AORTIC STENOSIS

INTRODUCTION

Aortic stenosis (AS) is a narrowing of the aortic valve that complicates the flow between the left ventricle (LV) and aorta. It is known that 1% to 2% of persons age 65 or older and 12% of persons 75 or older have aortic stenosis[1]. The aim of this article is to highlight the main etiologies and mechanisms of AS occurrence and to explain the main principles of ultrasound diagnostic of this disease.

AORTIC VALVE ANATOMY

To understand the basics of aortic stenosis we need to analyze the structure of the aortic root. The aortic root is a direct continuation of the left ventricular outflow tract (LVOT) and consists of sinuses of Valsalva, aortic annulus and aortic valve leaflets. The aortic annulus is a fibrous structure that connects the ventricular septum and the base of the aorta. Sinuses of Valsalva (coronary sinuses) are the anatomic spaces of the aortic root. The right coronary artery arises from the right (or anterior) coronary sinus and the left coronary artery from the left (or left posterior) sinus. The third sinus is noncoronary. The junction of the sinuses with the aorta is called the sinotubular junction[2] (Figure 1, from Circulation, 2008, Video 2).

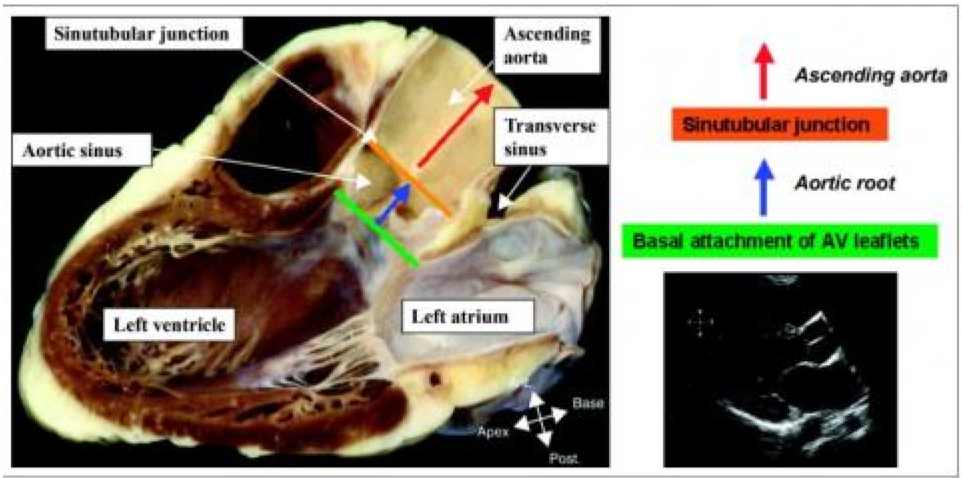


Figure 1

Video 2

The aortic valve is a semilunar valve that has three leaflets: left coronary, right coronary and noncoronary. Each leaflet has two free edges, both connected with the adjoining leaflets. Looking at the aortic valve in the transverse view you can see “peace sign” or “Mercedes sign”[1] (Figure 3 from Braunwald's Heart Disease, 2018, Video 4).

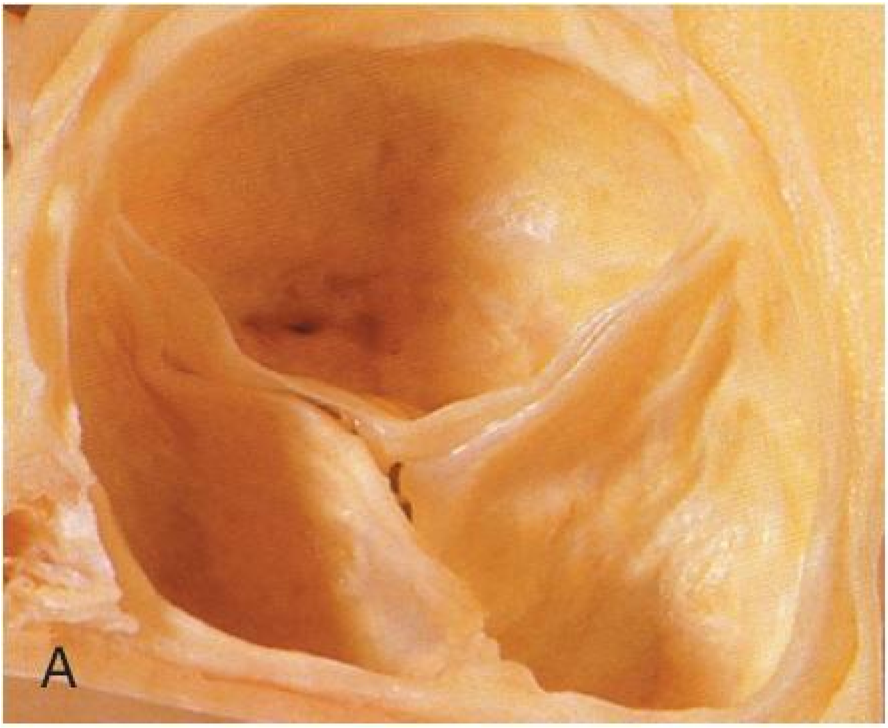


Figure 3

Video 4

Between the noncoronary and left coronary leaflets of the aortic valve and anterior leaflet of the mitral valve there is a fibrous sheet that is called aortomitral curtain.

ETIOLOGY OF AORTIC STENOSIS[3]

(Figure 5, From ASE Guidelines, 2017)

1. Rheumatic heart disease

Rheumatic heart disease is a cause of aortic valve stenosis, predominantly in developing countries. It results in thickening of the valve leaflets with fusion at the commissures and sometimes calcification. Rheumatic aortic valve stenosis is often associated with aortic valve regurgitation[4]. Rheumatic heart disease predominantly affects the mitral valve and should be evaluated in every case of rheumatic aortic valve disease.

2. Congenital aortic valve disease

Congenital aortic valve disease includes unicuspid, bicuspid, quadricuspid aortic valve. These anomalies are often associated with other congenital heart defects such as coarctation of aorta, ductus arteriosus, ventricular septal defect etc. that are often diagnosed at childhood.

In adulthood we are dealing predominantly with bicuspid aortic valve that can cause either regurgitation or stenosis of the aortic valve (or both). The prevalence of bicuspid valve is about 2% in population. In the vast majority of patients with bicuspid valve the ascending aorta is enlarged. The clinical symptoms in such patients usually develop with aging[5].

3. Calcification of the aortic valve

Calcification (degeneration) of the aortic valve is the leading cause of aortic valve stenosis especially in the elderly. The valve leaflets become stiff and immobile due to fibrosis and calcification. It results in valve area decrease and aortic stenosis development[6].

4. Infective endocarditis

Infective endocarditis with vegetation formation at the aortic valve leaflets leads predominantly to aortic valve regurgitation. In rare situations aortic valve stenosis can occur due to large vegetation sizes. In a case of aortic valve endocarditis there is high probability of mitral valve involvement[7].

5. Amyloidosis

Amyloidosis can lead to heart infiltration by different types of amyloid. It turns out that in patients with amyloidosis aortic valve stenosis occurs in 4-16% of cases. It is more pronounced in TTR (transthyretin) type of amyloidosis. The evaluation of amyloidosis in patients with severe aortic valve stenosis can change the diagnostic and treatment algorithm as the symptoms of heart failure can remain despite aortic valve surgery[8].

6. Radiation therapy of the chest

Radiation therapy of the chest can lead to progressive valve thickening and calcification that can result in aortic and mitral valves restriction and dysfunction with stenosis and\or regurgitation development[9].

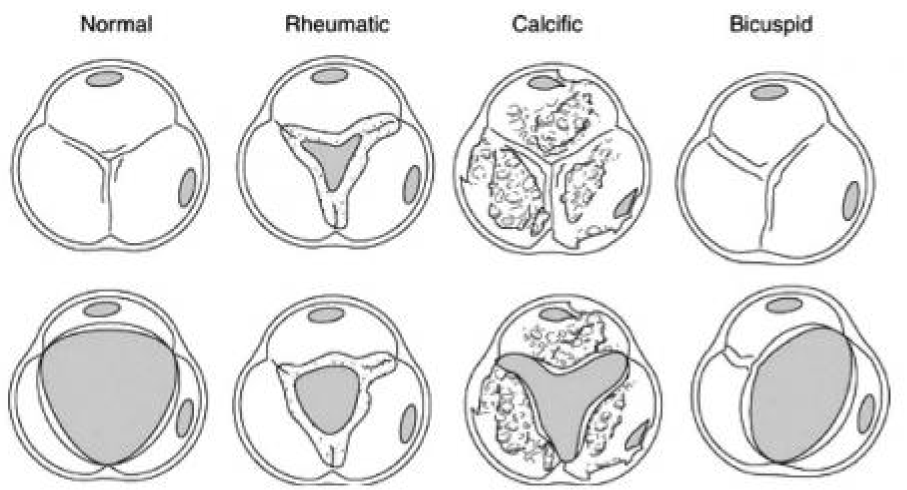


Figure 5

MEASUREMENTS AND CALCULATION PRINCIPLES

Echocardiography is the main method of aortic stenosis evaluation. It allows us to measure velocities and calculate volumes and gradients. To obtain these parameters we use the Doppler effect or Doppler principle[10]. The Doppler effect is the change of frequency of sound emitted or reflected by a moving object[11].

For AS evaluation we use three main types of Doppler mode[12,13]:

1. Pulsed wave doppler (PW);
2. Continuous wave doppler (CW);
3. Color doppler (CD) or color flow imaging (CFI) or color velocity imaging (CVI) or color mode.

PW and CW help us to evaluate velocity and direction of the flow in some point or along the line of the ultrasound beam. PW and CW images look like graphs with velocity and time on the axes (Figure 6).

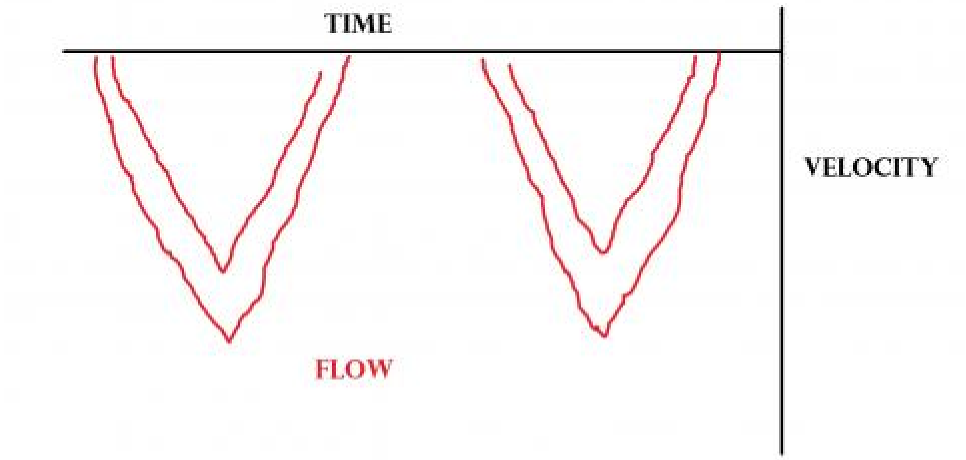


Figure 6

The ultrasound machine registers echo signals and shows as waveforms on a graph with waveforms above the baseline indicating flow towards the probe, and waveform below the baseline representing flow away from the probe (Figure 7).

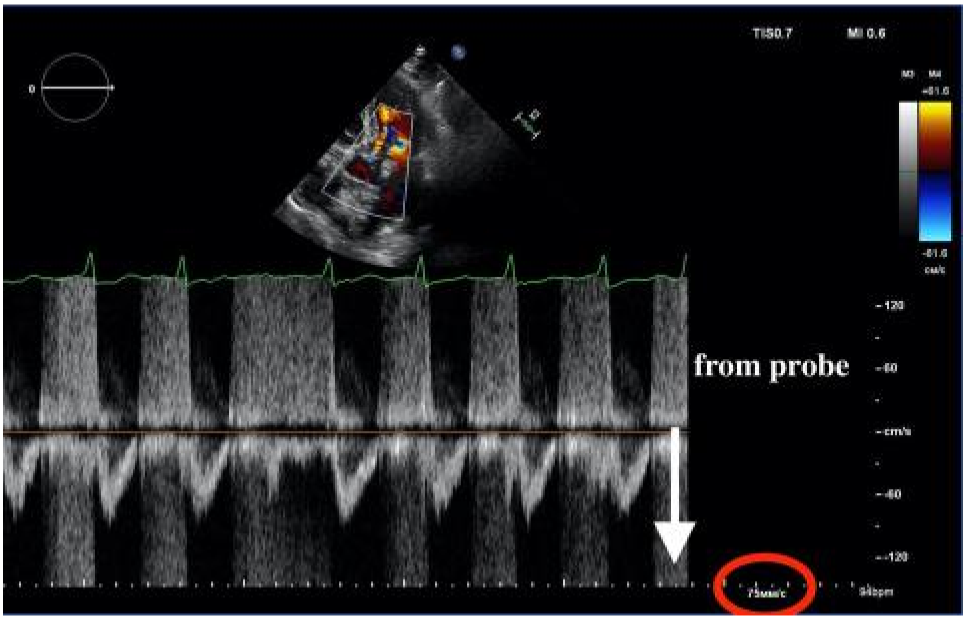


Figure 7

In cases of AS we use PW to obtain LVOT flow and calculate the stroke volume. PW is based on the work of a single piezoelectric element that sends the ultrasound signal to the target, then receives the signal when it is reflected back. Then the process repeats, one signal at a time. PW thereby estimates the velocity of blood flow in a small space, known as a sample volume. As an example, PW estimates flow velocity in LVOT, a few millimeters before the aortic valve (Figure 7). PW is not intended for high-velocity flows (> 1.7-2.0 m/s).

CW is used for measurements of the velocity and gradient through the aortic valve. CW is based on constant activity of two piezoelectric elements: one sends the ultrasound signal and the other receives it. CW estimates velocity of blood flow along the ultrasound beam and is intended for measurement of high velocity flows (> 1.7-2.0 m/s). For example, in Figure 8 we can see the flow of aortic stenosis. The main aim of blood flow measurements using PW or CW Doppler is the parallel alignment of the ultrasound beam to blood flow.

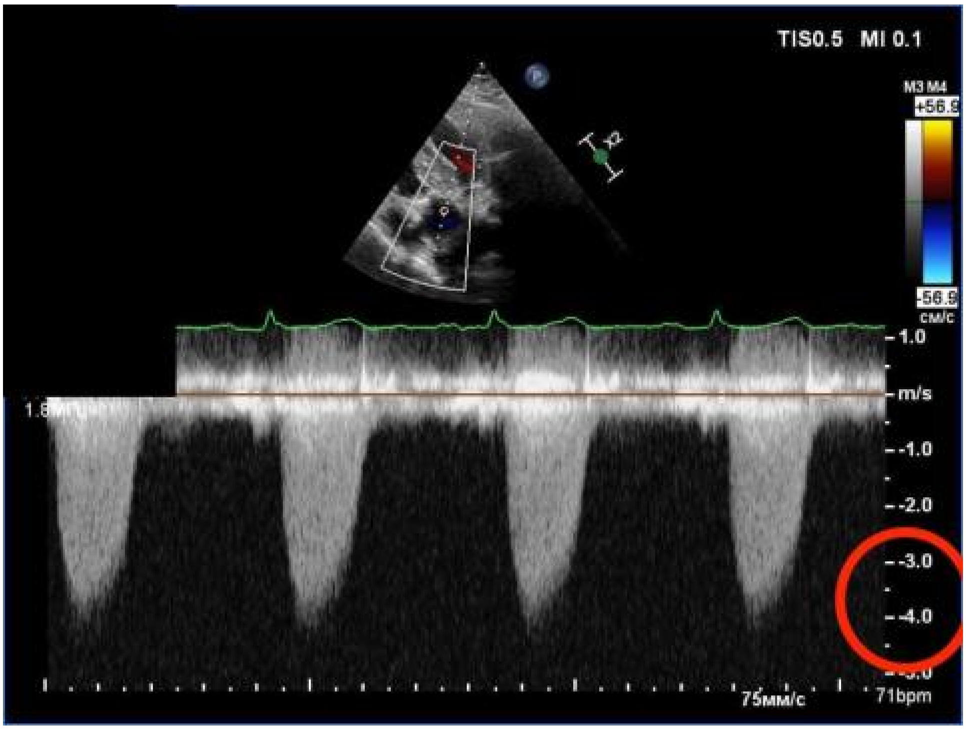


Figure 8

CD is used for better alignment of PW and CW modes. CD helps us to understand presence or absence of flow by letting us visualize the flow and evaluate its flow direction using color mapping. Instead of graphs CD uses colors for designation of flow directions. CD assigns different colors when blood is moving. Figure 9 illustrates the standard red and blue scale. Red is used to show the flow moving towards the probe (goes to upper part of the picture, figure 10), blue for flow moving away from the probe (goes to lower part of the picture) (Figure 11).

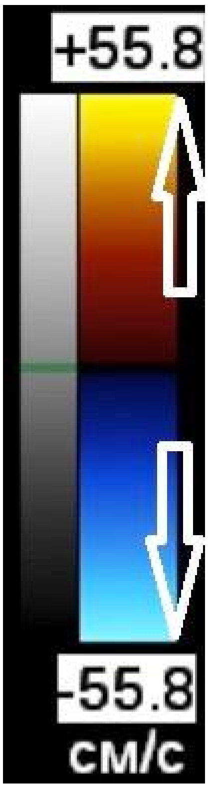


Figure 9

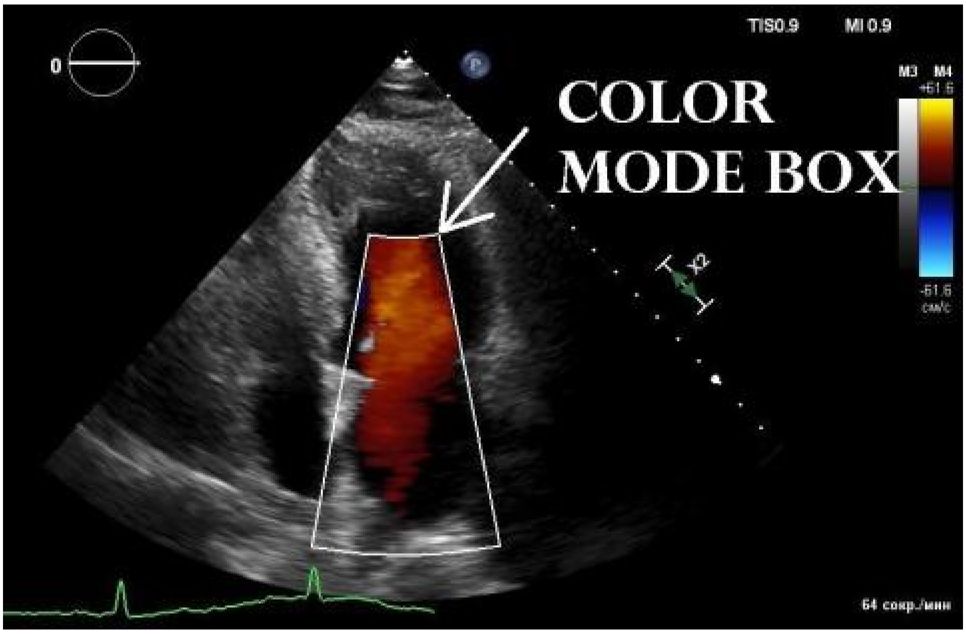


Figure 10

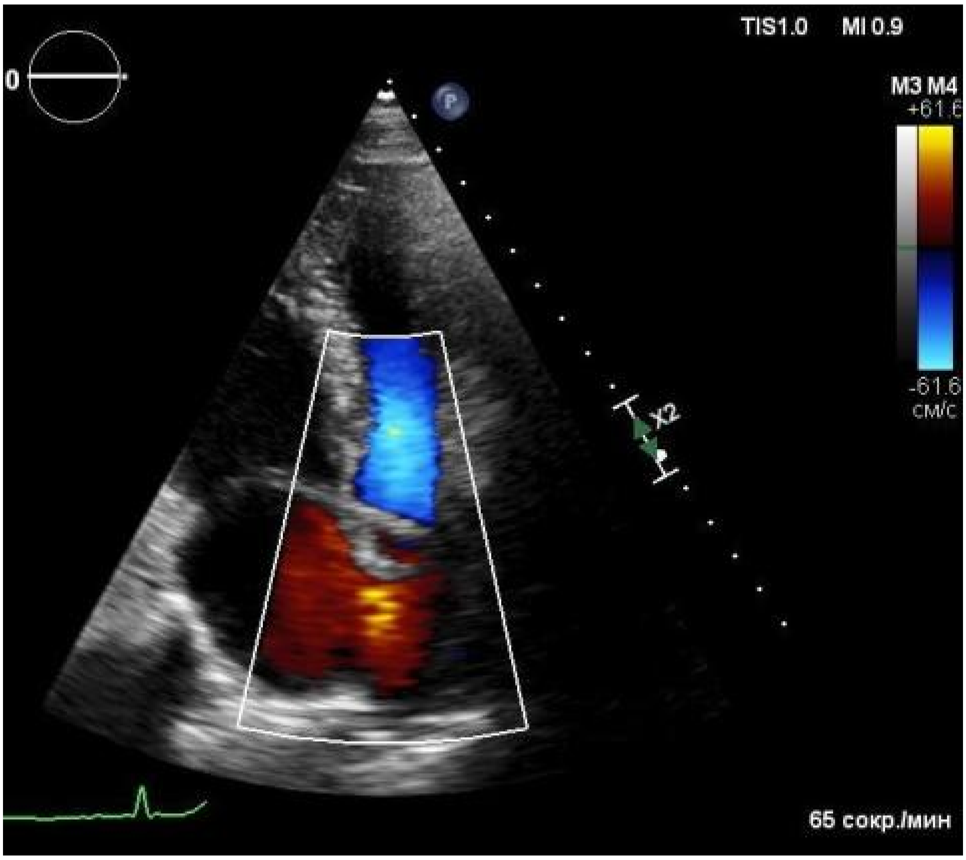


Figure 11

Let's look at some examples. To obtain the color view you need to activate the color mode box in the 2D image (Figure 10). You can move this box to receive information in the exact area of interest (for example, at the aortic valve or LV outflow tract) (Video 12). Flow in this box may look like a jet (Figure 13) and it is better delineated if flow is narrow and has a high velocity.

Video 12

Figure 13

In cases of AS we can see the pathological high velocity flow. The high gradient between LV and aorta is why the AS flow is well seen (Video 12).
Keep it in mind that the best way to correctly measure the flow across the valve is to align the ultrasound beam parallel to blood flow! (Figure 14).

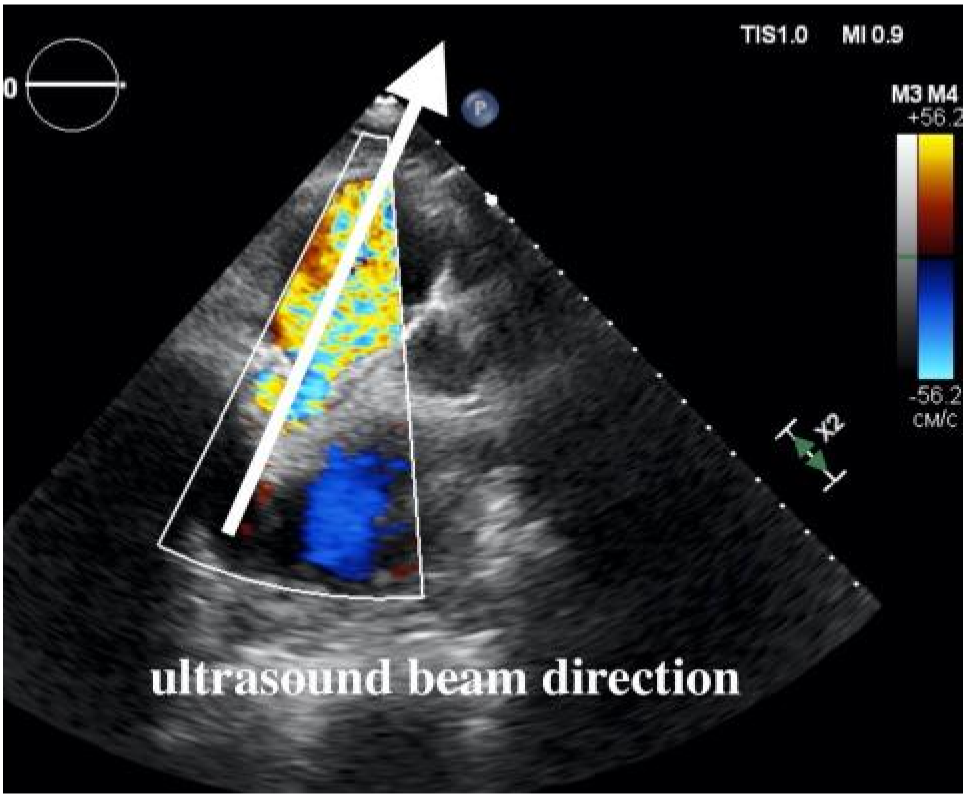


Figure 14

To estimate aortic valve stenosis, it is better to use the following sequence.

1. Visual assessment of leaflets mobility.

2. Measurement of LVOT diameter.
3. Registration of LVOT flow with PW doppler and evaluation of the flow status (low or normal) using stroke volume and stroke volume index.
4. Registration of the AS flow and calculation of the gradient and aortic valve area (AVA).
5. Additional parameters if needed.

TECHNICAL ASPECTS OF MEASUREMENTS AND CALCULATIONS[3,14]

We have to perform a number of measurements to obtain the necessary parameters. Let’s take a closer look and analyze some of them in detail.

1.Visual assessment

Visual assessment includes evaluation of number of valve leaflets, their mobility, annulus and leaflets echogenicity, from parasternal long and short axis view. This assessment allows us to understand that the problem with aortic valve really exists (Video 15,16).

Video 15

Video 16

2. Standard approach

The standard approach is to measure LVOT diameter in 2D mode parasternal long axis view (Figure 17, from ASE 2017). Optimize the ultrasound gain and frequency to obtain the best image quality. Use the linear measurement in mid systole.

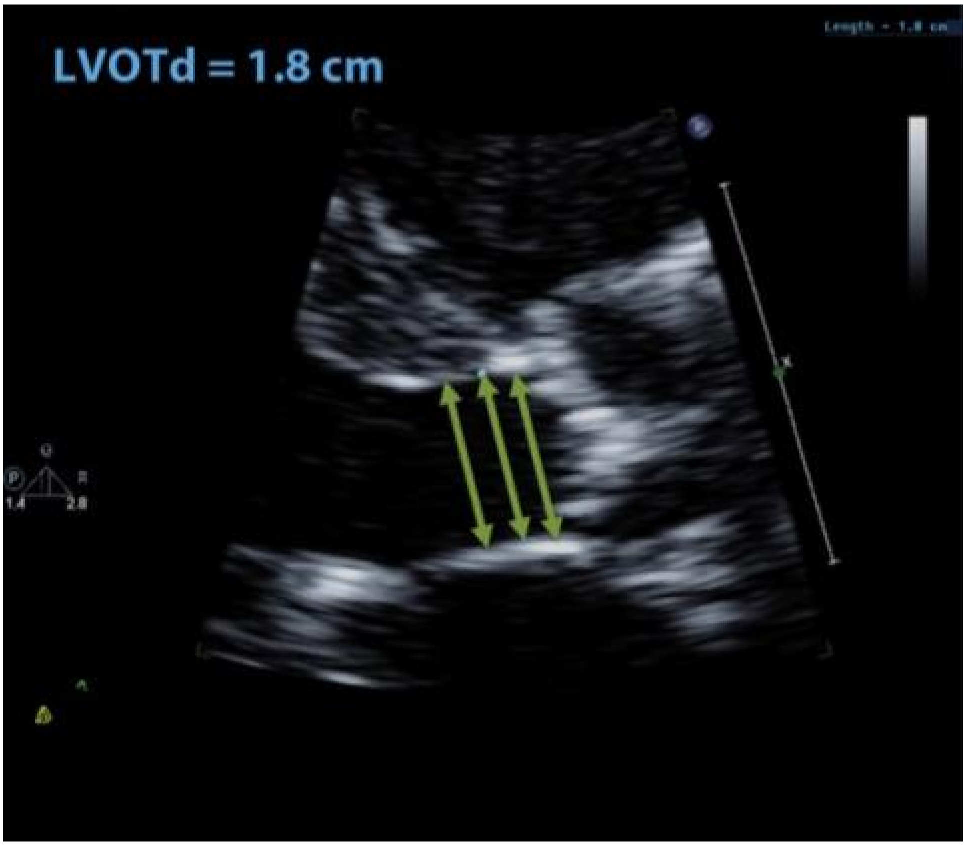
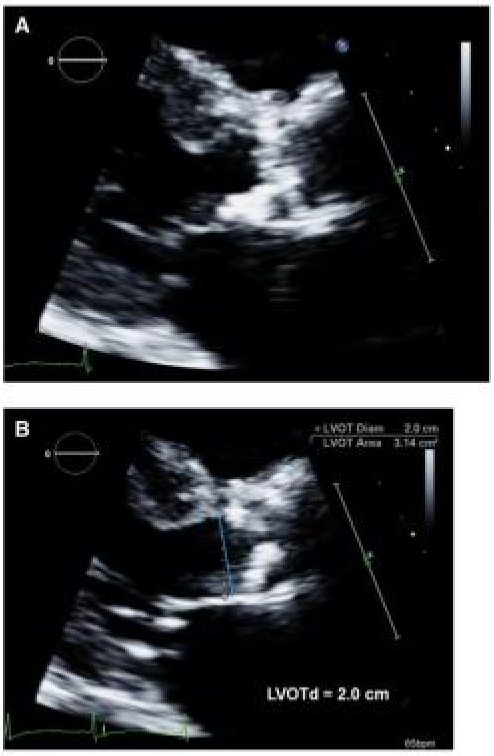


Figure 17

Measure the LVOT at the level of aortic valve annulus or deeper to the LVOT (up to 1 cm from the annulus). Different institutions use different approaches (Figure 17, 18 from ASE 2017) and it is preferable to use the same approach inside your practice for better reproducibility.



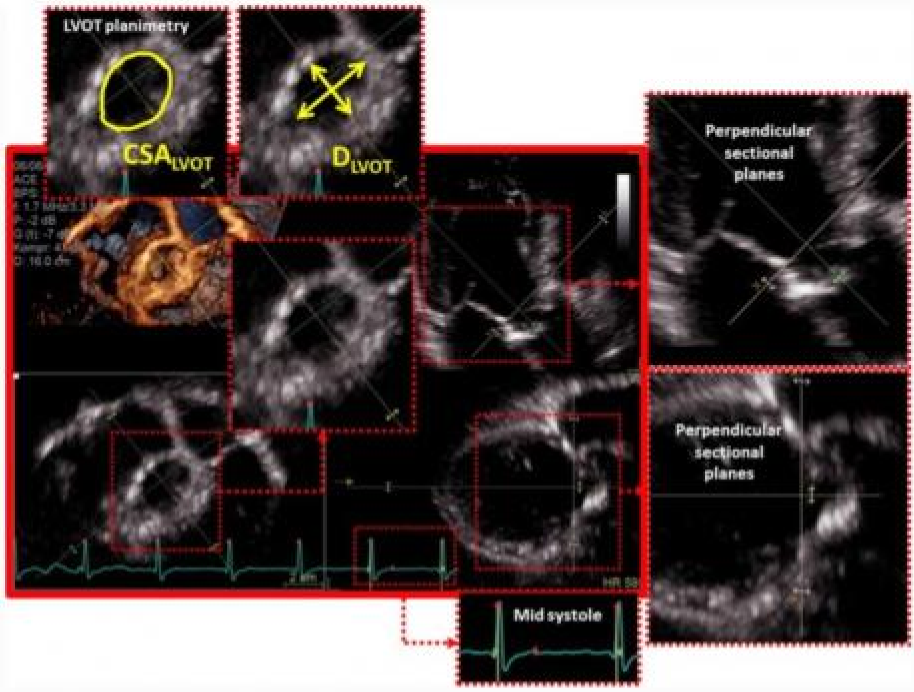
(**A**) A patient example in which calcification protruding into the LVOT might yield an incorrectly small LVOT diameter, because the calcium may not extend circumferentially around the annulus perimeter. (**B**) A slightly altered view avoids localized calcification and yields a larger and more accurate diameter. (With permission from Steve Goldstein from ASE's Comprehensive Echocardiography, Ch 95).

Figure 18

After the diameter measurement the ultrasound machine will automatically calculate LVOT cross-sectional area (CSA) using the formula:

$CSA = \pi \times d^2/4 = 0.785 \times d^2$

When in doubt, to check the results use the non-standard ways to measure CSA LVOT, like 3D or computed tomography LVOT cross-section area measurement (Figure 19, from Clinical Research in Cardiology, 2020). SV calculation based on 3D planimetry LVOT measurement allows us to obtain more accurate results[15].



Accurate—objective and transparent—LVOT planimetry and assessment of D_{LVOT} performed in the correct sectional plane at the correct time point using using 3D TTE

Figure 19

Do not forget: when you use the non-standard approaches, you have to interpret results carefully. LVOT CSA calculation is the main source of mistakes in AS evaluation.

3. PW doppler LVOT flow registration and SV calculation

The standard views for LVOT flow measurement are apical 5 and 3 chamber, but in case of any difficulties you can also visualize LVOT flow in subcostal, right parasternal views, etc. Use CD to find the flow in LVOT. It is better to put the PW doppler sample volume at the AV leaflets level and then carefully move it to the LVOT, toward the apex to obtain optimal laminar flow (Figure 20, from ASE guidelines 2017). It is important to perform flow registration parallel to the ejection jet (Figure 21 from Clinical Research in Cardiology, 2020).

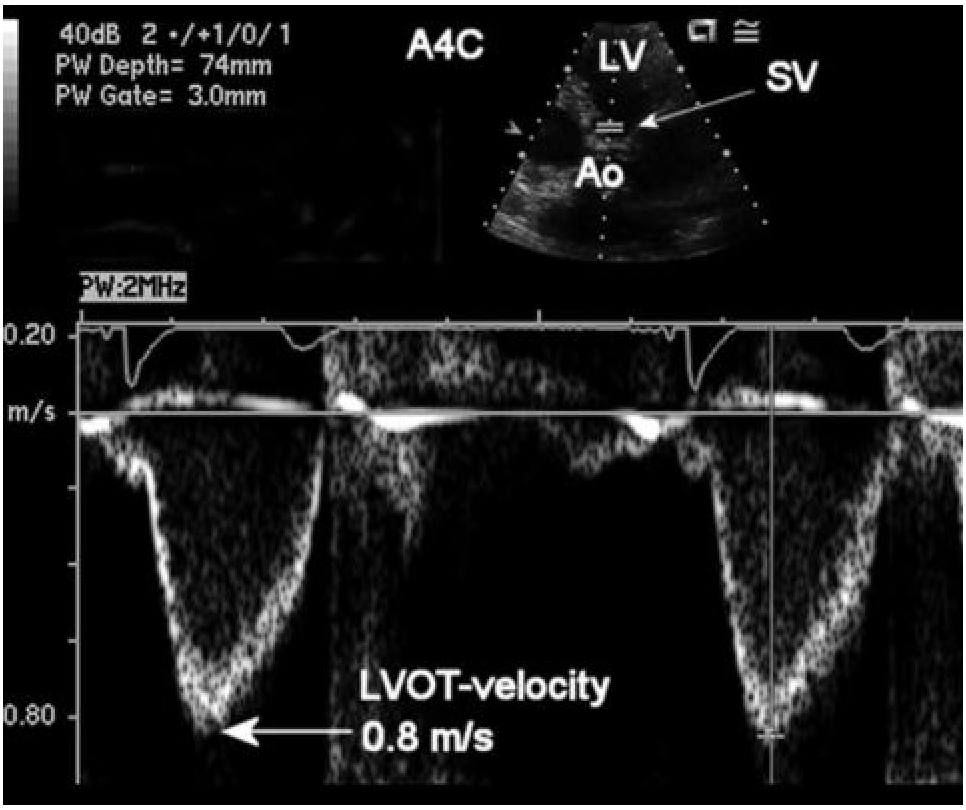


Figure 20

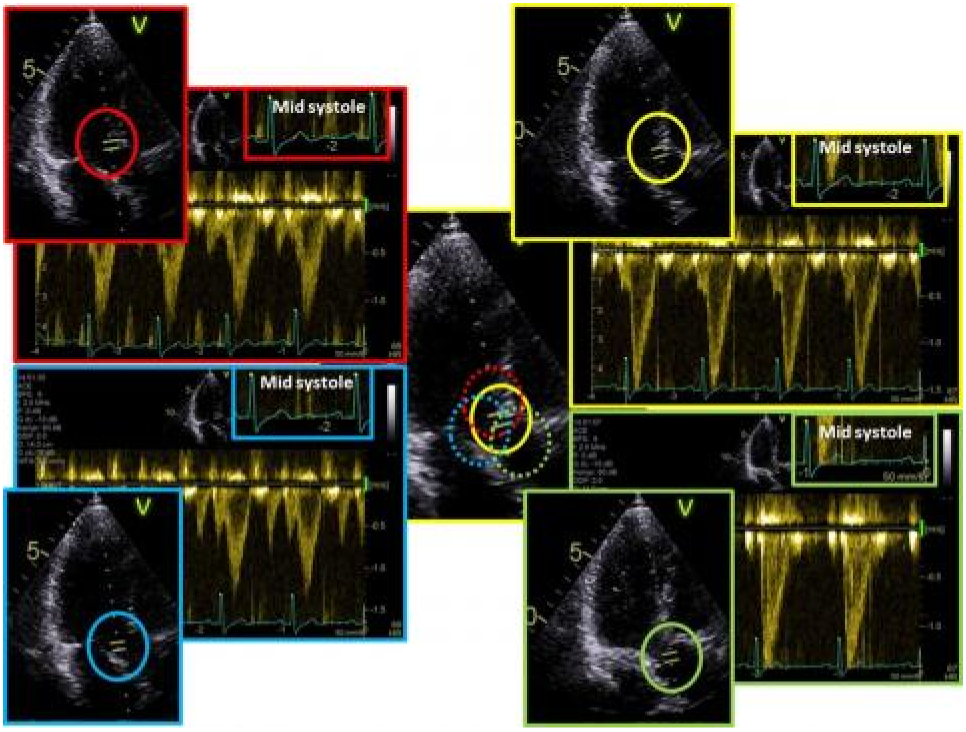


Figure 21

Adjust signal to noise ratio and use sweep speed of 50-100 mm/s. Use three beats in regular rhythm and five beats in irregular rhythm to perform calculations. In patients with rhythm disturbances and inconclusive results, for example high heart rate and/or severely irregular rhythm, consider measurements and calculations after rhythm normalization. After flow tracing the ultrasound machine will automatically calculate SV using formula:

$SV = CSA \times VTI = 0.785 \times d^2 \times VTI$

where SV-stroke volume, CSA- cross-section area, VTI- velocity time integral.
SV index is calculated by dividing SV by body surface area. In patients with AS we always need to calculate SV index to understand the flow status of the patient. If the SV index is less than 35 ml\m^2 the patient has the low flow state. If the SV index is more than 35 ml\m^2 the patient has a normal flow state. In case of turbulence, accelerated flow (LVOT obstruction) or other difficulties we can change sample volume position or use stroke volume calculation through 3D ejection fraction (3D EF) or cardiac magnetic resonance. Significant mitral regurgitation limits using of 3D EF SV.
4. AS flow registration, gradient and AVA calculation.
Use CD and different views (ie apical 5 chamber, apical 3 chamber, suprasternal, right parasternal, subcostal) to visualize the flow from left ventricle to aorta through the aortic valve (as example, see video from right parasternal view, Video 22). Perform CW flow registration parallel to ejection jet. Adjust signal to noise ratio, use sweep speed 50-100 mm/s. Trace the flow accurately to avoid the excessive noise registration and flow overestimation (Figure 23).

Video 22

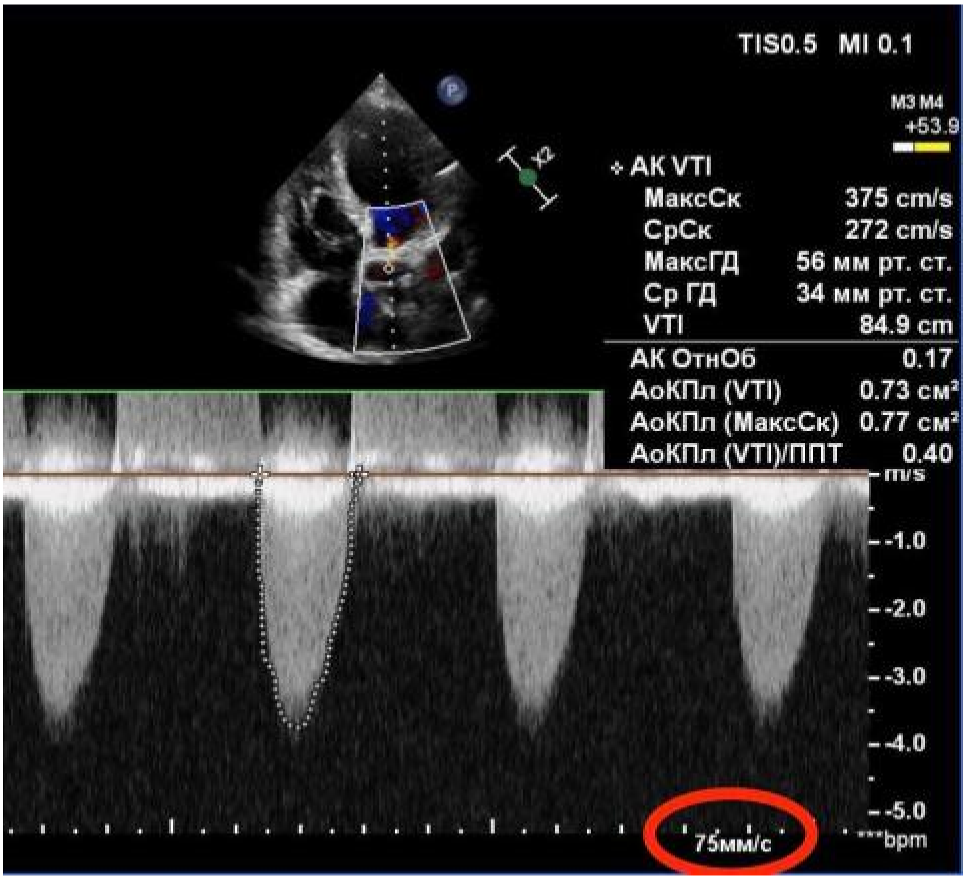


Figure 23

After the aortic valve flow tracing the ultrasound machine will calculate the peak velocity and mean gradient. Choose the highest velocity and gradient. It is better to use three beats in regular rhythm and five beats in irregular rhythm for calculations. In patients with rhythm disturbances and inconclusive results, for example high heart rate and/or severely irregular rhythm, consider measurements and calculations after rhythm normalization. Do not confuse high velocity flow in AS with flow in LVOT obstruction (Figure 24, from ASE guidelines, 2017, HOCM-hypertrophic obstructive cardiomyopathy). The last one usually has specific shape with the highest velocity in end-systole, “dagger-shape”. Also do not confuse AS flow with mitral regurgitation jet.

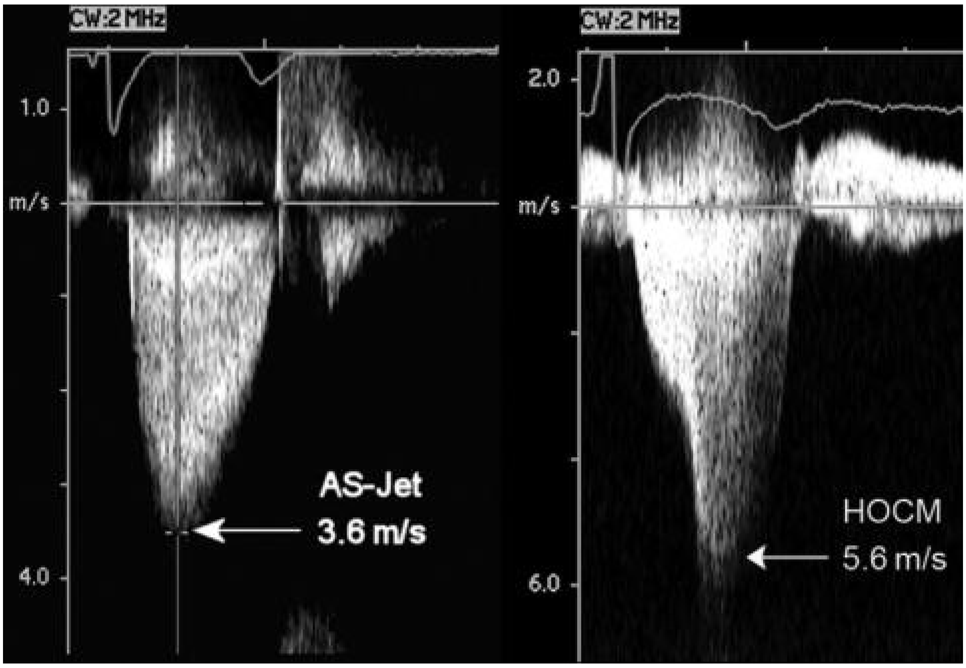


Figure 24

To measure the aortic valve area (AVA) we need to use the continuity equation principle. According to this principle the same volume goes through the LVOT and aortic valve. The cross-section areas and flow velocities through LVOT and aortic valve are different (Figure 25, from ASE guidelines 2017). If you know the stroke volume, the LVOT cross-section area and aortic valve flow you can calculate the aortic valve area (AVA).

SV AV = SV LVOT

where SV AV-stroke volume of aortic valve, SV LVOT- stroke volume of LVOT

SV AV= AVA × VTI AV

where VTI AVA- velocity time integral of AV

SV LVOT= CSA LVOT × VTI LVOT

where CSA LVOT- cross-section area of LVOT, VTI LVOT- velocity time integral of LVOT

AVA × VTI AV = CSA LVOT × VTI LVOT

AVA (VTI) = CSA LVOT × VTI LVOT/VTI AV

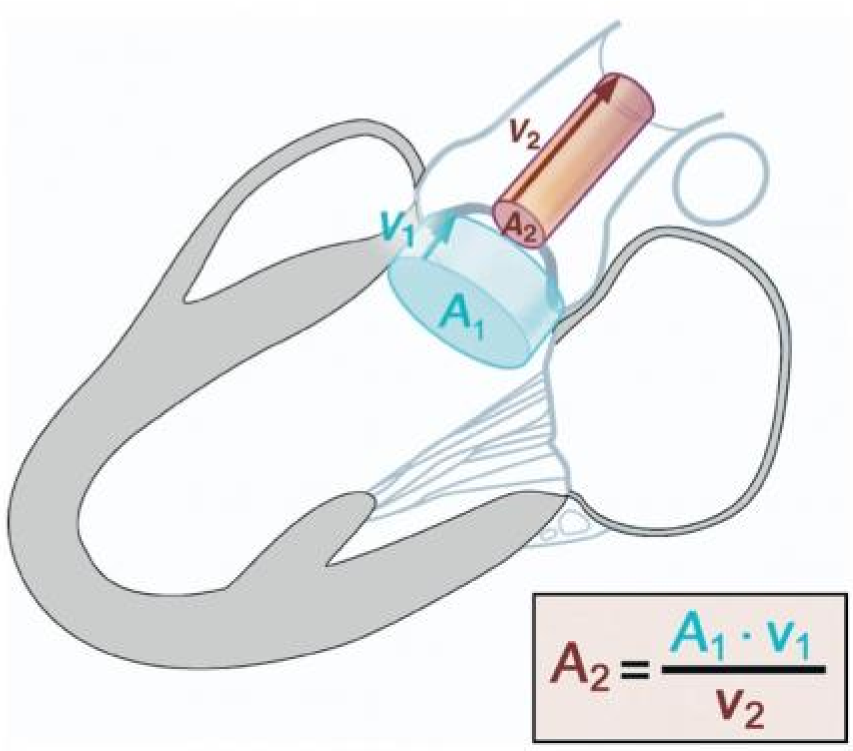
Knowing the LVOT diameter, LVOT flow and aortic valve flow, the ultrasound machine will automatically calculate the AVA

After AVA calculation it is possible to divide AVA by BSA to get indexed AVA.

5. You may use additional parameters for AS evaluation in case of inconclusive results of the standard measurements. The most frequently used additional parameters are dimensionless velocity index (DVI) or velocity ratio, simplified continuity equation AVA calculation (simplified AVA) and planimetry valve area calculation with 2D or 3D transthoracic (TTE) or transesophageal echocardiography (TEE).

To calculate DVI perform the same doppler measurements as described in steps 2-4. DVI is a ratio of LVOT velocity to aortic valve velocity. The ultrasound machine will automatically calculate it using formula:

DVI = V LVOT/V AV
where V LVOT-velocity in the LVOT

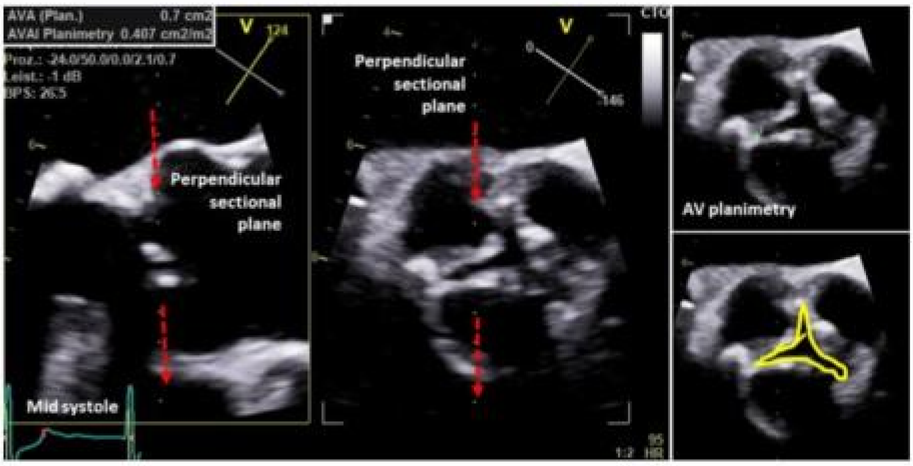


Schematic diagram of continuity equation.

Figure 25

Simplified continuity equation AVA calculation is almost the same as AVA calculation but instead of VTI the velocities are used:
AVA (velocity) = CSA LVOT × V LVOT/V AV

For planimetry valve area calculation we need to obtain a high quality image. Use 3D or short axis 2D without CD to perform measurements. It is better to use TEE because of its higher spatial resolution. Using high quality images, we can measure valve orifice area by direct planimetry trace (Figure 26, from Clinical Research in Cardiology, 2020).



Accurate—objective and transparent—AV planimetry of a tricuspid AV in severe AS performed in the correct sectional plane at the correct time point using using biplane 2D TEE

Figure 26

SEVERITY CRITERIA[3,16]

The main guideline approved criteria of aortic stenosis severity are mean gradient, peak flow velocity and AVA. Mean gradient ≥ 40 mm Hg, peak flow velocity ≥ 4 m\s and AVA (VTI) < 1 cm2 , AVA (VTI) index <0.6 cm^2\m^2 are considered to be criteria of severe aortic stenosis (Figure 27, from ASE guidelines 2017).

When using additional criteria consider DVI ≤ 0,25; AVA (velocity) < 1 cm^2; planimetry valve area < 1 cm^2 to be criteria of severe aortic stenosis.

Measures of AS severity obtained by Doppler-echocardiography

	Units	Formula/method	Cut-off for severe	Concept	Advantages	Limitations
AS jet velocity[13-15]	m/s	Direct measurement	4.0	Velocity increases as stenosis severity increases	Direct measurement of velocity. Strongest predictor of clinical outcome	• Correct measurement requires parallel alignment of ultrasound beam • Flow dependent.
Mean gradient[12-14]	mmHg	$\Delta P = \sum 4v^2/N$	40	Pressure gradient calculated from velocity using the Bernoulli equation	• Mean gradient is obtained by tracing the velocity curve • Units comparable to invasive measurements	• Accurate pressure gradients depend on accurate velocity data • Flow dependent
Continuity equation valve area[16-18]	cm^2	$AVA = (CSA_{LVOT} \times VTI_{LVOT})/VTI_{AV}$	1.0	Volume flow proximal to and in the stenotic orifice is equal	• Measures effective orifice area • Feasible in nearly all patients • Relatively flow independent	Requires LVOT diameter and flow velocity data, along with aortic velocity. Measurement error more likely
Simplified continuity equation[18,19]	cm^2	$AVA = (CSA_{LVOT} \times V_{LVOT})/V_{AV}$	1.0	The ratio of LVOT to aortic velocity is similar to the ratio of VTIs with native aortic valve stenosis	Uses more easily measured velocities instead of VTIs	Less accurate if shape of velocity curves is atypical
Velocity ratio[18,20]	None	$VR = \frac{V_{LVOT}}{V_{AV}}$	0.25	Effective AVA expressed as a proportion of the LVOT area	Doppler-only method. No need to measure LVOT size, less variability than continuity equation	Limited longitudinal data. Ignores LVOT size variability beyond patient size dependence
Planimetry of anatomic valve area[21,22]	cm^2	TTE, TEE, 3D-echo	1.0	Anatomic (geometric) CSA of the aortic valve orifice as measured by 2D or 3D echo	Useful if Doppler measurements are unavailable	Contraction coefficient (anatomic/effective valve area) may be variable. Difficult with severe valve calcification

Figure 27

FLOW STATUS[3]

AS gradients and velocities, in contrast to AVA, are flow dependent. This is the reason why we should evaluate the patient flow status in every case (see above) (Figure 28, from ASE guidelines 2017).

High gradient patients with AS can have high flow or normal flow state. Aortic regurgitation, thyrotoxicosis, shunts, anemia, intoxication or fever can explain high flow state. We have to re-assess such patients after flow status normalization (if normalization is possible).

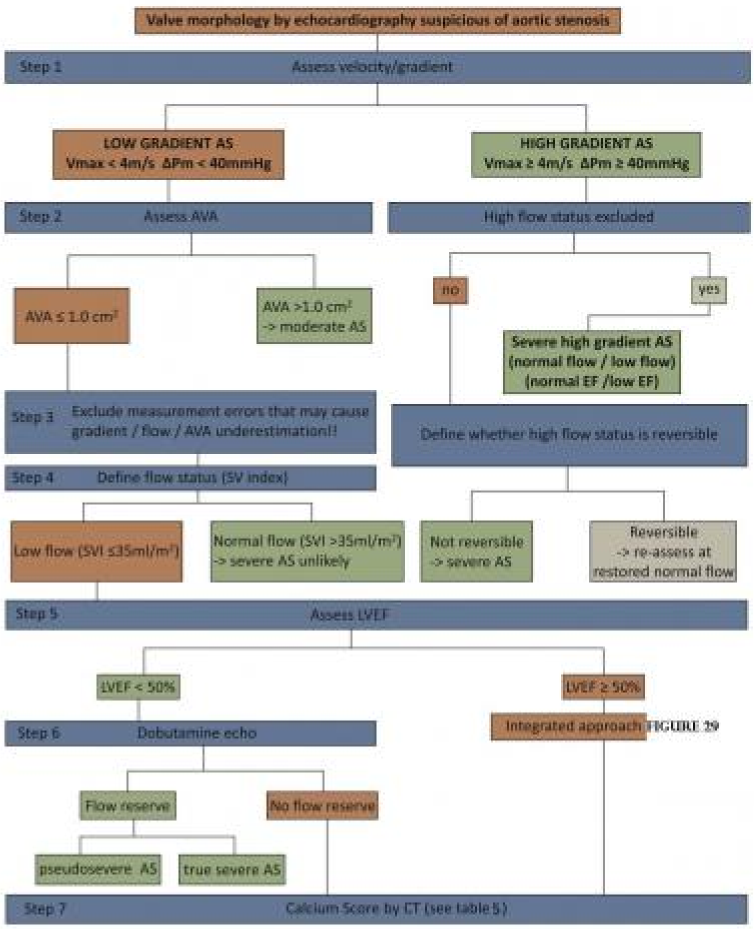


Figure 28

Low gradient patients with AS can have a low flow or normal flow state. In low gradient patients with suspected severe aortic stenosis we have to check or repeat measurements to exclude errors. Decreased left ventricle ejection fraction (LV EF), shunts, left ventricle hypertrophy with small cavity, significant mitral regurgitation can explain low flow state and low gradient. In low flow patients with decreased LV EF it is better to perform low-dose dobutamine stress echocardiography. If contractility and stroke volume increase (presence of contractility reserve) you can differentiate severe and pseudosevere low flow AS. In true severe AS gradient, velocity increase and AVA remains <1.0 cm^2, in pseudosevere AS - gradient, velocity increase and AVA also increases >1.0 cm^2. If LV is not able to increase its contractility and stroke volume (absence of contractility reserve) during dobutamine infusion the patient has a poor prognosis. We can use computed tomography (CT) calcium score to evaluate the possibility of severe aortic stenosis in such a case (in case of calcium score in men ≥ 3000, in women ≥ 1600 the severe aortic stenosis is very likely) (Figure 29, from ASE guidelines 2017). But absence of contractility reserve is a bad prognostic sign. In patients with low flow low gradient AS with normal LV EF we also can use CT calcium score and dobutamine stress test, but it’s less clear.

Criteria that increase the likelihood of severe AS in patients with AVA <1.0 cm^2 and mean gradient <40 mmHg in the presence of preserved EF		
(1) Clinical criteria:		
Physical examination consistent with severe aortic stenosis		
Typical symptoms without other explanation		
Elderly patient (>70 years)		
(2) Qualitative imaging data:		
LVH (additional history of hypertension to be considered)		
Reduced LV longitudinal function without other explanation		
(3) Quantitative imaging data:		
Mean gradient 30–40 mmHg*		
AVA ≤0.8 cm^2		
Low flow (SVi <35 mL/m^2) confirmed by other techniques than standard		
Doppler technique (LVOT measurement by 3D TEE or MSCT; CMR, invasive data)		
Calcium score by MSCT†		
Severe AS likely:	men ≥2000	women ≥1200
Severe AS very likely:	men ≥ 3000	women ≥1600
Severe AS unlikely:	men <1600	women <800

AS, Aortic stenosis; *AVA*, aortic valve area; *CMR*, cardiac magnetic resonance imaging; *EF*, ejection fraction; *LVOT*, left vetricular outflow tract; *MSCT*, multislice comptuted tomography; *SVi*, stroke volume index; *TEE*, transesophageal echocardiography.
*Haemodynamics measured when the patient is normotensive.
†Values are given in arbitrary units using Agatston method for quantification of valve calcification.

Figure 29

TREATMENT STRATEGY

Valve intervention is indicated in all patients with symptomatic severe aortic stenosis who do not have severe comorbidities that will affect the prognosis[16]. Patients with severe symptomatic aortic stenosis have poor prognosis without intervention. As long as the aortic valve gradient is ≥ 40 mm Hg and flow status is normal we can assume that LV function is almost normal and the patient will definitely benefit from intervention. In case of low flow low gradient aortic stenosis and low LV EF the situation is to be clarified. If during dobutamine stress-echocardiography the patient has a contractility reserve and true severe aortic stenosisn aortic valve replacement should be done. If the patient has contractility reserve and pseudosevere aortic stenosis he does not require intervention. In case of absence of the contractility reserve, aortic valve replacement will not give a clear benefit, the patient has poor prognosis (Figure 30, from ESC guidelines, 2017).

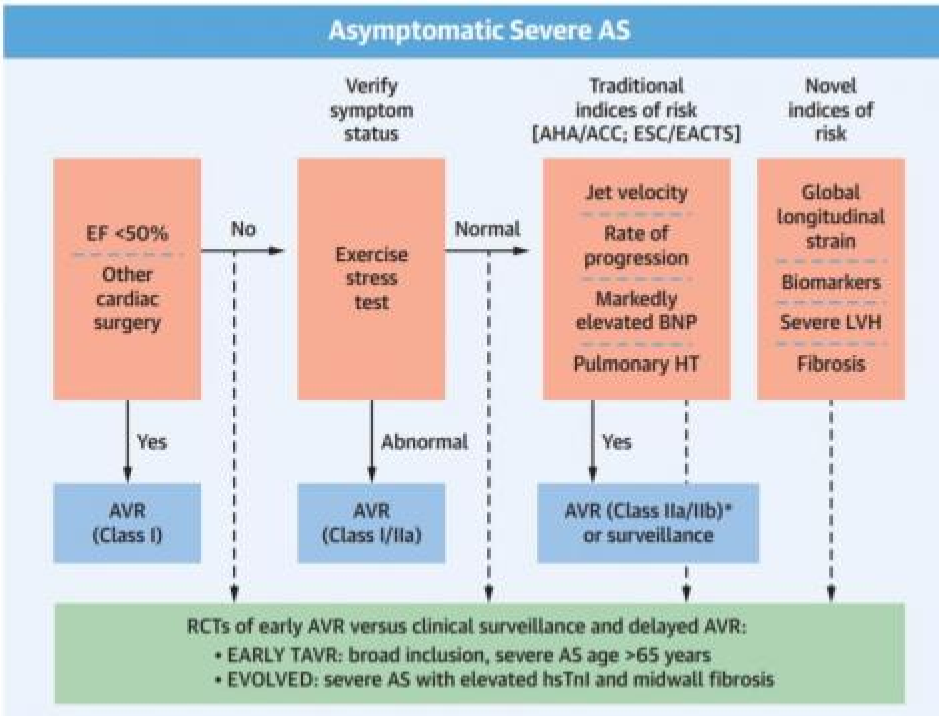


Figure 30

The most challenging question is how to deal with asymptomatic patients with severe aortic stenosis. First of all, we can perform exercise tests to evaluate whether the patient is truly asymptomatic. Moreover, even asymptomatic patients with severe aortic stenosis have poor prognosis. To stratify risk, we need to estimate the rate of progression, the NT-proBNP level, pulmonary hypertension, global longitudinal strain etc[17,18] (Figure 31, from JACC, 2019).

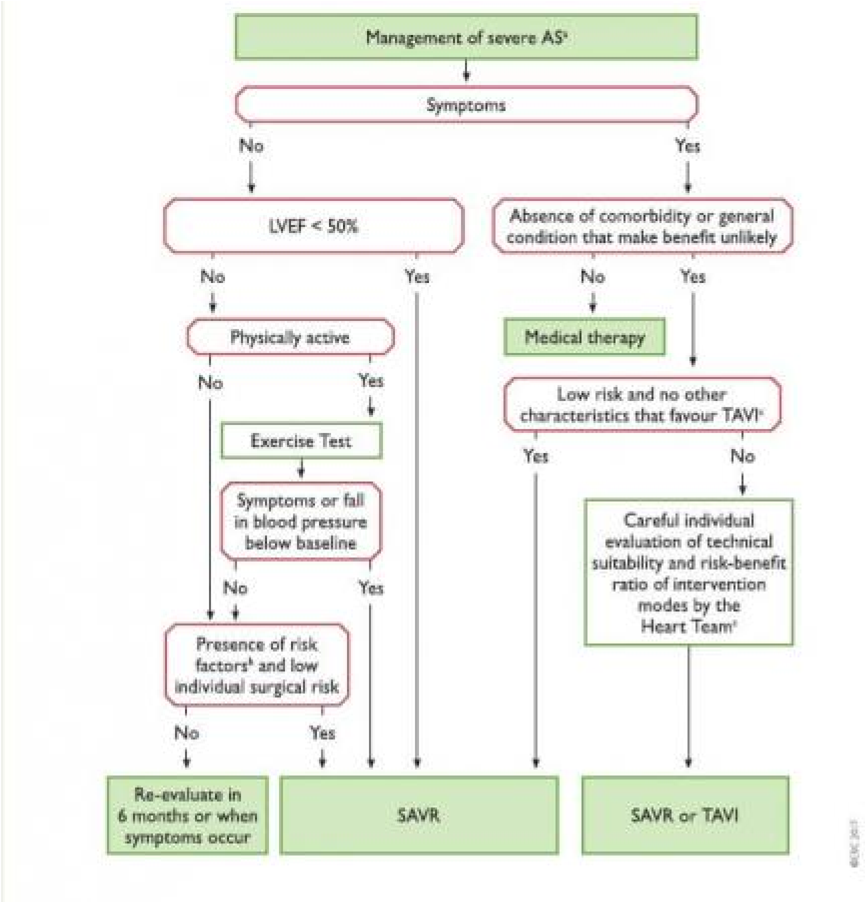


Figure 31

We have two main intervention options: surgical aortic valve replacement (SAVR) and transcatheter aortic valve replacement (TAVR)[19]. The choice of intervention depends on anatomical and technical aspects, clinical characteristics of the patient and additionally required heart or aorta surgery (Figure 32, from ESC guidelines 2017). We receive more and more evidence to use TAVR even in patients with low surgical risk[20].

	Favours TAVI	Favours SAVR
Clinical characteristics		
STS/EuroSCORE II <4% (logistic EuroSCORE I <10%)[a]		+
STS/EuroSCORE II ≥4% (logistic EuroSCORE I ≥10%)[a]	+	
Presence of severe comorbidity (not adequately reflected by scores)	+	
Age <75 years		+
Age ≥75 years	+	
Previous cardiac surgery	+	
Frailty[b]	+	
Restricted mobility and conditions that may affect the rehabilitation process after the procedure	+	
Suspicion of endocarditis		+
Anatomical and technical aspects		
Favourable access for transfemoral TAVI	+	
Unfavourable access (any) for TAVI		+
Sequelae of chest radiation	+	
Porcelain aorta	+	
Presence of intact coronary bypass grafts at risk when sternotomy is performed	+	
Expected patient–prosthesis mismatch	+	
Severe chest deformation or scoliosis	+	
Short distance between coronary ostia and aortic valve annulus		+
Size of aortic valve annulus out of range for TAVI		+
Aortic root morphology unfavourable for TAVI		+
Valve morphology (bicuspid, degree of calcification, calcification pattern) unfavourable for TAVI		+
Presence of thrombi in aorta or LV		+
Cardiac conditions in addition to aortic stenosis that require consideration for concomitant intervention		
Severe CAD requiring revascularization by CABG		+
Severe primary mitral valve disease, which could be treated surgically		+
Severe tricuspid valve disease		+
Aneurysm of the ascending aorta		+
Septal hypertrophy requiring myectomy		+

Figure 32

CONCLUSION

The correct assessment of aortic stenosis severity is the keystone of the treatment strategy. To perform accurate measurements you need to obtain a good image quality and summarize data from different views. If the obtained data is inconclusive you should use multimodal visualization.

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