TAVR-Update

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Disclosure

- Chiesi Pharma- Consultant

Objectives

- Review where TAVR is now
- Current Challenges
- TAVR Updates

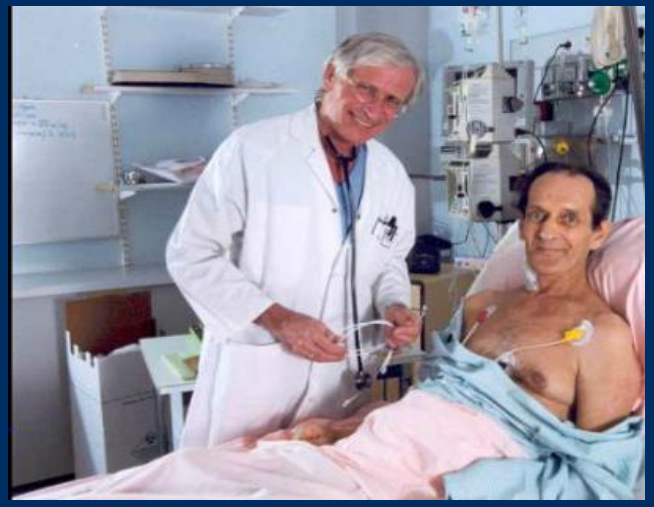
Background

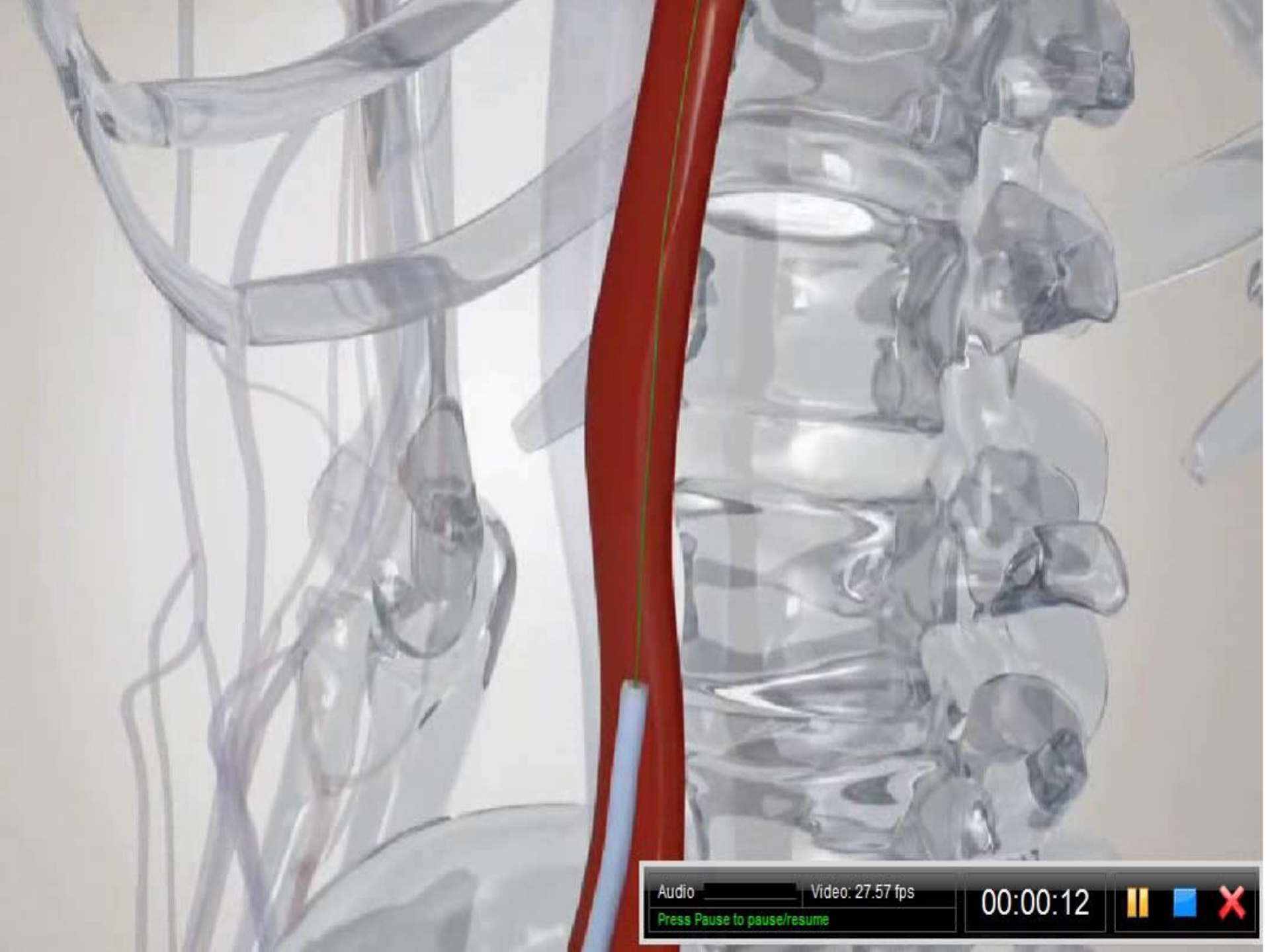
- Aortic valve stenosis
  - 15,000 deaths per year in North America
  - 85,000 valve procedures
  - AVR is indicated for severe AS and either symptoms or LV dysfunction
  - Over 500 TAVR programs open

2017

- 40th Anniversary of PCI
  - September 1977

- 15th Anniversary of TAVR
  - April 2002

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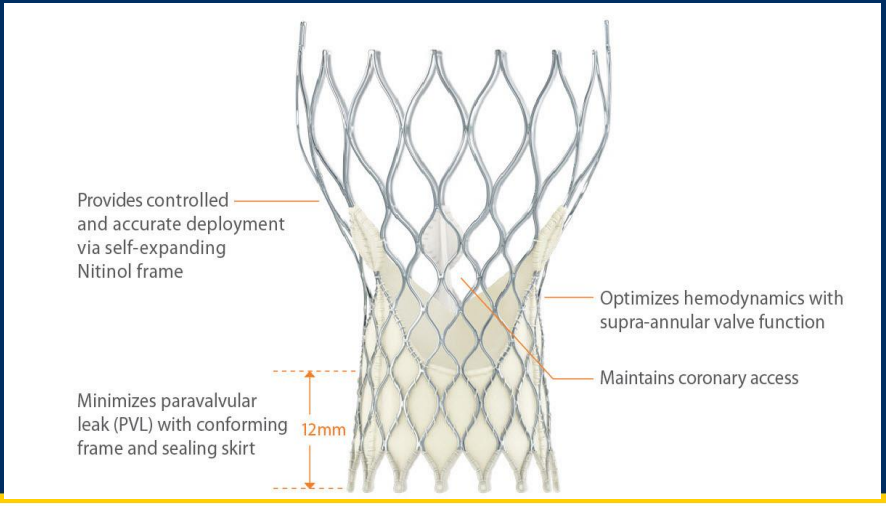
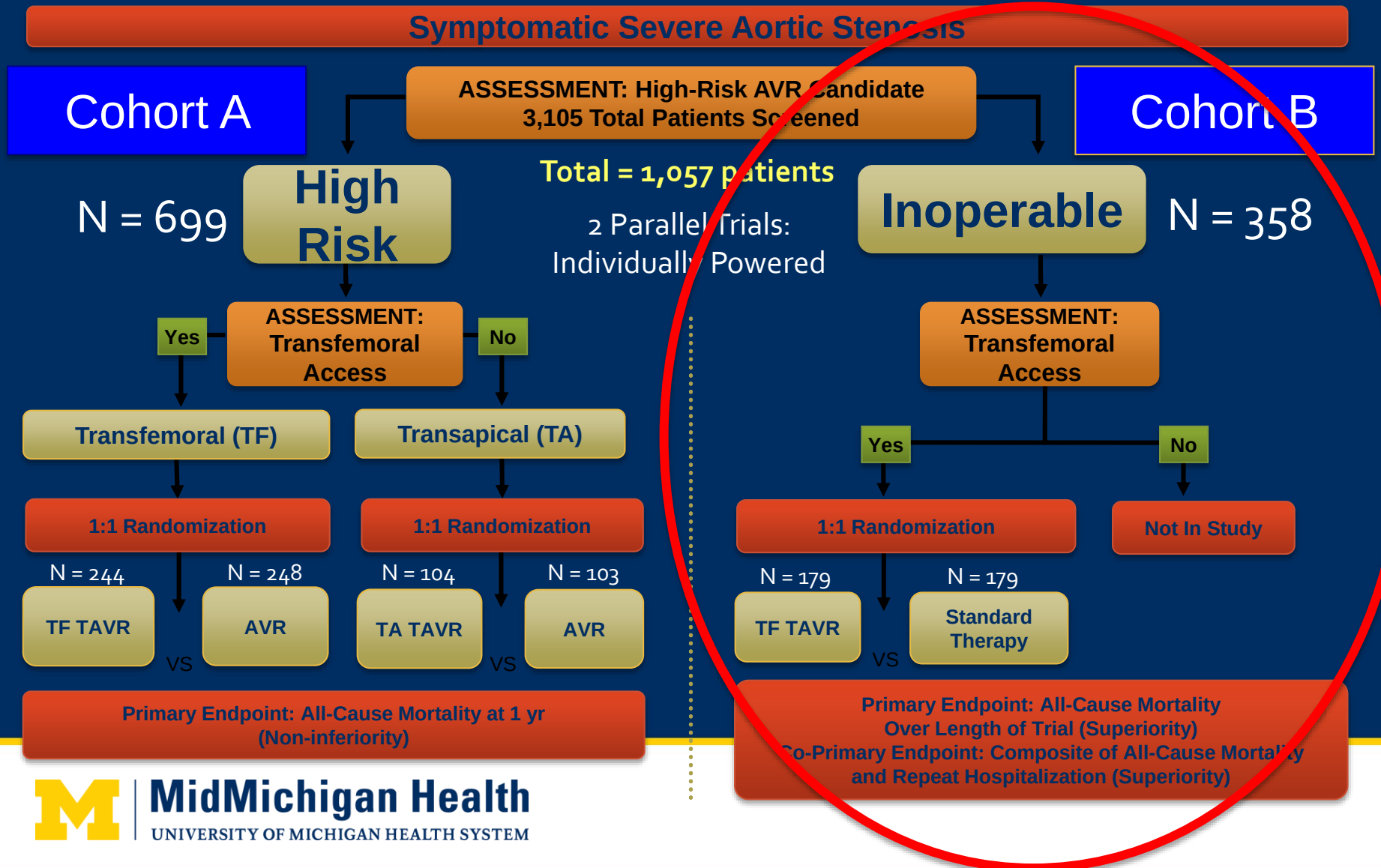
Two TAVR Options

- Edwards Sapien Valve
- Cobalt Chromium frame-balloon expandable (bovine)
- More Aortic Regurg, less AV block/PPM
- Better for severe bulky calcification.

- Medtronic CoreValve
- Nitinol Frame-self expanding
- Less Aortic Regurg, More heart block/PPM



PARTNER Study Design



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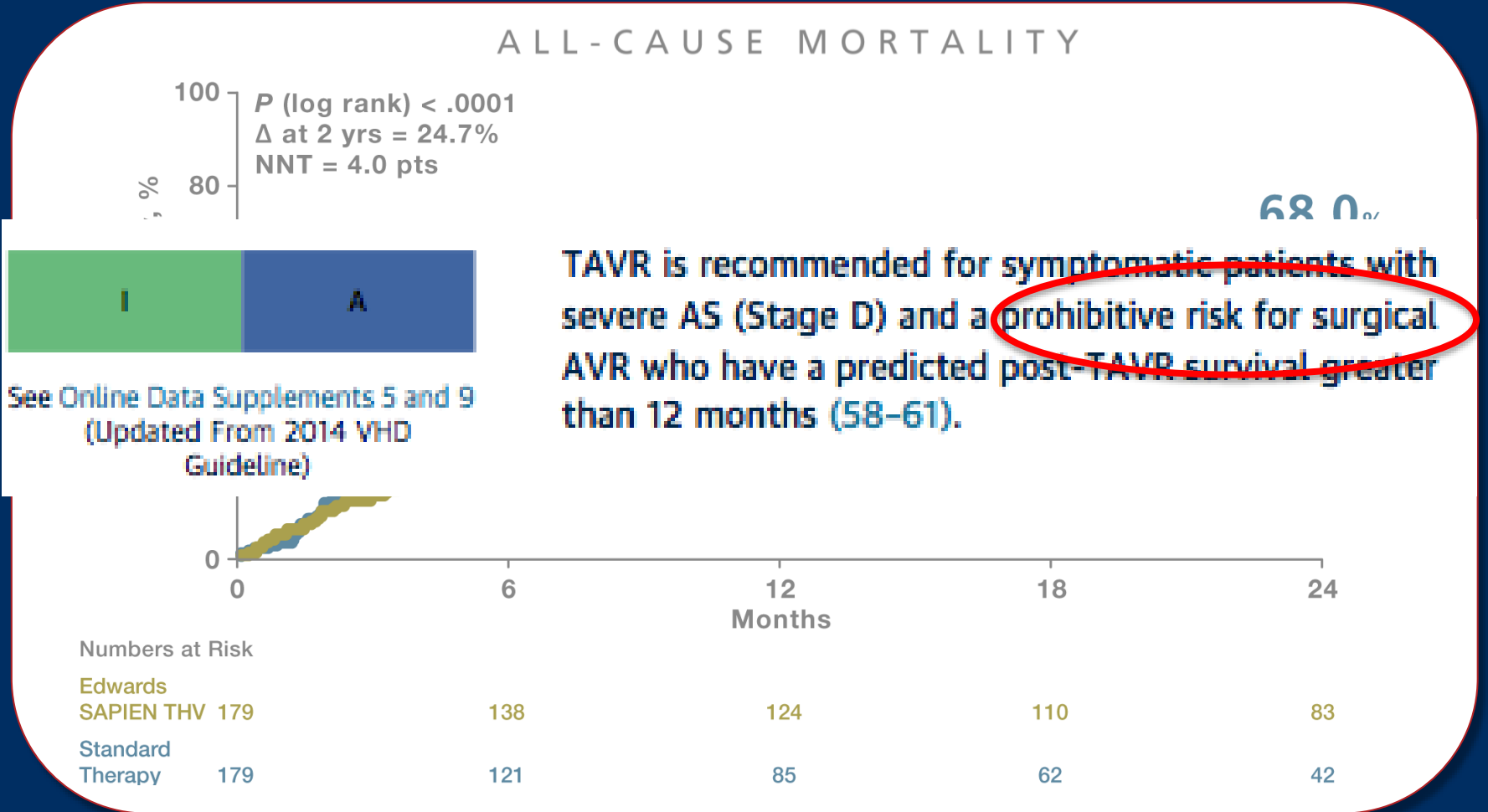
Cohort B Survival



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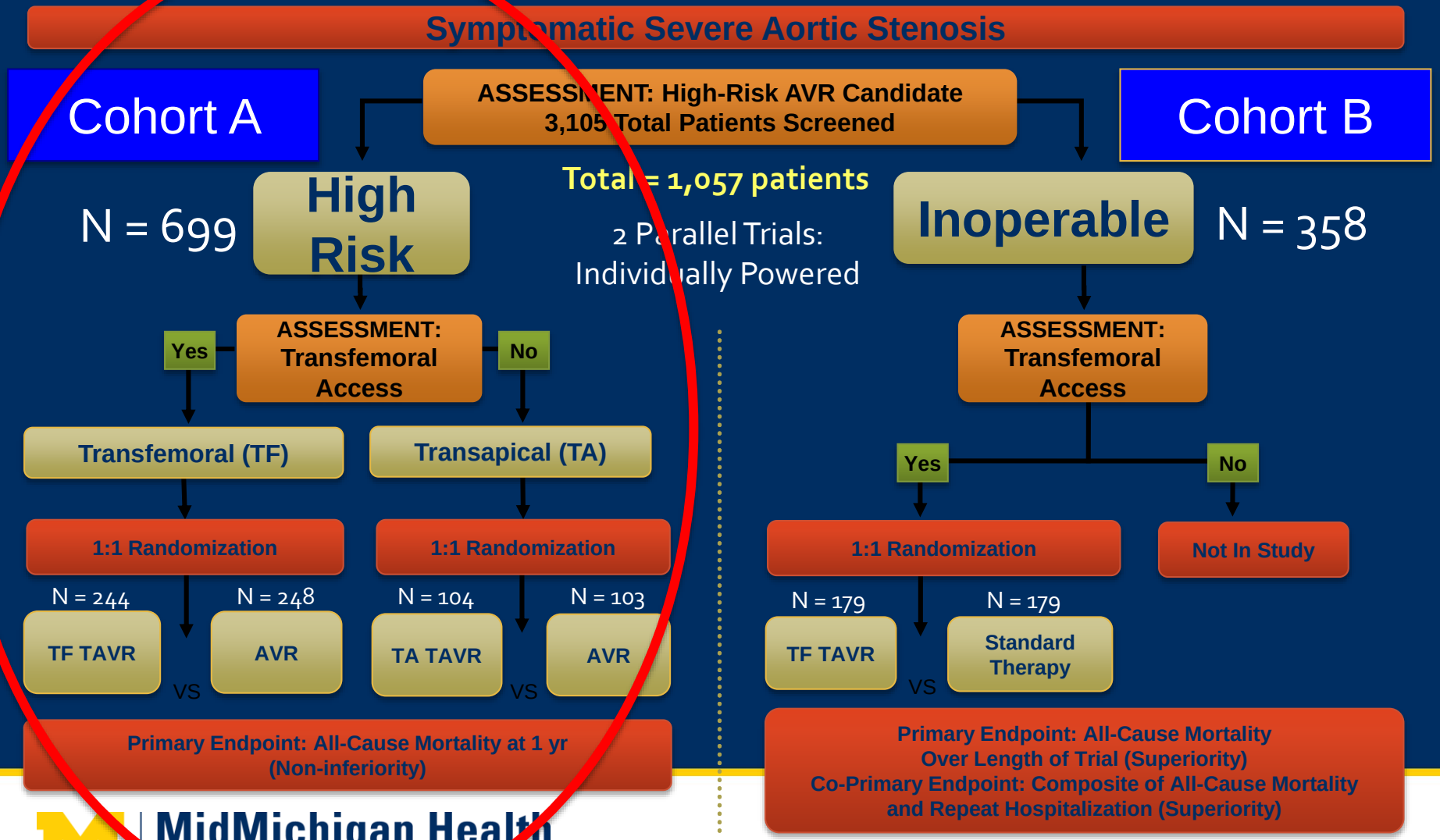
PARTNER Study Design



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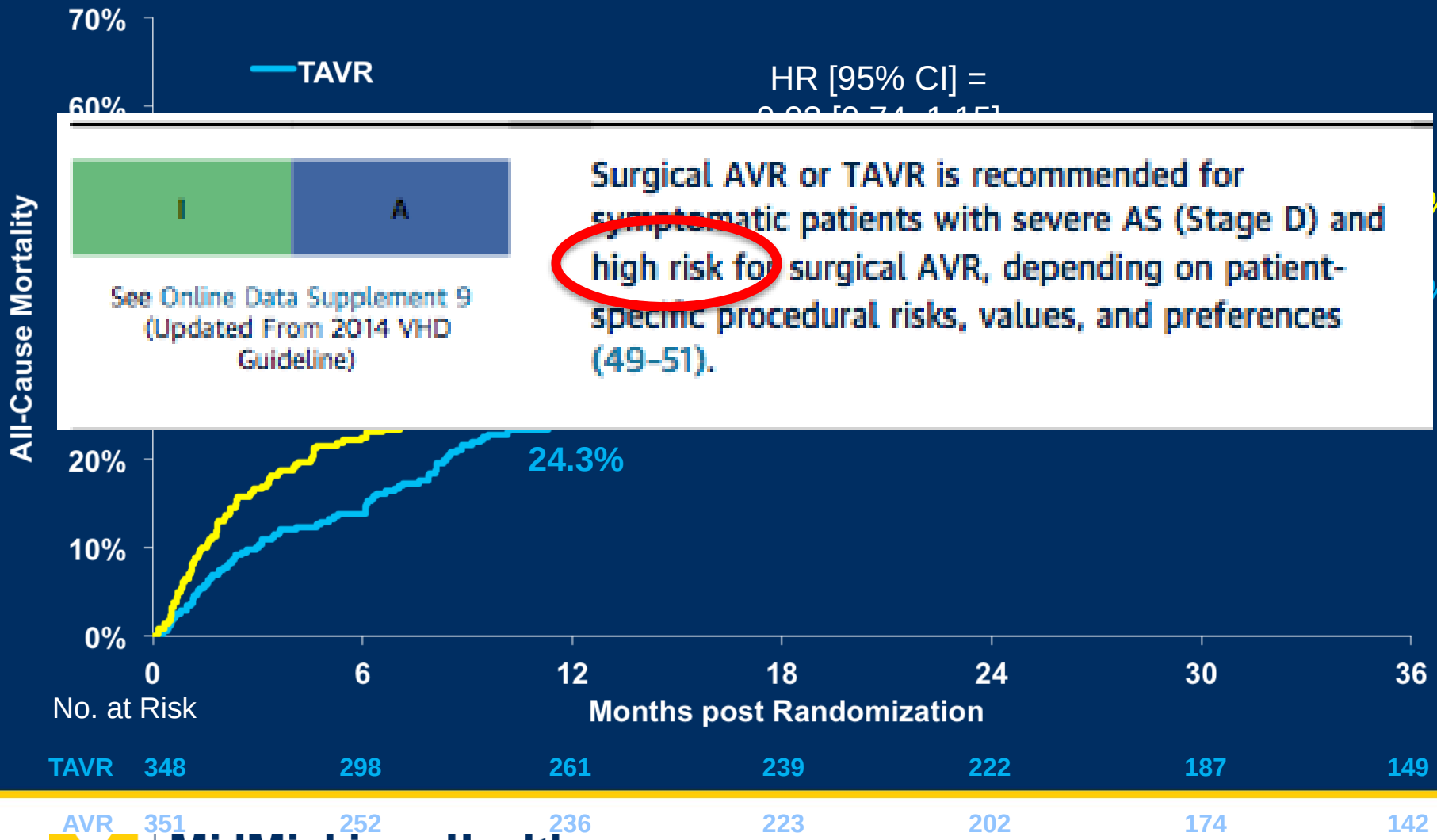
Cohort A: All-Cause Mortality



I | A

See Online Data Supplement 9 (Updated From 2014 VHD Guideline)

Surgical AVR or TAVR is recommended for symptomatic patients with severe AS (Stage D) and high risk for surgical AVR, depending on patient-specific procedural risks, values, and preferences (49–51).

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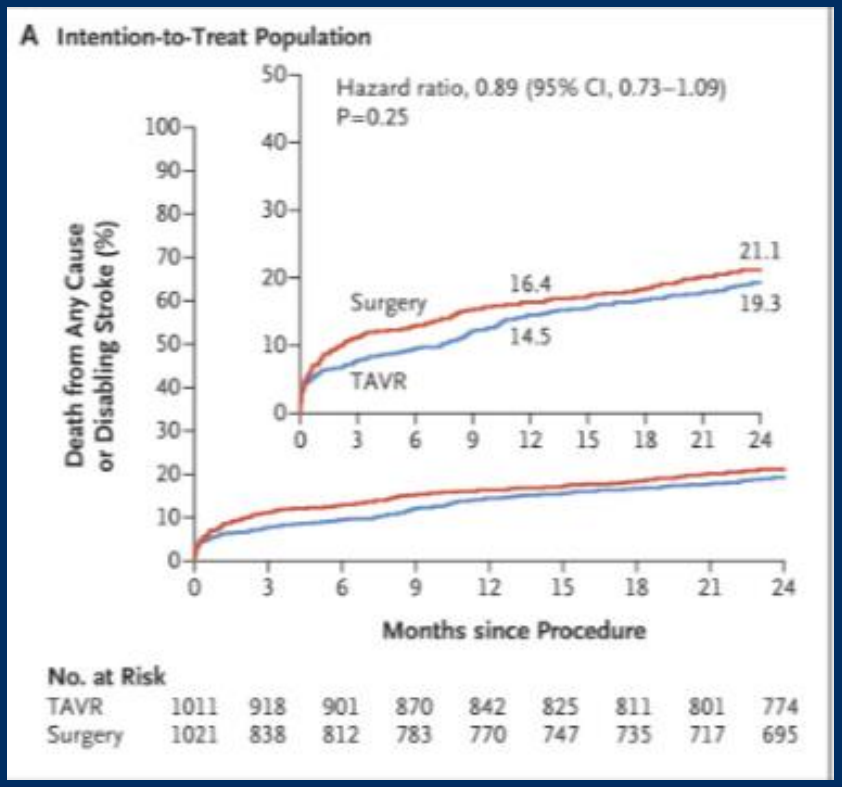
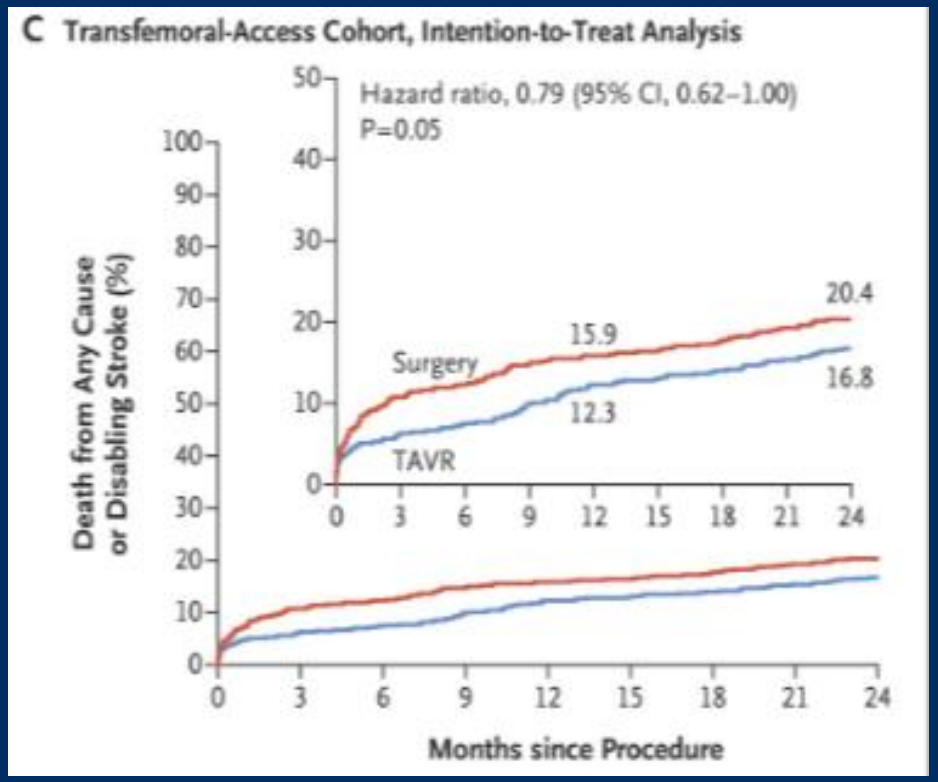
ORIGINAL ARTICLE

Transcatheter or Surgical Aortic-Valve Replacement in Intermediate-Risk Patients

Martin B. Leon, M.D., Craig R. Smith, M.D., Michael J. Mack, M.D., Raj R. Makkar, M.D., Lars G. Svensson, M.D., Ph.D., Susheel K. Kodali, M.D., Vinod H. Thourani, M.D., E. Murat Tuzcu, M.D., D. Craig Miller, M.D., Howard C. Herrmann, M.D., Darshan Doshi, M.D., David J. Cohen, M.D., et al., for the PARTNER 2 Investigators*





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N Engl J Med 2016; 374:1609-1620

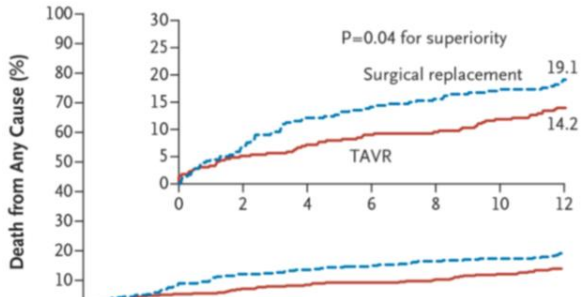
Core Valve

ORIGINAL ARTICLE

Transcatheter Aortic-Valve Replacement with a Self-Expanding Prosthesis

David H. Adams, M.D., Thomas C

3-Year Outcomes in High-Risk Patients Who Underwent Surgical or Transcatheter Aortic Valve Replacement



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ORIGINAL ARTICLE

Surgical or Transcatheter Aortic-Valve Replacement in Intermediate-Risk Patients

CONCLUSIONS

TAVR was a noninferior alternative to surgery in patients with severe aortic stenosis at intermediate surgical risk, with a different pattern of adverse events associated with each procedure. (Funded by Medtronic; SURTAVI ClinicalTrials.gov number, NCT01586910.)

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Table 2. Clinical End Points at 30 Days, 1 Year, and 2 Years.*

End Point	At 30 Days			At 1 Year			At 2 Years		
	TAVR (N=1011)	Surgery (N=1021)	P Value	TAVR (N=1011)	Surgery (N=1021)	P Value	TAVR (N=1011)	Surgery (N=1021)	P Value
	no. of patients (%)			*no. of patients (%)*			*no. of patients (%)*		
Death from any cause or disabling stroke	62 (6.1)	80 (8.0)	0.11	145 (14.5)	160 (16.4)	0.24	192 (19.3)	202 (21.1)	0.33
Death									
From any cause	39 (3.9)	41 (4.1)	0.78	123 (12.3)	124 (12.9)	0.69	166 (16.7)	170 (18.0)	0.45
From cardiac causes	33 (3.3)	32 (3.2)	0.92	70 (7.1)	77 (8.1)	0.40	97 (10.1)	104 (11.3)	0.38
Not from cardiac causes	6 (0.6)	9 (0.9)	0.41	53 (5.6)	47 (5.2)	0.71	69 (7.4)	65 (7.4)	0.98
Neurologic event									
Any event	64 (6.4)	65 (6.5)	0.94	99 (10.1)	93 (9.7)	0.76	121 (12.7)	103 (11.0)	0.25
Transient ischemic attack	9 (0.9)	4 (0.4)	0.17	23 (2.4)	16 (1.8)	0.38	34 (3.7)	20 (2.3)	0.09
Any stroke	55 (5.5)	61 (6.1)	0.57	78 (8.0)	79 (8.1)	0.88	91 (9.5)	85 (8.9)	0.67
Disabling stroke	32 (3.2)	43 (4.3)	0.20	49 (5.0)	56 (5.8)	0.46	59 (6.2)	61 (6.4)	0.83
Nondisabling stroke	23 (2.3)	18 (1.8)	0.43	30 (3.0)	24 (2.5)	0.44	33 (3.4)	27 (2.9)	0.51
Rehospitalization	64 (6.5)	62 (6.5)	0.99	142 (14.8)	135 (14.7)	0.92	183 (19.6)	156 (17.3)	0.22
Death from any cause or rehospitalization	99 (9.8)	101 (10.2)	0.78	234 (23.4)	225 (23.3)	0.97	303 (30.5)	281 (29.6)	0.67
Death from any cause, any stroke, or rehospitalization	140 (13.9)	153 (15.3)	0.37	274 (27.4)	276 (28.3)	0.64	344 (34.6)	326 (33.9)	0.75
Myocardial infarction	12 (1.2)	19 (1.9)	0.22	24 (2.5)	29 (3.0)	0.47	33 (3.6)	37 (4.1)	0.56
Major vascular complication	80 (7.9)	51 (5.0)	0.008	84 (8.4)	54 (5.3)	0.007	86 (8.6)	55 (5.5)	0.006
Life-threatening or disabling bleeding	105 (10.4)	442 (43.4)	<0.001	151 (15.2)	460 (45.5)	<0.001	169 (17.3)	471 (47.0)	<0.001
Acute kidney injury	13 (1.3)	31 (3.1)	0.006	32 (3.4)	48 (5.0)	0.07	36 (3.8)	57 (6.2)	0.02
New atrial fibrillation	91 (9.1)	265 (26.4)	<0.001	100 (10.1)	272 (27.2)	<0.001	110 (11.3)	273 (27.3)	<0.001
New permanent pacemaker	85 (8.5)	68 (6.9)	0.17	98 (9.9)	85 (8.9)	0.43	114 (11.8)	96 (10.3)	0.29
Endocarditis	0	0	—	7 (0.8)	6 (0.7)	0.84	11 (1.2)	6 (0.7)	0.22
Aortic-valve reintervention	4 (0.4)	0	0.05	11 (1.2)	4 (0.5)	0.10	13 (1.4)	5 (0.6)	0.09
Coronary obstruction	4 (0.4)	6 (0.6)	0.53	4 (0.4)	6 (0.6)	0.53	4 (0.4)	6 (0.6)	0.53

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N Engl J Med 2016; 374:1609-1620

Recurrent Theme:

TAVR

- More vascular complications
- More pacemakers
- More PVL
- Lower gradients and better EOA

SAVR

- More Bleeding
- More atrial fibrillation
- Acute kidney injury

Equipoise

Mortality, Stroke, MI, Aortic re-interventions?, durability (5 years)

Is TAVR now for everyone?

- Evidence base:
  - Inoperable patients
  - Extreme Risk patients
  - High Risk patients
  - Intermediate Risk patients
- On going Trials:
  - Low Risk Patient
- Uncertain Benefit
  - “Cohort C” Futility

TAVR

2017 AHA/ACC Focused Update of the 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 Clinical Practice Guidelines

Developed in Collaboration With the American Association for Thoracic Surgery, American Society of Echocardiography, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Anesthesiologists, and Society of Thoracic Surgeons

I A See Online Data Supplement 9 (Updated From 2014 VHD Guideline)	Surgical AVR or TAVR is recommended for symptomatic patients with severe AS (Stage D) and high risk for surgical AVR, depending on patient-specific procedural risks, values, and preferences (49–51).
I A See Online Data Supplements 5 and 9 (Updated From 2014 VHD Guideline)	TAVR is recommended for symptomatic patients with severe AS (Stage D) and a prohibitive risk for surgical AVR who have a predicted post-TAVR survival greater than 12 months (58–61).
IIa B-R See Online Data Supplements 5 and 9 (Updated From 2014 VHD Guideline)	TAVR is a reasonable alternative to surgical AVR for symptomatic patients with severe AS (Stage D) and an intermediate surgical risk, depending on patient-specific procedural risks, values, and preferences (62–65).

NEW: New RCT showed noninferiority of TAVR to surgical AVR in symptomatic patients with severe AS at intermediate surgical risk.

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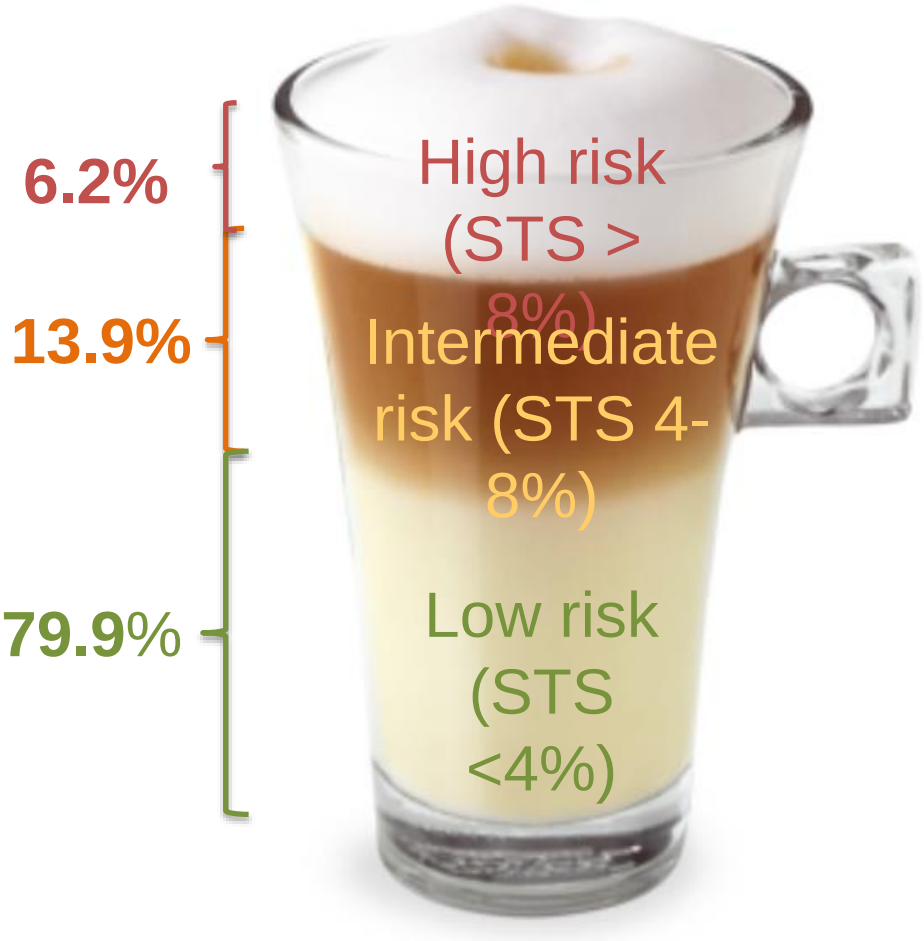
JACC.2017;70(2):252-89

STS database 2002-2010
(141,905 pts)



Courtesy of N. Piazza

What about Low Risk Patient?

- Notion Trial I and II
- Partner 3
- CoreValve Low Risk Trial
  - Sub-studies

Transcatheter Versus Surgical Aortic Valve Replacement in Patients With Severe Aortic Valve Stenosis

1-Year Results From the All-Comers NOTION Randomized Clinical Trial

Hans Gustav Hørsted Thyregod, MD,* Daniel Andreas Steinbrüchel, MD, DMSc,* Nikolaj Ihlemann, MD, PhD,† Henrik Nissen, MD, PhD,‡ Bo Juel Kjeldsen, MD, PhD,§ Petur Petursson, MD,‖ Yanping Chang, MS,¶ Olaf Walter Franzen, MD,† Thomas Engstrøm, MD, DMSc,† Peter Clemmensen, MD, DMSc,† Peter Bo Hansen, MD,# Lars Willy Andersen, MD, DMSc,# Peter Skov Olsen, MD, DMSc,* Lars Søndergaard, MD, DMSc†

ABSTRACT

BACKGROUND Transcatheter aortic valve replacement (TAVR) is an option in certain high-risk surgical patients with severe aortic valve stenosis. It is unknown whether TAVR can be safely introduced to lower-risk patients.

JACC 2015(65)20:2184-94

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
Logistic EuroSCORE II, %	1.9 ± 1.2	2.0 ± 1.3
Additive EuroSCORE, %	7.4 ± 1.4	7.5 ± 1.4
Diabetes mellitus	26/145 (17.9)	28/135 (20.7)
Creatinine level >2 mg/dl	2/145 (1.4)	1/135 (0.7)
History of hypertension	103/145 (71.0)	103/135 (76.3)
Peripheral vascular disease	6/145 (4.1)	9/135(6.7)
Prior cerebrovascular accident	24/145 (16.6)	22/135 (16.3)
Chronic lung disease	17/145 (11.7)	16/135 (11.9)
Cardiac risk factors		
Prior PCI	11/145 (7.6)	12/135 (8.9)
Pre-existing pacemaker	5/145 (3.4)	6/135 (4.4)
Prior MI	8/145 (5.5)	6/135 (4.4)
Prior AF/atrial flutter	40/144 (27.8)	34/133 (25.6)

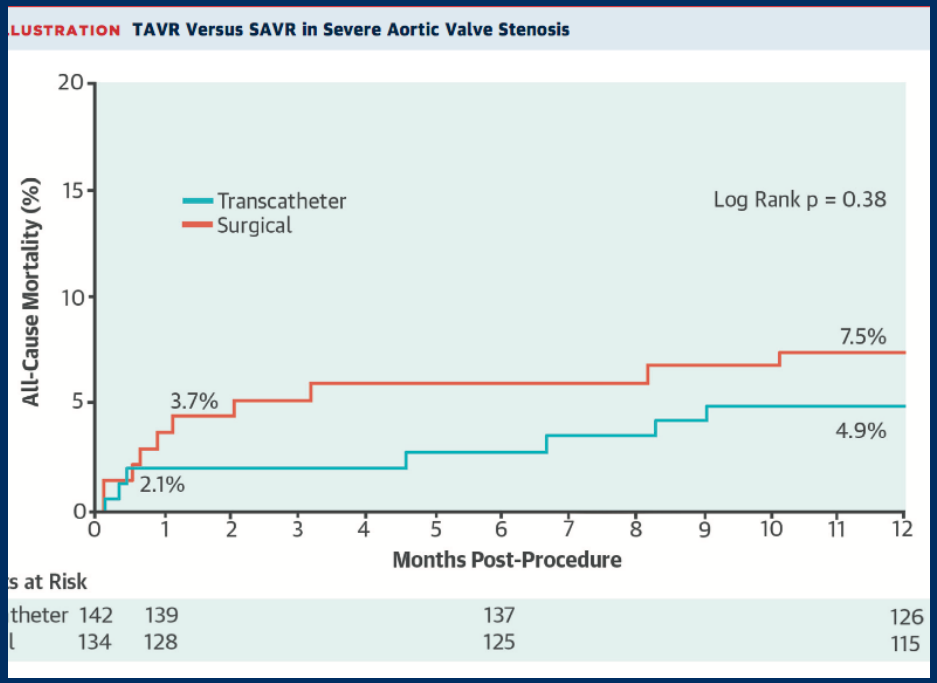
TABLE 2 Procedural Characteristics

TAVR	
Procedural success*	139/142 (97.9)
Total procedure time, min	90.3 ± 38.6
Local anesthesia	26/142 (18.3)
Use of inotropes	86/142 (60.6)
Implantation of >1 valve prosthesis	4/142 (2.8)
Conversion to surgery	3/142 (2.1)
Transfemoral access	137/142 (96.5)
Transsubclavian access	5/142 (3.5)
Valve size implanted	
23 mm	2/142 (1.4)
26 mm	57/142 (40.1)
29 mm	69/142 (48.6)
31 mm	14/142 (9.9)
SAVR	
Total procedure time, min	177.2 ± 39.8
Conversion to other procedure†	2/134 (1.5)
Use of inotropes	48/133 (36.1)
Valve size implanted	
19 mm	11/132 (8.3)
21 mm	42/132 (31.8)
23 mm	45/132 (34.1)
25 mm	32/132 (24.2)
27 mm	2/132 (1.5)

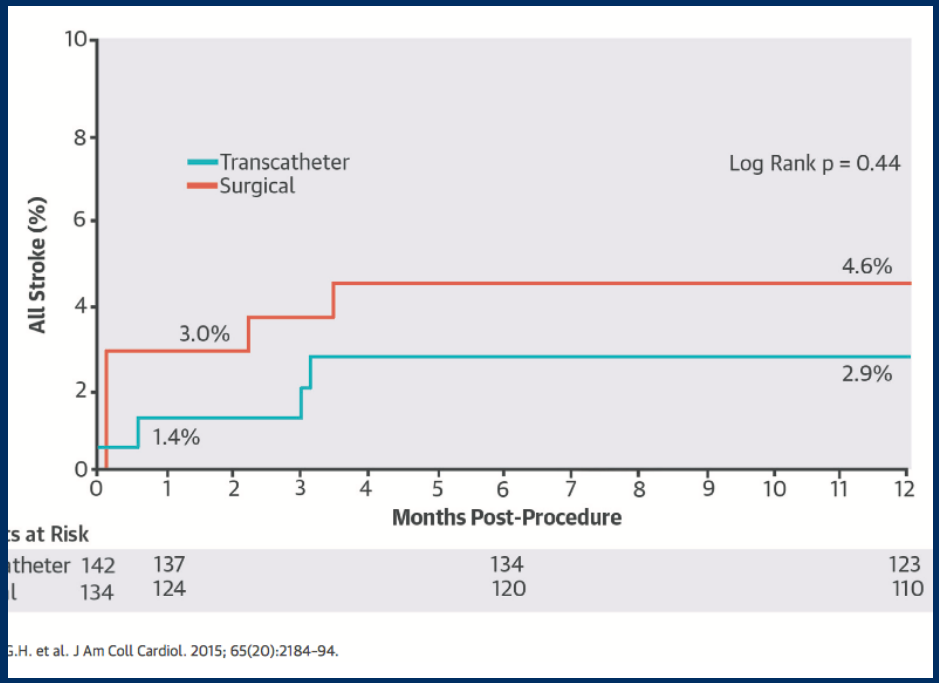
JACC 2015(65)20:2184-94

NOTION Trial (low Risk)

Mortality



Stroke



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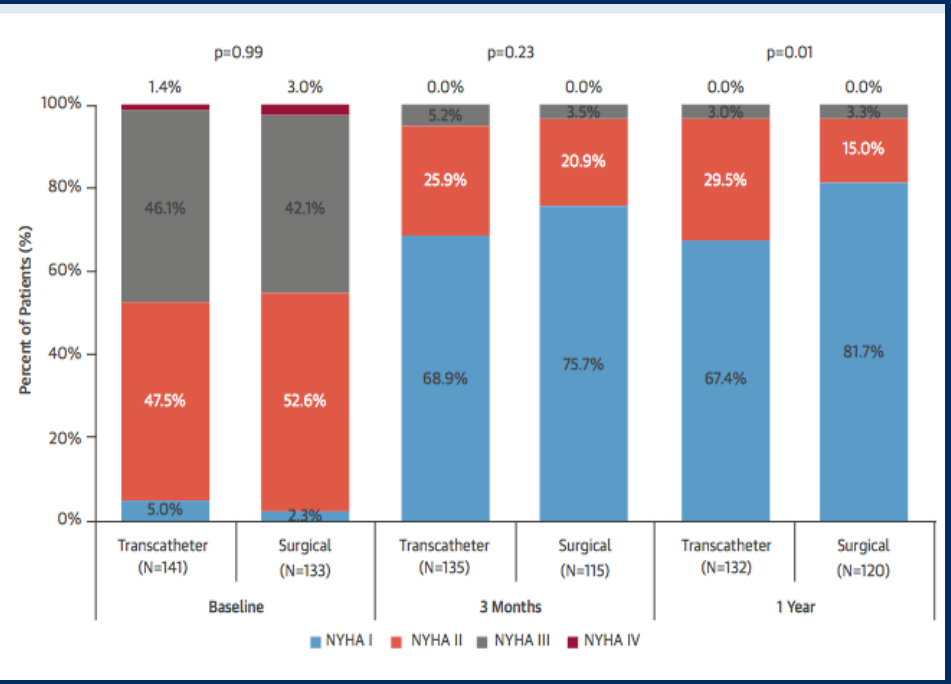
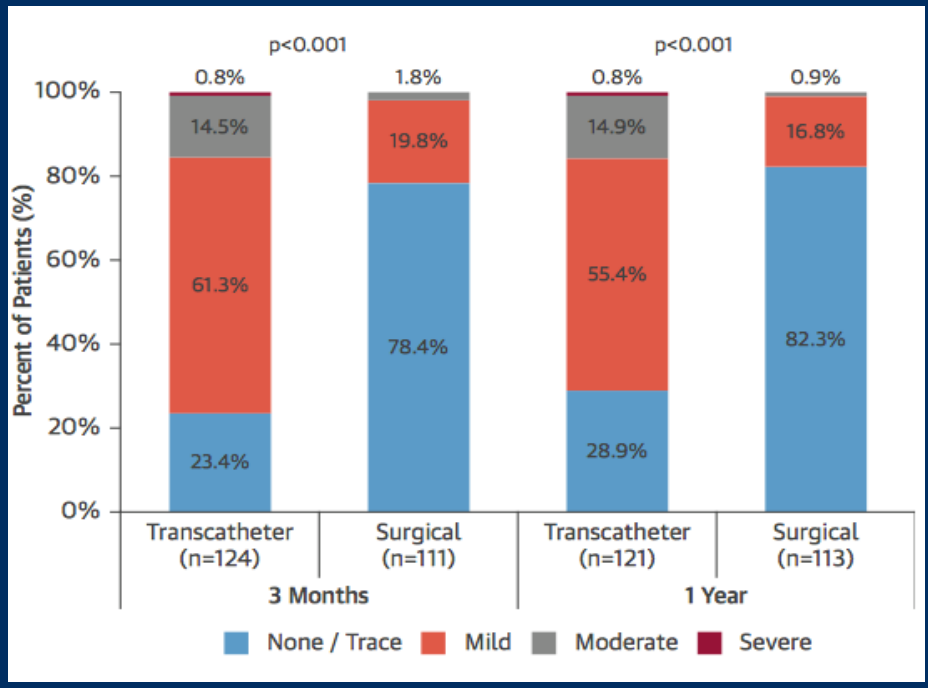
NOTION Trial

NYHA Classification



PVL



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JACC 2015(65)20:2184-94

Transcatheter Versus Surgical Aortic Valve Replacement in Patients With Severe Aortic Valve Stenosis

1-Year Results From the All-Comers NOTION Randomized Clinical Trial

METHODS Patients ≥70 years old with severe aortic valve stenosis and no significant coronary artery disease were randomized 1:1 to TAVR using a self-expanding bioprosthesis versus SAVR. The primary outcome was the composite rate of death from any cause, stroke, or myocardial infarction (MI) at 1 year.

CONCLUSIONS In the NOTION trial, no significant difference between TAVR and SAVR was found for the composite rate of death from any cause, stroke, or MI after 1 year. (Nordic Aortic Valve Intervention Trial [NOTION]; NCT01057173)
(J Am Coll Cardiol 2015;65:2184–94)

Clinical Outcomes

	Index Hospitalization* or 30 Days†			1 Year		
	TAVR	SAVR	p Value	TAVR	SAVR	p Value
Major, life threatening, or disabling bleeding*	16 (11.3)	28 (20.9)	0.03			
Cardiogenic shock*	6 (4.2)	14 (10.4)	0.05			
Major vascular complications*	8 (5.6)	2 (1.5)	0.10			
Acute kidney injury stage II or III*	1 (0.7)	9 (6.7)	0.01			
All-cause death†	3 (2.1)	5 (3.7)	0.43	7 (4.9)	10 (7.5)	0.38
Cardiovascular death†	3 (2.1)	5 (3.7)	0.43	6 (4.3)	10 (7.5)	0.25
Neurological events†	4 (2.8)	4 (3.0)	0.94	7 (5.0)	8 (6.2)	0.68
Stroke†	2 (1.4)	4 (3.0)	0.37	4 (2.9)	6 (4.6)	0.44
Transient ischemic attack†	2 (1.4)	0 (0)	0.17	3 (2.1)	2 (1.6)	0.71
MI†	4 (2.8)	8 (6.0)	0.20	5 (3.5)	8 (6.0)	0.33
Valve endocarditis†	1 (0.7)	0 (0)	0.33	4 (2.9)	2 (1.6)	0.47
New-onset or worsening AF†	24 (16.9)	77 (57.8)	<0.001	30 (21.2)	79 (59.4)	<0.001
Permanent pacemaker implantation†	46 (34.1)	2 (1.6)	<0.001	51 (38.0)	3 (2.4)	<0.001

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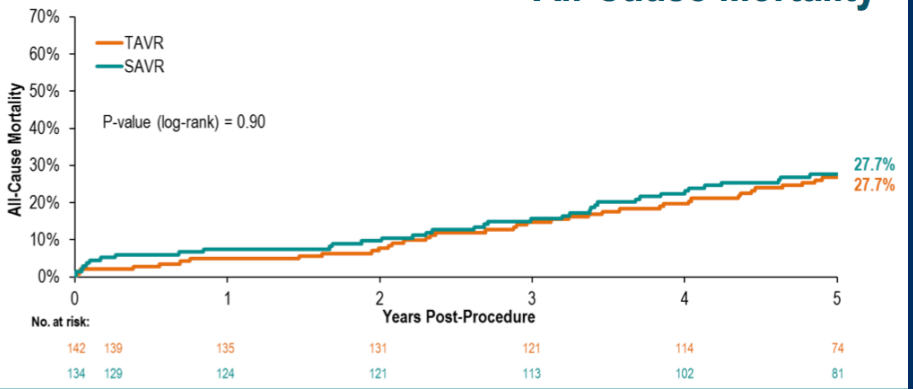
NOTION: 5-year Outcomes from the All-Comers Nordic Aortic Valve Intervention Randomised Clinical Trial in patients with Severe Aortic Valve Stenosis

Reported from the ACC Scientific Sessions 2018 (ACC.18) in Orlando, United States

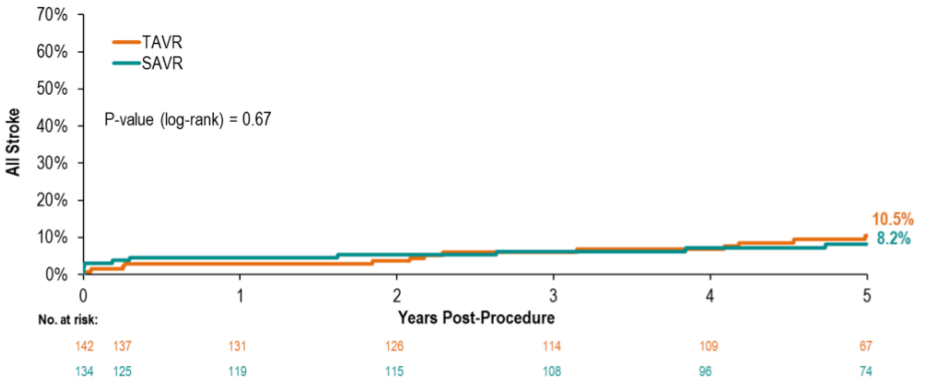
NOTION a prospective, multicentre, non-blinded, randomized trial compared TAVI vs. Surgery (TAVR versus SAVR) in all comer severe aortic stenosis patients aged 70 years and over who were suitable for self-expanding TAVI and surgery

All-Cause Mortality



ACC.18

Stroke



ACC.18

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NOTION: 5-year Outcomes from the All-Comers Nordic Aortic Valve Intervention Randomised Clinical Trial in patients with Severe Aortic Valve Stenosis

Reported from the ACC Scientific Sessions 2018 (ACC.18) in Orlando, United States

NOTION a prospective, multicentre, non-blinded, randomized trial compared TAVI vs. Surgery (TAVR versus SAVR) in all comer severe aortic stenosis patients aged 70 years and over who were suitable for self-expanding TAVI and surgery

Mortality with new PPM was higher in TAVI vs. no new PPM surgery patients (38.2% vs. 21.7%, p=0.07). The valve area and mean gradient was better with TAVI vs. surgical valve (1.66 vs. 1.23 cm2, p<0.001, Mean Gradient at 5 years 8.22 v 13.71 mm Hg, p<0.001). Severe AR was more with TAVI 8.2%, p<0.001. No difference in NYHA class at 1 year p=0.75. The authors concluded that Notion trial showed no difference in the primary endpoint. There was an increase in new PPM implantation with TAVI.

Potential Pitfalls in a low risk patient

- Need for PPM
  - Potential for TR regurgitation and RV dysfunction
- Stroke and embolic protection
- Future CAD and need for PCI
  - Won't usually present to TAVI centers
- Durability question
- Bicuspid AV and aortopathy

The PARTNER 3 Trial
Study Design

Symptomatic Severe Calcific Aortic Stenosis

Low Risk ASSESSMENT by Heart Team
(STS < 4%, TF only)

1:1 Randomization
(n=1228)

TF - TAVR
(SAPIEN 3)

- CT Imaging Sub-Study (n=200)
- Actigraphy/QoL Sub-Study (n=200)

Surgery
(Bioprosthetic Valve)

- CT Imaging Sub-Study (n=200)
- Actigraphy/QoL Sub-Study (n=200)

PARTNER 3 Registries

- Alternative Access (n=100) (TA/TAo/Subclavian)
- Bicuspid Valves (n=100)
- ViV (AV and MV) (n=100)

PRIMARY ENDPOINT:
Composite of all-cause mortality, all strokes, or re-hospitalization at 1 year post-procedure

Follow-up: 30 days, 6 mos, 1 year and annually through 10 years

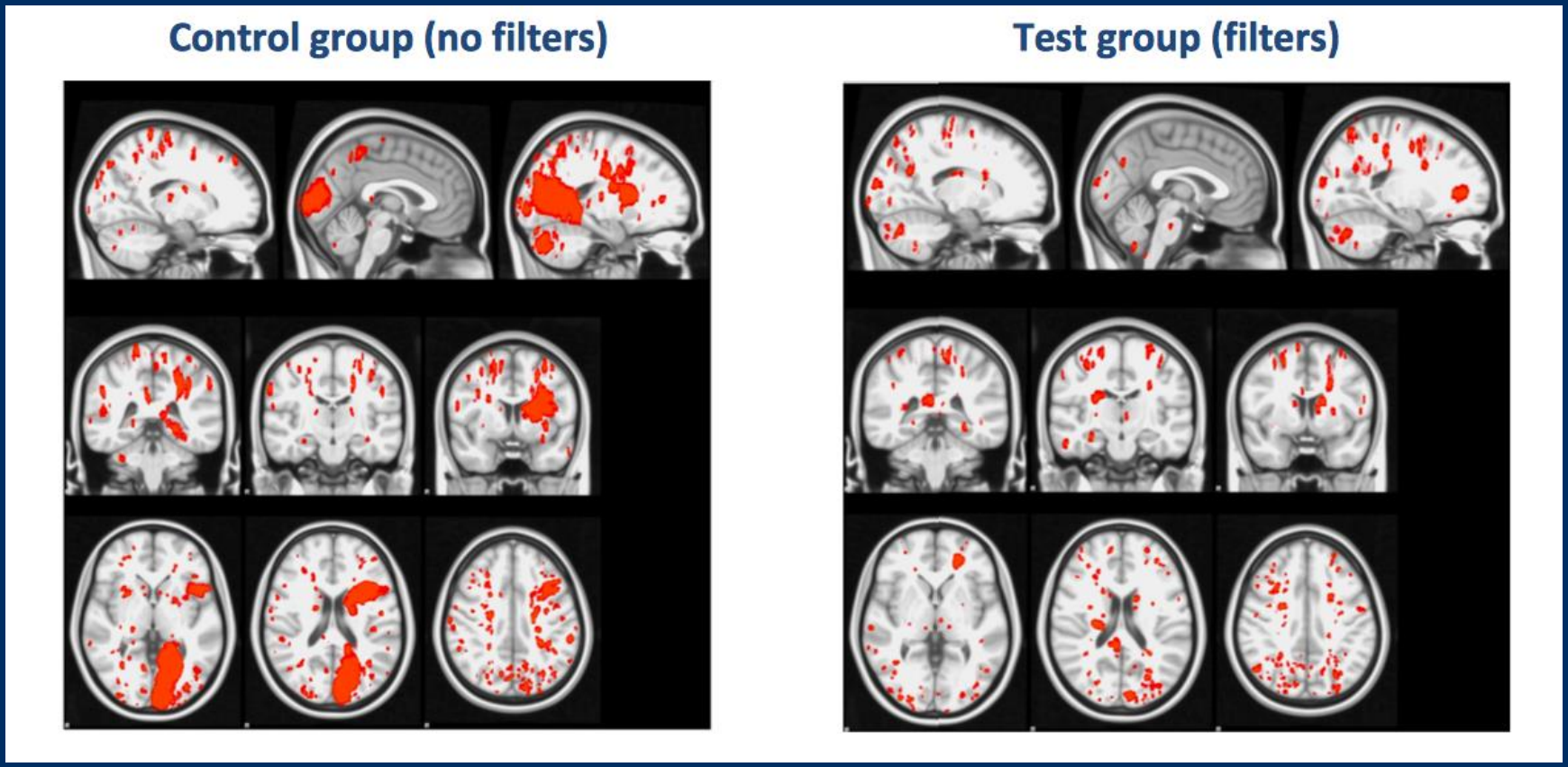
NEWS

FDA Gives Greenlight for Low-Risk TAVR Study With CoreValve

By Michael O'Riordan | February 21, 2016

- 1200 low-risk patients randomized to TAVR vs SAVR
- Primary end point of mortality and stroke at 2 years
- 400 patient sub-study on leaflet mobility

Strokes and Embolic protection



Strokes post AVR

- Likely underestimated
- Diffusion Weight MRI showed up 80% new ischemic lesion post AVR
- "Silent infarct"
  - 2-4 fold increase in future strokes
  - >3 fold increase in mortality
  - >2-fold increase in dementia
  - Cognitive decline

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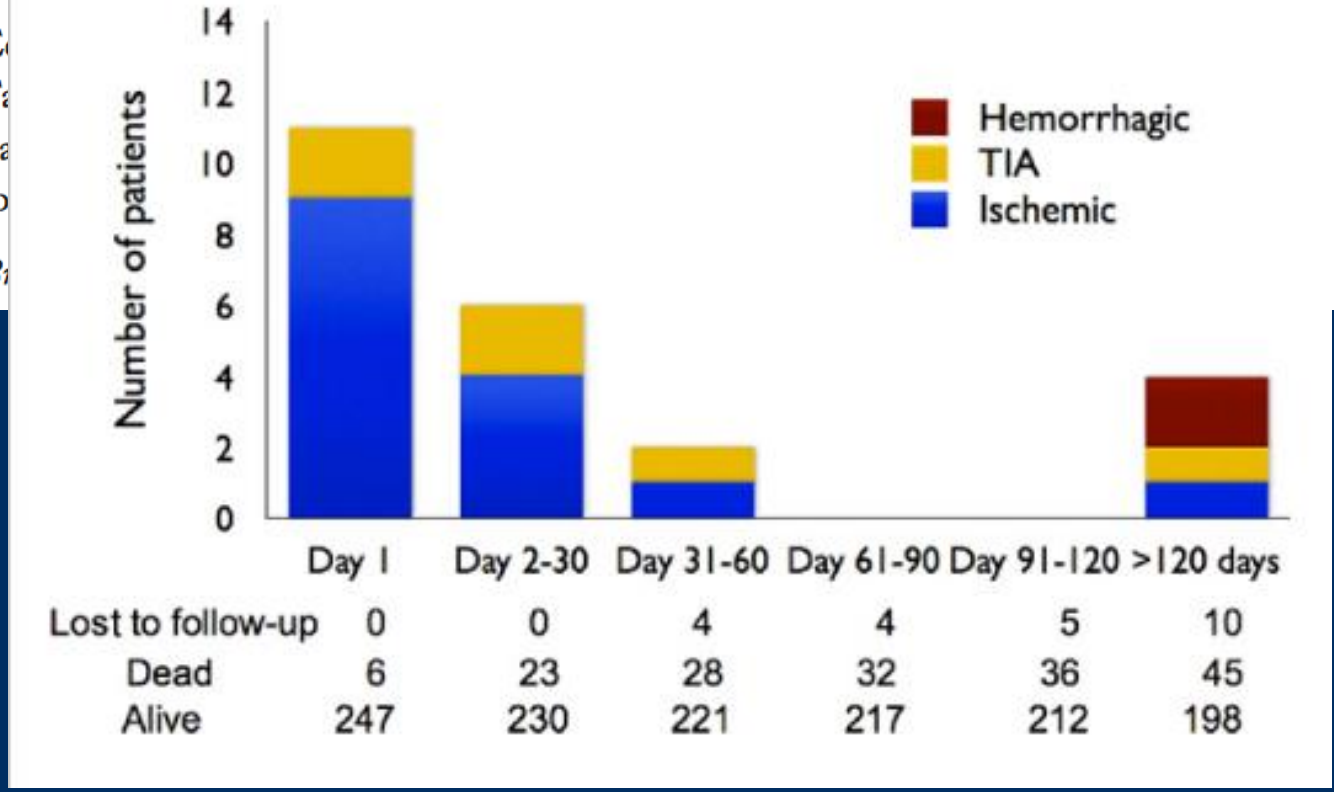
1. Sacco et al., Stroke 2013
2. Vermeer et al., Stroke 2003
3. Vermeer et al., New Engl J Med 2009

A High-Risk Period for Cerebrovascular Events Exists After Transcatheter Aortic Valve Implantation

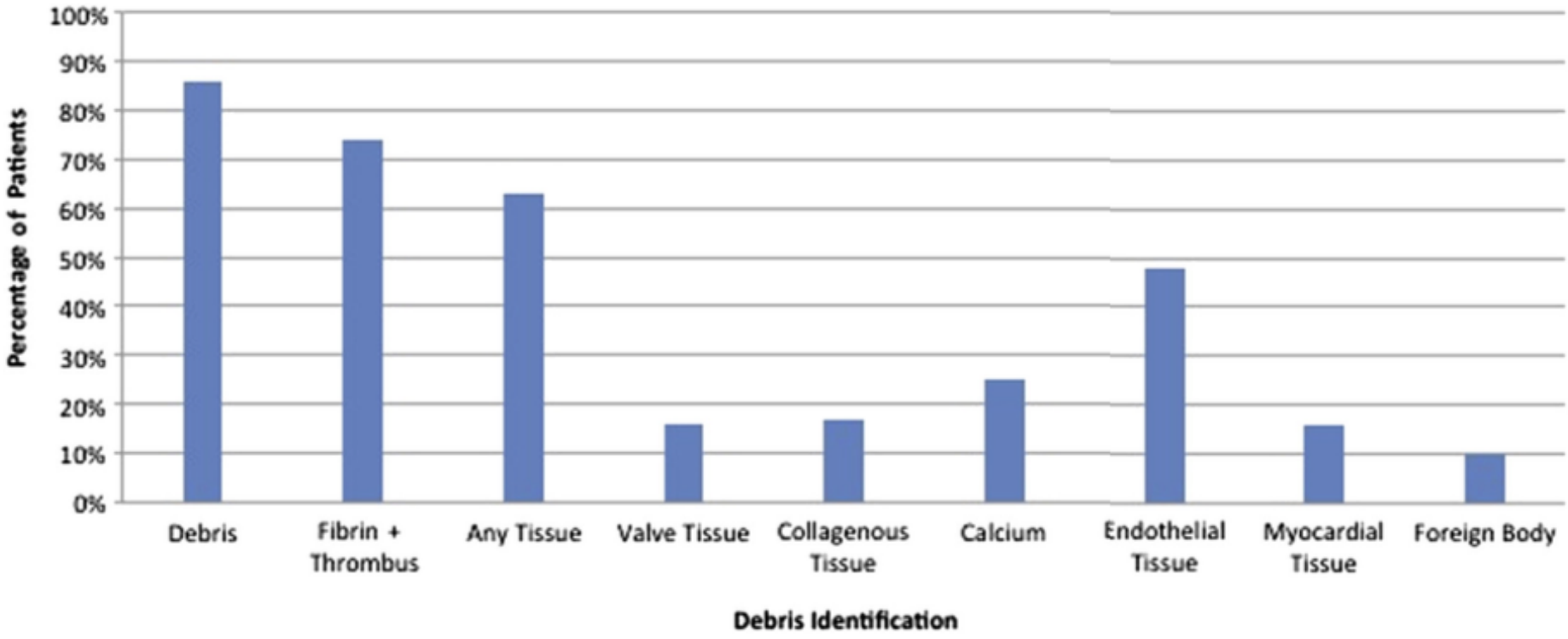
CME



Tay et al. JACC 2011;4(12):1290-97

Incidence and Predictors of Debris Embolizing to the Brain During

FIGURE 2 Identification and Frequency of Captured Debris



and more oversizing." (J Am Coll Cardiol Intv 2015;8:718-24) © 2015 by the American College of Cardiology Foundation.

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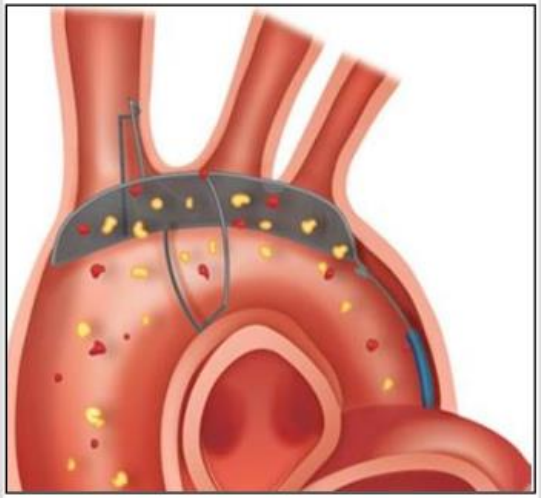
Van Mieghem et al. JACC 2015;8(5):718-24

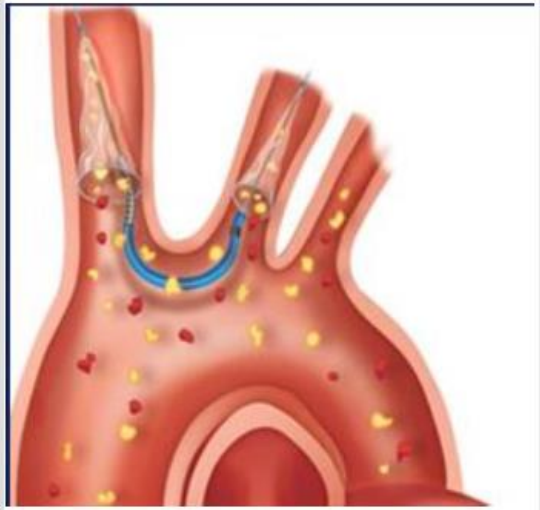
Embolic protection Devices

TriGuard Embolic Deflection Device (Keystone Heart)[1]



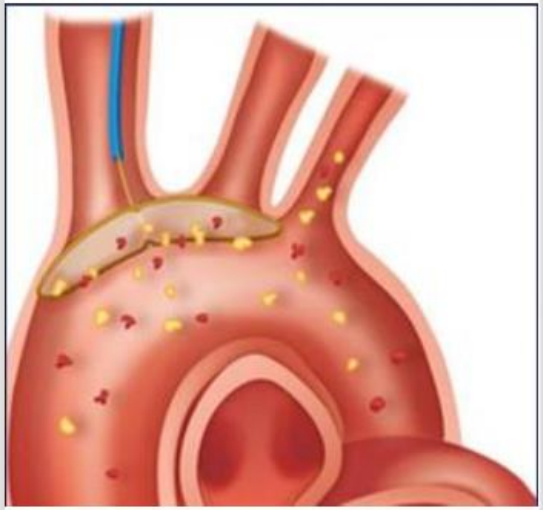
- ✓ Pore Size: 130 µm
- ✓ Delivery Sheath: 9F
- ✓ Access: Transfemoral
- ✓ Coverage: Brachiocephalic, left common carotid, left subclavian

Sentinel Cerebral Protection System (Claret Medical)[2]



- ✓ Pore Size: 140 µm
- ✓ Delivery Sheath: 6F
- ✓ Access: Brachial or radial
- ✓ Coverage: Brachiocephalic, left common carotid

Embrella Embolic Deflector System (Edwards Lifesciences)[3]

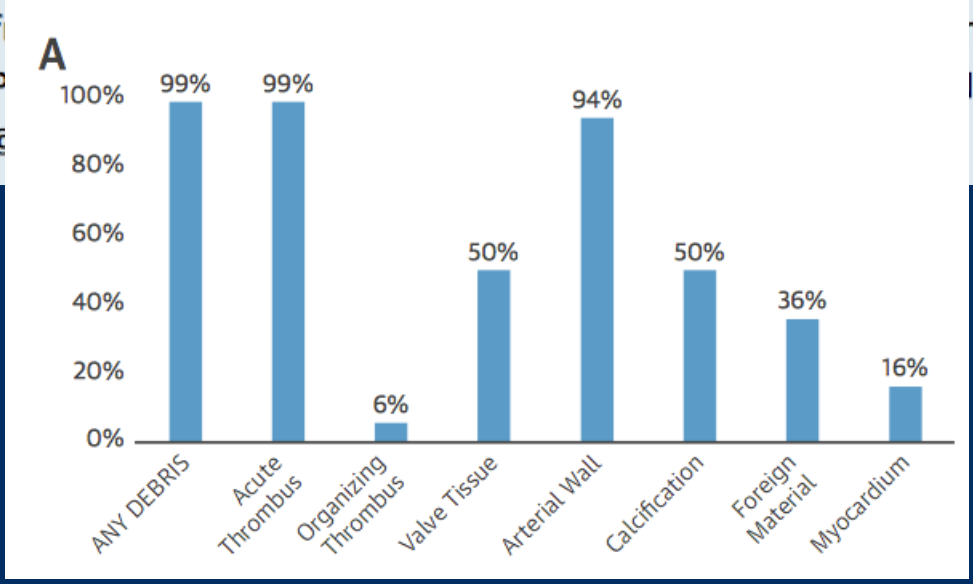


- ✓ Pore Size: 100 µm
- ✓ Delivery Sheath: 6F
- ✓ Access: Brachial
- ✓ Coverage: Brachiocephalic, left common carotid

Protection Against Cerebral Embolism During Transcatheter Aortic Valve Replacement

Samir R. Kapadia, MD,[a] Susheel Kodali, MD,[b] Raj Makkar, MD,[c] Roxana Mehran, MD,[d] Ronald M. Lazar, PhD,[b] Robert Zivadinov, MD, PhD,[e] Michael G. Dwyer, MD,[e] Hasan Jilaihawi, MD,[f] Renu Virmani, MD,[g] Saif Anwaruddin, MD,[h] Vinod H. Thourani, MD,[i] Tamim Nazif, MD,[b] Norman Mangner, MD,[j] Felix Woitek, MD,[j] Amar Krishnaswamy, MD,[a] Stephanie Mick, MD,[a] Tarun Chakravarty, MD,[c] Mamoo Nakamura, MD,[c] James M. McCabe, MD,[k] Lowell Satler, MD,[l] Alan Zajarias, MD,[m] Wilson Y. Szeto, MD,[h] Lars Svensson, MD, PhD,[a]

CONCLUSIONS TCEP was safe, captured embolic debris in 99% of patients, and did not change neurocognitive f… …nce scans was not statistically significant. (Cerebral P… …IEL]; NCT02214277) (J Am Coll Cardiol 2017;69:367–77) @



42% reduction in median new lesion volume

CLARET Device

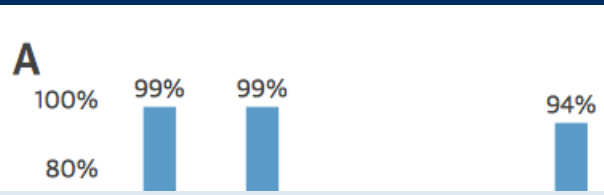
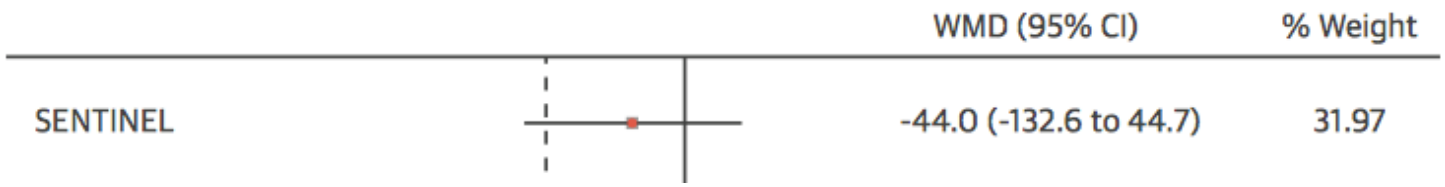
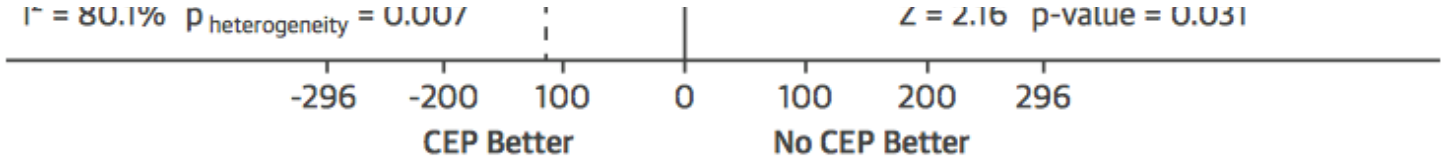


FIGURE 1 Meta-Analysis of Randomized Controlled Trials Investigating Claret (Claret Medical, Santa Rosa, California) Cerebral Protection Filters



CLARET MEDICAL RECEIVES FDA CLEARANCE TO MARKET SENTINEL CEREBRAL PROTECTION SYSTEM IN THE U.S.

The First and Only Embolic Protection Device Shown to Reduce TAVR Procedural Strokes by 63 Percent



Axel Linke, MD,[j,q] on behalf of the SENTINEL Trial Investigators

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Parachute use to prevent death and major trauma related to gravitational challenge: systematic review of randomised controlled trials

Gordon C S Smith, Jill P Pell

BMJ 2003

Parachutes reduce the risk of injury after gravitational challenge, but their effectiveness has not been proved with randomised controlled trials

Durability

Durability

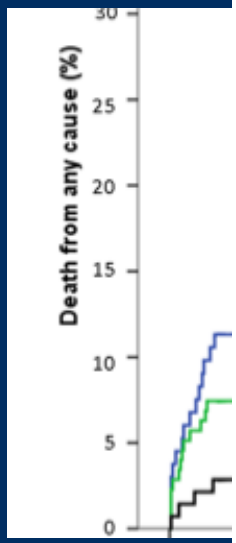
- Bio-prosthetic aortic valve degeneration
  - <1% at 1 year
  - 10-30% at 10 years
  - 20-50% at 15 years
- Trans-catheter Valve --?
  - Dvir et al. EuroPCR
  - ? 50% TAVI degenerate at 8 years (2/3 AI)

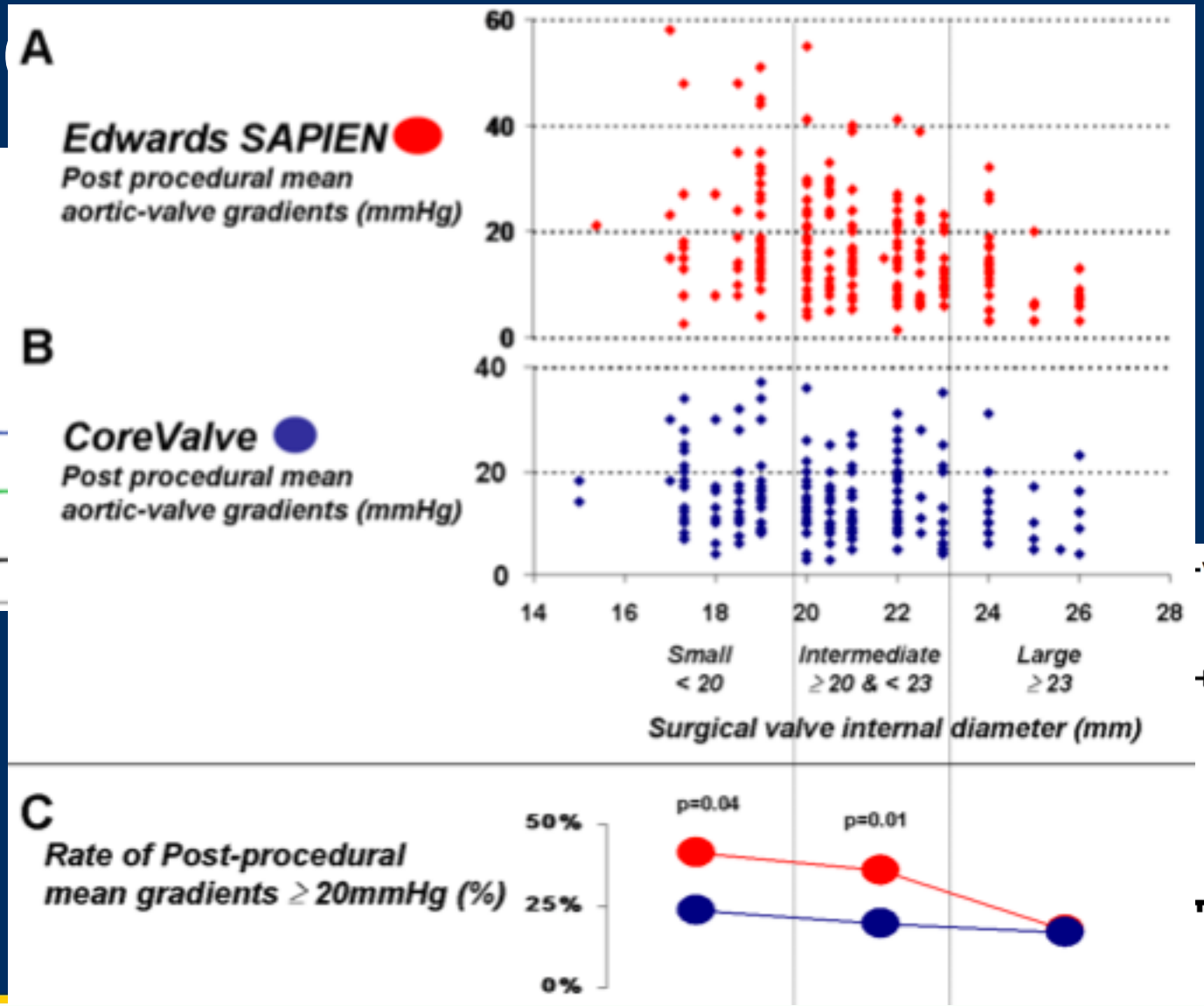
Interact Cardiovasc Thorac Surg 2014;19:36-40.
Pibarot P et al. Circulation 2009;119:1034-48.

TAVR degeneration

- Moderate AI and/or mean gradient >20 mmHg not present at 30 days post procedure (not comparable to definition of surgical valve degeneration)
- Sub-clinical leaflet immobility

Pati





-valve

p = 0.03

p < 0.001

p = 0.31

p = 0.97

10

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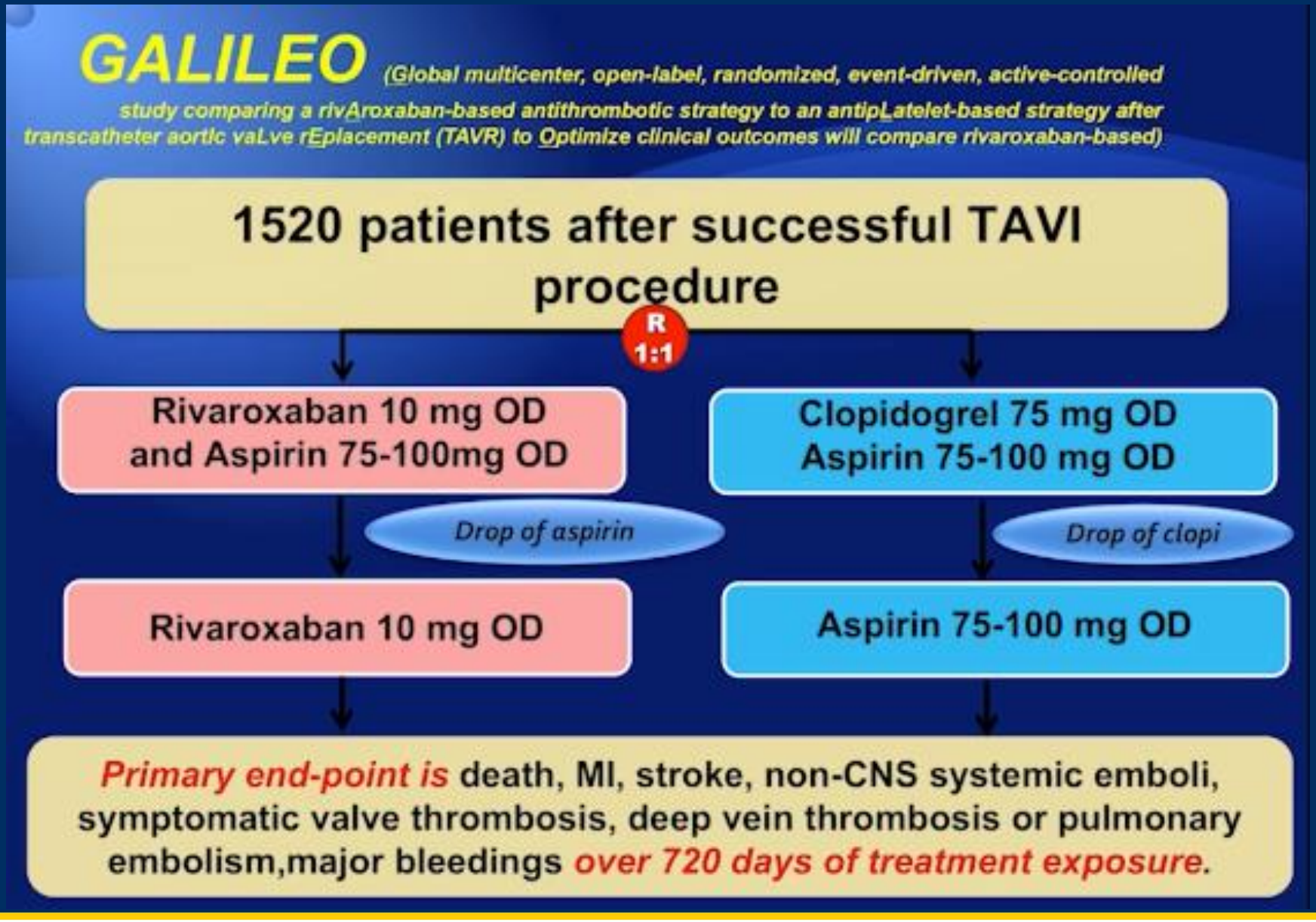
Dvir et al. JAMA 2014;312920:162-170

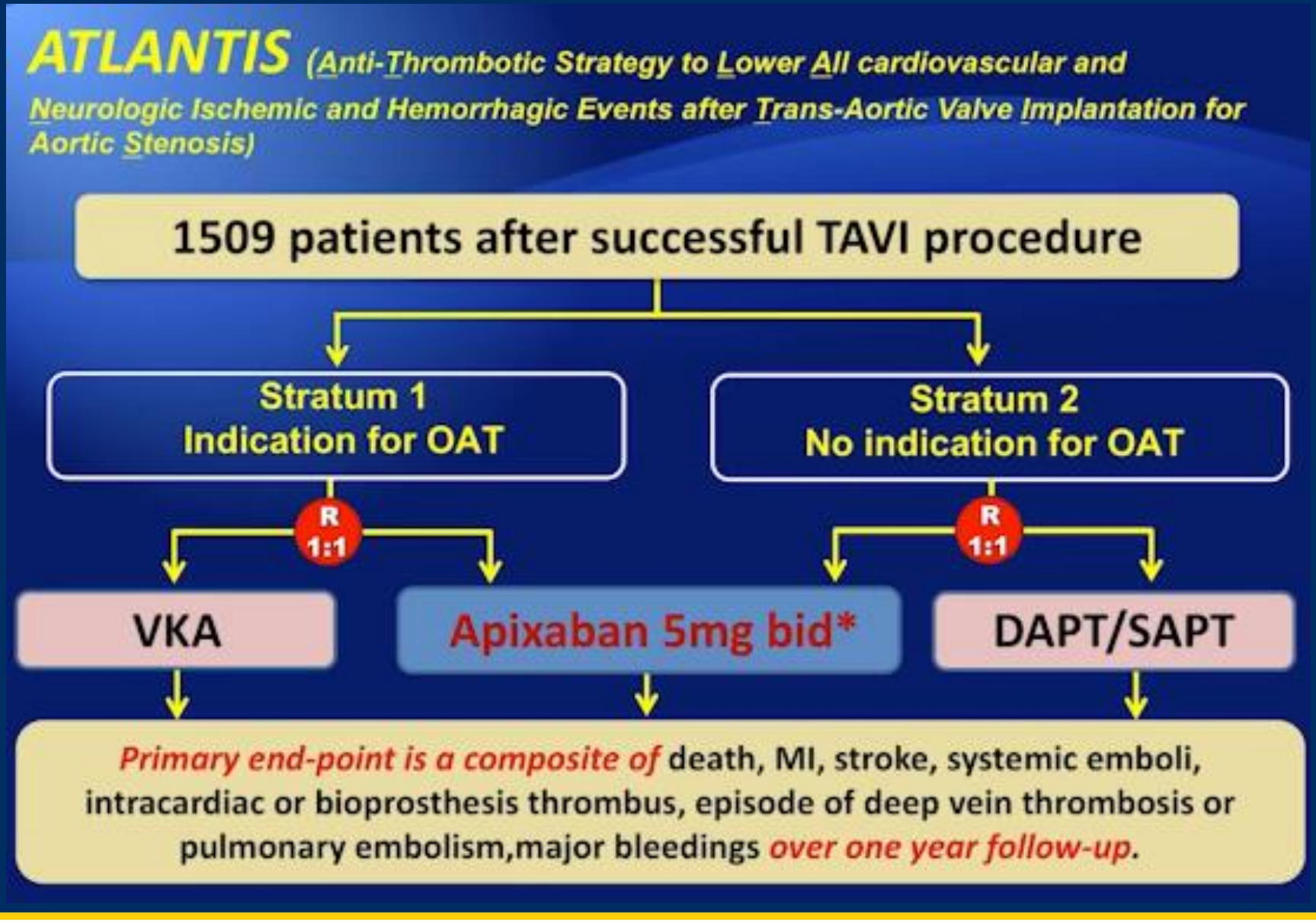
Subclinical leaflet thrombosis in surgical and transcatheter bioprosthetic aortic valves: an observational study

Tarun Chakravarty, MD, Prof Lars Søndergaard, MD, John Friedman, MD, Ole De Backer, MD, Prof Daniel Berman, MD, Klaus F Kofoed, MD, Hasan Jilaihawi, MD, Takahiro Shiota, MD, Yigal Abramowitz, MD, Troels H Jørgensen, MD, Tanya Rami, MS, Sharjeel Israr, MD, Gregory Fontana, MD, Martina de Knegt, MD, Andreas Fuchs, MD, Prof Patrick Lyden, MD, Prof Alfredo Trento, MD, Prof Deepak L Bhatt, MD, Prof Martin B Leon, MD, Prof Raj R Makkar, MD on behalf of the RESOLVE†, SAVORY Investigators†

RESOLVE and SAVORY Registries

- Assess prevalence of subclinical leaflet thrombosis
- 931 patients had 4D CT, ECHO
- 13% vs 4% thrombosis on TAVR vs SAVR (p=0.001)
- Resolution on anticoagulation (warfarin or NOAC)
- No stroke difference but more TIA
- Aortic gradients >20 mmHg or increase gradient >10 mmHg were seen more frequently in pts with leaflet thrombosis then not. 14% vs 1% p=<0.0001)


GALILEO
(Global multicenter, open-label, randomized, event-driven, active-controlled study comparing a rivAroxaban-based antithrombotic strategy to an antipLatelet-based strategy after transcatheter aortic vaLve rEplacement (TAVR) to Optimize clinical outcomes will compare rivaroxaban-based)
1520 patients after successful TAVI procedure
R 1:1
Rivaroxaban 10 mg OD and Aspirin 75-100mg OD
Clopidogrel 75 mg OD Aspirin 75-100 mg OD
Drop of aspirin
Drop of clopi
Rivaroxaban 10 mg OD
Aspirin 75-100 mg OD
Primary end-point is death, MI, stroke, non-CNS systemic emboli, symptomatic valve thrombosis, deep vein thrombosis or pulmonary embolism,major bleedings over 720 days of treatment exposure.



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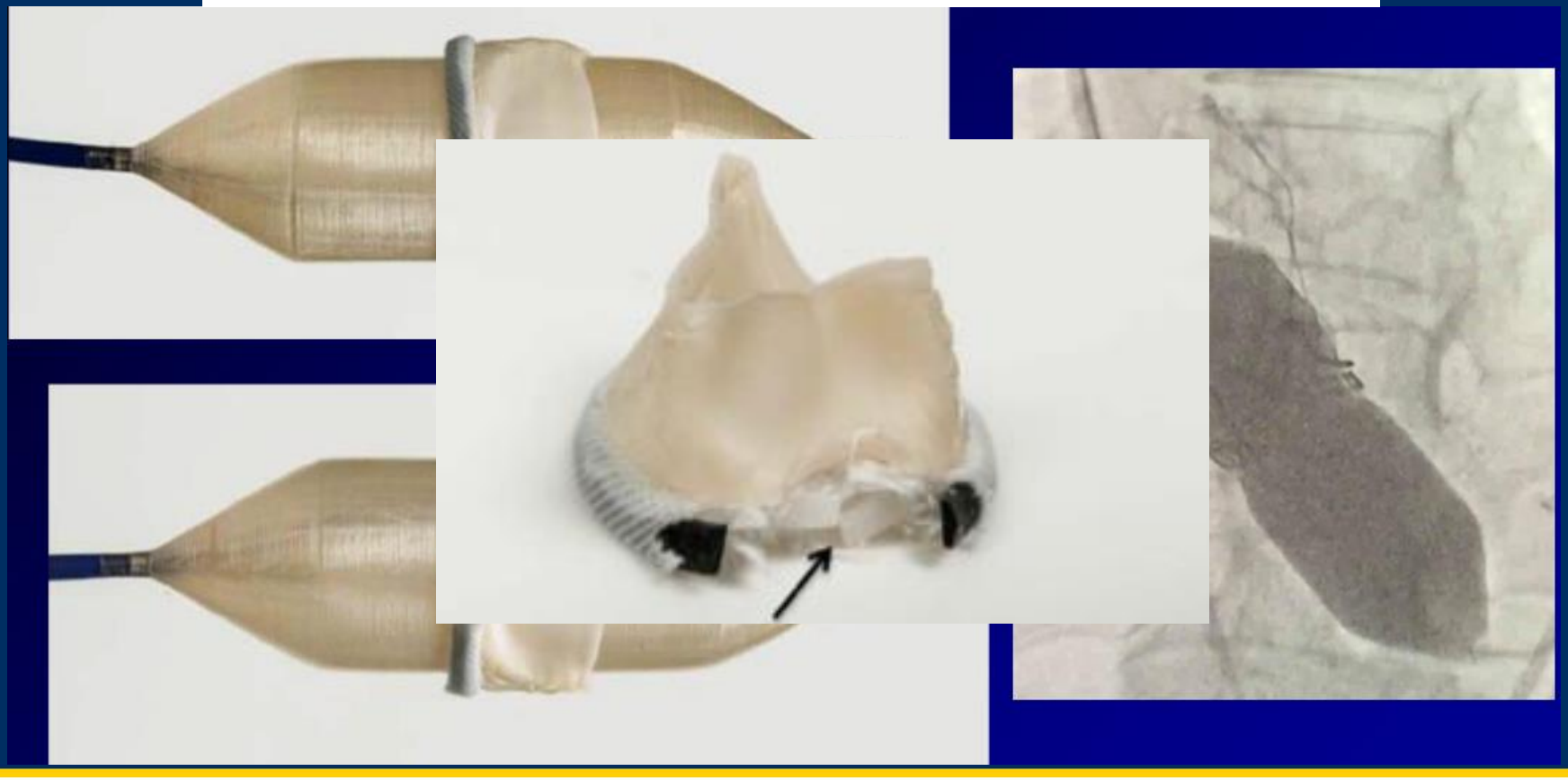
Ring

Fracturing the Ring of Small Mitroflow Bioprostheses by High-Pressure Balloon Predilatation in Transcatheter Aortic Valve-in-Valve Implantation

Jens Erik Nielsen-Kudsk, MD, DMSc; Evald Høj Christiansen, MD, PhD; Christian Juhl Terkelsen, MD, DMSc; Bjarne Linde Nørgaard, MD, PhD; Kaare Troels Jensen, MD, PhD; Lars Romer Krusell, MD; Mariann Tang, MD; Kim Terp, MD; Kaj-Erik Klaaborg, MD; Henning Rud Andersen, MD, DMSc



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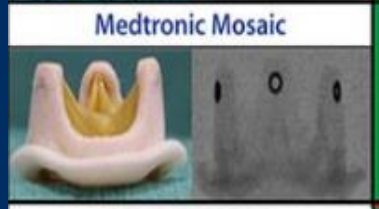
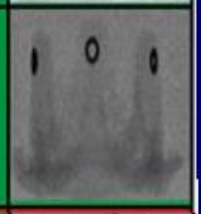
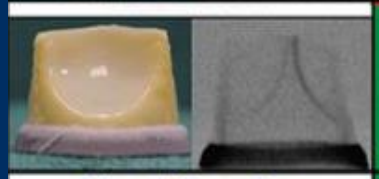
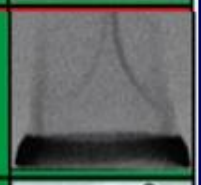
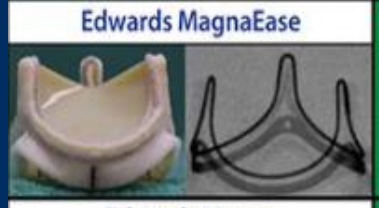
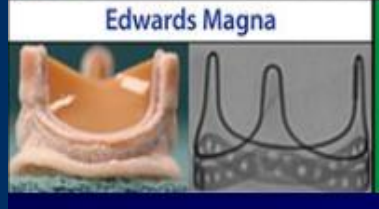
Circ Cardiovasc Inter. 2015;8:e002667

St. Jude Biocor Epic 	21 mm	YES / 8 ATM	YES / 8 ATM	
Medtronic Mosaic 	19 mm 21 mm	YES / 10 ATM YES / 10 ATM	YES / 10 ATM YES / 10 ATM	
	19 mm 21 mm	YES / 12 ATM YES / 12 ATM	YES / 12 ATM YES / 12 ATM	
Edwards MagnaEase 	19 mm 21 mm	YES / 18 ATM YES / 18 ATM	YES / 18 ATM YES / 18	
Edwards Magna 	19 mm 21 mm	YES / 24 ATM YES / 24 ATM	YES / 24 YES / 24	
St. Jude Trifecta 	19 mm 21 mm	NO NO	NO NO	
Medtronic Hancock II 	21 mm	NO	NO	

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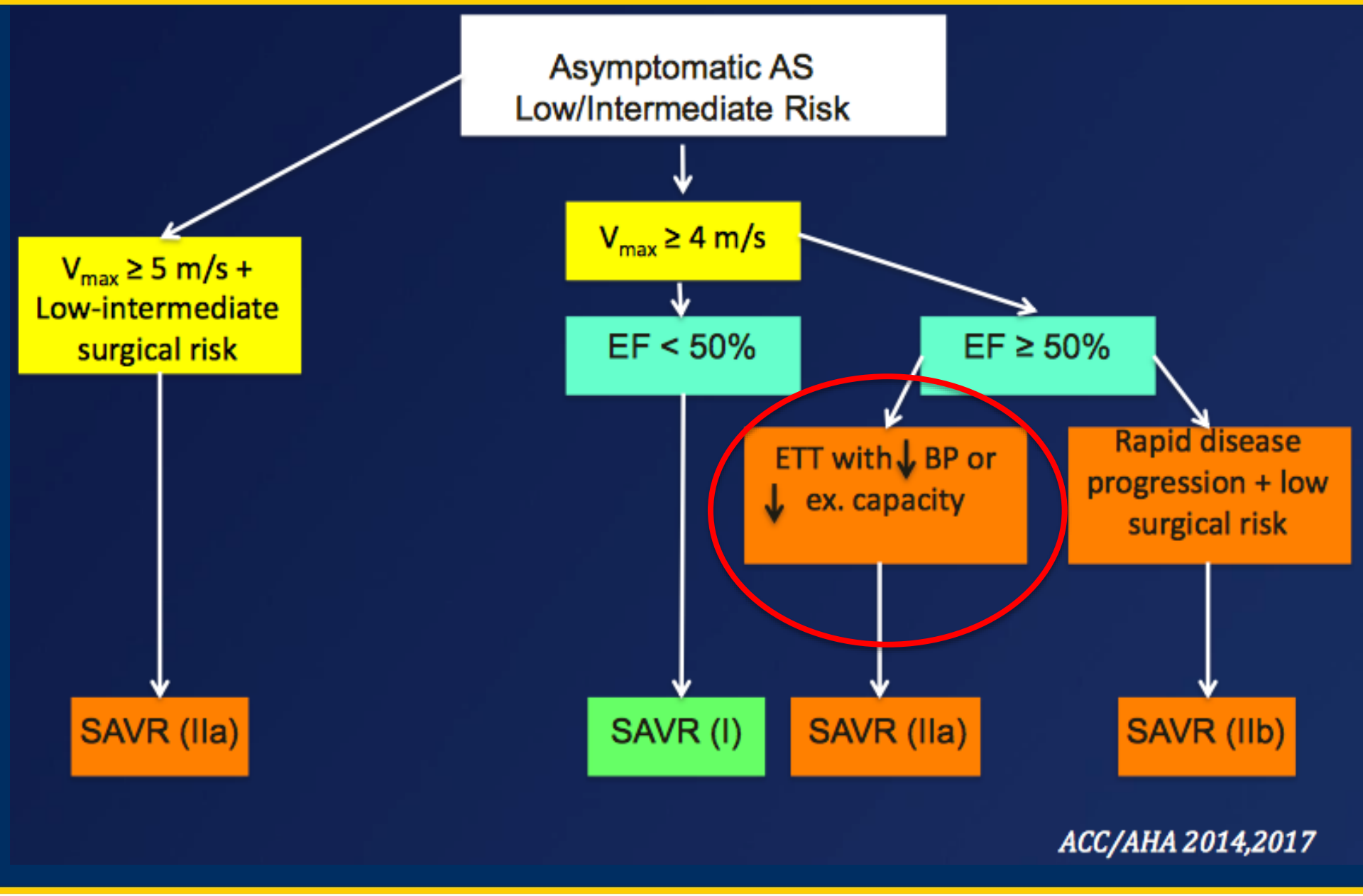
Asymptomatic aortic stenosis

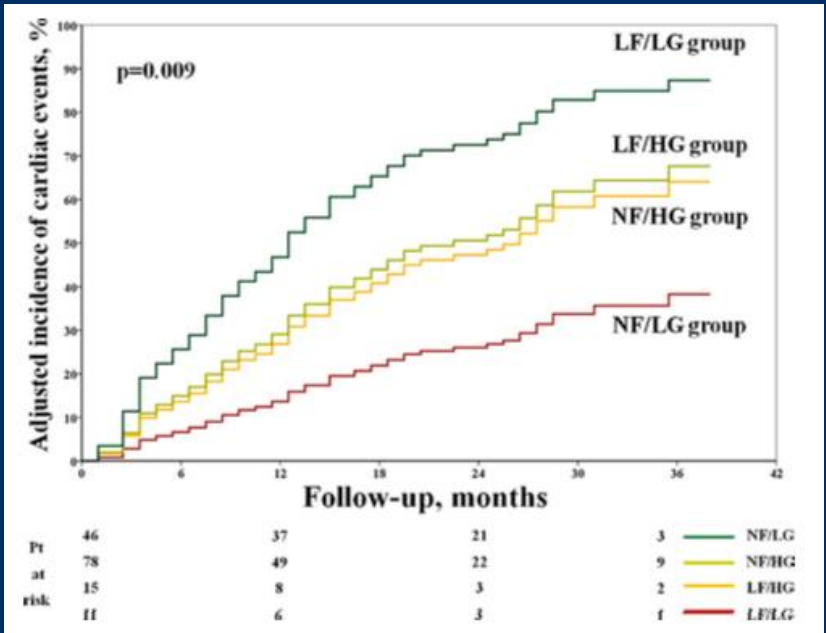
- True asymptomatic
- Under reported (Sx attributed to normal aging)
- Risk of SCD 1-2% vs surgery 1-5% mortality
  - No EQUIPOISE if considering SAVR
- Stress stress testing is indicated
  - ~5-6% doctors give stress tests (fear?)


Asymptomatic AS
Low/Intermediate Risk
V_{max} ≥ 5 m/s +
Low-intermediate
surgical risk
V_{max} ≥ 4 m/s
EF < 50%
EF ≥ 50%
ETT with ↓ BP or
↓ ex. capacity
Rapid disease
progression + low
surgical risk
SAVR (IIa)
SAVR (I)
SAVR (IIa)
SAVR (IIb)
ACC/AHA 2014,2017

Clinical Outcome in Asymptomatic Severe Aortic Stenosis

Insights From the New Proposed Aortic Stenosis Grading Classification

Patrizio Lancellotti, MD, PHD,* Julien Magne, PHD,* Erwan Donal, MD, PHD,† Laurent Davin, MD,* Kim O'Connor, MD,*‡ Monica Rosca, MD,* Catherine Szymanski, MD,* Bernard Cosyns, MD, PHD,§ Luc A. Piérard, MD, PHD*



- Asymptomatic AS
  - N= 150
  - Normal Stress Test
  - Mean F/up: 27 months
- **2-yr CV Events**
  - **CV death or Need for AVR: 51% (76/150)**
  - **Cardiac Death: 5.3% (8/150)**
- CV Events at F/up
  - 1 year: 29%
  - 2 years: 49%
  - 3 years: 60%

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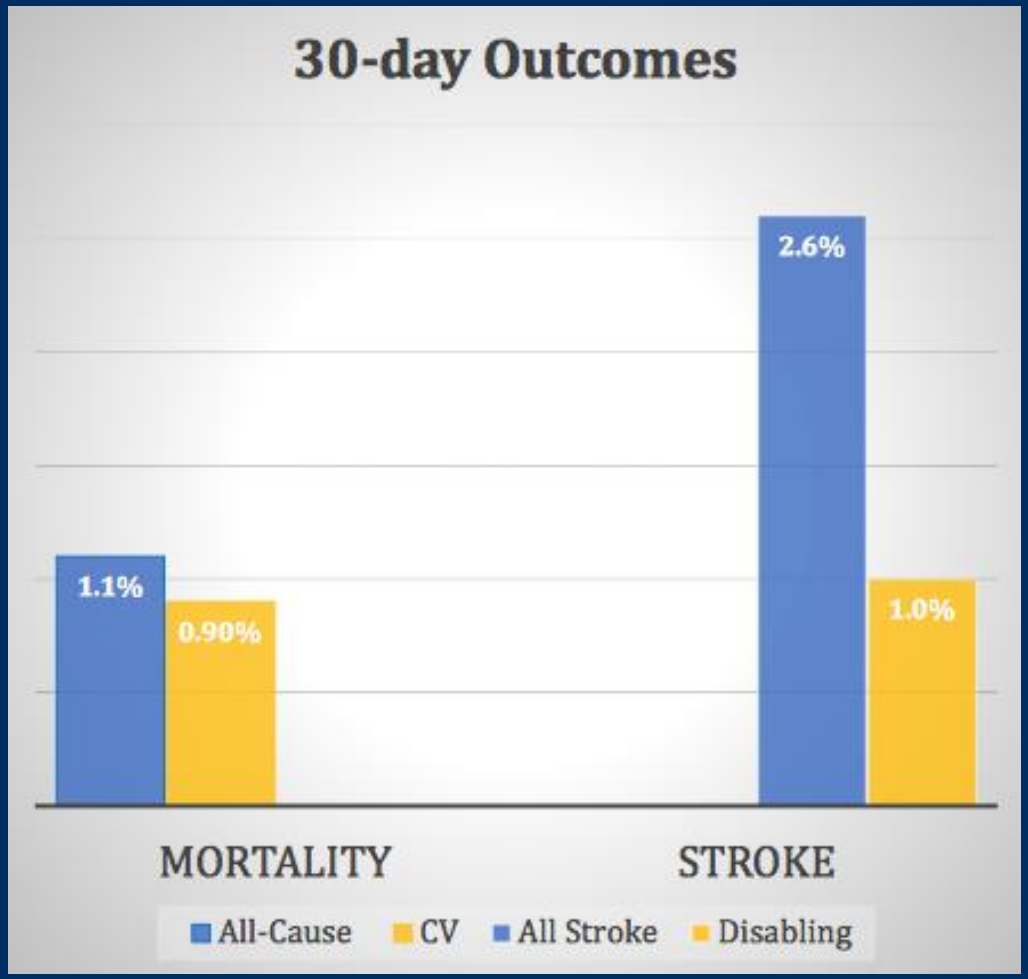
JACC 2012:59(3):235-43

SAPIEN 3 Trial



- N= 1078
- SAPIEN 3
- Mean Age: 82 yr
- Intermediate Risk
  - STS : 5.3%
- 30-day Outcomes
  - Mortality
    - All-cause: 1.1%
    - CV: 0.9%
  - Stroke
    - All Stroke: 2.6%
    - Disabling: 1.0%

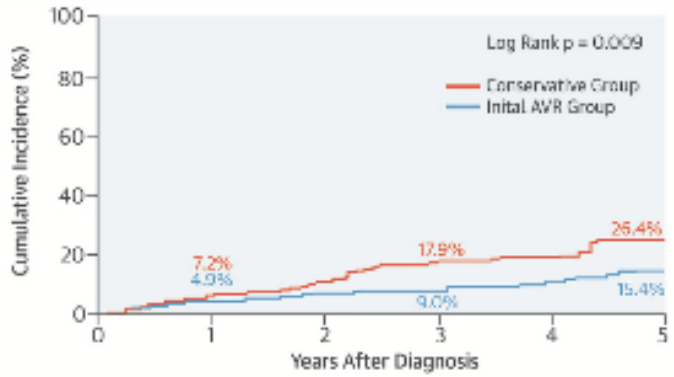
Kodali S et al. European Heart J 2016

Kodali et al. European Heart J 2016

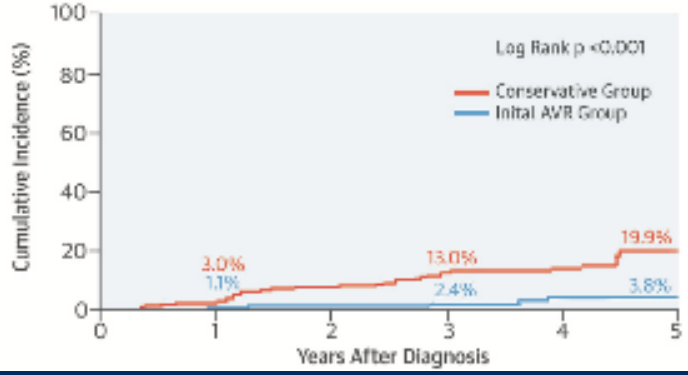
Initial Surgical Versus Conservative Strategies in Patients With Asymptomatic Severe Aortic Stenosis

ID, MPH,† Hiroki Shiomi, MD,* Kenji Ando, MD,‡

All-cause Death



Heart Failure Hospitalization



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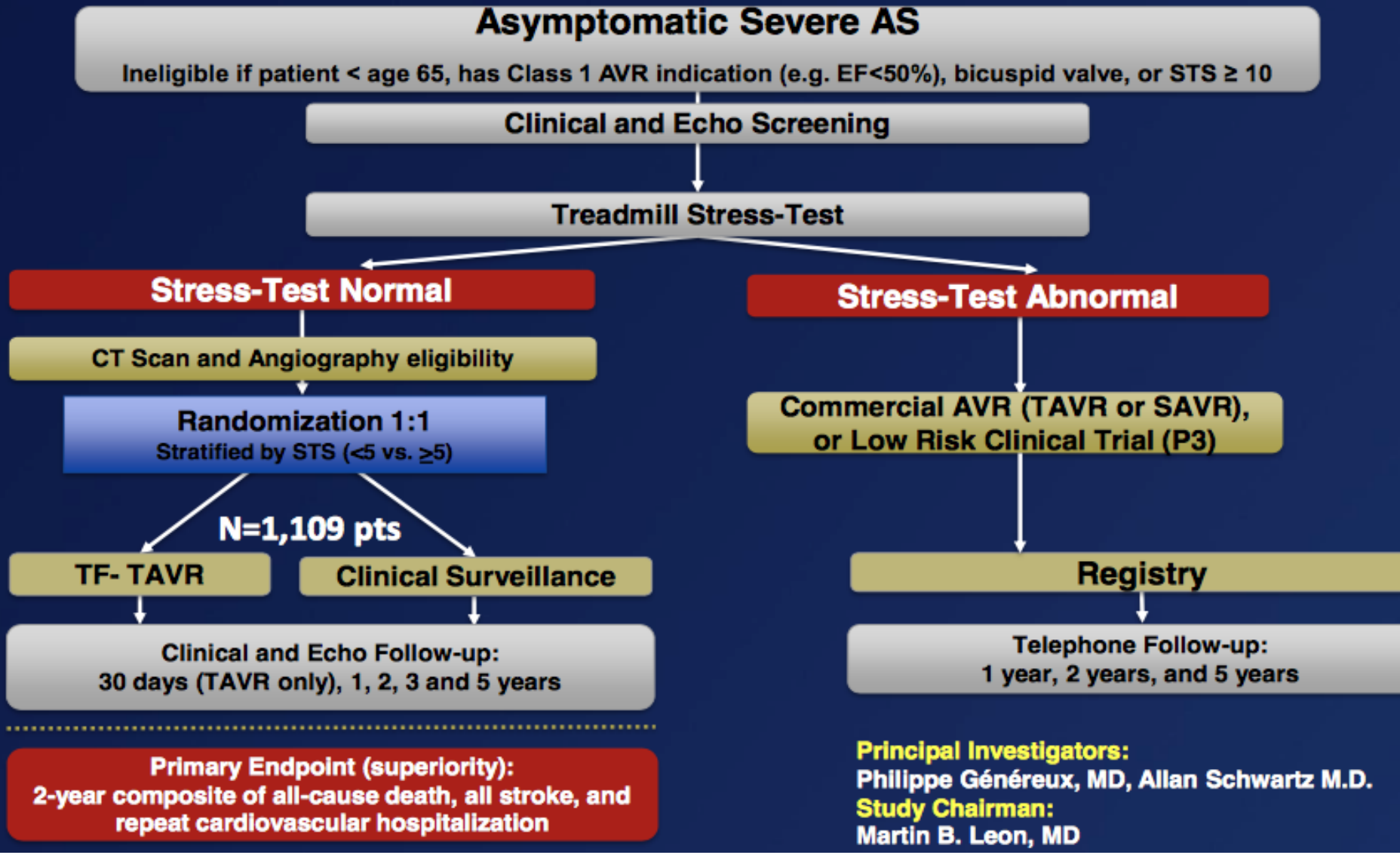
Taniguchi et al. JACC 2015;66:2827-38

EARLY TAVT Trial



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EARLY TAVR Trial

- Test the hypothesis that early TAVR will be superior to watchful waiting in patients with asymptomatic severe aortic stenosis

Early intervention with moderate AS and reduced EF?

European Heart Journal Advance Access published January 18, 2016

European Heart Journal
doi:10.1093/eurheartj/ehv701

CLINICAL RESEARCH
Valvular heart disease

Aortic valve surgery and survival in patients with moderate or severe aortic stenosis and left ventricular dysfunction

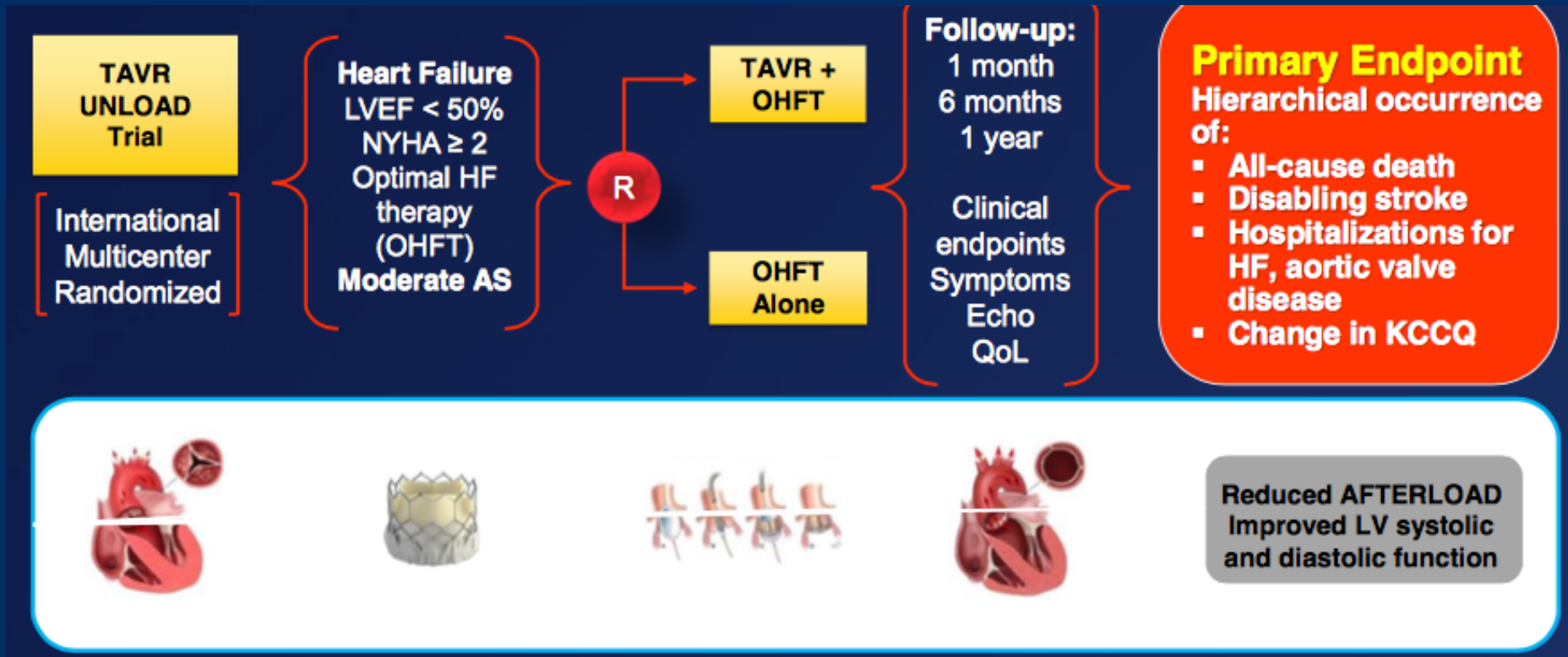
Zainab Samad[1]*, Amit N. Vora[1,2], Allison Dunning[2], Phillip J. Schulte[2], Linda K. Shaw[2], Fawaz Al-Enezi[1], Mads Ersboll[3], Robert W. McGarrah III[1], John P. Vavalle[1], Svati H. Shah[1,2,4], Joseph Kisslo[1], Donald Glower[1,5], J. Kevin Harrison[1], and Eric J. Velazquez[1,2]

[1]Division of Cardiology, Duke Medicine, Duke University, PO Box 3254, Rm 3347A Duke South, 200 Trent Drive, Durham, NC, USA; [2]Duke Clinical Research Institute, Durham, NC, USA; [3]Department of Cardiology, Rigshospitalet, Copenhagen, Denmark; [4]Duke Molecular Physiology Institute, Durham, NC, USA; and [5]Department of Surgery, Duke University,

Duke echo database identified 1634 pts with LV systolic dysfunction (EF ≤ 50%) and AS; 1090 (67%) with moderate AS (mean AV gradient ≥ 25-39 mmHg, mean AVA 1.08 cm2) and 544 (33%) with severe AS (mean AVA 0.72 cm2)

- Mean age 75yo and major co-morbidities included CAD 61%, DM 33%, and cerebrovascular disease 20%
- Pts followed at least 5 years after the index echo

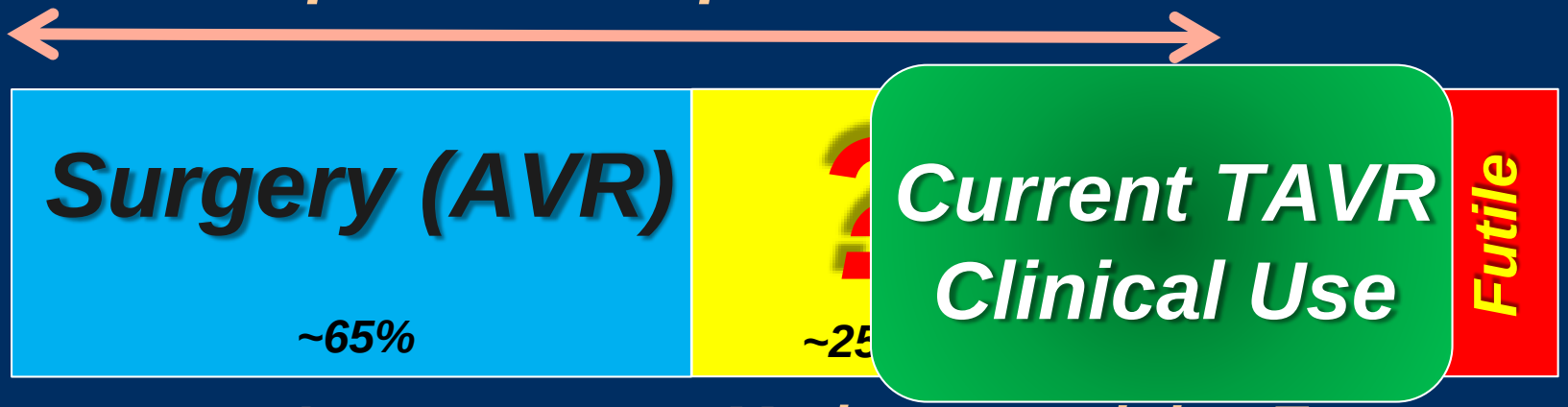
TAVR UNLOAD 600 pts, 1:1 randomization



TAVR Categories

(risk is a continuum)

Operable AS patients



TAVR in 2018

Evaluation in progress	Safe for TAVR But surgery also a good option	OK preferred	No

** Extreme (prohibitive) risk = "inoperable"*

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TAVR

- Over 500 TAVR programs in the US

2017 AHA/ACC Focused Update of the 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 Clinical Practice Guidelines

Developed in Collaboration With the American Association for Thoracic Surgery, American Society of Echocardiography, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Anesthesiologists, and Society of Thoracic Surgeons

I A See Online Data Supplement 9 (Updated From 2014 VHD Guideline)	Surgical AVR or TAVR is recommended for symptomatic patients with severe AS (Stage D) and high risk for surgical AVR, depending on patient-specific procedural risks, values, and preferences (49–51).	
I A See Online Data Supplements 5 and 9 (Updated From 2014 VHD Guideline)	TAVR is recommended for symptomatic patients with severe AS (Stage D) and a prohibitive risk for surgical AVR who have a predicted post-TAVR survival greater than 12 months (58–61).	
IIa B-R See Online Data Supplements 5 and 9 (Updated From 2014 VHD Guideline)	TAVR is a reasonable alternative to surgical AVR for symptomatic patients with severe AS (Stage D) and an intermediate surgical risk, depending on patient-specific procedural risks, values, and preferences (62–65).	NEW: New RCT showed noninferiority of TAVR to surgical AVR in symptomatic patients with severe AS at intermediate surgical risk.

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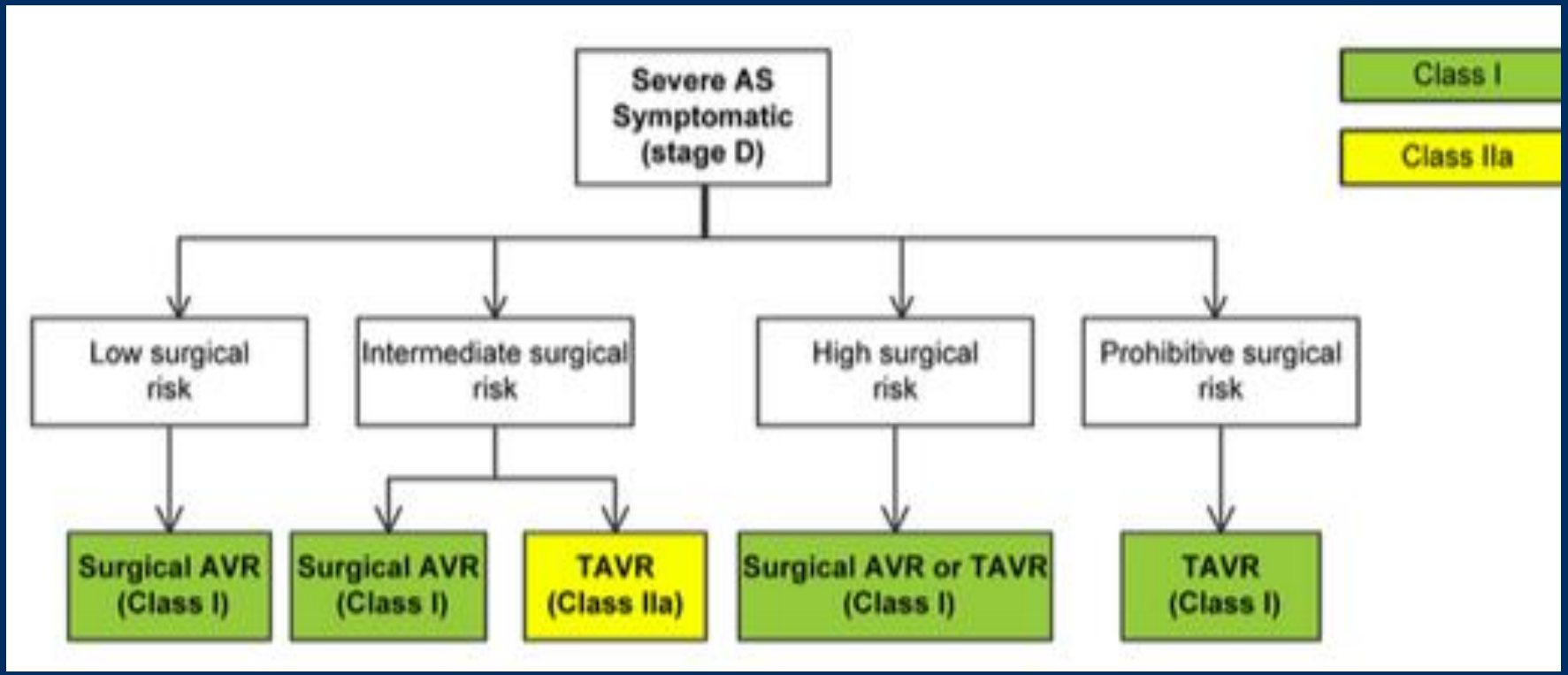
JACC.2017;70(2):252-89

Aortic Replacement Guidelines



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Valvular heart disease Focused Updated. JACC.2017;70(2):252-89

Questions:

- Intervention for asymptomatic aortic valve replacement is indicated:
  a. When mean valvular gradient falls by 20% with exercise
  b. Resting peak velocity of >5 m/sec
  c. Prior to moderate risk surgery
  d. New onset atrial fibrillation

- Intervention for asymptomatic aortic valve replacement is indicated:
  a. When mean valvular gradient falls by 20% with exercise
  b. Resting peak velocity of >5 m/sec
  c. Prior to moderate risk surgery
  d. New onset atrial fibrillation

- Sentinel Trial: The CLARET Device has shown to:
  a. Reduce mortality
  b. Statistically reduce major strokes
  c. Reduced major lesion volume by MRI
  d. Increase in vascular complication

- In the intermediate risk TAVR clinical trial SURTAVI: TAVR patients experienced more..

a. life threatening or disabling bleeding

b. atrial fibrillation

c. more acute kidney injury

d. vascular complications

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