



Conoscere⁸
e Curare
il Cuore 2018

SABATO 17 MARZO

STENOSI AORTICA MODERATA ED INSUFFICIENZA VENTRICOLARE SINISTRA. UNA BRUTTA ASSOCIAZIONE

Leonardo Bolognese

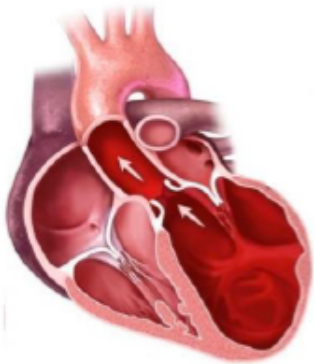
*Dipartimento Cardioneurovascolare
Azienda USL Toscana Sud - Est, Arezzo*



Moderate AS in Patients With LV Systolic Dysfunction: a new paradigm

Heart Failure

Leading cause of hospitalizations

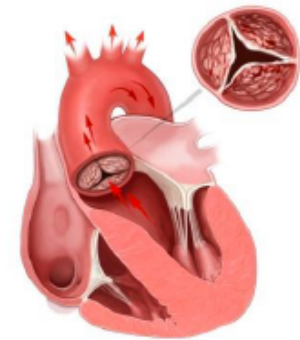


*Increased AFTERLOAD
(sympathetic activity)*

*Impaired LV systolic function
Diastolic dysfunction*

Aortic Stenosis

Most frequent valvulopathy



*Increased AFTERLOAD
(trans-valvular gradient)*

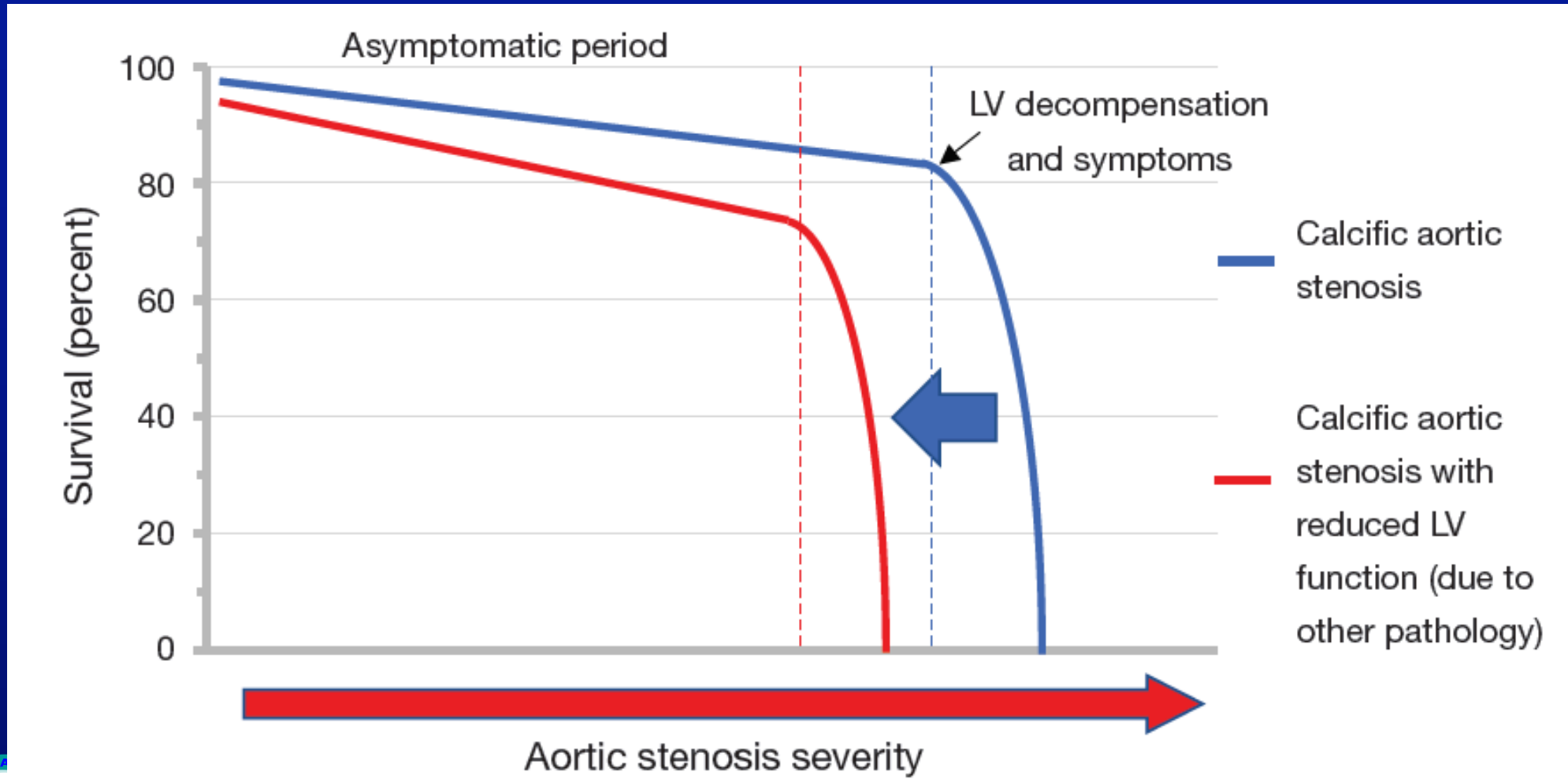
*Impaired LV systolic function
Diastolic dysfunction*

***Coexistence of
Heart Failure and
Moderate AS***

High risk population



The potential impact of coexistent LV dysfunction on the natural history of calcific AS

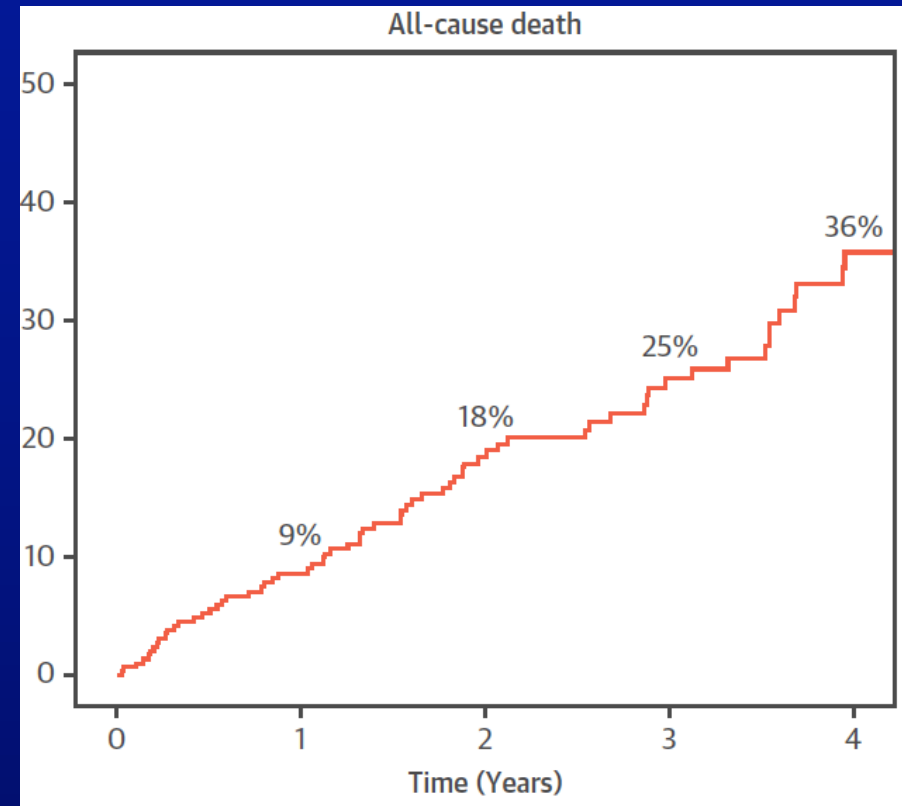
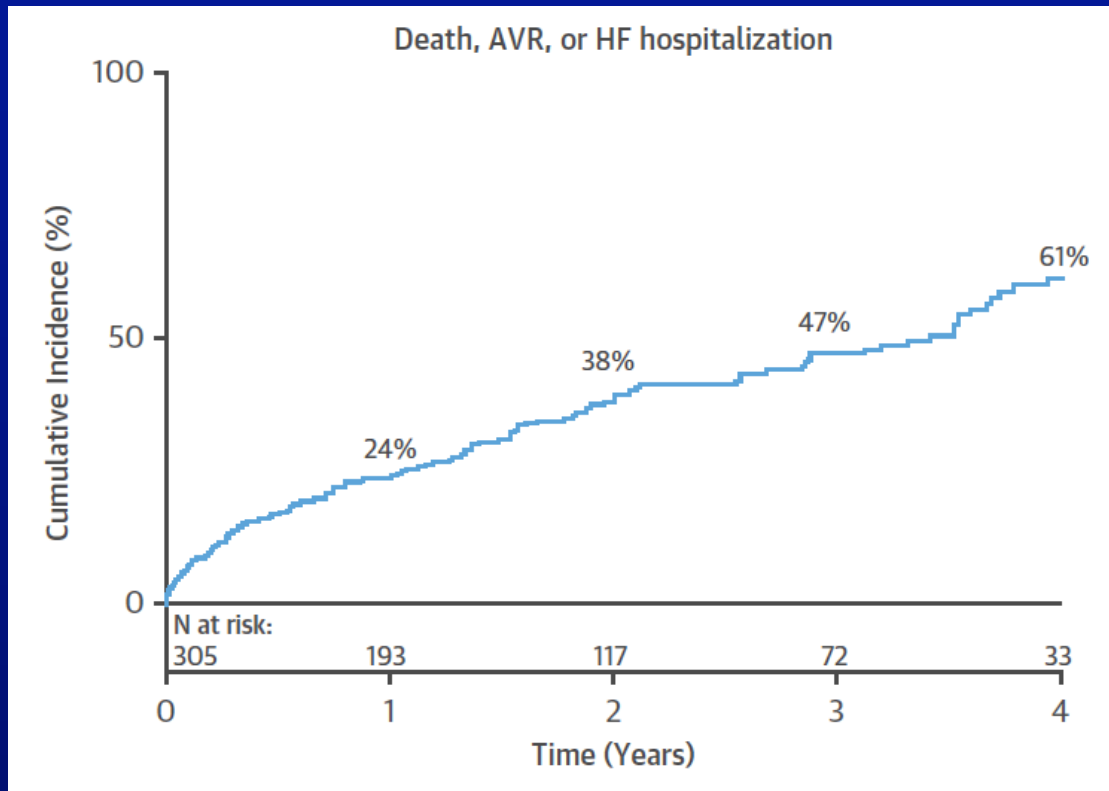


Everett RJ et al. J Thorac Dis 2017; 9:3560-3563



Prognostic Implications of Moderate AS in Patients With LV Systolic Dysfunction

305 pts from echo databases of 4 academic centers in the USA, Canada, and the Netherlands, between 2010 and 2015



van Gils L et al. J Am Coll Cardiol 2017;69:2383–92

Pitfalls of van Gils et al. Observational analysis

- The analysis included a heterogeneous population of pts: multiple underlying causes of LV dysfunction
- A third of pts in the study had moderate to severe AS
- Follow-up echo available in only 56% of pts
- 76% of pts were symptomatic but it is unclear to what extent symptoms and LV dysfunction were truly due to AS
- The decision-making process for timing and indications for AVR among the original study cohort are unclear



Moderate AS in Patients With LV Systolic Dysfunction: Key Issues

- *Is it truly moderate AS?*
- *What is the mechanism of LV dysfunction?*
- *Will SAVR or TAVR improve patient outcomes?*



Moderate AS Definition According to AVA, Gradient, LVEF, and Flow

Table 3 Recommendations for grading of AS severity

	Aortic sclerosis	Mild	Moderate	Severe
Peak velocity (m/s)	≤ 2.5 m/s	2.6–2.9	3.0–4.0	≥ 4.0
Mean gradient (mmHg)	–	< 20	20–40	≥ 40
AVA (cm ²)	–	> 1.5	1.0–1.5	< 1.0
Indexed AVA (cm ² /m ²)	–	> 0.85	0.60–0.85	< 0.6
Velocity ratio	–	> 0.50	0.25–0.50	< 0.25



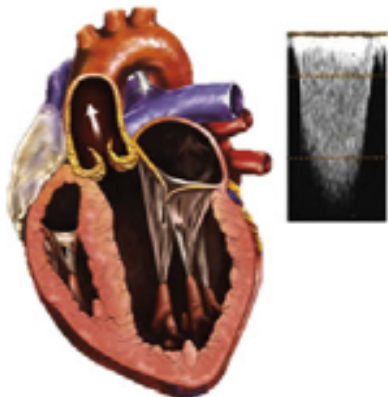
Baumgartner H et al, EHJ- Cardiovascular Imaging 2017;18: 254–275

Moderate AS

$AVA > 1.0 \text{ cm}^2$, $AVA_i > 0.6 \text{ cm}^2/\text{m}^2$
and $MG < 40 \text{ mm Hg}$



Moderate AS
Low LVEF
+ Symptoms
(Stage B2?)



Low Gradient AS

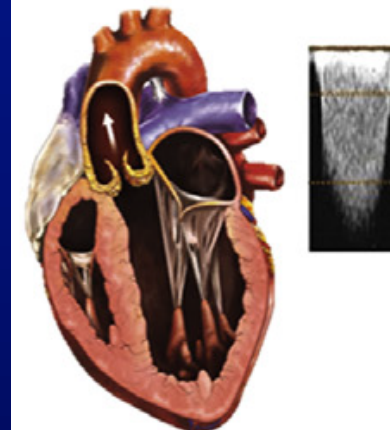
$AVA \leq 1.0 \text{ cm}^2$, $AVA_i \leq 0.6 \text{ cm}^2/\text{m}^2$
and $MG < 40 \text{ mm Hg}$



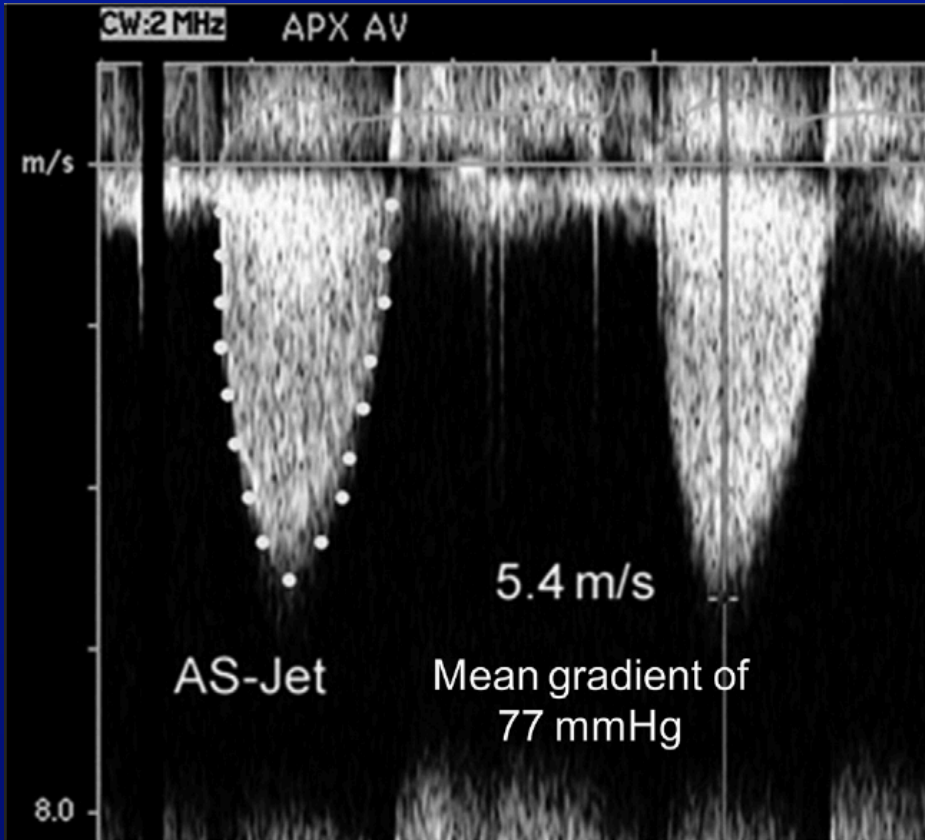
LVEF < 50%



«Classical»
Low-Flow
Low-Gradient
(Stage D2)

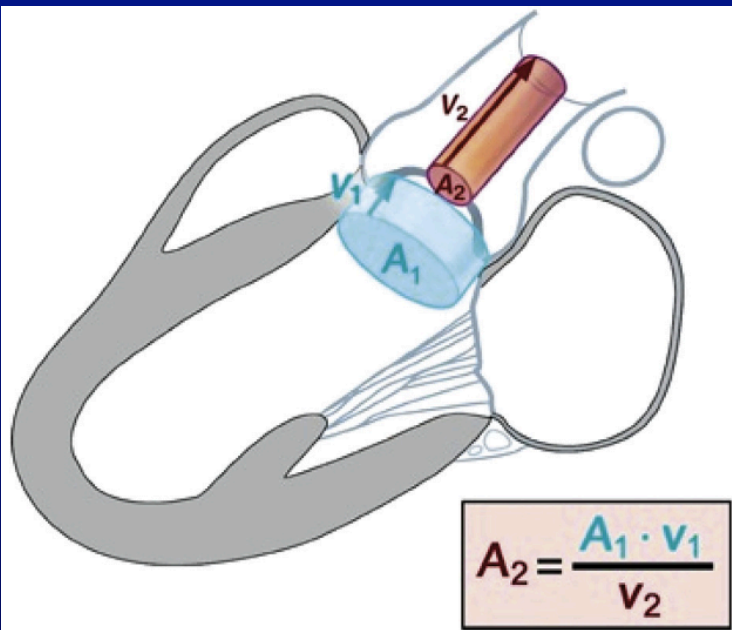
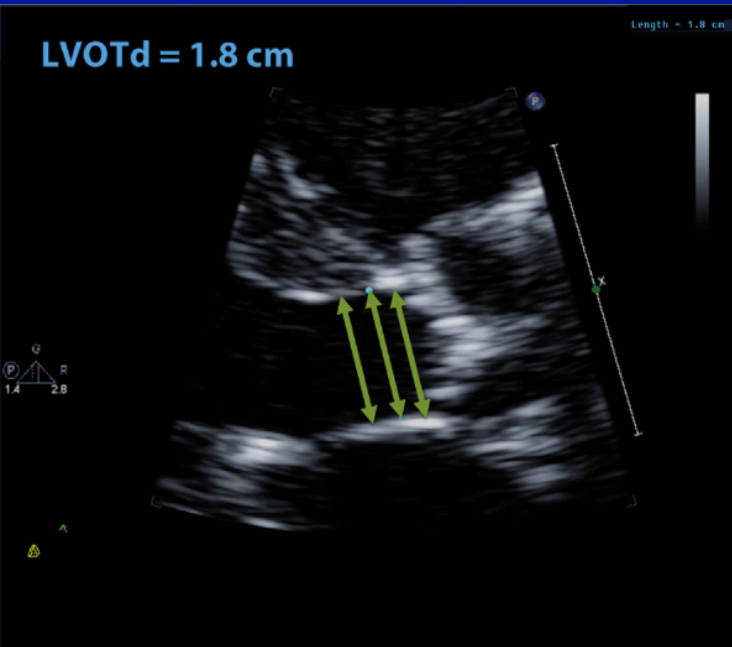


Mean gradient measurement



- Flow dependent
- A small error in this measurement may result in an important error in the evaluation of SA
- Optimal alignment of the CW Doppler beam with the direction of the aortic flow jet
- Multiwindow CW interrogation

LVOT diameter measurement



- The most problematic component of assessing valve area
- It assumes a circular shape of the LVOT that is, instead, often elliptical in shape
- A small error in this measurement may result in an important error in the calculation of the stroke volume and AVA

- 2D parasternal long-axis view
- Zoom mode
- Adjust gain to optimize the blood tissue interface

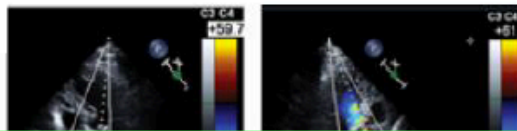
- Inner edge to inner edge
- Mid-systole
- Parallel and adjacent to the aortic valve or at the site of velocity measurement

$$A_2 = \frac{A_1 \cdot V_1}{V_2}$$

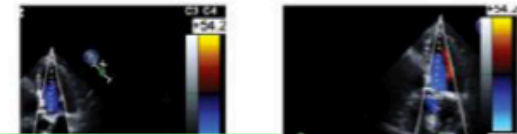
*Baumgartner H et al, EHJ- Cardiovascular Imaging
2017;18: 254–275*

Dobutamine Stress Echocardiography -Classical LF-LG AS -

true severe AS



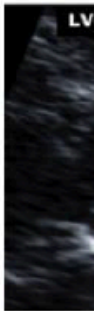
pseudo-severe AS



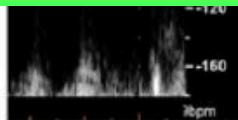
3 DSE Responses

- **True AS:** increased peak velocity and gradient with no significant change in AVA
- **Pseudo-severe AS:** increased AVA with minimal change in peak velocity or gradient
- **Uncertain:** resulting from failure of forward flow to increase with dobutamine

REST DO



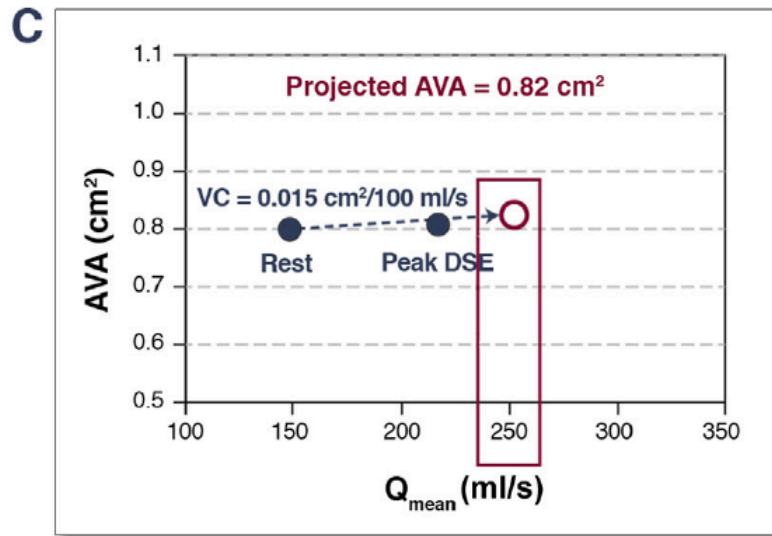
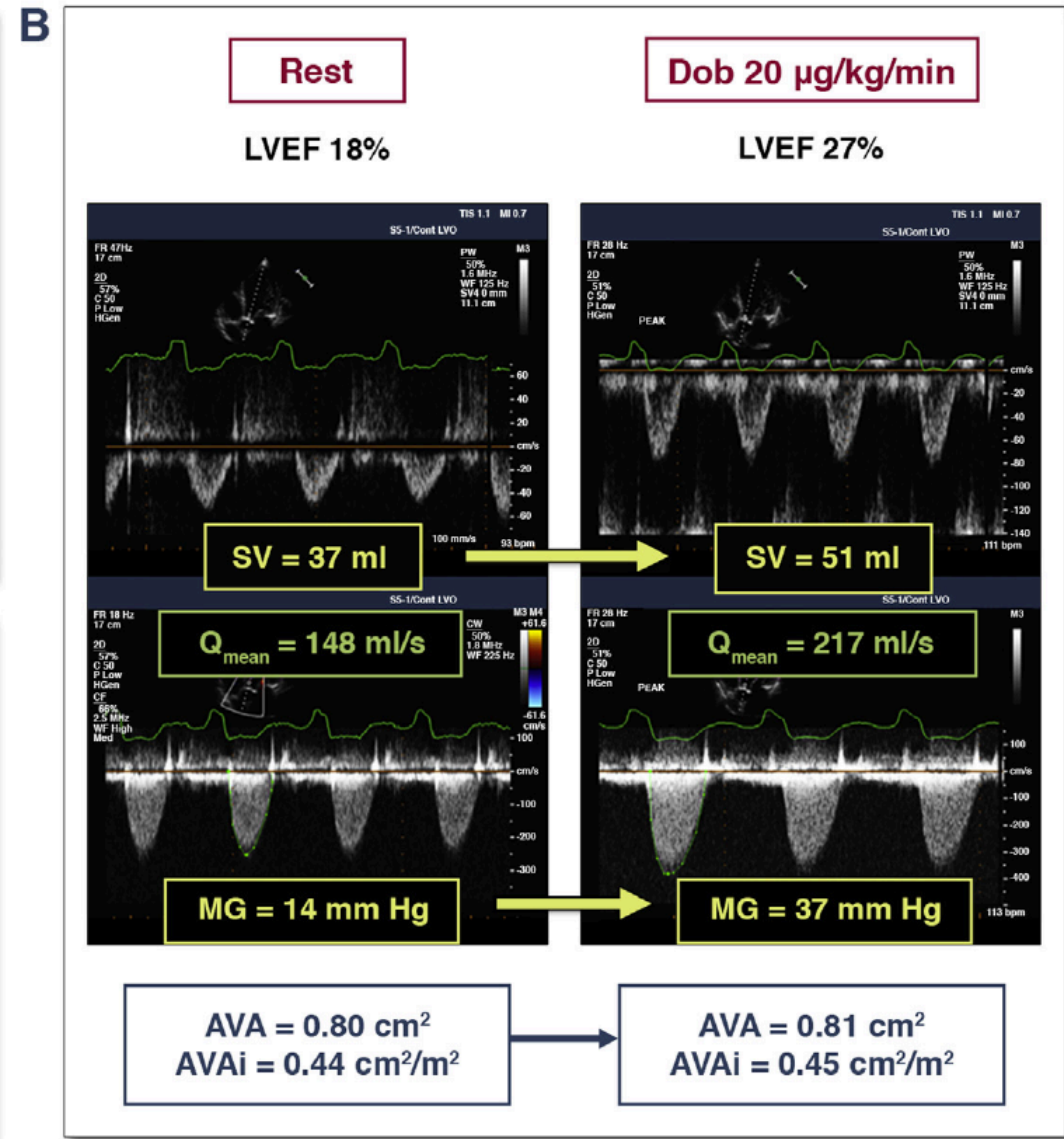
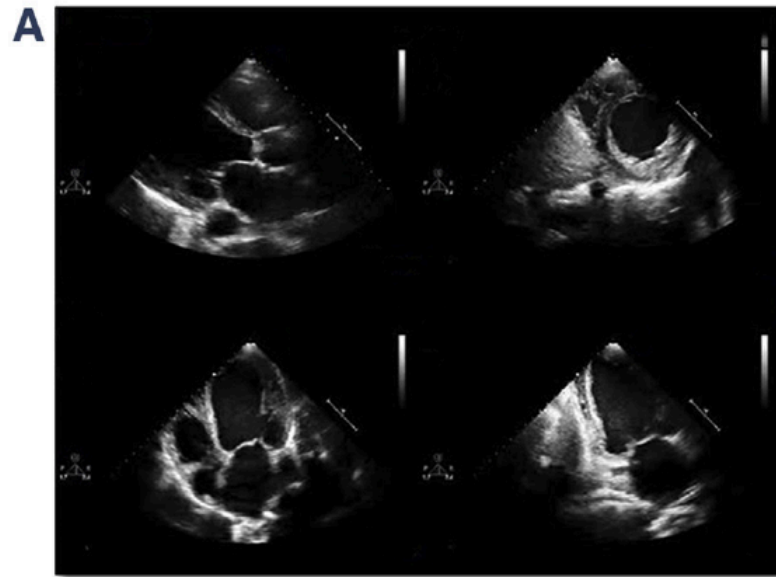
PEA



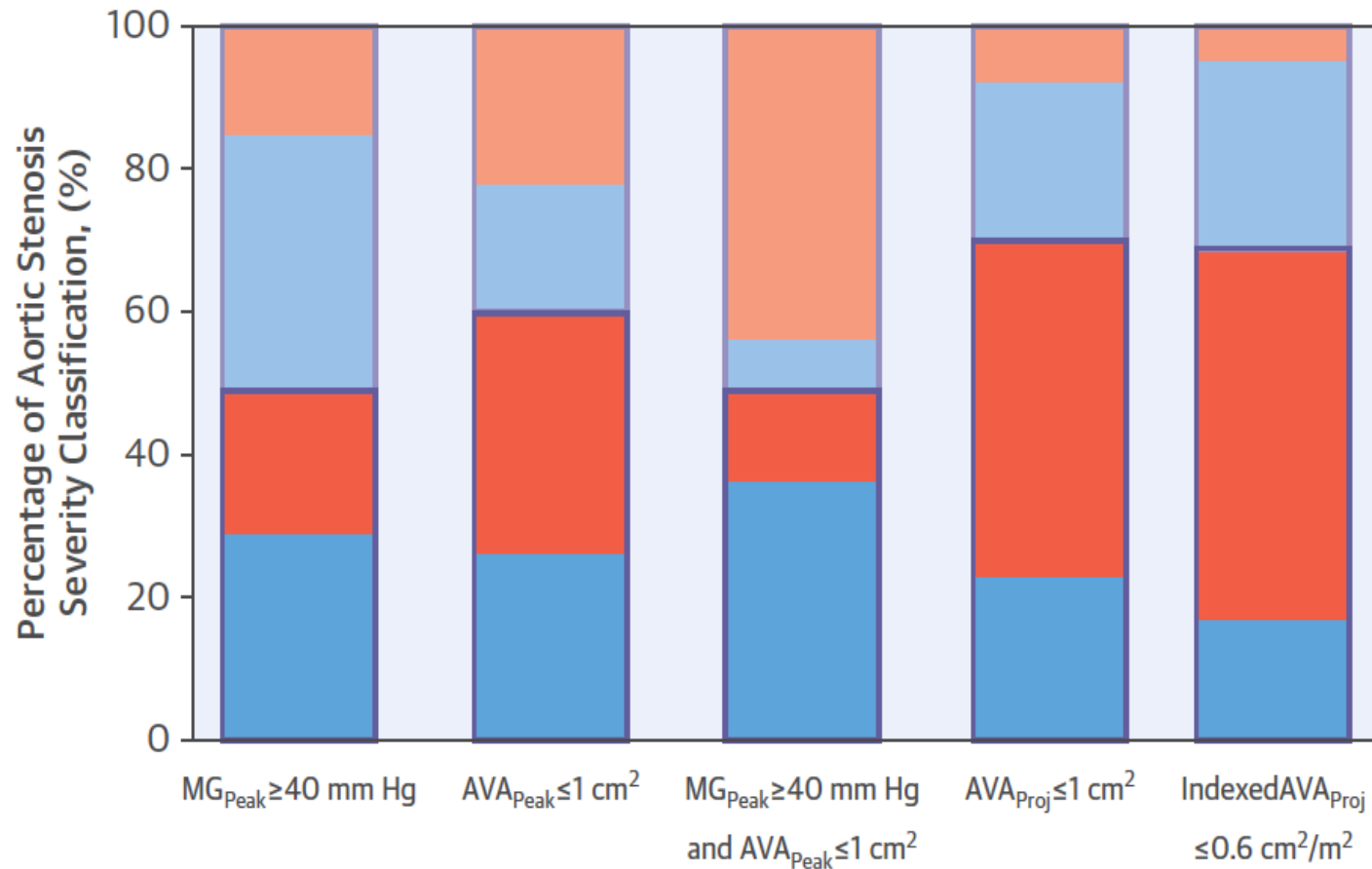
LVOT
TVI: 16 cm
SV: 60 ml

Aortic Valve
Vpeak: 266 cm/s
MG: 17 mmHg
TVI: 52 cm
AVA: 1.16 cm²

Multiparametric assessment of AS severity by DSE



Identification of Aortic Stenosis Severity by DSE Criteria: the TOPAS Registry



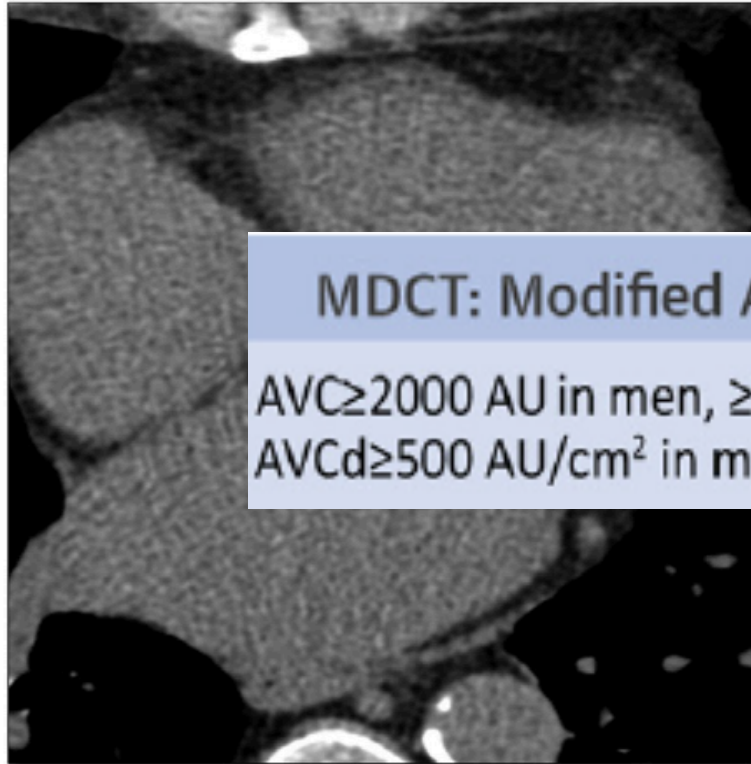
- Correctly Classified Pseudo-Severe AS
- Correctly Classified True-Severe AS
- Wrongly Classified Pseudo-Severe AS (True-Severe AS by DSE)
- Wrongly Classified Truly-Severe AS (Pseudo-Severe AS by DSE)

Annabi SM et al. J Am Coll Cardiol 2018;71:475–85

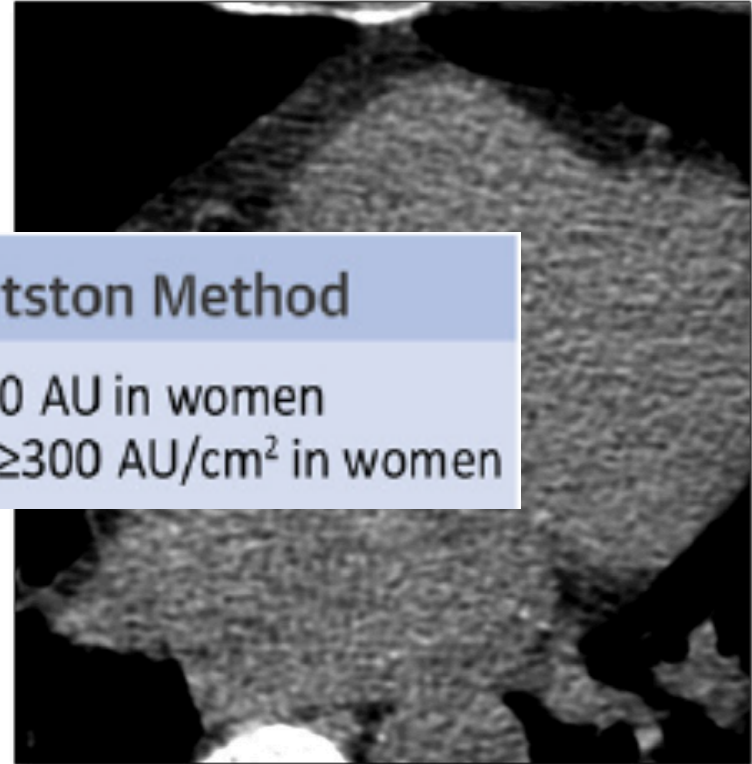


Quantitation of Aortic Valve Calcification by MDCT to Differentiate True Versus Pseudo-Severe Stenosis in Low-Gradient AS

Pseudo-Severe AS



True-Severe AS



MDCT: Modified Agatston Method

AVC ≥ 2000 AU in men, ≥ 1200 AU in women

AVCd ≥ 500 AU/cm² in men, ≥ 300 AU/cm² in women

AVC Score = 737 AU

AVC Density = 194 AU/cm²

AVA = 0.88 cm²; MG = 18 mm Hg

AVC Score = 3,127 AU

AVC Density = 753 AU/cm²

AVA = 0.64 cm²; MG = 26 mm Hg



Moderate AS in Patients With LV Systolic Dysfunction: Key Issues

- *Is it truly moderate AS?*
- *What is the mechanism of LV dysfunction?*
- *Will SAVR or TAVR improve patient outcomes?*

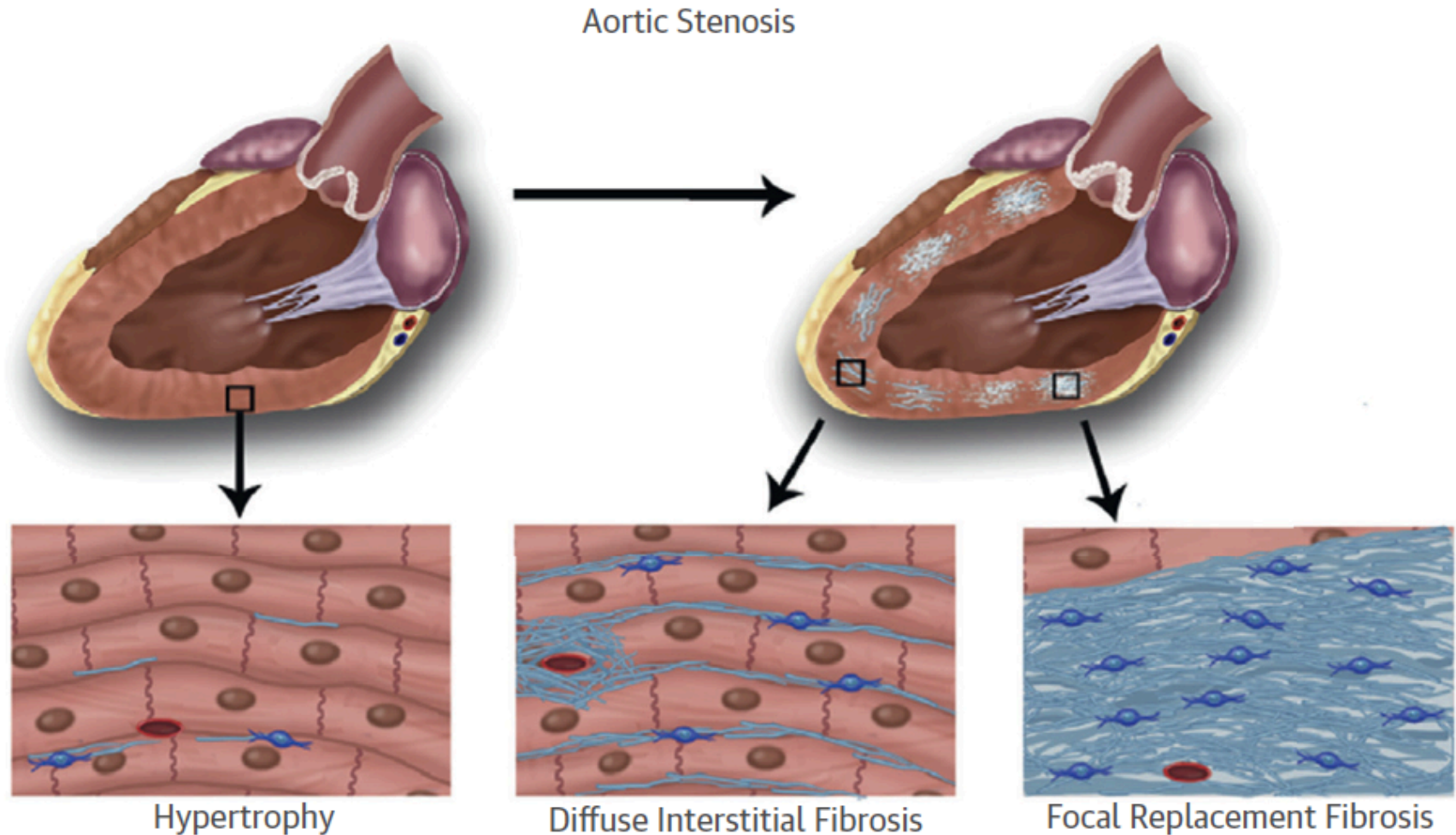


Causes of LV dysfunction in AS

- AS and associated afterload mismatch
- Co-existing conditions (hypertension, ischemic heart disease, etc)
- Mid-wall fibrosis
- Amyloidosis



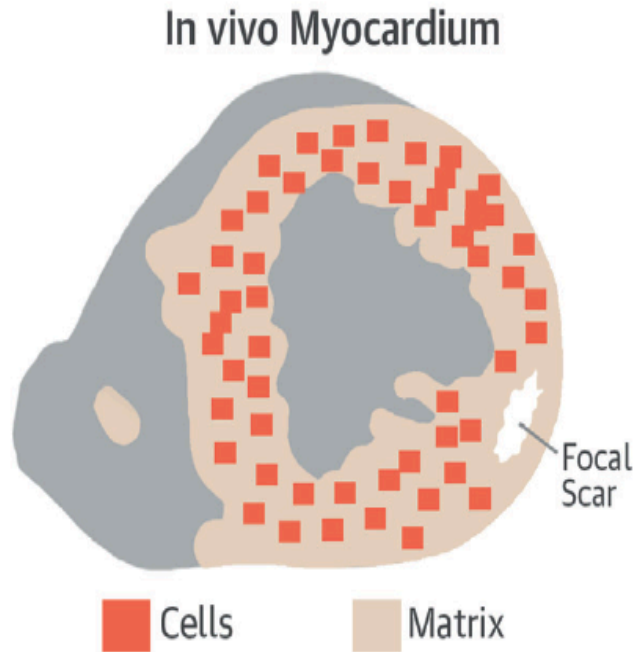
The remodeling response of the heart to the pressure overload



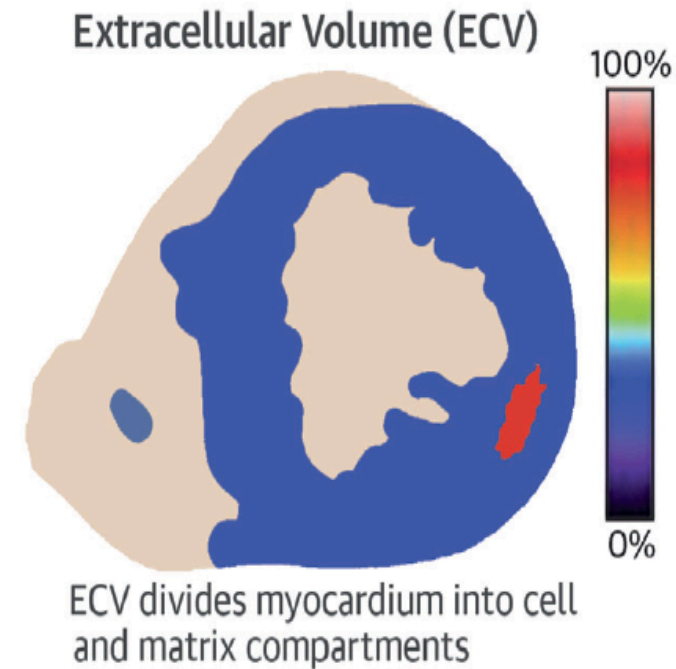
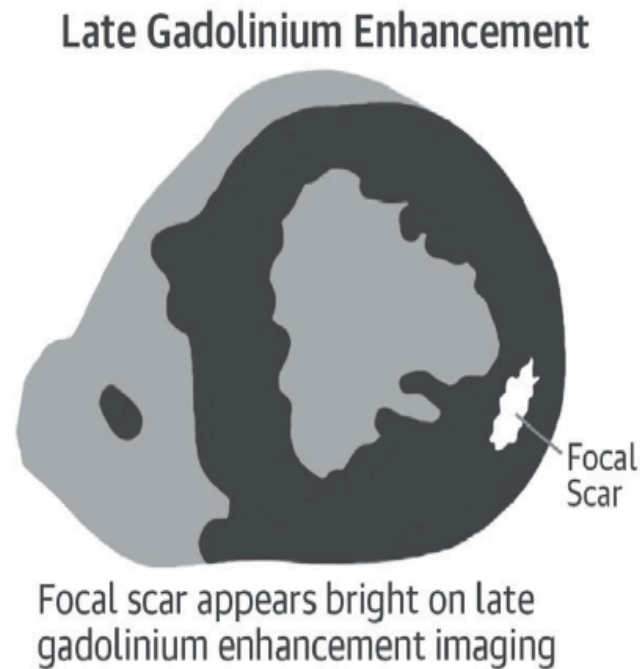
Steiner J et al J Am Coll Cardiol 2017;70:3026–41

CMR for quantification of focal and diffuse fibrosis

A. In vivo Myocardium



B. Cardiovascular Magnetic Resonance

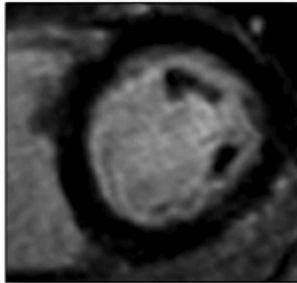
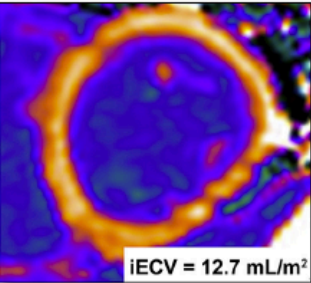


Treibel TA et al. J Am Coll Cardiol 2018;71:860–71

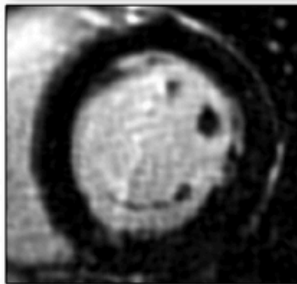
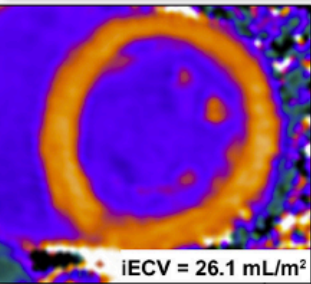
Myocardial Fibrosis and Cardiac Decompensation in AS

T1 Mapping for iECV Measurement

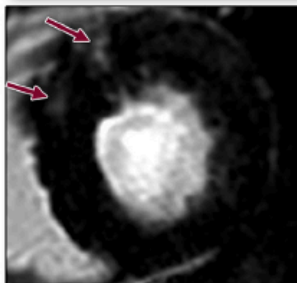
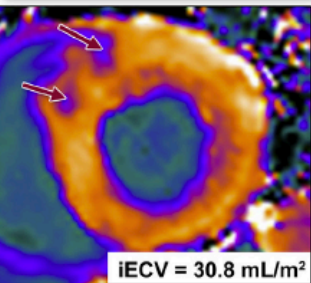
Late Gadolinium Enhancement



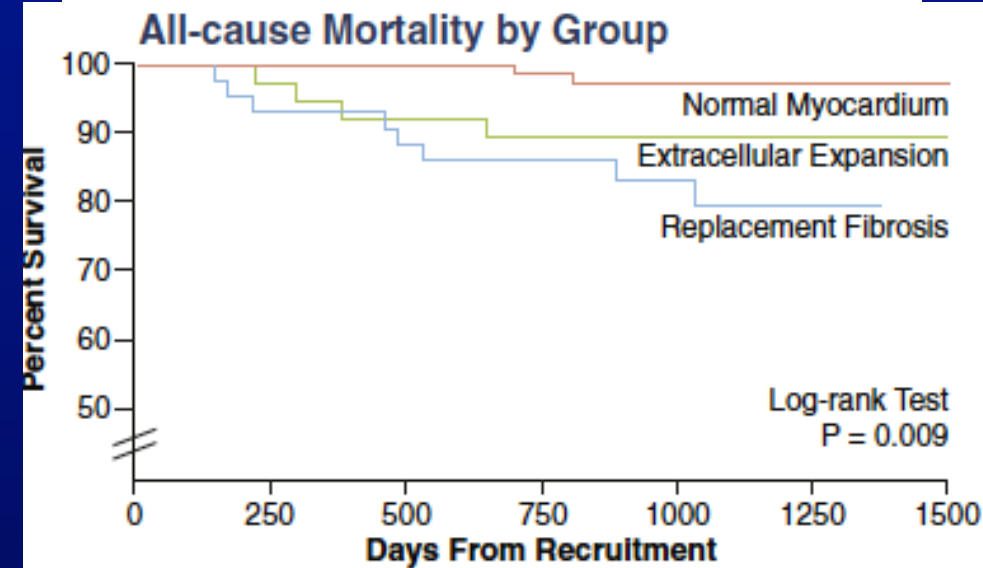
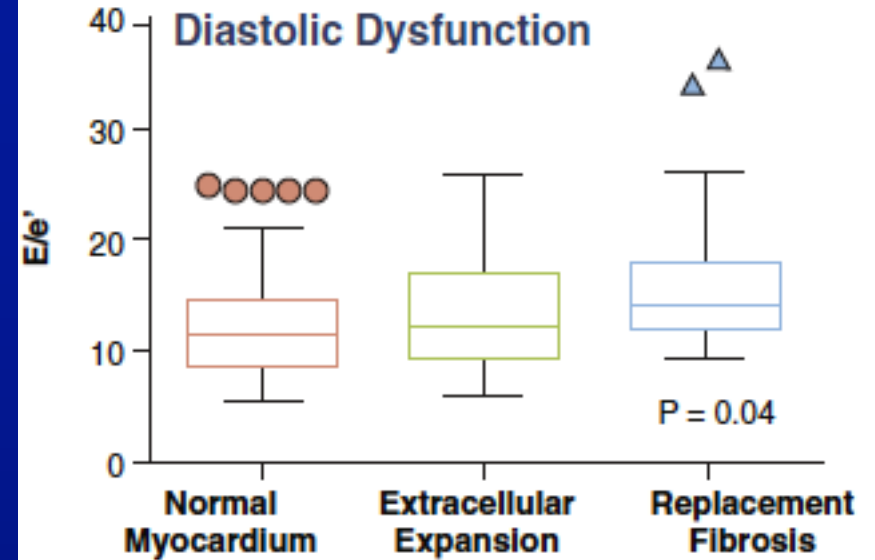
Normal Myocardium
(iECV < 22.5 mL/m²)
(N = 71)
No fibrosis
No mid-wall LGE



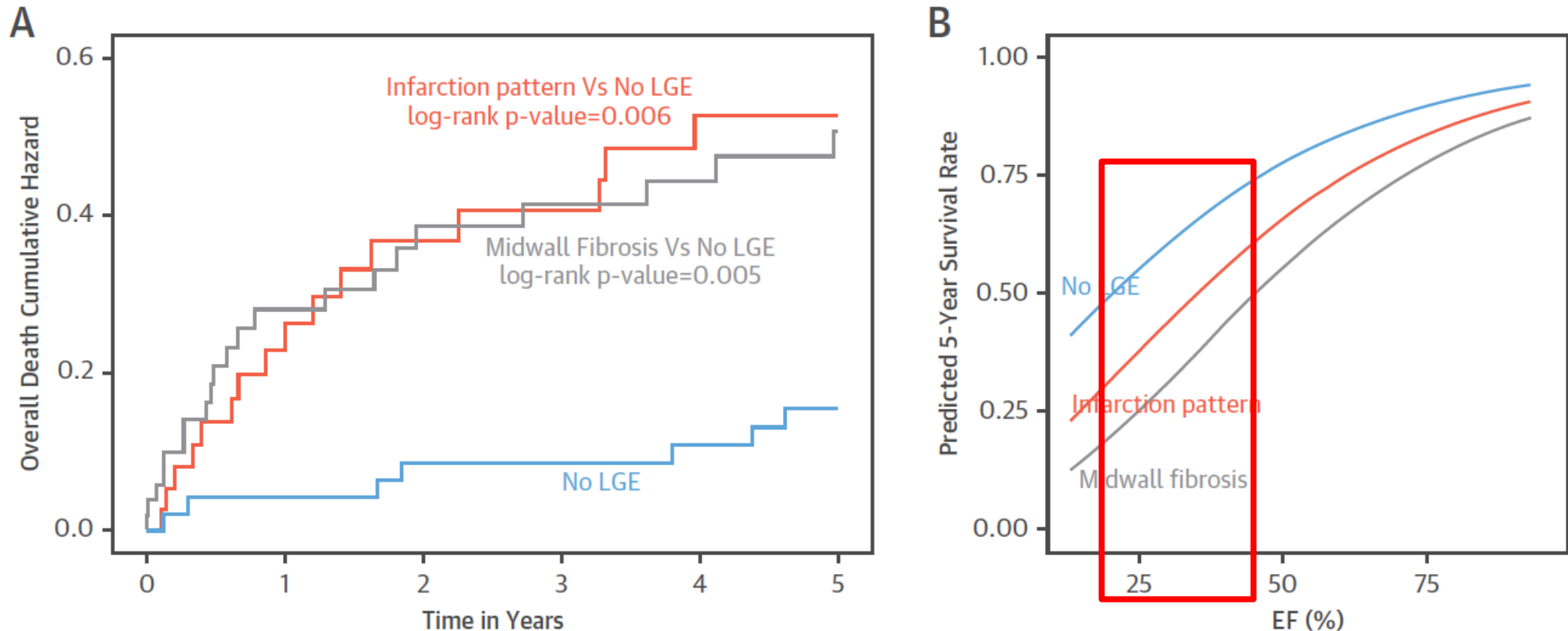
Extracellular Expansion
(iECV ≥ 22.5 mL/m²)
(N = 31)
Diffuse fibrosis
No mid-wall LGE



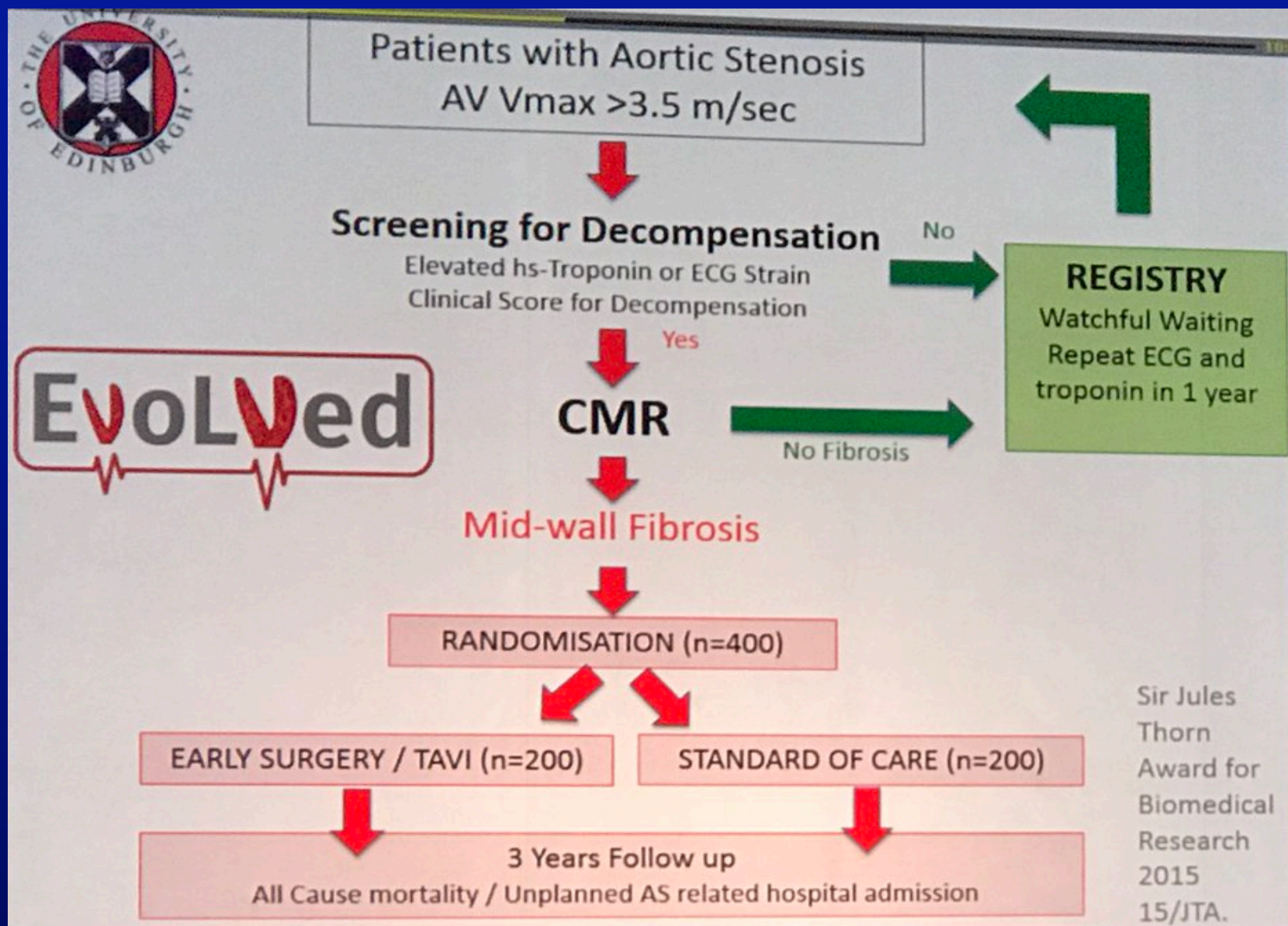
Replacement Fibrosis
(N = 37)
Mid-wall LGE present
(red arrows)



Midwall Fibrosis and 5-Year Outcome in Moderate and Severe Aortic Stenosis



AVR guided by Mid-wall Fobrosis



RESE



European Heart Journal (2016) 37, 3525–3531

EHJ BRIEF COMMUNICATION

Cardiomyopathies
Ac
wor

Cardiomyopathies



ESC

European Society
of Cardiology

European Heart Journal (2017) 38, 2879–2887

doi:10.1093/eurheartj/ehx350

CLINICAL RESEARCH

Heart failure/cardiomyopathy

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JACC: CARDIOVASCULAR IMAGING, VOL. 9, NO. 3, 2016

MARCH 2016:321–31

Coexistence of Degenerative Aortic Stenosis

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 71, NO. 4, 2018

Prevalence of Cardiac Amyloidosis in Patients Referred for Transcatheter Aortic Valve Replacement

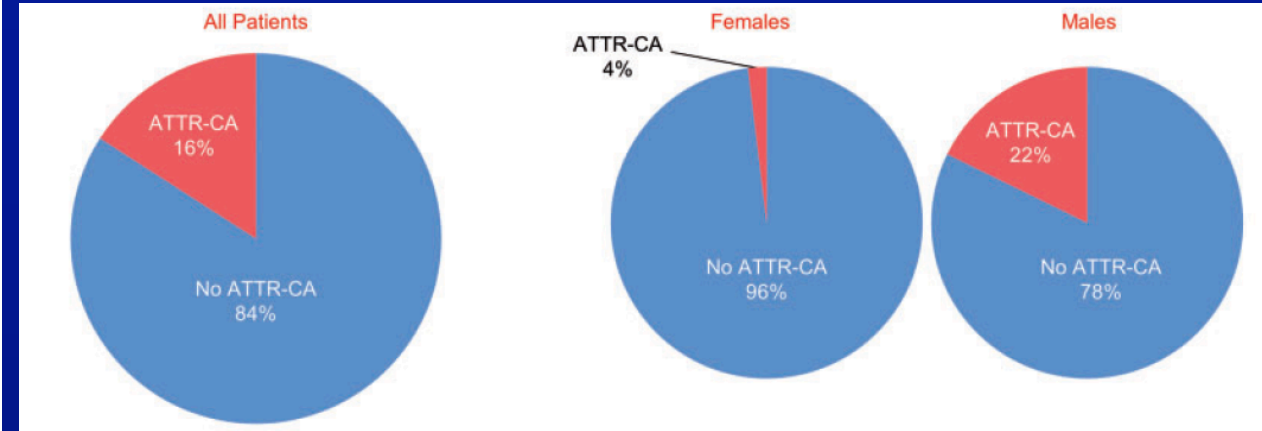
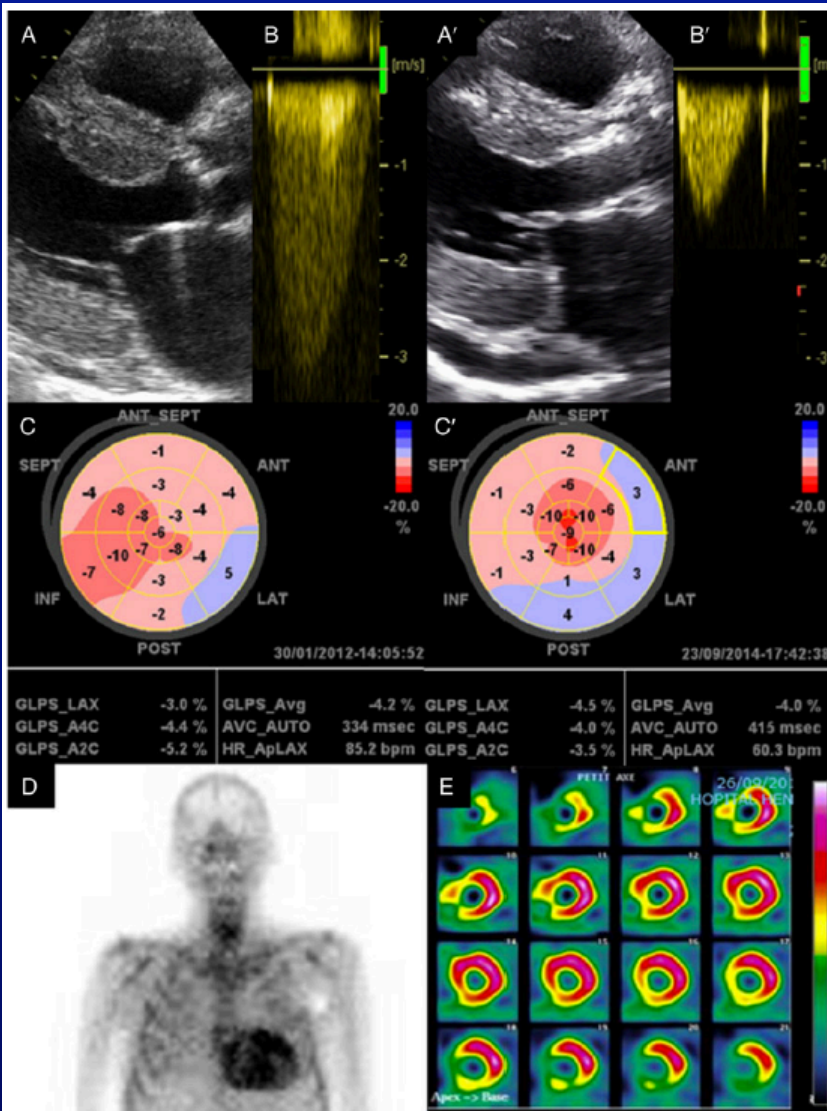


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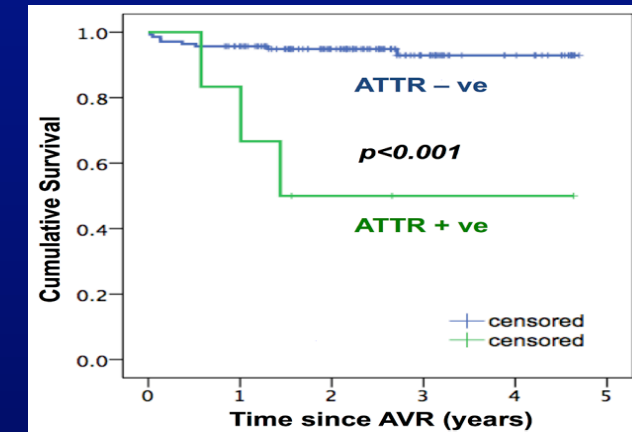
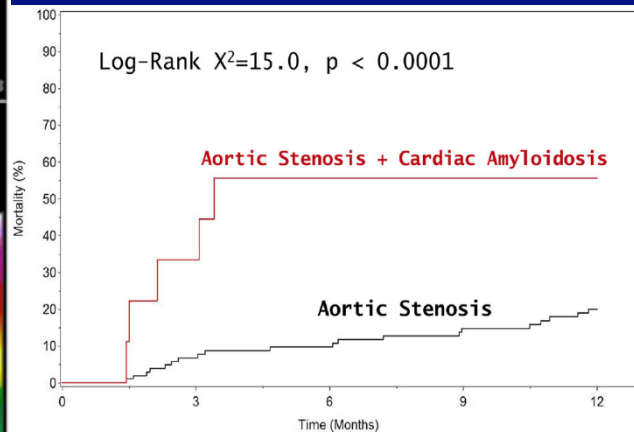


Transthyretin cardiac amyloidosis and AS

ATTR-CA is prevalent in 16% of patients with severe AS undergoing TAVR and is associated with a AS phenotype of low-flow low-gradient with mildly reduced EF



Castano A et al. Eur Heart J 2017; 38: 2879–2887



Treibel TA et al. Circ Cardiovasc Imaging. 2016
Cavalcante et al. J Cardiovasc Mag Res 2017; 19:98

Moderate AS in Patients With LV Systolic Dysfunction: Key Issues

- *Is it truly moderate AS?*
- *What is the mechanism of LV dysfunction?*
- ***Will SAVR or TAVR improve patient outcomes?***



**ESC**European Society
of CardiologyEuropean Heart Journal (2017) **00**, 1–53

doi:10.1093/eurheartj/ehx391

ESC/EACTS GUIDELINES

2017 ESC/EACTS Guidelines for the management of valvular heart disease

A) Symptomatic aortic stenosis	Class ^a	Level ^b
Intervention is indicated in symptomatic patients with severe, high-gradient aortic stenosis (mean gradient ≥ 40 mmHg or peak velocity ≥ 4.0 m/s). ^{91–93}	I	B
Intervention is indicated in symptomatic patients with moderate aortic stenosis and evidence of LV dysfunction.	I	C
Intervention is indicated in symptomatic patients with moderate aortic stenosis and evidence of LV dysfunction after medical treatment.	IIa	C
Intervention is indicated in symptomatic patients with moderate aortic stenosis and evidence of LV dysfunction after medical treatment.	IIa	C
Intervention should not be performed in patients with severe comorbidities when the intervention is unlikely to improve quality of life or survival.	III	C
SAVR should be considered in patients with <u>moderate aortic stenosis^e undergoing CABG or surgery of the ascending aorta or of another valve after Heart Team decision.</u>	IIa	C

Should AVR or TAVR be considered for patients with moderate AS and impaired LV function?

AVR for Moderate AS

Duke Echocardiographic Database

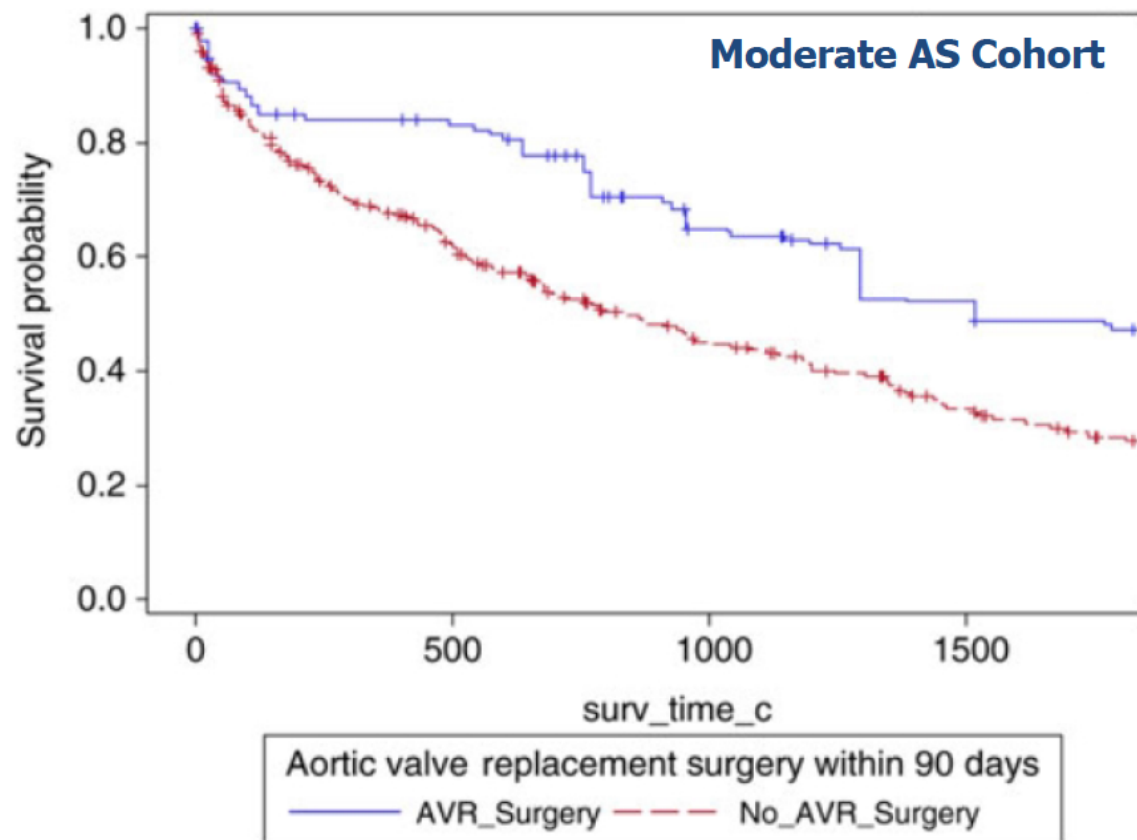
N = 132804

AS defined as $MG > 25$ mmHg or $v_{max} 3$ m/s

N = 1634 patients with AS

N = 1090 with moderate AS, 26% SAVR

N = 544 with severe AS, 48% SAVR



Transcatheter Aortic Valve Replacement to UNload the Left ventricle in patients with ADvanced heart failure (TAVR UNLOAD) trial

TAVR UNLOAD

INTERNATIONAL, RANDOMIZED, OPEN-LABEL TRIAL

Study Population

Patients with Moderate Aortic Stenosis and Symptomatic Heart Failure (NYHA \geq II) with Depressed Ejection Fraction ($<50\%$)

40 sites in 3 countries

Local Screening

Central Confirmation of Eligibility

N=600

1:1

R

TAVR plus OHFT

OHFT

Clinical follow-up & QoL
Echocardiography (TAVR only)

Clinical follow-up & QoL

Clinical follow-up & QoL

Echocardiography

Clinical follow-up & QoL

Echocardiography

1 m

6 m

12 m

24 m

Primary Endpoint: Hierarchical occurrence of all-cause death; disabling stroke; hospitalizations for heart failure, symptomatic aortic valve disease or non-disabling stroke; and, change in Kansas City Cardiomyopathy Questionnaire at one year



TAVR UNLOAD Trial: Key Considerations

- Is there a significant evidence base to justify any intervention in these patients?
- TAVR UNLOAD trial only randomizes patients to transfemoral TAVR
- Highly heterogeneous composite endpoint. The study will not be powered to assess survival
- Health policy implications and cost-effectiveness compared to more aggressive echocardiographic surveillance imaging



Take-home Messages

- Patients with moderate AS and LV dysfunction are a high-risk but heterogeneous and controversial group
- Observational data force us to re-consider our approach to these patients
- There is insufficient evidence to recommend SAVR or TAVR in all pts and would advocate a *patient stratified approach* after clarifying the severity of AS, the mechanism of LV dysfunction, and the likelihood of LV recovery post intervention
- Mechanical intervention for these patients is a pathophysiologically appealing approach to reducing afterload effectively; ongoing clinical trial will provide important data on outcome for these pts

