



Aortic Stenosis

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Disclosures

- ▶ No disclosures

Learning objectives

- ▶ Review prevalence and natural progression
- ▶ Recognize AS, understand echo findings, and know when to refer.
- ▶ Review ACC/AHA guidelines and timing of aortic valve replacement, SAVR vs TAVR

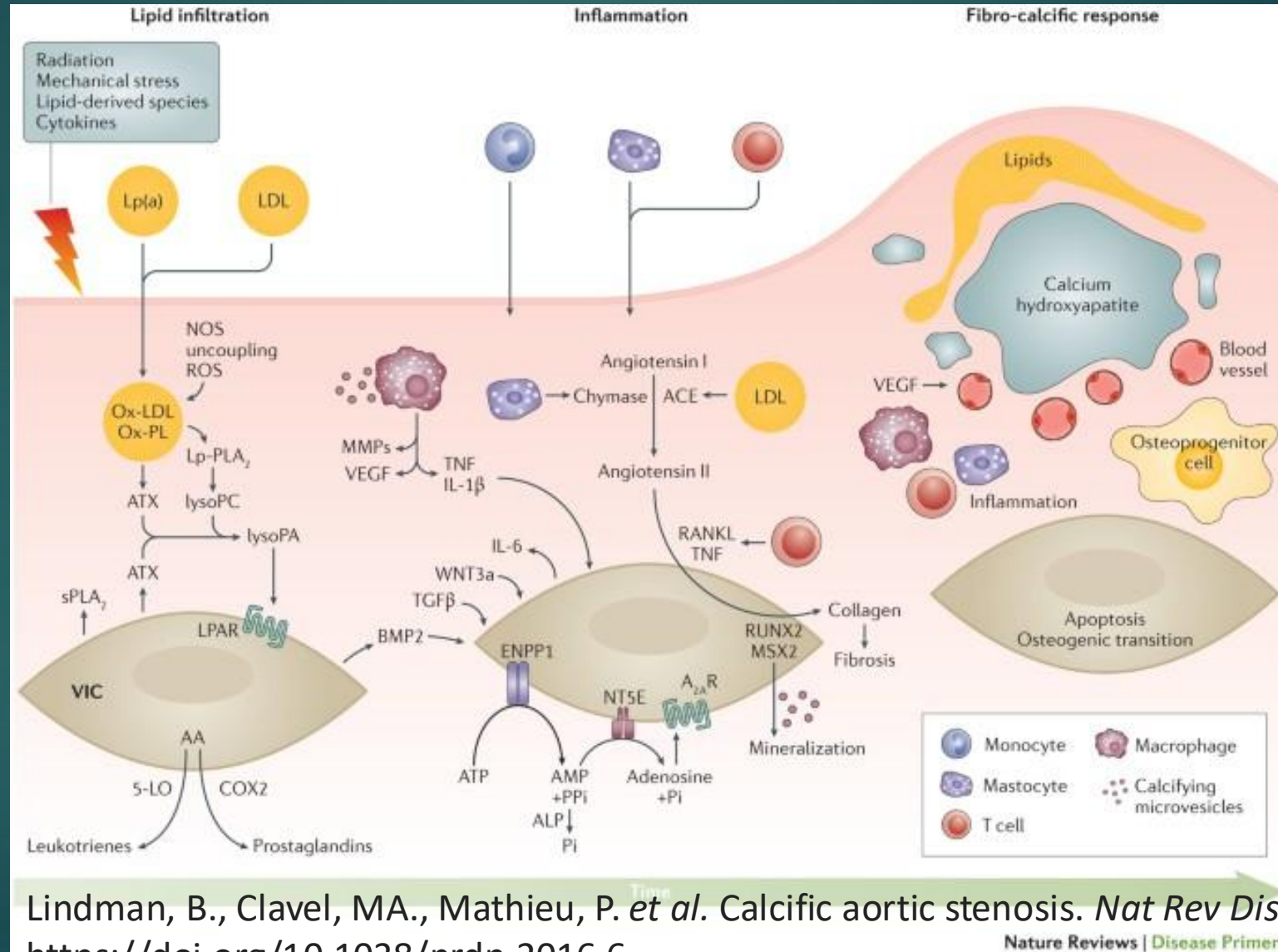
Prevalence

- ▶ AS is defined as valve leaflet disease leading to left ventricular outflow obstruction cause by progressive leaflet calcification.
- ▶ Affects ~ 12.5 million of people globally
- ▶ Aortic stenosis (AS) is the most frequent valvular heart disease in Western countries,¹ affecting ≈5% of individuals aged >65 year old
- ▶ For individuals above 80 years of age, the prevalence is ~ 10%, so it is the disease of the elderly.

Benjamin EJ, Virani SS, Callaway CW, Chamberlain AM, Chang AR, Cheng S, Chiuve SE, Cushman M, Delling FN, Deo R, et al. Heart disease and stroke Statistics-2018 update: a report from the American Heart Association. *Circulation*. 2018;137:e67–e492

Nkomo VT, Gardin JM, Skelton TN, Gottdiener JS, Scott CG, Enriquez-Sarano M. Burden of valvular heart diseases: a population-based study. *Lancet*. 2006;368:1005–1011.

Pathogenesis of the Aortic Stenosis



Lindman, B., Clavel, MA., Mathieu, P. *et al.* Calcific aortic stenosis. *Nat Rev Dis Primers* 2, 16006 (2016).

<https://doi.org/10.1038/nrdp.2016.6>

Nature Reviews | Disease Primers

Causes of AS

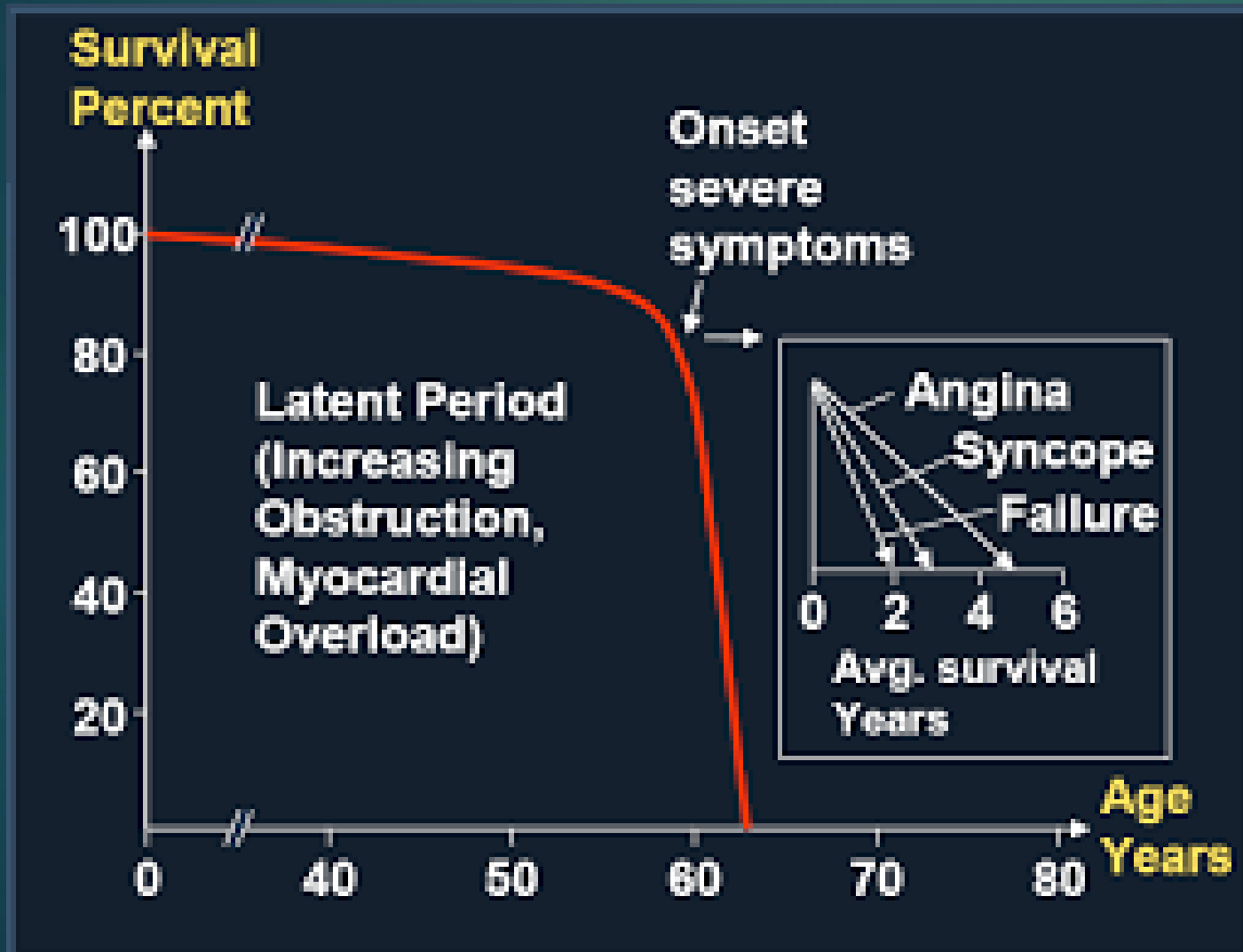
<5 %

50%

50%



History of the aortic stenosis

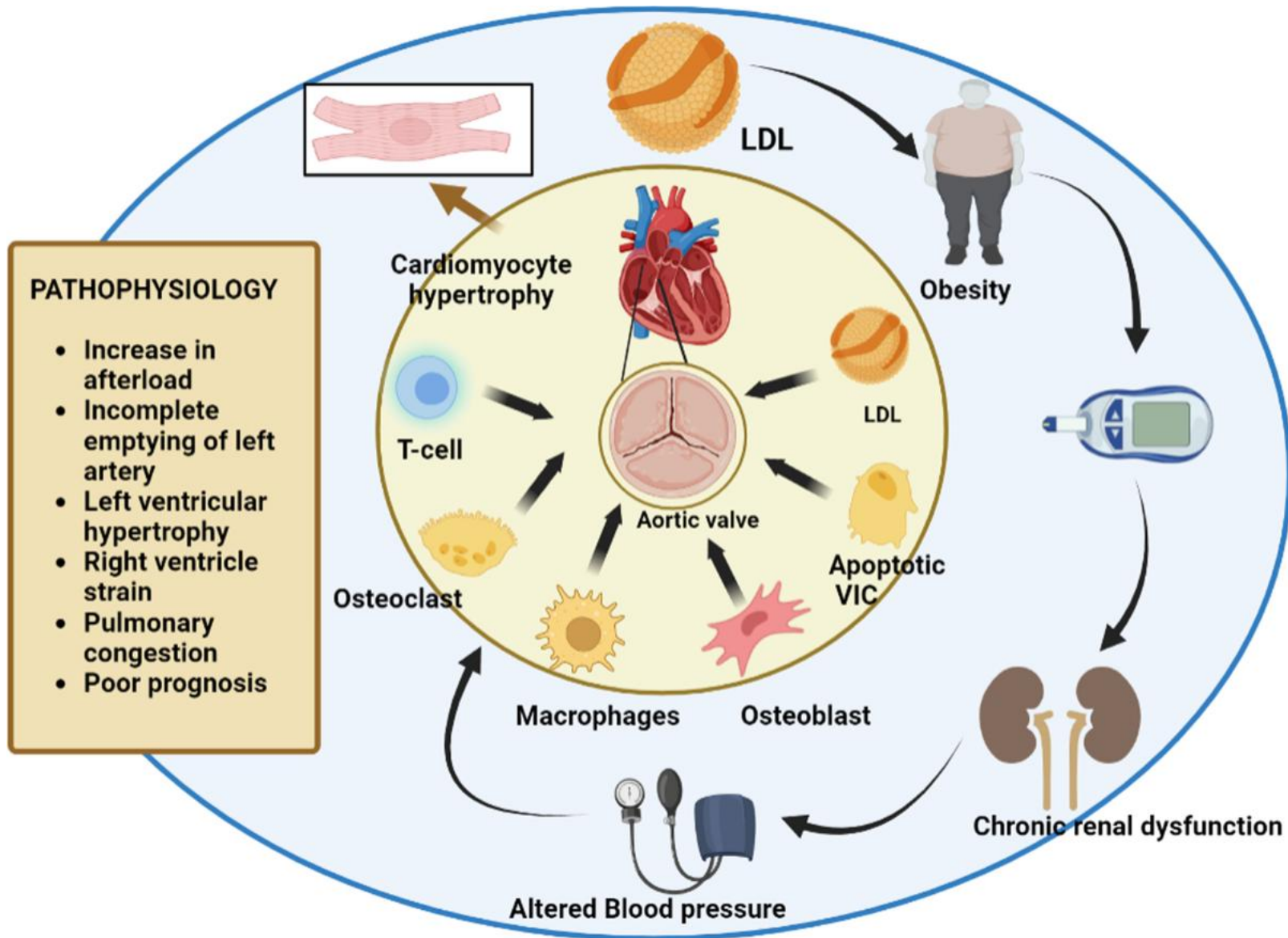


After severe symptom onset and if left untreated mortality is ~ 50% within 2-5 years.

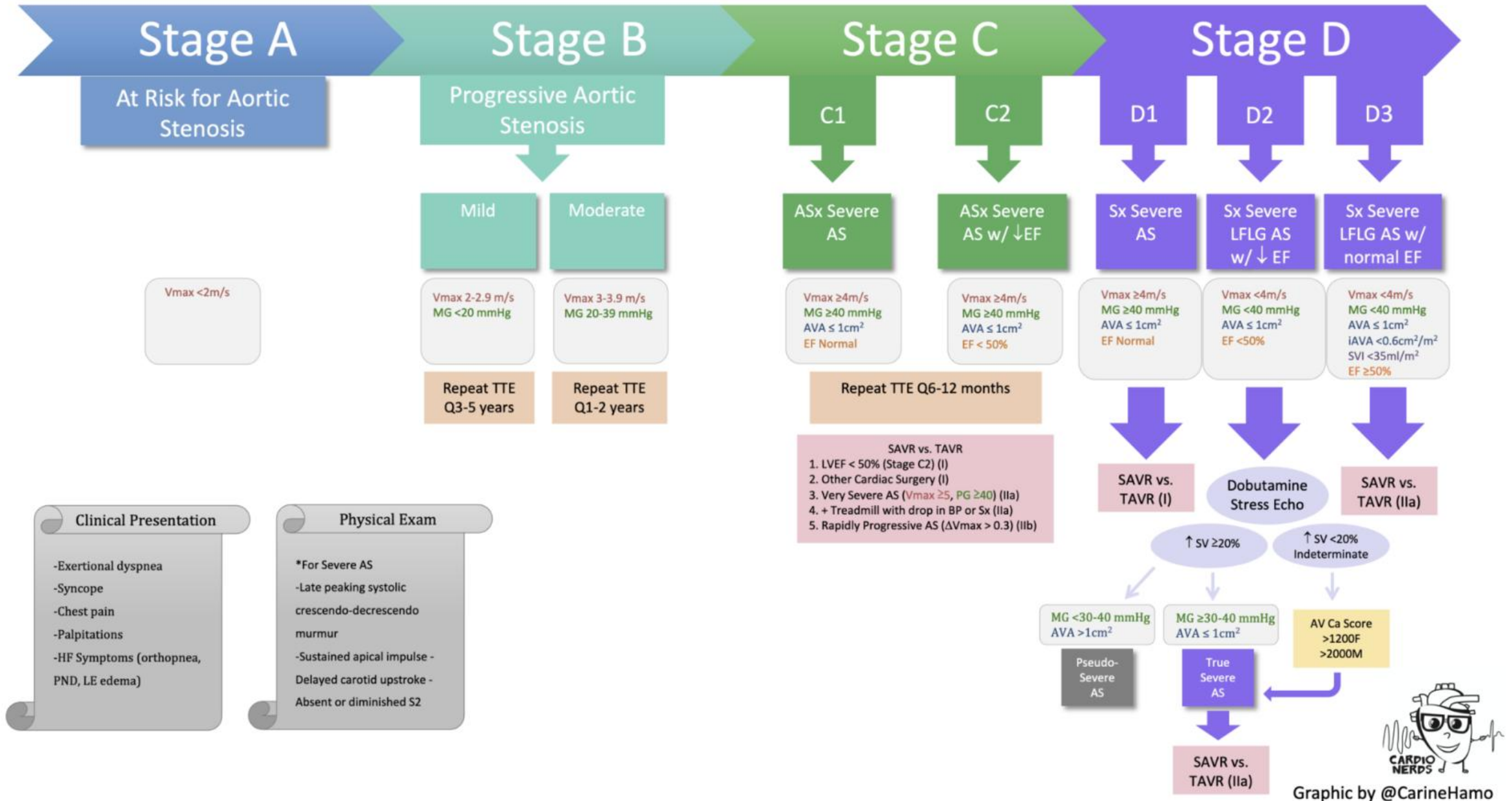
Important to educate patients on the symptoms and that timely intervention is needed.

Most common symptom in patients with severe AS?

--decrease in baseline exercise capacity or DOE.



AORTIC STENOSIS

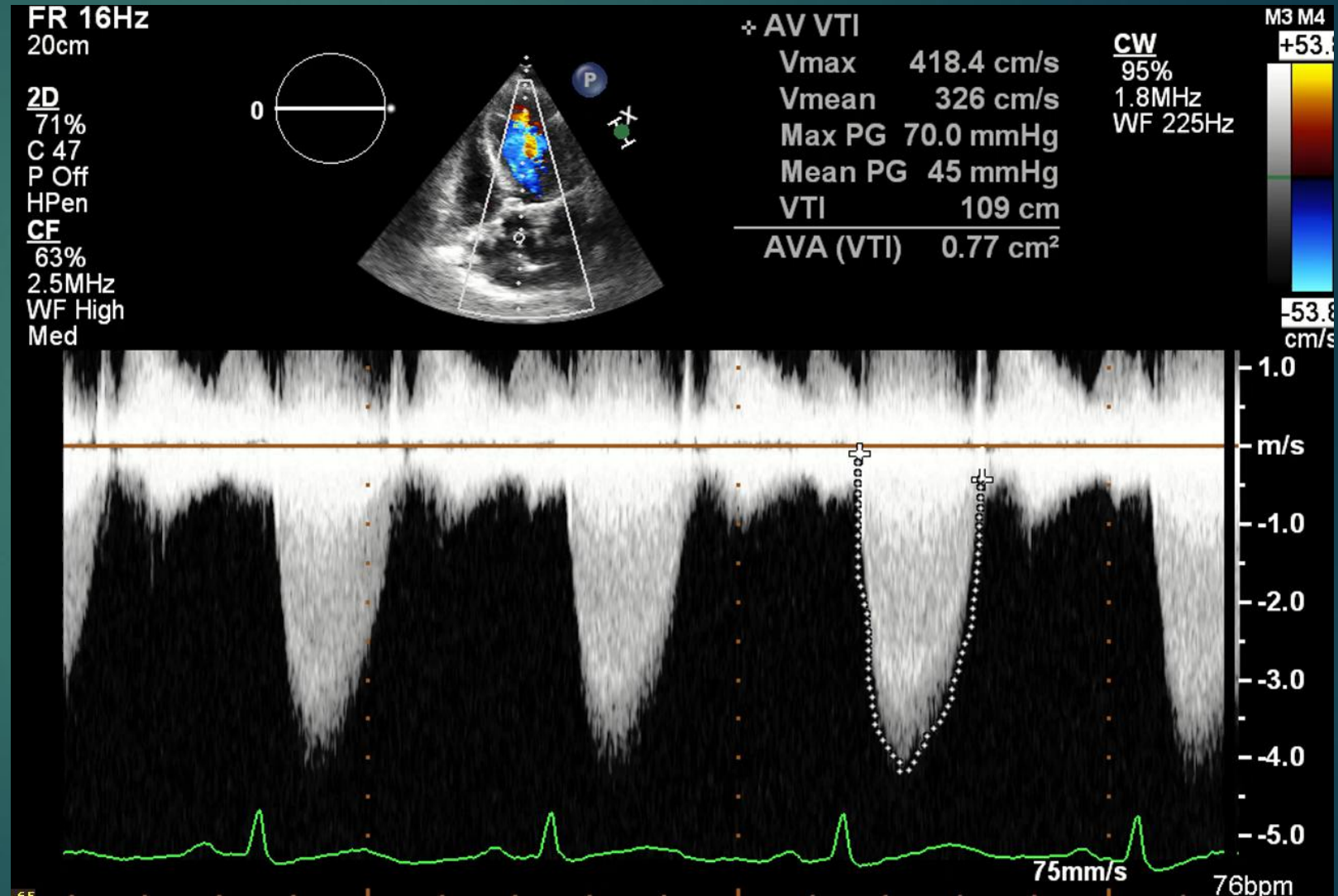


Physical Exam

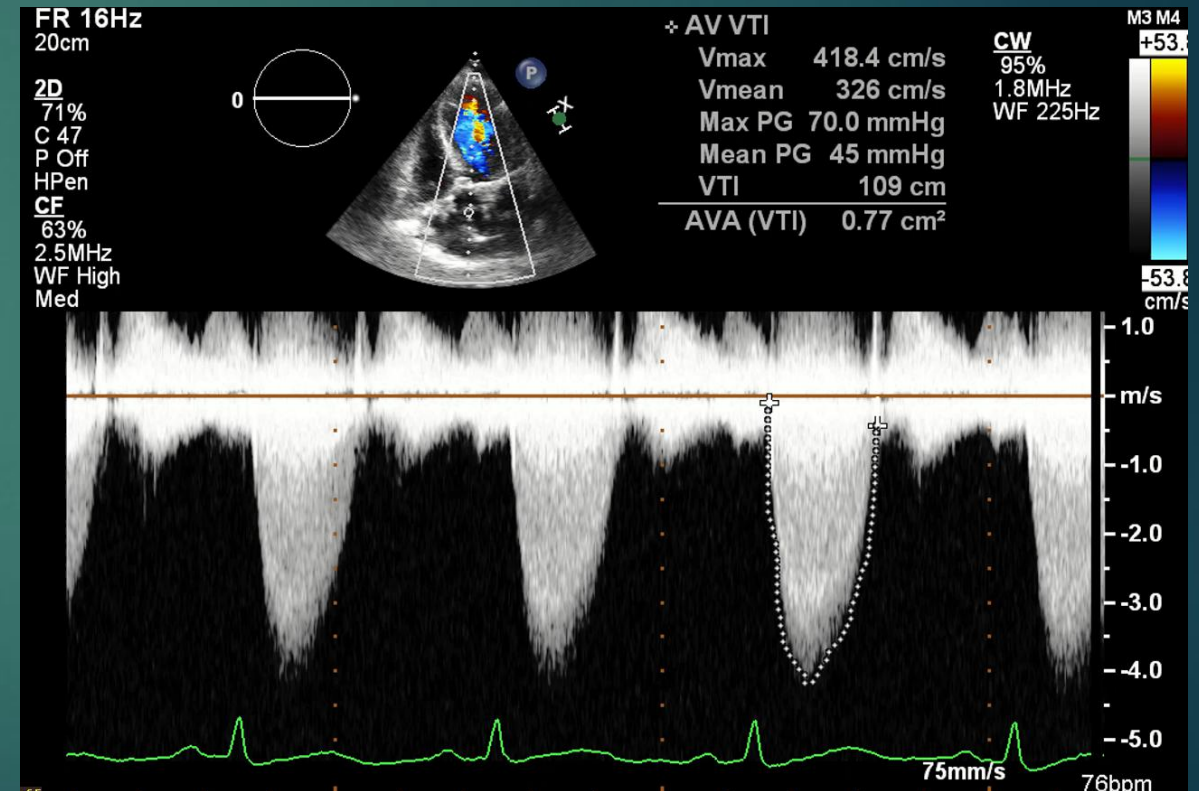
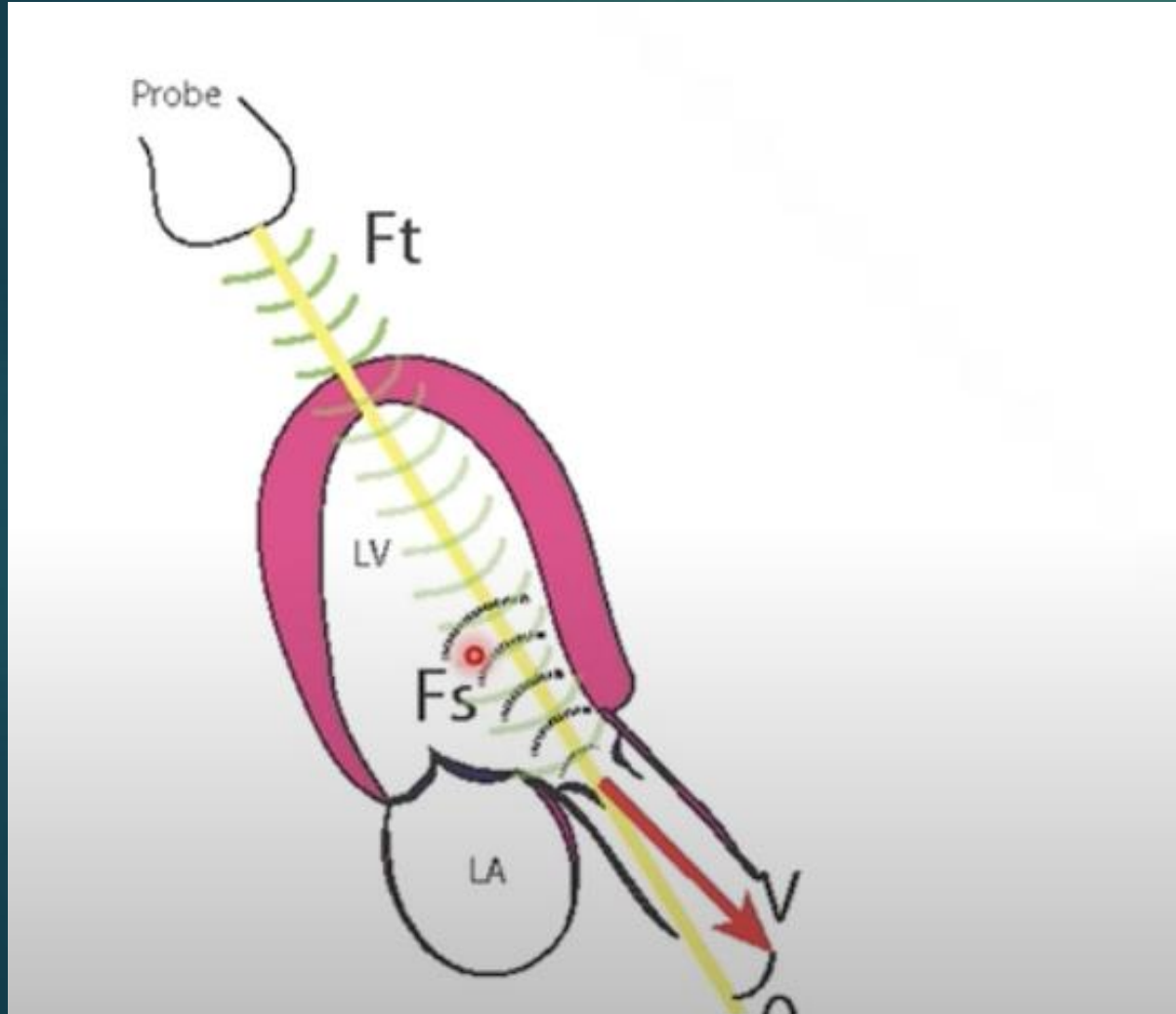
- ▶ Systolic murmur at the cardiac base: often grade 3/6, but 20% have a softer murmur.
- ▶ Diminished and delayed carotid upstroke is a specific finding (100%) for severe AS
- ▶ Late peaking systolic murmur, single quiet S2
- ▶ Sensitivity of murmur for diagnosis of any valvular disease is <50%
- ▶ Specificity is 70%
- ▶ Echo is a definitive test to diagnose AS

ECHO parameters

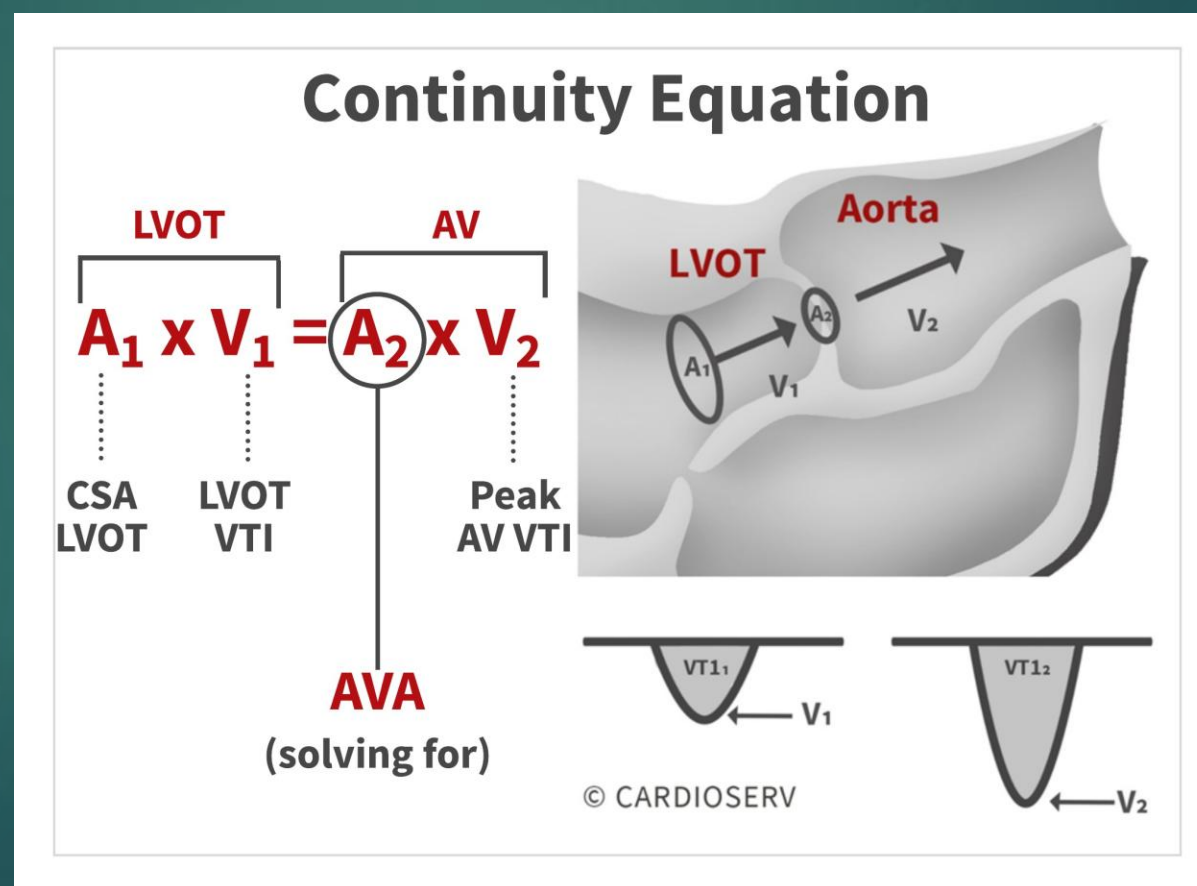
- ▶ Peak Velocity
- ▶ Mean gradient
- ▶ Aortic valve area
- ▶ LV function
- ▶ We use CW doppler to determine the Vmax and mean gradient



If you see that the doppler sample is not parallel and not on line with the aortic valve – it can underestimate the severity of AS

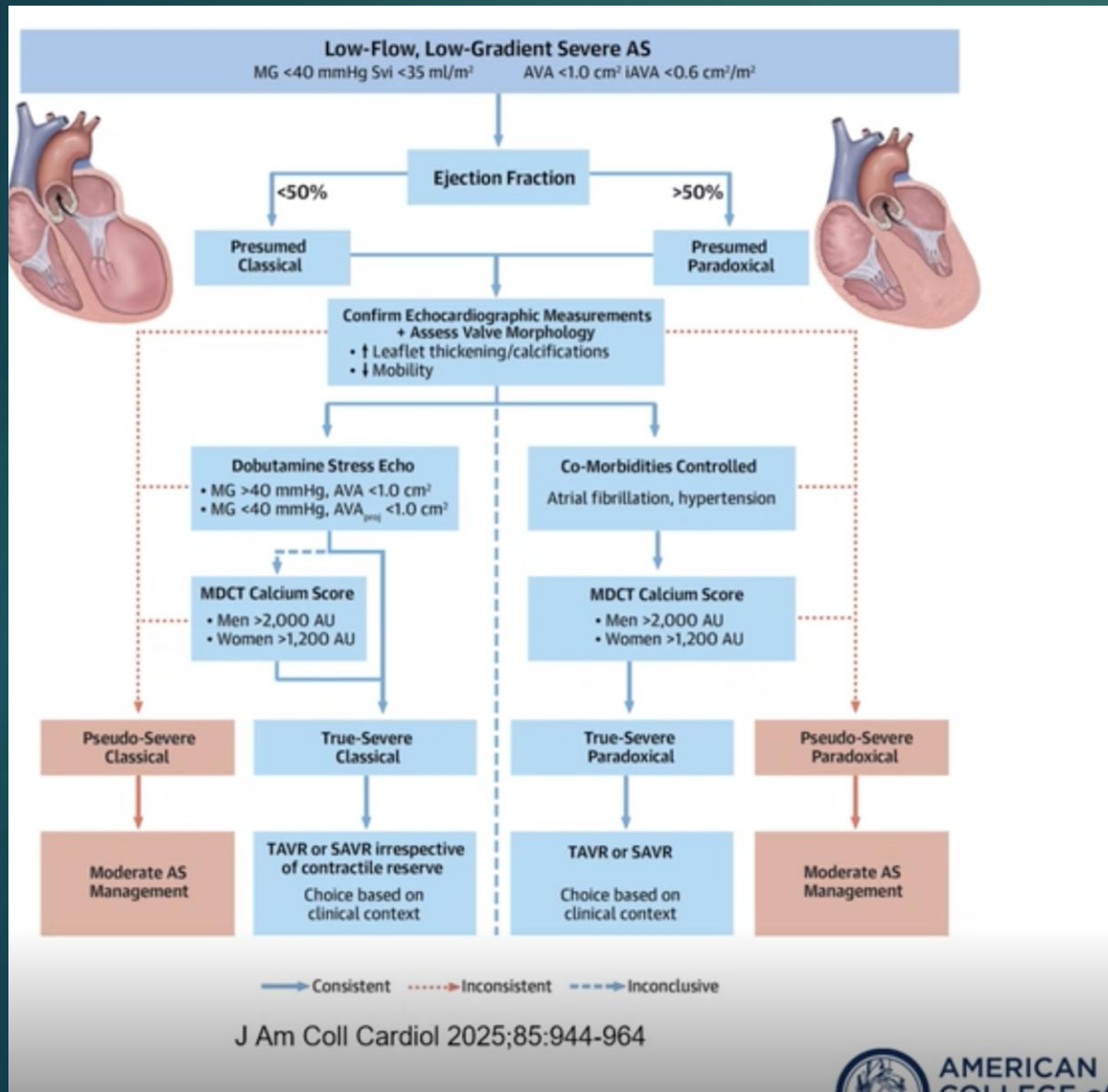


Calculating Aortic Valve area using the continuity equation



	Aortic Sclerosis	Mild	Moderate	Severe	Very Severe
Peak AV velocity (m/s)	< 2.0 m/s	2.0 - 2.9	3.0 - 3.9	≥ 4.0	≥ 5.0
Mean Gradient (mmHg)	--	< 20	20 - 39	≥ 40	≥ 60
AVA (cm ²)	--	> 1.5	> 1.0 - 1.5	≤ 1.0	≤ 0.60
Indexed AVA (cm ² /m ²)	--	> 0.85	> 0.60 - 0.85	≤ 0.60	
ECHO Surveillance		3-5yrs	1-2yrs	6months – 1yr	

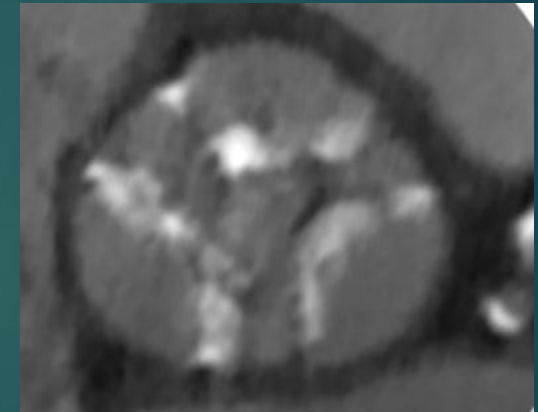
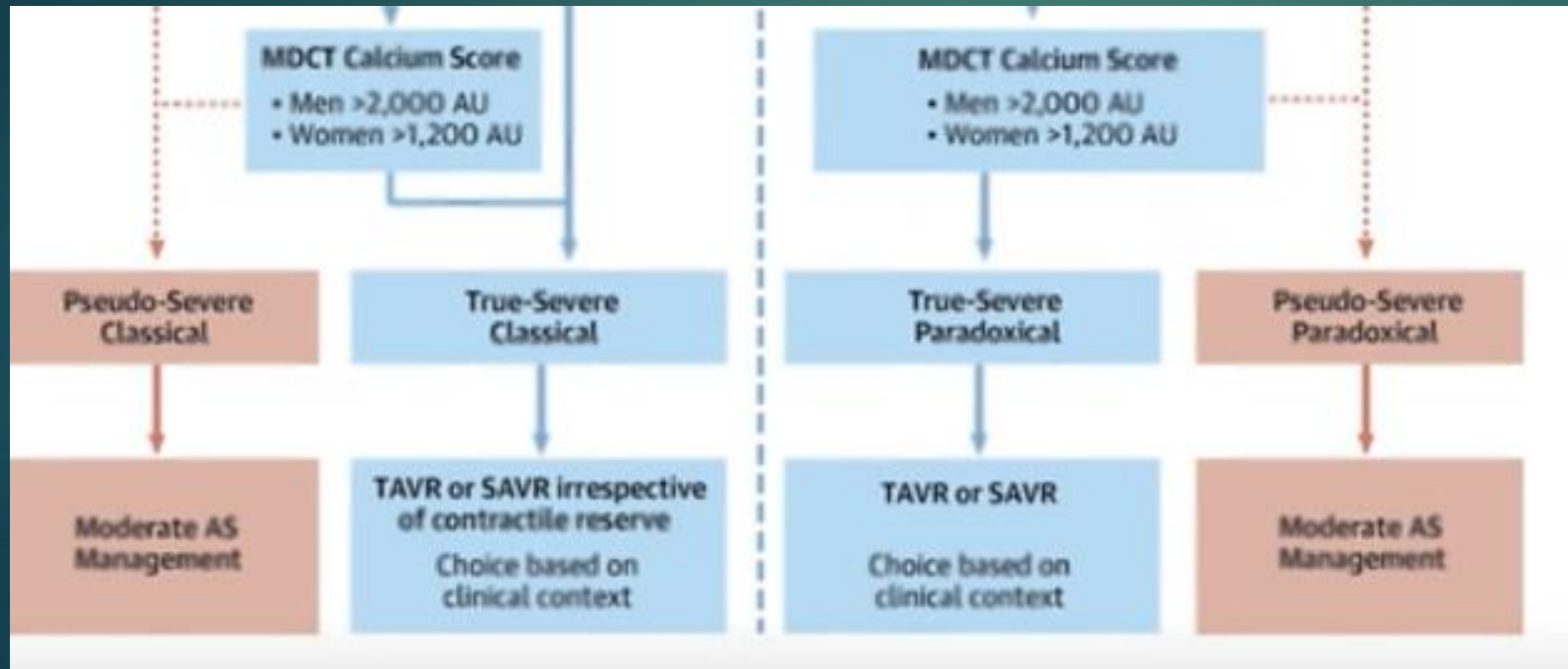
Low Flow State LFLG AS



When there is a discrepant data – pay attention to aortic valve area < 1.0 cm².

There is also Peak velocity of < 4 m/s;
Mean gradient < 40 mmHg

If data is inconsistent after dobutamine stress test – obtain Calcium Score



Stress testing in severe asymptomatic AS

Recommendations for Diagnostic Testing: Exercise Testing in Patients With AS		
Referenced studies that support the recommendations are summarized in Online Data Supplement 4 .		
COR	LOE	Recommendations
2a	B-NR	1. In asymptomatic patients with severe AS (Stage C1), exercise testing is reasonable to assess physiological changes with exercise and to confirm the absence of symptoms. ¹⁻⁴
3: Harm	B-NR	2. In symptomatic patients with severe AS (Stage D1, aortic velocity ≥ 4.0 m/s or mean pressure gradient ≥ 40 mm Hg), exercise testing should not be performed because of the risk of severe hemodynamic compromise. ⁵

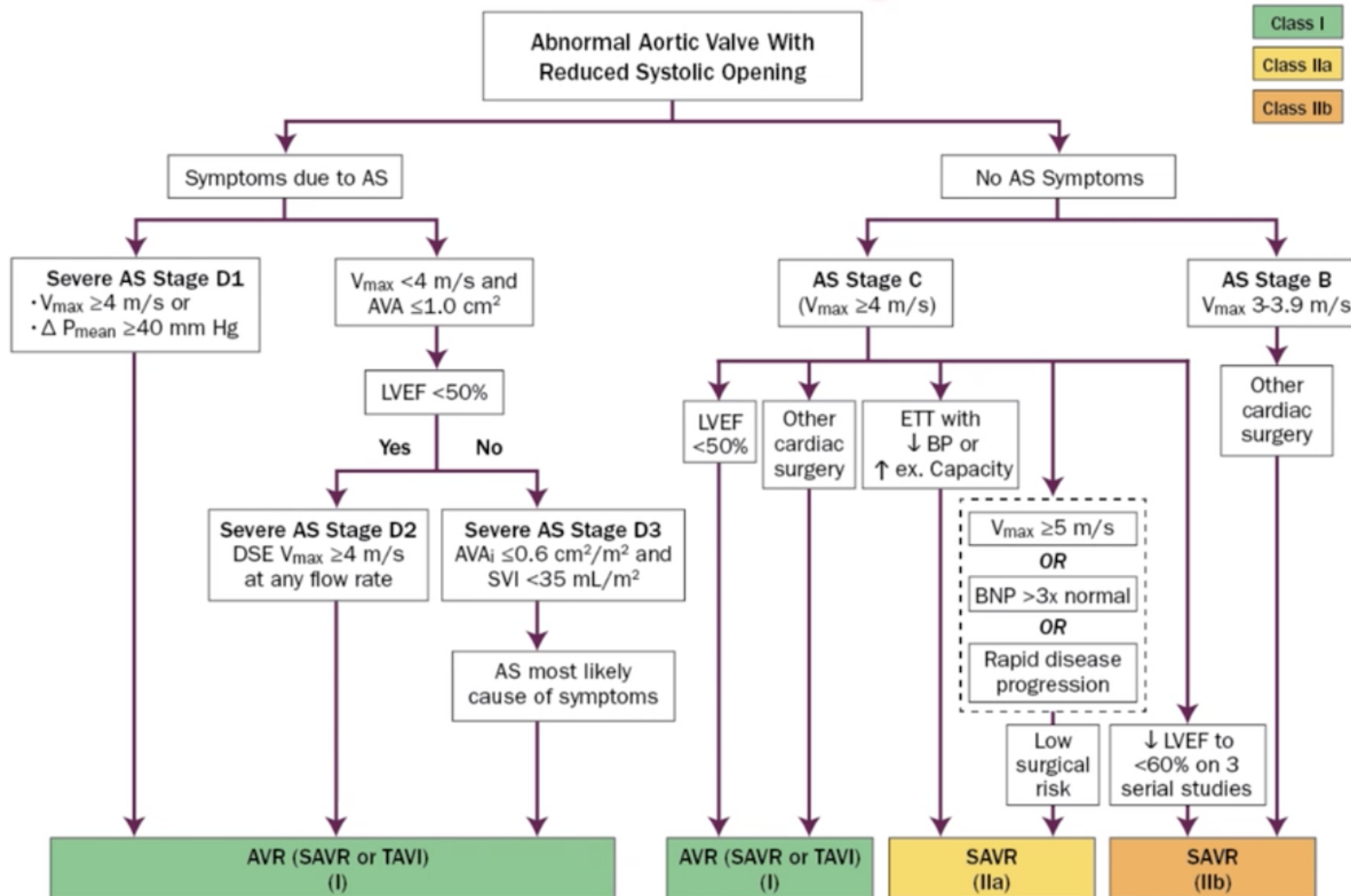
Medical therapy in AS

Recommendations for Medical Therapy of AS		
Referenced studies that support the recommendations are summarized in Online Data Supplement 5.		
COR	LOE	Recommendations
1	B-NR	1. In patients at risk of developing AS (Stage A) and in patients with asymptomatic AS (Stages B and C), hypertension should be treated according to standard GDMT, started at a low dose, and gradually titrated upward as needed, with appropriate clinical monitoring. ¹⁻³
1	A	2. In all patients with calcific AS, statin therapy is indicated for primary and secondary prevention of atherosclerosis on the basis of standard risk scores. ⁴⁻⁶
2b	B-NR	3. In patients who have undergone TAVI, renin-angiotensin system blocker therapy (ACE inhibitor or ARB) may be considered to reduce the long-term risk of all-cause mortality. ^{7,8}
3: No Benefit	A	4. In patients with calcific AS (Stages B and C), statin therapy is not indicated for prevention of hemodynamic progression of AS. ⁴⁻⁶

Treat HTN

Treat calcific AS with a statin

Indications and Timing for AVR



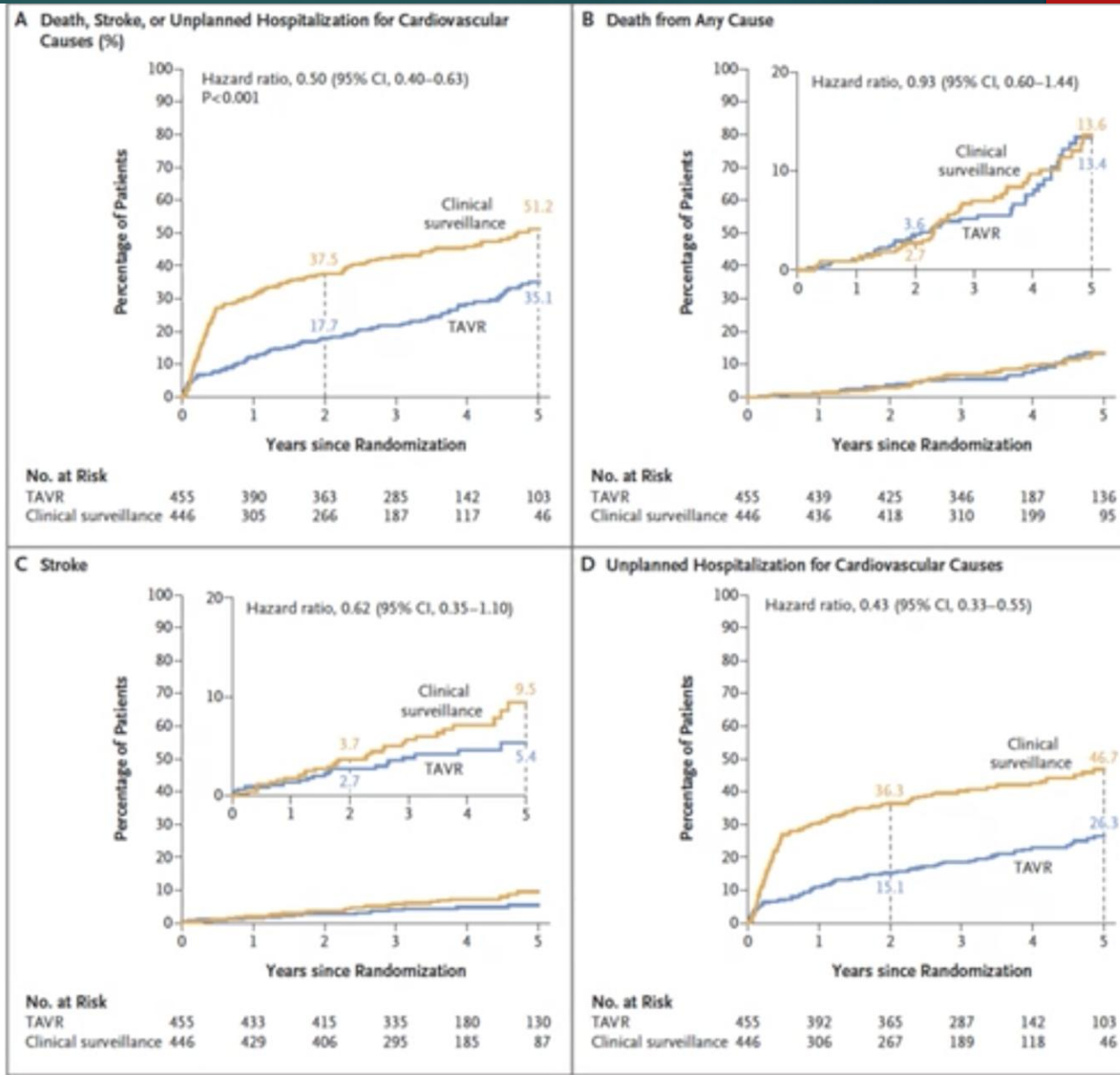
Early TAVR

Randomized~ 900 patients with severe asymptomatic AS to TAVI vs routine clinical surveillance

Primary endpoint of death, stroke unplanned hospitalization or cardiovascular cause showed that early TAVI patients did statistically better than those under clinical surveillance arm.

Primary endo-point occurred in 122 patients (26.8%) in the TAVR arm vs 202 patients (45.3%) in the clinical surveillance group

No difference in all cause mortality



TAVR vs SAVR

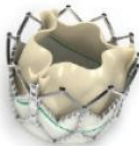
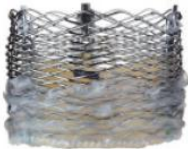
Summary of Transcatheter Aortic Valve Implantation (TAVI) Trials

Trial or study name	Dates of trial or study	Surgical risk	Study design	Valve implanted for TAVI	No. of patients	Study duration, y	Primary study end point	Results of primary study end point	Other events and comments
PARTNER 1B	May 2007 - Mar 2009	Inoperable	Randomized 1:1 to TAVI or standard therapy	Edwards SAPIEN (balloon-expandable valve)	179 in TAVI group; 179 in standard therapy group	1	Rate of death from any cause	30.7% in TAVI group vs 50.7% in standard therapy group; HR, 0.55 (95% CI, 0.40 to 0.74), $P < .001$	Major stroke: 7.8% in TAVI group vs 3.9% in standard therapy group ($P = .18$)
CoreValve Extreme Risk Pivotal ¹	Feb 2011 - Aug 2012	Inoperable	All received TAVI	CoreValve (self-expandable valve)	All 489 in TAVI group (no comparison group)	1	All-cause mortality or major stroke	26.0% vs 43.0% with the prespecified objective performance goal (upper 2-sided 95% CI boundary for 26.0%: 29.9%, $P < .0001$)	Major stroke: 4.3%
PARTNER 1A	May 2007 - Aug 28, 2009	High	Randomized 1:1 to TAVI or SAVR	Edwards SAPIEN (balloon-expandable valve)	348 in TAVI group; 351 in SAVR group	1	Rate of death from any cause	24.2% in TAVI group vs 26.8% in SAVR group ($P = .44$); 2-sided 95% CI, -9.3 to 4.1; upper 1-sided 95% CI boundary: 3.0 percentage points ($P = .001$ for noninferiority)	Major stroke: 5.1% in TAVI group vs 2.4% in SAVR group ($P = .07$)
CoreValve High Risk Pivotal ¹	Feb 2011 - Sep 2012	High	Randomized 1:1 to TAVI or SAVR	CoreValve (self-expandable valve)	390 in TAVI group; 357 in SAVR group	1	Rate of death from any cause	14.2% in TAVI group vs 19.1% in SAVR group; absolute reduction in risk, 4.9 percentage points; upper 95% CI boundary, -0.4 ($P < .001$ for noninferiority; $P = .04$ for superiority)	Major stroke: 8.8% in TAVI group vs 12.6% in SAVR group ($P = .10$)
PARTNER 2	Dec 2011 - Nov 2013	Intermediate	Randomized 1:1 to TAVI or SAVR	SAPIEN XT (balloon-expandable valve)	1011 in TAVI group; 1021 in SAVR group	2	Death from any cause or disabling stroke	No significant between-group difference: HR for the TAVI group, 0.89 (95% CI, 0.73 to 1.09, $P = .25$)	In the transfemoral cohort, the primary end point was lower in the TAVI group than in the SAVR group (HR for the intention-to-treat analysis, 0.79 [95% CI, 0.62 to 1.00], $P = .05$)
SURTAVI	Jun 2012 - Jun 2016	Intermediate	Randomized 1:1 to TAVI or SAVR	• CoreValve (84%) • Evolut R (16%) • Both are self-expandable valves	864 in TAVI group; 796 in SAVR group	2	Death from any cause or disabling stroke	12.6% in TAVI group vs 14.0% in SAVR group (95% Bayesian credible interval for difference, -5.2% to 2.3%; posterior probability of noninferiority, $P > .999$)	Higher rates of acute kidney injury and atrial fibrillation in SAVR group; higher rates of aortic regurgitation and pacemaker implantation in TAVI group
PARTNER 3 ²	Mar 2016 - Oct 2017	Low	Randomized 1:1 to TAVI or SAVR	SAPIEN 3 (balloon-expandable valve)	503 in TAVI group; 497 in SAVR group	1	Death from any cause, stroke, or rehospitalization	8.5% in TAVI group vs 15.1% in SAVR group; absolute between-group difference, -6.6 percentage points (95% CI, -10.8 to -2.5 percentage points, $P < .001$ for noninferiority); HR, 0.54 (95% CI, 0.37 to 0.79), $P = .001$ for superiority	No significant between-group differences for major vascular complications, pacemaker placement, and moderate to severe paravalvular regurgitation
Evolut Low Risk	Mar 2016 - Nov 2018	Low	Randomized 1:1 to TAVI or SAVR	• CoreValve (3.6%) • Evolut R (74.1%) • Evolut PRO (22.3%) • All 3 are self-expandable valves	734 in TAVI group; 734 in SAVR group	2	Death from any cause or disabling stroke	5.3% in TAVI group vs 6.7% in SAVR group (between-group difference, -1.4 percentage points; 95% Bayesian credible interval for difference, -4.9 to 2.1 percentage points; posterior probability of noninferiority $P > .999$)	Prespecified interim analysis: need for permanent pacemaker higher in TAVI group vs SAVR group (17.4% vs 6.1%, respectively; between-group difference, 11.3% [95% CI, 8.0% to 14.7%])

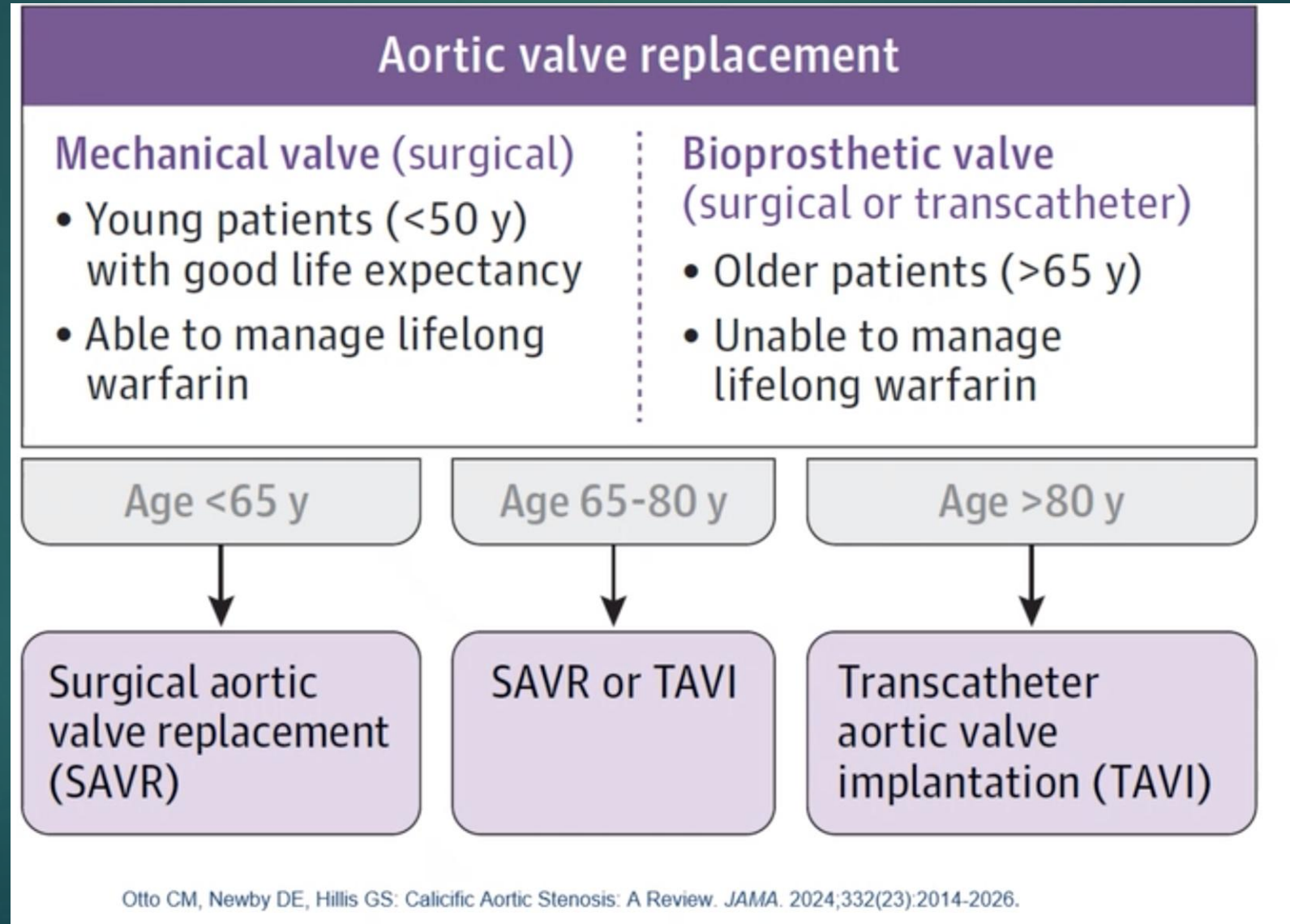
Abbreviations: Evolut Low Risk, Evolut Surgical Replacement and Transcatheter Aortic Valve Implantation in Low-Risk Patients; HR, hazard ratio; PARTNER, Placement of Aortic Transcatheter Valves; SAVR, surgical aortic valve replacement; SURTAVI, Surgical Replacement and Transcatheter Aortic Valve Implantation.

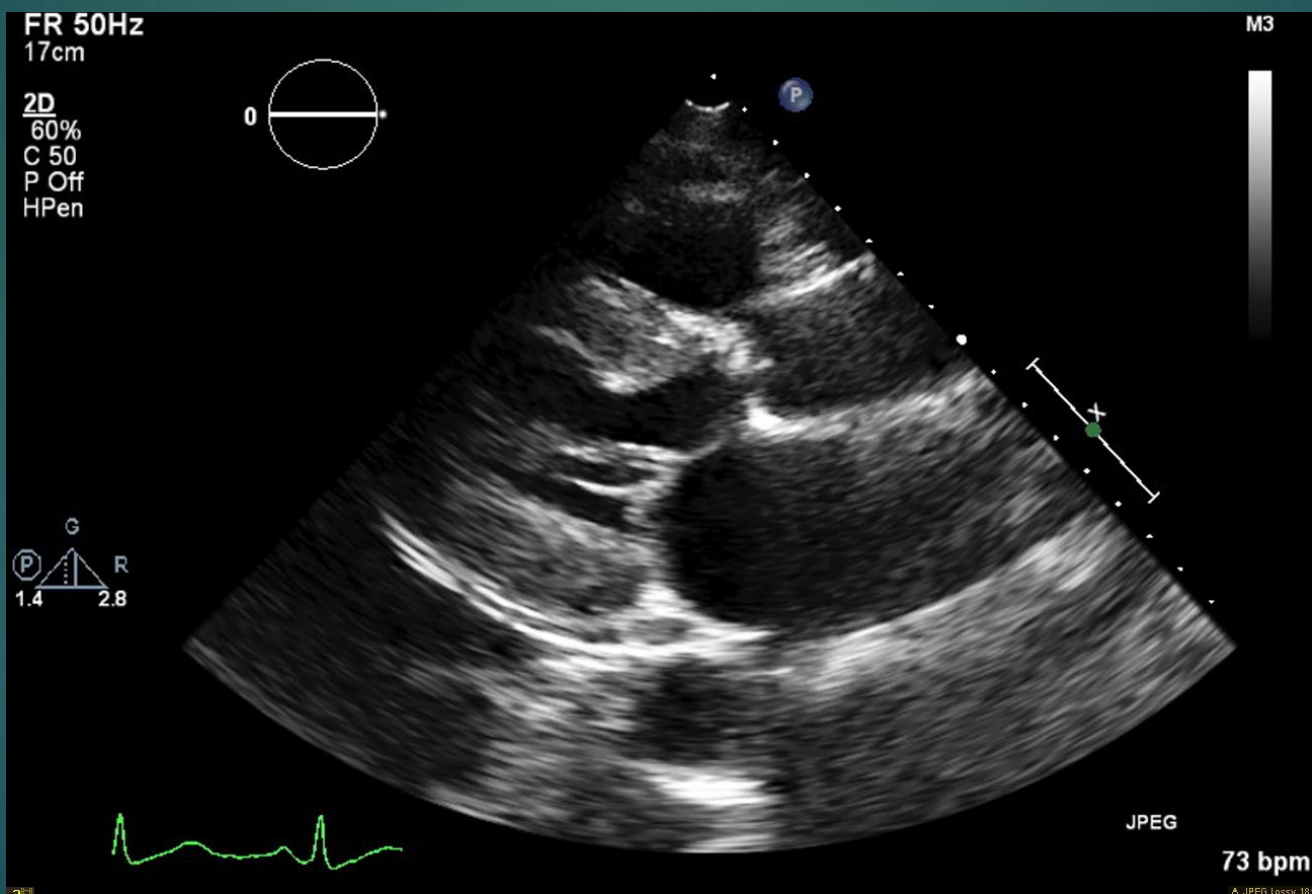
TAVR vs SAVR

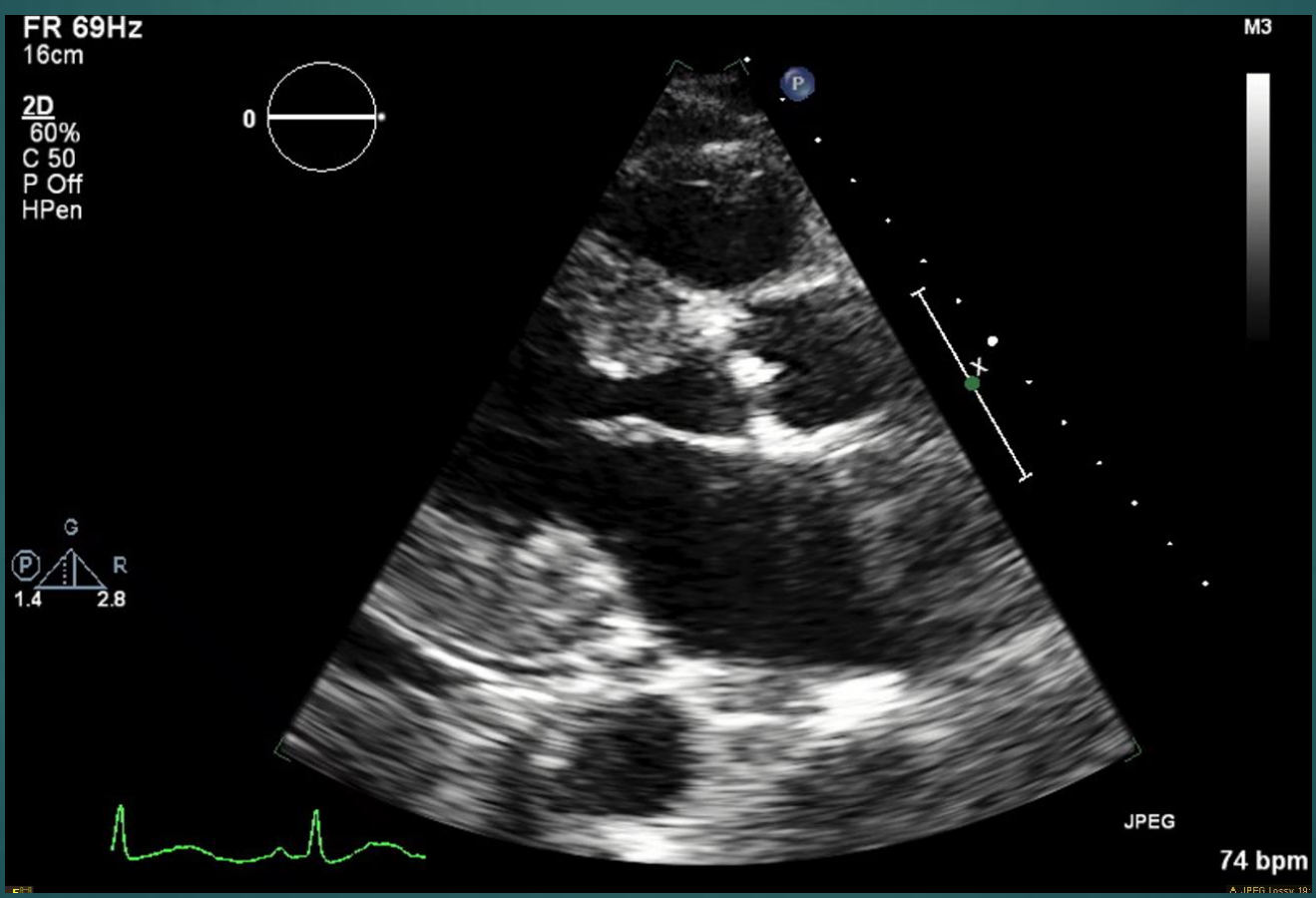
- ▶ No significant difference in mortality or stroke
- ▶ TAVR has less major bleeding, shorter hospital stay, more rapid return to activities, less pain, reduced onset of AF than in SAVR
- ▶ SAVR has less PVL, reduced PPM need, reduced vascular complications and decreased reintervention rates
- ▶ Surgical risk, durability patient age are important in patient selection

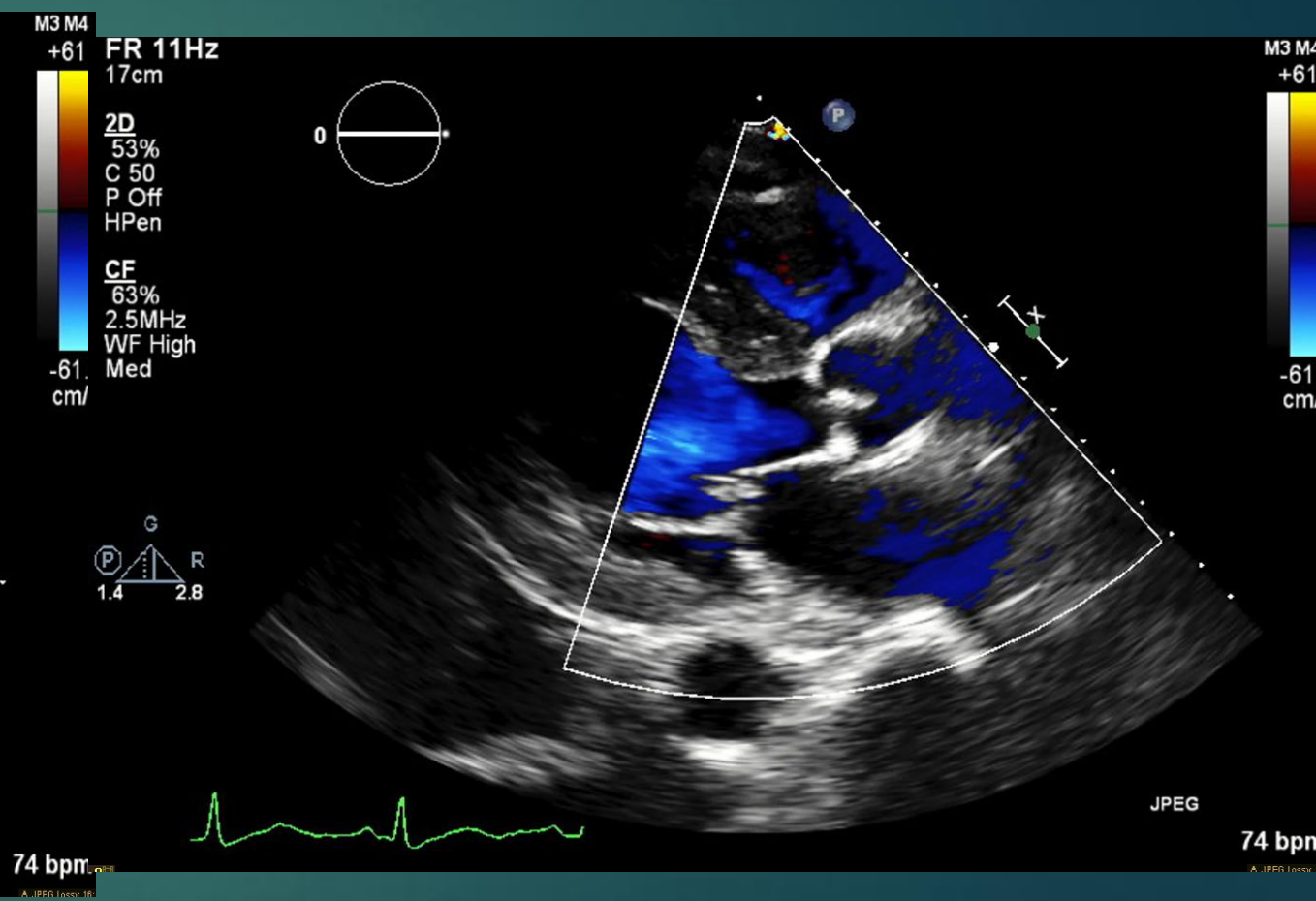
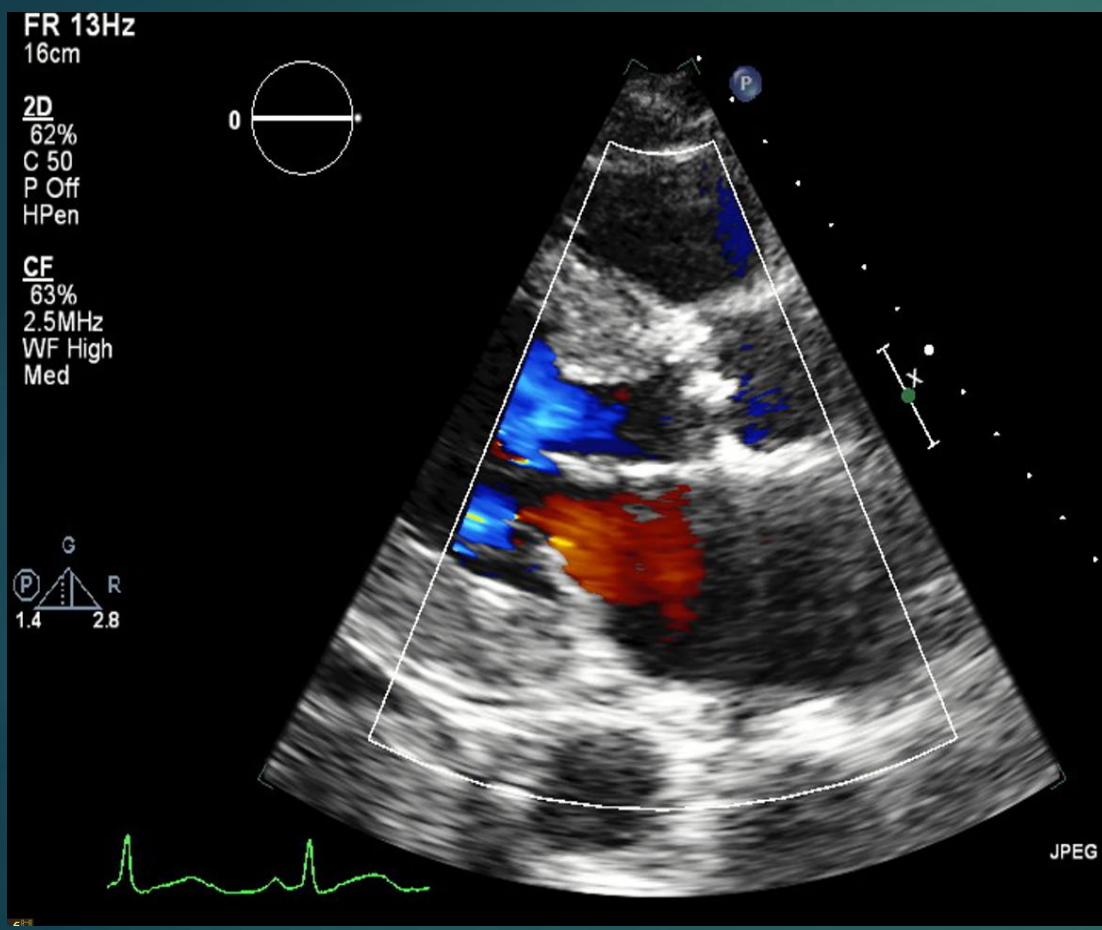
Balloon-expandable devices			
Sapien XT		Sapien 3	
			
Self-expanding devices			
Evolut R	Acurate Neo	Portico	Allegra
			
Mechanically-expandable devices			
Lotus			
			

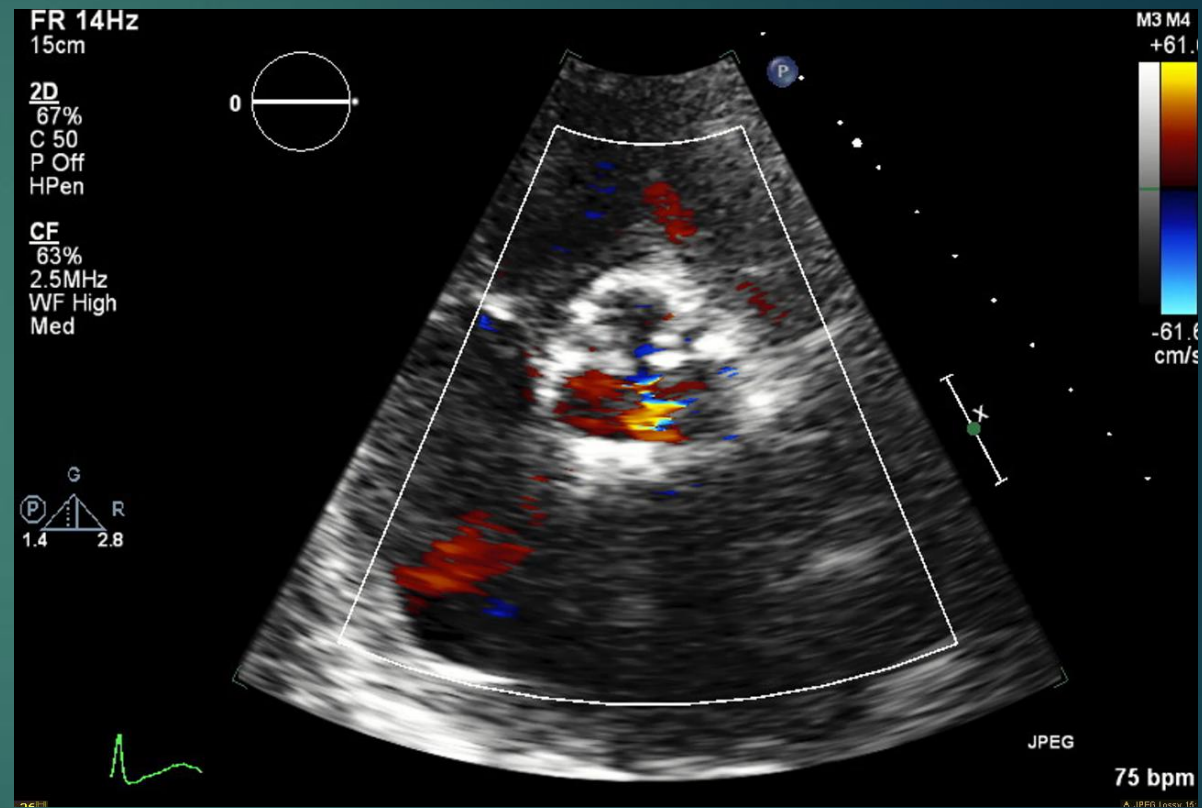
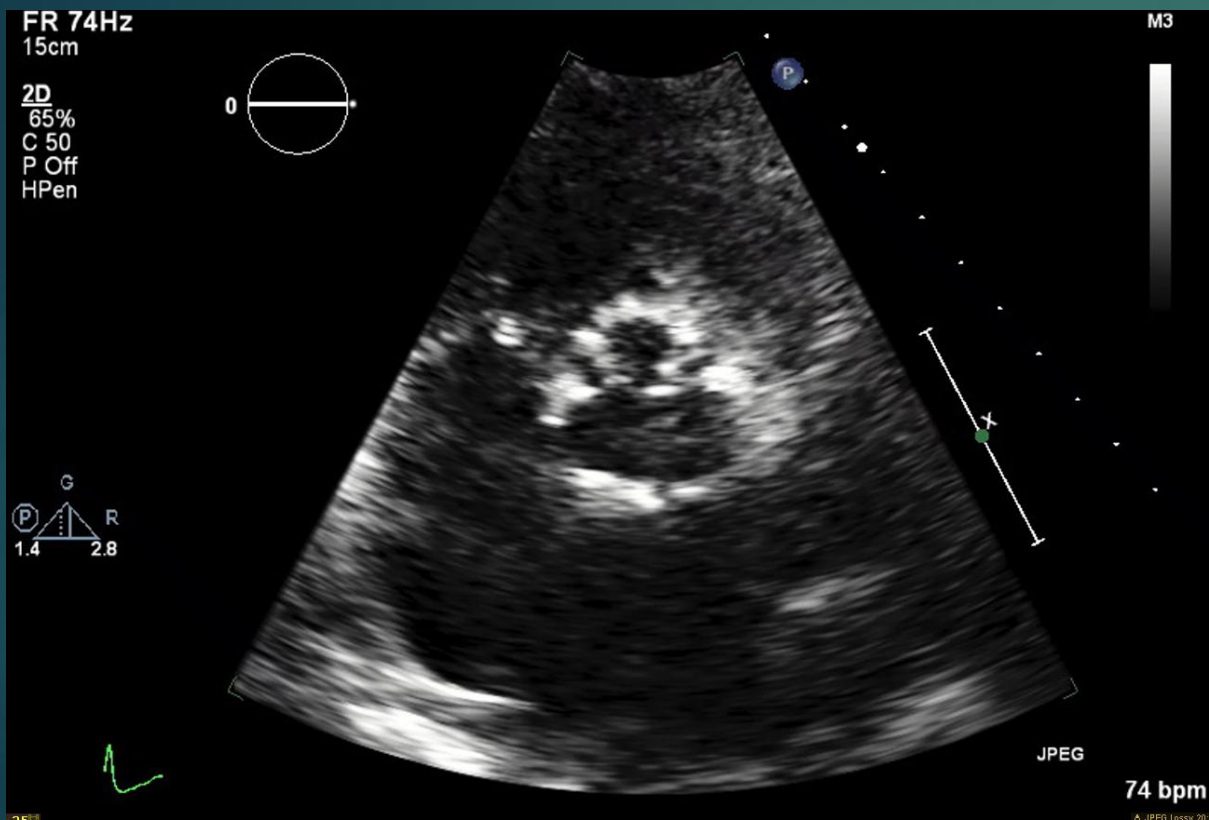
Shared decision making for AVR

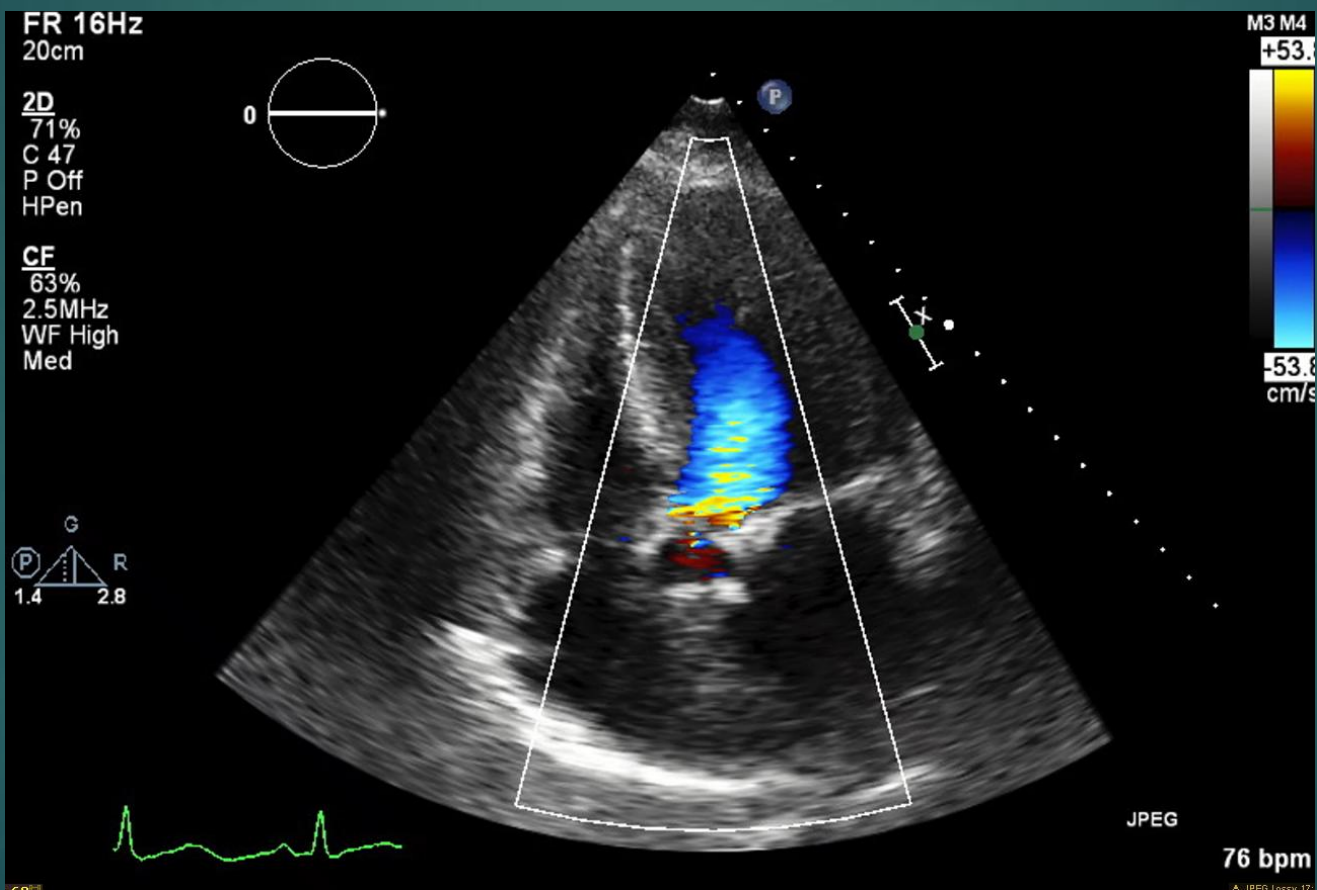












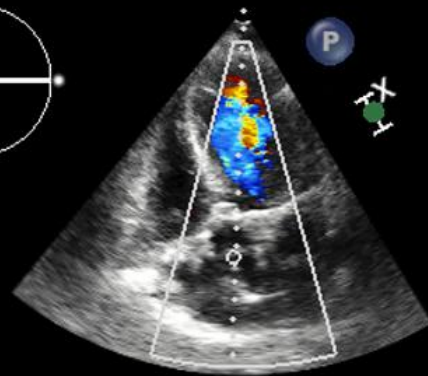
FR 16Hz
20cm

2D

71%
C 47
P Off
HPen

CF

63%
2.5MHz
WF High
Med



÷ AV VTI

Vmax 418.4 cm/s

Vmean 326 cm/s

Max PG 70.0 mmHg

Mean PG 45 mmHg

VTI 109 cm

AVA (VTI) 0.77 cm²

CW

95%

1.8MHz

WF 225Hz

M3 M4

+53.8

cm/s

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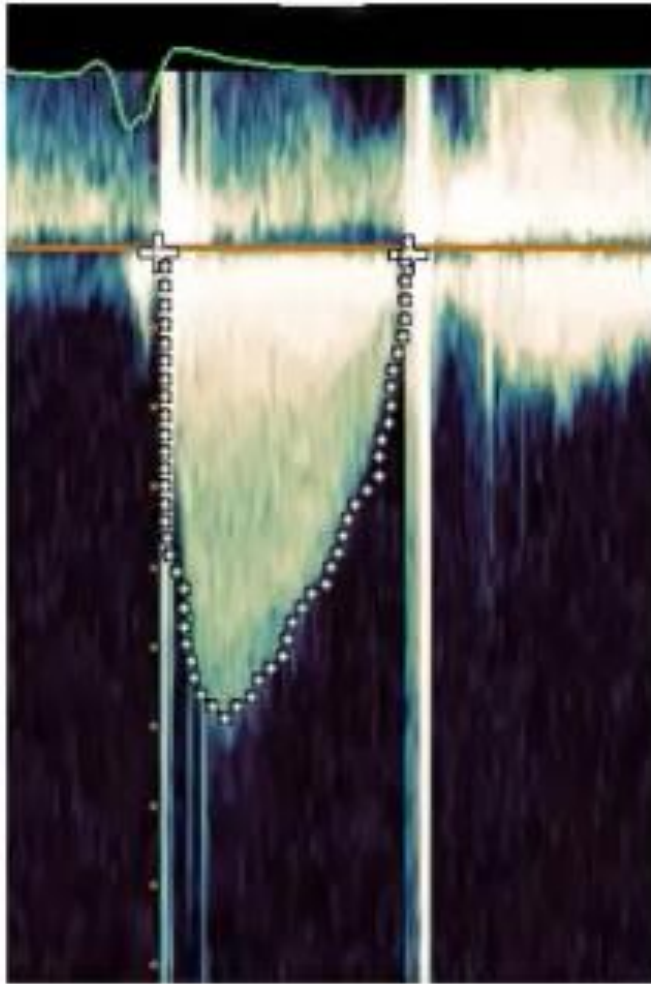
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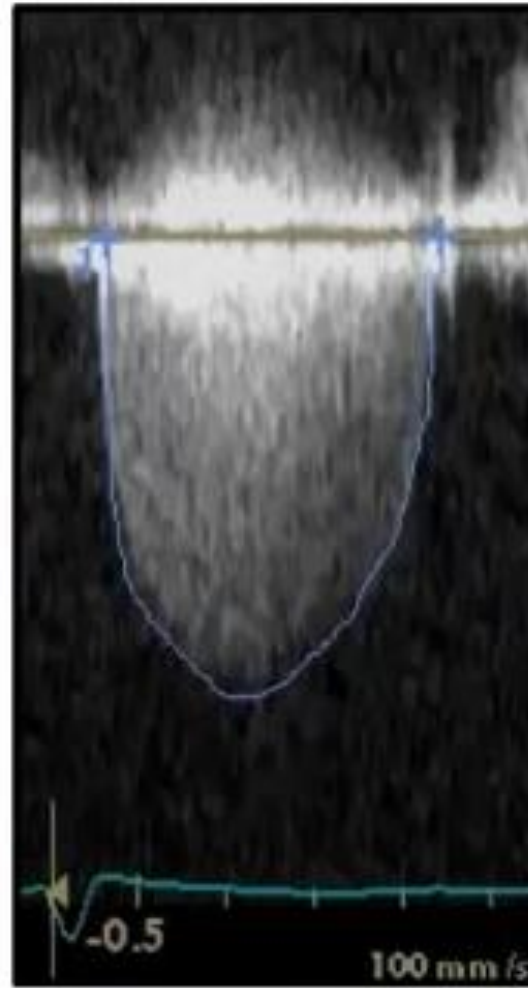
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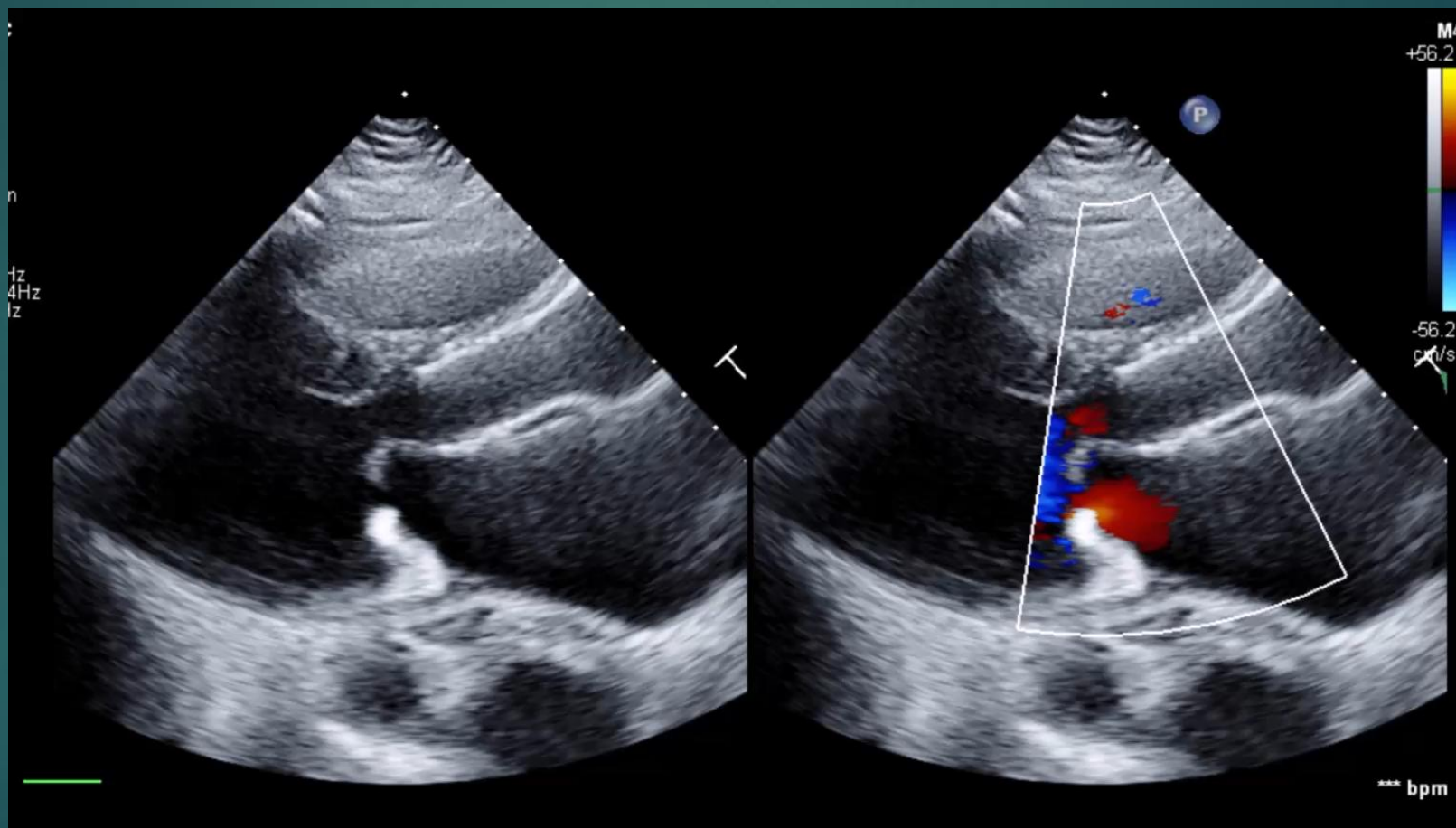


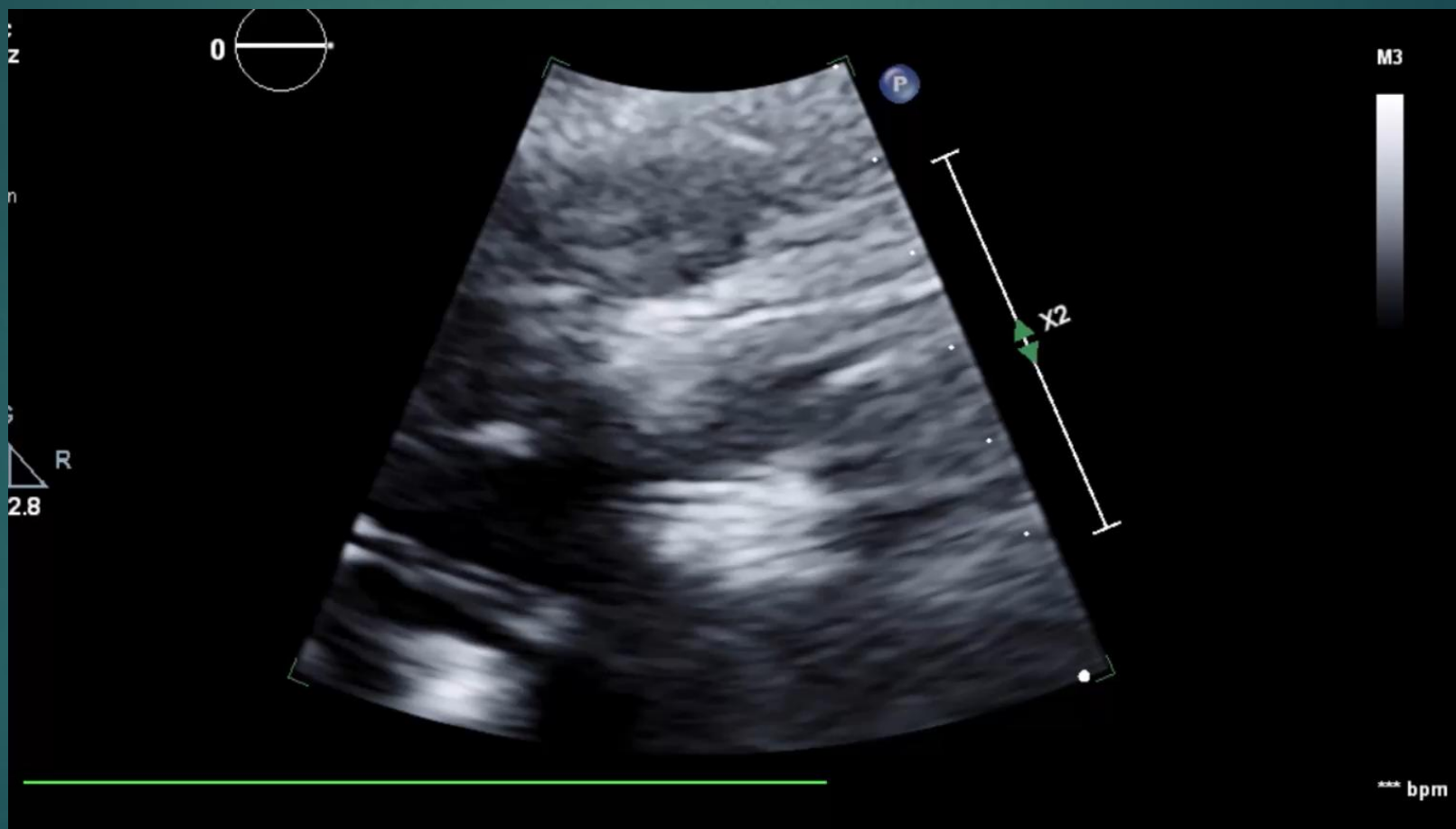


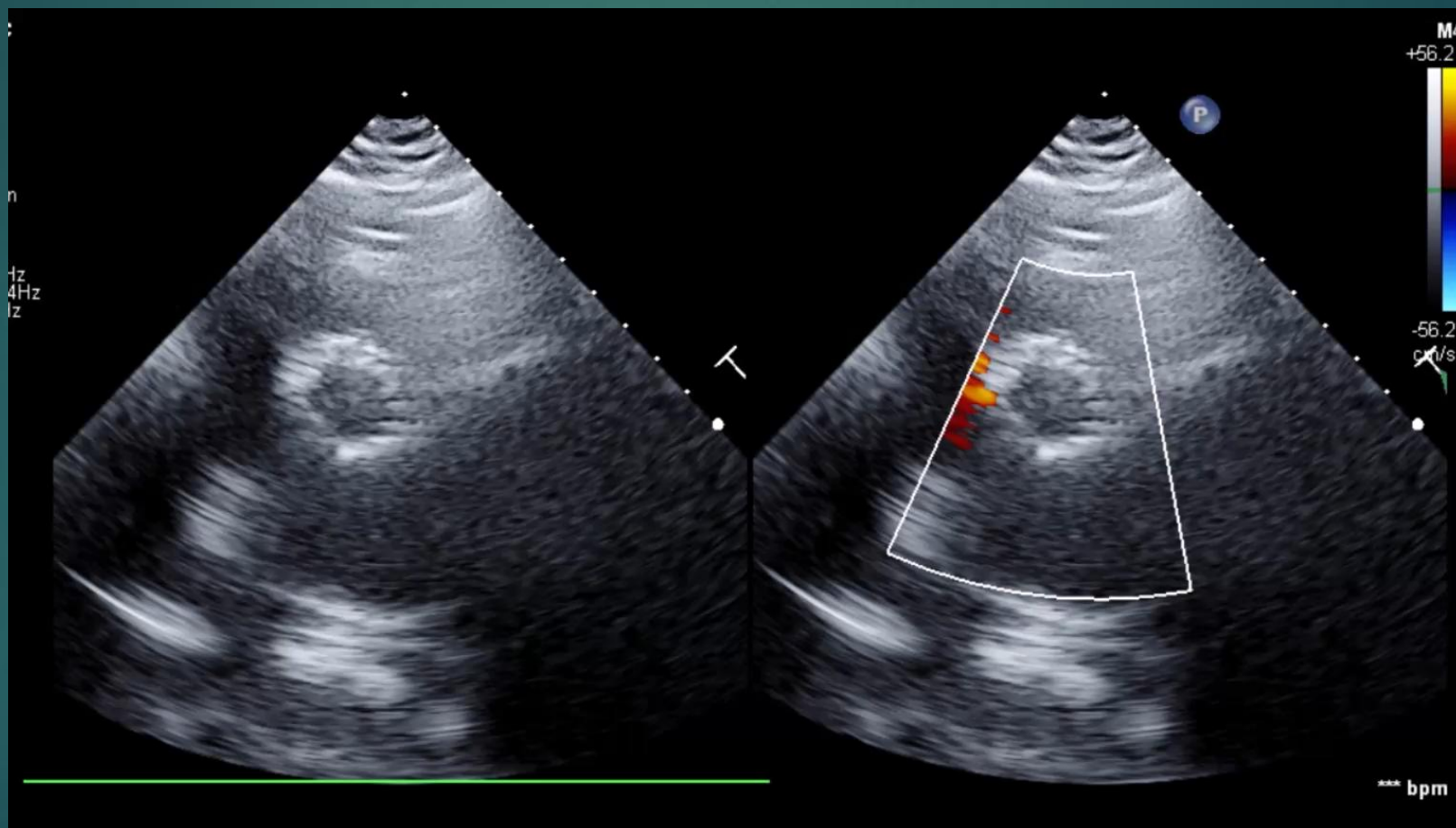
Mild AS



Severe AS







Summary

- ▶ AS is disease of the elderly
- ▶ Most common causes of AS are bicuspid aortic valve stenosis or normal tricuspid aortic valve calcifications
- ▶ Symptoms of severe AS DOE or reduced exercise capacity
- ▶ HF, syncope, angina are late manifestations
- ▶ Stages of AS are similar to stages of HF
- ▶ Severe AS: $V_{max} > 4$ m/s; Mean gradient > 40 mmHg, AVA < 1 cm².
- ▶ LFLG AS: $S_{vi} < 35$ ml/m², AVA < 1 cm²