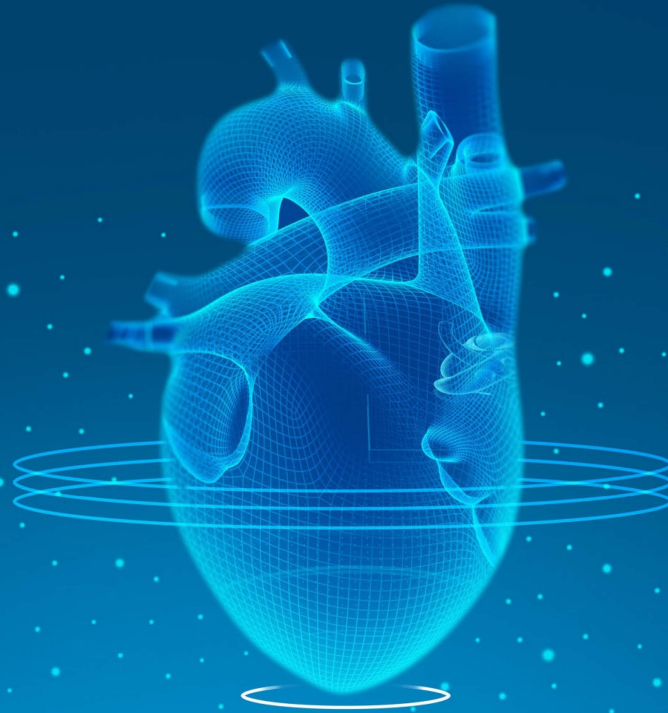




# GRAND ROUNDS



# Modern Definitions of Aortic Stenosis The Frontier

Nadira Hamid, MD  
Valve Science Center, Minneapolis Heart Institute Foundation  
Abbott Northwestern Hospital



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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<sup>2</sup>

PV ≥4 m/s

Mean grad >40 mmHg



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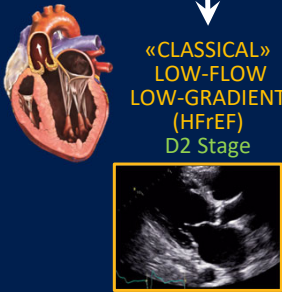
# Discordant Grading – Low Gradient AS

AVA≤1.0 cm<sup>2</sup>    MG<40 mmHg

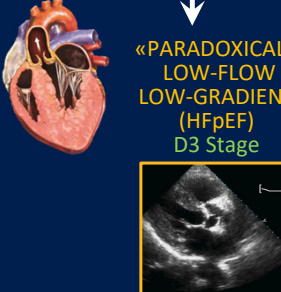
<50% ← LVEF → >50%

↓ SVi

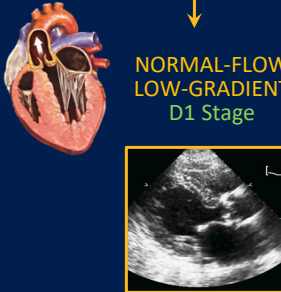
<35 mL/m<sup>2</sup> → >35 mL/m<sup>2</sup>




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



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




NORMAL-FLOW  
LOW-GRADIENT  
D1 Stage



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Courtesy of Philippe Pibarot



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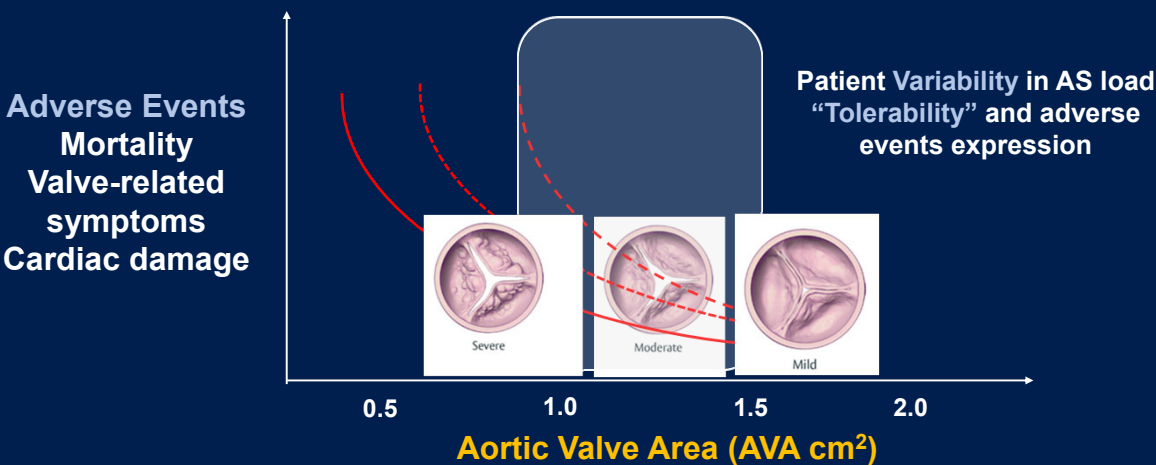
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# What is the Threshold For Adverse Events?



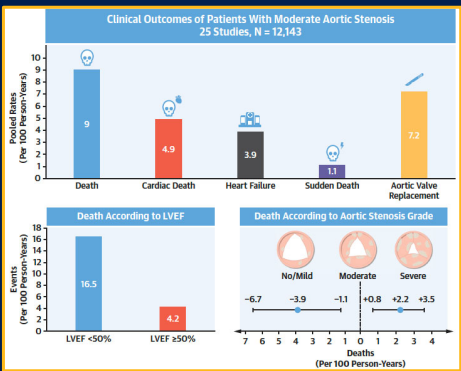
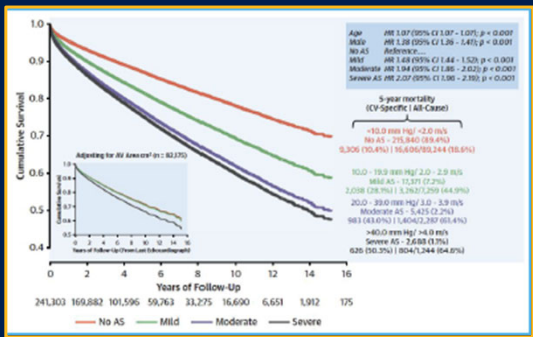
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# Is Moderate AS Bad?



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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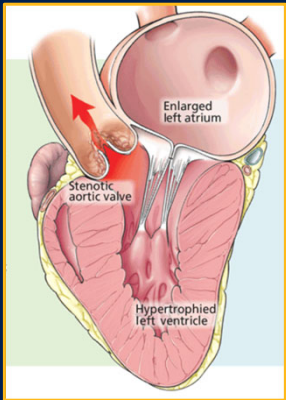
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# Why Moderate AS is Bad

## Cardiac Consequences

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



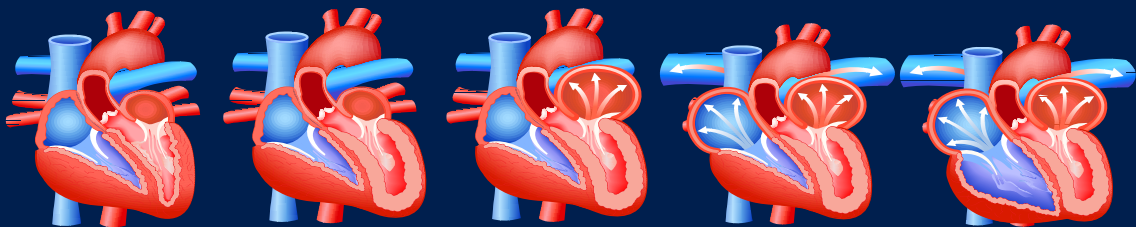
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# Cardiac Damage in AS Impairs Survival Often Silent



Stage 0 No damage	Stage 1 LV damage	Stage 2 LA/Mitral damage	Stage 3 PA/Tricuspid damage	Stage 4 RV damage
	Increased LV Mass Index >115 g/m <sup>2</sup> Male >95 g/m <sup>2</sup> Female	Indexed left atrial volume >34mL/m <sup>2</sup>	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)

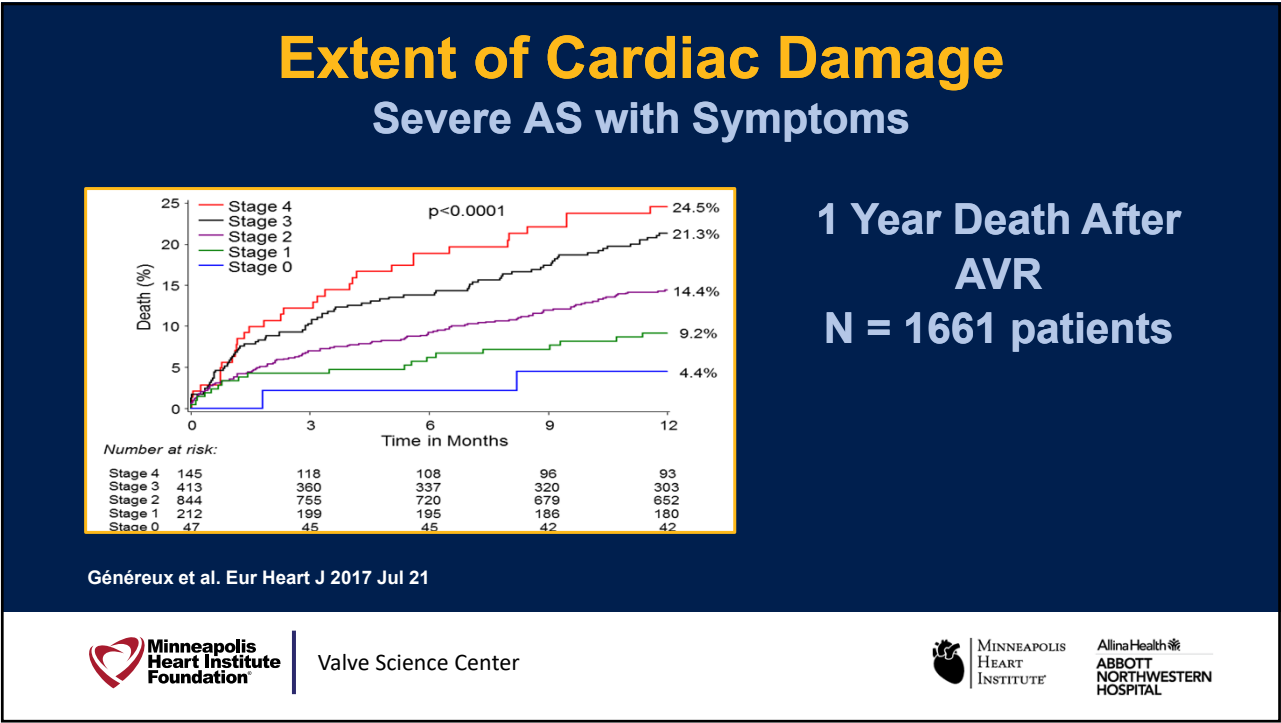


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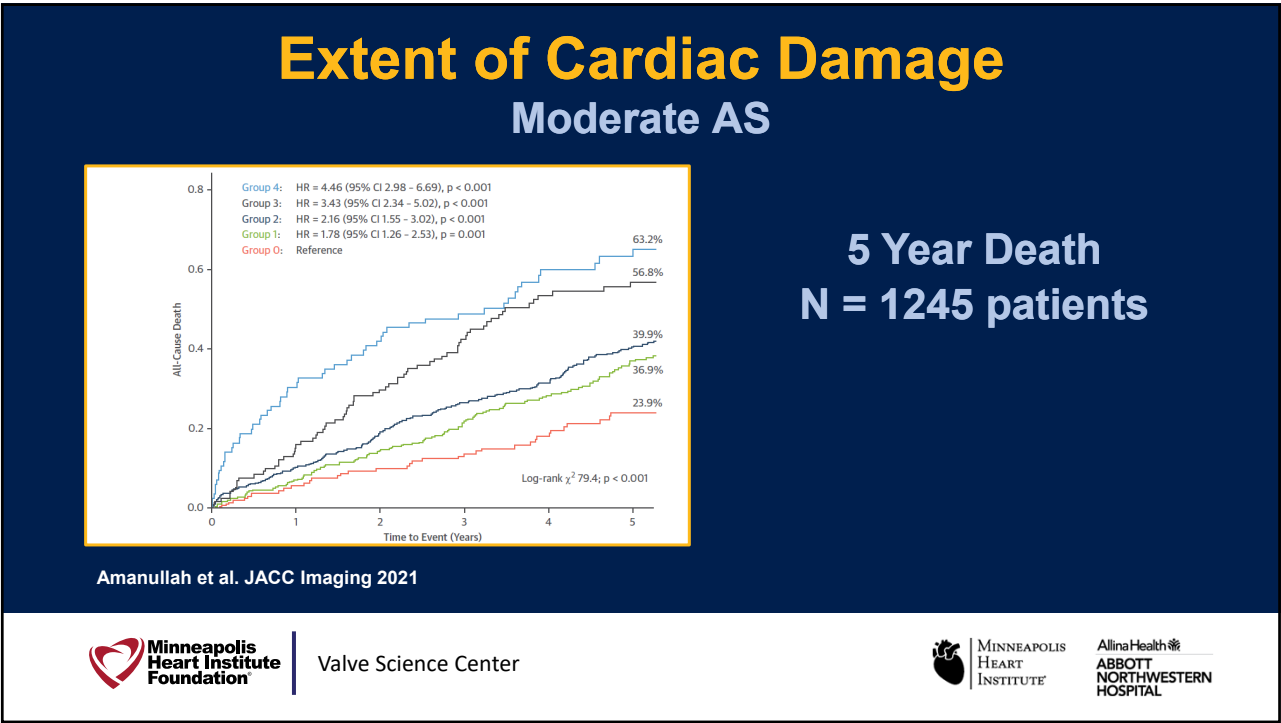


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# How do we improve detection of AS patients at risk?



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# Follow-up in Patients With Aortic Stenosis

Aortic Severity	Follow-up Recommendation
Mild ( $V_{max}$ 2.0–2.9 m/s)	Every 3-5 years
<b>Moderate (<math>V_{max}</math> 3.0–3.9 m/s)</b>	<b>Every 1-2 years</b>
Severe Asymptomatic ( $V_{max} \geq 4$ m/s)	Every 6-12 months

$V_{max}$  = 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<sup>2</sup>)
- 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



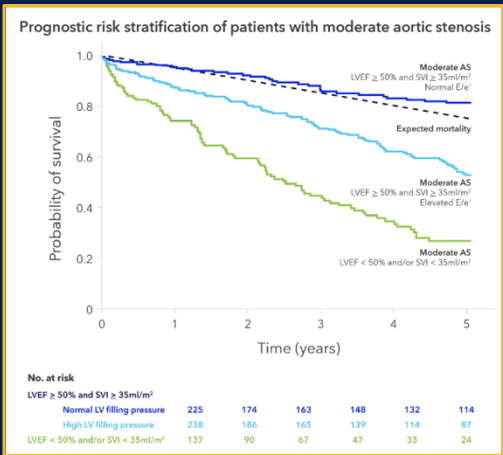
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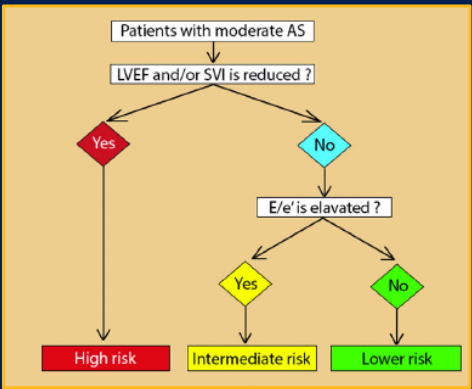
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# Beyond LVEF ...



Ito S et al. JASE 2020



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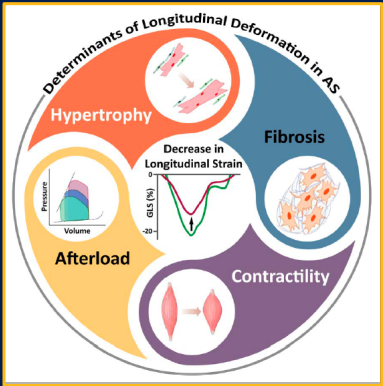


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# Global Longitudinal Strain



Speckle Tracking Echocardiography  
Gatekeeper for AS  
Prognostic value  
Early Intervention

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

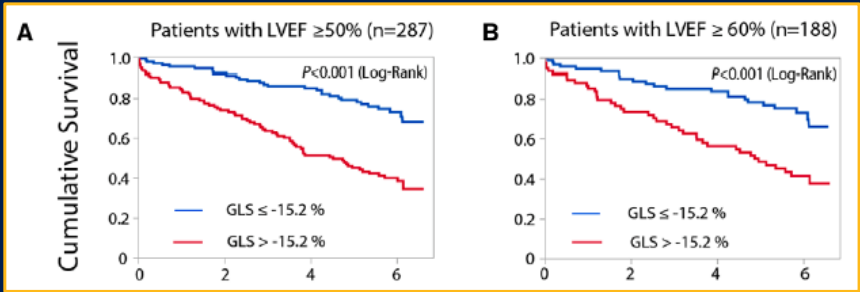


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# Global Longitudinal Strain Moderate AS



Higher Mortality  
GLS > -15.2%  
Including AVR  
pts

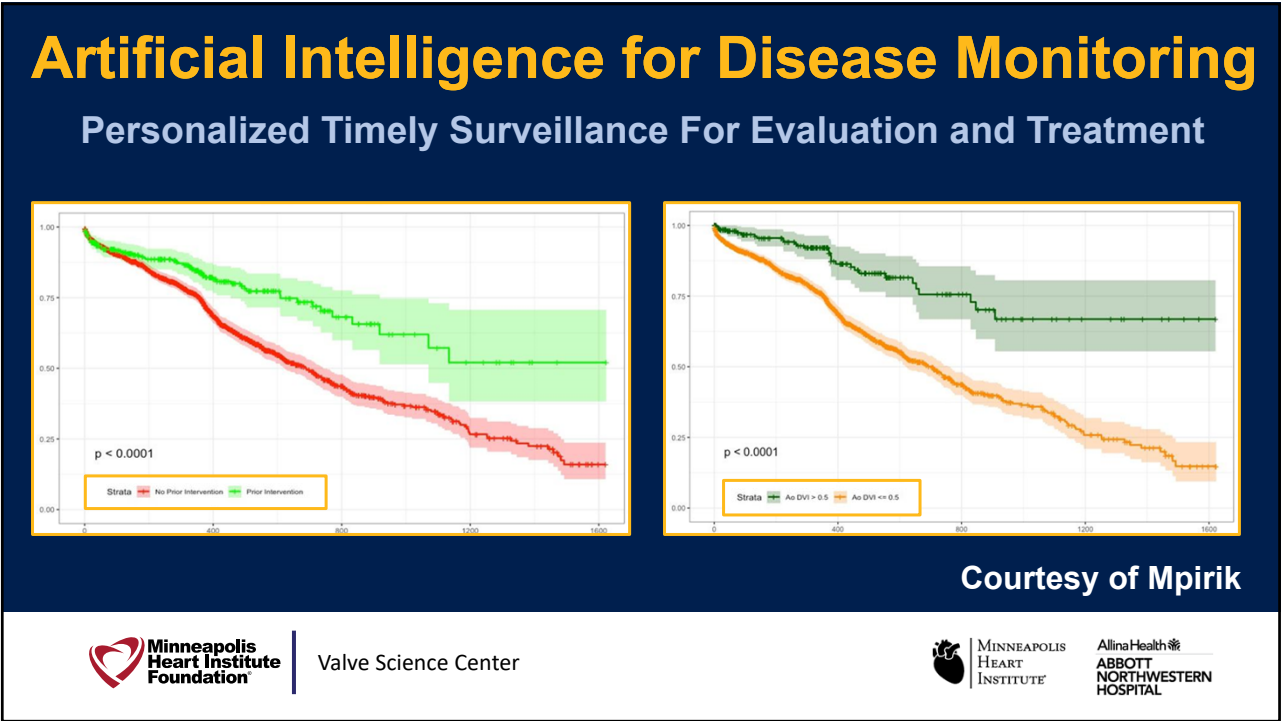
Zhu et al. Circ Cardiovascular Imaging 2020;13:e009958



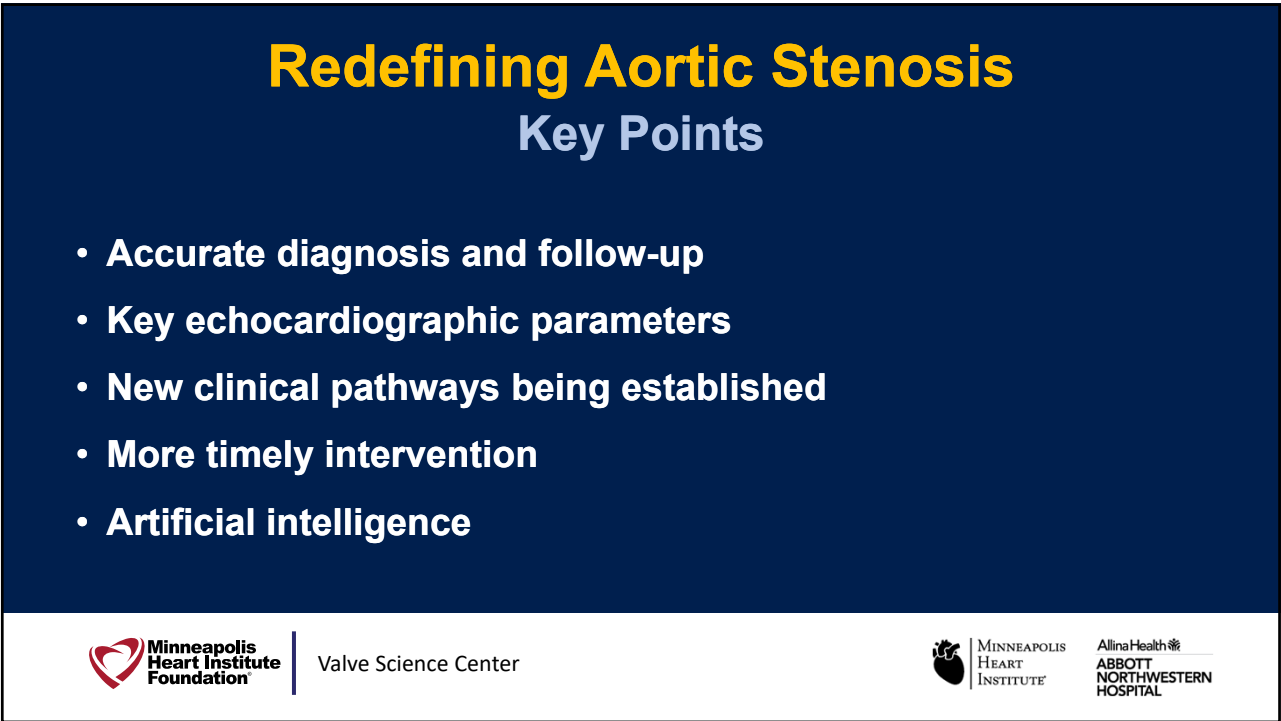
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Thank you!

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# The Rationale for TAVR in Moderate Aortic Stenosis



Paul Sorajja, MD  
Roger L. and Lynn C. Headrick Family Chair  
Valve Science Center, Minneapolis Heart Institute Foundation  
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?



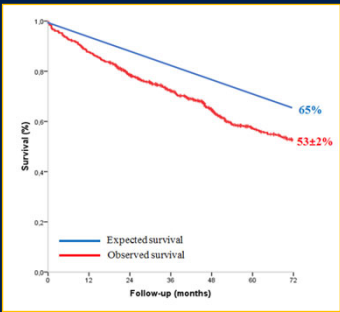
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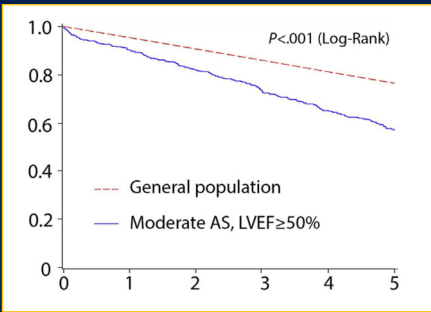
## Moderate Aortic Stenosis and Survival

AMIENS UNIVERSITY



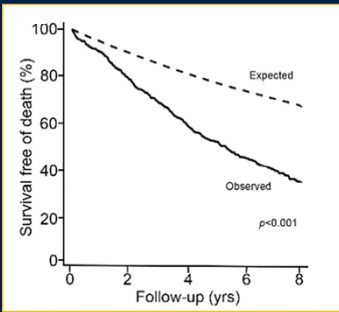
All Comers

MAYO CLINIC



Preserved EF

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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



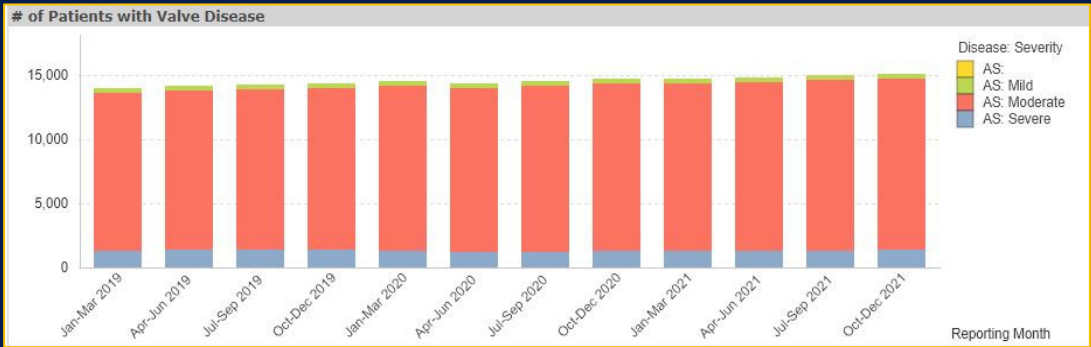
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# Prevalence of Moderate Aortic Stenosis

## Allina Health System



10x more than severe



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# Moderate Aortic Stenosis and HF

## 2020 Valve Guidelines for AVR

COE	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 mmHg 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).
2a	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).
2a	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 G  n  reux, 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

Vmax, ≥3.0 to <4.0 m/s  
Grad, ≥20 to <40 mmHg  
AVA, >1.0 to 1.5 cm<sup>2</sup>


#### Symptomatic

Dyspnea  
Angina  
Fatigue  
Syncope


#### At Risk

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 progression



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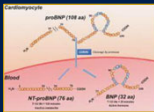
# Medical Instability Requiring Treatment

## Part of the Clinical Effectiveness Endpoint for EXPAND II

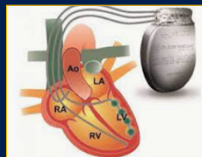



### Worse symptoms




### 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.

### NOVEL


LV mass  
SVI  
Diastology  
NT proBNP  
EF  
New AF



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# MHIF Leadership in EXPAND II



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



**Dr. Joao Cavalcante**  
CT/MRI Core Lab



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# Transcatheter AVR

Clinical Trials of TAVR vs. Surveillance for “moderate” AS

## PROGRESS (n=750)

P.I.'s: Philipp G  n  reux, 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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# Thank you!

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Tel: 507-513-1357



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