

Second, the timing of the iron assessment was not appropriately aligned with any therapeutic opportunity. The median interval between iron testing and surgery was only two days—far shorter than the 4–6 weeks recommended by the perioperative anemia management guidelines [2]. This brief window is physiologically insufficient for a meaningful erythropoietic response even with fast-acting intravenous iron formulations. Thus, the null finding may reflect a process limitation rather than biological futility.

Third, the study did not capture postoperative functional iron deficiency, a phenomenon that is increasingly being recognized after major surgery. Persistent inflammation elevates the levels of hepcidin and acute-phase proteins, promoting iron sequestration within macrophages and reducing bone marrow iron availability [3,4]. This “hidden” deficiency can delay hemoglobin recovery despite adequate total body iron stores. Recent evidence in cardiac surgery further shows that short-term preoperative intravenous iron in iron-deficient non-anemic patients fails to compensate for perioperative iron loss when administered too close to the time of surgery [5].

Taken together, the reported neutral direct association may be a compounded effect of the low-sensitivity model, suboptimal diagnostic timing, and unmeasured postoperative functional iron deficiency. Future prospective studies should incorporate a dynamic iron-deficit index integrating baseline status, estimated intraoperative iron loss, and postoperative inflammatory activity to better represent the true perioperative iron balance and recovery potential. For anesthesiologists, recognizing this hidden postoperative iron restriction may guide more effective timing of perioperative iron assessment and supplementation strategies.

Hsin-An Hsu, Wen-Ting Lin, Ming-Hui Hung

Department of Anesthesiology, National Taiwan University Hospital, Taipei, Taiwan

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Corresponding author: Ming-Hui Hung, M.D., M.S.

Department of Anesthesiology, National Taiwan University Hospital, No. 7 Chung-Shan South Road, Taipei 100225, Taiwan
Tel: +886-2-2312-3456
Email: mhhung@ntu.edu.tw

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Author Contributions: Hsin-An Hsu (Conceptualization; Data curation; Writing – original draft; Writing – review & editing); Wen-Ting Lin (Conceptualization; Data curation; Writing – original draft; Writing – review & editing); Ming-Hui Hung (Conceptualization; Data curation; Supervision; Writing – original draft; Writing – review & editing)

ORCID: Hsin-An Hsu, <https://orcid.org/0009-0004-1149-6555>; Wen-Ting Lin, <https://orcid.org/0009-0007-0971-8288>; Ming-Hui Hung, <https://orcid.org/0000-0002-2575-3004>

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Response to “Comment on Association between non-anemic iron deficiency and outcomes following off-pump coronary artery bypass surgery: a retrospective analysis”



Dear Editor,

We received a Letter to the Editor regarding our recent publication in the *Korean Journal of Anesthesiology* titled “Reassessing the role of preoperative non-anemic iron deficiency in off-pump cardiac surgery: insights beyond a negative association.” [1] We appreciate the readers’ thoughtful comments and the opportunity to clarify several important aspects of our study [2].

First, regarding the assertion that the surgical nature of off-pump coronary artery bypass grafting (OPCAB) may attenuate the detectable impact of iron deficiency (ID), we agree with their observation that OPCAB is an inherently “low-sensitivity” model for detecting iron-related vulnerabilities. However, this was precisely why we examined this specific cohort: the study was intentionally designed to evaluate ID within a patient- and surgery-specific context, in which cardiopulmonary bypass-related hemodilution and inflammation are minimized. Notably, similar findings have been reported even in on-pump and mixed types of cardiac surgeries [3], where physiological stressors are far more pronounced. Although these are findings from single-center retrospective studies, this consistency suggests that the neutral association may not be solely attributable to the OPCAB setting, but may instead reflect a broader characteristic of non-anemic ID in cardiac surgery patients.

Second, regarding the concern that the interval between iron assessment and surgery was too short (a median of two days) to allow any therapeutic intervention, we respectfully disagree that this represents a methodological limitation. Our aim was not to evaluate the efficacy of iron replacement, but rather to classify patients' baseline iron status as an exposure variable. In this context, the temporal proximity strengthens the internal validity of the study: a narrow interval reduces the likelihood of misclassification bias by ensuring that the iron profile closely reflects the patient's true preoperative physiological state. Thus, a short testing-to-surgery interval should be viewed as a design strength rather than a constraint.

Finally, regarding whether postoperative ID was considered in the interpretation of the results, we acknowledge that postoperative iron metabolism was not captured, which limits our ability to characterize postoperative functional ID. However, postoperative inflammation-driven iron sequestration is expected in most patients. Given that the type of surgery in our cohort was uniform, the magnitude and pattern of postoperative inflammation were likely more consistent than they would be in heterogeneous cardiac surgery cohorts. Moreover, although this phenomenon would likely have been more pronounced in those patients already iron deficient preoperatively, it did not translate into differences in prognosis. Even in cardiopulmonary bypass cases, in which nearly all patients develop postoperative ID [4], preoperative non-anemic ID was not associated with a worse 90-day DAOH (days alive and out of hospital) [5].

We hope that our response contributes to a more balanced understanding of the study results and underscores the need for future prospective investigations to better define the role of non-anemic ID in cardiac surgery.

Young-Lan Kwak

Department of Anesthesiology and Pain Medicine, Severance Cardiovascular Hospital, Anesthesia and Pain Research Institute, Yonsei University College of Medicine, Seoul, Korea

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Corresponding author: Young-Lan Kwak, M.D., Ph.D.

Department of Anesthesiology and Pain Medicine, Severance Cardiovascular Hospital and Anesthesia and Pain Research Institute, Yonsei University College of Medicine, 50 Yonsei-ro, Seodaemun-gu, Seoul 03722, Korea
Tel: +82-2-2228-8513 Fax: +82-2-2227-8063
Email: ylkwak@yuhs.ac

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ORCID: Young-Lan Kwak, <https://orcid.org/0000-0002-2984-9927>

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