Impact of fluid balance on intensive care unit mortality in critically ill patients with cardiovascular disorders

To the editor We read with interest the paper by Dr. Trejnowska et al., investigating the impact of positive fluid balance (FB) on clinical outcomes in critically ill patients with cardiovascular disorders. They concluded that achieving a positive FB of more than 1000 ml during each 24 hours within 3 days was significantly associated with increased intensive care unit (ICU) mortality. This study filled the gap in knowledge about the association between FB and mortality in critically ill patients with cardiovascular disorders; however, it is not free of limitations.

First, the novelty of the study is that the daily FB was analyzed in 24-hour intervals within 72 hours, using a cutoff value of 1000 ml. In clinical practice, fluid management is a continuous, dynamic process, while simply dividing FB by a 24-hour interval can lead to a biased conclusion. For instance, hypothetical patient A had a 24-hour FB of 1200 ml, 800 ml, and 1100 ml, and patient B reached 1100 ml, 1100 ml, and 1100 ml within the first 72 hours after ICU admission.

Second, according to other studies,2,3 positive FB had a dose-related impact on clinical outcomes. Thus, simply converting FB to a dichotomous variable could reduce statistical efficacy to detect a true association. For instance, according to the current study, we only know that achieving an FB of more than 1000 ml per day within 72 hours is associated with higher ICU mortality rates, compared with an FB of less than 1000 ml. However, what is the balance point: stable FB, more negative FB? Interestingly, in a retrospective study including 18 084 critically ill patients, Balakumar et al.4 reported that compared with stable FB, exposure to either positive or negative FB was associated with higher 1-year mortality. To explore the true association between FB and mortality in these patients, we performed a crude analysis using data from the MIMIC database. Only patients admitted to cardiac or cardiac surgical care unit were screened and patients with an ICU length of stay of less than 72 hours were excluded. A total of 4565 patients were included, and we used the LOWESS smoothing method to investigate the crude association between FB and ICU mortality (Figure 1). We noticed that the curve slope was much steeper on the side with an FB of more than 0, compared with the curve on the other side, which indicated different associations between an FB higher than 0, FB lower than 0, and mortality. However, more research is needed to validate these findings.

Third, in clinical practice, the volume of FB may be affected by numerous factors, especially disease severity. In patients with severe infection or under vasopressor support, a large

![FIGURE 1](image-url)
volume of fluids was often given during the fluid resuscitation stage. Thus, the association between FB and mortality may only reflect the severe clinical condition that was also related to high mortality. To draw a firm conclusion, these potential confounders should be carefully considered in the multivariable regression model. However, the confounder selection was unclear in the current study and only 3 factors were included as adjusting factors, which may increase the bias risk of these findings.

ARTICLE INFORMATION

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REFERENCES


Author’s reply  We would like to thank Si et al for their interest in our work and valuable comments. As stated in the manuscript, the aim of our study was to investigate whether a cumulative fluid balance (FB) affects mortality in critically ill patients hospitalized in the intensive care unit (ICU) due to cardiovascular disorders. We agree that fluid management is a continuous, dynamic process, but clinicians routinely establish fluid therapy based on, among others, patients’ response to treatment applied in previous days. Si et al noted that daily FB in our study was analyzed in 24-hour intervals. Similarly as in a study by Shum et al, we analyzed the amount of fluid input and output for 7 consecutive days, but a relationship between FB and mortality was seen only in the first 72 hours.

Regarding the definition of the term “day,” Shum et al stated that a day means a period from 12 PM to 12 PM on the next day. This method of calculating days does not emphasize the most important differences, which usually occur in the first hours of ICU treatment. The advantage of our study is that the treatment start was defined as the time and date of admission to the ward, and the following days were calculated as subsequent 24-hour intervals.

Due to the fact that patients were admitted at different times during the day, their “therapy day” could vary with respect to the number of hours. We eliminated these differences in our study. By introducing the amounts of fluid input, output, and FB to the database in 24-hour intervals, based on notes taken by care providers, we also minimized the possible error that may occur in a crude analysis of data from a large database.

Following the analysis of studies by Cronhjort et al and Lee et al, Si et al stated that positive FB had a dose-related impact on clinical outcomes. The fluid dose obtained in our study was 1000 ml in the first 72 hours after admission to the ICU. Si et al asked about the balance point: should it be stable or a more negative FB? To precisely answer these questions, a prospective study would be needed.

Si et al reported the results from their own study, in which they explored the actual association between FB and morality. They performed a crude analysis using data from the MIMIC database and LOWESS smoothing method, as Shen et al did in their analysis of critically ill patients with negative FB. The curve slope obtained by Si et al indicated different associations between an FB higher than 0, an FB lower than 0, and morality. The researchers concluded that more effort was needed to verify these findings.

Si et al raised concerns as to whether as few as 4 confounders can increase the risk of bias in the results. In our study, variables with a P value of less than 0.05 were included in the multivariate logistic regression analysis. The multivariate model was fitted using the stepwise method, where a P value of less than 0.05 was set as an inclusion and exclusion criterion. Therefore, only these data in which a statistical difference was found in the univariate analysis were included in the multivariate regression model. We analyzed many factors but managed to show a statistical difference between survival and mortality only for these 4 factors.

We agree with the conclusion by Si et al that numerous factors may affect FB, particularly, the disease severity, and that the relationship between FB and mortality may only reflect a severe clinical condition, which is also associated with high mortality. In our study, we aimed to draw clinicians’ attention to a group of patients who require more fluids in the first 3 days of hospitalization to achieve clinical stability and to show that mortality increases after reaching a certain threshold. However, further research is necessary to determine the effect of FB on mortality in this patient group.
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REFERENCES