See related editorial on pages 12-3.

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analysis better, such as with the use of image analysis for semi-quantitative assessment of the interpretation of the radiographic and histologic results, and with blinded assessment of the explanted valves as was done for the echocardiographic data. Flameng and colleagues³ should also clearly state that the explanted valve analysis was performed at their institution, and not by industry scientists. Unfortunately, they show bias toward the funding manufacturer's products, as witness by the unsubstantiated statement of "standard of care" when discussing the company's valves, both at the beginning and at the end of their discussion section.³

The authors are correct that if this technology is approved for commercial human use, there will be no long-term longitudinal studies of durability available initially for assessment, and we will have to go by studies such as theirs to make a decision on use. When the industry representative arrives at my office door with a brochure of research papers promoting this novel treatment relative to their second generation anticalcification product, I would hope that they will include studies with better objective design. Otherwise, I may suggest to them that this is just a *gimmick* or *new selling point*, and not choose the pudding. Rather, I may ask, "Where's the beef?"

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References

1. Mack MJ, Sade RM, American Association for Thoracic Surgery Ethics Committee; Society of Thoracic Surgeons Standards and Ethics Committee. Relations between cardiothoracic surgeons and industry. *J Thorac Cardiovasc Surg.* 2009;137:1047-9.
2. Schmoker J. Bioprosthetic valve durability: the proof is in the pudding. *J Thorac Cardiovasc Surg.* 2015;149:346-7.
3. Flameng W, Hermans H, Verbeken E, Meuris B. A randomized assessment of an advanced tissue preservation technology in the juvenile sheep model. *J Thorac Cardiovasc Surg.* 2015;149:340-5.

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STATE-OF-THE-ART SURGICAL CORONARY REVASCULARIZATION: MULTIPLE ARTERIAL CONDUITS, MINIMAL AORTIC MANIPULATION To the Editor:

In a recent issue, the Danish On-Pump Versus Off-Pump Randomization Study (DOORS) investigators reported a statistically significant

7% decrement in overall graft patency (defined as open and nonstenotic) assessed by angiography 6 months after off-pump coronary artery bypass graft (OPCAB) versus on-pump coronary artery bypass graft (ONCAB).¹ In the same issue, Takagi and colleagues² offer a meta-analysis of long-term survival after OPCAB versus ONCAB, reporting an adjusted hazard ratio of 1.07 (95% confidence interval, 1.03-1.11) for death $\geq$ 5 years following OPCAB compared with ONCAB. Smith³ and Lazar⁴ offered separate editorial commentaries, adding their clinical perspectives. They identified several important weaknesses and limitations of the DOORS trial¹ and the meta-analysis by Takagi and colleagues.²

Smith³ noted that the experience threshold for surgeons in the DOORS trial was relatively meager (at least 25 OPCAB cases with circumflex territory grafts) and that the predominance of single internal thoracic artery (ITA) plus saphenous vein grafts (SVGs) suggests something less than cutting-edge coronary surgery. Importantly, 57 of 446 (12.8%) OPCAB cases in the DOORS trial were converted to ONCAB, approximately 5-fold the rate of conversion reported in the Society of Thoracic Surgeons database (2.2%),⁵ perhaps suggesting an incomplete comfort level with OPCAB among some of the operating surgeons. Inexplicably, more perioperative bleeding was found in OPCAB patients than in ONCAB patients in the DOORS study, contrary to many previous reports.

The reported difference in occluded grafts did not reach significance ($P = .20$). Both OPCAB and ONCAB had 95% non-occluded left ITA grafts; the differences were in SVG, radial artery, and right ITA conduits. Moreover, in the 250 stenotic or occluded grafts, the obstruction was located at proximal anastomoses ($n = 121$), shaft lesions ($n = 65$), and distal anastomoses ($n = 96$). As Smith noted,³ in 74% of occluded/stenotic grafts, the problem was seen in sites (proximal anastomosis and midshaft lesions) that might not be expected to differ greatly between the 2 operative techniques.

Importantly, "The propensity to attend the follow-up angiography was unevenly distributed among groups."¹ Post-hoc adjustment for the propensity to attend the follow-up angiography suggested that the groups that had angiography were similar to their respective preoperative groups, but it is unclear whether sampling/selection bias at follow-up angiography could have confounded the study. Caution should be exercised in generalizing from this trial in which no primary end point was reported for almost half of enrolled patients.

We respectfully disagree with Smith's statement that OPCAB behaves like percutaneous coronary intervention (PCI) in multivessel disease or diabetes without the benefits of a truly noninvasive procedure. Indeed, it is important to note that when comparisons have been made between OPCAB and multivessel PCI, they have uniformly and strongly favored OPCAB over PCI.⁶⁻⁸ However, it is certainly true that the widespread use of SVG conduits, with their inevitable attrition, makes coronary artery bypass

grafting more vulnerable to competition from practitioners of multivessel PCI. Numerous large studies have confirmed the survival benefit of bilateral ITA^{9,10} and radial artery grafting.¹¹⁻¹³ Yet the percentage of contemporary coronary artery bypass graft cases in the United States performed with > 1 arterial conduit remains only approximately 5% to 10%,¹⁴ which is less than the approximately 10% to 15% rate in some European countries and much less than rates reported from Japan.¹⁵

Neither Smith³ nor Lazar⁴ mention the early advantages of OPCAB—numerous randomized and nonrandomized studies have reported reduced transfusion requirements, lower serum levels of myocardial enzymes, fewer perioperative neurologic events, and shorter hospital length of stay after OPCAB.^{5,16-18} They note that primary among the benefits of coronary artery bypass grafting is improved longevity and that survival after the procedure has been convincingly linked to completeness of revascularization. Thus, Lazar⁴ is correct in stating that OPCAB should not be performed when complete revascularization cannot be accomplished, unless a compelling risk factor such as porcelain aorta mandates a no-touch aortic technique for coronary revascularization. He is also correct in noting that no difference between OPCAB and ONCAB in regard to midterm survival has been noted in multiple randomized trials conducted by expert OPCAB practitioners.⁴ This observation drives home the operator-dependent nature of complex surgical procedures in general, and OPCAB in particular.

Smith³ and Lazar⁴ both recognize the increased technical difficulty of OPCAB relative to ONCAB and advocate for dedicated teams in which genuine expertise can be developed for this more challenging procedure. Just as complex mitral valve repair, aortic arch surgery, and thoracic transplantation have become the province of subspecialized teams, contemporary coronary artery bypass grafting in the era of multivessel PCI may also be sufficiently challenging to warrant dedicated teams that focus on achieving complete revascularization with multiple arterial conduits and minimal aortic manipulation.

Many patients at low risk for complications from cardiopulmonary bypass and aortic crossclamping can have ONCAB with fastidious cardioplegia, single aortic clamping, and multiple arterial conduits and enjoy excellent early outcomes as well as outstanding long-term survival. OPCAB uniquely offers the possibility of routinely minimizing or even completely avoiding aortic manipulation by use of clampless facilitating devices (such as the HeartString III [Maquet, Rastatt, Germany]) or utilizing bilateral ITAs alone for conduit inflow. This has been shown to reduce perioperative adverse neurologic events.¹⁹⁻²¹ However, clampless OPCAB with multiple or all-arterial conduits is a time-consuming and technically challenging operation that requires dedicated acquisition of individual and team skills beyond those necessary for on-pump left-ITA-plus-SVG grafting. Nonetheless, the fundamental

rationale for OPCAB holds: If complete and precise revascularization with optimal conduits can be accomplished without cardiopulmonary bypass, then the patient should benefit by avoiding the morbidities that can be attributed to aortic cannulation/clamping, cardiopulmonary bypass, hemodilution, hypothermia, and global myocardial ischemia/cardioplegia. Despite its serious flaws, the DOORS trial emphasizes the “if” in the above statement. OPCAB is technically demanding and individual patient variables may make it more so. It is not for every surgical team, nor for every patient.

Finally, Lazar's suggestion⁴ that our professional societies develop guidelines for the practice of OPCAB and mandate criteria for surgeon training, patient selection, and standardization of operative techniques would be difficult to implement. Nonetheless, there is a clear need for our profession to be able to systematically monitor clinical outcomes for all the procedures we perform beyond the 30-day interval presently reported in the Society of Thoracic Surgeons National Cardiac Database. Specifically, intense and concerted lobbying efforts should be made by our professional societies until government agencies allow a routine link between the Society of Thoracic Surgeons database and the National Death Index. This would provide all-cause mortality follow-up for every patient with a Social Security number, allowing us to better understand the effects of our surgical procedures on the long-term survival of our patients. Meanwhile, surgical coronary revascularization should be recognized as the technically demanding subspecialty that it is and evolution should be encouraged toward reference centers of excellence in which state-of-the-art surgical coronary revascularization will be reliably performed.

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References

1. Houliad K, Fenger-Grøn M, Holme SJ, Kjeldsen BJ, Madsen SN, Rasmussen BS, et al. Graft patency after off-pump coronary artery bypass surgery is inferior even with identical heparinization protocols: results from the Danish On-pump Versus Off-pump Randomization Study (DOORS). *J Thorac Cardiovasc Surg*. 2014;148:1812-9.
2. Takagi H, Umemoto T, All-Literature Investigation of Cardiovascular Evidence (ALICE) Group. Worse long-term survival after off-pump than on-pump coronary artery bypass grafting. *J Thorac Cardiovasc Surg*. 2014;148:1820-9.
3. Smith SR. #SLOPCAB: Is the party over? *J Thorac Cardiovasc Surg*. 2014;148:1788-9.
4. Lazar HL. Should off-pump coronary artery bypass surgery be abandoned? A potential solution. *J Thorac Cardiovasc Surg*. 2014;148:1829-31.
5. Puskas JD, Edwards FH, Pappas PA, O'Brien S, Peterson ED, Kilgo P, et al. Off-pump techniques benefit men and women and narrow the disparity in mortality after coronary bypass grafting. *Ann Thorac Surg*. 2007;84:1447-54.
6. Marui A, Kimura T, Tanaka S, Furukawa Y, Kita T, Sakata R, et al. Significance of off-pump coronary artery bypass grafting compared with percutaneous

- coronary intervention: a propensity score analysis. *Eur J Cardiothorac Surg.* 2012;41:94-101.
7. Jeong DS, Lee YT, Chung SR, Jeong JH, Kim WS, Sung K, et al. Revascularization in left main coronary artery disease: comparison of off-pump coronary artery bypass grafting vs percutaneous coronary intervention. *Eur J Cardiothorac Surg.* 2013;44:718-24.
 8. Yi G, Joo HC, Youn YN, Hong S, Yoo KJ. Stent versus off-pump coronary bypass grafting in the second-generation drug-eluting stent era. *Ann Thorac Surg.* 2013; 96:535-41.
 9. Weiss AJ, Zhao S, Tian DH, Taggart DP, Yan TD. A meta-analysis comparing bilateral internal mammary artery with left internal mammary artery for coronary artery bypass grafting. *Ann Cardiothorac Surg.* 2013;2: 390-400.
 10. Grau JB, Ferrari G, Mak AW, Shaw RE, Brizzio ME, Mindich BP, et al. Propensity matched analysis of bilateral internal mammary artery versus single left internal mammary artery grafting at 17-year follow-up: validation of a contemporary surgical experience. *Eur J Cardiothorac Surg.* 2012;41:770-5.
 11. Schwann TA, Tranbaugh RF, Dimitrova KR, Engoren MC, Kabour A, Hoffman DM, et al. Time-varying survival benefit of radial artery versus vein grafting: a multiinstitutional analysis. *Ann Thorac Surg.* 2014;97:1328-34.
 12. Shi WY, Hayward PA, Fuller JA, Tatoulis J, Rosalion A, Newcomb AE, et al. Is the radial artery associated with improved survival in older patients undergoing coronary artery bypass grafting? An analysis of a multicentre experience. *Eur J Cardiothorac Surg.* February 15, 2015 [Epub ahead of print].
 13. Tranbaugh RF, Dimitrova KR, Friedmann P, Geller CM, Harris LJ, Stelzer P, et al. Radial artery conduits improve long-term survival after coronary artery bypass grafting. *Ann Thorac Surg.* 2010;90:1165-72.
 14. Kappetein AP, Dawkins KD, Mohr FW, Morice MC, Mack MJ, Russell ME, et al. Current percutaneous coronary intervention and coronary artery bypass grafting practices for three-vessel and left main coronary artery disease. Insights from the SYNTAX run-in phase. *Eur J Cardiothorac Surg.* 2006;29:486-91.
 15. Kobayashi J. Current status of coronary artery bypass grafting. *Gen Thorac Cardiovasc Surg.* 2008;56:260-7.
 16. Zamvar V, Williams D, Hall J, Payne N, Cann C, Young K, et al. Assessment of neurocognitive impairment after off-pump and on-pump techniques for coronary artery bypass graft surgery: prospective randomised controlled trial. *BMJ.* 2002; 325:1268.
 17. Diegeler A, Hirsch R, Schneider F, Schilling LO, Falk V, Rauch T, et al. Neuro-monitoring and neurocognitive outcome in off-pump versus conventional coronary bypass operation. *Ann Thorac Surg.* 2000;69:1162-6.
 18. Keeling WB, Williams ML, Slaughter MS, Zhao Y, Puskas JD. Off-pump and on-pump coronary revascularization in patients with low ejection fraction: a report from the society of thoracic surgeons national database. *Ann Thorac Surg.* 2013; 96:83-8.
 19. Moss E, Puskas JD, Thourani VH, Kilgo P, Chen EP, Leshnower BG, et al. Avoiding aortic clamping during coronary artery bypass grafting reduces postoperative stroke. *J Thorac Cardiovasc Surg.* 2015;149:175-80.
 20. Calafiore AM, Di Mauro M, Teodori G, Di Giammarco G, Cirmeni S, Contini M, et al. Impact of aortic manipulation on incidence of cerebrovascular accidents after surgical myocardial revascularization. *Ann Thorac Surg.* 2002; 73:1387-93.
 21. Kim KB, Kang CH, Chang WI, Lim C, Kim JH, Ham BM, et al. Off-pump coronary artery bypass with complete avoidance of aortic manipulation. *Ann Thorac Surg.* 2002;74:S1377-82.

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OPCAB IS NOT FOR EVERY SURGEON AND NOT FOR EVERY PATIENT

Reply to the Editor:

Drs Yanagawa and Puskas have written a thorough, thoughtful, and articulate piece of effective advocacy in defense of off-pump coronary artery bypass (OPCAB), fortified by selective citation. I will not attempt to reply point by point.

I suspect we all agree that there are no perfect clinical trials. When meta-analyzers put the conclusions and imperfections of multiple trials in the salad spinner, out comes...salad. When differences between the modalities being compared are dramatic, none of that matters! The problem for OPCAB, now deep into its second decade of practice, is that convincingly demonstrated benefits have been illusory, and certain deficits (graft patency) have been stubbornly persistent.

When a procedure is called into question, a popular defense strategy used by surgeons is "not in my hands." I've used it myself! In the world of OPCAB, few surgeons bring as much legitimacy to that defense as Dr Puskas, whose randomized trials have been uniquely positive for OPCAB. But even Dr Puskas cannot be expected to perform every coronary artery bypass graft, and the super-expert is not a good solution to a public health problem the size of coronary disease.

A large part of me is disappointed by these developments. I have spent more than 15 years acquiring what I consider to be expertise in OPCAB. Certain technical benefits still have strong appeal. However, I agree completely with the authors' "not for every surgeon, not for every patient" precept, and I am dramatically expanding my application of the second "not."

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HARD ENDPOINTS FROM LARGE RANDOMIZED, CLINICAL TRIALS ARE MORE IMPORTANT THAN EARLY REPORTS OF SURROGATE ENDPOINTS FROM SMALL STUDIES

Reply to the Editor:

Thank you for the opportunity to comment on the letter by Yanagawa and Puskas, especially regarding our recent paper on graft patency in the Danish On-Pump versus Off-Pump Randomization Study (DOORS).¹

The conversion rate in DOORS was 12.8%,² similar to that in the American Randomized On-pump Off-pump Bypass (ROOBY) trial.³ Outside clinical trials, off-pump coronary artery bypass grafting (OPCAB) is often preferred to on-pump coronary artery bypass grafting (ONCAB) for patients who need relatively few grafts, tending to keep conversion rates low. Yanagawa and Puskas refer to a number of 2.2% as being the proportion of conversions in the Society of Thoracic Surgeons database, but the only reference