

## CORRESPONDENCE



## On-Pump versus Off-Pump CABG

**TO THE EDITOR:** In the Veterans Affairs Randomized On/Off Bypass (ROOBY) trial, Shroyer et al. (Nov. 5 issue)<sup>1</sup> assigned 2203 patients to receive coronary-artery bypass grafting (CABG) either with the use of cardiopulmonary bypass (on-pump CABG) or without such bypass (off-pump CABG). The trial enrolled low-risk male patients in whom avoidance of cardiopulmonary bypass was unlikely to greatly improve the expected excellent outcomes.<sup>2</sup> In a majority of patients, CABG was performed by surgical trainees under the supervision of attending surgeons who were remarkably inexperienced in the off-pump procedure and much more experienced in the on-pump procedure. The reported 12.4% rate of intraoperative conversion from planned off-pump CABG to on-pump CABG was five times the rate reported in the national database of the Society of Thoracic Surgeons<sup>3</sup> and is an explicit indictment of the off-pump inexperience of surgeons, trainees, and anesthesia-nursing teams participating in the ROOBY trial.<sup>4</sup> It is illogical to conduct a randomized trial comparing patient outcomes with alternative surgical techniques among surgical operators who have grossly asymmetric experience and expertise with the two procedures that are being compared. This is the “fatal flaw” of the ROOBY trial.

Off-pump CABG is a technically challenging surgical procedure that offers substantial benefit to patients at high risk for death and complications with on-pump CABG.<sup>3,5</sup> It remains a very important tool for surgical coronary revascularization.

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**TO THE EDITOR:** The findings of Shroyer et al. testify to the excellent contemporary results of CABG, whether on-pump or off-pump. However, even though the results largely reinforce the already well-established fact that there is no survival benefit to off-pump CABG in low-risk patients, this conclusion should not be generalized to higher-risk patients, for whom there is abundant evidence for superior outcomes with off-pump surgery.<sup>1</sup> Furthermore, the inexperience of the surgeons with respect to this more demanding surgical technique was particularly notable, since the 53 participating surgeons enrolled on average only eight patients per year during a 5-year period and had unacceptably high conversion rates to on-pump surgery (12%) and incomplete revascularization (18%). It is likely that their inexperience contributed to other less favorable clinical outcomes as well. Similarly, the failure to combine off-pump CABG with greater use of arterial grafts<sup>2</sup> and a “no-touch” aortic technique excludes the potential to minimize both overt and subclinical cerebral complications.<sup>3</sup>

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**TO THE EDITOR:** A randomized trial comparing two surgical techniques ought to include surgeons who are experienced in both procedures. Shroyer et al. conclude that patients who underwent off-pump CABG had worse composite outcomes and poorer graft patency at 1 year than did patients who underwent on-pump CABG. Disturbing was the assumption that performance of at least 20 off-pump CABG surgeries conferred “off-pump experience.” Although the prestudy off-pump experience averaged 120 cases, the median was only 50, indicating that some surgeons were quite experienced and the rest not so much. In 1313 of

2199 procedures (60%), a resident was the primary surgeon, with no difference in primary end points whether the resident or a staff member was the primary surgeon (perhaps because both were inexperienced?). A resident with possibly 100 cases under his or her belt faces a much steeper learning curve than a staff surgeon who has done several hundred. This study represents learning curves with respect to off-pump surgery for both residents and staff.

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**TO THE EDITOR:** It is unclear whether the adverse outcomes that were associated with off-pump CABG might have been associated with exposure to aprotinin or endoscopic saphenous-vein harvesting. Both of these perioperative variables have a significant effect on outcome after CABG.<sup>1,2</sup> This study raises important questions but should be interpreted in light of these possible confounders.

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No potential conflict of interest relevant to this letter was reported.

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**TO THE EDITOR:** The major impetus to develop off-pump CABG surgery stemmed from the observation that atherosclerotic aortas are a major source of embolism when clamped during cardiac bypass.<sup>1</sup> Atherosclerosis of the aorta is a major risk factor for the development of postoperative stroke and encephalopathy during on-pump CABG.<sup>2</sup> Off-pump surgery was reported to have a lower risk of stroke than bypass with aortic clamping.<sup>2</sup>

The status of the aorta (either during preoperative testing or intraoperative observation) was not mentioned in the article by Shroyer et al. or in the accompanying editorial by Peterson.<sup>3</sup> Knowledge of the presence, location, and severity of aortic disease — as well as the cardiac ejection fraction and the extent of coronary artery dis-

ease and lesions in neck and cranial arteries that supply the brain — would allow surgeons to selectively choose on-pump versus off-pump surgery, yet such detailed preoperative analysis is not routinely performed.<sup>4</sup>

The idea that one surgical strategy fits all is faulty. Much more sensible would be to evaluate patients as thoroughly as possible before surgery and then choose the most appropriate technique for that patient.<sup>4</sup>

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**THE AUTHORS REPLY:** The ROOBY trial showed better 1-year outcomes and graft patency among patients undergoing on-pump CABG than among those undergoing off-pump CABG. The correspondents raise important questions regarding the effect of surgeons' experience, the use of residents as primary surgeons, and conversions of surgical procedure on the trial's primary outcomes. Similar to previous trials, our study showed no difference in primary short-term or 1-year composite outcomes, regardless of the participating surgeon's experience (>50 or >100 previous off-pump cases) or whether the attending or a trainee was the primary surgeon (for details, see Table 1 in the Supplementary Appendix, available with the full text of this letter at NEJM.org).<sup>1-4</sup> These findings remained consistent in both the intention-to-treat analysis and after the exclusion of surgical conversions.

Regarding Taggart's question about our study's generalizability to subgroups of high-risk patients: we enrolled many patients with high-risk coexisting conditions. Among these subgroups, there was no difference in the 1-year composite end point between the two study groups. Worse short-term outcomes were seen among patients with diabetes who underwent the off-pump technique ( $P=0.01$ );

this difference did not persist after removal of patients who underwent surgical conversions ( $P=0.10$ ) (Table 1 in the Supplementary Appendix).

With respect to the comments of Augoustides regarding the use of aprotinin and endoscopic vein harvesting for saphenous-vein grafts: we agree that these processes of care may affect outcomes. Aprotinin was used in 6.0% of patients (4.3% of those who were not converted) in the off-pump group versus 28.6% (29.9% of those who were not converted) in the on-pump group. Further analysis of this aprotinin imbalance on the study's results appears warranted. Fifteen months after the initiation of our trial, data capture for endoscopic vein harvesting was initiated. For this period, the proportions of episodes of endoscopic vein harvesting were balanced between the two study groups ( $P=1.0$ ) and therefore should not have an effect on the study's conclusions.

Regarding Caplan's comments: our study was designed to assess the use of off-pump versus on-pump CABG, not other approaches, such as total arterial revascularization and aortic "no-touch" techniques. Our clinician team concurs that in some patients who undergo CABG, an aortic no-touch approach may be beneficial. In our study, there were 40 conversions of on-pump procedures to off-pump procedures (3.6%). Of these, 23 were due to surgeons' concerns related to calcification of the ascending aorta. It is important to note that there were no differences in overall neurocognitive outcomes between the two study groups.

In summary, these sensitivity analyses verify that our findings remain relevant to the majority of men at low-to-moderate risk of death at 30 days and perioperative complications, as well as to most cardiac surgical groups. For women, high-risk men, and other intraoperative surgical techniques, future research will be required to build an evidence base to optimally select patients for off-pump procedures.

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Since publication of their article, the authors report no further potential conflict of interest.

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**THE EDITORIALIST REPLIES:** I agree with Caplan's comments that aortic atherosclerosis is a risk factor for stroke after bypass surgery. In my editorial, I suggest that "future subgroup analyses are needed to determine whether there were specific

high-risk subpopulations for which the off-pump technique was particularly beneficial." Therefore, if Shroyer et al. have data regarding the extent of aortic calcification in study patients, then they should examine whether treatment outcomes varied as a function of this risk factor. Finally, I do not believe that my editorial supports a "one surgical strategy fits all" bottom line. Although the ROOBY trial did not support a general replacement of off-pump surgery with on-pump surgery, I conclude that off-pump surgery may be "a technique reserved for selected patients and skilled surgeon advocates."

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Since publication of his article, the author reports no further potential conflict of interest.

## A Controlled Trial of Initial Antiviral Regimens for HIV-1 Infection

**TO THE EDITOR:** Sax et al. (Dec. 3 issue)<sup>1</sup> found that abacavir–lamivudine was less potent than tenofovir disoproxil fumarate (DF)—emtricitabine among patients with human immunodeficiency virus type 1 (HIV-1) RNA levels of 100,000 copies per milliliter or more.

The authors report, but do not comment on, a significant heterogeneity of treatment effect according to sex and the availability or unavailability of genotype information at screening performed in cases of recent HIV infection. Minority drug-resistant mutations at baseline that were undetected by means of conventional genotyping could also explain the increased risk of virologic failure in the abacavir–lamivudine group,<sup>2</sup> particularly among the patients with thymidine-analogue minor mutations.<sup>3</sup>

A subgroup analysis according to HIV risk factors would be interesting because the risk of transmitted resistance is increased within the United States<sup>4</sup> and Western Europe<sup>5</sup> among men who have sex with men.

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Dr. Parienti reports receiving lecture fees from Abbott, Bristol-

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**TO THE EDITOR:** The study by Sax and colleagues comparing initial antiretroviral regimens for HIV-1 infection raises ethical concerns. The authors note that the data and safety monitoring board recommended that specific viral mutations detected by means of baseline resistance analysis not be disclosed. It is difficult to fathom what patient with even a basic understanding would choose to participate in such a study rather than receive standard care in which therapy is guided by genotype