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REVIEW

Aortic valve replacement in asymptomatic severe aortic stenosis. A focused review

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Abstract

Asymptomatic severe aortic stenosis (AS) has traditionally been managed with watchful waiting because of low annual sudden death rates (<1%) and concerns regarding procedural risk. Emerging randomized data indicate that irreversible myocardial injury may occur before symptom onset and that early aortic valve replacement (AVR) may improve outcomes. This review summarizes evidence from contemporary randomized controlled trials evaluating early surgical AVR (SAVR) or transcatheter AVR (TAVR) *vs* conservative management or surveillance in asymptomatic patients with severe AS and preserved left ventricular ejection fraction (LVEF). The RECOVERY trial randomized 145 asymptomatic patients with very severe AS (mean age 64 years) to early SAVR or conservative care. Over a median follow-up of 6.2 years, all-cause mortality occurred in 1% of the early surgery group *vs* 15% with conservative management (hazard ratio [HR] 0.09; 95% CI 0.01-0.67; *p*=0.003). The AVATAR trial included 157 asymptomatic patients with severe AS, preserved LVEF, and negative exercise testing (mean age approximately 67 years). Over a median follow-up of 32 months, the composite endpoint of all-cause death, myocardial infarction, stroke, or heart failure hospitalization occurred in 16.6% of patients assigned to early surgery compared with 32.9% in the conservative group (HR 0.46; 95% CI 0.23-0.90; *p*=0.02). The EARLY TAVR trial randomized 901 asymptomatic patients with severe AS and preserved LVEF to TAVR or clinical surveillance (mean age 75.8 years). After a median follow-up of 3.8 years, the primary composite outcome of death, stroke, or unplanned cardiovascular hospitalization occurred in 26.8% of the TAVR group *versus* 45.3% of the surveillance group (HR 0.50; 95% CI 0.40-0.63; *p*<0.001). Cardiovascular hospitalizations occurred in 20.9% *vs* 41.7%, all-cause mortality in 8.4% *vs* 9.2%, and stroke in 4.2% *vs* 6.7%, with no excess procedural complications in the early TAVR group. Randomized evidence demonstrates that early AVR, including both SAVR and TAVR, reduces mortality and major cardiovascular events in carefully selected asymptomatic patients with severe AS. The integration of clinical features with risk stratification tools, such as global longitudinal strain, cardiac magnetic resonance imaging, natriuretic peptides, and computed tomography-based valve calcification, supports timely intervention before irreversible myocardial damage occurs.

Key words: aortic stenosis; aortic valve replacement; watchful waiting.

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Current standard of care and the rationale behind watchful waiting

Severe aortic stenosis (AS) is a progressive and potentially fatal condition, marked by obstruction of blood flow across the aortic valve and increasing pressure overload on the left ventricle.[1] Traditionally, intervention has been reserved for symptomatic patients or those with signs of left ventricular dysfunction. This conservative approach assumes that asymptomatic individuals with severe AS have a relatively low annual risk of sudden cardiac death, estimated at less than 1%,[2] and that valve replacement carries significant procedural risks, particularly in older or comorbid patients.[3] However, this strategy has increasingly come under scrutiny. Myocardial fibrosis, subclinical dysfunction, and irreversible structural remodeling can begin before any symptoms manifest, potentially reducing the long-term benefit of valve replacement when treatment is delayed.[4,5] As our understanding of disease progression has ad-

vanced and procedural risks have declined, especially with transcatheter approaches, the timing of intervention in asymptomatic severe AS has become a critical point of debate.[6]

Emerging data supporting early aortic valve replacement

Recent randomized controlled trials have provided new insights that challenge the long-standing paradigm of watchful waiting. The *Randomized Comparison of Early Surgery versus Conventional Treatment in Very Severe Aortic Stenosis* (RECOVERY) trial[7] enrolled 145 asymptomatic patients with very severe AS, defined as an aortic valve area <0.75 cm² and peak velocity >4.5 m/s or mean gradient >50 mmHg. Patients were randomized to early surgery or conservative management. After a median follow-up of 6.2 years, early surgical AVR was associated with significantly lower all-cause mortality (1% *vs* 15%; HR 0.09; 95% CI, 0.01-0.67; *p*=0.003), with no perioperative deaths. Notably, the study cohort was relatively young (mean age ~64 years), with few comorbidities, and all patients underwent surgical aortic valve replacement (AVR), limiting the generalizability of its findings to broader, older populations. The *Aortic Valve Replacement Versus Conservative Treatment in Asymptomatic Severe Aortic Stenosis* (AVATAR) trial,[8] published in 2022, extended this evidence to a more diverse and representative population. Conducted across multiple European centers, the AVATAR trial included 157 asymptomatic patients with severe AS and preserved left ventricular ejection fraction (LVEF), all of whom had negative exercise stress tests to confirm the absence of exertional symptoms. Participants were randomized to early surgical AVR or conservative treatment. After a median follow-up of 32 months, the primary composite endpoint of death, myocardial infarction, stroke, or unplanned heart failure hospitalization, occurred in 16.6% of patients in the early surgery group, compared to 32.9% in the conservative arm (HR 0.46; 95% CI, 0.23-0.90; *p*=0.02). Importantly, the mean age of participants was slightly older (~67 years), and the trial more closely reflected routine practice settings. Despite a modest sample size, the AVATAR trial underscored the potential long-term advantages of intervening before symptom onset.

Additionally, there is growing interest in using transcatheter AVR (TAVR) for asymptomatic severe AS, particularly in older, low-risk patients, because of its less invasive nature and strong safety profile.[9] The *Evaluation of Transcatheter Aortic Valve Replacement Compared to Surveillance for Patients With Asymptomatic Severe Aortic Stenosis* (EARLY TAVR) trial[10] is the first randomized trial to assess early transcatheter intervention in this population. The trial randomized 901 asymptomatic patients with severe AS and preserved ejection fraction to either TAVR or clinical surveillance. The mean age of the patients was 75.8 years. Over a median follow-up of 3.8 years, the primary composite outcome of death, stroke, or unplanned cardiovascular hospitalization occurred in 26.8% of patients in the TAVR group compared to 45.3% in the surveillance group (HR 0.50; 95% CI, 0.40-0.63; *p*<0.001). Rates of death (8.4% *vs* 9.2%) and stroke (4.2% *vs* 6.7%) were also lower in the TAVR group, while cardiovascular hospitalizations were significantly reduced (20.9% *vs* 41.7%). Importantly, there was no increase in procedural complications among patients who underwent early TAVR compared to those who later crossed over from surveillance. These results provide robust evidence that early intervention with TAVR may improve clinical outcomes and reduce the burden of cardiac events in selected asymptomatic patients. The results of these trials are summarized in Figure 1 and Table 1.

It is noteworthy that all three trials reported substantial crossover from the conservative arm to the intervention during follow-up. In RECOVERY, 24% of patients in the conservative group eventually underwent AVR, while in AVATAR, over 75% had crossed over by 4 years. In EARLY TAVR, a similar

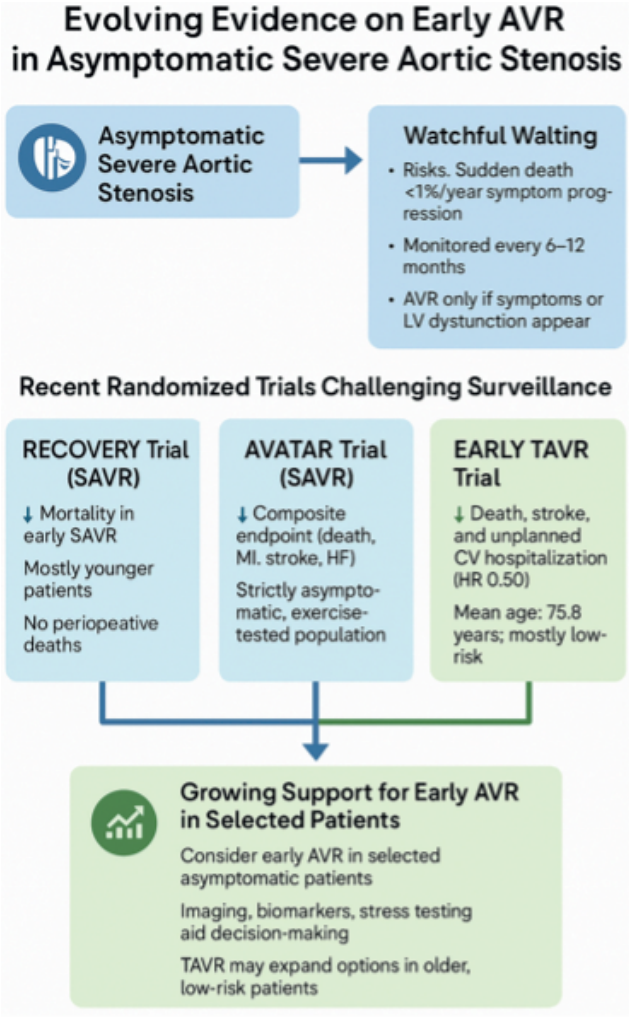

Figure 1. Early intervention *vs* conservative management for asymptomatic severe aortic stenosis.

Table 1. Summary of clinical trials.

	RECOVERY trial	AVATAR trial	EARLY TAVR trial
Year	2019	2024	2024
Randomized	Yes	Yes	Yes
No. of randomized patients	145	157	901
Follow-up time	6.2 years	5.3 years	3.8 years
Mean age	64.2 years	67 years	75.8 years
All-cause mortality	(HR 0.33; 95% CI, 0.12 to 0.90)	(HR 0.44; 95% CI, 0.23-0.85)	
CV mortality	(HR 0.09; 95% CI, 0.01 to 0.67)	(HR 0.54; 95% CI, 0.25-1.18)	

CI, confidence interval; HR, hazard ratio; CV, cardiovascular.

trend was observed, with most patients in the surveillance group receiving TAVR by the end of follow-up. These high crossover rates reflect the clinical reality that a significant proportion of asymptomatic patients eventually progress to requiring intervention, and they likely attenuate the observed benefit of early AVR in intention-to-treat analyses.

Further support comes from observational studies and meta-analyses.[11,12] A 2023 meta-analysis by Costa *et al.*,[13] which pooled data from 4,130 patients across twelve studies, reported that early AVR was associated with a 43% reduction in all-cause mortality (HR 0.57; 95% CI, 0.45-0.73; $p<0.001$) and a 52% reduction in heart failure hospitalization (HR 0.48; 95% CI, 0.29-0.80), without a statistically significant increase in stroke or perioperative death. These findings suggest that timely intervention may improve long-term outcomes in carefully selected patients. However, as with all observational data, these results are susceptible to residual confounding and selection bias, since healthier or more closely monitored patients may have been preferentially referred for early surgery.

Guideline recommendations and risk-based stratification

While data continues to accumulate, clinical guidelines have begun to evolve in response. The 2020 American College of Cardiology/American Heart Association (ACC/AHA) guidelines recommend AVR in asymptomatic patients with LVEF <50% (Class I), or in those undergoing other cardiac surgery.[14] Early AVR is considered reasonable (Class IIa) in patients with very severe AS (e.g., peak velocity ≥5.0 m/s), elevated brain natriuretic peptide (BNP) levels, rapid hemodynamic progression, or abnormal response to exercise testing. Similarly, the 2021 European Society of Cardiology (ESC) guidelines allow for early intervention in select asymptomatic patients, especially in high-volume centers with low surgical mortality.[15] These recommendations reflect a gradual but deliberate shift toward a more individualized and risk-based approach to early AVR.[16]

A key challenge lies in identifying which asymptomatic patients will benefit the most. Severe AS is not a homogeneous condition, and patient risk profiles vary widely.[17] Several clinical, imaging, and biomarker-based criteria can aid in stratifying risk.[18,19] Very severe AS, often defined by a mean gradient >60 mmHg or peak velocity >5.0 m/s, has been consistently associated with higher mortality, even in the absence of symptoms.[20] In such cases, myocardial function may already be impaired even without obvious symptoms. Subclinical left ventricular dysfunction, detected by reduced global longitudinal strain or cardiac magnetic resonance imaging evidence of fibrosis, can signal early myocardial injury not reflected by LVEF alone.[21] Elevated natriuretic peptide levels, particularly when adjusted for age and kidney function, are also linked to a higher risk of symptom onset, hospitalizations, and mortality.[22] Exercise testing can unmask exertional symptoms or hemodynamic instability that is not apparent at rest.[23] An abnormal test such as hypotension, arrhythmias, or limited exercise capacity has prognostic significance and can shift management toward earlier intervention.[24] Lastly, aortic valve calcification burden, as measured by computed tomography calcium scoring, has emerged as a robust predictor of rapid disease progression and adverse outcomes, particularly in patients whose hemodynamic parameters are borderline.[25]

The benefit of early AVR likely stems from the opportunity to intervene before the development of irreversible myocardial changes such as hypertrophy and fibrosis.[26] The *Early Valve Replacement Guided by Biomarkers of Left Ventricular Decompensation in Asymptomatic Patients with Severe Aortic Stenosis* (EVOLVED) trial employed cardiac magnetic resonance (CMR) based markers of myocardial fibrosis to risk-stratify asymptomatic patients, aiming to identify those who may benefit from early surgery.[27] Although the trial did not show a statistically significant mortality benefit, it highlighted the value of imaging biomarkers in guiding the timing of intervention.

Although early AVR offers potential benefits, it raises concerns about long-term valve management, particularly as interventions are considered at younger ages. Due to valve degeneration, younger patients undergoing AVR may require repeat procedures over their lifetime. This highlights the need for individualized decision-making, incorporating not only short-term risk but also long-term durability, patient preferences, and reintervention feasibility.

Conclusions

The longstanding strategy of deferring intervention until symptoms arise has guided management of severe AS for decades. However, it may not be suitable for all patients with severe AS. A growing body of evidence suggests that for many patients, waiting may mean missing a critical window for optimal intervention. Early AVR in selected individuals is now supported by clinical data and contemporary guidelines. While routine early intervention is not warranted for all, current evidence supports a more individualized approach that weighs procedural risks against the potential benefits of preserving cardiac function and optimizing long-term prognosis.

Contributions

All authors made a substantive intellectual contribution, read and approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

Conflict of interest

The authors declare that they have no competing interests, and all authors confirm accuracy.

Ethical approval

Not applicable.

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