



# Consider this strategy for upper GI bleeds

Patients with acute upper GI bleed are less likely to experience adverse events—and more likely to survive—when their care is governed by a restrictive transfusion policy.

## PRACTICE CHANGER

Do not order transfusions of red blood cells for patients with acute upper gastrointestinal bleeding unless their hemoglobin level <7 g/dL.

Villanueva C, Colomo A, Bosch A, et al. Transfusion strategies for acute upper gastrointestinal bleeding. *N Engl J Med*. 2013;368:11-21<sup>1</sup>

**A:** Based on a single randomized controlled trial (RCT) consistent with other RCTs on recommendations for transfusion.

## ILLUSTRATED CASE

An 82-year-old patient presents to the emergency department with several episodes of melena over the past week and one episode of hematemesis this morning. He denies any shortness of breath, dizziness, lightheadedness, or fatigue. He is tachycardic but normotensive. Lab results note a hemoglobin level of 8.3 g/dL. Should you order a transfusion of red blood cells?

**A**cute upper gastrointestinal bleeding (UGIB) commonly requires hospital admission, with approximately 61 cases per 100,000 population in the United States in 2009.<sup>2</sup> Gastroduodenal peptic ulcer disease accounts for the majority of these cases.<sup>3</sup> Although trends indicate an overall decrease in cases requiring hospitalization, UGIB remains a condition associated with a mortality rate of 2.5% and inpatient costs of \$2 billion annually.<sup>2,3</sup>

## Studies have been inconclusive—until now

An RCT published in 1999 showed a restrictive transfusion strategy (hemoglobin threshold of 7 g/dL) to be at least as effective as—and possibly superior to—a liberal strategy (threshold of 10 g/dL) in critically ill patients.<sup>4</sup> In 2010, an RCT demonstrated that a liberal transfusion strategy (also defined as a transfusion threshold of 10 g/dL) did not reduce the rates of death or in-hospital morbidity in elderly patients after hip surgery.<sup>5</sup> A recent Cochrane review of transfusion strategies for UGIB included only 3 small studies (N=93), so its authors could not draw any firm conclusions.<sup>6</sup> The results of a new RCT, detailed below, are more conclusive.

## STUDY SUMMARY

### Restrictive transfusion policy lowers mortality risk

Villanueva et al conducted a nonblinded RCT comparing outcomes in patients admitted to the hospital with moderate-risk acute UGIB transfused on a liberal vs a restrictive strategy.<sup>1</sup> The restrictive group used a transfusion hemoglobin threshold of 7 g/dL and a post-transfusion target of 7 to 9 g/dL; the liberal group used a threshold of 9 g/dL, with a post-transfusion target of 9 to 11 g/dL. Patients received one unit of red blood cells at a time until their hemoglobin was above the predetermined threshold.

CONTINUED

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➤ **Exercise caution before extrapolating the results of this study to patients with a history of cardiac disease.**

Patients were excluded if they declined blood transfusion; had massive exsanguinating bleeding, acute coronary syndrome, symptomatic peripheral vasculopathy, stroke, lower GI bleeding, or a transient ischemic attack; had received a transfusion within the previous 90 days; or had a recent history of surgery or trauma. Patients at low risk of rebleeding (as defined by the Rockall risk scoring system) were also excluded. Randomization was stratified by the presence or absence of cirrhosis of the liver.

Participants (N=921) had confirmed hematemesis and/or melena on admission. All underwent emergency gastroscopy within 6 hours of admission, with subsequent interventions based on endoscopic findings. In addition to established hemoglobin levels, patients received a transfusion anytime they developed signs or symptoms related to anemia, massive bleeding, or the need for surgery. Staff monitored hemoglobin levels every 8 hours during the first 48 hours, then daily thereafter.

Both groups had similar baseline characteristics, including hemoglobin on admission and source of bleeding. The authors used intention-to-treat analysis to identify the primary outcome: death from any cause at 45 days. Secondary outcomes were further bleeding and in-hospital complications.

During hospitalization, 49% of patients in the restrictive group and 86% of those in the liberal group received a blood transfusion ( $P<.001$ ). Thirty-two patients (17 from the restrictive group and 15 from the liberal group) withdrew from the study, leaving 889 patients for overall analysis.

At 45 days, overall mortality from any cause was 5% in the restrictive group and 9% in the liberal group ( $P=.02$ ; number needed to treat [NNT]=25). Sub-group analysis revealed a lower risk of death in patients with cirrhosis and Child-Pugh class A or B disease assigned to the restrictive transfusion group vs the liberal group. The results showed a trend toward a lower risk of death in patients with bleeding from varices or peptic ulcers for the restrictive group, as well.

In addition, the restrictive transfusion group had a significantly lower rate of adverse events (40% vs 48% for the liberal transfusion

group;  $P=.02$ , NNT=13), with a significant reduction in transfusion reactions (3% vs 9%;  $P=.001$ , NNT=17) and cardiac complications (11% vs 16%;  $P=.04$ , NNT=20). The restrictive group had a lower rate of further bleeding (10% vs 16% for the liberal transfusion group;  $P=.01$ , NNT=17), as well.

#### WHAT'S NEW

##### Many reasons to limit transfusions for acute upper GI bleed

This RCT provides evidence that patients with acute UGIB have improved survival rates and fewer adverse events when a restrictive transfusion strategy is used. In addition to improving patient outcomes, a restrictive strategy will likely reduce costs and overall use of blood products. Thus, the study, along with other recent evaluations, adds evidence to support more restrictive transfusion thresholds.

The AABB (formerly named the American Association of Blood Banks) recently released guidelines calling for restrictive transfusion thresholds (7-8 g/dL) in stable hospitalized patients.<sup>7</sup> In 2012, the American College of Gastroenterology published a practice guideline with a recommended target hemoglobin level of  $\geq 7$  g/dL in the management of patients who have ulcer bleeding but no signs of intravascular depletion or comorbidities such as coronary artery disease.<sup>8</sup>

#### CAVEATS

##### Results might differ when endoscopy is delayed

The patients in the study detailed here underwent emergency gastroscopy within 6 hours of admission, and both groups received the same therapies based on endoscopic findings. It remains unclear whether the benefits of a restrictive transfusion strategy would persist in patients who do not undergo endoscopy within that timeframe. And, because the reported baseline characteristics of the patients did not include the prevalence of cardiac disease, caution should be exercised before extrapolating these results to patients with underlying (active or historical) cardiac disease.

**CHALLENGES TO IMPLEMENTATION****Changing long-held policies may be difficult**

Although RCTs as well as clinical guidelines suggest that restrictive transfusion policies are safe and effective, changing long-held clinical practices is never easy. **JFP**

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**References**

1. Villanueva C, Colomo A, Bosch A, et al. Transfusion strategies for acute upper gastrointestinal bleeding. *N Engl J Med* 2013;368:11-21.
2. Laine L, Yang H, Chang SC, et al. Trends for incidence of hospitalization and death due to GI complications in the United States from 2001 to 2009. *Am J Gastroenterol* 2012; 107:1190-1195.
3. Gralnek IM, Barkun AN, Bardou M. Management of acute bleeding from a peptic ulcer. *N Engl J Med* 2008; 359:928-937.
4. Hebert PC, Wells G, Blajchman MA, et al. A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care. Transfusion Requirements in Critical Care Investigators, Canadian Critical Care Trials Group. *N Engl J Med* 1999; 340:409-417.
5. Carson JL, Terrin ML, Noveck H, et al. Liberal or restrictive transfusion in high-risk patients after hip surgery. *N Engl J Med* 2011; 365:2453-2462.
6. Jairath V, Hearnshaw S, Brunskill SJ, et al. Red cell transfusion for the management of upper gastrointestinal haemorrhage. *Cochrane Database of Systematic Reviews* 2010;CD006613.
7. Carson JL, Grossman BJ, Kleinman S, et al. Red blood cell transfusion: a clinical practice guideline from the AABB. *Ann Intern Med* 2012; 157:49-58.
8. Laine L, Jensen DM. Management of patients with ulcer bleeding. *Am J Gastroenterol* 2012; 107:345-360.