

## Editorial



# Reconsidering the Timing of Aortic Valve Replacement in Symptomatic Normal-Flow Low-Gradient Severe Aortic Stenosis

Hsin-Fu Lee , MD<sup>1,2,3,4</sup>

<sup>1</sup>Division of Cardiology, Department of Internal Medicine, New Taipei City Municipal Tucheng Hospital, New Taipei City, Taiwan

<sup>2</sup>The Cardiovascular Department, Chang Gung Memorial Hospital, Linkou, Taoyuan City, Taiwan

<sup>3</sup>College of Medicine, Chang Gung University, Taoyuan City, Taiwan

<sup>4</sup>Graduate Institute of Clinical Medical Sciences, College of Medicine, Chang Gung University, Taoyuan City, Taiwan

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### Correspondence to

Hsin-Fu Lee, MD

Division of Cardiology, Department of Internal Medicine, New Taipei City Municipal Tucheng Hospital, No. 6, Sec. 2, Jincheng Rd., Tucheng Dist., New Taipei City 23652, Taiwan.

Email: [hsinfu.lee@gmail.com](mailto:hsinfu.lee@gmail.com)

[8805033@cgmh.org.tw](mailto:8805033@cgmh.org.tw)

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### ORCID iDs

Hsin-Fu Lee 

<https://orcid.org/0000-0001-6955-2100>

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The recently published study, “Early Aortic Valve Replacement in Symptomatic Normal-Flow Low-Gradient Severe Aortic Stenosis: A Propensity Score–Matched Retrospective Cohort Study,”<sup>1)</sup> provides an insightful investigation into a critical yet understudied area of cardiovascular disease treatment. It is an important reminder of the dynamic nature of the field, where continuous review of established procedures is required to optimize patient outcomes.

A certain patient population, although exhibiting echocardiographic indications of severe aortic stenosis (AS) (with an aortic valve area of less than 1 cm<sup>2</sup>), does not fulfill the standard hemodynamic criteria needed for intervention, namely, an aortic valve mean gradient of 40 mmHg or more and/or a peak velocity of 4 m/s or higher. As a result, these patients are often categorized as having “low-gradient” severe AS.<sup>2)</sup> Patients are classified as having “low-flow, low-gradient” severe AS when this condition arises due to a reduced left ventricular (LV) stroke volume ( $\leq 35$  mL/m<sup>2</sup>). On the other hand, patients maintaining a normal LV stroke volume ( $> 35$  mL/m<sup>2</sup>) are designated as experiencing “normal-flow, low-gradient” (NFLG) severe AS.<sup>3)</sup> NFLG severe AS can sometimes be misidentified as moderate AS, that could explain why some patients diagnosed with moderate AS experience worse outcomes than others.<sup>4)</sup> Moreover, prognostic indicators, the criteria for intervention, and the potential benefits from surgical procedures for patients with NFLG remain uncertain due to conflicting data previously published on these matters.<sup>3)5)6)</sup>

The aforementioned study challenges this convention, suggesting that early intervention might be beneficial for patients with NFLG severe AS. Through robust propensity score matching, when comparing the early aortic valve replacement (AVR) group and conservative care group (excluding patients who underwent delayed AVR), the findings reveal a notably lower occurrence of composite end-points such as all-cause death and unplanned heart failure hospitalization in the early AVR group (5.0% vs. 15.1% per year; hazard ratio [HR], 0.47; 95% confidence interval [CI], 0.24–0.92;  $p=0.027$ ). The incidence of all-cause death also significantly reduced (2.5% vs. 7.9% per year; HR, 0.34; 95% CI, 0.14–0.83;  $p=0.017$ ). These outcomes present a persuasive argument in favor of early AVR, highlighting its

**Data Sharing Statement**

The data generated in this study is available from the corresponding author upon reasonable request.

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potential to improve patient prognosis without substantial complications, urging us to rethink the currently practiced wait-and-watch approach. However, while the evidence from the study is compelling, it is vital to proceed with caution. AVR, despite advancements, still carries considerable risk, and an overly aggressive treatment approach may lead to unnecessary complications. Therefore, a balance must be struck, and decision-making should be individualized, accounting for patient-specific factors such as age, overall health status, and comorbid conditions. Moreover, the propensity score matching employed in this study, although adept at controlling observed confounders, may not account for unmeasured or hidden biases. Hence, the results must be interpreted keeping this limitation in mind. Randomized controlled trials could provide more definitive answers, and we should advocate for such trials in the future.

In conclusion, the study opens a fascinating discourse on the management of NFLG severe AS. It brings to light the possibility that early AVR might be more beneficial than initially thought, possibly changing the course of how we view and treat this condition. Nevertheless, more extensive research is required to solidify these findings and to develop a more nuanced understanding of patient selection for early AVR.

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