ARCHIVES OF THE
TURKISH SOCIETY
OF CARDIOLOGY

Official journal of the
TURKISH
SOCIETY OF
CARDIOLOGY

Addressing the Survival Paradox, Procedural Learning Curve, and Pharmacological Confounding in Patients with Left Ventricular Systolic Dysfunction Undergoing Transcatheter Aortic Valve Replacement

Transkateter Aort Kapak Değişimi Uygulanan Sol Ventrikül Sistolik Disfonksiyonlu Hastalarda Hayatta Kalma Paradoksu, Prosedürel Öğrenme Eğrisi ve Farmakolojik Karıştırıcı Etkenlerin Ele Alınması

LETTER TO THE EDITOR
EDİTÖRE MEKTUP

To the Editor,

I read with great interest the article by Keskin et al.[1] comparing balloon-expandable valves (BEV) and self-expanding valves (SEV) in patients with left ventricular systolic dysfunction (LVSD) undergoing transcatheter aortic valve replacement (TAVR). While the authors provide valuable real-world evidence in this fragile population, several methodological considerations warrant further discussion.

First, the discrepancy between the higher crude long-term mortality in the BEV group and the non-significant Kaplan–Meier analysis deserves attention. While baseline risks (older age and higher European System for Cardiac Operative Risk Evaluation II [EuroSCORE II] in the BEV group) are primary drivers,[2] the numerically longer median follow-up in the BEV cohort (1,160 vs. 962 days; P = 0.09) represents an equally important confounder. In high-mortality cohorts, an additional 200 days of observation naturally accumulates more events independent of device performance. This temporal imbalance explains why the crude mortality difference disappears once appropriately accounted for in survival analyses.

Second, the "procedural learning curve" may have disproportionately affected the BEV cohort. As early procedures in the study program were predominantly BEV-based, the higher in-hospital mortality (12.5% vs. 6.0%) may reflect institutional maturation rather than intrinsic device-related risk. Center experience is a well-documented predictor of periprocedural outcomes;[3] therefore, adjusting for the era effect would allow for a more nuanced comparison.

Finally, a major underappreciated confounder is the threefold higher prevalence of sodium–glucose cotransporter-2 inhibitor (SGLT-2i) use in the SEV group (34.0% vs. 12.5%; P < 0.001). Although SGLT-2i use was non-significant in the multivariable Cox model, this finding may reflect limited statistical power. Recent data from Morel et al.[4] suggest that SGLT-2i therapy after TAVR is independently associated with reduced mortality and bioprosthetic valve failure. This pharmacological advantage in the SEV group—particularly relevant in LVSD patients who depend on myocardial recovery—represents a systematic bias. Sensitivity analyses restricted to SGLT-2i non-users could clarify whether this imbalance influenced the long-term outcomes.

In conclusion, the survival parity between BEV and SEV in this study is likely shaped by the convergence of baseline risk differences, follow-up duration, and the learning curve. These observations underscore the need for careful adjustment for pharmacological covariates in future prospective studies aimed at optimizing valve selection in patients with reduced ejection fraction.

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Received: March 23, 2026
Accepted: March 24, 2026

Cite this article as: Doğan M. Addressing the Survival Paradox, Procedural Learning Curve, and Pharmacological Confounding in Patients with Left Ventricular Systolic Dysfunction Undergoing Transcatheter Aortic Valve Replacement. *Turk Kardiyol Dern Ars.* 2026;54(4):374–375.

DOI: 10.5543/tkda.2026.63817

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Conflict of Interest: The author has no conflicts of interest to declare.

Funding: The author declared that this study received no financial support.

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