



Letters to the Editor

Assessing cardiac and kidney protective effects by remote ischemic preconditioning in cardiac surgery patients



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With great interest, we read the recent article published by Pinaud and colleagues [1] assessing cardiac and kidney protective effects by remote ischemic preconditioning in patients undergoing aortic valve surgery without coronary artery bypass grafting. They showed that remote ischemic preconditioning did not produce any protection against the postoperative acute myocardial cardiac and kidney injuries. Many things of this study were well done. Other than strict inclusion and exclusion criteria of patients, the authors had also tried to control most of the known risk factors that can affect acute cardiac and kidney injuries following cardiac surgery. Given acute myocardial and kidney injuries are associated with increased morbidity and mortality following cardiac surgery, we thank the authors for their endeavor to validate the protective efficiency of remote ischemic preconditioning on the vital organ injuries by conducting a randomized controlled clinical trial. However, we would like to ask some questions about their methodology.

First, as a preoperatively routine laboratory variable, preoperative hemoglobin level was not included in baseline characteristics of the study population. It has been shown that preoperative anemia is common among patients undergoing cardiac surgery and is associated with independently increased risks of postoperative adverse myocardial and renal events [2]. Furthermore, preoperative anemia has been independently associated with acute kidney injury following cardiac surgery.

Second, besides total cardiopulmonary bypass time and aortic cross-clamp time, we were not provided with other intraoperative risk factors affecting postoperative myocardial and kidney injuries, such as hemodynamic instability, hemodilution during cardiopulmonary bypass, blood transfusion, number of defibrillations, and need for placement of intra-aortic balloon pump. It has been

shown that postoperative myocardial injury correlates with changes in blood pressure and heart rate during cardiac surgery [3]. Furthermore, perioperative blood transfusion is associated with increased troponin I release after cardiac surgery. In addition, anemic patients presenting for cardiac surgery are more susceptible to transfusion-related acute kidney injury than nonanemic patients [4]. In particular, combination of intraoperative hemodilution anemia and hypotension can synergistically act to increase the risk of acute kidney injury after cardiac surgery. We are concerned that existence of any imbalance in the above risk factors would have confounded interpretation of their results.

Finally, in this study, acute kidney injury was defined according to the Acute Kidney Injury Network criteria as an increase in serum creatine level by more than 50% or more than 0.3 mg/dL from baseline within 72 h after surgery. However, the Acute Kidney Injury Network criteria require the use of a 48-h time window. Moreover, it was unclear whether the postoperative serum creatine level measured in this study had been corrected based on perioperative fluid balance. The data suggest that the Acute Kidney Injury Network criteria applied in cardiac surgery patients without correction of serum creatine level for fluid balance may lead to overdiagnosis of postoperative acute kidney injury, viz., a poor positive predictive value [5]. Thus, we cannot exclude the possibility that these factors would have confused incidence of postoperative acute kidney injury reported in this study.

Authors' contributions

Yi Liu had carefully read the manuscript of Pinaud *et al.*, analyzed their methods and data, suggested the comment points, and drafted this manuscript.

Fu-Shan Xue and **Rui-Ping Li** had carefully read the manuscript of Pinaud *et al.*, analyzed their methods and data, revised comment points and this manuscript, and the author **Fu-Shan Xue** is responsible for this manuscript.

Chao Sun had read the manuscript of Pinaud *et al.*, and helped to analyze their methods and data, and revise the comment points. All the authors have seen and approved the final manuscript.

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Yi Liu (MD)

Department of Anesthesiology, Shanxi Province Tumor Hospital,
Taiyuan and Wujiaqu People's Hospital, Wujiaqu City, Xinjiang, China

Fu-Shan Xue (MD)*

Rui-Ping Li (MD)

Chao Sun (MD)

Department of Anesthesiology, Plastic Surgery Hospital, Chinese
Academy of Medical Sciences and Peking Union Medical College,
Beijing, China

*Corresponding author at: Department of Anesthesiology, Plastic
Surgery Hospital, Chinese Academy of Medical Sciences and Peking
Union Medical College, 33 Ba-Da-Chu Road, Shi-Jing-Shan District,
Beijing 100144, China. Tel.: +86 13911177655;
fax: +86 10 88772106

E-mail addresses: xuefushan@aliyun.com,
fushan.xue@gmail.com (F.-S. Xue).

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Author's reply



We appreciate the interest and comments from Dr Liu and colleagues about our recently published RIPValve study [1]. We fully agree that many confounding factors may alter potential beneficial effects of conditioning strategies in the context of cardiac surgery. Among them, preoperative anemia is indeed known to influence the incidence of adverse cardiac and kidney events. In the RIPValve study, baseline hemoglobin concentration was not significantly different in both groups [13.5 ± 1.6 g/dL vs. 13.3 ± 1.6 g/dL in control and remote ischemic preconditioning (RIPC) groups, respectively]. Regarding other intraoperative parameters that may affect cardiac and kidney injuries, none was significantly different between groups: hemodynamic data, spontaneous resuscitation, number of defibrillations, number of blood

transfusions, etc. Of note, none of these low-risk patients experienced intra-aortic balloon pump implantation.

In a study recently published in *JAMA*, Zarbock and colleagues reported that RIPC significantly reduced the rate of acute kidney injury (AKI) and use of renal replacement therapy in high-risk patients undergoing cardiac surgery [2]. In this population, AKI occurred in 53% of the patients from the control group and in 37% of the patients receiving RIPC. Beside the definition of AKI, we believe that our population was at too low risk to take large advantage of RIPC in both kidney and heart (normal ejection fraction, short aortic cross-clamp duration in isolated aortic valve surgery, normal preoperative renal function). It is important to note that the large-scale multi-center ERICCA trial (ClinicalTrials.gov NCT01247545) testing RIPC in 1612 patients undergoing elective cardiac surgery, which presented preliminary results at the late breaker session of the American College of Cardiology Scientific Sessions 2015 [3] found no benefit of RIPC regarding AKI.

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Frédéric Pinaud (MD, PhD)

Jean-Jacques Corbeau (MD)

Christophe Baufreton (MD, PhD)

Jean-Patrice Binuani (MD)

Jean-Louis De Brux (MD)

Olivier Fouquet (MD)

Denis Angoulvant (MD, PhD)

Alain Furber (MD, PhD)

Fabrice Prunier (MD, PhD)*

Université Angers, “Cardioprotection, Remodelage, Thrombose”,
Angers, France

*Corresponding author at: Université Angers,
“Cardioprotection, Remodelage, Thrombose”, EA 3860,
rue Haute de Reculée, FR-49045 Angers, France.

Tel.: +33 241 355 147; fax: +33 241 354 004

E-mail address: faprunier@chu-angers.fr (F. Prunier).

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