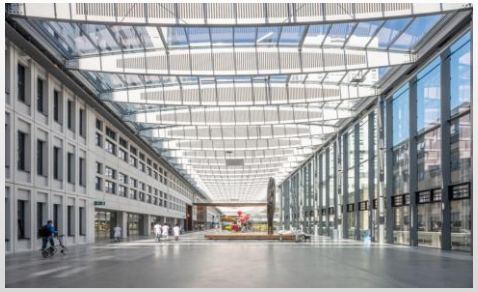

# Moderate AS in HFrEF

# Time to Treat is Now & Future Expectation from RCT

**Prof. Dr. Nicolas M. Van Mieghem**
**Professor and Director of Interventional Cardiology**
**Thoraxcenter, Cardiovascular Institute,**
**Erasmus University Medical Center**
**Rotterdam**

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# My Conflict of Interest

- Research Grant Support: Abbott, Boston Scientific, Edwards Lifesciences, Medtronic, PulseCath BV, Daiichi Sankyo , Teleflex, Astra Zeneca, HeartFlow
- Advisory board: Abbott, Ancora, Boston Scientific, Medtronic, PulseCath BV, Daiichi Sankyo, Abiomed, JenaValve, Anteris, Bolt Medical, Siemens, Pie Medical, Luma Vision, FEops, Materialise

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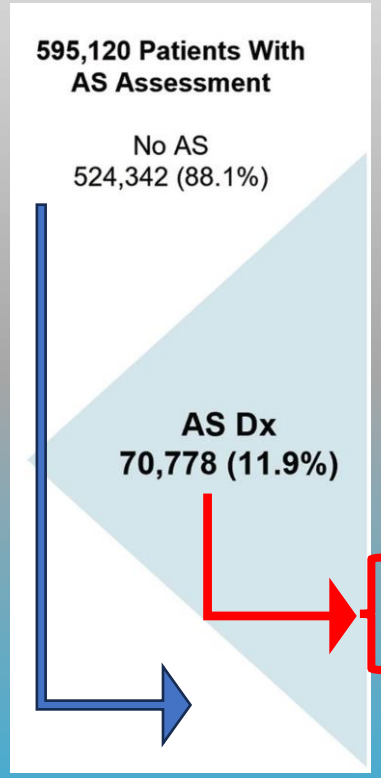
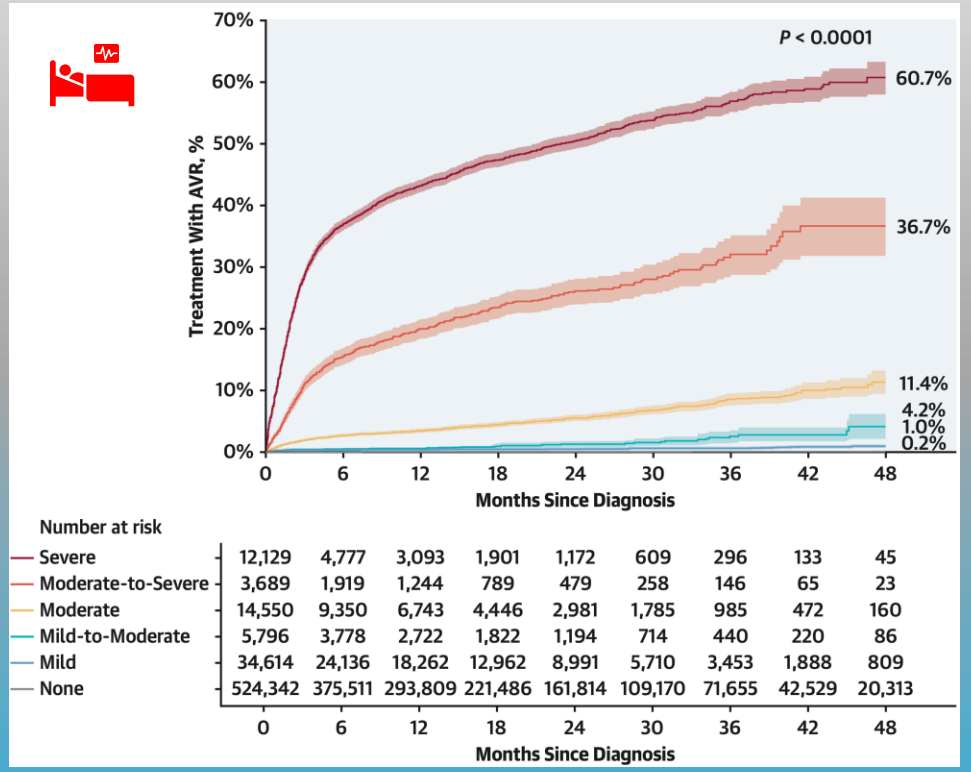
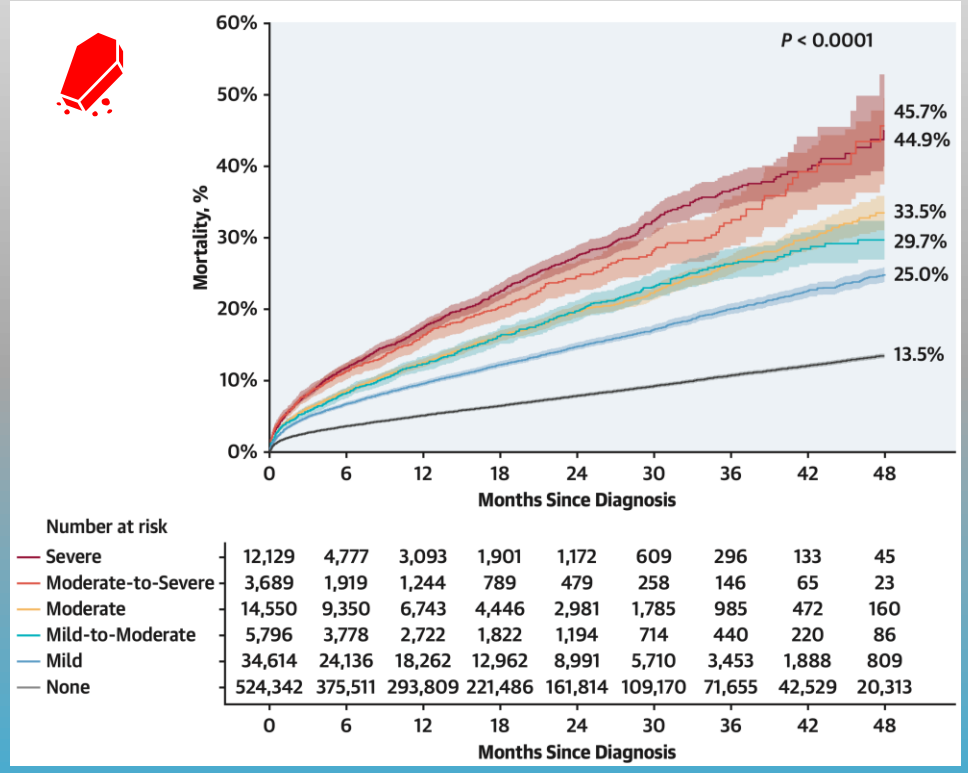
# Outcome after Echo diagnosis of Aortic Stenosis




**Real-world data set including 1,669,536 echocardiographic reports (1,085,850 patients) from 24 U.S. hospitals (egnite Database)**

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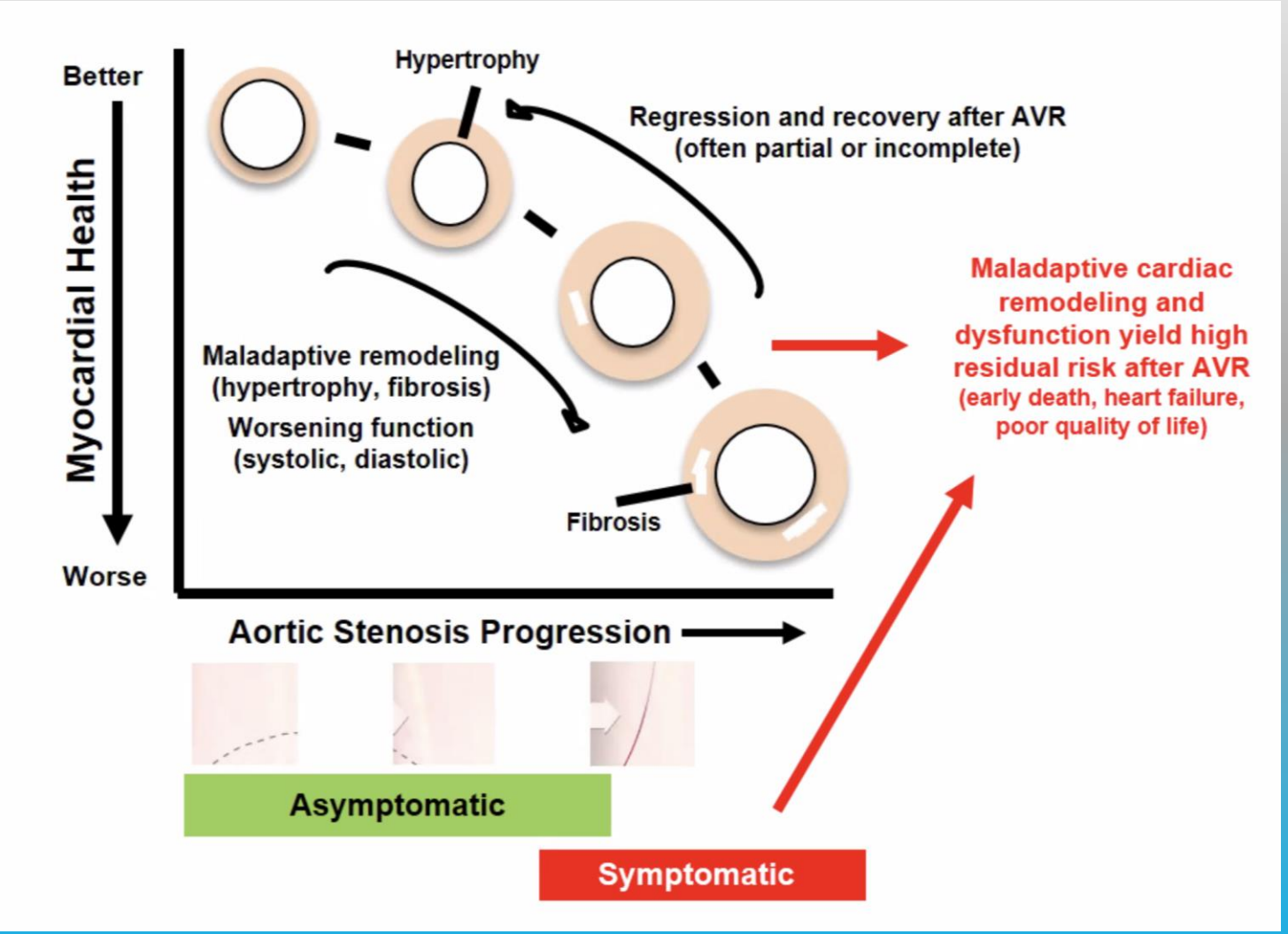
Genereux et al. JACC 2023;82:2101-09

# AS & maladaptive remodeling & fibrosis




Lindman et al. JACC CV Imaging 2020;13:481-93
Courtesy M Brenner & D Burkhoff

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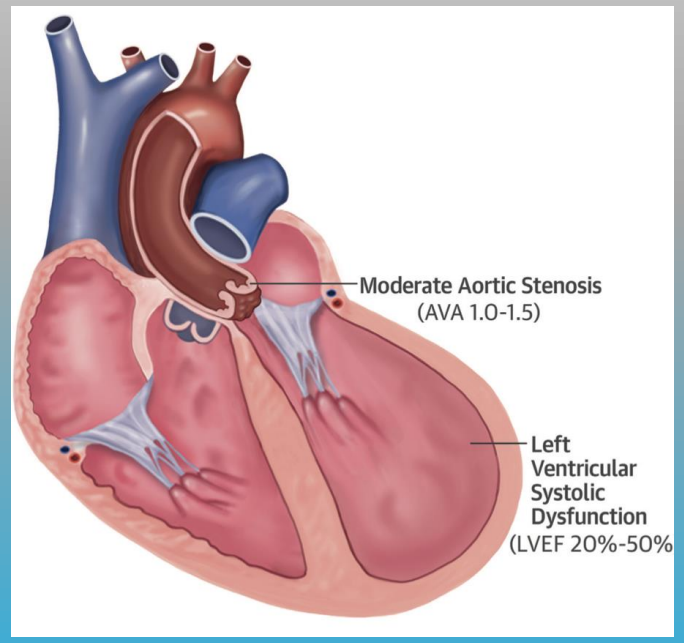
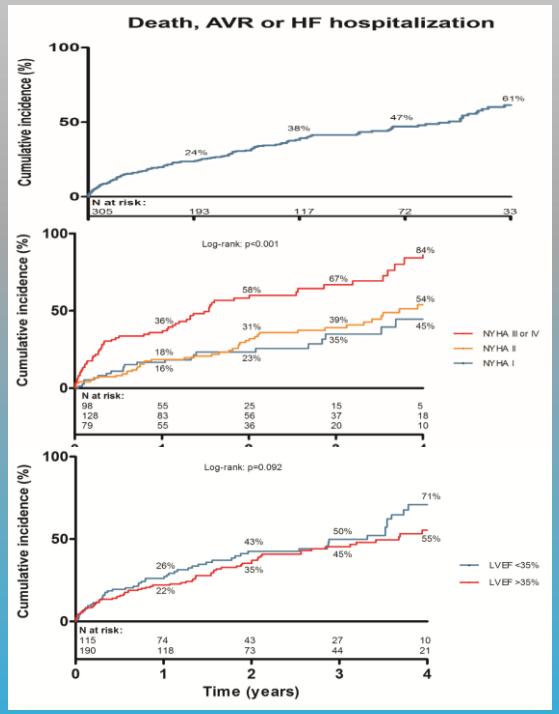
# Moderate AS & HFrEF

- ✓ Multi-center Collaboration
- ✓ 310 patients with HFrEF & moderate AS
- ✓ Mean age 73, mean EF 38%, AVA 1.24 $cm^2$



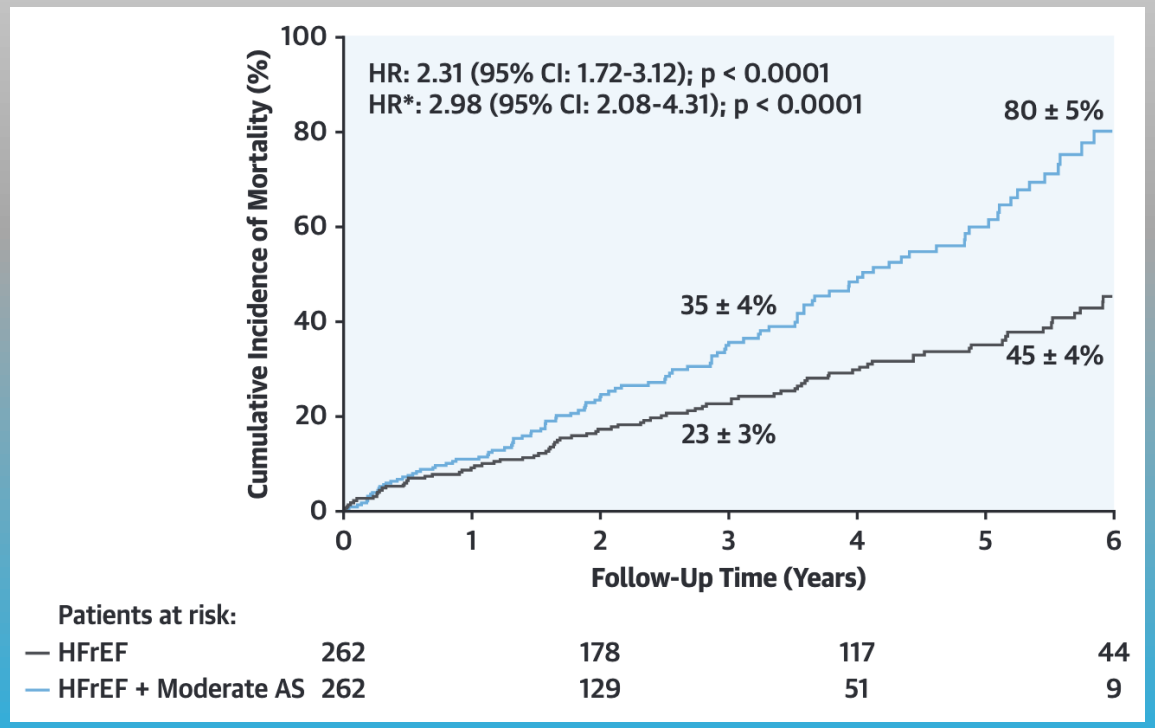

| | |
|---|---|
| NYHA I | 26% |
| NYHA II | 42% |
| NYHA III | 28% |
| NYHA IV | 4% |

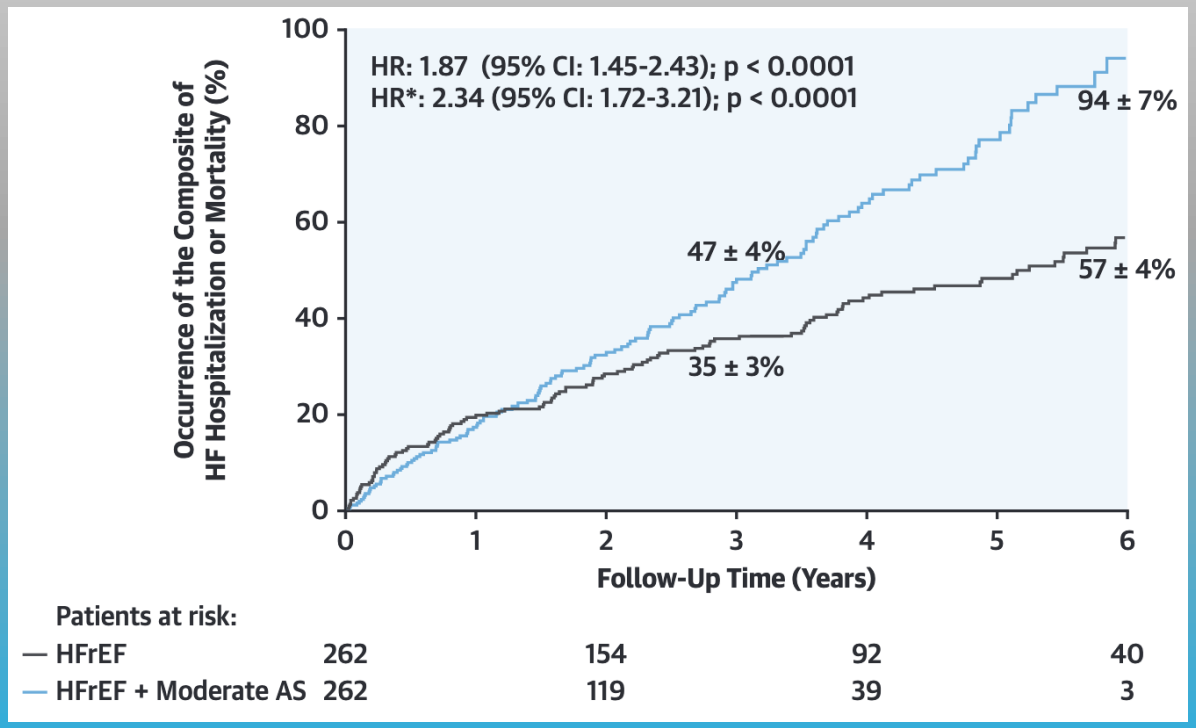



Van Gils et al. JACC 2017;69:2383-92

# Impact of Moderate AS in HFrEF

- ✓ **Multi-center Collaboration**
- ✓ **262 matched pairs of patients with HFrEF + or - moderate AS**



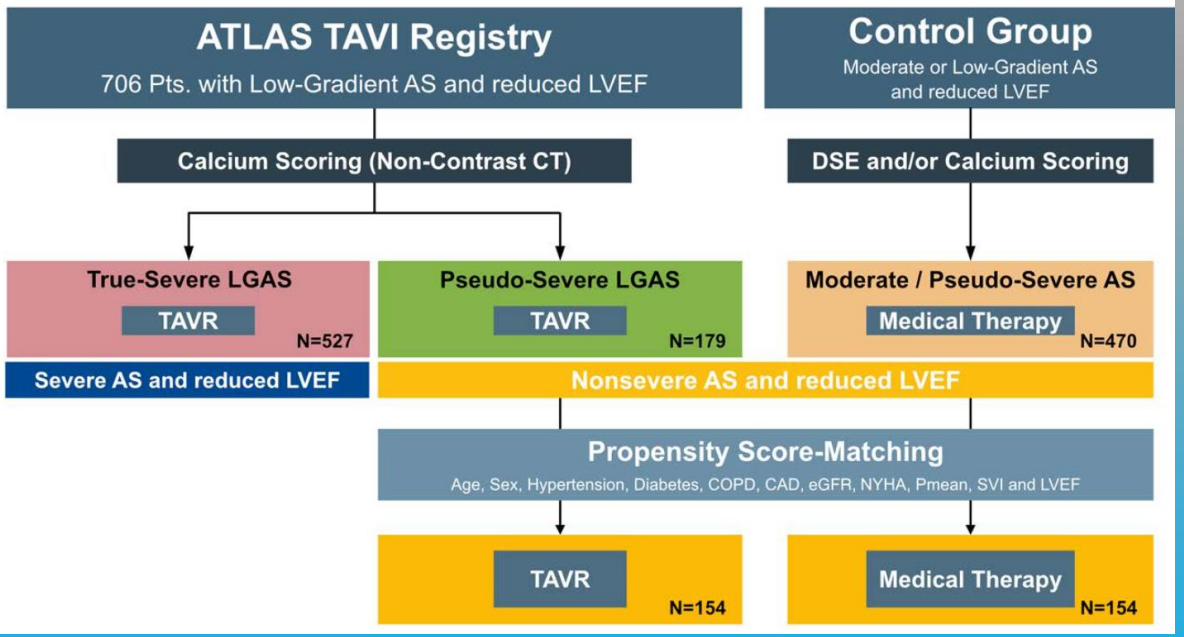



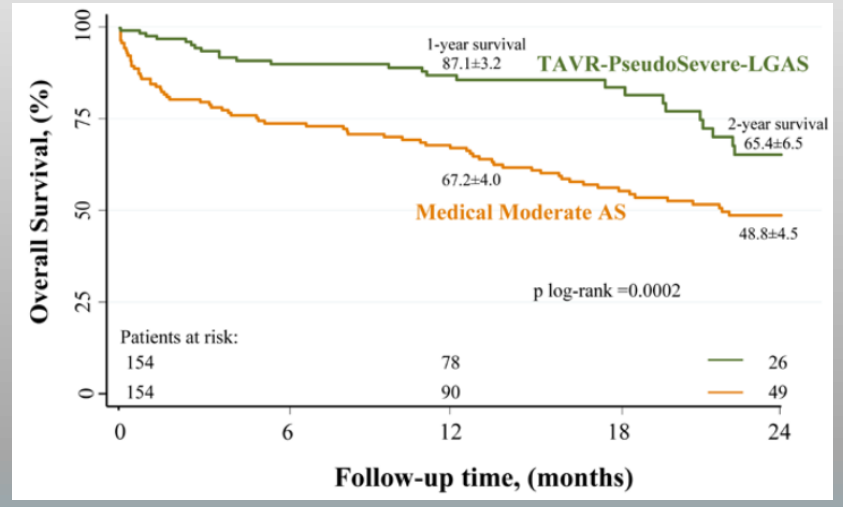

Jean et al. JACC 2021;77:2796-803

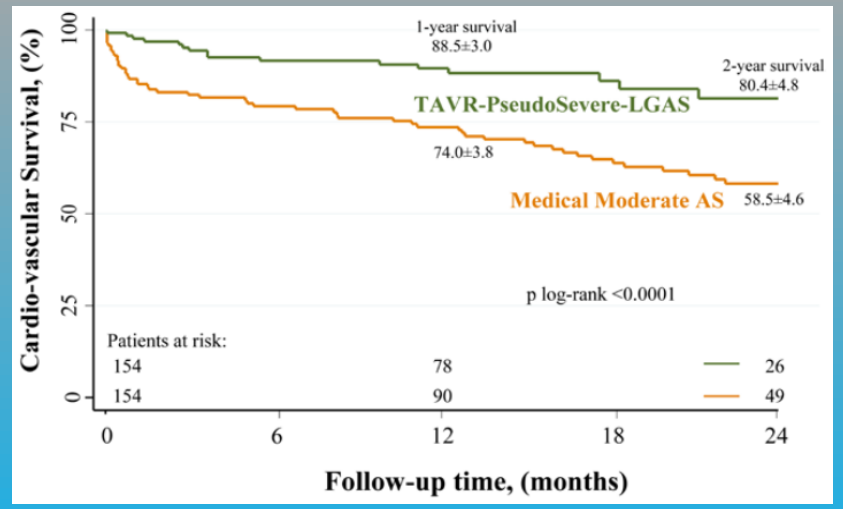
# TAVI for Moderate AS & HFrEF

## Transcatheter Aortic Valve Replacement in Patients With Reduced Ejection Fraction and Nonsevere Aortic Stenosis

Sebastian Ludwig, MD*; Niklas Schofer, MD*; Mohamed Abdel-Wahab, MD; Marina Urena, MD; Guillaume Jean, MD; Matthias Renker, MD; Christian W. Hamm, MD; Holger Thiele, MD; Bernard Iung, MD; Joris F. Ooms, MD; Maya Wiessman, MD; Nils S.B. Mogensen, MD; Benjamin Longère, MD; Nils Perrin, MD; Walid Ben Ali, MD, PhD; Augustin Coisne, MD, PhD; Jordi S. Dahl, MD, PhD; Nicolas M. Van Mieghem, MD; Ran Kornowski, MD; Won-Keun Kim, MD; Marie-Annick Clavel, DVM, PhD




Ludwig et al. Circ CVI 2023;16

# Beyond EF – The Cardiac Damage Concept

- ✓ N = 735 asymptomatic patients with at least moderate AS & EF > 50%
- ✓ N = 450 (61%) with severe AS

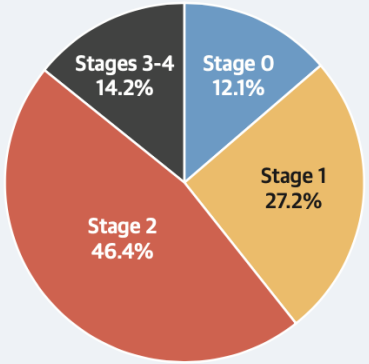
## Staging Classification

**Stages 3-4: Pulmonary or tricuspid valve damage, or RV damage or subclinical heart failure**
- Pulmonary hypertension (SPAP ≥60 mm Hg)
- Tricuspid regurgitation (≥moderate)
- RV systolic dysfunction (≥moderate)
- Moderate to severe low-flow (stroke volume index <30 ml/m²)

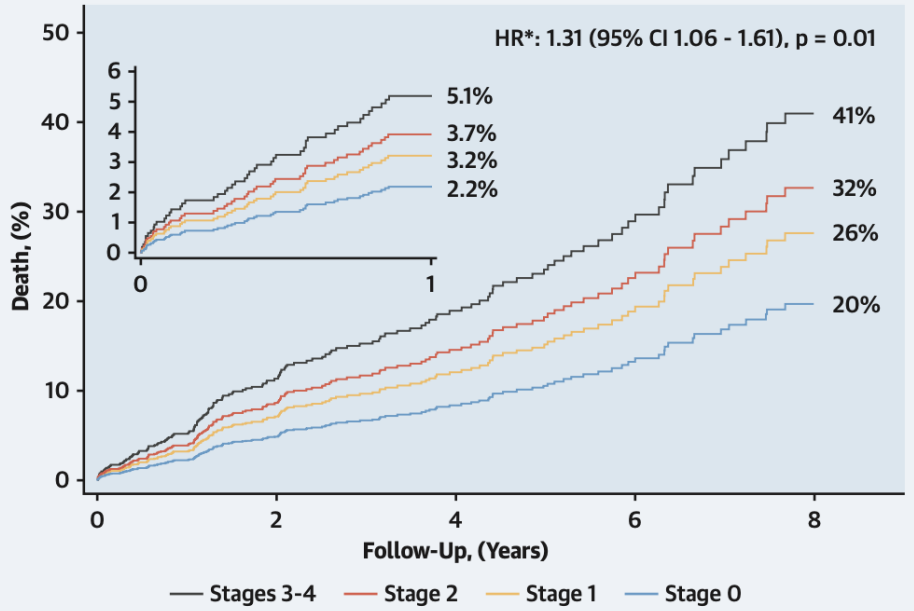
**Stage 2: LA or mitral valve damage**
- Left atrial enlargement (LA volume >34 ml/m²)
- Atrial fibrillation
- Mitral regurgitation (≥moderate)

**Stage 1: LV damage**
- LV hypertrophy (LV mass index >95 g/m² women; >115 g/m² men)
- Grade ≥ II LV diastolic dysfunction
- Impaired LV global longitudinal strain (≤|15%|)
- Subclinical LV systolic dysfunction (LVEF <60%)

**Stage 0: No cardiac damage**




## All-Cause Mortality




Tastet et al. JACC 2019;74:550-63

# RCT on TAVI in moderate AS

**TAVR UNLOAD study design**

- International, multicentre trial
- Study cohort: patients with heart failure with LVEF <5[illegible] and moderate aortic stenosis

domization 1:1

= 300

Transfemora[illegible] plus optimal [illegible] failure therapy

Optimal heart failure therapy

- Follow-up at 1 mo[illegible], 1 year and 2 years
- Clinical parameters[illegible] echocardiography and quality of life

Primary end point: composite of [illegible]th, disabling stroke, hospitalization due to hea[illegible]otomatic aortic valve disease or nondisablin[illegible]nd change in KCCQ relative to baseline

RESULTS @ TCT 2024

**PROGRESS study design**

Local Heart Team, Case Review Board & Core Lab Assessments

Moderate[illegible] ymptoms or cardiac damage / dysfunction [illegible]te for transfemoral access

[illegible]tion

TAVR
(SAPIEN 3 Valve Platform)

Clinical Surveillance
[illegible]tic valve replacement is allowed for [illegible] that develop severe AS)

Primary Endpoint: All-Cause Mortality, Stroke, and Unp[illegible] Hospitalization at 2 Years

Follow-up: Annually Through 10[illegible]

Enrollment complete 12/2023

**EXPAND TAVR II RCT**

**Patients with moderate AS, EF > 20%, NYHA≥2 &**

- **HF event < 1 calendar year prior to qualifying echo**
- **NT proBNP ≥ 600 pg/ml**
- **GLT ≤15% or**
- **E/e' ≥ 14.0**

**1:1 Randomization N = 650**

**TAVR + GDMT**

**GDMT**

- **Safety Composite rate @ 30 days of all-cause mortality, all-stroke, life threatening or fatal bleeding, acute kidney injury, hospitalization due to device or procedure-related complication, or valve dysfunction requiring reintervention.**
- **Efficacy Composite rate @ 2 years of all-cause mortality or unplanned procedure-related or aortic valve related hospitalization.**

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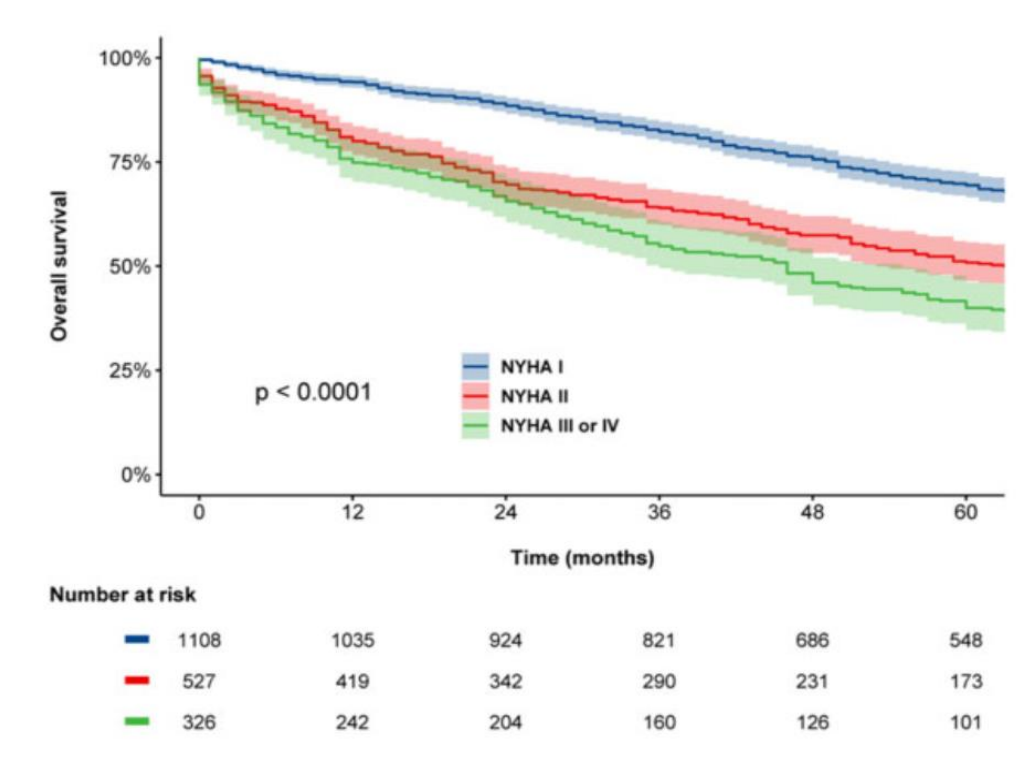
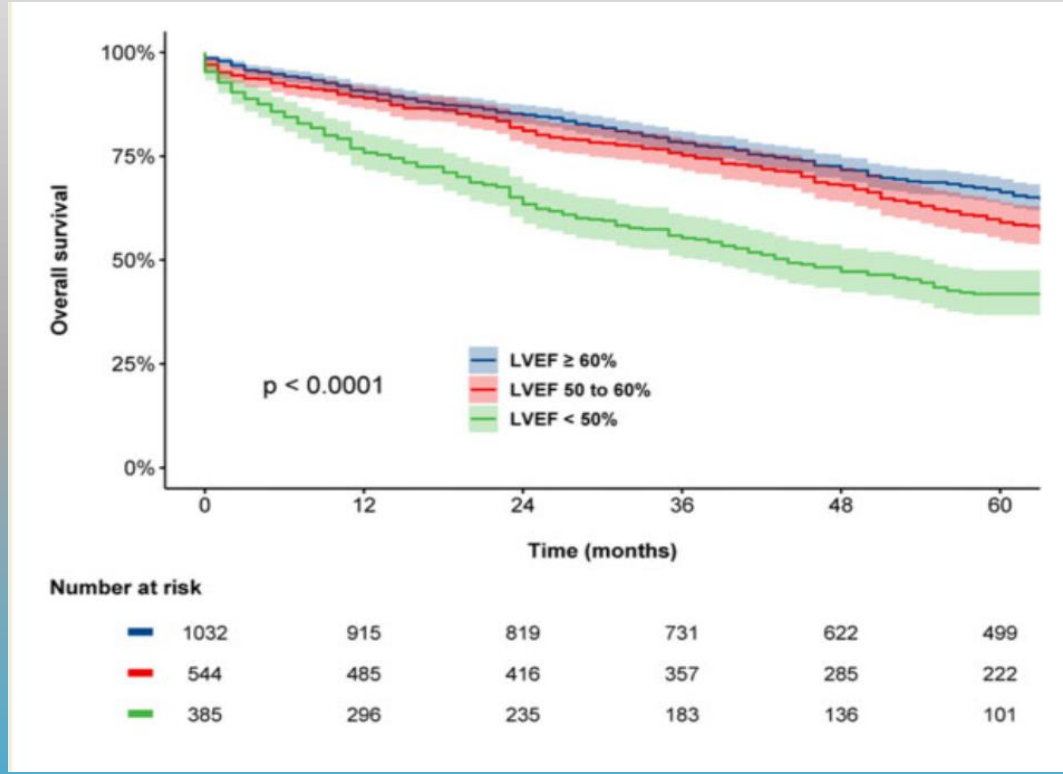
# Moderate AS – Impact of EF




**N = 1961 patients with moderate AS**
**EF < 50% in 385 patients (20%)**

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Stassen et al. EHJ CV Imaging 2022;23:790-9

# Immediate TAVI Effects on Hemodynamics

- 18 patients treated with TAVI
  - ✓ Moderate AS
  - ✓ EF 20 – 50%

| | |
|---|---|
| Age (years) | 77.4 ± 7.3 |
| Male sex (%) | 77.7 |
| LVEF (%) | 37.7 ± 12.7 |
| Agatston score, males | 1923 ± 737 |
| Agatston score, females | 1461 ± 666 |
| AOV annulus area ($mm^2$) | 472.7 ± 55.7 |
| SAPIEN3 size used (mm) | 26.7 ± 1.6 |
| Sapien3, 23mm (n) | 1 |
| Sapien3, 26mm (n) | 12 |
| Sapien3, 29mm (n) | 5 |

| Pre procedural TTE measurements | |
|---|---|
| AOV mean gradient (mmHg) | 20.5 ± 6.3 |
| AOV peak gradient (mmHg) | 34.4 ± 13.2 |
| AOV Vmax (m/s) | 3.0 ± 0.4 |
| AR grade (0-5) | 1.9 ± 1.4 |
| **Pre procedural invasive measurements** | |
| AOV mean gradient (mmHg) | 22.6 ± 8.6 |
| AOV peak gradient (mmHg) | 25.5 ± 9.4 |

| Post procedural TTE measurements | |
|---|---|
| AOV mean gradient (mmHg) | 10.3 ± 3.7 |
| AOV peak gradient (mmHg) | 16.4 ± 6.8 |
| AOV Vmax (m/s) | 2.0 ± 0.4 |
| AR grade (0-5) | 0.9 ± 1.3 |
| **Post procedural invasive measurements** | |
| AOV mean gradient (mmHg) | 4.0 ± 2.4 |
| AOV peak gradient (mmHg) | 8.2 ± 4.9 |

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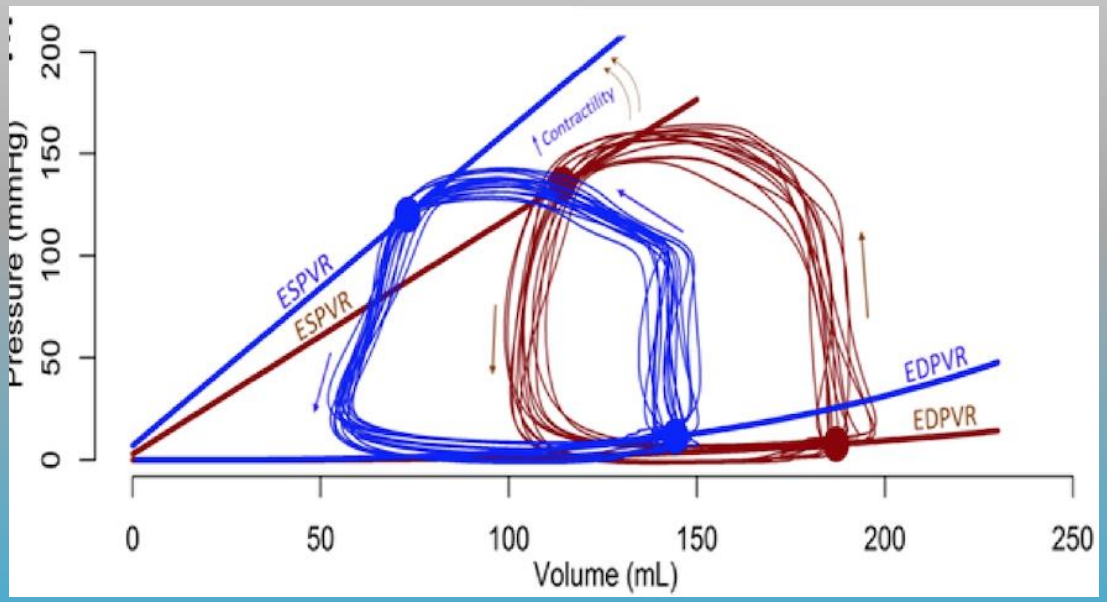
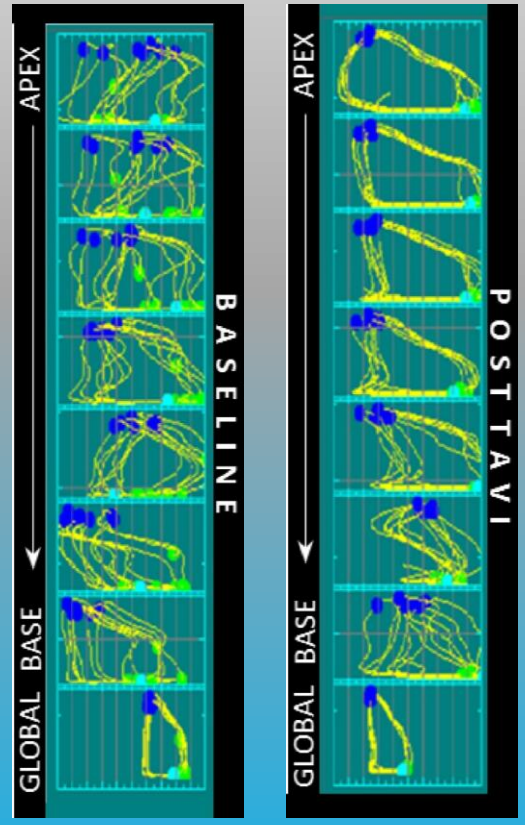
# Immediate TAVI Effects on LV Mechanics

**82 y/o male, EF 38% NYHA IV**

**Immediate LV Unloading & Contractility Increase**




**Segmental Resynchronization**

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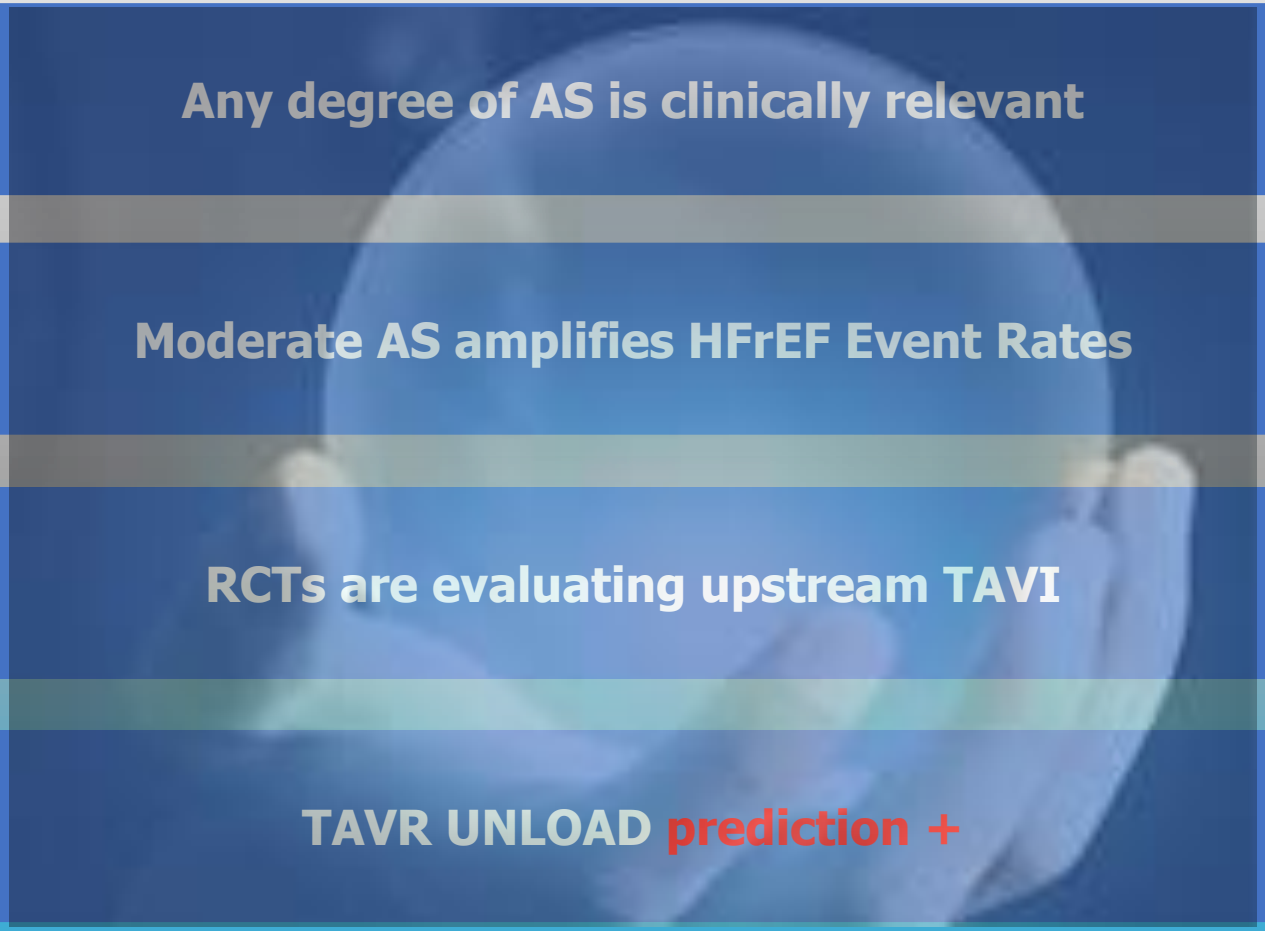
Bastos et al. JACC CVI 2019;12:684-6

# In conclusion



- Any degree of AS is clinically relevant
- Moderate AS amplifies HFrEF Event Rates
- RCTs are evaluating upstream TAVI
- TAVR UNLOAD prediction +

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