

# The negative influence and adverse outcome of blood transfusion in heart surgery patients

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**Osmar Antonio Centurion**Department of Health Sciences's Investigation, Sanatorio  
Metropolitano, Fernando de la Mora, Paraguay**Correspondence:** Osmar Antonio Centurion, Professor of  
Medicine, Asuncion National University, Department of Health  
Sciences's Investigation, Sanatorio Metropolitano, Teniente  
Ettiene 215 c/ Ruta Mariscal Estigarribia, Fernando de la Mora,  
Paraguay, Email osmarcenturion@hotmail.com**Received:** November 08, 2016 | **Published:** November 16,  
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## Editorial

There is compelling evidence indicating that blood transfusion (BT) is excessive and sometimes unnecessary. Nearly 14 million units of blood are donated annually in the USA, and about 4 million people receive BT every year.<sup>1,2</sup> Blood transfusion administration in surgical and critical care settings varies between 30-100% of patients. On the other hand, blood donations have significantly diminished mainly because of decreasing number of qualified donors.<sup>3-6</sup> This fact has resulted in a shortage of blood supply in blood banks worldwide which makes it necessary to seek out new treatment options.<sup>5</sup> Although, alternatives to BT and other treatment options exist, they are seldom utilized.

Despite many technological improvements and therapeutic advances, open heart surgery is still associated with the risks of bleeding and thrombotic events. It is relatively frequent to observe a decrease in plasma hemoglobin values under 10g/dL in the immediate period after heart surgery. In this context, some patients would receive blood transfusion (BT), especially if there are clinical signs of decreased plasma volume.<sup>7-11</sup> Although there is a clear evidence of change, since many decades ago it is believed that patients would benefit from a BT that increases the hemoglobin levels beyond 10g/dL and the hematocrit levels beyond 30%. There are several reasons to think this way. The transfused whole blood is an excellent plasma volume expander and stays in the intravascular space much longer than any other volume expander. Indeed, BT induces an increase in the plasma volume, a hemodynamic improvement, and an increase in the cardiac output and diuresis. Nevertheless, at the light of medicine based evidence, are these improvements correlated with decreased morbidity and lesser mortality?

Murphy et al.,<sup>7</sup> investigated the effects of BT in 8598 surgical patients during the post-operative period of coronary revascularization surgery.<sup>7</sup> They found no benefit from blood transfusion for hematocrits as low as 21% (hemoglobin of 7g/dL), and the risk of death within 30 days of surgery was almost 6 times greater for patients who received blood. Moreover, red blood cell transfusion in these heart surgery patients was linked as an independent variable to an increase in infections and ischemic complications such as myocardial infarction, renal compromise and failure, and stroke. Additionally, transfused patients had prolonged mechanical ventilation, higher incidence of atrial fibrillation, longer hospital length of stay, and higher morbidity and mortality.<sup>7</sup> Similar findings were demonstrated in several observational studies demonstrating clear association between red blood cell transfusion and adverse outcomes in cardiac surgery patients.<sup>7-11</sup> This adverse association between BT and cardiac surgery has been shown through the years in several studies and clinical observations.<sup>12-21</sup> Indeed, Denton Cooley demonstrated similar findings almost four decades ago.<sup>16</sup> It was also demonstrated that a single unit of red blood cell transfusion to a cardiac surgery patient is associated to a decreased survival at 10 years after the BT.<sup>21</sup>

The Society of Thoracic Surgeons and the Society of Cardiovascular Anesthesiologists guidelines emphasize that the benefits of transfusion have not been adequately demonstrated and that existing evidence is an imperfect guide to transfusion decisions. They suggest a transfusion trigger of hemoglobin less than 7g/dL in postoperative cardiac surgery patients with a class IIa level of indication.<sup>20</sup>

There are certain possible mechanisms responsible for the increased ischemic complications with red blood cell transfusion in heart surgery patients. A pro-inflammatory effect and storage defects contribute to the adverse effect of BT. Stored red blood cells are known to have decreased 2,3 DPG in the cell membrane, hence, they are less deformable, less likely to deliver oxygen to the tissues, and with greater tendency to produce capillary obstruction.<sup>18</sup> On the other hand, the mechanisms responsible for the increased incidence of infectious complications are due to the immunosuppressive effects of BT. Administration of blood products causes profound negative effects on the human immune system, a condition termed transfusion-related immune modulation. Mechanisms for this immune modulation include suppression of cytotoxic cell and monocyte activity, release of immunosuppressive prostaglandins, inhibition of interleukin-2 production, and increase in suppressor T-cell activity.<sup>22-29</sup> In addition, it is well known that BT was utilized against organ rejection in the beginnings of kidney transplantation in order to decrease the incidence of renal allograft rejection before effective immunosuppressant drugs became available.<sup>26</sup> Moreover, BT has been associated with cancer recurrence and death in patients with malignancy. Although, the utilization of universal leukoreduction has been recommended to reduce the rate of febrile nonhemolytic transfusion reactions, the risk of viral transmission, and the unresponsiveness of platelet transfusion after previous alloimmunization, it does not appear to play a role in the risk for cancer recurrence in specific subsets of surgical patients.<sup>30</sup>

Therefore, unnecessary blood transfusions should be avoided to further reduce the risk for infection and other complications. Indeed, there is a clear medicine based evidence of the shortcomings of BT in the setting of heart surgery. The evidence that BT carries significant risks points out to avoid BT when possible. In this context, Rawn JD from Harvard Medical School stated that "the experience with

Jehovah Witnesses demonstrates that when a commitment is made to avoid blood transfusion, the effort is successful in the vast majority of cases. Recognition that blood transfusion poses significant risk for what is frequently an uncertain benefit can inspire a similar level of commitment.<sup>21</sup>

## Conclusion

In conclusion, even one unit of blood transfusion during and immediately following heart surgery has been shown to be significantly associated with immediate and long-term adverse clinical outcomes, including increased infection, myocardial infarction, stroke, renal failure, prolonged ventilation and hospital stay, atrial fibrillation, multi-organ failure and death, as well as, increased overall healthcare costs. This is a serious call for attention to the medical community and a scientific motivation to perform a detailed and conscious revision of our routine daily medical practice.

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## Conflicts of interest

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