I know what the studies say, but what should I do for my patient?

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Threatening the remarkable progress in the treatment of cardiovascular disease is the virtual epidemic of obesity and the consequent increased incidence of diabetes. The prevalence of diabetes has more than doubled in the past decade, with current estimates predicting an incidence between 1 in 5 and 1 in 3 adults by the year 2050.¹ People with diabetes are more than twice as likely to have cardiovascular disease develop, and at least 65% will die of such disease. Diabetes affects vascular physiology on multiple levels and tends to manifest with diffuse, multivessel involvement.² It is perhaps for this reason that the more “vessel-directed” surgical rather than “lesion-directed” percutaneous coronary intervention (PCI) approach has proved more successful in this population. Both randomized, controlled trials and retrospective registry reviews have documented a survival benefit associated with surgical revascularization in patients with diabetes who have multivessel disease.³⁻⁹ The potential impact of newer generation drug-eluting stents on improving these results remains to be seen.¹⁰

The challenges of comparing procedure-related outcomes are considerable. Unlike a medication, which can be biochemically defined and whose dosage and pharmacokinetics can be quantified, each procedure is subject to subtleties of technique, nuances of clinical judgment, and intricacies of care that can vary in ways that defy even the most insightful of analytic approaches. It is in this gray zone of clinical ambiguity that many, if not most, patients actually reside. It is this very uncertainty that Nauffal and colleagues¹¹ seek to address in their report in this issue of the *Journal*. Retrospective analysis of 1583 patients with diabetes undergoing coronary artery bypass grafting (CABG) with triple-vessel disease in a single institution revealed 202 who had previously undergone PCI with stenting. Both Cox regression and propensity score-matching approaches demonstrated a clear association of previous stenting with diminished 5-year survival. Certainly, one conclusion that could be

drawn from these findings is that stenting in patients with diabetes compromises subsequent surgical options and actually deprives patients of the optimal benefit that might be achieved from CABG surgery. Unfortunately, the limitations of the available data did not permit Nauffal and colleagues¹¹ to explore the specific indications for stent deployment, the extent of disease at the time of stenting, the choice of stent (bare metal vs drug eluting and first vs second generation), the patient's SYNTAX score, or the interval between PCI and subsequent CABG. It is therefore unclear whether surgery at the time of PCI might have altered the patients' clinical course, or whether the surgical option would even have been appropriate. An equally plausible hypothesis might therefore suggest that the appropriate need for previous stenting distinguished a subset of patients with more aggressive disease who therefore died earlier.

It is therefore wise to permit clinical observation to be informed by physiologic reality. PCI addresses the obstructing atherosclerotic lesion, restoring circulation to the downstream vascular bed. If angioplasty is the art of controlled injury, stenting further manipulates the healing response to provide an open conduit. As Nauffal and colleagues¹¹ note in their discussion, local and systemic inflammatory responses, as well as endothelial injury, alterations of local shear stresses, and foreign-body reaction, have all been implicated in the body's response to stents. It should not be overlooked, however, that the marginal overall morbidity when compared with even the least invasive of surgical approaches is no small matter, especially in the emerging era of patient-centered outcomes. Surgical revascularization, by focusing on the downstream circulation directly, is somewhat immune to the complexity of the lesion itself. It is important to note, however, that not all graft conduits are created equal. A recent report from the Radial Artery Patency Study (RAPS) provides compelling evidence for the superiority of the radial artery relative to the saphenous vein in revascularization of the patient with diabetes.¹² Moreover, despite considerable surgical reluctance to risk deep sternal wound infection, several studies have documented improved long-term survival (with no increased sternal wound infection) associated with the use of bilateral internal thoracic arteries in patients with diabetes.^{13,14} Although the presumption regarding the superiority of internal thoracic artery grafting has classically centered around demonstrably improved graft patency, it should not be forgotten that among the reasons for this improved patency is the physiologic milieu favoring enhanced nitric oxide production, which therefore promotes vasodilatation, inhibits thrombosis and atherosclerosis, and supports the health and viability of the endothelium

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FIGURE 1. Stenting addresses the lesion directly, while the internal thoracic artery favors enhanced nitric oxide production, promoting downstream vasodilation, inhibiting thrombosis and atherosclerosis, and supporting the health and viability of the endothelium.

(Figure 1).¹⁵⁻¹⁷ These properties in fact may not only account for the improved graft patency but may also help to account for the relative absence of atherosclerotic progression in the vascular bed distal to the arterial grafts.¹⁸ These very properties may be particularly pertinent to the patient with diabetes, enhancing the ability of CABG to address not only the functional obstructions but the underlying pathophysiology. With the rising tide of diabetic vasculopathy, it will become increasingly important to consider both clinical utility and underlying physiology in navigating the uncertain path to optimal patient care.

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