TAVR: Optimizing the Choice of Prothesis and Patient. What is the Next Frontier?

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COI TAVR

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National Surgical PI

SurTAVI

Reprise III

Evolut R low risk trial

I am a cardiac surgeon

Portico NG

Study Chair

Reprise IV

Evolut Low Risk Bicuspid

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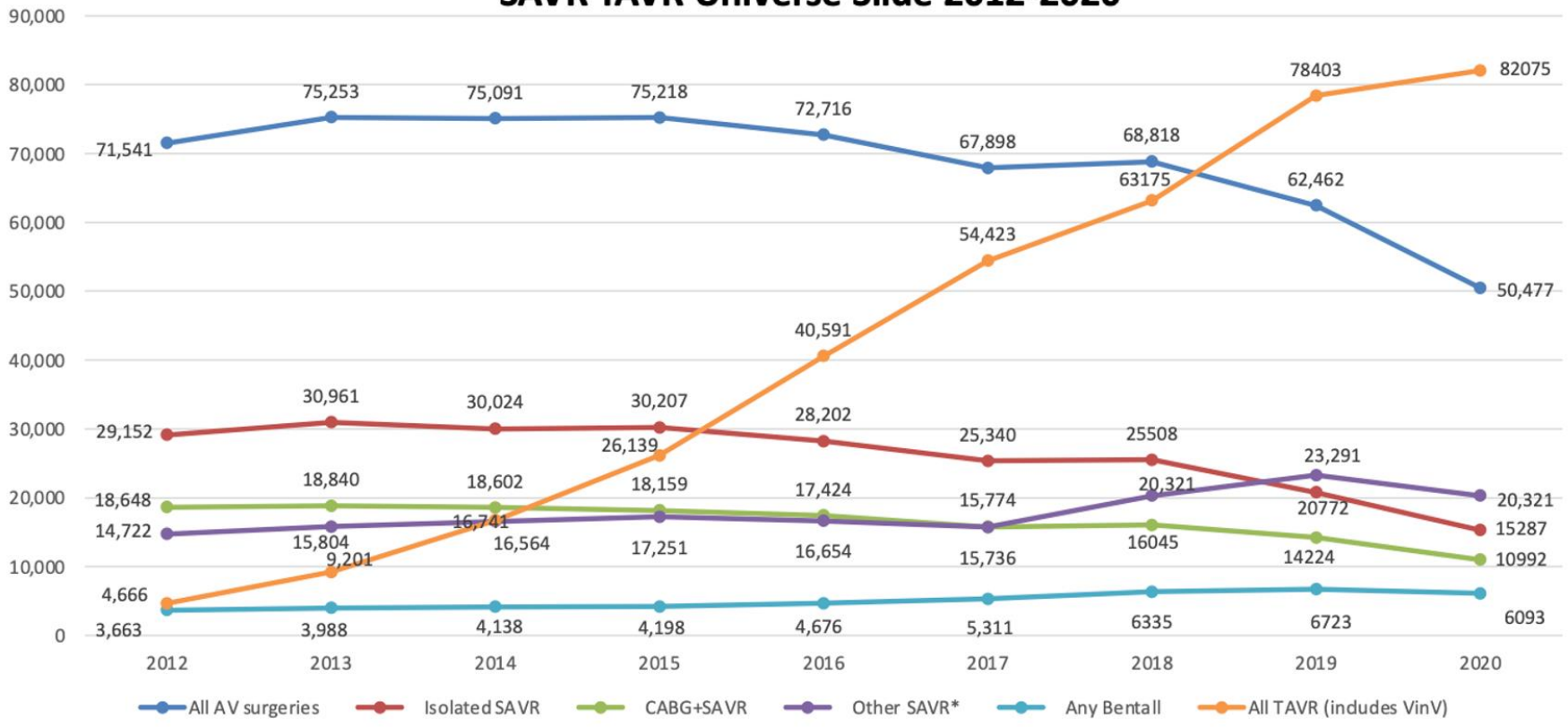
SAVR TAVR Universe Slide 2012-2020



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Circulation

ACC/AHA CLINICAL PRACTICE GUIDELINE

2020 ACC/AHA Guideline for the Management of Patients With Valvular Heart Disease: Executive Summary

A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines

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Circulation

3.2.4.2. Choice of SAVR Versus TAVI for Patients for Whom a Bioprosthetic AVR Is Appropriate

Recommendations for Choice of SAVR Versus TAVI for Patients for Whom a Bioprosthetic AVR Is Appropriate
Referenced studies that support the recommendations are summarized in Online Data Supplements 11 to 13.

COR	LOE	Recommendations
1	A	1. For symptomatic and asymptomatic patients with severe AS and any indication for AVR who are <65 years of age or have a life expectancy >20 years, SAVR is recommended.[123–125]
1	A	2. For symptomatic patients with severe AS who are 65 to 80 years of age and have no anatomic contraindication to transfemoral TAVI, either SAVR or transfemoral TAVI is recommended after shared decision-making about the balance between expected patient longevity and valve durability.[123,126–130]
1	A	3. For symptomatic patients with severe AS who are >80 years of age or for younger patients with a life expectancy <10 years and no anatomic contraindication to transfemoral TAVI, transfemoral TAVI is recommended in preference to SAVR.[123,126–132]

Otto CM, Nishimura RA, Bonow RO, Carabello BA, Erwin JP 3rd, Gentile F, Jneid H, Krieger EV, Mack M, McLeod C, O'Gara PT, Rigolin VH, Sundt TM 3rd, Thompson A, Toly C., 2020 ACC/AHA Guideline for the Management of Patients With Valvular Heart Disease: Executive Summary: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines., Circulation. 2020 Dec 17:PMID: 33332149

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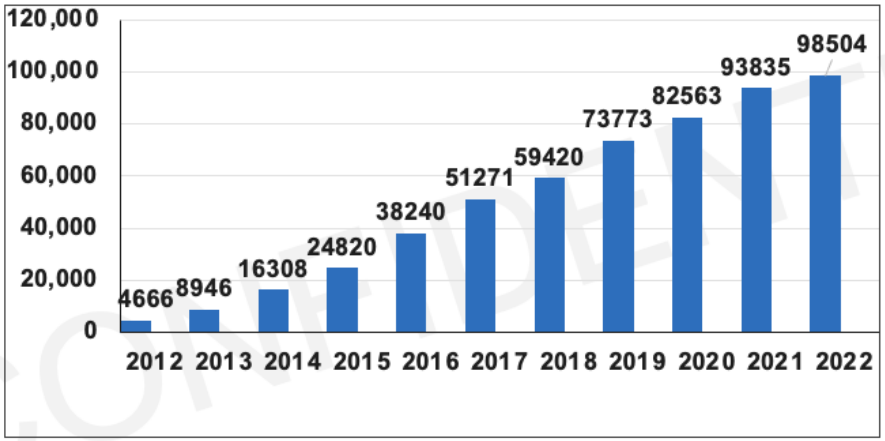
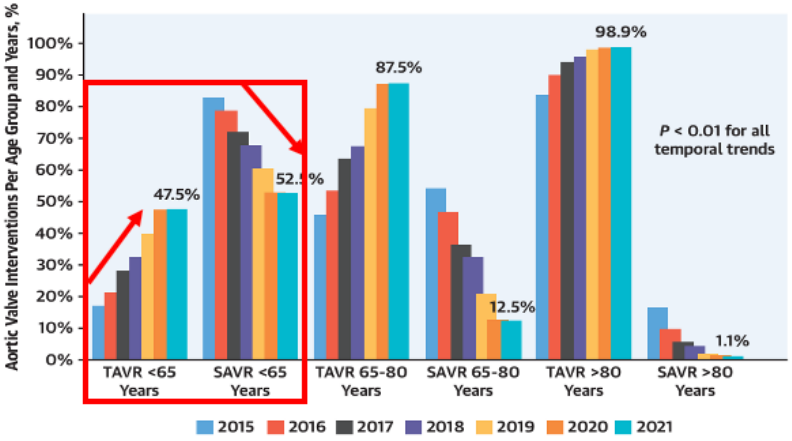
Commercial TAVR procedures in the U.S.



TAVR and SAVR procedures by age group in the U.S.



1. STS/ACC TVT Registry database. 2. Sharma T, et al. *J Am Coll Cardiol*. 2022;80:2054-2056.

What data are we missing?

Excluded patients from the randomized trials

Data on younger patients

Asymptomatic AS

Moderate AS with HF

AI

Who was excluded?

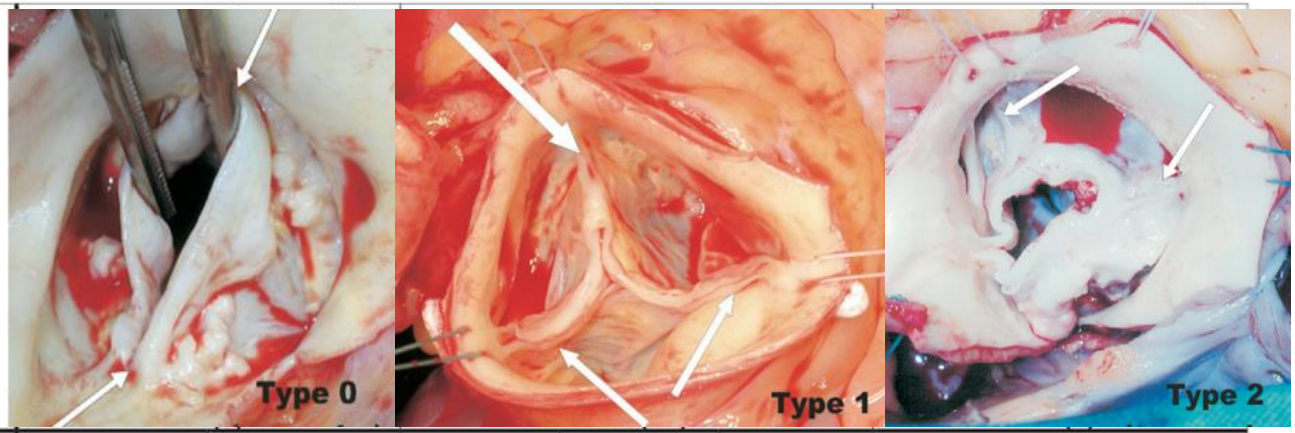
Bicuspid valves

Significant CAD

Unfavorable anatomy

Associated procedures

Appropriate for a mechanical valve



1. subcategory: spatial position of cusps in Type 0 and raphes in Types 1 and 2	lat 13 (4)	ap 7 (2)	L – R 216 (71)	R – N 45 (15)	N – L 8 (3)	L – R / R – N 14 (5)
2. subcategory: VALVULAR FUNCTION						
I	6 (2)	1 (0.3)	79 (26)	22 (7)	3 (1)	6 (2)
S	7 (2)	5 (2)	119 (39)	15 (5)	3 (1)	6 (2)
B (I + S)		1 (0.3)	15 (5)	7 (2)	2 (1)	2 (1)
No			3 (1)	1 (0.3)		

Sievers HH, Schmidtke C. A **classification** system for the bicuspid aortic valve from 304 surgical specimens., J Thorac Cardiovasc Surg. 2007 May;133(5):1226-33.

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Bicuspid Aortic Valve Morphology and Outcomes After Transcatheter Aortic Valve Replacement

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ABSTRACT

BACKGROUND Bicuspid aortic stenosis accounts for almost 50% of patients undergoing surgical aortic valve replacement in the younger patients. Expanding the indication of transcatheter aortic valve replacement (TAVR) toward lower-risk and younger populations will lead to increased use of TAVR for patients with bicuspid aortic valve (BAV) stenosis despite the exclusion of bicuspid anatomy in all pivotal clinical trials.

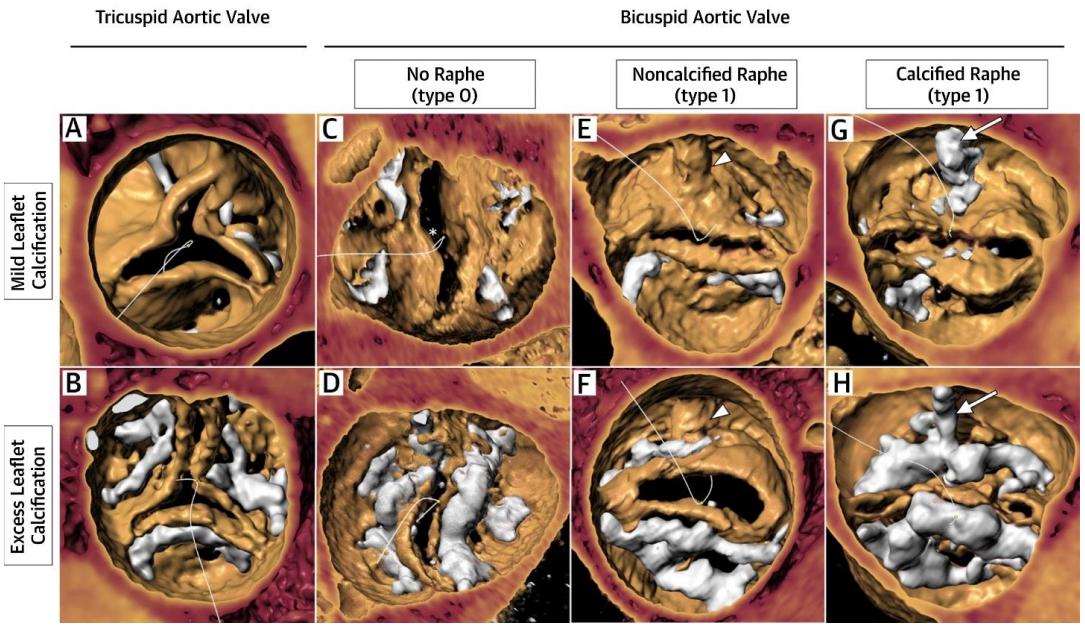
OBJECTIVES This study sought to evaluate the association of BAV morphology and outcomes of TAVR with the new-generation devices.

METHODS Patients with BAV confirmed by central core laboratory computed tomography (CT) analysis were included from the international multicenter BAV TAVR registry. BAV morphology including the number of raphe, calcification grade in raphe, and leaflet calcium volume were assessed with CT analysis in a masked fashion. Primary outcomes were all-cause mortality at 1 and 2 years, and secondary outcomes included 30-day major endpoints and procedural complications.

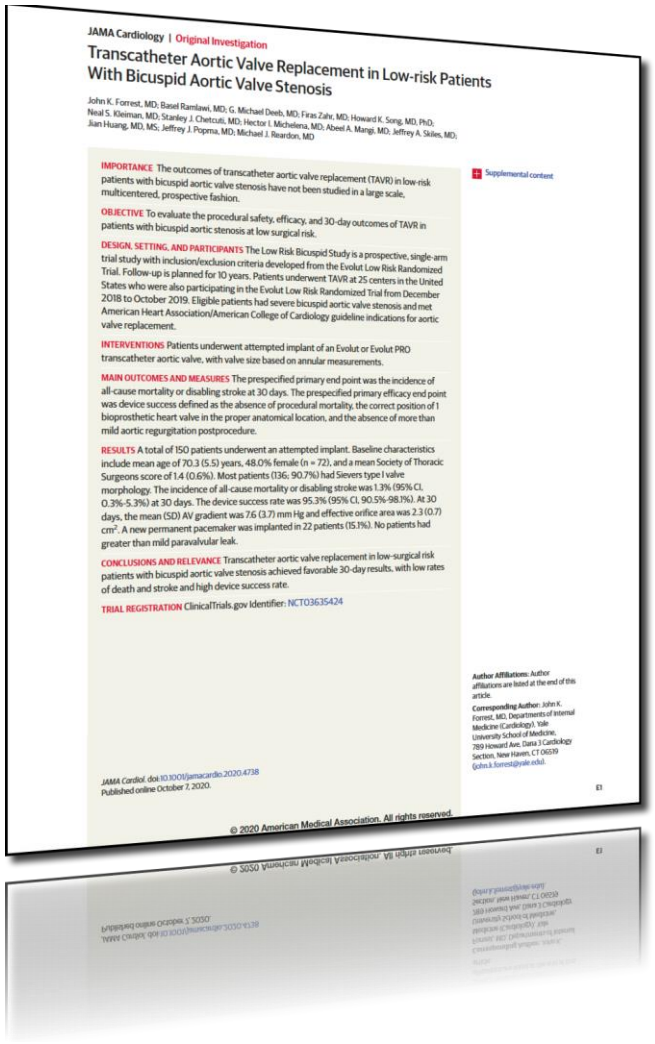
RESULTS A total of 1,034 CT-confirmed BAV patients with a mean age of 74.7 years and Society of Thoracic Surgeons score of 3.7% underwent TAVR with contemporary devices (n = 740 with Sapien 3; n = 188 with Evolut R/Pro; n = 106 with others). All-cause 30-day, 1-year, and 2-year mortality was 2.0%, 6.7%, and 12.5%, respectively. Multivariable analysis identified calcified raphe and excess leaflet calcification (defined as more than median calcium volume) as independent predictors of 2-year all-cause mortality. Both calcified raphe plus excess leaflet calcification were found in 269 patients (26.0%), and they had significantly higher 2-year all-cause mortality than those with 1 or none of these morphological features (25.7% vs. 9.5% vs. 5.9%; log-rank $p < 0.001$). Patients with both morphological features had higher rates of aortic root injury ($p < 0.001$), moderate-to-severe paravalvular regurgitation ($p = 0.002$), and 30-day mortality ($p = 0.016$).

CONCLUSIONS Outcomes of TAVR in bicuspid aortic stenosis depend on valve morphology. Calcified raphe and excess leaflet calcification were associated with increased risk of procedural complications and midterm mortality. (Bicuspid Aortic Valve Stenosis Transcatheter Aortic Valve Replacement Registry; NCT03836521)
(J Am Coll Cardiol 2020;76:1018-30)

Listen to this manuscript's audio summary by Editor-in-Chief Dr. Valentin Fuster on JACC.org.



Yoon SH, Kim WK, Dhoble A, Milhorini Pio S, …., Makkar RR; Bicuspid Aortic Valve Stenosis Transcatheter Aortic Valve Replacement Registry Investigators., Bicuspid Aortic Valve Morphology and Outcomes After Transcatheter Aortic Valve Replacement. J Am Coll Cardiol. 2020 Sep 1;76(9):1018-1030.



JAMA Cardiology | Original Investigation

Transcatheter Aortic Valve Replacement in Low-risk Patients With Bicuspid Aortic Valve Stenosis

John K. Forrest, MD; Basel Ramlawi, MD; G. Michael Deeb, MD; Firas Zahr, MD; Howard K. Song, MD, PhD; Neal S. Kleiman, MD; Stanley J. Chetcuti, MD; Hector I. Michelena, MD; Abeel A. Mangi, MD; Jeffrey A. Skiles, MD; Jian Huang, MD, MS; Jeffrey J. Popma, MD; Michael J. Reardon, MD

IMPORTANCE The outcomes of transcatheter aortic valve replacement (TAVR) in low-risk patients with bicuspid aortic valve stenosis have not been studied in a large scale, multicentered, prospective fashion.

OBJECTIVE To evaluate the procedural safety, efficacy, and 30-day outcomes of TAVR in patients with bicuspid aortic stenosis at low surgical risk.

DESIGN, SETTING, AND PARTICIPANTS The Low Risk Bicuspid Study is a prospective, single-arm trial study with inclusion/exclusion criteria developed from the Evolut Low Risk Randomized Trial. Follow-up is planned for 10 years. Patients underwent TAVR at 25 centers in the United States who were also participating in the Evolut Low Risk Randomized Trial from December 2018 to October 2019. Eligible patients had severe bicuspid aortic valve stenosis and met American Heart Association/American College of Cardiology guideline indications for aortic valve replacement.

INTERVENTIONS Patients underwent attempted implant of an Evolut or Evolut PRO transcatheter aortic valve, with valve size based on annular measurements.

MAIN OUTCOMES AND MEASURES The prespecified primary end point was the incidence of all-cause mortality or disabling stroke at 30 days. The prespecified primary efficacy end point was device success defined as the absence of procedural mortality, the correct position of 1 bioprosthetic heart valve in the proper anatomical location, and the absence of more than mild aortic regurgitation postprocedure.

RESULTS A total of 150 patients underwent an attempted implant. Baseline characteristics include mean age of 70.3 (5.5) years, 48.0% female (n = 72), and a mean Society of Thoracic Surgeons score of 1.4 (0.6%). Most patients (136; 90.7%) had Sievers type I valve morphology. The incidence of all-cause mortality or disabling stroke was 1.3% (95% CI, 0.3%-5.3%) at 30 days. The device success rate was 95.3% (95% CI, 90.5%-98.1%). At 30 days, the mean (SD) AV gradient was 7.6 (3.7) mm Hg and effective orifice area was 2.3 (0.7) cm^2. A new permanent pacemaker was implanted in 22 patients (15.1%). No patients had greater than mild paravalvular leak.

CONCLUSIONS AND RELEVANCE Transcatheter aortic valve replacement in low-surgical risk patients with bicuspid aortic valve stenosis achieved favorable 30-day results, with low rates of death and stroke and high device success rate.

TRIAL REGISTRATION ClinicalTrials.gov Identifier: NCT03635424

Supplemental content

Author Affiliations: Author affiliations are listed at the end of this article.

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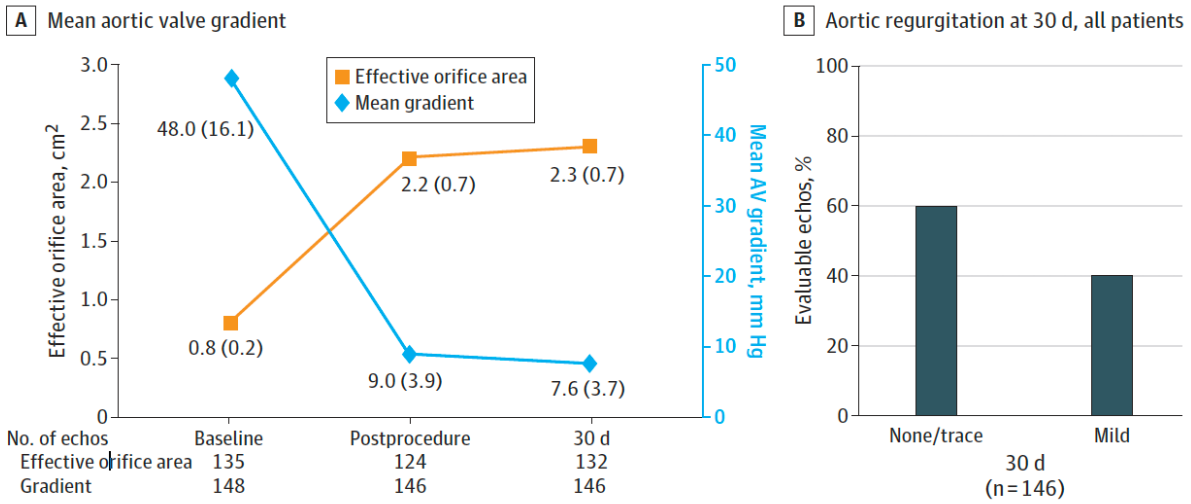
JAMA Cardiol. doi:10.1001/jamacardio.2020.4738
Published online October 7, 2020.



Forrest JK, Ramlawi B, Deeb GM, Zahr F, Song HK, Kleiman NS, Chetcuti SJ, Michelena HI, Mangi AA, Skiles JA, Huang J, Popma JJ, **Reardon MJ** , Transcatheter Aortic Valve Replacement in Low-risk Patients With BicuspidAortic Valve Stenosis., JAMA Cardiol. 2020 Oct 7:e204738. doi: 10.1001PMID: 33031491

BICUSPID TRIAL

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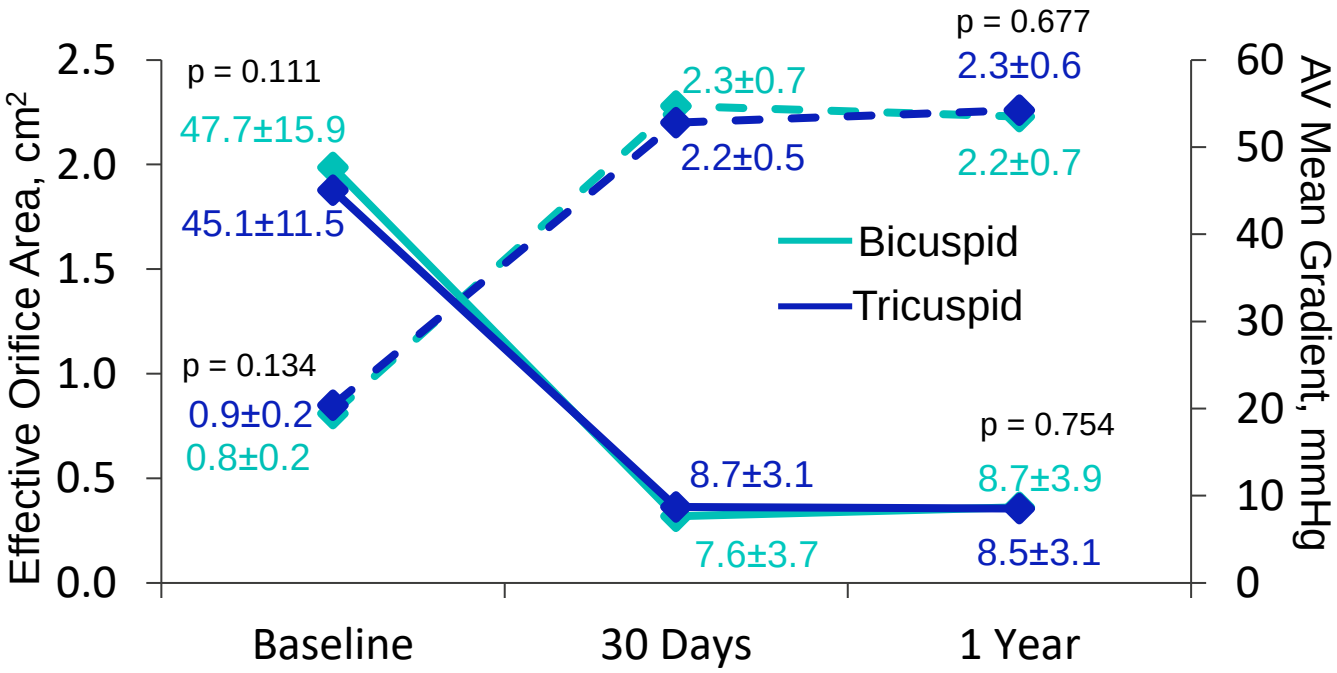
VALVE HEMODYNAMICS

- Core laboratory assessed effective orifice area (EOA) and mean AV gradient.
- Hemodynamics were similar between groups



John Forrest, M.D. TVT 2021

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Age less than 65

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Mean age

Sex

STS PROM

Baseline Patient Characteristics

THE PARTNER 3 TRIAL

% or mean ± SD

Demographics & Vascular Disease	TAVR (N=496)	Surgery (N=454)	Other Co-Morbidities	TAVR (N=496)	Surgery (N=454)
Age (years)	73.3 ± 5.8	73.6 ± 6.1	Diabetes	31.3%	30.2%
Male	67.5%	71.1%	COPD (any)	5.1%	6.2%
BMI – kg/m²	30.7 ± 5.5	30.3 ± 5.1	Pulmonary Hypertension	4.6%	5.3%
STS Score	1.9 ± 0.7	1.9 ± 0.6	Creatinine > 2mg/dL	0.2%	0.2%
NYHA Class III or IV*	31.3%	23.8%	Frailty (overall; > 2/4+)	0	0
Coronary Disease	27.7%	28.0%	Atrial Fibrillation (h/o)	15.7%	18.8%
Prior CABG	3.0%	1.8%	Permanent Pacemaker	2.4%	2.9%
Prior CVA	3.4%	5.1%	Left Bundle Branch Block	3.0%	3.3%
Peripheral Vascular Disease	6.9%	7.3%	Right Bundle Branch Block	10.3%	13.7%

*p = 0.01

Baseline Characteristics

Evolut™ Low Risk Trial

Mean ± SD or %	TAVR (N=725)	SAVR (N=678)
Age, years	74.1 ± 5.8	73.6 ± 5.9
Female sex	36.0	33.8
Body surface area, m²	2.0 ± 0.2	2.0 ± 0.2
STS PROM, %	1.9 ± 0.7	1.9 ± 0.7
NYHA Class III or IV	25.1	28.5
Hypertension	84.8	82.6
Chronic lung disease (COPD)	15.0	18.0
Cerebrovascular disease	10.2	11.8
Peripheral arterial disease	7.5	8.3

There are no significant differences between groups.

7% were < 65 years

6% were < 65 years

1.3% were < 60 years

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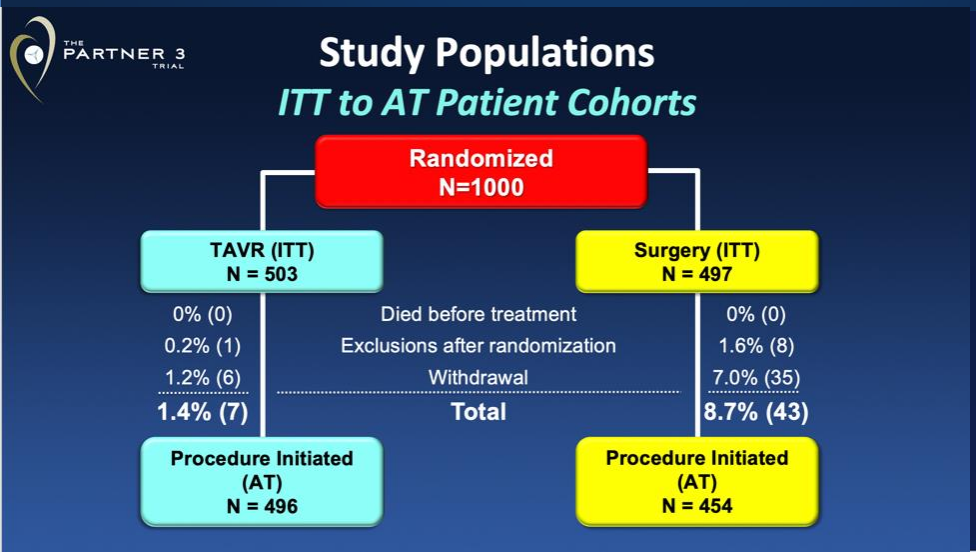
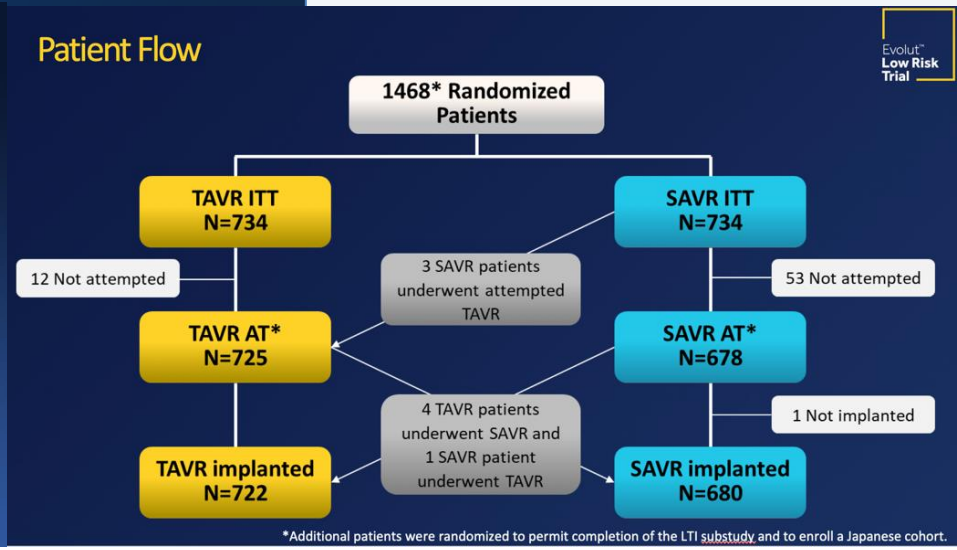
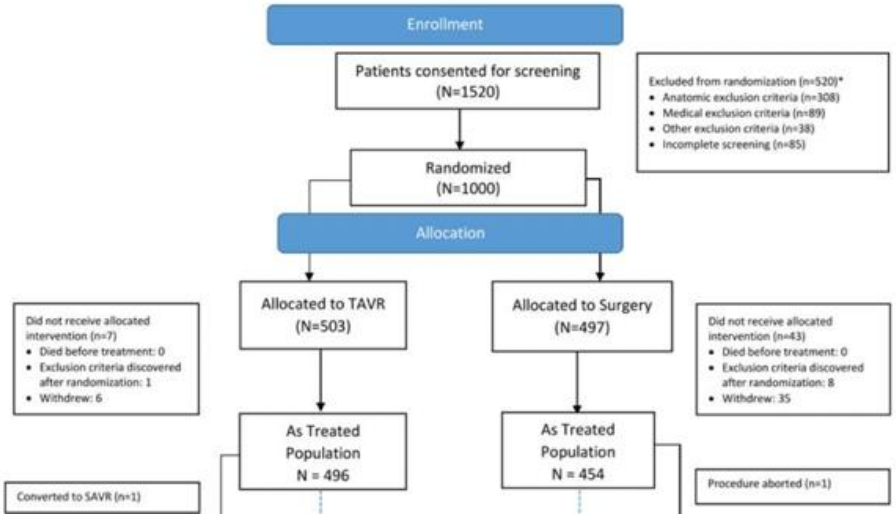
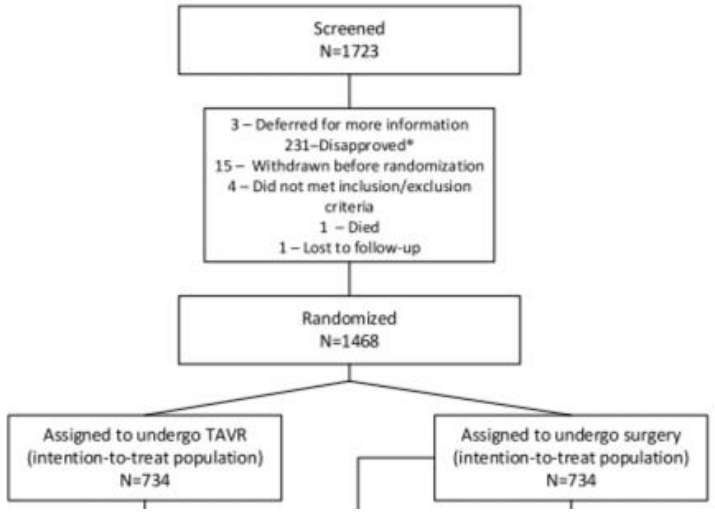






520/1,520 (34%) screen failed



255/1,723 (14.8%) screen failed

Significant CAD exclusion

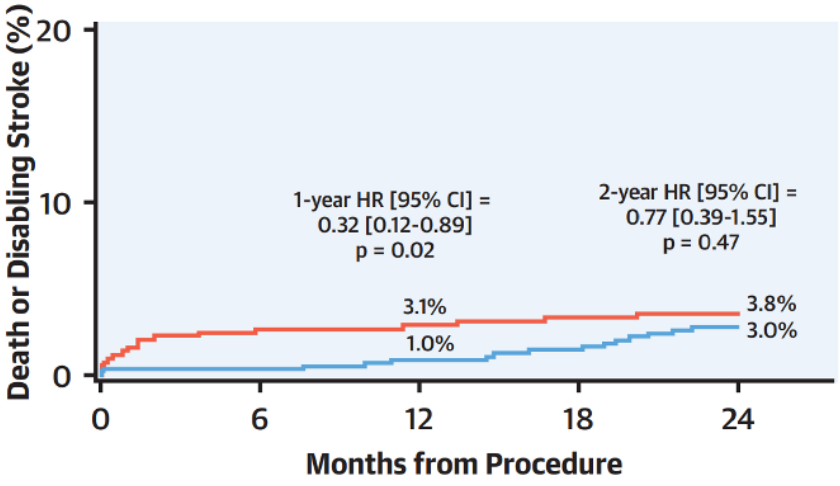
PARTNER III Syntax > 32

Evolut low risk Syntax > 22

Mean Syntax in Evolut was 7

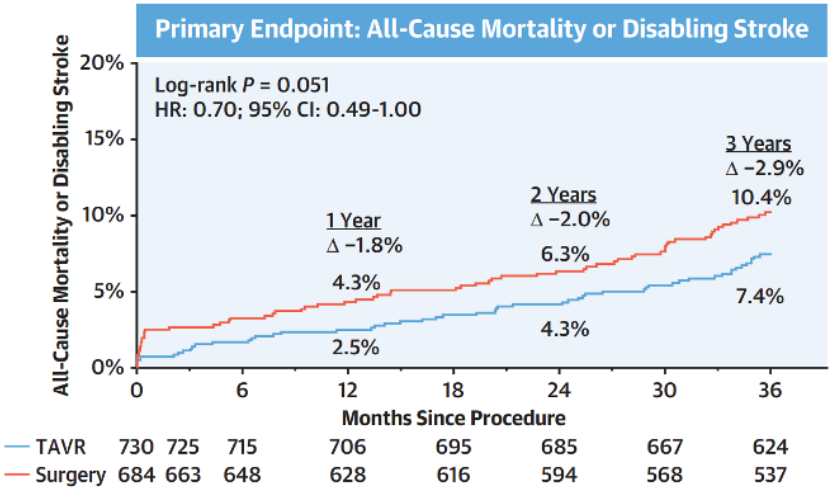
- Low risk studies of more contemporary balloon- and self-expanding valves have reported outcomes at 2 and 3 years, respectively.

PARTNER 3: All-cause mortality or disabling stroke through 2 years



Leon MB, et al. *J Am Coll Cardiol.* 2021;77:1149-1161.

Evolut Low Risk: All-cause mortality or disabling stroke through 3 years



Forrest JK, et al. *J Am Coll Cardiol.* 2023;81:1663-1674.

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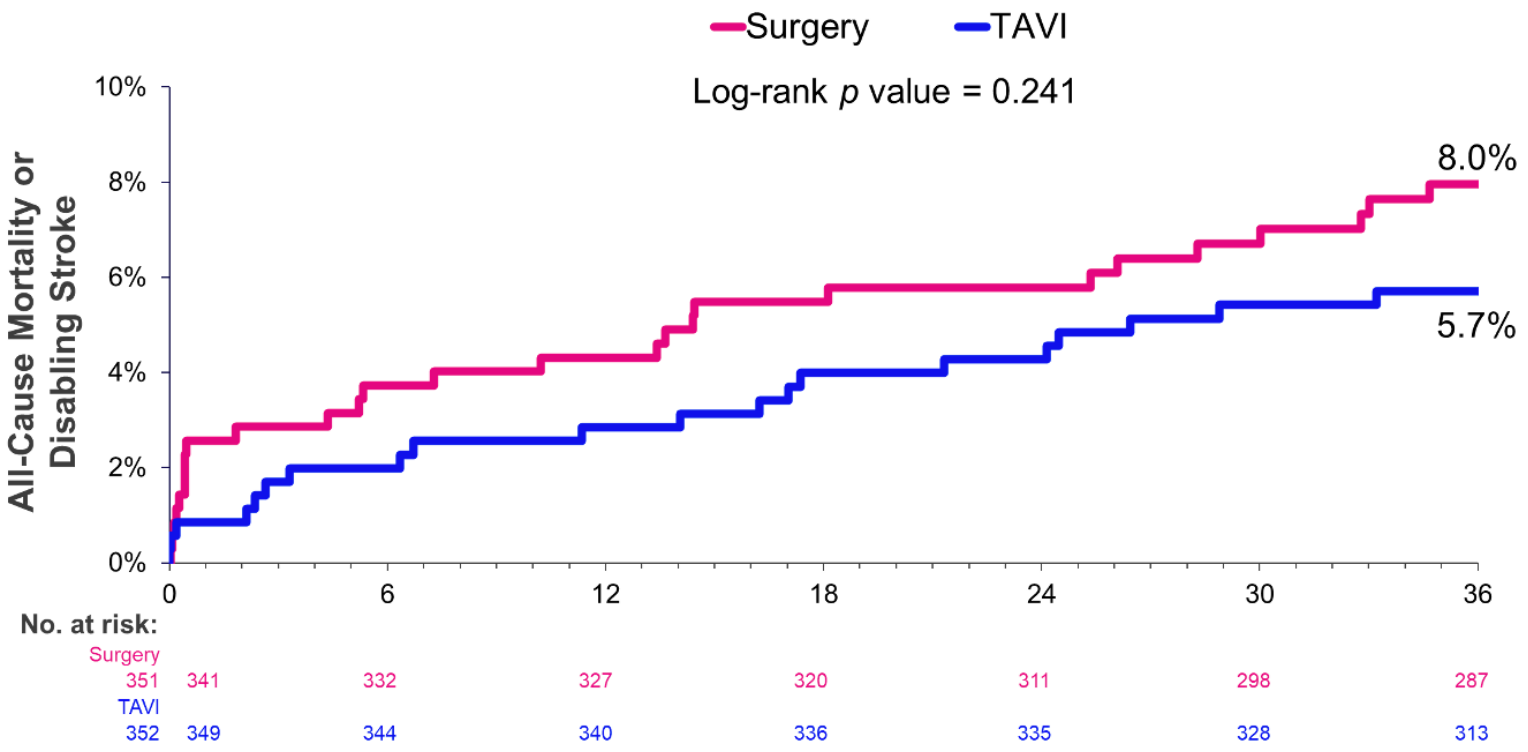
3-Year Outcomes following TAVI in Low Surgical Risk Patients under 75

Primary Endpoint: All-Cause Mortality or Disabling Stroke



Modine T, et al. Three-year outcomes following transcatheter versus surgical aortic valve replacement in low surgical risk patients under 75 years of age Presented at ESC; August 2023.

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TCT October 24

LBCT

Leon Partner 3 5-year data

Reardon Evolut low risk 4-year data

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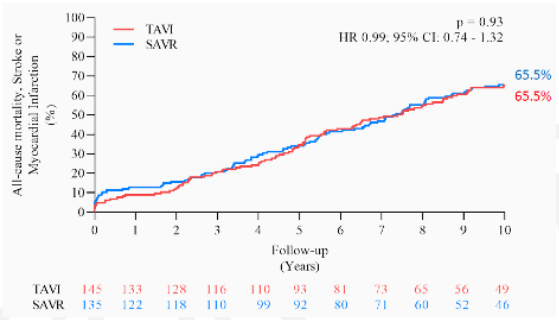
Notion 10 Year

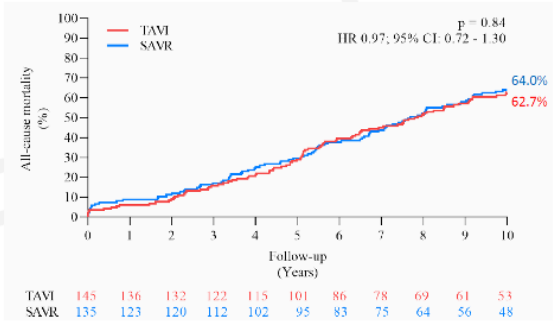
- Long-term data are limited in the low-risk population. Recent 10-year results from the NOTION trial[1] showed similar outcomes with TAVR vs SAVR for the primary endpoint and for all-cause mortality:

Notion 10 Year

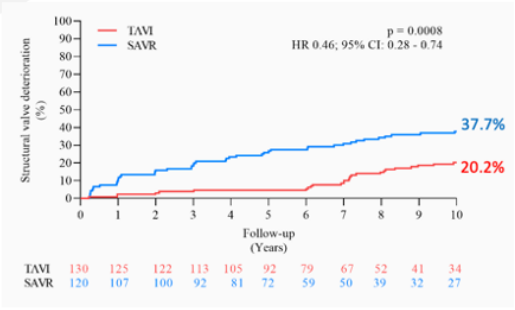
All-cause mortality, stroke, or MI



All-cause mortality



Structural Valve Durability



- However, the NOTION trial used first-generation CoreValves and included a slightly older (mean age, 79 years) and higher risk (mean STS score, ~3.0%) patient population compared with more contemporary studies of lower risk patients.

1. Jorgensen TH, et al. NOTION 10 years. Presented at ESC 2023, Aug 25-28, Amsterdam, Netherlands

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What is coming?

MODERATE AS WITH HF

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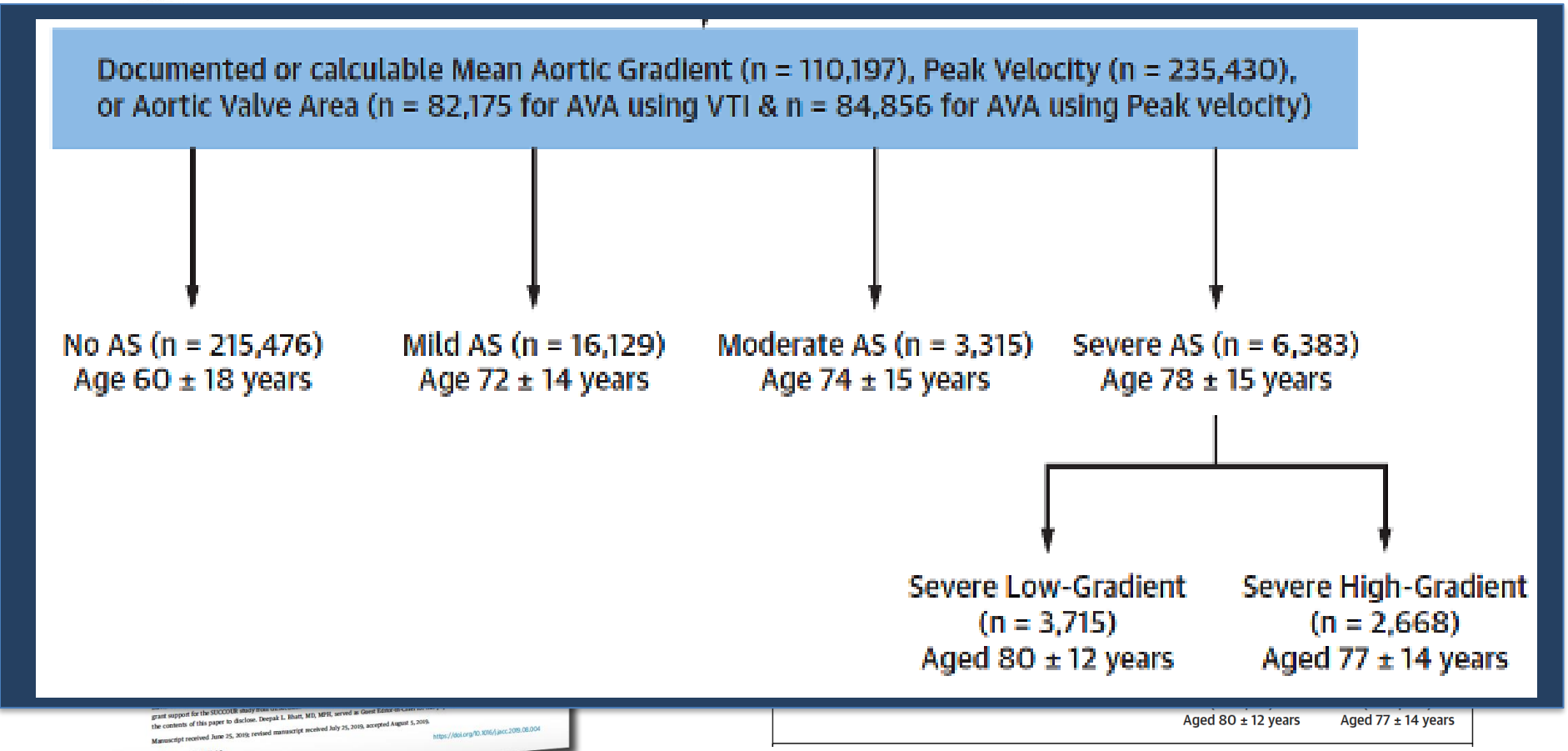

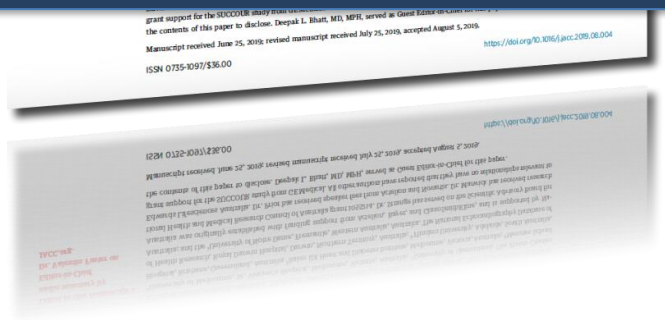

Poor Long-Term Survival in Patients With Moderate Aortic Stenosis.Strange G, Stewart S, Celermajer D, Prior D, Scalia GM, Marwick T, Ilton M, Joseph M, Codde J, Playford D; National Echocardiography Database of Australia contributing sites.J Am Coll Cardiol. 2019 Oct 15;74(15):1851-1863.

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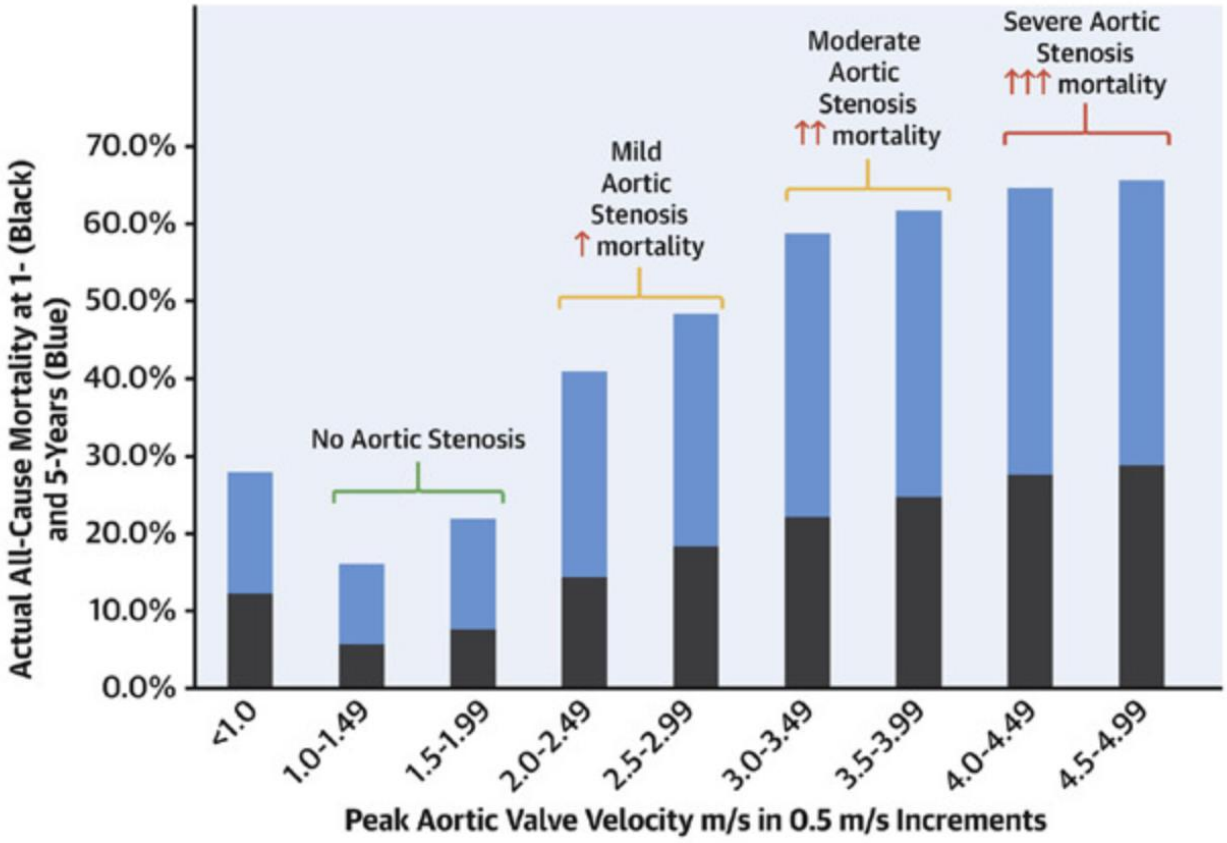
CENTRAL ILLUSTRATION: Moderate Native Valvular Aortic Stenosis and Long-Term Survival: 1- and 5-Year Mortality per Increment in Peak Aortic Valve Velocity



Strange, G. et al. J Am Coll Cardiol. 2019;74(15):1851-63.

MODERATE AS RCTS

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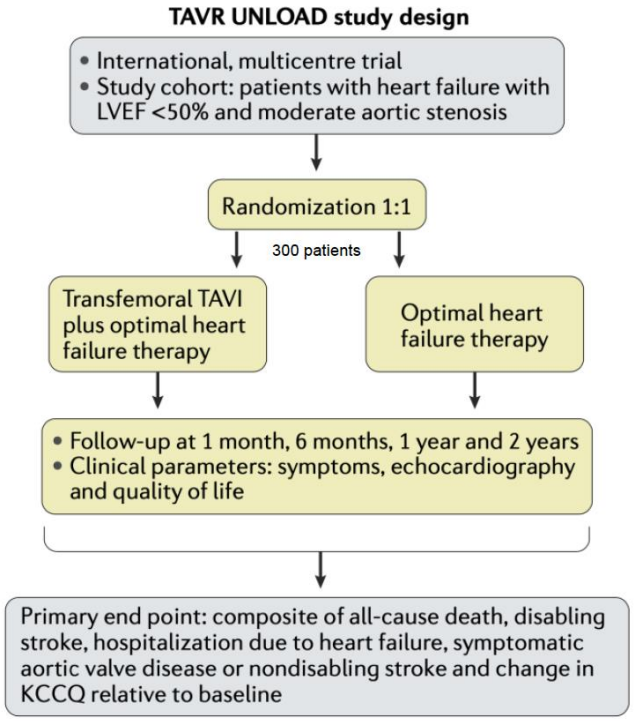
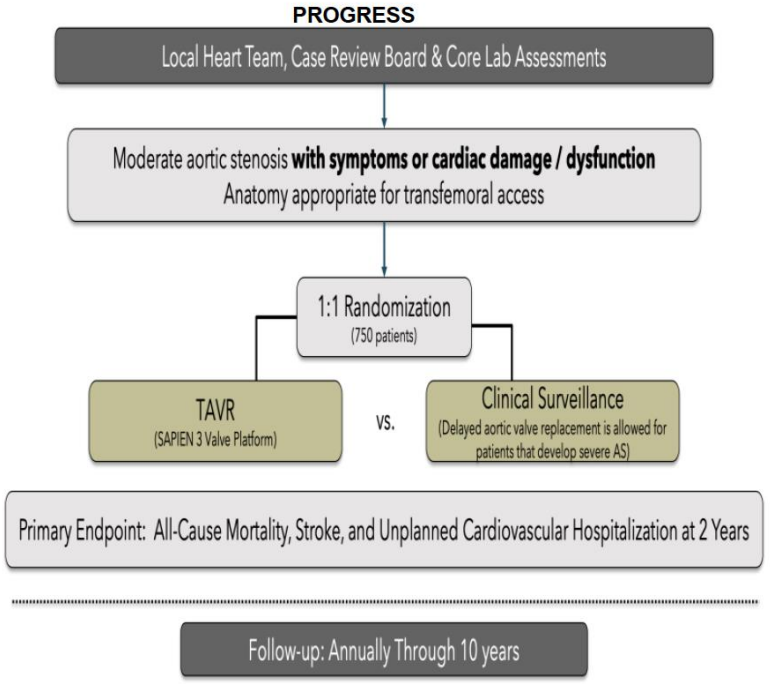
RCTs on TAVI in Moderate AS





ASYMPTOMATIC RCTS

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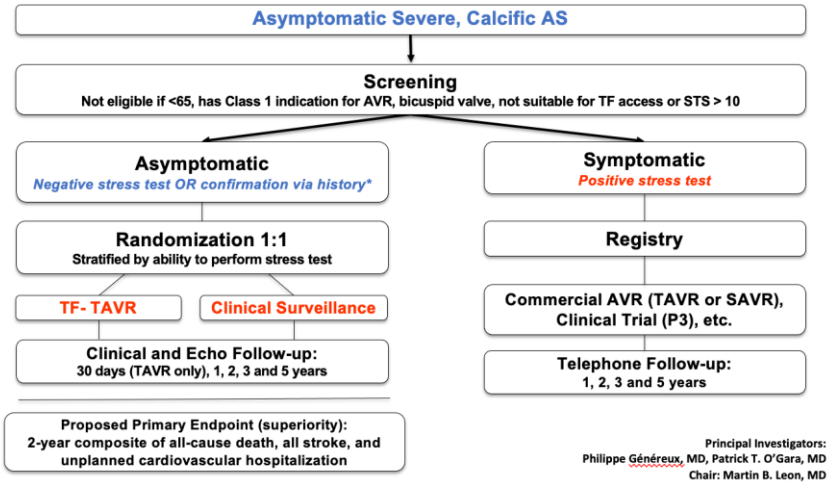
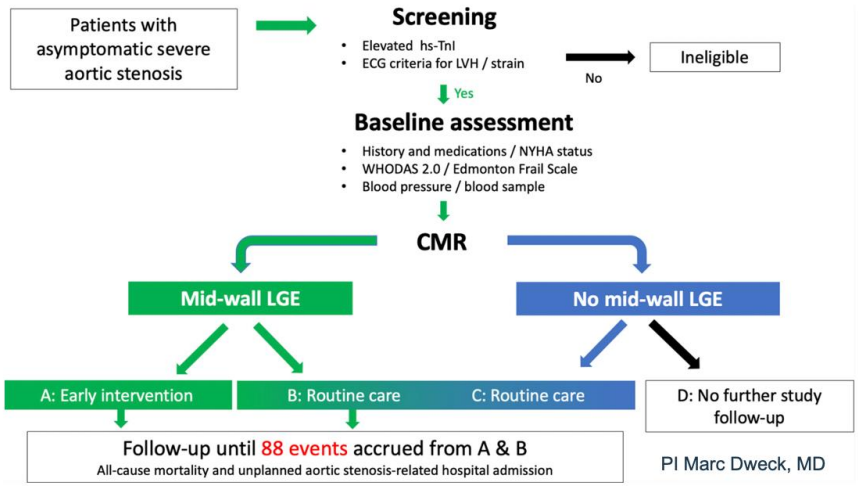
THE EARLY TAVR TRIAL



EVOLVED Trial

~80% SAVR, ~20% TAVR



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Early Surgery or Conservative Care for Asymptomatic Aortic Stenosis

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ABSTRACT

BACKGROUND
The timing and indications for surgical intervention in asymptomatic patients with severe aortic stenosis remain controversial.

METHODS
In a multicenter trial, we randomly assigned 145 asymptomatic patients with very severe aortic stenosis (defined as an aortic-valve area of ≤0.75 cm^2 with either an aortic jet velocity of ≥4.5 m per second or a mean transaortic gradient of ≥50 mm Hg) to early surgery or to conservative care according to the recommendations of current guidelines. The primary end point was a composite of death during or within 30 days after surgery (often called operative mortality) or death from cardiovascular causes during the entire follow-up period. The major secondary end point was death from any cause during follow-up.

RESULTS
In the early-surgery group, 69 of 73 patients (95%) underwent surgery within 2 months after randomization, and there was no operative mortality. In an intention-to-treat analysis, a primary end-point event occurred in 1 patient in the early-surgery group (1%) and in 11 of 72 patients in the conservative-care group (15%) (hazard ratio, 0.09; 95% confidence interval [CI], 0.01 to 0.67; P=0.003). Death from any cause occurred in 5 patients in the early-surgery group (7%) and in 15 patients in the conservative-care group (21%) (hazard ratio, 0.33; 95% CI, 0.12 to 0.90). In the conservative-care group, the cumulative incidence of sudden death was 4% at 4 years and 14% at 8 years.

CONCLUSIONS
Among asymptomatic patients with very severe aortic stenosis, the incidence of the composite of operative mortality or death from cardiovascular causes during the follow-up period was significantly lower among those who underwent early aortic-valve replacement surgery than among those who received conservative care. (Funded by the Korean Institute of Medicine; RECOVERY ClinicalTrials.gov number, NCT01161732.)

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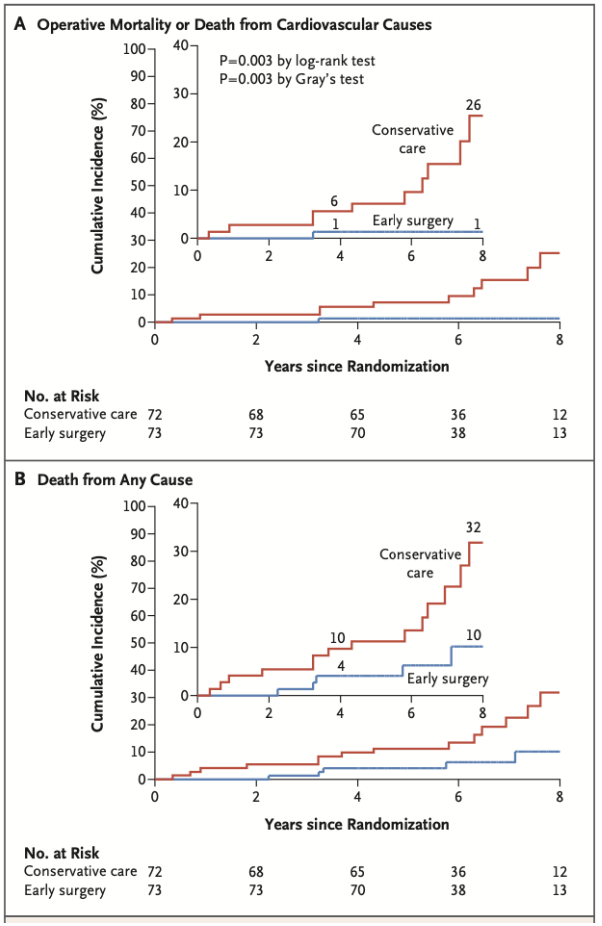

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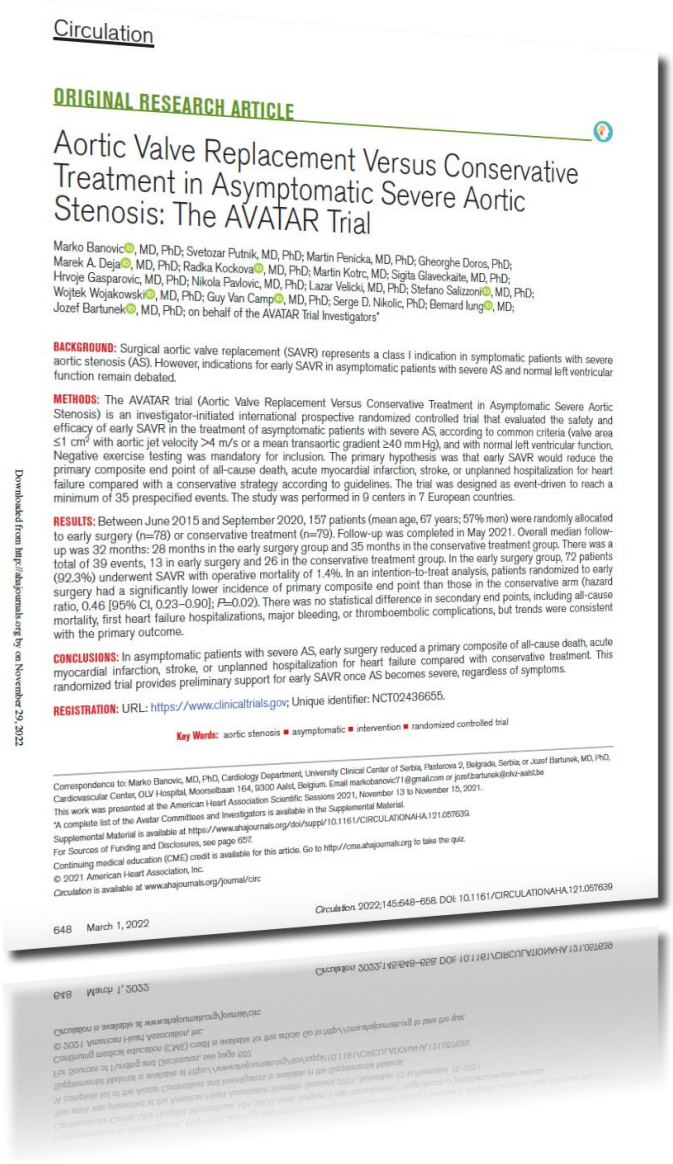

Circulation

ORIGINAL RESEARCH ARTICLE

Aortic Valve Replacement Versus Conservative Treatment in Asymptomatic Severe Aortic Stenosis: The AVATAR Trial

Marko Banovic, MD, PhD; Svetozar Putnik, MD, PhD; Martin Penicka, MD, PhD; Gheorghe Doros, PhD; Marek A. Deja, MD, PhD; Radka Kockova, MD, PhD; Martin Kotrc, MD; Sigita Glaveckaite, MD, PhD; Hrvoje Gasparovic, MD, PhD; Nikola Pavlovic, MD, PhD; Lazar Velicki, MD, PhD; Stefano Salizzoni, MD, PhD; Wojtek Wojakowski, MD, PhD; Guy Van Camp, MD, PhD; Serge D. Nikolic, PhD; Bernard Iung, MD; Jozef Bartunek, MD, PhD; on behalf of the AVATAR Trial Investigators*

BACKGROUND: Surgical aortic valve replacement (SAVR) represents a class I indication in symptomatic patients with severe aortic stenosis (AS). However, indications for early SAVR in asymptomatic patients with severe AS and normal left ventricular function remain debated.

METHODS: The AVATAR trial (Aortic Valve Replacement Versus Conservative Treatment in Asymptomatic Severe Aortic Stenosis) is an investigator-initiated international prospective randomized controlled trial that evaluated the safety and efficacy of early SAVR in the treatment of asymptomatic patients with severe AS, according to common criteria (valve area ≤1 cm^2 with aortic jet velocity >4 m/s or a mean transaortic gradient ≥40 mm Hg), and with normal left ventricular function. Negative exercise testing was mandatory for inclusion. The primary hypothesis was that early SAVR would reduce the primary composite end point of all-cause death, acute myocardial infarction, stroke, or unplanned hospitalization for heart failure compared with a conservative strategy according to guidelines. The trial was designed as event-driven to reach a minimum of 35 prespecified events. The study was performed in 9 centers in 7 European countries.

RESULTS: Between June 2015 and September 2020, 157 patients (mean age, 67 years; 57% men) were randomly allocated to early surgery (n=78) or conservative treatment (n=79). Follow-up was completed in May 2021. Overall median follow-up was 32 months: 28 months in the early surgery group and 35 months in the conservative treatment group. There was a total of 39 events, 13 in early surgery and 26 in the conservative treatment group. In the early surgery group, 72 patients (92.3%) underwent SAVR with operative mortality of 1.4%. In an intention-to-treat analysis, patients randomized to early surgery had a significantly lower incidence of primary composite end point than those in the conservative arm (hazard ratio, 0.46 [95% CI, 0.23–0.90]; *P*=0.02). There was no statistical difference in secondary end points, including all-cause mortality, first heart failure hospitalizations, major bleeding, or thromboembolic complications, but trends were consistent with the primary outcome.

CONCLUSIONS: In asymptomatic patients with severe AS, early surgery reduced a primary composite of all-cause death, acute myocardial infarction, stroke, or unplanned hospitalization for heart failure compared with conservative treatment. This randomized trial provides preliminary support for early SAVR once AS becomes severe, regardless of symptoms.

REGISTRATION: URL: https://www.clinicaltrials.gov; Unique identifier: NCT02436655.

Key Words: aortic stenosis ■ asymptomatic ■ intervention ■ randomized controlled trial

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This work was presented at the American Heart Association Scientific Sessions 2021, November 13 to November 15, 2021.
*A complete list of the Avatar Committees and Investigators is available in the Supplemental Material.
Supplemental Material is available at https://www.ahajournals.org/doi/suppl/10.1161/CIRCULATIONAHA.121.057639.
For Sources of Funding and Disclosures, see page 657.
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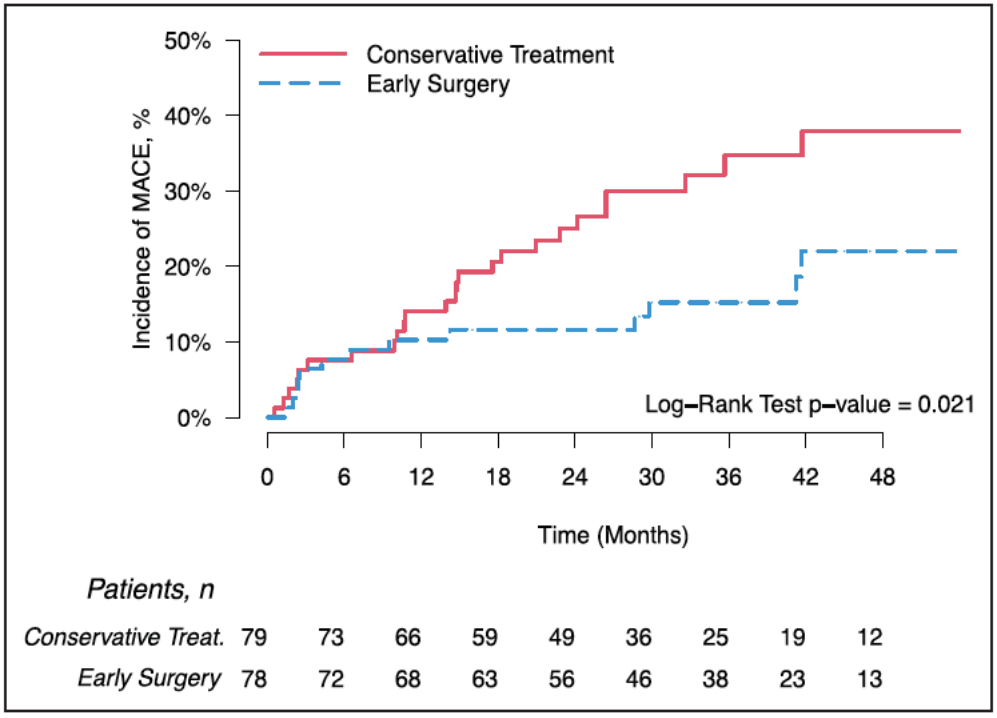

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Align trial TCT 2023
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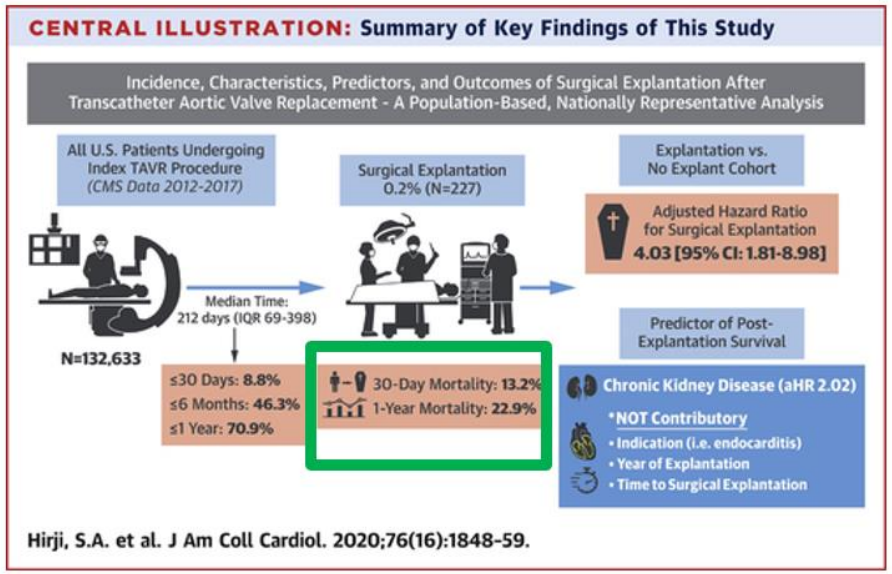
SURGICAL EXPLANT DATA

Associated with high 30-day operative mortality 10-13%



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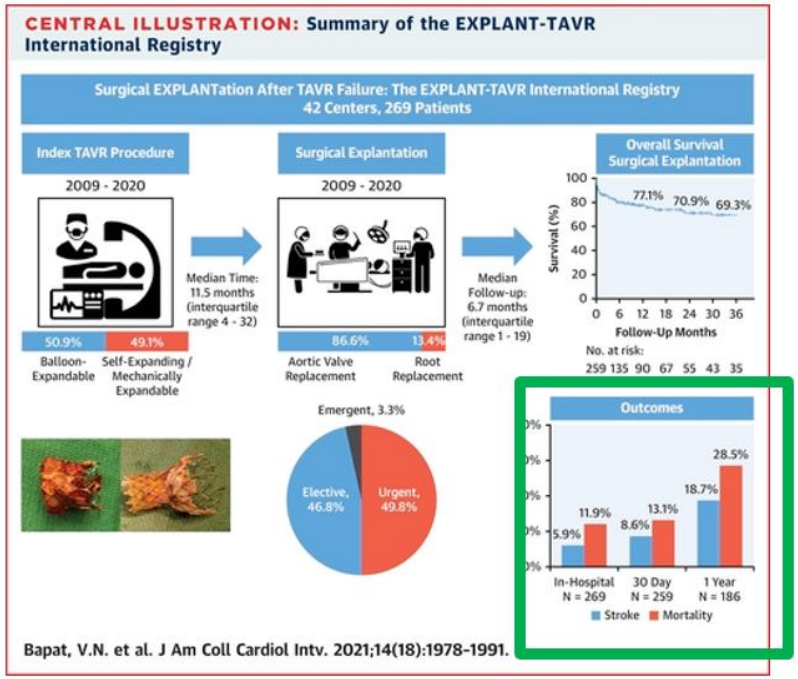

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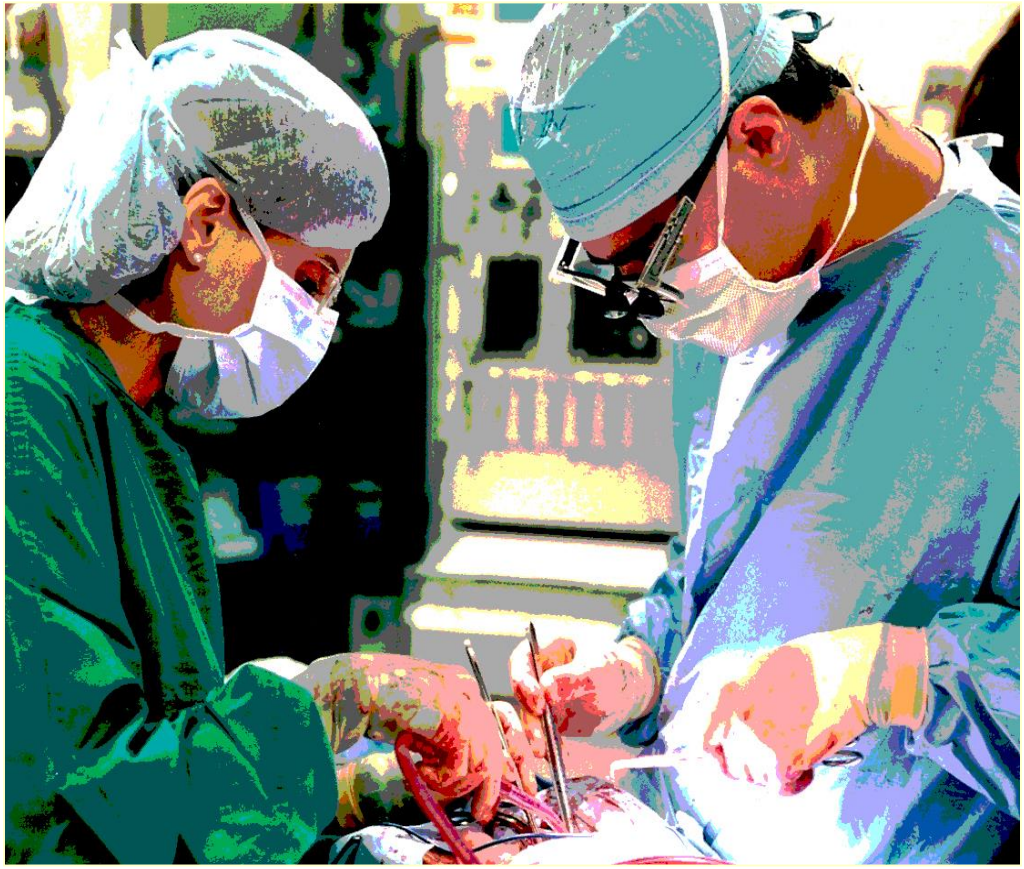

Thank You