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Key Words: red blood cell transfusion, cardiogenic shock, elderly, cardiac surgery

EDITORIAL COMMENTARY

Transfusion strategies in cardiac surgery: More pieces to the puzzle, more questions to be answered

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Blood management has emerged as an important aspect of perioperative cardiac surgical care and has evolved to become a key quality indicator.¹ Despite growing evidence of the risks and cost of blood transfusion, along with the physiologic rationale of improvement of oxygen delivery to tissues during hemorrhage and ischemia, the jury still out with respect to the optimal hemoglobin trigger for red blood cell transfusion in cardiac surgical patients, specifically in elderly patients, and how we define the concept of physiologic reserve, possibly to modify the transfusion threshold.

It is important, however, to recognize, that both anemia and transfusion are associated with poor outcomes and that both of these conditions are common among cardiac surgical patients. These patients frequently are seen with a myriad of comorbidities in different states of compensation and physiologic reserve that are difficult to control

for in large-scale studies. Moreover, the variability of the hemoglobin value in the perioperative care episode, as well as the frequency of rapid changes in blood volume during this period, make the issue of transfusion “trigger”

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Central Message

Elderly patients may benefit from a more liberal transfusion strategy. Studies are needed to balance benefit-risk-cost of transfusion.

See Article page 1314.

See Editorial page 1032.

extremely challenging to assess and standardize. Despite the best efforts to control for all these variables, we continue to have conflicting results with regard to which patients are the ones at risk, and who would benefit from a more liberal transfusion approach in the face of the known adverse outcomes with transfusion that have stirred the direction toward a generally restrictive strategy. With these challenges in mind, I will briefly describe two recent randomized controlled trials^{2,3} that evaluated restrictive versus liberal transfusion strategies in cardiac surgical patients. Active bleeding was not part of the exclusion criteria for either of the trials. The Transfusion Requirements After Cardiac Surgery (TRACS) trial² randomly allocated patients who underwent cardiac surgery under cardiopulmonary bypass ($n = 502$) to a restrictive (hematocrit $>24\%$) or a liberal (hematocrit $>30\%$) strategy. The primary outcome was a composite end point that included 30-day mortality and severe morbidity (including cardiogenic shock, adult respiratory distress syndrome, and acute kidney injury with need for dialysis). The occurrence of the primary end point was similar between both groups, and independent of the transfusion strategy, the quantity of transfused red blood cells was an independent risk factor for complications or death at 30 days. The Transfusion Indication Threshold Reduction (TITRe2) trial³ was a multicenter, parallel-group, randomized trial ($n = 2007$) that used lower transfusion thresholds (hemoglobin of 7.5 vs 9 g/dL). The TITRe2 investigators evaluated infectious complications and ischemic events, as well as health care costs, associated with both transfusion strategies. There were no significant differences in terms of the primary morbidity or health care cost between the groups. Furthermore, there were more deaths in the restrictive group. Although these later findings could be due to chance, these studies shed light on the complexities and variability found in cardiac surgical patients, despite clearly different transfusion thresholds between the mentioned studies.

In this issue of the *Journal*, Nakamura and colleagues⁴ demonstrate, in a subgroup analysis of the TRACS randomized, controlled trial,³ that cardiogenic shock was more frequent in elderly patients (defined as >60 years old) who underwent restrictive red blood cell transfusion,

compared with the liberal group. This study adds to the conflicting evidence as to how subsets of patients may benefit from a more liberal approach. Nevertheless, is early to generalize, and there are some aspects of the study that deserve mentioning. The transfusion rates in both groups were relatively high (70% in the liberal group vs 44% in the restrictive group), and the difference between the groups in final postoperative hemoglobin values was not significant, despite adequate adherence to protocol. The etiology of cardiogenic shock (postcardiotomy, ischemic, etc) was not disclosed, and there was not a clear time correlation with the nadir of hemoglobin. The larger number of patients with cardiogenic shock in the restrictive group deserve attention; however, association as opposed to causality is very difficult to discern. Moreover, 30-day mortality, adult respiratory distress syndrome, and acute kidney injury were similar between the groups, so the clinical impact of the higher frequency of cardiogenic shock in the elderly of the restrictive group was reduced to probable longer hospital stay and greater resource use.

These findings demonstrate that there is more to study on optimal transfusion strategies in cardiac surgical patients. The elderly population may represent a subset of patients with less physiologic reserve and a higher risk of complications from anemia when undergoing cardiac surgery. These findings, however, will need to be confirmed with larger studies.

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