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Patients with Massive Transfusion: Who are you?

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Transfusion of red blood cells (RBCs) is one of the most common medical procedures, occurring in 12% of U.S. hospital stays with a procedure¹. It also consumes valuable health care resources, with one analysis reporting a range of \$522 to \$1183 for the total cost per RBC unit administration². There is no doubt that the administration of stored allogeneic RBCs can be lifesaving in patients with profoundly low hemoglobin levels, for example 2 g/dL. However, many questions related to RBC transfusion remain unanswered.

A major unresolved controversy surrounding RBC transfusion is whether the administration of blood to patients with moderate levels of anemia (8–10 g/dL) is beneficial or even safe. The TRICC trial, which failed to show improved outcome in critically ill patients after liberal RBC transfusion, highlighted the point that “more is not always better” when it comes to allogeneic blood administration³. Another controversy involves the clinical relevance of the “storage lesion” that develops in banked RBCs.⁴ Recent randomized studies show that the administration of “young” RBCs is not better than “middle-aged” RBCs^{5, 6}, however, these trials did not address the safety and efficacy of “old” blood nearing the 42 day shelf life. RBC transfusion to increase arterial oxygen content and presumably tissue oxygenation has also been a component of goal directed therapy (GDT) in patients with sepsis. While the initial trial by Rivers et al. showed a benefit to this care⁷, subsequent large multicenter studies have failed to confirm a benefit of GDT including RBC transfusion^{8, 9}.

Another important aspect of transfusion medicine is massive transfusion, which is the focus of the study by Halmin et al. in this issue of *CCM*¹⁰. Massive transfusion, often defined as the administration of at least 10 units of RBCs in a 24 hour period,¹¹ is clearly associated with adverse outcome. It has been difficult, however, to tease out the extent to which the transfusions per se, independent of the underlying injury/illness, contribute to higher mortality in these patients. Trauma patients were the initial focus of studies and quality improvement initiatives (often called Massive Transfusion Protocol or MTP). MTPs focus on several processes of care including availability of adequate volumes of blood products

and in many cases a set ratio of RBC to plasma to platelets¹². It was widely believed (mostly anecdotal) that most massive transfusion was occurring in trauma and patients with obstetrical emergencies. Until now, there has been scant descriptive data addressing “Who are the patients with massive transfusion?”

Fortunately, the study by Halmin and colleagues¹⁰ makes an admirable start at addressing this gap in the literature. They leveraged large administrative databases in Sweden and Denmark to assess what types of patients received large numbers of RBC units, and the corresponding short (30 days) and long (>10 year) term mortality in these patients. Patients who received an RBC transfusion in Sweden from 1987 to 2010 were included as were those in Denmark from 1996 to 2010. The database (SCANDAT2) included 1,731,906 cases where at least 1 RBC unit was transfused (Supplementary Table). Of these cases, 92,057 (5.3%) received at least 10 RBC units within a 7 day period, and were deemed “massive transfusion” (MT) by the authors. In an attempt to allow some generalizability to previous studies of MT, they subdivided these cases into “acute” MT (n=53,836), defined as receiving at least 10 RBC units with 2 calendar days, vs “non-acute” MT (n=38,221) defined as receiving at least 10 RBCs units over a longer period of time (up to 7 days). The dataset did not contain the time (hour) of administration, which precluded use of the traditional definition of massive transfusion (10 units within 24 hours). Fortunately, their main results on the indication for MT are markedly consistent across acute and non-acute MT cases. Furthermore, a sensitivity analysis revealed that approximately half of the acute MT cases received the 10 RBC units within 1 calendar day supporting the notion that these cases involved acute bleeding.

The primary and most important finding is that major surgery was the most common indication for MT (61.2% of cases), with trauma playing a lesser role (15.4%), and obstetrical emergencies barely registering at only 1.8% of all MT cases. This important result was consistent across both acute and non-acute MT cases. Based on these data, investigators and quality experts should broaden the net for MT and include patients undergoing major surgery in particular. This is not to say that there is no need for massive transfusion protocols in obstetrics; rather, this study highlights the fact that efforts should certainly include other types of at-risk patients.

The study has other interesting findings. The incidence of MT occurred at a similar rate over the 13 year period (1987–2010, Figure 1), which may be disappointing but very useful news to those focused on efforts to reduce the likelihood of these events. The study’s mortality analyses has 2 main results. Death at 5 years was highly variable by indication and related to the patient’s underlying illness/condition, e.g. cancer. For example, 91.1% of patients who received MT in the setting of malignant disease (non-surgical) died within 5 years. In contrast, in cases of MT during obstetrical hemorrhage, which generally occurs in young and healthy individuals, mortality was only 1.7% through 5 years. In addition, they also found that standardized mortality ratios (indexed to the general population) remained quite high even out to 5 to 10 years after the massive transfusion. This, however, does not imply causation between the receipt of many units of RBCs, and long term mortality, because patients with more severe injury/illness who bleed significantly will certainly be at risk for complications, eg acute/renal failure, that will adversely impact their long term prognosis.

The authors were unable to assess whether the transfusions per se, independent of disease severity/comorbidities, were associated with adverse outcome.

Bleeding and the need for transfusion are still major issues affecting ICU patients. The study by Halmin and colleagues¹⁰ is a step in the right direction since it will help focus our research and quality improvement efforts on the patients in whom massive transfusion is occurring most frequently.

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