Title

Response: Postoperative Acute Kidney Injury and Blood Product Transfusion After Synthetic Colloid Use During Cardiac Surgery

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analysis and the large volume of higher quality evidence indicating harms of HES that have warranted regulatory restrictions and warnings. Overall, the outcomes of this retrospective observational study are of little value when a randomized controlled trial could have been feasable in elective cardiac surgery for adults undergoing coronary artery bypass grafting and/or valve replacement.

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Response: Postoperative Acute Kidney Injury and Blood Product Transfusion After Synthetic Colloid Use During Cardiac Surgery

To the Editor:

We thank Dr. Reinhart for his thoughtful comments on our publication titled "Postoperative AKI and Blood Product Transfusion After Synthetic Colloid Use During Cardiac Surgery."[1] In his letter, Dr. Reinhart highlights his concerns on study design and statistical methods used in this retrospective study. He also questioned the acute kidney injury (AKI) criteria from the Society of Thoracic Surgeons (STS). We agree with Dr. Reinhart that intraoperative synthetic colloid use still is controversial. However, the Food and Drug Administration warning was based on intensive care unit use in the critically ill patient population with high-volume synthetic colloid. Studies did not identify any differences in

the incidence of death or AKI in cardiac surgical patients receiving intraoperative synthetic colloid.[2–8]

Dr. Reinhart's group published a prospective study in 6,478 consecutive cardiac surgical patients.[9] With propensity matching, predominant use of hydroxyethyl starch (HES) 130/0.4 was associated with increased utilization of renal replacement therapy. He also cited a meta-analysis of 15 randomized trials with fewer than 1,000 patients evaluating perioperative HES administration; renal replacement therapy was increased by HES solutions as a class. Dr. Reinhart and his colleagues, based on these results, recommended a complete avoidance of HES solutions such as HES 130/0.4 in cardiac surgery.[10]

Dr. Reinhart and his colleagues have ignored the majority of the studies using synthetic colloid in cardiac surgery. Most of the studies referenced in his letter to the editor were not carried out in the cardiac surgical patient population. On the contrary, the majority of studies in the cardiac surgery population failed to find an association between the use of HES and postoperative AKI, blood loss, and mortality.[4–7] Even the HES 130/0.4 or 130/0.42 raw material has been studied and did not have a significant influence on perioperative blood loss. Moreover, the authors did not find any effect of tetrastarch raw material composition on short- and long-term renal function.[8]

The effects of HES use in cardiac surgery also have been studied in the pediatric population. Intraoperative use of HES was associated with a less positive fluid balance.[2,11–13] Perioperative hemostasis, blood loss, volume of red blood cells, and fresh frozen plasma administered, as well as the number of children who received transfusions, also were significantly lower in the HES group. No difference was observed regarding the incidence of postoperative renal failure requiring renal replacement therapy, morbidity, or mortality, especially with the intraoperative use of 6% HES 130/0.4 up to 30 mL/kg.[11–13] These results confirm that the use of HES for volume replacement in children during cardiac surgery with cardiopulmonary bypass is as safe as albumin. In addition, its use might be associated with less fluid accumulation.[12]

Another comment from Dr. Reinhart is about the AKI criteria we used in our study. Because we studied the effect of HES on postoperative AKI in cardiac surgical patients, we believe it is most appropriate to use STS criteria, and the STS definition is a more stringent definition adapted and modified from the failure stage of the Risk, Injury, Failure, Loss, End (RIFLE) criteria. However, there are studies that use other AKI criteria to evaluate postoperative AKI. In a recent study of 1,500 patients, the authors found that the use of HES 6% 130/0.4 for volume replacement had no association with the 30-day mortality and renal replacement therapy, even based on RIFLE classification, as Dr. Reinhart recommended, if the hydroxyethyl starch 6% 130/0.4 fluid were kept below 30 mL/kg,[14] which none of our patients exceeded. In another meta-analysis of 17 randomized studies with a total of 1,230 patients evaluating renal safety of hydroxyethyl starches 130/0.40 in surgical patients (9 of the 17 studies were in cardiac surgery), no evidence for renal dysfunction was observed using RIFLE and Acute Kidney Injury Network classifications.[2]

Abnormal bleeding occurs in more than 10% of patients undergoing cardiac surgery.[15] First-generation HES solutions are associated with increased bleeding and coagulopathy; however, recent evidence suggests that the effects of modern third-generation HES solutions on coagulation are similar to those of albumin and crystalloids in patients undergoing surgery.[15] Data from several large studies have demonstrated that third-generation HES solutions have greatly improved and do not increase risk of kidney injury, blood loss, transfusion, coagulopathy, or mortality in cardiac surgical patients.[15–17] Another study demonstrated that the administration of tranexamic acid in HES 130/0.4 prime solution study group decreased estimated blood loss and chest tube drainage in comparison to patients receiving Ringer prime solution with or without tranexamic acid postoperatively.[5] Even gelatins have a safety profile that is noninferior to crystalloids.[17] It has been suggested that third-generation HES solutions are safe and effective for plasma volume expansion during cardiac surgery.[15]

The other comments from Dr. Reinhart were on the study design and statistical methods used in this study. Our study clearly defined the study goals of comparing 2 different types of 6% HES and their effects on the development of postoperative AKI and the need for blood product transfusion in comparison to patients who did not receive HES. We used the propensity score methods, which allow one to design and analyze observational studies transparently.[1] A propensity-weighted and risk adjusted logistic regression model (using inverse probability of treatment weighting [IPTW]) was used in this study. Therefore, all the patients have a final propensity score. As per Austin's recent work, the IPTW is the best single method, because stratification requires careful attention to caliper widths to ensure that that important differences are not retained inadvertently within each stratum.[18] As we stated in the original study,[1] the following risk factors were entered in the model development as candidate variables for predicting postoperative outcomes with inverse propensity weighting of intraoperative colloids use: total HES/Voluvan/Hextend, age, sex, race, category of surgeries, emergency status, chronic kidney disease stage, crystalloids, body mass index, smoking, cerebrovascular accident, cerebrovascular disease, cardiogenic shock, circulatory arrest, previous cardiovascular intervention, previous coronary artery bypass graft, previous valve surgeries, other cardiac intervention, dialysis, last creatinine level, previous myocardial infarction, congestive heart failure, intra-aortic balloon pump, ejection fraction, and left main coronary artery disease. We believe that the statistical methods used in our study were the most vigorous methods for this type study.

In summary, the results from our study together with a large body evidence from other published studies as we presented here have suggested that the third-generation HES solutions have a better safety profile than the old generation HES solutions and do not increase the risk for postoperative kidney injury, blood loss, transfusion, or mortality in cardiac surgical patients.

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Transcatheter Aortic Valve Replacement With TandemHeart Support in a Patient With Cardiogenic Shock

To the Editor

Mechanical circulatory support devices are a new and developing class of therapy that requires unique and novel collaborations among cardiology, anesthesiology, and cardiac surgeons. In our recent case involving a 67-year-old male who presented in multisystem organ failure due to cardiogenic shock and was found to have severe aortic stenosis, moderate aortic insufficiency, and left ventricular thrombus, we gained experience working with maximal pharmacologic therapy, TandemHeart (Cardiac Assist, Inc, Pittsburgh, PA), percutaneous balloon aortic valvuloplasty, transcatheter aortic valve replacement, and an Impella device (Abiomed, Danvers, MA) for circulatory support.

A review by Nagpal et al delineates the criteria used to select appropriate circulatory support for these challenging patients. While the classic intra-aortic balloon pump, is easily inserted peripherally and is not anticoagulation dependent, we have many new and complex options. The Impella permits increased support up to 5-L/min with newer devices and off-loads the struggling left ventricle. However, it does require full anticoagulation, only allows single ventricle support per unit, and carries significant risk of hemolysis.[1] The TandemHeart has similar flow capacities to the Impella, yet it can also provide oxygenation support and is more forgiving of breaks in anticoagulation. It, similar to the abovementioned devices, requires frank immobility and a transseptal puncture by skilled, experienced interventionists.[1] TandemHeart and Impella have been demonstrated to produce up to 4.5-L/min of cardiac output in patients with cardiogenic shock.[2] However, when full support is mandatory, CentriMag (Thoratec, Pleasanton, CA) and extracorporeal membrane oxygenation are the only options. CentriMag allows patient mobility while supporting both ventricles and providing potential long-term support but requires surgical insertion and removal.[1]