

Severe Aortic Stenosis With No Symptoms

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Disclosures

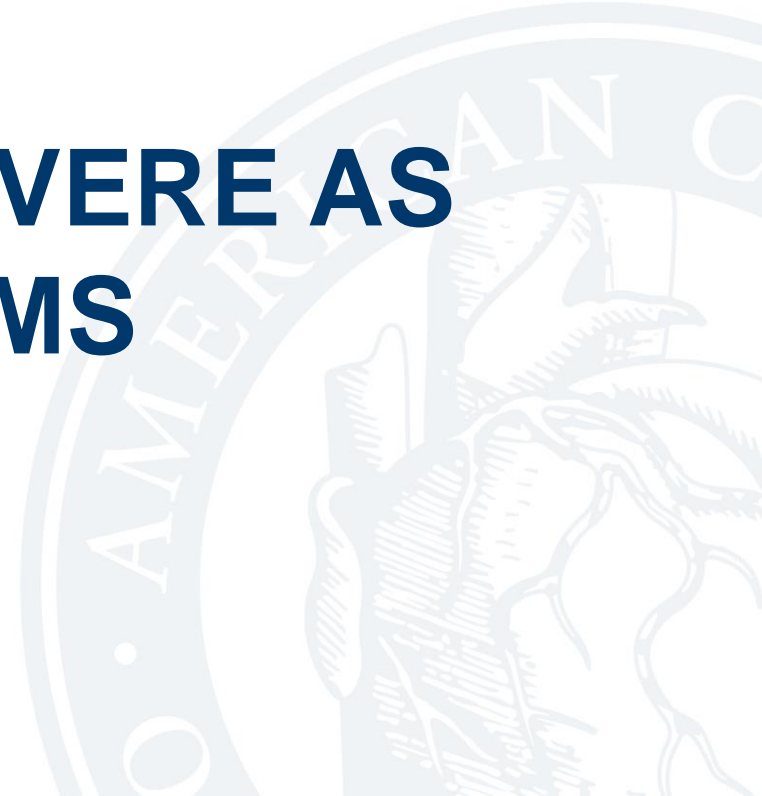
Abbott Vascular: Consultant, advisor, speaker Fees; Abiomed: Consultant, advisor, speaker fees; BioTrace Medical: Consultant, advisor, speaker Fees; Boston Scientific: Consultant; Cardiovascular System Inc.: Consultant, PI Eclipse Trial; Edwards LifeSciences: Consultant, advisor, speaker fees, proctor, research grant, PI EARLY-TAVR trial, PI PROGRESS trial; GE Healthcare: Consultant; iRythm Technologies: Consultant; Medtronic: Consultant, advisor, speaker fees; OpSens: Consultant; Pi-Cardia: Equity, consultant; Puzzle Medical: Equity, consultant; Saranas: Equity, consultant; Shockwave: Consultant, speaker fees; Siemens: Consultant; Soundbite Medical Inc.: Equity, consultant; Teleflex: Consultant; 4C Medical: Consultant, PI Feasibility study

Severe AS No Symptoms: Agenda

- Definition
- How to take a medical history
- Role of Stress Test
- Management 2020 Guidelines Updates
- Literature update and Ongoing Trials



DEFINITION OF SEVERE AS WITH NO SYMPTOMS



CLINICAL PRACTICE GUIDELINE: FULL TEXT

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



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

Developed in collaboration with and endorsed by 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

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†ACC/AHA Joint Committee on Clinical Practice Guidelines Liaison.

Severe AS with No Symptoms

TABLE 13 Stages of AS

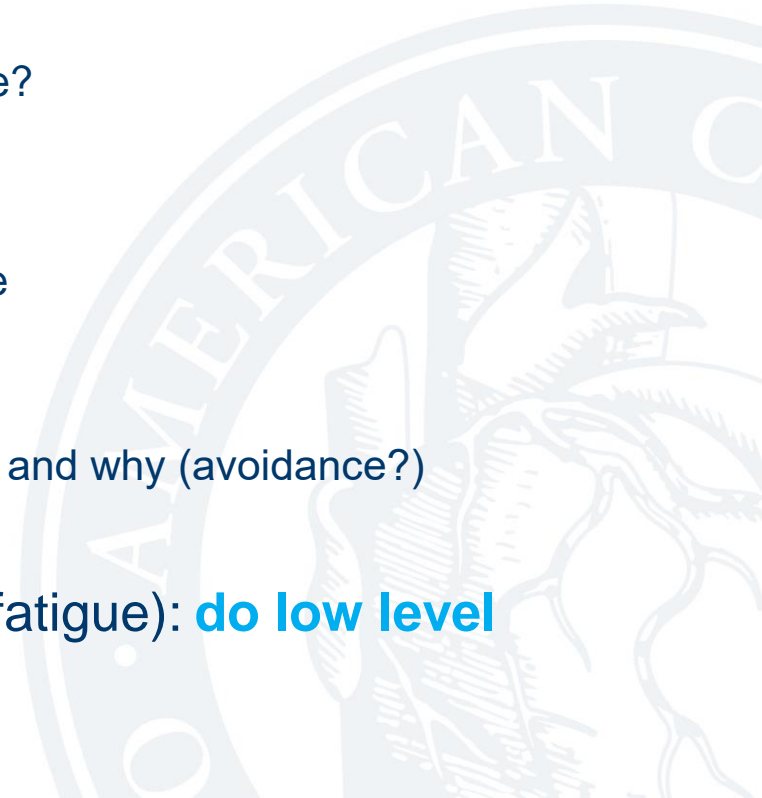
Stage	Definition	Valve Anatomy	Valve Hemodynamics	Hemodynamic Consequences	Symptoms
C: Asymptomatic severe AS					
C1	Asymptomatic severe AS	Severe leaflet calcification/fibrosis or congenital stenosis with severely reduced leaflet opening	<ul style="list-style-type: none"> ■ Aortic $V_{\max} \geq 4$ m/s or mean $\Delta P \geq 40$ mm Hg ■ AVA typically is ≤ 1.0 cm² (or AVAi 0.6 cm²/m²) but not required to define severe AS ■ Very severe AS is an aortic $V_{\max} \geq 5$ m/s or mean $P \geq 60$ mm Hg 	<ul style="list-style-type: none"> ■ LV diastolic dysfunction ■ Mild LV hypertrophy ■ Normal LVEF 	<ul style="list-style-type: none"> ■ None ■ Exercise testing is reasonable to confirm symptom status
C2	Asymptomatic severe AS with LV systolic dysfunction	Severe leaflet calcification/fibrosis or congenital stenosis with severely reduced leaflet opening	<ul style="list-style-type: none"> ■ Aortic $V_{\max} \geq 4$ m/s or mean $\Delta P \geq 40$ mm Hg ■ AVA typically ≤ 1.0 cm² (or AVAi 0.6 cm²/m²) but not required to define severe AS 	LVEF <50%	None

**TAKING MEDICAL HISTORY OF
PATIENTS WITH SEVERE AS
AND NO SYMPTOMS**

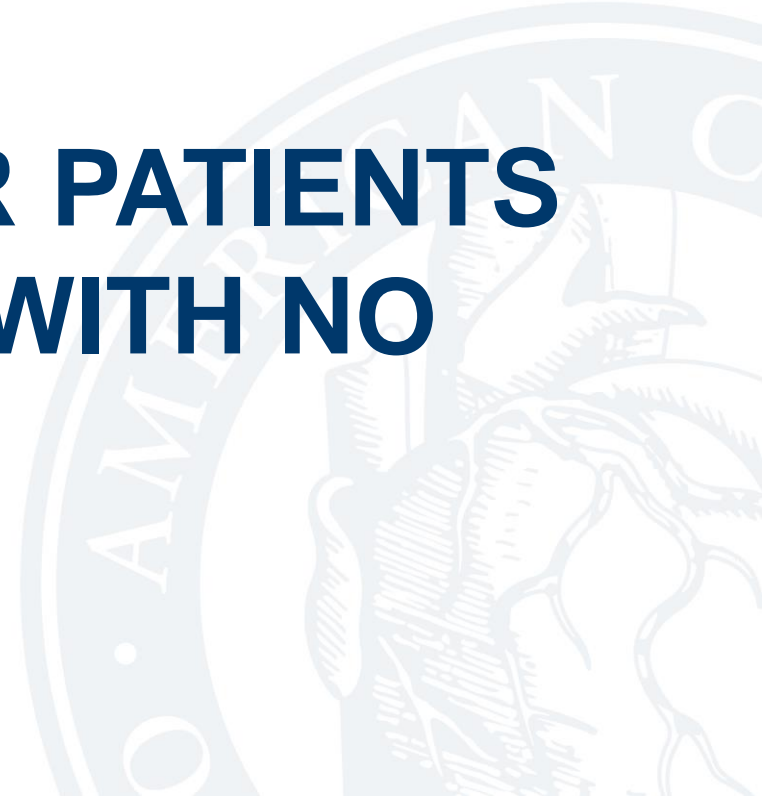


Taking Medical History of Patients with Severe AS and No Symptoms

- **Start with open questions**
 - What do you know about your heart valve issue?
 - How have you been feeling lately?
- **Then be more specific**
 - Ask about dyspnea, angina, dizziness, syncope
 - Ask to compare to 6-12 months ago
 - Ask if they slow down
 - Ask about activities that they don't do anymore and why (avoidance?)
- **Ask a family member**
- If no symptoms or vague symptoms (i.e. fatigue): **do low level stress test**



STRESS TEST FOR PATIENTS WITH SEVERE AS WITH NO SYMPTOMS



Exercise Testing Severe AS

Recommendations for Diagnostic Testing: Exercise Testing in Patients With AS

Referenced studies that support the recommendations are summarized in [Online Data Supplement 4](#).

COR	LOE	RECOMMENDATIONS
2a	B-NR	1. In asymptomatic patients with severe AS (Stage C1), exercise testing is reasonable to assess physiological changes with exercise and to confirm the absence of symptoms (1–4).
3: Harm	B-NR	2. In symptomatic patients with severe AS (Stage D1, aortic velocity ≥ 4.0 m/s or mean pressure gradient ≥ 40 mm Hg), exercise testing should not be performed because of the risk of severe hemodynamic compromise. (5)

How to do a Treadmill Stress Test for Severe AS Patients with No Symptoms?

- 1) Choose the *appropriate Treadmill Stress test protocol based on age and sex-gender* maximal predicted METs
- 2) Do it under close medical supervision
- 3) Stop the test when symptoms, drop of blood pressure, or arrhythmias occurred

Treadmill Stress Test: Limiting Dyspnea or Fatigue

Expected METs Adjusted for Age and Gender

Male

$18 - [0.15 \times \text{Age}]$

Female

$14.7 - [0.13 \times \text{Age}]$

Abnormal Treadmill Stress Test if ***test limiting***
dyspnea or fatigue (at **$\leq 60\%$ of Expected METs?***)

*Criteria use in the EARLY TAVR trial

Expected METs Adjusted for Age and Gender

Female		
Age	Expected METs	60% Expected METs
65	6.3	3.8
66	6.1	3.7
67	6.0	3.6
68	5.9	3.5
69	5.7	3.4
70	5.6	3.4
71	5.5	3.3
72	5.3	3.2
73	5.2	3.1
74	5.1	3.0
75	5.0	3.0
76	4.8	2.9
77	4.7	2.8
78	4.6	2.7
79	4.4	2.7
80	4.3	2.6
81	4.2	2.5
82	4.0	2.4
83	3.9	2.3
84	3.8	2.3
85	3.7	2.2
86	3.5	2.1
87	3.4	2.0
88	3.3	2.0
89	3.1	1.9
90	3.0	1.8
91	2.9	1.7
92	2.7	1.6
93	2.6	1.6
94	2.5	1.5
95	2.4	1.4
96	2.2	1.3
97	2.1	1.3
98	2.0	1.2
99	1.8	1.1
100	1.7	1.0

Male		
Age	Expected METs	60% Expected METs
65	8.3	5.0
66	8.1	4.9
67	8.0	4.8
68	7.8	4.7
69	7.7	4.6
70	7.5	4.5
71	7.4	4.4
72	7.2	4.3
73	7.1	4.2
74	6.9	4.1
75	6.8	4.1
76	6.6	4.0
77	6.5	3.9
78	6.3	3.8
79	6.2	3.7
80	6.0	3.6
81	5.9	3.5
82	5.7	3.4
83	5.6	3.3
84	5.4	3.2
85	5.3	3.2
86	5.1	3.1
87	5.0	3.0
88	4.8	2.9
89	4.7	2.8
90	4.5	2.7
91	4.4	2.6
92	4.2	2.5
93	4.1	2.4
94	3.9	2.3
95	3.8	2.3
96	3.6	2.2
97	3.5	2.1
98	3.3	2.0
99	3.2	1.9
100	3.0	1.8

*Criteria use in the EARLY TAVR trial

Treadmill Stress Test Protocols

- Protocol selection based on patient profile

- Modified Bruce Protocol (default)
- Naughton Protocol (~older, sedentary)
- Bruce Protocol (~young, active)

Modified Bruce Protocol 3-minute stages			
Stage	Speed	Incline Grade	METs
1	1.7 mph	0.0%	2
2	1.7 mph	5.0%	3
3	1.7 mph	10.0%	5
4	2.5 mph	12.0%	7
5	3.4 mph	14.0%	10
6	4.2 mph	16.0%	13
7	5.0 mph	18.0%	15
8	5.5 mph	20.0%	18
9	6.0 mph	22.0%	20

Naughton Protocol 2-minute stages			
Stage	Speed	Incline Grade	METs
1	1.0 mph	0.0%	2
2	2.0 mph	0.0%	3
3	2.0 mph	3.5%	5
4	2.0 mph	7.0%	6
5	2.0 mph	10.5%	7
6	2.0 mph	14.0%	8
7	2.0 mph	17.5%	10
8	3.0 mph	12.5%	11
9	3.0 mph	15.0%	13
10	3.0 mph	17.5%	14
11	3.0 mph	20.0%	15

Bruce Protocol, Standard 3-minute stages			
Stage	Speed	Incline Grade	METs
1	1.7 mph	10.0%	5
2	2.5 mph	12.0%	7
3	3.4 mph	14.0%	10
4	4.2 mph	16.0%	13
5	5.0 mph	18.0%	15
6	5.5 mph	20.0%	18
7	6.0 mph	22.0%	20

Note: METs, metabolic equivalents of task

What Represents a Positive Stress Test?

Usual criteria for Abnormal stress test:

- 1) **Limiting** symptoms (Angina-dyspnea-severe dizziness-syncope)
- 2) **Fall of >10mmhg of systolic blood pressure** from baseline to peak exercise (or lack of increase [$<20\text{mmhg}$] in SBP during exercise)
- 3) **Significant ventricular arrhythmias** (>3 consecutive ventricular premature beats)
- 4) $>2\text{mm}$ (vs. 5mm) ST-segment depression?

Male		
Age	Expected METs	60% Expected METs
78	6.3	3.8

78 yo Male
Severe AS
AVA 0.7cm²
PV 440 cm/s
LVEF 65%

ECG
sinus rhythm 70 bpm

NT Pro BNP 67

Modified Bruce protocol
Negative



Modified Bruce Protocol 3-minute stages			
Stage	Speed	Incline Grade	METs
1	1.7 mph	0.0%	2
2	1.7 mph	5.0%	3
3	1.7 mph	10.0%	5
4	2.5 mph	12.0%	7
5	3.4 mph	14.0%	10
6	4.2 mph	16.0%	13
7	5.0 mph	18.0%	15
8	5.5 mph	20.0%	18
9	6.0 mph	22.0%	20

*video used with permissions

Case Review: 87 yr old Female

History

S/p bladder cancer treated 10 yr ago

Osteoporosis

Intermediate risk based on Age/Frailty

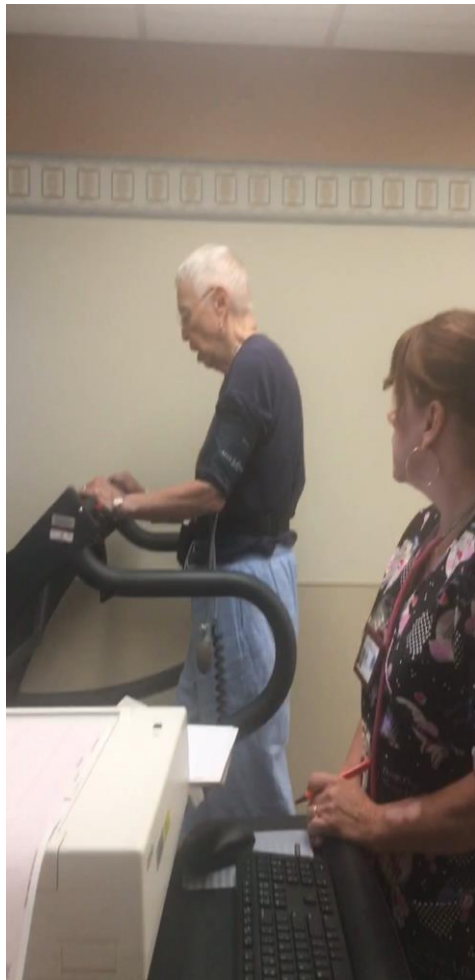
Naughton Protocol 2-minute stages			
Stage	Speed	Incline Grade	METs
1	1.0 mph	0.0%	2
2	2.0 mph	0.0%	3
3	2.0 mph	3.5%	5
4	2.0 mph	7.0%	6
5	2.0 mph	10.5%	7
6	2.0 mph	14.0%	8
7	2.0 mph	17.5%	10
8	3.0 mph	12.5%	11
9	3.0 mph	15.0%	13
10	3.0 mph	17.5%	14
11	3.0 mph	20.0%	15

Female		
Age	Expected METs	60% Expected METs
87	3.4	2.0

Treadmill Stress Test (TST) Summary:

- Baseline blood pressure: 130 / 60 mmHg
- Maximal blood pressure: 160 / 70 mmHg
- Overall condition:
 - Dizziness: No
 - Chest pain: No
 - Shortness of breath: No
 - Drop in SBP: No
 - Stress arrhythmias or conduction abnormalities: No

Naughton Stage 1



Female			
Age	Expected METs	60% Expected METs	
87	3.4	2.0	
Naughton Protocol 2-minute stages			
Stage	Speed	Incline Grade	METs
1	1.0 mph	0.0%	2
2	2.0 mph	0.0%	3
3	2.0 mph	3.5%	5
4	2.0 mph	7.0%	6
5	2.0 mph	10.5%	7
6	2.0 mph	14.0%	8
7	2.0 mph	17.5%	10
8	3.0 mph	12.5%	11
9	3.0 mph	15.0%	13
10	3.0 mph	17.5%	14
11	3.0 mph	20.0%	15

*video used with permissions

Naughton Stage 2



Abnormal Stress Test in Asx AS

	Moderate-Severe AS			Severe AS only		
	% Abnormal Stress Test	n	N	% Abnormal Stress Test	n	N
Takeda et al. 2001	27%	13	49			
Amato et al. 2001				67%	44	66
Alborino et al. 2002	60%	18	30			
Das et al. 2003	29%	19	65			

Abnormal Stress Test in Asx Severe AS:

~50% Abnormal Stress Test

Marechaux et al. 2010	27%	51	186			
Rajani et al. 2010	15%	3	20	39%	7	18
Donal et al. 2011	33%	69	207			
Levy et al. 2014				28%	12	43
Total		286	784		212	434

% Abnormal Stress test

Range: 15-66%

Pooled: 36.5%

Range: 28-67%

Pooled: 48.8%

Meta-Analysis of Prognostic Value of Stress Testing in Patients With Asymptomatic Severe Aortic Stenosis

Asim M. Rafique, MD^a, Simon Biner, MD^{a,b}, Indraneil Ray, MD^a, James S. Forrester, MD^a, Kirsten Tolstrup, MD^a, and Robert J. Siegel, MD^{a,*}

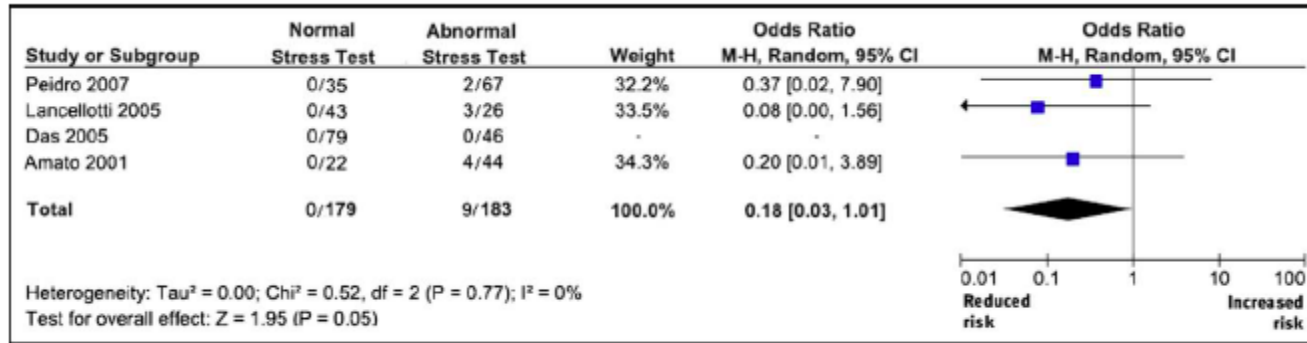
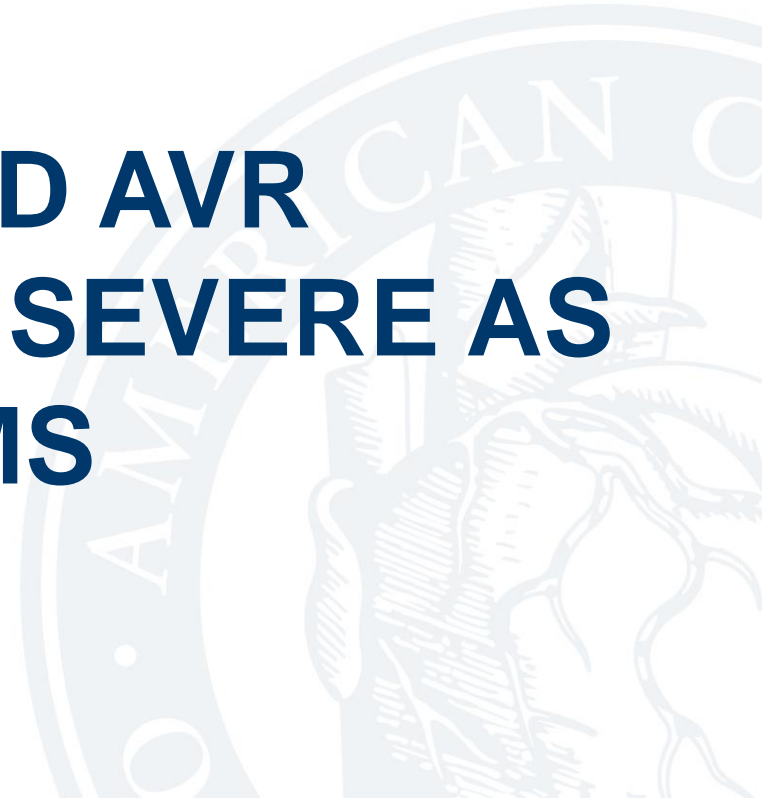


Figure 3. Pooled outcome estimates of risk for sudden cardiac death. None of the patients with normal stress test results experienced sudden death. Squares represent effect sizes; extended lines indicate 95% CIs; diamond represents total effect size.

**Abnormal stress test associated with
~6 fold increase in Cardiac Death**

MANAGEMENT AND AVR INDICATIONS FOR SEVERE AS AND NO SYMPTOMS



AVR for Severe AS no Sx

3 Class 1

4 Class 2a

1 Class 2b

COR	LOE	RECOMMENDATIONS
1	A	1. In adults with severe high-gradient AS (Stage D1) and symptoms of exertional dyspnea, HF, angina, syncope, or presyncope by history or on exercise testing, AVR is indicated (74-80).
1	B-NR	2. In asymptomatic patients with severe AS and an LVEF <50% (Stage C2), AVR is indicated (81-84).
1	B-NR	3. In asymptomatic patients with severe AS (Stage C1) who are undergoing cardiac surgery for other indications, AVR is indicated (57,63,85-87).
1	B-NR	4. In symptomatic patients with low-flow, low-gradient severe AS with reduced LVEF (Stage D2), AVR is recommended (88-95).
1	B-NR	5. In symptomatic patients with low-flow, low-gradient severe AS with normal LVEF (Stage D3), AVR is recommended if AS is the most likely cause of symptoms (96-98).
2a	B-NR	6. In apparently asymptomatic patients with severe AS (Stage C1) and low surgical risk, AVR is reasonable when an exercise test demonstrates decreased exercise tolerance (normalized for age and sex) or a fall in systolic blood pressure of ≥ 10 mm Hg from baseline to peak exercise (61,63,64,99).
2a	B-R	7. In asymptomatic patients with very severe AS (defined as an aortic velocity of ≥ 5 m/s) and low surgical risk, AVR is reasonable (86,100-104).
2a	B-NR	8. In apparently asymptomatic patients with severe AS (Stage C1) and low surgical risk, AVR is reasonable when the serum B-type natriuretic peptide (BNP) level is >3 times normal (101,105-107).
2a	B-NR	9. In asymptomatic patients with high-gradient severe AS (Stage C1) and low surgical risk, AVR is reasonable when serial testing shows an increase in aortic velocity ≥ 0.3 m/s per year (108,109).
2b	B-NR	10. In asymptomatic patients with severe high-gradient AS (Stage C1) and a progressive decrease in LVEF on at least 3 serial imaging studies to $<60\%$, AVR may be considered (81-84,102).
2b	C-EO	11. In patients with moderate AS (Stage B) who are undergoing cardiac surgery for other indications, AVR may be considered.

LITERATURE UPDATE AND ONGOING TRIALS



Natural History, Diagnostic Approaches, and Therapeutic Strategies for Patients With Asymptomatic Severe Aortic Stenosis



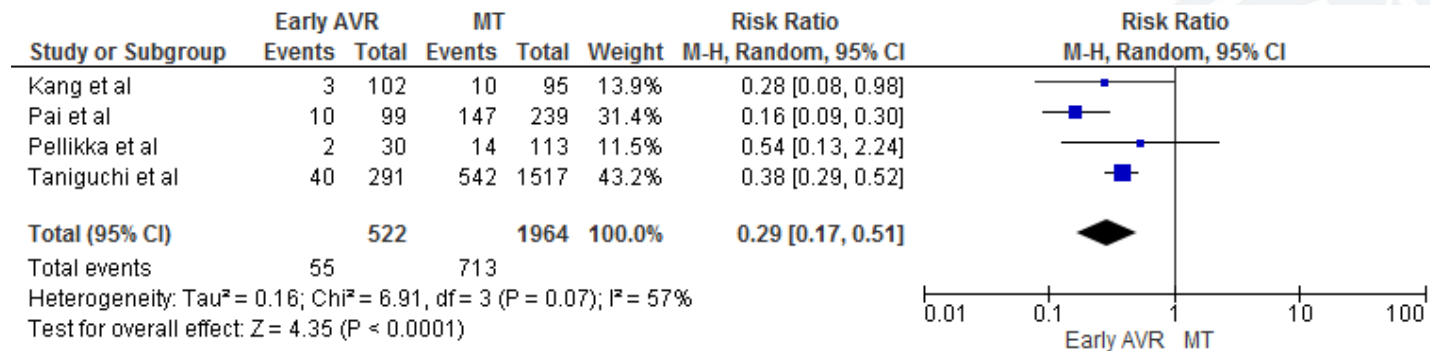
Philippe G n reux, MD,^{a,b,c} Gregg W. Stone, MD,^{a,b} Patrick T. O'Gara, MD,^d Guillaume Marquis-Gravel, MD,^c Bj rn Redfors, MD, PhD,^{b,e} Gennaro Giustino, MD,^f Philippe Pibarot, DVM, PhD,^g Jeroen J. Bax, MD, PhD,^h Robert O. Bonow, MD,ⁱ Martin B. Leon, MD^{a,b}

Studies Comparing AVR vs. Observation in Asymptomatic Severe AS Patients; N=2,486


Authors	AS definition	N	Age	Female	Follow-up (median)
Pellikka et al. 1990	Severe AS; Doppler PV ≥ 4 m/s	143 30 AVR 113 Medical	72 (mean) 40 to 94	38%	AVR 21 m Medical 20 m
Pai et al. 2006	Severe AS AVA < 0.8 cm ²	338 99 AVR 239 Medical	71 ± 15	49%	3.5 y
Kang et al. 2010	Very severe AS AVA ≤ 0.75 cm ² AND PV ≥ 4.5 m/s or a MG ≥ 50 mmHg	197: 102 AVR 95 Medical	63 ± 12	50%	AVR 1265 d Medical 1769 d
Taniguchi et al. 2015	Severe AS AVA: < 1 cm ² MG: > 40 mmHg PV: > 4 m/s	1808: 291 AVR 1517 Medical	AVR 71.6 ± 8.7 Medical 77.8 ± 9.4	60%	1361 d

All-Cause Mortality

AVR vs. Medical Therapy in Asymptomatic Severe AS; N=2,486



Unadjusted: ~3.5 fold increase in all-cause Mortality



Research

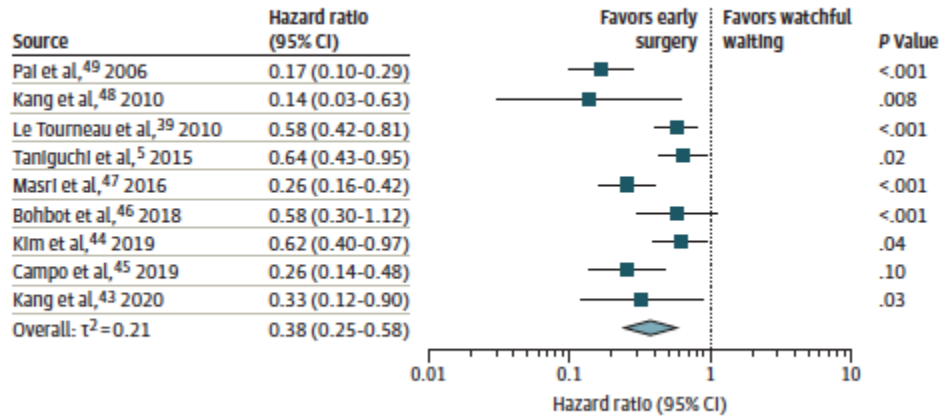
JAMA Cardiology | **Original Investigation**

Natural History of Asymptomatic Severe Aortic Stenosis and the Association of Early Intervention With Outcomes A Systematic Review and Meta-Analysis

Brigitta Gahl, PhD; Mevlüt Çelik, MD; Stuart J. Head, MD, PhD; Jean-Louis Vanoverschelde, MD, PhD;
Philippe Pibarot, DVM, PhD; Michael J. Reardon, MD; Nicolas M. van Mieghem, MD, PhD;
A. Pieter Kappetein, MD, PhD; Peter Jüni, MD; Bruno R. da Costa, PhD

9 studies; 3904 patients; median FU of 5.0 (3.7-5.7) years
~2.5 x Increase in Mortality with Clinical Surveillance

Figure 3. Meta-analysis on All-Cause Mortality of Surgery vs an Initial Conservative Treatment Strategy



HR, 0.38; 95% CI, 0.25-0.58

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*

Liège and Brussels, Belgium; Rennes, France; and Quebec, Canada

“Truly” Asymptomatic Severe AS

N=150 with **AVA <1cm²** (no gradient criteria)

Exclusion: 1) LVEF <55% 2) other moderate-severe valve disease 3) Atrial Fibrillation 4) COPD 5) **positive stress test** 6) incapacity to perform stress test

Endpoint: CV death or need for AVR motivated by the development of symptoms or LVEF<50%)

Clinical Outcome in Asymptomatic Severe Aortic Stenosis

Insights From the New Proposed
Aortic Stenosis Grading Classification

- 51% (76/150) events at mean follow-up **27 months**
- **6% (9/150) deaths**; 5.3% (8/150) cardiac deaths
- **2% (3/150) sudden deaths** without preceding symptoms
- **70 (47%) had indication for AVR:**
 - **Spontaneous symptoms: 58 (83%)**
 - Progressive AS: 2 (3%)
 - Positive stress test during follow-up: 8 (11%)
 - **LVEF <50%: 2 (3%)**

Valvular Heart Disease

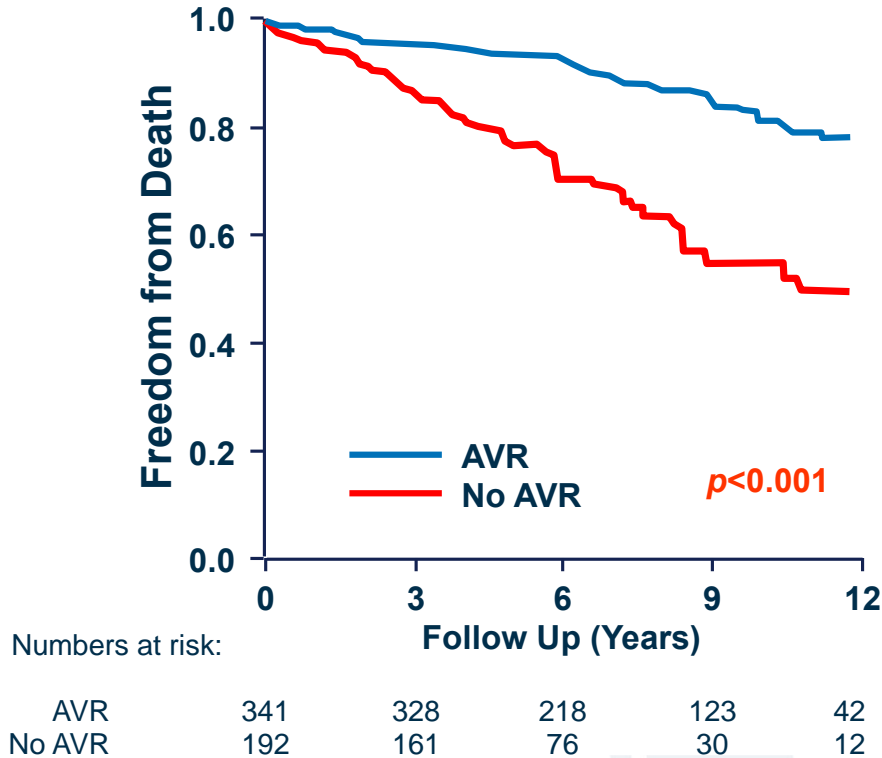
Predictors of Long-Term Outcomes in Asymptomatic Patients With Severe Aortic Stenosis and Preserved Left Ventricular Systolic Function Undergoing Exercise Echocardiography

Ahmad Masri, MD; Andrew L. Goodman, MD; Tyler Barr; Richard A. Grimm, MD;
Joseph F. Sabik, MD; A. Marc Gillinov, MD; L. Leonardo Rodriguez, MD;
Lars G. Svensson, MD, PhD; Brian P. Griffin, MD; Milind Y. Desai, MD

- 533 Asymptomatic Severe AS pts; mean STS 2.9%
- Single center, from January 2001 and December 2012
- **Exclusion:**
 - LVEF <50%
 - Severe tricuspid/mitral stenosis/regurgitation
 - Underwent TAVR
 - Incapacity to perform stress test
- Endpoint: All-cause mortality

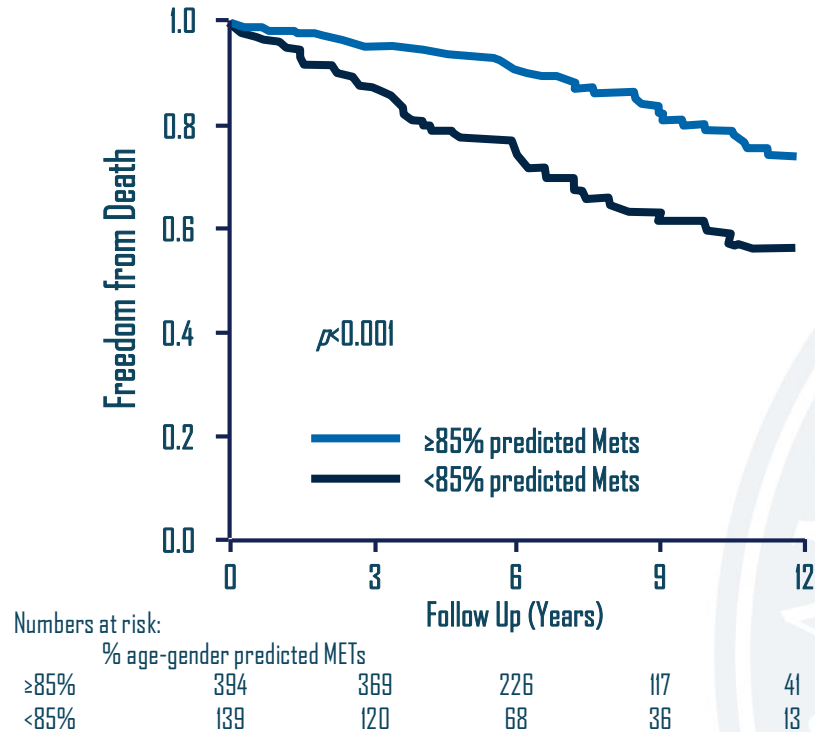
Severe Asymptomatic AS; n=533 pts.

Mortality According to AVR vs. no AVR



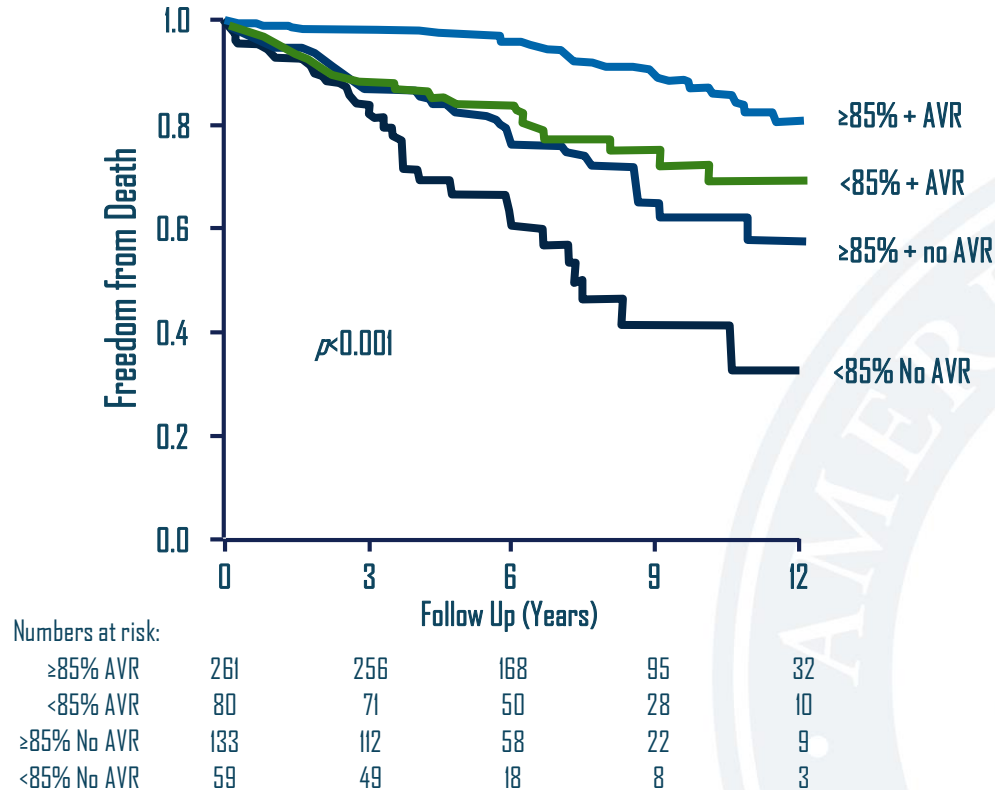
Severe Asymptomatic AS; n=533 pts.

Mortality According % Predicted Mets



Severe Asymptomatic AS; n=533 pts.

Mortality According % Predicted Mets and AVR



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Early Surgery or Conservative Care for Asymptomatic Aortic Stenosis

Duk-Hyun Kang, M.D., Ph.D., Sung-Ji Park, M.D., Ph.D., Seung-Ah Lee, M.D., Sahmin Lee, M.D., Ph.D.,
Dae-Hee Kim, M.D., Ph.D., Hyung-Kwan Kim, M.D., Ph.D., Sung-Cheol Yun, Ph.D., Geu-Ru Hong, M.D., Ph.D.,
Jong-Min Song, M.D., Ph.D., Cheol-Hyun Chung, M.D., Ph.D., Jae-Kwan Song, M.D., Ph.D.,
Jae-Won Lee, M.D., Ph.D., and Seung-Woo Park, M.D., Ph.D.

145 patients

Young

Bicuspid

Critical AS (PV~5.0)

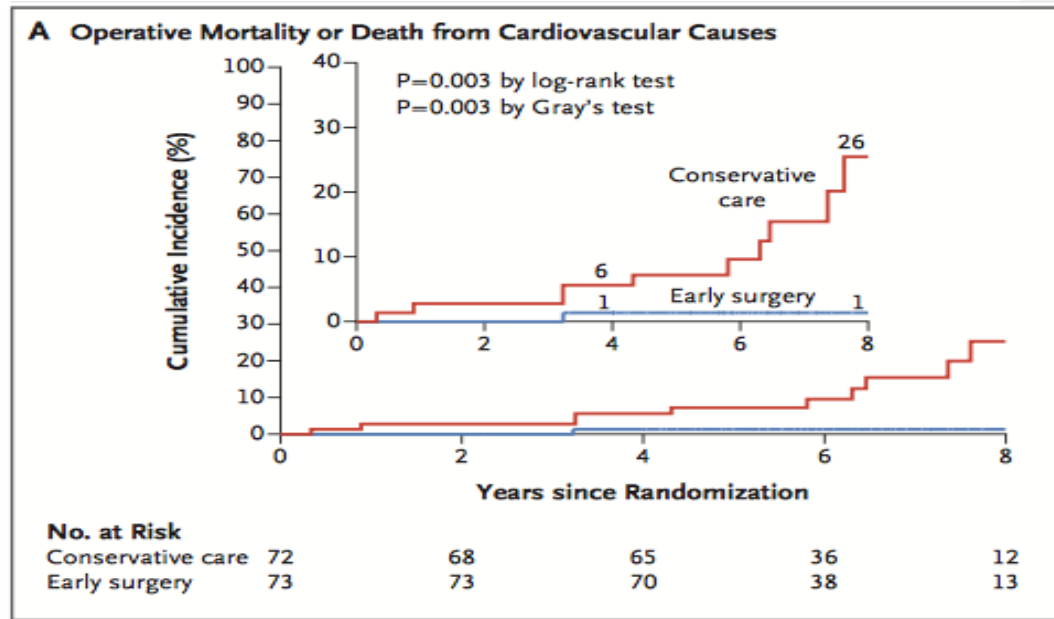
Normal EF

No treadmill stress test

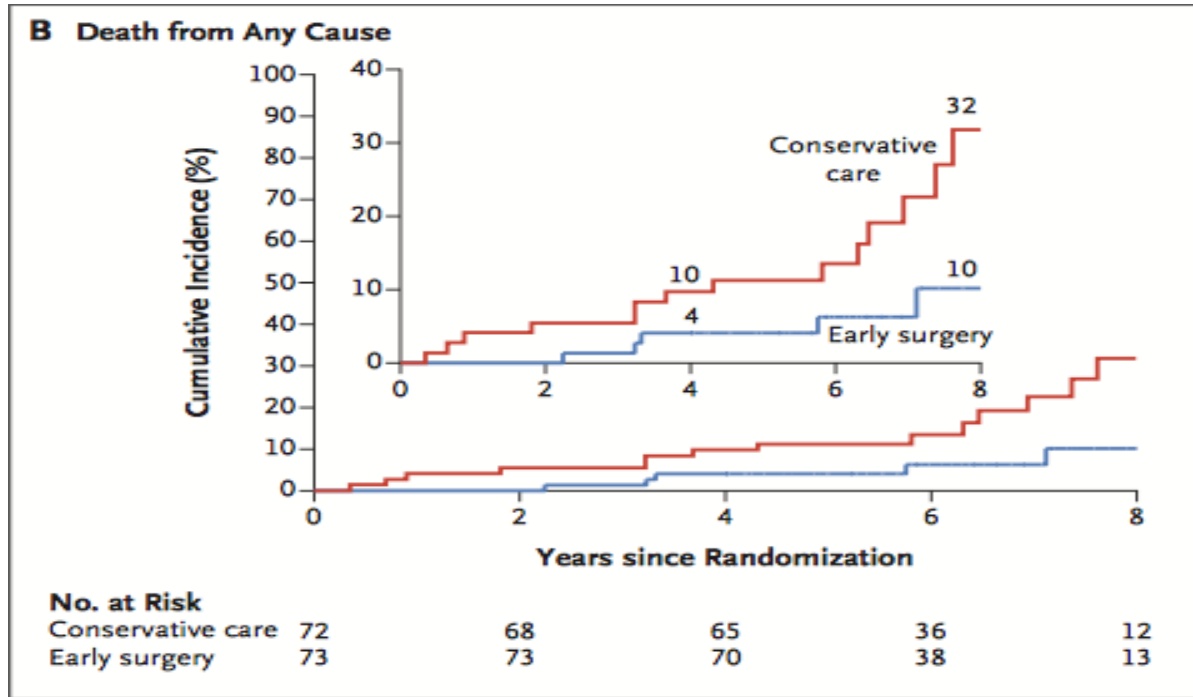
50% Mechanical valve

Table 1. Characteristics of the Patients at Baseline. ^a		
Characteristic	Conservative Care (N = 72)	Early Surgery (N = 73)
Age — yr	63.4±10.7	65.0±7.8
Male sex — no. (%)	34 (47)	37 (51)
Body-surface area — m ²	1.64±0.17	1.69±0.17
Body-mass index†	24.0±2.6	24.7±3.4
Diabetes — no. (%)	7 (10)	13 (18)
Hypertension — no. (%)	39 (54)	40 (55)
Smoking — no. (%)	21 (29)	19 (26)
Hypercholesterolemia — no. (%)	42 (58)	41 (56)
Coronary artery disease — no./total no. (%)‡	1/59 (2)	5/72 (7)
Previous PCI — no. (%)	1 (1)	3 (4)
Previous stroke — no. (%)	3 (4)	3 (4)
Peripheral vascular disease — no. (%)	2 (3)	1 (1)
Atrial fibrillation — no. (%)	6 (8)	3 (4)
Serum creatinine level — mg/dl	0.83±0.16	0.84±0.23
EuroSCORE II score — %§	0.9±0.4	0.9±0.3
Medication — no. (%)		
Angiotensin-converting-enzyme inhibitor	0	4 (5)
Angiotensin-receptor blocker	28 (39)	24 (33)
Calcium antagonist	20 (28)	19 (26)
Beta-blocker	8 (11)	13 (18)
Diuretic	17 (24)	13 (18)
Statin	32 (44)	34 (47)
Echocardiographic findings		
Cause of aortic stenosis — no. (%)		
Bicuspid aortic valve	39 (54)	49 (67)
Degenerative valvular disease	26 (36)	22 (30)
Rheumatic valvular disease	7 (10)	2 (3)
Peak aortic jet velocity — m/sec	5.04±0.44	5.14±0.52
Transaortic pressure gradient — mm Hg		
Peak	102.5±18.4	106.9±21.9
Mean	62.7±12.4	64.3±14.4
Aortic valve		
Area — cm ²	0.64±0.09	0.63±0.09
Area index — cm ² /m ²	0.39±0.07	0.38±0.06
Left ventricular mass index — g/m ²	133.7±31.1	135.6±38.2
Left ventricular ejection fraction — %	64.8±4.1	64.8±5.2

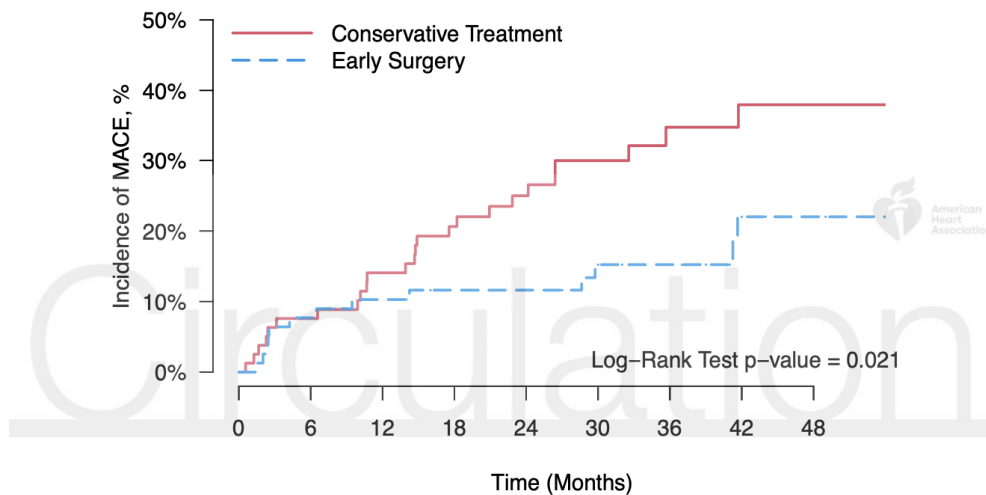
Early Surgery or Conservative Care for Asymptomatic
Aortic Stenosis



Early Surgery or Conservative Care for Asymptomatic
Aortic Stenosis



AVATAR Trial



<i>Patients, n</i>									
<i>Conservative Treat.</i>	79	73	66	59	49	36	25	19	12
<i>Early Surgery</i>	78	72	68	63	56	46	38	23	13

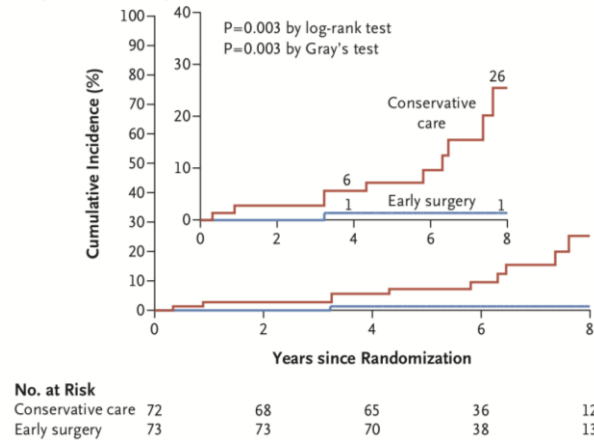
Bankovic et al. Circulation 2021
N=157 pts **SAVR only**

Severe AS with No Symptoms EARLY AVR vs. Clinical Surveillance



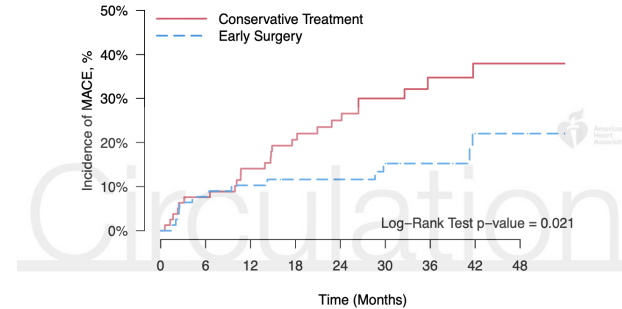
The NEW ENGLAND
JOURNAL of MEDICINE

A Operative Mortality or Death from Cardiovascular Causes



Kang et al. NEJM 2019
N=145 pts **SAVR only**
Critical AS
No stress test

Circulation



Patients, n

Conservative Treat.	79	73	66	59	49	36	25	19	12
Early Surgery	78	72	68	63	56	46	38	23	13

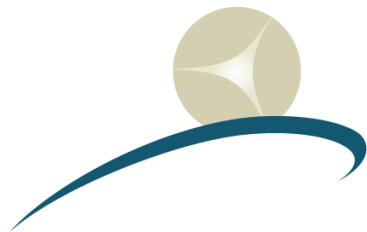
Bankovic et al. Circulation 2021
N=157 pts **SAVR only**

2 small randomized trials; SAVR only

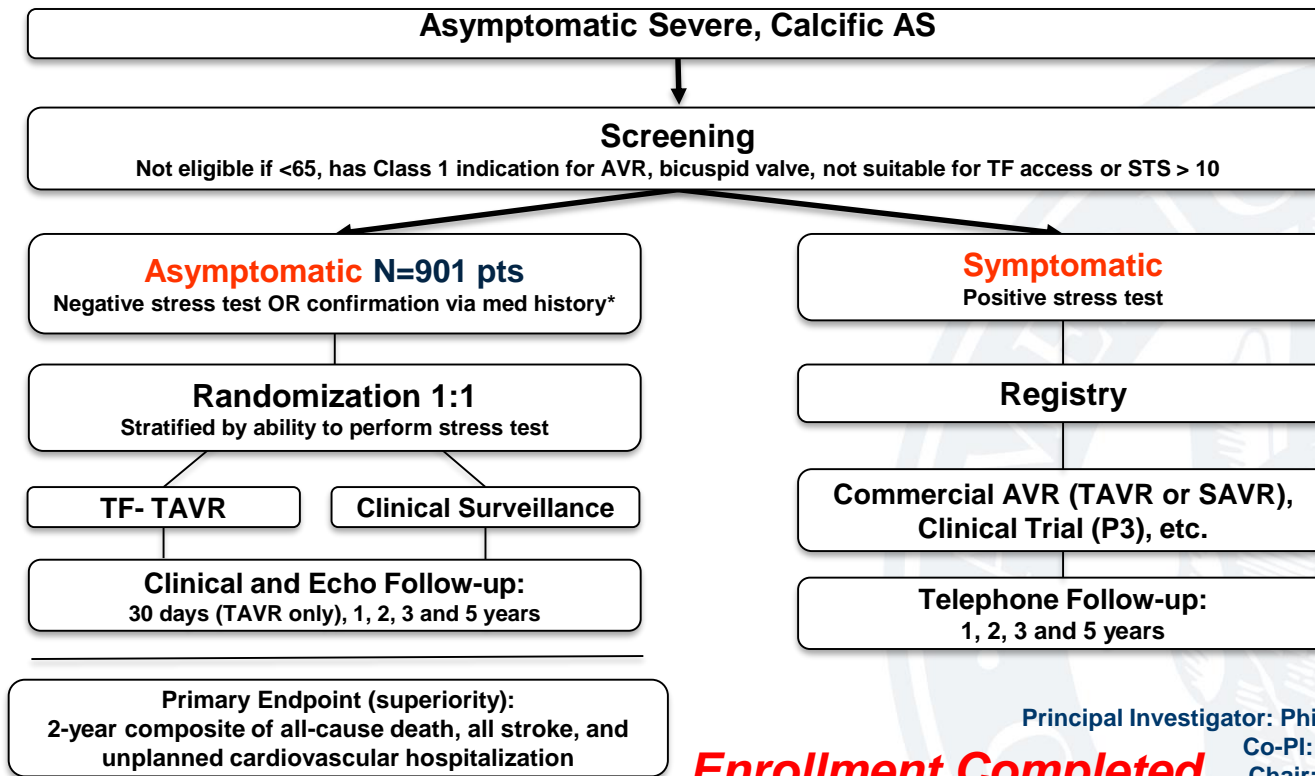
Severe AS No Symptoms: Ongoing Randomized Trials

- EARLY-TAVR trial
- EVOLVED trial
- ESTIMATE trial





THE EARLY TAVR TRIAL



Enrollment Completed

Principal Investigator: Philippe Généreux, MD

Co-PI: Allan Schwartz, MD

Chair: Martin B. Leon, MD