



# Is early transcatheter aortic valve replacement for asymptomatic aortic stenosis justified? – critical analysis of the strategy

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## Introduction

A recent study by Généreux *et al.* demonstrated that among patients with asymptomatic severe aortic stenosis, an early transcatheter aortic valve replacement (TAVR) strategy was superior to clinical surveillance in reducing the incidence of death, stroke, or unplanned hospitalization for cardiovascular causes (1). This finding represents a significant advancement in the management of this condition. The question that arises is: what prompted the initiation of this study?

Two previous randomized controlled trials (RCTs) demonstrated the benefits of early surgical aortic valve replacement (SAVR) in patients with asymptomatic severe aortic stenosis (2,3). Although there are differences between SAVR and TAVR, these findings provided the rationale for conducting a RCT to evaluate the role of TAVR. Another contributing factor was the study by Mack *et al.*, which reported low rates of bioprosthetic valve failure and a low incidence of significant paravalvular regurgitation in low-risk patients at five-year follow-up (4). Furthermore, while the composite endpoint of death, stroke, or rehospitalization favored TAVR over SAVR at one year, the difference was no longer significant at five years. The authors concluded

that these findings should inform the role of TAVR in the treatment of severe aortic stenosis, particularly in patients who are not candidates for surgery (4,5).

## Strengths and limitations of the study

This study was a large-scale RCT that included 901 patients. As expected, the control group exhibited rapid clinical deterioration, highlighting the need for a more refined risk stratification system to identify patients most likely to deteriorate and prioritize them for early TAVR (6). The need for a more refined risk stratification system includes criteria such as valve durability, conduction abnormalities, paravalvular leak, reintervention rates, and concomitant treatment of coronary artery disease (5). Interestingly, another RCT, the EVOLVED trial, which investigated a similar comparison, yielded different results. While early intervention reduced unplanned hospitalizations, it did not improve survival. Therefore, enthusiasm for early intervention should be tempered by the recognition that although quality of life may improve due to fewer unplanned hospitalizations, survival remains unaffected. Consequently, there is no consensus regarding the widespread adoption of

early intervention, and long-term survival data are needed to better guide clinical decision-making (7).

Other studies, such as those by Huded *et al.* and Dimitriadis *et al.*, have raised concerns about the findings of this study. Dimitriadis *et al.* noted that the rate of procedural complications was similar to that observed in patients with symptomatic aortic stenosis (8.1% *vs.* 9.9%). Given that sudden death rates in the symptomatic cohort were below 1%, he questioned whether early TAVR poses an undue risk of serious complications (8-10). Like many others, these authors emphasized the need for more robust criteria to detect disease progression (9).

A recent RCT, the AVATAR trial, arrived at similar conclusions to those of Génèreux *et al.* (1,11). However, Ennezat *et al.* criticized the AVATAR study for inadequately assessing the control group, suggesting that serial exercise testing should have been included, as proposed by Taniguchi *et al.* Notably, exercise testing every six months has been shown to reveal symptoms in approximately 30% of patients previously classified as asymptomatic (12,13).

Collectively, multiple researchers have pointed out the lack of robust control group criteria, including strict echocardiographic parameters, six-monthly exercise testing, and comprehensive comparisons of complications between study arms. Importantly, studies such as AVATAR also failed to demonstrate a significant mortality benefit with early intervention, suggesting that the primary advantage of early TAVR lies in improved quality of life. The key question remains whether this improvement alone justifies the widespread adoption of early TAVR.

### Challenges in implementing early TAVR in clinical practice

One major limitation of early TAVR is that although the composite primary endpoint included mortality, stroke, and unplanned hospitalization, when mortality was analyzed independently, it was similar between the groups (1). While quality of life was better at two years, the question remains whether this benefit justifies the risks of early TAVR, including procedure-related complications and potential mortality (2). Another major limitation is that 90% of patients in the control group eventually underwent TAVR during the study period, suggesting that the “control” group effectively represented a delayed intervention strategy rather than true clinical surveillance. Given that early TAVR did not improve all-cause mortality at four years, it is unlikely to significantly alter current clinical practice (14).

A key limitation of this study is the duration of follow-up. In the RECOVERY trial, survival curves only began to diverge after four years, with a clear separation occurring after six years of follow-up (2). Additionally, early TAVR in this study was performed in a relatively low-risk elderly population. Therefore, a comprehensive evaluation of associated risks is necessary, including valve durability, conduction abnormalities, paravalvular leak, reintervention rates, and concomitant treatment of coronary artery disease (15).

### Is early TAVR ready for routine implementation?

The primary benefit of early TAVR was a reduction in unplanned hospitalizations at five years, with no significant impact on mortality or stroke rates. Moreover, the level of patient monitoring in this trial was likely superior to that encountered in routine clinical practice (16). Given the numerous limitations identified, it is premature to introduce early TAVR as a standard of care.

### Conclusions

At present, early TAVR for asymptomatic severe aortic stenosis offers clear advantages over clinical surveillance in terms of reducing unplanned hospitalizations and improving quality of life. However, given the limitations of current evidence, including the lack of mortality benefit and uncertainties regarding long-term outcomes, further data are required before this approach can be widely adopted in clinical practice.

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