The authors did not provide the reasons for ICU admission of patients. It was also unclear what reasons resulted in such significant decreases in postoperative hemoglobin levels within a short 3-day period after ICU admission. We are concerned that any imbalance in these factors would have confounded interpretation of their results.

Finally, a limitation of this study design is that the decision to perform postoperative transfusions is mainly based on the hemoglobin levels rather than on a patient's status. In clinical practice, it may be unrealistic to use the hemoglobin threshold as the only endpoint to guide decisions regarding transfusion. The coexisting morbidities (*e.g.*, coronary artery disease) also are major determinants of the need for transfusion.[10] In the studies by Carson *et al.*,[2,3] the restrictive transfusion strategy allows transfusion for symptoms of anemia, which are chest pain thought to be cardiac in origin, symptoms and signs of congestive heart failure, or hypotension or tachycardia unresponsive to fluid challenge. Thus, we consider that for ICU patients with physiological instability, this study limitation may be one of the reasons for poorer short-term outcomes with a restrictive transfusion strategy.

## Competing Interests

The authors declare no competing interests.

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*(Accepted for publication May 21, 2015.)*

# Adding a New Piece to the Transfusion Puzzle in Oncologic Surgery Patients

*To the Editor:*

We read with interest the recent article by Pinheiro de Almeida *et al.*[1] regarding transfusion requirements in patients undergoing surgery for intraabdominal malignancies.

In contrast to the results from multiple other large-scale, randomized controlled trials, which did not show substantial differences in outcomes between restrictive and liberal blood transfusion strategies in a variety of different patient cohorts, the current study reports improved outcomes in patients that were transfused at a higher hemoglobin threshold (9 g/dl).[2–4] It is unclear whether this improvement is unique to this particular patient population (patients undergoing surgical resection for solid intraabdominal tumors) or whether the results could be generalized to all patients undergoing surgery for resection of solid tumors.

The authors suggest that the improved outcomes could be related to utilization of leukodepleted blood as well as shorter duration of blood storage compared with other studies. However, there are no convincing data to date that transfusion of leukodepleted blood is associated with improved mortality or reduced incidence of cancer recurrence.[5,6] Similarly, an association between the duration of erythrocyte storage and meaningful clinical outcomes such as increased mortality or long-term morbidities remains uncertain at this time.[7–9] It is noteworthy that the mortality difference was driven by the incidence of septic shock (24 of 31 patients), suggesting the possibility that higher hemoglobin concentrations may protect against septic shock physiology. However, the larger prospective trial by Holst *et al.*,[3]

which was specifically focused on patients with septic shock, failed to demonstrate any advantage to liberal transfusion.

One concern is whether the study by Pinheiro de Almeida *et al.*[1] had a sufficient number of patients upon which to set transfusion policies. Although the study was powered to assess a difference in primary outcome, it was not necessarily powered to achieve balance by randomization. For example, we note that the restrictive strategy group had twice the number of Whipple-type procedures, had a higher incidence of intraabdominal infections, twice the number of radical cystectomies, and a higher incidence of coronary artery disease and congestive heart failure. Imperfect randomization is a natural consequence of a smaller sample size. Furthermore, a large number of patients were excluded from this study, which further questions the generalizability of the study results.

Finally, there are potentially two distinct risk periods following major cancer surgery; the first is the intraoperative and immediate postoperative period when there is an increased risk of death due to blood loss and dilutional anemia. This risk may possibly be mitigated by blood transfusion as anemia in the early postoperative period is associated with increased risk of mortality in patients with cancer.[1,10] The second risk period occurs after discharge from hospital when patients may be at increased risk of cancer recurrence. Although blood transfusion is the mainstay therapy for perioperative anemia, there is the hypothesis that transfusion leads to a nonspecific immunosuppression and increased the risk of cancer recurrence.[10–12] However, this phenomenon has not been studied prospectively and remains controversial. Clearly, if a patient does not survive the immediate postoperative period, then cancer recurrence is not a relevant outcome. The critical unanswered question is where the "risk/benefit" threshold lies. Unfortunately, the authors do not provide data on long-term outcomes and cancer recurrence in their study population and only address early postoperative outcomes.

At this time, it remains unclear what criteria should be used to make the decision to transfuse or not, in order to balance the benefit of transfusion regarding perioperative mortality against the potential risk of transfusion regarding cancer recurrence. This balance likely varies based on a variety of factors including patient comorbidites, cancer type, and the extent of disease.[11] We will need additional prospective trials to refine the indications for blood transfusion following cancer surgery. Although Pinheiro de Almeida *et al.*[1] should be commended for their well-conducted study, which provides important new information in the perioperative transfusion literature, the practical question of whom and when to transfuse patients undergoing oncologic surgery to achieve "best outcomes" remains unanswered.

## Competing Interests

The authors declare no competing interests.

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*(Accepted for publication May 21, 2015.)*