

Are we on the verge of a paradigm shift in transfusion decision-making?

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Based on numerous trials that have reported the non-inferiority of a restrictive transfusion strategy (low haemoglobin (Hb) threshold, usually between 7 and 8 g/dl) in comparison with a liberal transfusion strategy (high Hb threshold, usually between 9 and 10 g/dl) in terms of mortality and/or morbidity and a decrease in patients transfused and RBC transfused per patient,¹ guidelines recommend a low haemoglobin threshold, unless specific conditions as acute coronary syndrome.^{2,3} At the same time, experts agree that anaemia tolerance must be integrated in the transfusion decision making process.³ However, symptoms of anaemia in critically ill or post-surgical patients are not specific and most often impossible to discriminate from other reasons. The benefit of integrating physiological transfusion triggers as the ScvO₂ in the transfusion decision process remains unknown and poorly explored in interventional studies. Physiological transfusion triggers aim to assess the balance between oxygen delivery (DO₂) and oxygen consumption (VO₂) that is likely to change along patient's clinical course.

The pilot randomised trial performed by Marine Saour et al., published in this issue of *The Lancet Regional Health - Europe*, compared two strategies of anaemia management in the perioperative setting of cardiac surgery from the day before surgery to hospital discharge or 28 days after surgery, in a University Hospital in France.⁴ Patients with a high risk of transfusion (TRUST score equal to or higher than 3) were randomised prior to surgery to receive either subcutaneous erythropoietin (600 IU/kg, maximum 40,000 U) associated to intravenous (IV) ferric carboxymaltose the day of surgery if their Hb was ≤ 13 g/dl, and after surgery RBC transfusion if Hb was ≤ 8 g/dl and ScvO₂ $\leq 65\%$ or if Hb was < 7 g/dl. If ScvO₂ was $> 65\%$ and Hb was ≤ 8 g/dl, erythropoietin and IV iron could be administered if they had not been given in the previous 7 days. Patients who were randomised in the controlled group received RBC transfusion when Hb was ≤ 8 g/dl or 200 or 300 mg of IV iron sucrose if the Hb was ≥ 8 g/dl.

The study primary outcome was the proportion of patients transfused with RBC after surgery up to hospital discharge or 28 days after surgery. Nine of the 62 (14.5%) patients in the interventional group required RBC transfusion by hospital discharge or day 28 after surgery compared to 19/61 (31.2%) in the controlled group (odds ratio 0.37 [95% CI, 0.15–0.91], $p = 0.03$),⁴ similar results were obtained when considering only anaemic patients at randomization and patients not transfused during surgery. There was more anaemic patients at day 28 and 3 months in the controlled group while the rate of severe adverse events were similar between groups.

This pilot trial is original and interesting by many aspects. First, it considers the perioperative period as a continuum for anaemia management. The second interesting point is the use of a bundle of measures including IV iron, erythropoietin and RBC transfusion, to treat anaemia. Although, patient blood management (PBM) programs include multimodal approach for anaemia prevention and management, randomized trials on PBM are commonly and until recently investigating only one measure (i.e. transfusion, iron, erythropoietin or tranexamic acid) at a specific time (before, during or after surgery). Last and not the least, Marine Saour et al., have included ScvO₂ in the transfusion decision making process, when patients were hemodynamically stable. ScvO₂ is a surrogate of the oxygen extraction ratio and then of the oxygen reserve (i.e. the balance between VO₂ and DO₂). A cut off of 65% of ScvO₂ has been reported to predict a response to RBC transfusion in a non-bleeding and hemodynamically stable patients with a good positive predictive value of 85% and a good specificity of 88% (95%CI, 75.7–94.7) after cardiac surgery.⁵

Two pilot trials have compared ScvO₂ to Hb as a trigger for RBC transfusion after cardiac surgery.^{6,7} However, in these studies, a Hb threshold of 9 g/dl was used while European guidelines strongly recommended a lower Hb threshold of 7.5 g/dl in this setting, questioning these studies findings.³ The trial by Marine Saour et al. has the specificity to integrate both ScvO₂ and Hb level in the transfusion decision making.

Future large randomized trials should consider, as Marine Saour et al. did, anaemia as a continuum along the clinical course and a multimodal approach of anaemia management. They should also investigate the benefit of a more personalised transfusion strategy



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integrating physiological triggers when possible to avoid unnecessary RBC transfusion and optimise RBC administration to patients' needs. Such future trials should integrate in both groups what is already known to be beneficial. Indeed, we could question why patients in the controlled group of the trial by Marine Saour et al., did not receive any pre-operative anaemia treatment. Finally, future research must integrate long term and functional outcomes.

Declaration of interests

CA gave lectures for MSD and CSL VIFOR.

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