

# Interpreting Blood Transfusion in Hip Fracture Surgery: Marker of Severity Rather Than Mediator of Harm? [Letter]

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## Dear editor

We read with great interest the recent article by Al-Husinat et al<sup>1</sup> examining risk factors for post-operative blood transfusion and associated outcomes following hip fracture surgery in a multicentre cohort of 1,040 patients. The authors are to be commended for providing important regional data and for demonstrating that, although transfusion was associated with ICU admission and prolonged hospital stay, it was not independently associated with all-cause mortality after multivariable adjustment. Notably, the authors conclude that transfusion may represent a marker of higher clinical acuity or complexity rather than a direct cause of adverse outcomes, underscoring the importance of careful risk adjustment when interpreting observational associations. We agree that this distinction is critical and warrants further emphasis.

In observational hip fracture populations, transfusion is often intertwined with baseline physiological vulnerability. Variables not captured in the present analysis including pre-fracture functional status, formal frailty indices, intraoperative estimated blood loss and perioperative hemodynamic instability, plausibly influence both transfusion requirement and downstream outcomes. Frailty and comorbidity burden independently predict short-term mortality and postoperative escalation following hip fracture surgery,<sup>2</sup> and transfusion may therefore function primarily as a surrogate for limited physiological reserve rather than a mediator of deterioration. This is consistent with emerging work in older adult populations highlighting the central role of biological vulnerability in clinical decision-making, as well as objective measures of physiological reserve such as sarcopenia.<sup>3,4</sup> Similarly, the temporal relationship between transfusion and ICU admission remains unclear. ICU transfer may precede transfusion or reflect evolving postoperative complications, making causal direction difficult to establish without time-dependent or mediation modelling. While the authors appropriately adjusted for measured confounders, residual confounding from unmeasured markers of severity remains likely in retrospective analyses. This is further supported by genome-wide association studies demonstrating that genetic predisposition contributes to heterogeneity in disease risk and outcomes, reinforcing the importance of accounting for underlying biological vulnerability beyond routinely measured clinical variables.<sup>5,6</sup> In this context, the finding that transfusion did not independently predict mortality strengthens the interpretation that it reflects underlying complexity rather than drives poor outcome.

The study's identification of low preoperative haemoglobin, clopidogrel use and unstable intertrochanteric fractures as predictors of transfusion is clinically important and aligns with contemporary Patient Blood Management (PBM) principles. Early recognition and optimisation of anaemia, careful perioperative coordination of antiplatelet therapy and strategies to minimise intraoperative blood loss remain central to improving outcomes in this population.<sup>7</sup> However, additional perioperative factors known to influence transfusion risk including quantified intraoperative blood loss and the use of antifibrinolytics such as tranexamic acid were not reported and may introduce residual confounding.<sup>8</sup> Clarification

regarding transfusion timing (intraoperative versus postoperative), number of units administered and intercentre variability would further contextualise the reported transfusion rate of 35.8%, which appears higher than that described in other national cohorts.<sup>9</sup> From a methodological standpoint, reliance on stepwise logistic regression based on p-value thresholds may risk model instability and reduced generalisability;<sup>10</sup> prespecified variable selection with internal validation techniques could enhance robustness in future analyses.

Overall, this study contributes valuable data and appropriately cautions against interpreting transfusion as a causal determinant of mortality. Framing transfusion within a broader model of geriatric vulnerability, integrating frailty, physiological reserve and perioperative blood management, may further clarify its role within contemporary hip fracture pathways. We congratulate the authors on their important work and look forward to further research refining risk stratification and optimisation strategies in this high-risk population.

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## Disclosure

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