

## Detection, evaluation, and management of anemia in elective surgery\*

L. T. Goodnough



### Interdisziplinäre Hämotherapie

Previously undiagnosed anemia is identified in 5 % to 75 % of elective surgical patients [1], depending on the associated comorbidity. In a national audit of elective orthopedic surgery [2], 35 % of patients were found to have hemoglobin <13 g/dL at preadmission testing. Other studies have indicated that the large majority of such patients are women and that approximately one third of these are the result of iron deficiency [3]. The remainder of anemias, although poorly characterized, is usually attributed to anemia of chronic disease.

Preoperative anemia has been associated with increased morbidity after surgery [4], most commonly related to blood transfusion therapy [2], including increased rates of postoperative infection [5-7] and mortality [8]. Gruson et al. [4] assessed the relationship between admission hemoglobin levels and long-term postoperative morbidity, mortality, and functional recovery in an elderly population with hip fractures. This study found that patients at risk for poor outcomes could be identified by measuring hemoglobin levels at hospital admission. Dunne et al. [9] found a frequent incidence of preoperative anemia in surgical patients and that blood transfusion in the first 24 h after trauma was associated with increased

risk for systemic inflammatory response syndrome, intensive care admission, and death. Halm et al. [10] recommended the diagnosis and correction of nutritional anemia with iron, vitamin B<sub>12</sub>, folate supplementation, or administration of recombinant human erythropoietin (rHuEPO). Shorter length of stay and decreased odds of death were associated with higher preoperative hemoglobin levels. Because preoperative anemia is associated with perioperative risks of blood transfusion, as well as increased perioperative morbidity and mortality, a standardized approach for the detection, evaluation, and management of anemia in this setting was identified as an unmet medical need.

A panel of multidisciplinary physicians was convened by the Society for Blood Management ([www.sabm.org](http://www.sabm.org)) to develop a clinical care pathway for anemia management in the elective surgical patient for whom blood transfusion is a probability (defined as any procedure for which a preoperative blood type and crossmatch is requested) [11]. The panel evaluated the current best practices with regard to screening for preoperative anemia, anemia evaluation, and anemia therapy. The goal of this forum was to develop a clinical care pathway for the detection, evaluation, and management of anemia in the elective surgery patient.

**SABM Recommendation 1:** Whenever clinically feasible, elective surgical patients should have a hemoglobin level tested a minimum of 30 days before the scheduled surgical procedure.

The Circular of Information [12] for blood and blood products has recommended that iron, vitamin B<sub>12</sub>, folic acid, and erythropoietin be used “instead of blood transfusion” if the clinical condition of the patient permits sufficient time for these agents to promote erythropoiesis, with the key phrase relevant to this recommendation being “sufficient time...to promote erythropoiesis.”

Based on the time interval required for anemia evaluation and management, the panel considered a 30-day interval to be optimal in the elective surgical patient. The panel further recommended that the patient's target hemoglobin before elective surgery should be within the normal range (normal female  $\geq 12$  g/dL, normal male  $\geq 13$  g/dL).

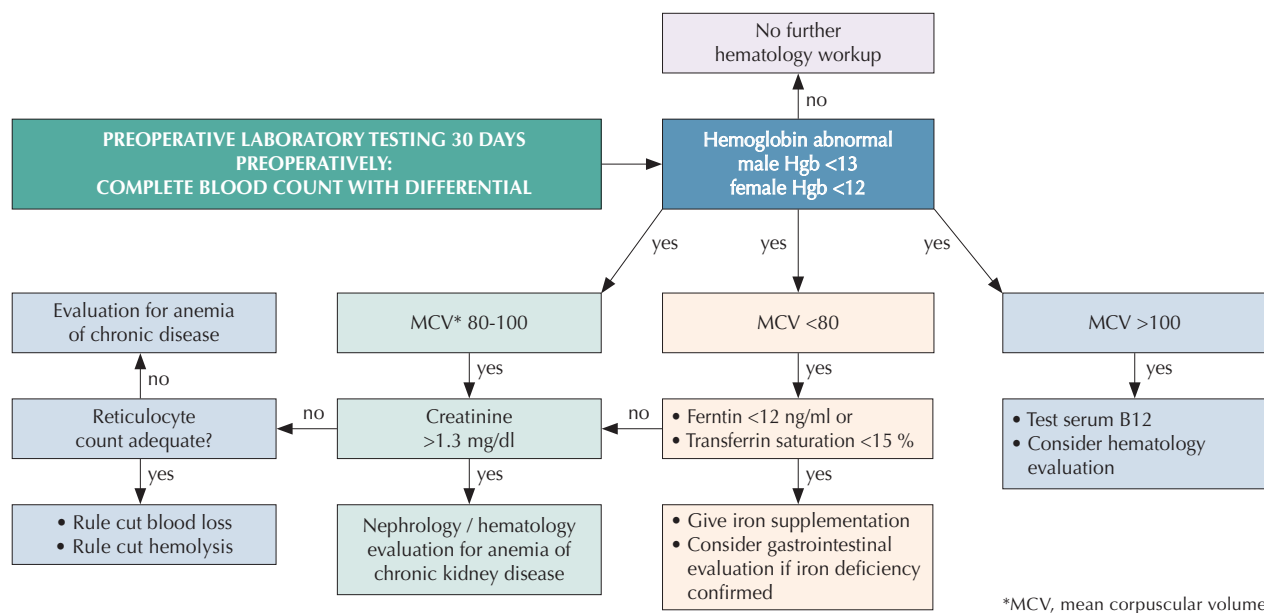
**SABM Recommendation 2:** Unexplained anemia should always be considered as secondary to some other process and, therefore, elective surgery should be deferred until an appropriate diagnosis is made.

To serve the patient's best interests, efforts should be made to identify the underlying etiologic factor or factors causing anemia and correct or manage the condition appropriately. Clinical and functional outcomes improve with the recognition of anemia as a symptom of an underlying condition. To facilitate this, the panel recommended that an effort be made to identify the underlying disorder causing the anemia and to correct or manage the disorder.

A clinical care pathway (Figure 1) was developed to provide guidance for

\* Dieser Artikel wurde in ähnlicher Form mit dem Titel „Management of preoperative anaemia in patients undergoing elective surgery“ bereits publiziert: ISBT Science Series (2010) 5, 120–124.

Figure 1



Clinical care pathway for identification and evaluation of anemia in elective surgical patients [16] - Mit freundlicher Genehmigung aus Anesth Analg. 2005 Dec;101(6):1858-61.

preoperative evaluation in the elective surgical patient anticipated to have significant blood loss. Currently, limiting preadmission testing to within several days before the scheduled operative procedure precludes the opportunity to evaluate and manage the patient with unexplained anemia. The recommended timeframe of laboratory testing 30 days before the scheduled elective procedure ensures that anemia can be detected, evaluated, and managed appropriately before elective surgery.

The diagnosis of an unexplained anemia in patients scheduled for elective surgery in which significant blood loss is anticipated should be considered an indication for rescheduling surgery until the clinical care pathway is completed. Anemia should be viewed as a significant clinical condition, rather than simply an abnormal laboratory value [14]. Morbidity and mortality after surgery is significantly associated with the presence of preoperative anemia [15], thus warranting this recommendation. Use of

the SABM clinical care pathway for anemia management in the elective surgical patient will improve patient outcomes through the identification, evaluation and management of unexpected anemia in this clinical setting [16].

More recently, the Network for the Advancement of Transfusion Alternatives (NATA) has focused on the development of practice guidelines in patients undergoing elective orthopaedic surgery. This has been particularly timely given the recent publication of two large, retrospective studies that have identified preoperative anemia as predictors of postoperative morbidity and mortality for elective surgical patients [17,18].

In a large retrospective analysis of 300,000 elderly patients undergoing noncardiac surgery, a preoperative hematocrit of 39 % or less was associated with a statistically significant increase in 30-day postoperative mortality [17]. This finding was confirmed by a subsequent retrospective study of 8,000 patients undergoing non-cardiac surgery, in which

40 % of patients had preoperative anemia, which was associated with a five-fold increase in 90-day postoperative mortality [18].

A multidisciplinary panel of physicians with expertise in orthopedic surgery, orthopedic anesthesia, hematology and epidemiology was convened by NATA with the aim of developing practice guidelines for the detection, evaluation and management of preoperative anemia in elective orthopedic surgery. The Medline database was searched using the MeSH keywords "anemia," "orthopedics," and "blood transfusion," and the abstracts of the retrieved references were reviewed to identify the relevant studies. A critical evaluation of the evidence was then performed and recommendations were formulated according to the method proposed by the Grades of Recommendation Assessment, Development and Evaluation (GRADE) Working Group, (19) using the modified grading system adopted by the American College of Chest Physicians [20].

## Detection of anemia

### NATA Recommendation 1:

**Elective surgical patients should have an Hb level determination as close to 28 days before the scheduled surgical procedure as possible.**

The Circular of Information for Blood and Blood Products [21] has recommended that iron, vitamin B<sub>12</sub>, folic acid, and erythropoietin be used instead of blood transfusion, "if the clinical condition of the patient permits sufficient time for those agents to promote erythropoiesis..." The key phrase relevant to this recommendation is, "sufficient time... to promote erythropoiesis." Detection of anemia as close to 28 days before surgery is recommended for sufficient time for evaluation and management.

### NATA Recommendation 2:

**The patient's target Hb before elective surgery should be within the normal range (normal female  $\geq 12$  g/dL, normal male  $\geq 13$  g/dL), according to WHO criteria.**

This recommendation is a suggestion, indicating a lack of consensus on whether elective surgical procedures should be cancelled, representing best practices, for patients who are identified to be anemic.

## Evaluation of anemia

### NATA Recommendation 3:

**Laboratory testing should be performed to further evaluate anemia for nutritional deficiencies, chronic renal insufficiency, and/or chronic inflammatory disease.**

Unexplained anemia should be considered as secondary to some other process, [22,23] and the cause of the anemia must be evaluated.

Once the screening blood count demonstrates anemia, evaluation begins with an assessment of iron status. When ferritin and/or iron saturation levels indicate absolute iron deficiency, referral to a gastroenterologist to rule out a

gastrointestinal malignancy as a source of chronic blood loss may be indicated.

When ferritin and/or iron saturation values rule out absolute iron deficiency, serum creatinine and glomerular filtration rate (GFR) determination may indicate chronic kidney disease (CKD) and the need for referral to a nephrologist.

When ferritin and/or iron saturation values are in determinant, further evaluation to rule out absolute iron deficiency versus inflammation/chronic disease is necessary. A therapeutic trial of iron would confirm absolute iron deficiency. No response to iron therapy would indicate the anemia of chronic disease, suggesting that ESA therapy be initiated.

## Management of anemia

### NATA Recommendation 4:

**Nutritional deficiencies should be treated.**

Iron supplementation is indicated in the presence of confirmed iron-deficiency anemia, as documented by the following laboratory values: transferrin saturation and/or serum ferritin  $< 30$  ng/mL [24,25]. Gastrointestinal evaluation for potential malignancy is recommended for any patient except possibly menstruating women.

A NATA expert panel recently reviewed the role of intravenous iron in the management of preoperative anemia and suggested that perioperative intravenous iron should be administered perioperatively in patients undergoing orthopedic surgery [26].

### NATA Recommendation 5:

**Erythropoiesis-stimulating agents (ESA) should be used for anemic patients in whom nutritional deficiencies have been ruled out and/or corrected.**

The use of ESA therapy in patients undergoing major, elective surgery is well-established on the basis of controlled, randomized trials and is approved for use in this setting.

However, recent concerns regarding the relative risk/benefit of these agents and

their appropriate use in patients with chronic kidney disease, [28] in patients with anemia related to cancer or chemotherapy, [27] and in patients undergoing elective surgery, [29] have resulted in a 'suggested' recommendation.

Patients should receive iron supplementation throughout any course of ESA therapy, in order to optimize the dose and response relationship for ESA therapy and red blood cell production in the presurgical setting [30].

## Conclusion

These recommendations are intended to provide guidance for preoperative evaluation in the elective surgical patient. Limiting preadmission testing to within several days before the scheduled operative procedure precludes the opportunity to evaluate and manage the patient with unexplained anemia. The recommended time frame of testing 4 weeks before the scheduled elective procedure ensures that anemia can be detected, evaluated, and managed appropriately before elective surgery.

Anemia should be viewed as a serious and treatable medical condition, rather than as simply an abnormal laboratory value. Anemia is a common condition in surgical patients and is independently associated with increased mortality. The diagnosis of an unexpected anemia in patients scheduled for elective surgery in which significant blood loss is anticipated should be considered an indication for rescheduling surgery until the evaluation is completed. The presence of preoperative anemia is significantly associated with morbidity and mortality after surgery, thus warranting this recommendation. Treatment of postoperative anemia should be the focus of investigations for the reduction of perioperative risk. Implementation of anemia management in the elective surgery setting will improve patient outcomes.

## References

1. Bierbaum BE, Callaghan JJ, Galante JO, et al. An analysis of blood management in patients having a total hip or knee arthroplasty. *J Bone Joint Surg Am* 1999;81:2-10.
2. Wilson A, Yu HT, Goodnough LT, Nissenson AR. Prevalence and outcomes of anemia in rheumatoid arthritis: a systematic review of the literature. *Am J Med* 2004;116:50S-7.
3. Goodnough LT, Vizmeg K, Sobecks R, et al. Prevalence and classification of anemia in elective orthopedic surgery patients: implications for blood conservation programs. *Vox Sang* 1992;63:90-5.
4. Gruson KI, Aharonoff GB, Egol KA, et al. The relationship between admission hemoglobin level and outcome after hip fracture. *J Orthop Trauma* 2002;16:39-44.
5. Edna TH, Bjerkeset T. Association between blood transfusion and infection in injured patients. *J Trauma* 1992;33:659-61.
6. Shander A. Anemia in the critically ill. *Crit Care Clin* 2004;20:159-78.
7. Triulzi DJ, Vanek K, Ryan DH, Blumberg N. A clinical and immunologic study of blood transfusion and postoperative bacterial infection in spinal surgery. *Transfusion* 1992;32:517-24.
8. Engoren MC, Habib RH, Zacharias A, et al. Effect of blood transfusion on long-term survival after cardiac operation. *Ann Thorac Surg* 2002;74:1180-6.
9. Dunne JR, Malone D, Tracy JK, et al. Perioperative anemia: an independent risk factor for infection, mortality, and resource utilization in surgery. *J Surg Res* 2002;102:237-44.
10. Halm EA, Wang JJ, Boockvar K, et al. The effect of perioperative anemia on clinical and functional outcomes in patients with hip fracture. *J Orthop Trauma* 2004;18:369-74.
11. Goodnough LT, Brecher ME, Kanter MH, AuBuchon JP. Transfusion medicine. Second of two parts—blood conservation. *N Engl J Med* 1999;18;340:525-33.
12. US Food and Drug Administration. Circular of information Web site. Available at: <http://www.fda.gov/laneproxy.stanford.edu/cber/gdlns/crcrlr.pdf>. Accessed November 3, 2004.
13. Weiss G, Goodnough LT. Anemia of chronic disease. *N Engl J Med* 2005;352:43-55.
14. Goodnough LT, Dubois RW, Nissenson AR. Anemia: not just an innocent bystander? *Arch Int Med* 2003;163:1400-2; correction appears in *Arch Int Med* 2003;163:1820.
15. Carson J, Duffa, Poses RM et al. Effect of anaemia and cardiovascular disease on surgical mortality and morbidity. *Lancet* 1996;348:1055-60.
16. Goodnough LT, Shander A, Spivak JL, Waters JH, Friedman AJ, Carson JL, Keating EM, Maddox T, Spence R. Detection, evaluation, and management of anemia in the elective surgical patient. *Anesth Analg*. 2005 Dec;101(6):1858-61.
17. Wu WC, Schiffner TL, Henderson WG, et al. Preoperative hematocrit levels and postoperative outcomes in older patients undergoing noncardiac surgery. *JAMA* 2007;297: 2481-8.
18. Beattie WS, Karkouti K, Wijeyesundera DN, Tait G. Risk associated with preoperative anemia in noncardiac surgery: a single-center cohort study. *Anesthesiology* 2009;110:574-81.
19. Atkins D, Best D, Briss PA, et al. Grading quality of evidence and strength of recommendations. *BMJ* 2004;328:1490.
20. Guyatt GH, Cook DJ, Jaeschke R, et al. Grades of recommendation for anti-thrombotic agents: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). *Chest* 2008;133:123S-31S.
21. Circular of information for the use of human blood and blood components. Bethesda, MD: American Association of Blood Banks, 2000.
22. Guralnik JM, Eisenstaedt RS, Ferrucci L, et al. Prevalence of anemia in persons 65 years and older in the United States: evidence for a high rate of unexplained anemia. *Blood* 2004;104:2263-8.
23. Weiss G, Goodnough LT. Anemia of chronic disease. *N Engl J Med* 2005; 352:1011-23.
24. Adamson JW. Iron deficiency and other hypoproliferative anemias. In: Braunwald, Fauci, Kasper, et al., eds. *Harrison's Principles of Internal Medicine*. New York: McGraw-Hill;2001:660-6.
25. Mast AE, Blinder MA, Gronowski AM, et al. Clinical utility of the soluble transferrin receptor and comparison with serum ferritin in several populations. *Clin Chem* 1998;44:45-51.
26. Beris P, Munoz M, Garcia-Erce JA, et al. Perioperative anaemia management: consensus statement on the role of intravenous iron. *Br J Anaesth* 2008;100: 599-604.
27. KDOQI Clinical Practice Guideline and Clinical Practice Recommendations for anemia in chronic kidney disease: 2007 update of hemoglobin target. *Am J Kidney Dis* 2007;50:471-530.
28. Rizzo JD, Somerfield MR, Hagerty KL, et al. Use of epoetin and darbepoetin in patients with cancer: 2007 American Society of Hematology/American Society of Clinical Oncology clinical practice guideline update. *Blood* 2008;111:25-41.
29. FDA. Erythropoiesis-stimulating agents. March 9, 2007 [monograph on the internet]. Available from: [www.fda.gov/AboutFDA/CentersOffices/CDER/ucm129253.htm](http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm129253.htm)
30. Goodnough LT. The new iron age: Evaluation and management of iron-restricted erythropoiesis. *Sem Hematol* 2009; In Press.

Korrespondenz-  
adresse

**Professor of Pathology & Medicine  
Lawrence Tim  
Goodnough, MD**



Department of Pathology Stanford  
University Medical Center 300  
Pasteur Dr., Room H-1402, 5626  
Stanford, CA 94305, USA  
Tel.: 001 650-723-5848  
Fax: 001 650-723-9178