also present in the other studies on this subject. In addition, physicians in the trial could decide to give a blood transfusion out of protocol in life-threatening situations.

We agree with Drs. Hall and Sharifpour that there is still a shortage of robust evidence from large RCTs that leukodepleted blood and shorter duration of blood storage can improve outcomes in surgical patients. As mentioned in the article, we agree with Dr. Sharifpour that despite the apparent benefits of a liberal strategy of erythrocyte transfusion in cancer patients undergoing abdominal surgery on short-term outcomes, the effects of this therapy on long-term outcomes such as cancer recurrence are not known.

As pointed out by von Heymann *et al.*, anemia may represent a heavy burden in oncologic patients with severe comorbidities and a substantial postoperative risk. Our RCT clearly showed that in a well-balanced population of cancer patients, a restrictive strategy of postoperative transfusion was associated with worse outcomes after abdominal surgery. This specific group of patients may not adapt well to anemia, presenting a higher incidence of complications, including 30-day cardiovascular events and mortality. Our results are in agreement with other data reported in the literature.

Competing Interests

The authors declare no competing interests.

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(Accepted for publication May 21, 2015.)

Heparin for Cardiac Surgery: Old and Forgotten?

To the Editor:

We read with interest the article by Karkouti *et al.*[1] published in the March 2015 issue regarding a transfusion algorithm based on point-of-care coagulation tests in cardiac surgery.

We wish to shed light on an issue that was not touched upon in the article but represents the first step in their algorithm and, without dispute, the first and most important single intervention in managing postcardiopulmonary bypass coagulopathy.

The dose of the heparin neutralization by protamine is shown in the algorithm as a ratio of milligrams to milligram. It has long been recommended that heparin should not be quantified in milligram, but in units.[2–4] In fact, to our knowledge, none of the currently available commercial heparins display its potency in milligram. This quantification of heparin in milligram introduces risk if the ordering physician is unfamiliar with the milligram to unit conversion.

The impression that 1 mg unfractionated heparin currently contains 100 units is widely accepted but dated and

erroneous. One milligram heparin has contained 130 units of heparin at least since the Second International Standardization in 1968.[2,5] More recently, after contamination issues, the Food and Drug Administration and U.S. Pharmacopeia have mandated a new reference standard for heparin, and 1 mg heparin now contains not less than 180 units.[6,7] We do not think this change in heparin formulation is recognized widely and hence advocating heparin use in milligram may lead to a variable interpretation and dosing.

Furthermore, the Society of Thoracic Surgeons and Society of Cardiac Anesthesiologists Practice Guidelines for Blood Transfusion and Conservation in Cardiac Surgery (2007, updated in 2011)[8,9] have recommend using either a low-dose protamine protocol (50% of heparin dose) or a titrated protamine dose guided by activated clotting time response testing to neutralize heparinization in the postcardiopulmonary bypass patient. Although the evidence in favor is not strong, we wonder if adherence to above guidelines may have impacted the data presented.

Advances in technology such as point-of-care coagulation testing should be embraced in a timely manner, but we must acknowledge that age-old drugs such as heparin and protamine have not yet been evaluated systematically in cardiac surgery.

Competing Interests

The authors declare no competing interests.

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(Accepted for publication June 15, 2015.)

In Reply:

We appreciate the letter by Bulatovic and Taneja on our study[1] and agree that it would have been more accurate to state heparin dose in units rather than in milligrams in our algorithm. We also agree that heparin management, which encompasses heparin dosing, monitoring of effect, and reversal with protamine, is an important component of cardiac surgery that is incompletely understood and requires further investigation. Given that our algorithm was not aimed at optimizing or even modifying heparin management, we made no attempts to alter or audit heparin management practice. The milligram to milligram representation of the protamine to heparin dose is consistent with a low-dose protamine practice.[2] Because heparin management at our institution was not altered with protocol implementation, this is not likely to have had an impact on our results.

Our algorithm was aimed at optimizing coagulation management by incorporation of point-of-care coagulation testing into routine practice, and the results suggest that we succeeded in reducing transfusions and some adverse outcomes. We are looking forward to the results of our large, multicenter study to see whether our findings are generalizable (ClinicalTrials.gov Identified NCT02200419).

Nevertheless, we do believe that additional benefits in coagulation management can be achieved by optimizing heparin management. We have noticed that in some of our patients who bleed unexpectedly, there is a profound deterioration in coagulation status, particularly platelet count and function, from rewarming to postprotamine periods, suggesting a contributory effect of protamine to the coagulopathy.[3] Perhaps, these patients would not have bled if heparin management was optimized by, for example, using mathematical models[4,5] or point-of-care heparin–protamine titration systems.[6]

We therefore agree with Bulatovic and Taneja that systematic studies on heparin management in cardiac surgery are required, as we do not seem to be much ahead of where we were in the 1970s.[7] Perhaps, with optimized heparin