

Iron Deficiency Anemia in the Surgical Patient

Summary

- Anemia is prevalent in the preoperative setting and should be treated.
 - Perioperative anemia is associated with increased morbidity and mortality.
 - Diagnosis and treatment of anemia and iron deficiency should commence early to improve patient readiness for surgery.
 - Iron therapy choice should be based on patient's iron status, tolerance of oral iron and timescale before surgery.
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Introduction

Some of the questions to consider when contemplating the role of iron for anemia in surgical patients are as follows: Is anemia common in surgical patients? Is it morbid? If so, can the morbidity be decreased with intervention? What role should iron play in the intervention? The short answer is that anemia is both common and morbid in surgical patients and that there is a role for iron therapy in many of these patients. There are a number of non-evidence-based misconceptions regarding prevalence, consequences, diagnosis and treatment of iron deficiency in the perioperative patient addressed below.

Is anemia common in surgical patients?

Anemia is prevalent in the preoperative setting with rates ranging from 11% to 76% according to one systematic review.¹ Many of the studies related to the evaluation and management of perioperative anemia are in patients undergoing major orthopedic surgery where one analysis found that 35% of patients had hemoglobin levels less than 13 g/dl at preadmission testing.² Of course, the prevalence varies depending on the surgical population, with the prevalence approaching 75% in patients undergoing surgery for colon cancer.

Is anemia morbid in surgical patients?

Both preoperative and postoperative anemia is associated with increased morbidity and mortality.³⁻⁵ Adverse outcomes become more common as the degree of anemia increases. Patients with cardiovascular disease have worse outcomes with similar degrees of anemia relative to patients without cardiovascular disease. However, randomized

clinical trials comparing restrictive versus liberal transfusion strategies have favored a restrictive approach even in the presence of cardiovascular disease.⁶⁻⁷

Is there a role for iron as an intervention in perioperative anemia?

Preoperative assessment and management of anemia including the use of oral or intravenous iron has been shown to improve postoperative hemoglobin and decrease exposure to allogeneic blood.⁸

An international consensus statement was published in 2017 on the perioperative management of anemia and iron deficiency.⁹ This statement provides formal guidance on the diagnosis and management of preoperative anemia. Their formal recommendations for best clinical practice are as follows:

1. Physicians should consider preoperative anemia and iron deficiency as an indication for a perioperative care pathway that stretches from the decision to operate until complete recovery from surgery.
2. The presence of anemia should be investigated in all surgical procedures with expected moderate-to-high blood loss (> 500 ml).
3. Serum ferritin level < 30 ng/ml is the most sensitive and specific test used for the identification of absolute iron deficiency. However, in the presence of inflammation (C-reactive protein > 5 mg/L and/or transferrin

saturation < 20%, a serum ferritin level < 100 ng/ml is indicative of iron deficiency.

4. Major, non-urgent surgery should be postponed to allow the diagnosis and treatment of anemia and iron deficiency.
5. When treating anemia preoperatively, the target hemoglobin concentration should be ≥ 13 g/dL in both sexes, to minimize the risk of transfusion associated unfavorable outcomes.
6. Oral iron replacement should be targeted to patients with iron deficiency with or without anemia whose surgery is scheduled 6–8 weeks after diagnosis, preferably by the primary care physician (General Practitioner).
7. Daily (40–60 mg) or alternate-day (80–100 mg) treatment with oral iron and nutritional advice should be initiated immediately in patients with iron deficiency and no contra-indications.
8. Sufficient data exist to support intravenous iron as efficacious and safe. Intravenous iron should be used as front-line therapy in patients who do not respond to oral iron or are not able to tolerate it, **or if surgery is planned for < 6 weeks after the diagnosis of iron deficiency.**
9. The diagnosis and treatment of anemia and iron deficiency should commence as early as possible in the peri-operative period, and ideally as soon as the decision to undertake surgery is made.

The preponderance of published evidence indicates that intravenous iron is safe, supporting a greater and earlier role in treating iron deficiency and **raising the question of whether parenteral iron should be considered front-line therapy in situations where oral iron will predictably fail** (e.g. when there is an inflammatory co-morbidity.) Time to surgery is rarely greater than 4-6 weeks in the United States, also suggesting a greater role for intravenous iron.

It is worth noting that we know even less about the optimal approach in patients with post operative

anemia who were not anemic preoperatively. Anemia is common after major surgery. Multiple small studies have failed to show a benefit with postoperative oral iron supplementation.¹¹⁻¹⁵ However, this shouldn't be surprising as we know that oral iron absorption may be compromised by inflammation in the postoperative setting.^{16,17} It stands to reason that there is a role for parenteral iron in certain postoperative populations. A small study looking at IV iron with or without recombinant erythropoietin in postoperative anemia without preoperative anemia did show an increase in erythropoiesis at post operative day 7 although no change in hemoglobin.¹⁶

In a recent review of intravenous iron for treatment of anemia in the 3 perisurgical phases, Peters *et al* note that anemia at discharge was associated with a severity-dependent, increased risk for 30-day readmission.¹⁸ Postoperative anemia was found to be common: the PREPARE study included in the review revealed a prevalence of 83.3% in 1534 orthopedic patients who were preoperatively non-anemic.

A small number of studies in patients undergoing a variety of different surgical procedures have shown an increase in erythropoiesis and hemoglobin and, in some studies, a reduction in transfusion. Altogether the number of trials is still low and further research is needed to give a distinct recommendation for postoperative intravenous iron treatment.¹⁸ However, the risks of intravenous iron appear low while the incidence of persistent anemia and iron deficiency is high. Further, the risks of anemia and iron deficiency are well described, arguing for postoperative intervention and follow-up after discharge to ensure postoperative anemia does not persist.

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