ASE: Echo Florida
10/9/2017
7:45 AM-8:20 AM

BASIC AND ADVANCED ASSESSMENT OF AORTIC STENOSIS

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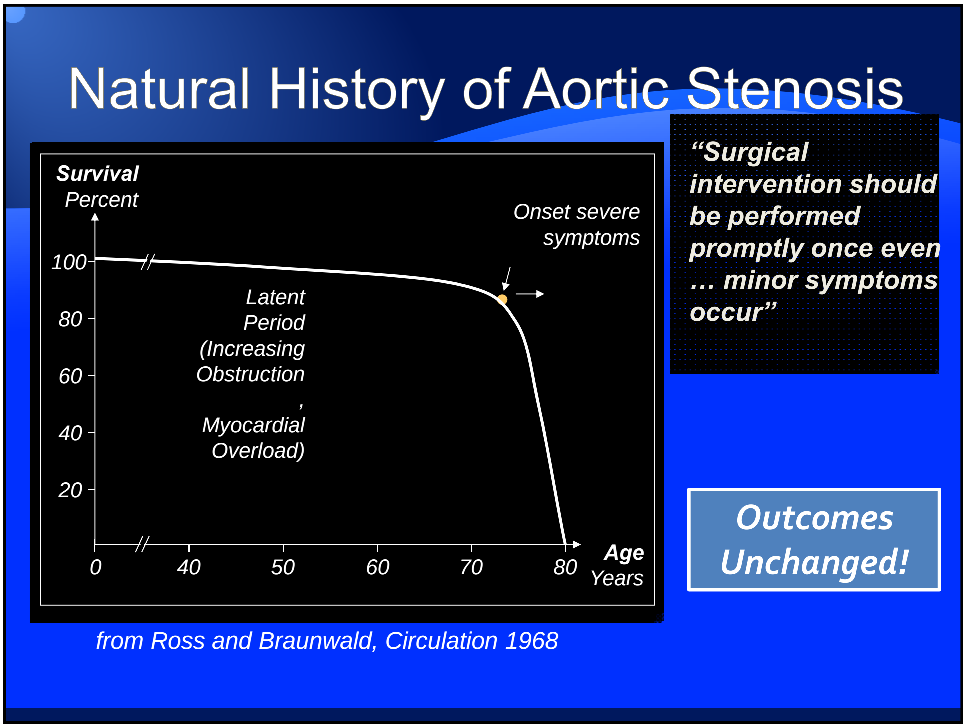
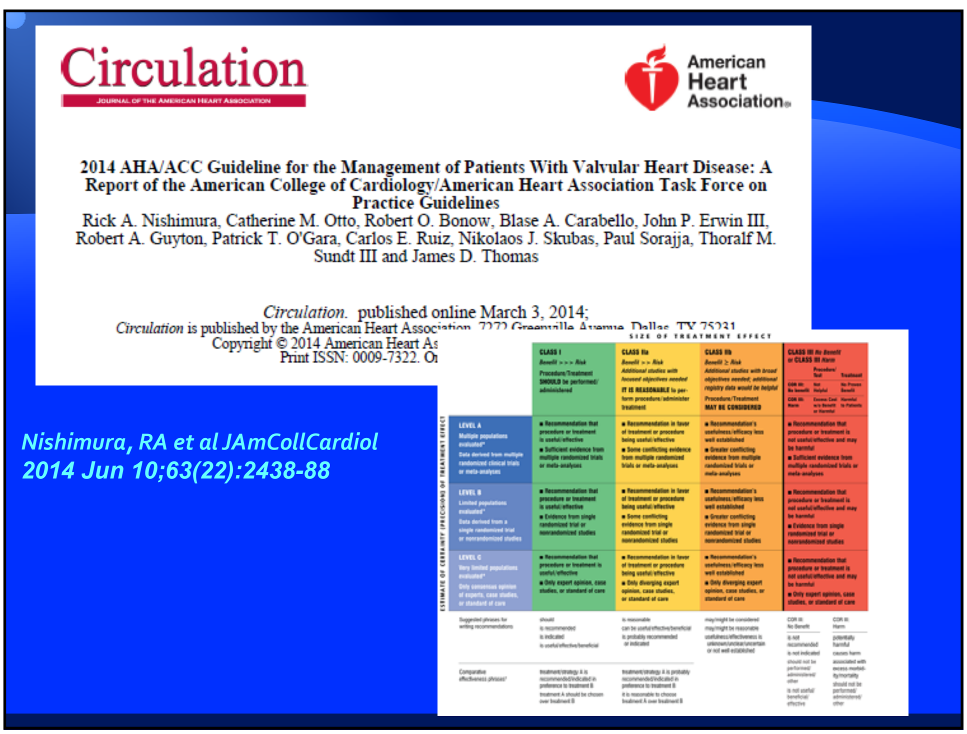
Disclosures

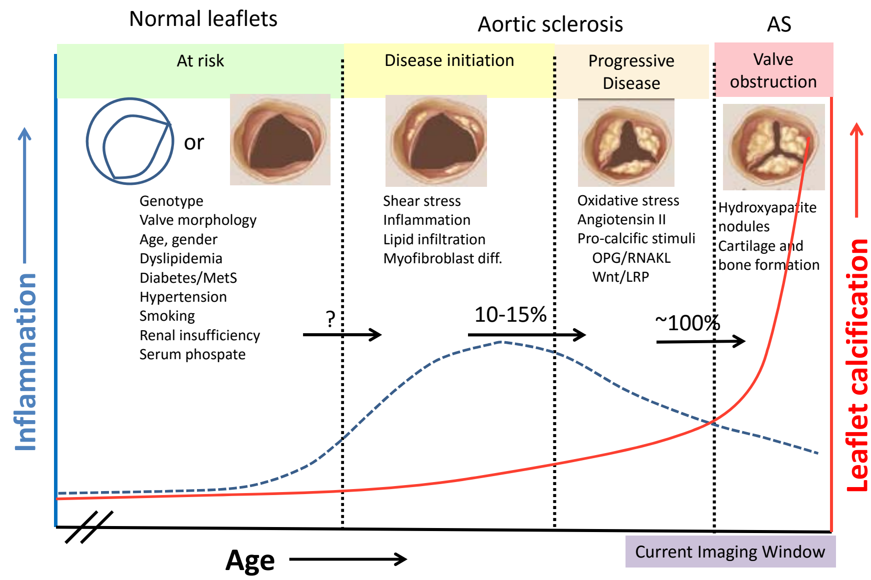
- *Core Lab Director for multiple tricuspid device trials for which I receive no direct compensation:*
  - *SCOUT Trial*
  - *Triluminate Trial*
  - *Tri-Repair Trial*
- *Speaker: Abbott Structural, GE, Philips, Boston Scientific*
- *Consultant: Gore&Associates, NaviGATE, Abbott Structural, GE, Philips*


Natural History of Aortic Stenosis
Survival
Percent
100
80
60
40
20
0
40
50
60
70
80
Age
Years
Onset severe
symptoms
Latent
Period
(Increasing
Obstruction
,
Myocardial
Overload)
"Surgical intervention should be performed promptly once even … minor symptoms occur"
Outcomes Unchanged!
from Ross and Braunwald, Circulation 1968


Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION
American Heart Association
2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines
Rick A. Nishimura, Catherine M. Otto, Robert O. Bonow, Blase A. Carabello, John P. Erwin III, Robert A. Guyton, Patrick T. O'Gara, Carlos E. Ruiz, Nikolaos J. Skubas, Paul Sorajja, Thoralf M. Sundt III and James D. Thomas
Circulation. published online March 3, 2014;
Nishimura, RA et al JAmCollCardiol
2014 Jun 10;63(22):2438-88

2014 ACC/AHA Valve Guidelines

Concept of Valve Disease Stages

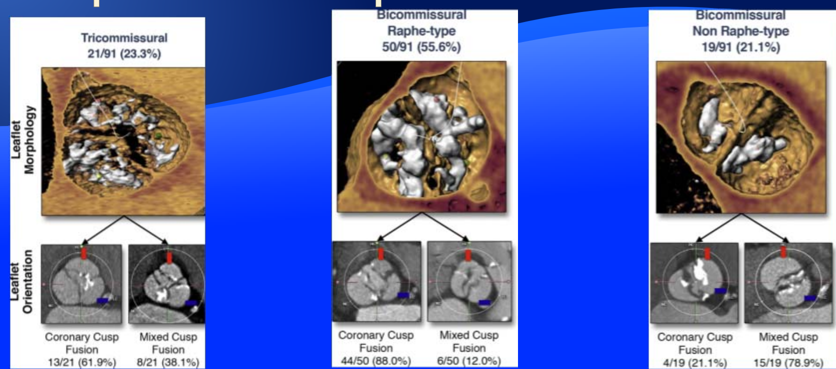


Stages of Valvular AS

Stage	Definition	Valve Anatomy	Valve Hemodynamics
A	At risk	• Bicuspid aortic valve (or other congenital valve anomaly) • Aortic valve sclerosis	• Aortic Vmax <2 m/s
B	Progressive	• 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 Vmax 2.0–2.9 m/s or mean ΔP <20 mm Hg • Moderate AS: Aortic Vmax 3.0–3.9 m/s or mean ΔP 20–39 mm Hg *(Typically AVA > 1.0 cm²)*

Nishimura, RA et al JAmCollCardiol 2014 Jun 10;63(22):2438-88

Proposed TAVR-specific Classification



Tricommissural (1 commissure completely fused between 2 cusps, often referred to as "functional" or"acquired" [functional/acquired] BAV by the surgical and interventional community [in this morphology, fusion is not seen in the basal third of the sinus

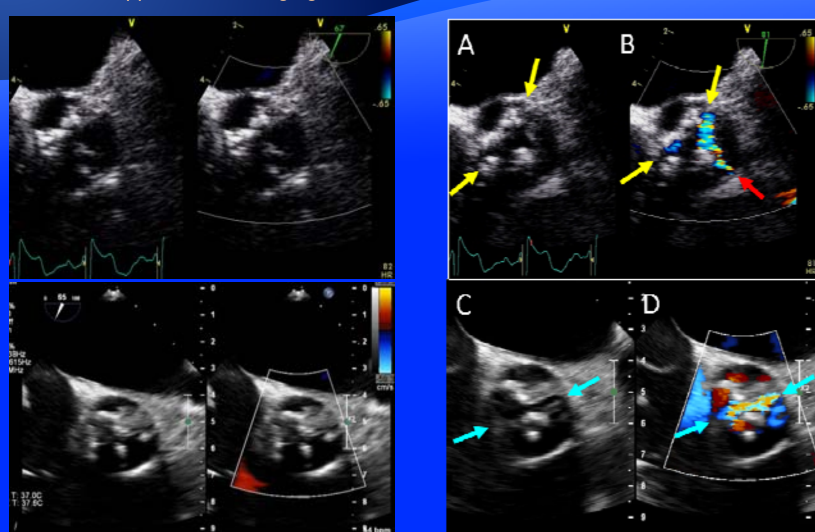
Bicommissural raphe type (in which 2 cusps fused by a fibrous or calcified ridge of various heights, does not reach the height of the commissure [in this morphology, fusion of cusps occurs at or proximal to the basal third of the sinus

Bicommissural non-raphe type (2 cusps completely fused from their basal origin by no visible seam [in this morphology, there are only 2 commissures with no raphe or third commissure

Jilaihawi H et al JACC Img 2016

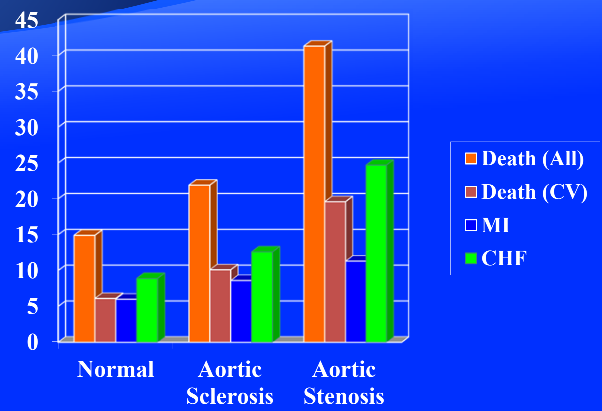
Trileaflet vs Bileaflet Valve

- *Submitted for review: bicuspid valve suspected on CT scan*
- *Color Doppler: clear imaging of flow into 3 commissures*



Hahn RT. Color Doppler to Differentiate Trileaflet From Bicuspid Aortic Stenosis. http://www.acc.org. Aug 31, 2016.

Prognosis of Aortic Sclerosis



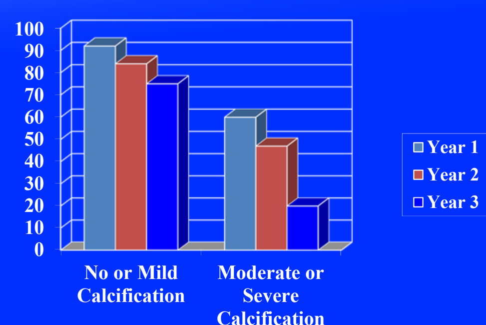
- Increased risk (up to 50%) of death from cardiovascular causes and risk of myocardial infarction even in the absence of a significant hemodynamic load

Otto CM et al. NEJM 1999;341:142-7

Prognosis of Calcification

- The extent of aortic valve calcification was a strong predictor of subsequent events (p<0.001) and event-free survival
- Calcification Score
  - 1 = no calcification
  - 2 = mildly calcified (small isolated spots)
  - 3 = moderately calcified (multiple larger spots)
  - 4 = heavily calcified (extensive thickening and calcification of all cusps)

Event-free Survival in Patient (n = 128) with Asymptomatic AS by Calcification



Rosenhek R, Binder T, Porenta G, et al. Predictors of outcome in severe, asymptomatic aortic stenosis. N Engl J Med 2000;:611-7.

Stages of Valvular AS

Stage	Definition	Valve Anatomy	Valve Hemodynamics
C1	Asymptomatic severe	• Severe leaflet calcification or congenital stenosis with severely reduced leaflet opening	• Aortic Vmax ≥4 m/s or mean ΔP ≥40 mm Hg • AVA typically is ≤1.0 cm2 (or AVAi ≤0.6 cm2/m2) • Very severe AS is an aortic Vmax ≥5 m/s or mean ΔP ≥60 mm Hg
C2	Asymptomatic Severe with LV dysfunction	• Severe leaflet calcification or congenital stenosis with severely reduced leaflet opening	• Aortic Vmax ≥4 m/s or mean ΔP ≥40 mm Hg • AVA typically is ≤1.0 cm2 (or AVAi ≤0.6 cm2/m2)

Nishimura, RA et al JAmCollCardiol 2014 Jun 10;63(22):2438-88

Stages of Valvular AS

Stage	Definition	Valve Anatomy	Valve Hemodynamics
D1	Symptomatic severe high-gradient AS	Severe leaflet calcification or congenital stenosis with severely reduced leaflet opening	• Aortic Vmax ≥4 m/s or mean ΔP ≥40 mm Hg • AVA typically is ≤1.0 cm2 (or AVAi ≤0.6 cm2/m2) but may be larger with mixed AS/AR

Nishimura, RA et al JAmCollCardiol 2014 Jun 10;63(22):2438-88

Severity of AS: Criteria

Severity	Peak Velocity (m/s)	Mean gradient (mm Hg)	AV area (cm²)	AVA Index (cm²/m²)	LVOT:AV VTI Index (DVI)
Mild	< 3.0 (2.6-2.9)*	<20 (<30)†	>1.5	>0.85* (<1.2)‡	>0.5
Moderate	3.0-4.0	20-40* (30-50)†	1.0-1.5	0.6-0.85*	0.25-0.50*
Severe	>4.0	>40 * or 50†	<1.0	<0.6	< 0.25
Critical	> 5.0	>60		<0.6	<0.4*

Note: Aortic valve sclerosis velocity ≤ 2.5 m/s

** EAE/ASE Recommendations*
† ESC Guidelines
‡ Non ACC/ESC guidelines

Nishimura, RA et al JAmCollCardiol 2014 Jun 10;63(22):2438-88

New ASE Guidelines

EACVI/ASE CLINICAL RECOMMENDATIONS

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

CrossMark

Helmut Baumgartner, MD, FESC, (Chair), Judy Hung, MD, FASE, (Co-Chair), Javier Bermejo, MD, PhD, John B. Chambers, MB BChir, FESC, Thor Edvardsen, MD, PhD, FESC, Steven Goldstein, MD, FASE, Patrizio Lancellotti, MD, PhD, FESC, Melissa LeFevre, RDCS, Fletcher Miller Jr., MD, FASE, and Catherine M. Otto, MD, FESC, *Muenster, Germany; Boston, Massachusetts; Madrid, Spain; London, United Kingdom; Oslo, Norway; Washington, District of Columbia; Liege, Belgium; Bari, Italy; Durham, North Carolina; Rochester, Minnesota; and Seattle, Washington*

Baumgartner H et al. J Am Soc Echocardiogr 2017;30:372-92

New ASE Guidelines

Table 2 Measures of AS severity obtained by Doppler-echocardiography

	Units	Formula/method	Cut-off for severe	Concept	Advantages	Limitations
AS jet velocity[12-15]	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[19,20]	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

(1) appropriate in all patients with AS (yellow);
(2) reasonable when additional information is needed in selected patients (green)

Baumgartner H et al. J Am Soc Echocardiogr 2017;30:372-92

New ASE Guidelines

(3) not recommended for clinical use (blue).

Table 2 Measures of AS severity obtained by Doppler-echocardiography

	Units	Formula/method	Cut-off for severe	Concept	Advantages	Limitations
LV % stroke work loss[23]	%	$\%SWL = \frac{\Delta P}{\Delta P + SBP} \cdot 100$	25	Work of the LV wasted each systole for flow to cross the aortic valve, expressed as a % of total systolic work	Very easy to measure. Related to outcome in one longitudinal study	Flow-dependent. Limited longitudinal data
Recovered pressure gradient[24,25]	mmHg	$P_{desc} - P_{vc} = 4 \cdot v^2 \cdot 2 \cdot \frac{AVA}{AoA}\left(1 - \frac{AVA}{AoA}\right)$	-	Pressure difference between the LV and the aorta, slightly distal to the vena contracta, where distal pressure has increased	Closer to the global haemodynamic burden caused by AS in terms of adaptation of the cardiovascular system. Relevant at high flow states and in patients with small ascending aorta	Introduces complexity and variability related to the measurement of the AoA. No prospective studies showing real advantages over established methods
Energy loss index[26]	cm^2/m^2	$ELI = \frac{(AVA \cdot AoA)/(AoA - AVA)}{BSA}$	0.5	Equivalent to the concept of AVA but correcting for distal recovered pressure in the ascending aorta	(As above) Most exact measurement of AS in terms of flow-dynamics. Increased prognostic value in one longitudinal study	Introduces complexity and variability related to the measurement of the AoA
Valvulo-arterial impedance[27]	$mmHg/mL/m^2$	$Z_{VA} = \frac{\Delta P_{net} + SBP}{SVi}$	5	Global systole load imposed to the LV, where the numerator represents an accurate estimation of total LV pressure	Integrates information on arterial bed to the haemodynamic burden of AS, and systemic hypertension is a frequent finding in calcific-degenerative disease	Although named 'impedance', only the steady-flow component (i.e. mean resistance) is considered. No longitudinal prospective study available
Aortic valve resistance[28,29]	$Dynes/s/cm^5$	$AVR = \frac{\Delta P}{Q} =$ [illegible] $\cdot 1333$	280	Resistance to flow caused by AS, assuming the hydrodynamics of a tubular (non flat) stenosis	Initially suggested to be less flow-dependent in low-flow AS, but subsequently shown to not be true	Flow dependence. Limited prognostic value. Unrealistic mathematic modelling of flow-dynamics of AS
Projected valve area at normal flow rate[30]	cm^2	$AVA_{proj} = AVA_{rest} + VC \cdot (250 - Q_{rest})$	1.0	Estimation of AVA at normal flow rate by plotting AVA vs. flow and calculating the slope of regression (DSE)	Accounts for the variable changes in flow during DSE in low flow, low gradient AS, provides improved interpretation of AVA changes	Clinical impact still to be shown. Outcome of low-flow AS appears closer related to the presence/absence of LV contractility reserve

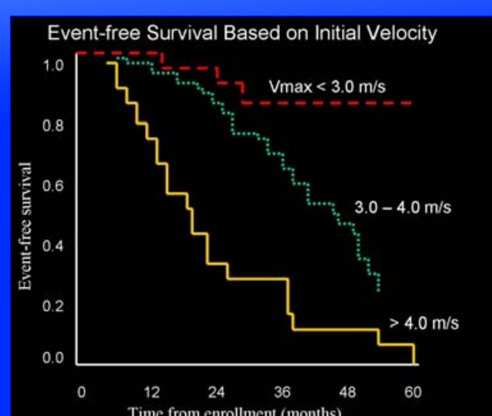
AoA, Crossectional area of the ascending aorta; *AS*, AS jet; *AVA*, continuity-equation-derived aortic valve area; AVA_{proj}, projected aortic valve area; AVA_{rest}, AVA at rest; *AVR*, aortic valve resistance; *BSA*, body-surface area; *DP*, mean transvalvular systolic pressure gradient; *DSE*, dobutamine stress echocardiography; *ELI*, energy-loss coefficient index; *LVOT*, LV outflow tract; *N*, number of instantaneous measurements; P_{desc}, pressure at the ascending aorta; P_{vc}, pressure at the vena contracta; Q, mean systolic transvalvular flow-rate; Q_{rest}, flow at rest; *SBP*, systolic blood pressure; *SWL*, stroke work loss; *TTE and TEE*, transthoracic and transesophageal echocardiography; *TVI*, timevelocity integral; v, velocity; *VC*, valve compliance derived as the slope of regression line fitted to the AVA versus Q plot; *VR*, velocity ratio.
Recommendation for clinical application: (1) appropriate in all patients with AS (yellow); (2) reasonable when additional information is needed in selected patients (green); and (3) not recommended for clinical use (blue).

Baumgartner H et al. J Am Soc Echocardiogr 2017;30:372-92

Appropriate in All Patients

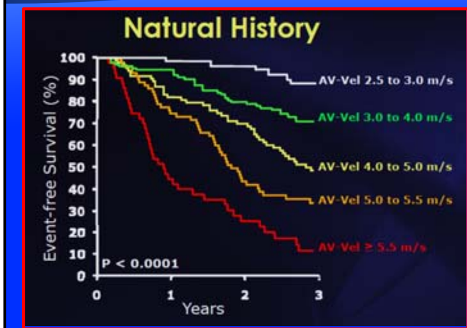
Prognosis of Velocity

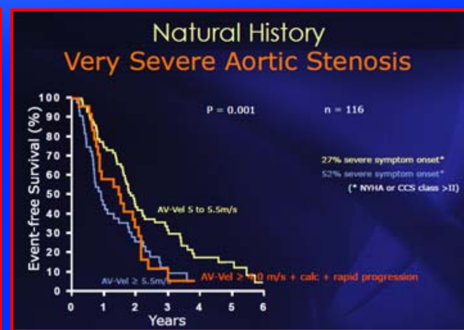
- High rate of clinical events, defined as death or aortic valve surgery for "asymptomatic" aortic stenosis
- On multivariate analysis, only **baseline aortic jet velocity, functional status score, and the rate of change in aortic jet velocity** were predictive of clinical outcome.



Otto C et al. Circulation 1997;95:2262

Spectrum of Aortic Stenosis

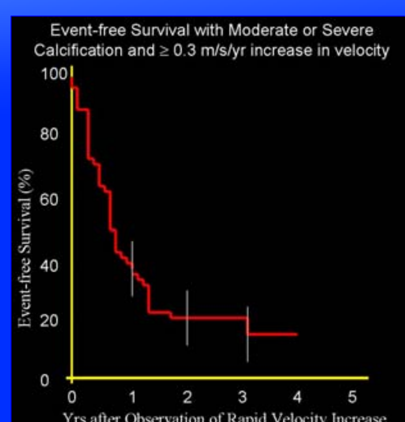




Rosenhek R et al. Eur Heart J 2004;25:199-205
Rosenhek R et al. N Engl J Med 2000;343:611-617
Rosenhek R et al. Circulation 2010;121:151-156

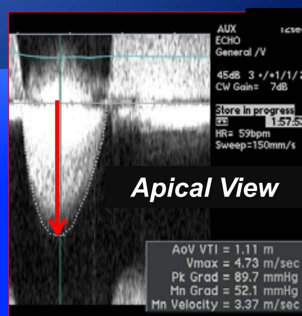
Prognosis of Rate of Velocity Increase

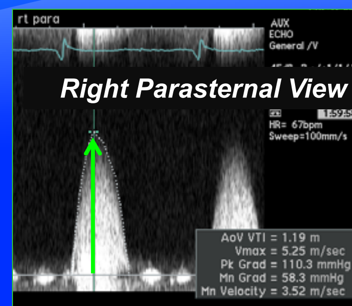
- Of the patients with moderately or severely calcified aortic valves whose aortic jet velocity **increased by 0.3 m/s or more within one year,** 79% underwent surgery or died within two years.



Rosenhek R, Binder T, Porenta G, et al. Predictors of outcome in severe, asymptomatic aortic stenosis. N Engl J Med 2000;:611-7.

Technical Pearl: Peak Velocity





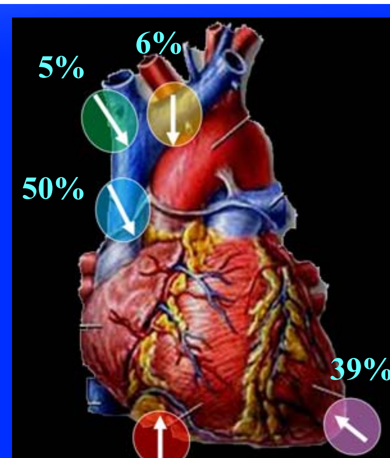
Transaortic Velocity or VTI

1. *Image peak velocity from at least two different windows*
   - *Use of a non-imaging CW probe, particularly for the right parasternal view*
2. *Use the highest velocity profile*
   - *Consider use of contrast to enhance Doppler signals*

Doppler Imaging in Aortic Stenosis: The Importance of the Nonapical Imaging Windows to Determine Severity in a Contemporary Cohort

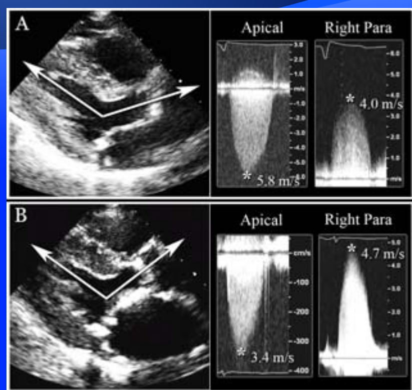
Jeremy J. Thaden, MD, Vuyisile T. Nkomo, MD, MPH, Kwang Je Lee, MD, PhD, and Jae K. Oh, MD, *Rochester, Minnesota and Seoul, Korea*

- V_{max}
  - RPS window in 50%,
  - apex in 39%,
  - suprasternal notch in 6%,
  - right supraclavicular in 5%

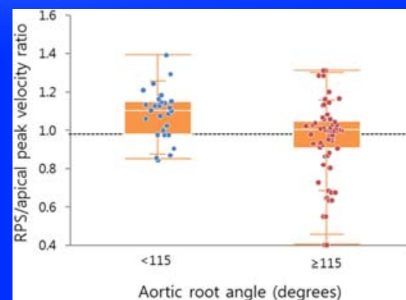


J Am Soc Echocardiogr 2015;28:780-5.

Optimal Doppler Velocity Location Depends on Aortic Root Angulation



J. Thaden and J. Oh et al



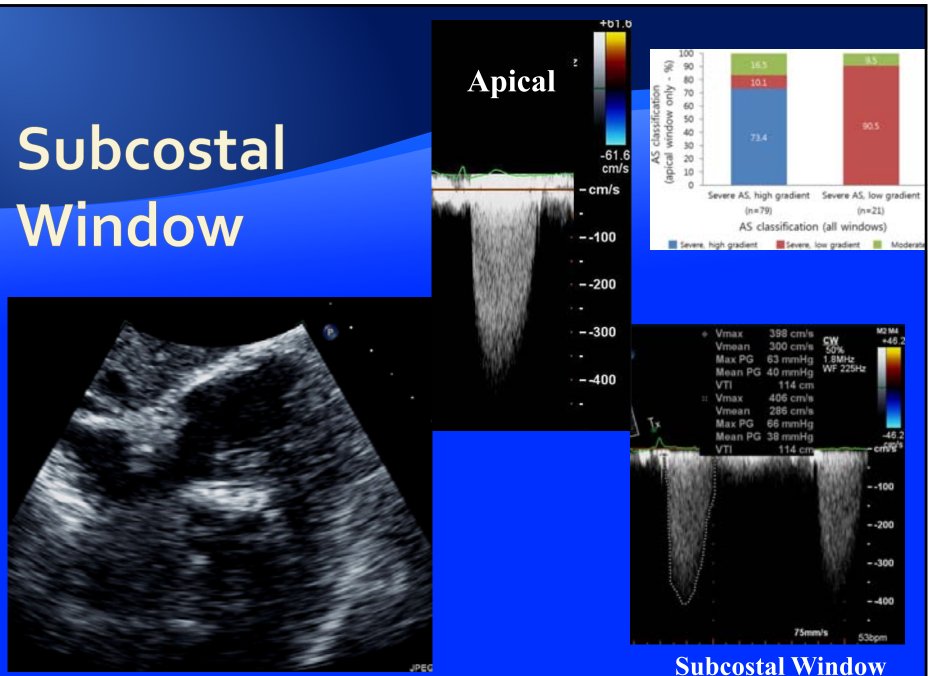
- Overall, the highest AV velocity comes from RPS in 50%
- If the angle<115 degree, it is from RPS in 67%
- AS is underestimated in 15% if only apex is used

Thadden et al. J Am Soc Echocardiogr 2015;28:780-5.

Right Parasternal Window

- Use color Doppler to help determine if right parasternal view is most appropriate

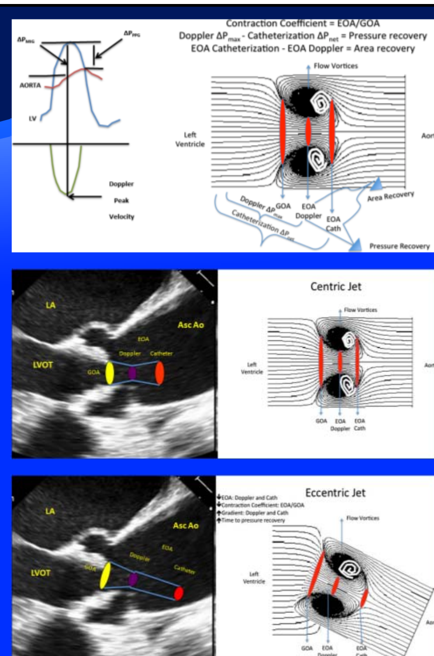
Subcostal Window



Reverse Area Gradient Mismatch

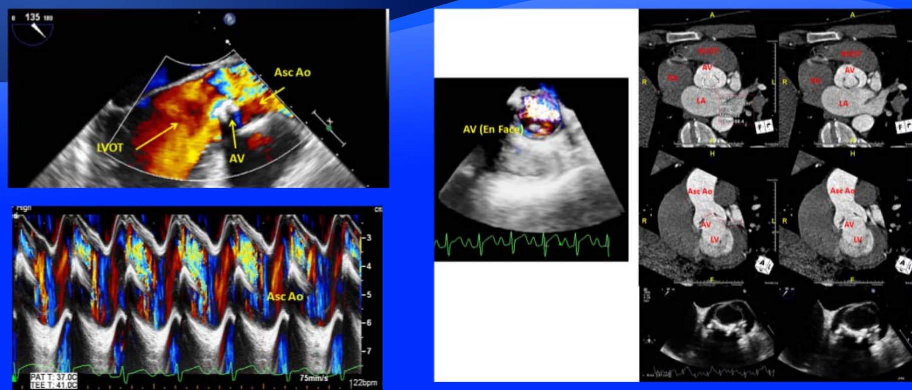
- In patients with aortic stenosis (AS) and eccentric transaortic flow, greater pressure loss occurs as the jet collides with the aortic wall together with delayed and diminished pressure recovery. This leads to the elevated transaortic valve pressure gradients noted on both Doppler and cardiac catheterization

Abbas AE et al. Echocardiography 2015;32:372–382



Bicuspid AV

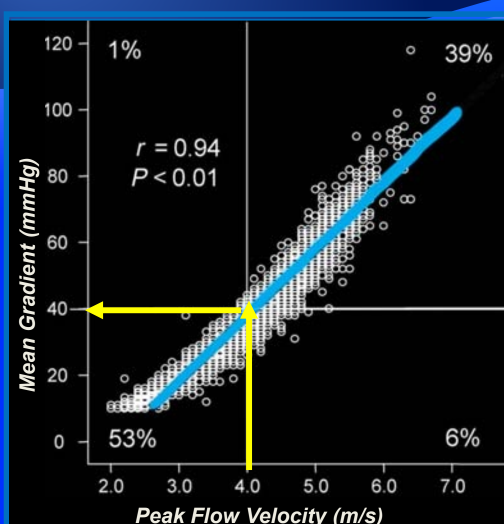
- GOA is determined by aortic valve planimetry using echocardiography, CTA, or MRI imaging.

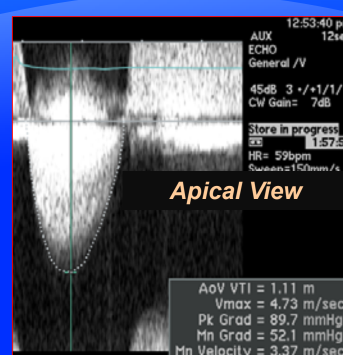


A 23-years-old with known bicuspid aortic valve disease and elevated gradients (mean 57 mmHg, peak 92 mmHg, EOA 1.0 cm2) underwent TEE for further evaluation. TEE imaging confirmed the presence of a bicuspid aortic valve; however, despite single leaflet calcification there was no significant overall valve restriction.

Abbas AE et al. Echocardiography 2015;32:372–382

Peak Velocity and Mean Gradient





Peak transaortic velocity of 4.0 m/s corresponds to a mean gradient of 40 mmHg

Minners, J. et al. Eur Heart J 2008 29:1043-1048

Pitfall of Velocity and Gradient

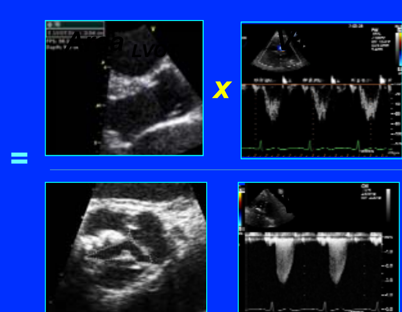
- Velocity and Gradient ignore the influence of cardiac output
  - High cardiac output (stroke volume index >58 cc/m²) → high gradient
    - Aortic regurgitation
    - Hyperdynamic function
  - Low cardiac output (stroke volume index < 35 cc/m²) → low gradient
    - Low flow/reduced EF
    - Low flow/normal EF
      - Small ventricular cavity
      - Significant MR
      - High BP
      - Abnormal contractile function (EF poor measure)

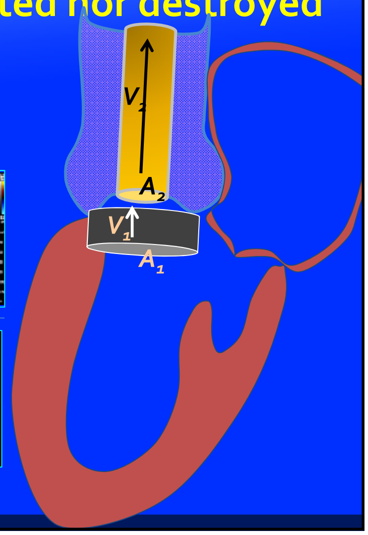
Continuity Equation

- Continuity Equation utilizes the conservation of mass theory

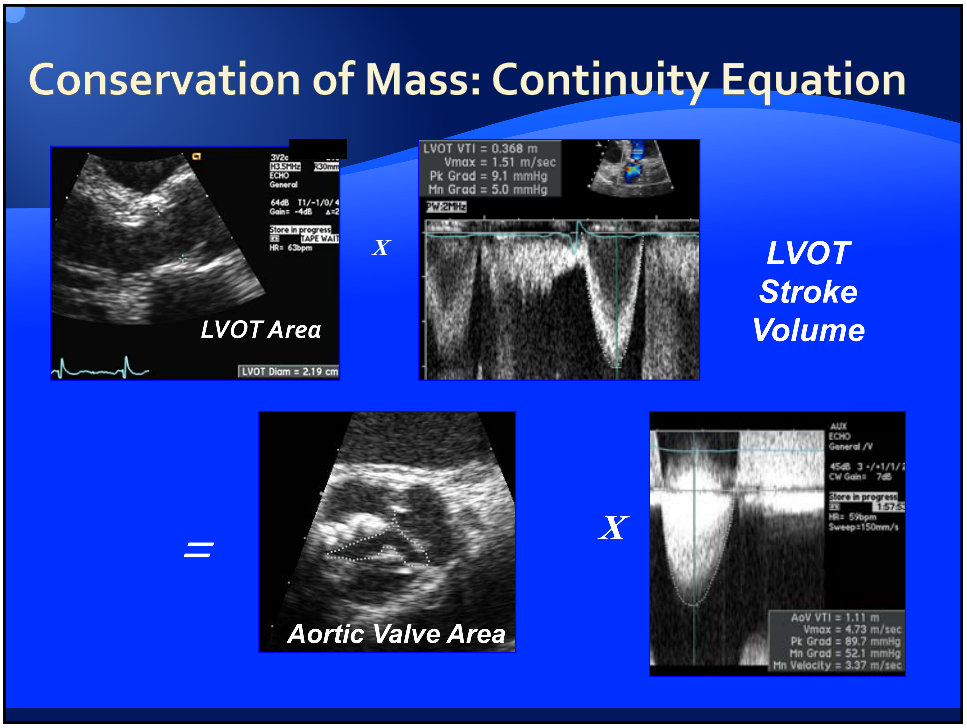
"Mass can be neither created nor destroyed"

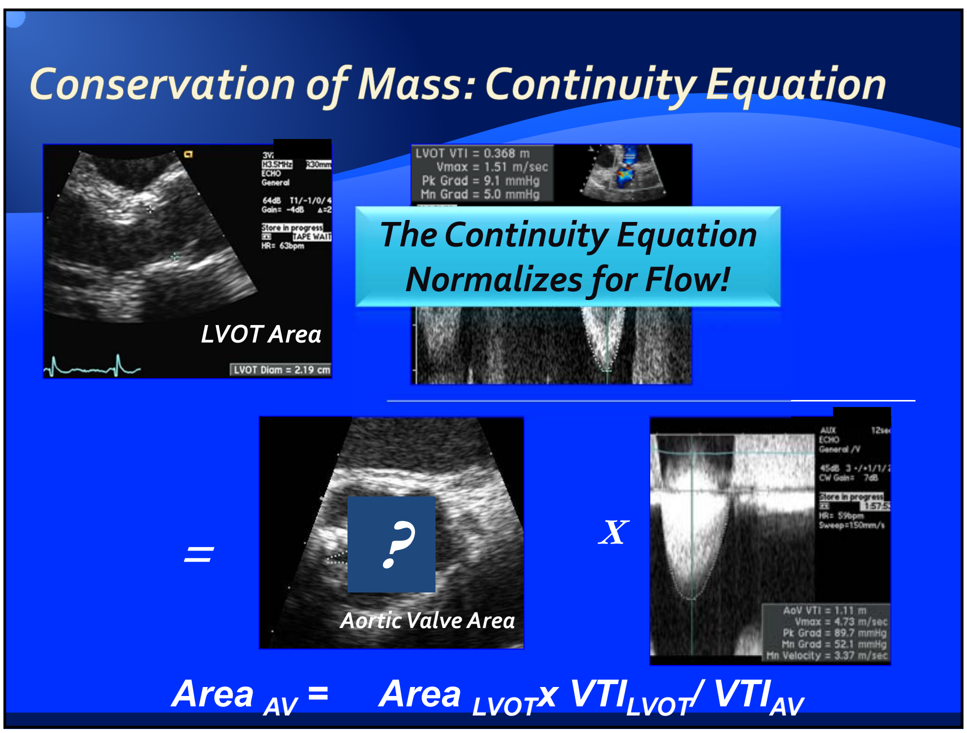
- Stroke Volume$_1$ = Stroke Volume$_2$
- (Area x TVI)$_1$ = *(Area x TVI)$_2$*





NOTE: use of VTI is preferred over Velocity in the Continuity Equation

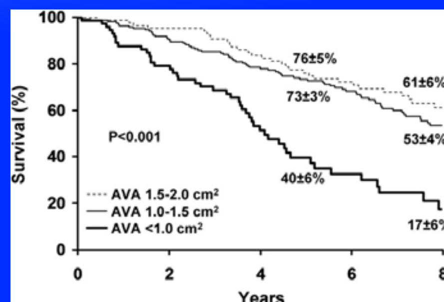

Conservation of Mass: Continuity Equation
LVOT Area
LVOT Diam = 2.19 cm
x
LVOT VTI = 0.368 m
Vmax = 1.51 m/sec
Pk Grad = 9.1 mmHg
Mn Grad = 5.0 mmHg
LVOT
Stroke
Volume
=
Aortic Valve Area
X
AoV VTI = 1.11 m
Vmax = 4.73 m/sec
Pk Grad = 89.7 mmHg
Mn Grad = 52.1 mmHg
Mn Velocity = 3.37 m/sec


Conservation of Mass: Continuity Equation
LVOT Area
LVOT Diam = 2.19 cm
LVOT VTI = 0.368 m
Vmax = 1.51 m/sec
Pk Grad = 9.1 mmHg
Mn Grad = 5.0 mmHg
The Continuity Equation
Normalizes for Flow!
=
?
Aortic Valve Area
X
AoV VTI = 1.11 m
Vmax = 4.73 m/sec
Pk Grad = 89.7 mmHg
Mn Grad = 52.1 mmHg
Mn Velocity = 3.37 m/sec
Area AV = Area LVOT x VTI LVOT / VTI AV

Prognosis of AVA

- Cardiac symptoms were frequent (59%) and unassociated with the AS severity (all P>.13)
- 67% had low gradient/severe AS

- *Excess mortality (vs expected) with AVA< 1.0 cm2*
  - *Symptomatic AS*
    - *Risk ratio, 1.78; [CI 1.33–2.35]; P<.001)*
  - *Asymptomatic AS*
    - *Risk ratio, 1.65; [CI, 1.05–2.47]; P=.02*



Severe AS <1cm² is likely highly sensitive but non-specific

Mean AVA of patients with <1.0 cm² = 0.79 ± 0.14

Malouf, J et al. J Thorac Cardiovasc Surg 2012;-:1-7

Aortic Stenosis:
Pitfalls of the Continuity Equation

- Accuracy of the LVOT diameter
  - error is squared

Variability 5-8%

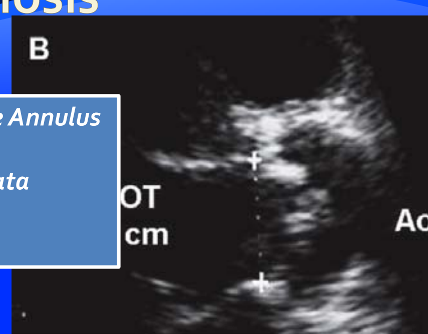
- LVOT velocity
  - angle θ
  - Use laminar flow before pre-stenotic acceleration
- CW aortic velocity inaccuracy
  - measure signal at multiple windows
  - Distinguishing AS from MR
- Nonsimultaneous measurement of LVOT and peak velocities
  - Varying cycle lengths

ASE Guidelines

- Left ventricular outflow tract diameter (LVOTd) is measured in a zoomed parasternal long-axis view in midsystole from the white-black interface (inner-to-inner) of the septal endocardium to the anterior mitral leaflet, parallel to the aortic valve plane.
- Some experts prefer to measure within 0.3– 1.0 cm of the valve orifice whereas others prefer the measurement at the annulus level

Baumgartner H et al. J Am Soc Echocardiogr 2017;30:372-92

LVOT measurement in Aortic Stenosis



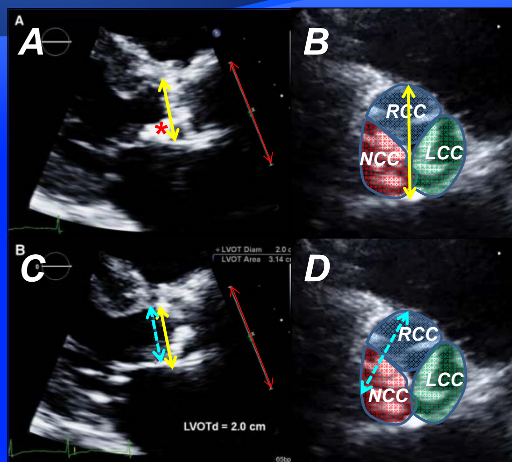
Editorial Comment on measuring at the Annulus for CE (ALL PATIENTS):

1. *Associated with strong outcomes data*
2. *Less variability with cardiac cycle*
3. *More reproducible and accurate*

- Methods:
- With appropriate gain and processing adjustments, the LVOTd was measured in the parasternal long-axis view using a zoomed freeze-frame at early to mid-systole, **inner edge to inner edge, from where the anterior cusp meets the ventricular anteroseptum, to the point where the posterior cusp meets the anterior mitral leaflet**

Michelena HI et al. Heart 2013 Jul;99(13):921-31

Editorial Comment

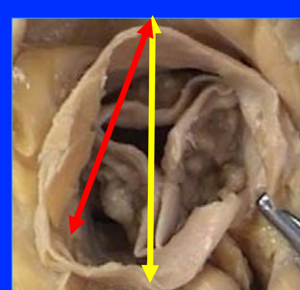


Hahn and Pibarot JASE 2017

- The maximum diameter of the annulus bisects a trigone on one side, and a cusp on the other side (**Yellow arrow**)
- When equal cusps are imaged in LAX view the LVOT and annular diameters may be underestimated (**Blue arrow**)

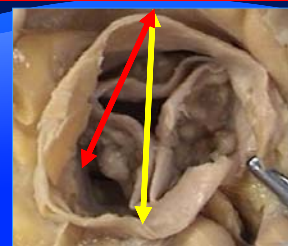
Aortic Valve Anatomy

- The scalloped configuration of the hingelines of the leaflets leave fibrous interleaflet triangles or trigones between the sinuses
- The virtual annulus marks the hingepoints of the cusps (Blue Line)
- The maximum diameter of the annulus bisects a trigone on one side, and a cusp on the other side (Yellow arrow)
  - When equal cusps are imaged in LAX view the LVOT and annular diameters may be underestimated (Red arrow)

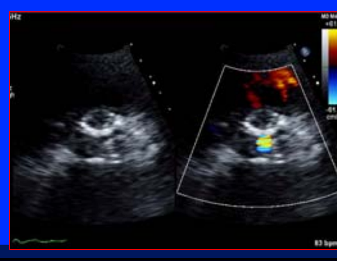


LVOT and Annular Measurement Pearls

- Short-axis (SAX) views may thus be helpful in characterizing the appearance of the valve and aligning the LAX view perpendicular to the largest LVOT diameter



1. *Use the pattern of calcification and valve opening*
2. *Color Doppler jets (systolic and diastolic) may help align the LAX view*



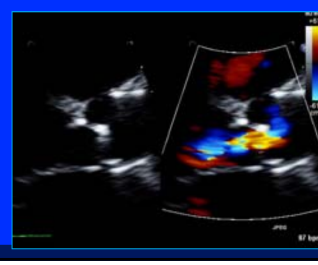


Table 1 Checklist for verification of the accuracy of the measurement of LVOT area for the calculation of AVA for the assessment of aortic stenosis severity

Actions	Interpretation and caveats
Use the midsystolic image that bisects the largest dimension of the aortic annulus: i.e., the plane that bisects the right coronary cusp hinge point anteriorly and the interleaflet triangle between the left and noncoronary cusps posteriorly (see Figure 1B)	If two leaflets are well visualized both anteriorly and posteriorly, this may not be the plane providing the largest diameter, and LVOTd may be underestimated from this view (see Figures 1C and 1D).
Measure LVOTd at the aortic annulus: not 0.5 to 1 cm below	Look for the hinge point of the right coronary cusp anteriorly and measure to the mitral-aortic curtain, perpendicular to the long-axis of the aorta (see Figure 1A).
In the presence of LVOT ectopic calcification: use the plane that bisects the largest diameter but excludes the calcification from the LVOTd measurement (see Figure 1A)	
Calculate predicted LVOTd using the formula: $LVOTd = (5.7 \times BSA) + 12.1$	If the LVOTd measured at the annulus is 2 mm smaller or larger than the predicted LVOTd, suspect error in the measurement of LVOTd. Note that the formula may overestimate LVOTd in obese individuals.
Calculate the DVI: $DVI = VTI_{LVOT}/VTI_{AoV}$	If AVA is $<1.0\ cm^2$ and indexed AVA is $<0.6\ cm^2/m^2$ but DVI is >0.25, suspect underestimation of LVOTd.
Corroborate the calculation of LVOT area obtained by 2D TTE with other modalities:	
3D TTE or TEE	Accuracy of 3D TTE determined by the echogenicity of the patient.
MDCT	Planimetered LVOT by MDCT area may be larger than LVOT area calculated using a linear diameter.
Corroborate the measure of LVOT stroke volume by other methods:	
Biplane Simpson	Biplane Simpson may underestimate stroke volume.
3D TTE volumes	Accuracy of 3D TTE determined by the echogenicity of the patient.
Corroborate the measure of AVA by other methods:	
Planimetry of AVA by TTE or TEE	The "anatomic" AVA measured by planimetry is often larger than the "effective" area measured by the continuity equation because of the flow contraction that occurs downstream of the valve orifice.
Hybrid MDCT-Doppler: LVOT area is measured by MDCT and used in the continuity equation to calculate the "hybrid" AVA	The hybrid method systematically measures larger AVAs, and therefore a larger cutoff value (i.e., <1.2 instead of $1.0\ cm^2$) should be used to define severe aortic stenosis.[6]
In the presence of discordant grading (small AVA with low gradient), calculate indexed AVA: AVA/BSA (cm^2/m^2)	A small AVA in a small patient may correspond to moderate AS. In such patients, the AVA is $<1.0\ cm^2$, suggesting severe AS, but the indexed AVA is $>0.6\ cm^2/m^2$, with a low gradient (<40 mm Hg), suggesting that the stenosis is in fact not severe. The indexed AVA may overestimate the severity of AS in obese patients.

AoV, Aortic valve; *AS*, aortic stenosis; *BSA*, body surface area; *DVI*, Doppler velocity index; *LVOTd*, LVOT diameter; *MDCT*, multidetector computed tomography; *TEE*, transesophageal echocardiography; *3D*, three-dimensional; *TTE*, transthoracic echocardiography.

Hahn and Pibarot JASE 2017

Journal of Cardiovascular Computed Tomography 8 (2014) 52–57

Available online at www.sciencedirect.com
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journal homepage: www.JournalofCard

Original Research Article

Effect of the ellipsoid shape of the lef outflow tract on the echocardiograph of aortic valve area in aortic stenosis

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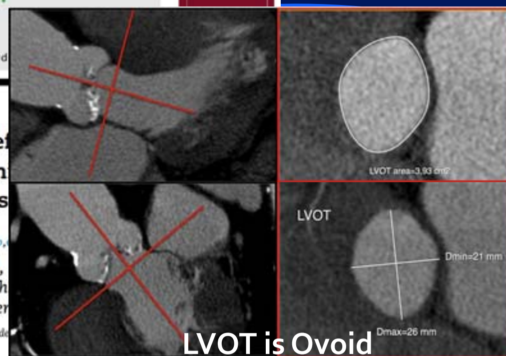

- Assuming that LVOT area is circular with TTE results in constant underestimation of the AVA with the continuity equation compared with MDCT planimetry
- The elliptical not circular shape of LVOT largely explains these discrepancies

J Cardiovasc CT 2014;8:52-57

JACC: CARDIOVASCULAR IMAGING VOL. 8, NO. 3, 2015
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Aortic Valve Area Calculation in Aortic Stenosis by CT and Doppler Echocardiography

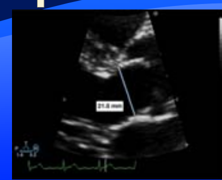
Marie-Annick Clavel, DVM, PhD,* Joseph Malouf, MD,* David Messika-Zeitoun, MD, PhD,†‡ Phillip A. Araoz, MD,* Hector I. Michelena, MD,* Maurice Enriquez-Sarano, MD*

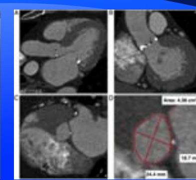
- 269 patients with isolated calcific AS
- Doppler and MDCT at same episode of care
- AVA was calculated by echocardiography (AVAEcho) and by MDCT (AVACT) using each techniquemeasurement of LVOT area.
- And measured by planimetry (AVAPlani).

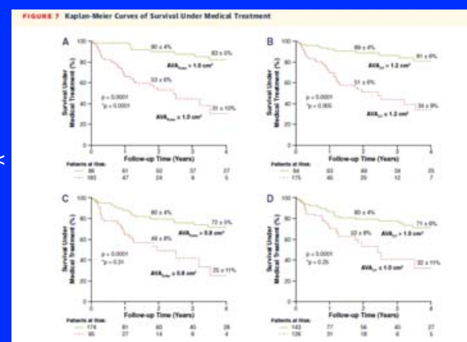
Clavel MA, Malouf J, Messika-Zeitoun D, Araoz PA, Michelena HI, Enriquez-Sarano M. Aortic valve area calculation in aortic stenosis by CT and Doppler echocardiography. JACC Cardiovasc Imaging. 2015;8(3):248-57.

Head-to-head Comparison

- AVACT was larger than AVAEcho (difference 0.12± 0.16 cm2; p < 0.0001) but **did not improve outcome prediction.**
- **Correlation gradient-AVA was slightly better with AVAEcho than AVACT** (r = 0.65 with AVAEcho vs. 0.61 with AVACT; p = 0.01), and discordant gradient-AVA was not reduced.
- For long-term survival, after multivariable adjustment, **AVAEcho or AVACT were independently predictive** (hazard ratio [HR]: 1.26, 95% confidence interval [CI]: 1.13 to 1.42; p < 0.0001 or HR: 1.18, 95% CI: 1.09 to 1.29 per 0.10 cm2 decrease; p < 0.0001) with a similar prognostic value (p ≥ 0.80).
- **Thresholds for excess mortality differed between methods: AVAEcho ≤1.0 cm2** (HR: 4.67, 95% CI: 2.22 to 10.50; p < 0.0001) **versus AVACT ≤1.2 cm2** (HR: 3.16, 95% CI: 1.64 to 6.43; p = 0.005),

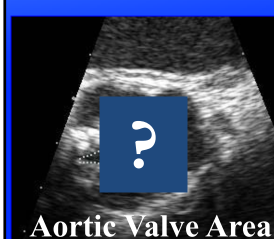






(Clavel et al. J Am Coll Cardiol Img 2015;8:248–57)

Doppler Index (Dimensionless Index)



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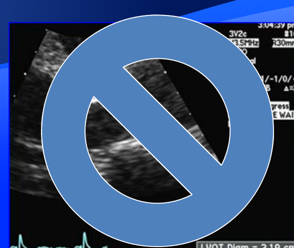
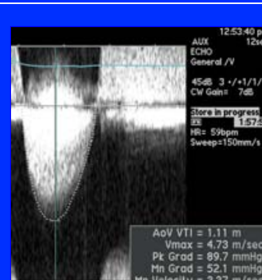


X



Doppler Index (DI)

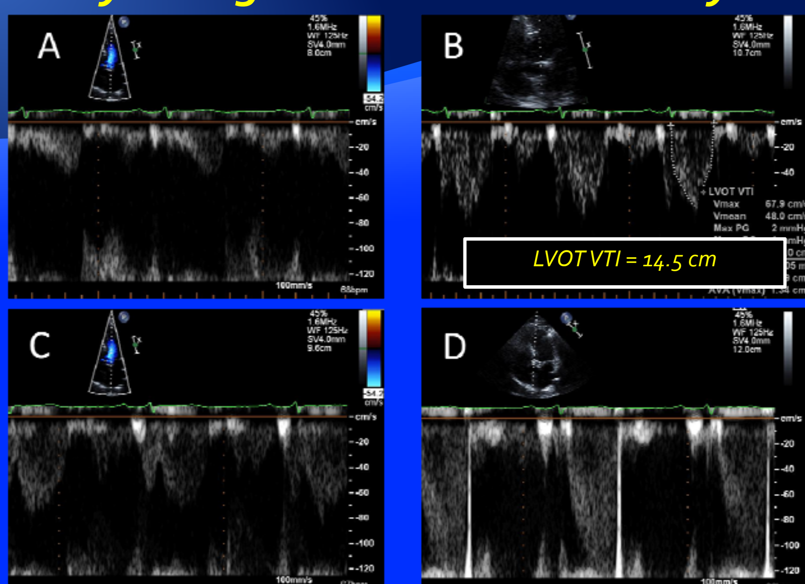
Criteria for severe is a DI < 0.25.

For TAVR patients, DI < 0.2

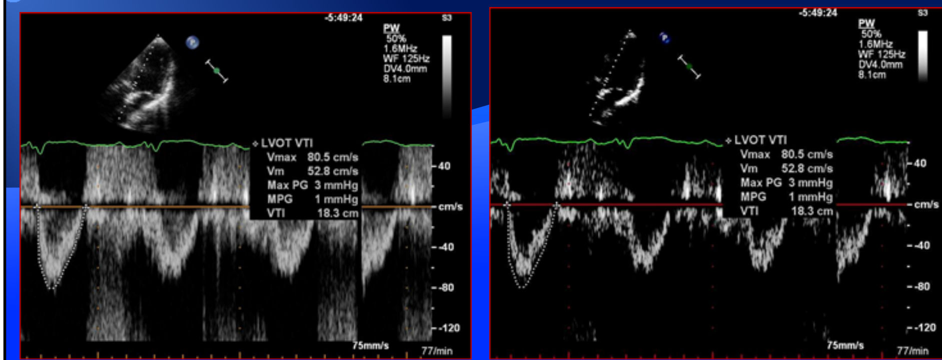
Aortic Stenosis:
Pitfalls of the Continuity Equation

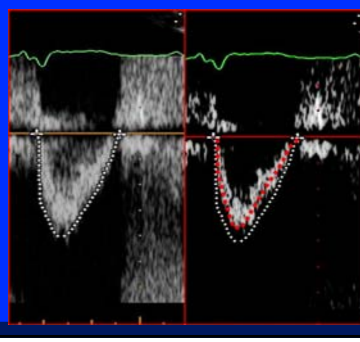
- Accuracy of the LVOT diameter
  - error is squared
- LVOT velocity
  - Angle θ
  - Use laminar flow before pre-stenotic acceleration
- CW aortic velocity inaccuracy
  - measure signal at multiple windows
  - Distinguishing AS from MR
- Nonsimultaneous measurement of LVOT and peak velocities
  - Varying cycle lengths

Key: Image Correct LVOT Velocity Profile



Use laminar flow before pre-stenotic acceleration



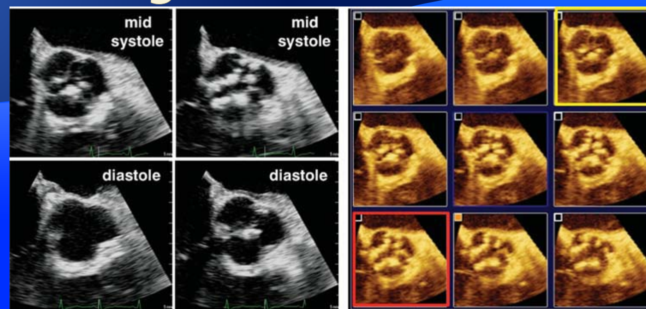


- **MODAL velocity**
  - *Not the maximum velocities of a few blood cells*
  - *Rather the most frequent value in a distribution*
    - *Lower gain and/or increase reject*

Planimetry of AVA: When Doppler not available

- Transthoracic echo
  - Limitations of transthoracic resolution
    - **Feasible in 76% of patients (range in literature 13-85%)**
    - Highly calcified (more severe stenosis), more difficult
    - **Lower window for short-axis views**
    - **Small range of mild to severe stenosis (0.25 cm²) makes small errors unacceptable**

2D TEE vs 3D TEE for AVA



- Aortic annulus moves cranially during early systole and caudally during the remainder of systole and isovolumic relaxation.
  - This motion affects the 2D TEE measurement of area
- Although AVA correlated well between 2DTEE and 3DTEE methods (r = 0.95), 2DTEE showed a significantly larger AVA compared with 3DTEE method

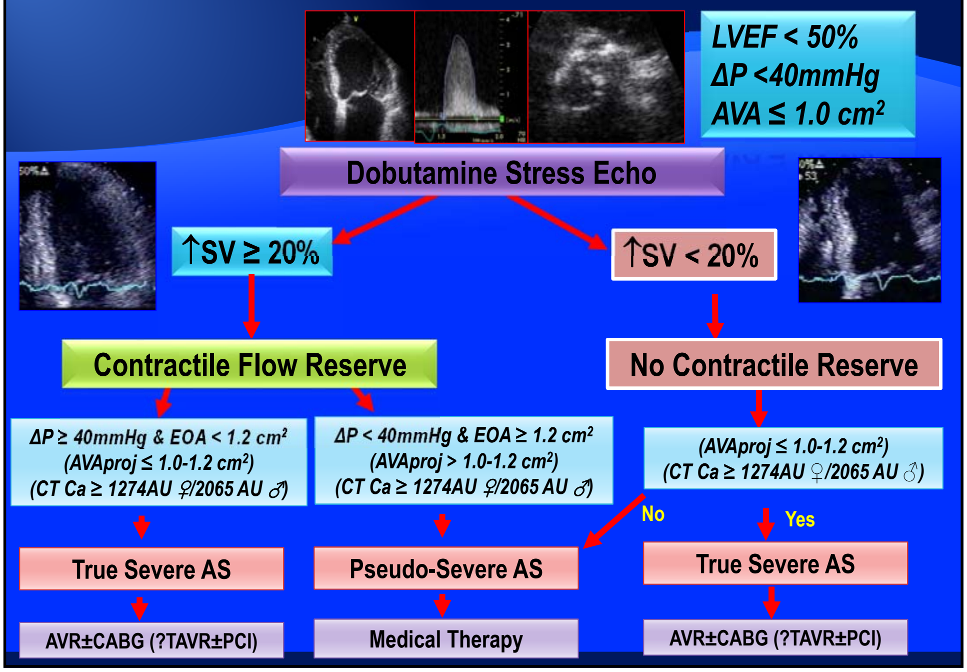
Nakai H et al. Eur J Echo 2010;11:369–376

Stages of Valvular AS

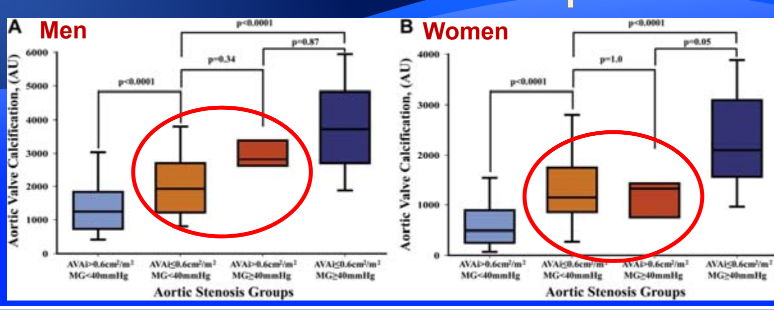
Stage	Definition	Valve Anatomy	Valve Hemodynamics
D1	Symptomatic severe high-gradient AS	Severe leaflet calcification or congenital stenosis with severely reduced leaflet opening	• Aortic Vmax ≥4 m/s or mean ΔP ≥40 mm Hg • AVA typically is ≤1.0 cm2 (or AVAi ≤0.6 cm2/m2) but may be larger with mixed AS/AR
D2	Symptomatic severe low-flow/low-gradient AS with reduced LV EF	Severe leaflet calcification with severely reduced leaflet opening	• AVA ≤1.0 cm2 with Aortic Vmax <4 m/s or mean ΔP <40 mm Hg • Dobutamine stress echocardiography shows AVA ≤1.0 cm2 with Vmax ≥4 m/s at any flow rate
D3	Symptomatic severe low-gradient AS with normal LVEF or paradoxical low-flow severe AS	Severe leaflet calcification with severely reduced leaflet opening	• AVA ≤1.0 cm2 with Aortic Vmax <4 m/s or mean ΔP <40 mm Hg • AVAi ≤0.6 cm2/m2 and • Stroke volume index <35 mL/m2 • Measured when patient is normotensive (systolic BP <140 mm Hg)

Nishimura, RA et al JAmCollCardiol 2014 Jun 10;63(22):2438-88

D2: Approach to Low-Flow, Low-Gradient AS, Low EF



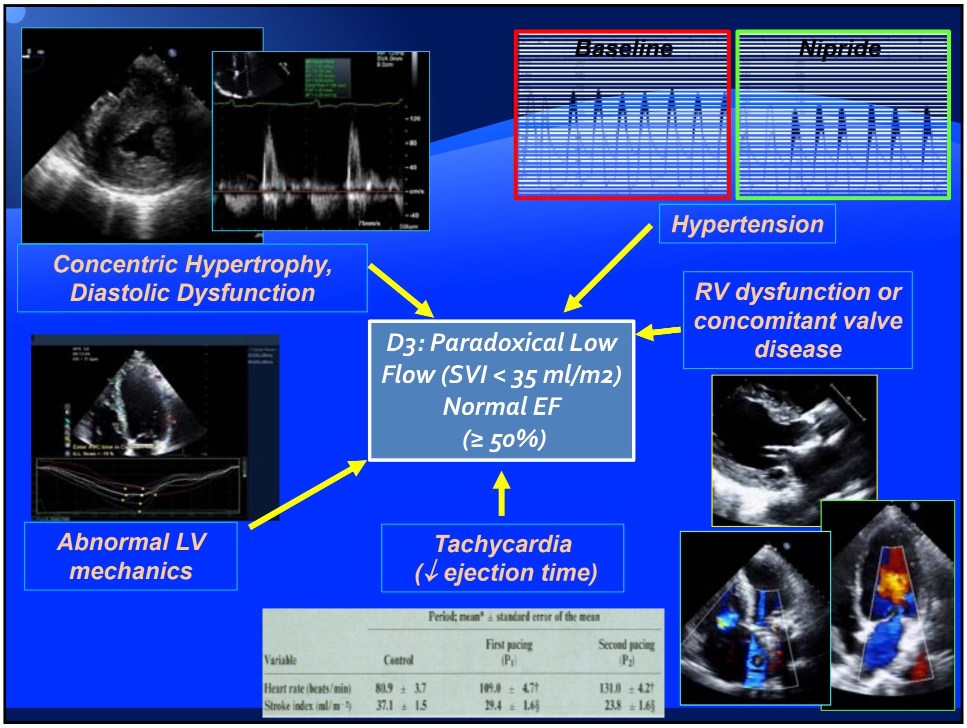
Distribution of Aortic Valve Calcification by Sex in the Various AS Groups



1. Range of AVC load in patients with "Discordant Gradient" is wide, suggesting that this group is heterogeneous.
2. Half of these patients had evidence of severe calcified aortic valve disease on the basis of AVC load measured by MDCT

	Women	Men
AVC	1,274 AU	2,065 AU
AVC density	292 AU/cm2	476 AU/cm2

(Note: AVC density = AVC indexed to annulus cross-sectional LVOT area)



D3 Patients

Table 5 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.

Don't forget the appearance of the valve on Echo

Baumgartner H et al. J Am Soc Echocardiogr 2017;30:372-92

Classification of AS

- In patients with a valve area <1.0 cm2, further classification based on the combinationof velocity (gradient), transvalvular SV, and LV ejection fraction is recommended as follows:
  - high gradient (velocity≥4 m/s or mean gradient ≥ 40 mmHg) vs. low gradient (mean gradient <40 mmHg);
  - normal flow (SVi ≥ 35 mL/m2) vs. low flow (SVi <35 mL/m2);
  - preserved ejection fraction (≥ 50%) vs. reduced ejection fraction (<50%).

Baumgartner H et al. J Am Soc Echocardiogr 2017;30:372-92

Flow and Gradient

LF/HG and NF/HG AS patterns raise less controversy and are encountered in up to 70% of patients. In these categories, AVR improves outcomes

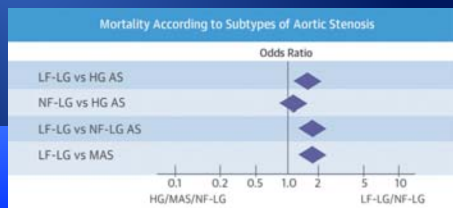
Gradient \ Flow	Normal	Low
High	NF/HG	LF/HG
Low	NF/LG	LF/LG

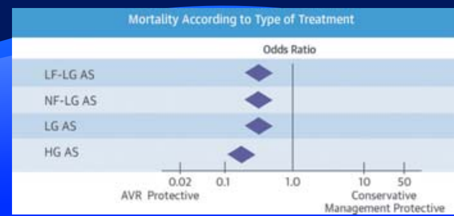
Hemodynamic profile and pattern of myocardial adaptation to pressure load similar to moderate AS HOWEVER aree outcomes similar to HG AS?

Associated with the reduced SVi, worse NYHA class, and poor survival at 3 years, improved survival with AVR

Dayan V et al, J Am Coll Cardiol. 2015;66::2594-603

Low Gradient Aortic Stenosis





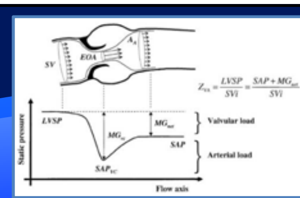
- Patients with LF-LG AS have increased mortality compared with
  - Moderate AS (hazard ratio [HR]: 1.68; 95% confidence interval [CI]: 1.31 to 2.17)
  - NF-LG (HR: 1.80; 95% CI: 1.29 to 2.51),
  - High-gradient (HR: 1.67; 95% CI: 1.16 to 2.39) AS.
- AVR was associated with
  - Reduced mortality in patients with LF-LG (HR: 0.44; 95% CI: 0.25 to 0.77).
  - Similar beneift in patients with NF-LG (HR: 0.48; 95% CI: 0.28 to 0.83).

Compared with patients with high-gradient AS, those with LF-LG were less likely to be referred to AVR (odds ratio: 0.32; 95% CI: 0.21 to 0.49).

Dayan V et al J Am Coll Cardiol 2015;66:2594–603

Not Recommended for Clinical Use (?)

Pressure Recovery in Aortic Stenosis



- Catheterization AVA by Gorlin formula is derived from recovered pressures.
- In these patients EOA by Doppler may lead to an overestimation of the severity of AS
  - **Pressure recovery depends on the ratio of EOA_{Dop} and Ao_A**
  - **The smaller the EOA_{Dop} relative to the A_A, the more flow turbulence will occur and the less pressure recovery**

Garcia D et al. J Am Coll Cardiol 2003;41:435–42
Pibarot and Dumesnil.J Am Coll Cardiol 2012;60:169–80

Pressure Recovery

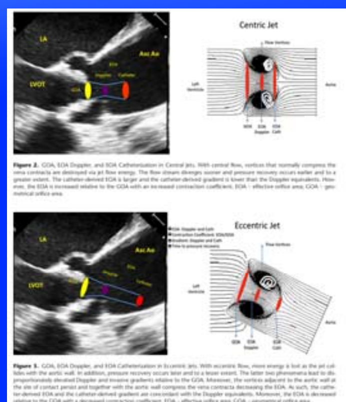
- **Pressure recovery becomes most relevant**
  - **Moderate to severe AS (Doppler EOA between 0.8 cm² and 1.2 cm²)**
  - **Small aortas (diameter at the sinotubular junction < 30 mm)**

$$P_{distal} - P_{VC} = 4v^2 x\ 2\ x\ (EOA / Ao_A)\ x\ (1- [EOA/Ao_A])$$

Pibarot and Dumesnil.J Am Coll Cardiol 2012;60:169–80.

Pressure Recovery in Bicuspid Aortic Stenosis

- **Eccentric jets have less pressure recovery since reconvertable energy is lost when an eccentric jet hits the aortic wall.**



- The Geometric Orifice Area (GOA) is determined by aortic valve planimetry using echocardiography, CTA, or MRI imaging with good correlation.
- The planimetered GOA was significantly larger (1.19 ± 0.35 cm^2) than EOA (0.89 ± 0.29 cm^2) in the bicuspid AS group (r = 0.71, P < .001, Δ = 0.29 ± 0.25 cm^2). This difference is not seen with trileaflet valves.

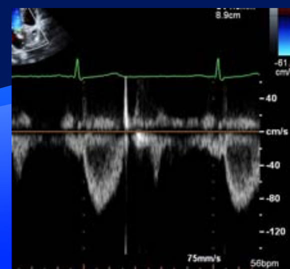
Abbas A et al Echocardiography 2015;32:372–382

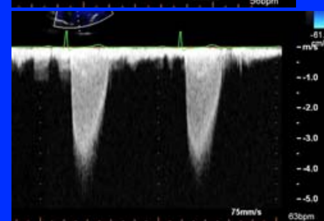
Donal E, et al. J Am Soc Echocardiogr. 2005;18(12):1392-8.

Bicuspid AV

Systolic Ascending Aorta diameter = 2.8 cm

Pressure Recovery in AS

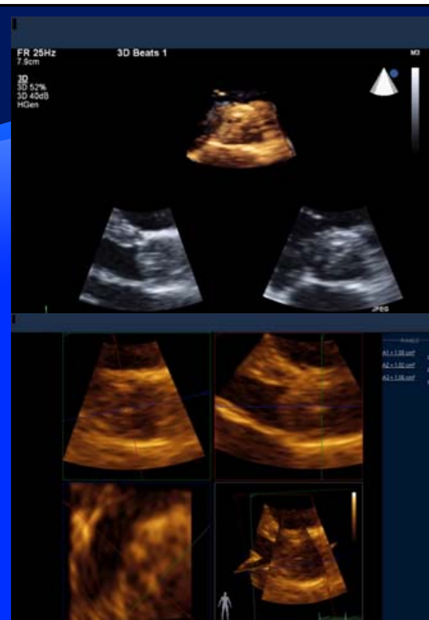




- *AVA = 0.85 cm2, DI = 0.26*
- *Energy Loss Index*
  $= [(EOA \times A_A)/(A_A\text{-}EOA)]/BSA$

  $= [(0.85\ cm^2 \times 6.15\ cm^2)/(6.15\ cm^2 - 0.85\ cm^2)]/BSA$
  $= 5.23\ cm^4/5.30\ cm^2]/1.56\ m^2$
  $= 0.99\ cm^2/1.56\ m^2$
  $= 0.63\ cm^2/m^2$

- *MODERATE AS*



Planimetered AVA = $1.02 cm^2$
$= 0.65\ cm^2/m^2$

Note: Patient exercised on Bruce Protocol for 14 min without symptoms

Energy Loss Index

- The energy loss coefficient (ELCo) provides an accurate estimation of the energy loss (EL) due to aortic stenosis using the calculated EOA_{Dop} and the cross-sectional area of the ascending aorta in systole (Ao_A).
- Energy loss index Advantages:
  - Takes into account the effects of both pressure recovery and body size.
  - In a substudy of the SEAS (Simvastatin Ezetimibe in Aortic Stenosis) trial 47.5% of patients classified as having severe AS by indexed EOA were reclassified to nonsevere AS when using energy loss index.

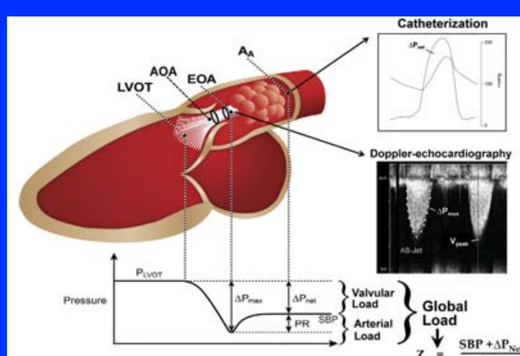
Energy loss index = $[(EOA \times A_A)/(A_A - EOA)]/BSA$

≤ 0.5–0.6 cm2/m2 suggests severe

Bahlmann E et al J Am Coll Cardiol Img 2010;3:555– 62

Global Load: Zva

- Valvuloarterial impedance (Zva)
  - Zva = SBP+ ΔP_{Mean} /SVI
  - > 4.5 $mmHg^{-1} \cdot m^{-2}$ suggests severe



- ***$\Delta P_{mean} = \Delta P_{NET}$ in the absence of significant pressure recovery***
- ***ΔP_{NET} + SBP = Global Load***

Paradoxical Low-Flow, Low-Gradient Severe Aortic Stenosis Despite Preserved Ejection Fraction Is Associated With Higher Afterload and Reduced Survival

Zeineb Hachicha, MD; Jean G. Dumesnil, MD; Peter Bogaty, MD; Philippe Pibarot, DVM, PhD

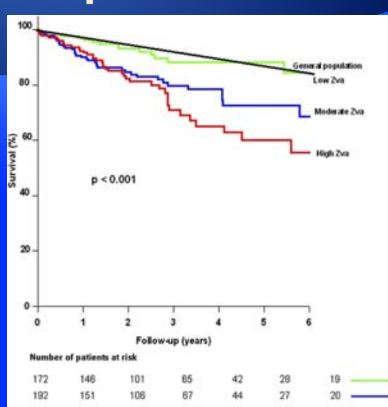
$$Zva = \frac{SAP + MG}{SVI}$$

Paradoxical Low Flow patient:

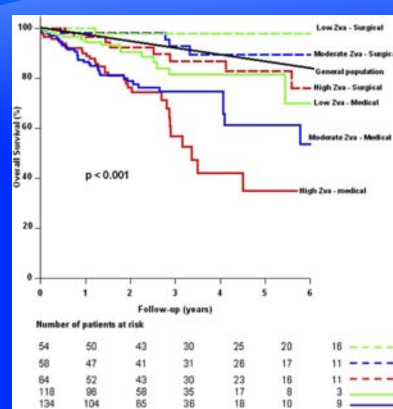
1. *Lower transvalvular gradient*
2. *Lower LV diastolic volume index*
3. *Lower LV ejection fraction (62.8% versus 68.7%; P<0.001)*
4. *Higher level of LV global afterload reflected by a higher valvulo-arterial impedance (5.3 ±1.3 versus 4.1 ±0.7 mm Hg · mL^{-1} · m2; P<0.001)*

Hachicha, Z. et al. Circulation 2007;115:2856-2864

Prognostic Importance of Impedance



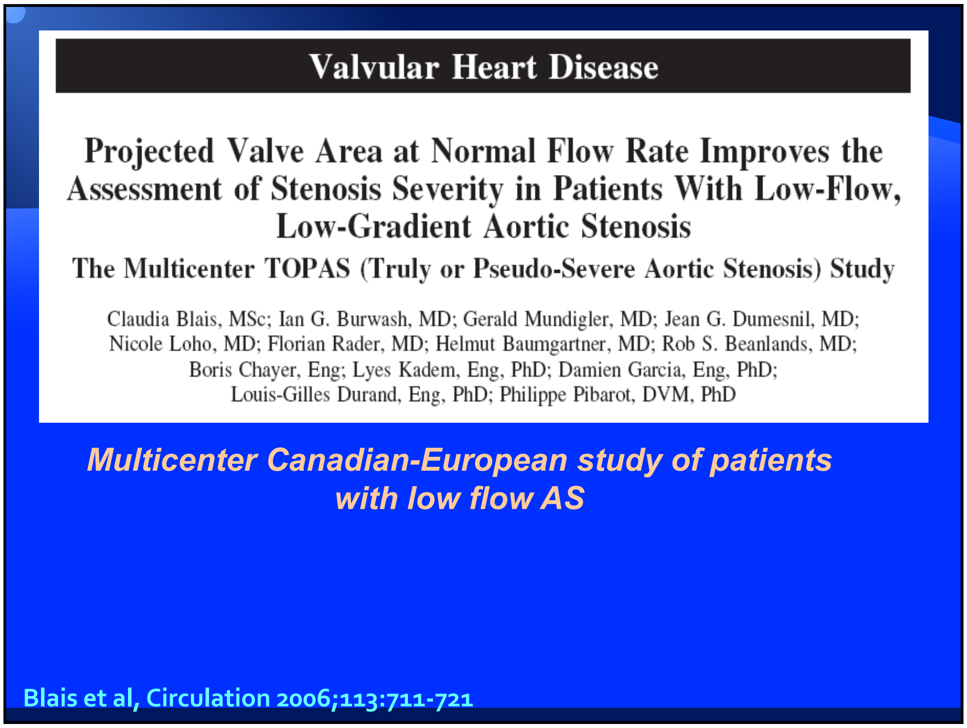
Overall Survival Versus Zva

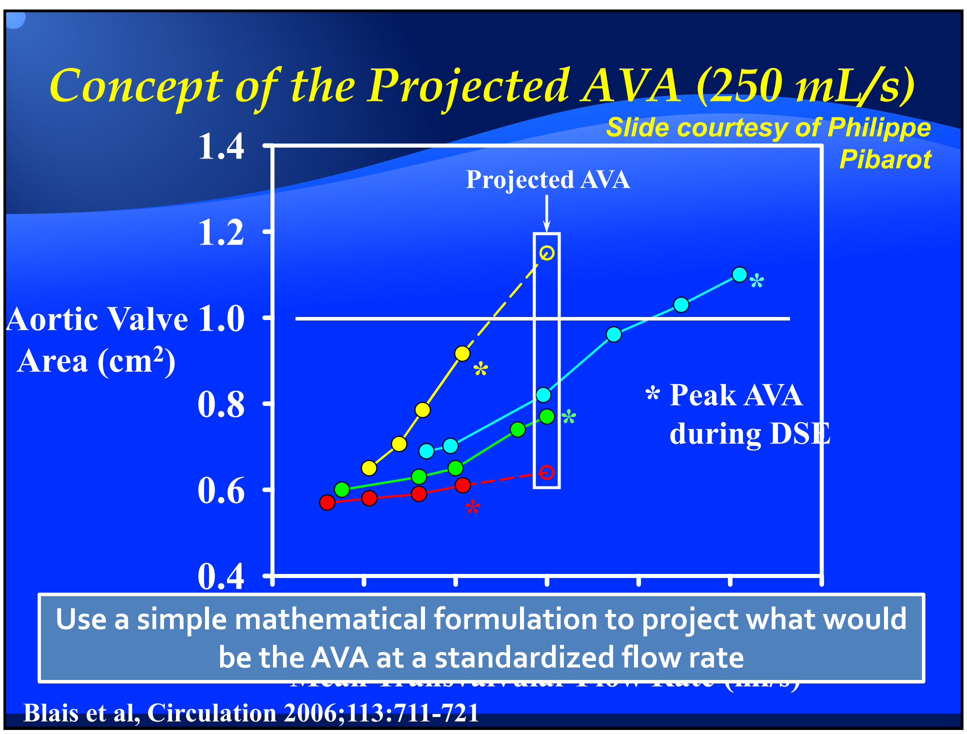


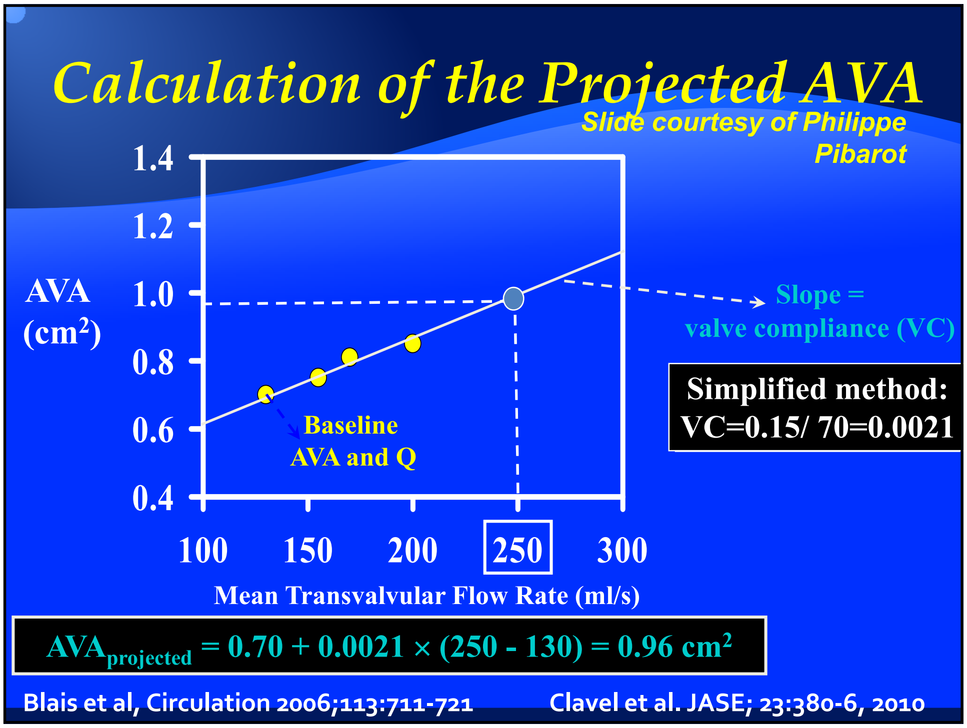
Overall Survival Versus Zva and Type of Treatment

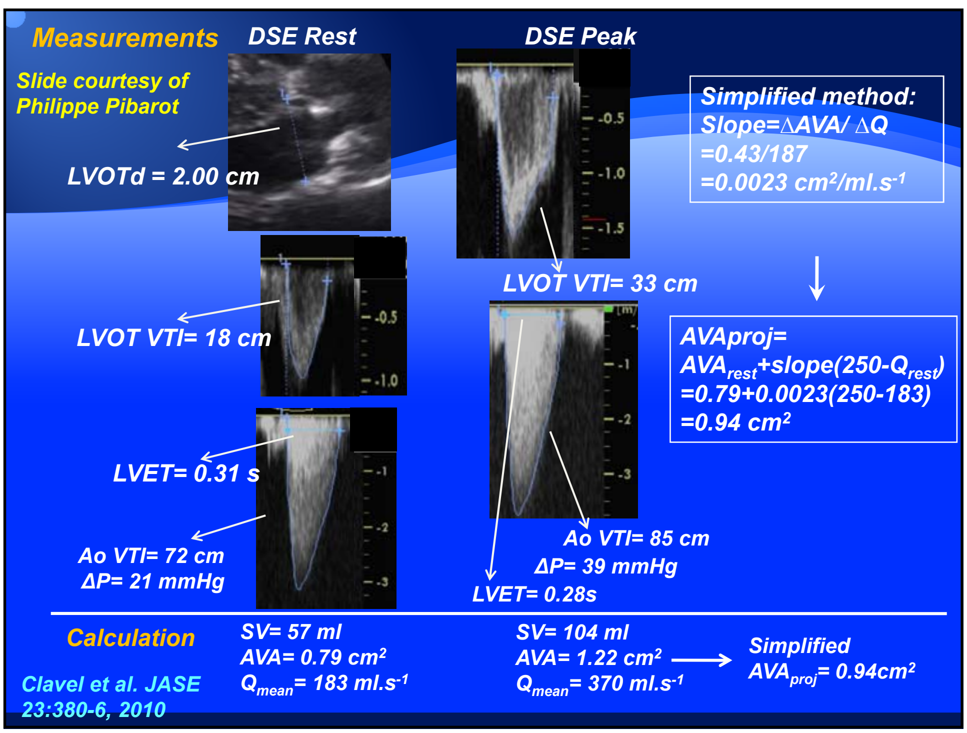
PLF: Lower overall 3-year survival (76% versus 86%; P=0.006).

Hachicha Z et al. J. Am. Coll. Cardiol. 2009;54;1003-1011

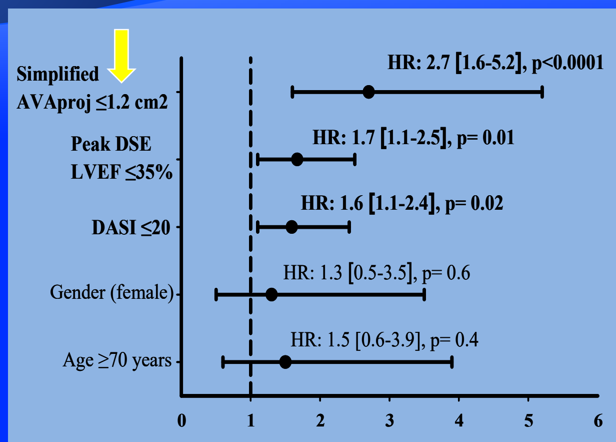

Valvular Heart Disease
Projected Valve Area at Normal Flow Rate Improves the Assessment of Stenosis Severity in Patients With Low-Flow, Low-Gradient Aortic Stenosis
The Multicenter TOPAS (Truly or Pseudo-Severe Aortic Stenosis) Study
Claudia Blais, MSc; Ian G. Burwash, MD; Gerald Mundigler, MD; Jean 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
Multicenter Canadian-European study of patients with low flow AS
Blais et al, Circulation 2006;113:711-721


Concept of the Projected AVA (250 mL/s)
Slide courtesy of Philippe Pibarot
Projected AVA
Aortic Valve Area (cm²)
1.4
1.2
1.0
0.8
0.6
0.4
* Peak AVA during DSE
Use a simple mathematical formulation to project what would be the AVA at a standardized flow rate
Blais et al, Circulation 2006;113:711-721


Calculation of the Projected AVA
Slide courtesy of Philippe Pibarot
AVA (cm²)
1.4
1.2
1.0
0.8
0.6
0.4
Slope = valve compliance (VC)
Simplified method:
VC=0.15/ 70=0.0021
Baseline AVA and Q
100
150
200
250
300
Mean Transvalvular Flow Rate (ml/s)
AVAprojected = 0.70 + 0.0021 × (250 - 130) = 0.96 cm²
Blais et al, Circulation 2006;113:711-721
Clavel et al. JASE; 23:380-6, 2010


Measurements
DSE Rest
DSE Peak
Slide courtesy of Philippe Pibarot
LVOTd = 2.00 cm
Simplified method:
Slope=ΔAVA/ ΔQ
=0.43/187
=0.0023 cm²/ml.s-1
LVOT VTI= 33 cm
LVOT VTI= 18 cm
AVAproj=
AVArest+slope(250-Qrest)
=0.79+0.0023(250-183)
=0.94 cm²
LVET= 0.31 s
Ao VTI= 72 cm
ΔP= 21 mmHg
Ao VTI= 85 cm
ΔP= 39 mmHg
LVET= 0.28s
Calculation
SV= 57 ml
AVA= 0.79 cm²
Qmean= 183 ml.s-1
SV= 104 ml
AVA= 1.22 cm²
Qmean= 370 ml.s-1
Simplified
AVAproj= 0.94cm²
Clavel et al. JASE 23:380-6, 2010

Predictors of Mortality in Patients with Low-EF, Low-Flow, Low-Gradient AS Treated Medically – TOPAS Study



Clavel et al. Circulation 2008 JASE 2010

What is moderate AS for a good ventricle may be severe for a depressed ventricle

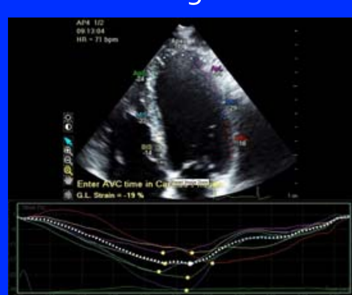
Other Measures of Aortic Stenosis Severity

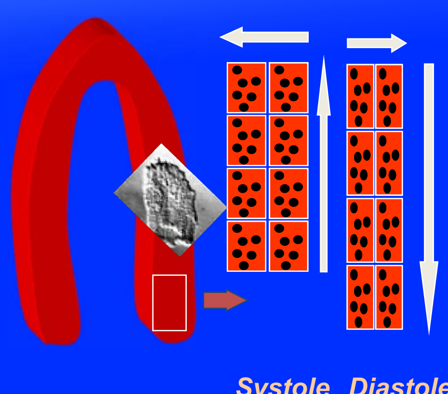
- SWL= 100 x (ΔP_{Mean} /SBP+ ΔP_{Mean})
  - Flow and AVA dependent
  - May lead to underestimation of AS severity
  - >25% suggests severe
- Systemic arterial compliance
  - SAC = SVI/SBP-DBP
  - ≤0.6 $ml \cdot mmHg^{-1} \cdot m^{-2}$ suggests severe
- Systemic vascular resistance
  - SVR = 80 xMBP/CO
  - >2,000 $dyne \cdot s \cdot cm^{-5}$ suggests severe

Other Prognostic Tools

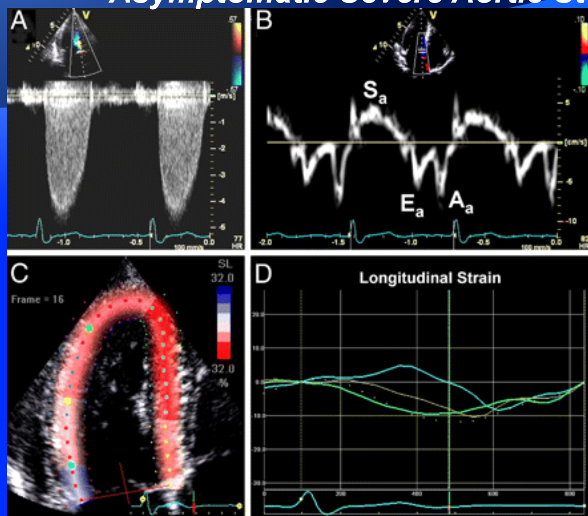
Myocardial Mechanics: Strain

- Strain (ε)= deformation
- Strain Rate = rate at which deformation occurs
- Longitudinal systolic strain of the left ventricle is shortening, normalized for diastolic length





Longitudinal Left Ventricular Mechanics in Asymptomatic Severe Aortic Stenosis



Reduced global strain = 12%.

Marker of LVH and fibrosis?

Dal-Bianco, J. P. et al. J Am Coll Cardiol 2008;52:1279-1292

JACC

Original Article

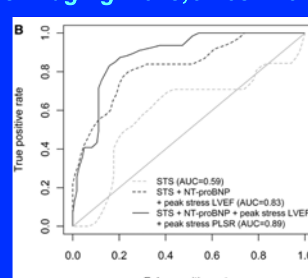
Two-Dimensional Strain for the Assessment of Left Ventricular Function in Low Flow–Low Gradient Aortic Stenosis, Relationship to Hemodynamics, and Outcome

A Substudy of the Multicenter TOPAS Study

Philipp Emanuel Bartko, MD; Georg Heinze, PhD; Senta Graf, MD; Marie-Annick Clavel, DVM, PhD; Aliasghar Khorsand, PhD; Jutta Bergler-Klein, MD; Ian Gordon Burwash, MD; Jean Gaston Dumesnil, MD; Mario Sénéchal, MD; Helmut Baumgartner, MD; Raphael Rosenhek, MD; Philippe Pibarot, DVM, PhD; Gerald Mundigler, MD

Bartko PE et al.Circ Cardiovasc Imaging. 2013;6:268-276.

1. *In patients (N = 47) with low flow–low gradient aortic stenosis, 2-dimensional strain parameters are strong predictors of outcome.*
2. *Peak stress SR may add incremental prognostic value beyond what is obtained from N-terminal pro–B-type natriuretic peptide and peak stress left ventricular ejection fraction.*



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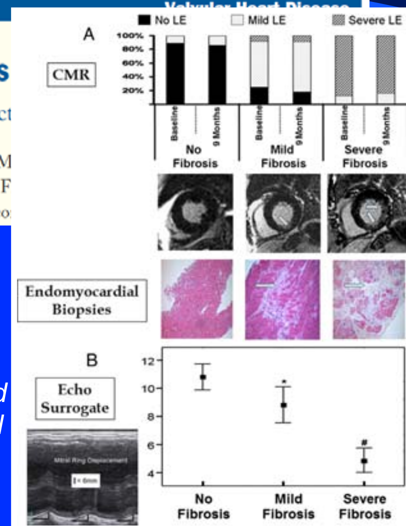
ISSN 0735-1097/$36.00
doi:10.1016/j.jacc.2011.02.059

Low-Gradient Aortic Valve Stenosis

Myocardial Fibrosis and Its Influence on Funct

Sebastian Herrmann, MD,*† Stefan Störk, MD, PHD,*† M
Volkmar Lange, MD,§ Jörg M. Strotmann, MD,* Stefan F
Stefan Gattenlöhner, MD,‡ Wolfram Voelker, MD,*† Geo

- *In low-gradient groups, more interstitial fibrosis in biopsy samples and more late enhancement MRI segments were observed.*
- *A close inverse correlation was found between interstitial fibrosis and mitral ring displacement (r = 0.79, p < 0.0001).*



Herrmann S et al. J Am Coll Cardiol 2011;58:402–12

European Heart Journal (2009) 30, 3037–3047
doi:10.1093/eurheartj/ehp351

CLINICAL RESEARCH

Strain analysis in patients with
stenosis and preserved left ventricular ejection

Abnormal Strain and Strain rate improve post SAVR in patient with normal EF

HEART

Myocardial de
stenosis: relat

Dana Cramariuc, Eva

2009

In patients with AS, lower average longitudinal strain is related to higher LV mass, concentric geometry and more severe AS.

European Journal of Echocardiography Advance Access published March 4, 2010

European Journal of Echocardiography
doi:10.1093/ejechocard/jeq014

Impact of global lef
ven
aor
tra

Patriz
Marie

Intrinsic myocardial dysfunction is common in patients with ↑global LV afterload, especially in low-flow AS.

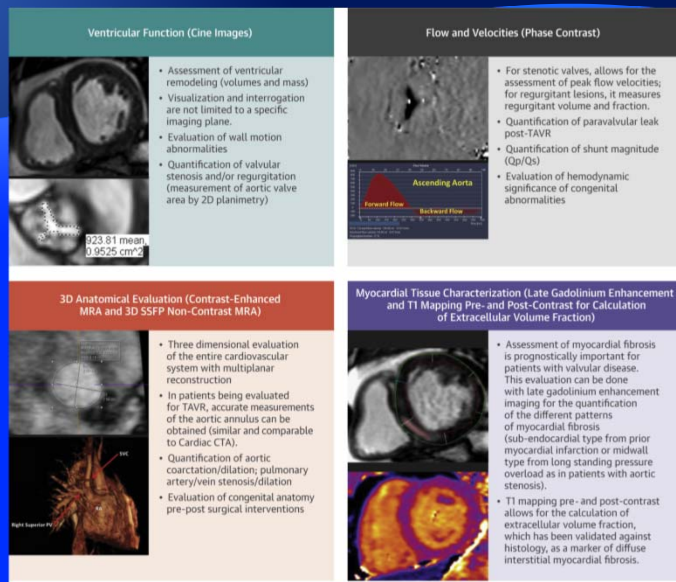
Original Article

Two-Dimensional Strain for the Assessment of Left
Ventri
Sten

Philipp Emar
Jean Gaston

1. *In patients (N = 47) with low flow–low gradient aortic stenosis, 2-dimensional strain parameters are strong predictors of outcome.*
2. *Peak stress PLSR may add incremental prognostic value*

Role of CMR



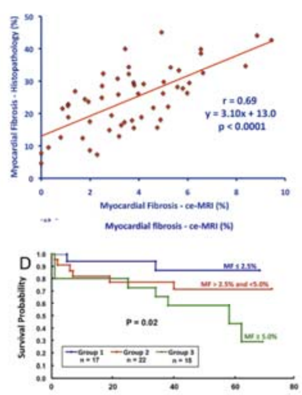
Calvacante, J et al. J Am Coll Cardiol Intv 2016;9:399–425

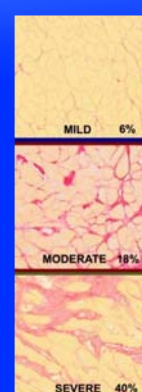
CMR: Late-Gadolinium Enhancement

Late gadolinium enhancement in AS & AR

n=54 (50% AS, 50% AR)

- Good correlation: histology vs CMR
- Fibrosis (histology or CMR) associated with
  - worse improvement post op
  - worse long-term survival.
- Age and Fibrosis were independent predictors of all-cause mortality.

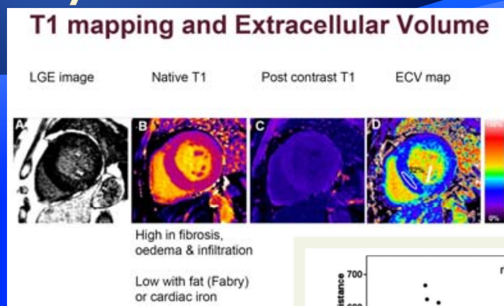




Azevedo et al JACC 2010

LGE for histologic fibrosis but is poor at determining interstitial fibrosis (which is potentially reversible).

Extracellular Volume: Diffuse Myocardial Fibrosis



Extracellular volume fraction (ECV), which corrects for blood pool and the plasma gadolinium volume of distribution, offers the best reproducibility and can predict outcomes

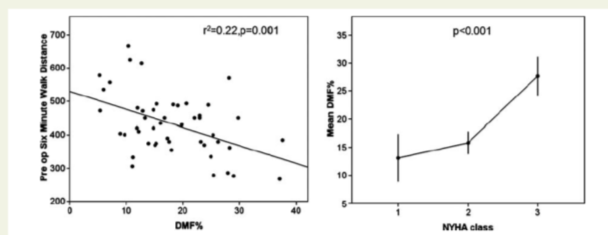


Figure 2 DMF and symptoms in AS. Baseline diffuse fibrosis (DMF%) (n = 63) correlates with symptoms in patients with AS—both 6MWT performance (Pearson's test, left) and NYHA (ANOVA, right). Error bars represent 95% confidence intervals.

Flett AS, Sado DM, Quarta G, et al. Eur Heart J Cardiovasc Imag. 2012;13: 819–26

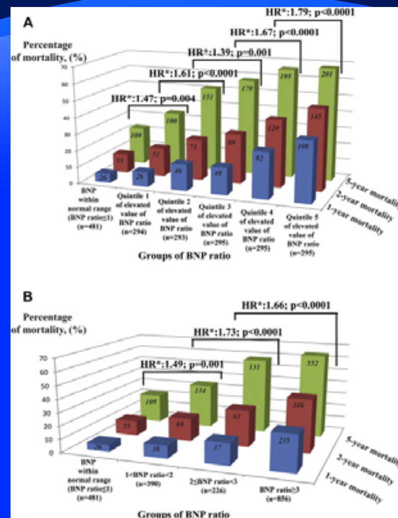
Outcomes with CMR T1 and ECV

- Native T1 mapping provides a noninvasive estimation of diffuse myocardial fibrosis and correlates with subclinical myocardial dysfunction in asymptomatic patients with AS [1].
- Symptomatic patients were more likely to demonstrate increased T1 values compared to asymptomatic patients [2].
- Patients with severe fibrosis were less likely to show improvement in symptoms, LV function and LVH after surgery compared with those patients with mild to moderate fibrosis [3].
- Differing patterns of remodeling, with both native T1 and ECV correlate with prognostic markers such as NT-pro-BNP [4]

1. Lee ST, Lee W, Lee JM et al. Radiology 2015;274(2):359-69
2. Flett AS, Sado DM, Quarta G, et al. Eur Heart J Cardiovasc Imag. 2012;13: 819–26
3. Milano AD, Faggian G, Dodonov M, et al. J Thorac Cardiovasc Surg. 2012;144(4):830–7.
4. Treibel T, Fontana M, Reant P, et al. J Cardiovasc Magn Reson. 2015;17

BNP and Outcomes in AS

- BNP ratio (measured BNP/maximal normal BNP value specific to age and sex) >1 defined BNP clinical activation
- BNP ratio >1 independently predicted mortality after diagnosis (p < 0.0001; hazard ratio [HR]: 1.91; 95% CI: 1.55 to 2.35) and provided incremental power to the survival predictive model
- Link to survival was confirmed in **asymptomatic** patients with normal EF
  - BNP ratio >1: adjusted HR: 2.35 [95% CI: 1.57 to 3.56]
  - BNP ratio 1-2.0: adjusted HR = 2.10 [95% CI: 1.32 to 3.36]
  - BNP ratio 2.0-3.0: adjusted HR = 2.25 [95% CI: 1.31 to 3.87]
  - BNP ratio of ≥3: adjusted HR = 3.93 [95% CI: 2.40 to 6.43]

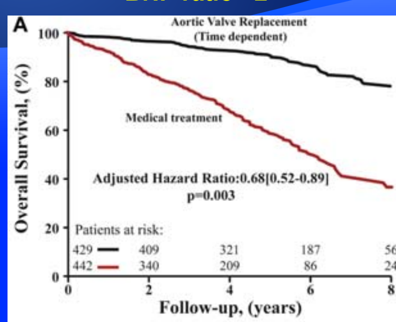


N = 1953

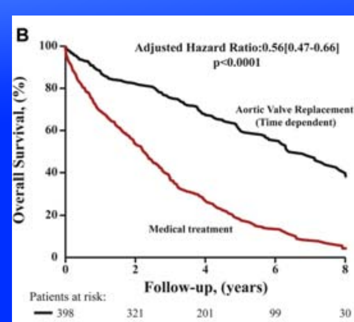
Clavel MS, Malof J, Michelena HI et al. J Am Coll Cardiol 2014,20;63(19):2016-25

BNP and Outcomes in AS

BNP ratio <2



BNP ratio ≥2

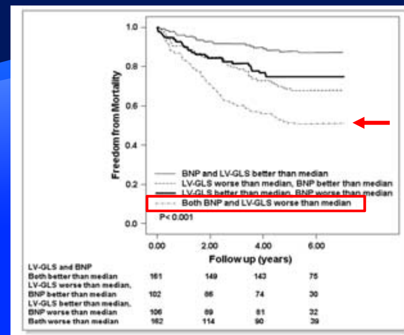


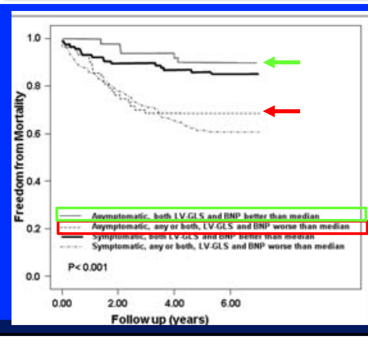
- AVR is independently associated with markedly improved prognosis in patients with clinically activated BNP

Clavel MS, Malof J, Michelena HI et al. J Am Coll Cardiol 2014,20;63(19):2016-25

Strain and BNP

- Patients with significant AS and preserved LVEF, a combination of BNP and LV-GLS provides synergistic risk stratification, independent of symptoms, risk factors, and echocardiographic variables.
- Asymptomatic patients had significantly worse survival, in the setting of abnormal LV-GLS and/or BNP
- LV-GLS and BNP become abnormal earlier in the disease cascade, as compared to flow-dependent markers such as LV-SVI





Goodman A. et al. J Am Heart Assoc. 2016;5:e002561 doi: 10.1161/JAHA.115.002561

Aortic Stenosis Toolbox

Aortic Stenosis →

Echocardiographic Assessment of Valvular Burden
1. *Peak velocity, Mean gradient and AVA*
2. *Net Valvular Load: Energy Loss Index*
3. *Global arterial load: Zva*

Echocardiographic Assessment of Size and Function
1. *LV mass and RWT*
2. *Systolic and Diastolic function*

Left ventricular remodeling + LV systolic and diastolic Fx + Flow →

Stroke Volume Index

D2: Low Flow Reduced EF → *1. Dobutamine Stress, 2. Projected Valve Area*; → *3. CT Calcium Score*

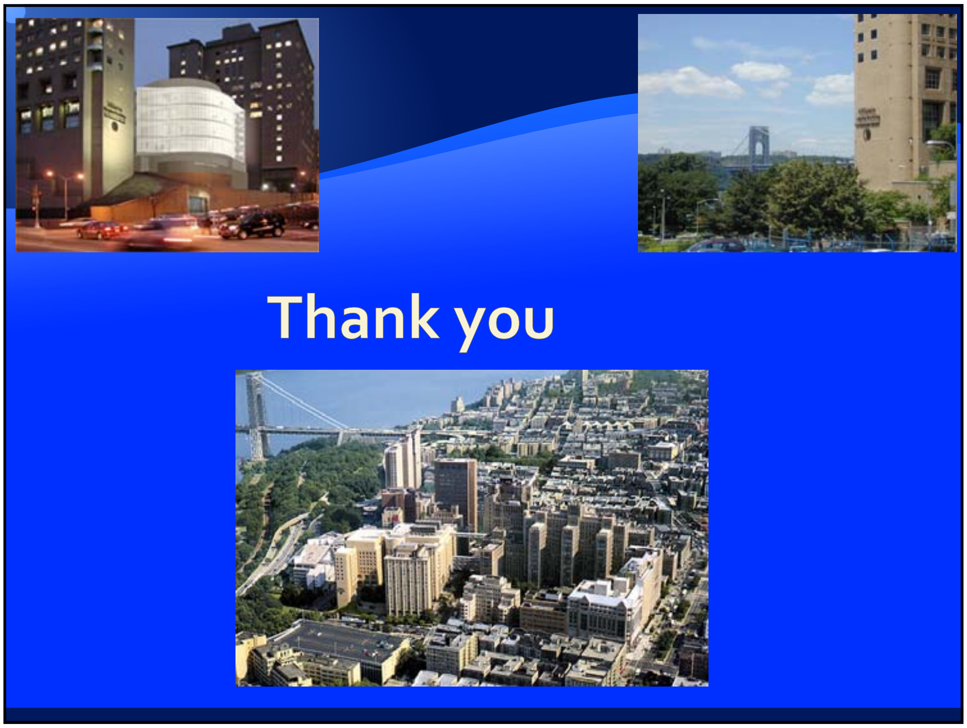
D3: Low Flow normal EF → *3. CT Calcium Score*; → *Myocardial Mechanics*

Asymptomatic →

Stress Echo
1. *EKG, BP, Symptom*
2. *Δ mean >20 mmHg)*

Biomarkers (BNP)

Myocardial Mechanics:
1. *Strain imaging (Echo, CMR)*
2. *LGE (CMR)*
3. *T1 mapping/ECV (CMR)*


Thank you