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Which asymptomatic patients with severe aortic valve stenosis should follow the route of early TAVR?

Pedro Villablanca MD, MSc, FACC, FSCAI

Fellowship Director Structural Heart Disease

Interventional Cardiology

Structural Heart Interventions

Endovascular Interventions

New Paradigm in AS Disease Management

- What are the risks/benefits of waiting?
- What are the risks/benefits of preemptive management?
- **When** is the optimal timing for more proactive care?

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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.

ORIGINAL ARTICLE

Transcatheter Aortic-Valve Replacement for Asymptomatic Severe Aortic Stenosis

P. Généreux, A. Schwartz, J.B. Oldemeyer, P. Pibarot, D.J. Cohen, P. Blanke, B.R. Lindman, V. Babaliaros, W.F. Fearon, D.V. Daniels, A.K. Chhatriwalla, C. Kavinsky, H. Gada, P. Shah, M. Szerlip, T. Dahle, K. Goel, W. O'Neill, T. Sheth, C.J. Davidson, R.R. Makkar, H. Prince, Y. Zhao, R.T. Hahn, J. Leipsic, B. Redfors, S.J. Pocock, M. Mack, and M.B. Leon, for the EARLY TAVR Trial Investigators*

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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*

JAMA | Original Investigation

Early Intervention in Patients With Asymptomatic Severe Aortic Stenosis and Myocardial Fibrosis

The EVOLVED Randomized Clinical Trial

Krithika Loganath, MD; Neil J. Craig, MD; Russell J. Everett, PhD; Rong Bing, PhD; Vasiliki Tsampasian, MD; Patrycja Molek, MD; Simona Botezatu, MD; Saadia Aslam, MD; Steff Lewis, PhD; Catriona Graham, MSc; Audrey C. White; Tom MacGillivray; Christopher E. Tuck; Phillip Rayson, (BA)Hons; Denise Cranley; Sian Irvine, PhD; Ruth Armstrong; Lynsey Milne; Calvin W. L. Chin, PhD; Graham S. Hillis, PhD; Timothy Fairbairn, PhD; John P. Greenwood, PhD; Richard Steeds, PhD; Stephen J. Leslie, PhD; Chim C. Lang, PhD; Chiara Bucciarelli-Ducci, PhD; Nikhil V. Joshi, PhD; Vijay Kunadian, PhD; Vassilios S. Vassiliou, PhD; Jason N. Dungu, PhD; Sandeep S. Hothi, PhD; Nicholas Boon, PhD; Sanjay K. Prasad, PhD; Niall G. Keenan, MD; Dana Dawson, PhD; Thomas A. Treibel, PhD; Mani Motwani, PhD; Christopher A. Miller, PhD; Nicholas L. Mills, PhD; Ronak Rajani, PhD; David P. Ripley, PhD; Gerry P. McCann, MD; Bernard Prendergast, MD; Anvesha Singh, PhD; David E. Newby, MD; Marc R. Dweck, PhD; for the EVOLVED investigators

Asymptomatic/Prompt Intervention Evidence

The EARLY TAVR Trial
Primary Results

Early vs Delayed TAVR

Biomarkers

Cardiac Damage

Impact of Age

4 RCT
Meta-analysis

RCT + Observational
Meta-analysis

Cost of AVS

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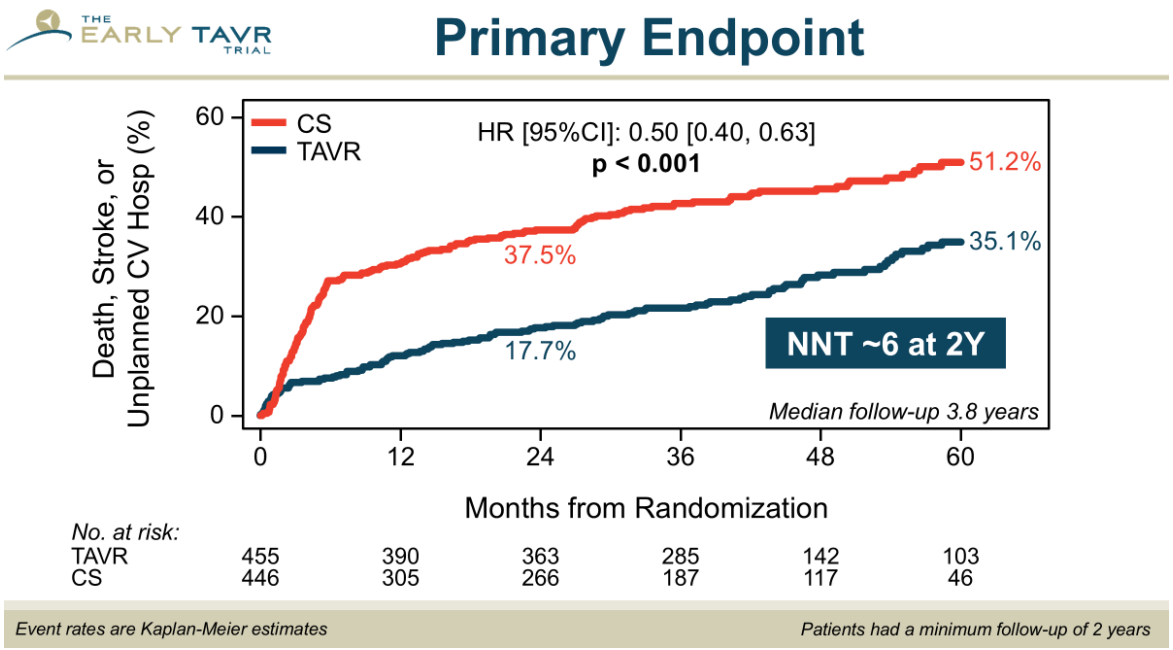
Question: Should we wait for symptoms to treat severe AS?



Prompt SAPIEN 3 TAVR was proven superior to guideline recommended surveillance in the EARLY TAVR trial

50% reduction in the risk of the composite endpoint: death, stroke, or unplanned cardiovascular hospitalization vs clinical surveillance through 5 years

Answer:

No. The risk of AVR intervention has decreased significantly since "watch and wait" was established. There is now robust evidence demonstrating no mortality or stroke penalty for intervention and even superiority of prompt TAVR compared to clinical surveillance.

Cardiac Damage/Injury

- Risks of waiting knowing that the pathophysiology of disease progression is occurring

Downstream Effects

- STAGE 1: LV enlargement to compensate for narrowing Aortic valve - Hypertrophy
- STAGE 2: LA enlargement and Mitral impact → Atrial Fib
- STAGE 3: Pulmonary Hypertension and Tricuspid
- STAGE 4: RV dysfunction

Should we Wait for Symptoms????

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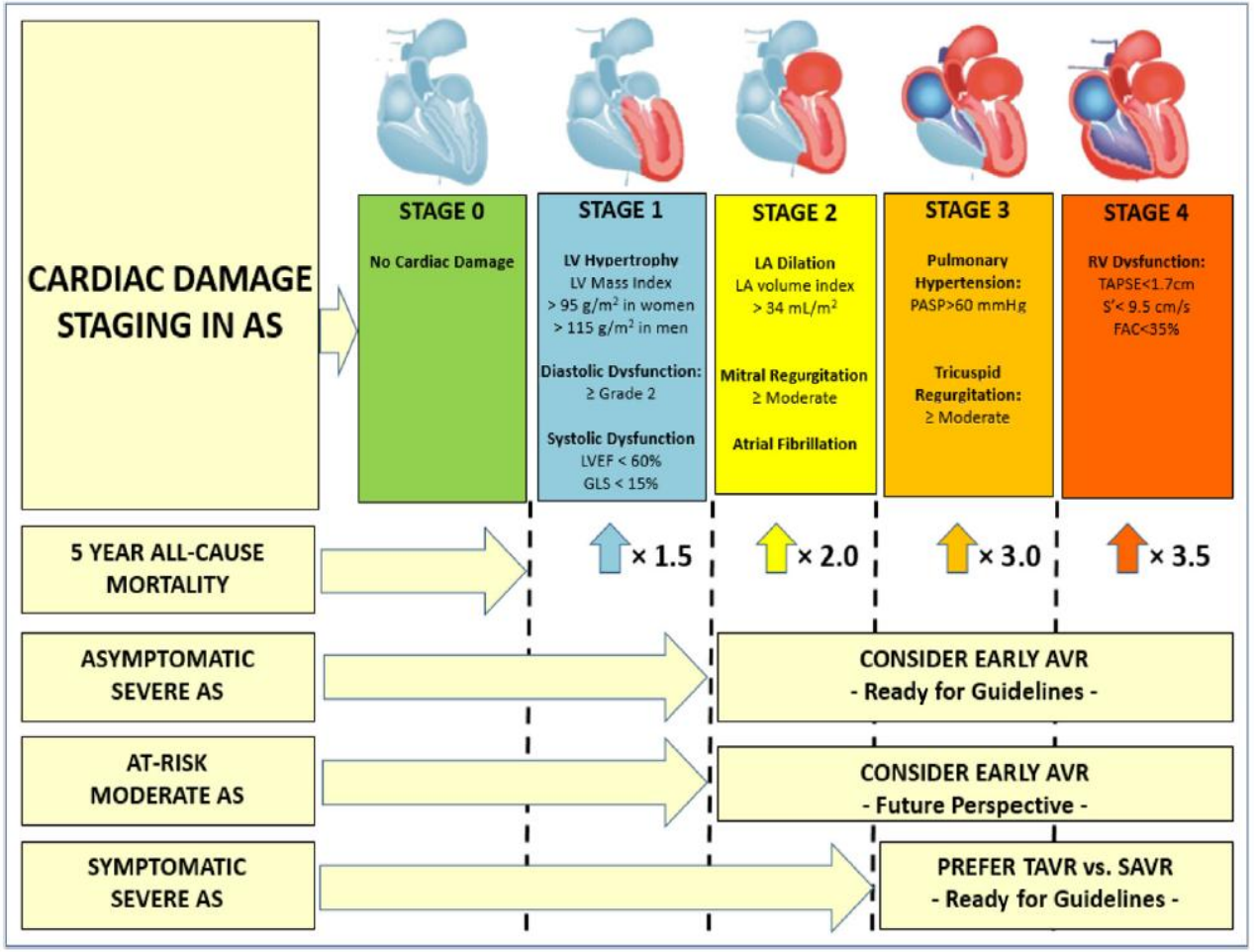
FIGURE 1 Clinical Implications of CD Staging in AS

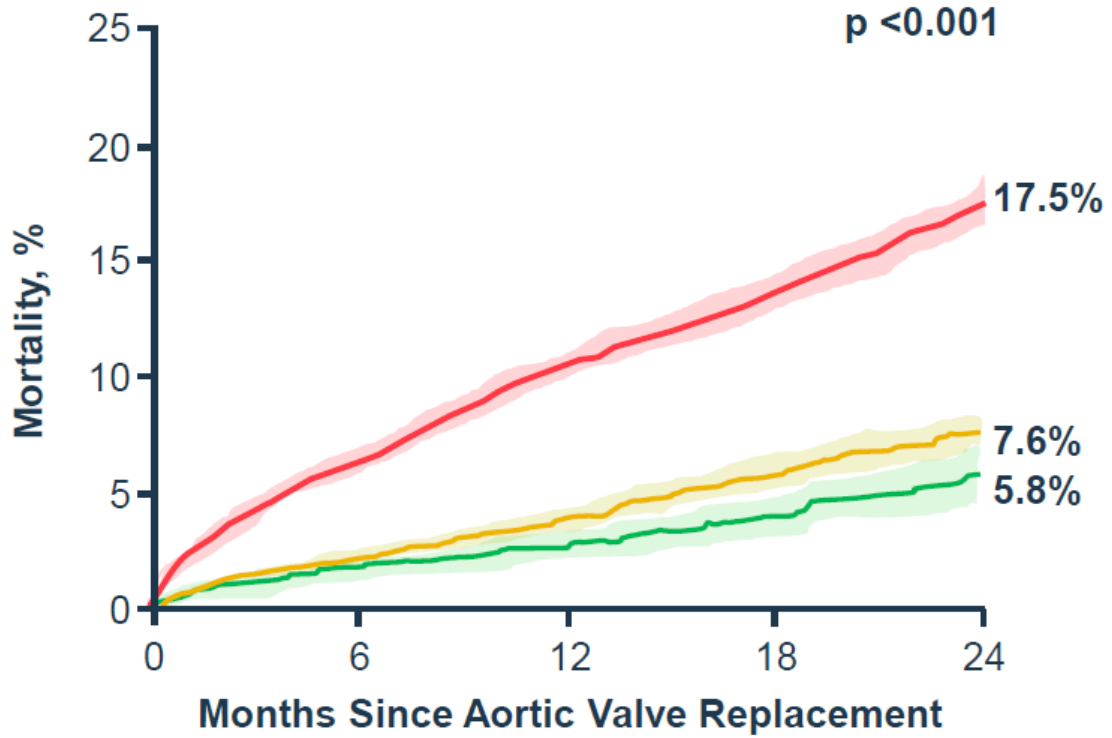


AS = aortic stenosis; AVR = aortic valve replacement; CD = cardiac damage; FAC = fractional area change; GLS = global longitudinal strain (absolute value); LA = left atrial; LV = left ventricular; LVEF = left ventricular ejection fraction; PASP = pulmonary arterial systolic pressure; RV = right ventricular; SAVR = surgical aortic valve replacement; S' = tricuspid annulus systolic wave peak velocity; TAPSE = tricuspid annulus plane systolic excursion; TAVR = transcatheter aortic valve replacement.

Pressure Imbalances Lead to Maladaptive Responses

2-Year Mortality After AVR Per Clinical Presentation

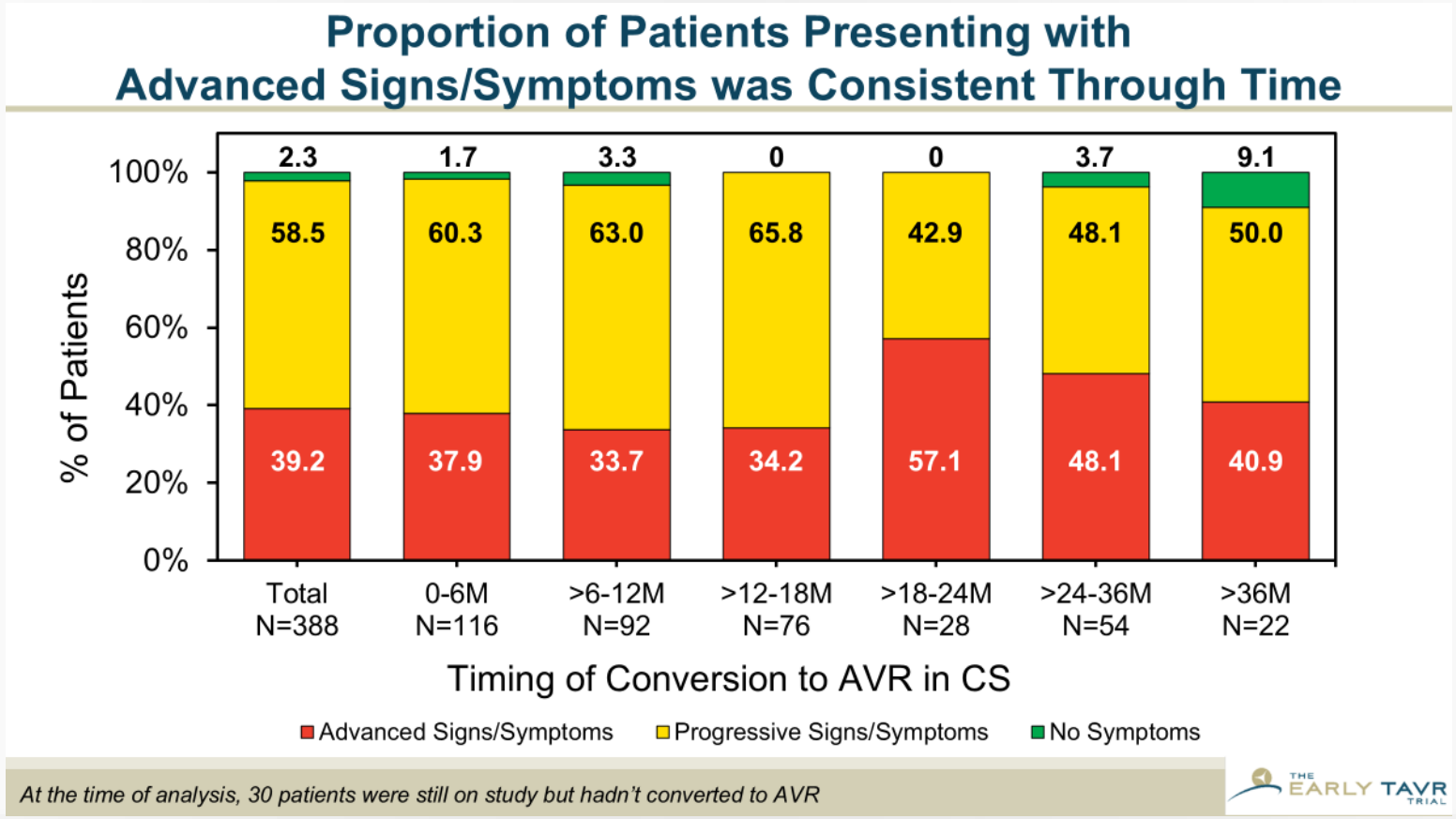
ASx vs. Progressive vs. Acute Valve Syndrome



No. at Risk

Asymptomatic	2504	1859	1540	1176	934
Progressive	6116	4710	3867	2871	2147
Acute	9218	6667	5243	3702	2700

Over 30% of Patients Presented With Advanced Signs Or Symptoms At The Time of AVR Conversion

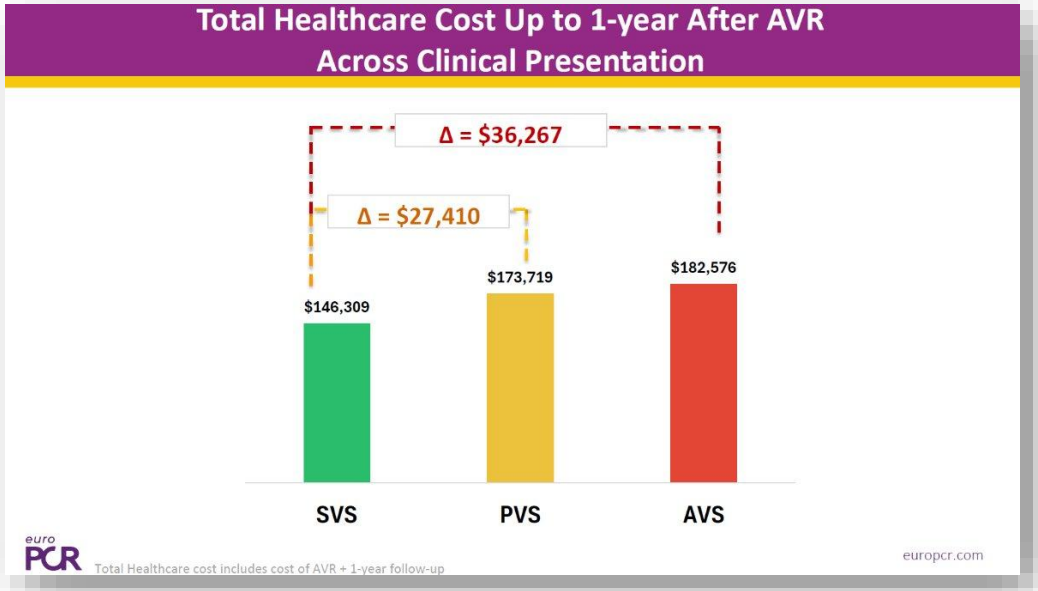


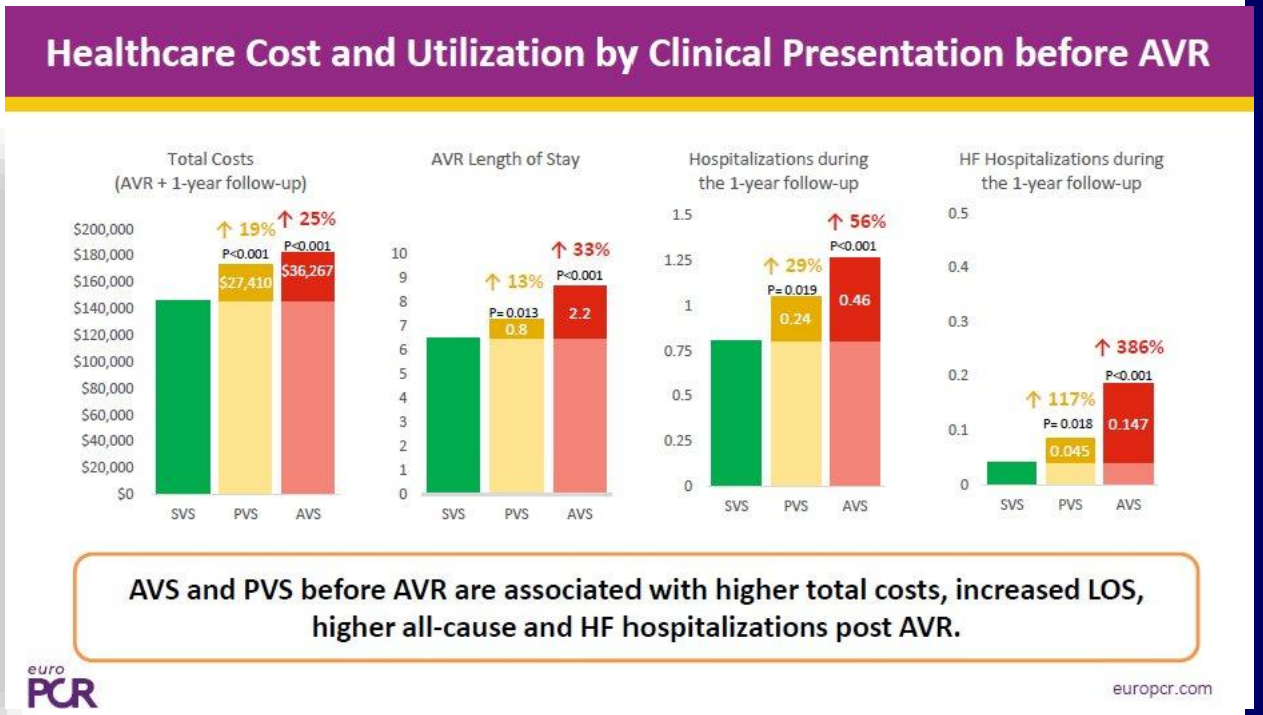
This disease progresses rapid and unpredictably

1. TAVR for Asymptomatic Severe Aortic Stenosis: Results of The EARLY TAVR Trial. Presented by P Genereux, TCT 2024.
2. Philippe Genereux MD et al. Transcatheter Aortic Valve Replacement for Asymptomatic Severe Aortic Stenosis NEJM In Press Oct 28, 2024

Question: What is the benefit of prompt intervention?

4 Economic Cost

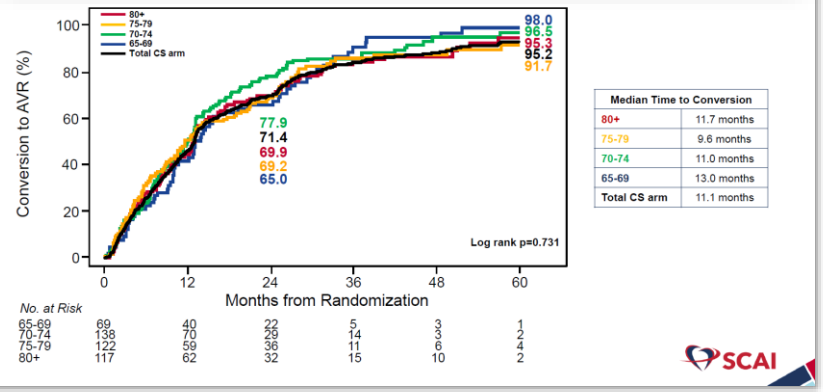




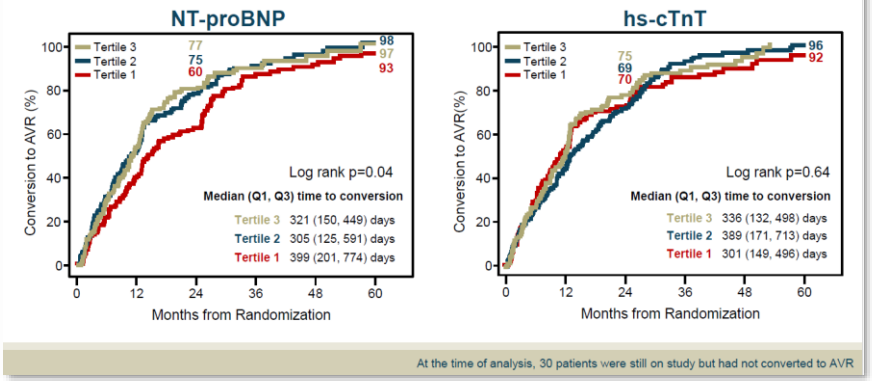
Answer:
Symptomatic (Both acute and progressive valve syndrome) AVR leads to a significant increase in healthcare costs compared to prompt intervention

Question: Can I predict WHEN patients will develop symptoms? No

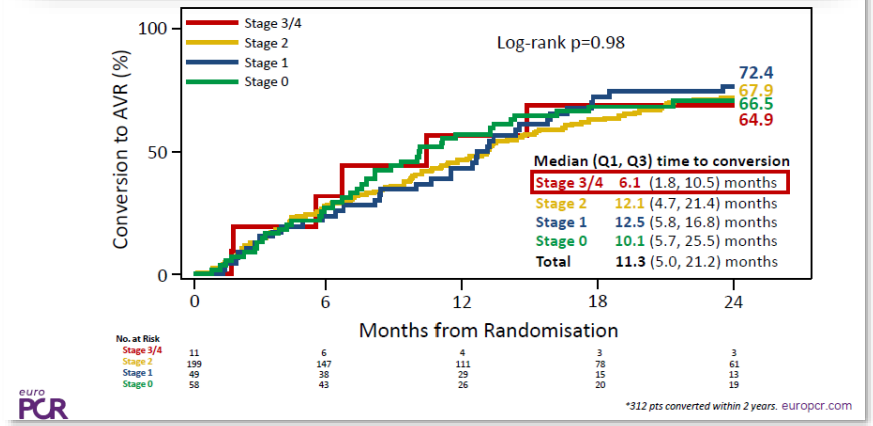
Impact of Age[1]



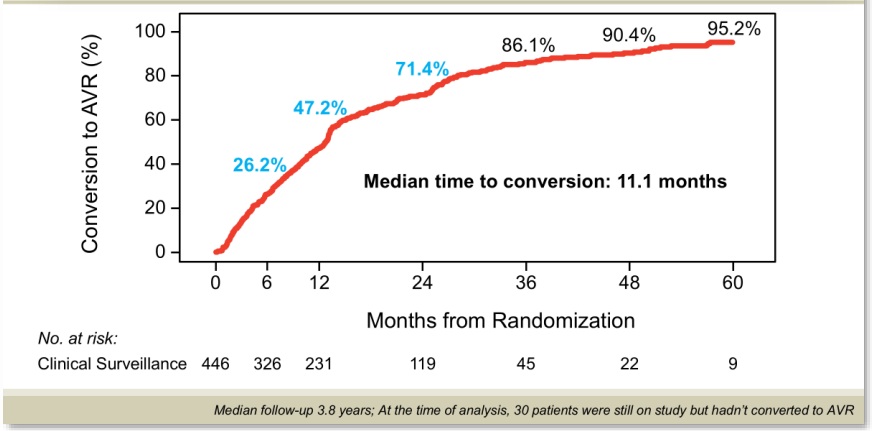
Biomarkers[2]



Cardiac Damage[3]



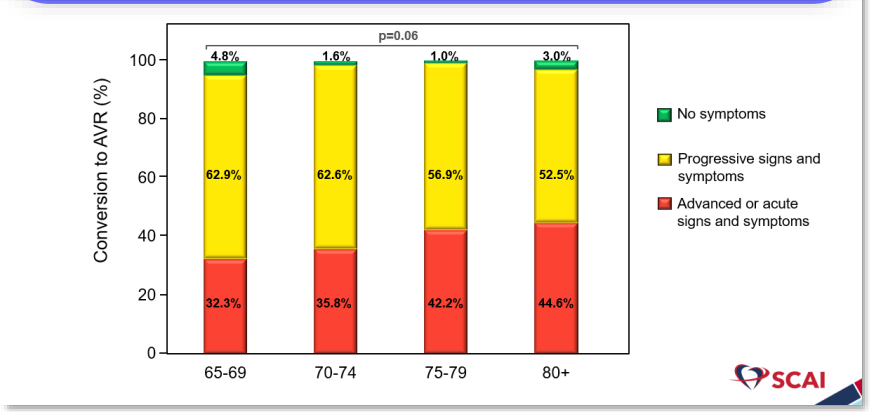
EARLY TAVR[4]



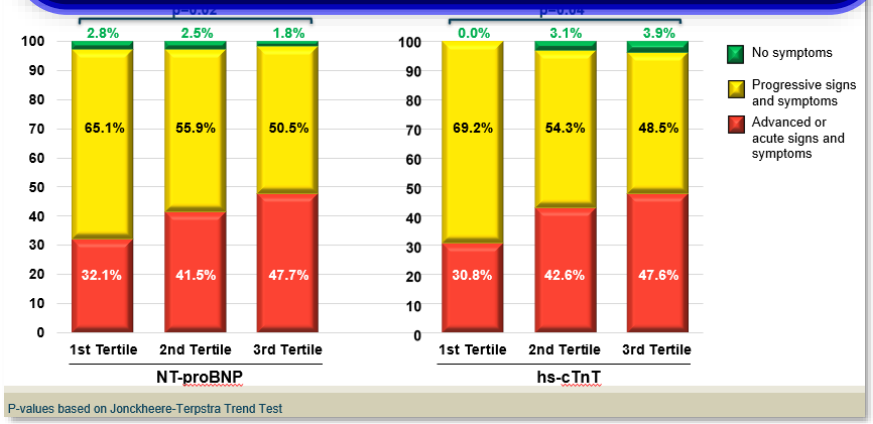
1. Impact of Age on Timing and Outcomes for Asymptomatic Severe Aortic Stenosis: Results from the EARLY TAVR Trial. Presented by P Genereux, SCAI 2025. 2. Cardiac Biomarkers in Patients with Asymptomatic Severe Aortic Stenosis. Presented by B Lindman, ACC 2025.
3. Incidence, Evolution and Impact of Cardiac Damage in Asymptomatic Severe Aortic Stenosis. Presented by P Genereux, EuroPCR 2025. 4. TAVR for Asymptomatic Severe Aortic Stenosis: Results of The EARLY TAVR Trial. Presented by P Genereux, TCT 2024

Question: Can I predict WHICH patients will develop acute valve syndrome? No.

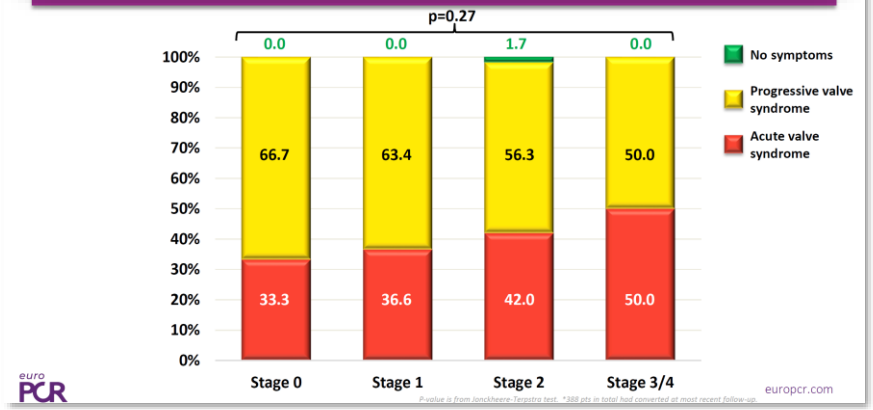
Impact of Age[1]



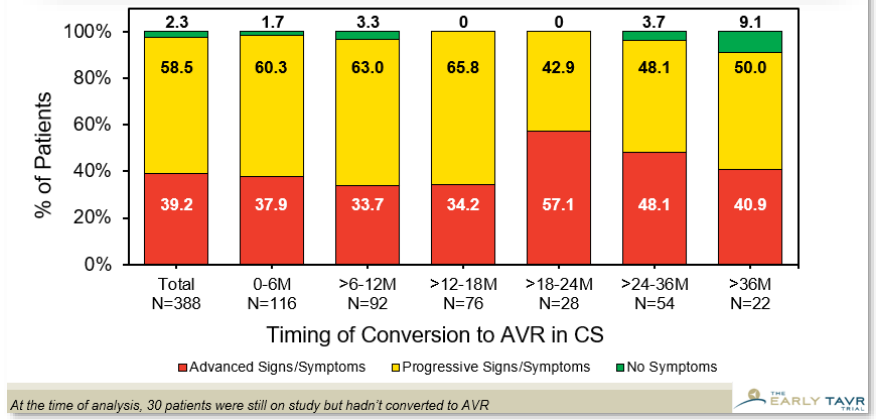
Biomarkers[2]



Cardiac Damage[3]



EARLY TAVR[4]



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Heart Team

What have we learned?

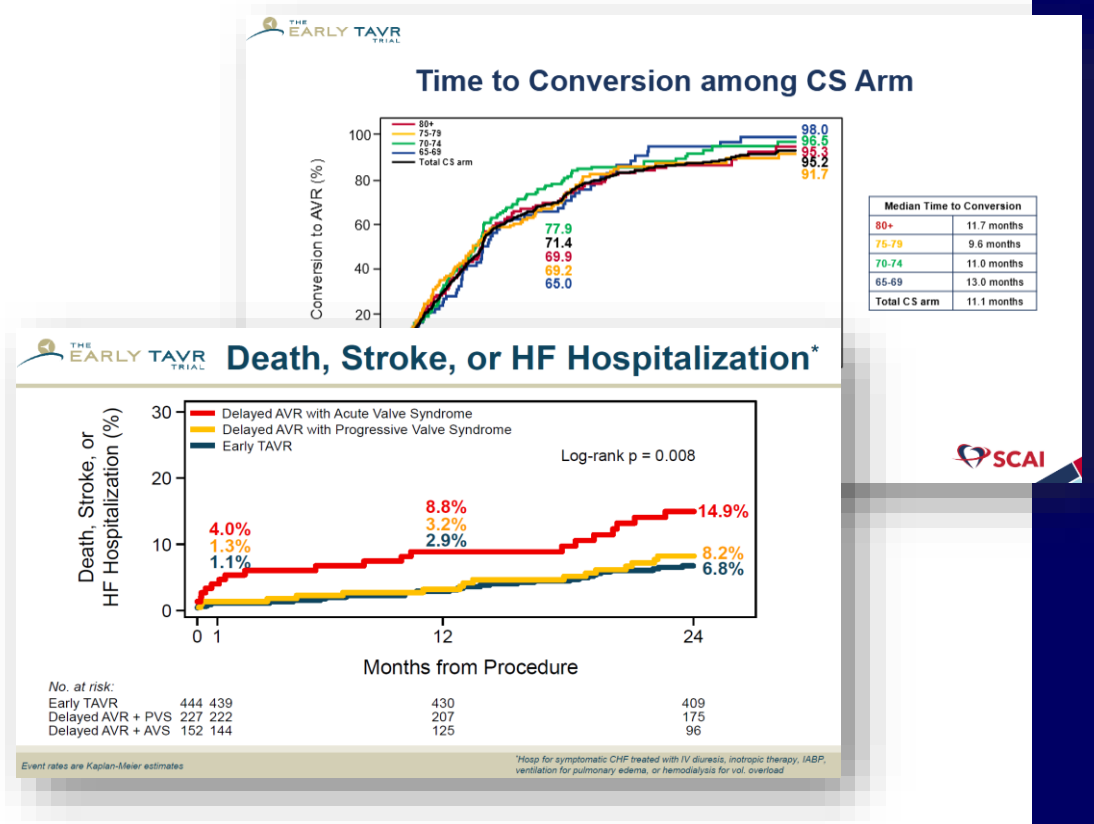
Who's Missing?

Shared Decision-Making

Patient Preferences

Durability – "I don't want to start the clock on the valve early"

- During a median follow-up of 3.8 years, 87% of patients in the clinical surveillance group underwent AVR
- We cannot predict how or when a patient will present with symptoms.
- The consequences of waiting and supporting data demonstrate: **Hospitalization, Mortality, Stroke, LV/LA health, Economic cost**



Median time from randomization to conversion to AVR was 11.1 months!

Note: Clinical surveillance arm starting point is from time of randomization to conversion to AVR, not from time of severe AS diagnosis

Anatomy Based Decision

65 yo ≠ 65 yo

Physician Perspective: What should be recommended for patients with asymptomatic severe AS?

3 RCTs have shown superiority of prompt AVR on the primary endpoint

Meta-analysis shows significantly lower rate of HF hospitalization and stroke and favorable trends on mortality with prompt AVR

There is no mortality or stroke penalty for prompt intervention

There appear to be benefits to LV/LA health which may further mitigate downstream HF risk

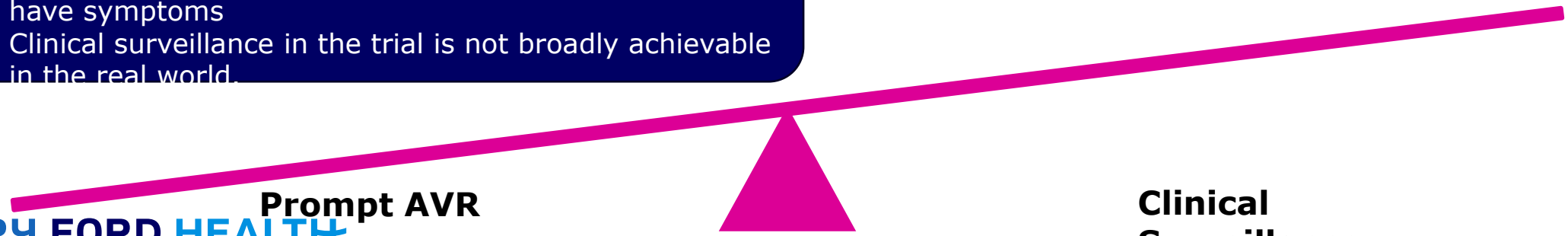
The benefits seen in the EARLY TAVR trial are conservative and almost certainly under-estimate what would occur in the real world

- Many patients thought to be asymptomatic actually have symptoms
- Clinical surveillance in the trial is not broadly achievable in the real world.

Anatomical feature that increases risk of procedural complication
Usually if one approach is anatomically higher risk, the alternative approach can mitigate the risk

Starting the clock earlier on valve durability
The clock doesn't appear to start all that much differently, so age or uncertainty about durability timeline should not be a deterrent to a prompt intervention strategy

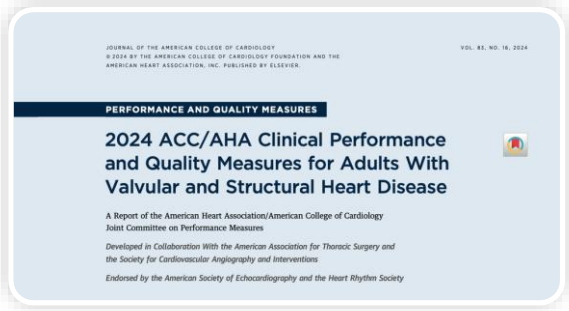
Patients who think they lack symptoms may not perceive how AVR will help them
We already have a Class I indication for AVR for asymptomatic patients when LVEF is <50%



The Impact of an Asymptomatic Indication: Simplification of the Patient Pathway for All Severe AS Patients

GC Visit → **Echo with Severe AS** → **Refer to Heart Team** → **TAVR**

≤ 90 Days


JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 83, NO. 16, 2024

PERFORMANCE AND QUALITY MEASURES

2024 ACC/AHA Clinical Performance and Quality Measures for Adults With Valvular and Structural Heart Disease

A Report of the American Heart Association/American College of Cardiology Joint Committee on Performance Measures

Developed in Collaboration With the American Association for Thoracic Surgery and the Society for Cardiovascular Angiography and Interventions

Endorsed by the American Society of Echocardiography and the Heart Rhythm Society

American Heart Association®
Target: Aortic Stenosis™

Patients with an echo indicating severe AS can be directly referred to the Heart Team for evaluation

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When I push for therapy

- Low EF
- Strain damage
  - LA dilation
  - MR
  - PAF
- Velocity >5
- Good Lifetime management
- Need for other surgery

Take Home Points

- Complete Work up:
  - CT
  - IC
  - CTS
- Lifetime management
- Patient Focus
- Define anatomy TYPE A, B, C TAVR

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