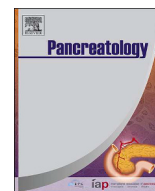




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Letter to the Editor

Comment on “Effect of albumin infusion in patients with predicted severe acute pancreatitis: A randomized controlled trial”

Dear Editor,

We read with great interest Shu et al.'s recent randomized controlled trial investigating albumin infusion in patients with predicted severe acute pancreatitis (SAP) [1]. This single-center study addresses a long-underexplored question in SAP management, providing valuable preliminary evidence for albumin's potential role. However, three critical limitations require further discussion to strengthen the clinical relevance of its findings and guide future research.

A major limitation is the lack of patient stratification by acute pancreatitis severity or baseline serum albumin levels, which substantially weakens the interpretability of the negative primary outcomes (no differences in SIRS remission or 60-day mortality). Although the authors noted that fewer than 5 % of enrolled patients had moderately severe AP, they did not subclassify SAP cases—for example, according to the presence of persistent organ failure as per the Atlanta 2012 criteria [2]. This is a significant oversight, since Petrov et al. demonstrated that clinical outcomes and treatment responses in AP vary considerably depending on the timing and type of organ failure [3]. Furthermore, no subgroup analysis was performed to evaluate patients with baseline hypoalbuminemia, despite evidence from the ALBIOS trial indicating that albumin supplementation confers the greatest benefit in septic patients with severe hypoalbuminemia (<25 g/L) or refractory hypotension [4]. Without such stratification, it remains possible that albumin may improve outcomes in specific SAP subgroups—an effect potentially obscured by the aggregate analysis.

Additionally, the use of a fixed albumin dosage (30 g/day of 5 % albumin for 3 days) lacks both mechanistic rationale and clinical individualization. Shu et al. employed a uniform regimen without adjusting for baseline albumin concentration or hemodynamic status, even though individualized albumin dosing—guided by serial measurements and clinical parameters—is increasingly

supported in critical care settings. For instance, the ALBIOS trial adopted a targeted strategy aimed at maintaining serum albumin ≥ 30 g/L, which aligns with the 2021 Surviving Sepsis Campaign recommendations and has been associated with more consistent hemodynamic stabilization [5,6]. By contrast, a fixed-dose approach risks underdosing severely hypoalbuminemic patients while exposing those with normal levels to unnecessary therapy, which may partly explain the absence of overall benefit.

Finally, the single-center design and small sample size (initially 60 patients, with only 32 versus 28 analyzed) limit the external validity and statistical power of the study. Single-center trials are susceptible to local practice biases and may not reflect the heterogeneity of SAP management across different settings. Moreover, the limited sample reduces the ability to detect clinically meaningful differences in secondary outcomes, such as the observed reduction in sepsis incidence (10 % vs. 36.7 %, $P = 0.01$), which was based on only 3 versus 11 events. Future trials should adopt multicenter designs with larger, more diverse populations to enhance generalizability and robustness.

In summary, Shu et al.'s study lays groundwork for albumin research in SAP, but addressing stratification, individualized dosing, and generalizability will advance clinical practice. We encourage large-scale, multicenter RCTs incorporating these elements to clarify albumin's role in SAP.

Ethics declarations

This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

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Competing interests

The authors declare that they have no known competing financial interests or personal relationships that could have influenced the work reported in this paper.

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