Priming Cardiopulmonary Bypass in Pediatric Surgery: Comment

To the Editor:

We read with great interest the article of Dieu *et al.*[1] regarding cardiopulmonary bypass (CPB) priming strategy in pediatric cardiac surgery. In this double-blind randomized controlled study, the authors reported that priming with fresh frozen plasma or balanced crystalloids does not result in a different risk of postoperative bleeding and transfusion of allogeneic blood components. The authors clearly have to be congratulated for addressing a very relevant clinical question in a study with a high level of methodologic quality. However, several points need to be taken into account when interpreting the reported results.

First, the studied population is probably not at a high risk of postoperative bleeding requiring the transfusion of hemostatic agents such as fresh frozen plasma. Indeed, most patients enrolled in the trial were small children (above 1 yr of age) undergoing low- to moderate-risk surgery (Risk Adjustment for Congenital Heart Surgery score, 1 to 3), whereas neonates and infants with cyanotic disease have been shown to be especially at higher risk of significant postoperative blood loss.[2] The results of the present study do not help to define the best CPB priming strategy in these high-risk populations.

Second, the authors decided to treat all the blood remaining in the circuit after CPB weaning with a cell saver, eliminating platelets and coagulation factors in the autologous blood retransfused to the patients. The use of cell salvage has been recommended to reduce perioperative transfusion.[3] However, to our point of view, because one of the primary outcome of this study was postoperative bleeding, it would have been more rational to use ultrafiltration and/or modified ultrafiltration to reduce the positive fluid balance at the end of surgery, thus keeping coagulation factors in the autologous blood returned to the children. Also, the authors stated that the cell salvage blood at the end of the procedure could be administered when necessary: could it be that this autologous blood was discarded in some patients?

Third, there is some evidence that adding albumin to CPB priming could be beneficial for the patient in terms of perioperative fluid balance and weight gain. As demonstrated in several randomized controlled studies, 6% hydroxyethyl starch 130/0.4 could be a cost-effective alternative to albumin for CPB priming in pediatric cardiac surgery.[4–6] Although we could agree that the evidence in favor of hydroxyethyl starch is not as high, there is also no clear evidence from the literature proving that a balanced crystalloid solution is effective and safe in this population.

Fourth, the authors advocated the double-blind design to justify the systematic transfusion of packed erythrocyte in the CPB prime. The author stated that the minimum desired hematocrit during CPB was 30% for patients with cyanotic heart disease and 25% for those with noncyanotic heart disease, which is not fully in line with actual transfusion guidelines in the field of pediatric patient blood management.[3] Could it be that some patients received allogeneic blood in the CPB, although they should have achieved the desired hematocrit without transfusion? Also, the transfusion triggers used in the postoperative period are much higher than those actually recommended.[3,7] To alleviate the problem regarding the maintenance of the double-blind design, the authors might have stratified the studied population according to the size of the CPB circuit, allowing study of a much broader population.

Because of these different elements, we think the study of Dieu *et al.*[1] addresses the problem only partially, and further works are required to help clinicians in defining the best strategy to manage CPB priming in pediatric cardiac surgery.

Competing Interests

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Priming Cardiopulmonary Bypass in Pediatric Surgery: Reply

In Reply:

We thank Dr. Schmartz *et al.*[1] for their interest in our randomized clinical trial comparing fresh frozen plasma *versus* crystalloid for priming cardiopulmonary bypass (CPB) circuit in pediatric surgery.[2] The authors are right in noting that our studied population does not belong to the group of patients at the highest risk of postoperative bleeding, *i.e.* neonates and small infants. However, up to now, no single double-blind study has evaluated this issue in older infants and small children. From an ethical point of view this question needed to be analyzed in this population before conducting a similar study in a very high-risk population. As a matter of fact, the recent published guidelines on patient blood management in pediatrics undergoing cardiac surgery concluded that in infants and children, no recommendations can be made regarding the addition of fresh frozen plasma to the CPB because of the absence of evidence in the matter.[3]

Dr. Schmartz *et al.* ask why we did not use conventional and/or modified ultrafiltration that both help in preserving the coagulation factors in the autologous blood returned to the children. Ultrafiltration techniques are routinely performed in many centers performing congenital heart surgery. These techniques, especially modified ultrafiltration, have shown many advantages including reduced positive fluid balance and reduced transfusion of allogeneic blood products.[4] However, studies showing benefits from modified ultrafiltration are all greater than 10 yr old,[4] and it has been shown that modified ultrafiltration is no longer necessary when small circuit sizes and priming volumes are used.[5] In addition, modified ultrafiltration can result in significant complications.[5] We routinely use normothermic CPB with warm blood cardioplegia. We therefore do not apply modified ultrafiltration and use conventional ultrafiltration only sporadically. At this stage the administration of cell salvage is the best option in our population.

Dr. Schmartz *et al.* ask whether cell-salvage blood was discarded in some patients. This question refers to our statement that cell-salvage blood at the end of procedure could be administered when necessary. We of course did not discard this autologous blood, but the administration took place either in the operating theatre or in the intensive care unit whenever it was necessary.

Dr. Schmartz *et al.* point out that there is no clear evidence from the literature that the balanced crystalloid as used in our trial is as effective and as safe as balanced hydroxyethylstarch solutions. We have highlighted in our manuscript why we opted not to use hydroxyethylstarch solutions. A meta-analysis of randomized controlled trials in pediatrics has moreover shown that these solutions significantly decrease platelet count as compared with other fluids.[6] This may result in increased postoperative bleeding and would have adversely influenced our results. Moreover, comparing fresh frozen plasma to a solution that is not the standard of care in our hospital would not have been approved by our local ethical committee.

Dr. Schmartz *et al.* note that our perioperative transfusion trigger for red blood cells is higher than what is currently recommended.[3] These current guidelines are based on two randomized studies.[7,8] Both studies were conducted with moderate to deep hypothermic CPB, and the randomization was aimed to obtain a hematocrit level of 20% *versus* 30%[7] or 25% *versus* 35%[8] at the onset of low-flow CPB. The question is whether the results of these studies can be extrapolated to our normothermic CPB management. Interestingly, the same group combined the data from these two trials to investigate the relationship between continuous hematocrit levels and postoperative outcomes.[9] They concluded that a hematocrit level at the onset of low-flow CPB of approximately 24% or higher is associated with higher Psychomotor Developmental Index scores and reduced lactate levels. Kussman *et al.*[10] analyzed the regional cerebral oximetry data of the trial that compared a hematocrit of 25% with a hematocrit of 35%.[8] They showed that perioperative periods of decreased cerebral oxygen delivery, as indicated by cerebral oximetry, are associated with lower Psychomotor Developmental Index scores and greater risk of hemosiderin on brain magnetic resonance imaging. We routinely use intraoperative regional cerebral oximetry and treat any cerebral oxygen desaturation based on established algorithms. We therefore have higher transfusion criteria.

Dr. Schmartz *et al.* assert that we should have included a broader population by stratifying the studied population according to the size of CPB circuit. As stated earlier, we aimed to investigate the CPB prime strategy in older infants before conducting the same study in neonates and younger infants. In conclusion, we agree that further well conducted studies are required in higher-risk patients. Meanwhile, our group has answered an important clinical question in a specific category of pediatric patients undergoing open heart surgery.

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Competing Interests

The authors declare no competing interests.

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