Reply to the Editor:

We appreciate Ji and Undar's kind appraisal of our study on the benefits of pulsatile cardioplegia in failing hearts, because their input to the importance of pulsatile cardiopulmonary bypass is well recognized.¹ They propose that energy equivalent pressure (EEP) and surplus hemodynamic energy (SHE) should be reported when studying the effect of pulsatile flow, because the difference between EEP and mean arterial pressure (MAP) conveys the extra energy generated by each pulsatile wave. EEP and MAP are identical and the difference is zero when the pressure wave is perfectly harmonic.

Our study did not report those values,² because EEP and MAP were not significantly different for the waveforms used. A recent study by Huo and Kassab³ quantitatively demonstrated this point computationally, based on a full analysis of steady state versus pulsatile flow in the entire coronary arterial tree based on measured anatomical data and experimentally to validate the model. The inlet pressure waveform measured from a porcine model was input into an isolated heart to verify the model predictions and showed excellent agreement between the model and the experiment. Mean flow of both pulsatile and steady-state experiments and mathematical model were not statistically different and were consistent with normal heart microsphere measurements.² The EEP, MAP, and SHE were 75.38 mm Hg, 73.54 mm Hg and 1.84 mm Hg, respectively, providing only a 2.4% SHE/EEP ratio.

These calculations and this discussion reflect why our study did not focus on the EEP and SHE parameters. Rather, we believe that a different mechanism is at play because changes occurred only in failing hearts, because no significant changes were found between pulsatile and nonpulsatile cardioplegic flow existed in normal hearts. More importantly, vascular resistance rose in failing hearts in both the beating and cardioplegic states (with and without pulsation) such that factors responsible for initiating such pulsatility effect, such as altered number of vessels, lumen diameter, and vascular length, must be understood as ventricular geometry becomes expanded and spherical. This pulsatility dependency observation implies that dilated heart failure may have impaired coronary flow reserve capacity by limiting coronary autoregulation. This implication reinforces the

need to ensure increased perfusion pressure during myocardial protection strategies with the beating and pulsatile or nonpulsatile cardioplegia delivery.

Here, a method of pulsatile cardioplegia delivery was introduced to demonstrate the capacity to overcome this limitation of nonpulsatile cardioplegia in failing hearts. Our findings underscore the value of coronary pulsation, either by compression of vessels by the beating heart or by internal stretching by pulsatile cardioplegic flow. Our findings support the work of Undar relating to the significance of pulsatile flow in the use of cardioplegia for cardiac protection. Furthermore, our observations reinforce the importance of studying models that reflect clinical entities, such as heart failure, because the observed enhancement of subendocardial muscle perfusion would have gone undetected in studies of normal hearts.

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Note: The following *Reply to the Editor* refers to a letter to the editor published in a previous issue of the *Journal*: Kulik A, Rubens FD, Ruel M. Intraoperative indocyanine green angiography: Ready for prime time? *J Thorac Cardiovasc Surg* 2007;133:592-3.

Reply to the Editor:

We thank Dr. Kulik and colleagues for their interest in our prospective study comparing transit-time ultrasound flow (TTF) and indo-

cyanine green angiography (ICG).¹ We appreciate the opportunity to elaborate on the three issues they raise:

1. Methods to improve visualization with ICG angiography
2. Appropriate TTF criteria for graft assessment
3. Cost Effectiveness

Regarding the first issue, indocyanine green angiography is a method of fluorescent dye-contrast angiography that uses near infrared laser as the energy source. We have previously demonstrated poorer visualization of thick pedicled arterial grafts with this technique due to limited penetration of the laser into thicker tissues.² To improve visualization, we ensure that there is no pedicle covering the area of the anastomosis itself and we routinely expose the native vessel for approximately 1 cm beyond the anastomosis. We do not skeletonize the entire graft. Our evaluation of patency is based on both anatomic visualization of the anastomosis itself and the opacification characteristics (ie, TIMI flow) of the native circulation. Also, further experience with the technique has led us to perform selective angiograms directly into the grafts which allows for improved visualization of the distal anastomosis versus injections into the central venous line which can be confounded by native flow.²

Regarding the second issue, whereas criteria for pulsatility index (PI) and diastolic flow fraction (DFF) are standard, there is little agreement on cut-off values that distinguish between normal and abnormal mean flow values. Although most surgeons would agree that a flow of less than 5 ml/min is definitely abnormal and will often prompt revision, flows between 5 to 40 ml/min could potentially represent abnormal grafts. There is no clear consensus regarding cutoff values that determine graft problems and little prospective data on the subject. The study by Di Giammarco and colleagues, who recommend a 15 ml/min mean flow cutoff, was retrospective in design.³ Because patients who had follow-up angiograms were generally symptomatic, their study design could not accurately assess the false positive rate. The study by Walpoth and colleagues, who recommend a 20ml/min mean flow cutoff, had no angiographic controls to determine sensitivity or specificity.⁴ In our study, surgeons were permitted to intervene on any graft they deemed to be poorly functioning, even if it

was "normal" by the prespecified TTF criteria (mean flow > 10 ml/min), but this did not occur in any cases. Indeed, as clearly stated in the manuscript, the mean flow in abnormal (>50% occluded) grafts was 24.4 ± 8.6 ml/min and was 16.4 ± 23.0 ml/min in grafts deemed to be totally occluded by the reference standard. In secondary analyses, if we used a cutoff mean flow of 15 ml/min, we would have identified no additional true positives and 6 false positives. Using a mean flow cutoff of 20 ml/min, we would have identified only one additional true positive and 10 false positives. Our findings are in agreement with the only other prospective comparison of these two techniques by Taggart, who demonstrated that up to 10% of patients may receive erroneous graft revisions based on false positive TTF findings.⁵

Hence, our cutoff value of 10 ml/min minimizes false positives while identifying nearly all true positives and may be an ideal reference value when used in conjunction with PI and DFF. Higher mean flow cutoffs appear to have too many false positives to be reliable measures, and many surgeons are unlikely to revise grafts based on higher flow values for this reason.⁶ This is especially true if revision means reinstating cardiopulmonary bypass.

Finally, in regard to cost effectiveness, we have not performed such a comparison, because this was a clinical effectiveness study. It is unlikely that either technology will be highly cost effective in terms of Quality Adjusted Life Years (QALY) which is the generally accepted measure, but there may be cost benefits from non-fatal events.

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Temporary coronary artery occlusion during off-pump surgery and endothelial vessel dysfunction: Is it still an unresolved mystery?

To the Editor:

We read with great interest the article by Bouchot and associates.¹ We would like to congratulate the authors for this well-designed study, but we would also add some comments. The aim was to determine the usefulness and safety of the poloxamer P407 gel (LeGoo; Pluromed, Woburn, Mass) to ensure a hemostatic effect at the anastomotic site during off-pump surgery in a porcine model. Twenty Landrace Yorkshire pigs, after median sternotomy, underwent internal thoracic artery off-pump grafting to the left anterior descending artery, the right coronary artery, or both by using the P407 gel to control the anastomotic-site bleeding. The major finding of the study was that the intracoronary injection of P407 gel allows a successful occlusion of the coronary vessel during grafting while preserving the endothelial function. The main limitation of the study protocol is essentially related to the health of the coronary artery tree used as a benchmark. Therefore, the presence of native atherosclerotic lesions might indicate the presence of further and otherwise undiscovered intimal injuries.

We maintain that shunting and snaring during off-pump coronary artery bypass

grafting are both risky procedures,² and thus the opportunity to use a gel effective in bleeding control without impairing the endothelial function might have a relevant effect on coronary artery bypass grafting surgery. Therefore, because there is a higher hazard of damage to the coronary wall during vessel manipulation with a more diseased atherosclerotic vessel, we suggest that testing the gel effects on the coronary arteries of patients affected by ischemic cardiomyopathy before heart transplantation and before the start of cardiopulmonary bypass should additionally be performed.

As clinicians continuing to educate ourselves on the benefits of new technologies, we conclude that a more carefully conducted study on a human model might resolve the issue of whether one technique is more suitable than another.

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Reply to the Editor:

We thank Dr Bottio and collaborators for their kind comments and insightful remarks concerning our recent article in the *Journal* on temporary coronary occlusion with the new poloxamer P-417 (LeGoo; Pluromed, Woburn, Mass) for off-pump coronary artery bypass grafting. We concur with them that one of the limitations of the porcine model used is the presence of normal coronary endothelial coverage and function,