Valvular Heart Disease for the Primary Care Provider

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Disclosure

Consultant: AbbVie; Corcept; Novo Nordisk

Research Grant: Cleerly; Janssen; Massachusetts General Hospital/PCORI; Novartis; Novo Nordisk

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Case Presentation

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43-year-old physician presents to establish care for prevention.

- Known murmur “since he was a kid”
- Competitive tennis player
- No complaints

Physical Exam

- BP 126/82, pulse 74
- Normal rhythm - short, systolic murmur best heard at the LUSB
- Lungs clear
- Radial pulses normal
- No edema

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Outline

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- *Approach to patient with a murmur*
- **Aortic valve disease (stenosis and regurgitation)**
- **Mitral valve regurgitation**
- **Tricuspid regurgitation**

Otto CM et al. Circulation. 2021;143: e72-e227

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Approach to a Patient with a Murmur

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A structured, five-step approach:

- **History & physical exam** — identification of symptoms (if any), characterization of the murmur
- **Innocent vs. pathologic** — recognize benign flow murmurs vs. those associated with pathology
- **Dynamic auscultation** — maneuvers to narrow the differential
- **Echocardiography** — know the Class I indications for TTE
- **Further workup** — TEE, CT, or CMR as indicated

Otto CM et al. Circulation. 2021;143: e72-e227

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Step 1: History & Physical Examination

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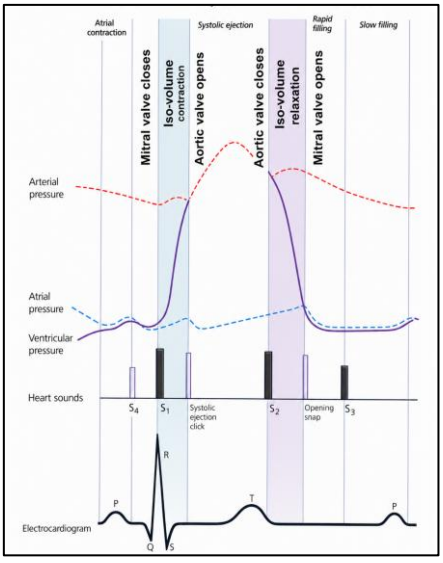
Every patient with a murmur deserves a careful history and physical exam. Key features to characterize:

- **Symptom** — presence or absence of cardiac symptoms (syncope/presyncope, SOB, chest pain, PND/orthopnea, lower extremity edema)
- **Timing in the cardiac cycle** — systolic, diastolic, or continuous
- **Location & radiation** — location gives clues to which valve involve, radiation to the neck, back, or axilla
- **Intensity** — graded 1 to 6
- **Associated findings** — ejection clicks, abnormal S2 splitting, thrills



Otto CM et al. Circulation. 2021;143: e72-e227

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Step 1: History & Physical Examination

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Valve Area (APT M)	Landmark on Chest	What to Listen For
Aortic	**Right upper sternal border** — 2nd–3rd intercostal space, right of sternum	Aortic stenosis (crescendo-decrescendo systolic murmur); aortic regurgitation (early diastolic murmur)
Pulmonic	**Left upper sternal border** — 2nd–3rd intercostal space, left of sternum	Pulmonic stenosis (systolic ejection murmur); pulmonic regurgitation (Graham Steell murmur)
Erb's Point	**Left middle sternal border** — 3rd intercostal space, left of sternum	Aortic regurgitation (often best heard here); also useful for detecting aortic stenosis radiation
Tricuspid	**Left lower sternal border** — 4th–5th intercostal space, left of sternum	Tricuspid regurgitation (holosystolic murmur, increases with inspiration — Carvallo sign); tricuspid stenosis
Mitral (Apex)	**Apex** — 5th intercostal space, midclavicular line	Mitral regurgitation (holosystolic murmur radiating to axilla); mitral stenosis (low-pitched diastolic rumble with opening snap)

Otto CM et al. Circulation. 2021;143: e72-e227

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Step 2: Innocent vs. Pathologic Murmurs

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Innocent murmur — typical features

- Grade 1–2 intensity at the left sternal border
- Midsystolic (ejection) pattern
- Normal S2 intensity and splitting
- No clicks, thrills, or added murmurs
- No increase with Valsalva or standing
- Common in high-output states (anemia, pregnancy)

Assume pathologic — always evaluate

- Diastolic murmurs — virtually always pathologic
- Most continuous murmurs (exceptions: venous hums, mammary souffles)
- Any murmur with symptoms or other abnormal findings

Otto CM et al. Circulation. 2021;143: e72-e227

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Step 3: Dynamic Auscultation

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Bedside maneuvers change loading conditions and help narrow the differential.

Maneuver	Physiologic effect	Murmurs that increase	Murmurs that decrease
Valsalva / Standing	↓ Preload	HCM, MVP	AS, MR, innocent murmurs
Squatting / Leg raise	↑ Preload	Most murmurs (AS, MR)	HCM, MVP
Handgrip / Arterial occlusion	↑ Afterload	MR, AR, VSD	HCM, AS
Inspiration	↑ Venous return	Right-sided (TR, PS)	—
Post-PVC / Long R–R	↑ Ventricular filling	Semilunar valves (AS, PS)	AV regurgitation unchanged

HCM, hypertrophic cardiomyopathy; MVP, mitral valve prolapse; AS, aortic stenosis; MR, mitral regurgitation; AR, aortic regurgitation; VSD, ventricular septal defect; TR, tricuspid regurgitation; PS, pulmonic stenosis.

Otto CM et al. Circulation. 2021;143: e72-e227

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Step 4: When to Order Echocardiography

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Transthoracic echo (TTE) is the first-line imaging test for evaluation of cardiac murmurs. ECG can also provide important information.

Class I — recommended

- Diastolic, continuous, holosystolic, or late-systolic murmurs
- Murmurs with ejection clicks or radiation to the neck/back
- Grade ≥3 midsystolic murmurs
- Any murmur with heart failure, syncope, angina, thromboembolism, or suspected endocarditis

Class IIa — should consider

- Murmurs with other abnormal cardiac findings or an abnormal ECG/CXR

Class III — not recommended

- Grade ≤2 midsystolic murmurs confidently judged innocent by an experienced examiner

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Step 5: Further Workup

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If TTE confirms significant valvular disease, consider:

- TEE, cardiac CT, CMR, stress testing, or diagnostic catheterization — guided by the specific lesion

Key caveat
Trivial or physiologic regurgitation (mitral, tricuspid, or pulmonic) is commonly detected by color Doppler in normal hearts without murmurs — do not overinterpret it.

Otto CM et al. Circulation. 2021;143: e72-e227

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Top 10 Take Home Messages from Valve Guidelines

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Disease stages should be classified on the basis of symptoms, valve anatomy, the severity of valve dysfunction, and the response of the ventricle and pulmonary circulation into Stages A, B, C, and D

Otto CM et al. Circulation. 2021;143: e72-e227

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Valve Disease Stages

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Stage	Definition	Description
A	At risk	Patients with risk factors for development of VHD
B	Progressive	Patients with progressive VHD (***mild to moderate severity and asymptomatic***)
C	***Asymptomatic severe***	Asymptomatic patients who have the criteria for severe VHD: C1: Asymptomatic patients with severe VHD in whom the LV or RV remains compensated space C2: asymptomatic patients with severe VHD with decompensation of LV or RV
D	Symptomatic severe	Patients who have developed ***symptoms*** as a result of VHD

Otto CM et al. Circulation. 2021;143: e72-e227

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Outline

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- **Approach to patient with valve disease**
- ***Aortic valve disease (stenosis and regurgitation)***
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Aortic Valve Pathology

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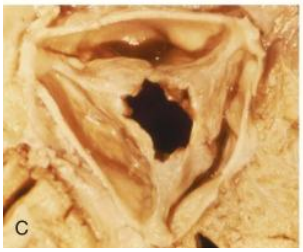
Normal Aortic Valve

Bicuspid Aortic Valve

Rheumatic Aortic Valve



Calcific (Senile) Aortic Valve

Robbins, Cotran & Kumar. Pathologic basis of disease.

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Natural Progression of Aortic Stenosis

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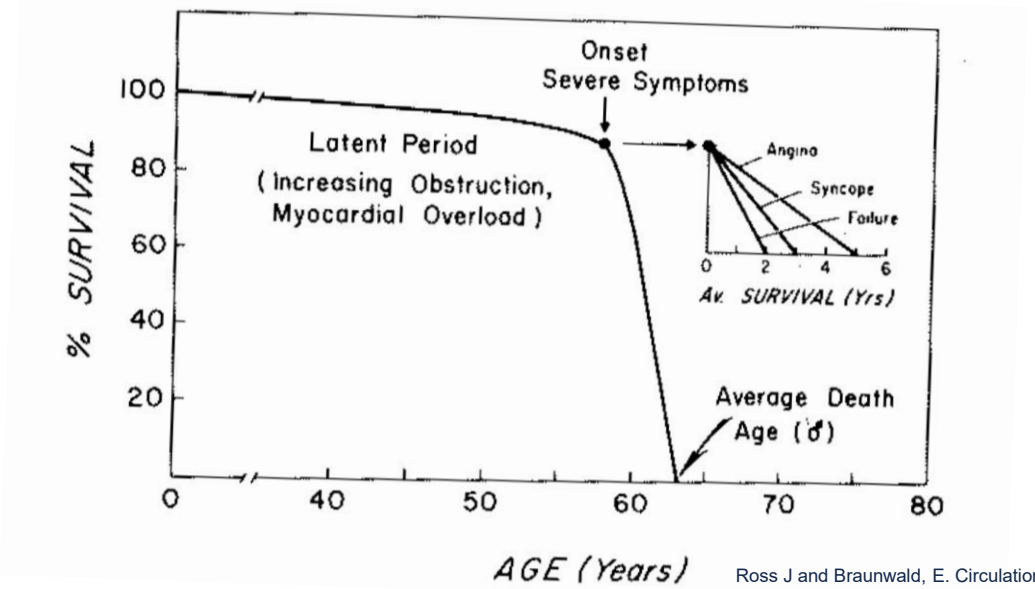

Ross J and Braunwald, E. Circulation. 38: 61, 1961

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Echocardiographic Evaluation of Aortic Valve Disease

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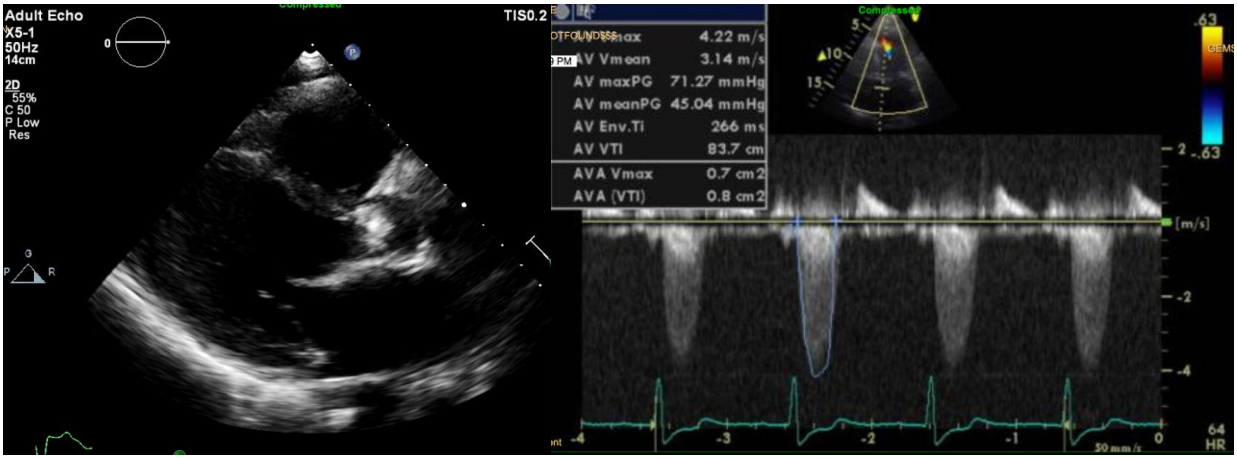

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Table 13. Stages of Valvular Aortic Stenosis

Stage	Definition	Valve Anatomy	Valve Hemodynamics	Hemodynamic Consequences	Symptoms
A	At risk of AS	• BAV (or other congenital valve anomaly) • Aortic valve sclerosis	Aortic V_{max} <2 m/s with normal leaflet motion	None	None
B	Progressive AS	• Mild to moderate leaflet calcification/fibrosis of a bicuspid or trileaflet valve with some reduction in systolic motion or • Rheumatic valve changes with commissural fusion	• **Mild AS**: aortic V_{max} 2.0–2.9 m/s or **mean ΔP <20 mm Hg** • **Moderate AS:** aortic V_{max} 3.0–3.9 m/s or **mean ΔP 20-39 mm Hg**	• Early LV diastolic dysfunction may be present • Normal LVEF	None

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Table 13. Stages of Valvular Aortic Stenosis

Stage	Definition	Valve Anatomy	Valve Hemodynamics	Hemodynamic Consequences	Symptoms
C: Asymptomatic Severe AS					
C1	Asymptomatic severe AS	Severe leaflet calcification/ fibrosis or congenital stenosis with severely reduced leaflet opening	• Aortic V_{max} ≥4 m/s or mean ΔP ≥40 mm Hg • AVA typically is ≤1.0 cm^2 (or AVAi 0.6 cm^2/m^2) but not required to define severe AS • Very severe AS is an aortic V_{max} ≥5 m/s or mean P ≥60 mm Hg	• LV diastolic dysfunction • Mild LV hypertrophy • Normal LVEF	• None • Exercise testing is reasonable to confirm symptom status
C2	Asymptomatic severe AS with LV systolic dysfunction	Severe leaflet calcification/fibrosis or congenital stenosis with severely reduced leaflet opening	• Aortic V_{max} ≥4 m/s or mean ΔP ≥40 mm Hg • AVA typically ≤1.0 cm^2 (or AVAi 0.6 cm^2/m^2) but not required to define severe AS	LVEF <50%	None

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Table 13. Stages of Valvular Aortic Stenosis

Stage	Definition	Valve Anatomy	Valve Hemodynamics	Hemodynamic Consequences	Symptoms
D: Symptomatic severe AS					
D1	Symptomatic severe high-gradient AS	Severe leaflet calcification/fibrosis or congenital stenosis with severely reduced leaflet opening	• Aortic V_{max} ≥4 m/s or mean ΔP ≥40 mm Hg • AVA typically ≤1.0 cm^2 (or AVAi ≤ 0.6 cm^2/m^2) but may be larger with mixed AS/AR	• LV diastolic dysfunction • LV hypertrophy • Pulmonary hypertension may be present	• Exertional dyspnea, decreased exercise tolerance, or HF • Exertional angina • Exertional syncope or presyncope
D2	Symptomatic severe low-flow, low-gradient AS with reduced LVEF	Severe leaflet calcification/fibrosis with severely reduced leaflet motion	• AVA ≤1.0 cm^2 with resting aortic V_{max} <4 m/s or mean ΔP <40 mm Hg • Dobutamine stress echocardiography shows AVA <1.0 cm^2 with V_{max} ≥4 m/s at any flow rate	• LV diastolic dysfunction • LV hypertrophy • LVEF <50%	• HF • Angina • Syncope or presyncope

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Table 13. Stages of Valvular Aortic Stenosis

Stage	Definition	Valve Anatomy	Valve Hemodynamics	Hemodynamic Consequences	Symptoms
D: Symptomatic severe AS					
D3	Symptomatic severe low-gradient AS with normal LVEF or paradoxical low-flow severe AS	Severe leaflet calcification/fibrosis with severely reduced leaflet motion	• AVA ≤1.0 cm^2 (indexed AVA ≤0.6 cm^2/m^2) with an aortic V_{max} <4 m/s or mean ΔP <40 mm Hg AND Stroke volume index <35 mL/m^2 • Measured when patient is normotensive (systolic blood pressure <140 mm Hg)	• Increased LV relative wall thickness • Small LV chamber with low stroke volume • Restrictive diastolic filling • LVEF ≥50%	• HF • Angina • Syncope or presyncope

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Natural Progression of Aortic Stenosis

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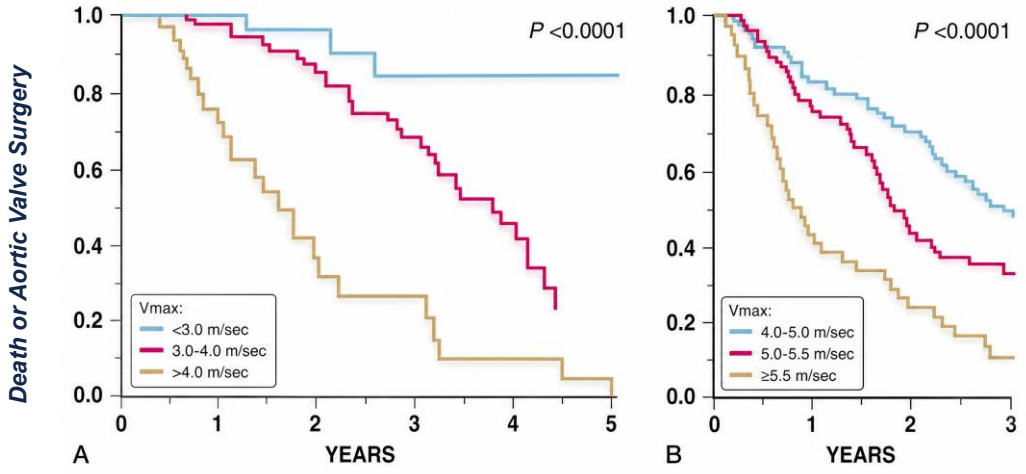

Otto CM, et al. *Circulation.* 95: 2262, 1997
Rosenhek R,, et al. *Circulation.* 121:151, 2010

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Outcomes with Early Surgery

n=145 Patients with Asymptomatic AoV Stenosis (>4.5 m/s or >50 mmHg)

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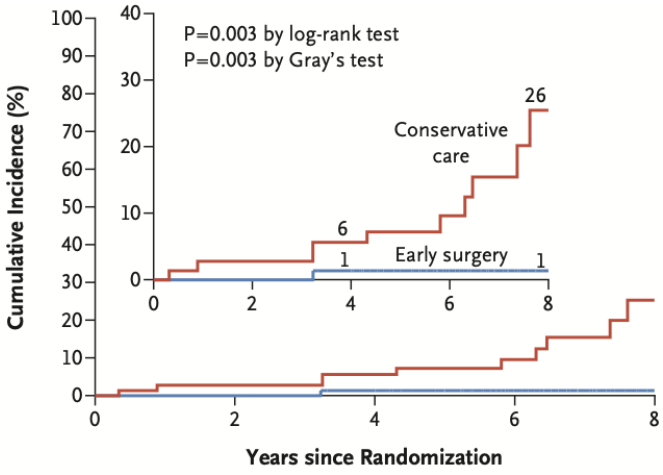

HR 0.09
95%CI 0.01-0.67
P=0.003

- 95% of those randomized to surgery had treatment within 2 months
- No operative mortalities
- 5/73 deaths in the early surgery (7%)
- 15/72 deaths in the conservative (15%)
- Limitation - small study performed at 4 centers in South Korea

No. at Risk

Conservative care	72	68	65	36	12
Early surgery	73	73	70	38	13

Kang et al. *N Engl J Med* 2020;382:111

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Timing of Intervention of AS

American Heart Association.

AMERICAN COLLEGE of CARDIOLOGY FOUNDATION

COR	LOE	Recommendations
1	A	1. In adults with severe high-gradient AS (Stage D1) and symptoms of exertional dyspnea, HF, angina, syncope, or presyncope by history or on exercise testing, AVR is indicated.
1	B-NR	2. In asymptomatic patients with severe AS and an *LVEF <50%* (Stage C2), AVR is indicated.
1	B-NR	3. In asymptomatic patients with severe AS (Stage C1) who are undergoing cardiac surgery for other indications, AVR is indicated.

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Timing of Intervention of AS

COR	LOE	Recommendations
1	B-NR	4. In symptomatic patients with low-flow, low-gradient severe AS with reduced LVEF (Stage D2), AVR is recommended.
1	B-NR	5. In symptomatic patients with low-flow, low-gradient severe AS with normal LVEF (Stage D3), AVR is recommended *if AS is the most likely cause of symptoms.*

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ARS Question #1

Aortic Valve Replacement Should Be Considered for All of the Following Except:

A. Asymptomatic, Aortic Valve Velocity >5 m/s
B. Symptomatic, Aortic Valve Velocity >4 m/s
C. Symptomatic, Aortic Valve Velocity >3.0 m/s
D. Asymptomatic, Aortic Valve Velocity <4 m/s

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Treatment of Aortic Stenosis

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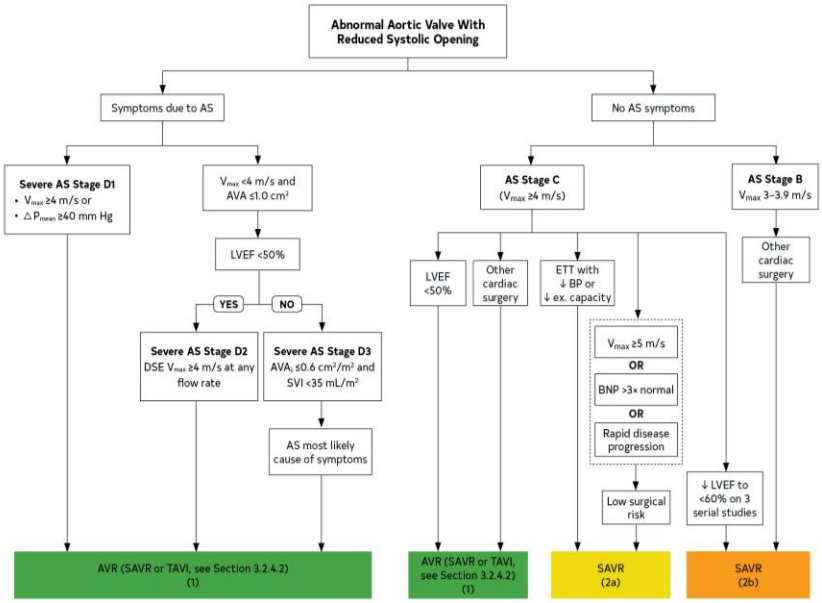

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Mechanical vs Bioprosthetic Valve

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Feature	Mechanical Valve	Bioprosthetic Valve
Durability	Designed to last a lifetime	Structural deterioration over time (15-yr reoperation risk: ~22% at age 50, ~30% at age 40, ~50% at age 20)
Anticoagulation	Lifelong VKA required (INR 2.0–3.0 for aortic; 2.5–3.5 for mitral)	Not required unless other indication (e.g., AF)
Lifestyle impact	Dietary restrictions, medication interactions, activity limitations, frequent INR monitoring	Fewer restrictions; no routine INR monitoring after initial period
Pregnancy	VKA therapy poses teratogenic risk; complex anticoagulation management during pregnancy	Preferred in women desiring future pregnancy (avoids VKA in pregnancy)
Valve-in-valve option	Not applicable	Transcatheter valve-in-valve (ViV) replacement available
Hemodynamics	Smaller effective orifice area in smaller sizes	TAVI bioprostheses may offer larger effective orifice areas in smaller sizes (less patient–prosthesis mismatch)

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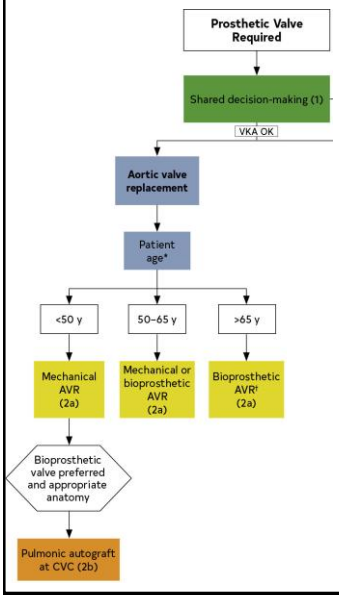
ACC/AHA Guidelines Mechanical vs. Bioprosthetic



Age <50 y	Age >65
High incidence of bioprosthetic valve dysfunction - 15-y risk: 30% for age 40 - 15-y risk: 50% for age 20	Low incidence of bioprosthetic valve dysfunction - 15-y risk: <10% for age >70 y
Lower risk of anticoagulation complications	Higher risk of anticoagulation complications
Preference – avoid reintervention	Preference - avoid risk/inconvenience of VKA
High-risk reintervention (porcelain aorta, prior radiation therapy)	Access to transcatheter ViV replacement
Small aortic root size for AVR (may preclude ViV procedure in future)	TAVI valves have larger effective orifice areas for smaller valve sizes (avoid patient–prosthesis mismatch)

J Am Coll Cardiol. 2021; 77: e25–e197

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Choice of Intervention: Mechanical Versus Bioprosthetic AVR

COR	LOE	Recommendations
1	C-EO	1. In patients with an indication for AVR, the choice of prosthetic valve should be based on a shared decision-making process that accounts for the patient's values and preferences and includes discussion of the indications for and risks of anticoagulant therapy and the potential need for and risks associated with valve reintervention.
1	C-EO	2. For patients of any age requiring AVR for whom VKA anticoagulant therapy is contraindicated, cannot be managed appropriately, or is not desired, a bioprosthetic AVR is recommended.
2a	B-R	3. For patients <50 years of age who do not have a contraindication to anticoagulation and require AVR, it is reasonable to choose a mechanical aortic prosthesis over a bioprosthetic valve.

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Table 10. Median Operative Mortality Rates for Specific Surgical Procedures (STS Adult Cardiac Surgery Database, 2019)

Procedure	Mortality Rate (%)
AVR	2.2
AVR and CABG	4
AVR and mitral valve replacement	9
Mitral valve replacement	5
Mitral valve replacement and CABG	9
Mitral valve repair	1
Mitral valve repair and CABG	5

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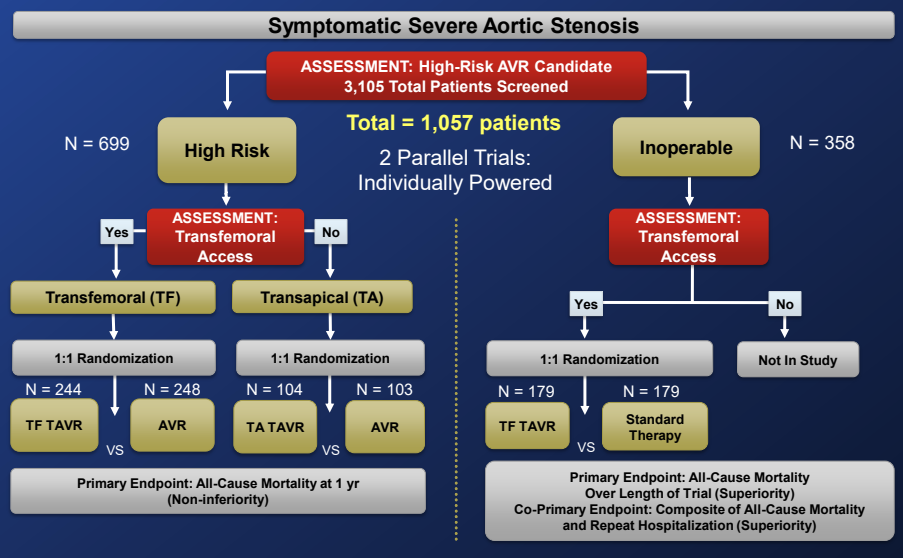
PARTNER Study Design



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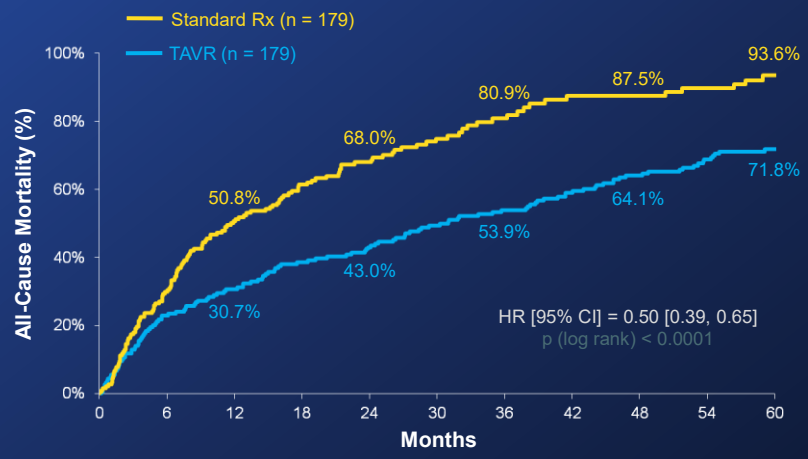
All-Cause Mortality (ITT)
Crossover Patients Censored at Crossover



** In an age and gender matched US population without comorbidities, the mortality at 5 years is 40.5%.*

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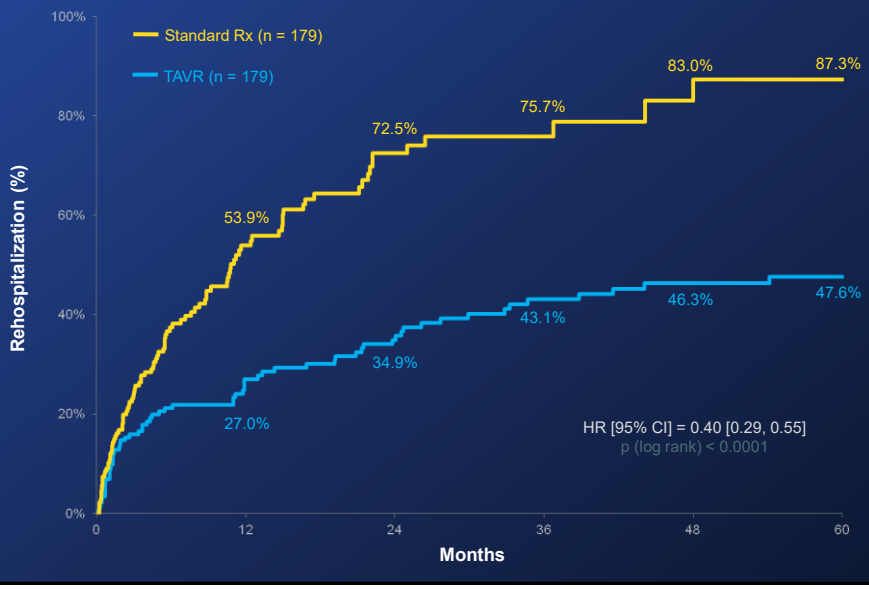
Repeat Hospitalization (ITT)



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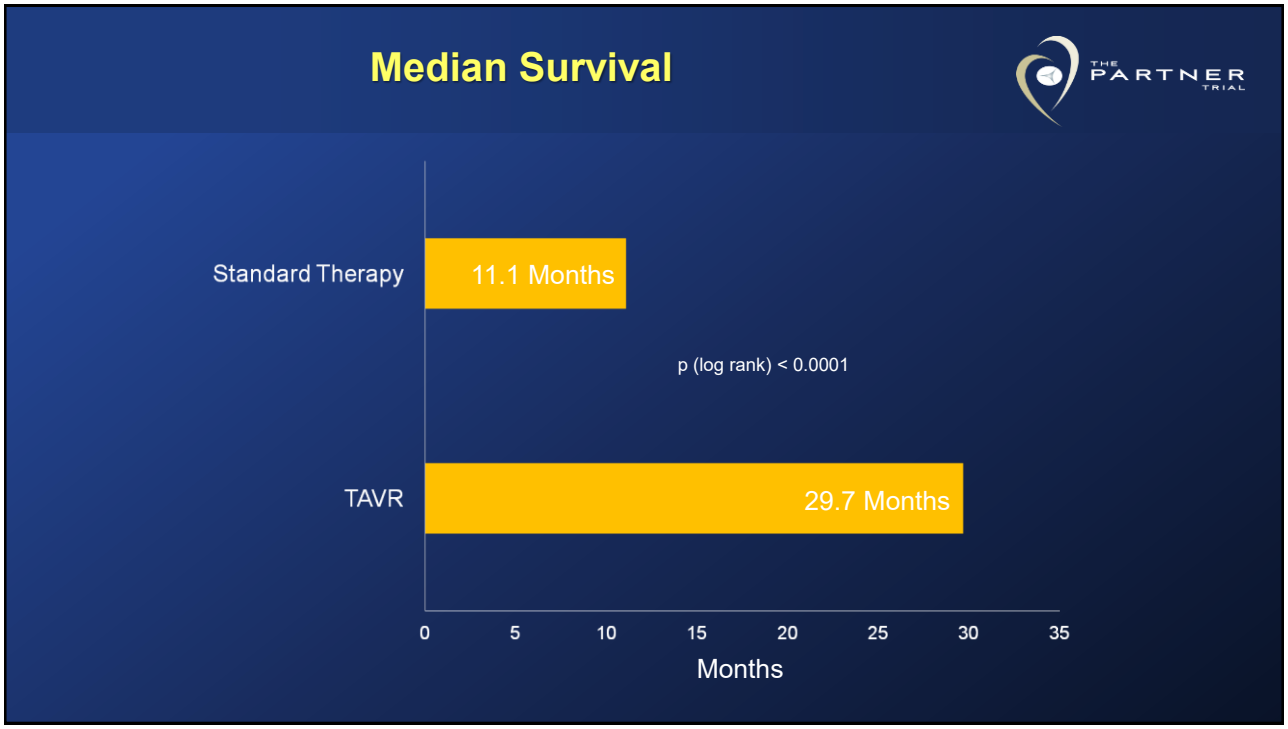

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Outcomes in Low-Risk Patients

n=1000 Patients Randomized to SAVR or TAVR

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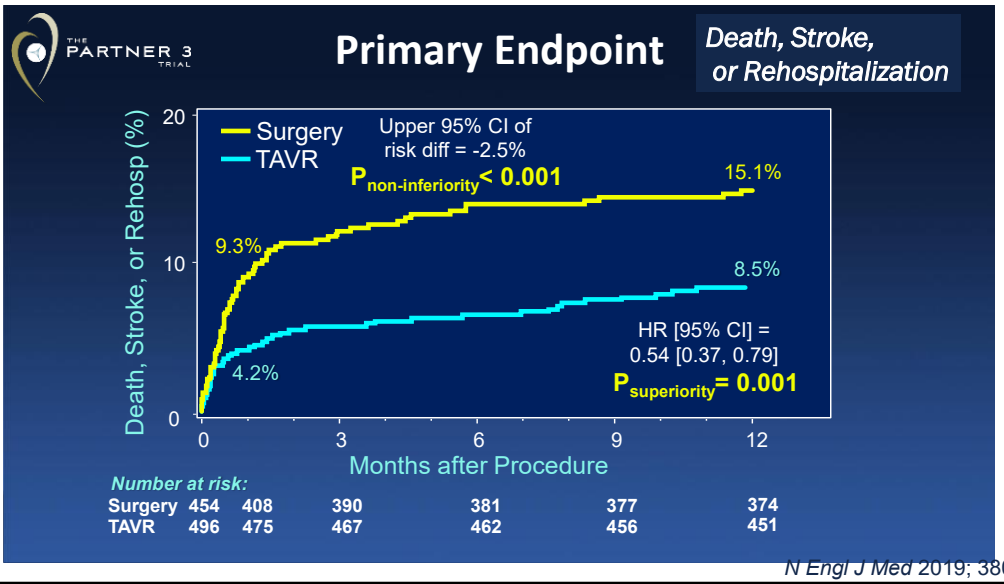

N Engl J Med 2019; 380:1695-1705

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Outcomes in Low-Risk Patients

n=1000 Patients Randomized to SAVR or TAVR

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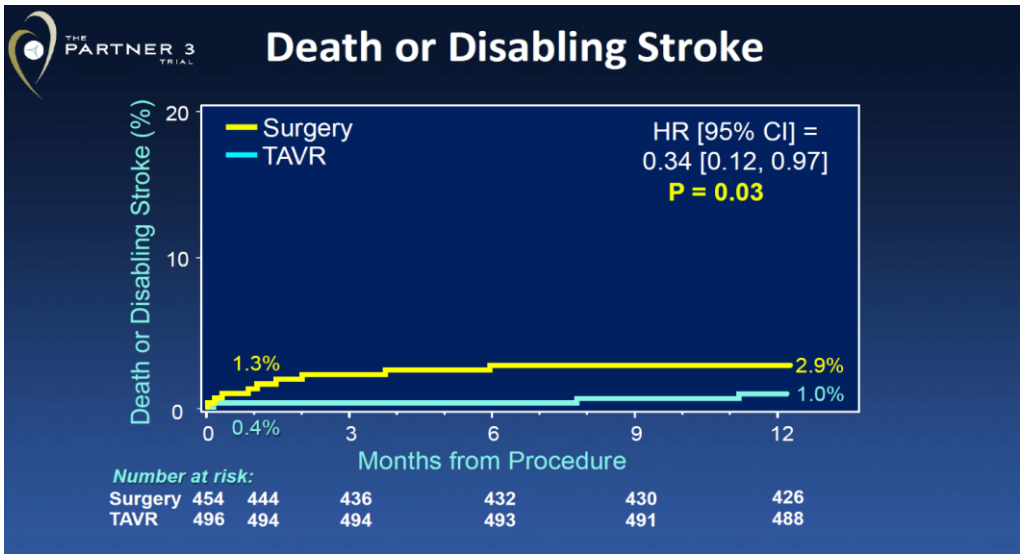

N Engl J Med 2019; 380:1695-1705

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Outcomes with Aortic Valve Replacement in Low-Risk Surgical Patients

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Outcome	SAPIEN 3 (PARTNER 3)	Evolut (Evolut Low Risk)	SAVR (PARTNER 3 / Evolut)
30-day mortality	0.4%	0.5%	1.1–1.3%
30-day all stroke	0.6%	3.4%	2.4–3.4%
30-day life-threatening/major bleeding	~3.6%	2.4%	7.5%
30-day new pacemaker	6.6%	17.4%	4.1–6.1%
1-year mortality	1.0%	2.4%	2.5–3.0%
1-year all stroke	2.0%	4.1%	3.6–4.3%
1-year life-threatening/disabling bleeding	~5%	3.2%	8.9%
1-year new pacemaker	~7.3%	19.4%	6.7–7.0%

N Engl J Med 2019;380:1695-1705 J Am Coll Cardiol 2021; 77: 1149-1161
N Engl J Med 2019;380:1706-1715 N Engl J Med 2023;389:1949-1960

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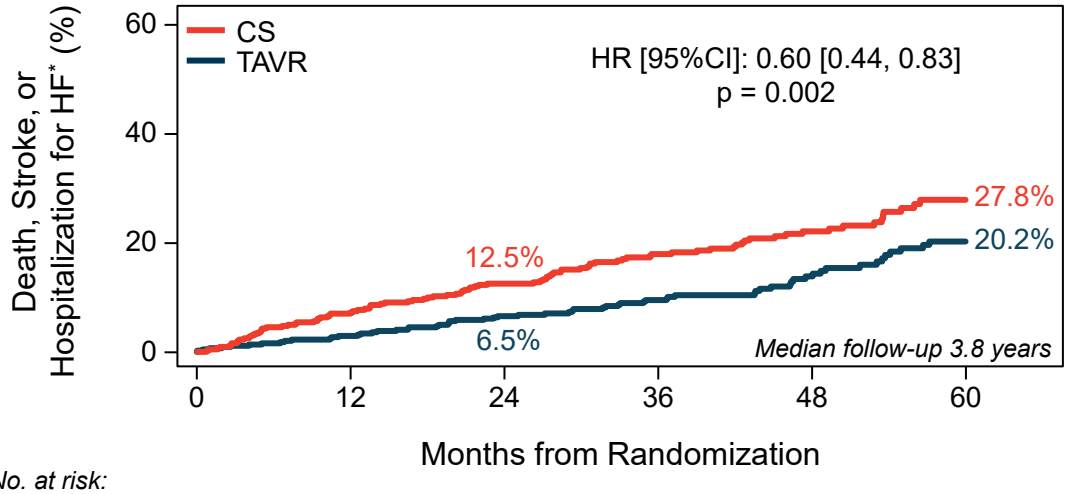
THE EARLY TAVR TRIAL

Death, Stroke, or Hosp. for HF*



No. at risk:

TAVR	455	431	412	331	175	128
CS	446	410	376	268	163	77

*Hosp for symptomatic CHF treated with IV diuresis, inotropic therapy, IABP, ventilation for pulmonary edema, or hemodialysis for vol. overload

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Outcomes in Low-Risk Patients (NOTION-2)

n=370 Patients with Bicuspid or Tricuspid Valve "Suitable" for SAVR or TAVR

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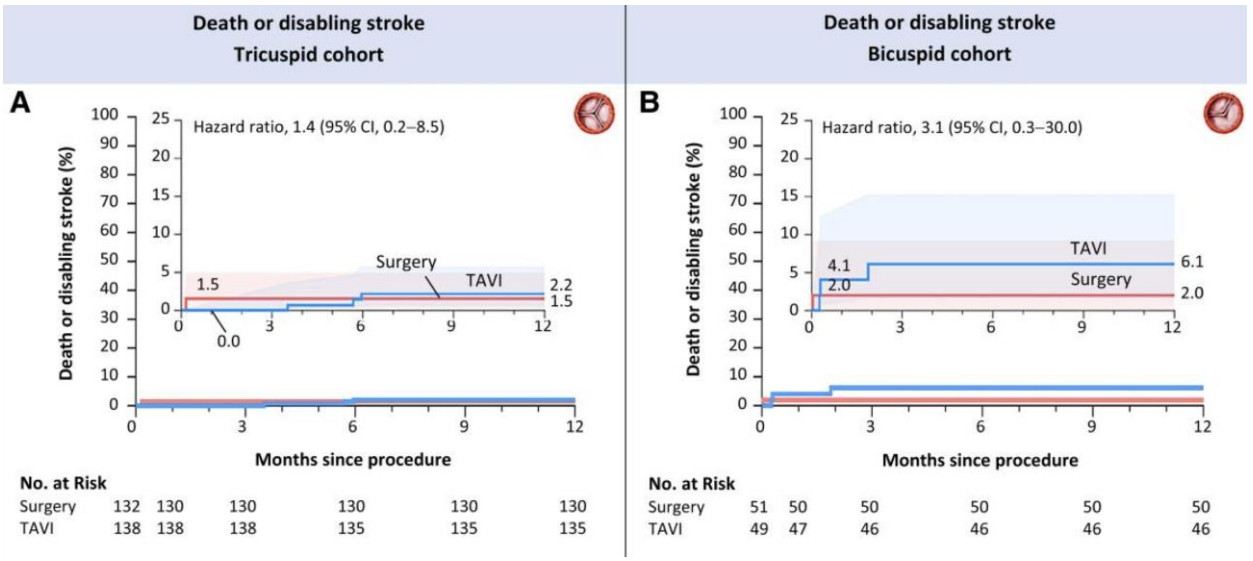

Jørgensen et al. European Heart Journal 2024; 45: 3804–3814

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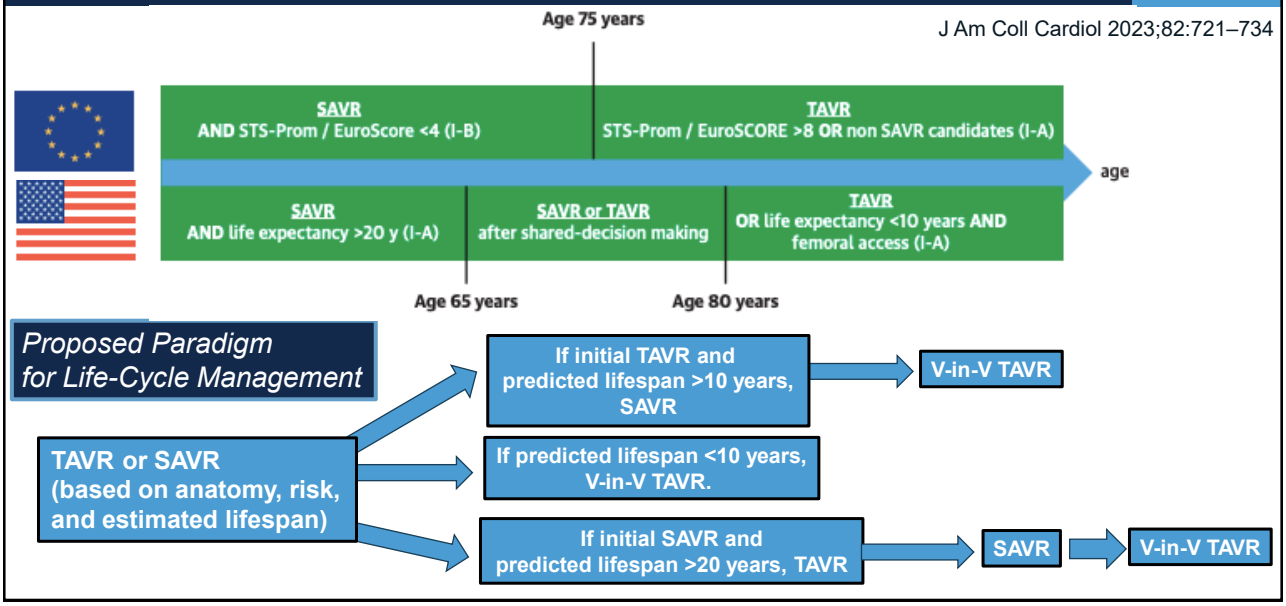
Current Guideline Recommendations for Life-Cycle Management of Severe Aortic Stenosis

J Am Coll Cardiol 2023;82:721–734



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Guideline Recommendation – Shared Decision Making

Recommendation for Evaluation of Surgical and Interventional Risk

COR	LOE	RECOMMENDATION
1	C-EO	1. For patients with VHD for whom intervention is contemplated, individual risks should be calculated for specific surgical and/or transcatheter procedures, using online tools when available, and discussed before the procedure as a part of a shared decision-making process.

SAVR	TAVI
Technical or anatomic	
▪ Prior mediastinal radiation ▪ Ascending aortic calcification (porcelain aorta may be prohibitive)	▪ Aorto-iliac occlusive disease precluding transfemoral approach ▪ Aortic arch atherosclerosis (protuberant lesions) ▪ Severe MR or TR ▪ Low-lying coronary arteries ▪ Basal septal hypertrophy ▪ Valve morphology (eg, bicuspid or unicuspid valve) ▪ Extensive LV outflow tract calcification

Comorbidities

- Severe COPD or home oxygen therapy
- Pulmonary hypertension
- Severe RV dysfunction
- Hepatic dysfunction
- Frailty*

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Mitral valve repair and CABG	5

J Am Coll Cardiol. 2021; 77: e25–e197

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ARS Question #2

As Compared to Surgery, Transcatheter Aortic Valve Replacement Results in All of the Following Except:

A. Lower morbidity and mortality
B. Lower rates of stroke
C. Shorter length of stay, higher quality of life (at 30 days)
D. Lower rates of pacemaker

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Echocardiogram of Aortic Insufficiency

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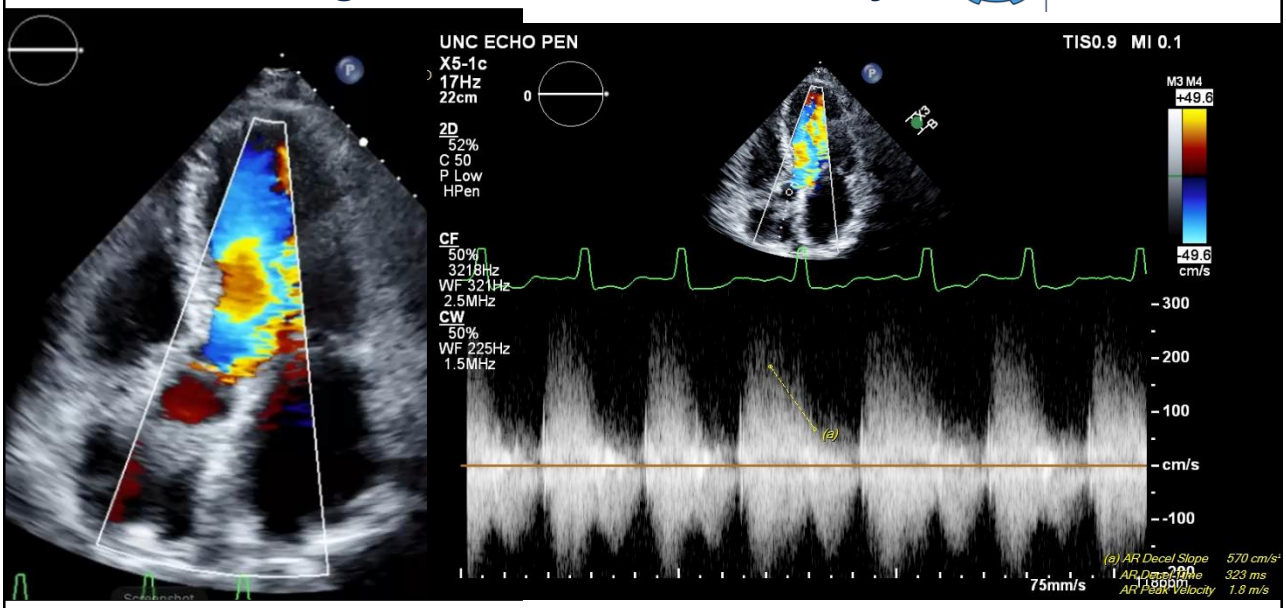
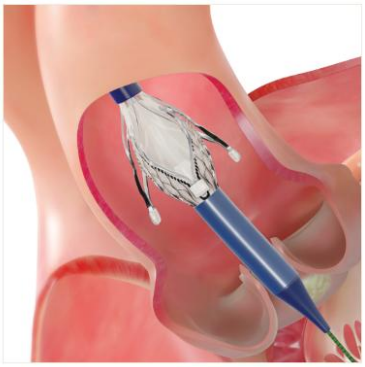


44

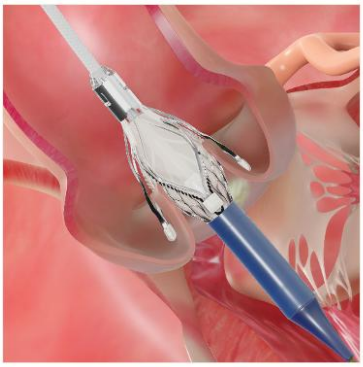
Trilogy Valve for Aortic Insufficiency

School of Medicine



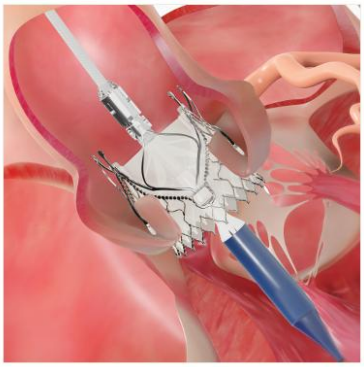
Alignment

- Aligns THV with native cusps



Positioning/Anchoring

- Locators "clip" onto native leaflets forming a natural seal and stable securement

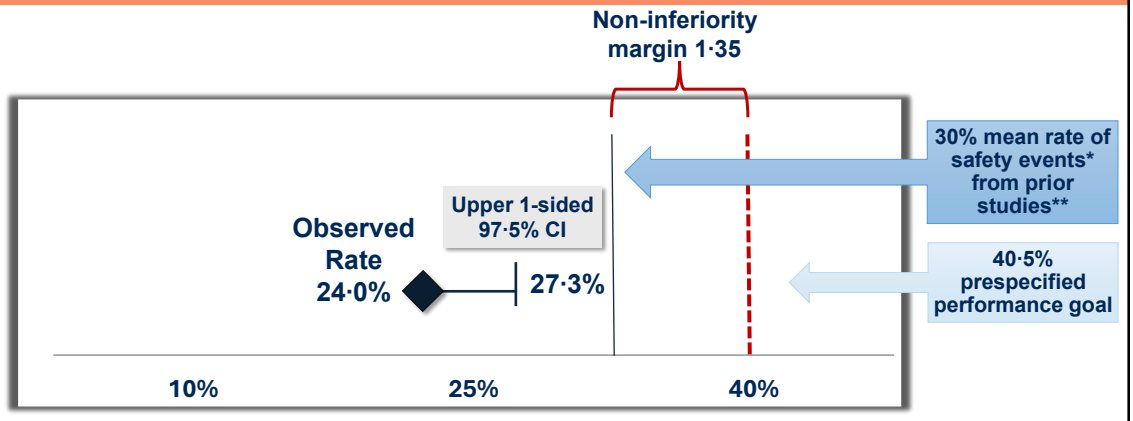


Deployment

- Large open cells provide access to low coronaries
- Flared sealing ring conforms to annulus

45

Primary Safety Endpoint* at 30 Days



$p_{noninferiority}<0·0001$

*Composite of 30-day all-cause mortality, any stroke, life-threatening/major bleeding, major vascular complication, AKI ≥2 or dialysis, valve intervention, new permanent pacemaker, ≥ moderate valvular regurgitation

** 1. Feldman TE, Reardon MJ, Rajagopal V, et al. The REPRISE III Randomized Clinical Trial. *JAMA.* 2018; 319: 27-37.
2. Makkar RR, Cheng W, Waksman R, et al. Self-expanding intra-annular versus commercially available transcatheter heart valves in high and extreme risk patients with severe aortic stenosis (PORTICO IDE): a randomised, controlled, non- inferiority trial. *Lancet.* 2020; 369: 669-683.
3. Thiele H, Kurz T, Feistritzer H-J, et al. Comparison of newer generation self-expandable vs. balloon-expandable valves in transcatheter aortic valve implantation: the randomized SOLVE-TAVI trial. *Eur Heart J.* 2020; 41:1890-1899.

PCR london VALVES

pcrlondonvalves.com

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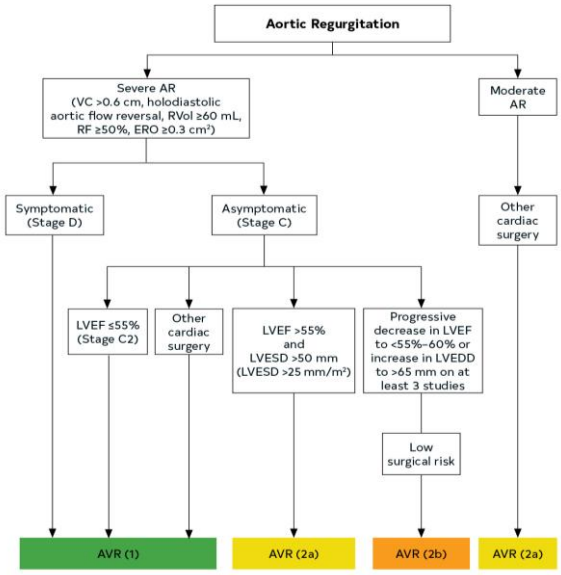
Echocardiogram of Aortic Insufficiency

School of Medicine



COR	LOE	Recommendations
1	B-NR	In asymptomatic patients with chronic AR (Stages B and C), treatment of hypertension (systolic blood pressure >140 mm Hg) is recommended.
1	B-NR	In patients with severe AR who have symptoms and/or LV systolic dysfunction (Stages C2 and D) but a prohibitive surgical risk, GDMT for reduced LVEF with ACE inhibitors, ARBs, and/or sacubitril/valsartan is recommended.

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Outline

School of Medicine

- Approach to patient with valve disease
- Aortic valve disease (stenosis and regurgitation)
- *Mitral valve regurgitation*
- Tricuspid regurgitation

Otto CM et al. Circulation. 2021;143: e72-e227

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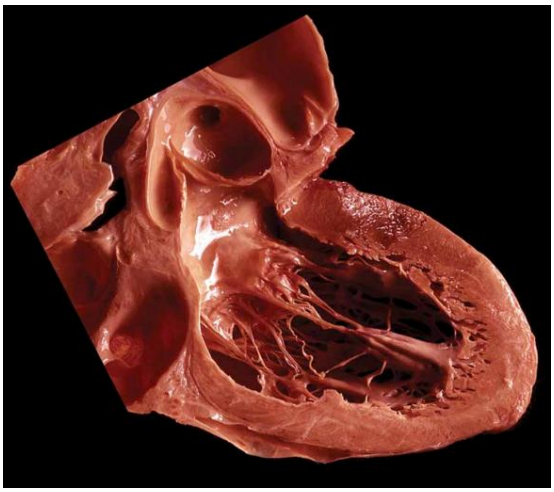
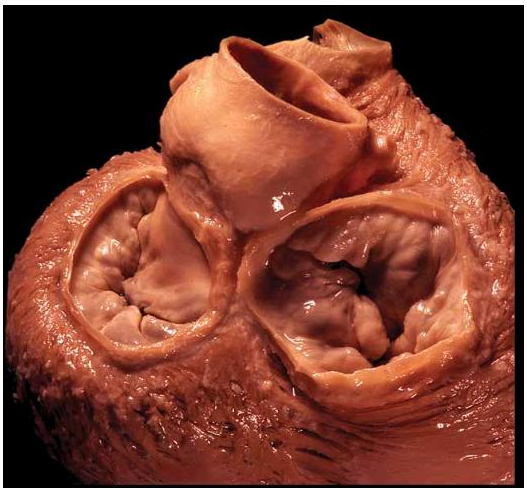
Mitral Valve

School of Medicine





Mori, Shivkumar *Atlas of Cardiac Anatomy*, Digital Edition 2022

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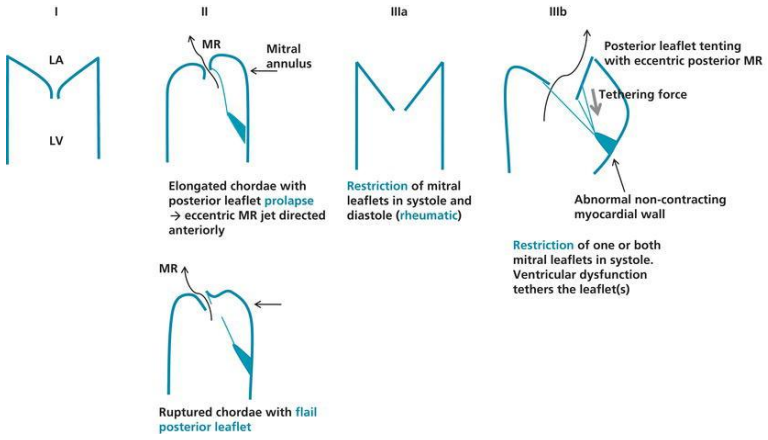
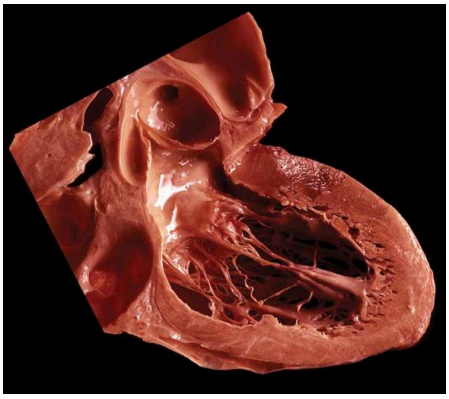
Primary Mitral Regurgitation

School of Medicine

Carpentier Classification of Mitral Valve Regurgitation





Mori, Shivkumar *Atlas of Cardiac Anatomy*, Digital Edition 2022
Valvular Disorders. Practical Cardiovascular Medicine 2e

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Table 17. Stages of Chronic Primary MR

Grade	Definition	Valve Anatomy	Valve Hemodynamics*	Hemodynamic Consequences	Symptoms
A	At risk of MR	• Mild mitral valve prolapse with normal coaptation • Mild valve thickening and leaflet restriction	• No MR jet or small central jet area <20% LA on Doppler • Small vena contracta <0.3 cm	• None	None
B	Progressive MR	• Moderate to severe mitral valve prolapse with normal coaptation • Rheumatic valve changes with leaflet restriction and loss of central coaptation • Prior IE	• Central jet MR 20%–40% LA or late systolic eccentric jet MR • Vena contracta <0.7 cm • Regurgitant volume <60 mL • Regurgitant fraction <50% • ERO <0.40 cm^2 • Angiographic grade 1+ to 2+	• Mild LA enlargement • No LV enlargement • Normal pulmonary pressure	None

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Table 17. Stages of Chronic Primary MR

Footnote text located on the next slide

Grade	Definition	Valve Anatomy	Valve Hemodynamics*	Hemodynamic Consequences	Symptoms
C	Asymptomatic severe MR	• Severe mitral valve prolapse with loss of coaptation or flail leaflet • Rheumatic valve changes with leaflet restriction and loss of central coaptation • Prior IE • Thickening of leaflets with radiation heart disease	• Central jet MR >40% LA or holosystolic eccentric jet MR • Vena contracta ≥0.7 cm • Regurgitant volume ≥60 mL • Regurgitant fraction ≥50% • ERO ≥0.40 cm^2 • Angiographic grade 3+ to 4+	• Moderate or severe LA enlargement • LV enlargement • Pulmonary hypertension may be present at rest or with exercise • **C1:** LVEF >60% and LVESD <40 mm • **C2:** LVEF ≤60% and/or LVESD ≥40 mm	• None
D	Symptomatic severe MR	• Severe mitral valve prolapse with loss of coaptation or flail leaflet • Rheumatic valve changes with leaflet restriction and loss of central coaptation • Prior IE • Thickening of leaflets with radiation heart disease	• Central jet MR >40% LA or holosystolic eccentric jet MR • Vena contracta ≥0.7 cm • Regurgitant volume ≥60 mL • Regurgitant fraction ≥50% • ERO ≥0.40 cm^2 • Angiographic grade 3+ to 4+	• Moderate or severe LA enlargement • LV enlargement • Pulmonary hypertension present	• Decreased exercise tolerance • Exertional dyspnea

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Table 10. Median Operative Mortality Rates for Specific Surgical Procedures (STS Adult Cardiac Surgery Database, 2019)

Procedure	Mortality Rate (%)
AVR	2.2
AVR and CABG	4
AVR and mitral valve replacement	9
Mitral valve replacement	5
Mitral valve replacement and CABG	9
Mitral valve repair	1
Mitral valve repair and CABG	5

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What Keeps Patients from Surgical Mitral Valve Replacement/Repair?

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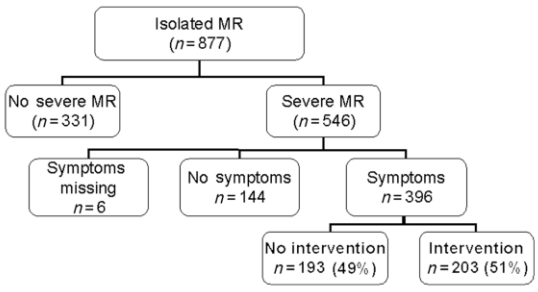
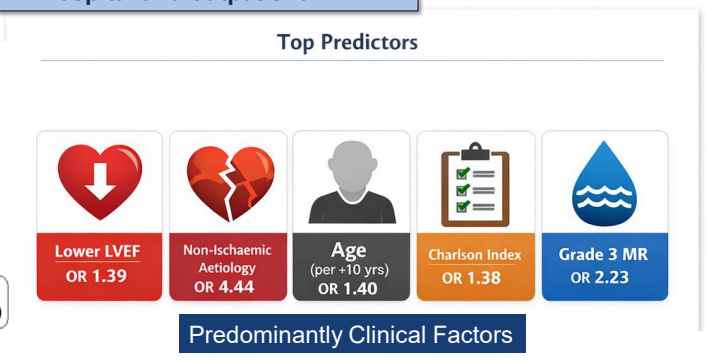
Euro Heart Survey on valvular heart disease (April-July 2001)
92 centers from 25 European countries
Recruitment both in-hospital and outpatient





1 out of 2 patients with severe, symptomatic mitral regurgitation were turned down for surgery

Mirabel M, et al. Eur Heart J. 2007:1358-65

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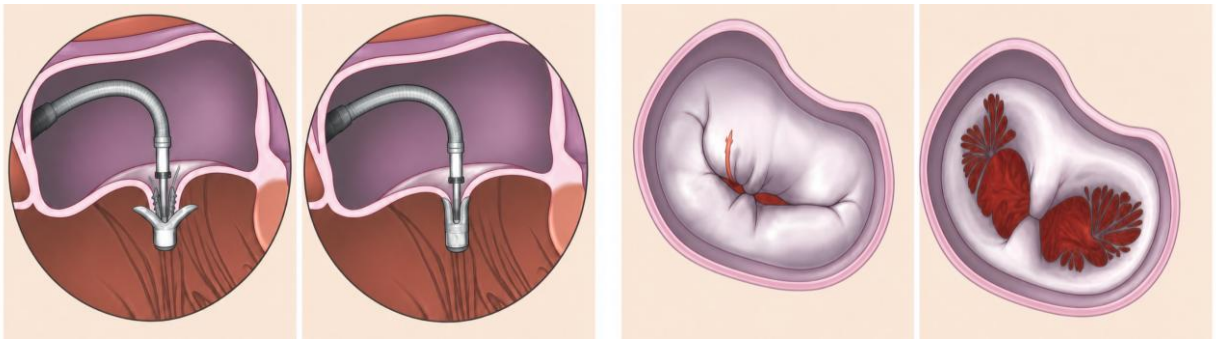
Edge to Edge Repair of Mitral Valve

School of Medicine



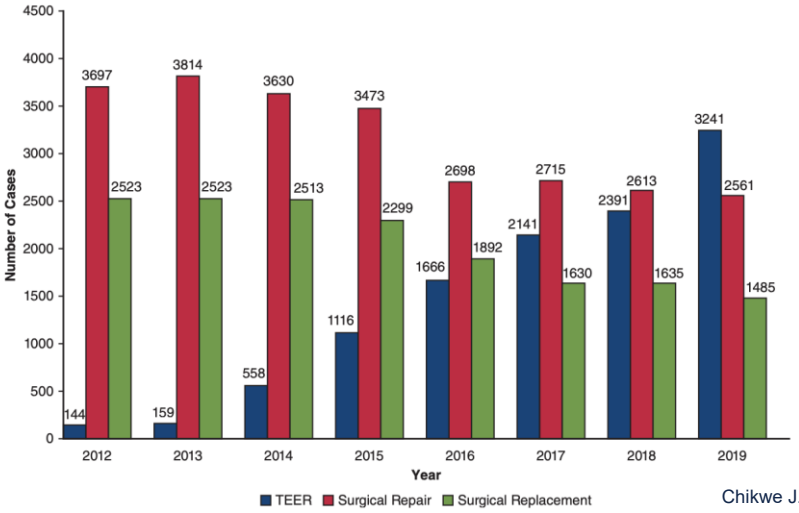
N Engl J Med 2011;364:1395-406

55

State of the Union – Mitral Valve Interventions

School of Medicine

Centers for Medicare and Medicaid Services data (2012-2019), 53,117 mitral valve interventions



Rates of M-TEER are increasing while rates of surgical repair and replacement are declining

Chikwe J. et al, J Thorac Cardiovasc Surg 2025;169:80-8

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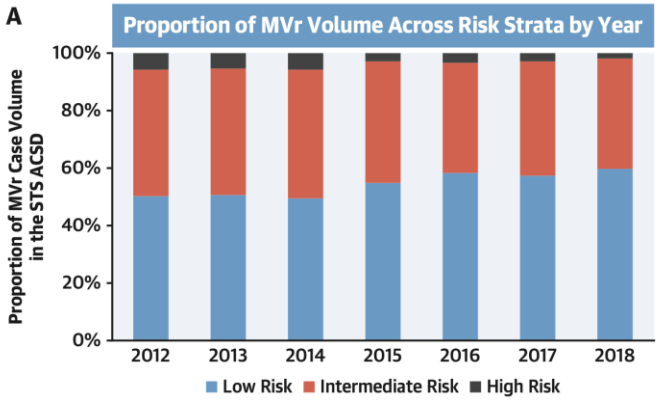
State of the Union – Mitral Valve Interventions

School of Medicine

STS database linked with Medicare administrative claims (July 2011-December 2018)



The introduction of TEER was associated with **improved surgical outcomes**:

- Median STS predicted mortality decreased from 1.5% to 1.2% after TEER availability
  - ✓ 30-day operative mortality decreased significantly
  - ✓ 5-year mortality after surgical repair decreased
- Improvements persisted even after controlling for temporal advances in surgical technique
- Mechanism appears to be **improved patient selection**—higher-risk "borderline" surgical candidates were increasingly referred for TEER once available, leaving a lower-risk cohort for surgery

Lowenstern AM et al. J Am Coll Cardiol 2023;81:521–532

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Intervention for Patients with Chronic Primary MR

American Heart Association.

AMERICAN COLLEGE of CARDIOLOGY FOUNDATION

COR	LOE	Recommendations
1	B-NR	1. In symptomatic patients with severe primary MR (Stage D), mitral valve intervention is recommended irrespective of LV systolic function.
1	B-NR	2. In asymptomatic patients with severe primary MR and LV systolic dysfunction (LVEF ≤60%, LVESD ≥40 mm) (Stage C2), mitral valve surgery is recommended.
1	B-NR	3. In patients with severe primary MR for whom surgery is indicated, mitral valve repair is recommended in preference to mitral valve replacement when the anatomic cause of MR is degenerative disease, if a successful and durable repair is possible.
2a	B-NR	4. In asymptomatic patients with severe primary MR and normal LV systolic function (LVEF ≥60% and LVESD ≤40 mm) (Stage C1), mitral valve repair is reasonable when the likelihood of a successful and durable repair without residual MR is >95% with an expected mortality rate of <1%, when it can be performed at a Primary or Comprehensive Valve Center.

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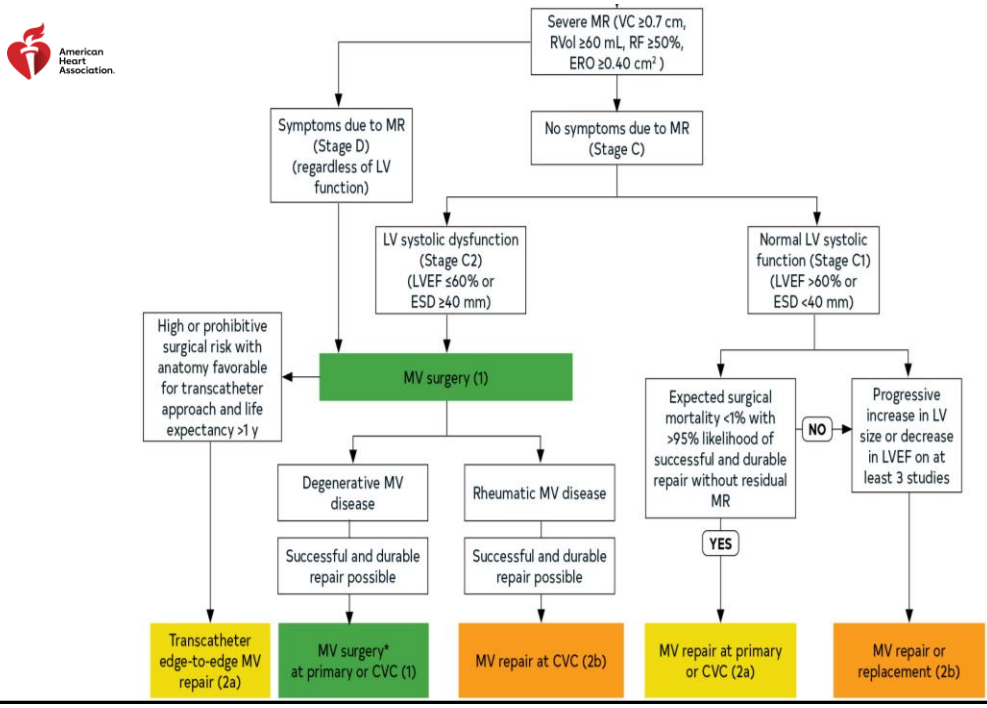

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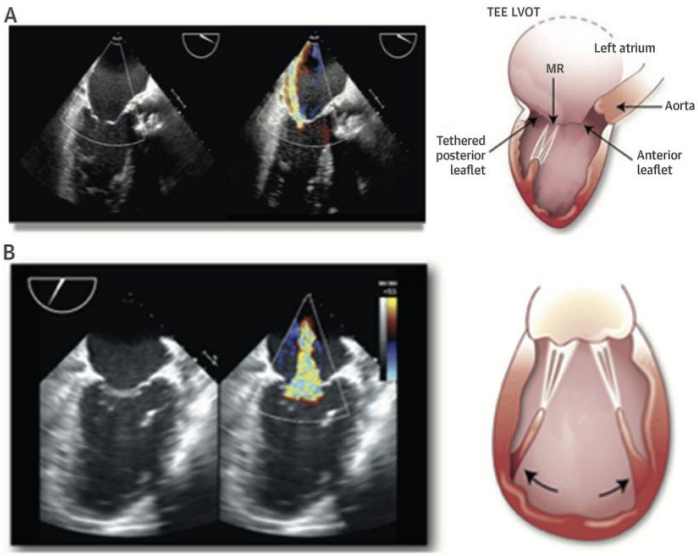
Functional Mitral Regurgitation Is a Problem with the Left Ventricle

School of Medicine

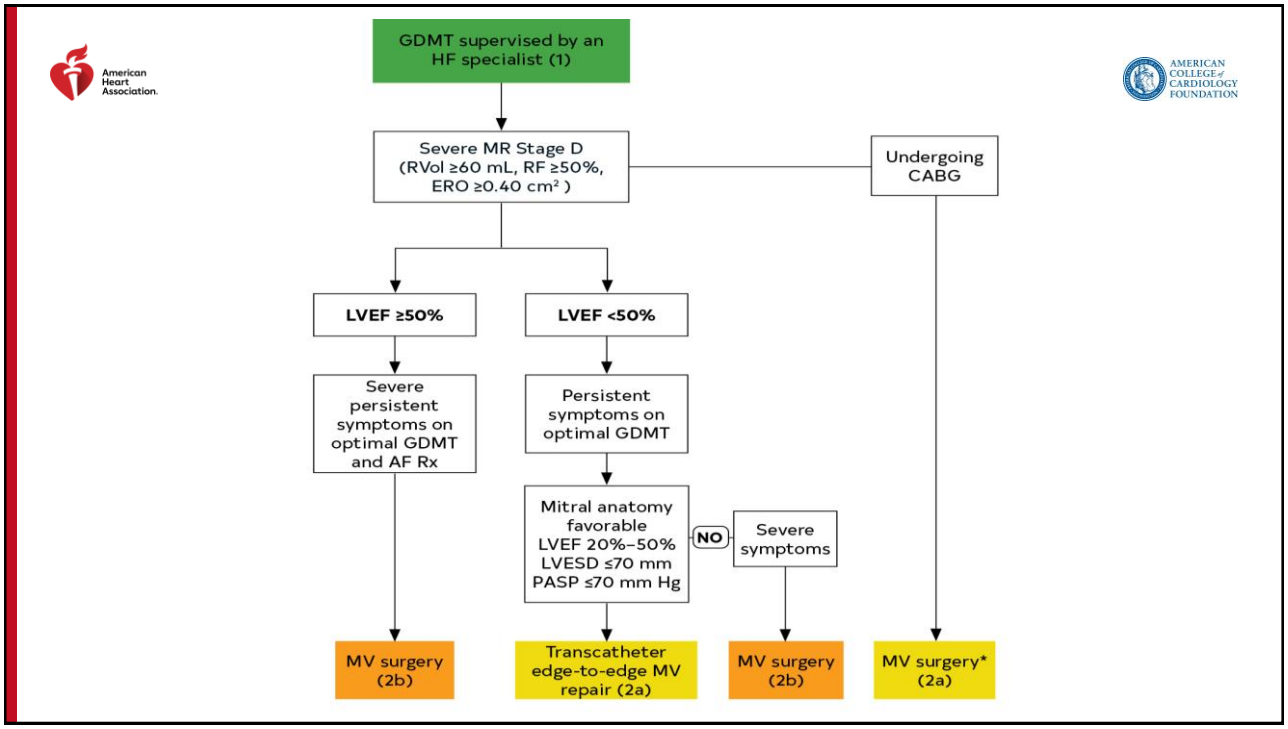


Tethered posterior leaflet seen with ischemic heart disease

Dilated cardiomyopathy resulting in a central jet due to lateral and apical displacement of the papillary muscles

Asgar A et al. J Am Coll Cardiol 2015;65:1231–48

60



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Diagnosis of Secondary MR

COR	LOE	Recommendations
1	B-NR	1. In patients with chronic secondary MR (Stages B to D), TTE is useful to establish the etiology and to assess the extent of regional and global LV remodeling and systolic dysfunction, severity of MR, and magnitude of pulmonary hypertension.
1	C-EO	2. In patients with chronic secondary MR (Stages B to D), noninvasive imaging (stress nuclear/PET, CMR, or stress echocardiography), coronary CT angiography, or coronary arteriography is useful to establish etiology of MR and to assess myocardial viability.
1	B-NR	3. In patients with chronic secondary MR with severe symptoms (Stage D) that are unresponsive to GDMT who are being considered for transcatheter mitral valve interventions, TEE is indicated to determine suitability for the procedure.
1	C-EO	4. In patients with chronic secondary MR undergoing transcatheter mitral valve intervention, intraprocedural guidance with TEE is recommended.

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Medical Therapy for Secondary MR

COR	LOE	Recommendations
1	A	1. Patients with chronic severe secondary MR (Stages C and D) and HF with reduced LVEF should receive standard GDMT for HF, including ACE inhibitors, ARBs, beta blockers, aldosterone antagonists, and/or sacubitril/valsartan, and biventricular pacing as indicated.
1	C-EO	2. In patients with chronic severe secondary MR and HF with reduced LVEF, a cardiologist expert in the management of patients with HF and LV systolic dysfunction should be the primary MDT member responsible for implementing and monitoring optimal GDMT.

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Key Trials in Mitral Valve Interventions
CLASP-2D 2 Year Outcomes

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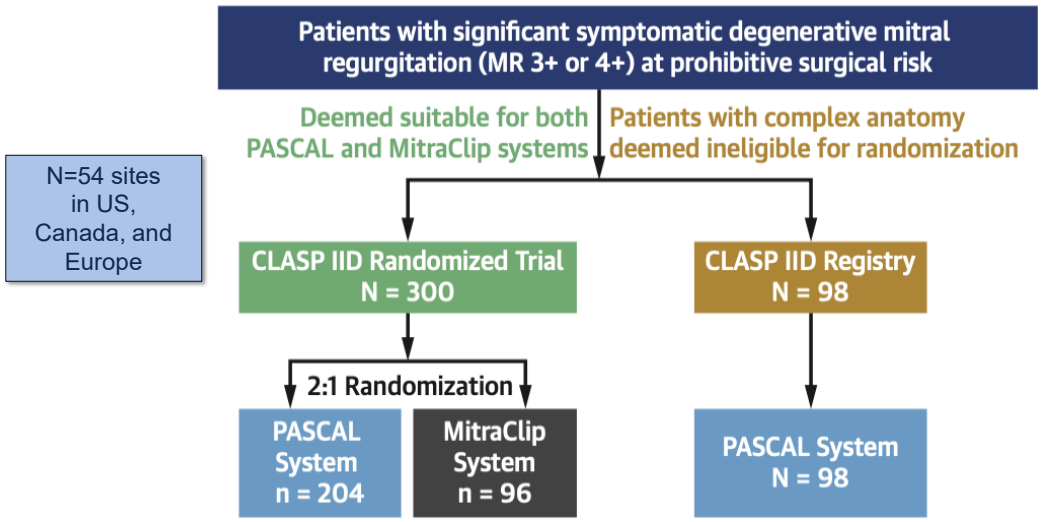

Makkar et al. *JACC Cardiovasc Interv*. 2025;18:2392

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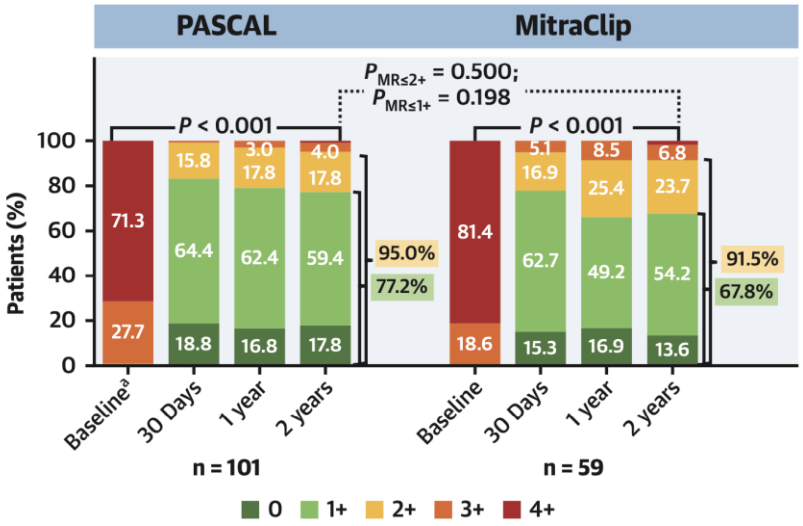
Key Trials in Mitral Valve Interventions

CLASP-2D 2 Year Outcomes (Mitral Regurgitation)

School of Medicine



Makkar et al. *JACC Cardiovasc Interv*. 2025;18:2392

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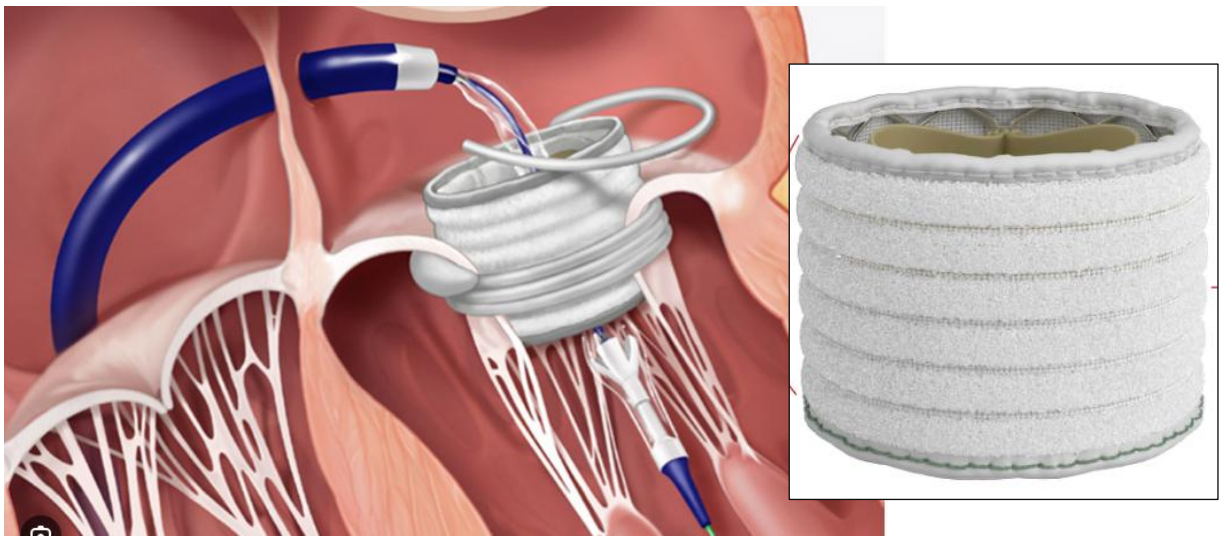
Edwards Sapien M3 (29mm)

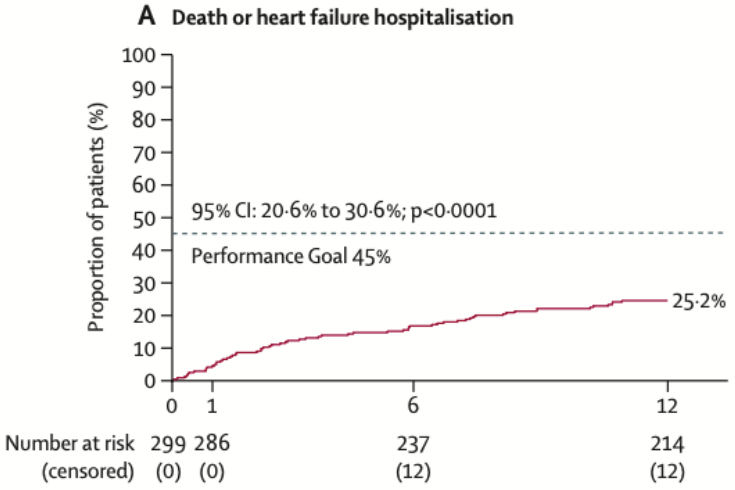
UNC SCHOOL OF MEDICINE



66

ENCIRCLE Trial

- ***Design*** **-** prospective, multicenter, single-arm, study
- ***Patients*** **-** symptomatic, moderate-to-severe or severe mitral regurgitation who were not suitable for surgery or TEER
- ***Primary endpoint*** **-** composite of all-cause mortality and heart failure rehospitalisation at 1 year in the as-treated population, compared with a prespecified performance goal of 45%



Lancet. 2025; 406(10519): 2541-2550

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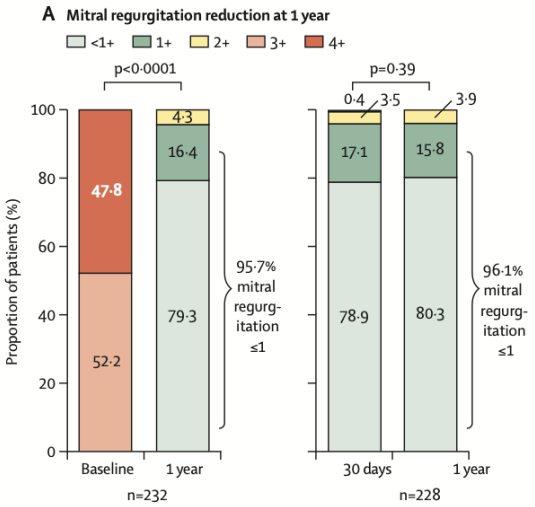
ENCIRCLE Trial
Improved Mitral Regurgitation and QoL



Lancet. 2025; 406(10519): 2541-2550

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Outline

School of Medicine

- Approach to patient with valve disease
- Aortic valve disease (stenosis and regurgitation)
- Mitral valve regurgitation
- *Tricuspid regurgitation*

Otto CM et al. Circulation. 2021;143: e72-e227

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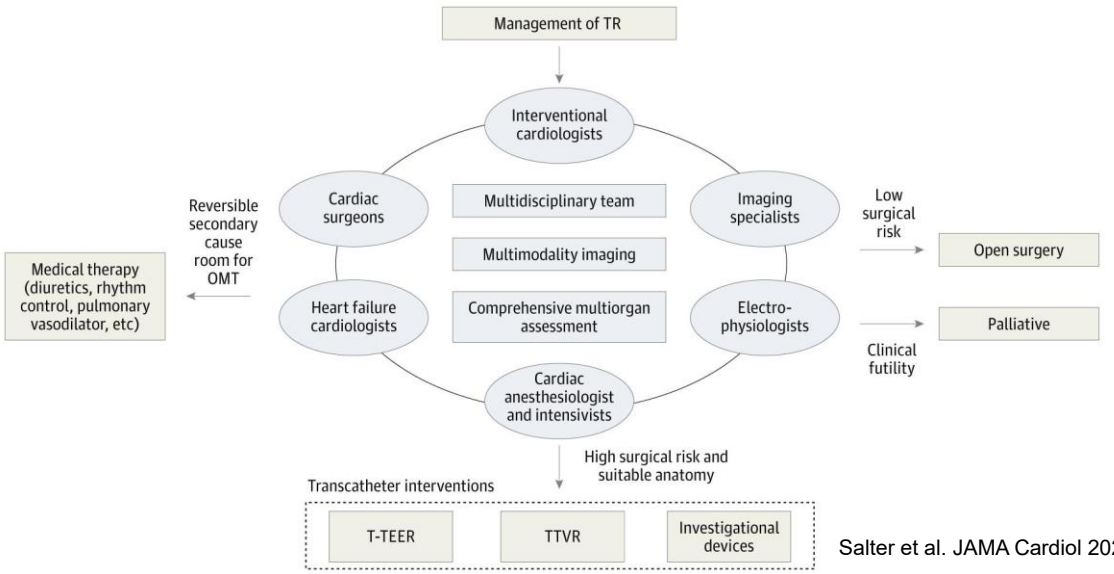
Tricuspid Valve Regurgitation Algorithm

UNC SCHOOL OF MEDICINE



Salter et al. JAMA Cardiol 2026;11;(1):98-10

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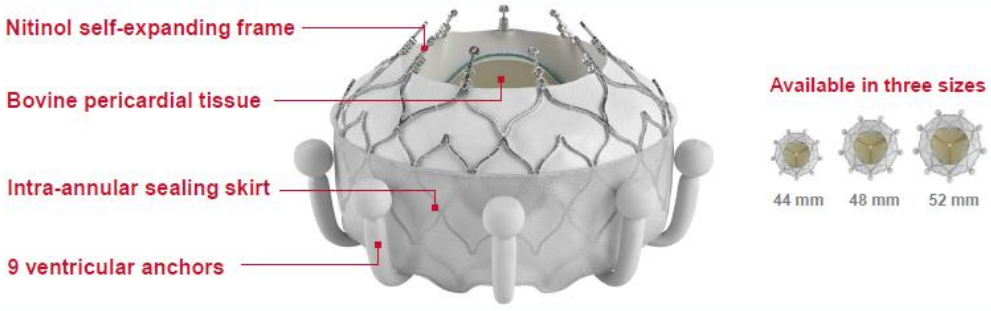
EVOQUE Transcatheter Tricuspid Valve Replacement System

EVOQUE Valve



EVOQUE Delivery System

CAUTION: Investigational device. Limited by Federal (or United States) law to investigational use.

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Tricuspid Valve ***Replacement*** for Severe TR

UNC SCHOOL OF MEDICINE

Indications

- Severe TR (either functional and/or degenerative) assessed using a 5-grade classification
- Signs/symptoms of TR ***OR*** prior heart failure hospitalization from TR despite optimal medical therapy including stable oral diuretics

Relative Contraindications

- LVEF < 25%
- Severe right ventricular dysfunction
- PASP >60 mmHg by echo or PASP >70 mmHg by RHC
- Pulmonary Vascular Resistance (PVR) >5 Wood units by RHC and systolic BP >85 mmHg after vasodilator challenge)

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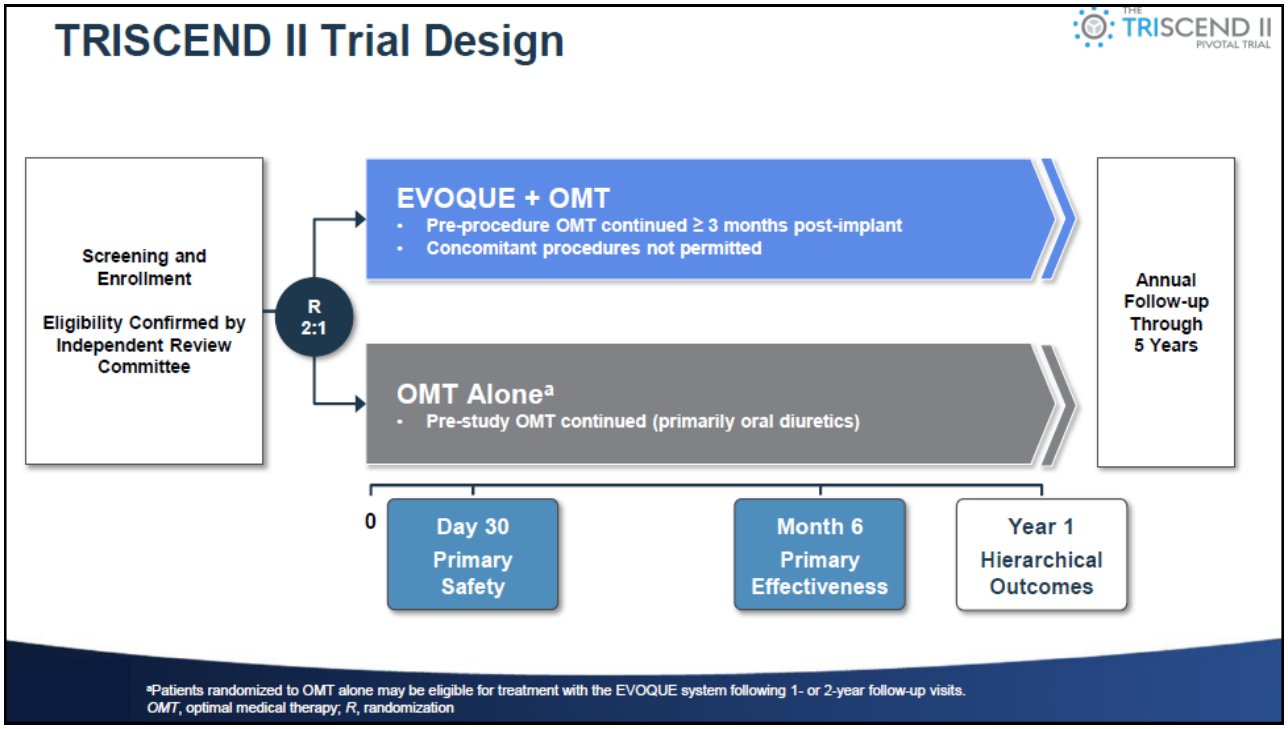
TRISCEND II Trial Design
THE TRISCEND II PIVOTAL TRIAL
Screening and Enrollment
Eligibility Confirmed by Independent Review Committee
R 2:1
EVOQUE + OMT
Pre-procedure OMT continued ≥ 3 months post-implant
Concomitant procedures not permitted
OMT Alone[a]
Pre-study OMT continued (primarily oral diuretics)
Annual Follow-up Through 5 Years
0
Day 30 Primary Safety
Month 6 Primary Effectiveness
Year 1 Hierarchical Outcomes
[a]Patients randomized to OMT alone may be eligible for treatment with the EVOQUE system following 1- or 2-year follow-up visits.
OMT, optimal medical therapy; R, randomization

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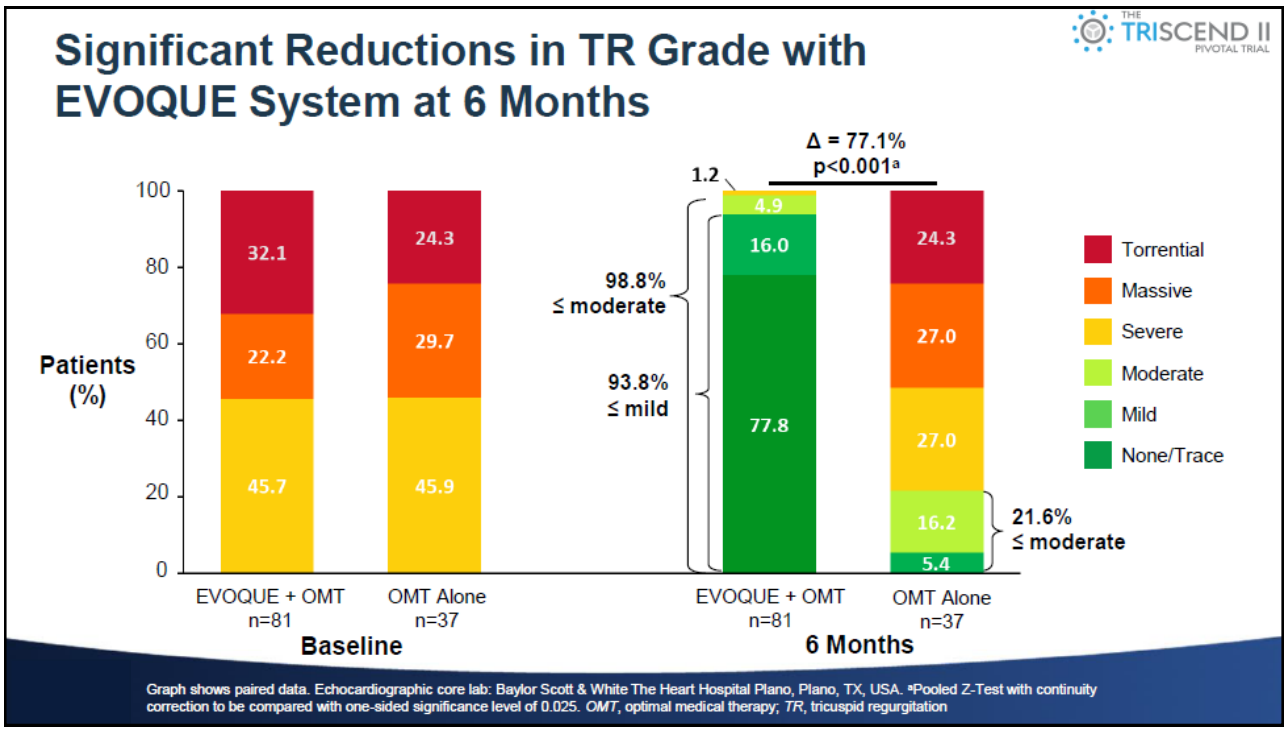
Significant Reductions in TR Grade with EVOQUE System at 6 Months
THE TRISCEND II PIVOTAL TRIAL
Patients (%)
100
80
60
40
20
0
32.1
22.2
45.7
24.3
29.7
45.9
EVOQUE + OMT n=81
OMT Alone n=37
Baseline
Δ = 77.1%
p<0.001[a]
1.2
4.9
16.0
77.8
98.8% ≤ moderate
93.8% ≤ mild
24.3
27.0
27.0
16.2
5.4
21.6% ≤ moderate
EVOQUE + OMT n=81
OMT Alone n=37
6 Months
Torrential
Massive
Severe
Moderate
Mild
None/Trace
Graph shows paired data. Echocardiographic core lab: Baylor Scott & White The Heart Hospital Plano, Plano, TX, USA. [a]Pooled Z-Test with continuity correction to be compared with one-sided significance level of 0.025. OMT, optimal medical therapy; TR, tricuspid regurgitation

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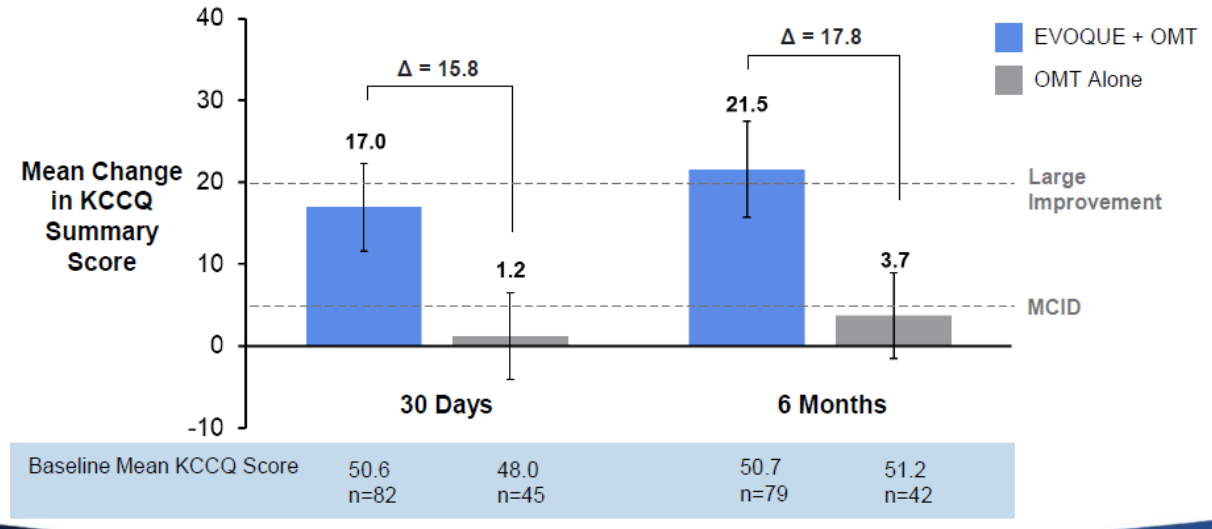
Changes in KCCQ at 30 Days and 6 Months



Graphs show paired analysis. Error bars show 95% CI. *KCCQ*, Kansas City Cardiomyopathy Questionnaire; *MCID*, Minimal Clinically Important Difference; *OMT*, optimal medical therapy

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2-Year TRISCEND II Outcomes

All-Cause Mortality

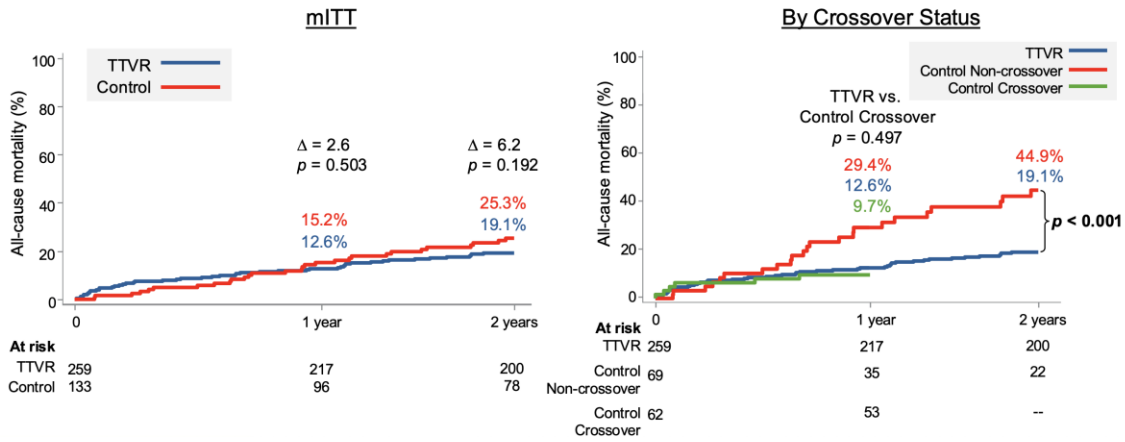

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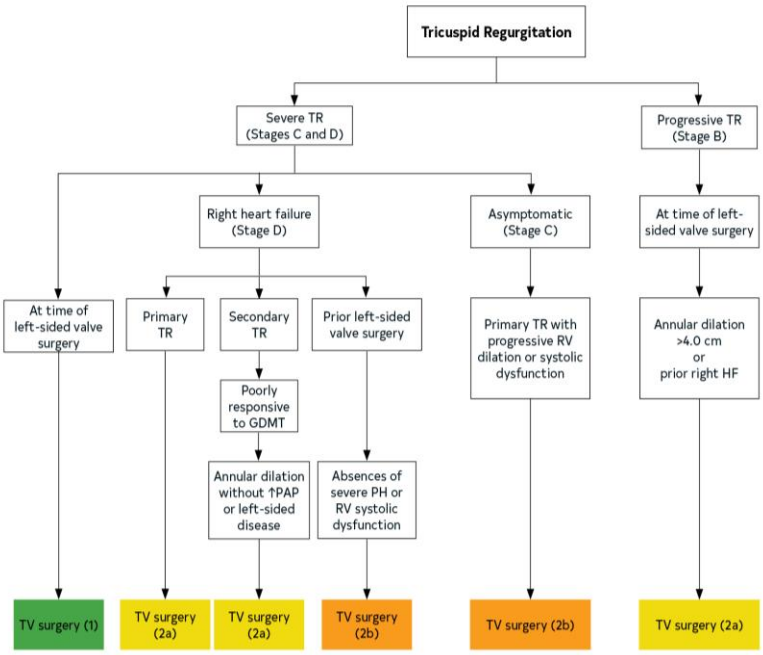
Figure 10. Tricuspid Regurgitation

Colors corresponds to Table 2



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Summary and Conclusions

School of Medicine

1. **Every murmur needs a focused H&P.** Characterize timing, intensity, location, and radiation, and screen for symptoms (syncope, dyspnea, angina).
2. **Diastolic and continuous murmurs are almost always pathologic.** Innocent murmurs are soft (grade 1–2), midsystolic, with a normal S2 and no added sounds.
3. **TTE is the first-line test.** Order it for any diastolic/continuous murmur, a loud or symptomatic systolic murmur, or abnormal ECG/exam findings.
4. **Don't overinterpret trivial/mild regurgitation.** trace mitral, tricuspid, or pulmonic flow on color Doppler is common in normal hearts.
5. **Stage disease.** Use symptoms, valve anatomy, severity of dysfunction, and ventricular/pulmonary response; correlate exam with imaging.
6. **Refer aortic stenosis early.** Symptom onset (angina, syncope, HF) marks a steep rise in mortality; severe AS may warrant referral before symptoms.
7. **TAVR is now indicated for all levels of risk (including low-risk)**. Refer severe AS to a valve team for shared decision-making.
8. **Valve choice is a shared decision.** Mechanical = durable but needs lifelong anticoagulation (younger); bioprosthetic = no long-term anticoagulation (older).
9. **In severe primary MR, refer before LV dysfunction.** TEER is an option at high surgical risk; secondary MR is an LV problem so optimize GDMT first.
10. **Don't forget about the tricuspid valve.** Now have better options for severe TR (including transcatheter).

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