Tri-City Cardiovascular Symposium

August 17, 2024

Shashank Jain, MD, MPH, FACC

- Board certified in Cardiology, Echocardiography, Nuclear Cardiology, Interventional Cardiology, and Internal Medicine.
- Completed a Cardiology training at Thomas Jefferson University Hospital in Philadelphia, PA.
- Clinical interests include percutaneous management of shock, coronary and valvular diseases, and various procedures such as coronary angioplasty, TAVR, TMVR, MitraClip, left atrial appendage occlusion, and PFO/ASD closure.

TRI-CITY
CARDIOLOG

Management of Valvular Heart Disease: Recent Developments

TRI-CITY
CARDIOLOG

Objectives

Aortic stenosis

- Revisit the symptoms associated with Aortic stenosis
- Understand the current unaddressed needs in patient management
  - Approach to patients at low surgical risk & severe AS;
  - Lifetime management of AS.

- Evolving concepts in management of Asymptomatic SAS and Moderate AS

  - Role of Cardiac staging in the patients with aortic stenosis
  - Do we need to treat some of the subgroups earlier?

- Role of medical therapy

Aortic Regurgitation

Tricuspid regurgitation

TRI-CITY
CARDIOLOG

Aortic stenosis

- Aortic stenosis is the most common heart valve disease encountered in clinical practice and affects 2% to 5% of older adults
- The prevalence has been estimated to be 12.4% in patients ≥75 years of age and is set to increase as a result of aging populace
- The etiology of AS can be accounted for by congenital, degenerative, and rheumatic processes
- Congenital Aortic Stenosis: Symptoms can appear in infancy or childhood, especially with severe malformations like unicuspid valves. However, many individuals with bicuspid valves may remain asymptomatic until adulthood.
- Calcific Aortic Stenosis: Typically manifests later in life, often in individuals over 65 years old, as it is associated with age-related degenerative processes

Aortic stenosis

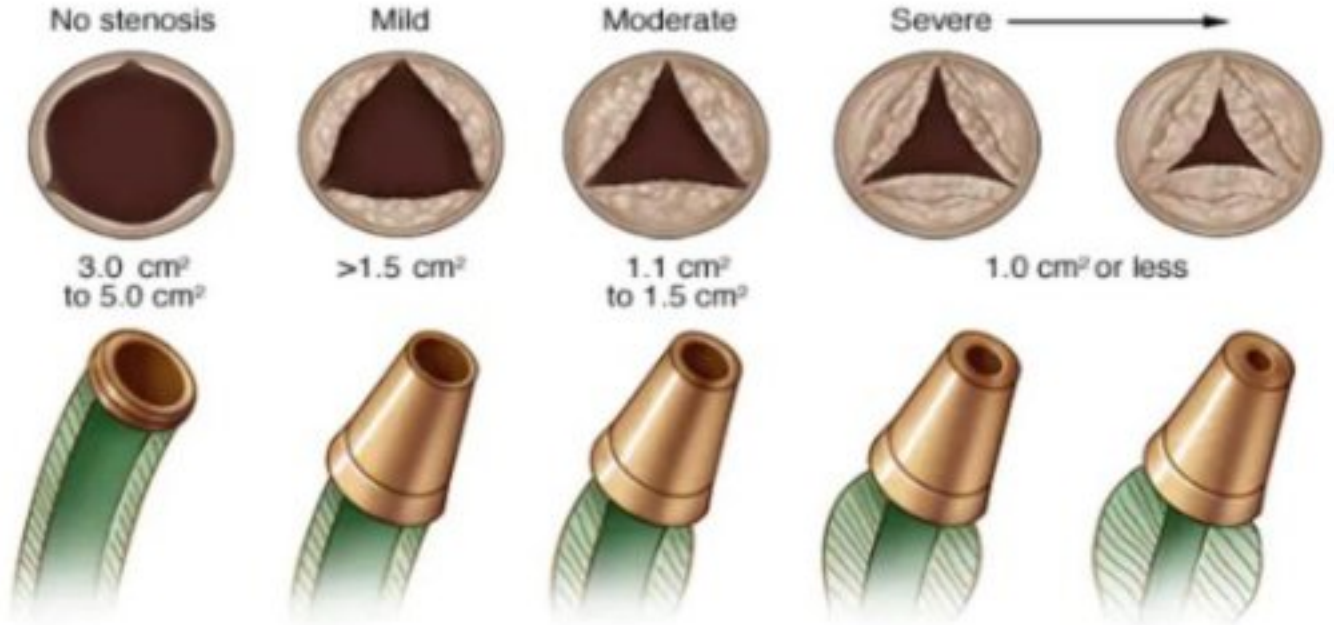
Physical examination

- Systolic murmur that is harsh, medium-pitched, and crescendo-decrescendo.
- It's usually loudest in the second right intercostal space, or aortic area, and can also be heard in the third and fourth interspaces along the left sternal border.
- The murmur radiates to the carotid arteries and right clavicle, and is often louder in the left carotid.
- It has a characteristic "diamond shape" in a phonocardiogram

	Mild AS	Moderate AS	Severe AS
Vmax (m/s)[a]	2.0–2.9	3.0–3.9	≥4.0
Mean gradient (mmHg)[a]	<30	30–49	≥50
AVA (cm^2)	>1.5	1.0–1.5	<1.0
AVAi (cm^2/m^2 BSA)	≥1.0	0.6–0.9	<0.6

[a]At normal transvalvular flow.
AS = aortic stenosis; AVA = aortic valve area; AVAi = indexed AVA; BSA = body surface area; Vmax = maximum Doppler velocity.

Aortic stenosis



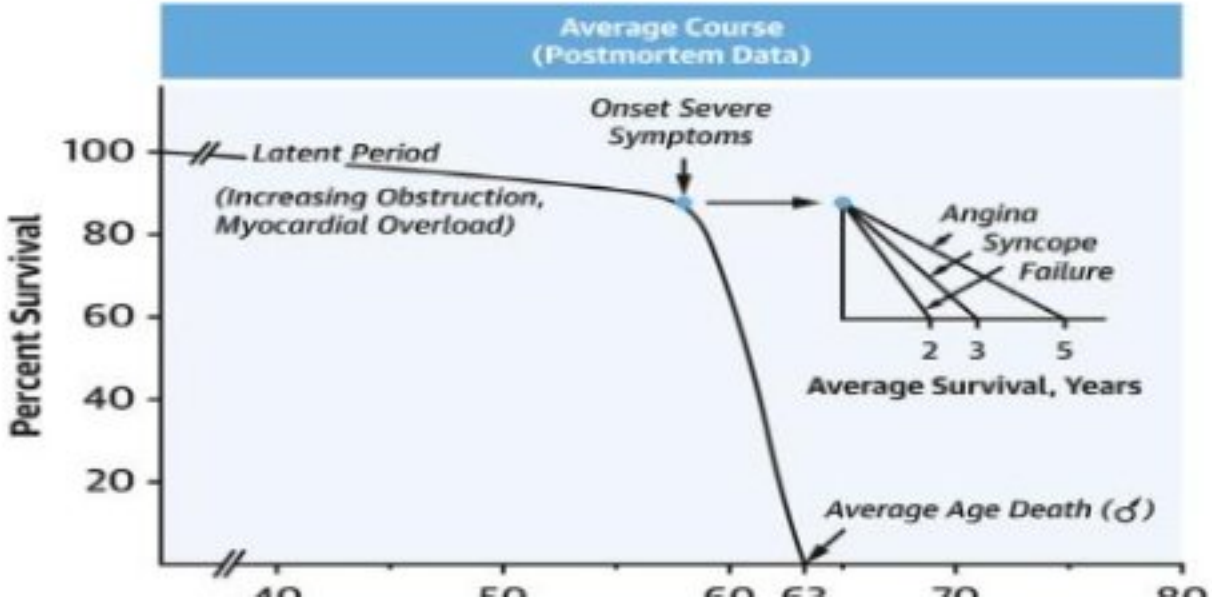
What are the symptoms of aortic stenosis

- Chest pain or discomfort, which may worsen with activity and radiate to the arm, neck, or jaw.
- Rapid, fluttering heartbeat or palpitations.
- Shortness of breath, DOE
- Dizziness or light-headedness, which can lead to presyncope, syncope.
- Difficulty walking short distances or a decline in activity level – gradual decline in exercise tolerance
- Fatigue, especially upon exertion

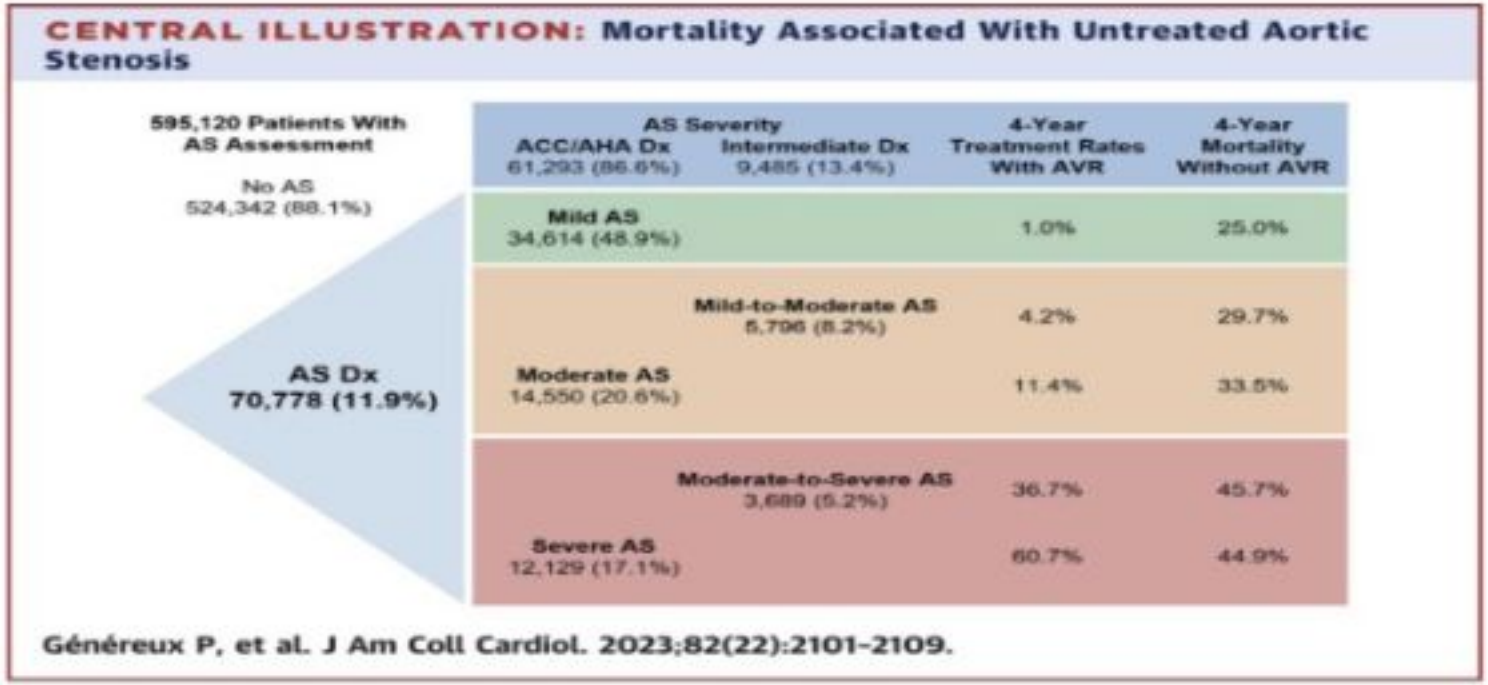
TRI-CITY
CARDIOLOG

Management philosophy of AS

- Vigilant management in which **intervention is triggered by the development of symptoms or LV systolic dysfunction** has heretofore appeared safe even for patients with severe or very severe AS followed up longitudinally with clinical and echocardiographic monitoring



The Mortality Burden of Untreated Aortic Stenosis



Généreux P, et al. J Am Coll Cardiol. 2023;82(22):2101-2109.

Case 1.

67 yo female patient, smoker, HTN, works at Walmart & up-until recently doing ok.

Presented with lightheadedness , heart failure, chest pain.

Informed us that "have been told that she has a loud murmur" but nothing to do as was asymptomatic.

Echo – EF 63%, Moderate LVH, severe AS with peak velocity of 5.5 m/sec velocity,

STS risk was low (<4%)

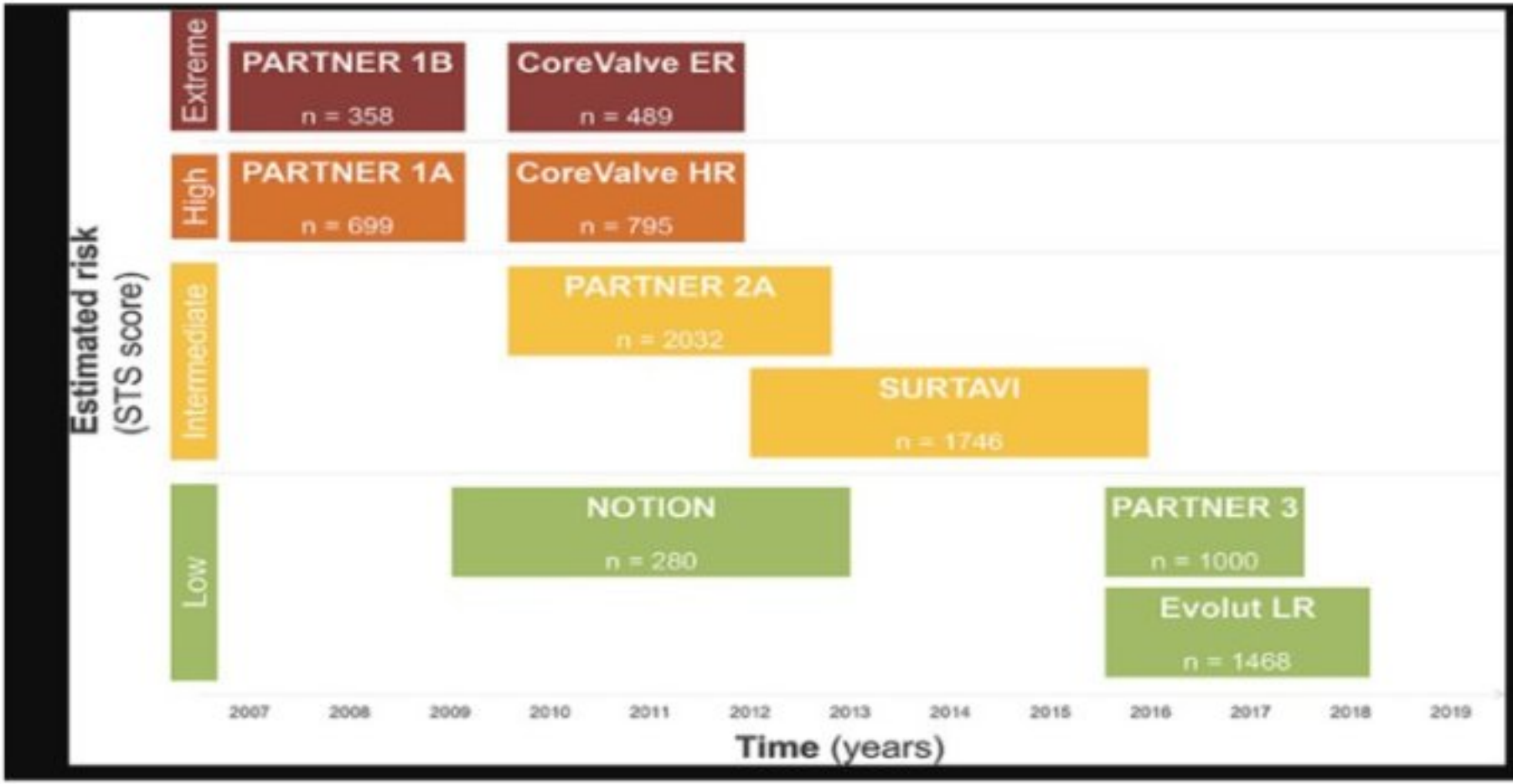
Patient preference : undergo TAVR

TRI-CITY
CARDIOLOG

Severe symptomatic aortic stenosis

- Aortic valve replacement - Transcatheter AVR vs Surgical AVR
  - Risk profile

TRI-CITY
CARDIOLO

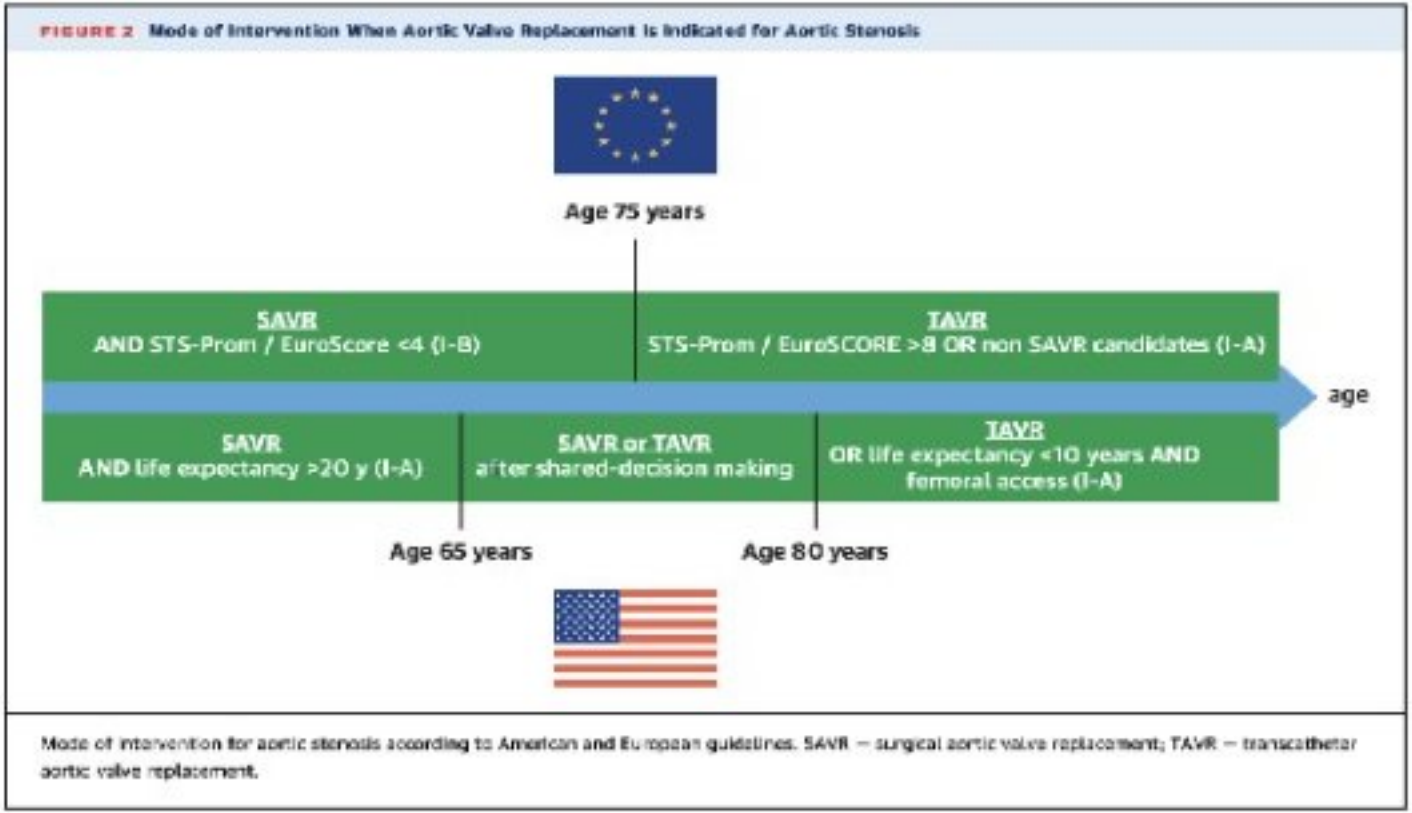

Estimated risk (STS score)
Extreme
High
Intermediate
Low
PARTNER 1B
n = 358
CoreValve ER
n = 489
PARTNER 1A
n = 699
CoreValve HR
n = 795
PARTNER 2A
n = 2032
SURTAVI
n = 1746
NOTION
n = 280
PARTNER 3
n = 1000
Evolut LR
n = 1468
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018
2019
Time (years)

Severe symptomatic aortic stenosis

- AVR - TAVR vs SAVR
  - Risk profile
    - TAVR data
      - PARTNER 1 trials included high risk and inoperable patients
      - PARTNER 2 Trial studies Intermediate-risk patients.
      - PARTNER 3 Trial studied Low-risk patients
      - Similar results for Evolut valve trials.
      - Overall, these trials have established TAVR as a strong alternative to SAVR across various risk profiles, demonstrating its effectiveness and safety in high, intermediate, and low-risk patients with severe AS. These findings have influenced clinical guidelines and expanded the eligible patient population for TAVR.
- Age

TRI-CITY
CARDIOLO

Severe symptomatic Aortic Stenosis



Mode of intervention for aortic stenosis according to American and European guidelines. SAVR = surgical aortic valve replacement; TAVR = transcatheter aortic valve replacement.

Severe symptomatic aortic stenosis

- AVR - TAVR vs SAVR
  - Risk profile
    - TAVR data
      - PARTNER 1 trials included high risk and inoperable patients
      - PARTNER 2 Trial studies Intermediate-risk patients.
      - PARTNER 3 Trial studied Low-risk patients
      - Similar results for Evolut valve trials.
      - Overall, these trials have established TAVR as a strong alternative to SAVR across various risk profiles, demonstrating its effectiveness and safety in high, intermediate, and low-risk patients with severe AS. These findings have influenced clinical guidelines and expanded the eligible patient population for TAVR.
  - Age
  - Anatomy

TRI-CITY CARDIOLO

Case 1.

67 yo female patient, smoker, HTN, works at Walmart up-until recently doing ok.
Presented with lightheadedness , CHF, one episode of Syncope.

"have been told that she has a loud murmur" but nothing to do, as no symptoms

Echo – EF 63%, Moderate LVH, severe AS with 5.5 m/sec velocity,

STS risk was low (<4%)

Patient had strong preference towards undergoing TAVR

Heart team discussion : because of high-risk anatomy underwent SAVR

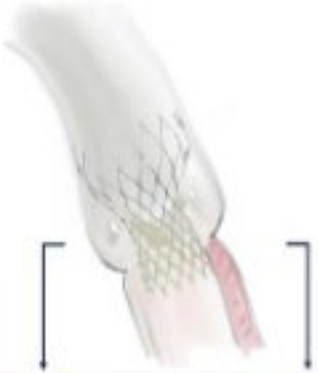
TRI-CITY
CARDIOLOG

Severe symptomatic aortic stenosis

- AVR - TAVR vs SAVR
  - Risk profile
    - TAVR data
      - PARTNER 1 trials included high risk and inoperable patients
      - PARTNER 2 Trial studies Intermediate-risk patients.
      - PARTNER 3 Trial studied Low-risk patients
      - Similar results for Evolut valve trials.
      - Overall, these trials have established TAVR as a strong alternative to SAVR across various risk profiles, demonstrating its effectiveness and safety in high, intermediate, and low-risk patients with severe AS. These findings have influenced clinical guidelines and expanded the eligible patient population for TAVR.
- Age
- Anatomy
- Lifetime management - planning for what comes next

TRI-CITY
CARDIOLO

Lifetime management of aortic stenosis

1st procedure	TAVR		SAVR		Ross	
						
2nd procedure	TAVR	TAVR explant + SAVR	TAVR	Redo SAVR	TAVR	Redo SAVR
	Minimally invasive procedure	Possible 3rd procedure	Wide experience with TAVR-in-SAVR Easy Coronary reaccess after SAVR Surgery at young age	Possible 3rd procedure	Minimally invasive procedure Possible 3rd procedure	Complex procedure
	Risk of coronary obstruction Difficult coronary reaccess Few options for 3rd procedure	Poor experience with TAVR explant Possible concomitant aortic repair	Few options for 3rd procedure	Higher operative risk	Possible need for two valves intervention	

Case number 2.

87 yo male patient with h/o CAD with CABG,HTN,PPM in place

- Aortic stenosis being monitored closely
- Stress test in 2018 – walked for 9 minutes on the bruce protocol
- Goes to the gym 3/week with NO symptoms

Echo 02/2023

- Ef- 60 %, RV dilated, mild LVH
- Trace MR , Mild TR.
- RVSP – 28 mmHG, LA - 27
- AS – valve area of – 0.6 cm2, PV – 4.0 m/sec

Echo 3/2024

- Ef- 55 %, grade 1 DD, LVH
- Dilated RV, reduced RV function, Mild MR, Moderate TR .
- RVSP - 35 mmHG, LA- 29
- AS – with valve area of 0.58, PV – 4.14

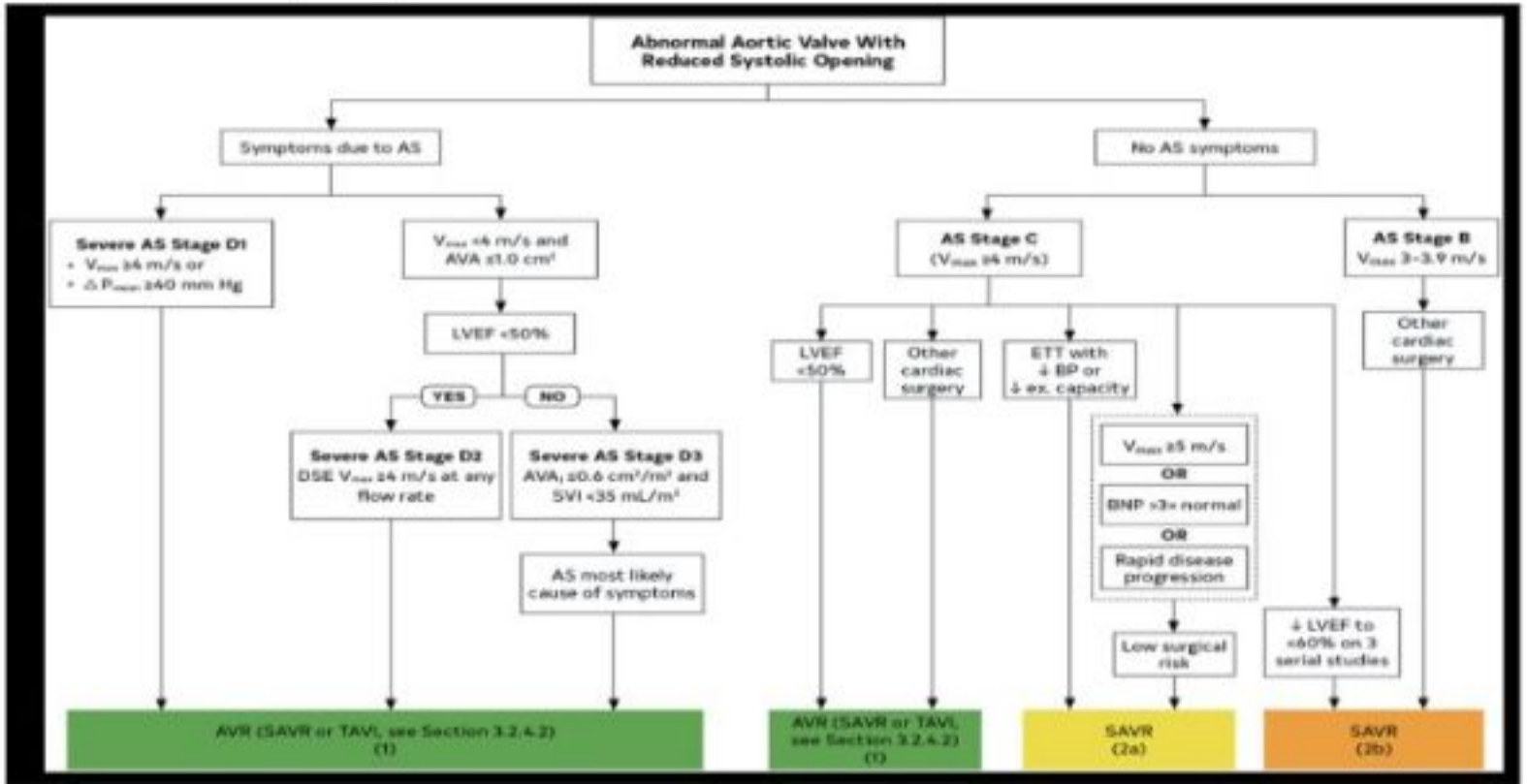
TRI-CITY
CARDIOLOG

Asymptomatic severe aortic stenosis

- Class 1 Indications for AVR
  - Peak velocity > 5 m/sec
  - EF < 50%
- Other subcategories that benefit from AVR
  - ETT – look for exercise capacity, drop in BP
  - **Unexplained** Systolic pulmonary artery pressure >60 mmHg
  - Rapid progression on serial monitoring (peak jet velocity increase >0.3 m/s/year)
  - Elevated BNP (BNP RATIO >3)
  - Someone undergoing other cardiac surgery

TRI-CITY CARDIOLOG

Asymptomatic severe aortic stenosis



What are the risks of waiting too long for valve replacement in asymptomatic patients with severe disease

1. Sudden cardiac death

2. Irreversible structural heart damage: severe left ventricular hypertrophy or reduction in global strain

3. Impaired exercise capacity

4. Higher surgical risk

5. Worsen valvular calcification – worsening anatomy

Management philosophy of AS

- A strategy of expectant but vigilant management in which intervention is triggered by the development of symptoms or LV systolic dysfunction has heretofore appeared safe even for patients with severe or very severe AS followed up longitudinally with clinical and echocardiographic monitoring
- **Conservatively managed asymptomatic patients with severe AS have fared less well**
- **Given the low periprocedural mortality and morbidity rates for isolated AVR in contemporary practice, especially for TAVR, earlier intervention has been increasingly advocated**

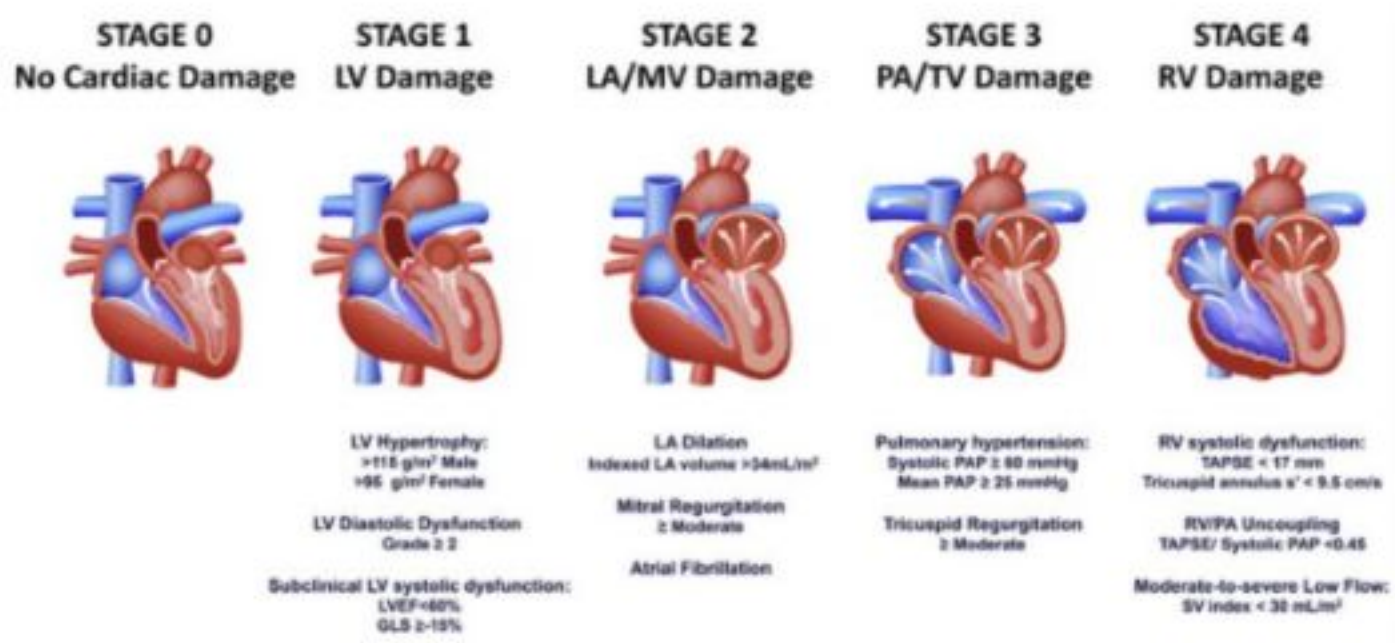
Asymptomatic severe aortic stenosis

Areas of active research

- Can we change the disease course with earlier and avoid irreversible damage
- Can we quantify cardiac damage - Role of staging patients with aortic stenosis
- EF < 6o% (Class II b in current guidelines)
- Role of CMR – to define myocardial fibrosis
- Role of GLS – strain imaging

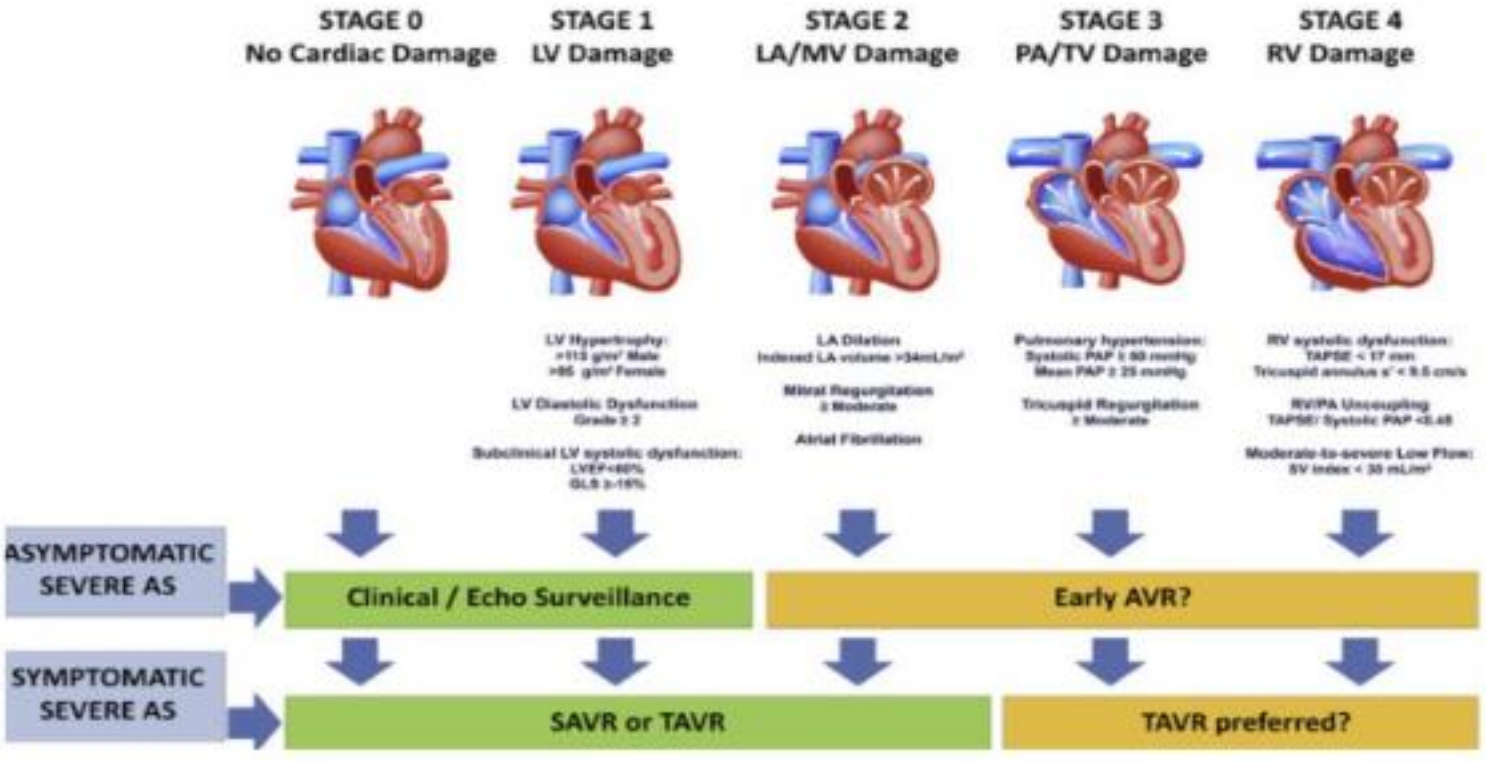
TRI-CITY
CARDIOLOG

Cardiac staging/damage in Aortic stenosis



Genereux P., Pibarot P., Redfors B., et al. "Staging classification of aortic stenosis based on the extent of cardiac damage". Eur Heart J 2017;38:2351-2359.

Cardiac damage/staging in Aortic stenosis



Case number 2.

87 yo male patient with h/o CAD with CABG,HTN,PPM in place

- Aortic stenosis being monitored closely
- Stress test in 2018 – walked for 9 minutes on the bruce protocol
- Goes to the gym 3/week with NO symptoms

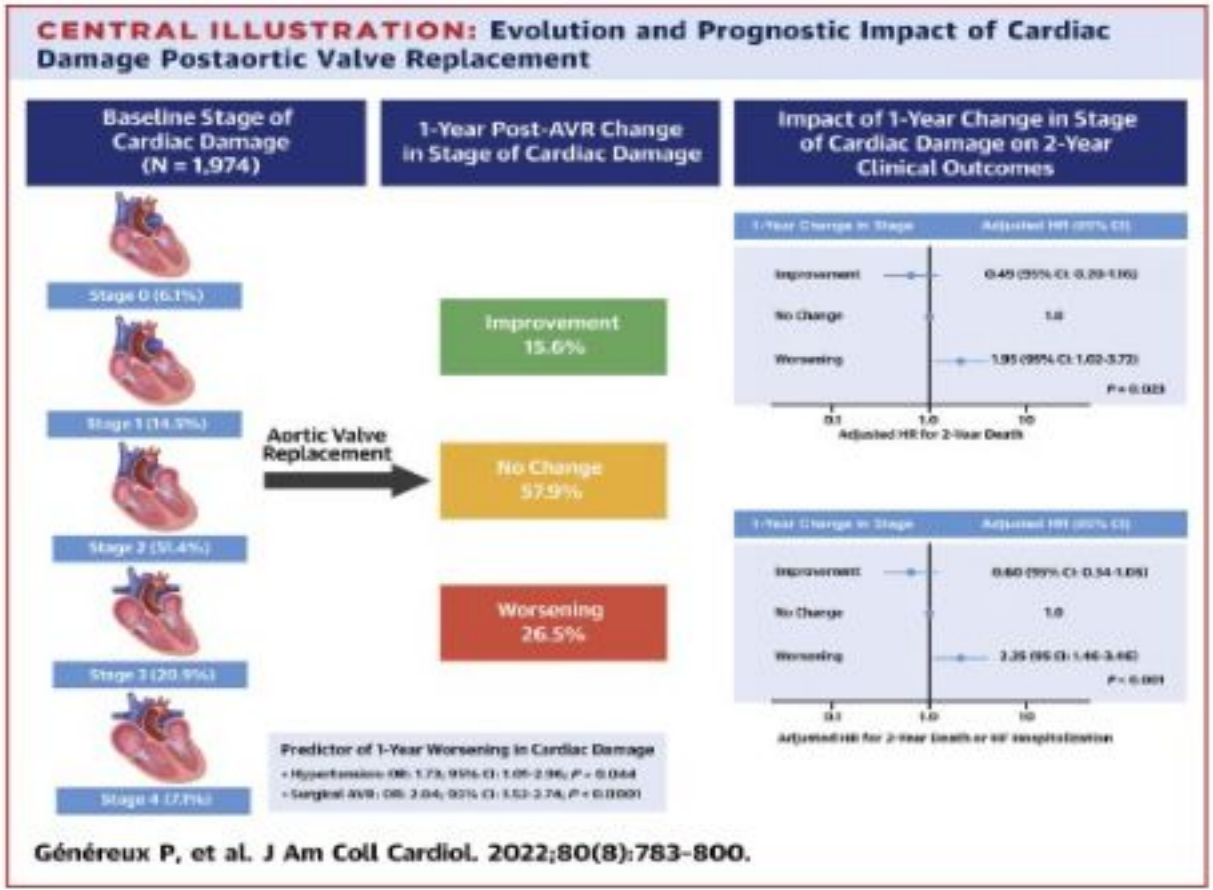
Echo 02/2023

- Ef- 60 %, RV dilated, mild LVH
- Trace MR , Mild TR.
- RVSP – 28 mmHG, LA - 27
- AS – valve area of – 0.6 cm2, PV – 4.0 m/sec

Echo 3/2024

- Ef- 55 %, grade 1 DD, LVH
- Dilated RV, reduced RV function, Mild MR**, Moderate TR .**
- RVSP - 35 mmHG, LA- 29
- AS – with valve area of 0.58, PV – 4.14

TRI-CITY
CARDIOLOG



Généreux P, et al. J Am Coll Cardiol. 2022;80(8):783-800.

Impact of TAVR on AS

- The change in cardiac damage stage at 1 year was independently associated with mortality and heart failure hospitalization at 2 years.
- Compared to no change, improvement in cardiac damage stage was associated with lower risk (adjusted HR 0.49 for mortality, 0.60 for death/heart failure), while worsening was associated with higher risk (adjusted HR 1.95 for mortality, 2.25 for death/heart failure)
- Factors associated with no change or worsening in cardiac damage stage after AVR included **diabetes mellitus, chronic kidney disease, and concomitant tricuspid and mitral regurgitation**
- The findings suggest that earlier detection of aortic stenosis and intervention before the development of irreversible cardiac damage may improve cardiac function and prognosis

TRI-CITY
CARDIOLOG

Case no. 3

- 87 yo male patient with h/o Myeloma, HTN, HLD presented with CHF (IV) . On work up found to have Severe AS, presenting weight was 176 pounds
- 10/2023 – Normal EF,LVH, Severe AS , moderate MR and mild TR, Right ventricle function decreased, RVSP 43 mmhg,

- Months of medical therapy, difficult to control sx

- TAVR 12/23

- Multiple follow ups for HF – now NYHA 2 with weight goal of 156 pounds, GDMT et al.
- Weight now (05/2024) – 156 pounds, on GDMT, Lasix et al.

- Echo 3/2024 - EF – 62%, RA enlarged , Normal RV function. Moderate MR, RVSP – 22 mmHG ,LAE

TRI-CITY
CARDIOLOG

Ongoing trials in Assymptomatic Severe AS

Early TAVR trial

- Severe asymptomatic aortic stenosis.
- Early TAVR versus clinical surveillance with deferred TAVR when symptoms develop. Bicuspid valves with suitable anatomy are included.

EVOLVED trial

- In asymptomatic patients with severe AS and midwall LGE, early AVR would improve outcomes when compared to the current standard of care.

TRI-CITY
CARDIOLOG

Moderate Aortic stenosis

Current guidelines-

- AVR may be considered in patients with moderate AS who are undergoing surgery for other indications.[
- Current guidelines suggest that patients with moderate AS (defined as peak transaortic velocity of 3.0–3.9 m/s or mean gradient [MG] of 20–39 mmHg) should undergo surveillance yearly, and AVR deferred until the AS becomes severe.

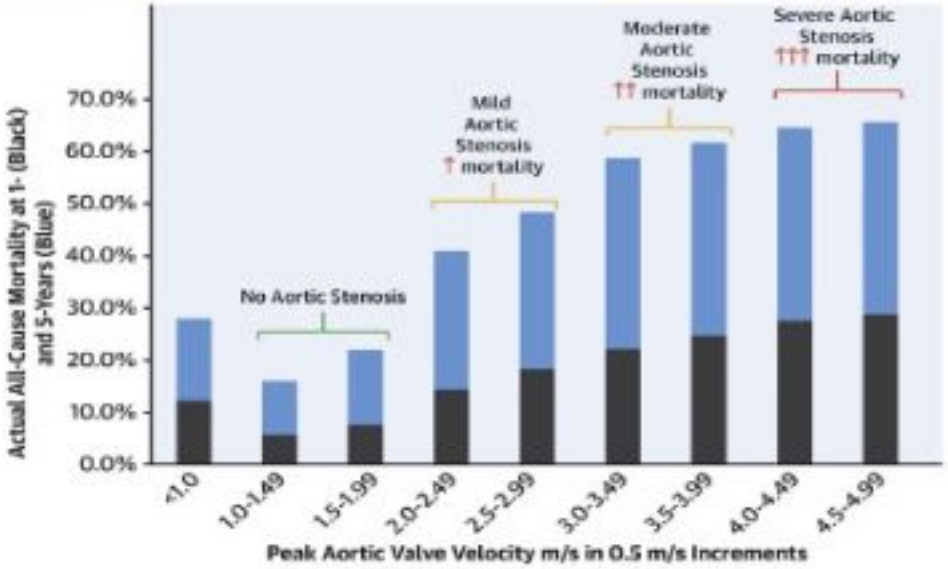
What is the mortality and morbidity in people with symptomatic Moderate Aortic stenosis

Focus on Moderate AS and LV dysfunction- There's growing interest in treating moderate AS patients with left ventricular systolic dysfunction, as this group shows high morbidity and mortality.

Moderate Aortic stenosis

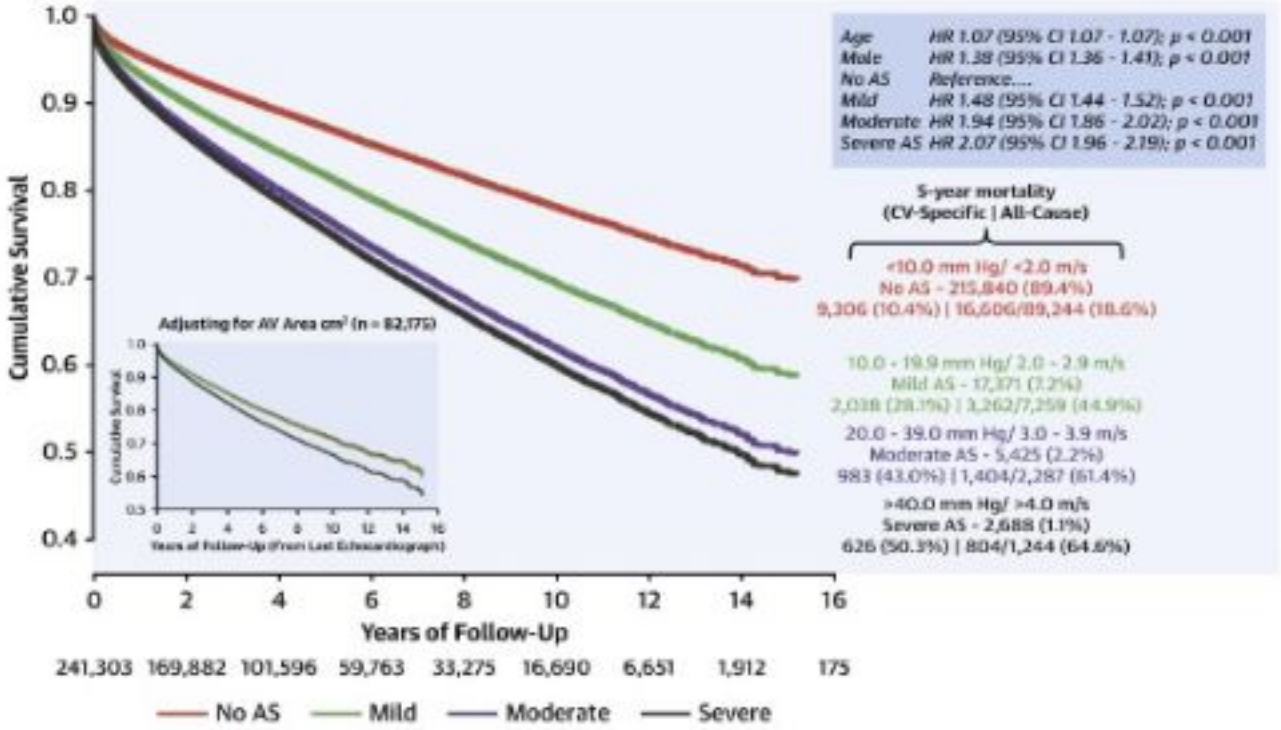
- Observational data from a large Australian registry evaluated Echocardiographic findings from 3,315 patients with moderate AS.
- The 5-year mortality was 56%, after adjusting for age, sex, left ventricular systolic or diastolic dysfunction and aortic regurgitation.
- The risk of dying in the longer term was similar to the risk in patients presenting with severe AS at baseline.

CENTRAL ILLUSTRATION: Moderate Native Valvular Aortic Stenosis and Long-Term Survival: 1- and 5-Year Mortality per Increment in Peak Aortic Valve Velocity



Strange, G. et al. J Am Coll Cardiol. 2019;74(15):1851-63.

TRI-CITY CARDIOLOG

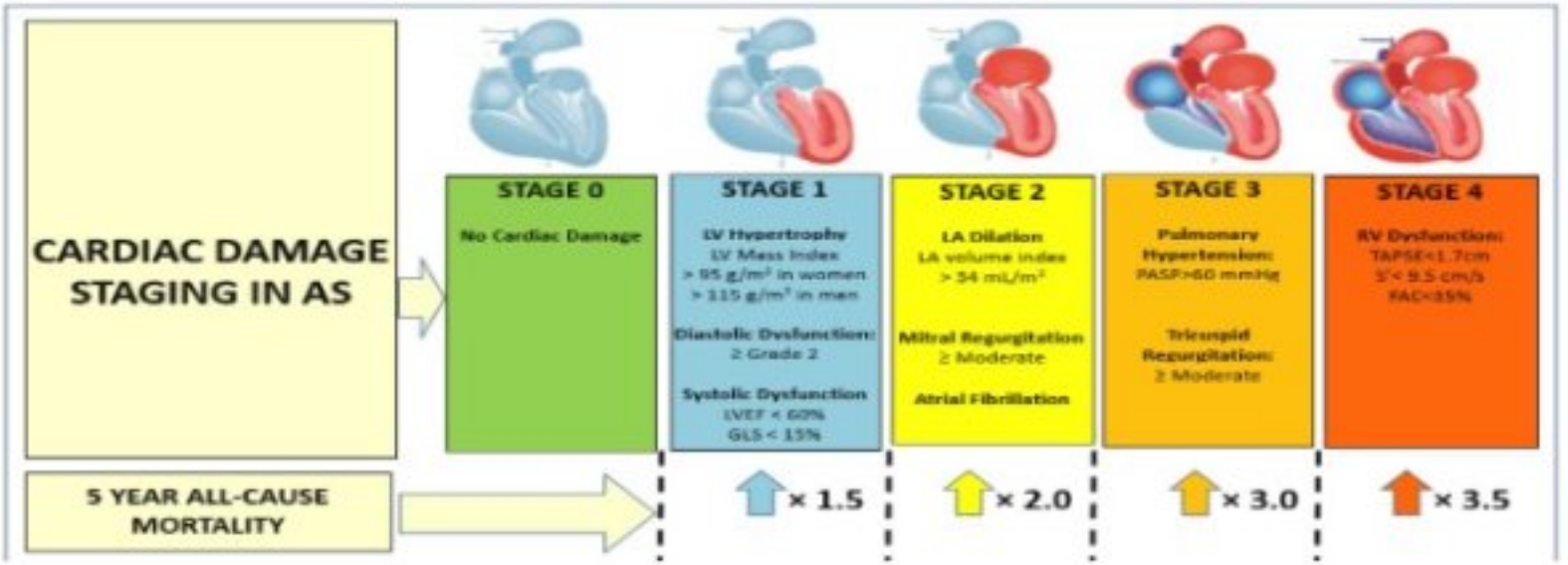


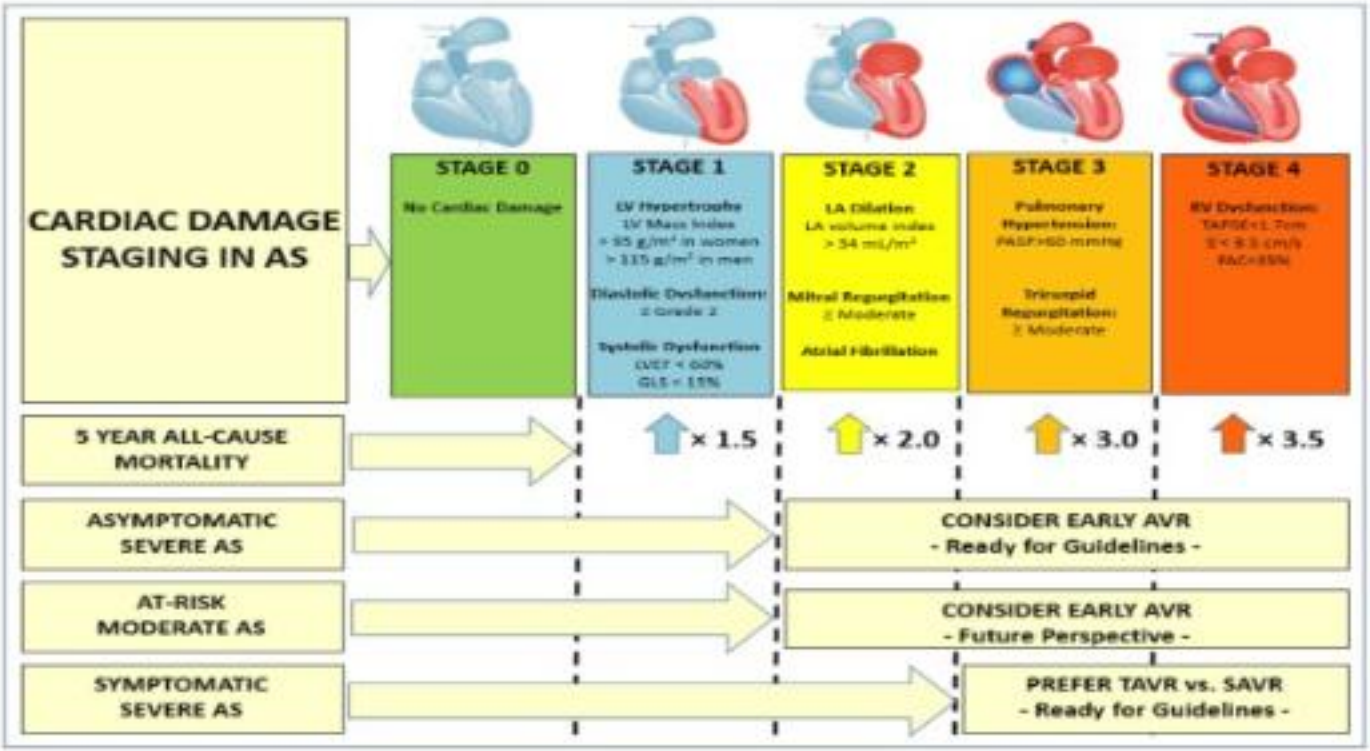
Adjusted Long-Term Survival According to Severity of AS Derived From Mean AV Gradient and Peak AV Velocity Levels

Moderate Aortic Stenosis- ongoing trials

- The TAVR UNLOAD trial is examining the effect of transcatheter aortic valve replacement (TAVR) in patients with moderate AS and heart failure with reduced LVEF.

- The PROGRESS trial and the Evolut EXPAND TAVR II Pivotal trial are investigating whether TAVR could improve outcomes in patients with moderate AS who have symptoms or evidence of cardiac damage/dysfunction


CARDIAC DAMAGE STAGING IN AS
STAGE 0
No Cardiac Damage
STAGE 1
LV Hypertrophy
LV Mass Index
> 95 g/m² in women
> 115 g/m² in men
Diastolic Dysfunction:
≥ Grade 2
Systolic Dysfunction
LVEF < 60%
GLS < 15%
STAGE 2
LA Dilation
LA volume index
> 34 mL/m²
Mitral Regurgitation
≥ Moderate
Atrial Fibrillation
STAGE 3
Pulmonary Hypertension:
PASP>60 mmHg
Tricuspid Regurgitation:
≥ Moderate
STAGE 4
RV Dysfunction:
TAPSE<1.7cm
S'< 9.5 cm/s
FAC<35%
5 YEAR ALL-CAUSE MORTALITY
× 1.5
× 2.0
× 3.0
× 3.5


CARDIAC DAMAGE STAGING IN AS
STAGE 0
No Cardiac Damage
STAGE 1
LV Hypertrophy
LV Mass Index
> 95 g/m² in women
> 115 g/m² in men
Diastolic Dysfunction:
≥ Grade 2
Systolic Dysfunction
LVEF < 60%
GLS < 15%
STAGE 2
LA Dilation
LA volume index
> 34 ml/m²
Mitral Regurgitation
≥ Moderate
Atrial Fibrillation
STAGE 3
Pulmonary Hypertension:
PASP>60 mmHg
Tricuspid Regurgitation:
≥ Moderate
STAGE 4
RV Dysfunction:
TAPSE<1.7cm
S' < 9.5 cm/s
RAZ<45%
5 YEAR ALL-CAUSE MORTALITY
× 1.5
× 2.0
× 3.0
× 3.5
ASYMPTOMATIC SEVERE AS
CONSIDER EARLY AVR
- Ready for Guidelines -
AT-RISK MODERATE AS
CONSIDER EARLY AVR
- Future Perspective -
SYMPTOMATIC SEVERE AS
PREFER TAVR vs. SAVR
- Ready for Guidelines -

Medical therapy

Statins

- While statins have proven benefits for atherosclerotic cardiovascular disease, their effectiveness in specifically slowing aortic stenosis progression appears to be limited based on current evidence.
- However, research is ongoing, and there may be potential benefits in certain patient subgroups that require furt investigation

- Appropriate treatment of Hypertension = ACE I

Which subgroup benefits the most?

- Mild to moderate

TRI-CITY
CARDIOLOG

Medical therapy

PCSK9i

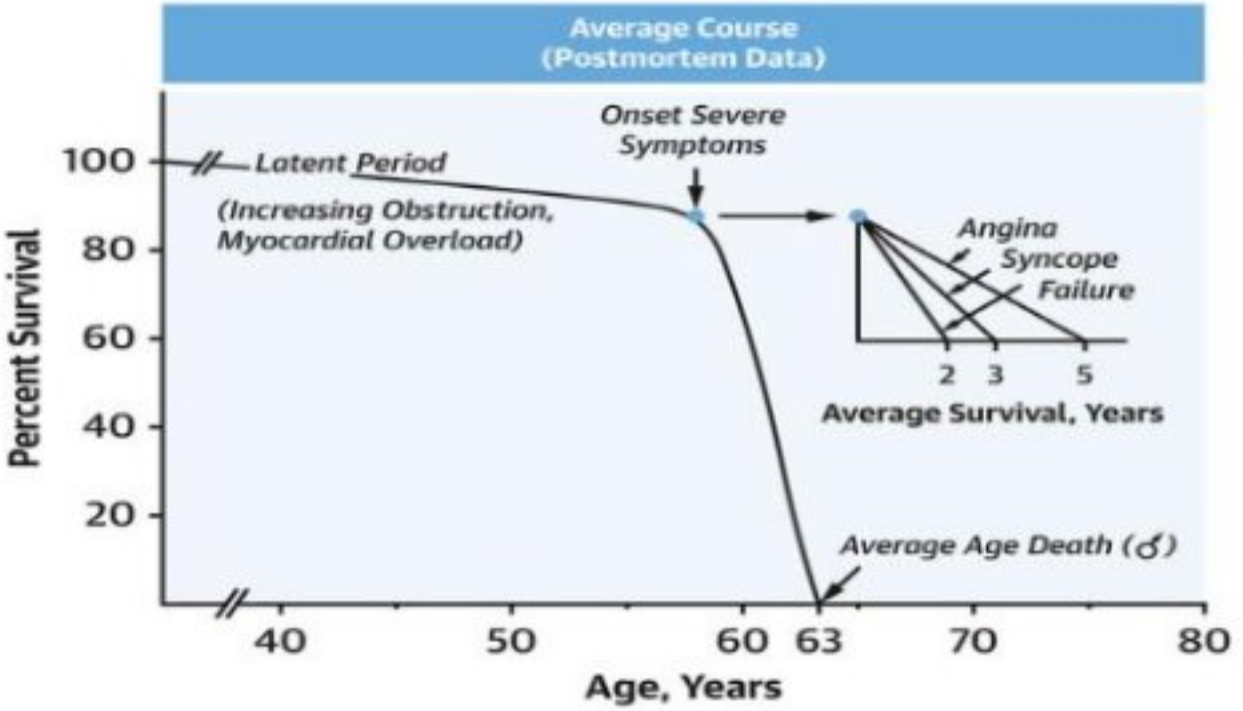
- Reduction of LDL-C levels
- Lowers Lpl A
- Direct Effects on Aortic Valve Cells - PCSK9 may directly influence the calcification process in aortic valve
- Trial underway

LPLa

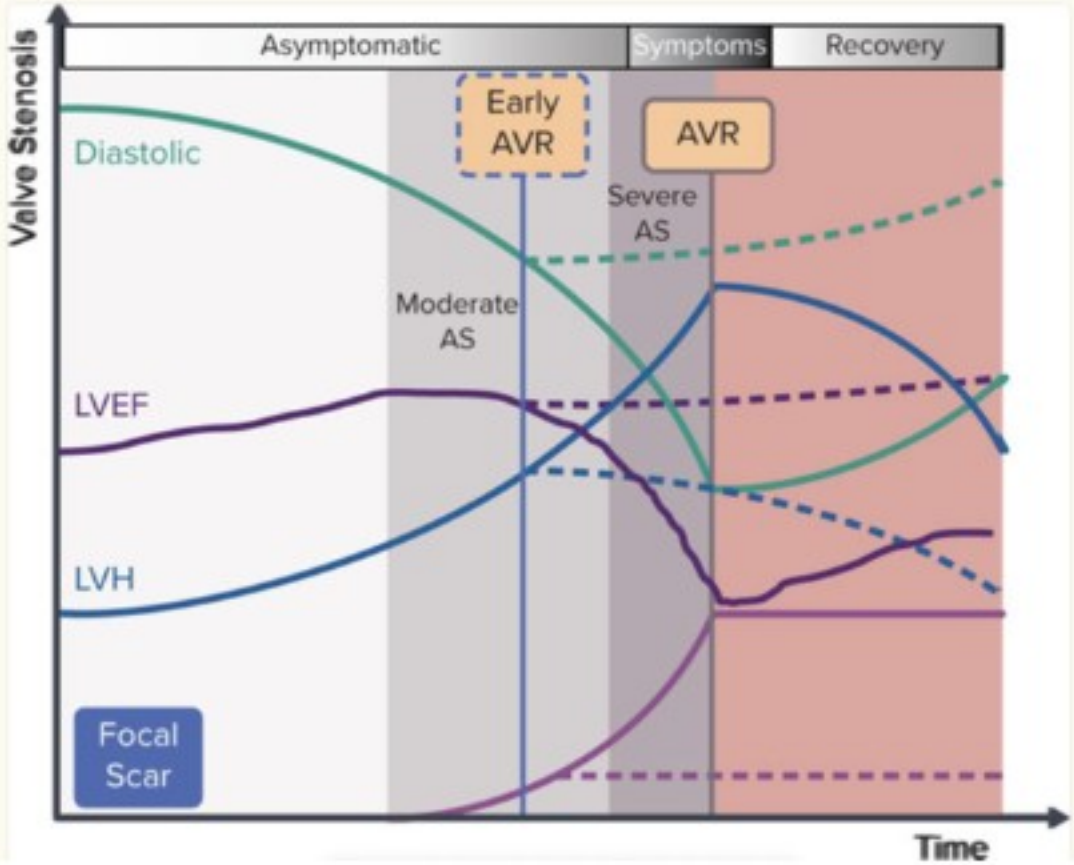
- strong association between elevated Lp(a) levels and aortic valve calcification, a primary driver of aortic stenosis.
- Elevated Lp(a) levels have been correlated with faster progression of aortic valve narrowing and an increased nee aortic valve replacement.
- It binds to the endothelial surface, infiltrates the aortic valve promoting inflammation and calcification

- Olpasiran and pelacarsen, for instance, have shown promise in reducing circulating Lp(a) levels by 85-90% in early phase trials. Phase 3 studies are ongoing to evaluate their efficacy in reducing cardiovascular events, including th related to aortic stenosis

Aortic Stenosis- Summary



Eugene Braunwald et al. *JACC* 2023; 82:2110-2112.


Asymptomatic
Symptoms
Recovery
Valve Stenosis
Early AVR
AVR
Diastolic
Severe AS
Moderate AS
LVEF
LVH
Focal Scar
Time

Summary

- Mortality increases in patients with mild ,moderate – severe aortic stenosis
- In the moderate and severe that AVR was carried out in only 36.7% and 60.7% of those 2 subgroups.
- Not only symptomatic but asymptomatic patients carry a burden of worse outcome
- Recognizing the signs and symptoms earlier and get these patient to earlier management

Bicuspid Aortic valve

- **Current standard of care –** The primary treatment for symptomatic severe aortic stenosis in BAV patients is aortic valve replacement.
- TAVR in this population has some anatomical challenges leading to higher complications **like paravalvular leak**
- Ongoing research - Advancements in transcatheter aortic valve replacement (TAVR) techniques for bicuspid aortic valves (BAV) have been significant, addressing the unique anatomical challenges posed by BAV.
- Newer generations of transcatheter heart valves (THVs) have been developed with design modifications that accommodate the elliptical and larger annular dimensions typical of BAVs.

Aortic regurgitation

- Current standard of care – The primary treatment for symptomatic severe aortic regurgitation is patients is aortic valve replacement.

- Expansion of TAVR Indications
  - not candidates for surgical aortic valve replacement (SAVR) due to high surgical risks
  - Failed Bioprosthesis

- Technological Innovations in the valves (Jena valve platform) that are being studied for this indication

- Studies have shown that self-expanding TAVR, particularly through the transfemoral route, achieves lower in-hospital mortality and complication rates compared to SAVR.

Tricuspid regurgitation

Transcatheter Edge-to-Edge Repair (TEER) –

- Severe TR,
- NYHA II,III,IV
- Surgical turn down,
- On optimized medical medical therapy,
- Systolic pulmonary artery pressure (sPAP) < 70 mm Hg
- Ef - > 20 %

- The TRILUMINATE study demonstrated that the TriClip significantly reduces TR severity and improves quality of life and NYHA functional class in patients with severe TR

TRI-CITY
CARDIOLOG

Tricuspid regurgitation

- Transcatheter Tricuspid Valve Replacement (TTVR):The EVOQUE tricuspid valve replacement device is part of ongoing clinical trials, such as **TRISCEND II**.

- Early results suggest it is safe and effective, potentially improving symptoms and longevity for patients with severe TR

    - At six months, 98.8% of patients achieved a reduction in TR grade to moderate or less, and 93.8% achieved a reduction to mild or less.
    - The EVOQUE system demonstrated substantially superior quality-of-life and functional outcomes compared to OMT alone

Tricuspid regurgitation

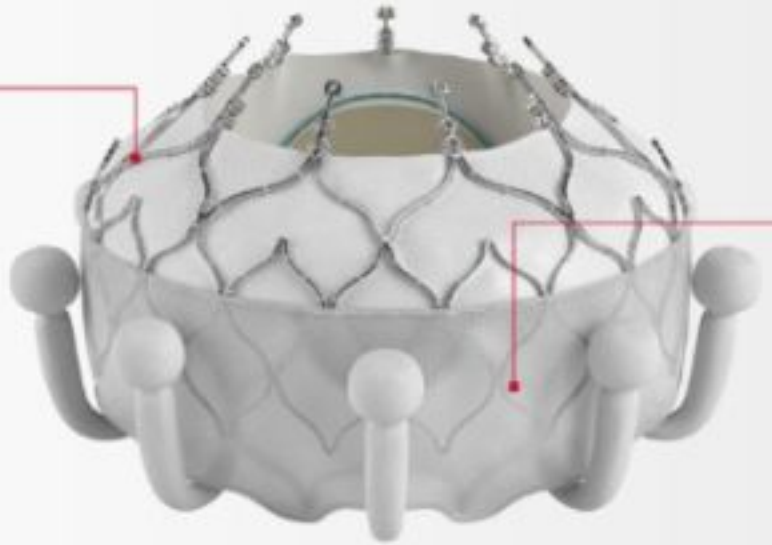
TEE views

- Key TEE Views: There are four essential TEE views used to guide tricuspid valve clip implantation: the 4-chamber, bicommissural, transgastric, and grasping views.
- Grasping View: This view is particularly important as it shows the leaflets to be treated and the clip with its arms wide open. Correct alignment at the transgastric level is critical to finding the best grasping view, which is one of the most complex steps during the procedure
- Transgastric View: This view is critical for aligning the clip with the valve leaflets. It provides a short-axis view of the valve and helps ensure the clip is perpendicular to the leaflets for proper grasping.

The EVOQUE transcatheter tricuspid valve replacement is a system designed with your patients in mind

Designed for anatomical compatibility

Self-expanding, shape memory nitinol frame designed to conform to native valve anatomy



Designed to seal within the native tricuspi annulus

Intra-annular sealing sk and frame

EVOQUE Tricuspid Valve Replacement Procedural Animation

Conclusions

- Burden of Aortic stenosis is set to increase
- We are starting to realize that earlier interventions in the disease process can lead to minimizing the damage – trials underway
- In 5-10 years the play-book might look different

- For Bicuspid valves and Aortic regurgitation – SAVR remains standard
- For those who need it, transcatheter technology is evolving to accommodate the need

- Tricuspid regurgitation
- We are on the cusp of starting to offer this therapy in our own practice

Any Questions?

Please use the QR code to submit your questions.

TRI-CITY
CARDIOLOG

Thank You For Attending the Tri-City Cardiovascular Symposium

TRI-CITY
CARDIOLOG

Figure 1. Pathophysiology of Aortic Stenosis by disease stage. In this figure, an illustration of the progression of AS is provided with particular emphasis on the pathophysiological basis for the occurrence of functional mitral and tricuspid regurgitation.