Low Flow Low Gradient Aortic Stenosis – Challenges in Diagnosis and Management

HKCC ASC 2020

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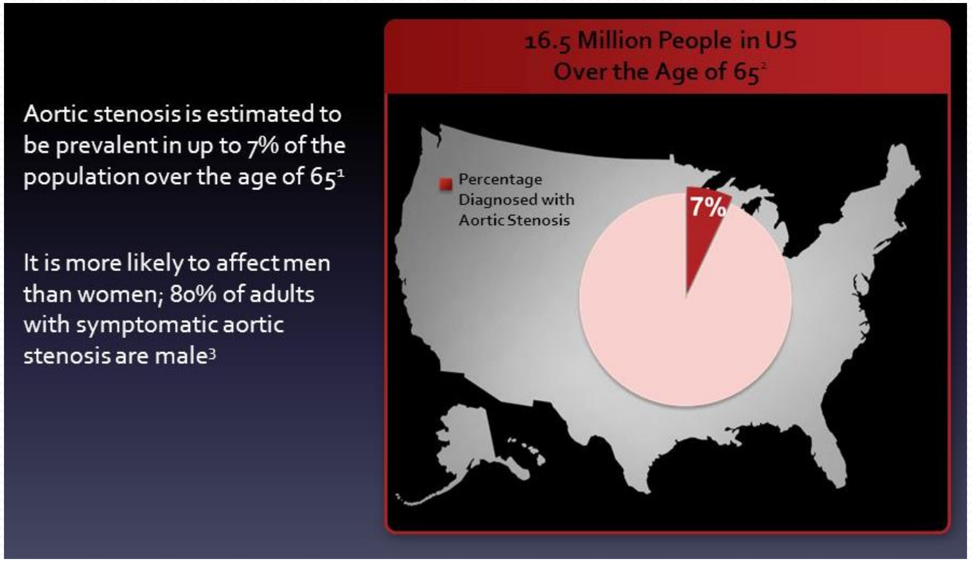
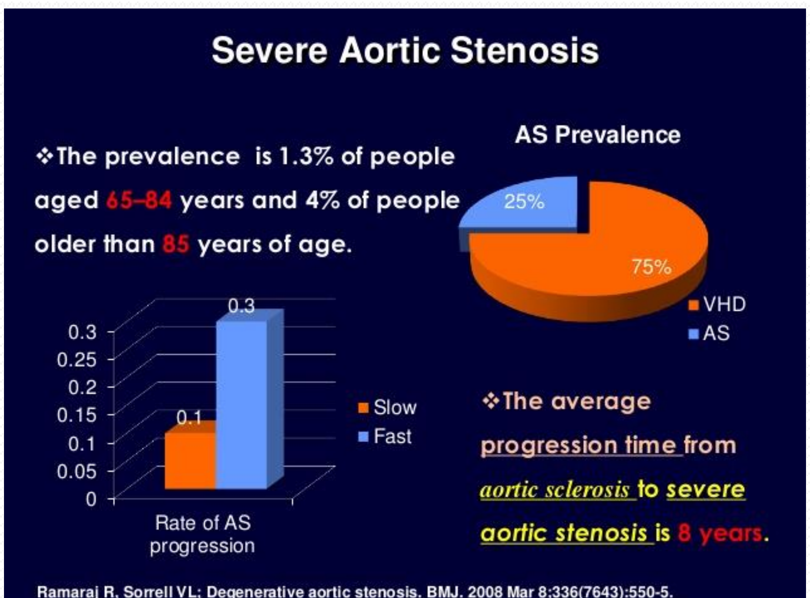
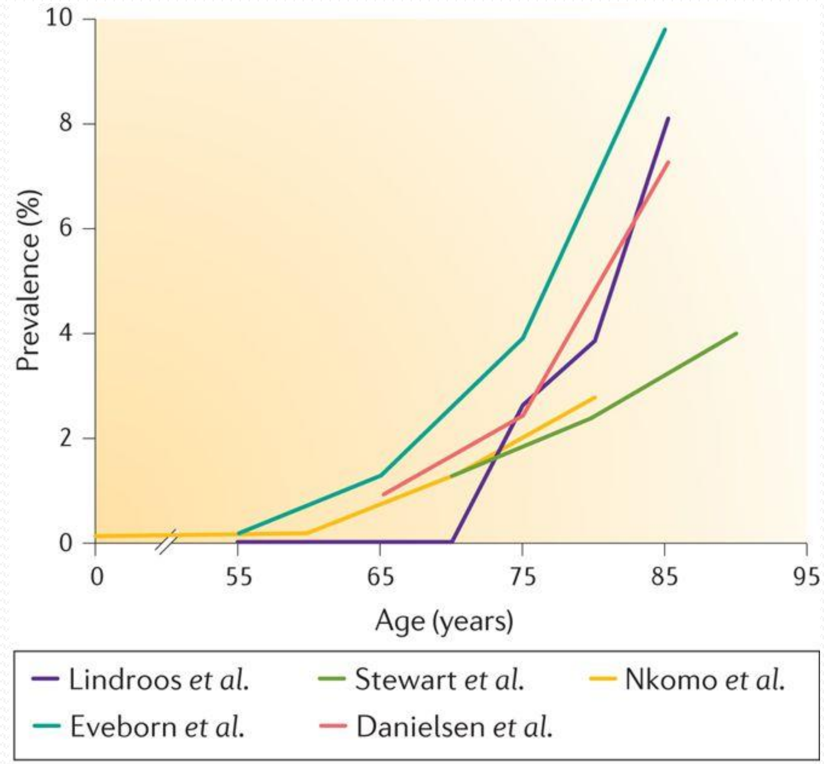
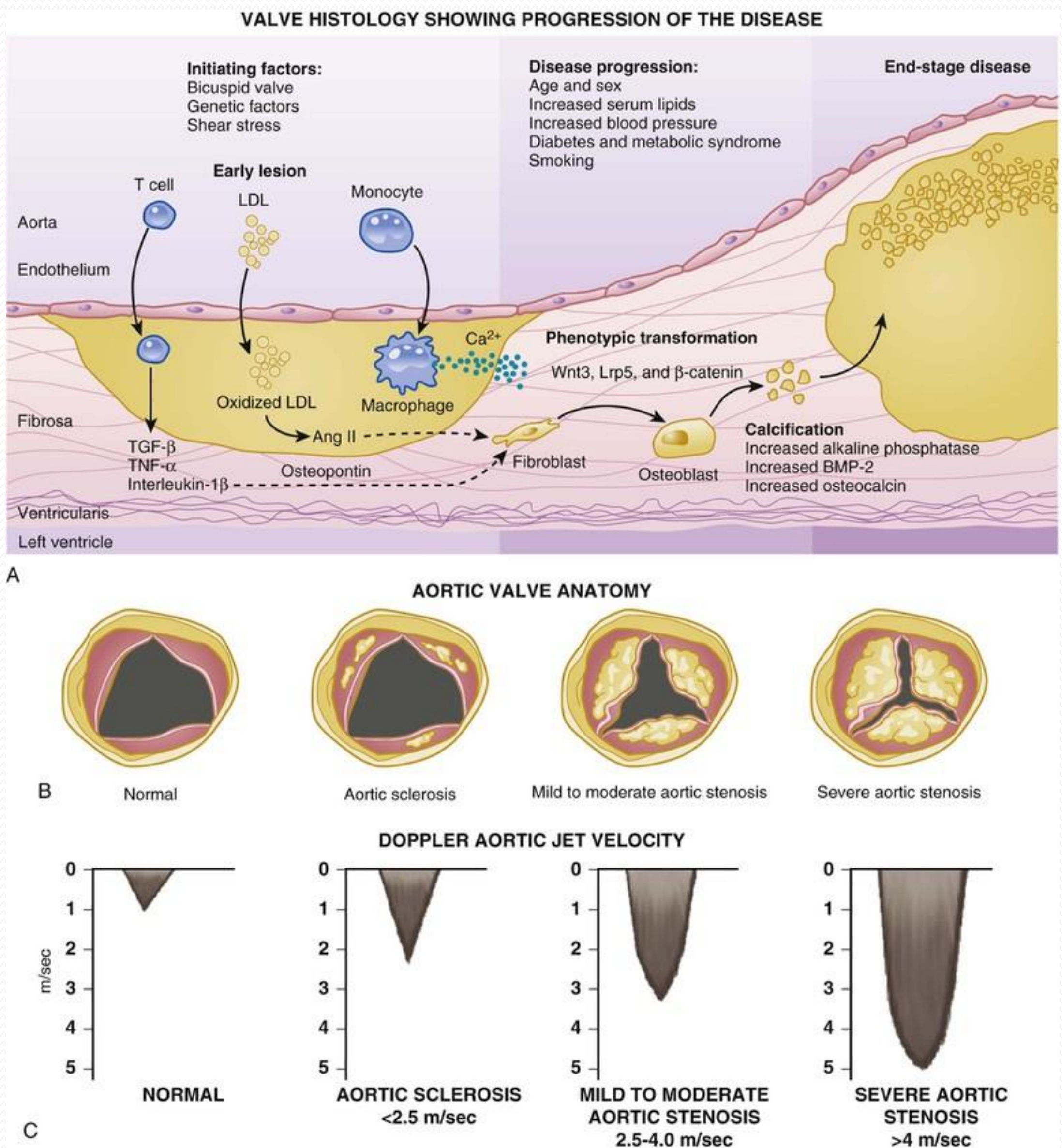
Prevalence


Aortic stenosis is estimated to be prevalent in up to 7% of the population over the age of 65[1]
It is more likely to affect men than women; 80% of adults with symptomatic aortic stenosis are male[3]
16.5 Million People in US Over the Age of 65[2]
Percentage Diagnosed with Aortic Stenosis
7%


Severe Aortic Stenosis
❖The prevalence is 1.3% of people aged 65–84 years and 4% of people older than 85 years of age.
AS Prevalence
25%
75%
VHD
AS
0.3
0.25
0.2
0.15
0.1
0.05
0
0.3
0.1
Slow
Fast
Rate of AS progression
❖The average progression time from aortic sclerosis to severe aortic stenosis is 8 years.
Ramaraj R, Sorrell VL; Degenerative aortic stenosis. BMJ. 2008 Mar 8;336(7643):550-5.

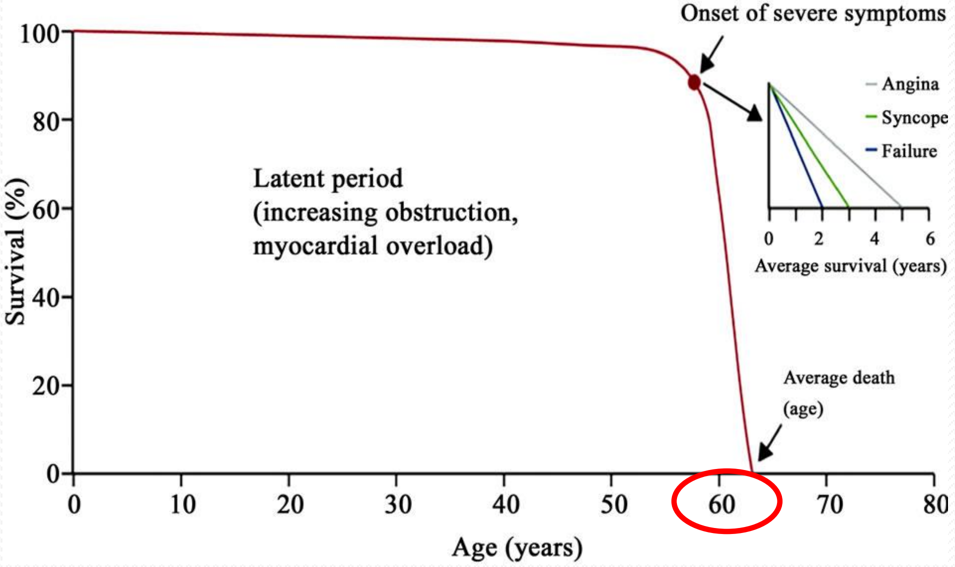

Prevalence (%)
10
8
6
4
2
0
0
55
65
75
85
95
Age (years)
Lindroos et al.
Stewart et al.
Nkomo et al.
Eveborn et al.
Danielsen et al.

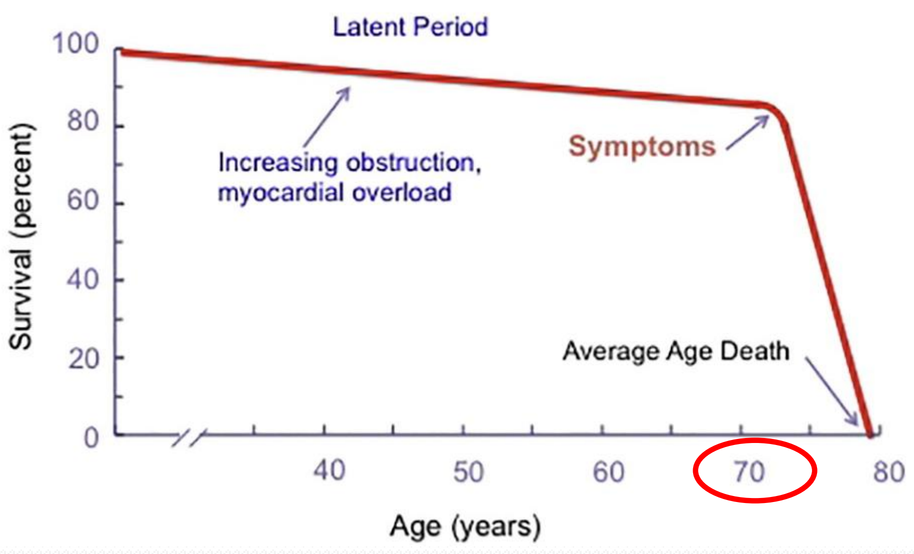
Pathophysiology



Natural History

- Asymptomatic for many years
- Symptoms develops with critically narrowed valve and LV dysfunction
  - Bicuspid – 5th-6th decade
  - Degenerative – 7th-8th decade
- Classical triad
  - Angina
  - Syncope
  - Heart failure
  - (Sudden death)





Aortic Stenosis - Causes

- Most common :-
  - Bicuspid aortic valve with calcification
  - Senile or Degenerative calcific AS
  - Rheumatic AS

General Approach by Echo

- Morphology
- Etiology
- Colour Doppler
- Quantitative assessment
- Effect on chamber size and function

- **Put everything together and see if the parameters are concordant**

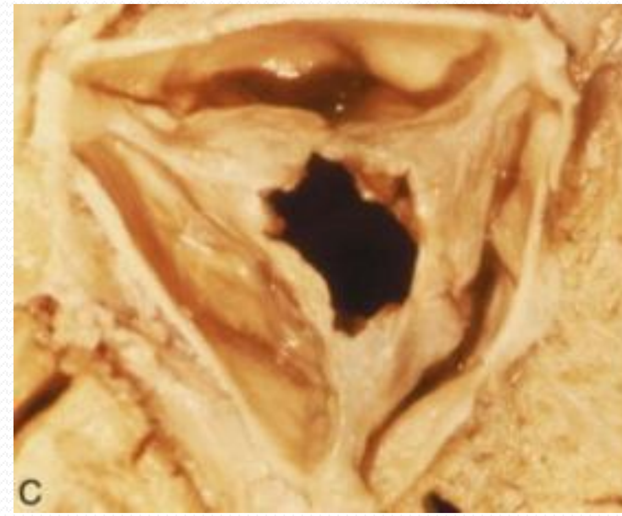
Anatomic Evaluation

- Combination of short and long axis images to identify
  - Number of leaflets
  - Describe leaf mobility, thickness, calcification

- Combination of imaging and Doppler allows the determination of the level of obstruction; sub-valvular, valvular, or supra-valvular.

Calcific vs. Rheumatic Aortic Stenosis

BICUSPID AORTIC VALVE



- Nodular calcific masses on aortic side of cusps
- No commissural fusion
- Free edges of cusps are not involved
- Stellate-shaped systolic orifice

- Commissural fusion
- Triangular systolic orifice
- Thickening +/- calcification
- Accompanied by rheumatic mitral valve changes

Classification of progression of Valvular Heart Diseases

Table 3. Stages of Progression of VHD

Stage	Definition	Description
A	At risk	Patients with risk factors for development of VHD
B	Progressive	Patients with progressive VHD (mild-to-moderate severity and asymptomatic)
C	Asymptomatic severe	Asymptomatic patients who have the criteria for severe VHD: C1: Asymptomatic patients with severe VHD in whom the left or right ventricle remains compensated C2: Asymptomatic patients with severe VHD, with decompensation of the left or right ventricle
D	Symptomatic severe	Patients who have developed symptoms as a result of VHD

VHD indicates valvular heart disease.

J Am Coll Cardiol. March 2014

Stages of Aortic Stenosis

Stage	Definition	Valve Anatomy	Valve Hemodynamics	Hemodynamic Consequences	Symptoms
A	**At risk of AS**	• Bicuspid aortic valve (or other congenital valve anomaly) • Aortic valve sclerosis	• Aortic V_{max} <2 m/s	• None	• None
B	**Progressive AS**	• Mild-to-moderate leaflet calcification of a bicuspid or trileaflet valve with some reduction in systolic motion or • Rheumatic valve changes with commissural fusion	• Mild AS: Aortic V_{max} 2.0–2.9 m/s or mean ΔP <20 mm Hg • Moderate AS: Aortic V_{max} 3.0–3.9 m/s or mean ΔP 20–39 mm Hg	• Early LV diastolic dysfunction may be present • Normal LVEF	• None

Stage	Definition	Valve Anatomy	Valve Hemodynamics	Hemodynamic Consequences	Symptoms
C - Asymptomatic severe AS					
C1	**Asymptomatic severe AS**	• Severe leaflet calcification or congenital stenosis with severely reduced leaflet opening	• Aortic V_{max} ≥4 m/s or mean ΔP ≥40 mm Hg • AVA typically is ≤1 cm^2 (or AVAi ≤0.6 cm^2/m^2) • Very severe AS is an aortic V_{max} ≥5 m/s, or mean ΔP ≥60 mm Hg	• LV diastolic dysfunction • Mild LV hypertrophy • Normal LVEF	• None– exercise testing is reasonable to confirm symptom status
C2	**Asymptomatic severe AS with LV dysfunction**	• Severe leaflet calcification or congenital stenosis with severely reduced leaflet opening	• Aortic V_{max} ≥4 m/s or mean ΔP ≥40 mm Hg • AVA typically is ≤1 cm^2 (or AVAi ≤0.6 cm^2/m^2)	• LVEF <50%	• None

Stage	Definition	Valve Anatomy	Valve Hemodynamics	Hemodynamic Consequences	Symptoms
D - Symptomatic severe AS					
D1	**Symptomatic severe high-gradient AS**	• Severe leaflet calcification or congenital stenosis with severely reduced leaflet opening	• Aortic V_{max} ≥4 m/s, or mean ΔP ≥40 mm Hg • AVA typically is ≤1 cm^2 (or AVAi ≤0.6 cm^2/m^2), but may be larger with mixed AS/AR	• LV diastolic dysfunction • LV hypertrophy • Pulmonary hypertension may be present	• Exertional dyspnea or decreased exercise tolerance • Exertional angina • Exertional syncope or presyncope
D2	**Symptomatic severe low-flow/low-gradient AS with reduced LVEF**	• Severe leaflet calcification with severely reduced leaflet motion	• AVA ≤1 cm^2 with resting aortic V_{max} <4 m/s or mean ΔP <40 mm Hg • Dobutamine stress echo shows AVA ≤1 cm^2 with V_{max} ≥4 m/s at any flow rate	• LV diastolic dysfunction • LV hypertrophy • LVEF <50%	• HF, • Angina, • Syncope or presyncope

Stage	Definition	Valve Anatomy	Valve Hemodynamics	Hemodynamic Consequences	Symptoms
D - Symptomatic severe AS					
D3	**Symptomatic severe low-gradient AS with normal LVEF or paradoxical low-flow severe AS**	• Severe leaflet calcification with severely reduced leaflet motion	• AVA $\leq$1 cm^2 with aortic V_{max} <4 m/s, or mean ΔP <40 mm Hg • Indexed AVA $\leq$0.6 cm^2/m^2 and • Stroke volume index <35 mL/m^2 • Measured when the patient is normotensive (systolic BP <140 mm Hg)	• Increased LV relative wall thickness • Small LV chamber with low-stroke volume. • Restrictive diastolic filling • LVEF ≥50%	• HF, • Angina, • Syncope or presyncope

Diagnostic dilemma

- The diagnosis of "severe aortic stenosis" can be confidently established when the data are congruent with each other
  - Normal flow, Normal EF, High gradient (Stage D1)

- What if there are mismatch of information??
  - "severe AS by AVA" but low gradient, low EF
  - "mild AS by AVA" but high gradient, normal EF

- ***Always review the measurements first before jumping to conclusion***

Doppler Assessment of AS

- The primary haemodynamic parameters recommended
  - Peak transvalvular velocity
  - Mean transvalvular gradient
  - Valve area by continuity equation (LVOT diameter measured)

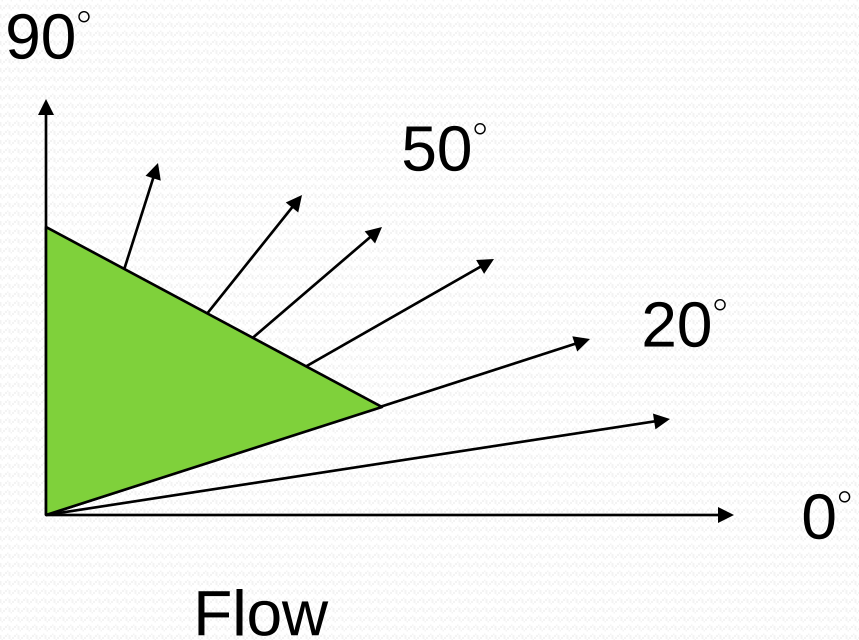
Peak Transvalvular Velocity Peak/Mean Gradient

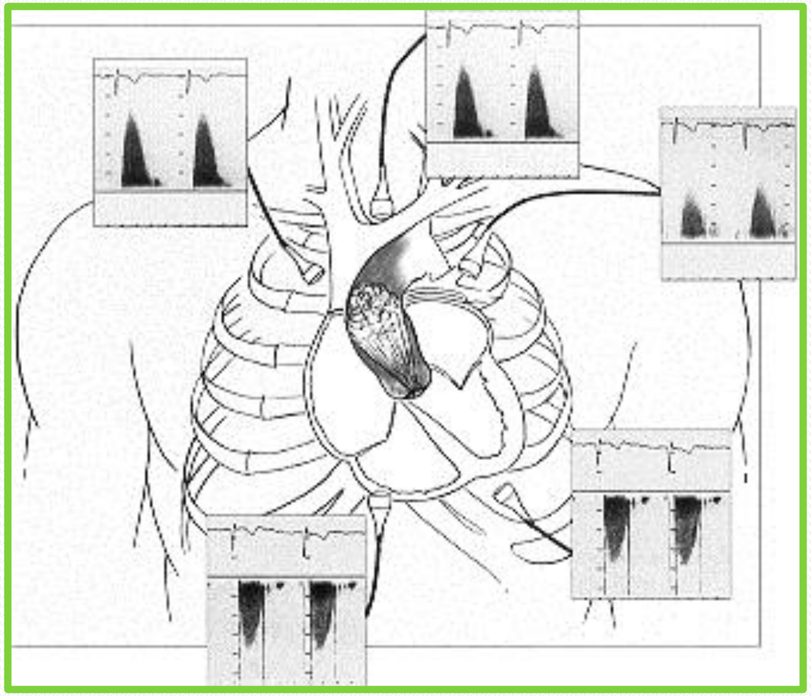
- Continuous-wave Doppler ultrasound
- Multiple acoustic windows
  - Apical and suprasternal or right parasternal most frequently yield the highest velocity
  - rarely subcostal or supraclavicular windows may be required
- The peak gradient is calculated from maximum velocity by Bernoulli equation
  - $\Delta P\ max = 4v^2\ max$
- The mean gradient is calculated by averaging the instantaneous gradients over the ejection period

Doppler Angle

GOAL: Parallel to flow

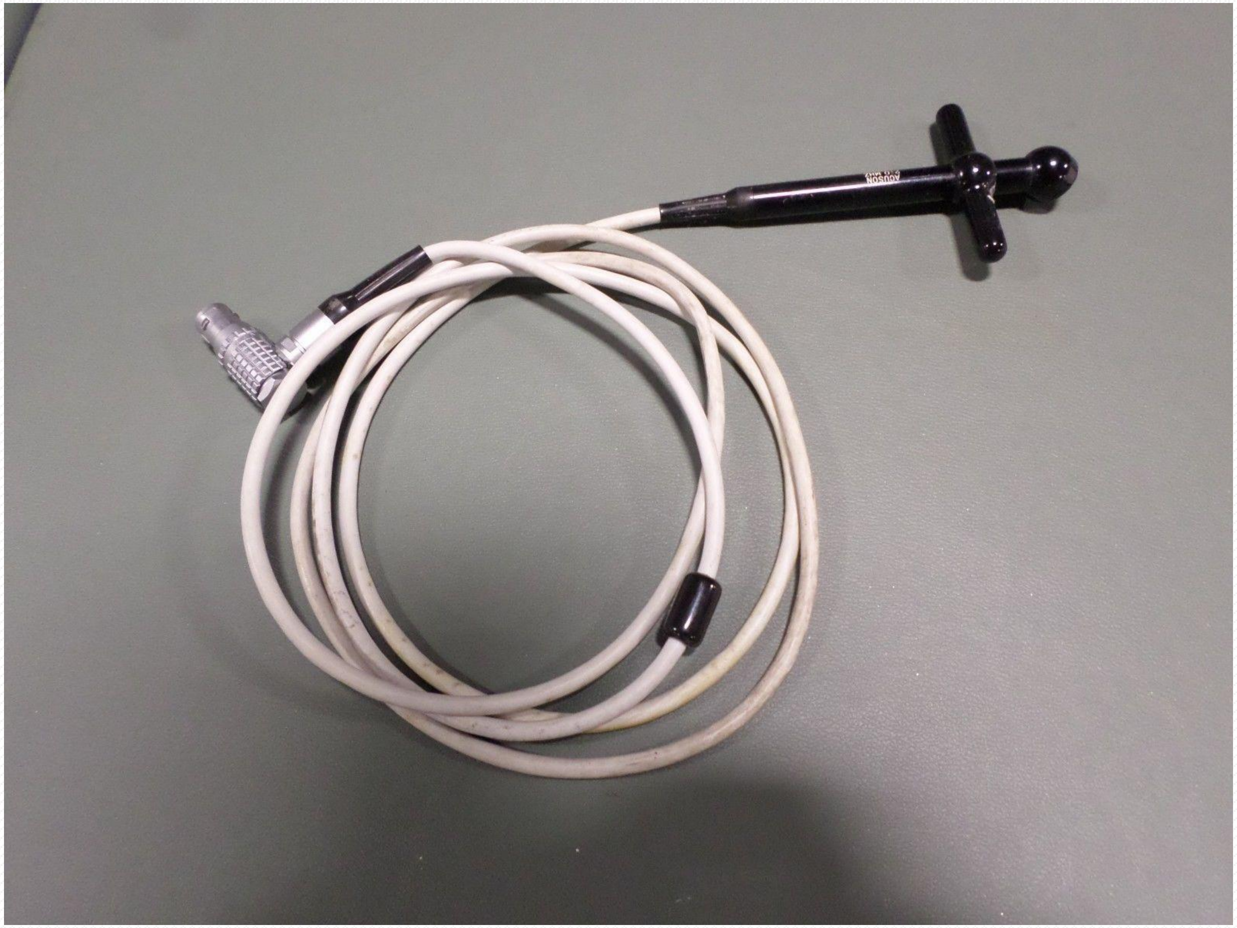
As angle increases, velocity underestimated



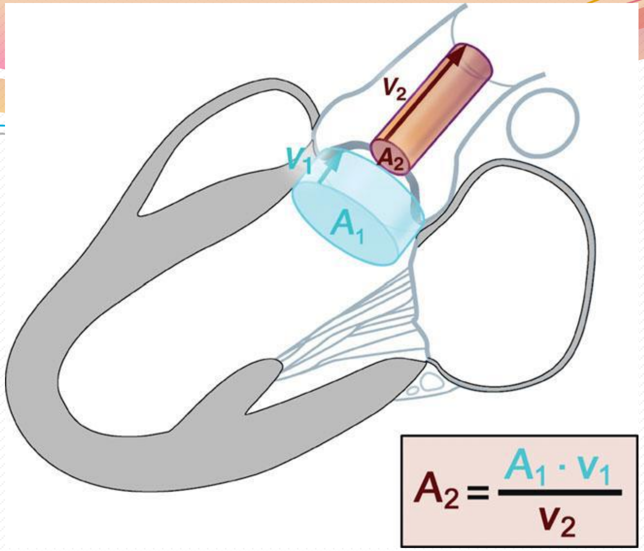


~20% cases peak velocity are not obtained from usual apical windows

Non-imaging probe (CW only)



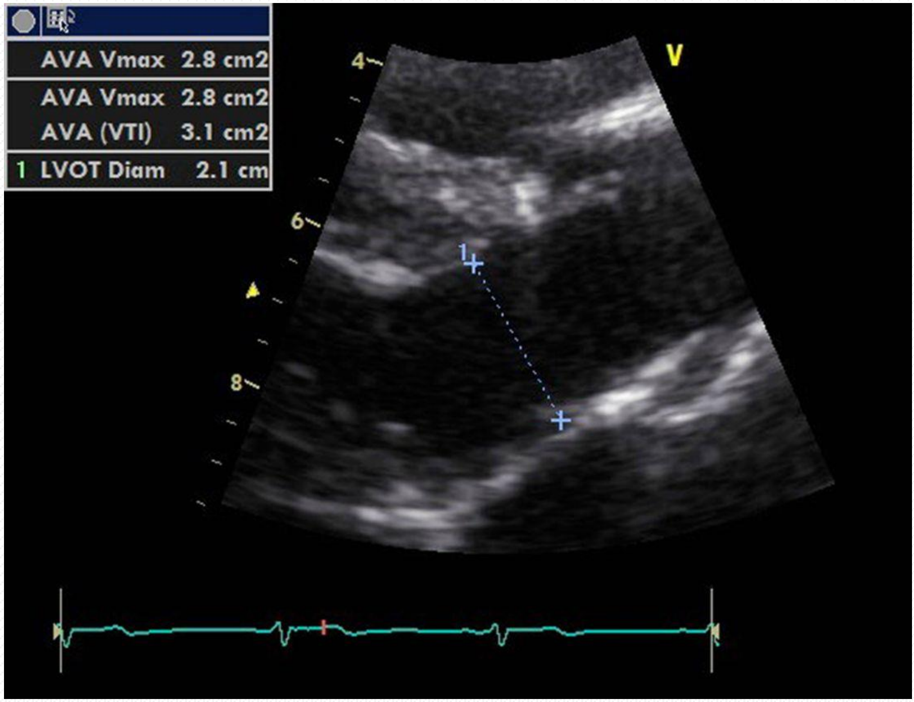
Aortic Valve Area
Continuity Equation



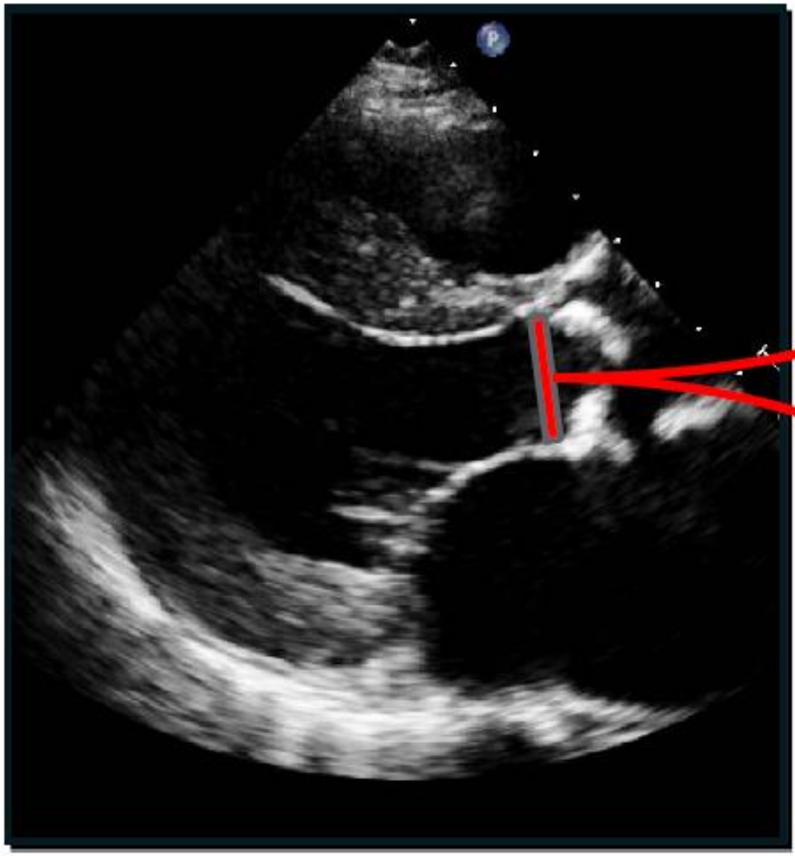
- **AVA = $CSA_{LVOT} \times VTI_{LVOT} / VTI_{AV}$**
- Calculation requires three measurements
  - AS jet velocity time integral (VTI) by CWD
  - LVOT diameter for calculation of a circular CSA
  - LVOT VTI recorded with pulsed Doppler
- ***Index for BSA especially for small built patient***
  - AVAi < 0.6 cm2/m2 BSA – severe stenosis

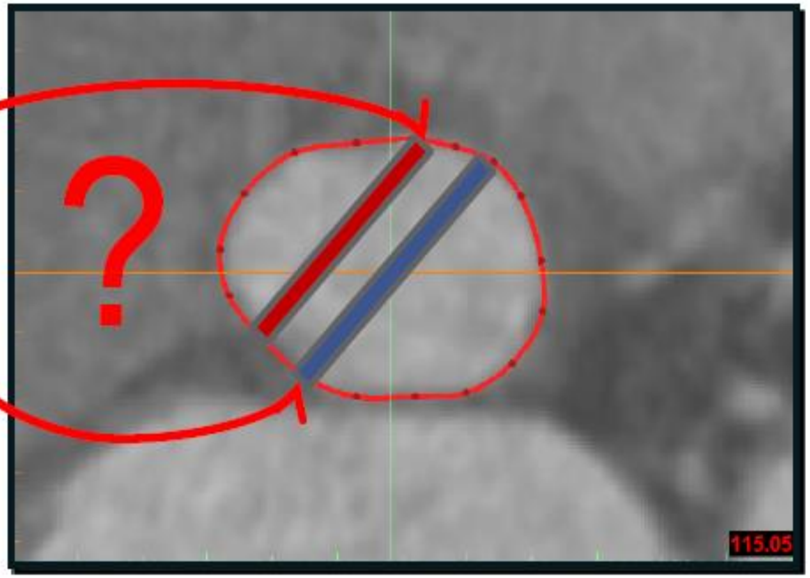
LVOT diameter

- LVOT diameter is measured from the inner edge to inner edge of the septal endocardium, and the anterior mitral leaflet in mid-systole
- ZOOM-IN, multiple measurement
- ***Largest source of error in AVA calculation (error would be squared)***



2D Echo LVOT measurement- Limitation





Conditions affecting flow (thus gradient)

- Increase flow
  - Anaemia
  - Thyrotoxicosis
  - Fever
  - Severe AR
- Decrease flow
  - Poor LV
  - Severe MR
  - Severe MS
  - Severe TR

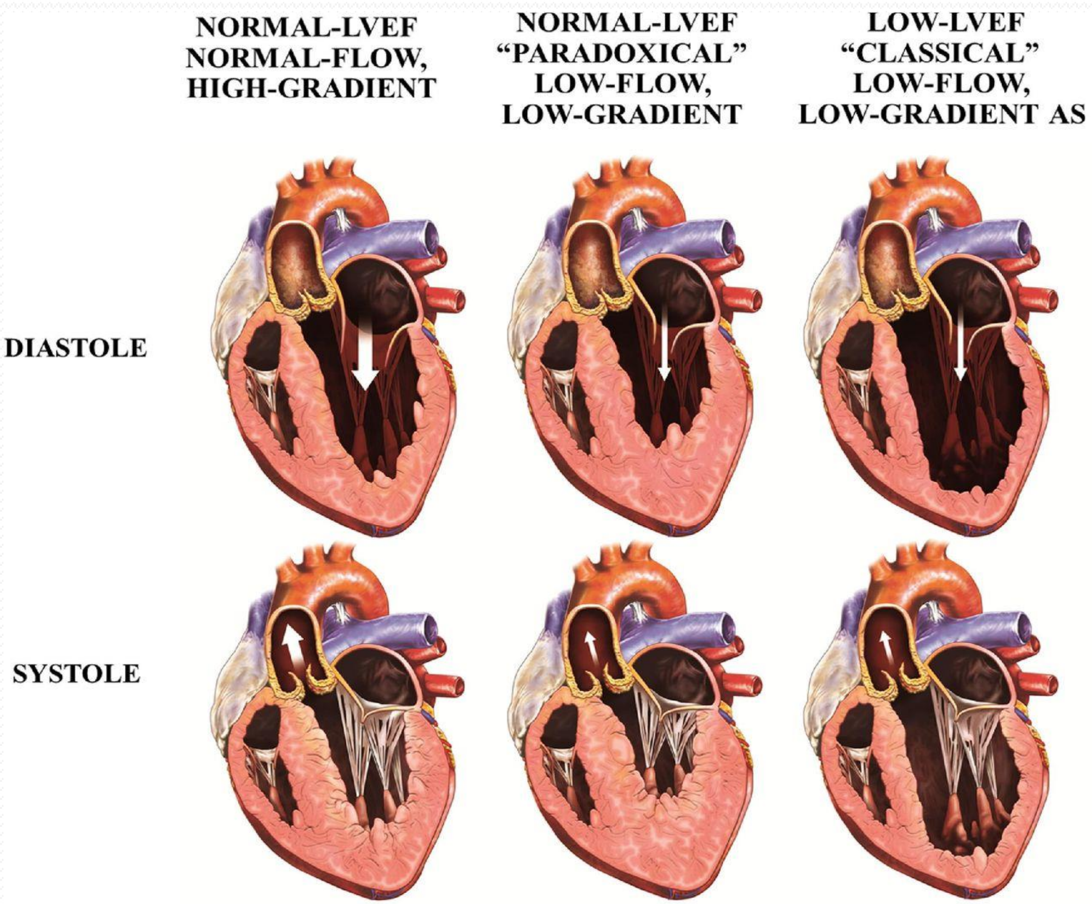
Check for proportionate change of LVOT TVI

Do not just report gradient without calculating AVA

LVOT/AV TVI ratio

- Dimensionless index
- Error of LVOT diameter measurement “ignored”
- Suboptimal CW or PW beam angle “ignored”
- Effect of high flow “ignored”
- Provide an alternative if AVA difficult to assess
- < 0.25 – severe aortic stenosis

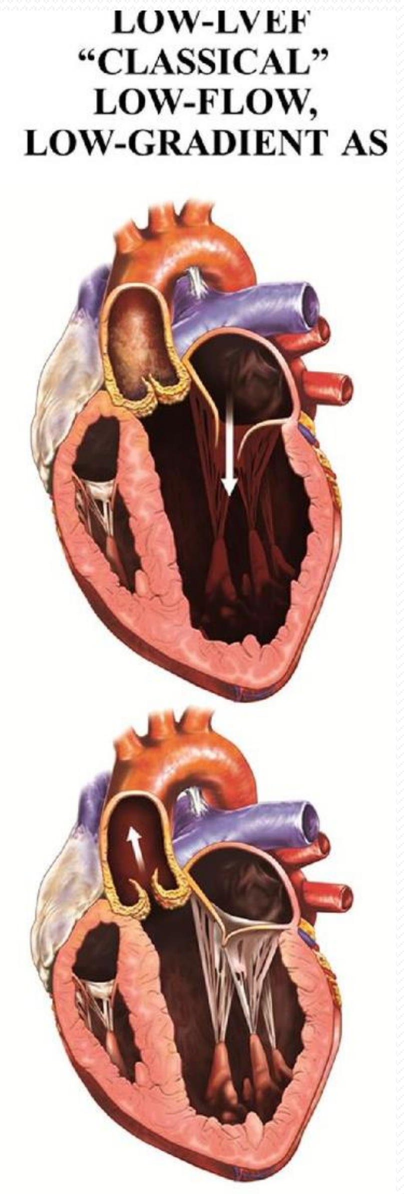
Low-Flow Low-Gradient (LFLG) AS



- Low flow Low gradient AS with Low EF (Classical, D2)
- Low flow Low gradient AS with Normal EF (Paradoxical, D3)
- Normal-Flow, Low-Gradient AS (?Measurement error, ??D4)

Classical LFLG AS (D2)

- Low Flow secondary to Low EF due to myocardial dysfunction
  - secondary to AS
  - secondary to other causes
  - primary myocardial disease
- “Psedo-severe” AS with impaired LVEF
  - DCMP(Primary Myocardial Dysfunction)
  - Ischemic Heart Disease
  - HT Heart Disease (After load mismatch)

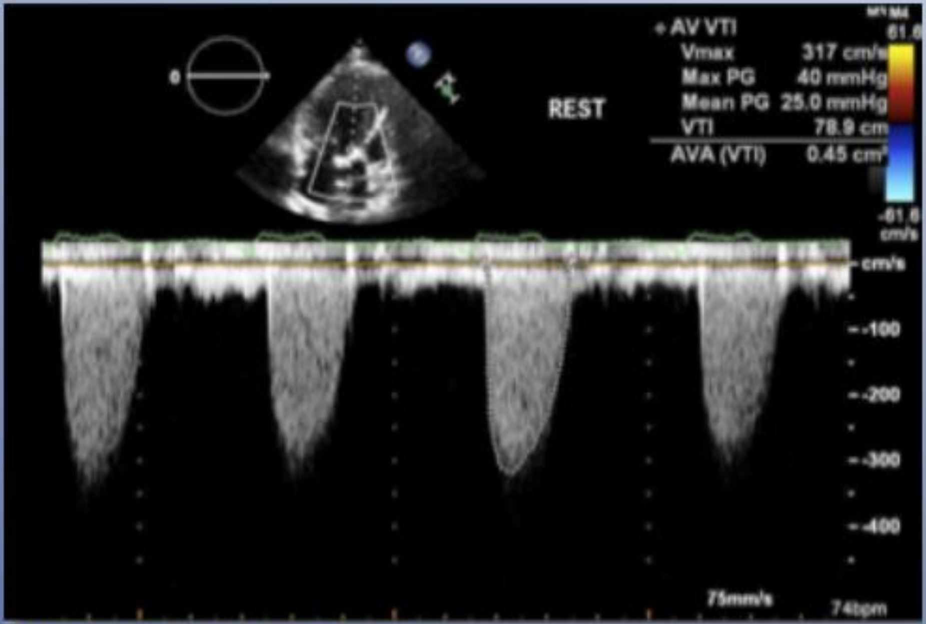


Dobutamine Stress Echo (DSE)

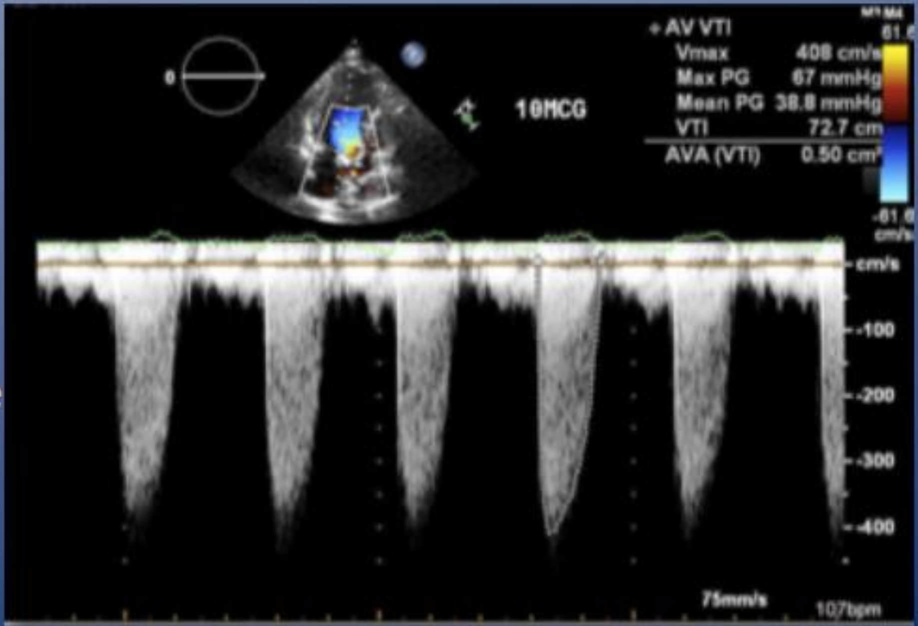
- Measure of the contractile response to dobutamine
- Assess for flow reserve, change in EOA and change in Gradient and velocity
- Low dose protocol up to 20 µg/kg/min

- Stress findings of true severe stenosis
  - AVA < $1cm^2$
  - Jet velocity > 4m/s
  - Mean gradient >40 mmHg
    - ***Nishimura RA et al. Circulation 2002;106:809-13.***
- Lack of contractile reserve-
  - Failure of LVEF to ↑ by 20% is a poor prognostic sign
    - ***Monin JL et al. Circulation 2003;108:319-24.***

Dobutamine stress ECHO in patient with LGSAS

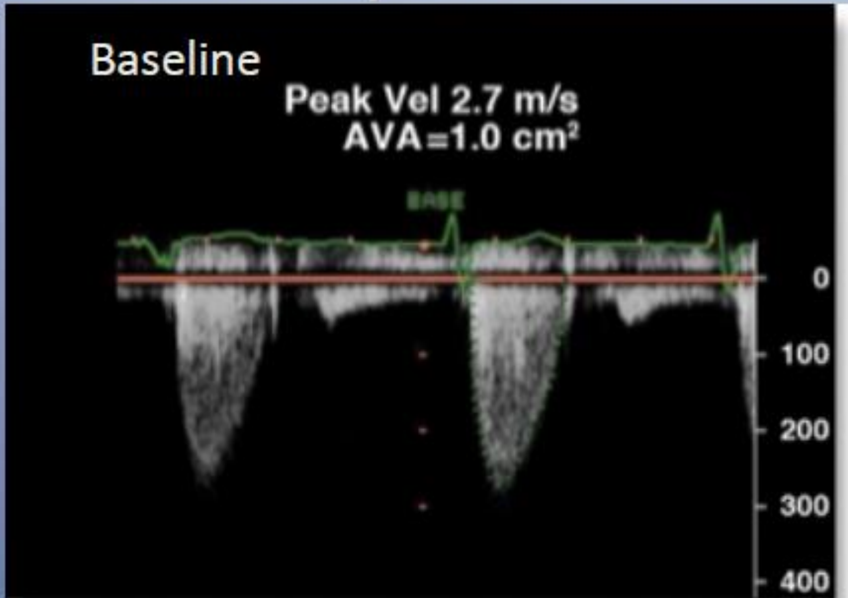


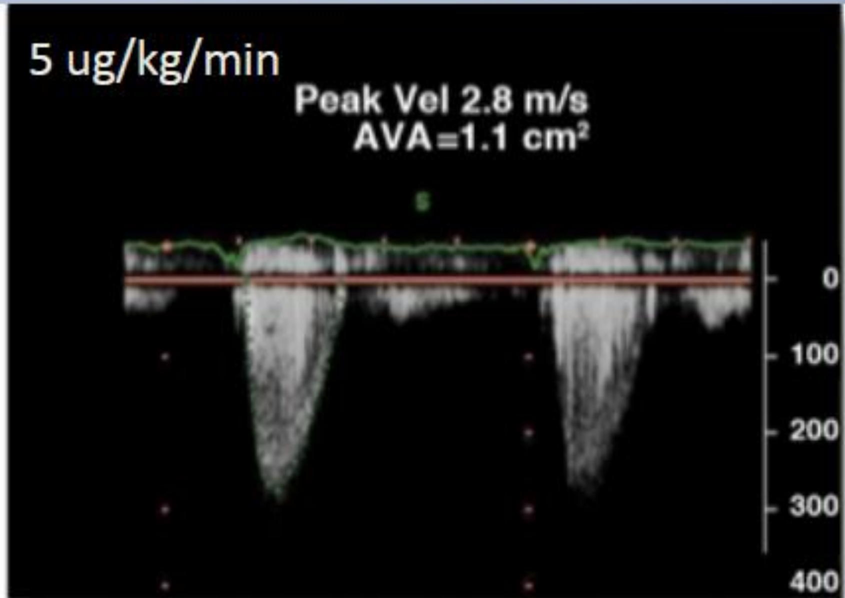
Baseline CW tracing:
Peak velocity 3.2 m/s
Mean grad 25 mmHg
AVA 0.45 cm^2



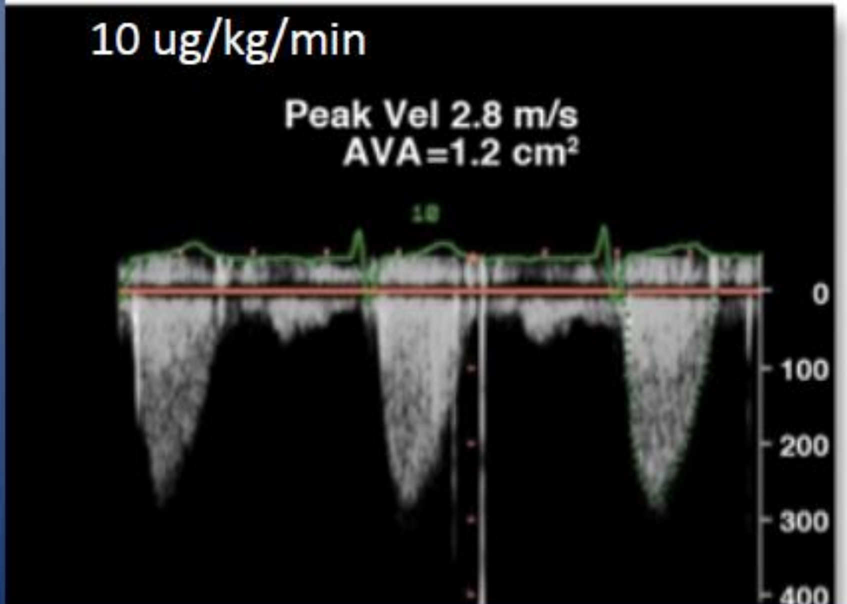
CW 10ug/kg/min dobutamine
Peak velocity 4.1 m/s
Mean grad 39 mmHg
AVA 0.5 cm^2

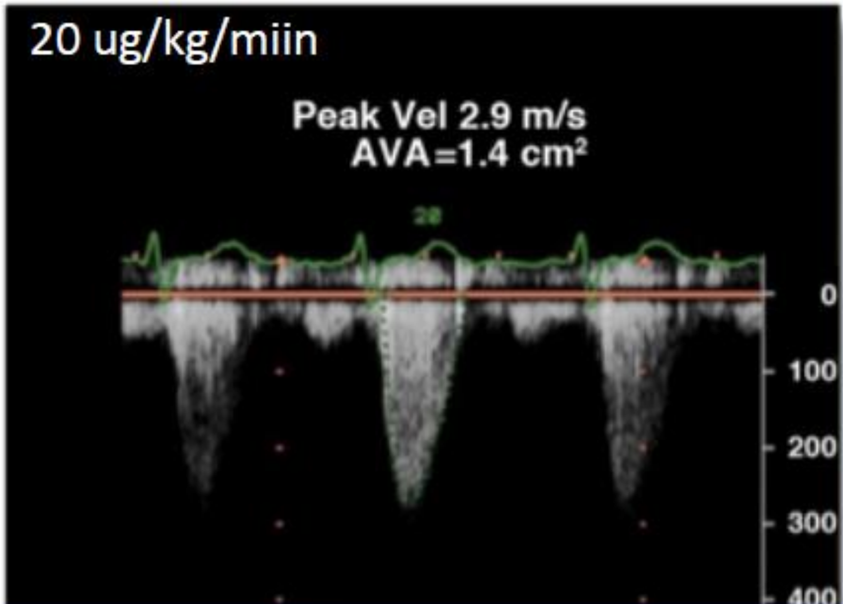
DSE in a patient with Pseudo-severe AS





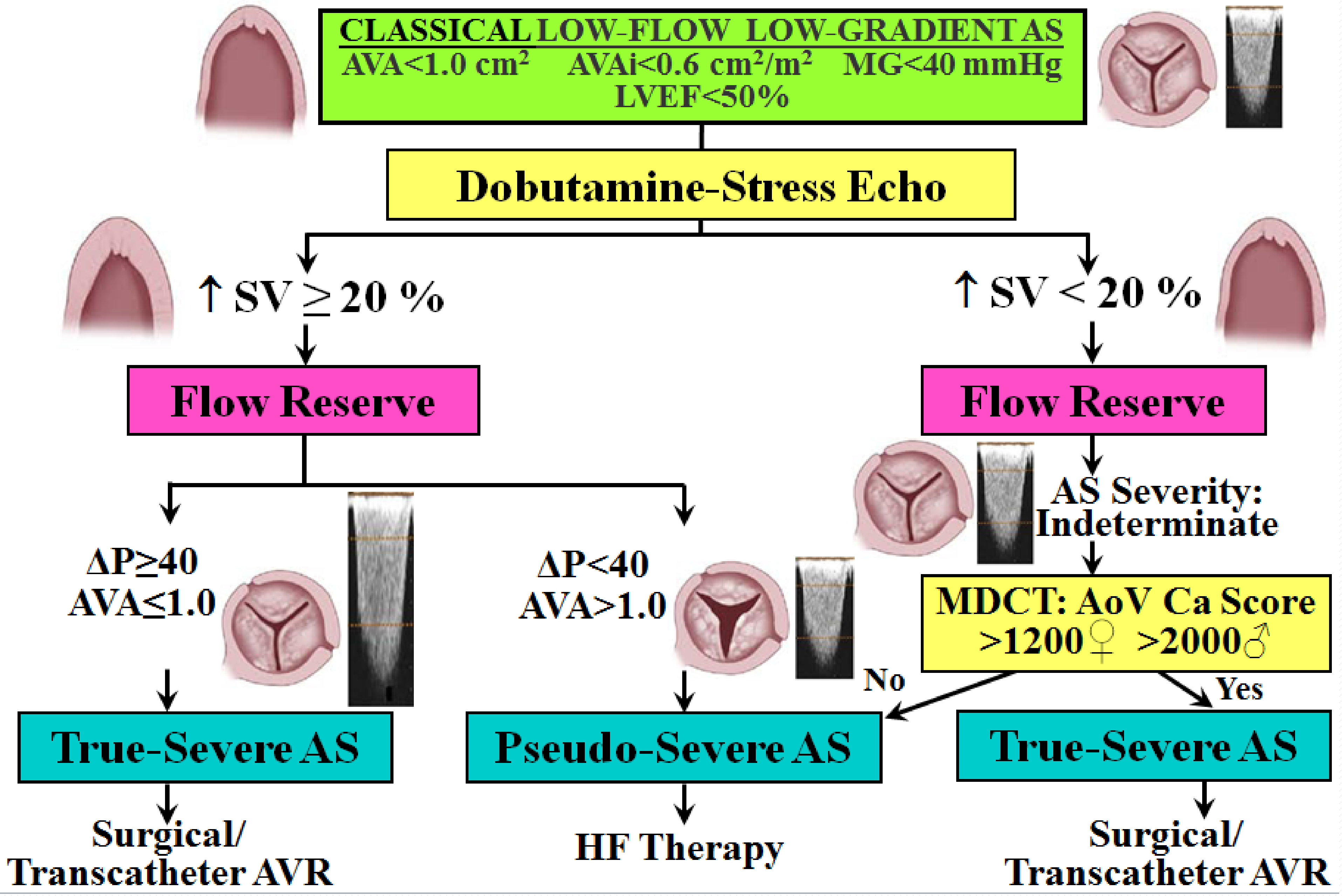
Peak velocity stable, AVA increased, contractile reserve +, absence of severe AS





Lack of Contractile Reserve

- Defined by increase in SV <20% during DSE or catheterization
- Higher operative mortality (22% to 33%) than those with flow reserve (5% to 8%).
- Higher prevalence of multivessel CAD
- Yet, ***should NOT preclude consideration of AV surgery*** in symptomatic subjects with severe AS



CLASSICAL LOW-FLOW LOW-GRADIENT AS
AVA<1.0 cm² AVAi<0.6 cm²/m² MG<40 mmHg
LVEF<50%
Dobutamine-Stress Echo
↑ SV ≥ 20 %
↑ SV < 20 %
Flow Reserve
Flow Reserve
AS Severity: Indeterminate
ΔP≥40
AVA≤1.0
ΔP<40
AVA>1.0
MDCT: AoV Ca Score
>1200♀ >2000♂
No
Yes
True-Severe AS
Pseudo-Severe AS
True-Severe AS
Surgical/
Transcatheter AVR
HF Therapy
Surgical/
Transcatheter AVR

Projected Valve Area at Normal Flow Rate Improves the Assessment of Stenosis Severity in Patients With Low-Flow, Low-Gradient Aortic Stenosis

The Multicenter TOPAS (Truly or Pseudo-Severe Aortic Stenosis) Study

Claudia Blais, MSc; Ian G. Burwash, MD; Gerald Mundigler, MD; Jean G. Dumesnil, MD;
Nicole Loho, MD; Florian Rader, MD; Helmut Baumgartner, MD; Rob S. Beanlands, MD;
Boris Chayer, Eng; Lyes Kadem, Eng, PhD; Damien Garcia, Eng, PhD;
Louis-Gilles Durand, Eng, PhD; Philippe Pibarot, DVM, PhD

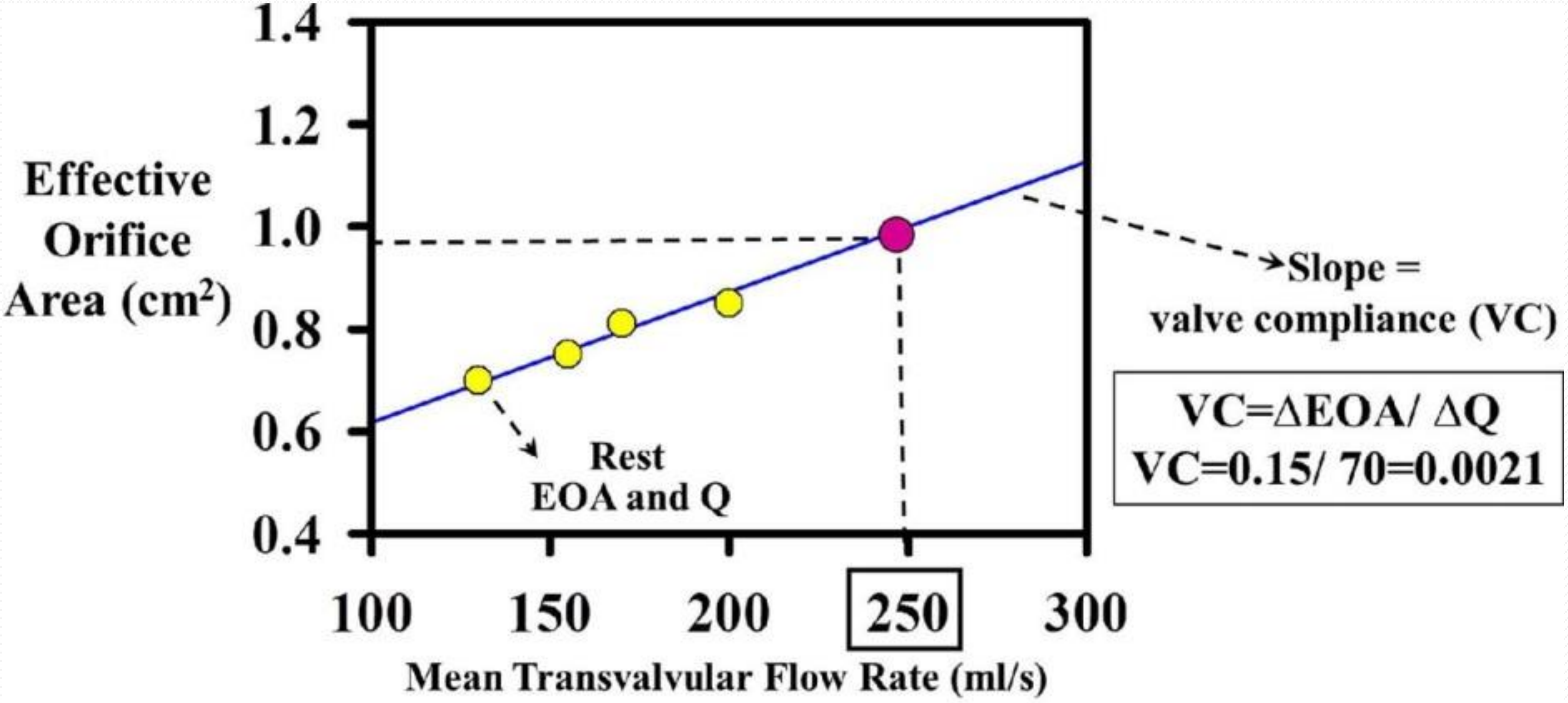
Background—We sought to investigate the use of a new parameter, the projected effective orifice area (EOA_{proj}) at normal transvalvular flow rate (250 mL/s), to better differentiate between truly severe (TS) and pseudo-severe (PS) aortic stenosis (AS) during dobutamine stress echocardiography (DSE). Changes in various parameters of stenosis severity have been used to differentiate between TS and PS AS during DSE. However, the magnitude of these changes lacks standardization because they are dependent on the variable magnitude of the transvalvular flow change occurring during DSE.

Methods and Results—The use of EOA_{proj} to differentiate TS from PS AS was investigated in an in vitro model and in 23 patients with low-flow AS (indexed EOA <0.6 cm^2/m^2, left ventricular ejection fraction $\leq 40\%$) undergoing DSE and subsequent aortic valve replacement. For an individual valve, EOA was plotted against transvalvular flow (Q) at each dobutamine stage, and valve compliance (VC) was derived as the slope of the regression line fitted to the EOA versus Q plot; EOA_{proj} was calculated as $EOA_{proj}=EOA_{rest}+VC\times(250-Q_{rest})$, where EOA_{rest} and Q_{rest} are the EOA and Q at rest. Classification between TS and PS was based on either response to flow increase (in vitro) or visual inspection at surgery (in vivo). EOA_{proj} was the most accurate parameter in differentiating between TS and PS both in vitro and in vivo. In vivo, 15 of 23 patients (65%) had TS and 8 of 23 (35%) had PS. The percentage of correct classification was 83% for EOA_{proj} and 91% for indexed EOA_{proj} compared with percentages of 61% to 74% for the other echocardiographic parameters usually used for this purpose.

Conclusions—EOA_{proj} provides a standardized evaluation of AS severity with DSE and improves the diagnostic accuracy for distinguishing TS and PS AS in patients with low-flow, low-gradient AS. (***Circulation*. 2006;113:711-721.**)

Key Words: aortic valve stenosis ■ echocardiography ■ hemodynamics ■ surgery ■ valves

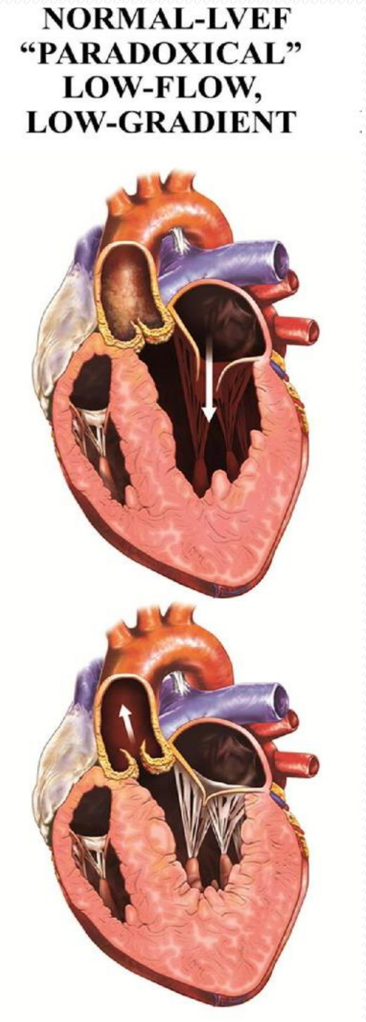
Projected EOA



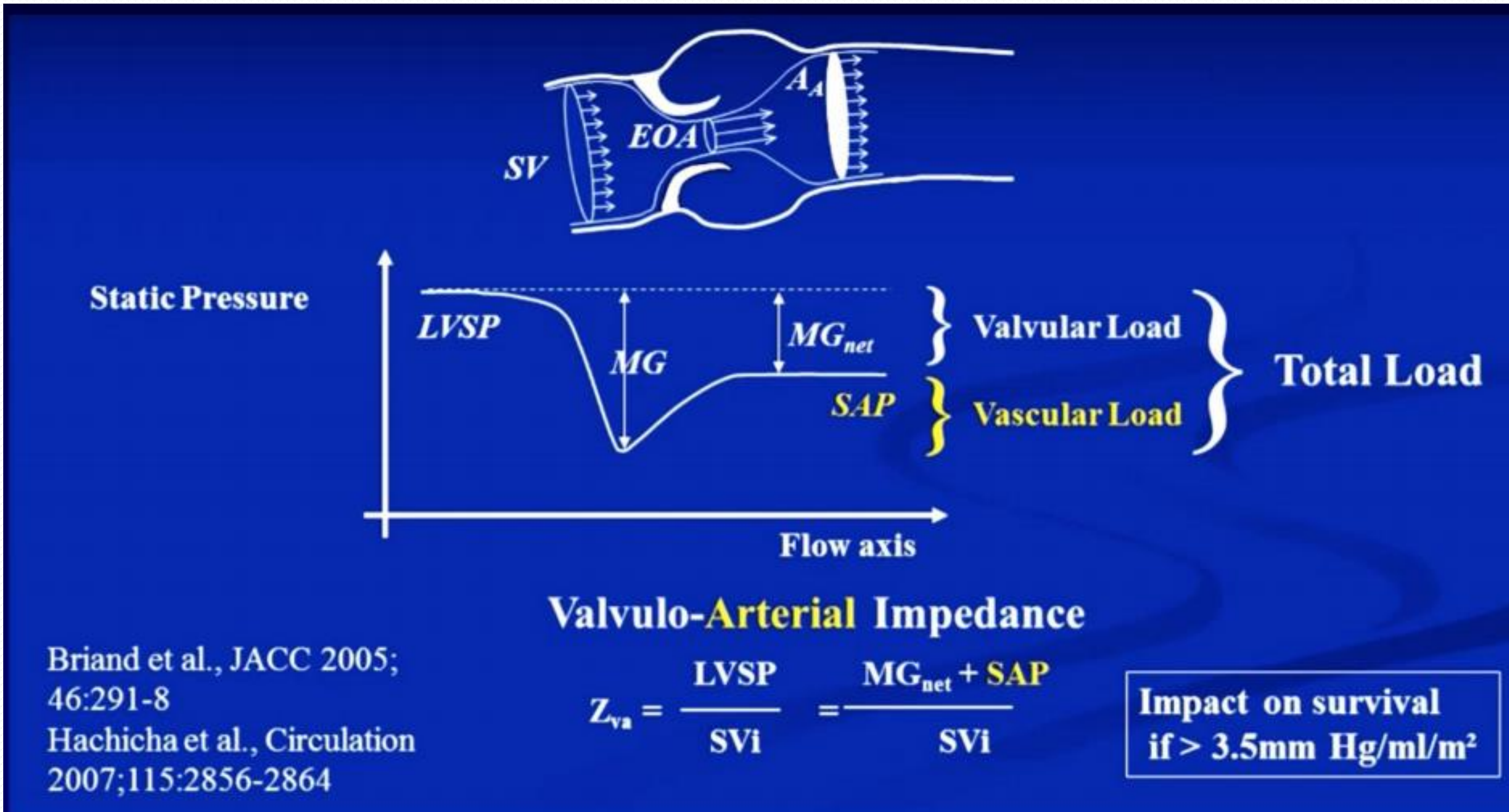
$$EOA_{Projected} = EOA_{Rest} + VC \times (250 - Q_{Rest})$$
$$= 0.70 + 0.0021 \times (250 - 130) = 0.97\ cm^2$$

Paradoxical LFLG AS (D3) - essentials

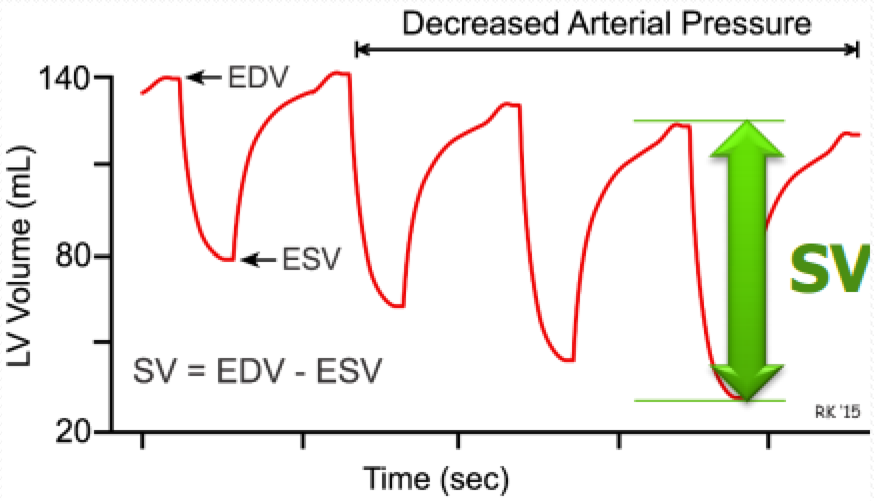
- Old, female, concomitant HT
- Pronounced LV concentric remodeling
- Small LV with restrictive filling
- Higher valvulo-arterial impedance (Zva)
- (Small body size – index AVA may be helpful but not for obese patient)

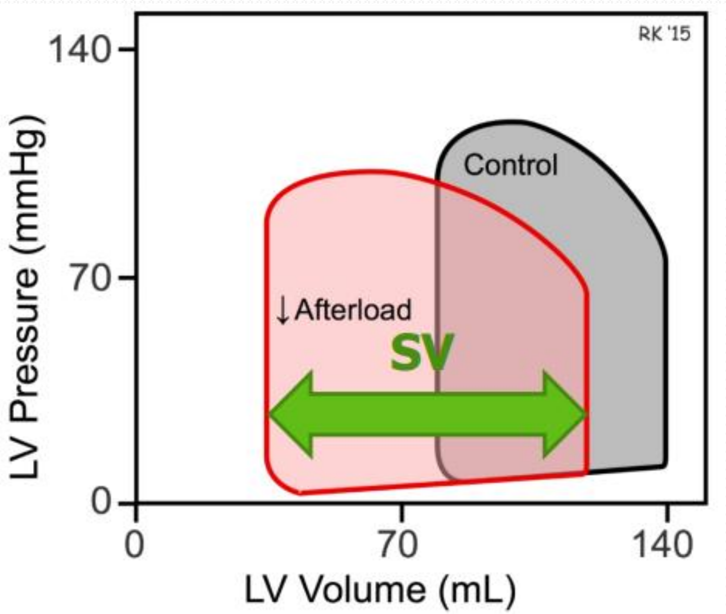


Valvulo-arterial Impedance (Zva)



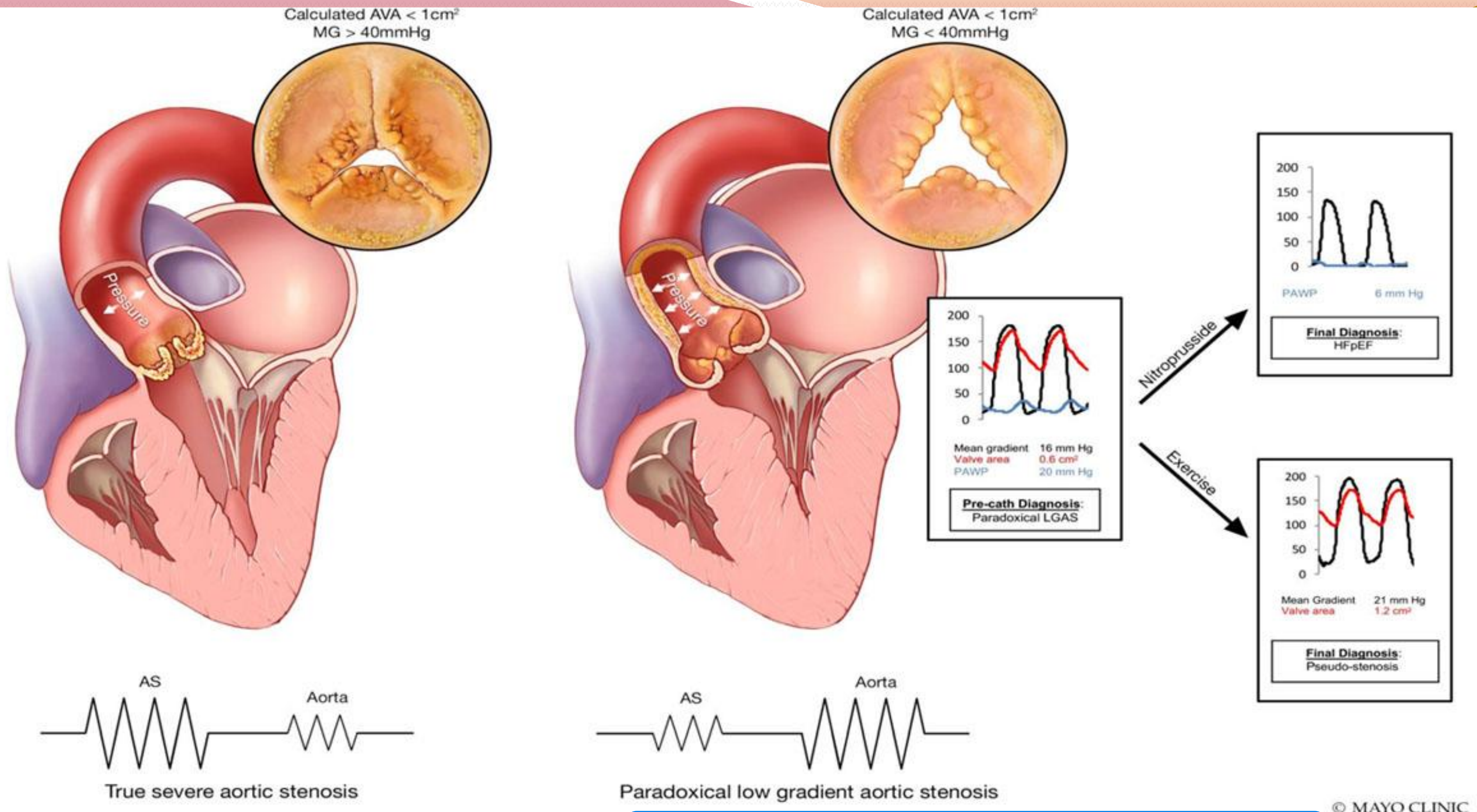
Decreasing blood pressure





Increase SV -> Increase transvalvular gradient

Try to assess AS severity at normotensive state



Primary resistor at vascular level

Nitroprusside

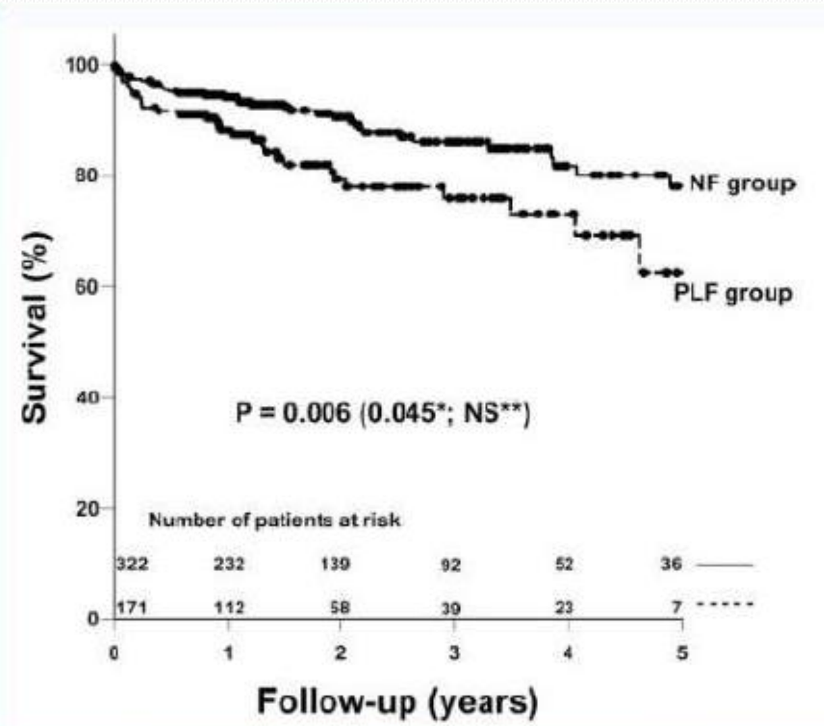
MG	SV	PAWP	Diagnosis	Treatment
>40 mmHg	↑	N/A	True AS	AVR
<30 mmHg	↑	↓	Pseudo AS	Medical
N/A	=	N/A	Uncertain	Further evaluation

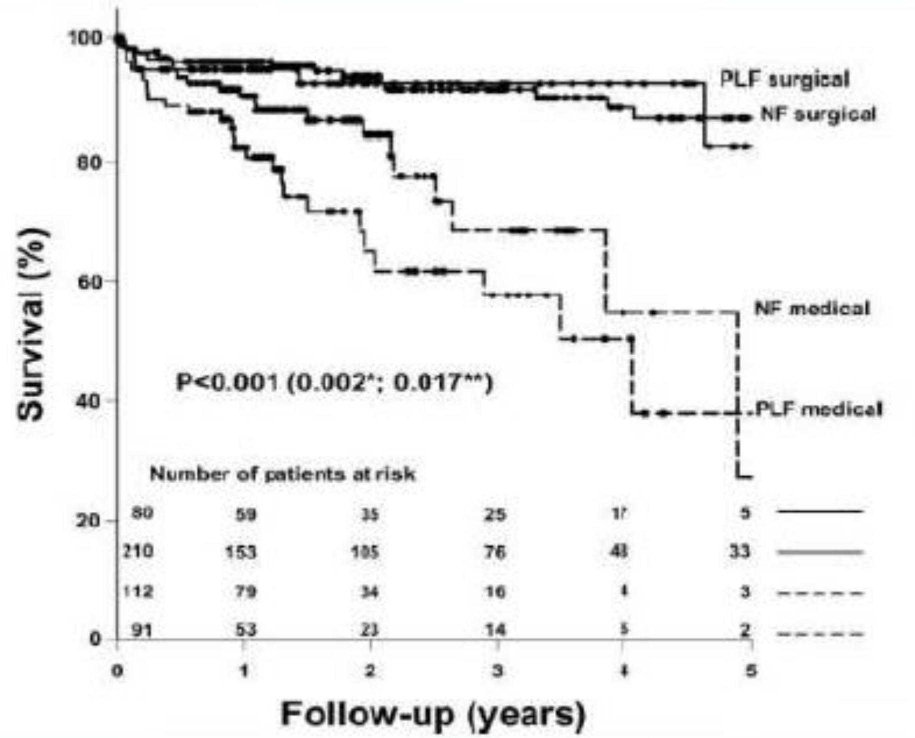
Exercise

MG	SV	PAWP	Diagnosis	Treatment
>40 mmHg	↑	↑	True AS	AVR
<30 mmHg	↑	↑	Pseudo AS	Medical
N/A	↑	Normal	Noncardiac	Rx underlying cause

Yogesh N.V. Reddy. Circulation.
Paradox of Low-Gradient Aortic Stenosis, Volume: 139, Issue: 19, Pages: 2195-2197

Worse prognosis the NF severe AS if treated medically

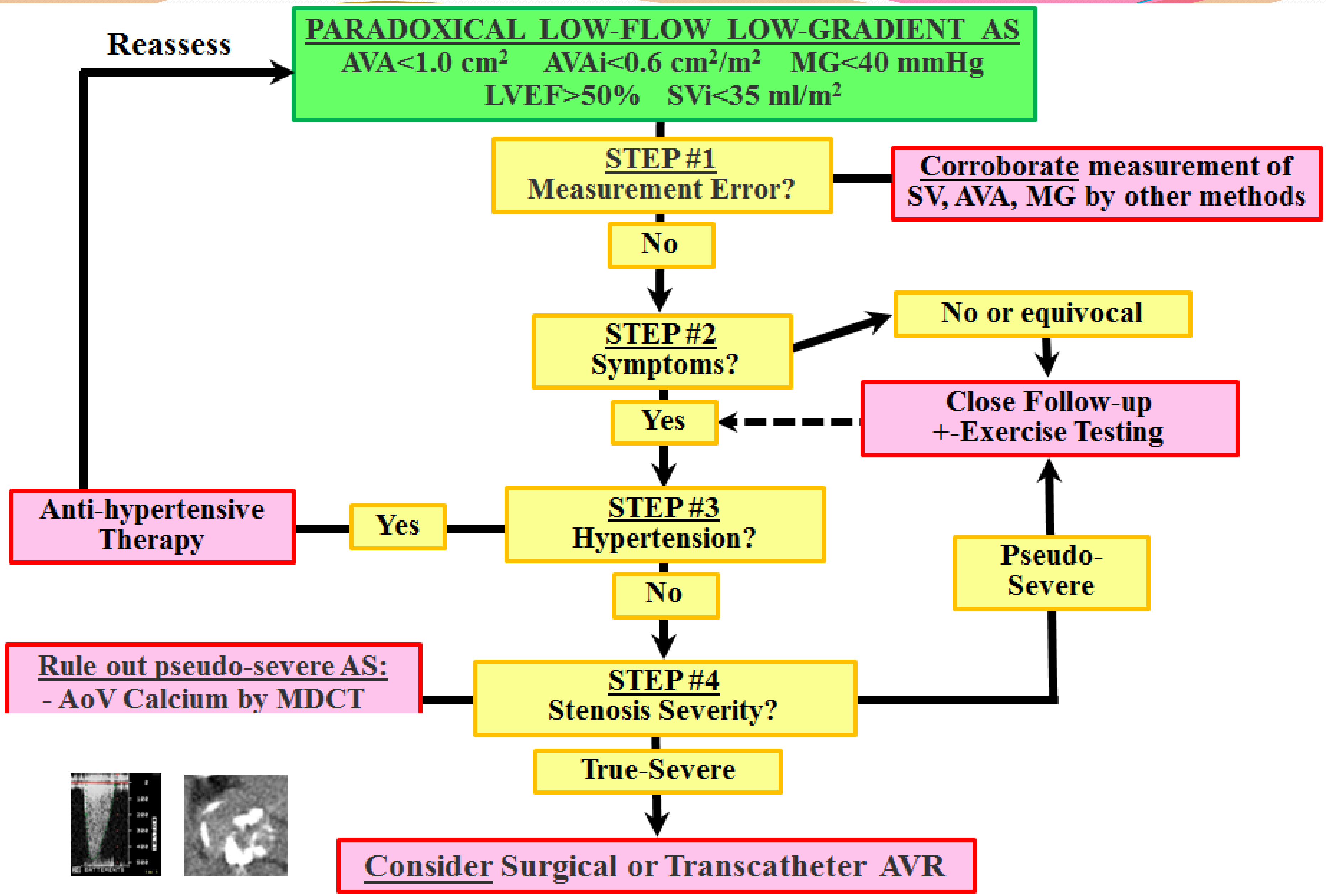


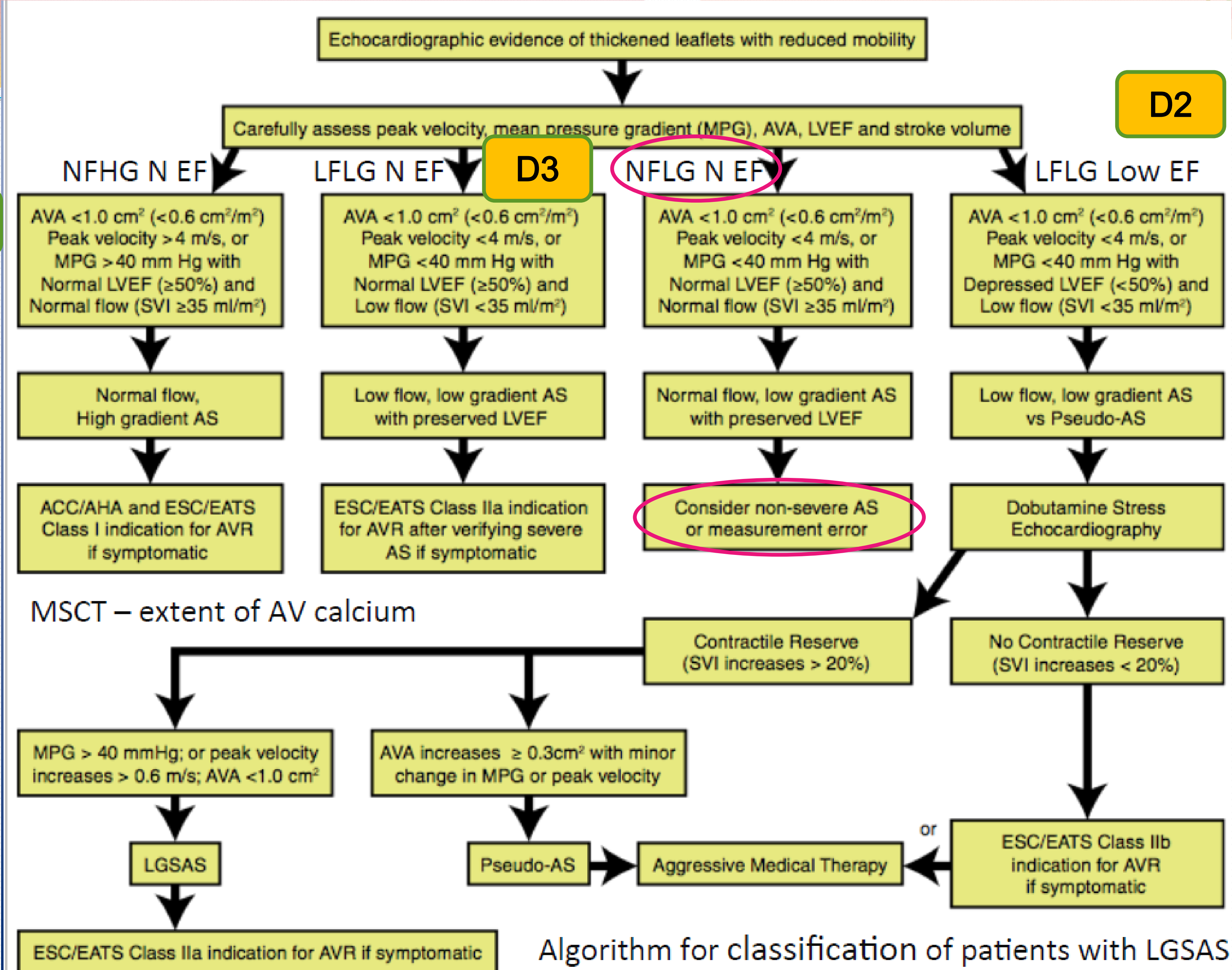


Hachicha et al. Circulation. 2007;115:2856 -64

Prognosis

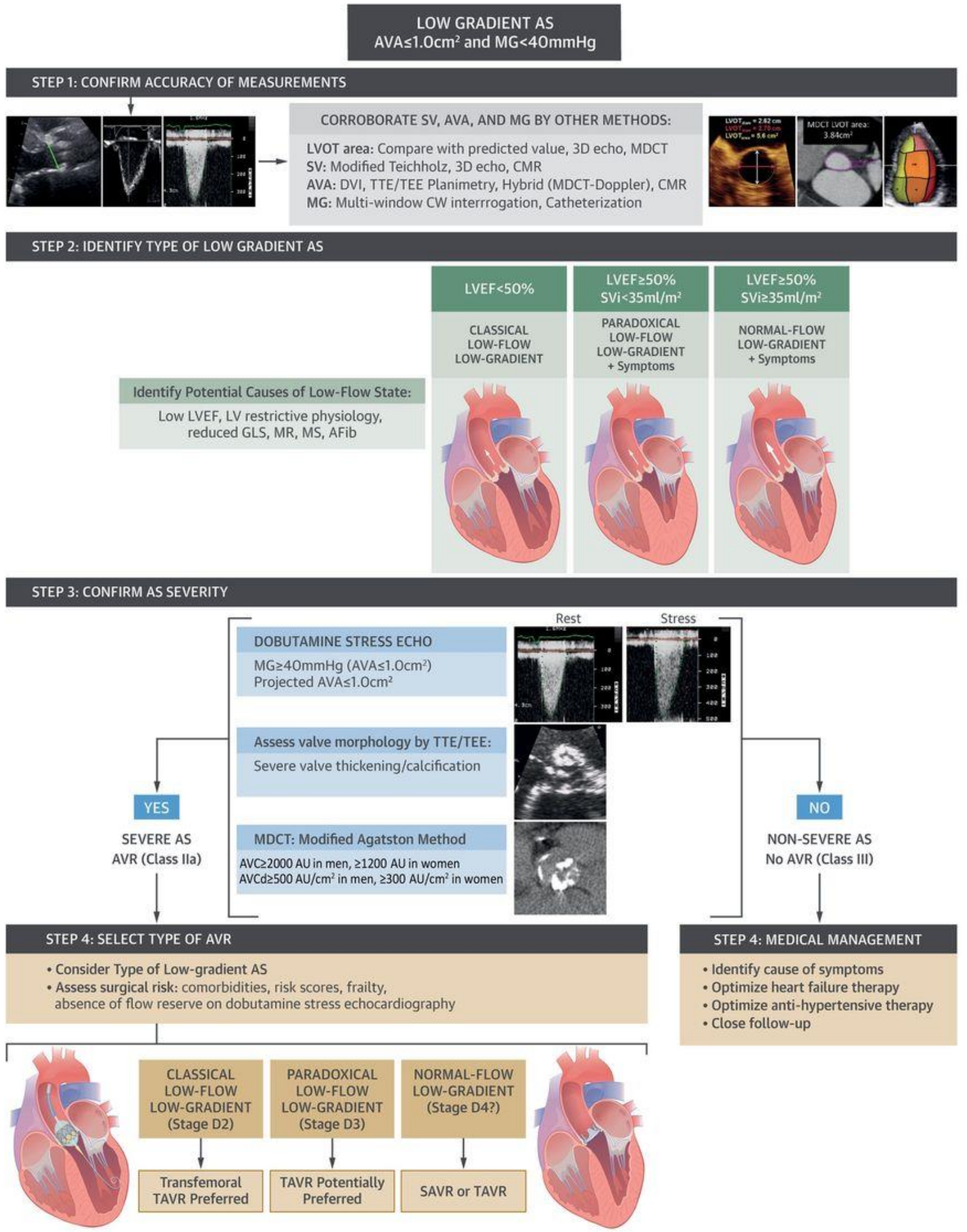
- Worse than moderate AS (albeit contradictory reports)
- Worse than severe AS with high gradient group
- Lower overall 3-year survival (76% versus 86%)
  - ($p < 0.006$ in 512 patients By Hacicha et al.)
- Two-fold increase in mortality and an almost **50% lower referral rate** (?undertreated) for AVR in the low gradient AS compared to the high gradient group (Barasch et al)


PARADOXICAL LOW-FLOW LOW-GRADIENT AS
AVA<1.0 cm² AVAi<0.6 cm²/m² MG<40 mmHg
LVEF>50% SVi<35 ml/m²
Reassess
STEP #1
Measurement Error?
Corroborate measurement of SV, AVA, MG by other methods
No
STEP #2
Symptoms?
No or equivocal
Close Follow-up
+-Exercise Testing
Yes
STEP #3
Hypertension?
Yes
Anti-hypertensive Therapy
No
Pseudo-Severe
STEP #4
Stenosis Severity?
Rule out pseudo-severe AS:
- AoV Calcium by MDCT
True-Severe
Consider Surgical or Transcatheter AVR



Algorithm for classification of patients with LGSAS

CENTRAL ILLUSTRATION: Algorithm for the Management of Low-Gradient AS



Clavel, M.-A. et al. J Am Coll Cardiol Img. 2017;10(2):185-202.

Typical characteristics of 3 different entities of AS

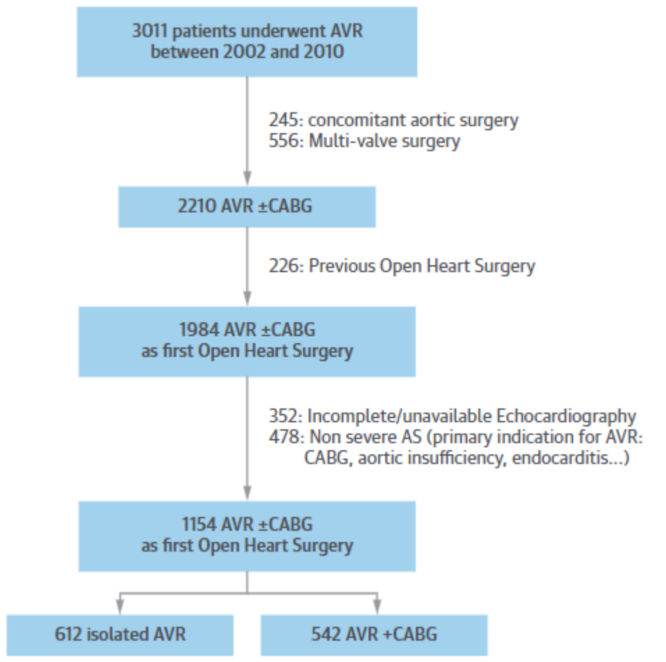
	Normal-Flow, High-Gradient	Preserved LVEF (Paradoxical), Low-Flow, Low-Gradient	Reduced LVEF, Low-Flow, Low-Gradient
Aortic valve area, cm^2	≤1.0	≤1.0	≤1.0
Indexed aortic valve area, cm^2/m^2	<0.6	<0.6	<0.6
Mean gradient, mm Hg	>40	<40	<40
Z_{va}, $mm\ Hg \cdot ml^{-1} \cdot m^2$	>4.5	>4.5	>4.5
LV end-diastolic diameter, mm	45–55	<47	>50
Relative wall thickness	>0.43	>0.50	0.35–0.55
LVEF, %	>50	>50	<50
Mitral ring displacement, mm	5–15	<8	<8
Global longitudinal strain, %	14–20	<14	<14
Stroke volume index, ml/m^2	>35	<35	<35
Mean flow rate, ml/s	>200	<200	<200
Myocardial fibrosis	+	++	+++
CT valve calcium score, AU	>1,650	>1,650	>1,650
Plasma NT-proBNP, pg/ml	<1,500	>1,500	>1,500

Impact of Classic and Paradoxical Low Flow on Survival After Aortic Valve Replacement for Severe Aortic Stenosis

sAVR

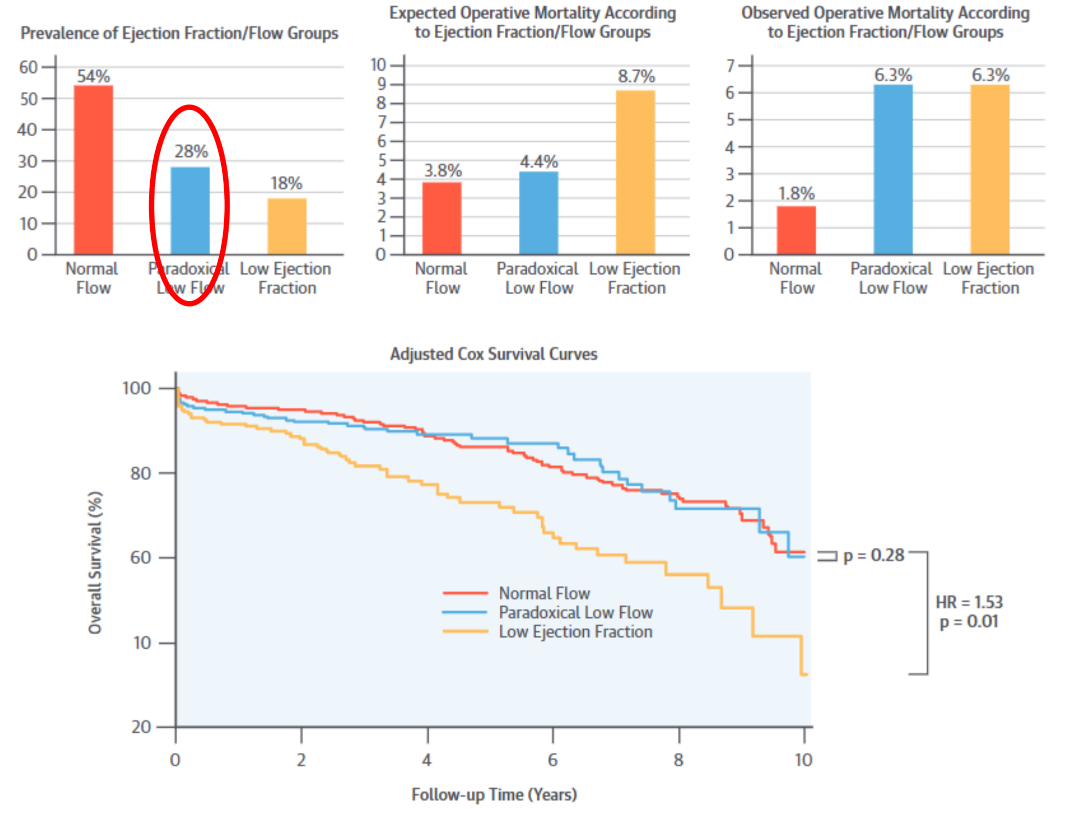
Marie-Annick Clavel, DVM, PhD, Maxime Berthelot-Richer, MD, Florent Le Ven, MD, MSc, Romain Capoulade, PhD, Abdellaziz Dahou, MD, MSc, Jean G. Dumesnil, MD, Patrick Mathieu, MD, Philippe Pibarot, DVM, PhD

FIGURE 1 Study Flow Chart



AVR = aortic valve replacement; AS = aortic stenosis; CABG = coronary artery bypass graft.

CENTRAL ILLUSTRATION Impact of Flow and Ejection Fraction After Aortic Valve Replacement



Clavel, M-A. et al. J Am Coll Cardiol. 2015; 65(7):645-53.

Prevalence for patient groups, 30-day mortality, and overall survival in normal flow **(red line)**, paradoxical low flow **(blue line)**, and low ejection fraction **(orange line)** patients. Survival is shown by Cox survival curves adjusted for age, female sex, New York Heart Association functional class III or IV, atrial fibrillation, chronic kidney failure, diabetes, coronary artery disease, chronic obstructive pulmonary disease, left ventricular mass index, and mean gradient.

TAVI

Transcatheter Aortic Valve Replacement in Patients With Low-Flow, Low-Gradient Aortic Stenosis

The TOPAS-TAVI Registry

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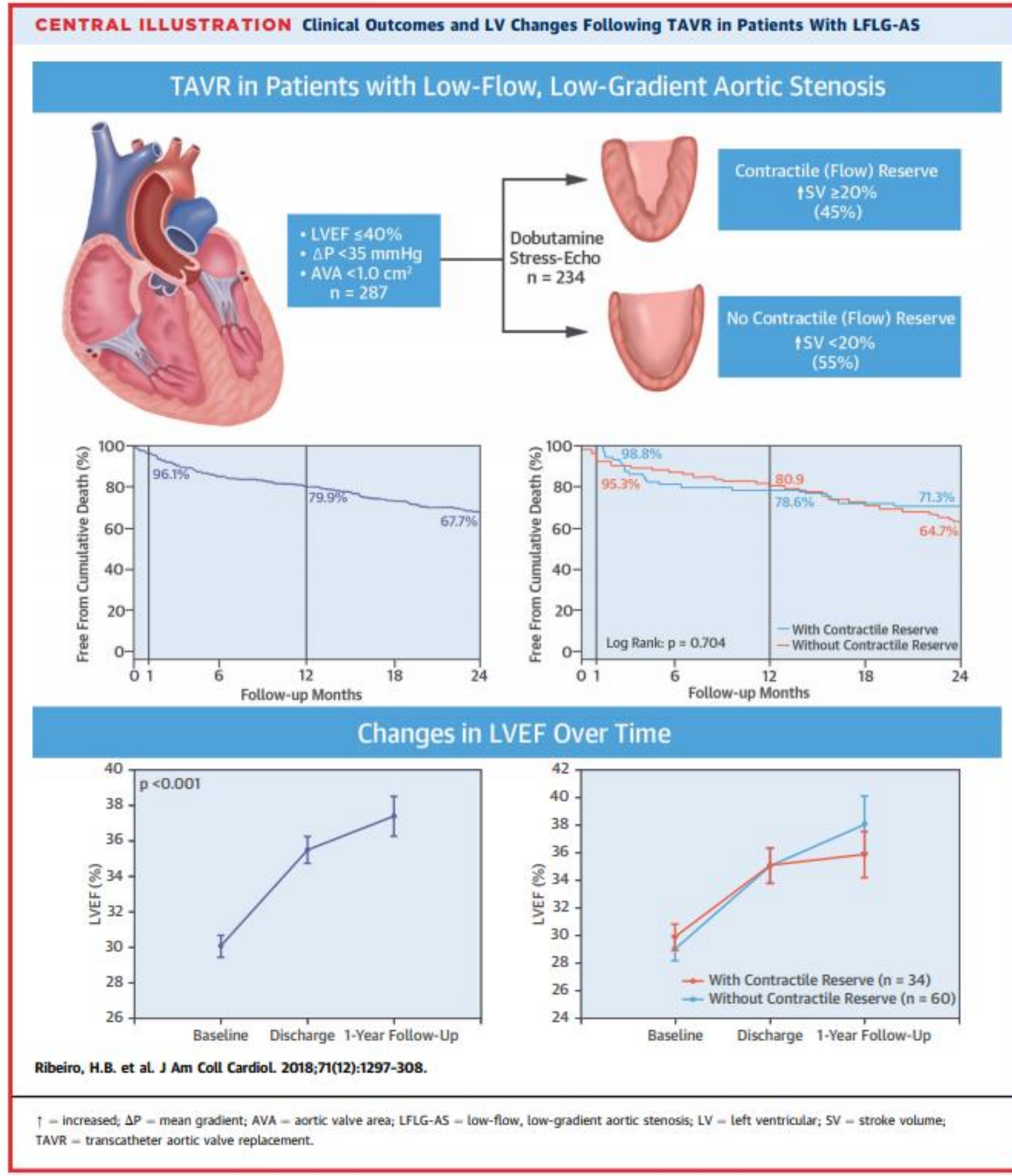
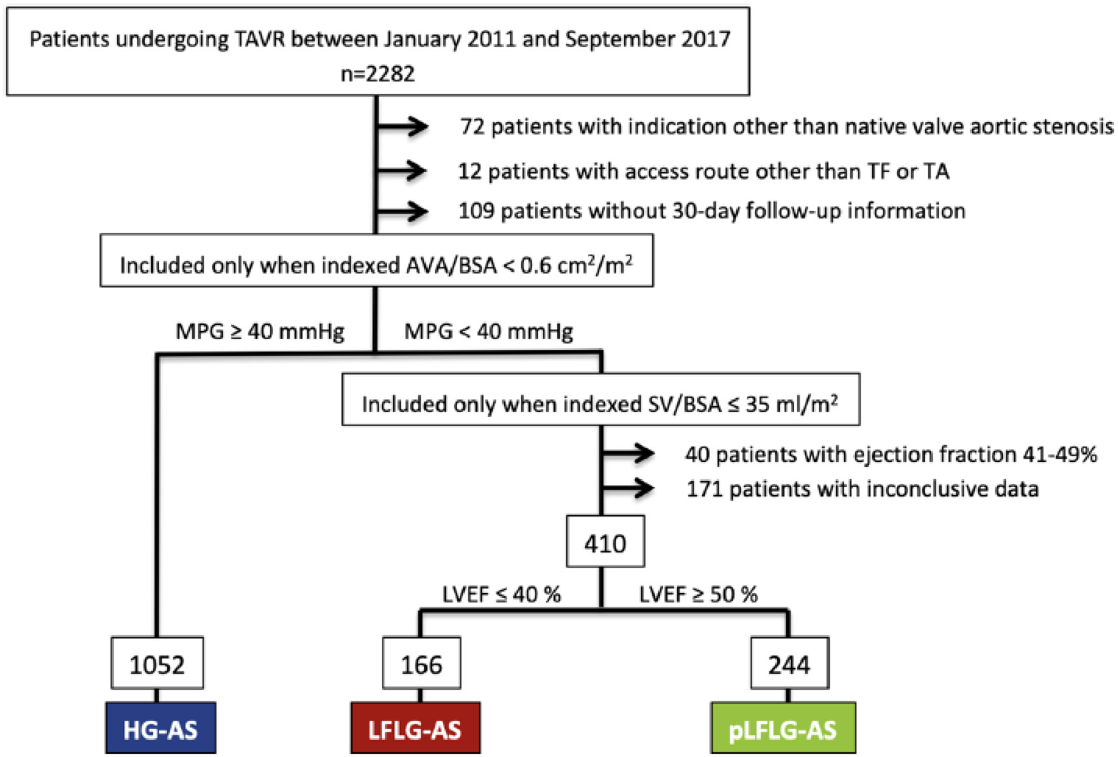
CONCLUSIONS
TAVR was associated with good periprocedural outcomes in patients with LFLG-AS.
LVEF improved following TAVR, but DSE failed to predict clinical outcomes or LVEF changes over time.



1-Year Survival After TAVR of Patients With Low-Flow, Low-Gradient and High-Gradient Aortic Valve Stenosis in Matched Study Populations

Ulrich Fischer-Rasokat, MD, PhD,[a,b] Matthias Renker, MD,[a,c,d] Christoph Liebetrau, MD, PhD,[a,b,d] Arnaud van Linden, MD,[c,e] Mani Arsalan, MD,[c,e] Maren Weferling, MD,[a] Andreas Rolf, MD, PhD,[a,b,d] Mirko Doss, MD, PhD,[c] Helge Möllmann, MD, PhD,[f] Thomas Walther, MD, PhD,[c,d,e] Christian W. Hamm, MD, PhD,[a,b,d] Won-Keun Kim, MD[a,b,c]

FIGURE 1 Flow Chart Illustrating the 3 Groups Derived From the Entire Patient Population

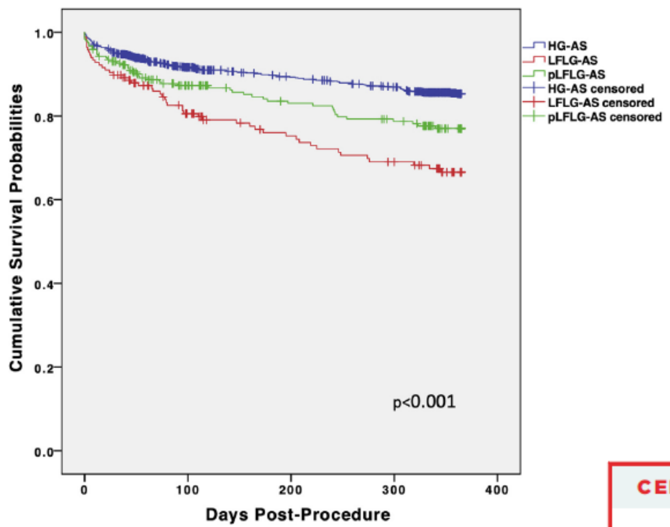


AVA = aortic valve area; BSA = body surface area; MPG = transvalvular mean pressure gradient; HG-AS = high-gradient aortic stenosis; LFLG-AS = low-flow, low-gradient aortic stenosis; LVEF = left ventricular ejection fraction; pLFLG-AS = paradoxical low-flow, low-gradient aortic stenosis; SV = stroke volume; TA = transapical; TF = transfemoral; TAVR = transcatheter aortic valve replacement.

J Am Coll Cardiol Intv 2019;12:752–63

Unmatched

FIGURE 2 Survival Curves Based on All-Cause Mortality for Patients in the Overall (Unmatched) Study Population

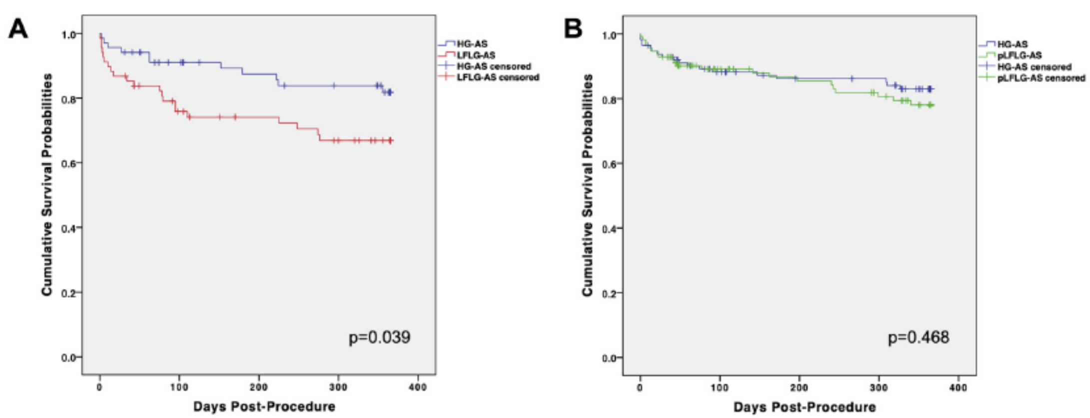


No. at risk					
HG-AS	1052	803	722	684	501
LFLG-AS	166	115	96	89	69
pLFLG-AS	244	176	155	144	117

Kaplan-Meier survival estimates for all-cause mortality. Abbreviations as in Figure 1.

Matched

CENTRAL ILLUSTRATION Survival Curves of Matched Study Populations



A

No. at risk					
HG-AS	68	55	49	45	37
LFLG-AS	68	46	41	36	29

B

No. at risk					
HG-AS	113	91	83	82	62
pLFLG-AS	113	79	71	65	55

Fischer-Rasokat, U. et al. J Am Coll Cardiol Intv. 2019;12(8):752-63.

Kaplan-Meier survival estimates for all-cause mortality of matched patients with **(A)** high-gradient aortic stenosis (HG-AS) and low-flow, low-gradient aortic stenosis (LFLG-AS) and **(B)** HG-AS and paradoxical low-flow, low-gradient aortic stenosis (pLFLG-AS).

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TABLE 5 Clinical Outcomes

	HG-AS (n = 68)	LFLG-AS (n = 68)	p Value	HG-AS (n = 113)	pLFLG-AS (n = 113)	p Value
30-day clinical outcomes						
Overall mortality	4 (5.9)	9 (13.2)	0.145	8 (7.1)	8 (7.1)	NS
In-hospital mortality	3 (4.4)	8 (11.8)	0.116	8 (7.1)	6 (5.3)	0.581
Cardiovascular mortality	4 (5.9)	8 (11.8)	0.281	7 (6.2)	5 (4.4)	0.531
Major stroke	1 (1.5)	3 (4.4)	0.310	3 (2.7)	5 (4.4)	0.472
Major vascular complication	4 (5.9)	4 (5.9)	NS	6 (5.3)	9 (8.0)	0.423
New pacemaker implant	11 (16.2)	12 (17.6)	0.819	24 (21.2)	13 (11.5)	0.048
Acute kidney injury						
Stage 1	7 (10.3)	3 (4.4)		11 (9.7)	4 (3.5)	
Stage 2	1 (1.5)	3 (4.4)	0.352	7 (6.2)	3 (2.7)	0.068
Stage 3	2 (2.9)	4 (5.9)		2 (1.8)	6 (5.3)	
Any event according to VARC-2 criteria	26 (38.2)	27 (39.7)	0.860	51 (45.1)	42 (37.2)	0.224
EF unchanged or improved*	40 (100)	26 (78.8)	0.002	41 (65.1)	44 (68.8)	0.660
1-yr clinical outcomes						
Overall mortality	11 (16.2)	21 (30.9)	0.043	18 (15.9)	21 (18.6)	0.597
Cardiovascular mortality	9 (13.2)	16 (23.5)	0.122	14 (12.4)	16 (14.2)	0.864
Major stroke	1 (1.5)	3 (4.4)	0.310	3 (2.7)	8 (7.1)	0.122
New pacemaker implant	12 (17.6)	18 (26.5)	0.215	25 (22.1)	14 (12.4)	0.053
Decompensation after 30-day follow-up	3 (4.4)	5 (7.4)	0.466	2 (1.8)	5 (4.4)	0.249

Values are n (%). *In survivors with echocardiographic exam 30 days after transcatheter aortic valve replacement.

EF = ejection fraction; VARC-2 = Valve Academic Research Consortium-2; other abbreviations as in Tables 1 and 4.

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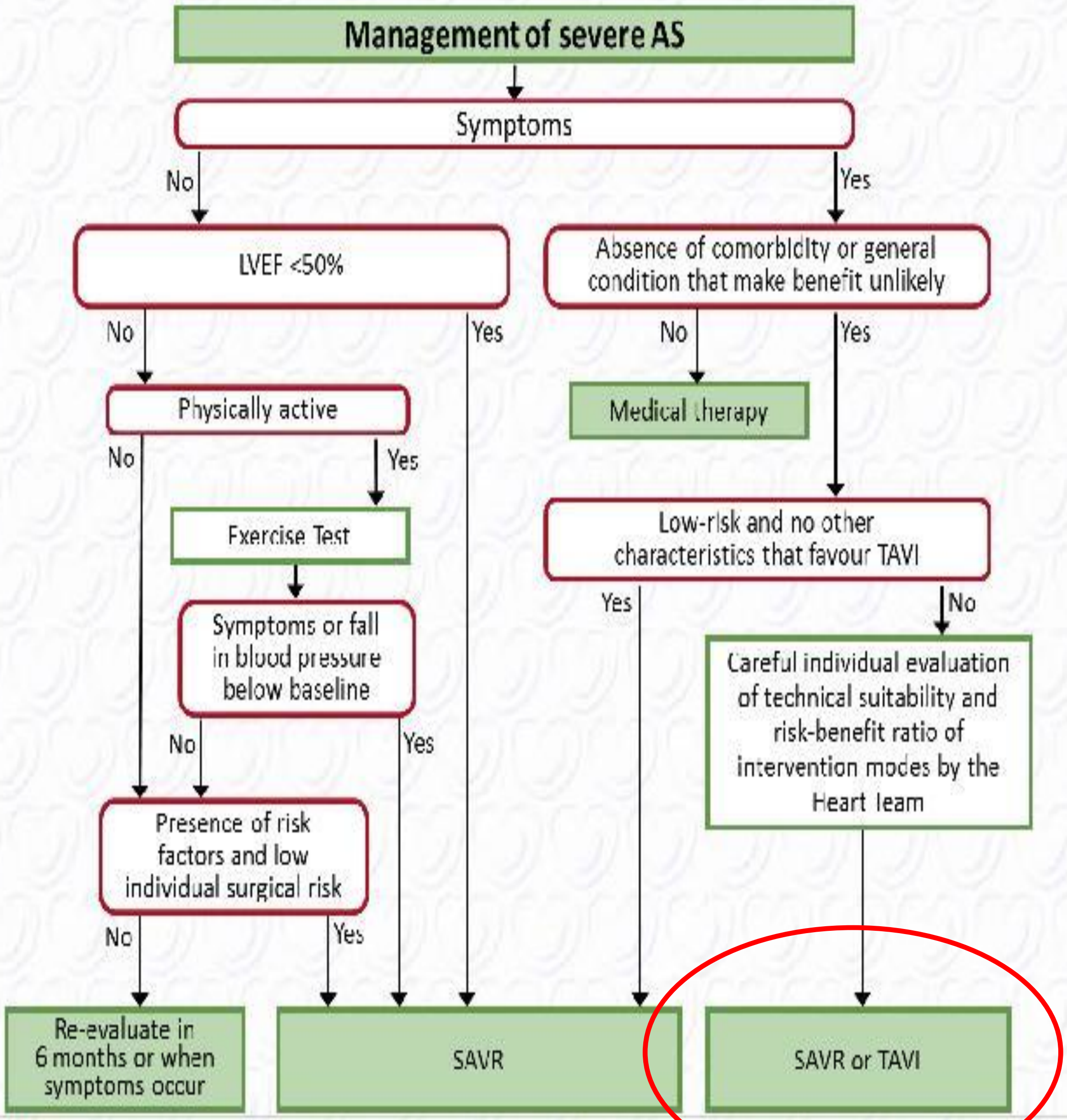
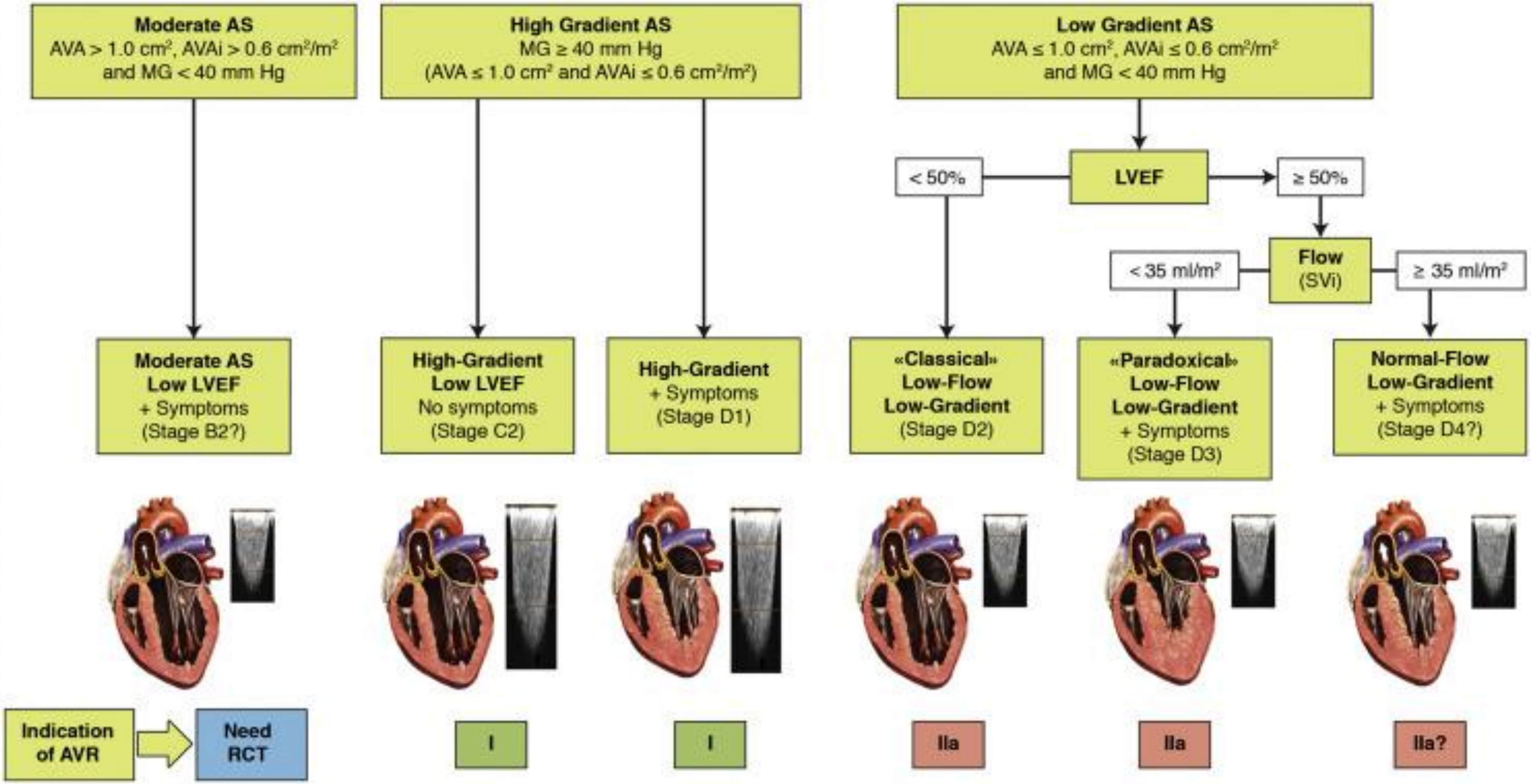
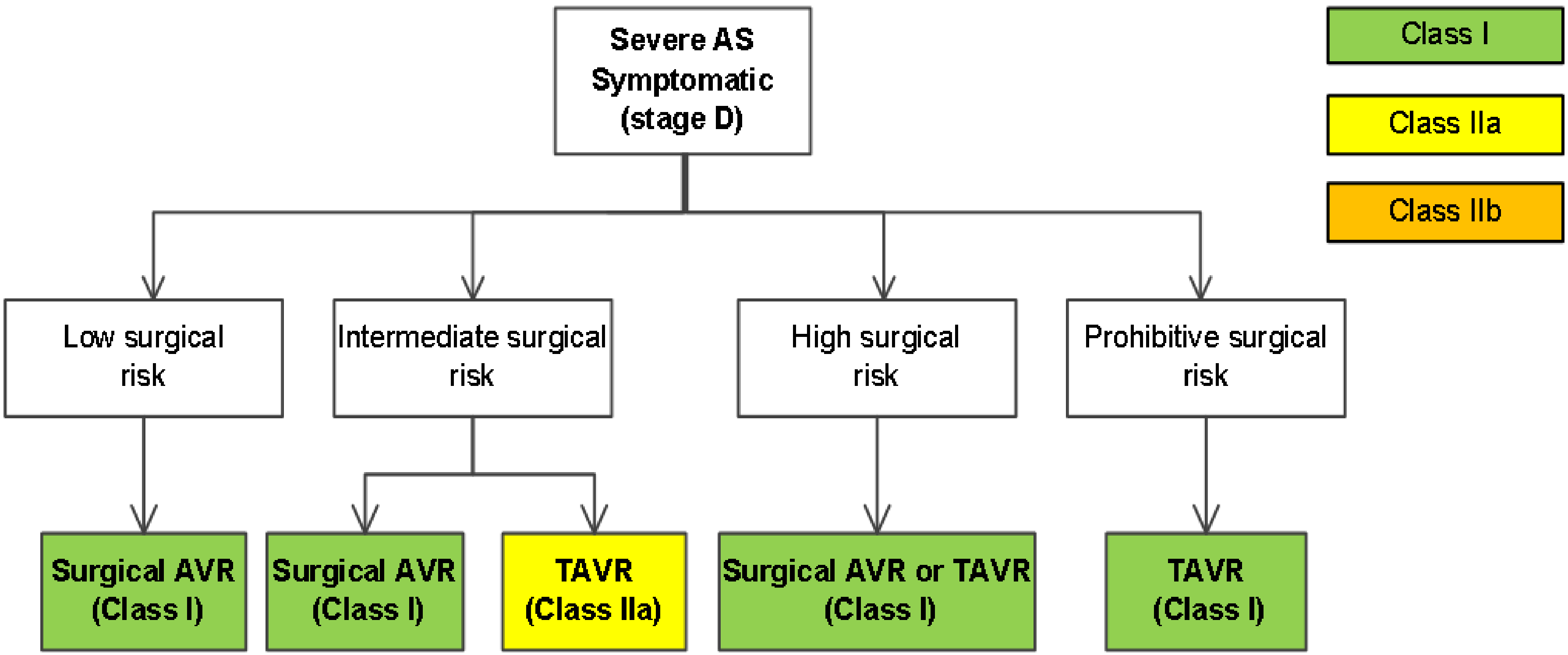

Management of severe AS
Symptoms
No
Yes
LVEF <50%
Absence of comorbidity or general condition that make benefit unlikely
No
Yes
No
Yes
Physically active
Medical therapy
No
Yes
Exercise Test
Low-risk and no other characteristics that favour TAVI
Yes
No
Symptoms or fall in blood pressure below baseline
Careful individual evaluation of technical suitability and risk-benefit ratio of intervention modes by the Heart Team
No
Yes
Presence of risk factors and low individual surgical risk
No
Yes
Re-evaluate in 6 months or when symptoms occur
SAVR
SAVR or TAVI



Moderate AS
AVA > 1.0 cm², AVAi > 0.6 cm²/m² and MG < 40 mm Hg
High Gradient AS
MG ≥ 40 mm Hg
(AVA ≤ 1.0 cm² and AVAi ≤ 0.6 cm²/m²)
Low Gradient AS
AVA ≤ 1.0 cm², AVAi ≤ 0.6 cm²/m² and MG < 40 mm Hg
LVEF
< 50%
≥ 50%
Flow (SVi)
< 35 ml/m²
≥ 35 ml/m²
Moderate AS Low LVEF + Symptoms (Stage B2?)
High-Gradient Low LVEF No symptoms (Stage C2)
High-Gradient + Symptoms (Stage D1)
«Classical» Low-Flow Low-Gradient (Stage D2)
«Paradoxical» Low-Flow Low-Gradient + Symptoms (Stage D3)
Normal-Flow Low-Gradient + Symptoms (Stage D4?)
Indication of AVR
Need RCT
I
I
IIa
IIa
IIa?

Choice of TAVR Versus Surgical AVR in the Patient With Severe Symptomatic AS (Modified)



Take Home Message

- Understand different subtypes of severe AS
- Exclude measurement errors and other concomitant flow conditions first
- Optimal hemodynamic condition during Echo assessment
- Integrated approach, additional imaging modalities
- Correlate with patient's symptoms
- "Dichotomous" cutoff values in guideline – apply with cautions
- Emerging role of TAVI in subtype D2 (classical LFLG) and D3 (paradoxical LFLG)