Anemia in critical care patients: Incidence, etiology, impact, management, and use of treatment guidelines and protocols

RONALD J. DEBELLIS

Purpose. The incidence, etiology, impact, and management of anemia in critical care patients and the development of treatment guidelines and protocols for the management of anemia in this patient population are discussed.

Summary. Most patients in intensive care units develop anemia as a result of blood losses, nutritional deficiencies, hemolysis, myelosuppression, renal insufficiency, inflammation, infection, or another disease process. Anemia can have an adverse impact on critically ill patients with severe ischemic heart disease or cerebrovascular disease and patients undergoing surgery. The use of blood conservation measures and restrictive blood transfusion strategies can circumvent problems associated with transfusion. Epoetin alfa increases hemoglobin concentrations and reduces the need for transfusion in critical care patients, including surgical patients with large anticipated blood losses. Epoetin alfa also appears to be effective for managing anemia in patients with multiple organ dysfunction syndrome. Iron supplementation is needed by most patients receiving erythropoietic therapy. Iron supplementation without erythropoietic therapy is inadequate to correct anemia unrelated to iron deficiency. Concerns have been raised about a possible increased risk for infection when parenteral iron therapy is used in critical care patients. Developing treatment guidelines or protocols for managing anemia in critical care patients can minimize the need for transfusions and improve prescribing of erythropoietic therapy.

Conclusion. Epoetin alfa can play an important role in managing anemia in critical care patients, thereby minimizing patient exposure to transfusion-related risks and optimizing the use of the limited blood supply. There is currently no data available for use of darbepoetin in this manner.

Index terms: Anemia; Blood; Combined therapy; Critical illness; Epoetin alfa; Erythropoietic agents; Infections; Iron preparations; Protocols; Toxicity

Anemia is a common problem in critically ill patients.1-3 Nearly 95% of patients in intensive care units (ICUs) develop anemia within 3 days after admission.2

The hemoglobin concentration or hematocrit used to define anemia and classify its severity in critical care patients is unclear. Published anemia severity classification schemes (see the supplement introduction) are not specific for the critical care patient population. Moreover, critical care patients are a heterogeneous group with various underlying diseases and conditions.

Etiology

Anemia in critical care patients may be the result of a variety of causes (Table 1), including blood losses from phlebotomy, trauma, or surgery and ongoing seepage from wounds or indwelling tubes used to drain fluids after surgery.1,4-6 The magnitude of blood losses due to phlebotomy in the ICU setting can be substantial. In 50 hospitalized patients who spent part or all of their stay in an ICU, the mean volume of blood drawn daily was 42 mL and the total volume drawn over the course of the hospitalization was 762 mL.7 The total volume drawn was higher in ICU patients with arterial lines (944 mL) than in ICU patients without such lines (301 mL).
patients developed bleeding after admission to the ICU. The gastrointestinal (GI) tract was the most common site of bleeding. The likelihood of death was significantly higher in patients with bleeding than in those who did not bleed. Risk factors for bleeding included the use of anti-ulcer medication or antiocoagulants, acute renal failure, malnutrition, and the use of mechanical ventilation.

Anemia in critical care patients may be the result of diminished erythropoiesis (red blood cell formation) in the bone marrow due to exposure to certain drugs or toxins, nutritional deficiencies of substrates required for erythropoiesis (e.g., iron, folate, vitamin B₁₂), or tumor infiltration or fibrosis of the bone marrow (see the preceding article by Schwartz in this supplement). Multiple drugs used in the ICU may cause decreased bone activity (e.g., corticosteroids, antibiotics, select antifungals, histamine H₂ blockers, and others). Vitamin B₁₂ deficiency is common in elderly patients with chronic alcoholism. Iron deficiency is not a common cause of anemia in such patients, especially if they receive blood transfusions because iron is supplied by transfusions. Up to 200 mg of elemental iron may be supplied by a blood transfusion.

Anemia in critical care patients may be attributed to a relative or absolute deficiency of erythropoietin, the renal hormone that stimulates erythropoiesis in the bone marrow. Possible causes of this deficiency include renal insufficiency or failure and infectious and inflammatory processes that result in a blunted erythropoietic response to low hemoglobin concentrations and hypoxia (i.e., failure of hypoxia to stimulate the production of erythropoietin by the kidneys).

Serum erythropoietin concentrations and hematocrit values were compared in 36 critically-ill patients without hypoxia, including 22 patients with sepsis, who stayed in an ICU for more than 7 days and 18 ambulatory patients with iron-deficiency anemia who served as a control group. A significant inverse correlation between serum erythropoietin concentration and hematocrit (i.e., high erythropoietin levels at low hematocrit values and low erythropoietin levels at high hematocrit values) was found in the control patients, but not in the critically-ill patients, except in a subgroup of 10 patients without sepsis or acute renal failure. In the control group, the mean hematocrit was 30% and the mean serum erythropoietin concentration was 845 IU/L. The hematocrit was similar in critically ill patients with or without sepsis (29% and 30%, respectively), but the mean serum erythropoietin concentration was substantially lower (124 IU/L and 199 IU/L, respectively). These findings reflect a blunted erythropoietin response to low hematocrit values.

Inflammatory cytokines associated with inflammation and infection (e.g., interleukin-1, interferon, tumor necrosis factor-α, transforming growth factor-β) inhibit erythropoietin gene transcription in renal juxtaglomerular cells (i.e., erythropoietin production in the kidneys) and the response to erythropoietin in the bone marrow (i.e., the proliferation of erythroid progenitors). The cytokines also increase iron sequestration in macrophages and suppress iron release from storage sites.

In clinical practice, serum erythropoietin concentrations typically are not measured in critically ill patients, but iron study results provide valuable clues about the etiology of anemia. Serum ferritin, a measure of total body iron stores, is elevated by inflammation. The anemia in critical care patients often resembles what is referred to as the anemia of chronic disease, which is characterized by a low serum iron concentration and total iron binding capacity (TIBC) and a normal or elevated serum ferritin concentration. By contrast, iron

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### Table 1. Etiology of Anemia in Critical Care Patients

| Blood losses | Phlebotomy | Trauma | Surgery | Stress-related GI bleeding
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**Hemolysis**

- Certain drugs
- Certain toxins
- Certain diseases

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*GI = gastrointestinal.*
deficiency anemia is characterized by a low serum iron concentration, high TIBC, and low serum ferritin concentration. TIBC is a measure of how much iron is available to bind to transferrin, a protein that transports iron in the blood.

Hemolysis can cause or contribute to anemia in critical care patients. It may be caused by various drugs (e.g., certain antibiotics), toxins, and diseases. Disease-related hemolysis may be caused by an autoimmune process, metabolic defect (e.g., glucose-6-phosphate dehydrogenase deficiency), erythrocyte membrane abnormality, or microangiopathy (i.e., mechanical disruption of erythrocytes in the circulation).

Endocrine disorders can cause anemia through various mechanisms (e.g., reduced oxygen demand and erythropoietin production in hypothyroidism, decreased erythropoietin production or impaired erythroid progenitor proliferation in hyperparathyroidism). Anemia also is associated with diabetes mellitus, especially in patients who also have renal impairment. Renal impairment is generally one of the sequelae of diabetes mellitus. As the disease worsens, the renal failure worsens as does the anemia.

Impact

Anemia can be particularly problematic for patients with severe ischemic heart disease or cerebrovascular disease. Decreased blood viscosity is associated with anemia, and a reduction in viscosity can lead to increases in cardiac output, stroke volume, heart rate, and myocardial oxygen consumption. Compensatory mechanisms that increase oxygen delivery to vital tissues include improvements in the microcirculation and increases in the oxygen extraction ratio (i.e., oxygen extraction by tissues).

Anemia also can affect platelet function and interactions between platelets and the vascular wall. Fewer platelets are available to adhere to sites of endothelial injury and prevent bleeding in patients with anemia compared with healthy patients.

The ability to tolerate anemia depends on circulatory status. Patients with an adequate volume in their circulatory system can tolerate lower hemoglobin concentrations than can hypovolemic patients.

In surgical patients, the effects of postoperative anemia include fatigue, confusion (especially in elderly patients), reduced vigor (i.e., muscle strength and functional ability during recuperation), cardiac morbidity, and delayed wound healing and rehabilitation. Preoperative anemia may affect survival in patients with cardiac disease undergoing coronary artery bypass grafting.

Management

The first step in managing anemia in critical care patients is to detect and correct to the extent possible underlying causes (e.g., nutritional deficiencies, renal insufficiency, endocrine disorders, occult blood loss, infection, inflammation). Baseline laboratory studies should include a complete blood count and serum iron, folate, ferritin, and vitamin B<sub>12</sub> concentrations. Patients should be screened for occult blood in the stool, and sites of chronic or acute blood loss (e.g., the GI or genitourinary tract, lungs) should be identified. Iatrogenic causes of anemia (i.e., unnecessary phlebotomy) should be eliminated.

Acute anemia usually is managed with blood transfusions or the administration of colloidal fluids. The management of chronic anemia depends on the etiology; it may involve the use of erythropoietic agents, iron supplementation, or both.

Transfusions

In 2001 (the most recent year for which data are available), more than 15 million units of whole blood and red blood cells were collected in the United States and 4.9 million patients in U.S. hospitals received nearly 14 million units (4% of collected blood is for the donor’s use and nearly 2% is discarded based on the results of laboratory screening tests). The number of units transfused is increasing at the rate of 6% per year. Blood donations have declined over the past two decades and could threaten the U.S. blood supply.

Transfusions are commonly used in critical care patients. In an open, prospective study in a 24-bed medical ICU at a tertiary-care university hospital, 74 (77%) of 96 patients treated in the ICU for more than three days received transfusions.

In a retrospective chart review at a tertiary-care center, 121 (85%) of 142 patients with an ICU stay lasting more than one week received transfusions. The daily blood loss due to phlebotomy (40–70 mL) accounted for 30% of the blood transfused.

Indications for transfusions included surgery or bleeding (24%), a hematocrit <25% (19%), and low cardiac output (14%). Approximately 40% of transfusions occur for no apparent reason.

In a larger prospective, multicenter observational cohort study of 4992 critically ill ICU patients who were followed for up to 30 days or until hospital discharge or death, 44% of patients were transfused, including 63% of patients with an ICU length of stay of seven days or longer and 33% of patients with a shorter ICU length of stay. Larger numbers of transfusions were associated with increases in organ dysfunction, mean ICU length of stay, hospital length of stay, and duration of mechanical ventilation compared with smaller numbers of transfusions.

Transfusions are administered to promptly increase red blood cell mass and blood volume, often in the case of acute blood loss or active bleeding. Transfusions also are used to increase oxygen delivery.
and alleviate the symptoms associated with anemia (e.g., fatigue, confusion). However, blood transfusions administered in ICUs often contain erythrocytes that have aged because of the time that elapses between donation and distribution to tertiary care centers.32 Aged erythrocytes lose the enzyme 2,3-diphosphoglycerate and adenosine triphosphate, resulting in decreased cytoskeleton oxidation and impaired oxygen off loading.25,26 As erythrocytes age, they also become less deformable and more rigid, increasing the likelihood of microcirculatory “sludging” (i.e., reduced blood flow due to thickening) and multiorgan dysfunction.

Blood transfusions can be life saving in patients with severe, acute blood losses. However, blood is a scarce and costly resource, and some patients refuse transfusions because of religious beliefs. Disadvantages of the use of allogeneic blood transfusions include the potential for transmission of infection, circulatory overload, and other transfusion-related reactions (see Table 3 in the Schwartz article in this supplement).27 Allogeneic blood transfusion in critically ill patients appears to cause immunosuppression, which can lead to transfusion-related graft-versus-host disease and other autoimmune diseases.28 Prolongation of the hospital stay has been associated with the use of allogeneic transfusions in patients undergoing hip or knee replacement surgery.29 Increased mortality was associated with the use of blood transfusions in patients with acute coronary syndrome who developed bleeding, anemia, or both during their hospital stay.30

The Serious Hazards of Transfusion (SHOT) scheme for monitoring the safety of blood transfusions was implemented in 1996 in the United Kingdom. An analysis of six years of SHOT data revealed that 64% of 1630 adverse events associated with blood transfusions involved an incorrect blood component.31 Other commonly reported adverse events include acute transfusion reactions (12%), delayed transfusion reactions (12%), and transfusion-related acute lung injury (6%). Acute lung injury is characterized by dyspnea, hypoxia, and pulmonary infiltrates within 24 hours after transfusion with no other apparent cause.

Thus, efforts to minimize the use of transfusions and consider alternatives to transfusions are needed for the management of chronic, stable anemia in critical care patients. Possible measures to reduce the need for transfusions include reducing blood sample size via the use of pediatric blood draw tubes, the use of blood conservation devices inserted into arterial lines (these devices measure hemoglobin and hematocrit and serve as an indirect calculator of oxygen delivery), returning dead space blood losses (i.e., cell-saver technology in which the patient’s own blood is gathered from drains and rein- fused), reducing the number of indwelling intravenous (i.v.) catheters, and eliminating standing orders for blood tests.25,32

The transfusion of autologous blood donated by the patient preoperatively (i.e., giving the patient his or her own blood) may be an option for patients undergoing elective surgery if the patient does not have cardiovascular disease or another comorbid condition that would be compromised in the short term by the loss of red blood cells when donating blood. The use of autologous blood instead of allogeneic blood can circumvent some of the complications associated with allogeneic blood transfusion (e.g., transmission of infection, graft-versus-host disease, allergic transfusion reaction), although the potential for other complications (e.g., circulatory overload) remains as well as creating a baseline anemia at the time of surgery or hospital discharge. Moreover, nearly half of autologous blood donated for hip or knee replacement surgery is wasted.29 However, the concern is not about wasted blood but rather about decreasing the patient’s hemoglobin and hematocrit prior to surgery. In patients with myocardial ischemia, dropping the hemoglobin and hematocrit below 10 and 30, respectively, has been associated with increased morbidity secondary to ischemic complications.

In some cases, transfusions are given primarily because of a clinician’s medical training to maintain a hemoglobin concentration of approximately 10 g/dL or a hematocrit of around 30% in accordance with the so-called “10/30 rule” rather than a patient’s physiologic needs.33 Such treatment by the numbers instead of according to the patient’s clinical status can be harmful. Moreover, the validity of the 10/30 rule, which was the standard of care for decades since it was first put forth in the 1940s, was questioned in the 1980s.20 The use of a restrictive transfusion strategy where patients with hemoglobin values between 7–9 gm/dL would be transfused has been suggested to minimize patient exposure to the risks associated with transfusions, although the use of such strategies might be limited to patients without active ischemic heart disease or cerebrovascular disease because of safety concerns.34

A restrictive transfusion strategy was compared with a liberal strategy in the Transfusion Requirements in Critical Care (TRICC) trial, a randomized, controlled trial of 838 critically ill patients who had baseline hemoglobin concentrations of less than 9 g/dL.35 The restrictive strategy allowed transfusions only if the hemoglobin concentration decreased below 7 g/dL, and the target hemoglobin concentration was 7–9 g/dL. The liberal strategy allowed transfusions if the hemoglobin concentration decreased below 10 g/dL (i.e., patients randomized to the liberal strategy were immediately eligible for transfusion), with a target
hemoglobin concentration of 10–12 g/dL. There was no significant difference between the two strategies in the cumulative 30-day survival (81% with the restrictive strategy, and 77% with the liberal strategy).

In a subset of 357 patients with cardiovascular disease who participated in the TRICC trial, there was no significant difference between the two transfusion strategies in 30-day survival. However, in 257 patients with severe ischemic heart disease, a nonsignificant trend toward reduced survival was associated with the restrictive strategy compared with the liberal strategy. These were secondary outcomes and not statistically significant; however, Kaplan-Meier curves trended in the appropriate direction. Thus, the optimal transfusion strategy for critically ill patients has not yet been definitively determined, and additional clinical research is needed.

**Blood substitutes**

Various blood substitutes have been developed and are under clinical investigation, primarily to reduce the need for blood transfusion in patients with anemia due to surgery or trauma. Perflubron emulsion is a perfluorocarbon (i.e., a carbon-fluorine compound) that is chemically and biologically inert and has a high capacity for carrying dissolved oxygen and carbon dioxide. It is in phase III clinical trials.

PolyHeme, a human-based temporary oxygen-carrying red blood cell substitute is in phase III clinical trials for the treatment of life-threatening acute blood loss when an oxygen-carrying fluid is required and red blood cells are not available. Hemoglobin glutamer-250, a modified bovine hemoglobin, has been used in adult surgical patients with anemia in South Africa for several years. In 2002, the manufacturer submitted a biologic license application to the Food and Drug Administration (FDA) for use in orthopedic surgical patients, and clinical trials in animals are under way to address questions from the FDA about the safety and efficacy of the product.

Blood substitutes may be an option in the future during blood shortages or for patients who refuse transfusions because of religious beliefs (e.g., Jehovah’s Witnesses). However, none of these products is currently available. The safety, efficacy, and cost-effectiveness of blood substitutes remain to be determined.

**Erythropoietic therapies**

Epoetin alfa and darbepoetin alfa have been used extensively to treat anemia in cancer patients with chemotherapy-induced anemia, but there is limited clinical experience with epoetin alfa and there are no published reports of experience with darbepoetin alfa in critical care patients. These medications are not approved by the FDA for the treatment of anemia in cancer patients due to other factors (e.g., iron or folate deficiency, hemolysis, GI bleeding). Epoetin alfa is approved by FDA to reduce the need for allogeneic blood transfusions in anemic patients scheduled to undergo elective, noncardiac, nonvascular surgery who are at high risk for perioperative transfusions because of anticipated blood losses, although the drug is not indicated for patients willing to donate autologous blood. Neither epoetin alfa nor darbepoetin alfa is approved by FDA for the treatment of anemia in critical care patients.

The efficacy of epoetin alfa in treating anemia in critical care patients was evaluated in a randomized, double-blind, placebo-controlled, pilot study of 160 patients who were admitted to the ICU at one of three academic tertiary care medical centers. Patients received epoetin alfa 300 units/kg or placebo subcutaneously (s.c.) once daily for five days beginning on the third day in the ICU, followed by the same dose every other day. The target hematocrit was 38%.

Treatment was continued for 2–6 weeks, until discharge from the ICU. The number of units of blood transfused over the course of the study was significantly lower in the epoetin alfa group (166) than in the placebo group (305). Each group contained 80 patients. Compared with placebo, epoetin alfa produced a significantly greater increase from baseline in hematocrit (4.8% versus 1.4%) and a significantly higher final hematocrit (35% versus 32%). The percentage of patients who received a blood transfusion between day 8 and day 42 or died before day 42 was 45% in the epoetin alfa group and 55% in the placebo group.

Multiple organ dysfunction syndrome (MODS) occurs secondary to acute illness in ICU patients and is characterized by altered organ function, anemia, and low endogenous erythropoietin concentrations due to the inhibitory effect of inflammatory cytokines associated with the illness. The production of cytokines in addition to potential renal failure due to MODS plays a role in impairing erythropoietin production. In a prospective, randomized, controlled study, 19 patients with this syndrome received epoetin alfa 600 units/kg or a saline placebo i.v. three times weekly for three weeks. The reticulocyte count, a measure of how rapidly erythrocytes are made in the bone marrow and released into the bloodstream, in the epoetin alfa group was significantly higher after three weeks of treatment than at baseline and compared with the placebo group at both baseline and after three weeks of treatment. There were no significant differences between treatment groups in ICU or hospital length of stay. These findings suggest that epoetin alfa is effective for managing anemia in patients with multiple organ dysfunction syndrome. Additional research is needed in larger numbers of patients.

The preoperative use of epoetin alfa was compared with preoperative
autologous blood donation in 490 patients undergoing total hip or knee replacement surgery in a multicenter, randomized, open-label, parallel-group study. A hemoglobin concentration of 11–13 g/dL at baseline (i.e., three weeks before surgery) was an inclusion criterion. The mean hemoglobin concentration at baseline was similar in the two treatment groups. Patients in the epoetin alfa group received 600 units/kg s.c. 21 days, 14 days, and 7 days before surgery and on the day of surgery. Both groups received anticoagulation therapy. The mean hemoglobin concentrations measured preoperatively, postoperatively on day 1, and at discharge visits were significantly higher in the epoetin alfa group than in the preoperative autologous blood donation group. Allogeneic blood transfusions were required in a significantly lower percentage of patients in the epoetin alfa group (13%) than in the preoperative autologous blood donation group (19%). Thus, epoetin alfa is useful for reducing the need for allogeneic blood transfusions in surgical patients with large anticipated blood losses. The recommended dose of epoetin alfa in such patients is 300 units/kg/day s.c. for 10 days before surgery, on the day of surgery, and for 4 days after surgery, or 600 units/kg s.c. 21 days, 14 days, and 7 days before surgery and on the day of surgery.

Iron supplementation

Iron supplementation is recommended to correct iron deficiency in critical care patients. Most patients receiving erythropoietic therapy eventually require iron supplementation because adequate iron stores are required for erythropoiesis, and demand usually exceeds the supply from stores.

In a randomized, open trial, 36 critically ill patients with anemia (hemoglobin concentration <11.2 g/dL or <12.1 g/dL if cardiac disease was present) were randomized to one of three treatment groups receiving: 1) a three-drug combination of epoetin alfa (300 units/kg) s.c. on days 1, 3, 5, 7, and 9; iron saccharate 20 mg/day i.v. for 14 days; and folic acid 1 mg/day i.v.; 2) a two-drug combination of folate and iron using the same dosage regimens; or 3) folate 1 mg/day i.v. alone. Patients with iron-deficiency anemia were excluded from the study. A significant increase from baseline in the reticulocyte count was observed only in the group receiving the three-drug combination of epoetin alfa, iron saccharate, and folate. Thus, iron therapy alone without erythropoietic therapy may be insufficient to generate an adequate amount of erythropoiesis.

The use of oral iron supplements can pose problems for critical care patients because of drug interactions, adverse effects (e.g., abdominal pain), and patient nonadherence (see the Schwartz article in this supplement). Parenteral iron is an alternative to oral therapy. However, concerns have been raised about whether parenteral iron therapy is beneficial or harmful for critical care patients, especially patients with or at risk for infections.

Iron is required for microbial growth. Inflammatory cytokines increase the synthesis of ferritin, which may serve a protective function by binding iron and reducing its availability for microbial growth. Excessive iron therapy could interfere with these antimicrobial effects. Iron appears to stimulate bacterial virulence, an effect thought to be mediated by hydroxyl free radicals. Impaired cellular immunity and inhibition of phagocytosis by neutrophils are associated with iron overload. Research is needed to clarify whether parenteral iron therapy increases the risk for infection or impedes recovery in patients with infections.

Treatment guidelines and protocols

Guidelines and protocols for the management of anemia in critical care patients should address blood-conservation practices and the use of blood transfusions, erythropoietic therapies, and iron supplementation. These guidelines should be evidence-based to the extent possible and take into consideration current local practices. Multidisciplinary input should be obtained in guideline development.

Developing guidelines and protocols for managing anemia in critical care patients is less straightforward than for patients with cancer (see the Schwartz article in this supplement) because the critical care patient population is smaller and less well studied. Few authoritative guidelines for the management of anemia in critically ill patients have been published.

Guidelines should outline the screening processes used to detect and assess the severity and etiology of anemia in critical care patients. Guidelines also should facilitate treatment decisions. Treatment guidelines should be as specific as possible about the type of patients to which they apply (e.g., surgical versus nonsurgical ICU patients), goals of treatment, and parameters for monitoring response to treatment. Threshold and target hemoglobin or hematocrit values for transfusions and the use of erythropoietic therapy should be established. Appropriate dosages (dose and frequency), route of administration, and duration of therapy for erythropoietic agents also should be specified in guidelines. For example, the identification of anemic ICU patients with an anticipated ICU stay of more than five days and the use of epoetin alfa 40,000 units s.c. once weekly beginning no earlier than the third day of the ICU stay and continuing until no longer indicated have been recommended.

Treatment guidelines and protocols for managing anemia in critical care patients should be periodically reevaluated and updated to reflect current practice and recent research.
was designed to decrease laboratory blood draws and blood transfusions by eliminating unnecessary procedures. In 123 ICU patients in whom blood draws were evaluated after implementation of the blood-conservation program, there were 31 discontinuations and 36 reductions in blood draws. A significant reduction in the mean number of units of blood transfused per patient was observed after implementation of the epoetin alfa protocol and blood-conservation program (7 after implementation versus 17 before implementation). The mean number of units transfused per ICU day also decreased significantly from 0.5 before implementation to 0.3 after implementation. There were no significant differences in ICU length of stay, mortality rate, or the average number of days of mechanical ventilation before and after implementation of the protocol. Thus, the evidence-based protocol and blood-conservation program at OSUMC increased rational prescribing of epoetin alfa, reduced blood losses due to phlebotomy, and optimized the use of the blood supply. Additional research in larger numbers of patients is needed to demonstrate a favorable impact on survival and other patient outcome measures.

Conclusion
Epoetin alfa is effective for managing anemia in critical care patients, including patients undergoing surgery. Use of the drug can help conserve the limited blood supply and avoid problems associated with transfusions.

References
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