Update on Blood Conservation for Cardiac Surgery

Bhanu P. Nalla, MBBS, FRCA,* John Freedman, MD, FRCPC,† Gregory M.T. Hare, MD, PhD, FRCPC,*‡ and C. David Mazer, MD, FRCPC*‡

PATIENTS UNDERGOING CARDIAC SURGERY are at risk of excessive bleeding, leading to increased usage of allogeneic blood and hemostatic blood products. Although this patient population represents a relatively small proportion of surgical patients, cardiac surgery consumes about 20% of the available blood supply in the United States,[1] with similar numbers reported worldwide.[2,3] The potential for beneficial effects of transfusing blood to maintain tissue oxygen perfusion and prevent organ ischemia may be greatest in patients with cardiovascular disease.[4] Indeed, life-threatening hemorrhage, an absolute indication for blood transfusion, may be relatively frequent in these patients, with repeat surgery for bleeding occurring in up to 5% of patients.[5,6] In addition, the risks of preexisting anemia and acute perioperative hemodilution have become more apparent.[7,8] However, there is a lack of clinical outcome data to support the liberal use of blood transfusion in cardiac surgery.[9]

In contrast, there is a growing body of evidence demonstrating that blood product transfusion is associated with an increased risk of morbidity and mortality.[10-12] The considerable variability in the transfusion of blood and blood products (8% to 98%) among institutions[13-15] and countries[13,14,16] may reflect the lack of a clear understanding of the risk/benefit ratio of transfusion in this high-risk patient population. However, convincing data are unavailable to assess the relative risk associated with anemia/hemodilution compared with that of allogeneic transfusion.

A broad approach to blood conservation is one way to minimize the risk. Limiting the use of blood and blood products in cardiac surgery is a multimodal strategy that involves a combined effort among all disciplines involved in patient care. This review focuses on strategies and recent interventions that can be employed to augment red cell mass and decrease red blood cell (RBC) and other blood product transfusions.

RISK OF ANEMIA AND HEMODILUTION ON CARDIOPULMONARY BYPASS

Using the World Health Organization criteria (hemoglobin [Hb] <13 g/dL for men, <12 g/dL for women), the prevalence of preoperative anemia is reported to be as high as 28%. For the purposes of this review, anemia is defined as any decrease in RBC mass or blood Hb concentration.

For decades, physiologists and physicians have emphasized that the main function of the RBC is to maintain adequate oxygen delivery to tissue.[17-19] Conversely, the lack of RBC Hb has been associated with decreased blood oxygen content and inadequate tissue oxygen delivery and increased mortality.[20-23] Recent clinical and experimental studies have supported the hypothesis that tissue hypoxia remains a likely primary mechanism of organ injury and mortality during acute and chronic anemia.[20,21,24-28] In further support of this hypothesis, recent clinical publications have continued to identify anemia as an independent risk factor for adverse events, including organ failure and increased mortality.[7,29-31] Furthermore, the risk of anemia appears to be increased in patients with cardiovascular disease.[4,22] The risk of preoperative anemia in cardiac and noncardiac surgeries includes renal failure, stroke, myocardial infarction, and increased mortality.[7,8,29,31] These risks carry over into the operative period during acute hemodilution on cardiopulmonary bypass (CPB), during which nadir hematocrit (Hct) levels <20% have been associated with increased risks of renal failure,[32-34] stroke,[35] and mortality.[36-39] It is, however, unclear from any of these studies whether treating perioperative anemia with blood transfusion would improve the patients' outcomes. Indeed, some investigators have suggested that a low Hct during CPB may be a surrogate marker for blood transfusion and its associated morbidity.[40,41] Thus, it becomes important to determine the balance of these risks and the crossover point at which the risk of anemia exceeds the potential risk of transfusion (Fig 1).

One primary reason to transfuse RBCs is to restore adequate tissue oxygen delivery. However, until recently, methods have not been available to measure tissue oxygen tension accurately after transfusion. New techniques for assessing the adequacy of tissue oxygen delivery after RBC transfusion include near-infrared

*From the Departments of *Anesthesia and †Hematology, Laboratory Medicine and Pathobiology, Keenan Research Center in the Li Ka Shing Knowledge Translation Institute of St Michael's Hospital, University of Toronto, Toronto, Ontario, Canada; and the ‡Department of Physiology, University of Toronto, Toronto, Ontario, Canada.*

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Address reprint requests to C. David Mazer, MD, FRCPC, Department of Anesthesia, St Michael's Hospital, 30 Bond Street, Toronto, ON M5B 1W8, Canada. E-mail: mazerd@smh.ca

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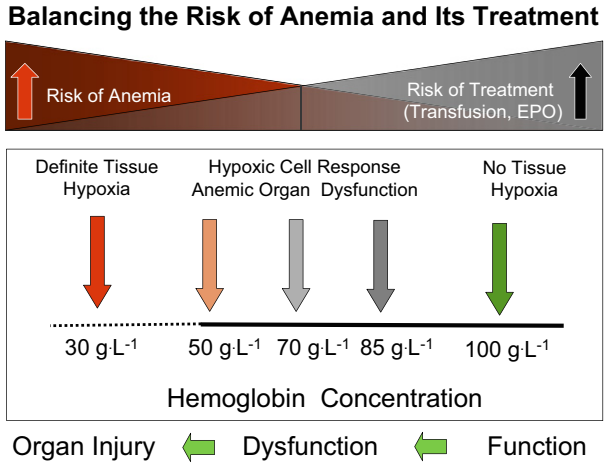

Fig 1. The risks of anemia include inadequate tissue oxygen delivery leading to organ dysfunction and increased mortality. These risks are low at hemoglobin concentrations >~100 g/L. As hemoglobin levels decrease, there is increasing evidence of organ dysfunction and injury. In experimental models, increased hypoxic cellular responses (hypoxia-inducible factor) are observed below a hemoglobin threshold of 85 g/L. These responses are tissue specific, occurring sooner in the kidney and liver compared with the heart and brain. Clear evidence of tissue hypoxia is not observed in all organs until very low hemoglobin concentrations are reached. These risks always must be matched against the risks associated with allogeneic red blood cell transfusion, which also include organ injury and increased mortality. The line balancing these two relative risks has not been established clearly in patients undergoing cardiac surgery. EPO, erythropoietin. (Color version of figure is available online.)

spectroscopy,[21,42-45] positron emission tomography,[46] and invasive oxygen electrodes.[20,47,48] These methods assess tissue oxygen tension directly or the degree of oxygen extraction. Some studies have demonstrated improved oxygen delivery and tissue partial pressure of oxygen with transfusion,[42-45,47,48] whereas other studies have not.[21,44,49] In addition, the age of the blood may influence the effect of transfusion on tissue oxygen delivery.[49] Although the benefit of transfusion to improve tissue oxygen tension still is not established clearly, it certainly has value in the setting of life-threatening hemorrhage which is considered an absolute indication for blood transfusion. Such events may be relatively more frequent in cardiac surgical patients.

EVOLUTION AND PRESUMED BENEFIT OF RBC TRANSFUSIONS

The potential benefits and risks of blood transfusion have been debated for >150 years in Western medical societies.[50,51] In more modern times, after World Wars I and II, and with the knowledge of ABO blood groups, transfusion was regarded as a life-saving modality.[52] Interestingly, a recent report has identified that donor allogeneic white blood cells may have survived within recipient World War II veterans up to 60 years after transfusion.[53] Although potential risks associated with transfusion continued to be a concern, the trend for liberal blood transfusion continued for several decades. This trend was offset by new and real concerns of transmission of viral disease in the 1980s, leading to a decreased confidence in the supply of banked blood and the promotion of transfusion avoidance.[54] Three randomized trials in adults and children demonstrating that lower Hb thresholds were well tolerated in critically ill patients and cardiac surgical patients contributed to the trend to decrease transfusions and tolerate lower Hb thresholds.[55-57] Furthermore, the physiologic premise that acute hemodilution optimized blood rheology and favored perfusion led to several clinical approaches that further decreased RBC mass in many clinical settings, including CPB.[58] The collective impact of these influences has promoted a clinical attitude of tolerance for acute and chronic anemia.

UNDERSTANDING THE RISKS OF BLOOD TRANSFUSIONS

An essential step in striving to conserve blood and decrease transfusion requirements in cardiac surgery is to weigh critically the expected benefits of blood and blood products against the risks associated with them. The potential benefits of blood transfusion include an increased oxygen-carrying capacity, volume support of cardiac output, and improved hemostasis associated with blood products.[59,60] Although blood transfusion has been a widely accepted practice for many decades, there are few randomized trials to support the use of blood products to treat disease. In fact, the two completed randomized trials in noncardiac critically ill patients have favored a lower Hb threshold.[56,57]

The risks associated with the transfusion of blood and blood products have been recognized for many decades (Table 1). Fortunately, with advances in screening, collection, and preparation techniques, the transmission of disease (bacterial, viral, or prion) and hemolytic transfusion reac-

Table 1. Current Estimated Risks of Transfusion

Infectious		Noninfectious	
HIV	1:2-8 million	Febrile reaction	1:1,000
Hepatitis B	1:155,000-350,000	TRALI	1:2,000-5,000
Hepatitis C	1:2-2.3 million	Transfusion error	1:38,000
HTLV	1:3-4.3 million	Hemolysis	1:100,000
Bacterial contamination	1:500,000	GVHD	1:1 million
Other (*Yersinia*, West Nile virus, malaria, etc)	1:1 million	Death	1:1.8-5.6 million

Abbreviations: GVHD, graft-versus host disease; HIV, human immunodeficiency virus; HTLV, human lymphotropic virus; TRALI, transfusion-related lung injury.