

Transcatheter Aortic Valve Replacement (TAVR): Past, present, and future

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Disclosures

None

Objectives

- Discuss the prevalence of valvular heart disease
- Aortic valve disease causes
- Physical exam / symptoms of severe AS
- Testing modalities
- Therapies

Louvre Museum, Paris, Fr



Basilica of SacreCoeur de Montmartre



Mr GQ

- 81 year old man with a history of hypertension
- Presents to his PCP for annual visit
- CC: Worsening SOB
- Baseline activity: 1 year ago can walk around Pena Adobe (Lagoon Valley) 2.5 miles
- Now: Difficulty walking to his mailbox
- Physical exam:
 - BP 129/64 mmHg, HR 78 bpm
 - Appears younger than stated age
 - 3/6 SEM RUSB +pulsus parvus et tardus, +S1, no
 S2

DDx for DOE + systolic murmur?

Aortic Valve Stenosis



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Aortic valve stenosis

Leonardo da Vinci (1512)









Alain Cribier and the first patient with TAVI, Rouen, 16 April 2002

HEART VALVE DISEASE





Most heart valve problems involve the **aortic & mitral valves.**

-AORTIC VALVE

between the left ventricle and the main artery (aorta)

• MITRAL VALVE between the left atrium and the left ventricle

SIGNS & SYMPTOMS

May vary, but often include:

- Heart murmur or unusual heartbeat
- Shortness of breath
- Swelling in the legs
- Chest pain
- Unusual fatigue
- Feeling dizzy or fainting
- HEART VALVE DISEASE happens when at least 1 of the 4 valves in the heart no longer works the way it should.

Prevalence of valvular heart disease

А 14 Prevalence Of Moderate Or Severe Valve Disease (%) 7 1 1 All valve disease valve disease valve disease 6 2 0. <45 45-54 65-74 ≥75 55-64 Age (years) В 14 Severe 12 Prevalence Of Moderate Or • Disease (%) 9 8 8 6 Valve 4 2 0 65-74 ≥75 <45 45-54 55-64 Age (years)

Prevalence of Valvular Heart Disease With Age

Nkomo VT, Gardin JM, Skelton TN, et al. Burden of valvular heart diseases: a population-based study. Lancet 2006; 368:1005-11.

2.5%

 % population develop valvular heart disease (industrialized countries)

Increasing age

 Prevalence of moderate or severe aortic and mitral valve disease increases with age

Severe aortic stenosis here in Solano County

1,400 Solano County residents

- Living with severe AS
- 440,000 people living in Solano County
- 16% older than age 65
- 2-5% prevalence of severe AS in pts > 65 years old

Impact of disease and survival



Moderate or severe VHD has a negative impact on survival

Nkomo VT, Gardin JM, Skelton TN, et al. Burden of valvular heart diseases: a population-based study. Lancet 2006; 368:1005-11.

Causes of valvular aortic



Figure 1 Aortic stenosis aetiology: morphology of calcific AS, bicuspid valve, and rheumatic AS. (Adapted from C. Otto, Principles of Echocardiograpy, 2007).

Baumgartner et al. Echo of aortic valve stenosis: JASE Apr 2017

- 1. Calcification of a tricuspid aortic valve
- 2. Calcification (secondary) of a bicuspid aortic valve
- 3. Rheumatic aortic valve disease



Krishnamurthy et al. J CV Trans Research, Dec 2014

Rheumatic Heart Disease

- Untreated, acute rheumatic fever can lead to rheumatic heart disease
- Pathophysiology poorly understood
- Largely eliminated in wealthy nations

Bicuspid aortic valve disease



Krishnamurthy et al. J CV Trans Research, Dec 2014

- Most common congenital abnormality of the aortic valve
- 3:1 male predominance
- Dominates in younger patients with AS
- Ascending aortic aneurysm present in 50% of cases
- >50% of coarctation patients have bicuspid aortic valves

Degenerative aortic valve disease

- Most common form of AS
- "Disease of the elderly"
 - Worsens with age



Degenerative aortic valve disease RISK FACTORS

Atherosclerotic Risk Factors:

- 1) Lipids
- 2) Hypertension
- 3) Male Gender
- 4) Metabolic Syndrome
- 5) Smoking
- 6) Diabetes
- 7) Renal Failure
- 8) Elevated CRP
- 9) Hyperhomocysteinemia

Genetic Factors:

- 1) Vitamin D Receptor
- 2) Apoplipoproteins A1, B and E
- 3) Estrogen Receptor Alpha Gene
- 4) Notch1
- Angiotensin Converting Enzyme
 Interleukin 10
- 7) Connective Tissue Growth Factor
- 8) Chemokine Receptor 5(CCR5)

Osteoblast Phenotype:

- 1) Anigogenesis and apoptosis
- 2) Bone Matrix Protein Expression: OPN, OCN, ON, Alk Phos, GAG, Collagen, FN
- 3) Transcription Factors: Cbfa1, Msx2, Sox9, Egr1
- 4) Cartilage: Hypertrophic Chondrocytes
- 5) Bone: Endochondral Ossification
- 6) Signaling Markers: Lrp5/Wnt, TGFbeta, TNFalpha, FGF, PDGF, IL6, RANKL, VEGF
- 7) Osteoclast Bone Resporption
- 8) MMP/Tenascin/ Purine Nucleotides
- 9) Inflammatory Cells and Lipids



Calcified Aortic Valve

Nalini M. Rajamannan. Arteriosclerosis, Thrombosis, and Vascular Biology. Calcific Aortic Stenosis, Volume: 29, Issue: 2, Pages: 162-168, DOI: (10.1161/ATVBAHA.107.156752)

Normal Aortic Valve

Murmur

- Systolic ejection murmur
- Loudest at the RUSB
- Radiates to both carotids or apex
- Pulsus parvus et tardus: carotid pulse, low in amplitude and delayed

AS Symptoms and Survival



Symptoms

- Initial: Exertional dyspnea or reduced exercise capacity
- Patients can augment activity to minimize symptom burden
- Angina, HF, and syncope = classic late manifestations of severe AS

Stages of disease

- Stage A: At risk population
- Stage B: Progressive (mild-mod) AS
- Stage C: Asymptomatic severe AS
- Stage D: Symptomatic severe AS



Patrizio Lancellotti et al. J Am Coll Cardiol Img 2016; 9:1264-1266.

Echo testing

- Severe AS:
 - Peak aortic valve velocity > 4 m/s
 - Mean aortic valve gradient > 40 mmHg (when flow is nml)
 - Valve area < 1 cm2



Treadmill stress testing

- Asymptomatic patients
- Functional capacity
- Confirm/refute asymptomatic status
- 1/3 of such asx pts have symptoms limiting exercise
- Decrease in SBP > 10 mmHg at peak exercise suggests imminent symptom onset



https://www.bhf.org.uk/informationsupport/heart-matters-magazine/medical/tests/stress-test

Cardiac Catheterization

- Measurement of the LV and aortic pressures
- Rarely needed to confirm AS severity
- Used when echo data inconclusive



Medical Treatment

- Primary prevention
 - Smoking cessation
- HTN
 - Especially important
 - AS + HTN increase load to the LV
- Activity prescription for severe AS:
 - Avoid strenuous activity
 - Avoid competitive sports
- Decompensated heart failure
 - Difficult to manage
 - Often needs hospitalization e.g. invasive hemodynamic monitoring

Aortic Valve Replacement (AVR)

- Class I indications for AVR:
 - Severe symptomatic pts
 - Severe, asymptomatic pts with reduced LVEF (<50%)
 - Those requiring other cardiac surgery
- Only effective therapy for severe AS
- When to replace?

Assess risk for AVR

- Determines patient longevity
- Society of Thoracic Surgeons (STS) predicted risk of mortality (PROM)
- Imperfect risk score; does not include frailty, other organ disease (e.g. PH), procedure specific (e.g. prior radiation)

- Low risk
 - STS-PROM < 4%
 - Non frail
- Intermediate risk
 - STS-PROM 4-8% or
 - Frail
 - 1 major organ system compromise
- High risk
 - STS-PROM > 8% or
 - Frail
 - >2 major organ system compromise
- Prohibitive
 - >3 major organ systems compromise
 - Severely frail



• 85M with severe, symptomatic aortic stenosis



STS Short-term / Operative Risk Calculator Adult Cardiac Surgery Database - All Procedures

Answer All Questions that Apply for Accurate Estimates

Planned Surgery	Isolated AVR	
Surgery Incidence	● First CV surgery ▼	D
Surgical Priority	● Elective ▼	
Demographics		
Sex 0	Male 🔻	E
Age (years)	85	
Height (cm)	180	A
Weight (kg)	85	Te
BMI (kg/m²)	BSA (m²)	
Race 🚯	Select all that apply 🔻	С
Payor / 🚯	Select a maximum of 🗲	
Laboratory Values		(
Creatinine (mg/dL)	9 0.8	
Hematocrit (%)	6 45	
WBC Count (10 ^s /µL)	0 5	н
Platelet Count (cells/ µL)	0 225	N
Preoperative Medio	cations	Ρ

Risk Factors/Comorbidities					
Diabetes 🚯	Select 🔻				
Family Hx of CAD Hypertension Liver Disease	Dialysis Cancer ≤ 5 yrs				
Unresponsive State	Immunocompromised				
Endocarditis 0	Select -				
Illicit Drug Use 🚯	Select -				
Alcohol Use 0	Select -				
Tobacco Use 🚯	Select -				
Pulmonary					
Chronic Lung Disease 🚯	Select 💌				
Recent Pneumonia Sleep Apnea	Home O ₂				
Vascular					
Cerebrovascular Dis.	Select -				
Peripheral Artery Disease Right Carotid Sten. ≥ 80%	Prior Carotid Surgery Left Carotid Sten. ≥ 80%				
Cardiac Status					
Heart Failure 🚯	Yes - Chronic 🔺				
NYHA Classification	Class II 🔺				
PreOp Mech Circ Support	Select all that apply A				
Ejection Fraction (%)	60				

	Coronary Artery Disease		
	Prim. Coronary Symptom	0	None/Other 🕶
	Myocardial Infarction-when	6	
	No. of Diseased Vessels	0	Select -
mised	Valve Disease Aortic Stenosis Mitral Stenosis Aortic Regurgitation	Ao	rtic Root Abscess
	Mitral Regurgitation	6	Select -
	Tricuspid Regurgitation	6	Select -
	Arrhythmia		
	Atrial Fibrillation	6	Select 🕶
	Atrial Flutter	0	Select -
	V. Tach / V. Fib	0	Select -
	Sick Sinus Syn.	6	Select -
	2 nd Degree Block	0	Select -
irgery n. ≥ 80%	3 rd Degree Block	0	Select
	Previous Cardiac Interventio	ns (Selec	t all that apply) 🕄
/▲			

Clinical Summary (3) About

Simulated Patient Summary

Frocedure Type. Isolated AVN				
Perioperative Out	come	Estimate %		
Operative Mortality		1.85%		
Morbidity & Mortalit	y	5.47%		
Stroke		1.03%		
Hona Fanaro		0.001/0		
Reoperation		3.04%		
Prolonged Ventilation		2.12%		
Deep Sternal Wound Infection		0.035%		
Long Hospital Stay (>14 days) 2.3		2.35%		
Short Hospital Stay (<6 days)* 51.7%				
Clinical Summary	y	Сору		
Planned Surgery:	Isolated AVR, Elective, First card	Isolated AVR, Elective, First cardiovascular		
Demographics:	surgery 85 year old, male, 85kg, 180cm, BMI: 26.2 kg/m², BSA: 2.05 m²			
Lab Values:	Creatinine: 0.8 mg/dL, Hematocrit: 45%, WBC Count: 5 10³/µL, Platelet Count: 225000 cells/µL			
Risk Factors / Comorbidities:	Hypertension			
Cardiac Status:	Chronic heart failure, NYHA Clas Fraction = 60%	s II, Ejection		
Coronary Artery Disease:	None/Other			
Volumetric et al.	A			

TAVR

- Minimally invasive
- Cath-based procedure
- Bioprosthetic valve placed in the orifice of the aortic valve
- Transfemoral approach is most common (if possible)



TAVR

Access Sites



TAVR Procedure



Length of Stay (TF TAVR): < 72 hr in 55 % patients Kapadia et al. JACC, March 2019.

Complications of TAVR



Eberhard Grube et al. J Am Coll Cardiol Intv 2019; 12:370-372.

• TAVR

- Less major bleeding
- Shorter hospital length of stay
- Reduced incidence of stroke and a-fib

• SAVR

- Less paravalvular leak
- Less risk for pacemaker need
- Less vascular complications
- Decreased repeat procedure/surgery rates

TAVR Team



Amyloidosis

- 1 in 8 pts with aortic stenosis has concomitant cardiac amyloidosis
 - E.g. transthyretin amyloidosis
- Suspicion raised if:
 - Hx carpal tunnel syndrome
 - Hx lumbar spinal stenosis
 - Disproportionate findings of:
 - HF sx
 - BNP levels
 - Conduction abnormalities
 - Low voltage disproportionate to LV wall thickness
 - Classical LFLG AS
- Rapid pacing is poorly tolerated

Low flow, low gradient AS

 Defined as having a low stroke volume (< 35 mL/m2 or mean transvalvular flow rate < 210 mL/s)

Bicuspid aortic valve

- More marked LV remodeling
- Higher incidence of HF
- TAVR technically more challenging
 - Heavier calcification
 - Noncircular LV outflow tract

Future Studies

- Long-term data on durability of TAVR valves pending
- Multiple trials assessing safety of early TAVR vs watchful waiting
 - Asymptomatic severe AS
 - Moderate AS with low EF

Thank you!