MILAN
SEPTEMBER
21&22,2023

Session: Burning questions in TAVI

High Lifetime Management: valve and sequence selection

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Session: Burning questions in TAVI

No conflict of interest to declare

Burning questions

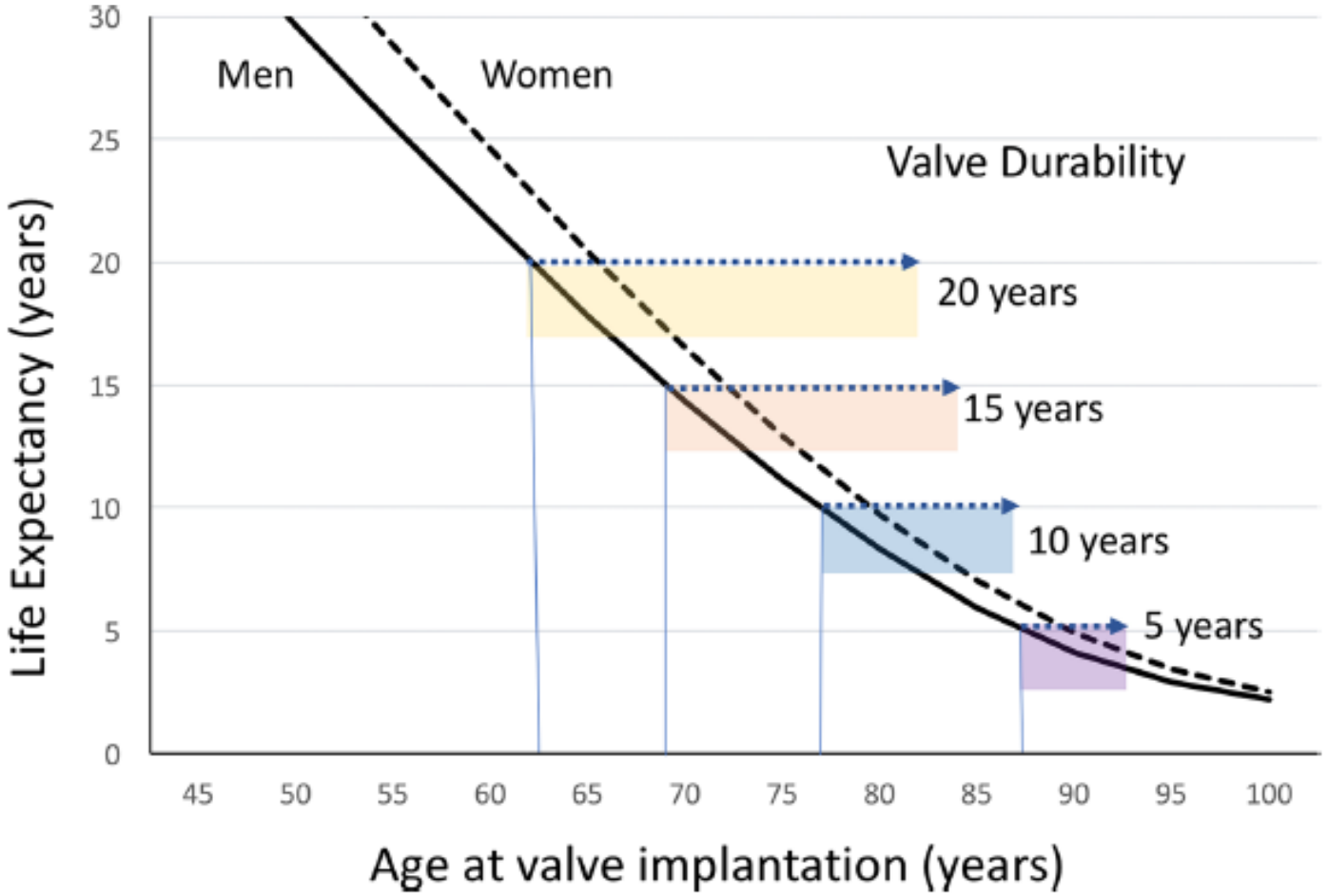
✓ All tissue valves have limited durability;

✓ It is unknown whether transcatheter and surgical valves have similar durability;

✓Valve durability is an increasingly important issue as TAVI expands to lower risk and younger populations with longer life expectancy

Importance of the valve durability-life expectancy ratio in selection of a prosthetic aortic valve

Rodrigo Bagur,[1,2,3] Philippe Pibarot,[4] Catherine M Otto[5]



Bagur R, et al. *Heart Month 2017 Vol 0 No 0*

Randomised trial TAVR vs surgery in younger patient at lower surgical risk

start

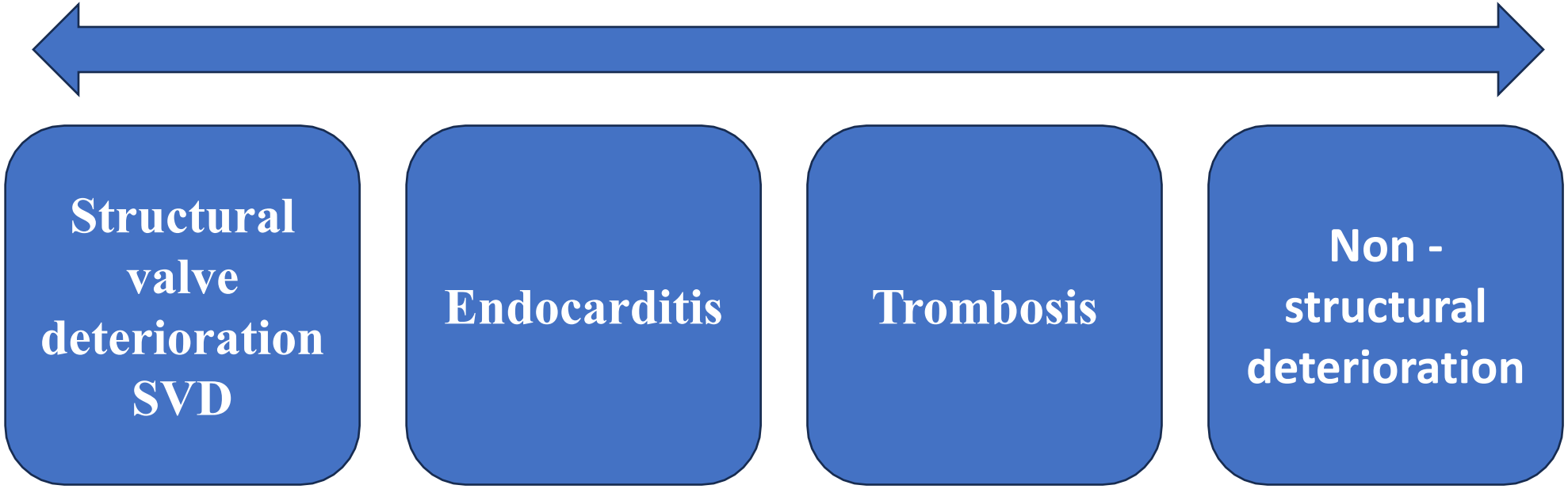
5 yrs

8 yrs

10 yrs

PARTNER 2	JACC 2020	Structural Deterioration of Transcatheter Versus Surgical Aortic Valve Bioprostheses in the PARTNER-2 Trial	Mean age 81±6 yrs
SURTAVI	JAMA 2022	**Self-expanding Transcatheter vs Surgical Aortic Valve Replacement in Intermediate-Risk Patients** 5-Year Outcomes of the SURTAVI Randomized Clinical Trial	Mean age 80±6 yrs
NOTION 3	EHJ 2021	Eight-year outcomes for patients with aortic valve stenosis at low surgical risk randomized to transcatheter vs. surgical aortic valve replacement	Mean age 79±5 yrs
PARTNER 3	ongoing		Mean age 73±6 yrs
EVOLUT LOW RISK	ongoing		Mean age 74±6 yrs

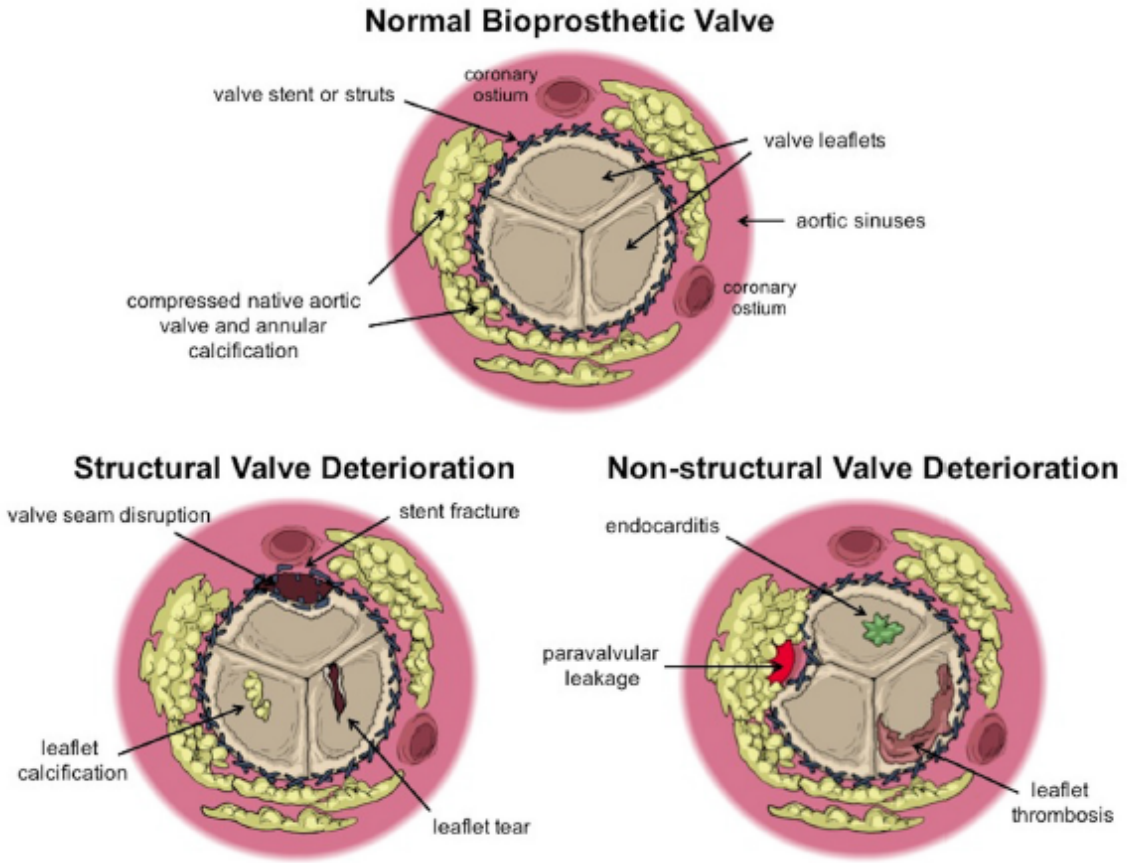
Etiology of Bioprosthetic Valve Dysfunction (BVD)



Intrinsic permanent changes of bioprothesis *(calcification, tears)*

Abnormalities not directly related to the bioprothesis *(mismatch, paravalvular leak)*

Determination of Etiology and Category of BVD by TTE, TEE, CT

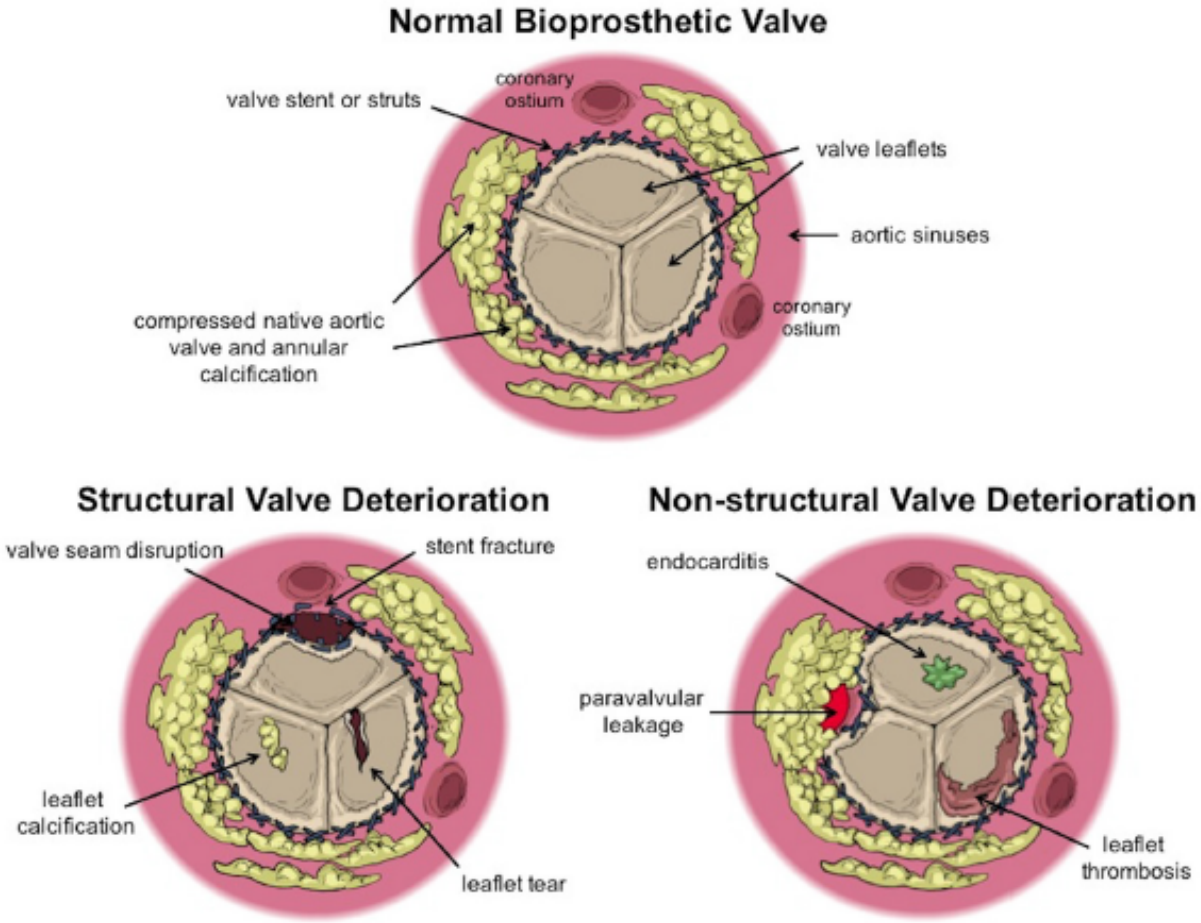


Structural BVD
Intrinsic permanent changes to the prosthetic valve, including:

- Wear and tear
- Leaflet disruption
- Flail leaflet
- Leaflet fibrosis and/or calcification
- Strut or stent fracture or deformation

Pibarot et al.; *JACC Vol.80, No. 5, 2022 – August 2,2022:545-561*

Determination of Etiology and Category of BVD by TTE, TEE, CT

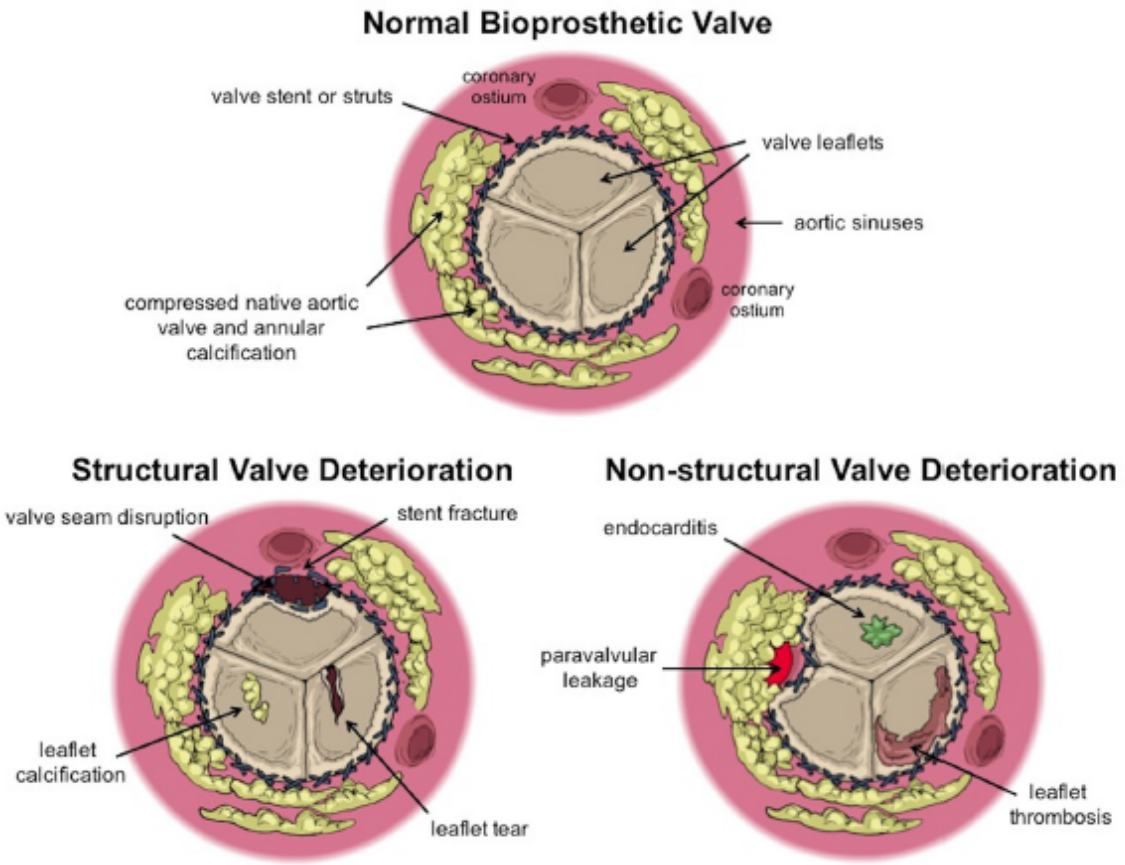


Nonstructural BVD
Any abnormality, **not** intrinsic to the prosthetic valve, resulting in valve dysfunction

- **Paravalvular Regurgitation**
- **Prosthesis-Patient Mismatch**
- **Other**
  May include: obstruction by pannus; inappropriate positioning or sizing, embolization; dilatation of the aortic root after stentless bioprostheses or aortic valve sparing operations

Pibarot et al.; *JACC Vol.80, No. 5, 2022 – August 2,2022:545-561*

Determination of Etiology and Category of BVD by TTE, TEE, CT



Thrombosis

Subclinical leaflet thrombosis:

Imaging findings of HALT/RLM with absent or mild hemodynamic changes and no symptoms/sequelae

Clinically significant valve thrombosis:

1) Clinical sequelae of thromboembolic event or worsening AS/AR and BVD Stage 2-3 or confirmatory imaging (HALT/RLM)
2) In the absence of clinical sequelae, both BVD Stage 3 and confirmatory imaging (HALT/RLM)

Endocarditis

Meeting at least 1 of the following criteria:
1) Fulfillment of the Duke endocarditis criteria
2) Evidence of abscess, pus, or vegetation confirmed as secondary to infection by histological or microbiological studies during re-operation
3) Evidence of abscess, pus, or vegetation confirmed on autopsy

Pibarot et al.; *JACC Vol.80, No. 5, 2022 – August 2,2022:545-561*

RED FLAGS of Aortic Bioprosthetic Valve Dysfunction (BVD)

- ✓ Reduced or excessive **leaflet mobility** and **leaflet thickening**
- ✓ **Color-flow Doppler** systolic restriction
- ✓ **Mean Gradient** ≥ 20 mmHg in high suspicious of BVD (≥ 30 mmHg) or increased in mean gradient ≥ 10 mmHg (≥ 20 mmHg) in high suspicious of BVD during follow-up.
- ✓ **EOA** < 1.1 cm^2 (< 0.8 cm^2) in high suspicious of BVD
- ✓ **DVI** < 0.35 (0.25) - **AT/LVET** > 0.32 (0.37)
- ✓ New onset or worsening of intraprosthetic **AR** ≥ mild
- ✓ New onset or worsening of **symptoms**

Pibarot et al.; *JACC Vol.80, No. 5, 2022 – August 2,2022:545-561*

Valve Academic Research Consortium 3: Updated Endpoint Definitions for Aortic Valve Clinical Research

Grading of BVD according Valve Academic Research Consortium 3

- ✓ **Stage 1:** Morphological valve deterioration: evidence without significant haemodynamic changes;
- ✓ **Stage 2:** Moderate haemodynamic valve deterioration;
- ✓ **Stage 3:** Severe haemodynamic valve deterioration;

Généreux, P. et al.; *J Am Coll Cardiol. 2021;77(21):2717–46.*

Valve Academic Research Consortium 3: Updated Endpoint Definitions for Aortic Valve Clinical Research

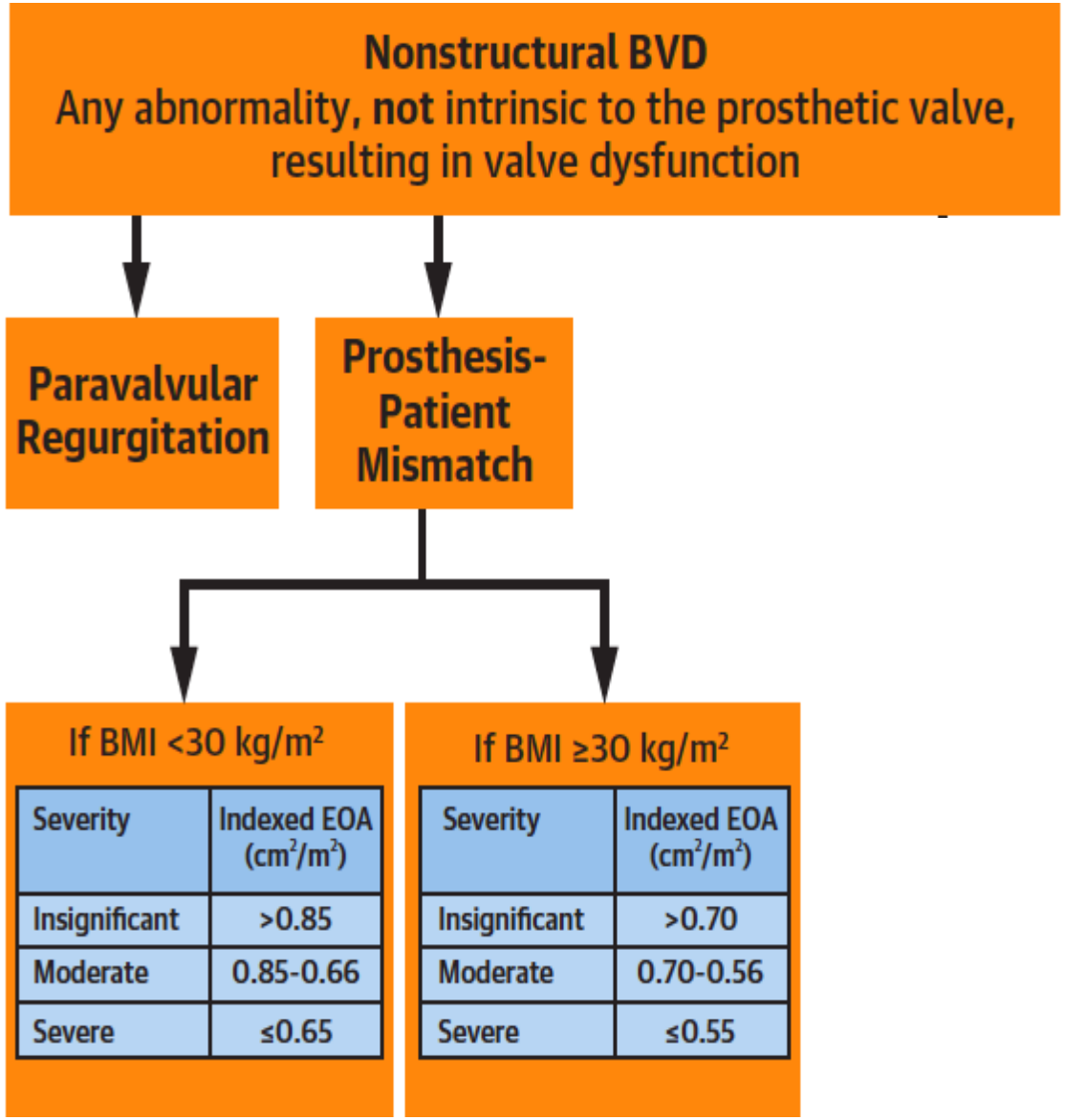
Stage	Moderate (stage 2)	Severe (stage 3)
Mean Gradient (mmHg)	≥ 20 mmHg	≥ 30 mmHg
Increase in mean Gradient to baseline (mmHg)	≥ 10 mmHg	≥ 20 mmHg
Decrease EOA ($cm^{2)}$	≥ 0.3 cm^2	≥ 0.6 cm^2
AR (occurence or increased)	Moderate	Severe

Généreux, P. et al.; *J Am Coll Cardiol. 2021;77(21):2717–46.*

Standardized Definitions for Bioprosthetic Valve Dysfunction Following Aortic or Mitral Valve Replacement

JACC State-of-the-Art Review

What about Prosthesis – Patient Mismatch ???

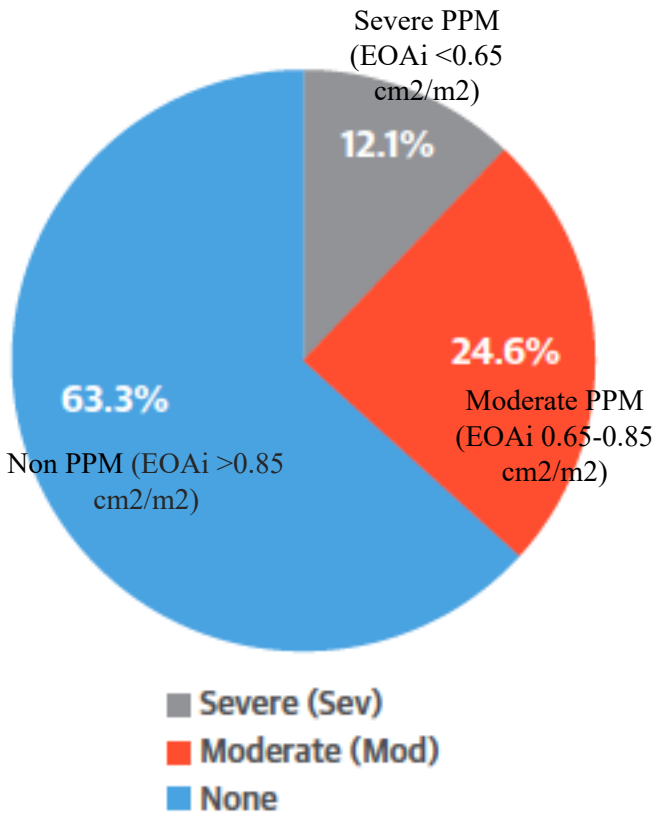


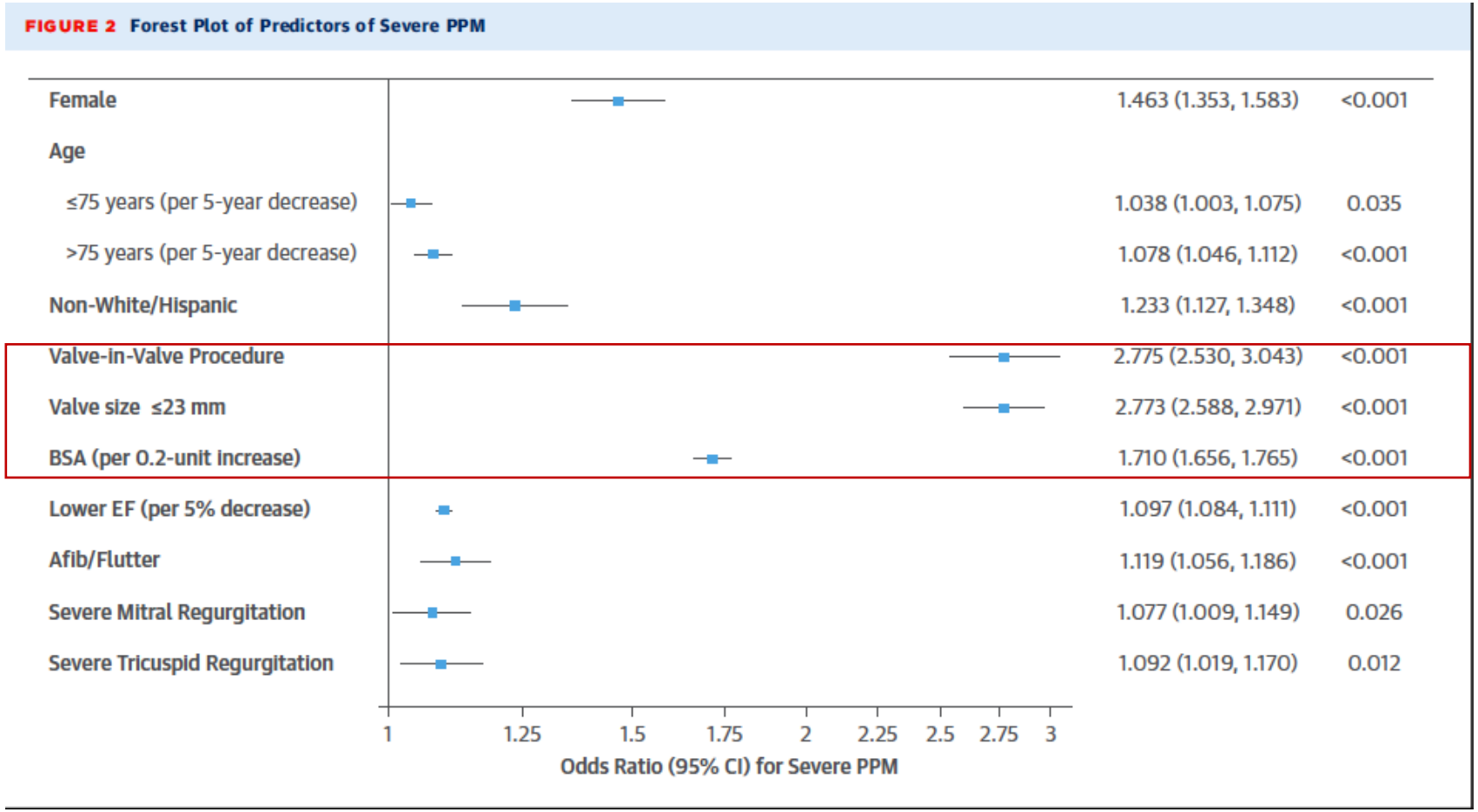
Pibarot et al.; *JACC Vol.80, No. 5, 2022 – August 2,2022:545-561*

Prosthesis–Patient Mismatch in Patients Undergoing Transcatheter Aortic Valve Replacement

From the STS/ACC TVT Registry

- ✓ Society of Thoracic Surgeons/American College of Cardiology TVT (Transcatheter Valve Therapy) registry to examine the frequency, predictors, and association with outcomes of PPM after TAVR in 62,125 patients enrolled between 2014 and 2017.

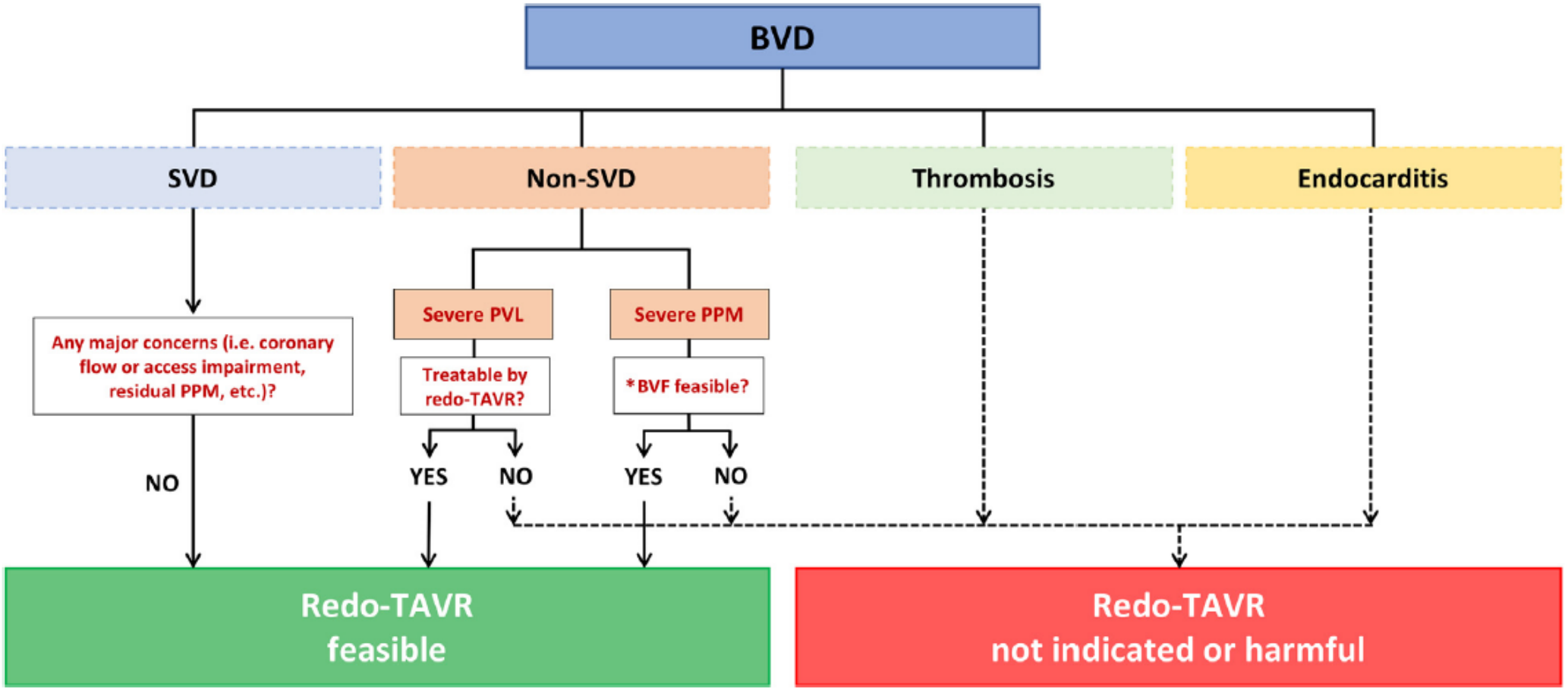




Herrmann, H.C. et al. *J Am Coll Cardiol. 2018;72(22):2701–11.*

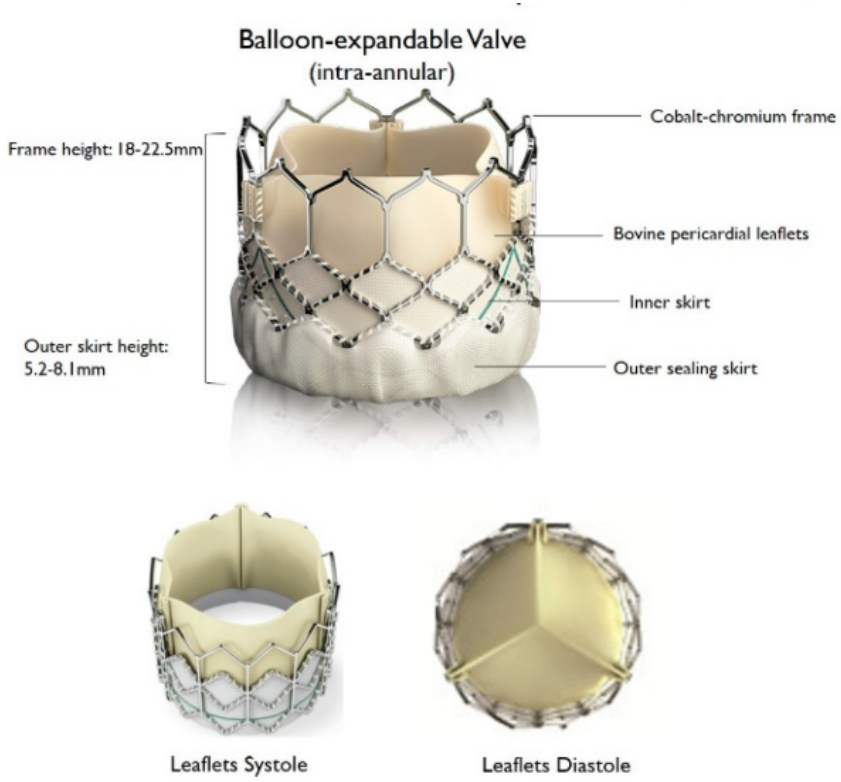
Transcatheter Aortic Valve Replacement in Failed Transcatheter Bioprosthetic Valves

…what about treatment?

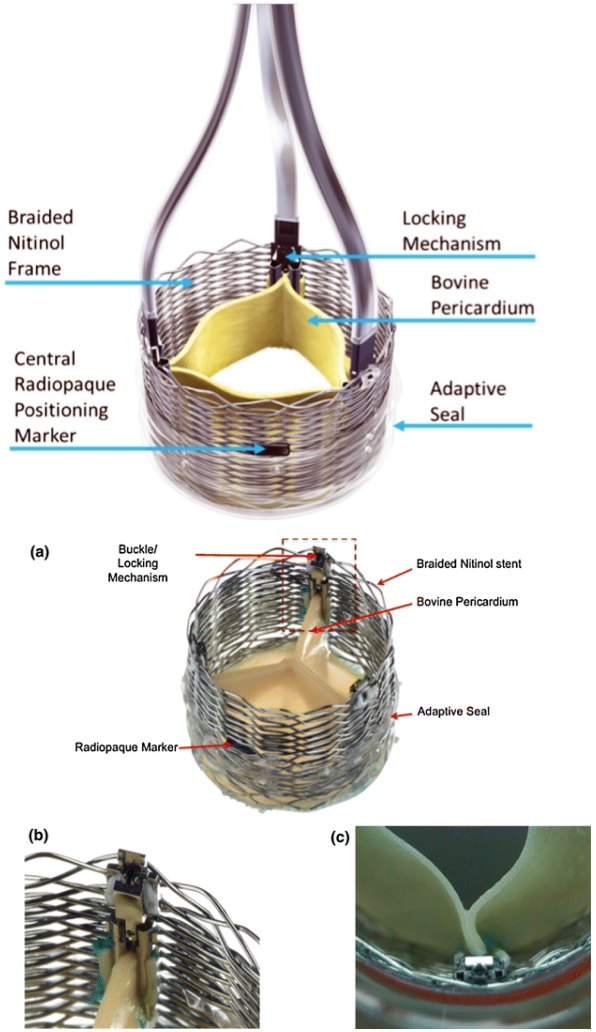


Tarantini et al:; *JACC Cardiovascular Interventions Vol.15,N. 18, September 26, 2022:1777-1793*

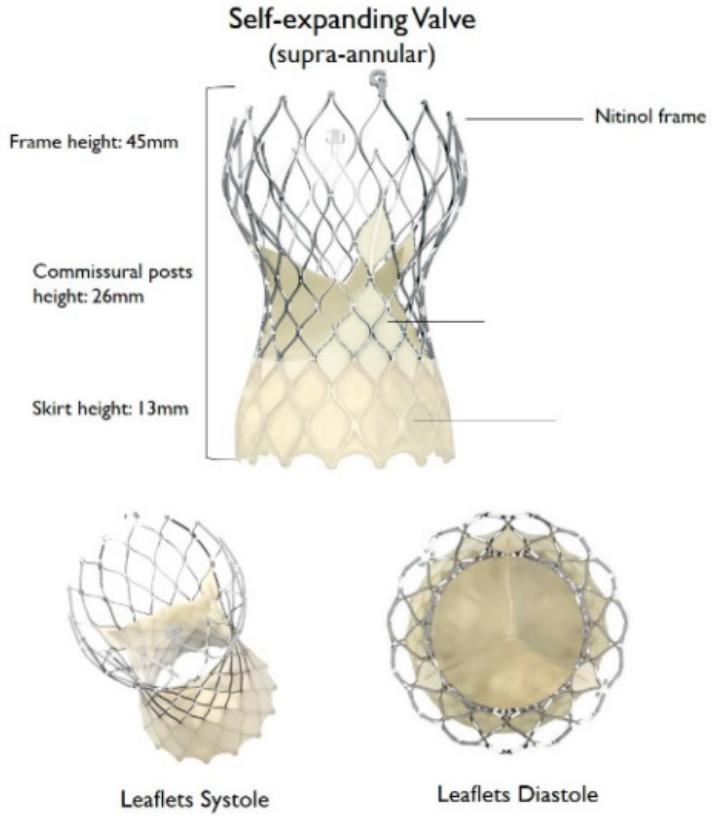
...the stars



Balloon Expandable Valve (BEV): Edwards



Mechanical Expandable Valve (MEV): Boston Scientific Lotus Valve

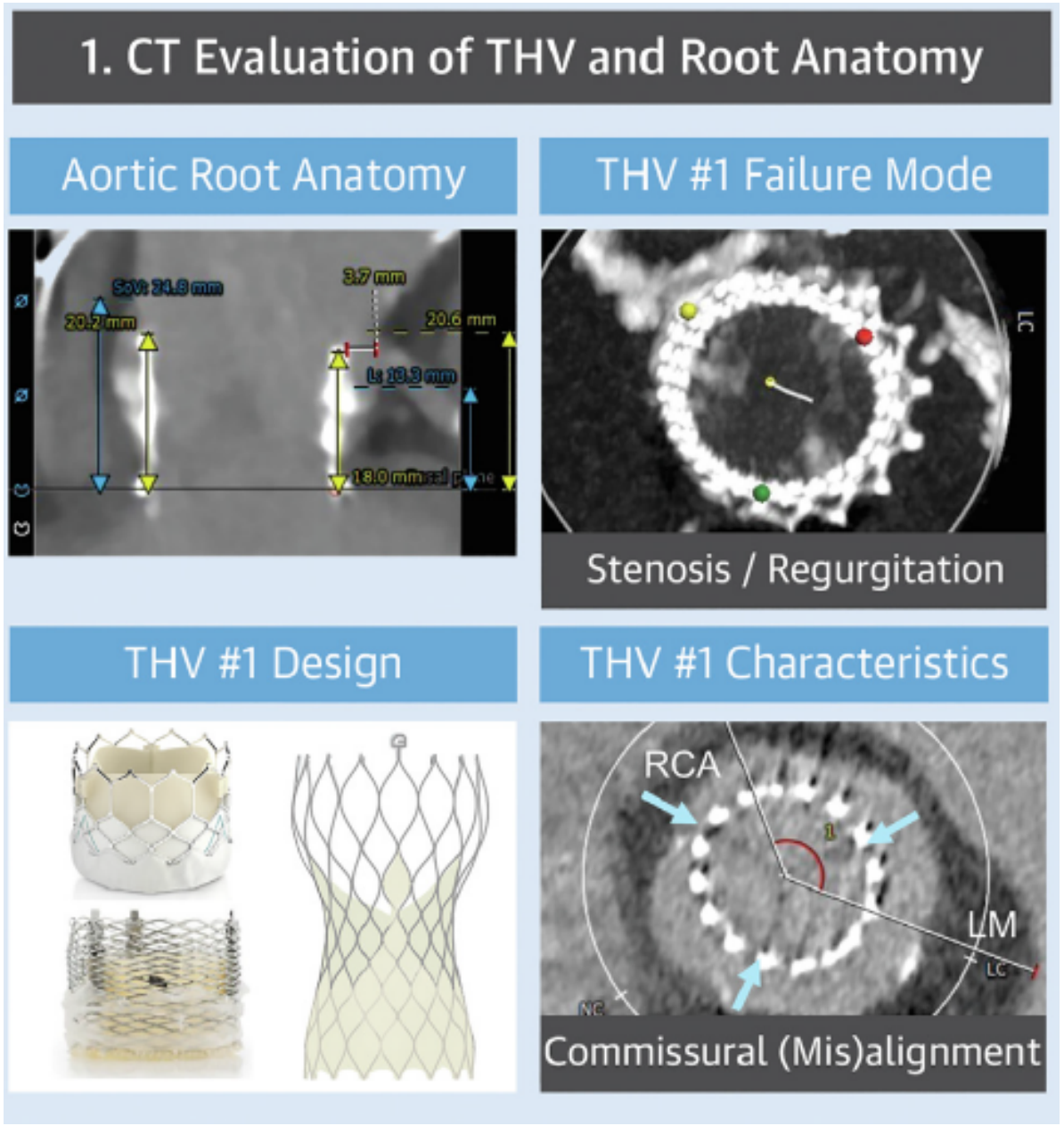


Self Expandable Valve (SEV): CoreValve Medtronic

Transcatheter Aortic Valve Replacement in Failed Transcatheter Bioprosthetic Valves

Key Steps for TAVR in TAVR

1. **CT evaluation of Transcatheter heart valve and root anatomy;**
2. Coronary obstruction risk assessment;
3. Transcatheter heart valve #2 sizing;
4. Trancatheter heart valve #2 positioning.



Tarantini et al:; *JACC Cardiovascular Interventions Vol.15,N. 18, September 26, 2022:1777-1793*

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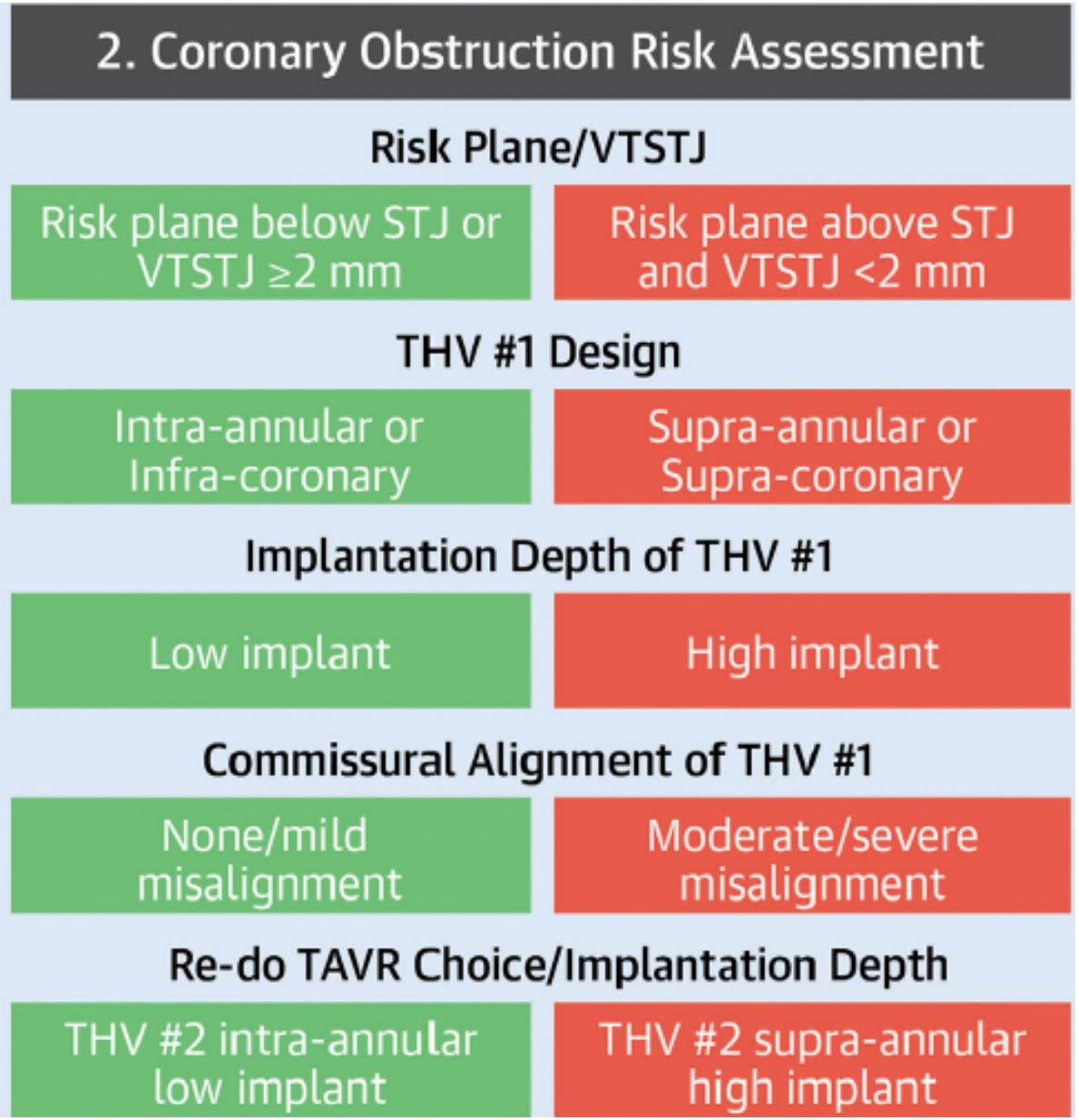

Tarantini et al:; *JACC Cardiovascular Interventions Vol.15,N. 18, September 26, 2022:1777-1793*

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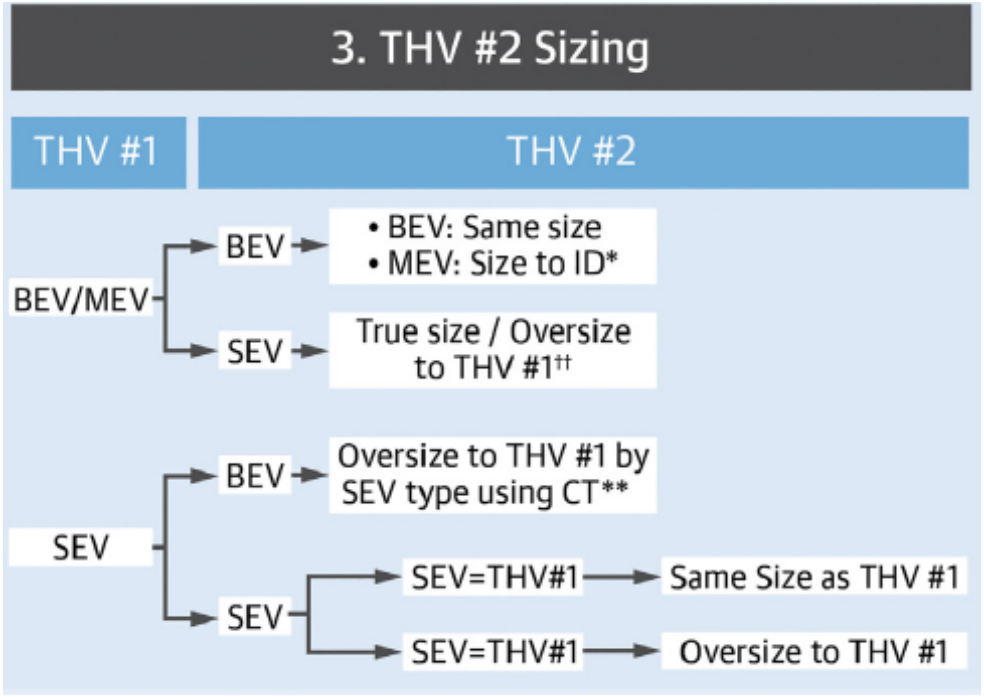
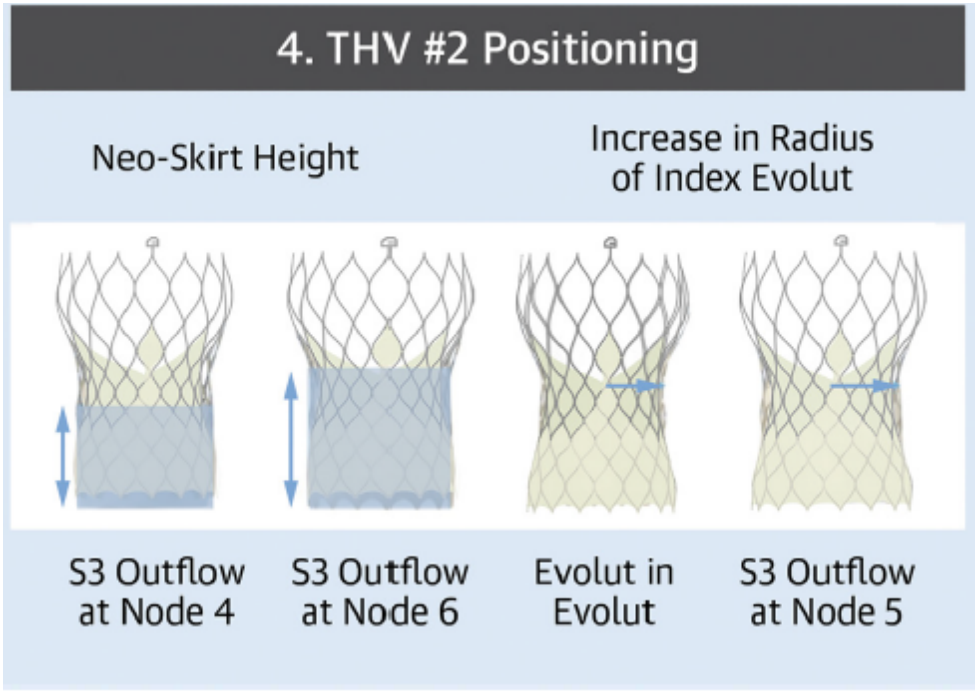
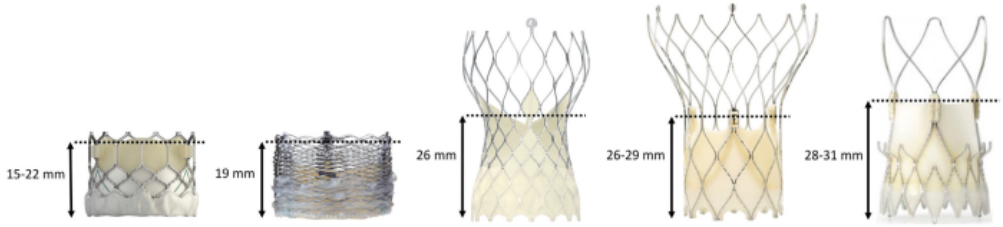




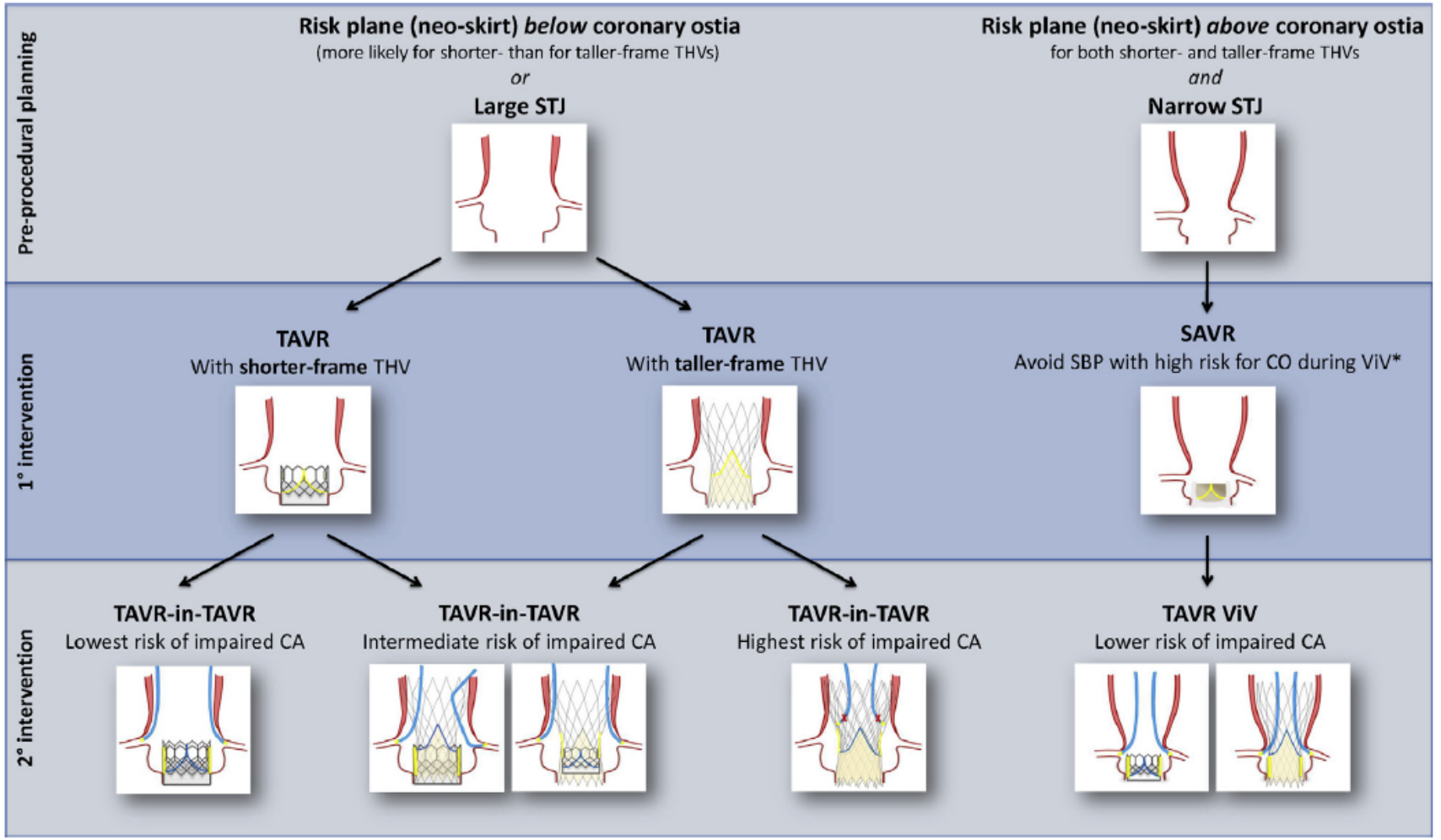
Tarantini et al:; *JACC Cardiovascular Interventions*
Vol.15,N. 18, September 26, 2022:1777-1793

Coronary Access and TAVR-in-TAVR

Don't Put Off Until Tomorrow What You Can Do Today*

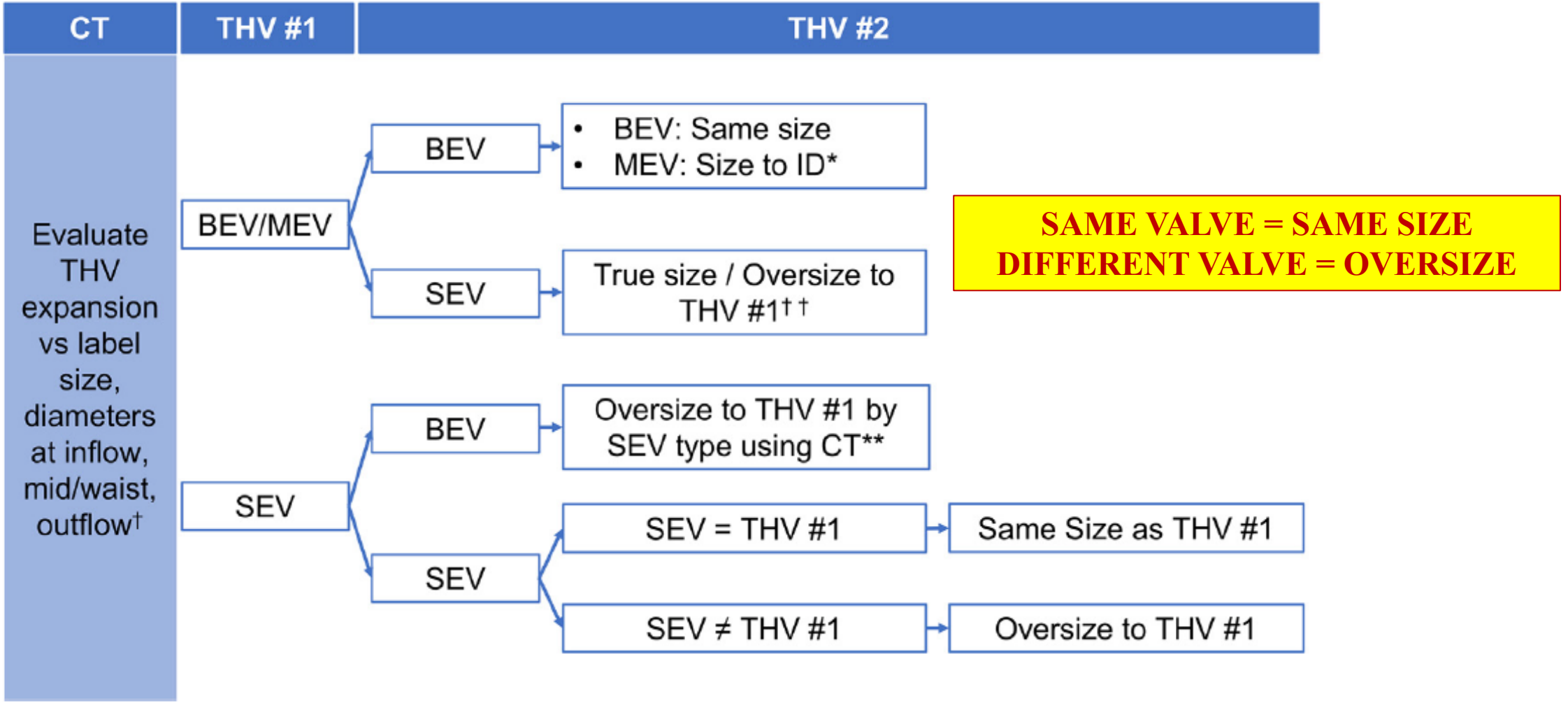


Treatment of AS in Younger Patients With Regard to Future Coronary Access



Giuseppe Tarantini et al. *J Am Coll Cardiol Intv 2020; 13:2539-2541*

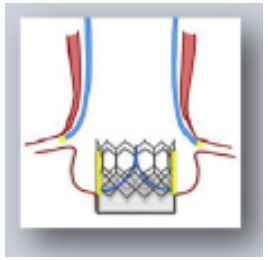
…what valve in valve?

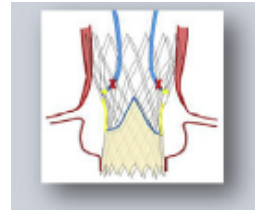


Tarantini et al:; *JACC Cardiovascular Interventions Vol.15,N. 18, September 26, 2022:1777-1793*

Transcatheter Aortic Valve Replacement in Failed Transcatheter Bioprosthetic Valves

Redo-TAVR or TAVR EXPLANT ?





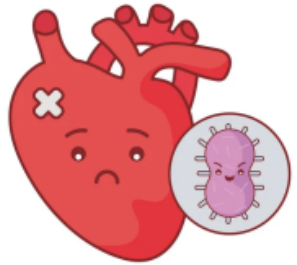


TABLE 1 Potential Factors Affecting Candidacy of Redo-TAVR Versus TAVR Explant

	Redo-TAVR Favored	TAVR Explant Favored
Patient		
Age	Older	Younger
Comorbidities/frailty	Present/multiple	Absent/few
Surgical risk	High/extreme	Low/intermediate
Lifetime management of aortic valve reintervention	Likely only 1 reintervention	Likely >1 reintervention
Anatomical		
Risk of coronary obstruction	Low/moderate	Moderate/high
Coronary reaccess after redo-TAVR	Easy	Difficult
Mechanism of THV failure		
Endocarditis	Absent	Present
Severe PPM	Absent	Present
Moderate/severe PVL	Absent or PVL amenable to percutaneous treatment	Present or PVL not amenable to percutaneous treatment
Need for other cardiac surgical procedures	No	Yes
Timing of THV failure	Late	Early

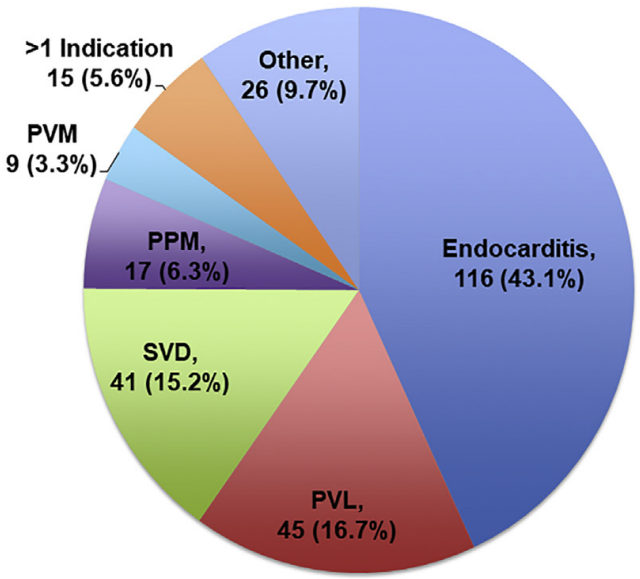
Tarantini et al:; *JACC Cardiovascular Interventions Vol.15,N. 18, September 26, 2022:1777-1793*

Surgical Explantation After TAVR Failure

Mid-Term Outcomes From the EXPLANT-TAVR International Registry

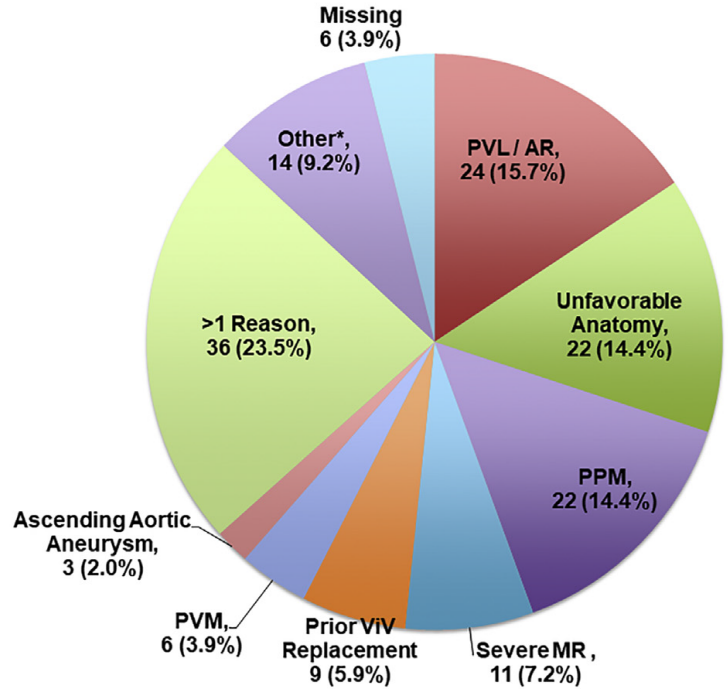
- ✓ A multicenter, international registry (EXPLANT-TAVR) of patients who underwent TAVR explantation;
- ✓ **269 patients** across 42 centers with a mean age of 72.7 +/- 10.4 years underwent TAVR explantation;

Primary Indications for TAVR Explantation (N=269)



>1 Indication, 5.6%		
	PPM	PVL
SVD	3.7%	1.1%
PVL	0.4%	
PVM	0.4%	

Primary Reasons for Exclusion from Redo-TAVR (N=153)



> 1 Reason, 23.5%			
	Unfavorable Anatomy	PPM	PVL
PPM	2%		
PVL	9.2%	0.7%	
PVM	1.3%	0.7%	
Prior ViV		1.3%	
Severe MR / MS			3.9%
Other	0.7%		3.9%

Bapat et al.; *JACC Cardiovascular Interventions Vol 14, N. 18, 2021 September 27, 2021: 1978 -1991.*

Surgical EXPLANTation After TAVR Failure: The EXPLANT-TAVR International Registry
42 Centers, 269 Patients

Index TAVR Procedure

2009 - 2020

50.9% Balloon-Expandable

49.1% Self-Expanding / Mechanically Expandable

Median Time: 11.5 months (interquartile range 4 - 32)

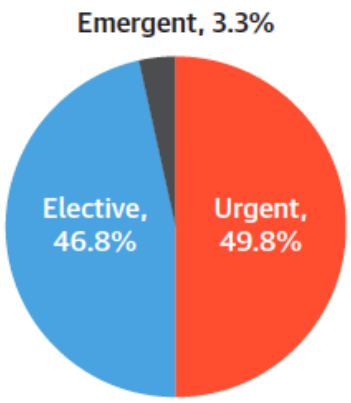
Surgical Explantation

2009 - 2020

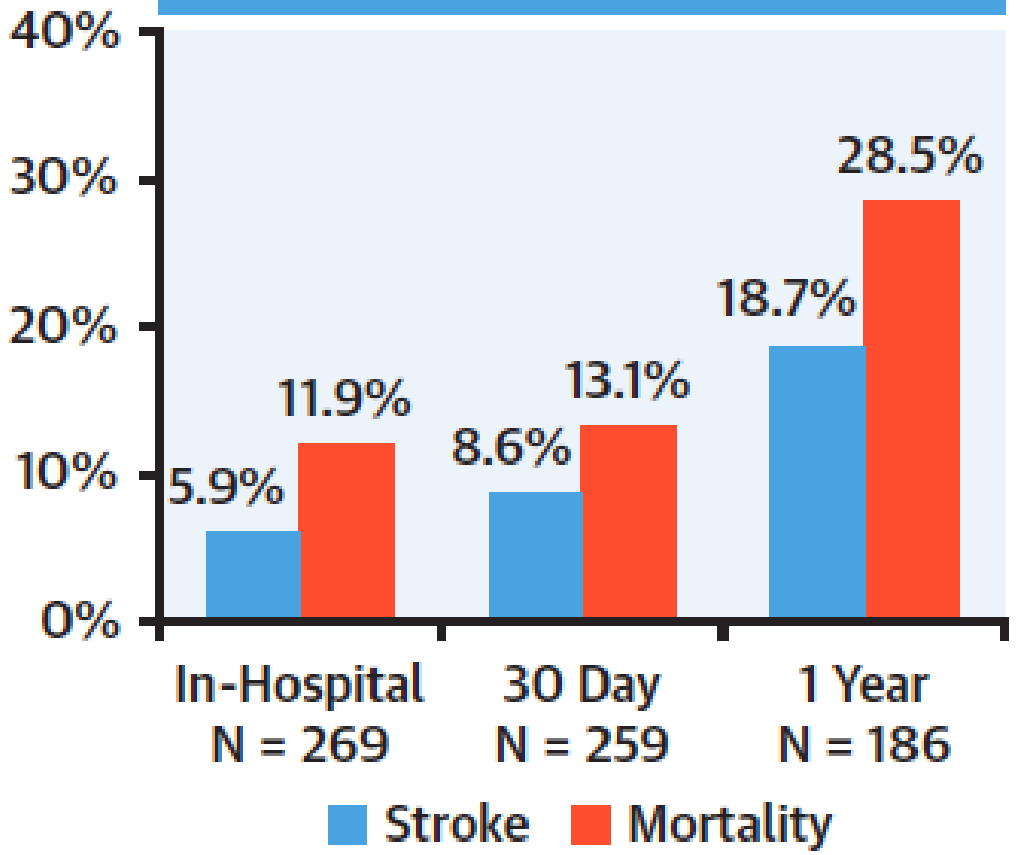
86.6% Aortic Valve Replacement

13.4% Root Replacement

Median Follow-up: 6.7 months (interquartile range 1 - 19)



Outcomes



Bapat et al.; *JACC Cardiovascular Interventions Vol 14, N. 18, 2021 September 27, 2021: 1978 -1991.*

Summary of reported TAVR Explant Studies

TABLE 4 Summary of Reported TAVR Explant Studies

First Author (Ref. #)	Study Period	N	Top Indications for Explant (%)	Outcomes (%)
Hirji et al[37]	1/2012-12/2017	227T	THV failure (79.3) Endocarditis (20.7)	30-day: mortality: 13.2 30-day stroke: 5.7 1-year mortality: 22.9
Jawitz et al[38]	7/2011-3/2015	123	Other (21.1) PVL (15.5) SVD (11.4) Endocarditis (9.8)	30-day mortality: 17.1 30-day stroke: 3.3
Fukuhara et al[8]	1/2012-12/2019	34	AI/PVL (50) SVD (38) Need for other cardiac surgery (18) Endocarditis (12)	30-day mortality: 15 30-day stroke: 0
Brescia et al[10]	1/2012-12/2019	46	Procedure-related failure (34.8) PVL (28.3) SVD[a] (26.1) Need for other cardiac surgery (26.1) Endocarditis (13.0)	30-day mortality: 20 30-day stroke: 4
Bapat et al[9]	11/2009-9/2020	269	Endocarditis (43.1) SVD (15.2) PVL (10.7) Other (9.7) PPM (6.3)	30-day mortality: 13.1 30-day stroke: 8.6 1-year mortality: 28.5 1-year stroke: 18.7

[a]Includes prosthetic stenosis and insufficiency.

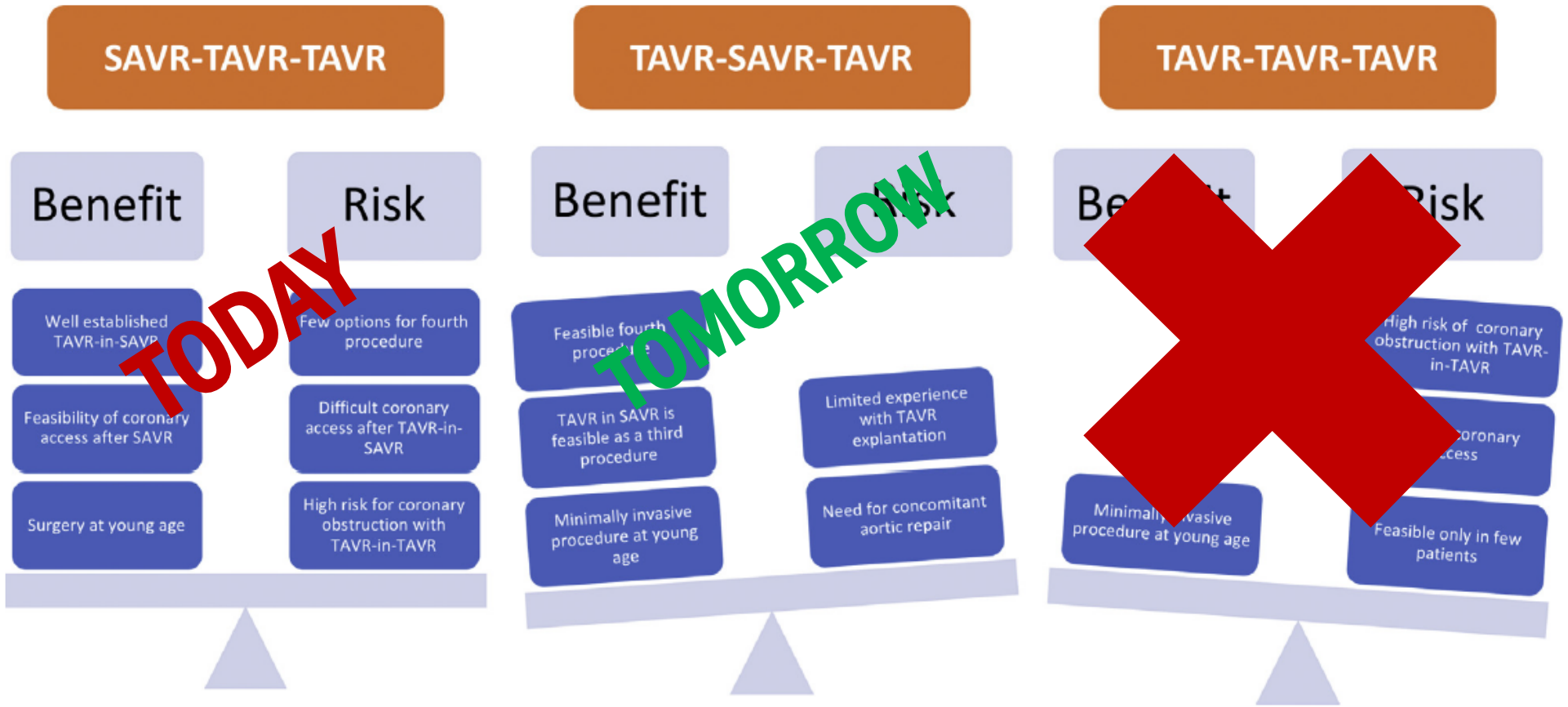
AI/PVL = aortic insufficiency/paravalvular leak; PPM = prosthesis-patient mismatch; SVD = structural valve degeneration; other abbreviations as in Table 1.

Tarantini et al:; *JACC Cardiovascular Interventions Vol.15,N. 18, September 26, 2022:1777-1793*

Which is the ideal planning for young patient with severe AS and at low surgical risk?

Which is the ideal planning for young patient with severe AS and at low surgical risk?

CENTRAL ILLUSTRATION Risks and Benefits of 3 Potential Strategies in the Lifetime Management of Severe Aortic Stenosis in Young Patients



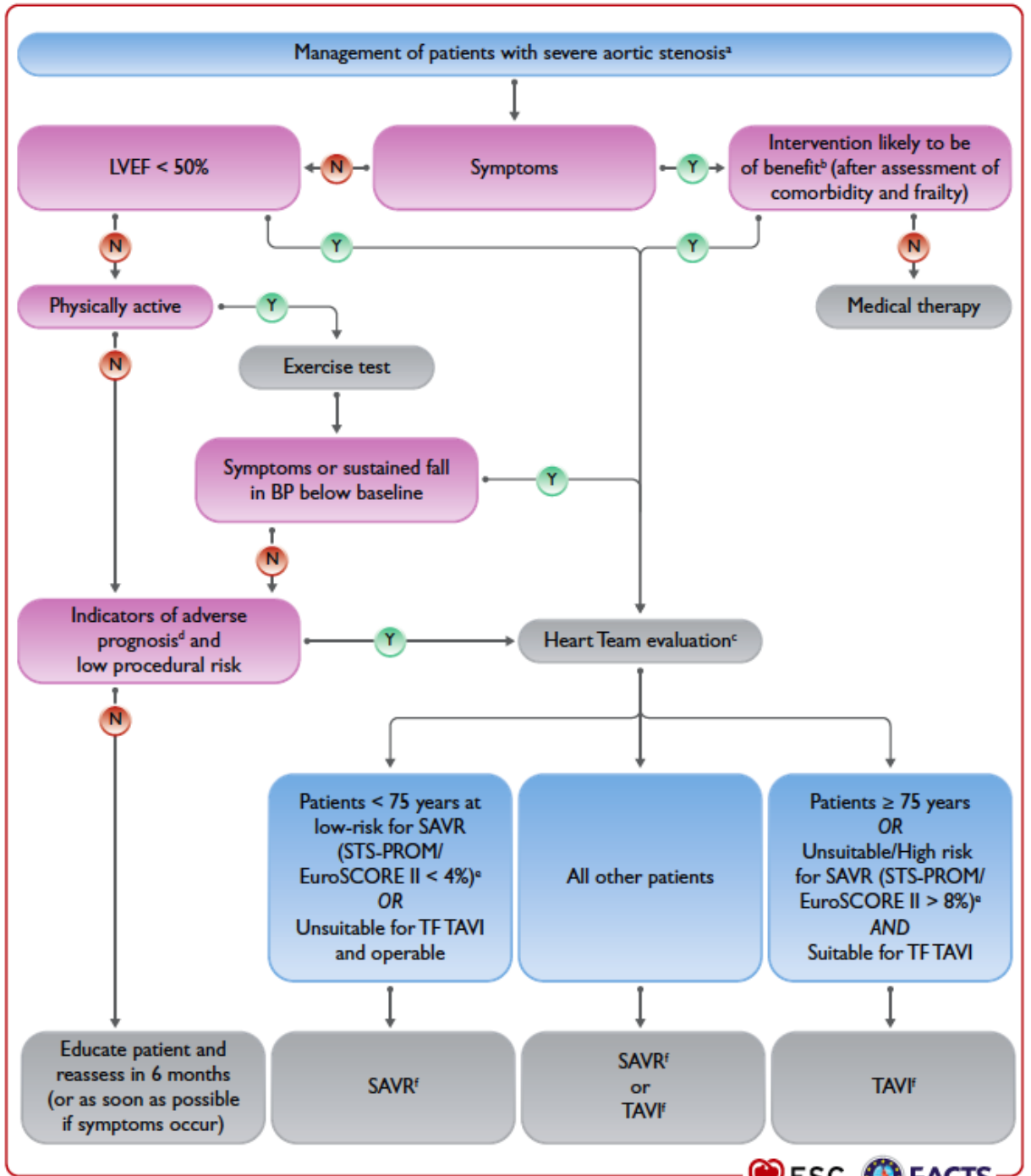
Yerasi, C. et al. J Am Coll Cardiol Intv. 2021;14(11):1169-80.

SAVR = surgical aortic valve replacement; TAVR = transcatheter aortic valve replacement.

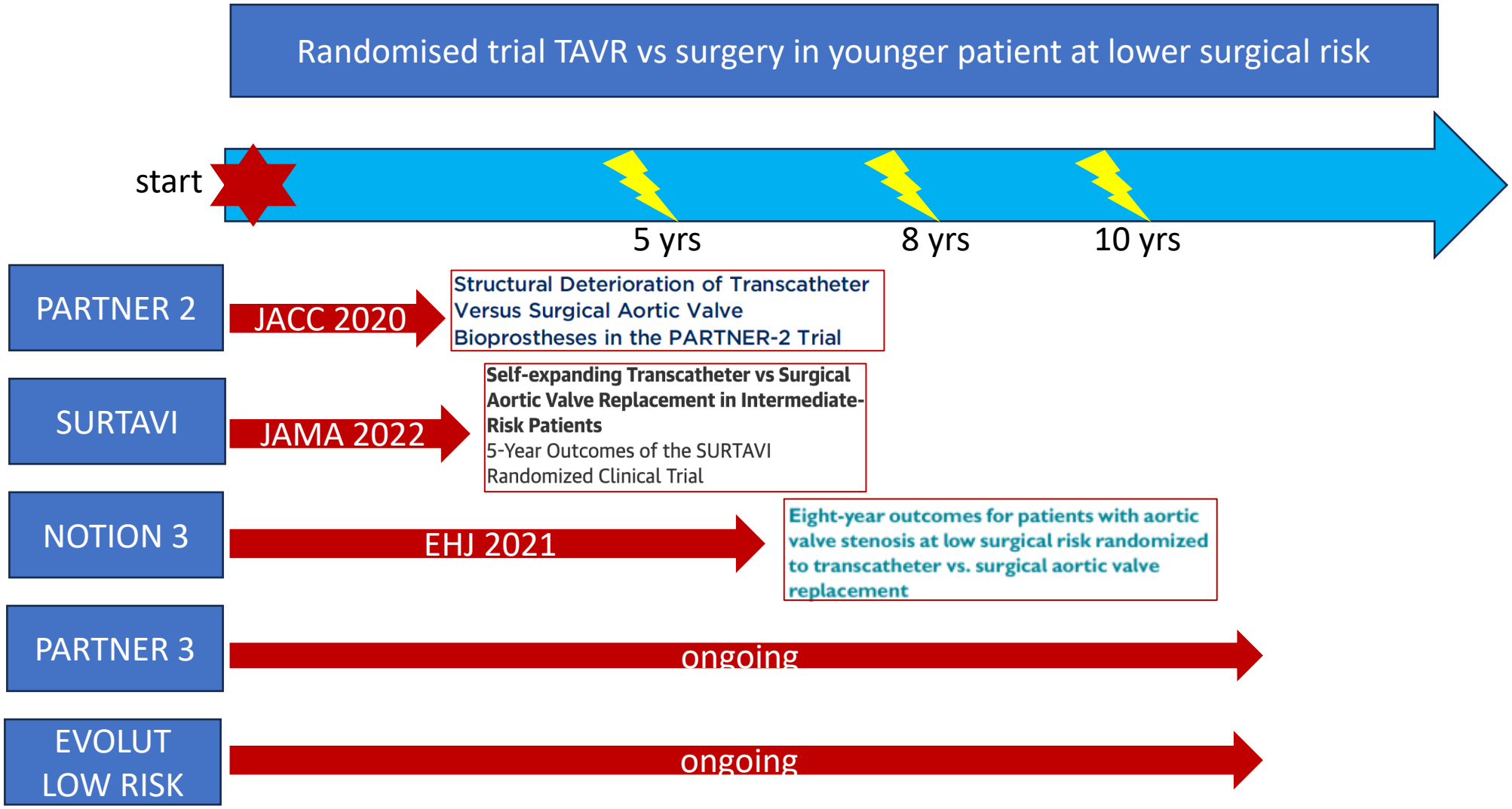
Take-home messages

- ✓ Definition of structural bioprosthetic valve deterioration requires confirmation by imaging and evaluation of hemodynamic deterioration;
- ✓ In patients with structural valve deterioration and PPM **redo TAVR** could be feasible;
- ✓ Key points for redoTAVR are evaluation of transcatheter heart valve and root anatomy, coronary obstruction risk assessment, transcatheter heart valve sizing and positioning of 2 valve;
- ✓ TAVR explant is technically more demanding than first-time or redo SAVR, with higher-than-expected mortality and stroke.
- ✓ **Sequencing** is an emerging concept which must be taken into account, especially in younger patients

2021 ESC/EACTS Guidelines for the management of valvular heart disease



Modificata


Randomised trial TAVR vs surgery in younger patient at lower surgical risk
start
5 yrs
8 yrs
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EVOLUT LOW RISK
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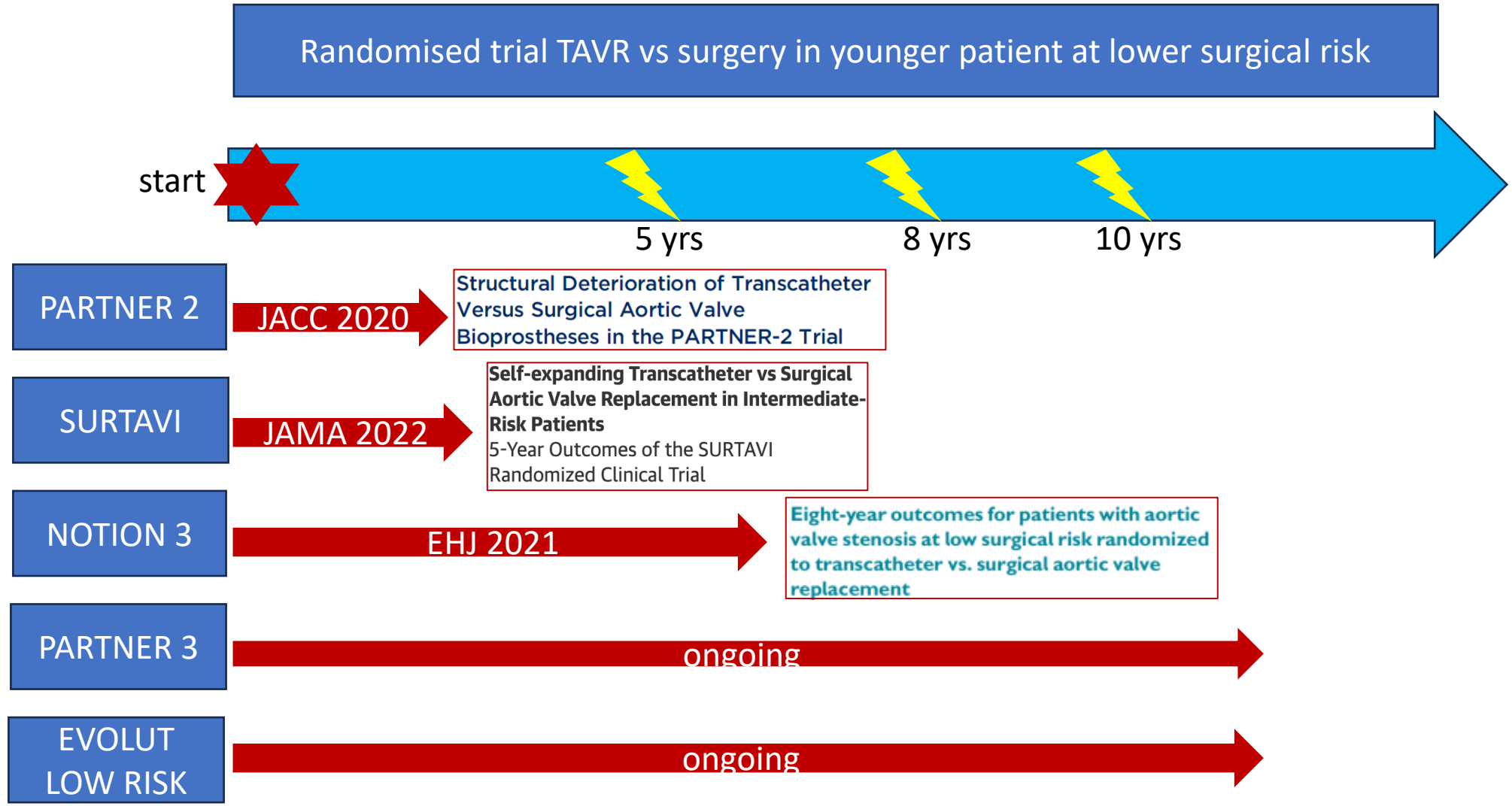
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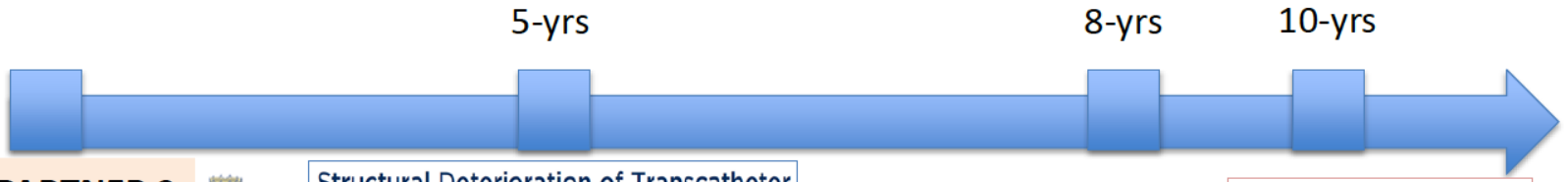
5-Year Outcomes of the SURTAVI Randomized Clinical Trial
NOTION 3
EHJ 2021
Eight-year outcomes for patients with aortic valve stenosis at low surgical risk randomized to transcatheter vs. surgical aortic valve replacement
PARTNER 3
ongoing
EVOLUT LOW RISK
ongoing

Da rifare per impaginazione

Data from randomised trials TAVI vs. Surgery



PARTNER 2

Structural Deterioration of Transcatheter Versus Surgical Aortic Valve Bioprostheses in the PARTNER-2 Trial

JACC 2020

Expected 2025-6

SURTAVI

JAMA Cardiology | Original Investigation

Self-expanding Transcatheter vs Surgical Aortic Valve Replacement in Intermediate-Risk Patients

5-Year Outcomes of the SURTAVI Randomized Clinical Trial

JAMA 2022

Expected 2026-7

NOTION 3

Eight-year outcomes for patients with aortic valve stenosis at low surgical risk randomized to transcatheter vs. surgical aortic valve replacement

Troels Højsgaard Jørgensen[1*†], Hans Gustav Hørsted Thyregod[2†], Nikolaj Ihlemann[3], Henrik Nissen[3], Petur Petursson[4], Bo Juel Kjeldsen[5], Daniel Andreas Steinbrüchel[6], Peter Skov Olsen[7], and Lars Søndergaard[1]

EHJ 2021

PARTNER 3

Expected 2023

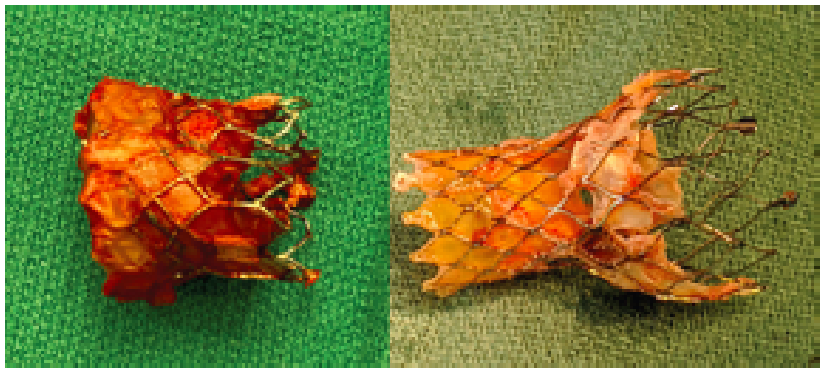
EVOLUT Low Risk

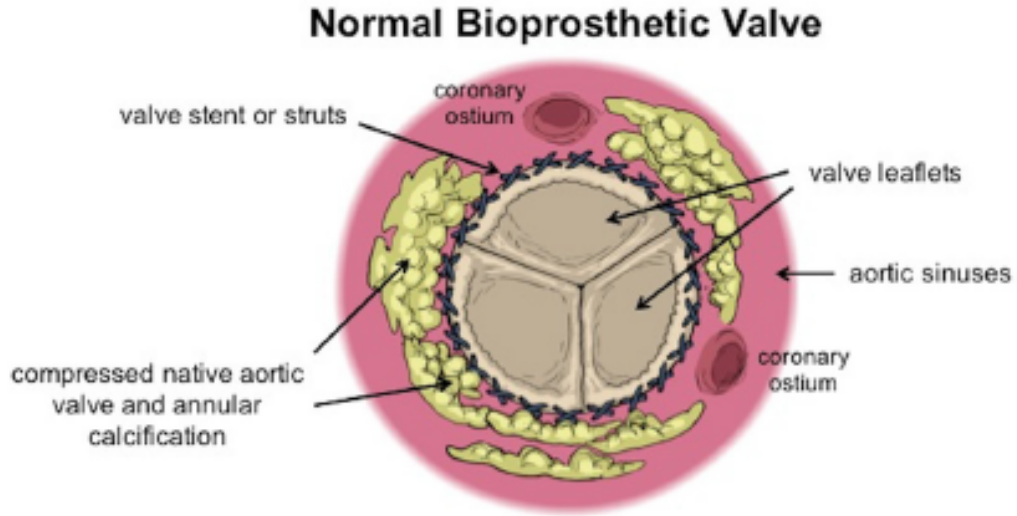
Expected 2024

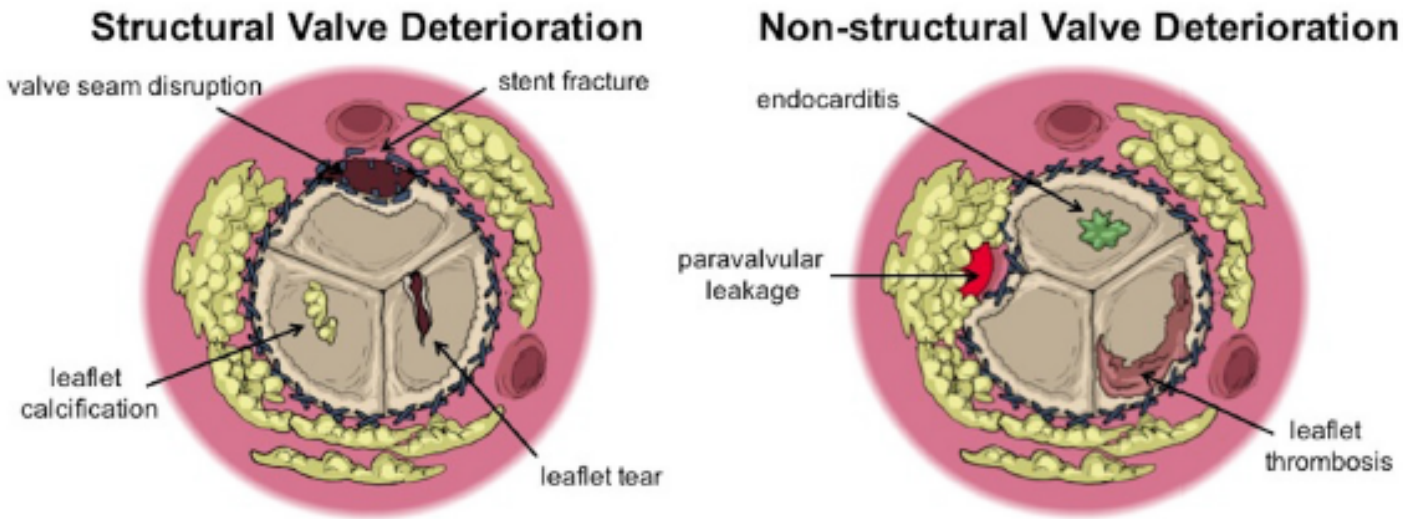
Younger patients with low surgical risk and Higher life expentancy

Importance of the valve durability-life expectancy ratio in selection of a prosthetic aortic valve

Rodrigo Bagur,[1,2,3] Philippe Pibarot,[4] Catherine M Otto[5]







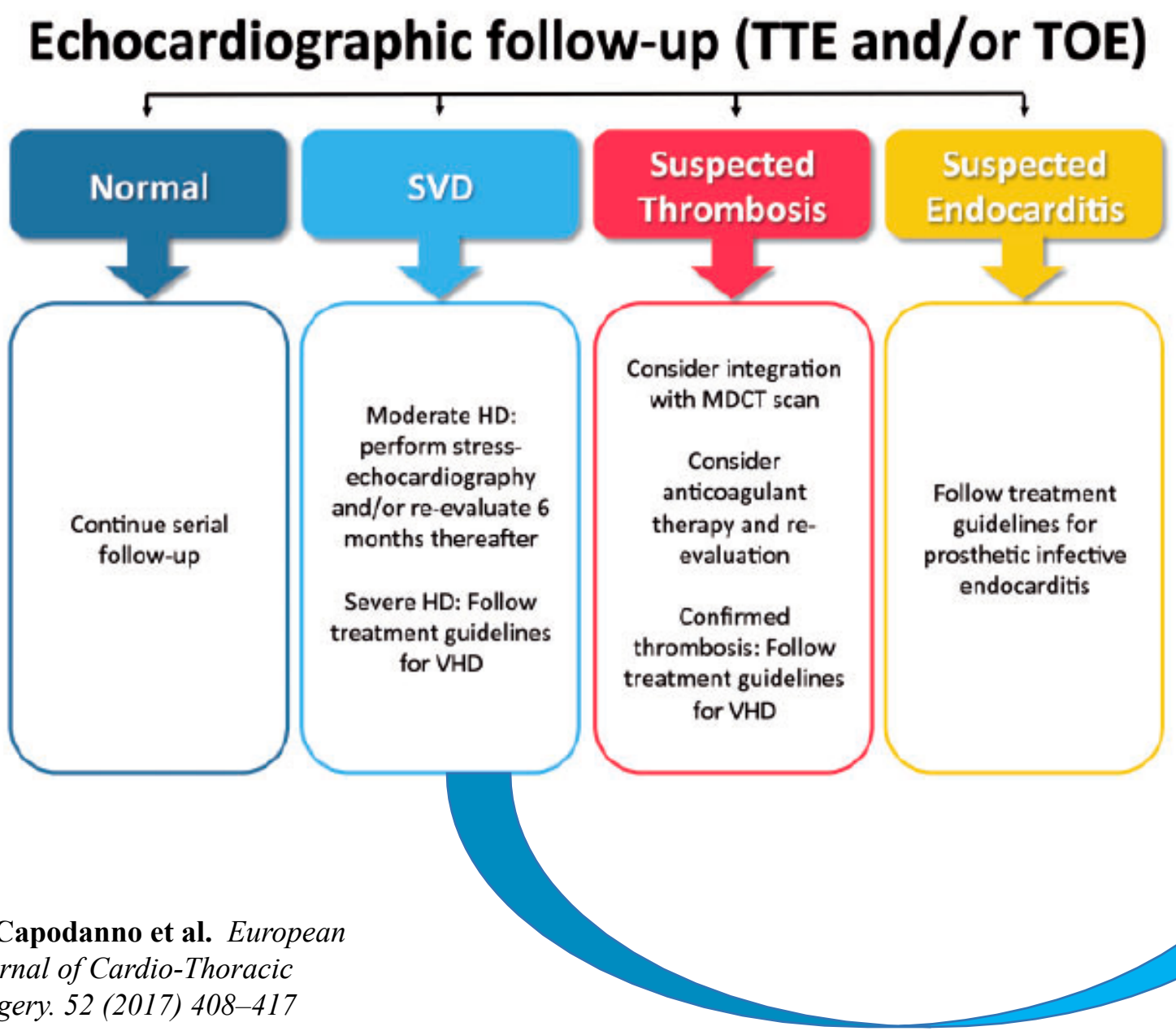


Table 3: Structural valve deterioration

Moderate haemodynamic SVD (any of the following)
Mean transprosthetic gradient ≥20 mmHg and <40 mmHg
Mean transprosthetic gradient ≥10 and <20 mmHg change from baseline
Moderate intra-prosthetic aortic regurgitation, new or worsening (>1+/4+) from baseline
Severe haemodynamic SVD (any of the following)
Mean transprosthetic gradient ≥40 mmHg
Mean transprosthetic gradient ≥20 mmHg change from baseline
Severe intra-prosthetic aortic regurgitation, new or worsening (>2+/4+) from baseline
Morphological SVD (any of the following)
Leaflet integrity abnormality (i.e. torn or flail causing intra-frame regurgitation)
Leaflet structure abnormality (i.e. pathological thickening and/or calcification causing valvular stenosis or central regurgitation)
Leaflet function abnormality (i.e. impaired mobility resulting in stenosis and/or central regurgitation)
Strut/frame abnormality (i.e. fracture)
Haemodynamic and morphological SVD

SVD: structural valve deterioration.

D. Capodanno et al. *European Journal of Cardio-Thoracic Surgery. 52 (2017) 408–417*

…and the future ?

Optimizing the first valve to avoid TAVR complications: *PVL, Conduction abnl*

Holographic Virtual Reality Guidance

Real-time assessment of patient specific anatomy

Implanter control of catheter

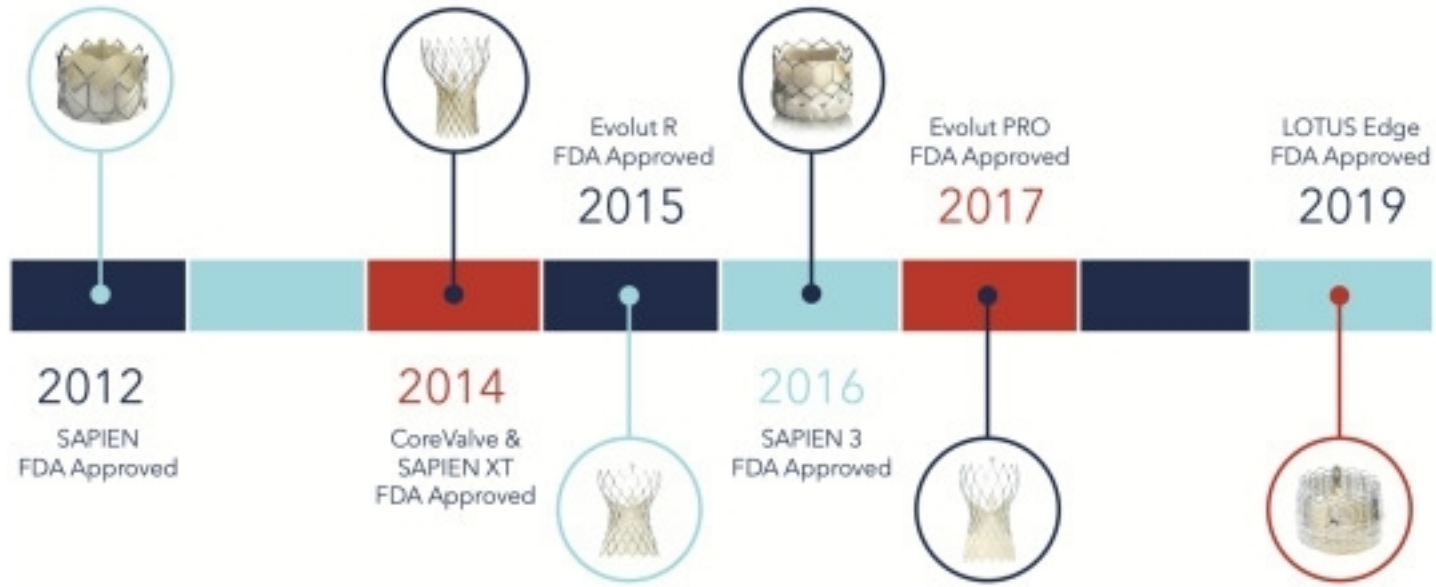
Less reliance on imaging / echo team

Ideal for 4D Intra-Cardiac Echo (ICE)

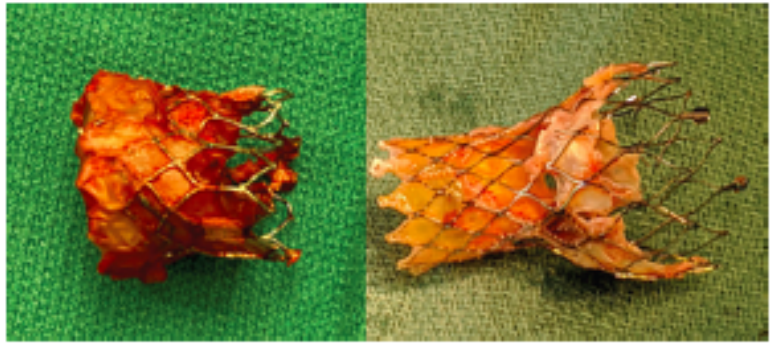
Can be used for procedural pre-planning

Dutcher J, Sander P. J Am Coll Cardiol. 2022 Mar; 79: 865.

U.S. TAVR Landscape



Durability of transcatheter aortic valve implantation: A translational review



Charles Fauvel et al.; *Archives of Cardiovascular Disease (2020)* ***113***, *209—221*

Pathophysiology of bioprosthesis valve deterioration
"Similitudes with native valve deterioration and differencies"

Fibrocalcification of the prosthesis tissue
- Traditional cardiovascular risk factors
- Phosphocalcic metabolism dysregulation
- Increased mechanical stresses (hypertension, mismatch, small sizing)
- Glutaraldehyde-based fixation : passive calcification with circulating phospholipids and calcium ions → collagen fixation : increase of rigidity

Lipid inflammatory-mediated process
- Macrophage infiltration, monocytes, T-cells
- Lp(a), oxidized phospholipids, PCSK9
- Osteoblastic differentiation

Valve thrombosis
- Increase local inflammation and fibrocalcifying process
- Lp(a) : pro-thrombosis property

5-years durability **
- Mack, MJ 0%
- Barbanti, M 1.4%
- Toggweiler, S 3.4%
- Didier, R 2.5%

Beyond 5-years durability **
- Eltchaninoff, H 3.2% at 8y
- Durand, E 4.2% at 7y
- Deutsch, MA 14.9% at 7y
- Holy, EM 0% at 8y
- Sondergaard, L 4.8% at 6y

Perspectives
Durability beyond 10-15 years and in low-risk patients ?
Decellularisation and/or anticalcification pre-treatment to reduce bioprosthesis failure ?
TAVI extension to low-risk patients in guidelines ?

TAVI indicated by heart team

TTE at discharge, 30 days, then yearly : structural valve deterioration (SVD) ? *

Date of implantation — **5 years** — **> 10 years**

Bioprosthesis deterioration biomarkers

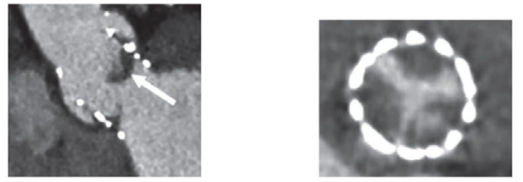
Circulating
- Lipids
- Renal insufficiency
- HOMA index
- Calcemia level
- Parathyroid hormone level
- CD14a level

Imaging
- Echocardiography
- MDCT
- PET-CT with ^{18}FDG
- Cardiac magnetic resonance

Identify a population at risk of early deterioration
- Dysmetabolic profile, insulin resistance
- Diabetes
- Renal insufficiency
- Age ? Female gender ?
- No anticoagulation at discharge, then long-term antcoagulation
- Valve sizing < 23-26 mm

SVD suspected by TTE during follow-up *

Bioprosthesis valve thrombosis (BVT) ?
Consider MDCT as soon as possible



BVT confirmed
Consider anticoagulation and repeated TTE

BVT excluded and SVD confirmed
Consider valve-in-valve TAVI

Key messages in TAVR explant

✓ **TAVR explant** is technically more demanding than first-time or redo SAVR, with higher-than-expected mortality and stroke, but with experience outcomes will improve;

✓ The need for **TAVR explant** should be discussed in young and low risk patients when redo TAVR is unlikely anatomically feasible, to better inform patient the pros and cons of index SAVR vs TAVR as 1° aortic valve intervention;

✓ Experience may guide decision-making in TAVR vs SAVR as first AV intervention as part of patient lifetime management strategy.

Importance of the valve durability-life expectancy ratio in selection of a prosthetic aortic valve

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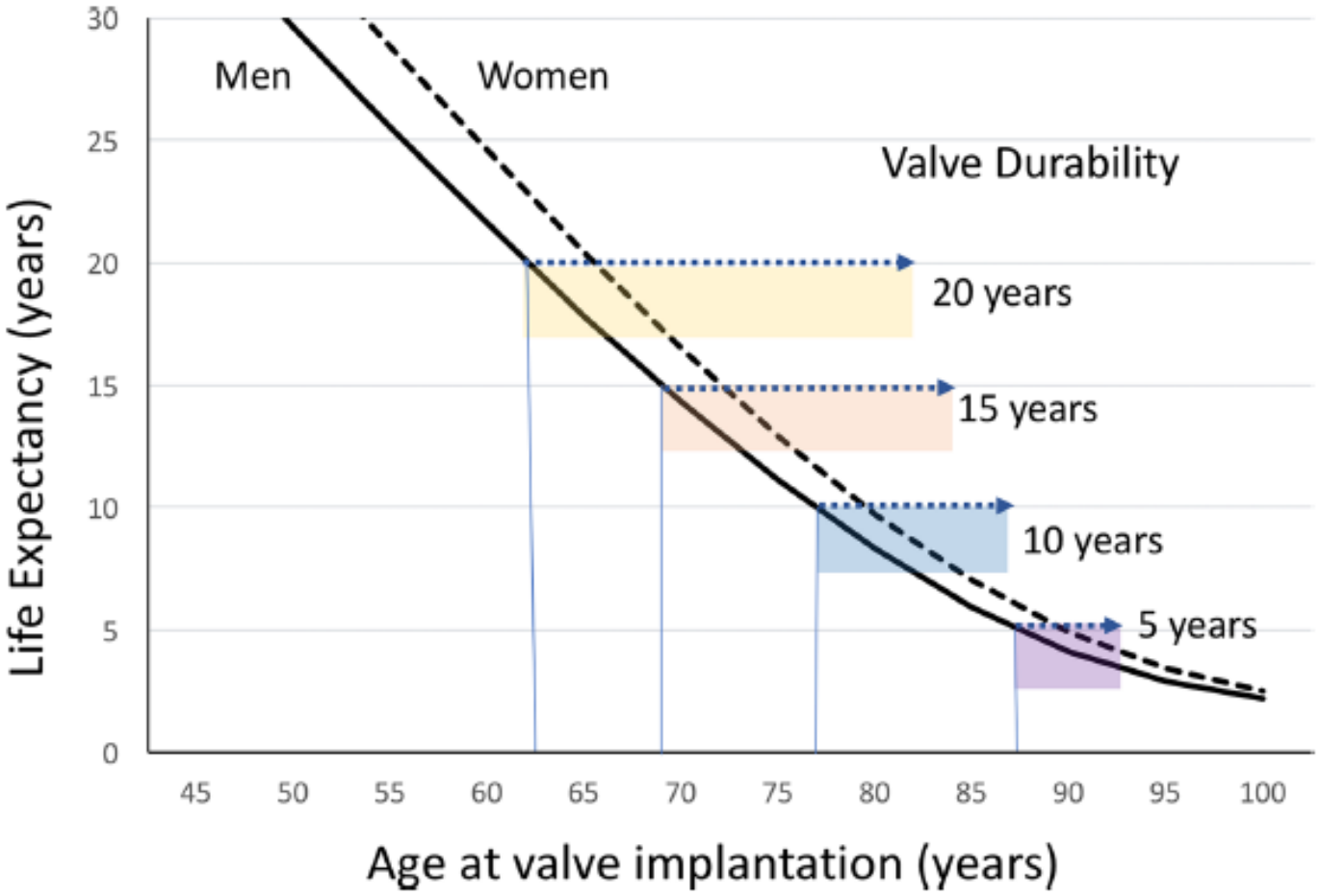


PURPOSE IN FIRST TAVR

In all patients need to consider the optimal first valve to minimize and avoid:

- ✓ Paravavular leak;
- ✓ New LBBB and pacemakers;
- ✓ HALT;
- ✓ Adverse hemodynamics and valve asymmetry that affect outcomes and durability;
- ✓ Optimize commissural alignment to preserve coronary access;

2) In young patients, need to also consider placement that «sets up» a future TAVR-in-TAVR procedure to avoid complications

Bagur R, et al. *Heart Month 2017 Vol 0 No 0*

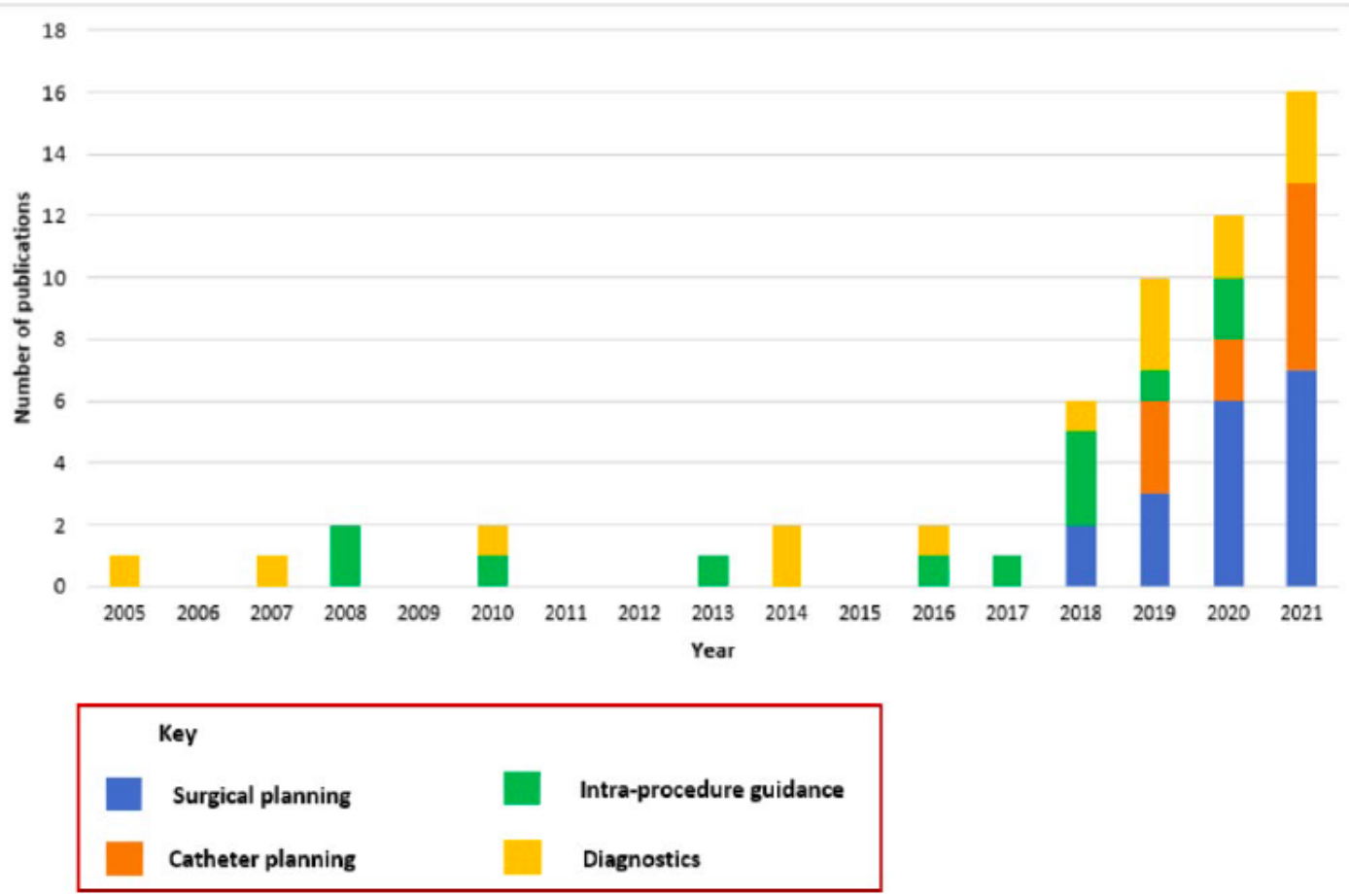
…and the future ?

Artificial Intelligence

- Real-time assessment of patient specific anatomy
- Implanter control of catheter
- Less reliance on imaging/echo team
- Ideal for 4D Intra-Cardiac Echo (ICE)
- Can be used for procedural pre-planning

Dutcher J and Sander P. *J Am Coll Cardiol. 2022 Mar, 79 (9_Supplement) 865*

Extended reality for procedural planning and guidance in structural heart disease – a review of the state-of-the-art



Natasha Stephenson et al.; *The International Journal of Cardiovascular Imaging (2023) 39:1405–1419*