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Interpreting Early Reticulocyte Response After Intravenous Iron Therapy in Heart Failure

LETTER TO THE EDITOR

To the Editor,

Kumral et al[1] evaluated whether an early reticulocyte rise after intravenous ferric carboxymaltose identifies short-term hematologic response in hospitalized heart failure with left ventricular ejection fraction below 50%.[1] The topic is clinically relevant because intravenous iron is recommended in symptomatic heart failure with iron deficiency, but treatment monitoring still relies on ferritin and transferrin saturation measured weeks after administration.[2]

However, the present data support early biological signal detection rather than a definitive treatment-response marker. First, 183 of 251 screened patients were excluded, mainly because baseline or follow-up laboratory data and clinical follow-up were unavailable.[1] This degree of post-screen exclusion can introduce substantial selection bias. The final analysis included only 68 patients, and the non-responder group was particularly small. Long-term comparisons based on such imbalanced subgroups are vulnerable to unstable event estimates.

Second, the 1-month hemoglobin increase is a post-baseline classification. Associations between this responder status and 2-year emergency visits or mortality should therefore be interpreted as prognostic associations, not as evidence that the early reticulocyte rise mediates later clinical benefit. In the same study, responders already had higher baseline reticulocyte values.[1] This pattern suggests that baseline marrow activity may identify a biologically fitter subgroup with greater erythropoietic reserve, independent of the treatment effect itself.

Third, the manuscript alternates between describing reticulocytes as a percentage of circulating red cells and reporting them in 10^9/L.[1] Clarification of whether the primary analyses used relative reticulocyte percentage, absolute reticulocyte count, or both would improve reproducibility. This distinction is relevant because anemia severity can alter percentage-based interpretation, whereas absolute reticulocyte indices are generally preferred for response assessment.[3]

The current findings justify prospective validation of early reticulocyte kinetics after intravenous iron. They do not yet establish reticulocyte rise as a surrogate for long-term clinical benefit in heart failure, particularly when larger trials of intravenous iron have shown more consistent effects on hospitalization than on mortality.[4,5]

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