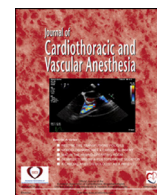




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Editorial

Caring for Jehovah's Witness Patients Undergoing Complex Cardiac Surgery

The transfusion of blood products is common in cardiac surgery. Jehovah's Witness (JW) patients generally do not accept the transfusion of "primary blood components" including allogeneic red blood cells (RBCs), platelets, and fresh frozen plasma on religious grounds. Cardiac surgery in patients refusing blood products represents a unique challenge for the cardiovascular anesthesiologist and intensivist, potentially resulting in a conflict between the patient's independence and the physician's duty to save the patient's life.¹⁻⁴ A recent review on the outcomes of cardiac surgery in JW patients concluded that the bloodless protocol for JW patients does not seem to significantly affect clinical outcomes when compared to non-JW patients with the possibility to transfuse blood products.² This conclusion was mainly based on 11 comparative studies including >750 JW patients undergoing cardiac surgery between 1990 and 2018.² Reported in-hospital mortality was 0%-to-19% in JW patients, and 0%-to-9% in control patients. Although there was no statistically significant difference in mortality within the included studies,² one study reported a 4- to 5-times higher in-hospital death rate in JW patients.⁵ Furthermore, Chambault and colleagues reported that morbidity including re-surgery for bleeding, acute kidney injury, stroke, and myocardial infarction, was similar or even higher in the controls as compared to JW patients.² Based on these findings, Chambault et al. suggested that the bloodless approach could potentially provide advantages to any patient undergoing cardiac surgery.²

In this issue of the *Journal of Cardiothoracic and Vascular Anesthesia*, Helwani, et al. presented their experiences with JW patients undergoing cardiac surgery at their institution over a 20-year period in a retrospective cohort analysis.⁶ They identified 48 adult JW patients, who were divided into a group with severe blood loss leading to anemia defined as any postoperative hematocrit <21% (n = 9) and a control group of patients with postoperative hematocrit ≥21% (n = 39). Postoperative anemia was associated with increased mortality at 30, 90, and 365 days after surgery and a trend to increased length of hospital stay.⁶

The findings of the present study are of interest, as they partially questioned previous data that cardiac surgery in JW patients might be as safe as in non-JW patients.² In agreement with formerly reported survival,² 1-year mortality was 0% in the group with postoperative hematocrit >21% in the present study. On the other hand, patients with hematocrit <21% had significantly worse outcomes, resulting in a 3-month mortality of 44%. In 3 out of 4 deaths, severe anemia appeared to be directly associated with cause of death (ie, stroke, multiorgan failure, cardiogenic shock).⁶ This raises the question as to the safety margin of postoperative hemoglobin values. In 2 large randomized controlled studies including 7,250 patients, cardiac surgery patients were randomized to a liberal and a restrictive transfusion strategy.⁷⁻⁹ In the Transfusion Requirements in Cardiac Surgery-III (TRICS-III) trial, patients were transfused with RBC when hemoglobin was <7.5 g dL⁻¹ in the restrictive group or when hemoglobin fell below 9.5 g dL⁻¹ in the intensive care unit and below 8.5 g dL⁻¹ on the ward in the liberal group.^{7,9} In the Transfusion Indication Threshold Reduction (TITRe-2) trial, RBCs were transfused with a hemoglobin level of <7.5 and <9.5 g dL⁻¹ after on-pump cardiac surgery in the restrictive and the liberal group, respectively.⁸ Both studies found no differences in mortality and major morbidity after 30 days between the 2 groups. However, the TITRe-2 study reported favorable survival after 90 days with the liberal transfusion strategy. In contrast, TRICS-III found no differences between the 2 groups after 6 months.¹⁰ Furthermore, younger patients seemed to have a better survival rate with liberal transfusion in both studies. When compared with the present study by Helwani et al.,⁶ the lowest hemoglobin values were relevantly lower in the acute bleeding group as compared to the restrictive groups in TRICS-III and TITRe-2. We might not exactly know the lowest hemoglobin values in the Helwani study, as measurement frequencies might have been reduced for blood-sparing reasons or due to missing consequences of very low hemoglobin values. Unfortunately, Helwani, et al. could not provide data on end-organ ischemia such as, for example, increased lactate values or low near-infrared spectroscopy values in the acute bleeding group.^{6,11} Furthermore, the exact mechanism of anemia in the present study was not clear.

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Obviously, increased blood loss during and after surgery might be the most common etiology. However, massive hemodilution might also have contributed to low hemoglobin values but not necessarily to reduced RBC mass.

What can perioperative physicians learn from this study? Jehovah's Witness patients have proved to be the ideal candidates for patient blood management (PBM)^{12,13} without an option to transfuse. Patient blood management aims to avoid unnecessary RBC transfusion by multiple interventions, thereby eventually improving patient outcome.¹¹ A strict PBM protocol, as suggested by recent guidelines,^{12,13} might allow for bloodless cardiac surgery even in patients at highest risk for bleeding.¹⁴ In JW patients, preoperative improvements of RBC mass and perioperative optimization of hemostasis seem to be most important. In a recent study including 137 JW patients undergoing different cardiac surgical procedures, successful hemoglobin optimization by adding iron/vitamins or erythropoietin to achieve a target hemoglobin $>12 \text{ g dL}^{-1}$ in combination with timely discontinuation of antiplatelet and anticoagulant agents were associated with fewer adverse events and lower mortality as compared to "nonoptimized" JW patients.¹⁵ Importantly, total RBC mass rather than absolute hemoglobin values might be more relevant.¹⁶ Different strategies have been recommended and studied. The administration of combined intravenous iron and erythropoiesis-stimulating agents (ESA) might be the most promising.¹⁷ Different studies have shown that such a strategy could reduce the perioperative need for RBC transfusion in non-JW patients.¹⁷ However, most studies could not show an effect on morbidity or mortality.¹⁷ Finally, even with such elaborate strategies, increased hemoglobin values are not always achievable.¹ In the above-mentioned study, only 93 of 137 patients (68%) achieved a preoperative hemoglobin value $>12 \text{ g dL}^{-1}$ despite interventions to improve RBC mass.¹⁵ Limitations in the preoperative treatment time must also be kept in mind,¹⁷ often leading to insufficient hemoglobin optimization. The worse outcome of patients with urgent surgery in the present study⁶ might be, at least, partially explained by such facts. It remains unclear whether nonanemic JW patients should be treated with ESA and/or intravenous iron before cardiac surgery. Total RBC mass should be kept in mind,¹⁶ as well as potential side effects of intravenous iron and ESA.¹⁷ However, given that most deaths in the present study might have been directly related to end-organ ischemia, means to increase RBC mass should potentially be considered also in nonanemic JW patients, especially in those undergoing complex cardiac surgery.

Of note, recent advances in PBM, such as coagulation management guided by viscoelastic testing,¹²⁻¹⁴ might not have been available or common in the early phase of the Helwani et al. study.⁶ Again, it would be interesting to know whether patient outcome has improved over the years. However, such an analysis might be limited by the low number of included patients in the Helwani et al. study.⁶

In summary, many JW patients can undergo major surgery by implementing a strict PBM protocol without an option to transfuse, but they may be at an increased risk of death in the case of extensive bleeding after complex cardiac surgery.

Preoperative optimization of RBC mass, intraoperative blood conservation, and meticulous hemostasis techniques are crucial. Over the years, different treatment options, such as ESA or factor concentrates, have become available, and are acceptable for many JW patients. The use of hemoglobin-based oxygen carriers as treatment options in JW patients has recently been described,¹⁸ but its availability is severely limited. In the future, additional treatments, such as platelet substitutes, might become optional for JW patients.¹⁹ Lastly, a minimally invasive cardiovascular surgical approach holds promise in lowering transfusion risk,²⁰ but PBM remains the guiding principle in optimizing overall clinical outcome.

Conflict of Interest

None.

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