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Alternatives to Preoperative Transfusion Should Be Preferred in Anemic Cardiac Surgical Patients Instead of Useless Transfusion

To the Editor:

We read with great interest the recent article published by Karkouti *et al.* about prophylactic erythrocyte transfusion in anemic patients scheduled for cardiac surgery.¹ We are very concerned by the concept of “prophylactic packed erythrocyte transfusion” before elective surgery.

The authors stated “this pilot study showed that in anemic cardiac surgical patients, prophylactic transfusion of 2 units of erythrocytes 1 to 2 days before surgery safely reduces perioperative anemia and erythrocyte transfusions, and may reduce plasma iron level.”

This statement is not in accordance with the title of the article. More importantly, it is not supported by the data presented.

On the one hand, the study was not powered to assess the safety of prophylactic transfusion in this population. According to the reported incidence of immediate complications associated with packed erythrocytes transfusion, a much higher number of patients had to be studied. As estimated by the authors, inclusion of 1,000 patients should be necessary to show a statistically significant improvement in renal function. With this larger population, side effects associated with erythrocyte transfusion might appear. These side effects may have potentially severe consequences for patients' outcome, especially if they have resulted in a report of the surgical intervention. Of note, the total number of erythrocyte units transfused in the perioperative period was not different between the two studied groups.

On the other hand, the statement that “the increase in postoperative iron and transferrin saturation levels was more pronounced in the control arm than in the treatment arm” could not be inferred from the statistical analysis used. Indeed, a two-way ANOVA test should have been performed to demonstrate an interaction between “group” and “time” effects. Moreover, as observed in the treatment arm, transferrin saturation levels may increase after cardiac surgery because of several other factors that have to be taken into account.

It is increasingly recognized that preoperative anemia and perioperative transfusion are both independently associated

with increased postoperative morbidity in cardiac surgery patients.^{2,3} Several alternatives have been proposed to treat preoperative anemia and to reduce intra- and postoperative transfusion, in particular intravenous iron and erythropoietin. In the subpopulation of patients in which iron status was evaluated, most patients in both groups exhibited preoperative functional iron deficit (*i.e.*, transferring saturation level less than 20%) that might have been corrected before surgery. The 2011 Updated Society of Thoracic Surgery and Society of Cardiovascular Anesthesiologists Blood Conservation Clinical Practice Guidelines stated that it is reasonable to use preoperative iron and erythropoietin several days before cardiac surgery to increase erythrocyte mass in patients with preoperative anemia (Class IIa recommendation).⁴

Although preoperative hemoglobin optimization requires some delay, which could not fit with the surgical schedule, several authors showed that even a very short preoperative erythropoietin administration seems to be a safe and easy method to reduce the need for erythrocyte transfusions in cardiac surgery patients.^{5,6} In particular, Yoo *et al.* showed very recently that a single intravenous administration of erythropoietin and iron supplementation 1 day before surgery significantly reduced the intra- and postoperative transfusion requirement in anemic patients undergoing valvular heart surgery.⁷ Even if the benefit to risk balance might be confirmed in a large multicenter randomized controlled trial, a combination of iron and erythropoietin appears to be an interesting alternative for preoperative anemia correction.

Regarding the management of cardiopulmonary bypass (CPB), the association between lowest hematocrit on CPB and adverse renal outcomes has been well demonstrated.⁸ However, maintenance of oxygen delivery to the tissues and in particular to the kidneys can be maintained by other treatments than packed erythrocytes transfusion. Ranucci *et al.* showed that the detrimental effect of a high hemodilution degree during CPB could be significantly reduced by increasing the oxygen delivery, notably to the kidneys, with an increased pump flow.⁹ This increase in pump flow can be achieved without significant increases in shear stress with the modern CPB circuitry, in particular the arterial line. In addition, ultrafiltration of the priming volume has been shown to be an efficient technique to reduce the degree of hemodilution during CPB.⁴

Finally, although the total number of erythrocytes units transfused in both groups throughout the studied period was not different between the two, the authors did not report if some patients in the control group were finally not transfused. If this was the case, then it implies that some patients in the “prophylactic” transfusion group might have been transfused unnecessarily.

In conclusion, the article published by Karkouti *et al.*¹ has to be interpreted with great caution. Based on the results presented, preoperative erythrocyte could not be considered as a strategy to decrease perioperative transfusion. A multimodal pre- and intraoperative approach should have been

preferred, and the effects of such strategies on patient postoperative outcome remain to be demonstrated through a large randomized controlled multicenter trial.

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