British Cardiovascular Society

'Promoting excellence in cardiovascular care'

Asymptomatic Severe Aortic Stenosis – Are We Moving Towards Earlier Intervention?

Dr Atmadeep Banerjee, MBBS, MRCP

Cardiology Registrar

Worthing Hospital, University Hospitals Sussex NHS Foundation Trust

Take Home Messages

- 2025 European Society of Cardiology (ESC) guidelines include a new Class IIa recommendation for considering intervention in asymptomatic patients with severe aortic stenosis, if the procedural risk is low.
- This recommendation is based on four trials comparing early intervention to conservative management in this patient group.
- Positive outcomes in these trials were driven mainly by a reduction in unplanned hospitalisations rather than mortality. A meta-analysis also demonstrated a reduction in stroke in the early intervention group.
- The studies were heterogenous and included several design limitations that have been explored in critical reviews. There is also a lack of data regarding patient selection for early intervention.

Introduction

Patients with severe aortic stenosis (AS) are often asymptomatic at the point of diagnosis (1,2). Guidelines have conventionally recommended close surveillance for truly asymptomatic patients who do not have left ventricular dysfunction or other features of very severe or progressive AS (3–6). Based on four randomised controlled trials (RCTs), 2025 European Society of Cardiology (ESC) guidelines include a new class IIa recommendation to consider intervention in these patients (1) (**Table 1**). However, this remains an area of active debate, with critical reviews examining study design and the real-world implications of these studies (7,8).

RECOVERY trial

The RECOVERY trial, conducted at 4 centres in South Korea, recruited 145 asymptomatic patients with very severe AS (9). Patients were randomised to either early surgical aortic valve replacement (SAVR) or conservative management, and were followed up for a median period of 6 years. Early surgery reduced the incidence of the primary composite endpoint of peri-operative death or cardiovascular death during the follow-up period (1% vs 15%; HR: 0.09 [95% CI: 0.01-0.67])(9).

The study lacked mandatory exercise testing, and included patients with very severe AS and echocardiographic parameters approaching existing guideline thresholds for intervention (3,5,9). The patients were relatively young (mean age 64 years), with a high proportion having bicuspid aortic valve (61%) rather than degenerative valve disease (33%) (9). There was a sharp increase in the mortality rate after 5 years, coinciding with the end of mandatory echocardiographic follow-up, suggesting a lack of strict surveillance in the control group and inadequate detection of disease progression (7).

AVATAR trial

The AVATAR trial enrolled 157 patients with asymptomatic severe AS and randomised them to early SAVR or conservative care (10). Over a median follow-up of 2.7 years, there was a reduction in the primary composite outcome of all-cause mortality, acute myocardial infarction, stroke, or unplanned heart failure hospitalisation in the SAVR group (15.2% vs 34.7%; HR: 0.46 [95% CI: 0.23-0.90]). This was driven mainly by a higher incidence of all-cause death and heart failure hospitalisation in the conservative group.

Though the trial recruited patients from 9 centres in 7 European countries, 73% of patients were recruited from a single centre reducing the generalisability (10). The mortality in the control arm was disproportionately high compared to other trials, suggesting that some of these deaths might have been due to undetected symptomatic progression due to inadequate close follow-up (7).

EARLY TAVR trial

The EARLY TAVR study, conducted in 75 centres in USA and Canada, randomised 901 patients with asymptomatic severe AS to early transcatheter aortic valve implantation (TAVI) or clinical surveillance (11). Over a median follow-up of 3.8 years there was a reduction in the primary composite endpoint of death, stroke, or unplanned cardiovascular hospitalisation (26.8% vs 45.3%; HR: 0.50 [95% CI: 0.40-0.63]), driven mainly by reduction in hospitalisation (20.9% vs 41.7%; HR: 0.43 [95% CI: 0.33-0.55]. There was no significant reduction in death (8.4% vs 9.2%; HR: 0.93 [95% CI: 0.60-1.44] or stroke (4.2% vs 6.7%; HR: 0.62 [95% CI: 0.35-1.10]). Early intervention also resulted in better symptom scores at 2 years (86.6% vs 68.0%; HR: 18.5 [95%CI: 12.6-24.3]).

There was significant crossover with 87% of control patients undergoing AVR (median time to conversion: 11.1 months) (11). 26.2% of control patients had AVR within the first 6 months, which were included as unplanned hospitalisations contributing to the primary endpoint (7,8,11). The high rate of AVRs in this group were driven mainly by new symptom-onset rather than acute decompensation (7,8,11). Previously asymptomatic control patients reported significantly worsening symptoms within 3 months, suggesting an effect of "subtraction anxiety" in this unblinded trial (7,8,12).

Table 1. Randomised controlled trials investigating early intervention in asymptomatic severe aortic stenosis

Trial	RECOVERY	AVATAR	EARLY TAVR	EVOLVED
Year published	2020	2022	2025	2025
Country/Region	South Korea	7 European countries	USA, Canada	UK, Australia
Participants (n)	145	157	901	224
Percentage female (%)	51	43	31	28
Median age (years)	64	67	76	73
Median follow-up (years)	6	2.7	3.8	3.5
Inclusion criteria for defining severe AS	• AVA ≤ 0.75cm^2, and • Vmax ≥ 4.5m/s or ΔPm ≥ 50mmHg	• AVA ≤ 1cm^2, or indexed AVA ≤ 0.6cm^2/ m^2, and • Vmax > 4m/s or ΔPm ≥ 40mmHg	• AVA ≤ 1cm^2, or indexed AVA ≤ 0.6cm^2/ m^2, and • Vmax ≥ 4m/s or ΔPm ≥ 40mmHg	• Vmax ≥ 4m/s, or • Vmax ≥ 3.5m/s with indexed AVA ≤ 0.6cm^2/ m^2
Exercise-testing to confirm asymptomatic status	Optional	Mandatory	Mandatory	Optional
Intervention	SAVR	SAVR	TAVI	SAVR or TAVI
Primary endpoint	Composite of peri-operative death or CV death	Composite of all-cause mortality, acute myocardial infarction, stroke, or unplanned HF-hospitalisation	Composite of death, stroke, or unplanned CV-hospitalisation	Composite of all-cause mortality or unplanned AS-related hospitalisation
Primary endpoint result	Met	Met	Met	Not met

RCTs = Randomised controlled trials, AS = Aortic stenosis, AVA = Aortic valve area, Vmax = Peak transvalvular velocity, ΔPm = Mean pressure gradient, SAVR = Surgical aortic valve replacement, TAVI = Transcatheter aortic valve implantation, CV = Cardiovascular, HF = Heart failure

EVOLVED trial

The EVOLVED RCT compared early AVR (SAVR or TAVI) to conservative management in an enriched cohort of patients with asymptomatic aortic stenosis and mid-wall myocardial fibrosis detected by late gadolinium enhancement on cardiac magnetic resonance imaging (CMR) (13). 224 patients were recruited across the UK and Australia. Median follow-up of 3.5 years showed no significant difference in the primary composite endpoint of all-cause mortality or unplanned AS-related hospitalisation (18% vs 23%; HR: 0.79 [95% CI: 0.44-1.43]). Analysis of secondary endpoints demonstrated a significant reduction in unplanned AS-related hospitalisations and lower symptom burden in the intervention group, which was suggested as hypothesis-generating. The study was underpowered due to disrupted recruitment from the Covid-19 pandemic (13,14). Patients randomised to early AVR also had a longer delay to intervention (median 5 months) (13–15).

Future research

A meta-analysis of these RCTs concluded a significant association between early AVR and reduction in unplanned hospitalisation and stroke, but no impact on mortality (15). Despite the use of random-effects modelling in this analysis, the pooled effects were influenced by the higher weight of the Early TAVR trial, and should be interpreted with caution. The mechanism of stroke reduction also remains unclear, with the study authors hypothesising possible reductions in valve-related thromboembolism or development of subclinical AF. Ongoing studies such as EASY-AS and DANAVR will help provide further evidence regarding the management of these patients (1,7,16).

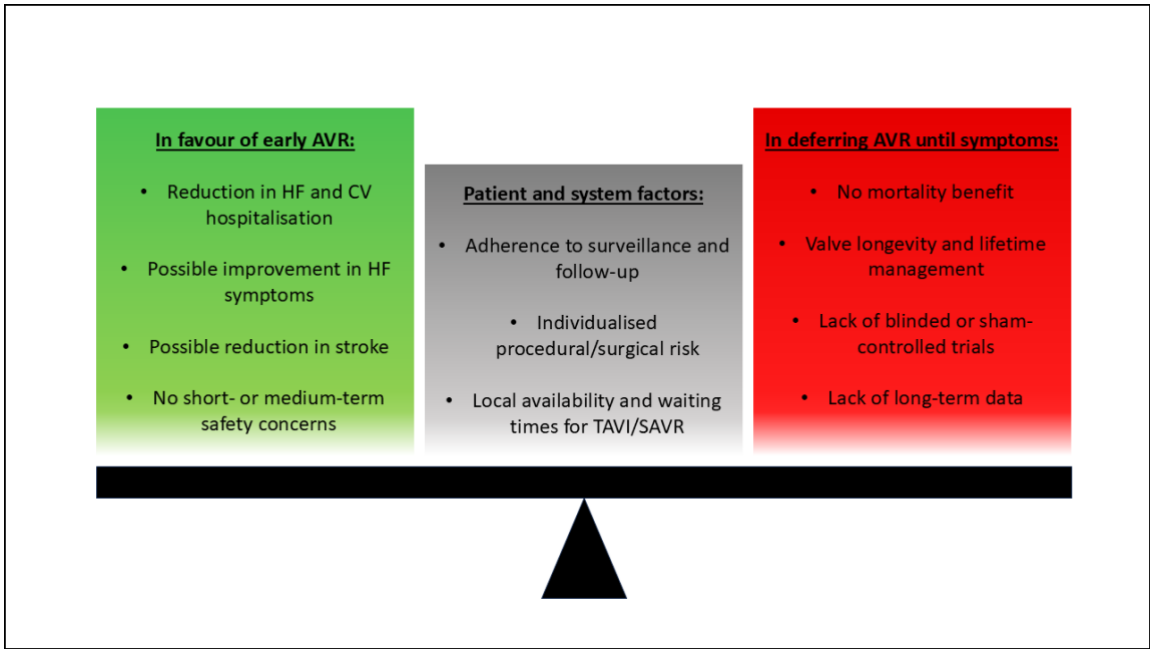
Further evidence is also needed to identify biomarkers and imaging parameters to guide patient selection. A pre-specified biomarker sub-study of Early TAVR showed an association between higher levels of NT-proBNP and hs-cTnT with higher event rates (17). However, baseline biomarkers failed to predict benefit from TAVI, time to conversion to AVR, or progression of symptom severity. Future studies might also investigate MRI markers of reversible cardiac remodelling to better identify patients who might benefit from earlier intervention (14).

Conclusions

Current guidelines and evidence support an individualised approach (1,7) (**Figure 1**). Systemic factors need to be considered, such as geographical variations in access to procedures and surgery (18).

Disclosures: The author declares no conflicts of interest related to this work.

Figure 1. Factors to consider in decision-making regarding early intervention in asymptomatic severe AS.
Original image by author, created using Microsoft Office.



References

1. Praz F, Borger MA, Lanz J, Marin-Cuartas M, Abreu A, Adamo M, et al. 2025 ESC/EACTS Guidelines for the management of valvular heart disease: Developed by the task force for the management of valvular heart disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). Eur Heart J. 2025 Aug 29;ehaf194.
2. Gahl B, Çelik M, Head SJ, Vanoverschelde JL, Pibarot P, Reardon MJ, et al. Natural History of Asymptomatic Severe Aortic Stenosis and the Association of Early Intervention With Outcomes: A Systematic Review and Meta-analysis. JAMA Cardiol. 2020 Oct 1;5(10):1102–12.
3. Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP, Guyton RA, et al. 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: Executive Summary. Circulation. 2014 June 10;129(23):2440–92.
4. Otto CM, Nishimura RA, Bonow RO, Carabello BA, Erwin JP, Gentile F, et al. 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. Circulation. 2021 Feb 2;143(5):e72–227.
5. Baumgartner H, Falk V, Bax JJ, De Bonis M, Hamm C, Holm PJ, et al. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. Eur Heart J. 2017 Sept 21;38(36):2739–91.
6. Vahanian A, Beyersdorf F, Praz F, Milojevic M, Baldus S, Bauersachs J, et al. 2021 ESC/EACTS Guidelines for the management of valvular heart disease: Developed by the Task Force for the management of valvular heart disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). Eur Heart J. 2022 Feb 14;43(7):561–632.
7. Victor Dayan MD, Mateo Marin-Cuartas MD, Raffaele De Caterina MD, Suzanne De Waha MD, Nicolas M. Van Mieghem MD, Michael A. Borger MD, et al. Early Intervention vs Conservative Management in

Severe Asymptomatic Aortic Stenosis: A Critical Review of Randomized Evidence. JACC Adv [Internet]. 2025 Oct 1 [cited 2025 Oct 1]; Available from: https://www.jacc.org/doi/10.1016/j.jacadv.2025.102178
8. Mandrola J. Medscape. [cited 2025 Sept 30]. A Positive Trial That Fails to Inform Clinical Decisions. Available from: https://www.medscape.com/viewarticle/early-tavr-positive-trial-fails-inform-clinical-decisions-2024a1000kec
9. Kang DH, Park SJ, Lee SA, Lee S, Kim DH, Kim HK, et al. Early Surgery or Conservative Care for Asymptomatic Aortic Stenosis. N Engl J Med. 2020 Jan 9;382(2):111–9.
10. Banovic M, Putnik S, Penicka M, Doros G, Deja MA, Kockova R, et al. Aortic Valve Replacement Versus Conservative Treatment in Asymptomatic Severe Aortic Stenosis: The AVATAR Trial. Circulation [Internet]. 2022 Mar 1 [cited 2025 Oct 1]; Available from: https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.121.057639
11. Généreux P, Schwartz A, Oldemeyer JB, Pibarot P, Cohen DJ, Blanke P, et al. Transcatheter Aortic-Valve Replacement for Asymptomatic Severe Aortic Stenosis. N Engl J Med. 2025 Jan 15;392(3):217–27.
12. Rajkumar CA, Nijjer SS, Cole GD, Al-Lamee R, Francis DP. 'Faith Healing' and 'Subtraction Anxiety' in Unblinded Trials of Procedures. Circ Cardiovasc Qual Outcomes. 2018 Mar;11(3):e004665.
13. Loganath K, Craig NJ, Everett RJ, Bing R, Tsampasian V, Molek P, et al. Early Intervention in Patients With Asymptomatic Severe Aortic Stenosis and Myocardial Fibrosis: The EVOLVED Randomized Clinical Trial. JAMA. 2025 Jan 21;333(3):213.
14. Bonow RO. Myocardial Fibrosis and Timing of Intervention for Aortic Stenosis. JAMA. 2025 Jan 21;333(3):207–9.
15. Philippe Généreux MD, Marko Banovic MD, Duk-Hyun Kang MD, Gennaro Giustino MD, Bernard D. Prendergast MD, Brian R. Lindman MD, et al. Aortic Valve Replacement vs Clinical Surveillance in Asymptomatic Severe Aortic Stenosis: A Systematic Review and Meta-Analysis. J Am Coll Cardiol [Internet]. 2025 Mar 11 [cited 2025 Oct 1]; Available from: https://www.jacc.org/doi/10.1016/j.jacc.2024.11.006
16. Beerkens FJ, Tang GHL, Kini AS, Lerakis S, Dangas GD, Mehran R, et al. Transcatheter Aortic Valve Replacement Beyond Severe Aortic Stenosis. JACC. 2025 Mar 11;85(9):944–64.
17. Lindman BR, Pibarot P, Schwartz A, Oldemeyer JB, Su YR, Goel K, et al. Cardiac Biomarkers in Patients With Asymptomatic Severe Aortic Stenosis: Analysis From the EARLY TAVR Trial. Circulation. 2025 June 3;151(22):1550–64.
18. Aktaa S, Ali N, Ludman PF, Curzen N, Goodwin AT, Hildick-Smith D, et al. Geographical Inequality in Access to Aortic Valve Intervention in England: A Report from the UK Transcatheter Aortic Valve Implantation Registry and National Adult Cardiac Surgery Audit. Interv Cardiol Rev Res Resour. 2024 Aug 28;19:e15.