXPAND II

Dr. Paul Sorajja
U.S. National P.I.

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Transcatheter AVR

Clinical Trials of TAVR vs. Surveillance for "moderate" AS

PROGRESS (n=750)
P.I.'s: Philipp Généreux, Raj Makkar, Jeroen Bax

2-yr composite of death, stroke, unplanned cv hospitalization

EXPAND II (n=650)
P.I.'s: Josep Rodes-Cabau, Paul Sorajja, Stephan Windecker

30-day MACE
2-yr composite of death, unplanned procedure/AV-related hospitalization

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Key Points for Moderate AS

- Rate of progression is variable
- May cause cardiac damage
- Associated with (or may cause) poor survival
- Randomized trials will determine benefit of AVR

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