ARCHIVES OF THE
TURKISH SOCIETY
OF CARDIOLOGY

Official journal of the
TURKISH
SOCIETY OF
CARDIOLOGY

Revisiting Iron Deficiency in Heart Failure: The Prognostic Value of Type 1 Iron Deficiency

Kalp Yetmezliğinde Demir Eksikliğini Yeniden Ele Almak: Tip 1 Demir Eksikliğinin Prognostik Değeri

LETTER TO THE EDITOR
EDİTÖRE MEKTUP

To the Editor,

I read with great interest the article by Çolluoğlu et al.,[1] titled "*Beyond the Guidelines: The Critical Role of Type 1 Iron Deficiency in Predicting Mortality in Patients with Heart Failure*," published in the April 2025 issue of the *Archives of the Turkish Society of Cardiology*. The authors provide compelling evidence that Type 1 iron deficiency (ID), defined as transferrin saturation (TSAT) ≤ 15–16% with anemia, is an independent predictor of one-year all-cause mortality in patients with heart failure (HF), unlike Type 2 or Type 3 ID or guideline-defined ID. This study highlights the need to refine ID classification to better identify high-risk HF patients.

The findings challenge the reliance on guideline-defined ID criteria, which primarily focus on ferritin and TSAT levels extrapolated from non-HF populations.[2] The higher mortality rate in Type 1 ID patients (38.3%) compared to those with Type 2 or Type 3 ID (22.7%) or guideline-defined ID (26.0%) underscores the prognostic value of this novel classification. We agree that Type 1 ID, reflecting reduced systemic iron availability, may better capture the iron demands of cardiomyocytes, as supported by the significant hazard ratios in both unadjusted (hazard ratio [HR]: 2.289, $P < 0.001$) and adjusted (HR: 1.543, $P = 0.020$) Cox regression analyses.[1]

However, I would like to raise a point for discussion. The study notes that patients with Type 1 ID had higher B-type natriuretic peptide (BNP) levels and lower estimated glomerular filtration rate (eGFR), suggesting more severe HF.[1] Could the increased mortality risk associated with Type 1 ID partly reflect an advanced disease state rather than ID alone? Including New York Heart Association (NYHA) class data, as acknowledged in the study's limitations, could have clarified this relationship.[3] Additionally, exploring hepcidin levels, which mediate functional ID by sequestering iron in HF, could further validate the mechanistic pathways proposed by Weber et al.[4,5] The absence of NYHA functional class data in the study by Çolluoğlu et al.[1] limits the ability to fully discern whether the elevated mortality risk in Type 1 ID patients is solely attributable to ID or reflects more advanced heart failure. Given that higher NYHA classes (III–IV) are associated with worse prognosis, their inclusion could have clarified whether the observed 38.3% mortality rate in Type 1 ID patients was partly driven by greater disease severity, as suggested by their higher BNP levels and lower eGFR. Incorporating NYHA class data in future studies could enhance the precision of risk stratification and strengthen the prognostic specificity of Type 1 ID in HF.

I commend the authors for their rigorous methodology and for emphasizing the potential of intravenous iron supplementation as a therapeutic strategy. Their findings advocate for revising ID diagnostic criteria in HF to improve risk stratification and patient outcomes. I look forward to future studies validating these results in larger, multicenter cohorts, and I believe these considerations may further strengthen future research on this topic.

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

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

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Received: June 19, 2025
Accepted: August 14, 2025

Cite this article as: Zorlu Ç. Revisiting Iron Deficiency in Heart Failure: The Prognostic Value of Type 1 Iron Deficiency. *Turk Kardiyol Dern Ars.* 2025;53(8):634–635.

DOI: 10.5543/tkda.2025.29473

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