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COMMENT & RESPONSE

Avoidable Blood Transfusions

To the Editor I read with much interest the article by Goel et al,[1] titled, "Association of Perioperative Red Blood Cell Transfusions With Venous Thromboembolism in a North American Registry." The authors should be congratulated for their efforts to find causes for postoperative deep vein thrombosis and, eventually, pulmonary embolism. They analyzed data from the American College of Surgeons National Surgical Quality Improvement Program registry regarding 750 937 patients who had surgery in 525 hospitals over a 1-year period. They found that there was a higher incidence of deep vein thrombosis and pulmonary embolism within 30 days from surgery in patients who had received perioperative blood transfusion. About 6.3% of the patients received at least 1 blood transfusion. In a retrospective analysis, they found that blood transfusion was an independent risk factor for thromboembolism and deep vein thrombosis.

I have concerns about their study. In the United States, training programs teach the importance of avoiding unnecessary blood transfusions. It is almost a dogma, and this is somewhat testified by the low number of patients who received blood transfusions in their data (6.3%). It is very difficult to compare patients retrospectively without an objective assessment of their general conditions and without the possibility to determine why those patients had blood transfusions. Data about preoperative hematocrit level were not available. Goel et al[1] performed retrospective propensity score matching; this analysis presents many drawbacks when it is not possible to determine all characteristics of the general status of the patients. Unfortunately, propensity score matching implies many inadvertent selection biases.

It is wise to accept the conclusions of Goel et al[1] that blood transfusions carry a significant risk, especially for other reasons than thromboembolism, like transmission of HIV, hepatitis C, and other unknown, unpredictable diseases. Still, I have doubts about the appropriateness of the correlation between blood transfusions and deep vein thrombosis; I think that the final messages of the authors are of paramount importance, and there is the need for clear guidelines about perioperative blood transfusions. Too often, surgeons feel much better if the patient's hematocrit level is in an acceptable range. National guidelines can support the decision in difficult clinical situations as well as support a legal defense in times when all of us are obliged to do more than required just to avoid future consequences.

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1. Goel R, Patel EU, Cushing MM, et al. Association of perioperative red blood cell transfusions with venous thromboembolism in a North American registry. 2018;153(9):826-833. doi:10.1001/jamasurg.2018.1565

In Reply We thank Sterpetti for his response and close attention to our study.[1] We agree with the author's assertion that in the United States, there has been an immense focus on reducing unnecessary blood transfusions, supported by clinical practice guidelines and patient blood management programs.[2] The effect of patient blood management initiatives in the United States is evident by recent data showing nationwide decreases in red blood cell (RBC) and plasma transfusions.[3]

Our study aimed to evaluate the association of perioperative RBC transfusions with postoperative new-onset/progressive venous thromboembolism (VTE). This study question stems from multiple translational and clinical studies that have suggested a relationship between transfused RBC and pathologic thrombosis.[4,5] As outlined in our article, multiple mechanistic pathways have been hypothesized to explain this potential association.[6] Although Sterpetti questions the appropriateness of our study question, we see value in exploring a potential association that is both biologically plausible and clinically relevant. It should be noted that this study was not intended to or designed to calculate causal effects.

We conducted a secondary analysis of data from the American College of Surgeons National Surgical Quality Improvement Program, a validated and widely recognized national registry for studying surgical outcomes. The registry includes participation from more than 500 academic and nonacademic hospitals. While the prospective design and large sample size of the registry make the data powerful, these data have

limitations, as we stated in the Discussion section of the article.[1] An inherent limitation of any retrospective observational study is the inability to account for unmeasured (or unmeasurable) covariates, regardless of the statistical method used to analyze the data (eg, multivariate regression or propensity score matching). For instance, the specific preoperative health conditions and indications for perioperative RBC transfusion were unknown. However, it is noteworthy that the association was observed across a number of surgical subspecialties independent of several factors related to severity of illness. We hope future prospective studies will account for potential confounders that could not be examined in our analysis.

As Sterpetti notes, the study did not provide data on preoperative hematocrit levels. For patients with available data, mean (SD) preoperative hematocrit levels were 39.8% (4.9) in the group that did not receive any perioperative RBC transfusion and 33.4% (6.4) in the group that received at least 1 perioperative RBC transfusion. Including preoperative hematocrit levels as a continuous variable in the fully adjusted model does not affect the findings reported in the primary analysis; any perioperative RBC transfusion remains significantly associated with the development of postoperative VTE (adjusted odds ratio, 2.1; 95% CI, 2.0-2.3) in the overall study population. Postoperative hematocrit levels are not available in the registry.

Ultimately, our retrospective study supports the hypothesis that perioperative RBC transfusions may be associated with development of new or progressive VTE within 30 days of surgery. These data support the need for prospective studies as VTE continues to be a public health problem.

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Prehospital Advanced Life Support for Out-of-Hospital Cardiac Arrest in Blunt Trauma Patients

To the Editor We thank Fukuda et al[1] for their study analyzing the association of prehospital advanced life support (ALS) with the outcomes of out-of-hospital cardiac arrest. The authors conclude that ALS by physicians resulted in a higher 30-day survival than ALS by emergency medical service (EMS) personnel and basic life support (BLS).

However, the implications of the study may be overstated. First, given the retrospective design of the study, there are multiple confounding factors that the authors have not accounted for. These mainly include patient demographic characteristics, like age and sex; modifiable predictors of survival outcomes, like body mass index; general health status as assessed by the American Society of Anesthesiologists index; and comorbidities present, as shown in Table 1.[1] Importantly, the extent of blunt injury (assessed by the Injury Severity Score or Abbreviated Injury Scale score) and etiology of cardiac arrest were not evaluated. A major predictor of survival was time to response,[2] which was statistically different between the various cohorts (Tables 1 and 3).[1] When comparing between EMS and physicians, it is pertinent to match their expertise, since physicians, unlike EMS, may have differing experience and hence success in providing life support.[3] Similarly, many patients who survive long enough to reach the hospital for ALS by physicians fare better because of other above-mentioned factors.

In addition to the differing sample sizes between the various cohorts, the authors do not know how patients were allocated to these cohorts. This introduces selection and allocation bias, especially since these are decisions guided by clinical findings. Similarly, patients often receive additional interventions, so using a composite end point such as 30-day survival is not necessarily a valid measure of the effectiveness of either ALS or BLS or who provides it. Instead, a more immediate assessment of ALS success as well as a comprehensive assessment of complications during hospital stay is necessary. Thus, while the study design improves the generalizability of the results, its decreases the internal validity of the conclusions.

Nevertheless, we agree and emphasize that the prompt provision of ALS or BLS by trained professionals is vital for optimizing survival in out-of-hospital cardiac arrest. Further work is required to determine if these results are observed in matched cohorts and, if so, to subsequently incorporate these findings into treatment guidelines.

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