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Reply to the Editor:

We thank Dr McKay for her comments regarding our article. We examined the relative safety in off-pump coronary artery bypass grafting (CABG) of two volume replacement fluids in widespread use at the time we conducted our study.¹ Dr McKay argues that the questions we investigated are moot, that the fluids whose safety we investigated are not in widespread contemporary use, and that there were methodologic flaws in our study conduct. We will now address each of Dr McKay's arguments, showing that the choice between the volume replacement fluids we studied remains clinically relevant, that her methodologic concerns are overstated, and that our findings raise a series of further questions.

Dr McKay states that there is existing evidence demonstrating that use of high molecular weight (HMW) hetastarch, one of the fluids we studied, is associated in both cardiac and noncardiac surgery with greater blood loss than is either low molecular weight (LMW) hetastarch or albumin. Dr McKay offers two examples of prior studies of bleeding risk in cardiac surgery. Unfortunately, whereas we examined bleeding risk in off-pump CABG, the first of the cardiac papers Dr. McKay cites² investigated the impact of hetastarch and albumin as pump prime in on-pump cardiac procedures, and the second³ examined the impact of hydroxyethyl starch (Voluven), an LMW hetastarch, in orthopedic procedures. Generalization of findings from either of these studies to the risk posed by HMW hetastarch in off-pump procedures is at best problematic. The differences between the hemodynamic properties of on-pump versus off-pump cardiac procedures are well documented.⁴⁻⁷ McKay also cites two prior reviews of the risks associated with volume replacement fluids in noncardiac surgery. The first⁸ cites 10 studies of volume replacement that actually examined the effects of its use in cardiac surgery. All of these

studies of cardiac surgery examined on-pump procedures and/or other use of fluids and/or postoperative fluid administration. None of these studies examined perioperative administration of hetastarch versus albumin in off-pump procedures. The second cited article⁹ again examined only on-pump cardiac procedures. Perhaps Dr McKay inadvertently switched the citations to Gandhi³ and Wilkes⁹ and their associates. That second article⁹ was actually one of the sparks for our decision to investigate risks associated with volume replacement fluid use in off-pump procedures. Parenthetically, that second article is considered by many to have established that the particular formulation of hetastarch carries too high a bleeding risk for it to be used routinely for volume replacement in CABG procedures performed on-pump. We instead examined the bleeding risk carried by HMW hetastarch in off-pump procedures. Approximately 20% of the CABG procedures in 2007 were performed off-pump.¹⁰ We note that the recently published results of a large-scale randomized clinical trial that favor on-pump over off-pump procedures may impact this practice pattern, contributing to an increase in the relative frequency of on-pump procedures.¹¹

Second, Dr McKay was not clear regarding the hetastarch formulation used in our study. Our study examined Hextend, a formulation of HMW hydroxyethyl starch 6% in a buffered electrolyte dextrose solution. This composition of the test solution infused is identified on our article's first page, and its administration is discussed in the section describing randomization and sample size. We inadvertently omitted mentioning this fluid a second time in the Clinical Protocol section of our article. We apologize for any confusion this may have caused for Dr McKay or other readers. Participants were randomly assigned to receive an initial infusion of 1000 mL of Hextend or 1000 mL of albumin. Any subsequent infusions of

colloid used only albumin. These subsequent infusions were provided at the discretion of the attending physicians.

Dr McKay next asks about blinding and transfusion practices. This portion of the protocol is presented in the article's section on Power Analysis. Intensivists providing postoperative care were blinded to the fluids infused, but the anesthesiologists infusing the fluids were not blinded. We followed this protocol for several reasons. Current requirements in this era of regulatory compliance call for transparent intravenous tubing. Given that albumin and hetastarch fluids have different appearances, it would have been difficult to assure a blinded process in the clinical setting of the operating room even if we had somehow covered the 500-mL containers from which the fluid was being infused. Dr McKay also complains that we do not present standardized (protocol or goal-driven) fluid administration. Presuming that Dr McKay is referring to fluid administered after the first liter (administered per protocol and described in our article's Statistical Power Analysis section), we state later in that section that the remaining standard operative regimen of crystalloids and blood products in the perioperative period were administered at the discretion of the anesthesiologist. We note in the following paragraphs on Clinical Protocol that postoperative fluid management was at the discretion of the attending intensivist according to each patient's clinical status. The fluid management policy in both periods was selected so that our study could examine the impact of the initial fluid used for volume replacement on vascular outcome in patients receiving the careful care provided following the protocols otherwise used to guide care in nonresearch environments.

Dr McKay also questions what factors (beyond infusion of the randomly assigned fluid) explain the increased blood loss and transfusion requirement in members of the hetastarch branch. She proposes that the 287.2-mL

greater infusion of colloid in the initial preoperative preparation explains the 165.0-mL greater postoperative chest tube drainage and the 0.73-unit greater transfusion of packed red blood cells. The hypothesized mechanism for this effect is the greater volume of colloid causing expanded plasma volume, increased clotting factor dilution, decreased blood viscosity, and increased venous return and cardiac output. These mechanisms might be believable if the 287.2-mL increase was from a baseline of 0 mL. Instead, it represents a 24.1% increase from the 1192.3 mL of colloid administered to those in the albumin arm (see Table 1). Combining colloid with crystalloid and cell salvage, those in the hetastarch arm were infused with 4944.9 mL while those in the albumin arm were infused with 4693.7 mL, a difference of 251.4 mL or 5.4% of the volume of fluids administered in the perioperative period. We do not think this 5.4% difference in fluid administered is clinically significant. We also note that albumin was the only fluid administered after the first liter.

We agree with Dr McKay that the question of which fluids should be considered optimal for volume replacement in CABG procedures is not settled. We are now actively involved in designing further studies using associations with the outcomes examined in our study and other outcomes to examine the effectiveness and risks of using albumin versus other fluids in this clinical context. We trust that these and other studies will provide a methodologically sound evidence base that can be used to guide future clinical decision-making in this area.

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REGIONAL WALL MOTION ABNORMALITIES AND SCARRING IN SEVERE FUNCTIONAL ISCHEMIC MITRAL REGURGITATION: A PILOT CARDIOVASCULAR MAGNETIC RESONANCE IMAGING STUDY

To the Editor:

We read with interest Flynn and colleagues' article¹ concerning preoperative evaluation with cardiac magnetic resonance imaging (MRI) in patients undergoing coronary artery bypass grafting and mitral valve annuloplasty for ischemic mitral valve regurgitation (IMVR).

In our experience, cardiac MRI has been advocated for preoperative routine evaluation of patients with