

Reply to the Letter to the Editor: "Interpreting Early Reticulocyte Response After Intravenous Iron Therapy in Heart Failure"

To the Editor,

We thank the authors¹ for their interest in our study² and for their constructive comments regarding the interpretation of early reticulocyte dynamics following intravenous iron therapy in patients with heart failure.

First, the authors note the high number of excluded patients. As stated in our manuscript, most exclusions were due to the absence of paired laboratory measurements within the predefined 72- to 120-hour window or incomplete follow-up data. Because early reticulocyte assessment is not routinely performed in clinical practice, requiring both baseline and early post-treatment measurements inevitably reduced the analyzable cohort. Nevertheless, this approach was necessary to evaluate early hematologic kinetics following intravenous iron therapy in a real-world clinical setting.

Second, we agree that classification based on a ≥ 1 g/dL hemoglobin increase at 1 month represents a post-baseline categorization and therefore associations with long-term outcomes should be interpreted cautiously. Our primary aim was to assess whether early reticulocyte dynamics could identify patients demonstrating an active erythropoietic response after intravenous iron therapy. Although responders had higher baseline reticulocyte levels, the predictive signal was not limited to baseline measurements. Importantly, the early dynamic change in reticulocyte levels (delta reticulocyte) was also significantly associated with subsequent hemoglobin increase.

Third, our analyses focused on the change in reticulocyte levels between baseline and 72-120 hours (delta reticulocyte). Receiver operating characteristic analysis identified a $>9\%$ increase in delta reticulocyte as the optimal threshold predicting a ≥ 1 g/dL hemoglobin increase at 1 month, and patients were categorized accordingly.

These findings suggest that early reticulocyte kinetics may represent a practical indicator of early hematologic responsiveness to intravenous iron therapy. While hypothesis generating, they highlight the potential value of early erythropoietic markers for treatment monitoring in patients with heart failure.

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LETTER TO THE EDITOR REPLY

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