

## Indications for Blood Transfusions: Too Complex to Base on a Single Number?

In this issue, the AABB (formerly the American Association of Blood Banks) presents a clinical practice guideline for red blood cell transfusion (1). The guideline nicely reports the risks associated with transfusions, and I do not want to challenge the conclusions reached by this distinguished group of experts. Indeed, it would be difficult to argue with their statement that “On the basis of data from all the randomized trials, the panel found little evidence to support a liberal transfusion strategy.” Certainly, ample evidence supports the assertion that, in general, less may be better when it comes to blood transfusion.

Yet, considering the supporting evidence and the questions the panel focused on, I do challenge the strict transfusion triggers provided by the panel. First, in developing the guidelines, the panel focused more on blood transfusion and its related problems than on the problems associated with anemia. In any decision to transfuse, one must weigh the risks and benefits associated with transfusion against those associated with anemia. Although blood transfusions have been associated with adverse outcomes, anemia is also associated with increased mortality rates (2–4). Second, the quality of blood has improved over the years. In particular, it is likely (although not definitely proven) that leukoreduction has helped decrease some of the harmful effects of blood transfusion (5). Observational studies in Europe have suggested that transfusion has become safer over time. For example, blood transfusion was an independent risk factor for mortality in the ABC (Anemia and Blood Transfusion in Critical Care) study conducted in 1999 (6) but not in the SOAP (Sepsis Occurrence in Acutely Ill Patients) study conducted several years later (7), although similar statistical techniques (including multivariable analyses and propensity scoring) were used in the 2 studies. Third and most important, the studies evaluating liberal versus conservative blood transfusion practices have usually addressed the simple question of number of transfusions, without taking into account particular characteristics of the patient populations, especially the presence of coronary artery disease (CAD) and patient age.

Perhaps the most influential of these studies was that by Hébert and colleagues (8), in which patients were assigned to a restrictive (transfusion if hemoglobin level <7 g/dL) or more liberal (transfusion if hemoglobin level <10 g/dL) strategy. Patients in the restrictive group had similar 30-day mortality rates (and even lower mortality rates in the subgroup of patients with higher disease severity [Acute Physiology and Chronic Health Evaluation II {APACHE II} score  $\leq 20$ ] and in patients younger than 55 years). This well-performed, multicenter study serves as the strongest basis for the AABB’s recommendation of a hemoglobin level of 7 g/dL as the threshold for transfusion. However,

several limitations of the study warrant consideration. First, it was conducted more than 10 years ago and blood preservation techniques have improved since then. In particular, leukoreduction was not in practice when the study was done. Second, the investigators enrolled only a small fraction (838 of 6451, or 13%) of evaluated patients, and the study was stopped early due to slow enrollment. These factors raise questions about the generalizability of the observations. Reanalyzing the data some years later, Deans and colleagues (9) highlighted that 30-day mortality was lower in the restrictive group than in the liberal group in patients without CAD (16% vs. 25%) but was higher in the restrictive group among patients with CAD (26% vs. 21%;  $P = 0.03$ ). The European SOAP group of investigators initiated but quickly aborted a study comparing hemoglobin thresholds of 7 versus 9 g/dL, because too many patients did not meet inclusion criteria and the enrollment rate was very slow. For example, clinicians were uncomfortable with the idea of assigning a young trauma patient after bleeding was controlled to the 9-g/dL group, or an elderly patient with CAD to the 7-g/dL group. The current AABB guidelines (1) consider the impact of CAD by providing a weak recommendation that the transfusion threshold should simply be increased from 7 g/dL to 8 g/dL for patients with preexisting cardiovascular disease.

The specific AABB transfusion thresholds are provided to help standardize transfusion practice (1). I believe this approach is too simplistic; basing the decision to transfuse on hemoglobin levels alone is insufficient. Admittedly, using such typical symptoms of anemia as fatigue, tachycardia, and dyspnea (or mechanical ventilation) to help in such decisions is not ideal because they are common indicators of severity of illness. The use of a low  $SvO_2$  (venous oxygen saturation) may be helpful, but this has not been fully established (10). Transfusion decisions need to consider individual patient characteristics, including age and the presence of CAD, to estimate a specific patient’s likelihood of benefit from transfusion. The decision to transfuse is too complex and important to be guided by a single number.

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