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Anesthesiology. Author manuscript; available in PMC 2017 August 01.

Published in final edited form as:

Anesthesiology. 2016 August ; 125(2): 438–439. doi:10.1097/ALN.0000000000001190.

Platelet Counts, Acute Kidney Injury, and Mortality After Coronary Artery Bypass Grafting Surgery

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We appreciate comments from Drs. Hui and Yu regarding our published manuscript titled "Platelet Counts, Acute Kidney Injury, and Mortality after Coronary Artery Bypass Grafting Surgery."[1] The letter indicated that "despite the elaborate statistical analysis and the innovative perspectives" they were concerned over "the study design and the interpretation of statistical results" of our study. More specifically, the letter highlighted that information on perioperative blood loss was not included in the logistic regression analysis, and "suggest focusing more attention on perioperative blood loss, rather than platelets reduction in future research studies on postoperative acute kidney injury." In support of their statement, Drs. Hui and Yu critiqued that significant blood loss is an independent risk factor for postoperative acute kidney injury (AKI) and in-hospital mortality after cardiac surgery. However, all studies cited in support of their statement did not directly test blood loss as a predictor of AKI. For example, one study defined significant blood loss as a need for large volume of blood transfusion (administration of ≥ 5 units of packed red blood cells within 1 day of surgery);[2] another reviewed risk factors and management of AKI without discussing the role of blood loss for predicting perioperative AKI;[3] or was conducted in patients undergoing non cardiac surgery and investigated the role of perioperative hemoglobin as a predictor of AKI;[4] and, the last citation, was a meta-analysis of studies about the effects of perioperative hemodynamic optimization for postoperative renal dysfunction.[5] Whereas

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The authors declare no competing interests.

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several studies have found transfusion and anemia to be associated with AKI in cardiac surgery, none have addressed blood loss itself as a predictor.[6-8] Further, the incidence of major bleeding requiring reoperation after elective coronary artery bypass grafting surgery is reported to be around 2.1%,[9] and therefore given this low incidence it is unlikely that major bleeding and/or blood loss accounted for a higher risk for acute kidney injury in our study. In addition, accurate measurement of blood loss intraoperatively in cardiac surgery with use of cardiopulmonary bypass has limitations. Similarly, chest tube outputs after surgery is not a reliable method of capturing blood loss because the hemoglobin content in the chest tube is not measured.

Drs. Hui and Yu also alluded that our study did not explore the functions of the whole set of serum coagulant components on AKI from a “broader view, other than focusing on the single variable of platelet count.” Again, in support of their statement, they reference two studies conducted in nonsurgical populations- one on increased fibrin formation and impaired fibrinolysis capacity in severe chronic kidney disease,[10] and the other, on the role of tissue factor and coagulation factor VII levels in patients with acute myocardial infarction.[11] We are not aware of any studies to date to indicate that increased fibrin formation, impaired fibrinolysis capacity, tissue factor or coagulation factor VII levels play a significant role in the development of postoperative AKI after cardiac surgery. Further, many of these factors of coagulation are not routinely measured during and after cardiopulmonary bypass in patients undergoing cardiac surgery. On the contrary, previous studies indicated that contact activation during and after cardiopulmonary bypass can lead to formation of circulating microaggregates (adhesions among leukocytes, activated platelets, and endothelial cells), and along with persistent thrombin generation, microaggregates may produce ongoing microvascular plugging that manifest clinically as end-organ injury such as AKI.[12] The involvement of activated platelets in the formation of these microaggregates can manifest in the reduction in platelet counts as reasoned in our study. Thus, measuring intra- and postoperative platelet counts, which is readily available and is a routinely performed laboratory test in patients undergoing cardiac surgery, may be used as an indicator of ongoing platelet activation/consumption that may prognosticate end-organ injury such as AKI.

Finally, the letter suggests, “readers to keep alerted of the conclusions” of our study “in order to avoid over reliance in the statistical results while neglecting the possible biologic implausibility.” It should be noted first that our hypothesis and our analysis strategy sought to reveal the independent effect of postoperative thrombocytopenia, separate from any overlap with patient- and procedure-related effects. Thus, using contemporary statistical methods for adjusting for those covariable effects on outcome is critically important. Second, as also highlighted in the accompanying editorial to our article,[13] platelets reflect biologic complexity of poorly buffered inflammation, and in depth research of that biocomplexity may allow hypothesis-driven studies to sprout out from the findings of our observational study. Of note, we agree that since we were not able to measure markers of inflammation and microthrombosis in our current study, future studies that are prospective in design and of sufficient size are needed to define the context of platelet activation, thrombocytopenia, and inflammation related ischemic complications in coronary artery bypass grafting surgery.[1]

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