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Patient Selection for TAVR

Expanding TAVR to intermediate Risk Patients

No conflict of interest to declare

In our cath lab, the last 2.5 years a total of 118 pts underwent ***118 TAVR*** procedures:

procedure success : 118 (100%)
mortality : 2 (1.8%)
stroke 0 (0%)
new pacemaker: 8 (9.5%)
Age: 83±5 years
Euroscore I: ≥25-28%

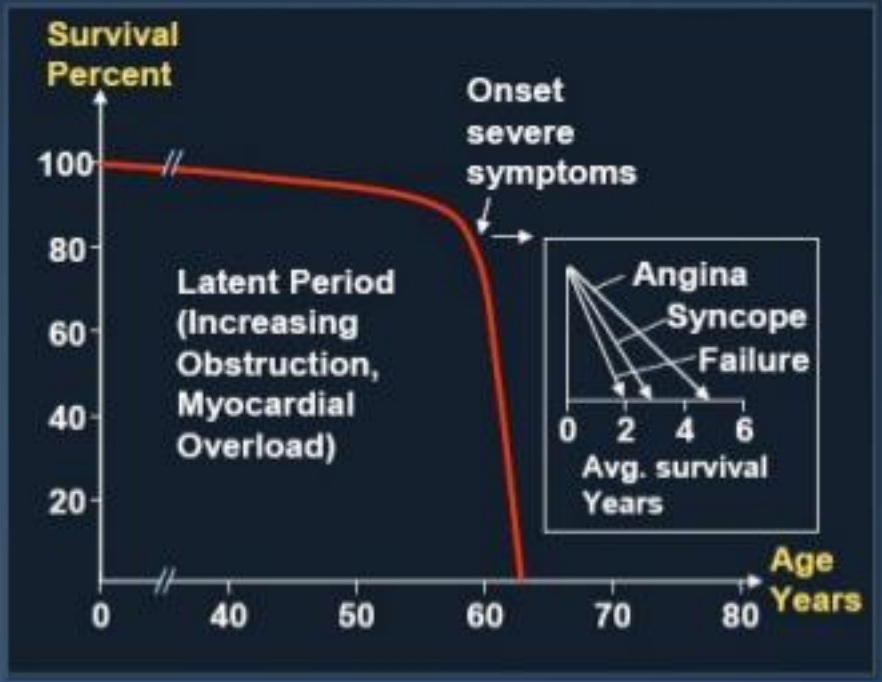
I. Patient Selection for TAVR

AORTIC STENOSIS

Aortic stenosis has become a major cause of morbidity and mortality among a growing population of older adults

Aortic Stenosis is Life-Threatening and Progresses Rapidly

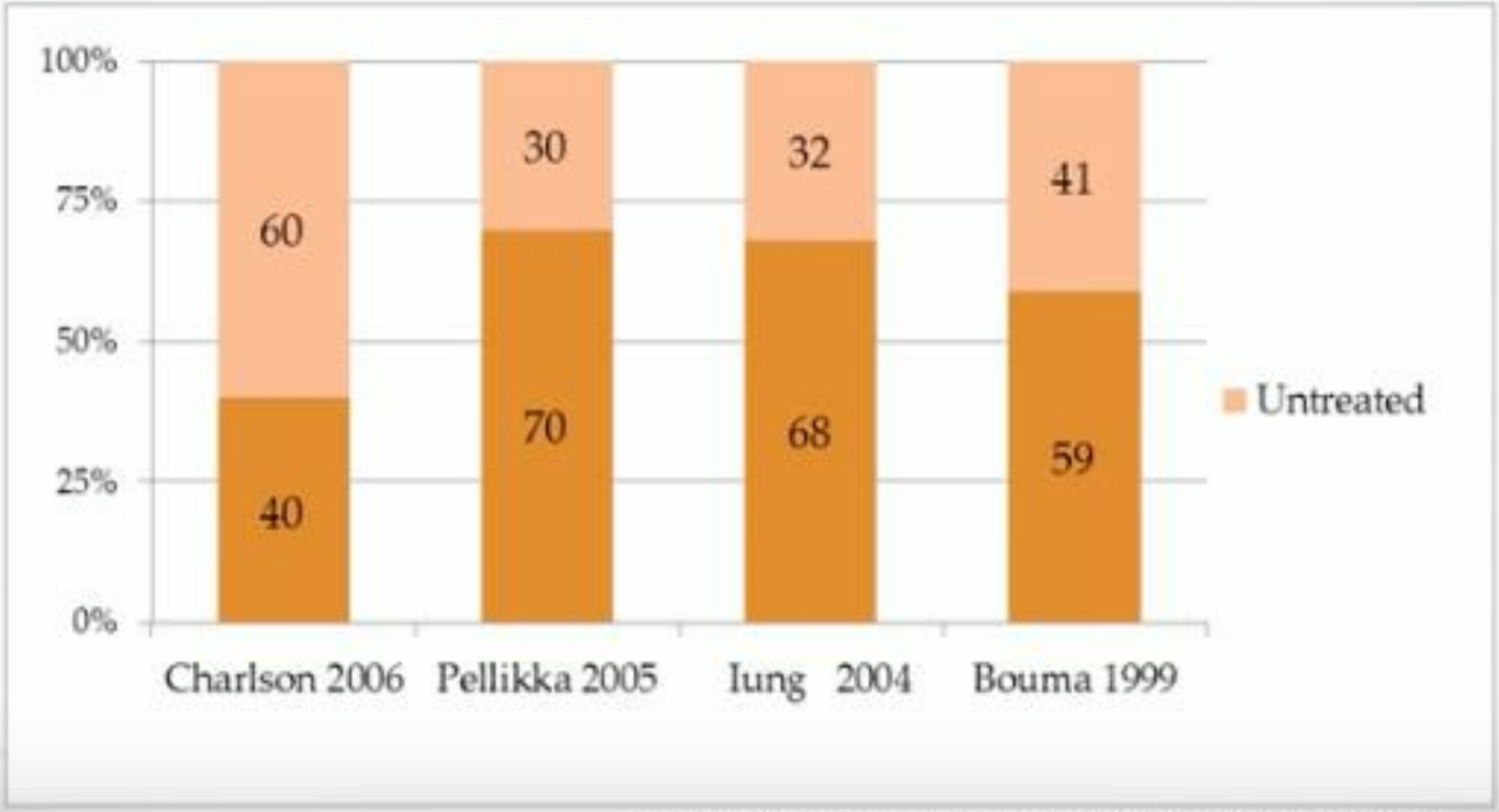
Treatment Options and Timing Matter



"Survival after onset of symptoms is 50% at two years and 20% at five years."[1]

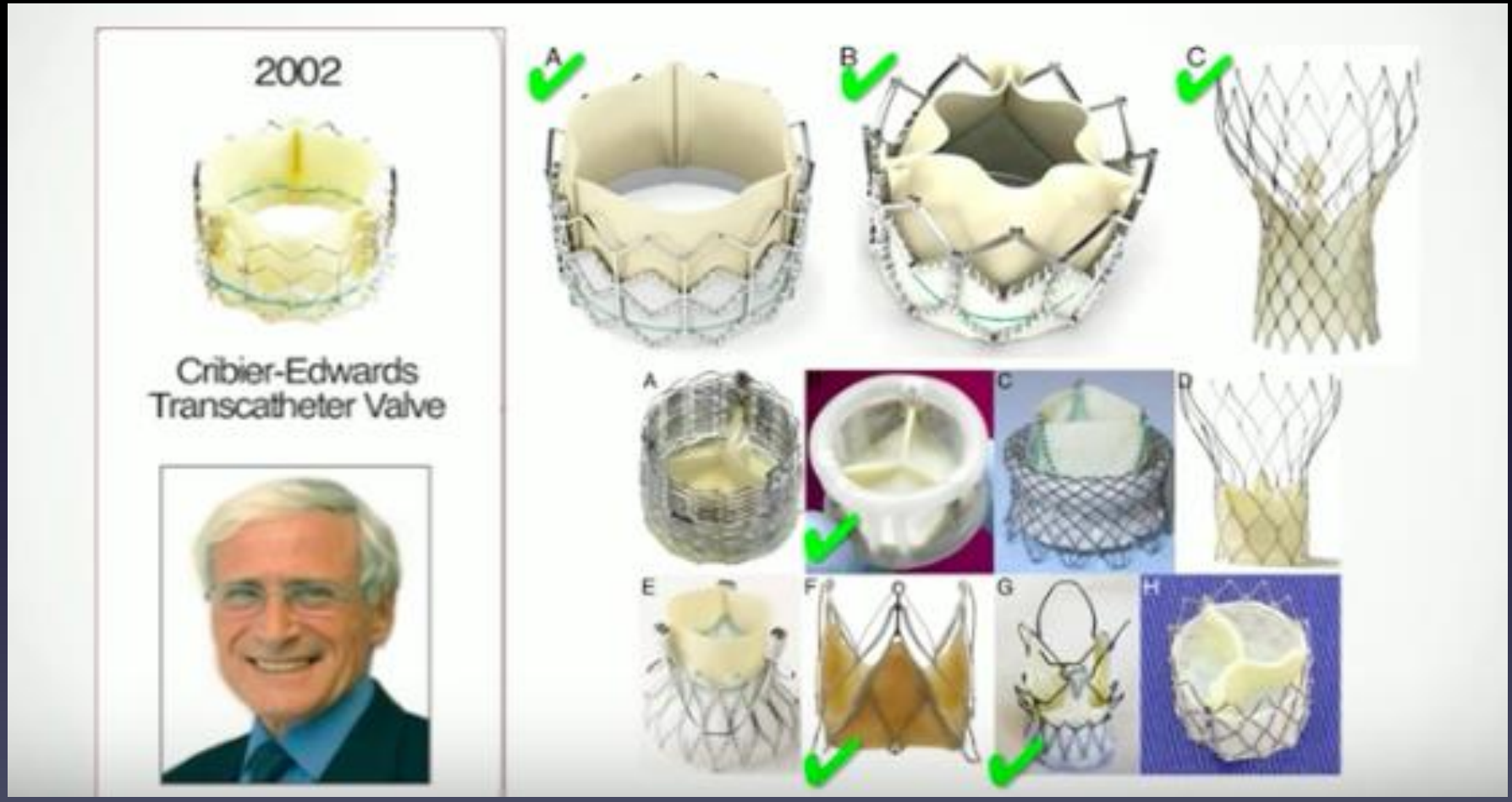
"Surgical intervention [for severe AS] should be performed promptly once even … minor symptoms occur."[2]

Many patients are not surgically treated!



J Heart Valve Dis2006;15:312-321; Circulation 2005;
European Heart Journal 2003;24:1231-1243;

An Estimated 400,000 TAVR have been Performed over 64 Countries since 2002



JACC 2013:62,S 1-10

Transcatheter aortic valve replacement **(TAVR)** has been validated as new therapy for patients affected by severe symptomatic aortic stenosis who are not eligible for surgical intervention

Patient selection:

requires a multidisciplinary team approach including interventional cardiologists, surgeons, anesthesiologists and imaging specialists in order to delineate risk profile (Heart team).

should be based not only on accurate assessment of aortic ***stenosis morphology, but also on several clinical and functional data.***

Patient Selection

Inclusion Criteria

Symptomatic severe AVS
Survival >12 mo
Prohibitive or high surgical risk
Gain improvement in quality of life
Frail, prior radiation, porcelain aorta, severe hepatic or pulmonary disease
Should be no absolute contraindication

Contraindications for transcatheter aortic valve implantation

Absolute contraindications
Absence of heart team or surgery on the site
Estimated life expectancy < 1 yr
Improvement of quality of life by TAVI unlikely because of comorbidities
Severe primary associated disease of other valves with major contribution to the patient's symptoms, that can be treated only by surgery
Inadequate annulus size (< 18 mm, > 29 mm)
Thrombus in the left ventricle
Active endocarditis
Elevated risk of coronary ostium obstruction (asymmetric valve calcification, short distance between annulus and coronary ostium, small aortic sinuses)
Plaques with mobile thrombi in the ascending aorta, or arch
For transfemoral/subclavian approach: inadequate vascular access (vessel size, calcification, tortuosity)
Relative contraindications
Bicuspid or non-calcified valves
Untreated coronary artery disease requiring revascularization
Haemodynamic instability
LVEF < 20%
For transapical approach: severe pulmonary disease, LV apex not accessible

TAVR Patient selection:

I. clinical evaluation

symptoms
surgical risc score
comorbidity
frailty

ASYMPTOMATIC PTS WITH SEVERE AVS

Risk of rapid progression and sudden death (2% annually)

Identifying those pts:

AVA<0.75 cm^2
Flow velocity >4 m/sec

"positive" stress test with symptoms during exercise
(masked asymptomatic)
decrease in LVEF
Hypotension or ventricular arrythmias

surgical risc score

Assessing risk for aortic valve surgery

- Society of Thoracic Surgery Predictive Risk of Operative Mortality (STS PROM) Calculator

Risk	PROM at 30 Days
Extreme	Inoperable
High	>8%
Intermediate	4-8%
Low	<4%

- Frailty Assessment

EUROSCORE I
(logistic) >20%

Patient related factors	
Age	
Gender	Male
Chronic pulmonary disease	No
Extracardiac arteriopathy	No
Poor mobility	No
Previous Cardiac Surgery	No
Creatinine	No
Active endocarditis	No
Critical preoperative state	No

Cardiac related factors	
Engina CCS Class IV	No
LV function	good
Recent MI	No
Pulmonary hypertension	No

Operation related factors	
Emergency	No
Other than isolated CABG	No
Surgery on thoracic aorta	No
Post infarct septal rupture	No

EUROSCORE II

>10%

Patient related factors	
Age	
Gender	Male
Chronic pulmonary disease	No
Extracardiac arteriopathy	No
Poor mobility	No
Previous Cardiac Surgery	No
Active endocarditis	No
Critical preoperative state	No
Renal impairment Creatinine Clearance	normal
Diabetes on insulin	No

Cardiac related factors	
Engina CCS Class IV	No
LV function	good
Recent MI	No
Pulmonary hypertension	No
NYHA	I

Operation related factors	
Surgery on thoracic aorta	No
Urgency	elective
Weight of the operation	isolated ca

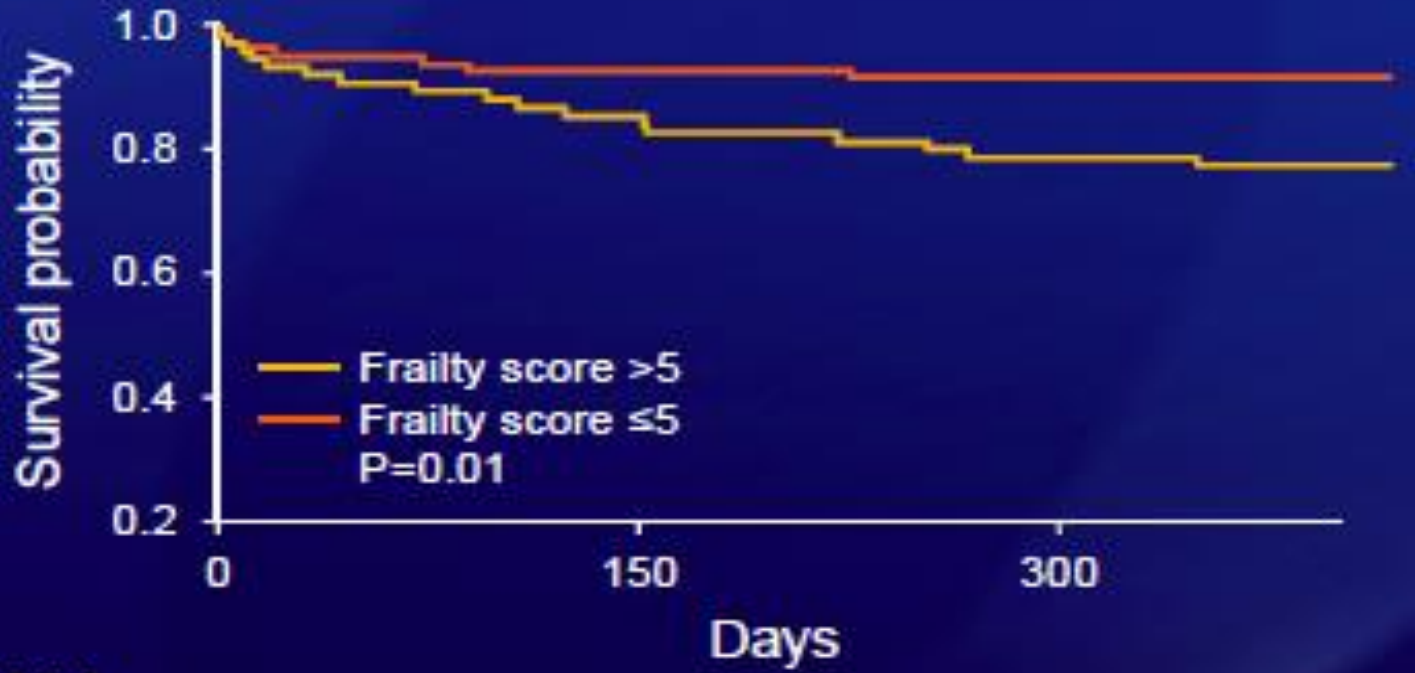
"Biological syndrome that reflects a state of decreased physiological reserve and vulnerability to stressors"

Components of Frailty Score

Frailty domain	Measure	Frailty score
Slowness	15-ft walk gait speed (m/s)	Quartiles (0–3)
Weakness	Grip strength (kg)	Sex-based quartiles (0–3)
Wasting and malnutrition	Serum albumin (g/dL)	Quartiles (0–3)
Inactivity	Katz activities of daily living	Any dependence = 3 Independent = 0

Green et al: JACC Intv 5:974, 2012

Kaplan-Meier Survival Estimates Stratified by Frailty Score



No. at risk			
Score >5	76	65	60
Score ≤5	83	77	76

Green et al: JACC Intv 5:974, 2012

Patient selection:
II. anatomical evaluation

** Severity of stenosis*

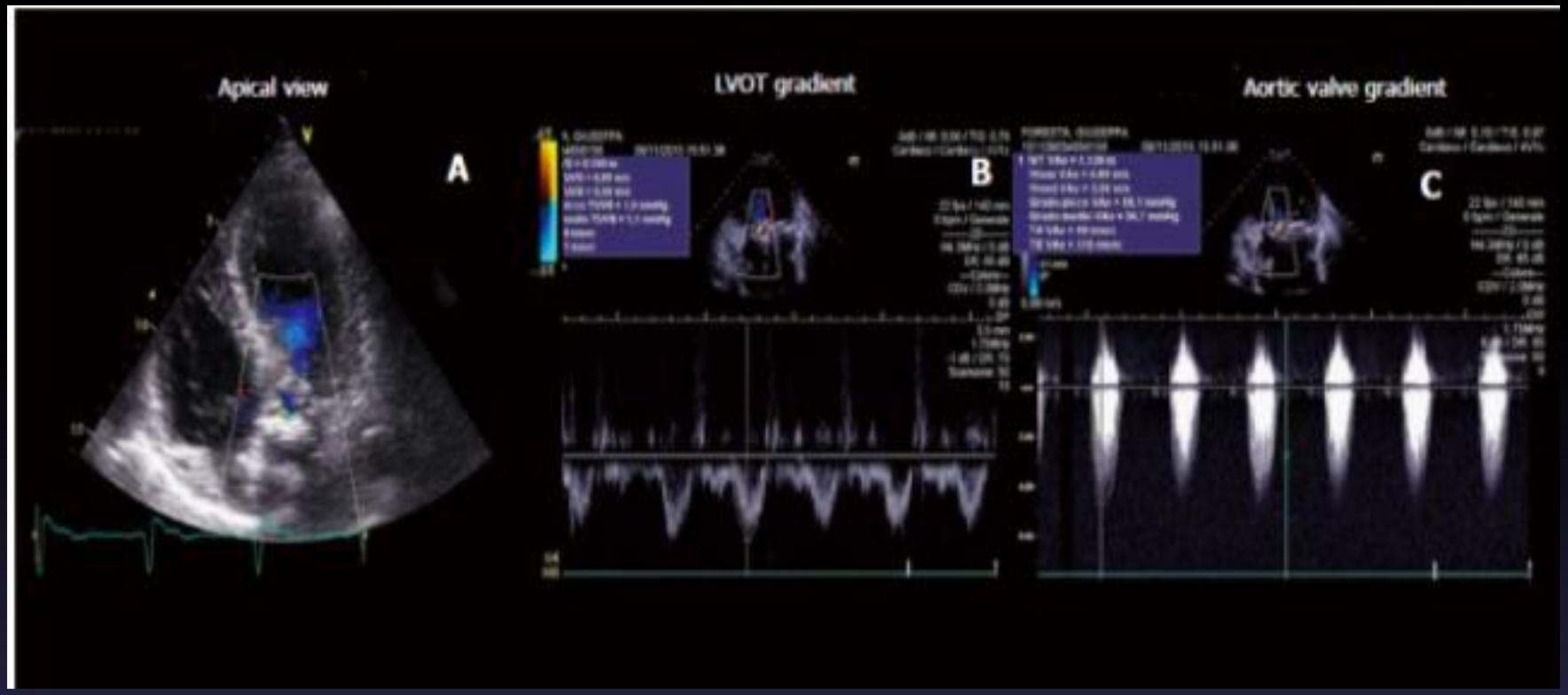
** AV morphology*
Annulus size
Sinus dimension
Number of valve cusps
Leaflet geometry
Calcification
Coronary ostia
LV outflow

(above the valve annulus)

Landing zone

**Basal septal hypertrophy*
**Mitral valve*
** Ascending aorta*

Severity of stenosis



Transthoracic echocardiography (TTE) gives detailed anatomic description of aortic valve complex and allows to estimate the haemodynamic entity of valvular stenosis.

Gives information about valve anatomy (bicuspid or tricuspid valve) and severity of impairment of cusp motion.

Provides an accurate evaluation of alterations in left and right ventricular morphology and function, MR, PASP.

Aortic valve stenosis - severity

Recommendations for classification of AS severity[1]

	Aortic sclerosis	Mild	Moderate	Severe
Aortic jet velocity (m/s)	≤2.5 m/s	2.6-2.9	3.0-4.0	>4.0
Mean gradient (mmHg)	-	<20 (<30[a])	20-40[b] (30-50[a])	>40[b] (>50[a])
AVA (cm^2)	-	>1.5	1.0-1.5	<1
Indexed AVA (cm^2/m^2)		>0.85	0.60-0.85	<0.6
Velocity ratio		>0.50	0.25-0.50	<0.25

- [a]ESC Guidelines.[2]
- [b]AHA/ACC Guidelines.[3]

Role of transoesophageal echocardiography

Transesophageal echocardiography (TEE) allows to better visualize aortic cusps, define etiology (bicuspid *vs* tricuspid) and directly measure aortic valve area by planimetry in doubt cases, when TTE is not conclusive.

TEE can be used in association with other imaging techniques for optimal pre-procedural planning in the setting of TAVI.

Annulus size

Very important information:

Overestimation = Risk of annulus rupture

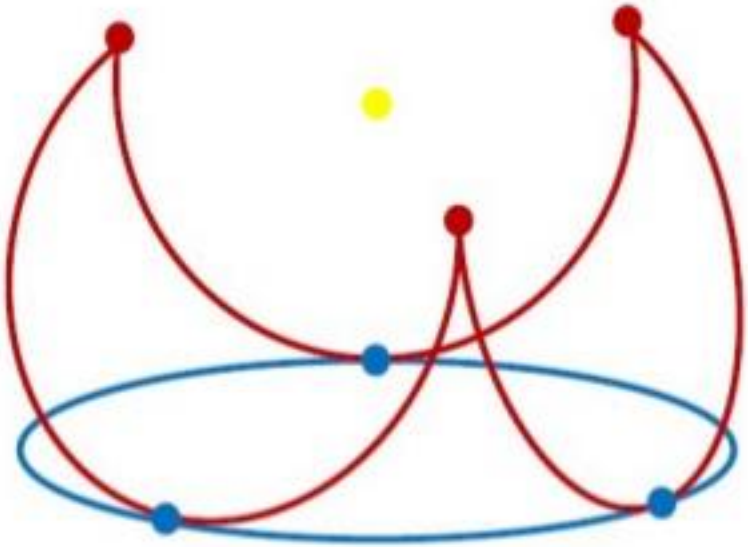
Valve dysfunction ?

Underestimation = Risk of embolization

Risk of Aotic regurgitation

Annulus is not an annulus...

It is a crown with 3 branches



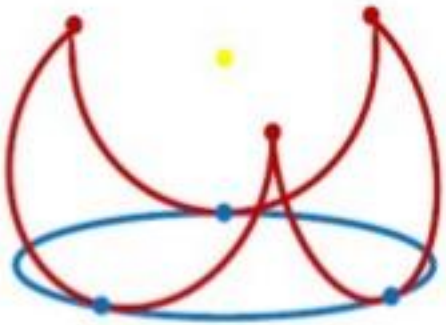
True Annulus = insertion of cusps

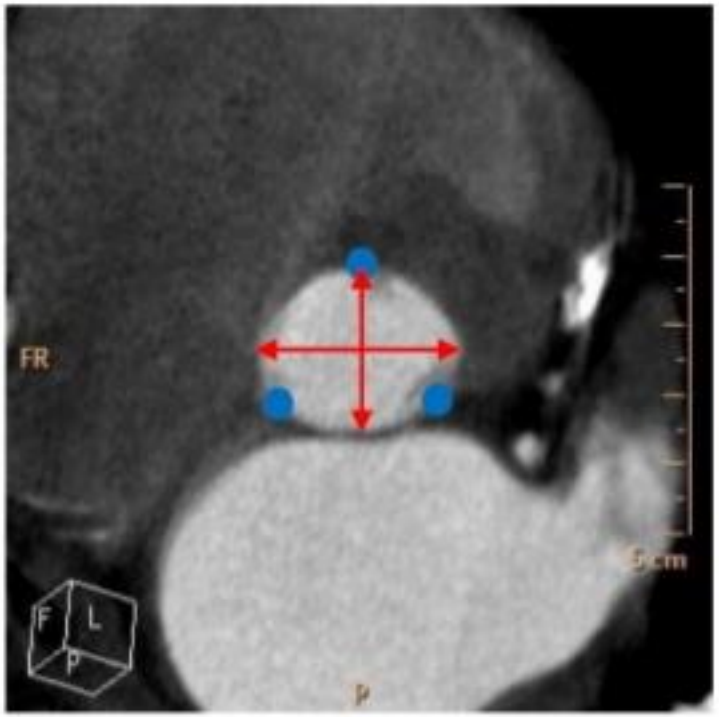
Aortic annulus for implantation

Commissures of the aortic valve

Lowest points of the aortic cups

...and this crown is not circular

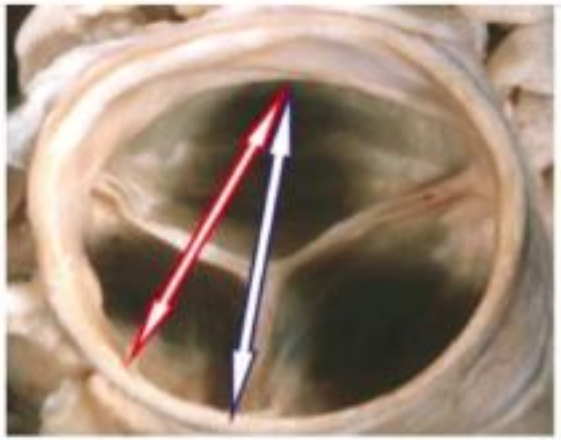


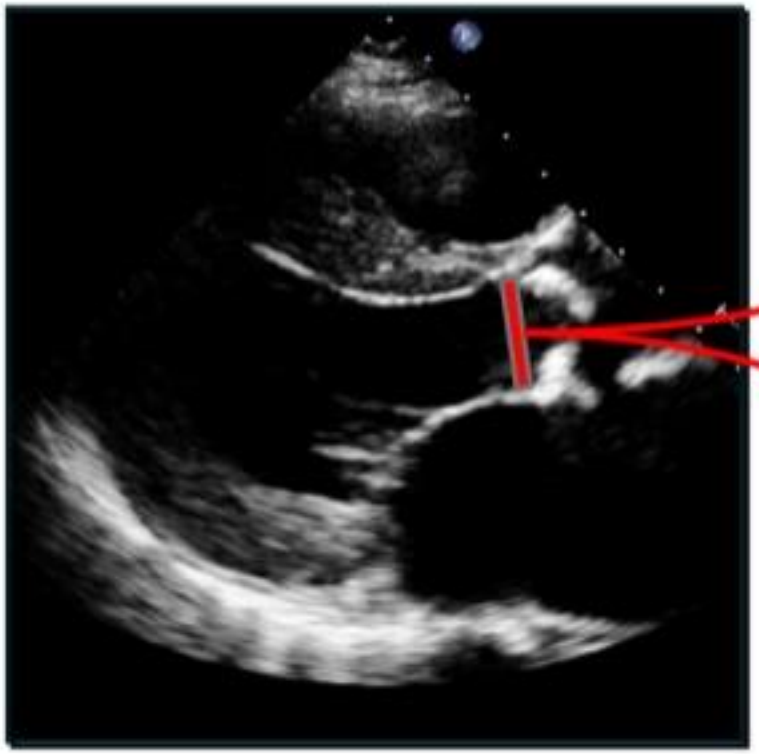


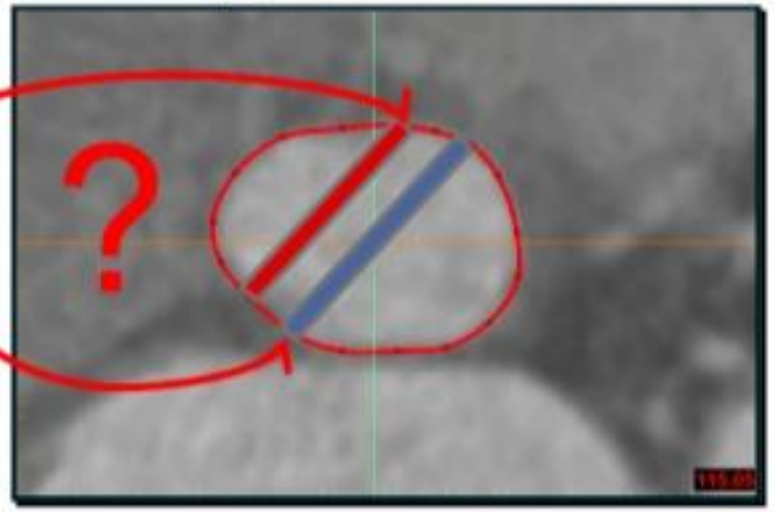
- ✓ Variable orientation (≤30°)
- ✓ Small diameter is often antero-posterior (= Echo)
- ✓ Large diameter grossly lateral
- ✓ Variability between the 2 diamètres (4-5mm, from 1 to 8mm)

A Limitation of Echo

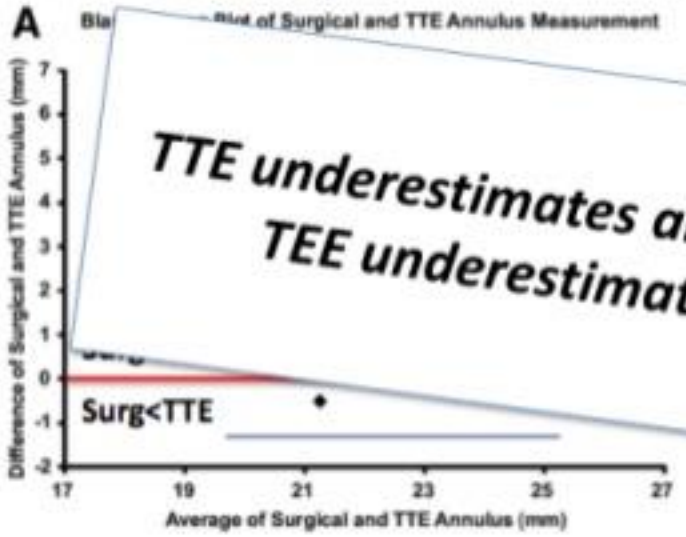
The imaging plane acquired may not be measuring the true annulus diameter





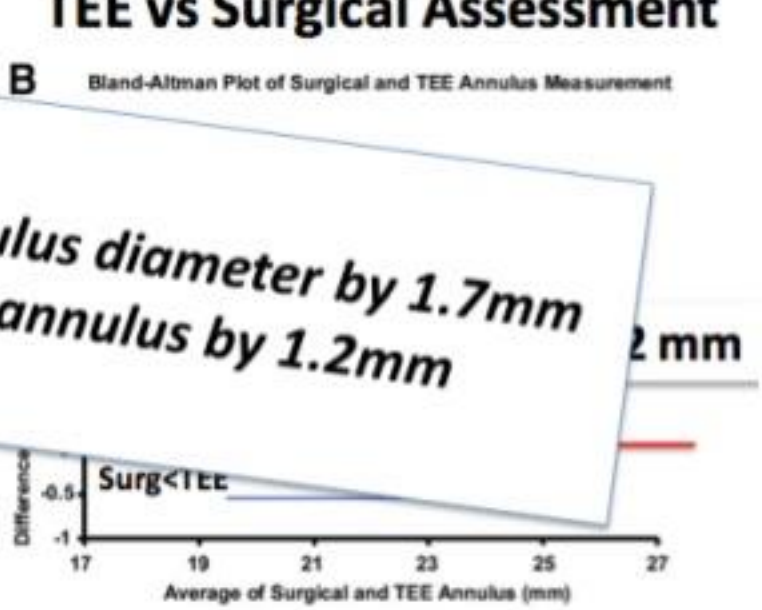


TTE vs Surgical Assessment



parasternal long-axis view

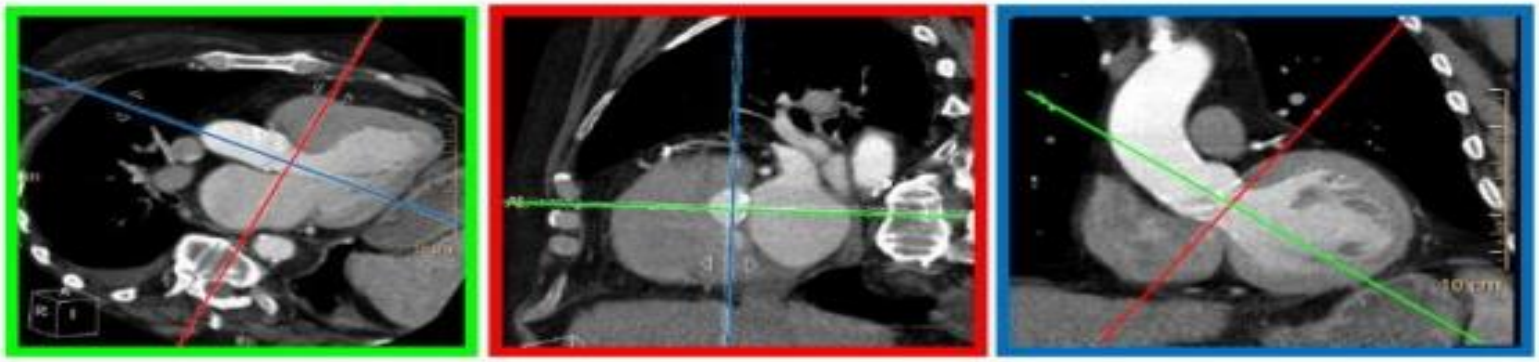
TEE vs Surgical Assessment



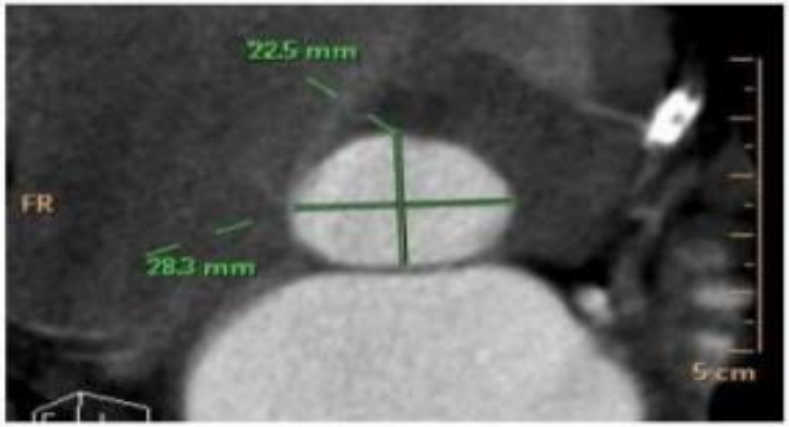
the 3-chamber, long-axis view

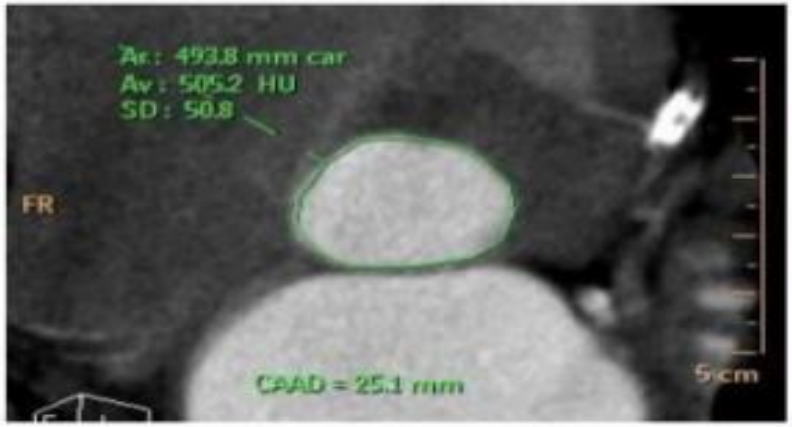
TTE underestimates annulus diameter by 1.7mm
TEE underestimates annulus by 1.2mm

CT scan is 3D & isotropic

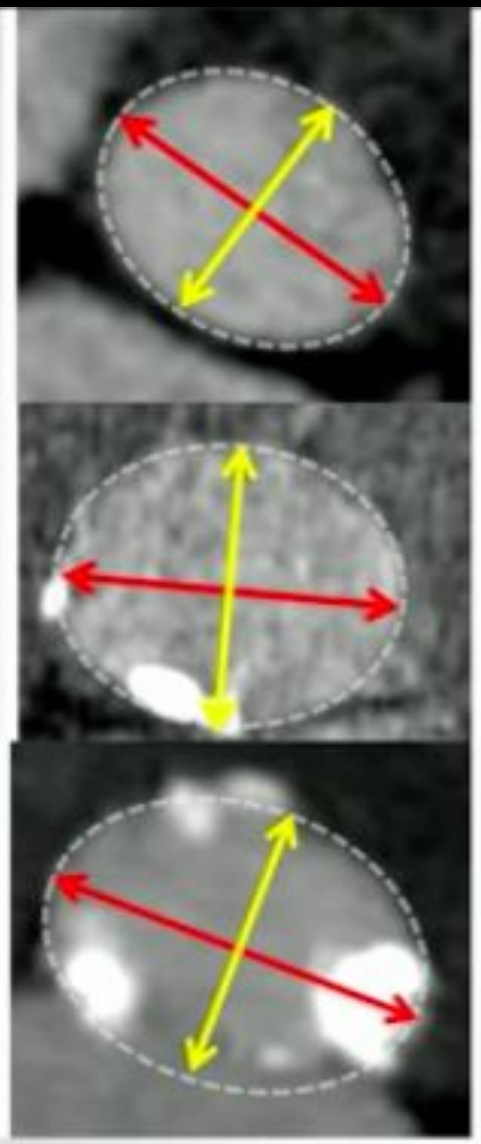


- Resolution = 0.5 mm in all directions
- May help to determine the optimal view

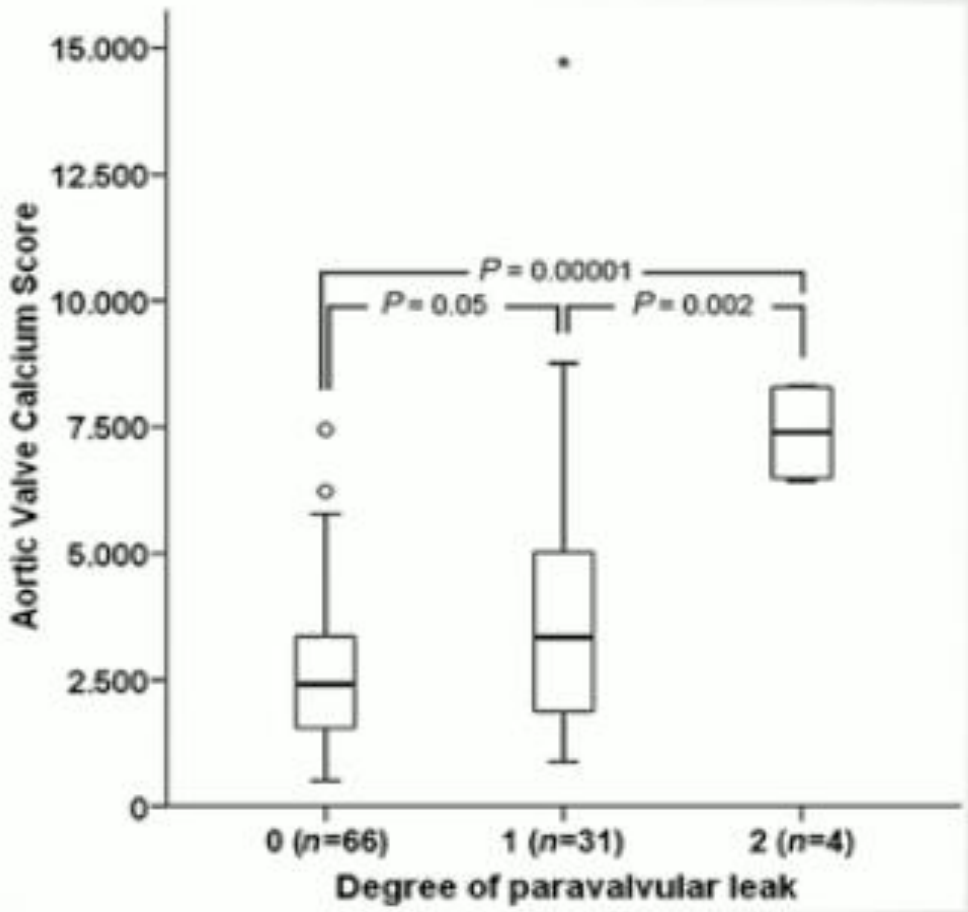




Multidetector scanners allow multiplanar reformation and 3-dimensional reconstruction of aortic root, ascending tract, arch and descending segments of aorta



Mean Aortic Valve Calcium Score as a Predictor of Paravalvular Leak

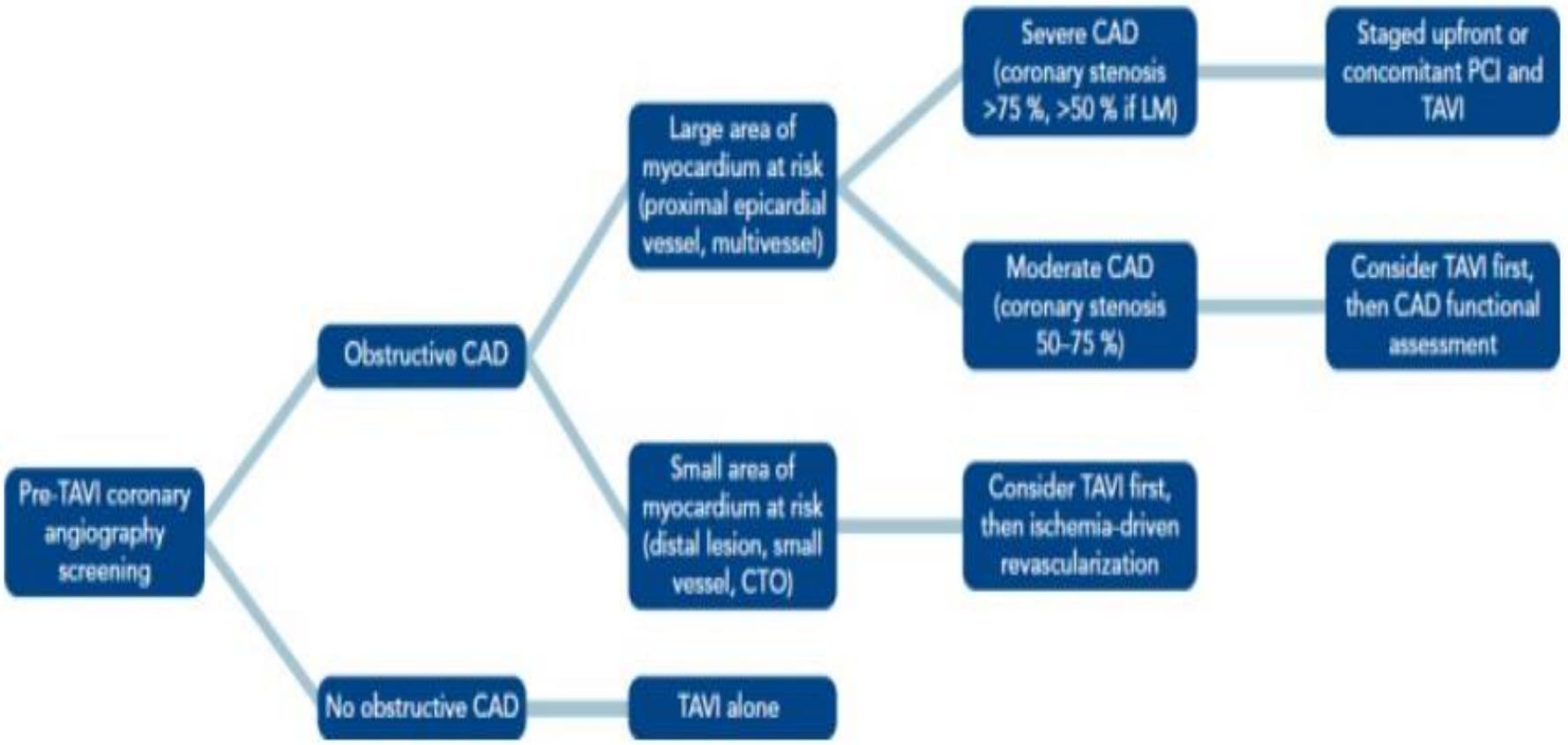


Haensig M et al. Eur J Cardiothorac Surg 2012;41:1234-1241

Patient selection:

III. Coronary angiography-PCI

Flow Chart of Suggested Strategies for Coronary Artery Disease Management in Transcatheter Aortic Valve Implantation Candidates



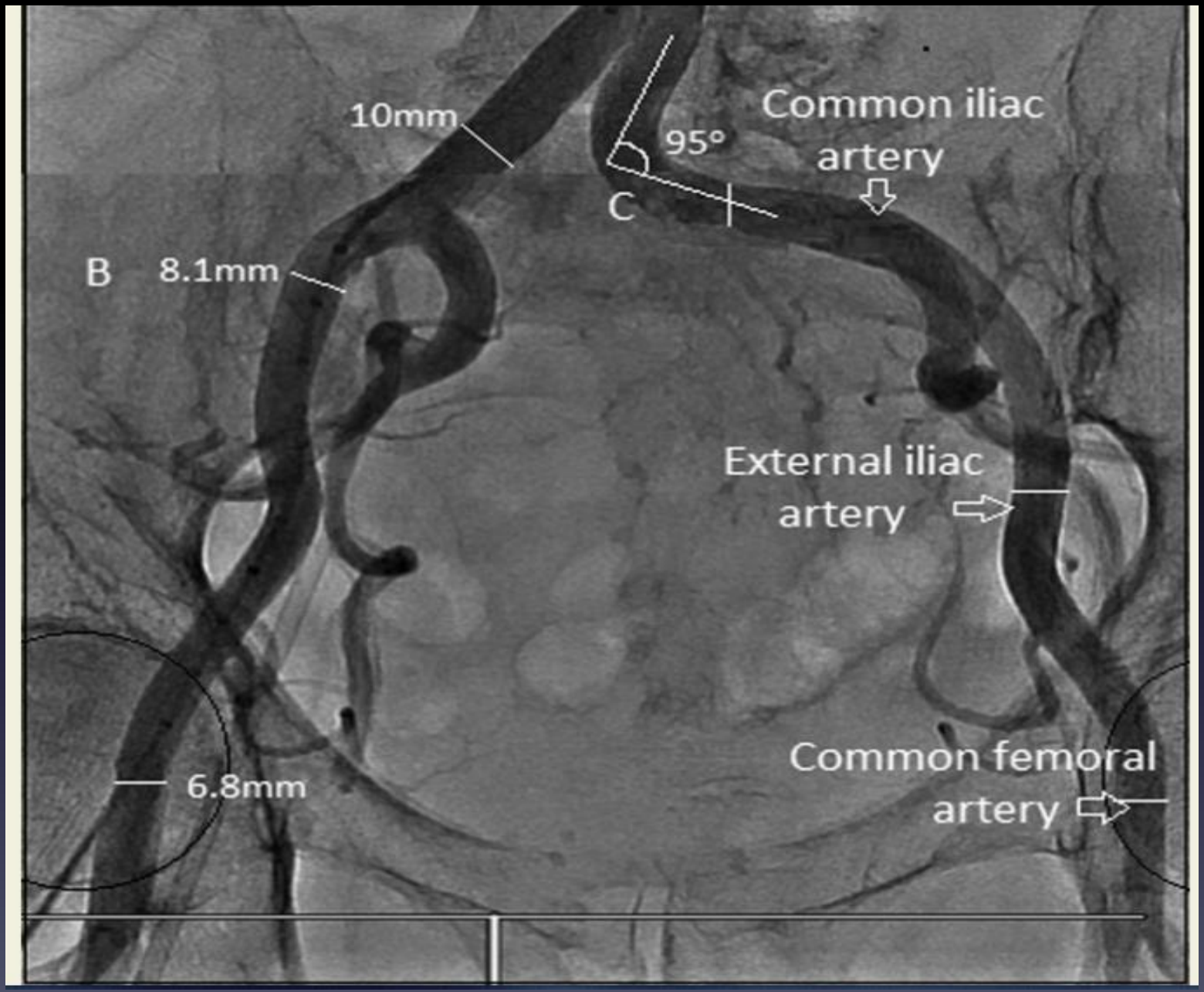
Εικόνα 1) Contrast aortography during BAV
Εικόνα 2) Τοποθέτηση stent στον πρόσθιο κατιόντα κλάδο της αριστερής στεφανιαίας αρτηρίας
Εικόνα 3) Απελευθέρωση- έκπτυξη της βαλβίδας και stent στην περισπωμένη αρτηρία
Εικόνα 4) Double Chimney Stent Technique
Εικόνα 5) Kissing stents
Εικόνα 6) Flaring the proximal stent segments

Patient selection:

IV. Peripheral access

Patient Evaluation

- CT Angiogram
  - Arterial calcification
  - Arterial tortuosity
  - Minimal luminal diameter


10mm
95°
Common iliac artery
C
B
8.1mm
External iliac artery
6.8mm
Common femoral artery

II. Expanding TAVR to intermediate Risk Patients

Several prospective randomized trials demonstrated non-inferiority for TAVR compared to SAVR in patients at high surgical risk.

(PARTNER 1A, CORE VALVE)

Current debates focus on the expansion of TAVI as the standard of care for the treatment of patients with AS and low to intermediate operative risk.

More recently, three additional trials reported non-inferiority of TAVR in intermediate-risk patients

(PARTNER 2A, NOTION, SURTAVI)

N Engl J Med. (2011) 364:2187–
N Engl J Med. (2014) 370:1790–8.
N Engl J Med.(2017) 376:1321–31
N Engl J Med. (2016) 374:1609–20.

REGISTRIES

German registry on aortic valve replacement (AQUA), the number of annual TAVI procedures in Germany increased 20-fold from 2008 to 2014 while the number of SAVR procedures slowly declined.
Operative risk decreased significantly over the years with a larger percentage of patients at low to intermediate risk

German Aortic Valve Registry (GARY)
15.964 pts 2011-2013
Significant regression in risk profiles (logES 20% to 16%)

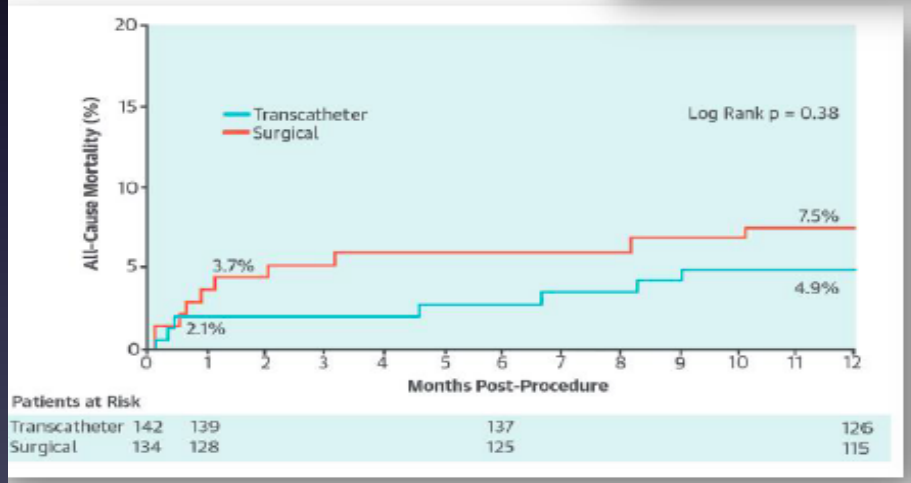
STS/TVT Am coll of Cardiology Registry
54.780 pts 2012-2015
TAVI procedures increased from 4.627 to 24.808
Significant regression in risk profiles (STS: 7% to 6%)

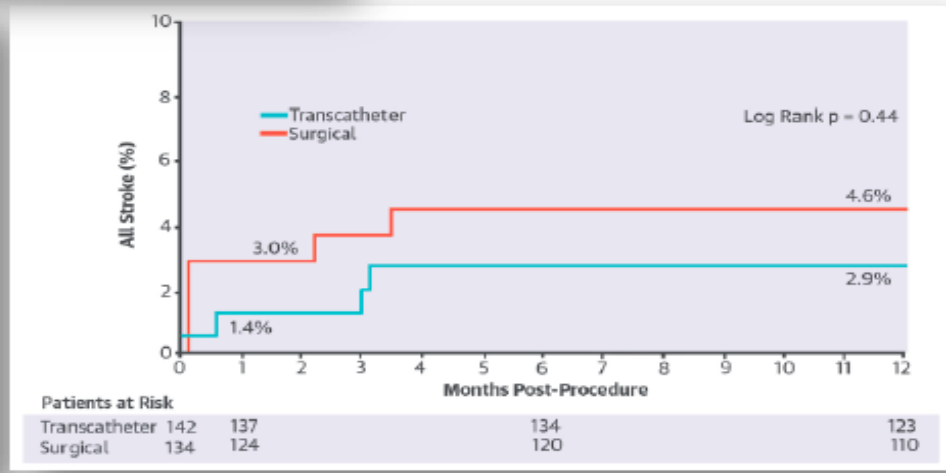
Eurointervention(2016) 11:1029–33.
J Am Coll Cardiol. (2017) 69:1215–30.
J Am Coll Cardiol (2015) 65:2173–80

NOTION : RCT trial
TAVI vs SAVR in low risk patients

TABLE 1 Baseline Characteristics

	TAVR* (n = 145)	SAVR* (n = 135)
Age, yrs	79.2 ± 4.9	79.0 ± 4.7
Male	78/145 (53.8)	71/135 (52.6)
NYHA functional classification		
I	7/144 (4.9)	3/134 (2.2)
II	67/144 (46.5)	70/134 (52.2)
III	67/144 (46.5)	57/134 (42.5)
IV	3/144 (2.1)	4/134 (3.0)
STS-PROM score, %	2.9 ± 1.6	3.1 ± 1.7
Logistic EuroSCORE, %	8.4 ± 4.0	8.9 ± 5.5





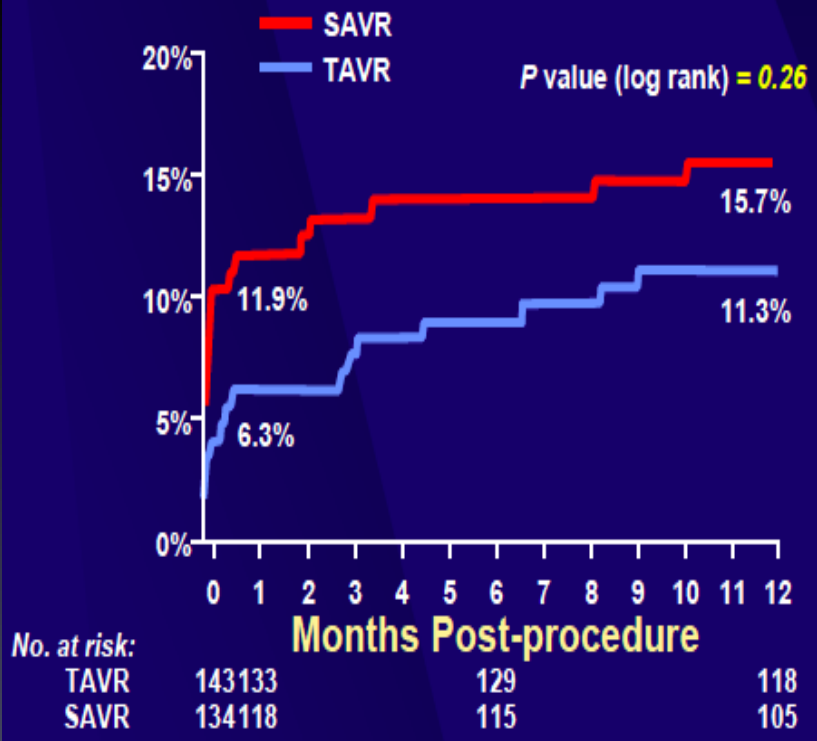
Thyregod et al, J Am Coll Cardiol 2015;65:2184-94

JACC (2015) 65:2184-94

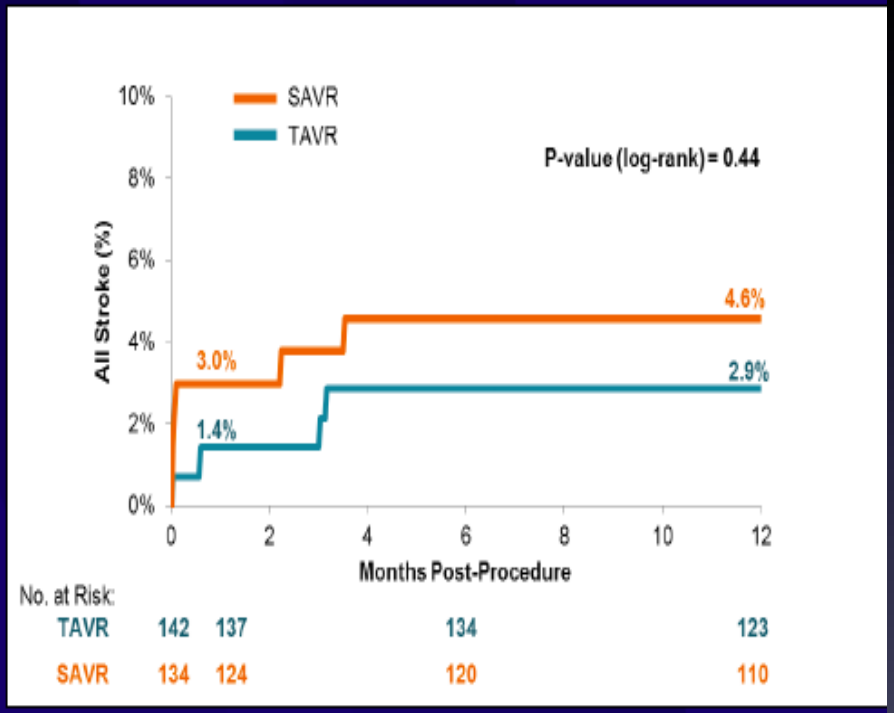
1-Year Results From the All-Comers

NOTION Randomized Clinical Trial

All-cause Mortality MI, or Stroke (%)



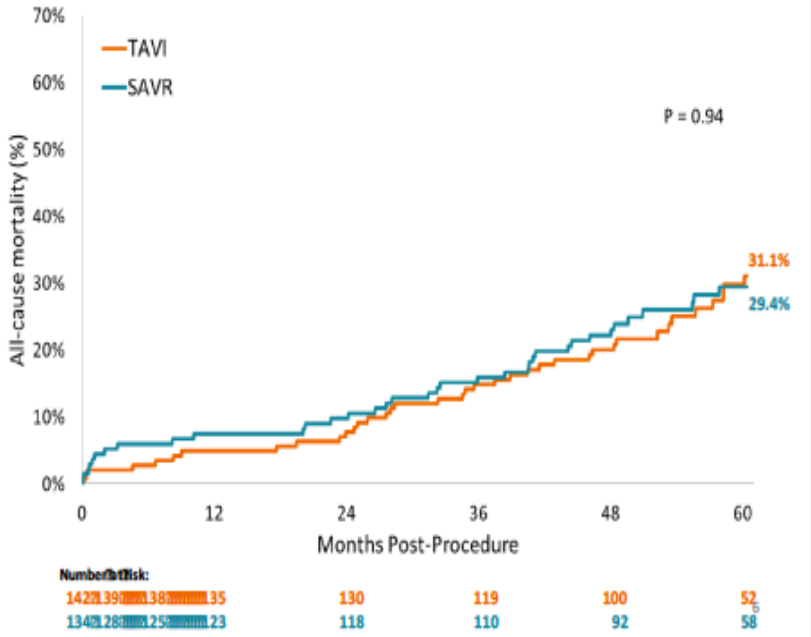
Stroke



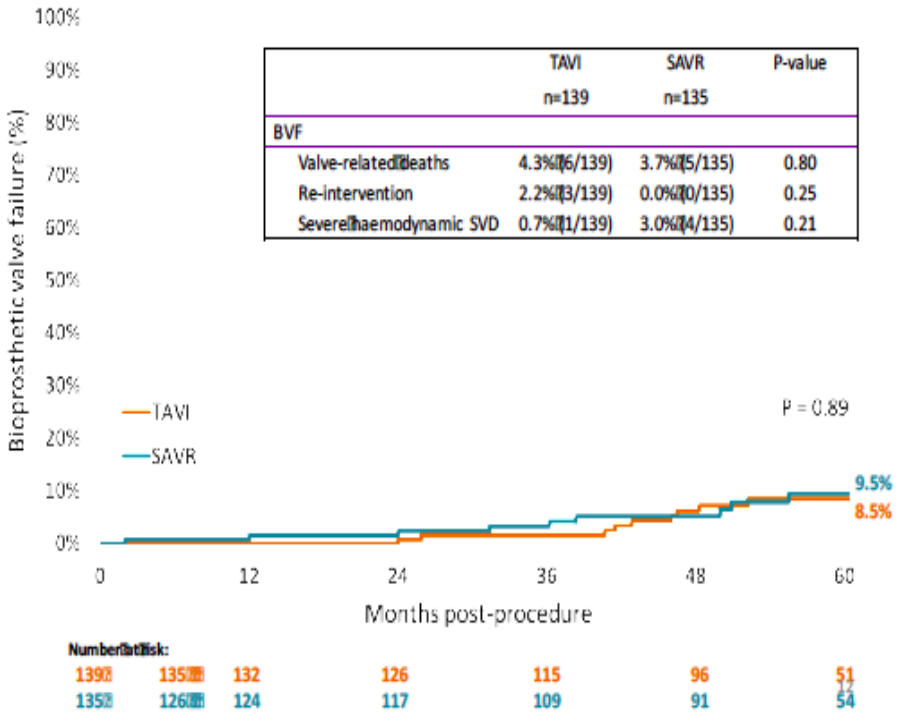
JACC (2015) 65:2184-94

CoreValve NOTION Trial: 4-year F-Up

All-Cause Mortality



Bioprosthetic valve failure

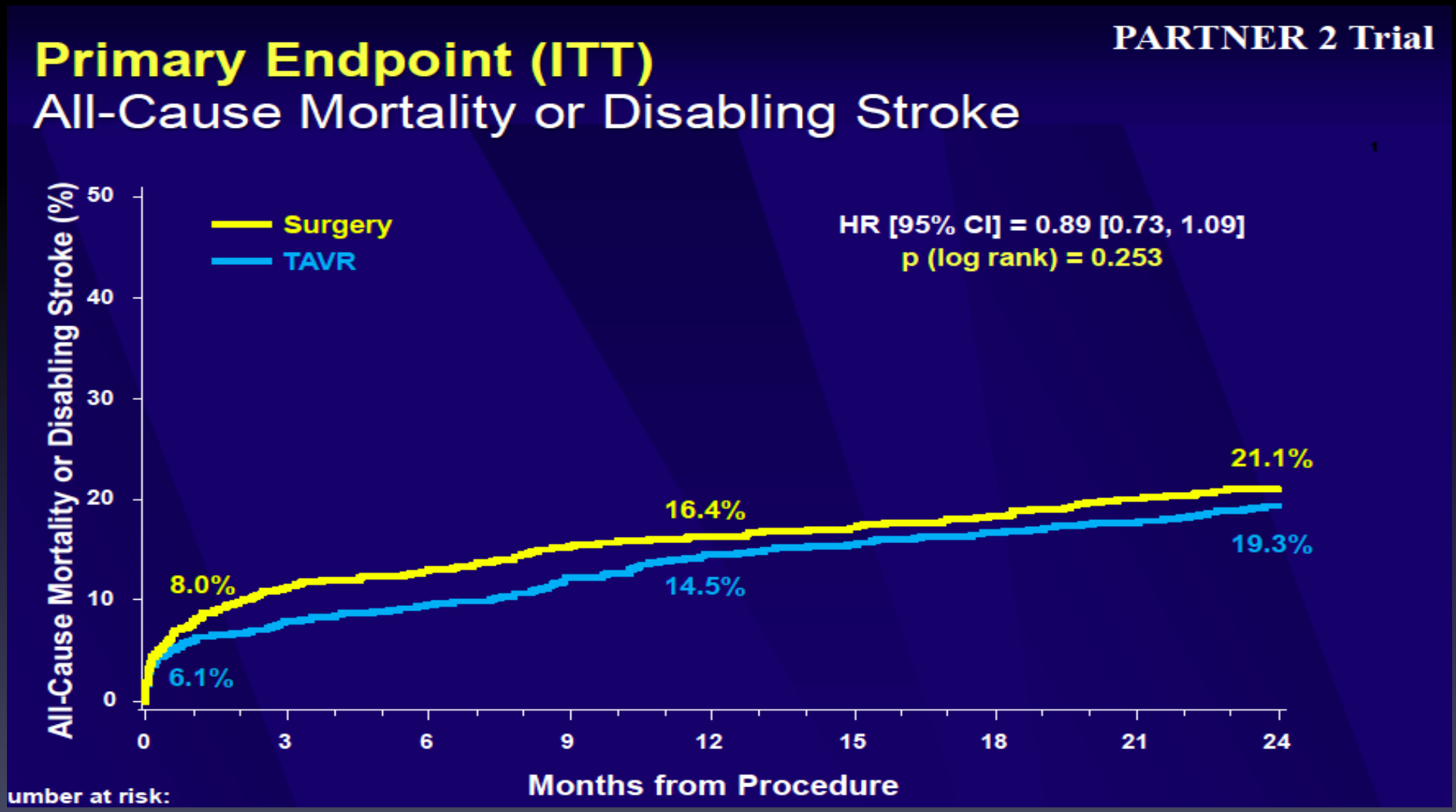


	TAVI n=139	SAVR n=135	P-value
BVF			
Valve-related deaths	4.3% (6/139)	3.7% (5/135)	0.80
Re-intervention	2.2% (3/139)	0.0% (0/135)	0.25
Severe haemodynamic SVD	0.7% (1/139)	3.0% (4/135)	0.21

JACC (2015) 65:2184-94

Partner 2A trial-

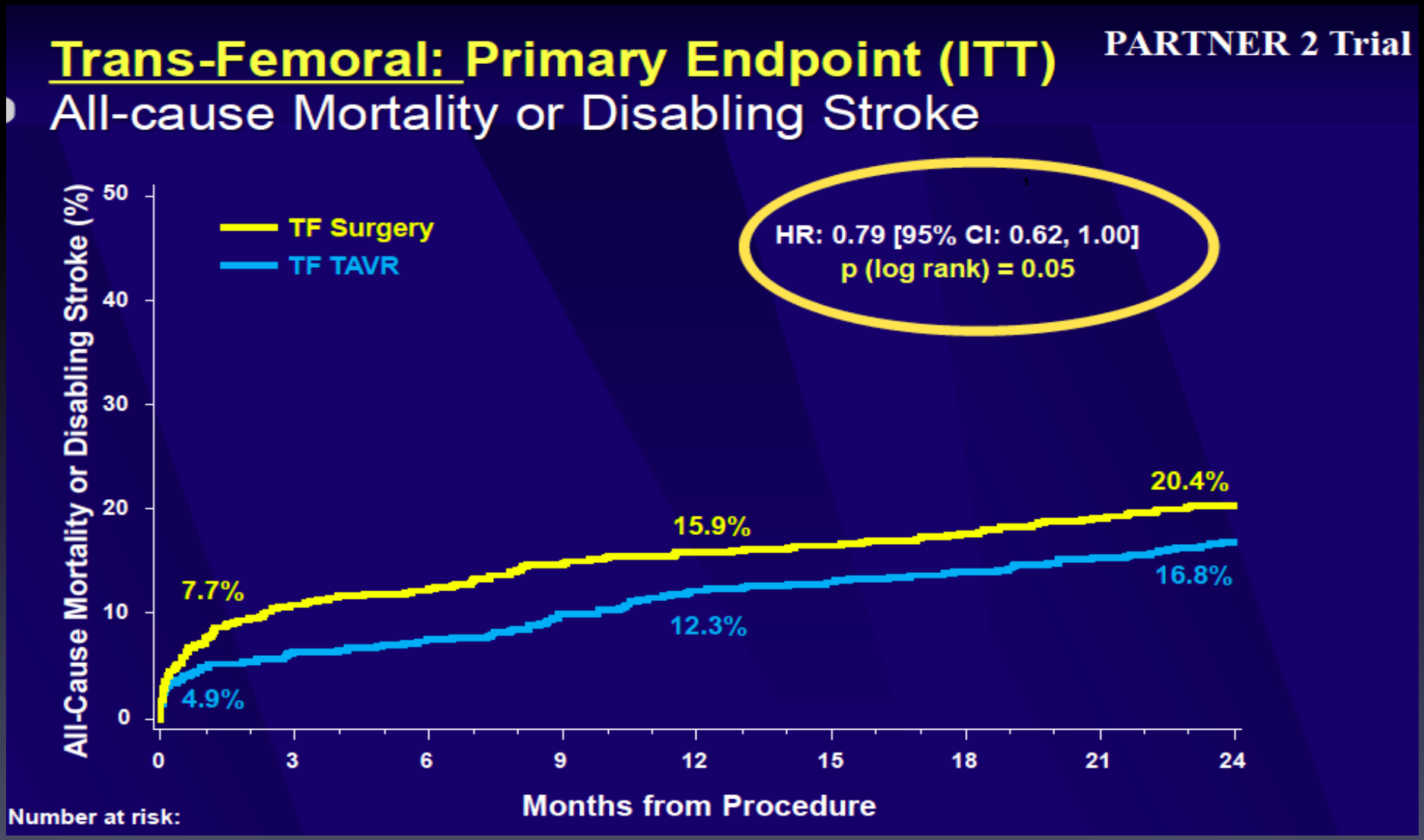
2032 pts : Intermediate risk STS: 4-8%



N Engl J Med 2016; 374:1609-1620

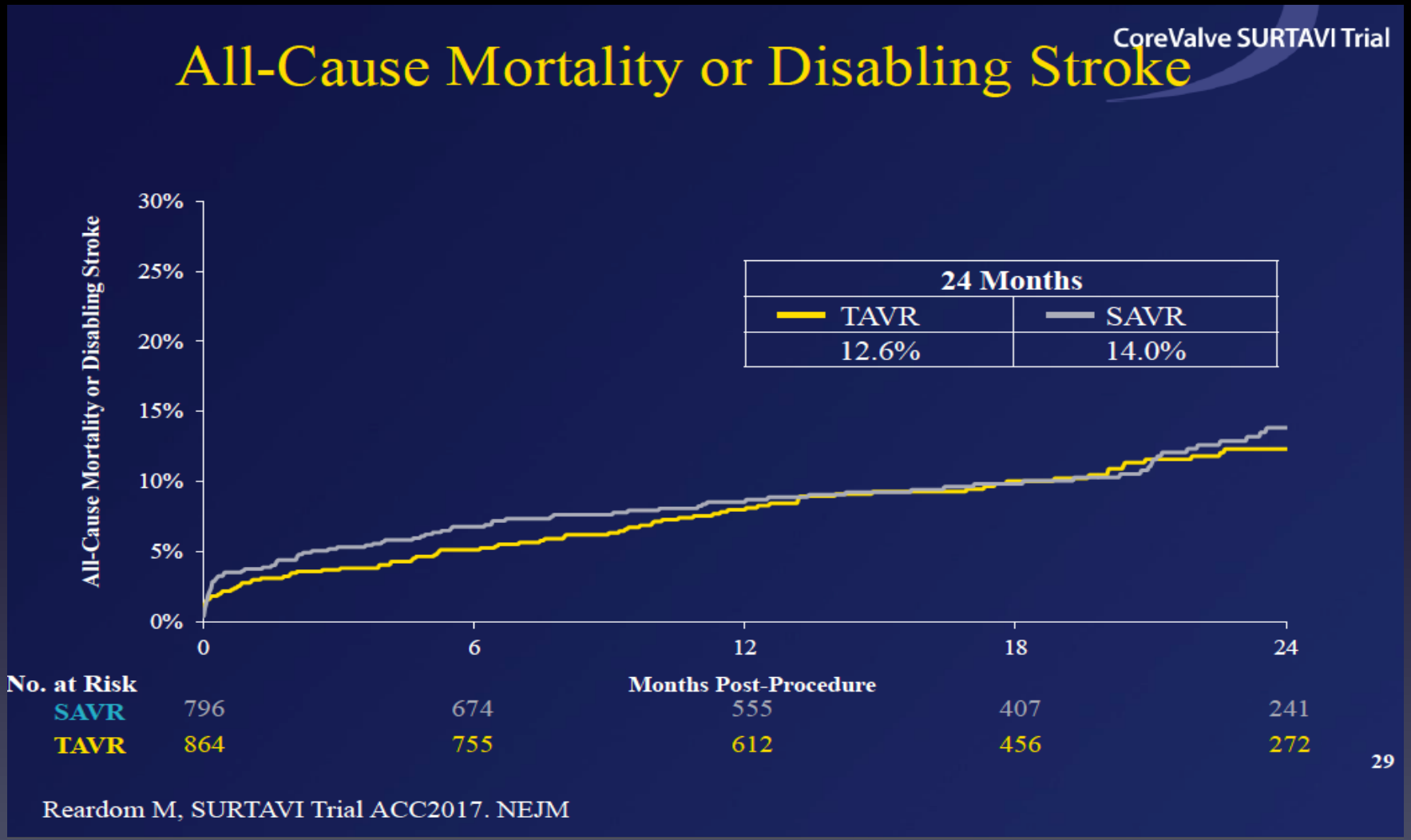
Partner 2A trial-

2032 pts : Intermediate risk STS: 4-8%



N Engl J Med 2016; 374:1609-1620

SURTAVI trial
1764 pts, Intermediate risk: STS: 4.5%



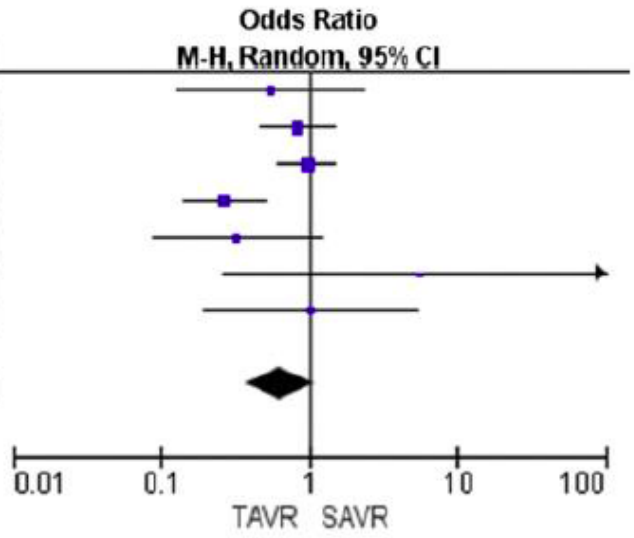
TAVR vs. SAVR in low to intermediate risk patients: A meta-analysis of randomized and observational studies

30 day mortality

Study or Subgroup	TAVR Events	TAVR Total	SAVR Events	SAVR Total	Weight	Odds Ratio M-H, Random, 95% CI
NOTION 2015	3	145	5	135	9.6%	0.55 [0.13, 2.34]
OBSERVANT 2015	20	650	24	650	22.3%	0.83 [0.45, 1.51]
PARTNER 2 2016	39	1011	41	1021	25.5%	0.96 [0.61, 1.50]
SAPIEN 3 2016	12	1077	38	944	21.2%	0.27 [0.14, 0.52]
Schymik 2015	3	216	9	216	10.8%	0.32 [0.09, 1.21]
STACCATO 2012	2	34	0	36	2.8%	5.62 [0.26, 121.32]
Tokarek 2015	3	39	3	40	7.8%	1.03 [0.19, 5.43]
Total (95% CI)		**3172**		**3042**	**100.0%**	**0.63 [0.37, 1.08]**
Total events	82		120			

Heterogeneity: Tau² = 0.25; Chi² = 13.78, df = 6 (P = 0.03); I² = 56%

Test for overall effect: Z = 1.67 (P = 0.09)



Conclusions: Comparing with SAVR in patients at low to intermediate surgical risk, TAVR has:

- Similar mortality rate and MACCE,
- Lower incidence of acute kidney injury and new-onset atrial fibrillation,
- Higher major vascular complications and permanent pacemaker implantation.

Zhou Y et al. Int J Cardiol. 2017 Feb 1;228:723-728

TABLE 2 | Overview of currently active randomized trials on TAVI vs. SAVR in low to intermediate risk patients with severe aortic stenosis.

	DEDICATE	NOTION 2	PARTNER 3	CoreValve low risk
Reference/NCT number	Clinicaltrials.gov/NCT03112980	Clinicaltrials.gov/NCT02825134	Clinicaltrials.gov/NCT02675114	Clinicaltrials.gov/NCT02701283
Study start date	2017	2016	2016	2016
Study status	Recruiting	Recruiting	Recruiting	Recruiting
Estimated study completion date	2024	2024	2027	2026
Patients' risk profile	STS-PROM 2-6%	Patient age ≤75 years and STS-PROM <4%	STS-PROM <4%	Operative risk <3%
Study arms	TAVI* vs. SAVR* (1:1 randomization)	TAVI* vs. SAVR* (1:1 randomization)	TAVI (SAPIEN 3) vs. SAVR* (1:1 randomization)	TAVI (CoreValve Evolut R) vs. SAVR* (1:1 randomization)
Estimated enrollment	1,600	992	1,328	1,200
Primary Outcome	• Efficacy endpoint: Overall survival at 5 years • Safety endpoint: Overall survival at 1 year and 196 deaths (event-driven)	All-cause mortality, myocardial infarction or stroke at 1 year	All-cause mortality, stroke, or re-hospitalization at 1 year	All-cause mortality or disabling stroke at 2 years
Follow up time	5 years	1 year	10 years	10 years

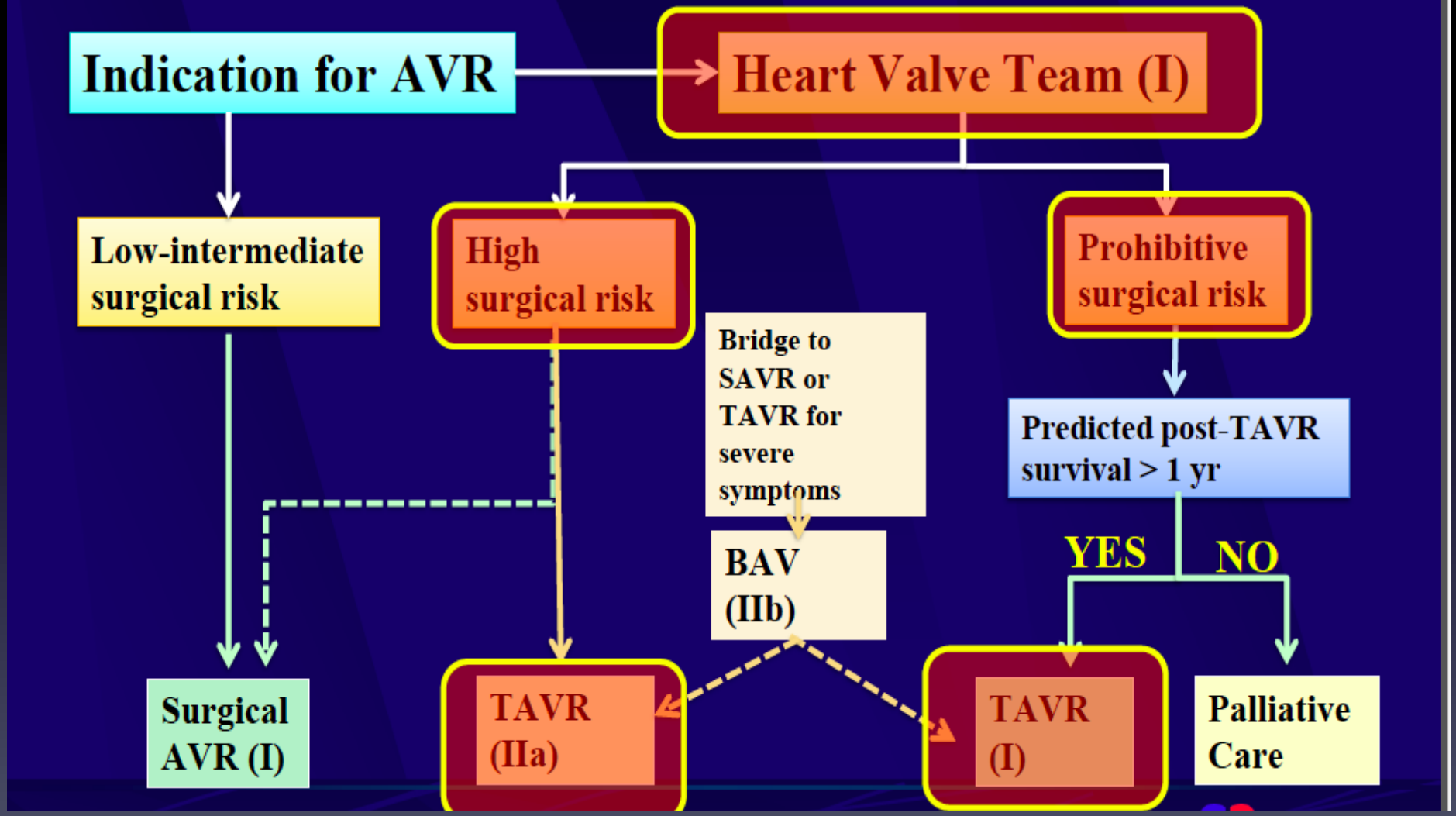
REVIEW published: 12 July 2018

2014 ACC/AHA Valve Guidelines

Intervention for AS

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



Intervention for Severe AS

Indications for TAVR vs surgical AVR:

AMERICAN COLLEGE of CARDIOLOGY

American Heart Association.

EUROPEAN SOCIETY OF CARDIOLOGY®

EACTS

	• Evaluation by a Heart Team	class I
	• Surgical AVR for patients at low surgical risk	class I
	• TAVR for patients with prohibitive surgical risk and life expectancy >12 months	class I
New 2017	• TAVR or SAVR for patients at high surgical risk	class I
New 2017	• TAVR or SAVR for patients at intermediate surgical risk	class IIa (ACC/AHA); class I (ESC/EACTS)

In Summary

- Patient selection for TAVR is based on accurate assessment of aortic stenosis, both clinical and anatomical.

  The Heart Team is key in the risk evaluation of this population.

  3D imaging modalities are preferred for assessing the anatomy and the dimensions of the aortic annulus.

- TAVR has become the standard treatment in patients at increased surgical risk and is increasingly being performed in patients at intermediate to low risk at current.