

## Rethinking red cell transfusion

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Story from the Front Lines:

A man in his 70s with a history of coronary artery disease, chronic kidney disease and type 2 diabetes was transferred to our facility for a high-risk PCI after NSTEMI at an outside facility. The day prior to transfer he was placed on a nitroglycerin drip after developing unstable angina, which was continued upon arrival. His hemoglobin was noted to be 7.9, and given the complexity of the PCI, as well as the potential to cause acute renal failure with a contrast load, he was given three units of packed red blood cells with the hope that his angina was due in part to anemia. He developed acute hypoxic respiratory failure overnight, requiring BiPAP, and a chest x-ray was consistent with TRALI. His oxygenation status further declined, ultimately developing ARDS requiring mechanical ventilation and a prolonged hospital stay.

Teachable Moment:

Controversy exists as to whether a restrictive or liberal transfusion strategy is better for patients undergoing acute coronary syndromes (ACS). Patients with coronary artery disease are at risk for anemia, given their long-term use of antiplatelet agents, anticoagulants or need for invasive procedures. It is generally accepted that in patients with ACS, transfusion to a hemoglobin of 8 is beneficial, as this leads to increased oxygen delivery to ischemic myocardium. Debate continues about whether a hemoglobin concentration of 8 is sufficient to meet this demand as compared to higher hemoglobin targets, but should this necessarily be the case?

Multiple studies have attempted to resolve the debate. The CRIT study<sup>1</sup> randomized patients to a liberal versus restrictive transfusion strategy in critically ill patients. In this study, a liberal transfusion strategy resulted in higher rates of in-hospital death, recurrent MI, and new or worsening heart failure. In a 2013 meta-analysis<sup>2</sup> reviewing liberal versus restrictive transfusion strategies in patients with acute MI, patients with an MI who received any transfusions, or patients who received liberal transfusion strategies had a higher rate of mortality (hazard ratio 2.25, compared to no or restrictive transfusion strategies). Similarly, a Cochrane review<sup>3</sup> in 2015 that reviewed 31 different trials found that restrictive transfusion strategies had no effect on mortality, overall morbidity or MI.

Transfusions are expensive, labor-intensive and may cause harm, including transfusion reactions, transmission of diseases, acute lung injury, circulatory overload and/or immunosuppression<sup>1</sup>. The most feared transfusion reaction is transfusion-related acute lung injury (TRALI), which occurs within six hours after transfusion. The true incidence of TRALI is unknown but can lead to significant morbidity and mortality. If TRALI develops into ARDS, management is supportive care, which can include noninvasive or mechanical ventilation, vasopressive medications and/or fluid resuscitation. In a study performed by Vlaar et al<sup>4</sup>, the mortality associated with TRALI was 53%.

Based on this data, what are we to do? Transfusions, with the potential for morbidity, should not be ordered without a thorough informed consent process and recognition that the best evidence does not mandate transfusion at a specific threshold in non-bleeding patients. Prior studies have argued that sicker patients may need more frequent transfusions if bleeding or hemodynamically unstable, leading to confounding of indication<sup>5</sup>. However, multiple studies have showed that there is not an increased rate of

cardiac events among patients who undergo a restrictive transfusion strategy compared to a liberal transfusion strategy. Given that we have the potential to cause harm with more frequent transfusions, we should reconsider routinely transfusing red cells in anemic patients with acute coronary syndromes.

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2. Chatterjee S, Wetterslev J, Sharma A et al. Review: Blood transfusions are associated with higher mortality than no or restricted transfusions in MI. *Jama Internal Medicine*. 2013;173:132-139.
3. Holst LB, Petersen MW, Haase N et al. Restrictive versus liberal transfusion strategy for red blood cell transfusion: systematic review of randomized trials with meta-analysis and trial sequential analysis. *BMJ*. 2015;350:h1354.
4. Vlaar AP, Binnekade JM, Prins D et al. Risk factors and outcome of transfusion-related acute lung injury in the critically ill: A nested case-control study. *Critical Care Medicine*. 2010; 38(3):771-778.
5. Carson JL, Brooks MM, Abbott JD et al. Liberal versus restrictive transfusion thresholds for patients with symptomatic coronary artery disease. *American Heart Journal*. 2013; 165(6)964-971.