# Safe Application of a Restrictive Transfusion Protocol in Moderate-Risk Patients Undergoing Cardiac Operations

Howard K. Song, MD, PhD, Christian von Heymann, MD, Christian M. Jespersen, MD, Keyvan Karkouti, MD, Wolfgang Korte, MD, Jerrold H. Levy, MD, Marco Ranucci, MD, Trine Saugstrup, MS, and Frank W. Sellke, MD

Division of Cardiothoracic Surgery, Oregon Health & Science University, Portland, Oregon; Department of Anaesthesiology and Intensive Care Medicine, Charité-Universitätsmedizin Berlin, Berlin, Germany; Safety Surveillance, Global Safety, Novo Nordisk, Bagsværd, Denmark; Department of Anesthesia and Toronto General Research Institute, Toronto General Hospital, University Health Network, University of Toronto, Toronto, Ontario, Canada; Center for Laboratory Medicine, St Gallen, Switzerland; Department of Anesthesiology and Critical Care, Duke University School of Medicine, Durham, North Carolina; Department of Cardiothoracic-Vascular Anesthesia and Intensive Care Unit, IRCCS Policlinico San Donato, San Donato Milanese, Milan, Italy; Biostatistics, Novo Nordisk A/S, Søborg, Denmark; and Department of Surgery, Rhode Island Hospital, Brown Medical School, Providence, Rhode Island

*Background.* **Perioperative red blood cell transfusion is associated with adverse outcomes after cardiac operations. Although restrictive transfusion protocols have been developed, their safety and efficacy are not well demonstrated, and considerable variation in transfusion practice persists. We report our experience with a restrictive transfusion protocol.**

*Methods.* **We analyzed the outcomes in 409 patients undergoing cardiac operations enrolled in a trial conducted at 30 centers worldwide. Blood products were administered on the basis of a transfusion algorithm applied across all centers, with a restrictive transfusion trigger of hemoglobin less than or equal to 6 g/dL. Transfusion was acceptable but not mandatory for hemoglobin 6 to 8 g/dL. For hemoglobin 8 to 10 g/dL, transfusion was acceptable only with evidence for end-organ ischemia.**

*Results.* **The patient population was moderately complex, with 20.5% having combined procedures and 29.6% having nonelective operations. The mean EuroSCORE for the population was 4.3, which predicted a substantial incidence of morbidity and mortality. Actual outcomes were excellent, with observed mortality of 0.49% and rates of cerebrovascular accident, myocardial infarction, and acute renal failure 1.2%, 6.1%, and 0.98%, respectively. The frequency of red blood cell transfusion was 33.7%, which varied significantly by center. Most transfusions (71.9%) were administered for hemoglobin 6 to 8 g/dL; 21.4% were administered for hemoglobin 8 to 10 g/dL with evidence for end-organ ischemia; 65.0% of patients avoided allogeneic transfusion altogether.**

*Conclusions.* **A restrictive transfusion protocol can be safely applied in the care of moderate-risk patients undergoing cardiac operations. This strategy has significant potential to reduce transfusion and resource utilization in these patients, standardize transfusion practices across institutions, and increase the safety of cardiac operations.**

**(Ann Thorac Surg 2014;■:■–■)**


Patients undergoing cardiac operations frequently experience anemia related to surgical blood loss, coagulopathy, and hemodilution [1]. Acute perioperative anemia is appropriately treated with red blood cell (RBC) transfusions to restore the oxygen-carrying capacity of the blood to adequate levels and avoid end-organ ischemia. However, RBC transfusion is itself associated with increased morbidity and mortality after cardiac operations [2–9]. In addition to the detrimental effect of RBC transfusion on the individual patient, transfusion and the treatment of the adverse events of transfusion represent a significant cost to the health care system. Patients undergoing cardiac operations receive 10% to 15% of the 14 million units of allogeneic RBCs transfused annually in the United States [10, 11].

Despite the widespread desire to avoid or limit perioperative transfusion in patients receiving cardiac operations, considerable variation in transfusion practice persists. In a recent Society of Thoracic Surgeons study of cardiac surgery centers in the United States, the rates of RBC transfusion ranged from 7.8% to 92.8% in patients undergoing isolated coronary artery bypass grafting (CABG) [12]. Restrictive transfusion protocols have been developed in an attempt to standardize transfusion practice, reduce the cost of transfusion, and improve the outcomes of cardiac operations [13, 14]. However, the safety of such protocols, especially in higher-risk populations receiving cardiac operations, has not been well demonstrated. In this study, we report our experience with a restrictive transfusion protocol in a moderate-risk population of patients undergoing cardiac operations.

Accepted for publication Dec 18, 2013.

Address correspondence to Dr Song, Division of Cardiothoracic Surgery, Oregon Health & Science University, Mail Code L353, 3181 SW Sam Jackson Park Rd, Portland, OR 97239; e-mail: songh@ohsu.edu.


Published by Elsevier Inc

0003-4975/$36.00
http://dx.doi.org/10.1016/j.athoracsur.2013.12.025

## Patients and Methods

This study represents a secondary analysis of 409 patients undergoing cardiac operations enrolled in a randomized, double-blinded, placebo-controlled, multinational, multicenter, phase II, dose-escalation trial to determine whether recombinant Factor XIII administration after cardiac operations reduces transfusion needs [15]. The original analysis concluded that although Factor XIII administration is safe, it has no effect on transfusion or reoperation in patients undergoing cardiac operations. The trial was conducted from July 27, 2009, to February 23, 2011. It was performed in accordance with the Declaration of Helsinki, International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use Good Clinical Practice, and was approved by the health authorities of each country involved and by the Ethics Committee or Institutional Review Board of each of the 31 cardiac surgery centers involved. The trial is registered at http://www.clinicaltrials.gov (Identifier NCT 00914589).

### *Patients*

Adult patients (18–80 years old) who were scheduled to undergo nonemergent CABG requiring cardiopulmonary bypass, single heart valve replacement or repair requiring cardiopulmonary bypass, or both of these surgical interventions were eligible for inclusion. All patients received intraoperative antifibrinolytic agents, and patients were required to be at moderate risk for transfusion. Moderate risk for transfusion was defined as meeting two or three of the following criteria: (1) nonelective operation, (2) redo operations, (3) combined CABG and valve operation, (4) age 69 years or older, (5) body surface area less than 1.9 $m^2$, (6) creatinine greater than 100 μmol/L if female and greater than 110 μmol/L if male, (7) platelet count less than 150,000/μL, and (8) hematocrit less than 36% if female and less than 39% if male. The validity of the transfusion risk model was confirmed before the trial by use of historical transfusion data from two of the centers involved with the study design. If only one criterion or more than three of the criteria were met, patients were not eligible for the study. Patients at low risk for transfusion were excluded because the original intent of the study was to detect whether recombinant Factor XIII administration reduced transfusion needs; the inclusion of low-risk patients would have made detection of such an effect less feasible.

### *Transfusion Management*

Autologous blood collection before operation and acute normovolemic hemodilution was not permitted. Shed blood collected in the operating room could be transfused washed or unwashed according to institutional practice. Transfusion of blood collected in mediastinal drains was not permitted.

Allogeneic transfusion was standardized across all centers participating in the study by the use of transfusion protocols developed by the trial Steering Committee (Appendix). The transfusion protocols were effective after patient randomization at the completion of cardiopulmonary bypass. RBC transfusion was mandatory for hemoglobin below 6.0 g/dL, optional for hemoglobin between 6.0 and 8.0 g/dL, acceptable for hemoglobin between 8.0 and 10.0 g/dL provided there was evidence for end-organ ischemia, and not permitted for higher hemoglobin values. Transfusions were administered 1 unit at a time, and the hemoglobin was rechecked after each transfused unit. Coagulation products were administered if after reversal of protamine patients bled 2 mL/kg or more over 30 minutes or 1.5 mL/kg or more per hour over 2 consecutive hours. Fresh frozen plasma (10–15 mL/kg) was administered if the international normalized ratio was 1.5 or greater. Platelets (1 apheresis unit or 4–6 pooled units) were transfused if the platelet count was $100 \times 10^9$/L or less. Fibrinogen concentrate (2 g) or cryoprecipitate (8–10 units) was transfused if the fibrinogen concentration was 1.5 g/L or less. An external adjudication committee was established to ensure compliance with the transfusion protocol at each center.

### *Laboratory Tests*

Standard laboratory tests (hematology, coagulation, and biochemistry) were measured before operation and approximately 30 minutes, 8 hours, 1 day, 2 days, 3 days, 7 days, and 5 to 7 weeks after separation from cardiopulmonary bypass.

### *Outcomes*

An external, independent safety data monitoring committee was established to ensure the safety of patients. Transfusion of any allogeneic blood product was recorded. Clinical outcomes including mortality and all adverse events were reported until postoperative day 7 or hospital discharge. Serious adverse advents were reported until the follow-up visit 5 to 7 weeks after operation. Prespecified critical adverse events were acute myocardial infarction (based on enzyme and electrocardiogram criteria adjudicated by an independent central laboratory), stroke or transient ischemic attack, peripheral artery occlusion, deep vein thrombosis, pulmonary embolism, renal dysfunction (doubling of creatinine or renal replacement therapy), reoperation, and death.

### *Statistical Analyses*

The 409 patients enrolled in the study were randomized to receive placebo or recombinant Factor XIII in two different doses after protamine reversal of heparin after cardiopulmonary bypass. Because the primary statistical analysis of this study showed no effect on transfusion and no safety concern for recombinant Factor XIII dosing, the three groups were combined for this secondary analysis to report our experience with the restrictive RBC transfusion protocol [16].

## Results

### *Patient Characteristics*

The patient characteristics and operative details are summarized in Table 1. The patients had a mean age of

*Table 1. Patient Characteristics and Operative Details*

| Patient Characteristics | Value |
|---|---|
| Age, y, mean (SD) | 68.8 (8.4) |
| Male sex, n (%) | 336 (82.2) |
| White race, n (%) | 371 (90.7) |
| Body surface area, $m^2$, mean (SD) | 1.88 (0.2) |
| Left ventricular ejection fraction, %, mean (SD) | 56.2 (10.0) |
| Hemoglobin, g/dL, mean (SD) | 13.7 (1.3) |
| Hematocrit, %, mean (SD) | 40.3 (3.6) |
| Creatinine, mg/dL, mean (SD) | 1.02 (0.3) |
| Platelet count, $\times 10^9$/L, mean (SD) | 210.8 (60.0) |
| INR, mean (SD) | 1.1 (0.1) |
| aPTT, sec, mean (SD) | 29.1 (9.9) |
| Fibrinogen, mg/dL, mean (SD) | 410.9 (139) |
| Operative details | |
| CABG, n (%) | 214(52.3) |
| Valve repair or replacement, n (%) | 111(27.1) |
| Combined CABG and valve, n (%) | 84(20.5) |
| Redo operations, n (%) | 13(3.2) |
| Nonelective operations, n (%) | 121 (29.6) |
| EuroSCORE, mean (SD) | 4.3(2.0) |
| TRUST score, mean (SD) | 2.54 (0.88) |

aPTT = activated partial thromboplastin time; CABG = coronary artery bypass grafting; INR = international normalized ratio of prothrombin time; SD = standard deviation; TRUST = Transfusion Risk Understanding Scoring Tool.

68.8 years and were predominantly male and of white race. The mean preoperative hematology values were in the normal range. Approximately half of the patients underwent isolated CABG, and half underwent a valve procedure or a valve procedure combined with a CABG. A significant proportion of patients (29.6%) underwent nonelective operations.

Patients were selected for inclusion in the study on the basis of their prospectively determined moderate risk for postoperative transfusion (Methods). The transfusion risk model used for this determination included several patient characteristics also associated with postoperative morbidity and mortality, including nonelective operations, redo operations, combined CABG and valve operations, advanced age, and renal impairment. Because of this selection mechanism, patients enrolled in the study had a moderately high risk for mortality. The mean EuroSCORE for the patient population predicted an operative mortality of 4.3%.

Although a unique transfusion risk model was used to select patients for inclusion in the original trial, for the sake of this secondary analysis it was desirable to calculate the transfusion risk for the patient population using a validated, widely accepted transfusion risk tool. A Transfusion Risk Understanding Scoring Tool (TRUST) score was therefore calculated [16]. The mean TRUST score for the study population was 2.54. This would predict a probability for blood transfusion for the study population on either the day of operation or the first postoperative day of approximately 55%.

### *Transfusion*

Approximately two thirds of patients (66.3%) avoided perioperative RBC transfusion (Table 2). Of those patients receiving perioperative RBC transfusion, the great majority received only 1 or 2 units. Perioperative transfusion of fresh frozen plasma or platelets was much rarer (<10%). Overall, 65.0% of patients in the study avoided any allogeneic perioperative transfusion.

The RBC transfusion was most commonly given for a patient whose hemoglobin was in the 6- to 8-g/dL range (Table 3). By the rules of the transfusion protocol, centers were allowed to administer RBC transfusion to patients with hemoglobin levels in this range without providing a medical justification. RBC transfusion was given for a patient whose hemoglobin was in the 8 to 10-g/dL range with medical justification in 21.4% of RBC transfusions. Compliance with the RBC transfusion protocol was excellent, with only 11 of 313 total units transfused given outside of the protocol rules. Despite the excellent compliance, transfusion practice varied significantly among study centers. In a logistic regression analysis, the study site was the only variable found to predict RBC transfusion avoidance ($p = 0.0009$).

### *Outcomes of Operations*

The observed clinical outcomes were excellent (Table 4). The incidence of myocardial infarction and other adverse events potentially caused or exacerbated by anemia and impaired oxygen delivery to end organs was low and within the range expected for the patient population.

*Table 2. Allogeneic Transfusions in the First Postoperative Week*

| Allogeneic Transfusion | No. of Patients (%) |
|---|---|
| RBC | |
| 0 units | 271 (66.3) |
| 1 unit | 62 (15.2) |
| 2 units | 41 (10.0) |
| 3 units | 11 (2.7) |
| 4 units | 9 (2.2) |
| 5 or more units | 15 (3.6) |
| FFP | |
| 0 units | 382 (93.4) |
| 1 unit | 1 (0.2) |
| 2 units | 9 (2.2) |
| 3 units | 9 (2.2) |
| 4 or more units | 8 (1.9) |
| Platelets | |
| 0 units | 386 (94.4) |
| 1 unit | 8 (2.0) |
| 2 units | 3 (0.7) |
| 3 or more units | 12 (2.9) |
| Any allogeneic transfusion | 143 (35.0) |
| No allogeneic transfusion | 266 (65.0) |

FFP = fresh frozen plasma; RBC = red blood cell.

*Table 3. Patient Hemoglobin Before to Red Blood Cell Transfusion*

| Patient Hemoglobin | No. of Units (%): 313 Total Units |
|---|---|
| ≤6 g/dL | 10 (3.2) |
| >6 g/dL, <8 g/dL[a] | 225 (71.9) |
| ≥8 g/dL, <10 g/dL[b] | 67 (21.4) |
| Off protocol | 11 (3.5) |

[a] Transfusion acceptable without medical justification, but not mandatory. [b] Transfusion acceptable with clinical evidence for inadequate oxygen delivery.

The observed mortality rate of 0.49% was substantially lower than that predicted by the mean patient EuroSCORE [17, 18].

## Comment

Numerous observational studies have shown that perioperative transfusion is associated with an increased risk of adverse events after cardiac operations. Perioperative RBC transfusion incrementally increases the risk of renal failure, respiratory failure, infection, and cardiovascular and neurologic adverse events in patients undergoing cardiac operations. Higher rates of short-term and long-term mortality have also been found to be associated with perioperative RBC transfusion [2–9]. There is a widespread desire to reduce perioperative transfusion because of the increasing awareness of its deleterious effects and its cost to the health care system. Professional societies have published blood conservation guidelines in an attempt to help achieve this goal [10, 19]. Despite this, transfusion rates continue to vary substantially, with RBC transfusion rates reported to be as high as 92.8% for patients undergoing isolated CABG [12]. RBC transfusion protocols have also been developed and have shown promise in reducing transfusion; however, these have typically been applied to low-risk patient populations, and their safety in higher-risk populations is not well documented [20]. The ideal transfusion trigger for patients undergoing cardiac operations has also not been delineated, and it often focuses primarily on RBC transfusion, not other blood components [20–23]. The most recent large study used a transfusion trigger of hemoglobin below approximately 8 g/dL and did not find a difference in outcomes in comparison with to a more liberal transfusion policy. Using a transfusion trigger of hemoglobin below 8 g/dL, these investigators reported an RBC transfusion rate of 47% [14].

*Table 4. Patient Outcomes*

| Adverse Events | Patients (%) |
|---|---|
| Myocardial infarction | 25 (6.1) |
| Cerebrovascular accident | 5 (1.2) |
| Renal failure | 4 (0.98) |
| Limb ischemia | 1 (0.24) |
| Deep vein thrombosis | 2 (0.49) |
| Reoperation due to postoperative hemorrhage | 9 (2.2) |
| Death | 2 (0.49) |

In this study we report our experience with a more restrictive RBC transfusion protocol (mandatory transfusion for hemoglobin <6 g/dL) applied to a moderate-risk population of patients undergoing cardiac operations. The protocol performed well, with RBC and overall transfusions limited to 33.7% and 35.0%, respectively, of the patient population. Although this was an observational study without a control group, our observed rates of transfusion are favorable in comparison with to the overall transfusion rate predicted by the study population TRUST score, which was 55%. Our results are also favorable compared with those of other published transfusion rates, including other studies of transfusion protocols [14]. The Society of Thoracic Surgeons National Database reported a perioperative transfusion rate of 56.1% for RBC transfusion among patients undergoing first time isolated CABG in 2008 [12].

Importantly, our observed clinical outcomes also were excellent, with low rates of adverse events and a mortality rate substantially lower than that predicted by EuroSCORE. It is true that clinical outcomes observed in the setting of randomized trials frequently exceed outcomes that are experienced in real-world practice because of careful patient selection. However, the comparison of our observed mortality with the expected mortality calculated by EuroSCORE alleviates the risk of selection bias somewhat. For instance, patients requiring emergency operations were excluded from the study, and the EuroSCORE algorithm takes this into account in the calculation of expected mortality. It is interesting to speculate that the excellent observed clinical outcomes are related to the high frequency with which patients in our study avoided allogeneic transfusion and its associated deleterious effects.

Despite excellent compliance with the transfusion protocol, there was significant variation in transfusion rates among participating centers. Much of the variation in transfusion practice likely occurred in the treatment of patients whose hemoglobins were in the 6- to 8-g/dL range, because this was the most common range in which transfusion occurred and no medical justification was required. Increasing the requirement for objective transfusion criteria for patients within this hemoglobin range will likely lead to additional improved transfusion protocol performance in the future. This is especially important for future prospective controlled trials, wherein limitation of intercenter variability in transfusion is desirable. The ideal transfusion trigger has not yet been delineated; however, our data suggest that this trigger can be a hemoglobin of less than 8 g/dL, at least in some patients, and that requiring objective medical justification will help to standardize transfusion practice across institutions in the future.

Differences in the management of hemodilution across centers may also have contributed to the variation observed in transfusion rates among participating centers. Centers with stringent hemodilution management

would be expected to trigger RBC transfusion less frequently, leading to lower transfusion rates even if the transfusion protocol were uniformly applied across centers.

Our experience with a restrictive transfusion protocol indicates that further prospective, randomized studies are needed to validate this approach. We found that a restrictive transfusion protocol can be safely and effectively applied in the care of moderate-risk patients undergoing cardiac operations. This strategy has significant potential to reduce the use of transfusion and resources in these patients, standardize transfusion practices across institutions, and increase the safety of cardiac operations.

This study was sponsored by Novo Nordisk A/S (Bagsvaerd, Denmark). The authors had full control of the design of the study, methods used, outcome parameters and results, analysis of data, and production of the written report for the initial study and this secondary analysis. The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree with the article as written.

## References

1. Mehta RH, Sheng S, O'Brien SM, et al. Reoperation for bleeding in patients undergoing coronary artery bypass surgery: incidence, risk factors, time trends, and outcomes. Circ Cardiovasc Qual Outcomes 2009;2:583–90.
2. Engoren MC, Habib RH, Zacharias A, Schwann TA, Riordan CJ, Durham SJ. Effect of blood transfusion on long-term survival after cardiac operation. Ann Thorac Surg 2002;74:1180–6.
3. Koch CG, Li L, Duncan AI, et al. Morbidity and mortality risk associated with red blood cell and blood-component transfusion in isolated coronary artery bypass grafting. Crit Care Med 2006;34:1608–16.
4. Koch CG, Li L, Duncan AI, et al. Transfusion in coronary artery bypass grafting is associated with reduced long-term survival. Ann Thorac Surg 2006;81:1650–7.
5. Koch CG, Li L, Sessler DI, et al. Duration of red-cell storage and complications after cardiac surgery. N Engl J Med 2008;358:1229–39.
6. Kuduvalli M, Oo AY, Newall N, et al. Effect of peri-operative red blood cell transfusion on 30-day and 1-year mortality following coronary artery bypass surgery. Eur J Cardiothorac Surg 2005;27:592–8.
7. Murphy GJ, Reeves BC, Rogers CA, Rizvi SI, Culliford L, Angelini GD. Increased mortality, postoperative morbidity, and cost after red blood cell transfusion in patients having cardiac surgery. Circulation 2007;116:2544–52.
8. Scott BH, Seifert FC, Grimson R. Blood transfusion is associated with increased resource utilisation, morbidity and mortality in cardiac surgery. Ann Card Anaesth 2008;11:15–9.
9. Surgenor SD, DeFoe GR, Fillinger MP, et al. Intraoperative red blood cell transfusion during coronary artery bypass graft surgery increases the risk of postoperative low-output heart failure. Circulation 2006;114:I43–8.
10. Ferraris VA, Brown JR, Despotis GJ, et al. 2011 update to the Society of Thoracic Surgeons and the Society of Cardiovascular Anesthesiologists blood conservation clinical practice guidelines. Ann Thorac Surg 2011;91:944–82.
11. Services UDoHaH. The 2007 Nationwide Blood Collection and Utilization Survey Report. Department of Health and Human Services, 2007.
12. Bennett-Guerrero E, Zhao Y, O'Brien SM, et al. Variation in use of blood transfusion in coronary artery bypass graft surgery. JAMA 2010;304:1568–75.
13. Bracey AW, Radovancevic R, Riggs SA, et al. Lowering the hemoglobin threshold for transfusion in coronary artery bypass procedures: effect on patient outcome. Transfusion 1999;39:1070–7.
14. Hajjar LA, Vincent JL, Galas FR, et al. Transfusion requirements after cardiac surgery: the TRACS randomized controlled trial. JAMA 2010;304:1559–67.
15. Karkouti K, von Heymann C, Jespersen CM, et al. Efficacy and safety of recombinant factor XIII on reducing blood transfusions in cardiac surgery: a randomized, placebo-controlled, multicenter clinical trial. J Thorac Cardiovasc Surg 2013;146:1–13.
16. Alghamdi AA, Davis A, Brister S, Corey P, Logan A. Development and validation of Transfusion Risk Understanding Scoring Tool (TRUST) to stratify cardiac surgery patients according to their blood transfusion needs. Transfusion 2006;46:1120–9.
17. Geissler HJ, Holzl P, Marohl S, et al. Risk stratification in heart surgery: comparison of six score systems. Eur J Cardiothorac Surg 2000;17:400–6.
18. Roques F, Michel P, Goldstone AR, Nashef SA. The logistic EuroSCORE. Eur Heart J 2003;24:881–2.
19. Ferraris VA, Ferraris SP, Saha SP, et al. Perioperative blood transfusion and blood conservation in cardiac surgery: the Society of Thoracic Surgeons and The Society of Cardiovascular Anesthesiologists clinical practice guideline. Ann Thorac Surg 2007;83:S27–86.
20. Reeves BC, Murphy GJ. Increased mortality, morbidity, and cost associated with red blood cell transfusion after cardiac surgery. Curr Opin Cardiol 2008;23:607–12.
21. Hebert PC, Wells G, Blajchman MA, et al. A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care. Transfusion Requirements in Critical Care Investigators, Canadian Critical Care Trials Group. N Engl J Med 1999;340:409–17.
22. Madjdpour C, Spahn DR, Weiskopf RB. Anemia and perioperative red blood cell transfusion: a matter of tolerance. Crit Care Med 2006;34:S102–8.
23. Vincent JL, Piagnerelli M. Transfusion in the intensive care unit. Crit Care Med 2006;34:S96–101.

*Appendix. Red Blood Cell Transfusion Protocol*

| Patient Hemoglobin | Response |
|---|---|
| Hemoglobin ≥10 g/dL | No transfusion |
| Hemoglobin ≥8 g/dL, <10 g/dL | Transfuse if there is medical justification[a, b] |
| Hemoglobin >6 g/dL, <8 g/dL | Transfusion is acceptable without medical justification, but not mandatory[a] |
| Hemoglobin ≤6 g/dL | Transfuse[a] |

[a] Remeasure hemoglobin after each red blood cell unit transfused to determine eligibility for next unit. [b] Medical justification for red blood cell transfusion includes one or more of the following: central venous saturation <60%, cardiac index <2.0 unresponsive to inotropic or mechanical support, signs/symptoms of end-organ ischemia such as electrocardiogram change or left ventricular wall motion abnormality.

*Non—Red Blood Cell Blood Component Transfusion Protocol If bleeding ≥1.5 mL/kg/hour for 2 consecutive hours or 4 mL/kg/hour for 30 minutes, consider transfusion.*

| Coagulation Parameter[a] | Response |
|---|---|
| International normalized ratio >1.5 | Fresh frozen plasma 10–15 mL/kg |
| Platelet count ≤100,000/μL | 1 U apheresis or 4–6 U pooled platelets |
| Fibrinogen ≤1.5 g/L | Fibrinogen 2 g or cryoprecipitate 8–10 U |
| Activated clotting time >10% or activated partial thromboplastin time >20% above normal limit | Consider protamine 25 mg |

[a] In patients with profuse microvascular bleeding, non—red blood cell products can be given before coagulation parameters are available.

ACT = activated clotting time; aPTT = activated partial thromboplastin time; INR = international normalized ratio.