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Commentary

Commentary: Revisiting the Effectiveness of Albumin Administration in Critical Care: Insights for Extracorporeal Membrane Oxygenation Patients with Cardiogenic Shock

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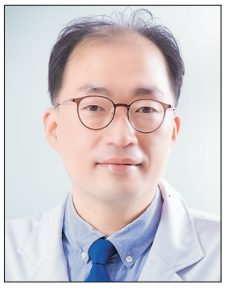

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Hypoalbuminemia is a well-known risk factor for mortality and poor outcomes in critically ill patients, including those with sepsis, decompensated heart failure, shock, and major surgery. Despite being frequently discussed in the literature, confusion persists regarding the pathogenesis and clinical significance of hypoalbuminemia in the critically ill. The pathophysiology of hypoalbuminemia in acute conditions is believed to be distinct from that in chronic disease. Although hypoalbuminemia in the acute setting can be attributed to a combination of factors, including reduced albumin synthesis, hemodilution from fluid administration, renal losses due to congestion, hemorrhage, and increased catabolism, the major cause of hypoalbuminemia may be capillary leakage into the interstitial space due to inflammatory processes [1,2]. In cardiogenic shock (CS), rapid hemodynamic correction may result in a minimal systemic inflammatory response. However, prolonged hypoperfusion states usually elicit marked systemic inflammatory responses, such as severe sepsis, and increase microvascular permeability, causing albumin leak from the plasma and albumin entrapment in the interstitial space. In patients with CS, the application of extracorporeal membrane oxygenation (ECMO) may exacerbate capillary leakage, as cardiopulmonary bypass and hemodilution could potentially worsen the condition [3].

In this issue of the journal, Jeon et al. [4] assessed the predictive value of the mean serum albumin level before ECMO support (pre-ECMO serum albumin) for 30-day mortality in patients with CS who underwent veno-arterial (VA) ECMO. They showed that the pre-ECMO serum albumin level was an independent predictor of 30-day mortality in a Cox regression analysis (hazard ratio, 0.25; 95% confidence interval [CI], 0.11–0.59; p=0.002). The area under the receiver operating characteristic curve for pre-ECMO serum albumin was 0.73 (95% CI, 0.63–0.81; p<0.001). The optimal cutoff value of serum albumin for predicting mortality was 3.4 g/dL. Dividing the groups based on a concentration of 3.4 g/dL, the cumulative incidence of mortality was significantly higher in the lower-albumin group than in the higher-albumin group (p<0.001). In the Discussion section, the authors described the effectiveness of albumin administration in critical care patients rather negatively, stating that there was no clear evidence for mortality improvement and that albumin administration would not be effective in restoring blood albumin concentration. In the Conclusion section, the authors stated that

"there was not a strong correlation between the amount of infused albumin and serum albumin levels." Although this study included a parameter called "albumin infusion, adjusted," it may not have fully reflected the actual administration and fluid management of albumin during the initial few days. It is difficult to accept this statement without a further detailed analysis to fully understand the relationship between albumin administration and serum albumin levels. I suggest that it may be worthwhile to re-evaluate the potential benefits and drawbacks of albumin administration by reviewing various relevant studies. Therefore, the subsequent discussion aims to explore whether albumin administration is truly effective in critically ill patients, including those with CS who are supported by ECMO.

Serum albumin is the main critical factor in colloid osmotic pressure, maintaining a balance between hydrostatic and colloid osmotic pressure within vessels. For this reason, one of the main topics regarding hypoalbuminemia in critically ill patients has been comparing albumin and crystalloid solutions for fluid resuscitation to maintain adequate intravascular volume during the early phase. However, albumin is not just a controller of plasma oncotic pressure—instead, it is also an actual plasma protein with complex physiological and pharmacological activity. It serves as a binding protein, a plasma buffer to maintain physiological pH levels, and an antioxidant associated with the pathogenesis of inflammatory diseases [5]. Thus, these functions of albumin, as suggested by early preclinical and preliminary data, could lead to favorable perceptions regarding the perceived advantages of albumin, which may influence its use in critically ill patients.

Around the year 2000, the administration of albumin was actually considered to be harmful. In 1998, a meta-analysis reported that the use of albumin solutions for resuscitation was linked to a 6% increase in the absolute risk of mortality compared to crystalloids [6]. A propensity score analysis of 339 patients from 3,147 individuals admitted to 198 intensive care units found that mortality rates were higher among those who received albumin than among those who did not [7]. However, subsequent studies demonstrating no significant difference or even lower mortality rates with the administration of albumin have led to a more favorable view of the use of albumin in critically ill patients. The Saline versus Albumin Fluid Evaluation study was a randomized controlled trial that involved 6,997 critically ill patients who received either 4% albumin or normal saline for their initial fluid administration [8]. The study found no significant differences between the 2 groups in terms of mortality, and a subgroup analysis suggested potential benefits of albumin administration in patients with severe sepsis. In 3 randomized trials comparing albumin with crystalloids in patients with severe sepsis, mortality was lower in the albumin group, and the corresponding relative risks were similar, ranging from 0.87 to 0.94 [9-12].

There are extremely limited studies on patients with CS who are supported by ECMO, but Wengenmayer et al. [13] reported a significant improvement in hospital survival with albumin fluid resuscitation in VA-ECMO. In their study, they compared a fluid resuscitation strategy using balanced crystalloids alone to a mixed regime with albumin and balanced crystalloids on a 1:2 volume basis, resulting in 10 g of albumin per liter of fluid therapy. Although there have been extremely limited clinical studies on this topic, and the pathophysiologic perspective on the trans-capillary escape rate of albumin and albumin entrapment in the interstitial space during ECMO has not been clearly elucidated, further clinical research is needed to better understand the potential benefits and risks associated with albumin administration in this patient population. I suggest that further research should consider the following points. (1) The optimal dose, timing (with a focus on the early phase), and concentration of albumin fluids, as well as the ratio of albumin and crystalloid administration, in patients with CS undergoing ECMO. (2) The development of a more sensitive indicator for the effects of administered albumin, such as ECMO weaning failure, duration of ECMO, and hemodynamic improvement (mean blood pressure, ECMO flow), that can better capture the potential benefits of albumin administration beyond mortality outcomes. (3) The effects of albumin administration on renal function in patients with CS undergoing ECMO.

Additional studies investigating the use of albumin in patients with CS who are supported by ECMO could provide valuable insights into the potential benefits and drawbacks of this therapy, and could inform clinical decision-making regarding the use of albumin.

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Conflict of interest

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