KEY CLINICAL QUESTIONS

When should a hospitalized patient be transfused?

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KEY POINTS SUMMARY

1. Many of the red blood cell transfusions in the hospital setting are unnecessary and potentially harmful.
2. Adverse transfusion reactions occur in an estimated 10% of red blood cell transfusions.
3. Patients symptoms, vital signs, and physical exam findings should guide the decision to transfuse.
4. Anemic patients with significant cardiac disease may benefit from a higher transfusion threshold to avoid ischemia.

ADDITONAL READING

- Corwin HL, Carson JL. Blood transfusion—when is more really less? *N Engl J Med*. 2007;356(16):1667-1669.
- Spiess BD. Red cell transfusions and guidelines: a work in progress. *Hematology/Oncology Clinics of North America*. 2007;21(1):185-200.
- Hebert PC, Fergusson DA. Do transfusions get to the heart of the matter? *JAMA*. 2004;292(13):1610-1612.
- Hearnshaw S, Travis S, Murphy M. The role of blood transfusion in the management of upper and lower intestinal tract bleeding. *Best Pract Res Clin Gastroenterology*. 2008;22(2):355-371.

Case

A 65-year-old male nursing home resident is sent to the emergency room with a productive cough, fever, and low blood pressure, and is diagnosed with community-acquired pneumonia. He has a history of tobacco abuse, hypertension, and a right middle cerebral artery stroke. His admission labs show a hemoglobin level of 9.0 g/dL. The day after admission his hypotension has resolved and he reports feeling much better after two liters of intravenous fluids and antibiotics. However, his hemoglobin level is 7.9 g/dL. There is no evidence of bleeding. Should this hospitalized patient be transfused?

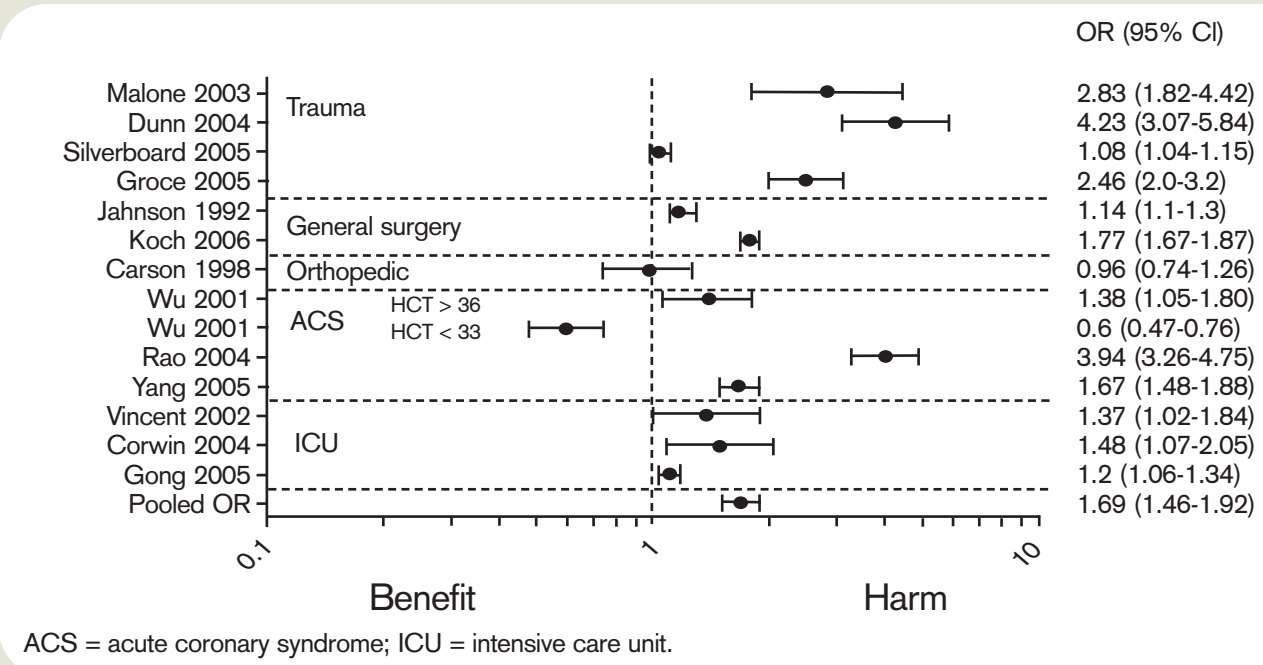
Overview

When to give a red blood cell transfusion is a clinical question commonly encountered by hospitalists. Individuals with acute blood loss, chronic blood loss, anemia of chronic disease, and hemolytic anemia often are given transfusions. Hospitalists serving as consultants may be asked when to transfuse patients perioperatively.

It is estimated up to 25% of the red blood cells transfused in the U.S. are inappropriate.[1-4] Many physicians transfuse based on a number, rather than on

A ROOM WITH VIEWS / ALAMY

Figure 1: Association between blood transfusion and the risk of death (odds ratio [*OR*] and 95% confidence interval).



ACS = acute coronary syndrome; ICU = intensive care unit.

Source: Marik PE, Corwin HL. Efficacy of red blood cell transfusion in the critically ill: a systematic review of the literature. *Crit Care Med*. 2008;36(9):2667-2674.

objective findings. Overuse is common because of the wide availability of red blood cells, the belief complications are infrequent, and an unfounded fear of adverse outcomes if a patient is not transfused.

Tachycardia, low blood pressure, and declining oxygen saturations are signs clinicians can use when making the decision to transfuse. Electrocardiographic changes associated with tissue hypoxia can occur at a hemoglobin level <5 g/dL in healthy adults. Studies show mortality and morbidity increase rapidly at levels <5.0 to 6.0 g/dL.[5] Currently, no diagnostic serological test exists for tissue hypoxia, which is the physiologic reason to give red blood cells.

Red blood cell transfusion can be a life-saving therapy; however, it is not a benign intervention. It is estimated 10% of transfusion reactions will have some adverse event.[6] Red blood cell use exposes patients to hemolytic transfusion reactions, infections, and transfusion related acute lung injury.[7,8] Additionally, unnecessary economic expenses are incurred and a scarce resource is diverted from other patients.

Hospitalists should be able to describe the indications for red blood cell transfusion and understand the evidence for and against its use. Physicians who appreciate the risks and benefits of red blood cell use tend to transfuse less blood that those who less informed. [9, 10]

Review of the Data

General outcomes: Despite the long history of red blood cell transfusion, which dates back to 1818, when James Blundell successfully saved a woman exsanguinating from a postpartum hemorrhage, little evidence has been accumulated for its appropriate use. In the 1980s, the discovery of the human immunodeficiency virus sparked blood product safety concerns. This stimulated research and a debate over red blood cell transfusion practices, with a growing body of literature unsupportive of transfusion for an arbitrary trigger, for example the "10/30 rule," which referred to 10 g/dL hemoglobin or hematocrit of 30%.[9]

Observational studies have raised concerns by linking morbidity and mortality to red blood cell use. Among 1,958 surgical patients who refused blood transfusion on religious grounds, there was an increase in mortality when hemoglobin levels were <6.0 g/dL. Hemoglobin levels higher than 7.0 g/dL showed no increased mortality.[11] A recent comprehensive review included 272,596 surgical, trauma, and ICU patients in 45 observational studies. The review included studies with end points, including mortality, infections, multiorgan dysfunction syndrome, and acute respiratory distress syndrome, and concluded transfusions are associated with a higher risk of morbidity and mortality.[12] (see Figure 1, p. 20)

Higher rates of infection associated with transfusions occurred in patients with post-operative trauma, acute injuries, gastrointestinal cancer undergoing surgery, coronary bypass surgery, hip surgery, burns, critical illness, and patients requiring ventilation. (see Figure 2, p. 21)[12] The increased infection risk likely is due to the transient depression of the immune system induced by red blood cell transfusion. Prolonged hospital stays in postoperative colorectal surgery patients and ICU patients have been associated with transfusions.[13]

A meta-analysis of the few randomized controlled trials favors the restrictive use of red blood cells. The preponderance of the evidence comes from the Transfusion Requirements in Critical Care (TRICC) trial.[14] This randomized control trial in critically ill medical and surgical patients demonstrated a restrictive strategy (transfusion trigger of <7.0 g/dL) and was as effective as a liberal transfusion strategy (transfusion trigger <10.0 g/dL). (see Figure 3, p. 22) Indeed, patients in the restrictive arm of the trial, who were less ill and under age 55 had a lower mortality rate than those who were transfused liberally.[15] To date, there are no hospital-based randomized control trials that evaluate outcomes of anemic non-ICU medical patients.

This evidence has created a growing consensus that a restrictive use of blood results in improved patient outcomes. In patients without cardiovascular disease the evidence suggests most patients tolerate a hemoglobin level of 7.0 g/dL.[5]

Cardiac Patients

Experimental and clinical evidence suggests patients with cardiovascular disease are less tolerant of anemia. Patients with coronary disease are more likely to have adverse outcomes than those without coronary disease, if they do not have a red blood cell transfusion.[11,16]

The myocardium has a higher oxygen extraction ratio compared to the tissue oxygen extraction ratio, making it more sensitive to anemia.[17,18] The presence of cardiac disease may require a higher threshold to transfuse blood; however, the precise recommended threshold remains controversial. A restrictive red blood cell transfusion strategy (maintaining the hemoglobin between 7.0 g/dL and 9.0 g/dL) appeared to be safe in most critically ill patients with cardiovascular disease.[14]

The data is more conflicting for patients with an acute coronary syndrome (ACS). Some studies have found increased mortality and another concluded ACS decreased with red blood cell use.[19-21] Further research is needed to determine when red blood cells should be given to patients with coronary disease.

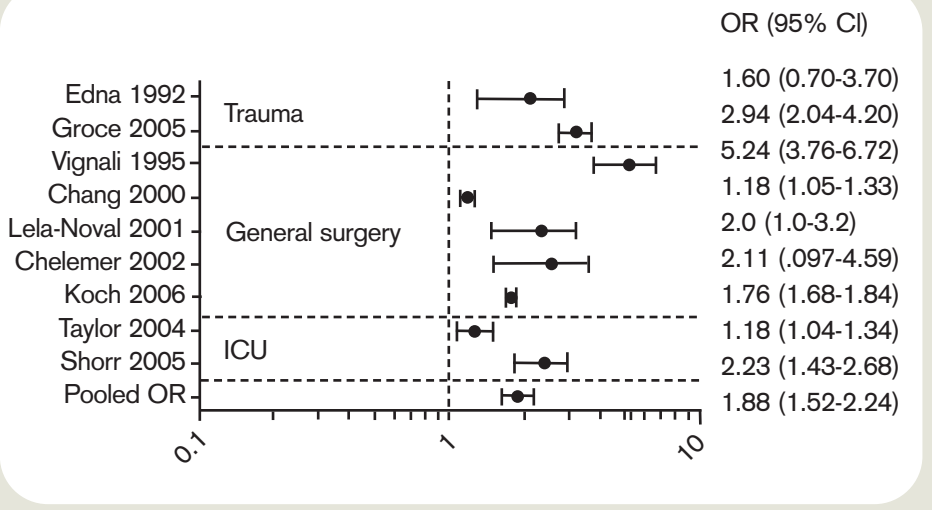
Gastrointestinal Bleeding

The decision to transfuse for gastrointestinal (GI) bleeding takes into account the site and etiology of the bleeding, availability of treatments, and risk of continued bleeding. Once the blood loss is controlled, a decision must be made on how to treat the anemia. Currently, no studies have looked at outcomes for patients who did and did not receive blood for an acute or chronic GI bleed.

Additionally, no studies have been conducted to delineate when to transfuse patients with chronic GI blood loss. Studies of patients with an acute GI bleed and cardiovascular disease have shown an increase in mortality, but it is unknown if the use of specific transfusion triggers affects outcomes in this group.

In patients with GI bleeding, experts feel the use of red blood cells should be guided by available evidence. For patients without cardiac disease, red blood cell transfusion is rarely required following definitive treatment and cessation of blood loss unless the hemoglobin is <7.0 g/dL.[22]

Figure 2: Association between blood transfusion and the risk of infectious complications (odds ratio [*OR*])



Source: Marik PE, Corwin HL. Efficacy of red blood cell transfusion in the critically ill: a systematic review of the literature. *Criti Care Med.* 2008;36(9):2667-2674.

Back to the Case

The patient described in our case should not be transfused unless he has clinical signs or symptoms of tissue hypoxemia. An appropriate workup for his anemia should be initiated and, if an etiology identified, definitive treatment or intervention applied.

Bottom Line

Unless there are clinical signs of tissue hypoxia, symptomatic anemia, or a hemoglobin of <7.0 g/dL, red blood cell transfusion is not recommended, unless

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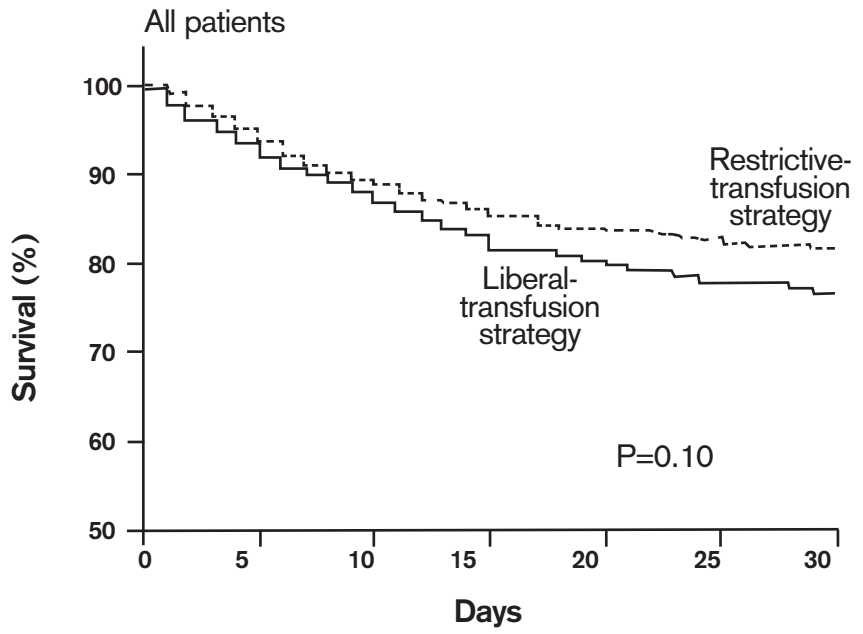
Figure 3: Kaplan-Meier estimates of survival in the 30 days after admission to the ICU in the restrictive-strategy and liberal-strategy groups



Source: 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(6):409-417

the patient has active ACS or significant underlying coronary disease. TH

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