

## **Preoperative anemia**

*Common, consequential and correctable in non-emergent surgery*

**By Kathrine Frey, MD**

Preoperative anemia is common, especially in patients undergoing non-emergent high-blood-loss surgical procedures such as joint replacement and cardiovascular (CV) surgeries, where loss of three or more grams of hemoglobin is not uncommon. Certain patients undergoing low-blood-loss surgeries, such as for endometrial abnormalities or colon cancer, often have severe anemia prior to the procedure due to disease-associated chronic bleeding. Anemia rates in pre-surgical patients range from 5 percent to 75 percent, depending on the procedure. Preoperative anemia is the strongest predictor of transfusion.

A recent study of nearly 230,000 patients undergoing non-CV surgery found that even mild preoperative anemia is associated with increased morbidity and mortality, irrespective of transfusion (Musallam K. et al., *Lancet*, 2011). Studies with similar findings have been done in CV surgery patients. (Karkouti K. et al, *Circulation*, 2008)

Many studies in general surgery and CV surgery have found that transfusion is associated with increased complications in a dose-dependent manner. These adverse effects include pulmonary complications, infections, and increased length of hospital stay, among others. (Vamvakis E.C. et al., *Blood*, 2009)

From an infectious disease transmission standpoint, allogeneic blood is safer than ever. However, non-infectious risks remain, including volume overload, which is under-reported and currently estimated to occur in as many as 1 in 100 transfusions. In addition, up to 40 percent of transfusions administered currently may not meet medical indications, as described in a large meta-analysis by members of the International Consensus Conference on Transfusion Outcomes in

2011. To many transfusion and patient safety experts, transfusion is now considered an “undesirable event.”

Risk factors for transfusion include female gender, age greater than 65 years, body weight less than 70 kg, creatinine greater than 1.2, multisite surgery, revision procedure, time to surgery of fewer than two weeks, and anemia. Unlike the other risk factors, anemia is generally correctable prior to surgery if it is identified with intent to treat and in a timely manner.

Prevalence of preoperative anemia varies by surgical procedure, with rates of approximately 30 percent in joint replacement patients and in patients having coronary artery bypass grafting, and in 65 percent of patients undergoing valve replacement. Anemia is more common in the elderly and in patients with comorbid conditions. Iron deficiency, the most common type of anemia, is identified in 30 percent of anemic patients, followed by anemia of chronic disease (25 percent) and renal disease-associated anemia (15 percent to 20 percent). Medications can play a role in partially effective hematopoiesis, including iron deficiency due to antacid use and decreased erythropoietin in patients taking beta blockers and other cardiac medications. Multifactorial anemia is very common.

### **Diagnosing preoperative anemia**

For patients undergoing high-blood-loss surgeries, laboratory testing for “blood health” should include more than a solitary hemoglobin value; this may not be necessary for low-blood-loss surgeries unless the risk of preoperative anemia is very high (e.g., for some GI and GYN surgeries). Iron depletion and iron deficiency precede anemia and, when present, impede the red cell regenerative response in the face of blood loss.

For example, an initial laboratory evaluation panel for applicable non-emergent preoperative patients would include complete blood count; reticulocyte count;

creatinine with GFR; and iron studies, including serum iron, percent saturation, iron binding capacity, and ferritin. Follow-on laboratory tests for patients with anemia or other hematologic abnormalities identified may include, but are not limited to, C-reactive protein, red cell folate, serum vitamin B12, soluble transferrin receptor, LDH, haptoglobin, direct antiglobulin test, leukocyte differential, and, sometimes, blood morphology. (Goodenough LT et al., *Anesth Analg*, 2005).

In addition to laboratory testing and knowing the patient's medications, it is helpful to know the patient's medical history, to correlate any blood health abnormalities with the known clinical situation. Consider the example of a diabetic female with chronic mild anemia and hemoglobin of 11.0 with low percent saturation, elevated ferritin, and elevated C-reactive protein inflammatory, whoshows findings of anemia of inflammation. This clinical picture makes sense. In comparison, a middle-aged male with hemoglobin of 11.0 with iron deficiency as a new finding raises suspicion for gastrointestinal or other bleeding; the cause of these findings should be determined prior to elective surgery, and the surgery postponed.

### **Transfusion for perioperative anemia**

Blood transfusion prior to surgery is not a solution for preoperative anemia, and post operative red cell transfusion is not advised in the absence of critical bleeding or symptoms of ischemia (increased heart rate not responsive to volume replacement or decreased oxygen saturation not responsive to oxygen therapy). There is ample medical evidence showing that a restrictive approach to transfusion ("permissive anemia"), such as holding transfusion until hemoglobin of 7.0 g/dL in non-critically bleeding, asymptomatic patients, is safer than

transfusion unless the patient has active heart disease (Hebert Paul C. et al., NEJM, 1999).

Pre- and postoperative anemia treatment strategies use the same therapeutic agents, namely, intravenous iron preparations and, sometimes, an erythrocyte stimulating agent (ESA). Oral iron is generally ineffective in treating anemia preoperatively unless there is a timeframe of several weeks to months to surgery, also noting that there is poor patient compliance with taking iron orally.

Approximately 30 percent of patients will be intolerant to oral iron, and the response (or not) to the iron will likely be determined on the day of surgery. However, oral iron is a good option in patients found to be iron deplete or deficient but without anemia.

Intravenous iron preparations are much safer now than they were years ago when anaphylactic reactions were a concern. Iron sucrose is commonly used in the perioperative setting. Unlike older IV preparations, iron sucrose and most other forms of IV iron cannot be given as a single dose, and divided doses totaling 1 g of iron are not uncommon. A rule of thumb is that 250 mg iron is needed to increase the Hgb by 1 gm,, with addition of another 500 mg for iron-deficient patients to restore iron stores. Effect on hemoglobin level usually occurs starting at one week, with maximal effect achieved at two weeks. Hypotension, arthralgia, abdominal discomfort, and back pain are potential side effects of IV iron.

In general, IV iron, especially the newer forms, is a safer alternative to blood transfusion. Death occurs at a much lower rate with iron than with blood transfusions (0.4/ million vs. 4/million, respectively); this is also true for life-threatening adverse events (4/million vs. 10/million, respectively), according a systematic review by the Network for Advancement of Transfusion Alternatives.

ESAs are FDA approved to treat anemia in several patient populations, but only epoetin alpha is approved by the FDA explicitly for use in patients undergoing major surgery with high anticipated blood loss. This agent is on label for joint replacement patients but currently is not used prior to cardiac surgery. Patients treated with ESAs must not be iron deficient prior to treatment, as the erythropoiesis-stimulating response requires the presence of iron for completion, and giving erythropoietin in the absence of iron will not produce red cells (some describe this as akin to stepping on the accelerator without any gas in the tank). Iron may be administered either orally or intravenously. It is important to note that ESAs are prothrombotic, so pharmacologic DVT prophylaxis should be considered.

### **Preoperative anemia evaluation: earlier is better**

Several surgical societies, including the Society of Cardiovascular Anesthesiologists and the Society of Thoracic Surgeons, as well as the Joint Commission, have weighed in in support of anemia evaluation 15–45 days prior to surgery. The Society of Thoracic Surgeons recommends preoperative hemoglobin of 13 g/dL for males and females prior to surgery. Some CV surgery programs now cancel cases the day of surgery if the patient is found to be anemic.

Formal preoperative evaluation for anemia 30 days prior to elective surgery is not currently a common practice. Patients often visit their primary care physician in the two weeks prior to surgery; if anemia is identified, the physician can be in an uncomfortable position in regard to delaying surgery. Many physicians are not aware of substantial hemoglobin loss in procedures like joint replacement, which averages four grams for knee and hip replacement. Similarly, they are not aware of transfusion variability for surgeons and other physicians, a phenomenon that is widely described in the medical literature. For example, a

recent large study of transfusion in primary hip surgery at the University of Pittsburgh Medical Center showed that one surgeon who performed 350 cases transfused 5 percent of patients, while another surgeon who also performed 350 cases transfused 95 percent of patients. This underscores the importance of evaluation for and correction of anemia preoperatively.

Assuring that patients presenting for surgery have maximized red cell mass and the ability to produce red cells after large amounts of blood are lost serves the patient, the hospital, and the community well, in a number of ways:

- Patients avoid complications associated with preoperative anemia as well as transfusion.
- Donor blood is used appropriately, assuring its availability for others in need.
- Hospitals don't use resources providing adverse event care and transfusion procedures that are avoidable.

Pre-surgical anemia is common, clinically significant – and treatable. Physicians who see patients preoperatively can improve care and outcomes by recognizing patients at risk for anemia and treating them in a timely manner.

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Pearls:

- Even mild preoperative anemia is associated with increased morbidity and mortality, irrespective of transfusion.

- There is a need for a preoperative “blood health” check for non-emergent patients having high-blood-loss procedures well in advance of surgery (three or more weeks).
- The blood health check should ensure that patient has maximized red cell mass and the ability to make red cells after blood is lost.
- In general, IV iron, especially the newer forms, is a safer alternative to blood transfusion.