Assessing Independent Effects of Anemia and Transfusion on Late Mortality

To the Editor:

In a retrospective analysis, Engoren and colleagues [1] showed that the anemia–transfusion interaction was associated with an increased risk of late mortality after coronary artery bypass graft surgery. The combined mortality risk of anemia and transfusion was nearly triple that of the nonanemic patient not receiving a transfusion. Furthermore, mortality risk associated with transfusion was increased in anemic patients compared with that in nonanemic patients. However, in this study 70 of the 922 operative survivors (8%) are dead in a long follow-up period, with a median duration of 2.45 years (interquartile range, 1.36 to 3.45 years). It is generally believed the mortality related to the surgery and anesthesia lasts only a month [2]. Thus, an important question is whether there is really a causal relation of perioperative anemia and transfusion with late mortality. Also, a limitation of this study is lack of evaluation for the association of perioperative anemia and transfusion with early mortality, which is more related to surgery and anesthesia than late mortality [2].

In general, early mortality after coronary artery bypass graft surgery is low [3]. In the longer term, the decline in patient survival most likely represents the natural process of aging [2]. In this study, patients who died are older and are more likely to have comorbidities. In our view, no matter how refined the adjustment is for differences in preoperative health status and comorbidities, it is never possible to ensure a complete adjustment for differences between decedents and survivors. Furthermore, Westenbrink and associates [4] demonstrate that postoperative anemia is common and frequently persists for months after coronary artery bypass graft surgery. When postoperative hemoglobin level is considered as a continuous variable, every 1 mg/dL decrease in hemoglobin level is associated with a 13% increase in adverse cardiovascular events and a 22% increase in all-cause mortality. Thus, statistical association of perioperative anemia and transfusion with late mortality in this study does not prove causality. We argue that late mortality more likely is attributable to the natural process of health status and pathologic developments of relevant morbidities.

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References

Reply

To the Editor:

Thank you for the opportunity to reply to Wang and colleagues [1]. They “argue that late mortality is more likely due to the natural process of health status and pathologic developments of relevant morbidities” and cite a Danish study comparing patients with osteoarthritis undergoing hip replacement surgery to the general population to suggest that mortality related to surgery and anesthesia lasts only 1 month [2]. In that study, however, the general population was sicker, particularly older patients with more cases of diabetes and cardiovascular and pulmonary diseases. The authors did not compare within the operative group to determine whether perioperative processes of care have an association with long-term outcomes, rather they found that healthier patients undergoing surgery live longer than sicker patients not undergoing surgery.

There is increasing evidence that perioperative processes of care and intermediate outcomes have an association with long-term outcomes. Small bumps in serum creatinine, even if postoperative creatinine levels return toward preoperative levels, are associated with increased long-term mortality after cardiac surgery [3]. Using bispectral index—a measure of cerebral suppression produced by general anesthesia—one study found that greater cerebral suppression was associated with increased mortality over the next several years [4]. While these studies and ours [5] are retrospective and can find only associations and not imply causation, a prospective randomized study evaluated the efficacy of removing versus not removing two units of autologous blood approximately 1 week before surgery for nonmetastatic colorectal cancer. Patients in both the autologous and control group received a transfusion, respectively, with autologous or homologous red cells for blood loss greater than 500 mL or hemoglobin less than 10.5 g/dL. When the authors compared patients without transfusion, the greater transient anemia in the predonation group than in the control group was associated with worse 20-year survival. The prospective design of this study suggests a causal role in a perioperative process of care, hemoglobin level, and late increased mortality [6].

Additional studies are needed to define how perioperative care affects long-term outcomes such as renal, cardiac, and cognitive function and mortality.

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