THE ANATOLIAN JOURNAL OF CARDIOLOGY

Official journal of the TURKISH SOCIETY OF CARDIOLOGY

Clarification Needed on Methodological Aspects of TAVR Outcomes Across Flow-Gradient and Ejection Fraction Profiles

LETTER TO THE EDITOR

To the Editor,

We read with interest the recent article by Yamashita et al[1] examining outcomes after transcatheter aortic valve replacement (TAVR) across distinct flow-gradient and ejection fraction profiles. The study addresses an important clinical question; however, several methodological issues may affect interpretation and merit clarification.

First, cardiovascular (CV) death is designated a primary endpoint, with outcome definitions stated to align with STS/TVT and VARC-3 criteria.[1,2] However, the manuscript does not detail how CV deaths were ascertained or adjudicated. This is particularly important given the discrepancy between Table 3 and Supplementary Table 1. In Table 3, the adjusted hazard ratio for CV death in the LF-LG with reduced ejection fraction (rEF) group is not significant (HR: 1.04, 95% CI: 0.50-2.16), whereas Supplementary Table 1 reports a significant association (HR: 1.94, 95% CI: 1.19-3.18).[1] Clarification regarding this divergence would be helpful.

Second, the study does not report post-TAVR use of heart failure guideline-directed medical therapy (GDMT) or atrial fibrillation (AF) therapies. Without these data, it is difficult to assess whether differences in medical management influenced outcomes, particularly in groups with reduced EF or high AF prevalence. Both GDMT- and AF-directed treatments are known to impact CV death, heart failure hospitalization, and stroke risk.[3,4]

Third, AF was excluded from final models despite prevalence as high as 71% in some subgroups; Supplementary Table 1 lists AF as "not selected" across all endpoints.[1] Atrial fibrillation's exclusion may thus confound phenotype-outcome associations and introduce measurement bias in flow-dependent groupings. Specifically, the left ventricular outflow tract time-velocity integral was averaged over five cardiac cycles in AF and three in sinus rhythm, introducing greater variability in stroke volume index among patients with AF.[1]

The small LF-HG with rEF cohort (n = 50) also limits precision for CV death estimates, as reflected in wide confidence intervals (Table 3). This imprecision likely contributes to the discrepancy between Table 3 and Supplementary Table 1.

These issues are central to interpreting the study's conclusions. We respectfully encourage the authors to clarify CV death adjudication methods, report GDMT and AF therapy use where available, and consider sensitivity analyses that force AF into the covariate set. These steps would enhance transparency and strengthen the study's contribution to clinical practice.

Hakan Tibilli[1]

Murat Abdulhamit Ercişli[2]

[1]*Department of Cardiology, Başkent University Adana Hospital, Adana, Türkiye*
[2]*Department of Cardiovascular Surgery, Gaziantep City Hospital, Gaziantep, Türkiye*

Corresponding author:
Hakan Tibilli
✉ khanofmed@yahoo.com

Cite this article as: Tibilli H, Ercişli MA. Clarification needed on methodological aspects of TAVR outcomes across flow-gradient and ejection fraction profiles. *Anatol J Cardiol.* 2026;30(2):133-134.

DOI:10.14744/AnatolJCardiol.2025.5747

Declaration of Interests: The authors have no conflicts of interest to declare.

Funding: The authors declare that this study received no financial support.

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