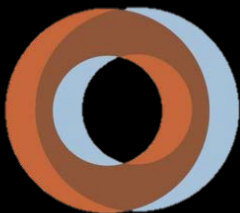


Low Gradient Severe? AS

Philippe Pibarot, DVM, PhD, FACC, FAHA, FESC, FASE
Canada Research Chair in Valvular Heart Diseases



Institut Universitaire de Cardiologie
et de Pneumologie de Québec /
Québec Heart & Lung Institute



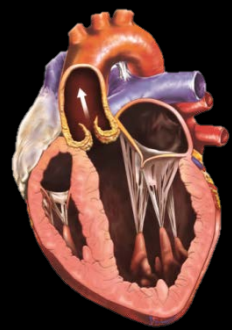
Université
LAVAL

Disclosure Statement

- **Edwards LifeSciences: Echo CoreLab for the PARTNER-II SAPIEN 3**
- **V-Wave: Echo CoreLab for FinM Experience**

LOW GRADIENT SEVERE? AS

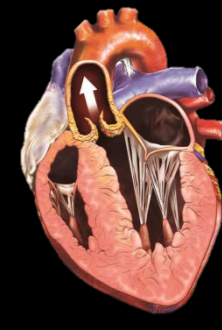
$AVA \leq 1.0 \text{ cm}^2$ $MG < 40 \text{ mmHg}$



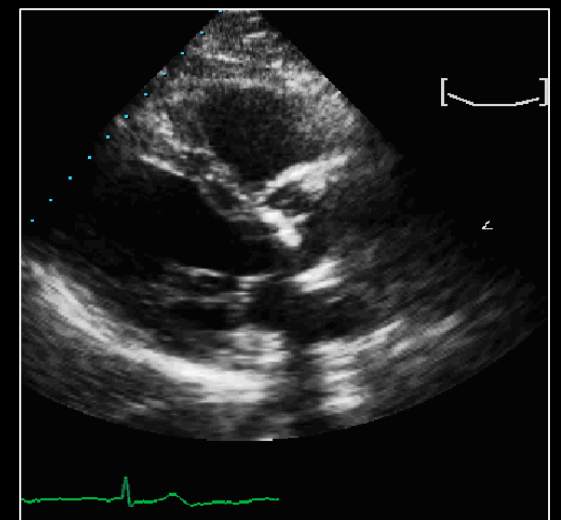
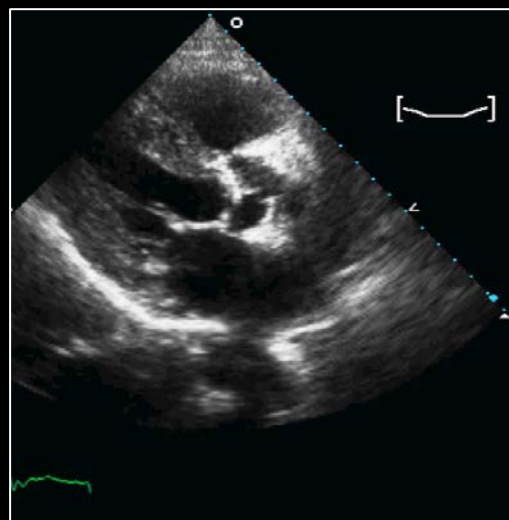
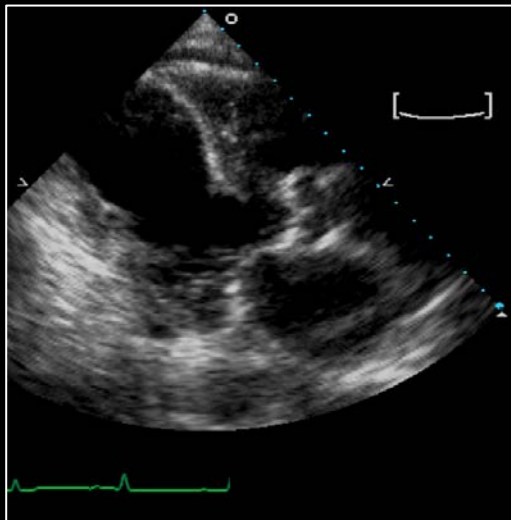
**«CLASSICAL»
LOW-FLOW
LOW-GRADIENT
D2 Stage**

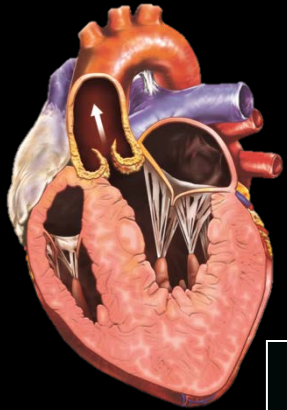


**«PARADOXICAL»
LOW-FLOW
LOW-GRADIENT
D3 Stage**

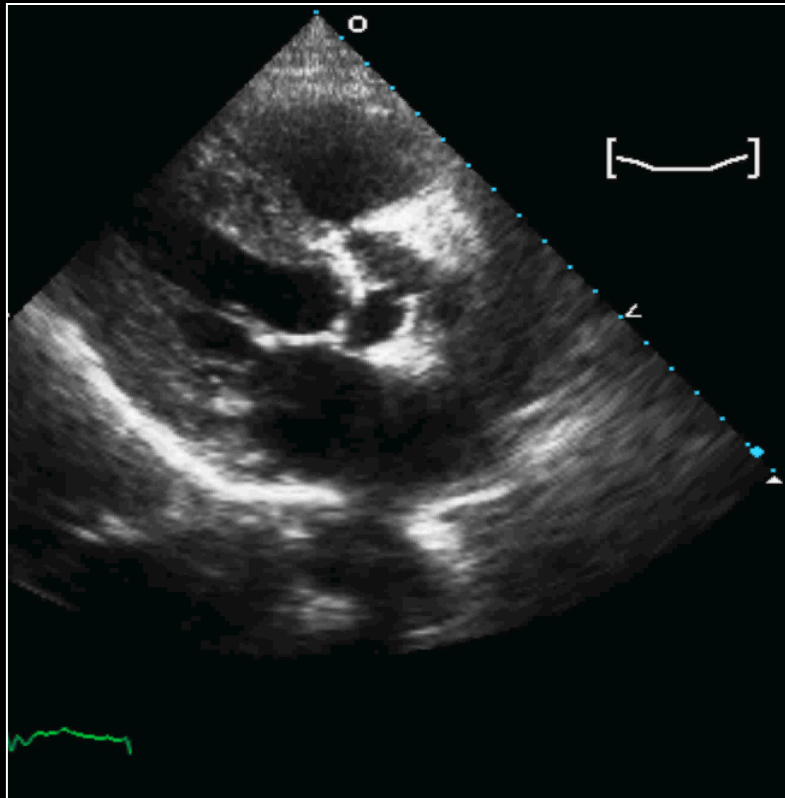


**NORMAL-FLOW
LOW-GRADIENT
D? Stage**



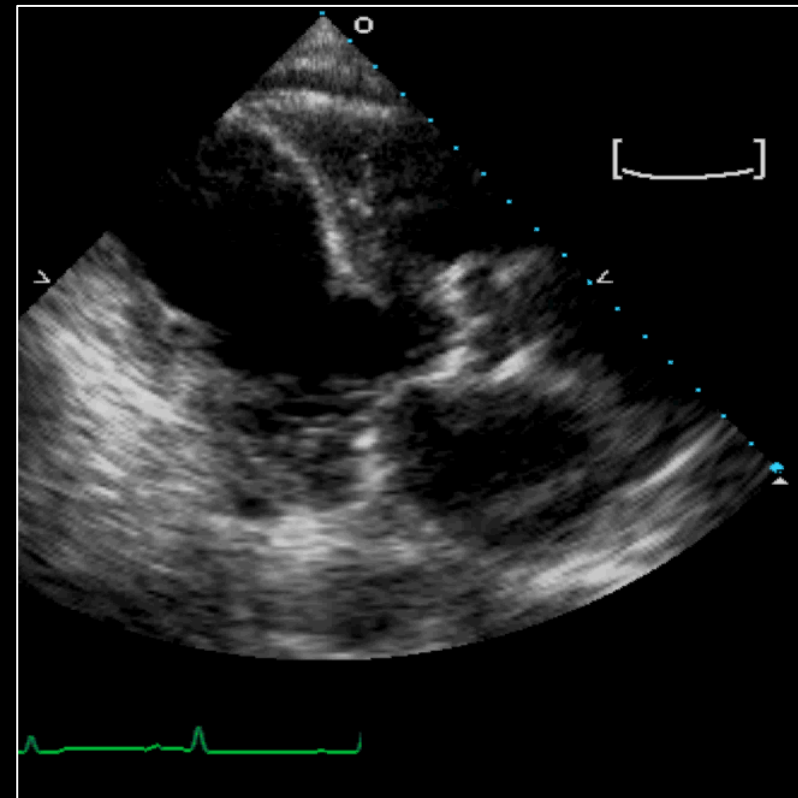
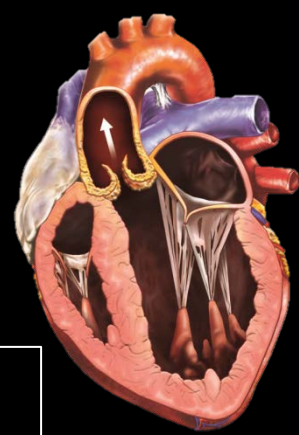


NORMAL-LVEF
«PARADOXICAL»
LOW-FLOW
LOW-GRADIENT



LVEF=60%
SV=46 mL
MG=29 mmHg

LOW-LVEF
«CLASSICAL»
LOW-FLOW
LOW-GRADIENT

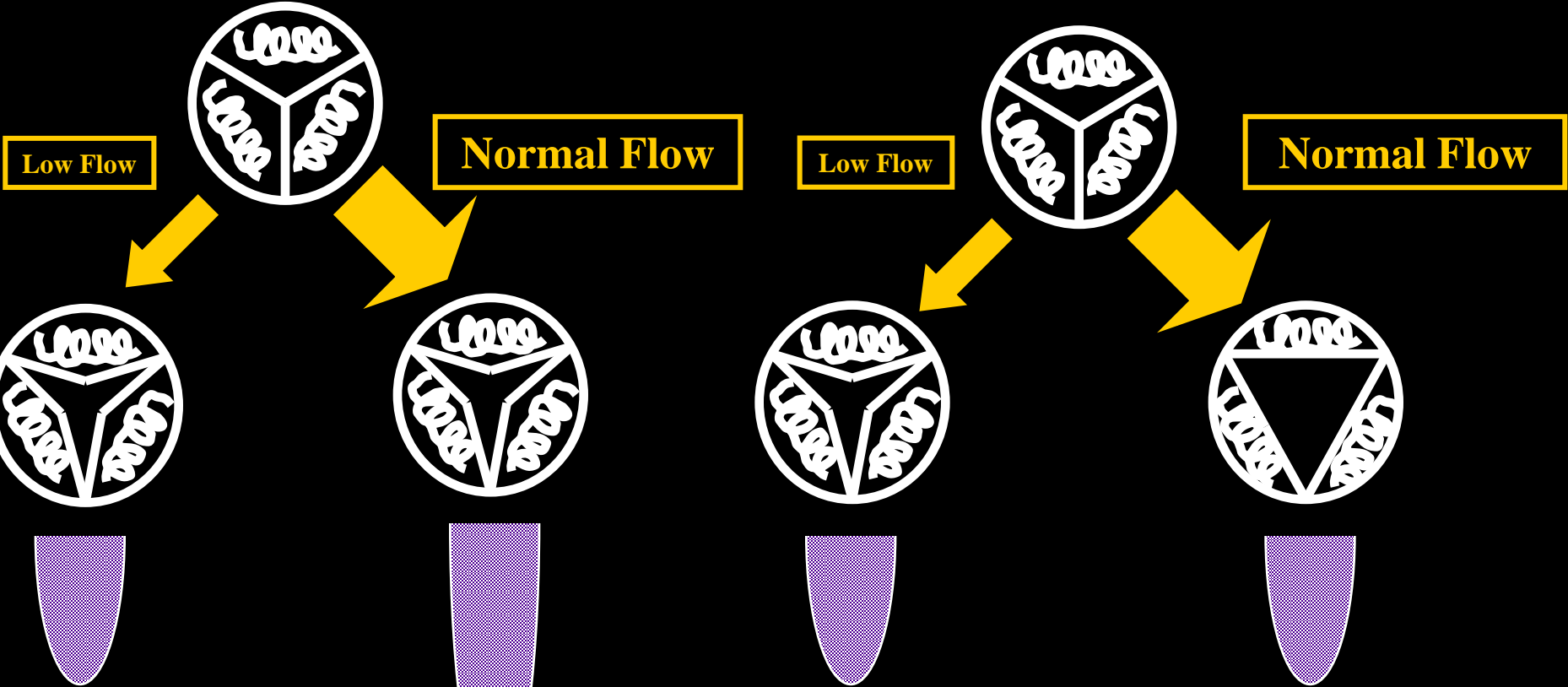


LVEF=25%
SV=42 mL
MG=25 mmHg

Low-Flow, Low-Gradient Severe(?) AS

True-Severe AS

Pseudo-Severe AS

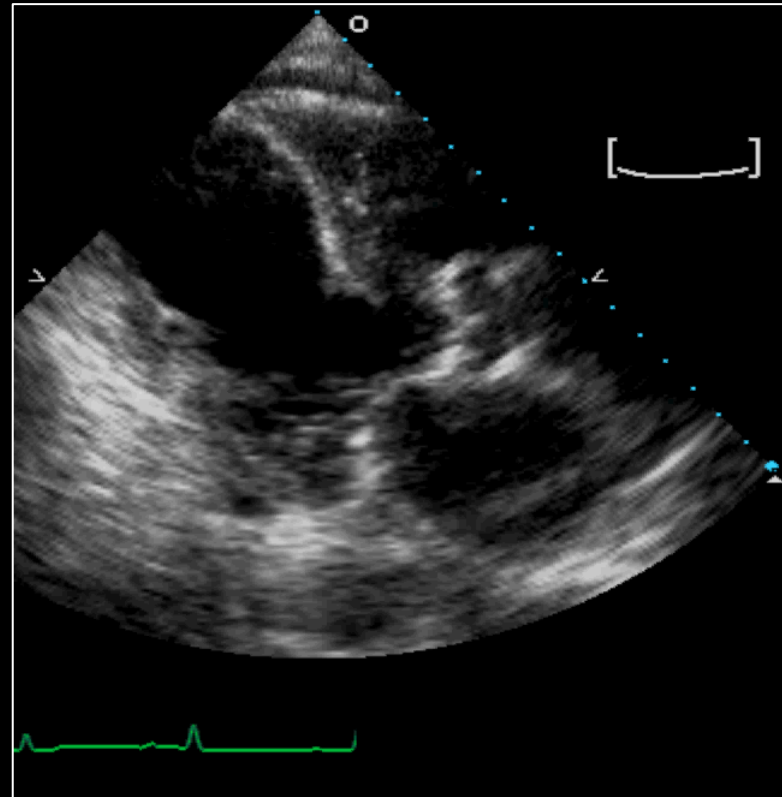
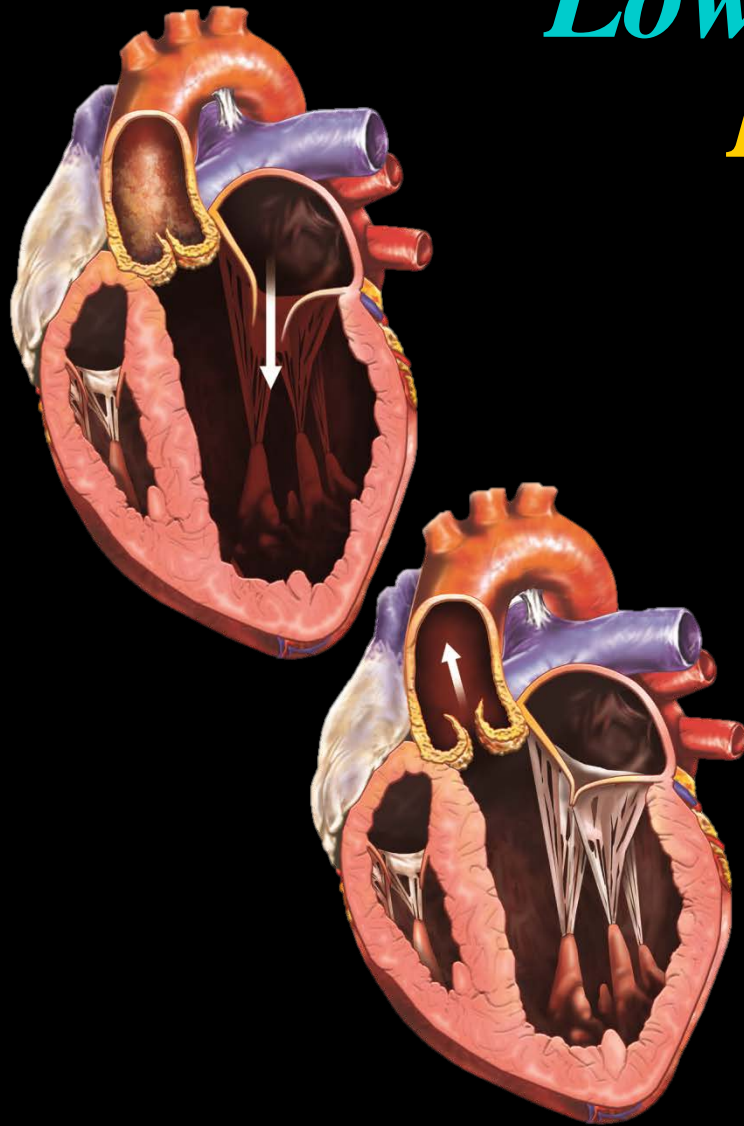


AVA

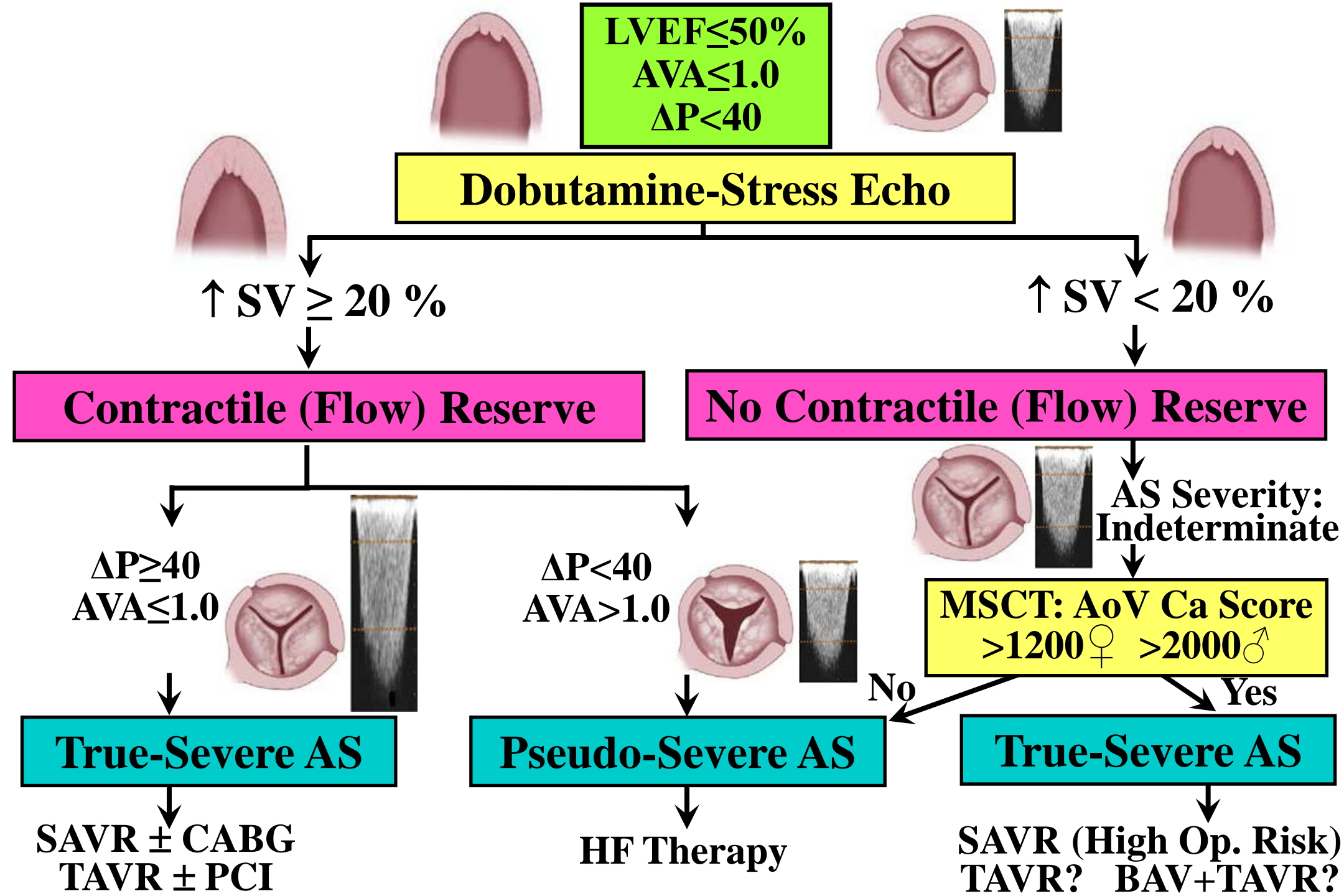
ΔP

$$\text{Gradient} = \frac{Q^2}{K \times AVA^2}$$

“Classical” Low-Flow, Low-Gradient AS with Reduced LVEF



LVEF=25%
SV=42 mL
MG=25 mmHg



2014 ACC/AHA Guidelines on Management of VHD: Indications for AVR in AS

Definition: AVA \leq 1.0 cm², Mean gradient $<$ 40 mmHg, LVEF $<$ 50%

Stage: D2

Recommendation	Class	Level
AVR is reasonable in symptomatic patients with low LVEF, low-flow/low-gradient severe AS with a DSE that shows a mean gradient \geq 40 mm Hg with an AVA \leq 1.0 cm ² at any dobutamine dose	IIa	B

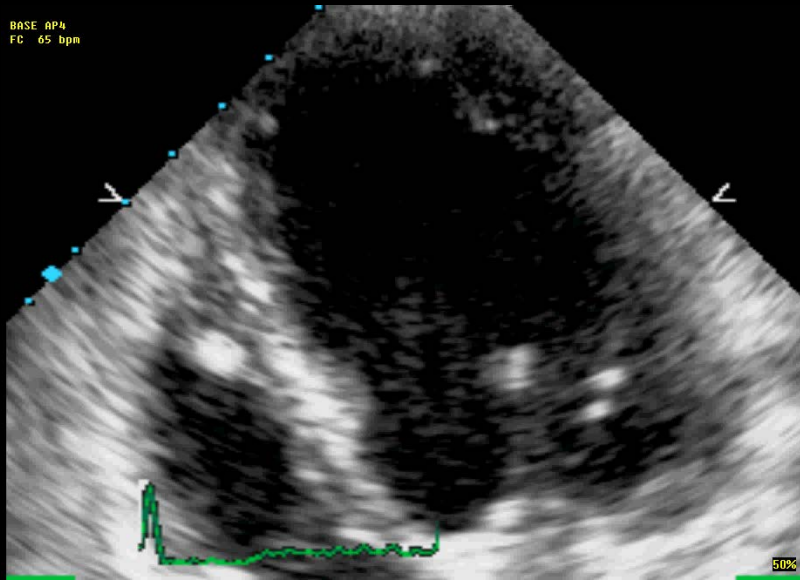
2012 ESC/EACTS Guidelines on Management of VHD: Indications for AVR in AS

**Severe AS on DSE: Increase in AVA $<0.2 \text{ cm}^2$ with final AVA $<1 \text{ cm}^2$;
mean gradient $>40 \text{ mmHg}$**

Flow reserve: $>20\%$ increase in stroke volume

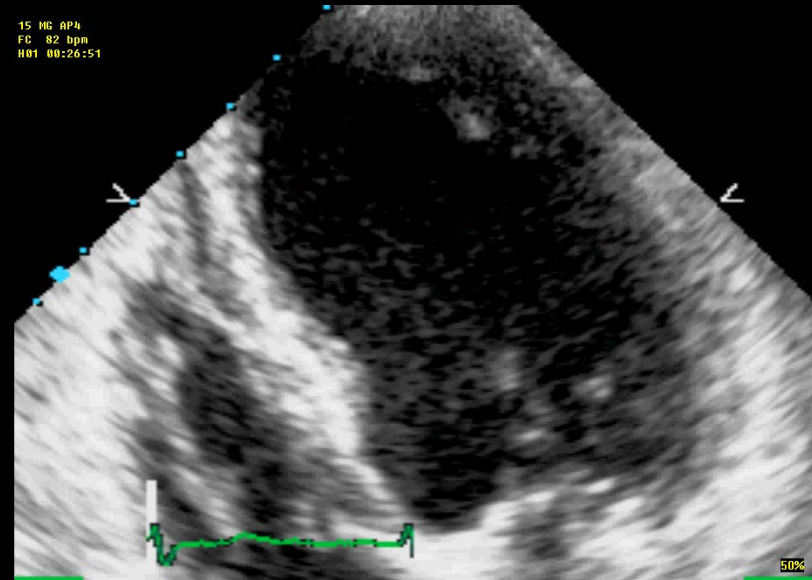
Case

Resting Echo

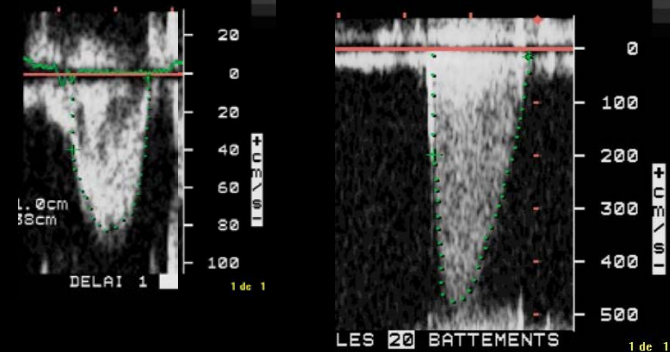
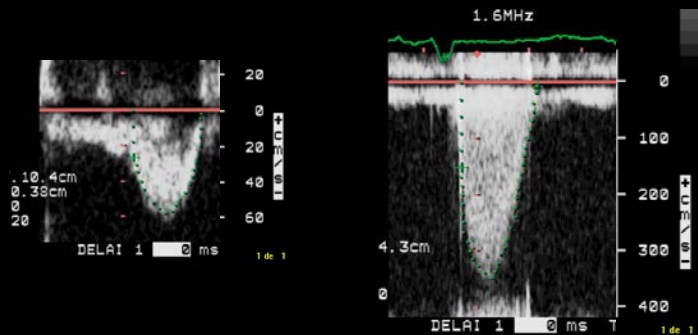


LVEF=40% SV= 53 ml
AVA= 0.77 cm²
 $\Delta P= 49 / 29$ mmHg

DSE



LVEF=50% SV= 73 ml
AVA= 0.75 cm²
 $\Delta P= 92 / 52$ mmHg



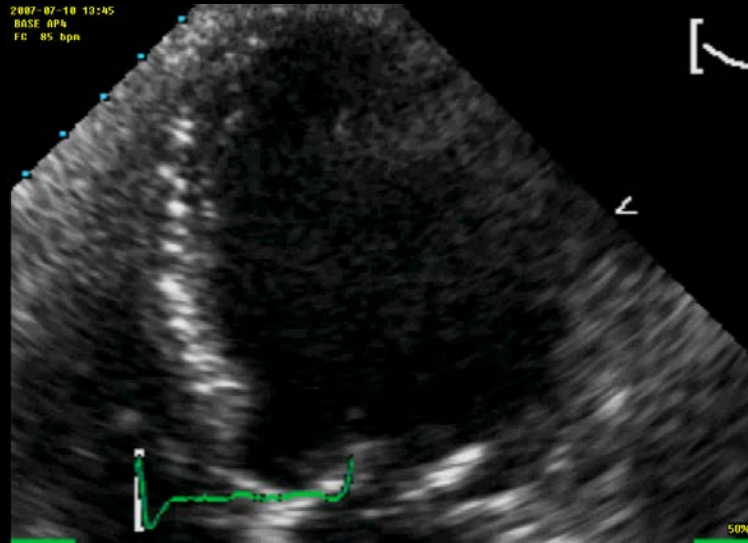
Case:

➤ *Contractile/flow reserve: Yes*

➤ *Stenosis severity: True-severe*

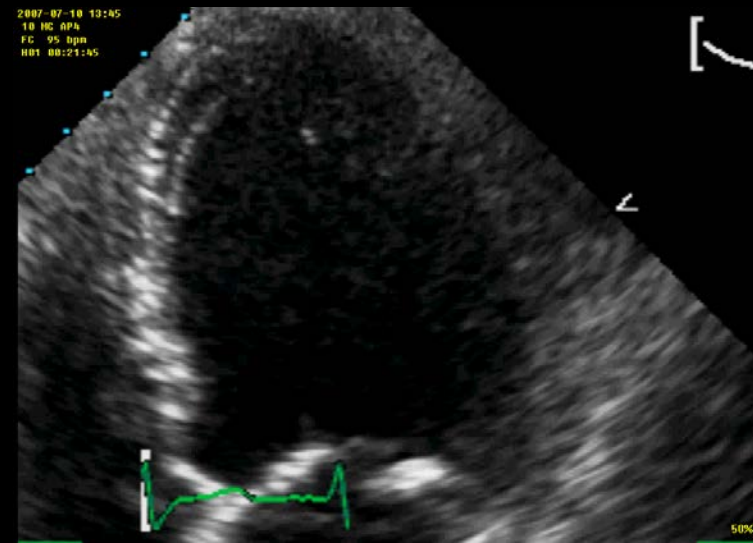
Case

Resting Echo

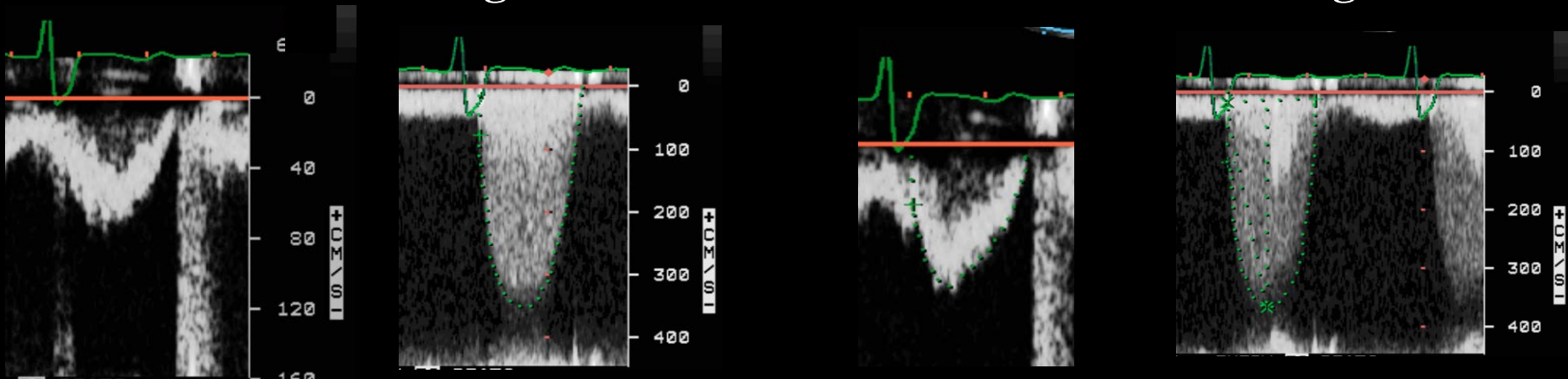


LVEF=25% SV= 51 ml
AVA= 0.8 cm²
 $\Delta P= 46 / 27$ mmHg

DSE



LVEF=30% SV= 57 ml
AVA= 0.8 cm²
 $\Delta P= 52 / 30$ mmHg



Case:

- *Contractile/flow reserve: No*
- *Stenosis severity: Indeterminate*

Usefulness of AoV Ca Scoring by MDCT to Differentiate True vs. Pseudo-Severe Stenosis in Low-Flow, Low-Gradient AS

Pseudo-Severe



AVC: 1034 AU

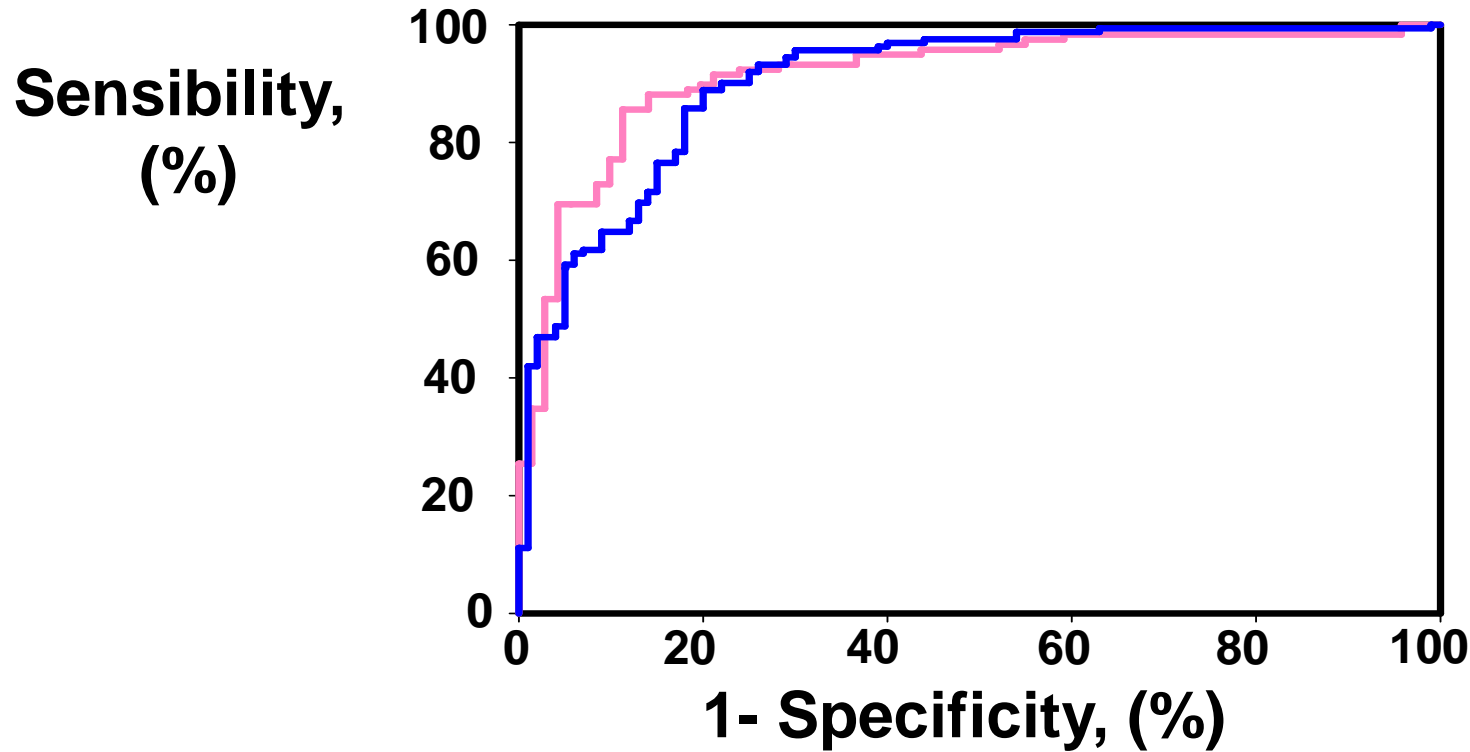
True-Severe



AVC: 4682 AU

*Clavel et al. JACC 2013: AVC Score to identify Severe AS: >1200AU in ♀
>2000 AU in ♂*

Mayo-Québec-Bichat Collaboration: Accuracy of AVC to identify severe AS

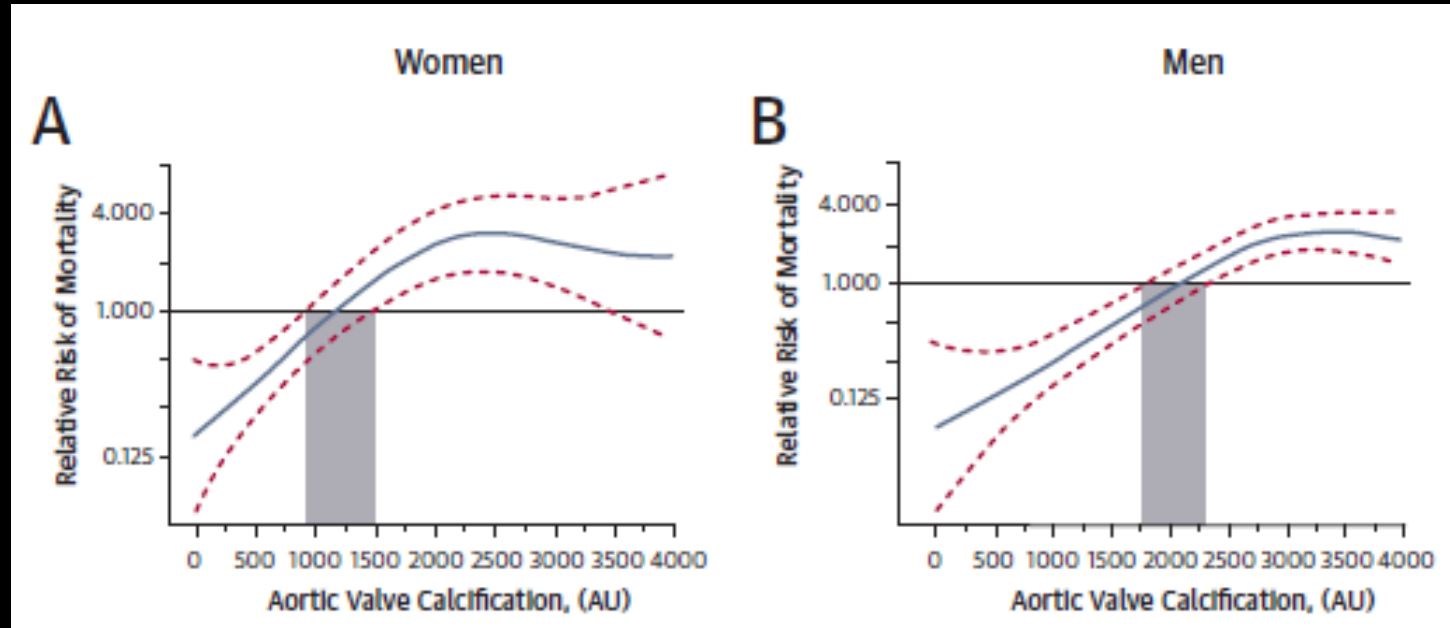


**Case:
2010 AU**

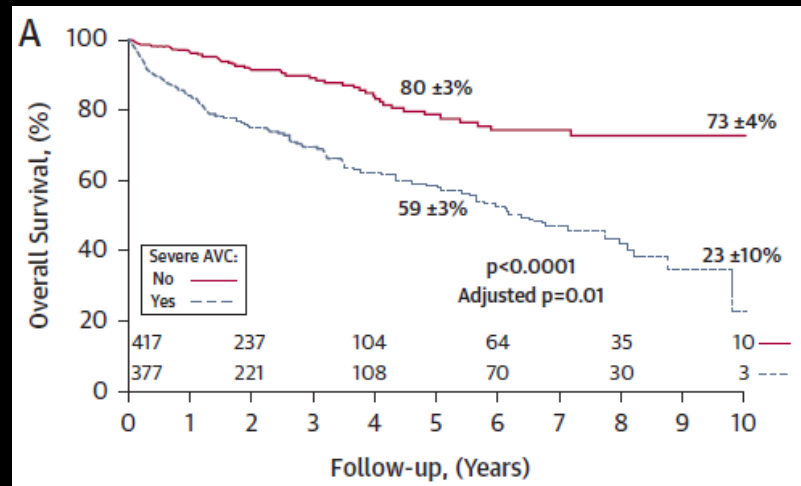
Gender	Threshold	AUC	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Women	1274 AU	0.91	89	86	93	79
Men	2065 AU	0.90	89	80	88	82

Mayo-Québec-Bichat Collaboration: Impact of AVC on Survival In patients with AS

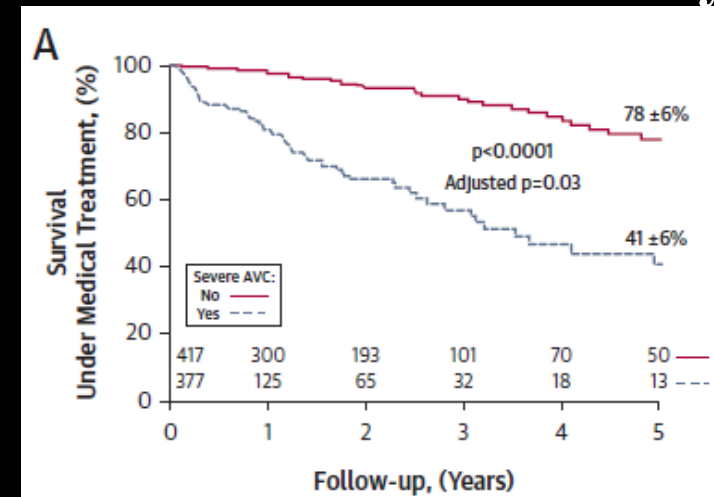
>1200AU in ♀
>2000 AU in ♂



Whole Cohort

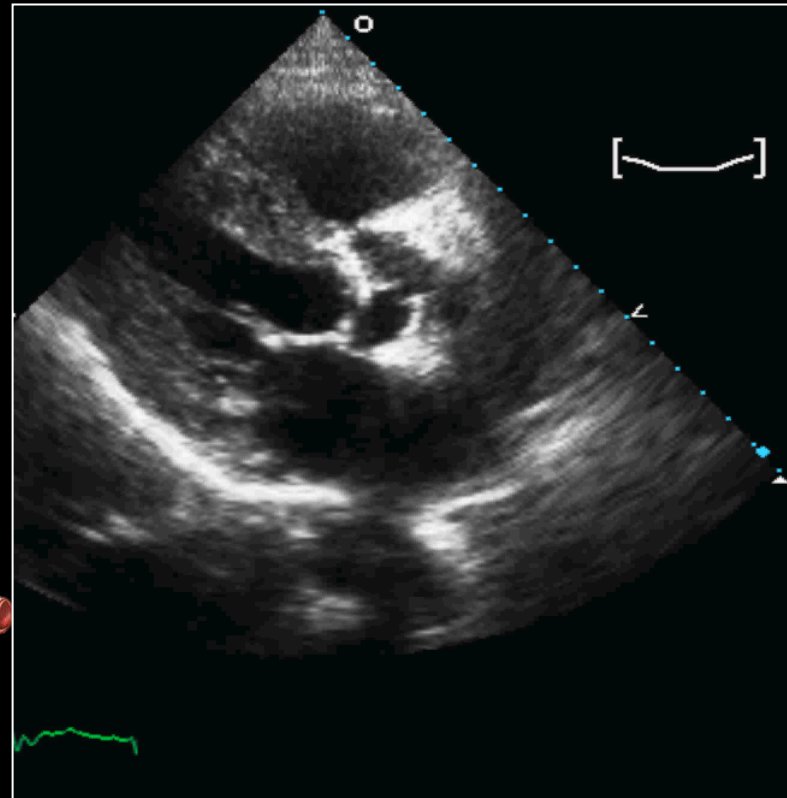
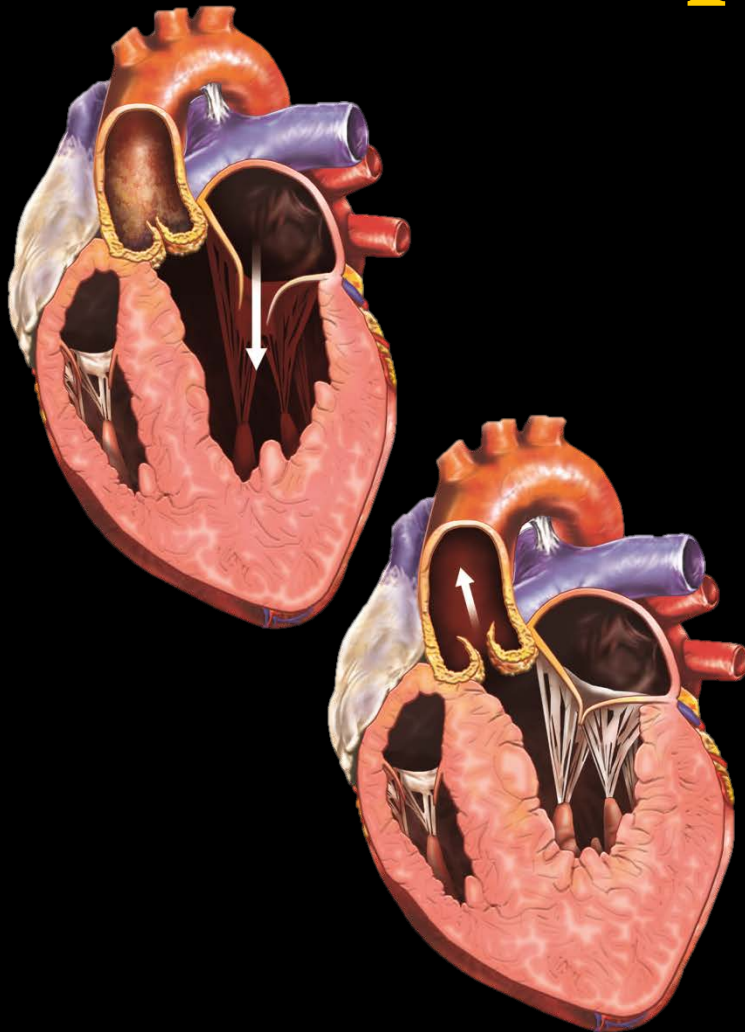


Patients treated Medically



Clavel et al.
JACC 2014

“Paradoxical” Low-Flow, Low-Gradient AS with Preserved LVEF

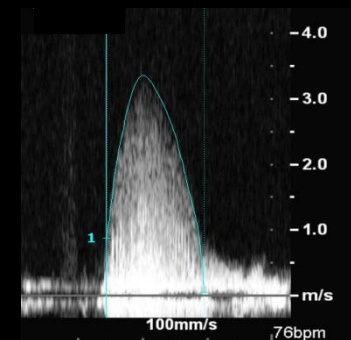
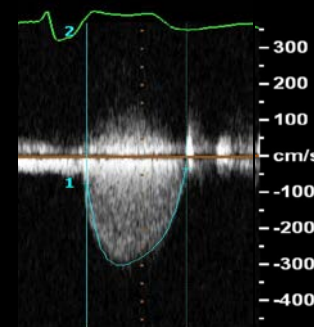
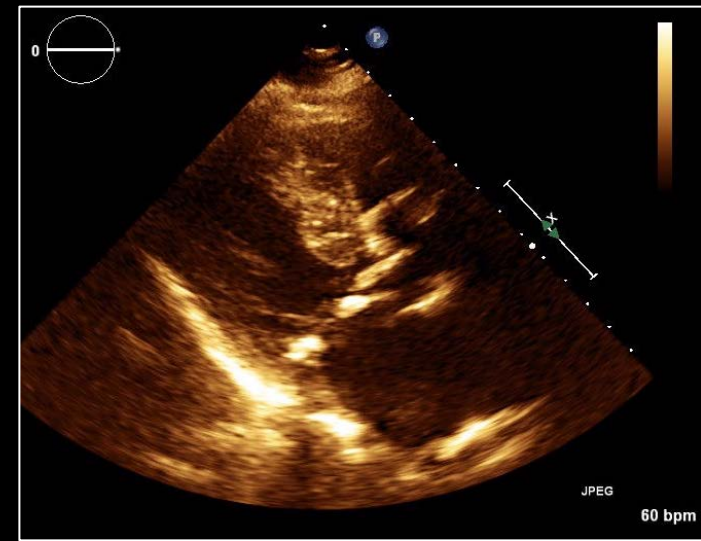


↑ Age
Women
Hypertension
MetS – Diabetes

LVEF=60%
SV=46 mL
MG=29 mmHg

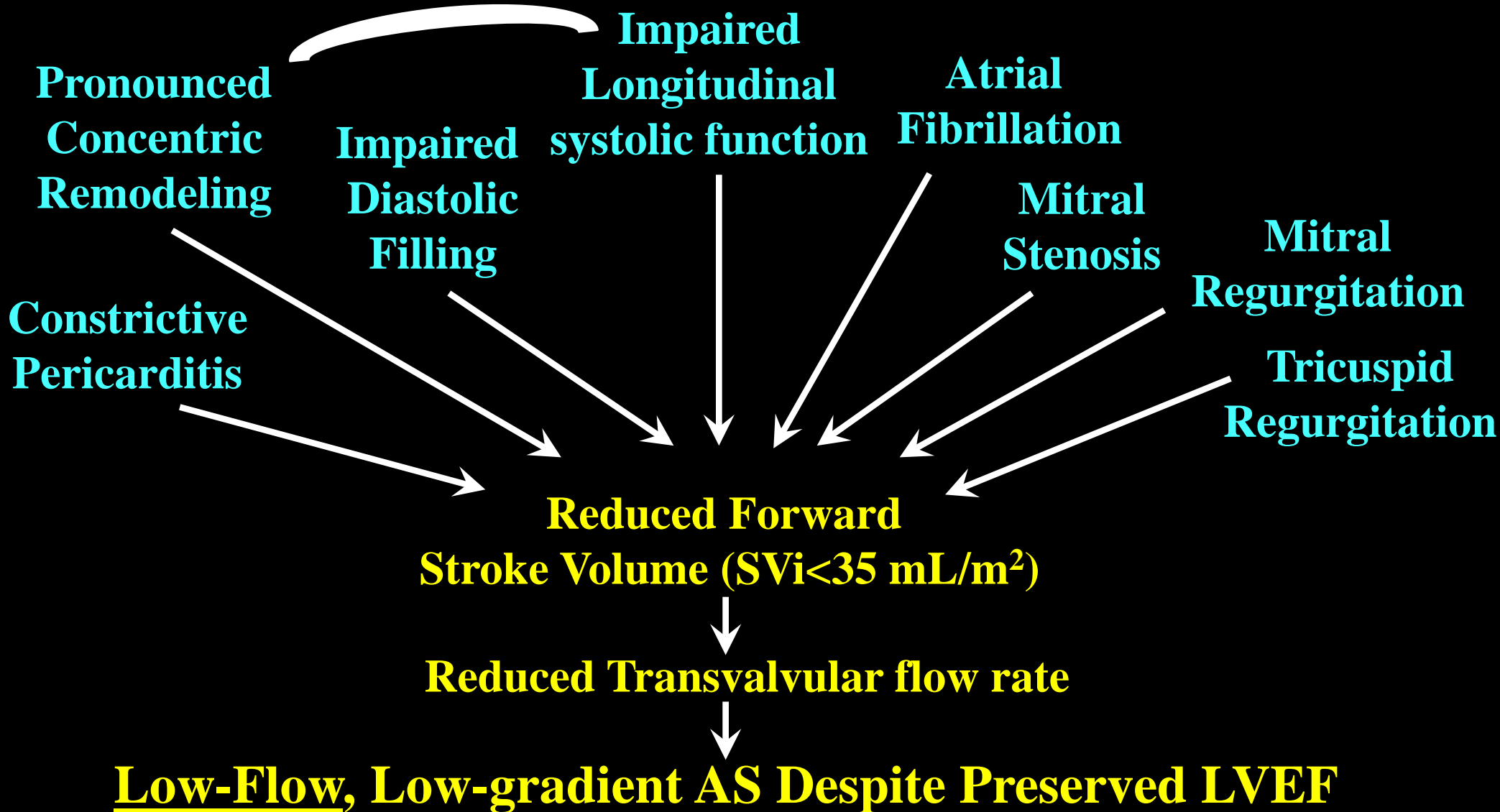
Case

- 82 y.o. woman
- Hypertension treated with ACEI
- No CAD
- NYHA III, HF hospitalization
- LVEF: 65%
- Severe Diastolic Dysf.
- AS severity on echo:
 - AVA: 0.64 cm^2 ; iAVA: $0.36 \text{ cm}^2/\text{m}^2$
 - Peak/mean gradient: **44/26 mmHg**
 - SV index: **29 ml/m²**

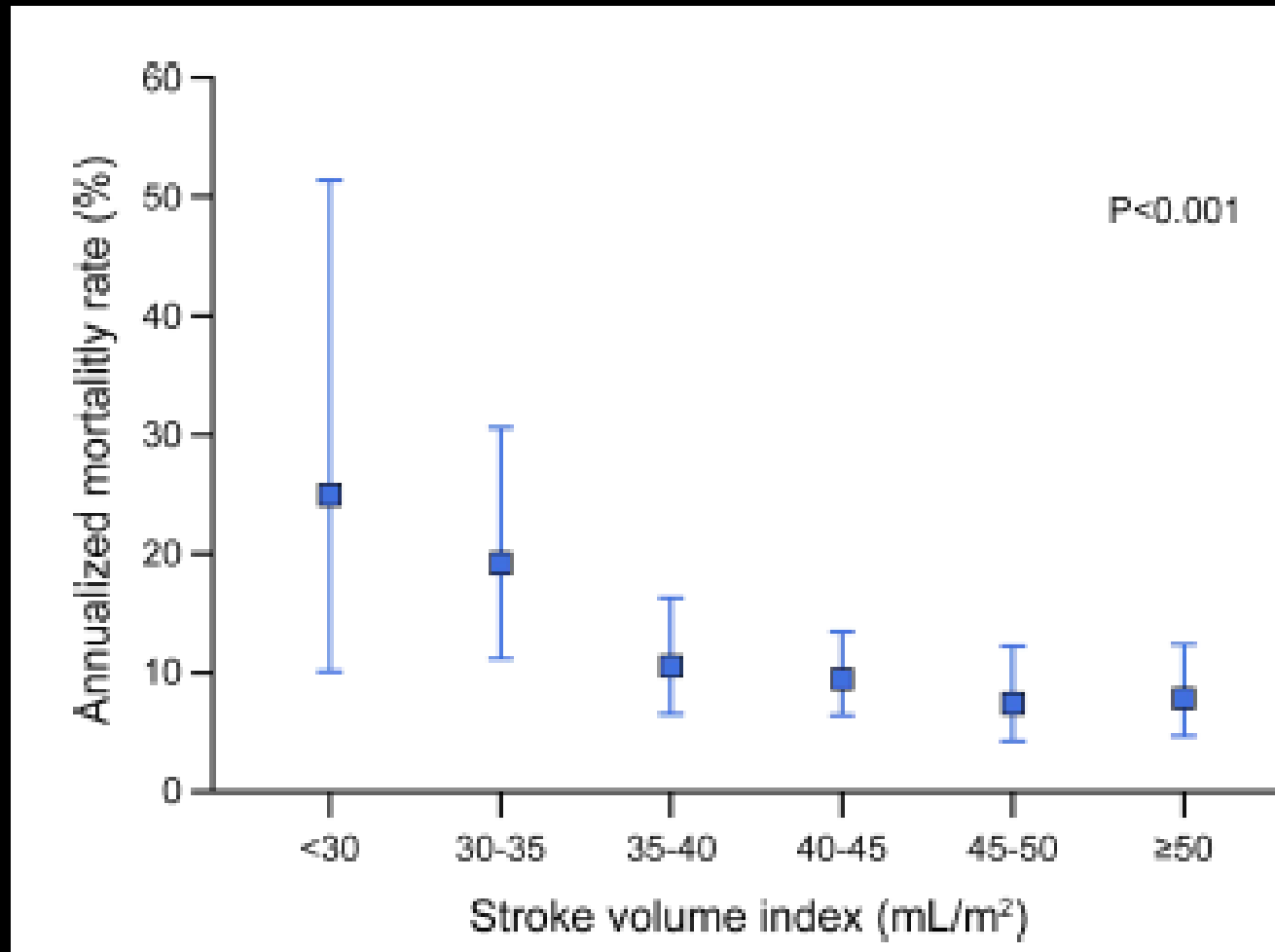


AORTIC STENOSIS

± HYPERTENSION

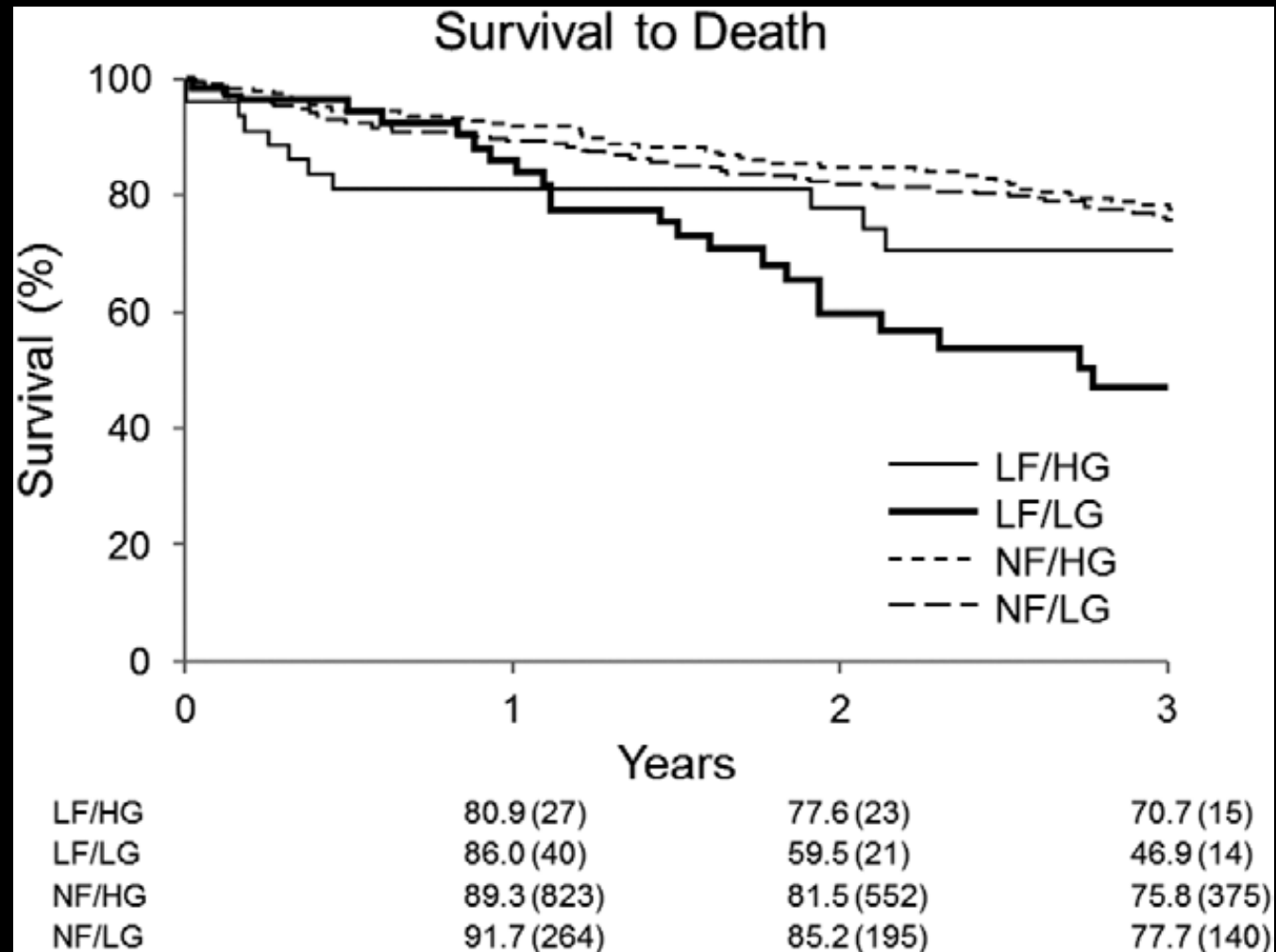


Survival by stroke volume index in patients with low-gradient normal LVEF severe aortic stenosis

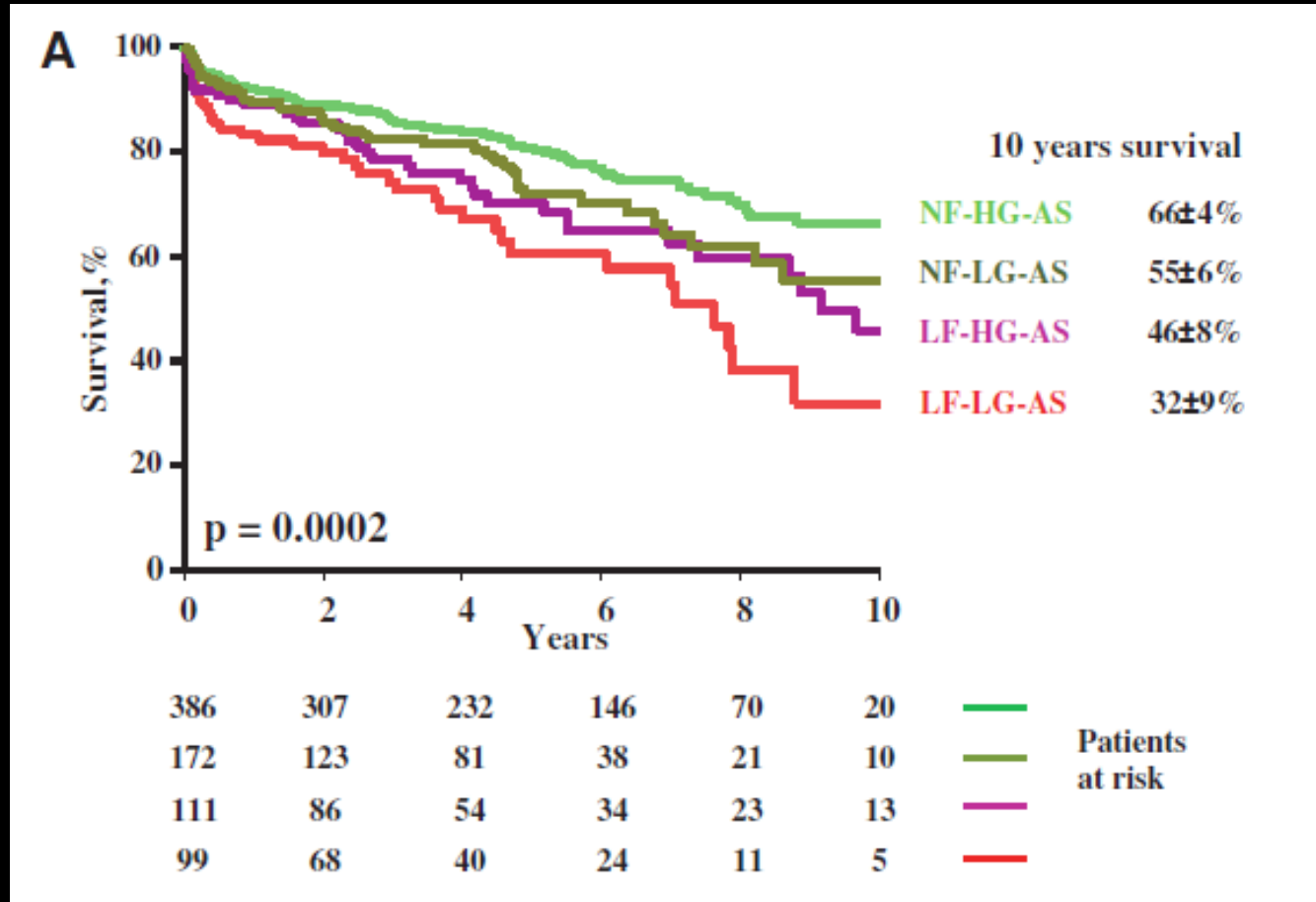


Eleid et al.
Heart 2014

Outcome of Patients with Low-Gradient AS



Outcome in Paradoxical Low-Flow, Low-Gradient Severe Aortic Stenosis and Preserved LVEF A Cardiac Catheterization Study

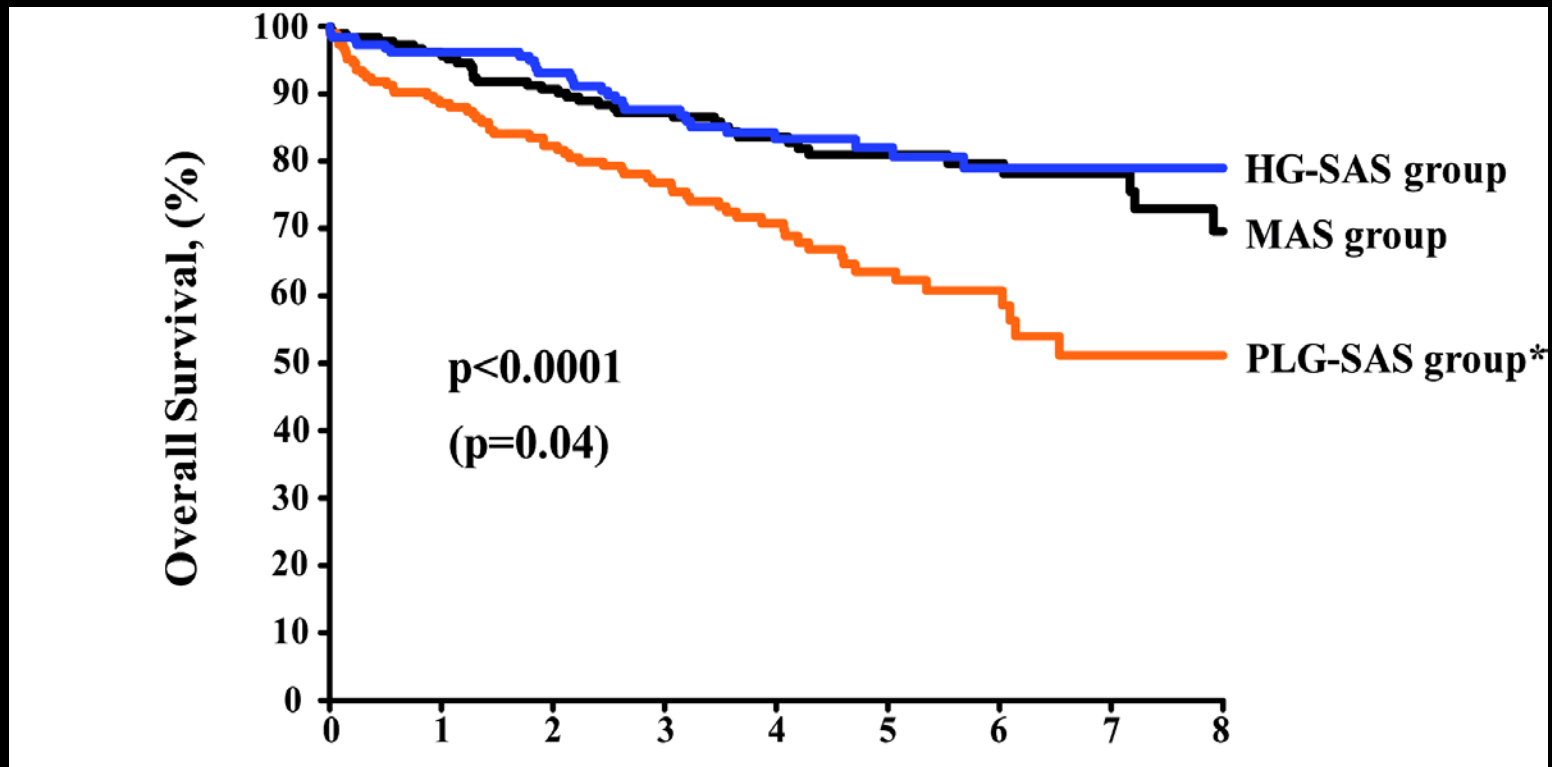


Mohty et al.

Circulation 2013

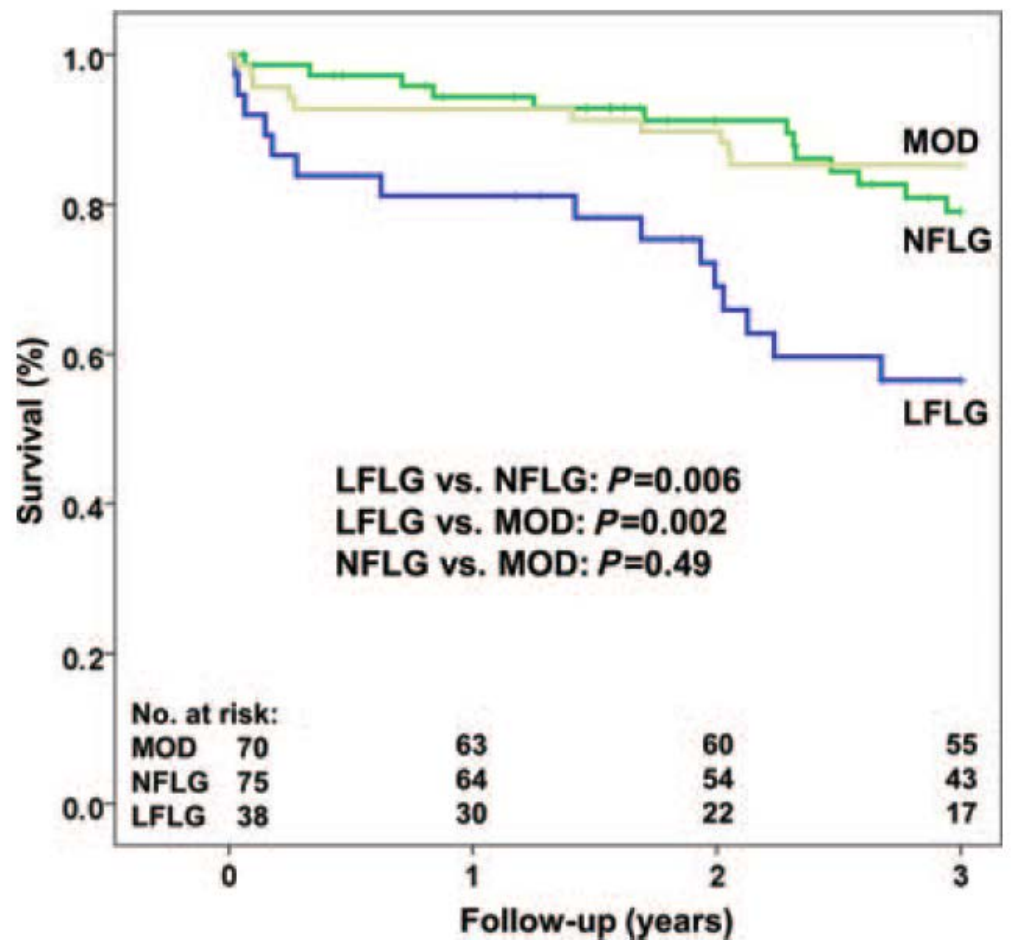
Outcome of Patients with Paradoxical Low-Flow, Low-Gradient AS

Case Match Study: 3 × 187 patients



Clavel et al.
JACC 2012

Outcome of Patients with Paradoxical Low-Flow, Low-Gradient AS

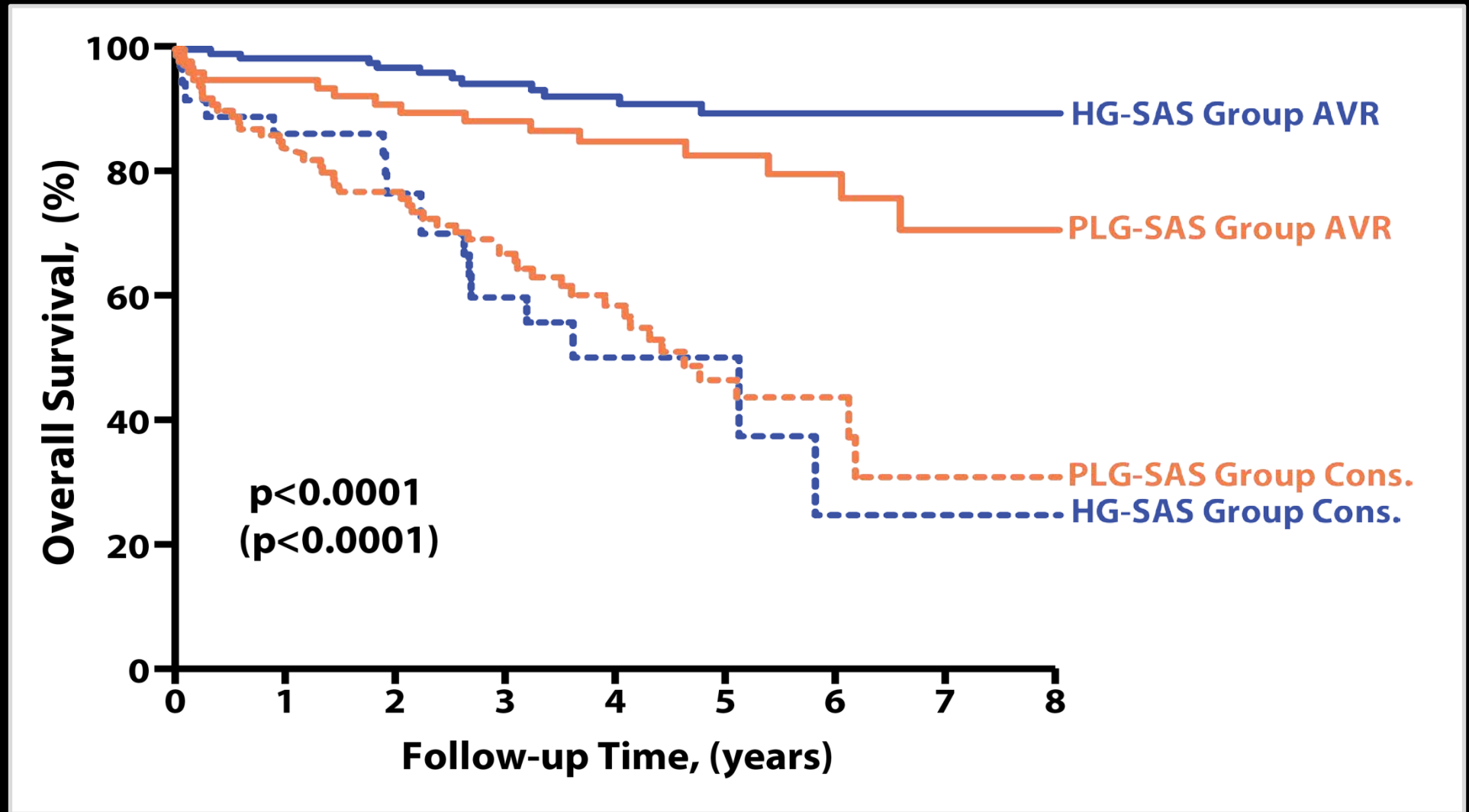


Conclusions:

Patients with paradoxical LFLG AS exhibit marked concentric remodelling, impaired LV longitudinal function and worse prognosis

Normal-flow, low-gradient AS patients have outcomes similar to moderate AS

Impact of AVR on Survival in Patients with Paradoxical Low-Flow, Low-Gradient AS



Impact of AVR on Outcome of Symptomatic Patients with Severe Stenosis, Low Gradient, and Preserved LVEF

1704 Patients

Table 5. Multivariable Predictors of All-Cause Mortality

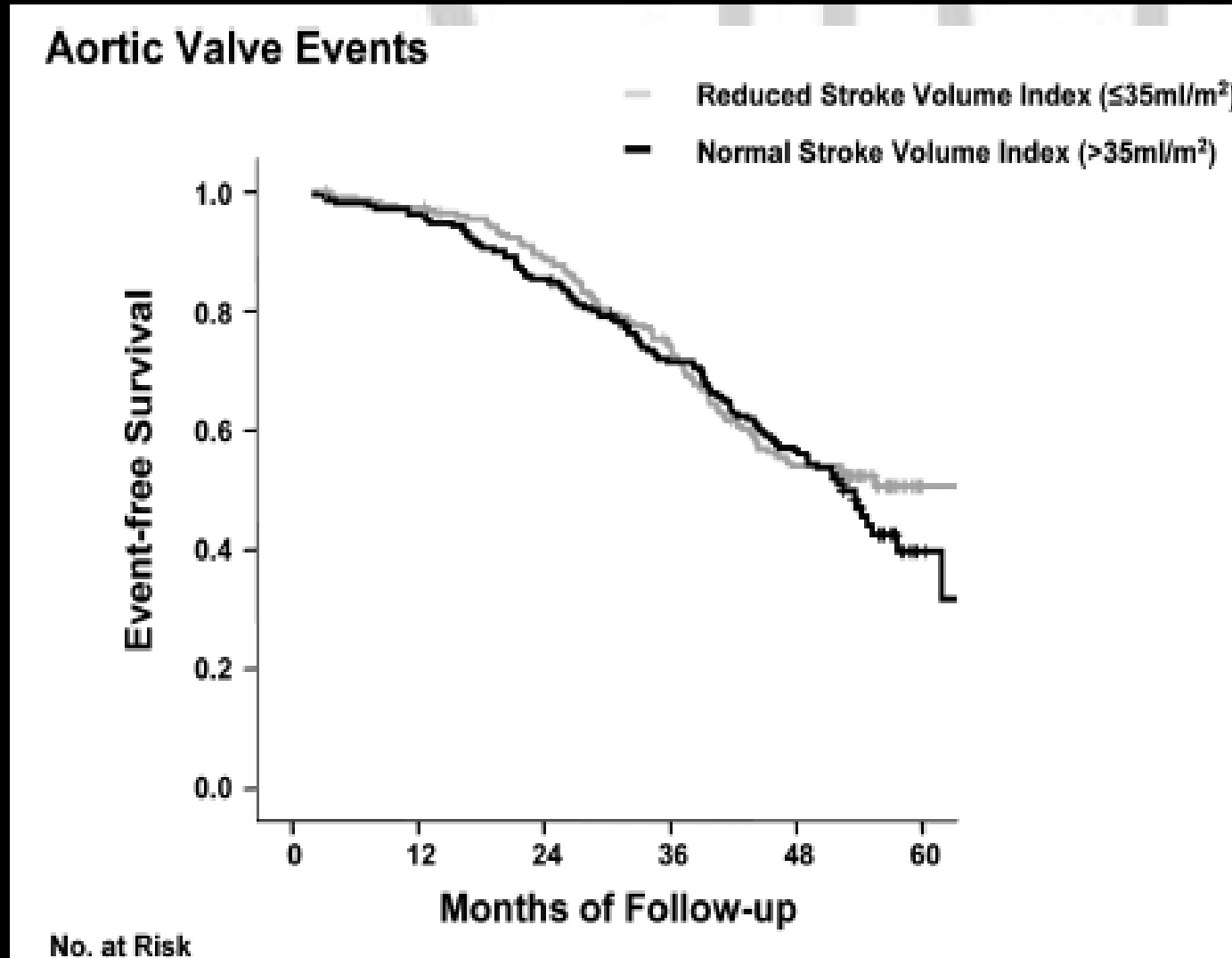
Variable	RR	Lower 95%	Upper 95%	P Value
Flow-gradient patterns				
NF/LG no AVR	1.00	Reference group		
NF/LG+AVR	0.86	0.518	1.414	0.54
LF/LG no AVR	3.26	1.713	6.217	0.0003
LF/LG+AVR	0.94	0.384	2.297	0.89
NF/HG no AVR	2.81	1.905	4.140	<0.0001
NF/HG+AVR	0.69	0.450	1.048	0.08
LF/HG no AVR	1.55	0.615	3.904	0.35
LF/HG+AVR	0.89	0.396	1.994	0.77
Clinical				
Age	1.02	1.012	1.034	<0.0001
Male sex	1.46	1.169	1.821	0.0008
Obesity	1.51	1.214	1.885	0.0002
Hypertension	1.42	1.076	1.868	0.01
Previous HF	1.29	0.984	1.684	0.07
Echocardiographic				
Aortic valve area	0.07	0.026	0.163	<0.0001
Ejection fraction	0.98	0.968	1.000	0.05

AVR indicates aortic valve replacement; HF, heart failure; HG, high gradient; LF, low flow; LG, low gradient; HG, high gradient; NF, normal flow; and RR, relative risk.

Eleid et al.
Circulation 2013

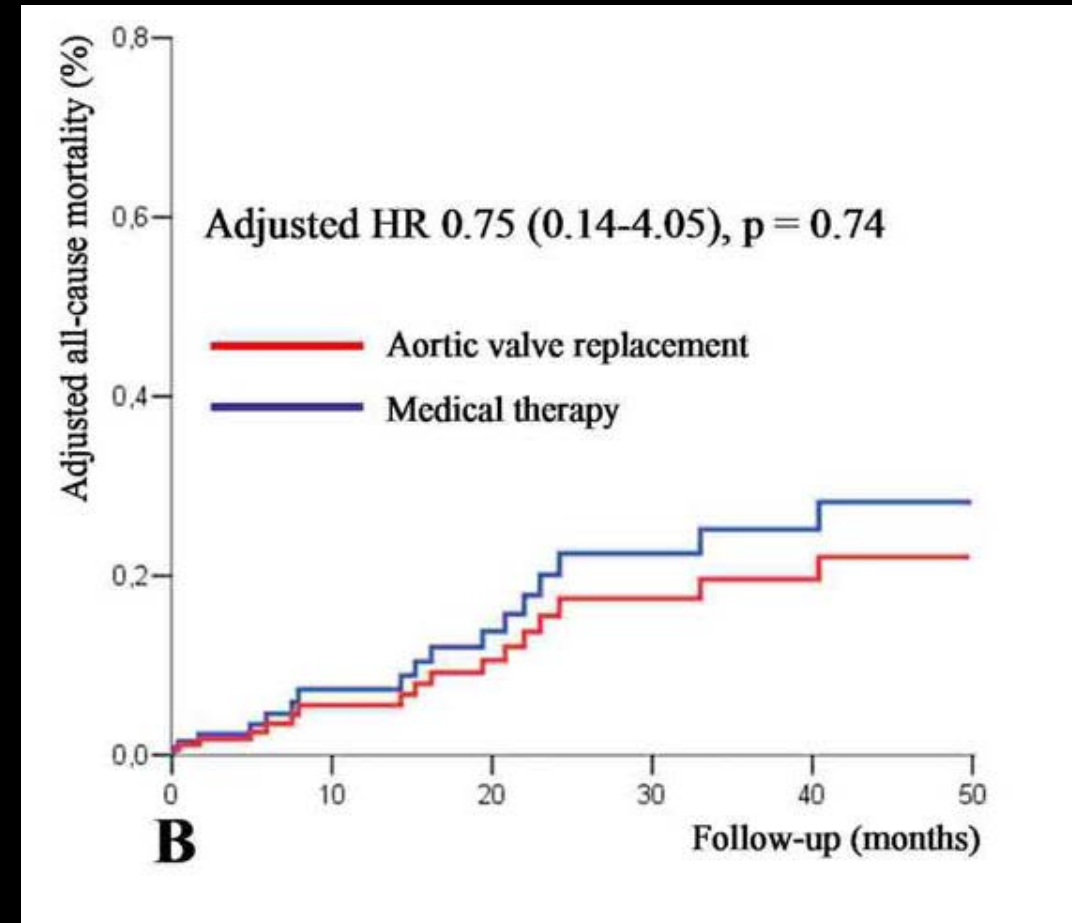
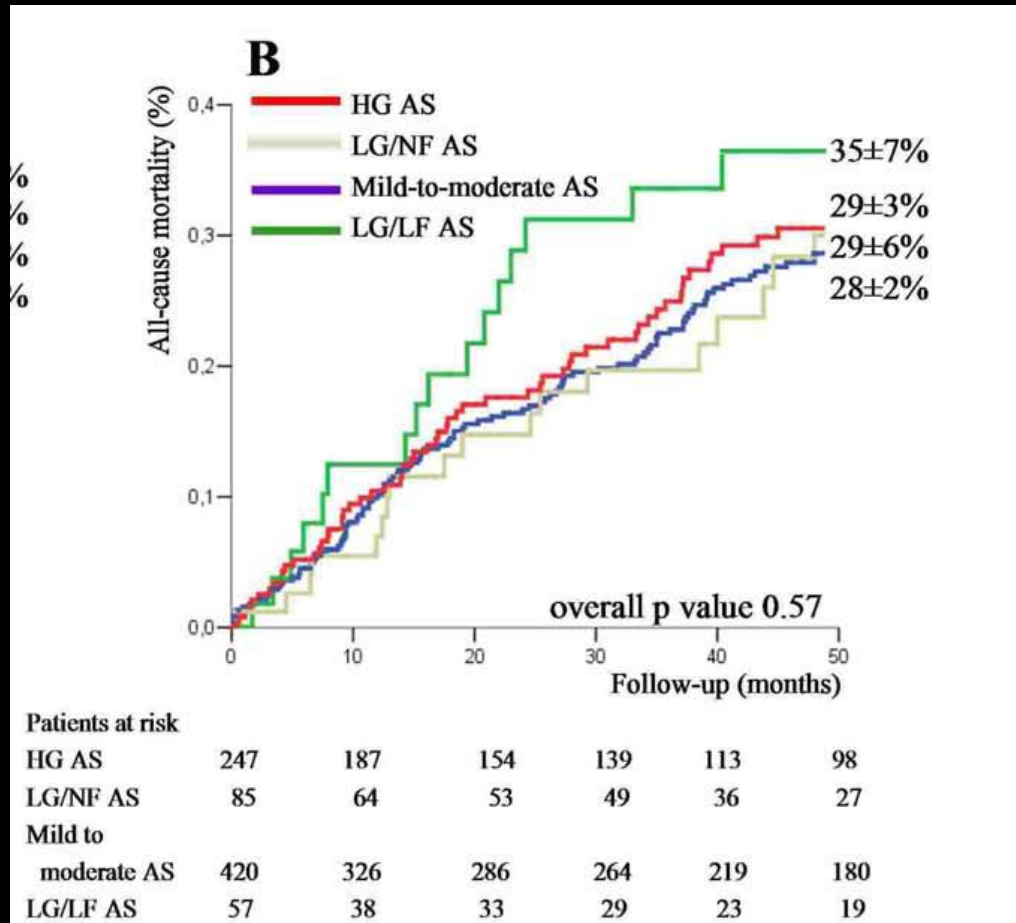
Outcome of Patients With Low-Gradient "Severe" Aortic Stenosis and Preserved LVEF

A Substudy of the SEAS trial

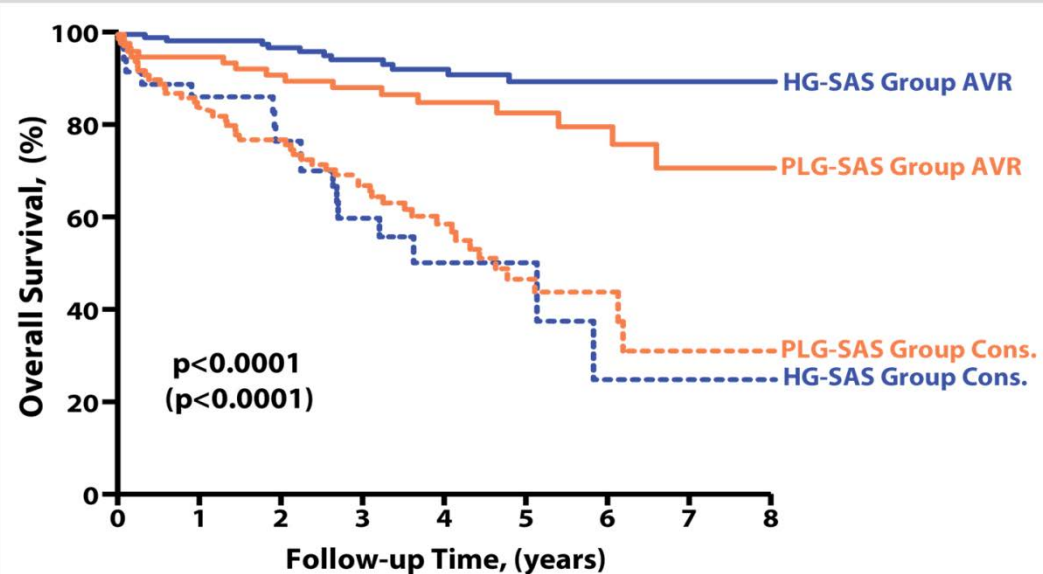
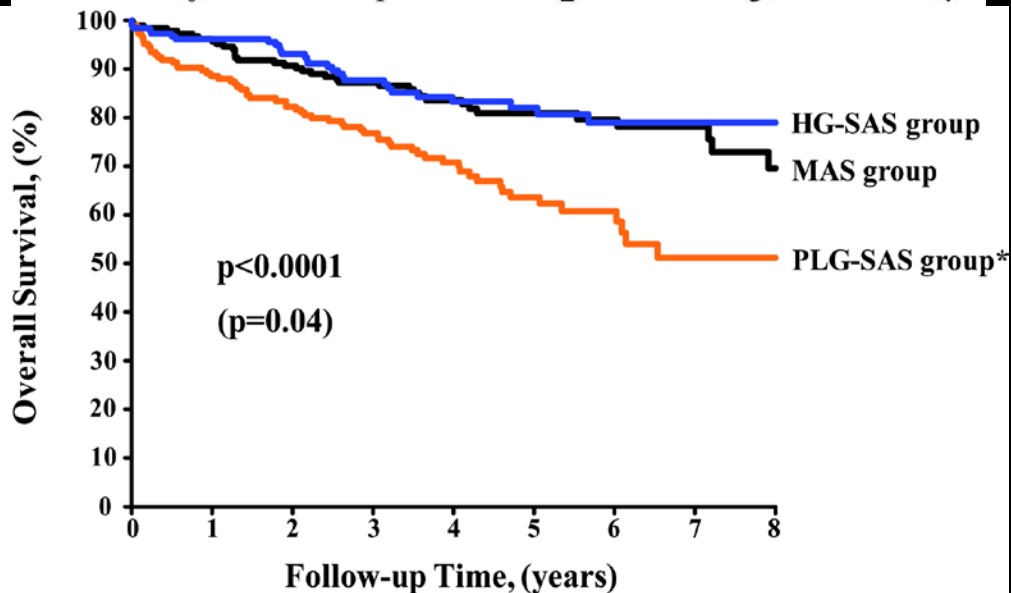
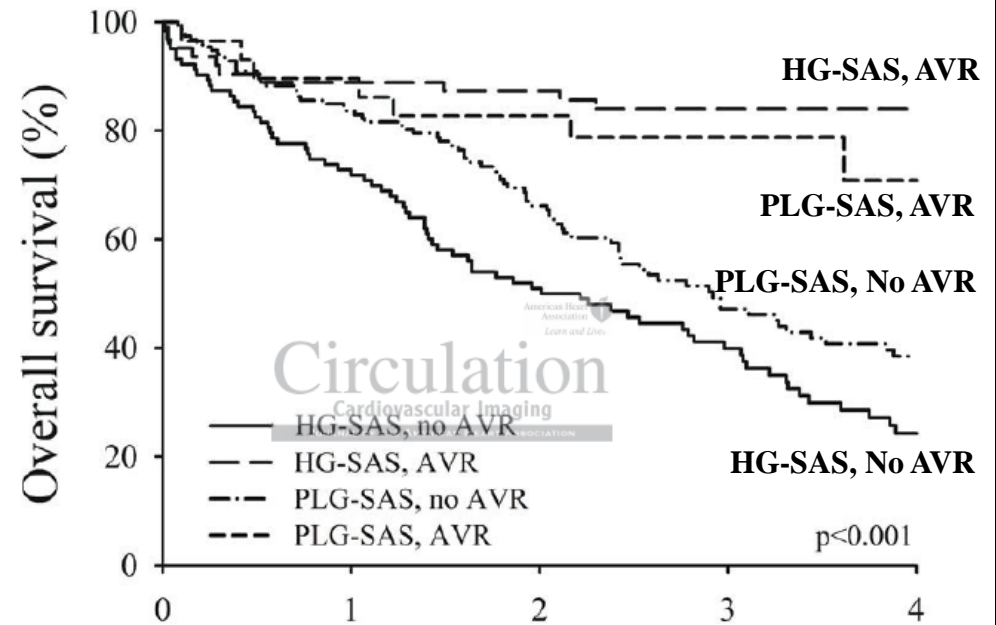
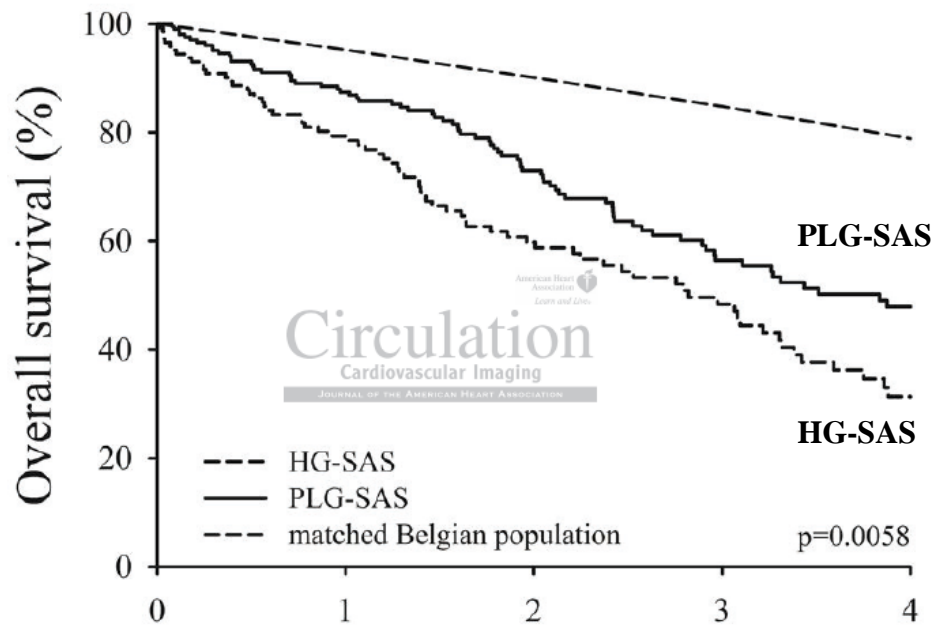


*Jander et al.
Circulation.
2011;123:887-895.*

Outcome of Patients with Paradoxical Low-Gradient AS and Impact of AVR



Outcome of Patients with Paradoxical Low-Gradient AS and Impact of AVR



Potential Causes of Discordance between AVA (e.g. 0.8) and gradient (e.g. 30) in Pts. With Preserved LVEF

➤ Measurement errors

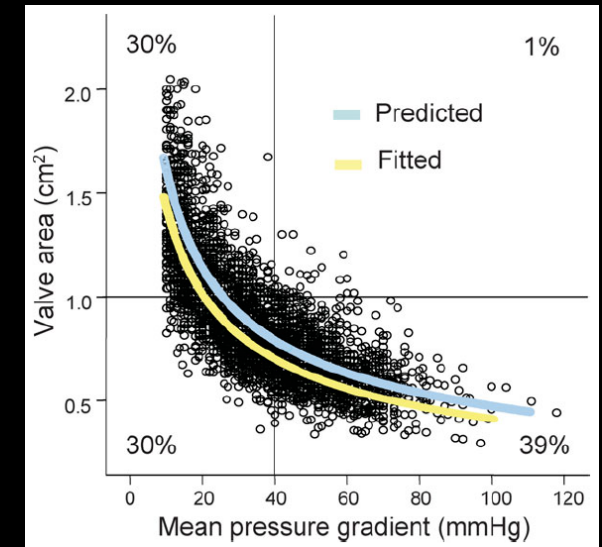
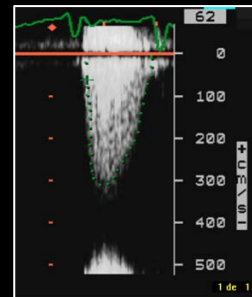


➤ Small body size



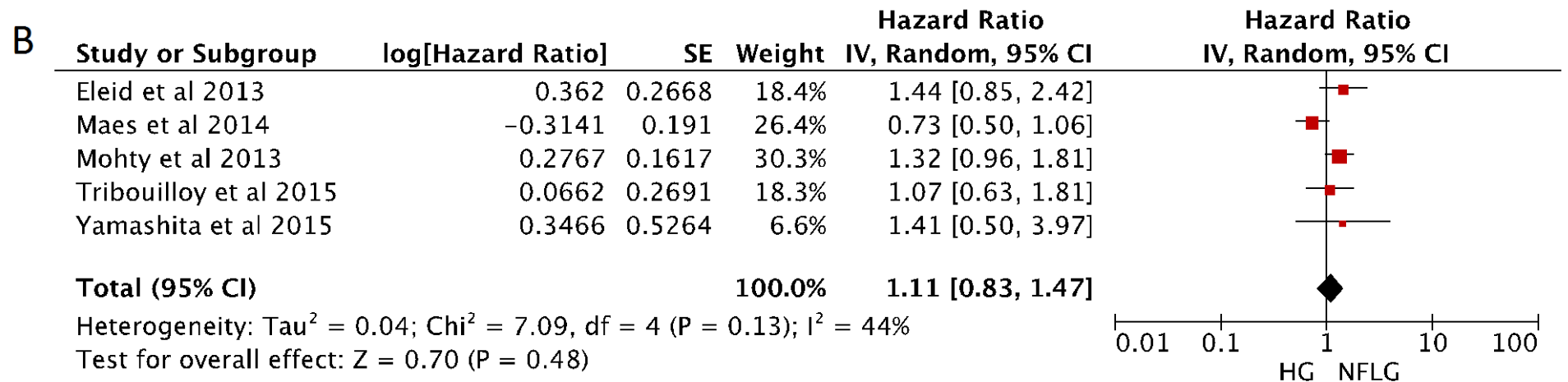
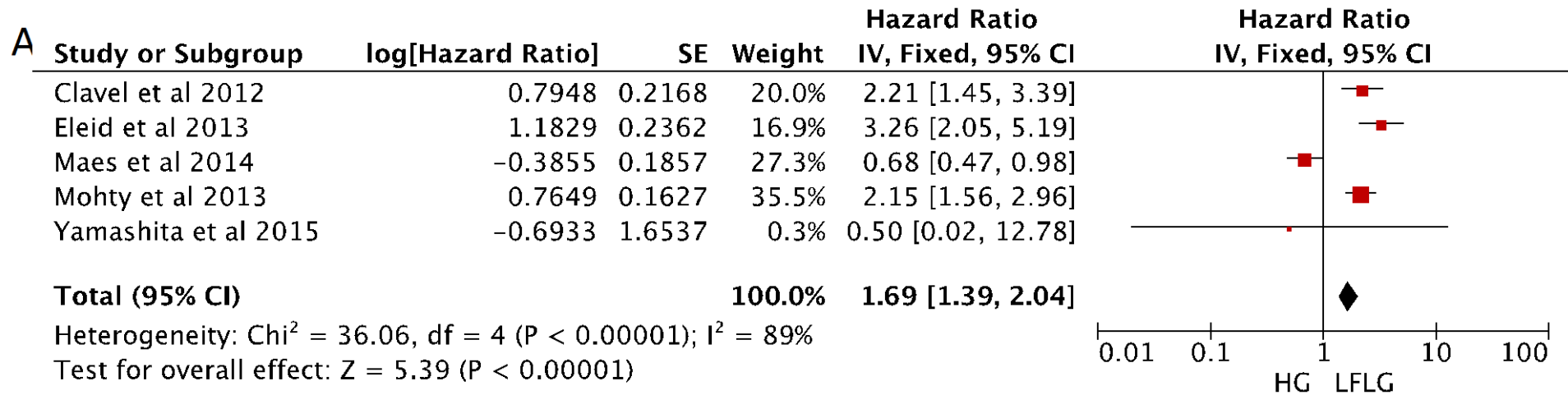
➤ Normal-flow, low-gradient AS
Inconsistency in guidelines criteria

➤ Paradoxical low-flow, low-gradient severe? AS

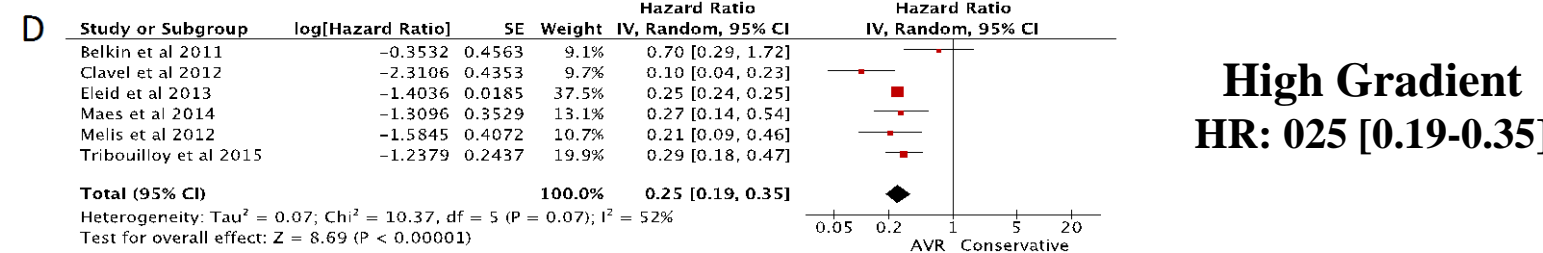
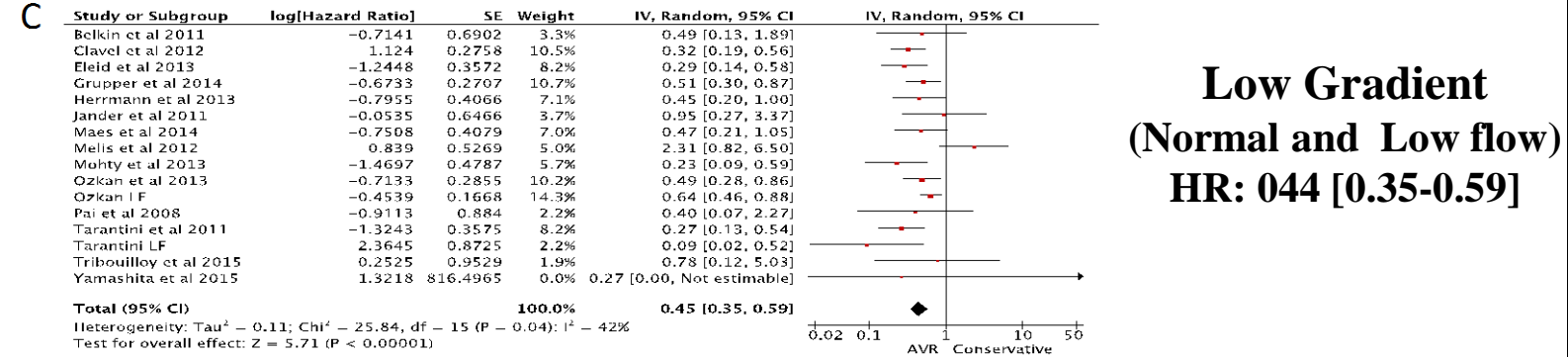
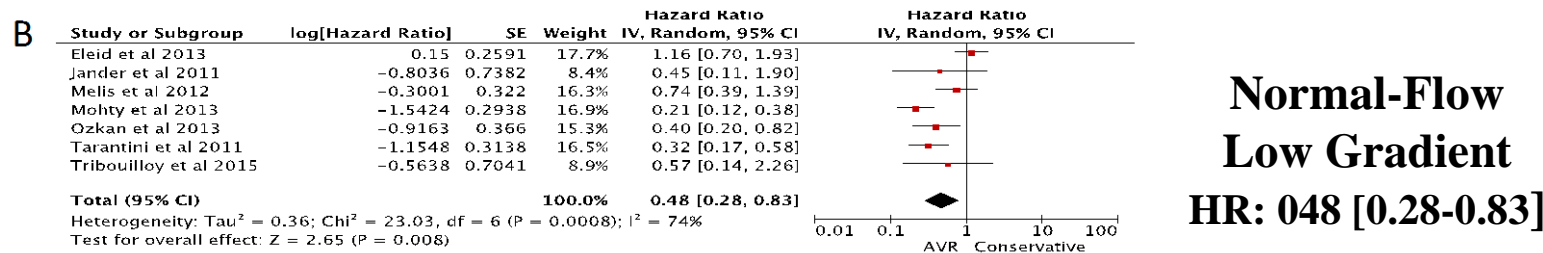
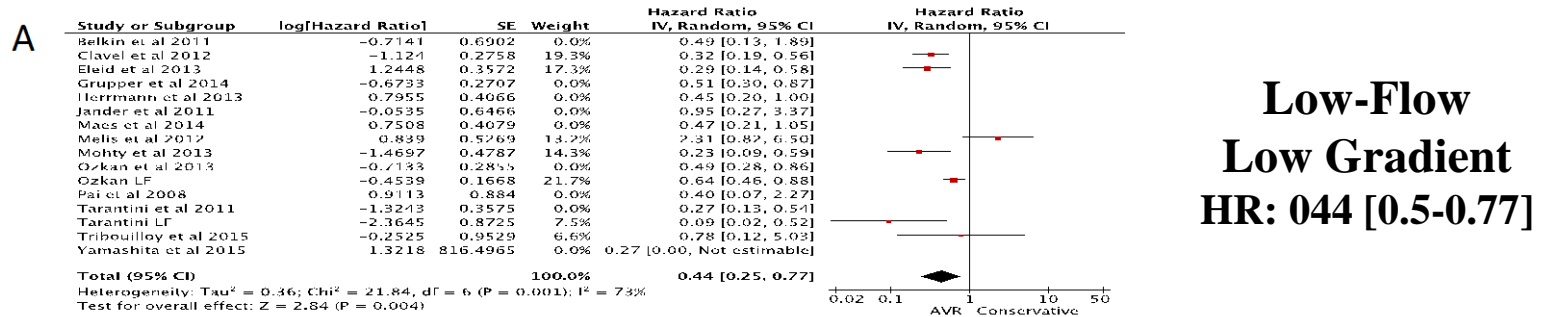


Minners et al.
Eur Heart J, 2008

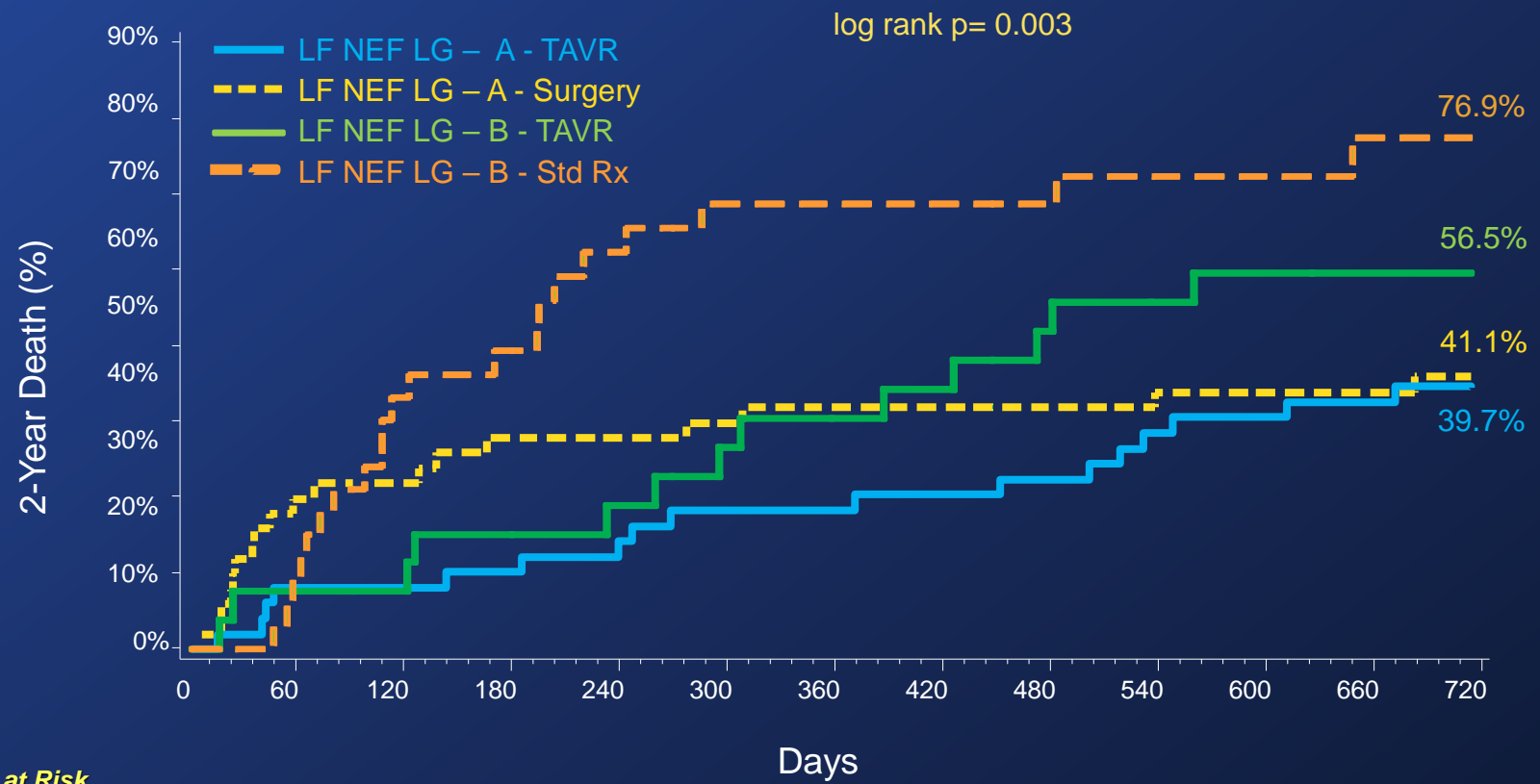
Outcome of Low-Flow / Low-Gradient AS: A Meta-Analysis



Benefit of AVR in Low-Flow / Low-Gradient AS: A Meta-Analysis



Treatment Comparison in Normal EF, Low-flow, low-gradient AS



Numbers at Risk

	0	60	120	180	240	300	360	420	480	540	600	660	720
A – TAVR	43	39	38	34	34	33	29	26	22				
A – Surgery	44	33	30	30	28	27	27	26	23				
B – TAVR	23	21	19	17	15	13	11	10	10				
B – Std Rx	29	22	15	10	9	9	6	5	4				

Guidelines on Management of VHD: Indications for AVR in Paradoxical Low-Flow, Low-Gradient AS

Definition: AVA \leq 1.0 cm², Indexed AVA \leq 0.6 cm²/m²
Mean gradient < 40 mmHg,
LVEF \geq 50%, SVi<35 mL/m²

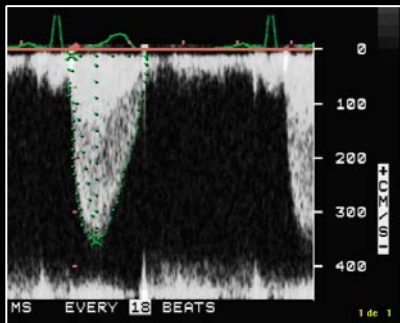
Stage: D3

Guidelines	Recommendation for AVR	Class
ESC-EACTS 2012	AVR should be considered in symptomatic patients with low flow, low gradient (<40 mmHg) AS with normal EF only after careful confirmation of severe AS .	IIa
ACC-AHA 2014	AVR is reasonable in symptomatic patients who have low-flow, low-gradient severe AS who are normotensive and have an LVEF \geq 50% if clinical, hemodynamic, and anatomic data support valve obstruction as the most likely cause of symptoms	IIa

Usefulness of Stress-Echocardiography to Differentiate True vs. Pseudo-Severe Stenosis in Paradoxical, Low-Flow, Low-Gradient AS

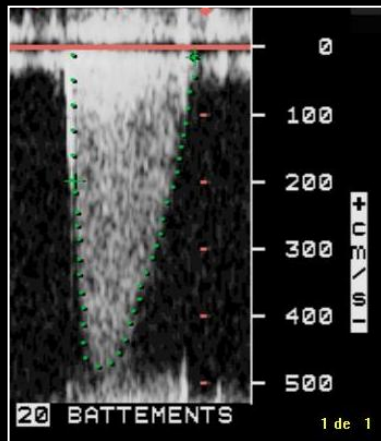
51 patients with PLF-LG

REST



DSE

15 $\mu\text{g}/\text{kg}/\text{min}$



Peak ΔP : 51

94 mmHg

Mean ΔP : 29

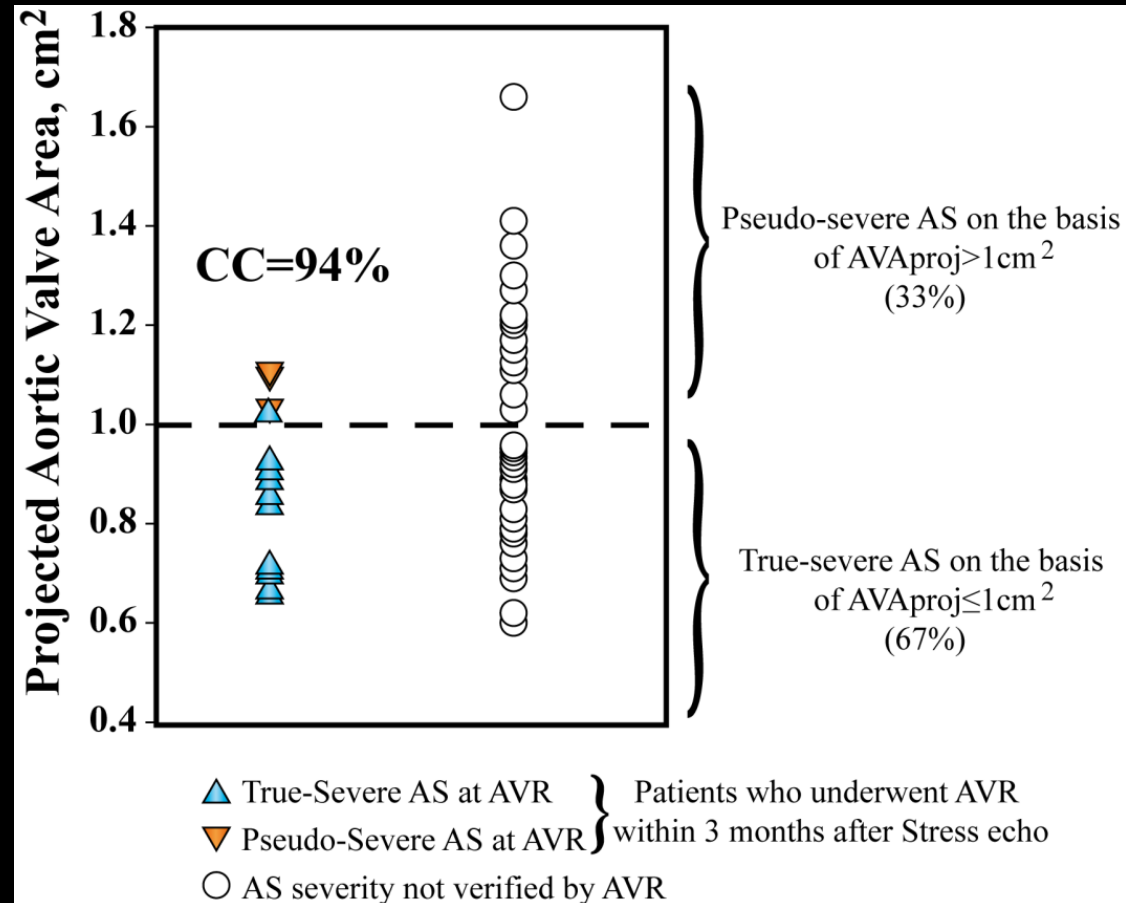
57 mmHg

AVA: 0.70

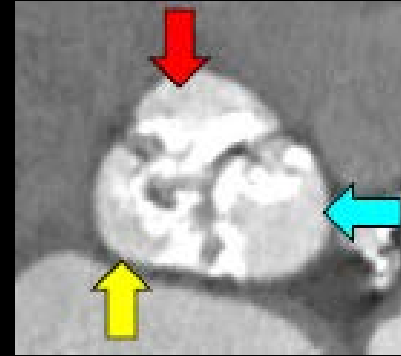
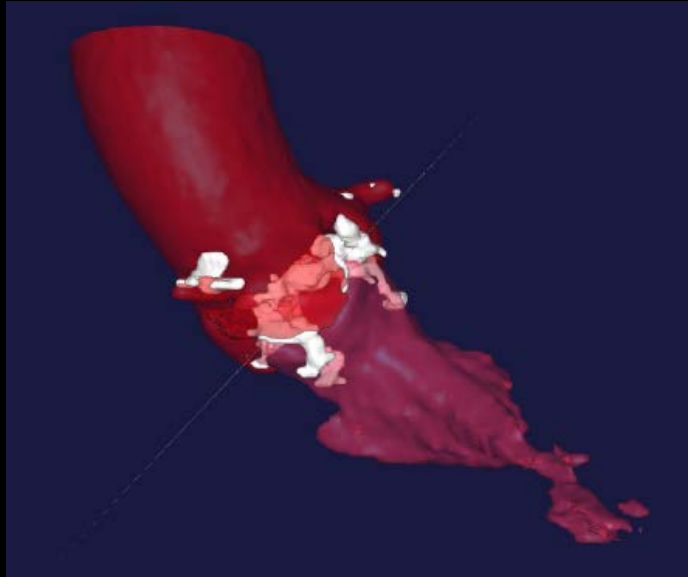
0.77 cm^2

LVEF: 60

65%



Case: Aortic Valve Calcium Scoring by MDCT



**AVC Score:
3200 AU**

EDITORIAL COMMENT

Management of Paradoxical Low-Flow, Low-Gradient Aortic Stenosis



Need for an Integrated Approach, Including Assessment
of Symptoms, Hypertension, and Stenosis Severity*

Philippe Pibarot, DVM, PhD, Marie-Annick Clavel, DVM, PhD

