PROTOCOL FOR RBC TRANSFUSION IN CRITICALLY ILL PATIENTS

This protocol is based upon medical literature review and expert opinion and is intended to provide recommendations for RBC Transfusions in the care of critically ill patients.

Best Practice Recommendations

No active bleeding without active coronary ischemia:

- **Hgb <7 g/dl:** Transfuse 1 unit of RBC and reassess patient’s clinical status. Maintain Hgb level at 7-9 g/dl. Reassess Hgb after blood product administration.
- **Hgb 7 to 9 g/dl:** Limit transfusions unless inadequate tissue O₂ delivery is documented (SvO₂<60, elevated lactate, chest pain, or hypotension or tachycardia unresponsive to crystalloid resuscitation).
- **Hgb >9 g/dl:** RBC transfusion is not indicated.

No active bleeding with evidence of ongoing symptomatic coronary ischemia:

- **Hgb <8 g/dl:** Transfuse 1 unit of RBC and reassess patient’s clinical status and Hgb level after blood product administration.
- **Hgb 8-10 g/dl:** Equipoise in the current available literature with studies showing harm and other studies showing protective effects with a restrictive (Hgb<8) vs. liberal (Hgb<10) transfusion strategy. Consider transfusion of 1 unit RBC and reassess patient’s clinical status.
- **Hgb >10 g/dl:** RBC transfusion is not indicated.

Active Bleeding:

- **Acute hemorrhage (hemodynamically unstable):** RBC transfusion should be guided by rate of bleeding and hemodynamic parameters rather than Hgb level.
- **Acute hemorrhage (hemodynamically stable):** Target Hgb 7 to 9 g/dl: Restrictive transfusion strategy unless inadequate tissue O₂ delivery is documented (SvO₂<60, elevated lactate, or hypotension or tachycardia unresponsive to crystalloid resuscitation).

Background Information and Literature Review

The risk and benefit ratio of blood product transfusion is debated in the literature. In regards to the benefits of blood product transfusion, anemia can lead to inadequate oxygen delivery to tissues. The deleterious effects of severe postoperative anemia were highlighted in a study where patients with a postoperative Hgb ≤8.0 g/dL refused blood transfusions due to religious reasons.
had an increased mortality.\(^1\) Mortality rates increased as Hgb levels decreased below 7.1 g/dL. On the other hand, blood product transfusion carries a significant risk such as transfusion reactions, transmission of infectious agents, transfusion related acute lung injury, volume overload, and immunomodulation.\(^2\) In addition, blood product resuscitation is independently associated with higher nosocomial infection rates, risk for worsening SIRS and sepsis, multiple organ failure, longer ICU and hospital length of stay, as well as, increased mortality.\(^3\)

Hebert et al.\(^4\) published the Transfusion Requirements In Critical Care (TRICC) trial, a landmark study in 1999, that compared a restrictive vs. liberal transfusion strategy in critically ill patients. The study demonstrated that patients restricted to a transfusion trigger of Hgb 7.0 g/dL with a target of 7.0 to 9.0 had lower in-hospital mortality than patients transfused at 10.0 with a target of 10.0 to 12.0. Overall, 30-day mortality favored the restrictive strategy but was not statistically significant (23% in the liberal group vs. 19% in the restrictive group). However, 30-day mortality rates were lower with the restrictive strategy in two predefined subgroups: (1) Patients who were less severely ill (APACHE II score ≤20; mortality 9 vs. 16%) and (2) Patients <55 years of age (mortality 6 vs. 13%).

Support for a restrictive transfusion strategy was also demonstrated in Functional Outcomes in Cardiovascular Patients Undergoing Surgical Hip Fracture Repair (FOCUS) trial.\(^5\) Patients with high cardiovascular risk factors were randomized into liberal vs. restrictive postoperative transfusion groups after hip repair surgery. The liberal transfusion group received immediate transfusion of one unit of RBCs plus subsequent transfusions to raise the Hgb level to >10 g/dL if decreased below this level. The restrictive transfusion group received a single unit only if they developed symptoms of anemia (defined as chest pain, orthostatic hypotension, tachycardia unresponsive to fluid resuscitation, or congestive heart failure) or, in the absence of symptoms, when the Hgb level fell below 8 g/dL. The study showed that there was not a difference in functional recovery (inability to walk 10 feet), 60-day mortality, in-hospital myocardial infarction, or unstable angina with liberal or restrictive transfusion strategies.

A restrictive transfusion threshold is further supported by a recent Cochrane systematic review (included 19 randomized control clinical trials involving more than 6000 patients) and meta-analysis of clinical trials of RBC transfusion.\(^6,7\) Important findings from these two reviews reported that restrictive strategies vs. liberal resulted in 1.19 fewer units transfused per patient, a trend towards a lower 30 day mortality and overall infection rate, and no difference in functional recovery, cardiac events, stroke, hospital or intensive care length of stay. Furthermore, another meta-analysis showed that a restrictive approach to product transfusion resulted in lower hospital-associated infections.\(^8\) Specifically, the pooled risk of all serious infections was 11.8% in the restrictive group and 16.9% in the liberal group. The greatest benefit was seen in patients undergoing orthopedic surgery and those who presented with sepsis.

In the setting of active coronary ischemia, there is equipoise in the current available literature with some studies showing harm and other studies showing protective effects with a restrictive vs. liberal transfusion strategy. The recent Cochrane review\(^9\) reported no increased risk of myocardial infarction (MI) when all trials were included, however, the two largest trials (TRICC and FOCUS)\(^4,5\) found opposite effects regarding the risk of MI with a restrictive transfusion strategy. Specifically, the TICC trial,\(^4\) a restrictive transfusion strategy was associated with a lower MI risk (0.7 vs. 2.9%); however, in patients with ischemic heart disease, there was a reversal in the trend in 30-day mortality, with the 30-day mortality slightly higher in the restrictive vs. liberal strategy group (26 vs. 21%). In the FOCUS trial,\(^5\) a restrictive transfusion strategy was associated with a higher risk of MI (3.8 vs. 2.3%), however the trend was not statistically significant. To further address the unresolved issue of appropriate blood transfusion in acute coronary ischemia, a single center pilot trial in 110 patients with acute coronary syndrome or
stable angina undergoing cardiac catheterization with Hgb <10 g/dL was recently performed.\textsuperscript{11} Patients in the liberal transfusion strategy received one or more units of blood to raise the Hgb level ≥10 g/dL. Patients in the restrictive transfusion strategy were permitted to receive blood for symptoms from anemia or for Hgb <8 g/dL. The liberal transfusion strategy was associated with a statistically non-significant trend for fewer major cardiac events and a statistically significant decrease in deaths at 30 days than the more restrictive strategy. To further highlight the conflicting landscape in the literature, a recent meta-analysis focusing on patients receiving blood transfusions in the setting of myocardial infarction concluded that all-cause mortality was increased with a strategy of blood transfusion vs. no blood transfusion (18.2 % vs. 10.2%).\textsuperscript{12} However, the mortality risk associated with blood transfusions was mitigated when the analysis was restricted to studies that included patients with a STEMI. It is important to note a major weakness of this meta-analysis:\textsuperscript{12} the report did not stratify pre-transfusion Hgb concentration to discern the risk of anemia vs. the risk of blood transfusions. Because of the conflicting reports in the literature, the benefits and harm of blood transfusions during active coronary ischemia remains controversial. At this time, we recommend targeting a Hgb level of 8-10 g/dL. Overall, multiple factors related to the patient’s clinical status, oxygen delivery, and pre-transfusion Hgb level should be considered in patients with coronary ischemia.

In regards to acute bleeding, there should not be a threshold for blood product transfusion in the \textit{hemodynamically unstable} patient. The pace of bleeding and degree of hemodynamic instability should guide blood product resuscitation.\textsuperscript{9} On the other hand, in a \textit{hemodynamically stable, bleeding} patient, a restrictive transfusion strategy is recommended. A recent single center clinical control trial randomized 921 patients with acute upper gastrointestinal bleeding to a restrictive or a liberal transfusion strategy (transfusion threshold of 7 g/dL vs. 9 g/dL).\textsuperscript{10} The study results demonstrated a lower percent of patients undergoing transfusion (49 vs. 86%), fewer complications (40 vs. 48%), less re-bleeding (10 vs. 16%), fewer deaths due to uncontrolled bleeding (0.7 vs. 3.1%), and fewer deaths from any cause (5 vs. 9%). Importantly, patients with massive bleeding, acute coronary syndrome, history of peripheral vascular disease or stroke, and Hgb >12 g/dL were excluded during randomization. This study suggests that in \textit{hemodynamically stable}, bleeding patients who are \textit{not high risk}, a restrictive transfusion strategy is safe.

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**Approval**

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