Sex matching and red cell safety

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Although transfusion can be lifesaving in severe acute blood loss, evidence of increased morbidity and mortality associated with transfusion continues to be reported.¹⁻⁶ These findings have resulted in an array of practices to not only improve the safety of the blood supply⁷ but also rationally limit transfusion. Because limiting transfusion means limiting transfusion risk, clinicians have sought evidence supporting specific transfusion practices. Although initial studies on restrictive versus liberal transfusion practices supported a lowering of most transfusion thresholds,^{2,8} more recent studies do not support these findings.⁹⁻¹³ Despite the conflicting data, the search continues for the safest transfusion.

Although some transfusion risks are related to the recipient, or the circumstances surrounding the transfusion, some arise from the donor unit itself. The red cell storage defect, which affects cell deformability and oxygen delivery, accounts for increased morbidity and mortality associated with increased storage age of the donor unit.¹⁴⁻¹⁷ Another example is the risk of transfusion-related acute lung injury associated with female donors, human leukocyte antigen class II antibody, and anti-human neutrophil antigen.^{18,19} In this month's issue of the *Journal*, Bjursten and colleagues²⁰ report another donor unit risk factor: Sex mismatch between the donor and the recipient (Figure 1). By using retrospective data from more than 11,000 cardiac surgery patients undergoing on-pump coronary artery bypass, aortic valve replacement, or both, the authors observe an independent association between sex-mismatched red cell transfusion and mortality.

Like any retrospective study, the current study carries the limitation of possible confounding. It is almost axiomatic that patients receive transfusions for specific reasons, without which they would not receive them. Therefore, it is difficult to completely separate the morbidity associated with transfusion from the morbidity associated with its indications by using epidemiologic data. Statistical approaches such as regression and propensity matching can sort out some independent confounders, but only those that we are able to identify and measure. But because

Is it important to sex match red cells?

Central Message

New evidence suggests that sex-mismatched red cells may be an important cause of transfusion-related morbidity. However, definitive conclusions await confirmation in other populations.

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transfusion almost always occurs without regard (or even knowledge) of the donor's gender, the assignment of patients to gender-matched or mismatched groups is practically random, or at least haphazard and blinded. This advantage in study design lends support to the authors' conclusions.

Bjursten and colleagues²⁰ also report increased 1-year mortality associated with small transfusion (1-2 units) of

FIGURE 1. Is it important to sex match red cells? Epidemiologic evidence suggests a survival advantage.

nonleukocyte-depleted red cells. Although the data on leukocyte-depleted transfusion are conflicting,²¹⁻²⁴ the trajectory of red cell transfusion in the United States is trending toward complete leukocyte depletion of the red cell inventory.^{24,25} Of note, the authors did not observe increased mortality associated with age of the donor unit.

These results add to the limited data regarding sex-mismatch transfusion. There is some evidence suggesting an association between sex-mismatch red blood cell units with mortality,²⁶ but this observation is not universal.²⁷ Reproducibility of these findings in other databases is a necessary first step for sex mismatch to become an established risk factor. A better mechanistic understanding of this risk is the next step. Both are probably needed before evidence-based practice recommendations can be made.

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