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EDITORIAL COMMENT

Is It Still Worth the Pain to "Drain" Stenosed Saphenous Veins?

Appraising Native Coronary Artery Versus Bypass Graft Percutaneous Coronary Interventions*

Rishi Puri, MBBS, PhD,[a,b] Olivier F. Bertrand, MD, PhD[a]

In 1967 while at the Cleveland Clinic, René Favaloro pioneered the use of saphenous vein grafts (SVGs) for performing coronary artery bypass graft (CABG) surgery (1), revolutionizing the treatment of obstructive coronary artery disease. CABG remains the benchmark mode of coronary revascularization for patients with multivessel and/or significant left main stem disease (2,3). However, the sobering reality is the systemic, progressive nature of atherosclerotic disease and its propensity to emerge and rapidly progress within venous conduits, often remanifesting as various facets of acute coronary syndromes. Culprit lesions in SVGs most often are complex and highly thrombotic. In fact, the 1-year SVG failure rate has been reported to be as high as 41% (4). Although total arterial surgical coronary revascularization is hailed as the novel surgical gold standard, SVGs remain workhorse conduits for bypassing most non-left anterior descending coronary lesions. As such, a growing number (presently nearly 20%) of all percutaneous coronary interventions (PCIs) occur in patients presenting with symptomatic coronary artery disease at various stages post-CABG, posing unique challenges for interventional cardiologists.

SVG PCI is associated with greater periprocedural myocardial infarction (MI) rates, in-hospital mortality, and restenosis rates compared with native coronary artery PCI (5). Distal embolization and slow flow or no reflow occurs in up to 15% of SVG PCIs, as a result of friable, ulcerated, thrombotic atheroma coupled with the release of a host of soluble vasoocclusive neurohumoral mediators that further propagate a thrombotic milieu. Furthermore, atheroma progression remote to prior stented segments occurs much more rapidly than observed in native coronary arteries (6), leading to greater revascularization rates. These associations have thus led many to query the benefits of PCI within SVGs, particularly in relation to the alternative strategy of performing PCI within the native coronary system of prior CABG recipients.

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With this in mind, in this issue of *JACC: Cardiovascular Interventions*, Brilakis et al. (7) report on the frequency, associations, and outcomes of PCI in native coronary arteries versus bypass grafts in prior CABG recipients, within the large U.S. Department of Veterans Affairs (VA) integrated health care system. Given the evolution in clinical practice, the investigators essentially chose to expand on their prior analysis capturing similar data within the National Cardiovascular Data Registry CathPCI registry from 2004 to 2009 (8). The present analysis provides data on longer term clinical outcomes (median follow-up period 3.1 years). Of the 60,000 reported PCIs performed across 67 VA hospitals from 2005 to 2013, just over 11,000 were undertaken in veterans with prior CABG. Native coronary arteries were intervened upon in nearly 75% of occasions; the remaining 25% of PCIs essentially were within SVGs. The SVG PCI group was generally older and more

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From the [a]Quebec Heart & Lung Institute, Laval University, Quebec City, Quebec, Canada; and the [b]Cleveland Clinic Coordinating Center for Clinical Research, Cleveland Clinic, Cleveland, Ohio. Both authors have reported that they have no relationships relevant to the contents of this paper to disclose.

likely diabetic with chronic kidney disease, whereas the native coronary artery PCI group was more likely to have presented with stable angina. The SVG PCI group was also less likely to receive drug-eluting stents (DES) relative to the native coronary artery PCI group. The use of an embolic protection device during SVG PCI was also relatively modest (~25%). The investigators appropriately used the third universal definition as a means of defining periprocedural MI. From the perspective of procedure-related outcomes, no reflow and periprocedural MI, mortality was assessed as being significantly greater in the SVG PCI cohort. The SVG PCI group also seemed to fare worse overall in the longer term, with a 30% greater chance of dying following hospital discharge, a 60% greater chance of a subsequent MI, and a 60% chance of requiring repeat coronary revascularization. The 1-year death and MI rates among the SVG PCI and native coronary artery PCI groups were 13.4% and 8.9%, respectively ($p < 0.001$), whereas revascularization rates were 22.7% and 14.4%, respectively ($p < 0.001$).

The investigators are indeed right to claim the present analysis to comprise the largest case series with the longest follow-up for evaluating outcomes between SVG PCI and native coronary artery PCI in CABG recipients, but several caveats of this analysis warrant consideration when attempting to place the clinical implications of these data in context. There were significant differences between the 2 populations in terms of not only baseline characteristics but also proportions, and to our reckoning, there was no propensity weighting or matching undertaken in an attempt to even out some of these inherent population differences. From a procedural perspective, several adjunct methods have been shown to improve patient outcomes when performing SVG PCI. These include the preference of DES over bare-metal stents (9), direct stenting (10), the use of embolic protection devices (11), and prompt and liberal pharmacological treatment to reverse slow flow or no reflow (12). However the use of DES in only 65% of SVG PCIs, the use of embolic protection devices in 26% of SVG PCIs, and the lack of information on the use of periprocedural pharmacology to optimize Thrombolysis In Myocardial Infarction flow during SVG PCI makes it difficult to truly interpret the relevance of these findings in relation to recognized standards for performing SVG PCI. It is also impossible to reconcile biases that undoubtedly were inherent during the decision to perform SVG versus native coronary artery PCI per patient. The absence of data adequately describing the complexity of coronary lesions as well as the fact that the rate of SVG PCI varied as a function of time elapsed post-CABG are areas in which treatment bias likely influenced study outcomes. Furthermore, these VA patients fared considerably worse in comparison with a contemporary German cohort of patients undergoing SVG PCI within the confines of the ISAR-CABG randomized controlled trial, whereby 1-year death, MI, and target vessel revascularization rates in the DES arm of ISAR-CABG were 5%, 4%, and 7% respectively (9). This compares with respective rates of 8.6%, 5.9%, and 22.7% noted in the SVG PCI group within the present VA analysis (7). Further international comparisons highlighted stent failure rates at 1 year post SVG PCI to vary between 6.6% and 10.8% of patients receiving DES and bare-metal stents, respectively, within the Western Denmark Heart Registry (13), and a prospective multicenter German registry evaluating DES during SVG PCI demonstrated a combined 1-year rate of death, MI, and stroke of 13.6% and a target vessel revascularization rates of 17.7% (14), all significantly lower than the equivalent endpoints demonstrated within the present VA registry. Finally, and perhaps just as important, the use of established medical therapies (i.e., high-intensity statins, type and duration of antiplatelet therapies) to optimize secondary prevention were not reported.

The investigators advocate that improved clinical outcomes could be achieved if interventional cardiologists would opt to revascularize native coronary lesions as opposed to performing SVG PCI in prior CABG recipients, and they further promote the femoral approach to more easily facilitate these PCIs. This assertion may be somewhat contrary to published data (15), especially given that the rate of chronic total occlusions in the native coronary artery PCI group was less than 5%, the presence of which has not been demonstrated to affect procedural success when undertaken transradially (16).

When faced with a patient with prior CABG presenting with SVG lesions with an appropriate indication for coronary revascularization, what should we as interventional cardiologists do? Despite its limitations, findings of the present analysis are consistent with a number of prior analyses and the general notion that intervening on SVG lesions poses unique challenges that associate with greater adverse events compared with the undertaking of native coronary revascularization in CABG recipients. Do these data, however, sound the death knell for SVG PCI? The answer in 2016 is simply “no.” A fundamental limitation of these analyses comparing SVG PCI with native coronary artery PCI in CABG recipients is the lack of a level playing field of baseline clinical and anatomic characteristics prior to embarking on the revascularization strategy. Furthermore, the adjunct

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steps required to optimize SVG PCI outcomes (i.e., DES use, direct stenting, embolic protection device use, and prompt pharmacotherapy to reverse slow-flow or no reflow) were either unreported or infrequently undertaken. This therefore sets the stage for the urgent need for appropriately designed prospective randomized trials to help guide clinical practice in this domain. A discussion, however, of potential trial designs is beyond the scope of this editorial. In the interim, given the appropriate clinical setting, interventional cardiologists should continue to treat CABG recipients requiring PCI on a case-by-case basis, understanding their own limitations regarding the complexity of native or SVG lesions, and to use the various strategies shown to optimize SVG PCI should this be the chosen approach for their specific patient. As Winston Churchill famously remarked, "This isn't the end. It is not even the beginning of the end. But it is, perhaps, the end of the beginning." Perhaps the same could be considered for evaluating PCI strategies in CABG recipients.

REPRINT REQUESTS AND CORRESPONDENCE: Dr. Olivier F. Bertrand, Quebec Heart & Lung Institute, 2725 Chemin Ste-Foy, Québec City, Québec G1V 4G5, Canada. E-mail: olivier.bertrand@criucpq.ulaval.ca.

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