

TRANSFUSION

Key points

1. Preoperative anemia is associated with increased postoperative mortality.
2. Optimum transfusion thresholds remain uncertain.
3. Transfusion is not purely a benign intervention—there is increasing concern for immunomodulatory effects.
4. Erythropoietin may be considered in patients who refuse transfusion, but there are significant risks associated with its use and uncertain benefit.

Perioperative patients may have anemia and thrombocytopenia from a multitude of causes, including underlying medical conditions, surgical bleeding, factor deficiencies, consumption, and drug reactions. Transfused blood products are considered a precious resource, providing incentive to minimize their use. There is also increasing concern that transfusion of packed red blood cells may pose risks beyond that of transfusion reactions. In this section we focus on the use of transfusion of packed red blood cells in the perioperative period.

Preoperative evaluation

- Identify preoperative anemia in patients at risk—In a natural history study of 1958 patients undergoing noncardiac surgery who refused transfusion for religious reasons:¹
 - Preop anemia was associated with increased 30 day mortality
 - Risk was minimal in patients without cardiovascular disease who suffered mild blood loss (less than 2 g/dl Hgb drop), but high in those with cardiovascular disease.
 - An unusual feature of this study was that “anemia” was the cause of death in 28% of cases—making applicability to a population that accepts transfusion less clear.
 - Anemia is a risk factor in many prognostic indices e.g. APACHE II, and cardiovascular disease is a risk factor in other perioperative risk indices, so this data is generally consistent with other studies.
- There is no data suggesting that correcting preoperative anemia with *transfusion* would reduce the risk.
- For patients with severe anemia intending to have purely elective surgery, it is reasonable to recommend working up and treating the anemia prior to surgery.
- Autologous blood: The potential advantage of autologous blood is avoidance of mismatch with allogeneic transfusion, and, for the patient, the feeling that they are receiving a known and “safe” source of blood. However, patients who donate autologous blood (typically 2-4 wks preop) may become anemic prior to surgery⁹, and anemia is a risk factor for perioperative complications (although anemia due specifically to donating blood has not been studied). If autologous blood is donated earlier prior to surgery to allow repletion of red blood cells, then there may be problems with efficacy of stored blood. Finally, most studies examined transfusion rates but not other clinical outcomes. Therefore, there is enough question of the efficacy of predonating autologous blood that we do not recommend it routinely, but we ultimately leave the decision to donate autologous blood to the patient and the surgeon. This is most commonly seen at UWMC in joint replacement surgery.

Postoperative management:

- Note that management of intraoperative transfusion is generally left to the surgical and anesthesia teams.
- Postoperative anemia is a risk factor for mortality: Patients undergoing surgery who refused transfusion had an increase in 30 day mortality at hemoglobin <7 (about 10%) and further at Hgb <5 (about 30-35%).³
- Transfusion thresholds:
 - Several studies investigated transfusion in patients undergoing CABG. One randomized trial did not show any outcome differences in patients who received transfusions at a Hgb of <8 g/dL compared with <9 g/dL.² (Note these patients all started with Hgb >12).

Hematology

- Critically ill patients randomized to a restrictive transfusion strategy triggering transfusion at a Hgb <7 g/dL versus Hgb <10 g/dL had no significant difference in 30 day mortality.⁴ Only a subset of these patients were surgical patients—in the subset of trauma patients there was no difference in outcomes.⁵ The authors ultimately recommended a Hgb goal of 7-9.
- The FOCUS trial seeks to study the differences in transfusion thresholds in anemia patients with cardiovascular disease post hip surgery.⁶ (trial ongoing)

In summary, there remains no definitive evidence in non-CABG surgical patients as to optimum transfusion thresholds. In patients with cardiovascular disease, it may be reasonable to target higher hemoglobins, but there is a wide range between Hgb 7-9 (corresponding roughly to Hcts 21-27) that appears acceptable.

Additional factors to consider:

- Regardless of the absolute number, is the patient tolerating this degree of anemia?
 - Is there expected additional blood loss? If the patient has copious drain output or active bleeding, then it is reasonable to transfuse sooner, expecting the next Hgb to drop further.
- Risks of transfusion: In addition to typical “transfusion reactions” and the very low risk of viral hepatitis and HIV, there are additional risks to transfused blood, including acute lung injury and infection due to bacterial contamination. Furthermore, there has been growing discussion regarding immunomodulation from transfused blood which may predispose to bacterial infection. In some studies transfused blood has been associated with increased mortality and multi-organ failure, although it has been difficult to separate the effect of transfusion from increased comorbidity. Some studies have implicated worsening problems with increased age of stored blood.^{7,8}

Transfusion Reduction

- Concerns regarding safety of allogeneic transfused blood, and the existence of populations who refuse blood transfusions for religious reasons (e.g. Jehovah’s Witnesses), have increased attempts to reduce perioperative transfusion.
- Surgical techniques such as cell savers and readministering filtered blood captured from operative bleeding sites and postoperative drains are likely beneficial, but beyond the scope of the internist’s practice. We appropriately leave these decisions to the surgical and anesthesia teams.
- Protocols involving erythropoietin have evolved. There are significant risks of erythropoietin including venous thromboembolism, antibody-mediated anemia, and increased mortality in cancer patients with higher hemoglobins. It remains a potential option with that is probably best reserved for patients with religious refusal of transfusion who are having surgery with high degree of expected blood loss in which the risk of erythropoietin might outweigh the risk of severe anemia.

Indication: Transfusion reduction, baseline Hgb <13 Protocol: Erythropoietin 600 units/kg SC once a week at 21, 14, 7 days before surgery and on the day of surgery + FeSO ₄ 324 mg po bid with vitamin C 250 mg po bid. Monitoring: Check Hct at 14 days preop. Discontinue therapy if Hgb >13 achieved.
--

*Local resources: Swedish Hospital Blood Management program 206-320-2358.

References

1. Carson JL, Duff A, Poses RM, et al. Effect of anaemia and cardiovascular disease on surgical mortality and morbidity. *Lancet*. 1996;348:1055–1060.
2. 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;39:1070-1077.
3. Carson JL, Noveck H, Berlin JA, et al. Mortality and morbidity in patients with very low postoperative Hb levels who decline blood transfusion. *Transfusion*. 2002;42:812-818.

4. Hebert PC, Wells G, Blajchman MA, et al. A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care. *N Engl J Med.* 1999;340:409-417.
5. McIntyre L, Hebert PC, Wells G, et al. Is a restrictive transfusion strategy safe for resuscitated and critically ill trauma patients? *J Trauma.* 2004;57:563-568.
6. Carons JL, Terrin ML, Magaziner J, et al. Transfusion trigger trial for functional outcomes in cardiovascular patients undergoing surgical hip fracture repair (FOCUS). *Transfusion.* 2006;46:2192-2206.
7. Gunst MA, Minei JP. Transfusion of blood products and nosocomial infection in surgical patients. *Curr Opin Crit Care.* 2007;13:428-432.
8. Vamvakas EC, Blajchman MA. Transfusion-related immunomodulation (TRIM): an update. *Blood Reviews.* 2007;21:327-348.
9. Lee GC, Cushner FD. The effects of preoperative autologous donations on perioperative blood levels. *J Knee Surg.* 2007;20:205-209.

