

EDITORIAL



Who should receive volume resuscitation with 20% albumin after cardiac surgery? It is probably more complex than just a lack of flair!

Patrick M. Honore^{1,2*} , Patrick R. Lawler^{3,4,5} and Alexander Zarbock⁶

© 2024 Springer-Verlag GmbH Germany, part of Springer Nature

Intravenous fluid bolus therapy is commonly performed after cardiac surgery to optimize intravascular volume and end-organ perfusion. Recent pilot data suggest that using 20% albumin for such fluid boluses, compared to crystalloid, may reduce vasopressor duration and dose, potentially achieving hemodynamic targets with less fluid and thereby minimizing the negative effects of volume overload and prolonged vasopressor therapy [2]. Accordingly, Wigmore et al. performed an open-label multicentre, parallel-group, open-label, randomised clinical trial (RCT) to evaluate the effect of fluid bolus therapy with 20% albumin on the duration of vasopressor therapy compared with crystalloid (the HAS FLAIR-II RCT) [1].

HAS FLAIR-I was a sequential period open-label pilot non-randomized study that included 100 cardiac surgery patients [2]. Although demographic characteristics between the groups were similar at baseline, treatment with 20% albumin fluid bolus therapy was associated with a less positive median fluid balance in the first 24 h, fewer episodes of fluid bolus therapy and a lesser volume of fluid bolus therapy. In addition, the intervention was associated with a decreased median overall dose of nor-epinephrine in the first 24 h. Recent narrative reviews which included four non-randomized studies did not clearly observe benefit with intravenous albumin for fluid bolus therapy after cardiac surgery [3–5].

The HAS FLAIR-II RCT showed that volume resuscitation with 20% albumine had no effect on vasopressor duration (primary outcome) or mortality [2]. However,

randomization to albumin bolus therapy was associated with a reduced positive fluid balance (a secondary outcome). In both studies, initiation of fluid bolus therapy was not standardized, but was performed by clinicians based on hemodynamic instability [1, 2].

It has been shown that hypoalbuminemia commonly occurs in cardiac patients, especially in elderly patients and those with chronic congestive heart failure, and it is associated with adverse events [6, 7], including atrial fibrillation postoperatively [7]. Accordingly, the treatment effect was assessed in a prespecified subgroup analysis according to pre-operative plasma albumin (≤ 37 g/L). There was no evidence of differential treatment effects on vasopressor duration stratified by baseline albumin, nor was there in the other pre-specified subgroup analysis based on stratification by baseline vasopressor use. By contrast, there may have been heterogeneity of treatment effect in a non-prespecified exploratory subgroup analysis based on sex, but in the context of an overall neutral trial these observations should be interpreted with caution. Prior studies have suggested that potential differences in mortality between men and women are nuanced [8], as preoperative profiles of women and men differ. However, in well-matched patients, female gender was not associated with increased mortality and had minimal impact on morbidity after coronary artery bypass grafting [8]. As such, these exploratory observations should be interpreted with caution.

In a recent study, Savadjian et al. showed that albumin 4% or 20% was still frequently used perioperatively in approximately 16% of patients [9]. In the HAS FLAIR-II RCT, more patients in the treatment arm received preoperative albumin as compared to the HAS FLAIR-I study, which may explain the overall neutral effect in HAS

*Correspondence: Patrick.Honore@CHU.UCL.Namur.UCLouvain.be

¹ ICU Department, CHU UCL Namur Godinne, UCL University, Campus Godinne, 1, Avenue Dr Gaston Therasse, 5530 Yvoir, Belgium
Full author information is available at the end of the article

FLAIR-II. It seems obvious that we should measure albumin levels more frequently and especially before surgery and immediately after ICU admission.

According to the results of the HAS FLAIR II study, should we restrict the use of 4% or 20% albumin only to sicker patients? For instance, Rabin et al. did use albumin only in three severe conditions: patients requiring more than 3 L crystalloids in the early post-operative period, hypoalbuminemic patients with a level below 38 g/L and patients considered fluid overloaded [10]. He demonstrates that albumin restriction in the cardiac surgery intensive care unit (ICU) was feasible and safe. Significant reductions in utilization and cost with no changes in morbidity or mortality were demonstrated [10, 11].

Despite Wigmore et al. wanting to publish about post cardiac surgery acute kidney injury (AKI) in a separate paper, we have some interesting insights from the literature regarding hypoalbuminemic patients. Indeed, Lee et al. [12] demonstrate the protective effect of preoperative correction of a low preoperative albumin level by administering human albumin solution, with the goal of preserving renal function in patients undergoing cardiac surgery. The study is a prospective, randomized, double-blind, placebo-controlled clinical trial and the findings of the study include the following: (i) supplementation of exogenous human albumin immediately before surgery predictably achieved the target concentration of albumin and (ii) correction of a low albumin concentration is apparently associated with a significant reduction in the incidence of AKI, from 26% in the control group to 13.7% in the albumin group. According to the accompanying editorial by Jiang et al. [12], the observations of Lee et al. are important. Scientifically, they validate previous reports [14, 15] that a preexisting low albumin level is an independent risk factor for AKI after non cardiac surgery. Clinically, restoring the target level of albumin is associated with a reduction in AKI in amplitude greater than that of any known intervention in patients undergoing off pump cardiac surgery. In fact, in the HAS FLAIR II study, on pump cardiac surgery was an inclusion and they were no off pump cardiac surgery patients. Nevertheless, it might be interesting they would find the same relationship between hypoalbuminemic patients and the administration of albumin is apparently associated with a significant reduction in the incidence of AKI.

Take-home message

The HAS FLAIR-II RCT did not observe a statistically significant reduction in the duration of vasopressor therapy with 20% albumin fluid bolus therapy as opposed to crystalloids, although albumin was associated with a significantly reduced overall fluid balance. Potential limitations of HAS FLAIR-II included the open label design,

lack of protocolization of any other aspects of care, and inclusion of patients who were not requiring vasopressors at baseline which meant that many patients' clinical course did not contribute to the continuous primary outcome. It is possible that a future larger RCT, considering these limitations, may provide definitive evidence for this question. Sex differences were noticed and require further evaluation. On top, questions arise about the role of 4% and 20% albumin as well as cost-effectiveness.

Author details

¹ ICU Department, CHU UCL Namur Godinne, UCL University, Campus Godinne, 1, Avenue Dr Gaston Therasse, 5530 Yvoir, Belgium. ² Faculty of Medicine and Experimental Research Laboratory Institute of the Catholic Louvain Medical School, Brussels, Belgium. ³ Cardiac Intensive Care Unit, McGill University Health Centre, Montreal, Canada. ⁴ Division of Cardiology, University of Toronto, Toronto, Canada. ⁵ Division of Critical Care Medicine, University of Toronto, Toronto, Canada. ⁶ Department of Anesthesiology, Intensive Care and Pain Medicine, University Hospital Münster, Münster, Germany.

Funding

None.

Data availability

Not applicable.

Declarations

Conflicts of interest

PMH, PR. Lawler and AZ report no conflicts of interest related to the content of this editorial.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Received: 4 June 2024 Accepted: 12 June 2024

Published: 2 July 2024

References

- Wigmore GJ, Deane A, Presnell JJ, Easwood G, Serpa Neto A, Maiden MJ, Bihari S, Baker RA, Bennetts JS, Anstey JR, Raman J, Bellomo R (2024). Twenty percent human albumin solution fluid bolus administration therapy in patients after cardiac surgery-II: a multicentre randomised controlled trial. *Intensive Care Med.* <https://doi.org/10.1007/s00134-024-07488-3>
- Wigmore GJ, Anstey JR, St. John A, Greaney J, Morales-Codina M, Presnell JJ, Deane AM, MacIsaac CM, Bailey M, Tatoulis J, Bellomo R (2019) 20% human albumin solution fluid bolus administration therapy in patients after cardiac surgery (the HAS FLAIR study). *J Cardiothorac Vasc Anesth* 33:2920–2927. <https://doi.org/10.1053/j.jvca.2019.03.049>
- Curtis S, Anwar S (2019) Fluid resuscitation after cardiac surgery: the quest for the ideal fluid. *J Cardiothorac Vasc Anesth* 33(11):3218. <https://doi.org/10.1053/j.jvca.2019.06.023>
- Otero TMN, Aljure OD, Yu S (2021) Postoperative resuscitation with hypertonic saline or hyperoncotic albumin in patients following cardiac surgery: a review of the literature. *J Card Surg* 36(3):1040–1049. <https://doi.org/10.1111/jocs.15233>
- Wigmore G, Anstey J, Deane A, Bellomo R, on behalf of the HAS FLAIR Investigators (2019) HAS FLAIR investigators reply to fluid resuscitation after cardiac surgery: the quest for the ideal fluid. *J Cardiothorac Vasc Anesth* 33(11):3218–3219. <https://doi.org/10.1053/j.jvca.2019.06.021>

6. Cutuli SL, Bitker L, Osawa EA, O'Brien Z, Canet E, Yanase F, Ancona P, Wilson A, Lucchetta L, Kubicki M, Cronhjort M, Cioccarl L, Peck L, Young H, Eastwood GM, Mårtensson J, Glassford NJ, Bellomo R (2020) Haemodynamic effect of a 20% albumin fluid bolus in post-cardiac surgery patients. *Crit Care Resusc* 22(1):15–25. <https://doi.org/10.51893/2020.1.oa2>
7. Shah A, Memon RA, Shirazi Z, Ishaq M (2023) Postoperative atrial fibrillation after coronary bypass surgery in patients having pre-operative hypoalbuminemia. *J Ayub Med Coll Abbottabad* 35(4):574–578. <https://doi.org/10.55519/JAMC-04-11891>
8. Koch CG, Khandwala F, Nussmeier N, Blackstone EH (2003) Gender and outcomes after coronary artery bypass grafting: a propensity-matched comparison. *J Thorac Cardiovasc Surg* 126(6):2032–2043. [https://doi.org/10.1016/s0022-5223\(03\)00950-4](https://doi.org/10.1016/s0022-5223(03)00950-4)
9. Savadjian AJ, Taicher BM, La JO, Podgoreanu M, Miller TE, McCartney S, Raghunathan K, Shah N, Mamoun N (2024) Reduce intraoperative albumin utilisation in cardiac surgical patients: a quality improvement initiative. *BMJ Open Qual.* 13(2):e002726. <https://doi.org/10.1136/bmjopen-2023-002726>
10. Rabin J, Meyenburg T, Lowery AV, Rouse M, Gammie JS, Herr D (2017) Restricted albumin utilization is safe and cost effective in a cardiac surgery intensive care unit. *Ann Thorac Surg* 104(1):42–48. <https://doi.org/10.1016/j.athoracsur.2016.10.018>
11. Mwaura L, Vuylsteke A (2019) Fueling the debate on albumin after cardiac surgery. *J Cardiothorac Vasc Anesth* 33(11):2928–2929. <https://doi.org/10.1053/j.jvca.2019.04.030>
12. Lee EH, Kim WJ, Kim JY, Chin JH, Choi DK, Sim JY, Choo SJ, Chung CH, Lee JW, Choi IC (2016) Effect of exogenous albumin on the incidence of post-operative acute kidney injury in patients undergoing off-pump coronary artery bypass surgery with a preoperative albumin level of less than 4.0 g/dl. *Anesthesiology* 124:1001–1011
13. Jiang Y, Shaw AD (2016) Albumin supplementation as a therapeutic strategy in cardiac surgery: useful tool or expensive hobby? *Anesthesiology* 124(5):983–985. <https://doi.org/10.1097/ALN.0000000000001052>
14. Moghadamyeghaneh Z, Hwang G, Hanna MH, Phelan MJ, Carmichael JC, Mills SD, Pigazzi A, Dolich MO, Stamos MJ (2015) Even modest hypoalbuminemia affects outcomes of colorectal surgery patients. *Am J Surg* 210:276–284
15. Adogwa O, Martin JR, Huang K, Verla T, Fatemi P, Thompson P, Cheng J, Kuchibhatla M, Lad SP, Bagley CA, Gottfried ON (2014) Preoperative serum albumin level as a predictor of postoperative complication after spine fusion. *Spine (Phila Pa 1976)* 39:1513–1519