Coronary bypass: Is it time to take the next step—the routine use of the second arterial graft?

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See related articles by Buxton et al on pages 1238-44, Deb et al on pages 1246-53, and Raza et al on pages 1257-66.

Despite mounting evidence of the long-term advantages of multiarterial grafting the overwhelming majority of patients undergoing coronary artery bypass grafting in 2014 are receiving only 1 arterial conduit.¹ Why? There are certainly barriers to adoption of a multiarterial strategy.

These barriers are multifactorial but readily apparent. For surgeons considering bilateral internal thoracic artery (BITA) grafting, the fear of sternal wound complications in an increasingly obese and diabetic population seems justified in light of recent societal and governmental actions. Mediastinitis, one of the key Society of Thoracic Surgeons quality metrics used in public reporting, is now deemed a “never” event, and readmission for these patients is no longer reimbursed by the Centers for Medicare and Medicaid Services. Public reporting of hospital and surgeon outcomes is becoming commonplace and is based on short-term, not long-term outcomes. BITA grafting is technically more challenging, may lead to more frequent reexploration, prolongs the operation, and is often outside the comfort zone of surgeons because it makes a relatively simple operation more complex. For radial artery (RA) grafting, conduit vasospasm and graft failure as a result of competitive flow are of concern, and additional time and often personnel are needed for conduit harvesting. For either additional arterial conduit, it is often unclear which patients will truly benefit and what coronary anatomy is suitable. Finally, remuneration to physicians or hospitals is not commensurate with the skill, effort, and time required for multiarterial grafting.

The superiority of traditional coronary artery bypass grafting with a single arterial graft combined with saphenous vein grafts (SVGs) to non-left anterior descending coronary artery targets relative to multivessel percutaneous

coronary intervention has been firmly established in both diabetic and nondiabetic populations in 2 large, multicenter, randomized, controlled trials: Future Revascularization Evaluation in Patients with Diabetes Mellitus; Optimal Management of Multivessel Disease (FREEDOM) and Synergy between Percutaneous Coronary Intervention and Cardiac Surgery (SYNTAX).^{2,3} But we surgeons can do better for our patients. Locker and colleagues⁴ recently showed that in propensity score–matched groups patients undergoing multiarterial revascularization had an estimated 15-year survival of 70%, versus 60% for patients undergoing a single internal thoracic artery (SITA) graft plus SVG (hazard ratio, 0.73; 95% confidence interval [CI], 0.59-0.90; $P = .003$). Dorman and colleagues⁵ used propensity score matching to compare median survival for patients undergoing BITA grafting with that of those undergoing SITA for multivessel disease (follow-up 6 weeks to 30 years; median, 8.9 years). The median survival for patients with SITA grafting was 9.8 years (95% CI, 8.6-10.5 years), versus 13.1 years (95% CI, 12.2-13.9 years) for patients undergoing BITA grafting ($P < .001$). In an updated meta-analysis of published studies comparing BITA versus SITA, the BITA group demonstrated significantly better long-term survival than did the SITA group receiving a left internal thoracic artery (LITA) graft (hazard ratio, 0.78; 95% CI, 0.72-0.84; $P < .00001$).⁶ In an analysis evaluating the effect of RA grafts relative to SVGs, SITA plus RA plus SVG had improved long-term survival relative to SITA plus SVG alone (83.1% vs 74.3%; $P < .001$).⁷

Superior patency of either arterial conduit relative to SVG has also been demonstrated. In a multicenter randomized study comparing RA versus SVG patency, the RA was randomized to be grafted to either the circumflex or the right coronary artery, with the SVG used for the other territory.⁸ The frequency of functional graft occlusion, defined as lack of Thrombolysis In Myocardial Infarction flow grade 3, was lower in RAs than in SVGs (28 of 234 [12.0%] vs 46 of 234 [19.7%]; $P = .03$). The frequency of complete graft occlusion was also significantly lower with RA compared with SVG (24 of 269 [8.9%] vs 50 of 269 [18.6%]; $P = .002$). In a recent meta-analysis of RA angiographic studies, Cao and colleagues⁹ demonstrated that the RA was significantly less likely to be associated with graft failure or complete occlusion than was SVG. Tatoulis and associates¹⁰ demonstrated an overall 10-year angiographic right internal thoracic artery (RITA) patency of 90%. The RITA had a patency equivalent to LITA patency when

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grafted to the same territory, had similar patency regardless of whether used as an in situ graft or a free graft, and had superior patency relative to the RA (10-year patency, 78%).

Not all reports, however, have been as supportive of a multiarterial grafting strategy. Midterm (5-year) results of the single center Radial Artery Patency and Clinical Outcomes randomized trial (RAPCO) revealed no significant difference in clinical outcome or graft patency when comparing the RA with the SVG in patients older than 70 years.¹¹ Similarly, Tranbaugh and colleagues¹² showed no significant survival or patency difference when the circumflex territory was bypassed with the RA relative to the RITA.

Despite numerous observational analyses suggesting a long-term survival advantage of BITA and RA grafting, randomized trial data are lacking. Long-term results of RAPCO will elucidate differences between RITA and RA grafting in patients younger than 70 years and between SVG and RA grafting in patients older than 70 years.¹¹ The 10-year multicenter Arterial Revascularization Trial (ART) of Taggart and associates¹³ provides much needed randomized clinical trial data about the long-term survival benefit of BITA grafting relative to SITA grafting to the left coronary circulation. It will also provide comparative effectiveness data for a LITA plus RA strategy in a subgroup of patients. In their 1-year ART results, Taggart and associates¹³ reported comparable short-term outcomes in terms of survival, myocardial infarction, stroke, and repeated revascularization. Importantly, the incidence of sternal wound complications requiring reconstruction was once again shown to be significantly higher in the BITA group, 1.9% versus 0.6%.

In this issue of *The Journal of Thoracic and Cardiovascular Surgery*, 3 important contributions provide additional evidence in support of a multiarterial grafting strategy. Raza and colleagues report The Cleveland Clinic experience spanning 40 years and investigate SITA and BITA grafting with or without additional grafts versus the SVG only grafting approach in patients with diabetes mellitus. After adjustment for baseline patient characteristics through multivariable logistic regression analysis, BITA versus SITA grafting was associated with a 21% lower late mortality (68% CI, 16%-26%). The incidence of deep sternal wound infection was again significantly higher after BITA versus SITA grafting (3.4% vs 2.1%; $P = .01$), a difference that persisted after multivariable adjustment ($P = .002$). Their conclusion is that BITA grafting and complete revascularization provided the optimal revascularization strategy to maximize long-term survival in patients with diabetes, although they urge careful patient selection. The RITA is rarely used for a right coronary lesion, and Lytle¹⁴ has stated that additional arterial grafts should be used for patients with a 10-year life expectancy.

In a second article in this *Journal*, a substudy of the multicenter Radial Artery Patency Study (RAPS) by Deb

and colleagues reports an examination of 5-year patency of RA versus SVG in patients with diabetes younger than 80 years. The within-patient randomization protocol, with the RA randomized to either the circumflex or right coronary territory (both with at least 75% proximal stenosis) and SVG used to the remaining territory, allowed patients to serve as their own controls. The proportion of complete graft occlusion was significantly lower for the RA (4/83 [4.8%]) than for SVGs (21/83 [25.3%]; $P = .0004$). Cumulative patency rates for RA grafts, irrespective of diabetes status, were similar for patients with and without diabetes, whereas cumulative patency rates of SVGs were worse for patients with diabetes, suggesting the improved durability of the RA relative to SVGs in this subset of patients. Notably, earlier publication of data from the overall RAPS study revealed that the patency superiority of the RA occurred primarily in targets with at least 90% proximal stenosis, with relative equipoise between RA and SVG in targets with 75% to 90% stenosis.⁸

In a third article, Buxton and associates report their examination in a multi-institutional observational analysis of the long-term effect of total arterial revascularization relative to LITA plus SVGs for patients with multivessel coronary disease. Patients receiving a mix of multiarterial grafts plus SVGs were excluded. Multivariable Cox proportional hazard modeling and propensity score-matched pairs were used to control for differences in preoperative risk. Total arterial revascularization yielded a superior survival advantage on Cox proportional hazard analysis, with a hazard ratio of 0.79 (95% CI, 0.70-0.90; $P < .001$). In 384 propensity-matched pairs, the total arterial revascularization patients had improved 15-year survival relative to the SITA patients (54% $\pm$ 3.3% vs 41% $\pm$ 3.0%; $P = .0004$). Again, this was a retrospective observational study. It was conducted in institutions with a bias toward arterial grafting, and one must believe that the very best candidates received total arterial grafts and there was some reason the patients who underwent SITA grafting did not get a second arterial graft.

Without compelling evidence from large randomized trials supporting a multiarterial grafting strategy in a broad population of patients undergoing coronary artery bypass grafting, what can we conclude from the studies in this issue of the *Journal*, as well as numerous other analyses? Is there sufficient evidence to force a change in the practice of surgical coronary revascularization? Despite complex statistical methods to adjust for preoperative variables in retrospective studies, including propensity score matching, there must remain concern about selection bias for patients undergoing a multiarterial revascularization strategy. For observational database studies, despite careful matching algorithms and risk-adjustment strategies, several important variables are simply missing, unavailable to the statistician, that viscerally influence a surgeon's judgment when

choosing the revascularization strategy for each patient. These include measures of frailty, the quality and size of target vessels, the severity and distribution of stenoses, the quality of conduit available, and, importantly, such infrequent but strongly influential factors as severe chronic obstructive pulmonary disease, previous radiation to the chest, cirrhosis, inflammatory bowel disease, and other comorbidities. Beyond selection bias, retrospective analyses are particularly subject to publication bias; equivalent outcomes with multiple arterial grafts are much more unlikely to reach publication. There are smaller randomized trials supporting multiarterial grafts, such as the previously mentioned RAPS trial.⁸ We would be remiss, however, if we did not also include the Veterans Affairs trial of RA versus SVG for the second-best coronary target, which failed to show an advantage of the RA as a second graft.¹⁵ Fortunately, there are larger randomized trials in progress, most notably ART,¹³ which will substantially help inform the decision.

It has been 15 years since Lytle and colleagues' flat-footed statement,¹⁶ "Two internal thoracic artery grafts better than one." Despite the absence of strong data from randomized trials, we believe that the combination of evidence from observational studies, evidence from smaller randomized trials, and data on the favorable effect of arterial grafts on the progression of atherosclerotic coronary occlusion¹⁷ has reached a level that demands a change in practice. Patients with a reasonable life expectancy (10 years), with a good second left-sided target and without a strong risk for mediastinitis (no severe peripheral vascular disease, no diabetes, no severe obesity) should in almost every case receive a second internal thoracic graft to the left system. In the context of shared decision making, the surgeon should very strongly recommend the second arterial graft for these patients. The RA can be used rather than the RITA for patients with a good distal target and at least 90% proximal stenosis, especially if there are factors predisposing toward mediastinitis. In less ideal cases, there is still a likely benefit such that the second arterial graft should be frequently recommended, if necessary with a discussion of an increased risk of wound infection. The benefit is sufficiently well established, and the additional risk is sufficiently low. In 2014, our patients deserve a palpable shift in our practice of coronary revascularization. The time has come.

References

1. ElBardissi AW, Aranki SF, Sheng S, O'Brien SM, Greenberg CC, Gammie JS. Trends in isolated coronary artery bypass grafting: an analysis of the society of thoracic surgeons adult cardiac surgery database. *J Thorac Cardiovasc Surg.* 2012;143:273-81.
2. Serruys PW, Morice MC, Kappetein AP, Colombo A, Holmes DR, Mack MJ, et al. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. *N Engl J Med.* 2009; 360:961-72.
3. Farkouh ME, Domanski M, Sleeper LA, Siami FS, Dangas G, Mack M, et al; FREEDOM Trial Investigators. Strategies for multivessel revascularization in patients with diabetes. *N Engl J Med.* 2012;367:2375-84.
4. Locker C, Schaff HV, Dearani JA, Joyce LD, Park SJ, Burkhart HM, et al. Multiple arterial grafts improve late survival of patients undergoing coronary artery bypass graft surgery: analysis of 8622 patients with multivessel disease. *Circulation.* 2012;126:1023-30.
5. Dorman MJ, Kurlansky PA, Traad EA, Galbut DL, Zucker M, Ebra G. Bilateral internal mammary artery grafting enhances survival in diabetic patients: a 30-year follow-up of propensity score-matched cohorts. *Circulation.* 2012;126:2935-42.
6. 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.
7. 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.
8. Deb S, Cohen EA, Singh SK, Une D, Laupacis A, Fremes SE; RAPS Investigators. Radial artery and saphenous vein patency more than 5 years after coronary artery bypass surgery: Results from RAPS (Radial Artery Patency Study). *J Am Coll Cardiol.* 2012;60:28-35.
9. Cao C, Manganas C, Horton M, Bannon P, Munkholm-Larsen S, Ang SC, et al. Angiographic outcomes of radial artery versus saphenous vein in coronary artery bypass graft surgery: a meta-analysis of randomized controlled trials. *J Thorac Cardiovasc Surg.* 2013;146:255-61.
10. Tatoulis J, Buxton BF, Fuller JA. The right internal thoracic artery: the forgotten conduit—5,766 patients and 991 angiograms. *Ann Thorac Surg.* 2011;92:9-15; discussion 15-7.
11. Hayward PA, Buxton BF. Mid-term results of the Radial Artery Patency and Clinical Outcomes randomized trial. *Ann Cardiothorac Surg.* 2013;2:458-66.
12. Tranbaugh RF, Dimitrova KR, Lucido DJ, Hoffman DM, Dincheva GR, Geller CM, et al. The second best arterial graft: a propensity analysis of the radial artery versus the free right internal thoracic artery to bypass the circumflex coronary artery. *J Thorac Cardiovasc Surg.* 2014;147:133-40.
13. Taggart DP, Altman DG, Gray AM, Lees B, Nugara F, Yu LM, et al. ART Investigators. Randomized trial to compare bilateral vs. Single internal mammary coronary artery bypass grafting: 1-year results of the Arterial Revascularisation Trial (ART). *Eur Heart J.* 2010;31:2470-81.
14. Lytle BW. Bilateral internal thoracic artery grafting. *Ann Cardiothorac Surg.* 2013;2:485-92.
15. Goldman S, Sethi GK, Holman W, Thai H, McFalls E, Ward HB, et al. Radial artery grafts vs saphenous vein grafts in coronary artery bypass surgery: a randomized trial. *JAMA.* 2011;305:167-74.
16. Lytle BW, Blackstone EH, Loop FD, Houghtaling PL, Arnold JH, Akhrass R, et al. Two internal thoracic artery grafts are better than one. *J Thorac Cardiovasc Surg.* 1999;117:855-72.
17. Dimitrova KR, Hoffman DM, Geller CM, Dincheva G, Ko W, Tranbaugh RF. Arterial grafts protect the native coronary vessels from atherosclerotic disease progression. *Ann Thorac Surg.* 2012;94:475-81.