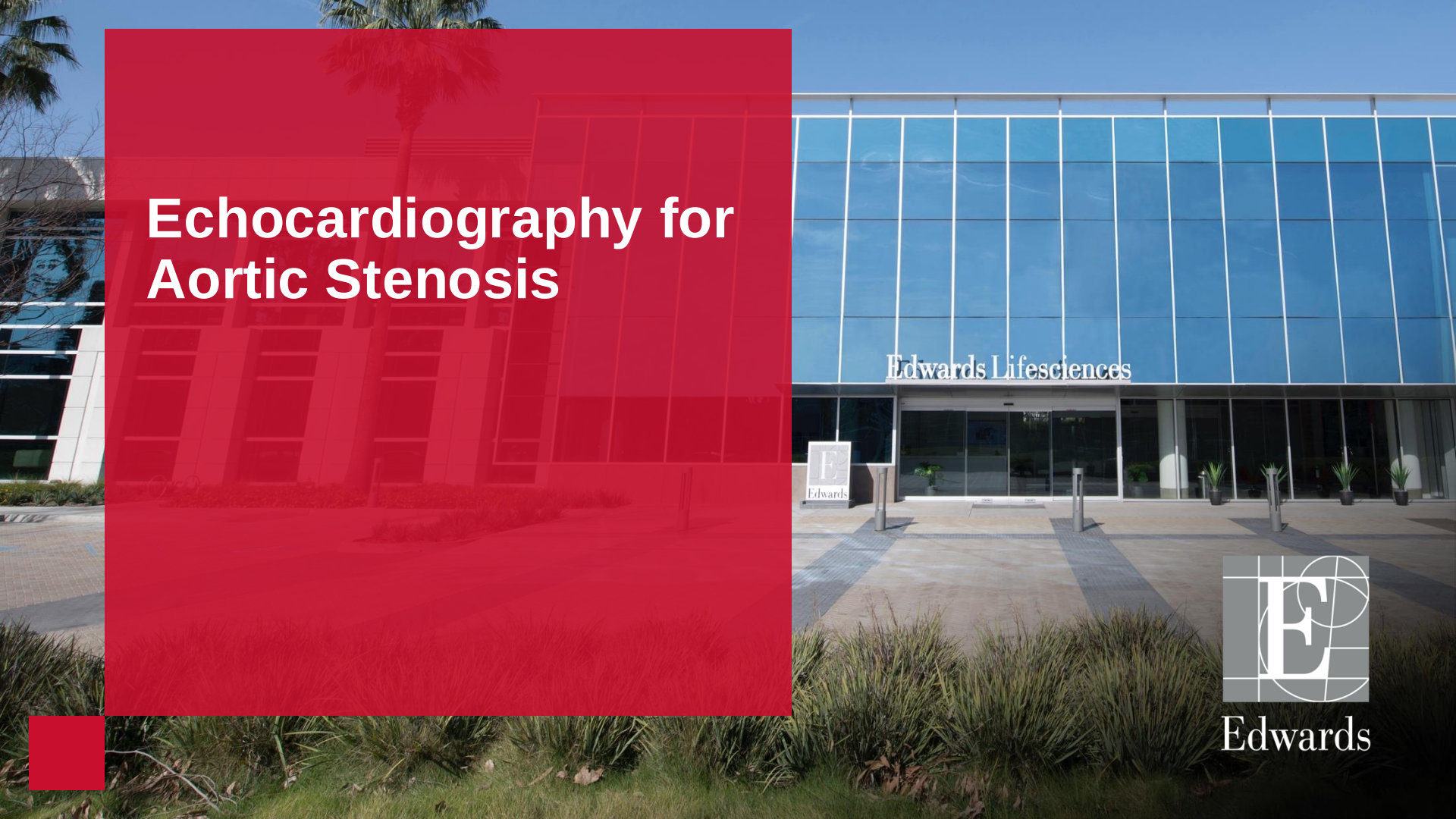
Echocardiography for Aortic Stenosis



Edwards

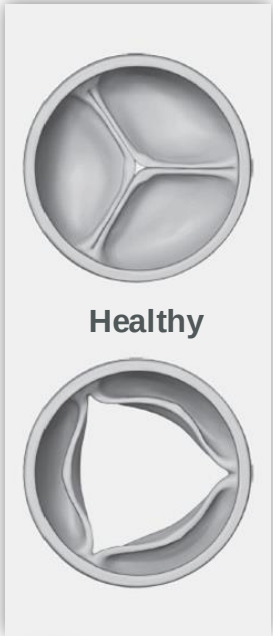
Agenda

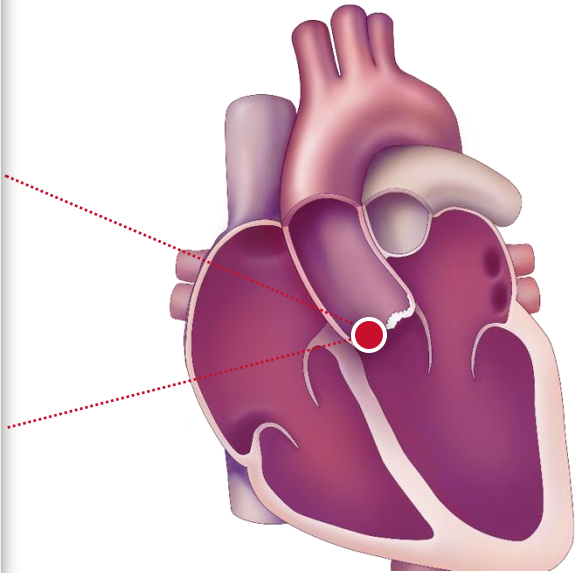
- Aortic stenosis (AS) and importance of diagnosis
- Severe AS imaging
- Calculations
- Low-flow low-gradient AS
- Post TAVR echocardiography

Aortic stenosis and the importance of diagnosis

Edwards

Aortic stenosis is a progressive disease





Aortic Stenosis: is a buildup of calcium deposits on the valve, which causes it to narrow and reduce blood flow to the rest of the body.

Images displayed are representative of aortic valves.

Burden of structural heart disease

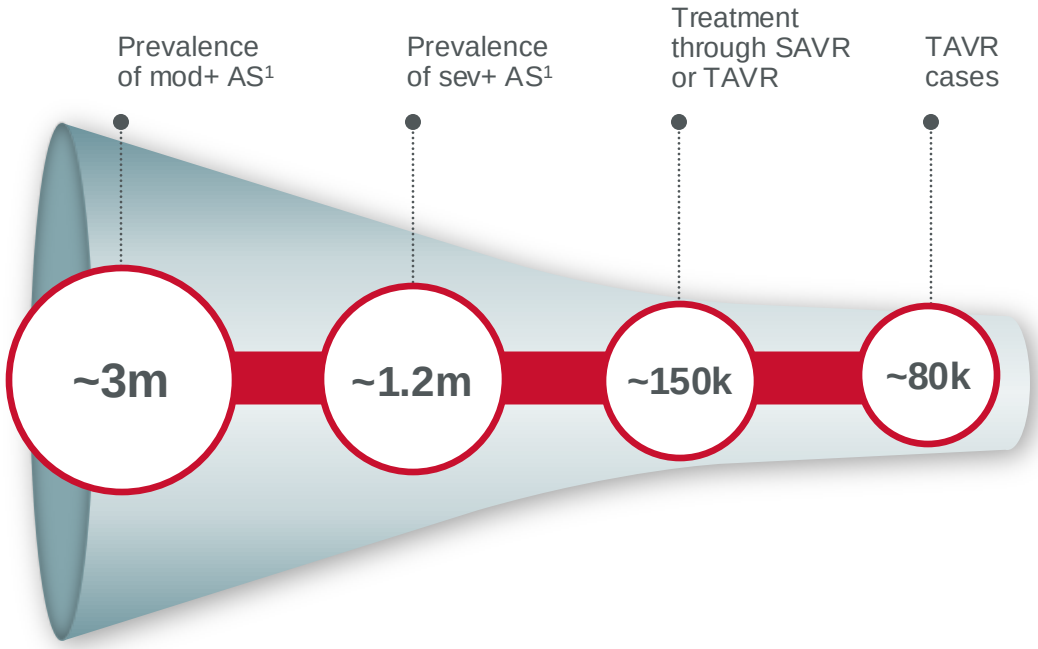
Survival after onset of symptoms for severe aortic stenosis (AS) is as low as **50% at two (2) years** and **20% at five (5) years.**[1]

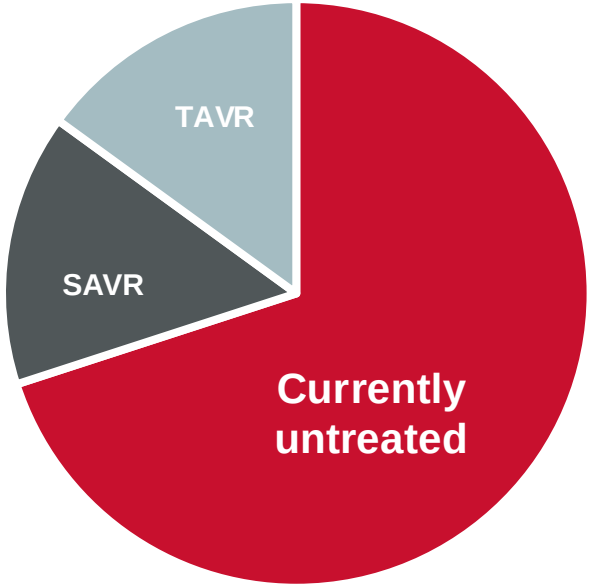
Treatment is critical for survival

Note: For historical series of patients before the availability of valve surgery and for a more recent series of patients who refused intervention for severe symptomatic AS

1. Otto C. Timing of aortic valve surgery. Heart. 2000;84(2):211–218.

High number of severe AS patients remain undertreated

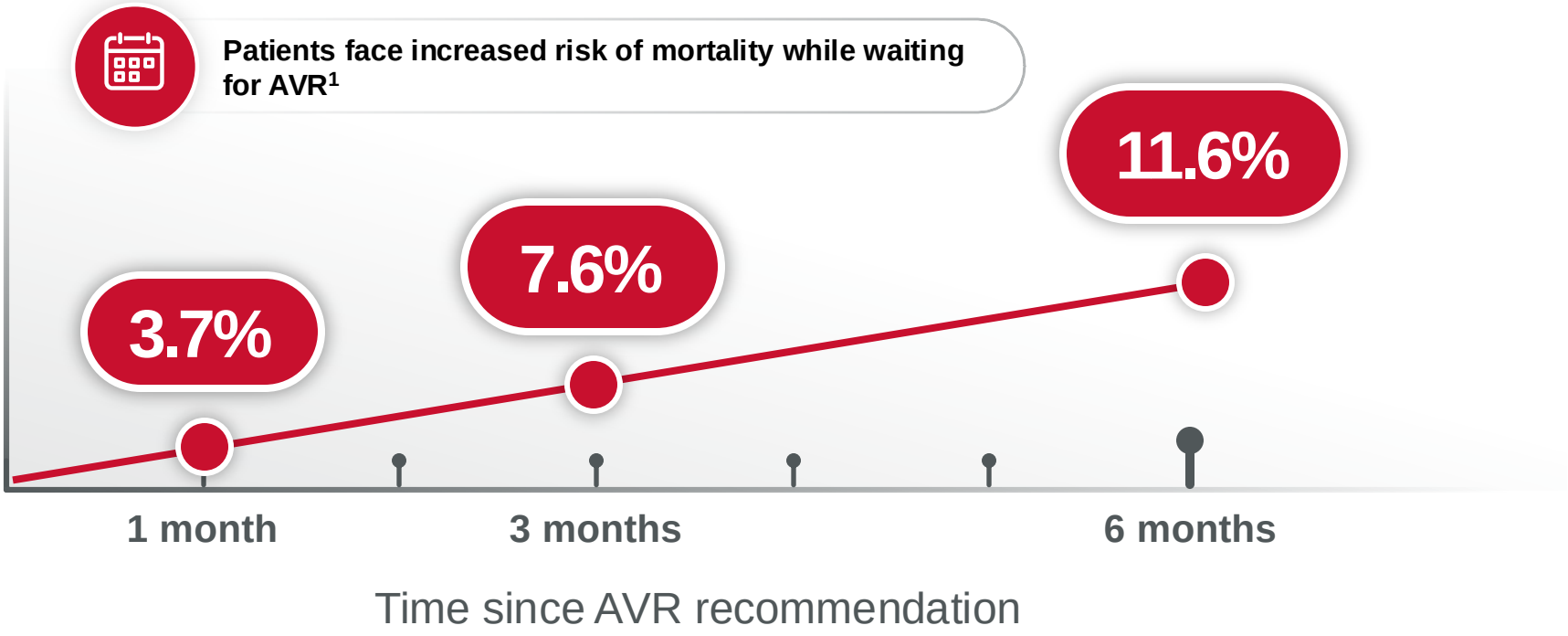




U.S. severe, symptomatic AS[2]

1. Nkomo 2006, Iivanainen 1996, Aronow 1991, Bach 2007, 2019 internal estimates
2. Goldsweig, A. The Evolving Management of Aortic Valve Disease; 2019 internal estimates

Severe AS is life threatening and treatment is critical



1. Malaisrie SC, et al. Mortality while waiting for aortic valve replacement. Ann Thorac Surg. 2014;98:1564-71.

Severe aortic stenosis imaging review

Transthoracic Echocardiogram

Edwards

Echocardiography in aortic stenosis

Why Echo in AS?[1]

TTE is indicated in patients with signs or symptoms of AS or a bicuspid aortic valve for:

- Accurate diagnosis of cause
- Hemodynamic severity, LV size, and systolic function to determine prognosis and timing of valve intervention

Class I Indication (AHA /ACC[1])

Echocardiography is the key tool for the diagnosis and evaluation of aortic stenosis.

Clinical decision making is based on the echocardiographic assessment of its severity.

Role of Echo in TAVR[2]

Pre-procedural assessment

- Severity of disease
- Role of stress testing

Intra-procedural imaging

- Risk assessment
- Procedure guidance
- Valve sizing

Post-procedural assessment

- Paravalvular leak
- EOA and gradients

1. 2020 AHA/ACC Guideline for the Management of Patients with Valvular Heart Disease
2. Hahn, R.(2018). Echocardiographic Imaging for Transcatheter Aortic Valve Replacement. JASE, 31(4), 405–433

Stages of aortic stenosis

Stage	Definition	Valve Hemodynamics			Hemodynamic Consequences
		Aortic Valve Area	Aortic V_{max}	Mean pressure gradient	
B	Progressive AS (Moderate)	 AVA > 1.0 cm^2	 3.0-3.9 m/s	 20-39 mm Hg	▪ Early LV diastolic dysfunction may be present ▪ Normal LVEF
C1	Asymptomatic severe AS				▪ LV diastolic dysfunction ▪ Mild LV hypertrophy ▪ Normal LVEF
C2	Asymptomatic severe AS with LV dysfunction	 AVA ≤ 1.0 cm^2 (or AVAi ≤0.6 cm^2/m^2)	 ≥ 4 m/s	 ≥ 40 mm Hg	▪ LVEF <50%
D1	Symptomatic severe high gradient AS				▪ LV diastolic dysfunction ▪ LV hypertrophy ▪ Pulmonary hypertension may be present

OR

D2 & D3: Covered in following sections

Based on the 2020 AHA/ACC Guideline for the Management of Patients with Valvular Heart Disease

Aortic valvular complex

How would you measure the LVOT?

How would you measure the Sinus of Valsalva diameter?

How would you measure the STJ?

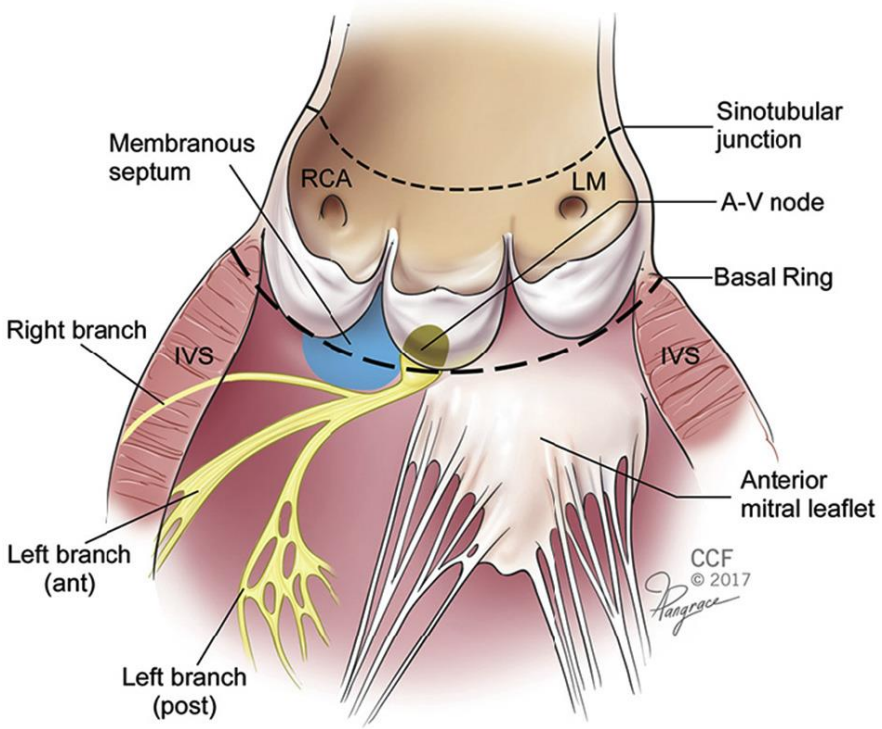
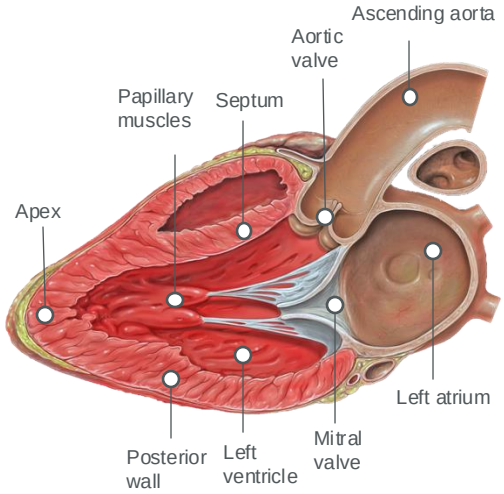
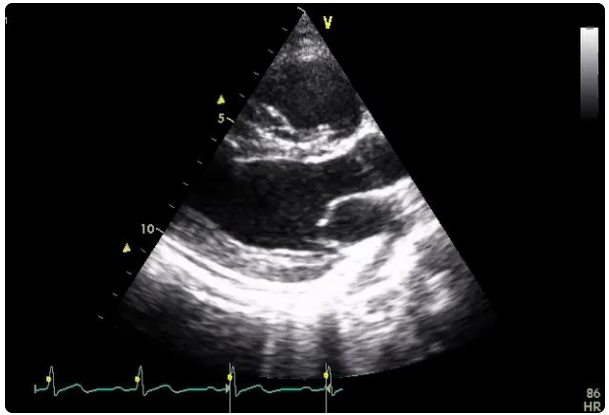


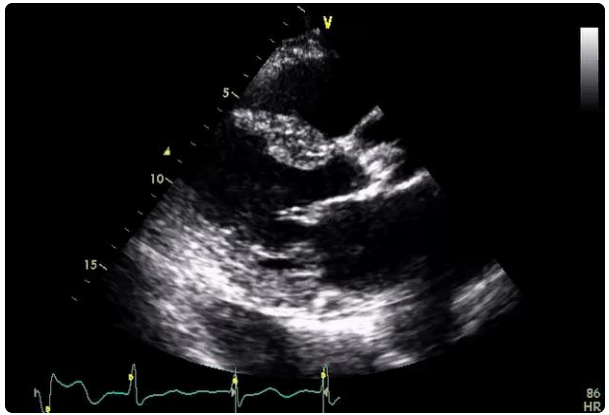
Image Source: Hahn, R.(2018). Echocardiographic Imaging for Transcatheter Aortic Valve Replacement. JASE, 31(4), 405–433

Parasternal long axis view





PLAX – normal

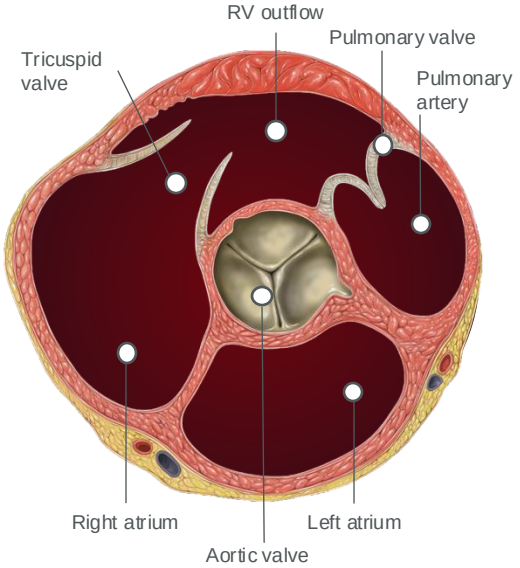


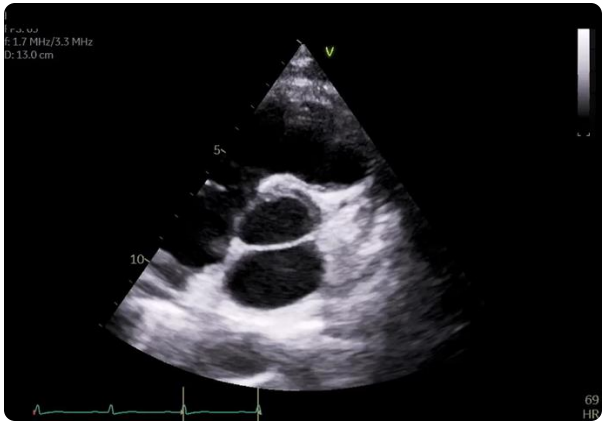
PLAX – with AS

Key structures and issues

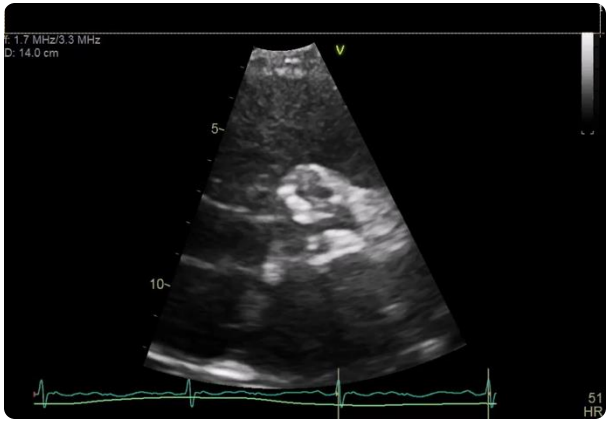
- Aortic valve anatomy
- Cusp mobility
- Valve calcification
- LVOT diameter
- LV/RV function
- Aortic root complex
- Aortic insufficiency

Parasternal short axis (aortic valve level)





PSAX – Normal AS

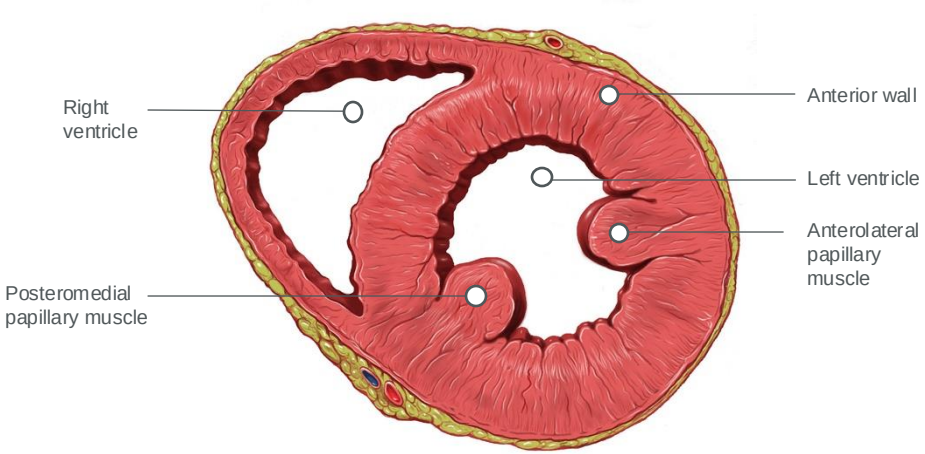


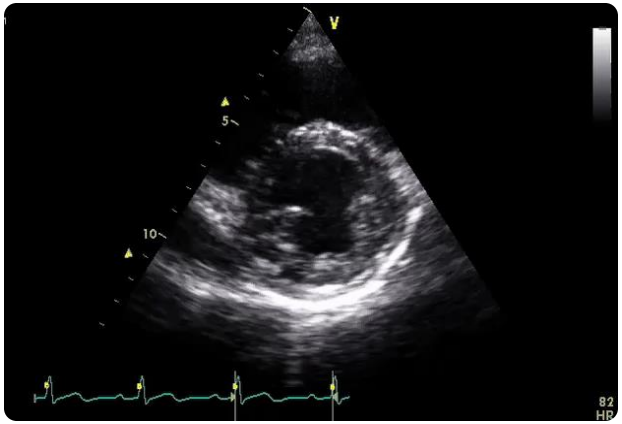
PSAX – Severe AS

Key structures and issues

- Number of cusps in systole
- Assess cusp mobility and commissural fusion
- Assess valve calcification
- Coronary flow
- Aortic insufficiency

Parasternal short axis (ventricular level)

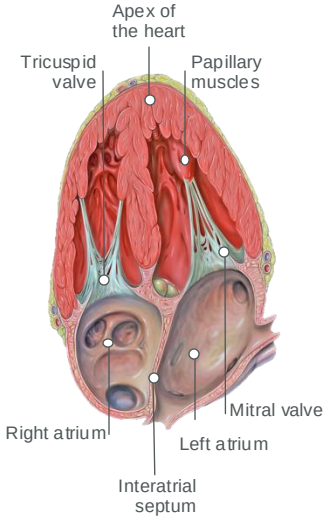


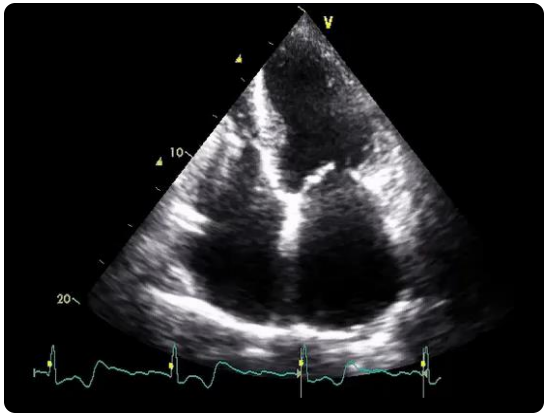


PSAX – Normal

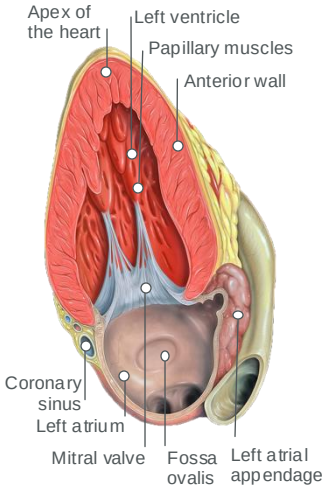
Key structures and issues		
	LV/RV size and function	Ventricular septal defect
	Wall motion abnormalities	Pericardial effusion

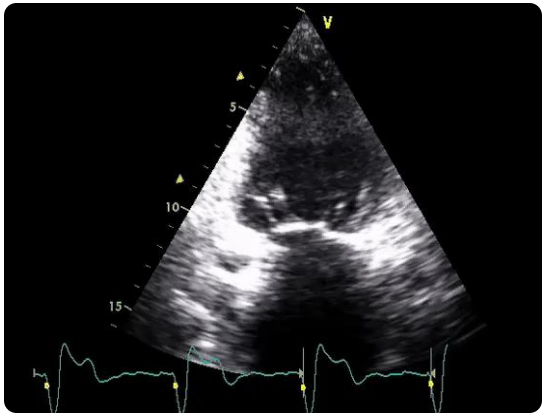
Apical four/two chamber views





Apical four chamber

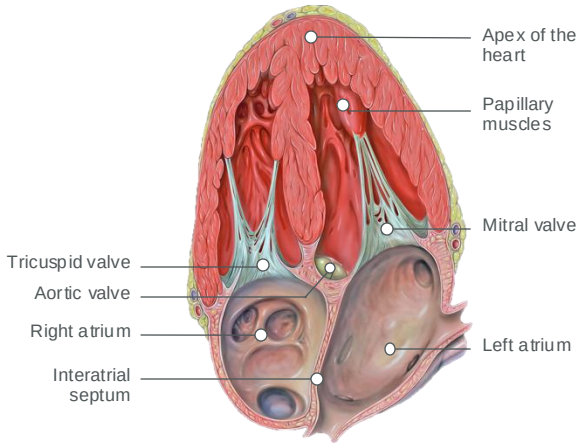


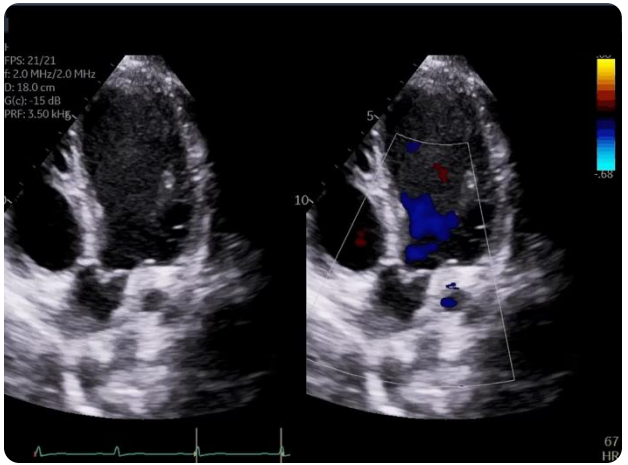


Apical two chamber

Key structures and issues		
	LV/RV size and function	Mitral and tricuspid valves
	Contractility, wall motion abnormalities	Pericardial effusion
	▪ Normal LVEF = 55-65%	Ventricular septal defect

Apical five chamber view

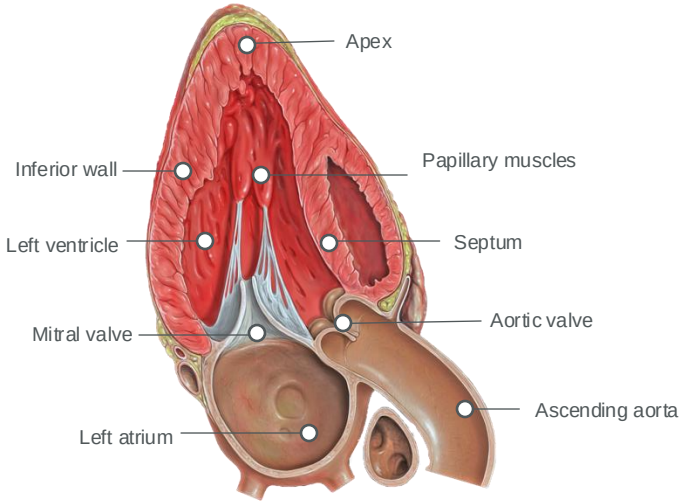


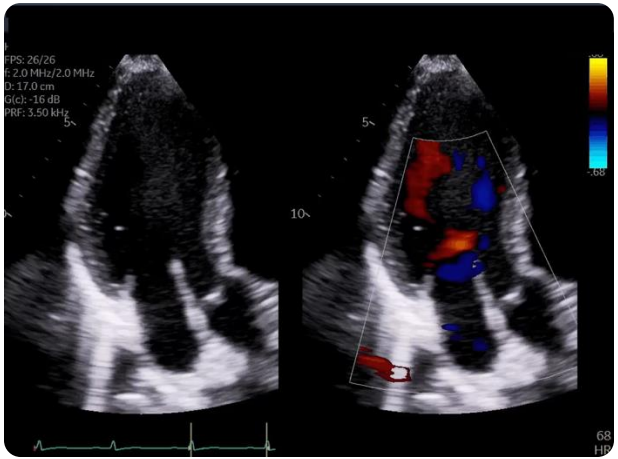


Key structures and issues

- **Aortic valve gradient flow/gradients**
- **LVOT obstruction**
- **LV/RV function**
- **Mitral valve complex**
- **MR/TR**
- **Aortic insufficiency**

Apical three chamber view





Key structures and issues

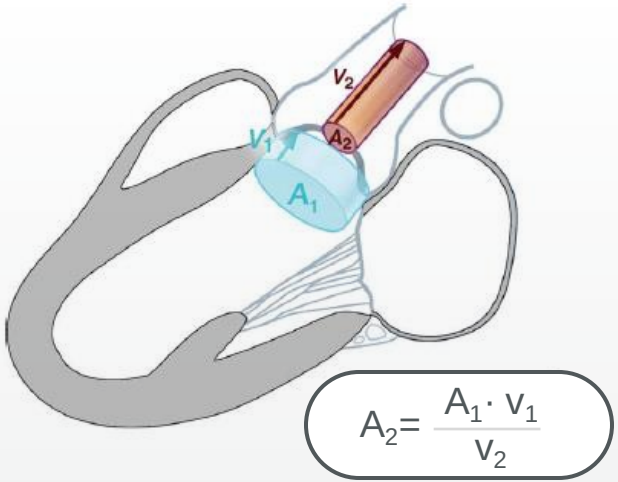
- **Aortic valve flow/gradients**
- **LVOT obstruction**
- **LV function**
- **Mitral valve complex**
- **Mitral regurgitation**
- **Aortic insufficiency**

Calculations

AVA, Peak-V, MPG & DI

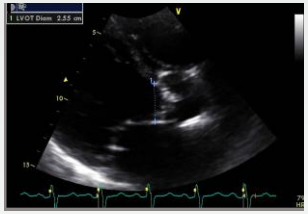
Edwards

Calculating aortic valve area – continuity equation

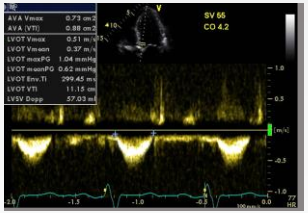


- Continuity equation is based on conservation of mass
- It assumes that the stroke volume ejected through the LV outflow tract all passes through the stenotic orifice

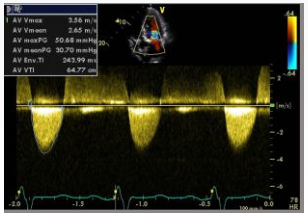
Requires the following measurements



A_1 = LVOT diameter
for calculation of circular cross sectional area



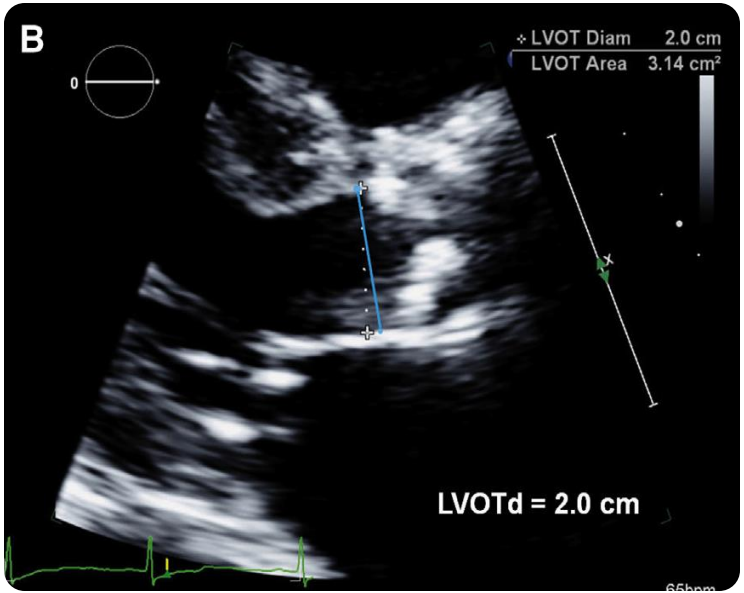
V_1 = LVOT (peak V & VTI)
recorded with PWD



V_2 = AV (peak V & VTI)
recorded with CWD

Source: Baumgartner, H. (2009). Echocardiographic assessment of valve stenosis: EAE/ASE recommendations for clinical practice. JASE, 22(1), 1-23

LVOT diameter (for cross sectional area)



Data acquisition[1]

- Record in the parasternal long axis view
- Zoom mode
- Adjust gain to optimize the blood tissue interface

Measurement[1]

- Inner edge of the septal endocardium and the anterior mitral leaflet in mid-systole.
- Parallel and adjacent to the aortic valve or at the site of velocity measurement
- Diameter is used to calculate a circular CSA

Watchouts[1,2,3,]

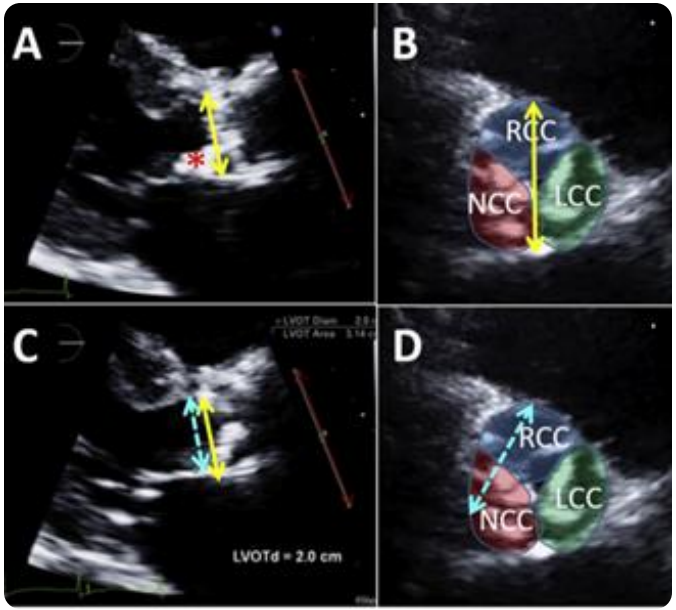
- LVOT becomes progressively more elliptical (rather than circular) in many patients, which may result in underestimation of LVOT CSA
- In presence of calcium, measure to the native leaflet
- Take multiple measurements

1. Baumgartner, H. (2009). Echocardiographic assessment of valve stenosis: EAE/ASE recommendations for clinical practice. JASE, 22(1), 1-23
2. Baumgartner, H. (2017). Recommendations on the Echocardiographic Assessment of Aortic Valve Stenosis: A Focused Update from the European Association of Cardiovascular Imaging and the American Society of Echocardiography. *JASE*, *30*(4), 372–392.
3. Hahn, R.(2018). Echocardiographic Imaging for Transcatheter Aortic Valve Replacement. JASE, 31(4), 405–433

LVOT measurement watchouts

A Yellow arrow is measurement of largest diameter by excluding ectopic calcium (red asterisk)

C The yellow arrow is larger suggested measurement (dashed blue arrow)



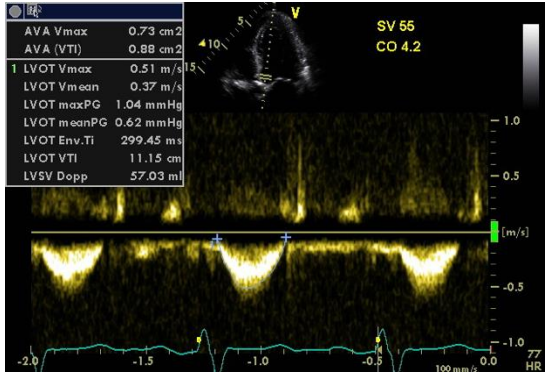
(**LCC**) left coronary cusp, (**LVOTd**) LVOT diameter, (**NCC**) noncoronary cusp, (**RCC**) right coronary cusp

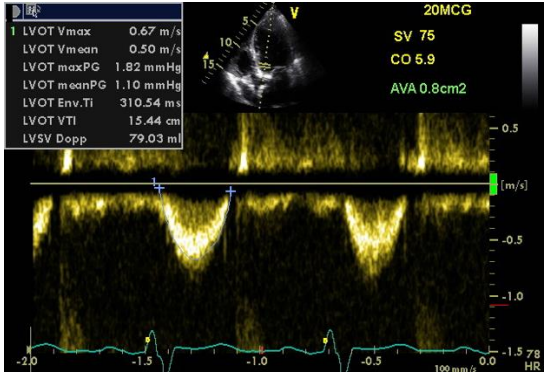
B Representation of measurement from short axis view

D Representation of where incorrect measurement would be taken from short axis view

Image Source: Hahn, R. T. (2017). Accurate Measurement of Left Ventricular Outflow Tract Diameter: JASE, 30(10), 1038–1041.

LVOT VTI – PW Doppler sample





LVOT VTI
can give you cardiac output

Stroke volume = LVOT area x LVOT VTI.
Cardiac output is = Heart rate x stroke volume.

Data acquisition

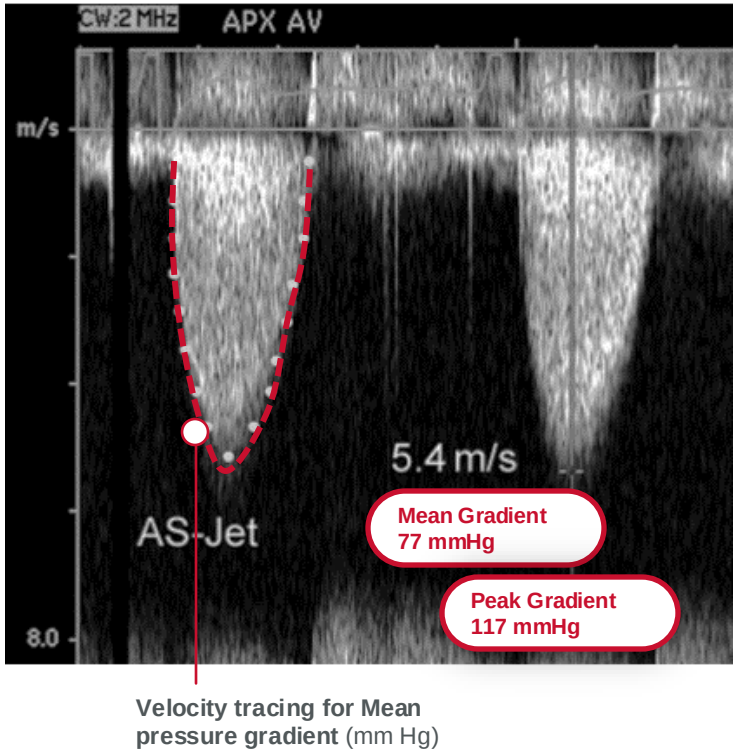
- Pulsed-wave Doppler (PW)
- Apical long-axis or five-chamber view
- Sample volume positioned just on the LV side of valve and moved carefully into the LVOT if required to obtain laminar flow curve
- Velocity baseline and scale adjusted to maximize size of velocity curve
- Time axis (sweep speed) 50-100 mm/s
- Low wall filter setting
- Smooth velocity curve with a well-defined peak and a narrow velocity range at peak velocity

Measurement

- Maximum velocity from peak of dense velocity curve
- VTI traced from modal velocity

Baumgartner, H. (2017). Recommendations on the Echocardiographic Assessment of Aortic Valve Stenosis: A Focused Update from the EACI and the ASE. JASE, 30(4), 372–392.

AV peak velocity and VTI – CW Doppler sample



Velocity tracing for Mean pressure gradient (mm Hg)

Data acquisition

- Continuous Wave Doppler (dedicated transducer)
- Multiple acoustic windows (e.g. apical, suprasternal, right-parasternal)
- Decrease gain, increase wall filter, adjust baseline curve and scale to optimize signal
- Gray scale spectral display with expanded time scale
- Velocity range and baseline adjusted so velocity signal fits but fills the vertical scale

Measurement

- Maximum velocity at peak of dense velocity curve. Avoid noise and fine linear signals
- VTI traced from outer edge of dense signal
- Mean gradient calculated from traced velocity curve
- Report window where maximum velocity obtained

Baumgartner, H. (2017). Recommendations on the Echocardiographic Assessment of Aortic Valve Stenosis: A Focused Update. JASE, 30(4), 372–392.

AV peak velocity and VTI considerations

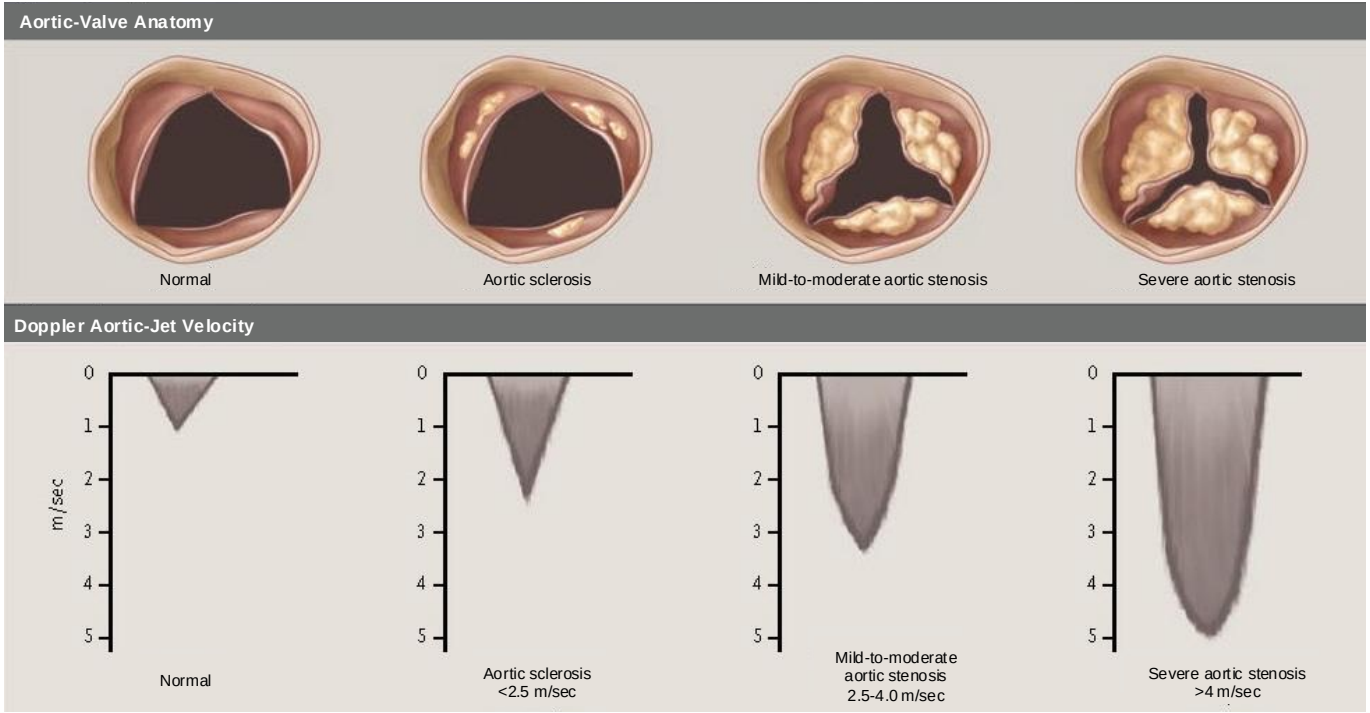
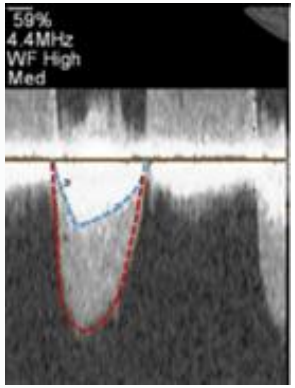


Image Source: Otto, C. M. (2008). Calcific Aortic Stenosis — Time to Look More Closely at the Valve. *NEJM*, *359*(13), 1395–1398.

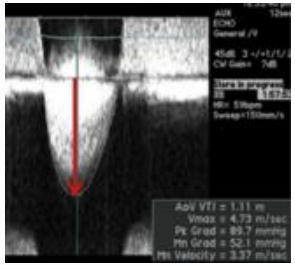
Pitfalls of CW Doppler acquisition

Pitfall & incorrect example[1]

- Off-axis imaging of the vena contracta (narrowest, highest velocity portion of the jet) will lead to underestimation of the severity of stenosis; seeing a “double envelope” of dense LVOT flow (blue trace), and fainter transaortic flow (red trace) may indicate that the insonation beam is angled away from the vena contracta.



- The direction of the transaortic jet may often be anterior and to the right; assuming the peak velocity from a single apical window will underestimate the severity of stenosis in up to 50% of patients.



Measurement Limitations[2]

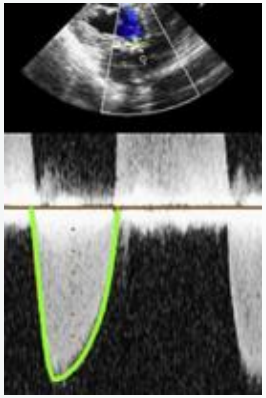
Velocity

- Correct measurement requires parallel alignment of US beam
- Flow dependent

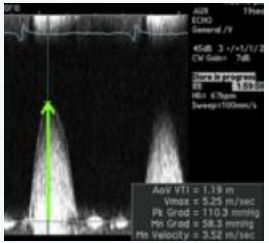
Mean gradient

- -Accurate pressure gradients depend on accurate velocity
- -Flow dependent

Correct measurement & example[1]



Adjust the imaging window to find the densest, most uniform continuous-wave spectral profile.

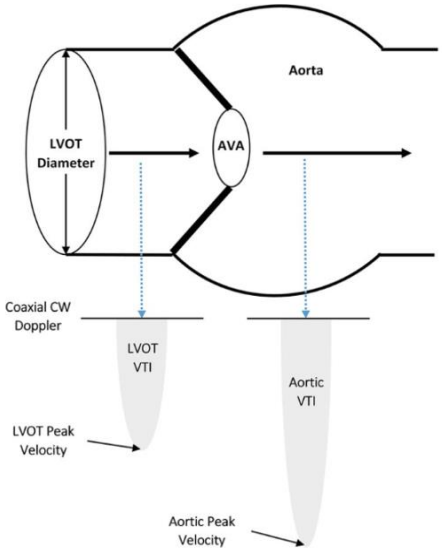


The right parasternal window in this patient showed peak velocities that were 0.5 m/sec higher; a multiwindow approach is always recommended.

Utilize multiple windows to assess the highest velocity jet

1. Hahn, R.(2018). Echocardiographic Imaging for Transcatheter Aortic Valve Replacement. JASE, 31(4), 405–433
2. Baumgartner, H. (2017). Recommendations on the Echocardiographic Assessment of Aortic Valve Stenosis: A Focused Update. JASE, 30(4), 372–392

Velocity Ratio and VTI ratio (Dimensionless Index)



	Mild	Moderate	Severe
AVA (cm²)	> 1.5	> 1.0-1.5	≤ 1.0
DI	> 0.50	0.25-0.50	< 0.25

- Dimensionless Index (DI) is another approach to reducing error related to LVOT area measurements (by removing LVOT CSA from continuity eqn.)

$$AVA\ (cm^2) = \frac{CSA_{LVOT} \times VTI_{LVOT}}{VTI_{AV}}$$

$$\text{Velocity ratio} = \frac{V_{LVOT}}{V_{AV}}$$

OR

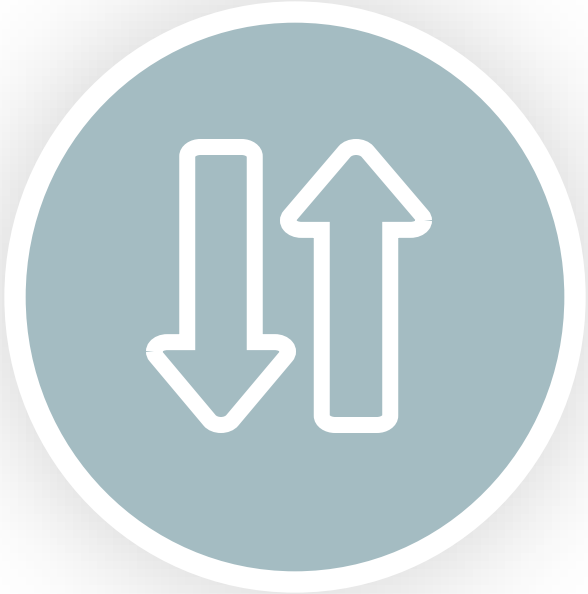
$$\text{VTI ratio*} = \frac{VTI_{LVOT}}{VTI_{AV}}$$

- Can use as alternative method to check AVA when there are discordant measurements.
- Use when AV prosthetic valve in place.

*VTI Ratio is also referred to as Dimensionless Index

Image Source: Otto, Catherine M. "Heartbeat: Time to Switch from Aortic Valve Area to Aortic Valve Index?" *Heart*, vol. 105, no. 2, 2019, pp. 89–91.
Baumgartner, H. (2017). Recommendations on the Echocardiographic Assessment of Aortic Valve Stenosis: A Focused Update. *JASE*, *30*(4), 372–392.

Low-flow low-gradient



Edwards

AHA/ACC VHD guideline – symptomatic severe AS

Symptoms include dyspnea or decreased exercise tolerance, heart failure, angina, syncope, and presyncope

Patients with severe aortic stenosis typically have an aortic valve area ≤ 1.0 cm^2

Stage	Definition	Valve hemodynamics	Hemodynamic consequences
D: symptomatic severe aortic stenosis			
D1	**High-gradient**	▪ Aortic **valve area typically ≤ 1.0 cm^2** ▪ Aortic **jet velocity ≥ 4m/s or mean gradient ≥ 40 mmhg** ▪ Aortic **valve area index ≤ 0.6 cm^2/m^2**	▪ Left ventricular diastolic dysfunction ▪ Left ventricular hypertrophy ▪ Pulmonary hypertension may be present
D2	**Low-flow/low-gradient with reduced left ventricular ejection fraction**	▪ Aortic **valve area ≤ 1.0 cm^2** ▪ Resting aortic **jet velocity < 4m/s or mean gradient < 40 mmhg** ▪ **Dobutamine stress** echocardiography shows aortic **valve area ≤ 1.0 cm^2 with** aortic **jet velocity ≥ 4m/s** at any flow rate	▪ Left ventricular diastolic dysfunction ▪ Left ventricular hypertrophy ▪ **Left ventricular ejection fraction < 50%**
D3	**Low-gradient with normal left ventricular ejection fraction or paradoxical low-flow**	▪ Aortic **valve area ≤ 1.0 cm^2** ▪ Aortic **jet velocity < 4m/s or mean gradient < 40 mmhg** ▪ Indexed aortic **valve area ≤ 0.6 cm^2/m^2** and ▪ **Stroke volume index < 35 ml/m^2 measured when patient is normotensive** (systolic blood pressure < 140 mmhg)	▪ Increased left ventricular relative wall thickness ▪ Small left ventricular chamber with low stroke volume ▪ Restrictive diastolic filling ▪ **Left ventricular ejection fraction ≥ 50%**

Based on the 2020 AHA/ACC Guideline for the Management of Patients with Valvular Heart Disease

LV morphology by severe symptomatic AS state

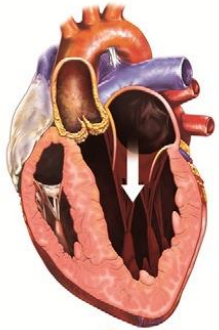
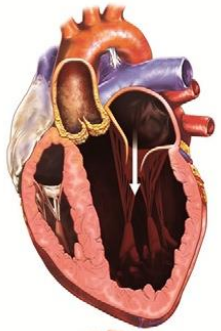
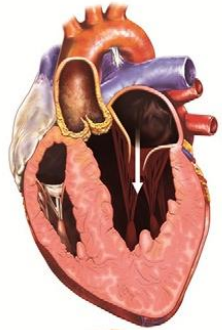
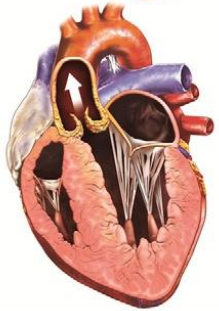
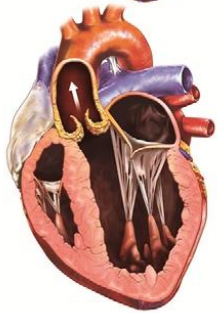
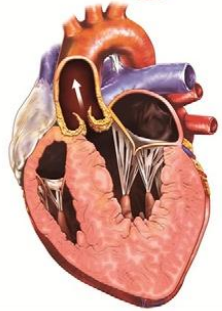
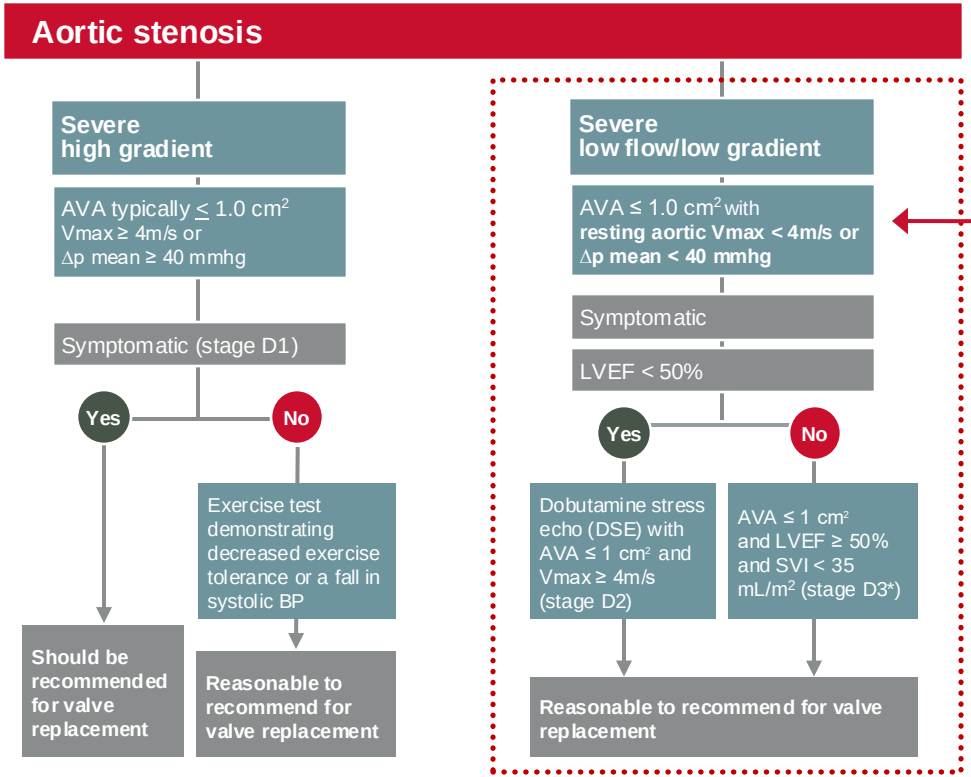
	D1	D2	D3
	High-gradient	Low-flow, low-gradient reduced-LVEF	"Paradoxical" low-flow, low-gradient, preserved-LVEF
Diastole			
Systole			

Image Source: Pibarot, P. (2012). Low-Flow, Low-Gradient Aortic Stenosis With Normal and Depressed Left Ventricular Ejection Fraction. JACC, 60(19), 1845–1853.

AHA/ACC guideline for aortic valve replacement



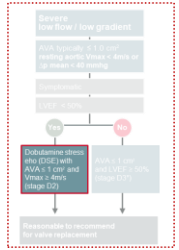
Special considerations of difficult subgroups

Measurement errors for all components (transaortic velocity, LVOT velocity, LVOT area) need to be carefully excluded, in particular the underestimation of LVOT area and thus underestimation of flowrate.

*AVR should be considered with stage D3 AS only if valve obstruction is the most likely cause of symptoms, stroke volume index is < 35 mL/m², indexed AVA is ≤ 0.6 cm²/m² and data are recorded when the patient is normotensive (systolic BP< 140 mm Hg).

Based on the 2020 AHA/ACC Guideline for the Management of Patients with Valvular Heart Disease

(D2) Low-flow low-gradient with reduced LVEF (classical)

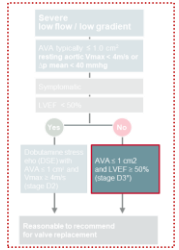


- **Stage D2 – Low-flow low-gradient with reduced LVEF[1]:**
  - Severe leaflet calcification with severely reduced leaflet motion
  - LVEF less than 50%
  - Calculated valve area ≤1.0 cm^2
  - Resting aortic V_{max} < 4.0 m/s **or** mean pressure gradient < 40 mm Hg

- **Low-dose dobutamine stress echocardiography can be used to differentiate between true and pseudo severe aortic stenosis (Class IIa)[2]**
  - Better define the severity of the aortic stenosis
  - Accurately assess contractile/pump reserve

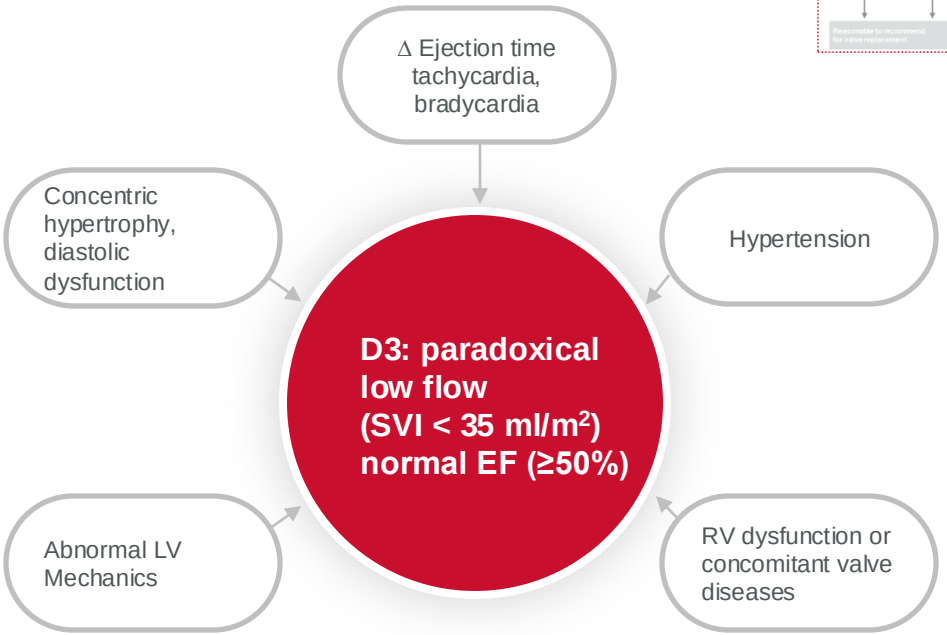
1. Baumgartner, H. (2017). Recommendations on the Echocardiographic Assessment of Aortic Valve Stenosis: A Focused Update. JASE, 30(4), 372–392.
2. 2020 AHA/ACC Guideline for the Management of Patients with Valvular Heart Disease

(D3) Low-flow low-gradient with preserved LVEF (paradoxical)



Some patients with severe aortic stenosis based on valve area have a lower than expected gradient (e.g. mean gradient < 30 mmHg) despite preserved LV ejection fraction (e.g. EF > 50%)

- These low gradients **often lead to an underestimation of the severity of the disease**, so many of these patients do not undergo surgical aortic valve replacement[1]



Stage D3 – Definition[2]

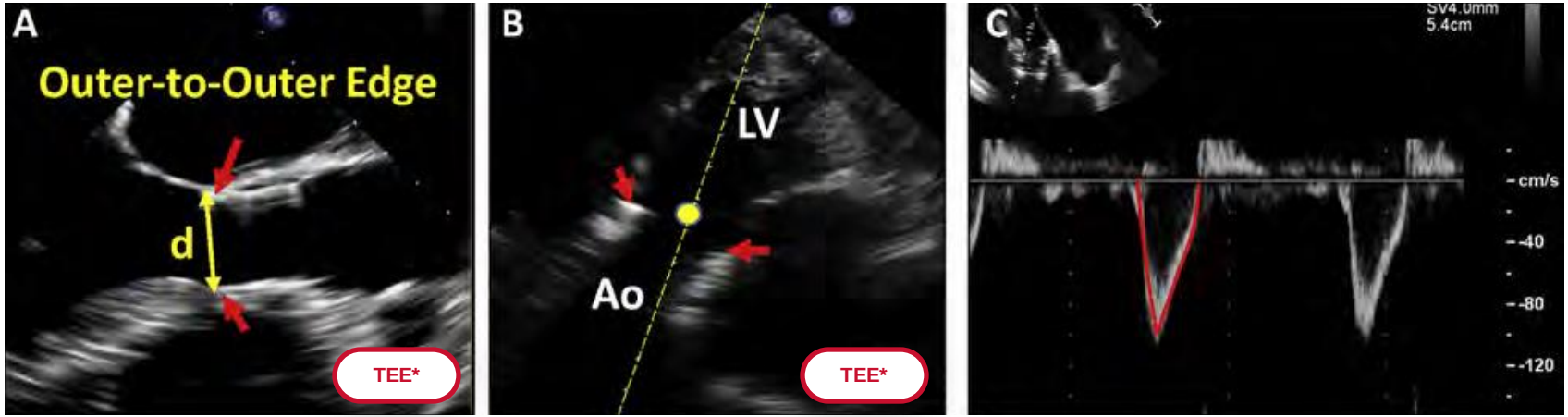
- AVA ≤1.0 cm^2 with aortic V_{max} <4 m/s or mean pressure gradient <40 mm Hg
- Indexed AVA ≤0.6 cm^2/m^2 and stroke volume index <35 mL/m^2
- Measured when patient is normotensive (systolic BP <140 mm Hg)

1. Dumesnil, J. G. (2009). Paradoxical low flow and/or low gradient severe aortic stenosis despite preserved left ventricular ejection fraction. EHJ, 31(3), 281–289.
2. 2020 AHA/ACC Guideline for the Management of Patients with Valvular Heart Disease

Post TAVR echocardiography

Edwards

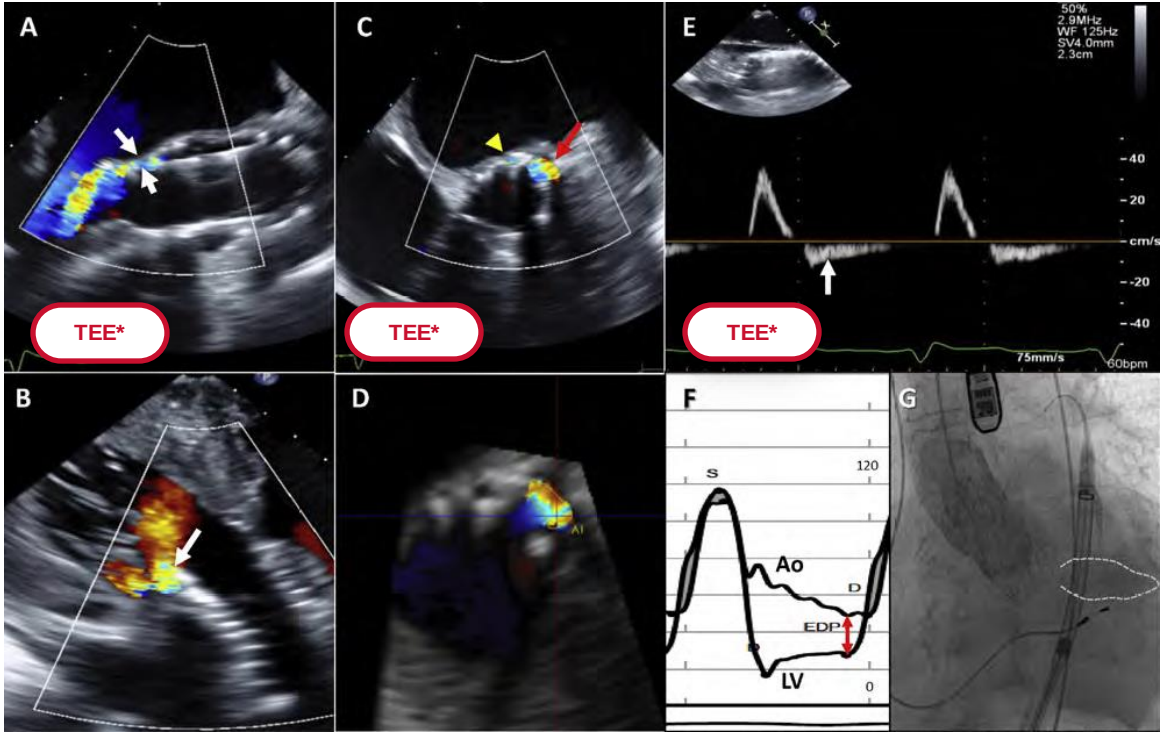
LVOT post measurement



These images detail the correct post-implantation measurements for LVOT diameter, placement of PW sample gate and LVOT VTI tracing.[1]

1. Zoghbi, W. A. (2019). Guidelines for the Evaluation of Valvular Regurgitation After Percutaneous Valve Repair or Replacement. JASE, 32(4), 431–475.

PVL assessment alternatives[1]

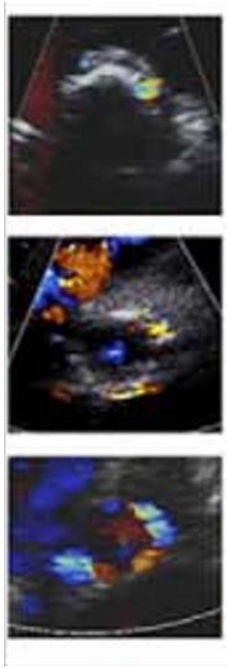


A. Vena contracta
B. Proximal flow convergence
C. Vena contracta area by 2D echo
D. Vena contracta area by 3D echo
E. Flow reversal in descending aorta
F. End diastolic pressure by cath
G. AR by fluoroscopy/ contrast injection

1. Zoghbi, W. A. (2019). Guidelines for the Evaluation of Valvular Regurgitation After Percutaneous Valve Repair or Replacement. JASE, 32(4), 431–475.

PVL assessment and grading

Scoring[1]



- Mild < 10%
- Mod < 29%
- Severe ≥ 30%

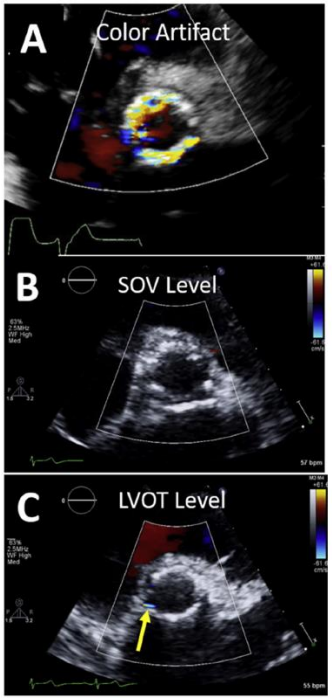
SAX: Number of jets and size at origin

LAX: Jet length and area used to confirm presence and location but not used to grade severity

Steps

1. To assess for the presence of PVL, image just below the stent frame
2. When attempting to quantify PVL severity, image closer to the jet origin

Watchouts[2]



1. Bloomfield, G. S. (2013). A Practical Guide to Multimodality Imaging of Transcatheter Aortic Valve Replacement. JACC, 442–455.
2. Hahn, R. T. (2015). Recommendations for Comprehensive Intraprocedural Echocardiographic Imaging During TAVR. JACC, 8(3), 261–287.

Aortic Stenosis echo recap

Standard TTE Considerations[1]

AS peak velocity (Peak-V)

Mean transvalvular pressure gradient (MPG)

Aortic valve area (AVA) by continuity equation

Additional considerations

- Dimensionless Index
  - Velocity ratio = V_{LVOT} /V_{AV}
- SVi
  - SV/BSA
- AVAi
  - AVA/BSA
- Ejection fraction

1. Baumgartner, H. (2017). Recommendations on the Echocardiographic Assessment of Aortic Valve Stenosis: A Focused Update. JASE, 30(4), 372–392.

Important Safety Information

Edwards SAPIEN 3 THV System and Edwards SAPIEN 3 Ultra THV System

Indications: The Edwards SAPIEN 3 and SAPIEN 3 Ultra Transcatheter Heart Valve system is indicated for relief of aortic stenosis in patients with symptomatic heart disease due to severe native calcific aortic stenosis who are judged by a Heart Team, including a cardiac surgeon, to be appropriatefor the transcatheter heart valve replacement therapy.

The Edwards SAPIEN 3 and SAPIEN 3 Ultra Transcatheter Heart Valve system is indicated for patients with symptomatic heart disease due to failing (stenosed, insufficient, or combined) of a surgical or transcatheter bioprosthetic aortic valve, a surgical bioprosthetic mitral valve, or a native mitral valve with an annuloplasty ring who are judged by a heart team, including a cardiac surgeon, to be at high or greater risk for open surgical therapy (i.e., predicted risk of surgical mortality ≥ 8% at 30 days, based on the Society of Thoracic Surgeons (STS) risk score and other clinical co-morbidities unmeasured by the STS risk calculator).

Contraindications: The valves and delivery systems are contraindicated in patients who cannot tolerate an anticoagulation/antiplatelet regimen or who have active bacterial endocarditis or other active infections, or who have significant annuloplasty ring dehiscence.

Warnings: Observation of the pacing lead throughout the procedure is essential to avoid the potential risk of pacing lead perforation. There may be an increased risk of stroke in transcatheter aortic valve replacement procedures, as compared to balloon aortic valvuloplasty or other standard treatments in high or greater risk patients. Incorrect sizing of the valve may lead to paravalvular leak, migration, embolization, residual gradient (patient-prosthesis mismatch), and/or annular rupture. Accelerated deterioration of the valve due to calcific degeneration may occur in children, adolescents, or young adults and in patients with an altered calcium metabolism. Prior to delivery, the valve must remain hydrated at all times and cannot be exposed to solutions other than its shipping storage solution and sterile physiologic rinsing solution. Valve leaflets mishandled or damaged during any part of the procedure will require replacement of the valve. Caution should be exercised in implanting a valve inpatients with clinically significant coronary artery disease. Patients with pre-existing prostheses should be carefully assessed prior to implantation of the valve to ensure proper valve positioning and deployment. Do not use the valve if the tamper-evident seal is broken, the storage solution does not completely cover the valve, the temperature indicator has been activated, the valve is damaged, or the expiration date has elapsed. Do not mishandle the delivery system or use it if the packaging or any components are not sterile, have been opened or are damaged (e.g., kinked or stretched), or if the expiration date has elapsed. Use of excessive contrast media may lead to renal failure. Measure thepatient's creatinine level prior to the procedure. Contrast media usage should be monitored. Patient injury could occur if the delivery system is not un-flexed prior to removal. Care should be exercised in patients with hypersensitivities to cobalt, nickel, chromium, molybdenum, titanium, manganese, silicon, and/ or polymeric materials. The procedure should be conducted under fluoroscopic guidance. Some fluoroscopically guided procedures are associated with a risk of radiation injury to the skin. These injuriesmay be painful, disfiguring, and long-lasting. Valve recipients should be maintained on anticoagulant/antiplatelet therapy, except when contraindicated, as determined by their physician. This device has not been tested for use without anticoagulation. Do not add or apply antibiotics to the storage solution, rinse solution, or to the valve. Balloon valvuloplasty should be avoided in the treatment of failing bioprostheses as this may result in embolization of bioprosthesis material and mechanical disruption of the valve leaflets. Do not perform stand-alone balloon aortic valvuloplasty procedures in the INSPIRIS RESILIA aortic valve for the sizes 19-25 mm. This may expand the valve causing aortic incompetence, coronary embolism or annular rupture. Transcatheter valve replacement in mitral annuloplasty rings is not recommended in cases of partial annuloplasty ring dehiscence due to high risk of PVL. Transcatheter valve replacement in mitral annuloplasty rings is not recommended in cases of partial (incomplete) annuloplasty rings in the absence of annular calcium due to increased risk of valve embolization. Transcatheter valve replacement in mitral annuloplasty rings is not recommended in cases of rigid annuloplastyrings due to increased risk of PVL or THV deformation. To prevent possible damage to the balloon shaft, ensure that the proximal end of the balloon shaft is not subjected to bending. Ensure there is no residual fluid left in the balloon to avoid potential difficulty with valve alignment during the procedure. Do not position the valve past the distal Valve Alignment Marker. This will prevent proper valve deployment. If valve alignment is not performed in a straight section, there may be difficulties performing this step which may lead to delivery system damage and inability to inflate the balloon. Utilizing alternate fluoroscopic views may help with assessing curvature of the anatomy. If excessive tension is experienced during valve alignment, repositioning the delivery system to a different straight section of the vasculature and relieving compression (or tension) in the system will be necessary.

Important Safety Information (cont.)

Precautions: Long-term durability has not been established for the valve. Regular medical follow-up is advised to evaluate valve performance. Limited clinical data are available for transcatheter aortic valve replacement in patients with a congenital bicuspid aortic valve who are deemed to be at low surgical risk. Anatomical characteristics should be considered when using the valve in this population. In addition, patient age should be considered as long-term durability of the valve has not been established. Glutaraldehyde may cause irritation of the skin, eyes, nose, and throat. Avoid prolonged or repeated exposure to, or breathing of, the solution. Use only with adequate ventilation. If skin contact occurs, immediately flush theaffected area with water; in the event of contact with eyes, seek immediate medical attention. For more information about glutaraldehyde exposure, refer to the Safety Data Sheet available from EdwardsLifesciences. If a significant increase is resistance occurs when advancing the catheter through the vasculature, stop advancement and investigate the cause of resistance before proceeding. Do not force passage, as this could increase the risk of vascular complications. To maintain proper valve leaflet coaptation, do not overinflate the deployment balloon. Appropriate antibiotic prophylaxis is recommended post-procedure in patients at risk for prosthetic valve infection and endocarditis. Additional precautions for transseptal replacement of a failed mitral valvebioprosthesis include, the presence of devices or thrombus or other abnormalities in the caval vein precluding safe transvenous femoral access for transseptal approach; and the presence of an Atrial SeptalOccluder Device or calcium or abnormalities in the atrial septum preventing safe transseptal access. Special care must be exercised in mitral valve replacement if chordal preservation techniques were used in the primary implantation to avoid entrapment of the subvalvular apparatus. Safety and effectiveness have not been established for patients with the following characteristics/comorbidities: non-calcified aortic annulus; severe ventricular dysfunction with ejection fraction < 20%; congenital unicuspid aortic valve; pre-existing prosthetic ring in the tricuspid position; severe mitral annular calcification (MAC); severe (> 3+) mitral insufficiency, or Gorlin syndrome; blood dyscrasias defined as leukopenia (WBC < 3000 cells/mL), acute anemia (Hb < 9 g/dL), thrombocytopenia (platelet count < 50,000 cells/mL), or history of bleeding diathesisor coagulopathy; hypertrophic cardiomyopathy with or without obstruction (HOCM); echocardiographic evidence of intracardiac mass, thrombus, or vegetation; a known hypersensitivity or contraindication to aspirin, heparin, ticlopidine (Ticlid), or clopidogrel (Plavix), or sensitivity to contrast media, which cannot be adequately premedicated; significant aortic disease, including abdominal aortic or thoracic aneurysm defined as maximal luminal diameter 5 cm or greater, marked tortuosity (hyperacute bend), aortic arch atheroma (especially if thick [> 5 mm], protruding, or ulcerated) or narrowing (especially with calcification and surface irregularities) of the abdominal or thoracic aorta, severe “unfolding” and tortuosity of the thoracic aorta; bulky calcified aortic valve leaflets in close proximity to coronary ostia; a concomitant paravalvular leak where the failing prosthesis is not securely fixed in the native annulus or is not structurally intact (e.g.,wireform frame fracture, annuloplasty ring dehiscence); or a partially detached leaflet of the failing bioprosthesis that in the aortic position may obstruct a coronary ostium. For Left axillary approach, a left subclavian takeoff angle ~ ≥ 90° from the aortic arch causes sharp angles, which may be responsible for potential sheath kinking, subclavian/axillary dissection and aortic arch damage. Ensure there is flow in Left Internal Mammary Artery (LIMA)/Right Internal Mammary Artery (RIMA) during procedure and monitor PA pressure in homolateral radial artery. Residual mean gradient may be higher in a “THV-in-failing prosthesis” configuration than that observed following implantation of the valve inside a native aortic annulus using the same size device. Patients with elevated mean gradient post procedure should be carefully followed. It is important that themanufacturer, model and size of the preexisting prosthesis be determined, so that the appropriate valve can be implanted and a prosthesis-patient mismatch be avoided. Additionally, pre-procedure imaging modalities must be employed to make as accurate a determination of the inner diameter as possible.

Potential Adverse Events: Potential risks associated with the overall procedure, including potential access complications associated with standard cardiac catheterization, balloon valvuloplasty, the potential risks of conscious sedation and/or general anesthesia, and the use of angiography: death; stroke/transient ischemicattack, clusters, or neurological deficit; paralysis; permanent disability; respiratory insufficiency or respiratory failure; hemorrhage requiring transfusion or intervention; cardiovascular injury including perforation or dissection of vessels, ventricle, atrium, septum, myocardium, or valvular structures that may require intervention; pericardial effusion or cardiac tamponade; thoracic bleeding; embolizationincluding air, calcific valve material, or thrombus; infection including septicemia and endocarditis; heart failure; myocardial infarction; renal insufficiency or renal failure; conduction system defect whichmay require a permanent pacemaker; arrhythmia; retroperitoneal bleed; arteriovenous (AV) fistula or pseudoaneurysm; reoperation; ischemia or nerve injury or brachial plexus injury; restenosis; pulmonary edema; pleural effusion; bleeding; anemia; abnormal lab values (including electrolyte imbalance); hypertension or hypotension; allergic reaction to anesthesia, contrast media, or device materials; hematoma; syncope; pain or changes (e.g., wound infection, hematoma, and other wound care complications) at the access site; exercise intolerance or weakness; inflammation; angina; heart murmur;and fever. Additional potential risks associated with the use of the valve, delivery system, and/or accessories include: cardiac arrest; cardiogenic shock; emergency cardiac surgery; cardiac failure orlow cardiac output; coronary flow obstruction/transvalvular flow disturbance; device thrombosis requiring intervention; valve thrombosis; device embolization; device migration or malposition requiring intervention; left ventricular outflow tract obstruction; valve deployment in unintended location; valve stenosis; structural valve deterioration (wear, fracture, calcification, leaflet tear/tearing fromthe stent posts, leaflet retraction, suture line disruption of components of a prosthetic valve, thickening, stenosis); device degeneration; paravalvular or transvalvular leak; valve regurgitation; hemolysis; deviceexplants; nonstructural dysfunction; mechanical failure of delivery system and/or accessories; and non-emergent reoperation.

Important Safety Information (cont.)

Edwards Crimper

Indications: The Edwards crimper is indicated for use in preparing the Edwards SAPIEN 3 Ultra transcatheter heart valve and the Edwards SAPIEN 3 transcatheter heart valve for implantation.

Contraindications: There are no known contraindications.

Warnings: The devices are designed, intended, and distributed for single use only. **Do not resterilize or reuse the devices.** There are no data to support the sterility, nonpyrogenicity, and functionality of the devices after reprocessing.

Precautions: For special considerations associated with the use of the Edwards crimper prior to THV implantation, refer to the THV Instructions for Use.

Potential Adverse Events: There are no known potential adverse events associated with the Edwards crimper.

CAUTION: Federal (United States) law restricts these devices to sale by or on the order of a physician.

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