Twenty-five years after its tentative beginnings, percutaneous coronary intervention (PCI) has become the dominant form of coronary revascularization. This year, the 800,000 PCI procedures are more than double the number of coronary artery bypass graft (CABG) surgeries. Although there had already been substantial growth throughout the 1980s and early 1990s as a result of improving equipment and techniques for conventional balloon angioplasty, the accelerated growth since 1994 has clearly been fueled by the rapid adoption of coronary stenting. Today, >80% of PCI procedures involve stent placement, supported by a series of randomized trials that have demonstrated better acute angiographic results, reduced emergency surgery, and reduced recurrence rates (restenosis) when stents are placed properly with an effective antiplatelet regimen. In practice, however, the excellent results in the circumscribed lesion types studied in the key randomized trials have been generalized to other lesion morphologies (eg, small vessel, diffuse disease, bifurcation lesions) for which the evidence supporting stent use is less clear. Over the past several years, there has been a concurrent increase in the use of platelet glycoprotein IIb/IIIa inhibitors as an adjunctive therapy during PCI. A plethora of randomized clinical trials demonstrate that these agents are very effective in reducing periprocedural myocardial infarction, defined as elevation of cardiac enzymes.1–3

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Taken together, these 2 advances have made PCI faster, safer, and more durable than in the pre-1990 era in which Plain Old Balloon Angioplasty (POBA) was the only form of PCI available. Emergency bypass surgery to treat an angioplasty-induced complication, in particular, has fallen by more than an order of magnitude (from 3% to ∼0.3%) during this period.4 But it is not clear whether the magnitude of these improvements is sufficient to move the “tipping point” for coronary revascularization between PCI and surgical revascularization in difficult patient subsets (like those with extensive multivessel coronary disease) in which bypass surgery has long been dominant.

The Present Report

The article in the present issue by Srinivas et al5 attempts to shed light on this question by comparing data from 2 historical data sets—904 multivessel-diseased patients randomized to angioplasty in the Bypass Angioplasty Revascularization Investigation (BARI) trial between 1988 and 1991, and 857 patients selected for the presence of BARI-like multivessel disease from within the National Heart, Lung, and Blood Institute Dynamic Registry between 1997 and 1999. Patients with left main disease, prior PCI, or prior bypass surgery and those undergoing treatment for acute myocardial infarction were excluded from both cohorts. Reflecting more current practice, the Dynamic Registry patients made substantial use of intracoronary stents (76%) and glycoprotein IIb/IIIa inhibitors (24%), neither of which were available to the BARI operators. As such, contemporary PCI was associated with improved angiographic success rates (from 72% in BARI to 91% in the Dynamic Registry), with dramatically reduced rates of abrupt vessel closures (from 9.5% to 1.5%, P = 0.001) and in-hospital CABG (from 10.2% to 1.9%, P = 0.001). Although there were no reductions in late death or myocardial infarction (MI), there was a markedly reduced need for repeat revascularization 1 year after the initial procedure, with late CABG falling from 22.7% to 8.6%, and late PCI falling from 22.5% to 12.4% (both P = 0.001). This report thus confirms our notion (based on multiple prospective randomized clinical trials) that the incorporation of new technologies and drugs has actually resulted in significant improvements in clinical outcomes for patients undergoing PCI.

Limitations of the Present Analysis

Despite the rigorous and standardized methods used in the present analysis, there are a number of potential challenges in any attempt to match data collected a decade apart from 2 distinct patient populations that used different methodology. For example, the observation that Dynamic Registry patients with multivessel disease had fewer lesions attempted (1.53, versus 2.56 lesions per patient in BARI), with the majority (59% versus 24% in BARI) having only a single lesion attempted, is subject to several caveats. One is the selective nature of the BARI randomized PTCA cohort, who represented only 44% of patients that met eligibility criteria. Other BARI-eligible patients refusing randomization were enrolled instead in a BARI Registry, wherein nearly two thirds
underwent PCI at the discretion of the operator, with more common 2- (rather than 3-) vessel disease than seen in the BARI Randomized cohort. Perhaps these BARI Registry patients (or at least the sum of BARI Randomized plus Registry patients) might be a more reasonable and representative group against which to compare the Dynamic Registry patients with multivessel disease chosen by their physicians to undergo PCI.

A second caveat in this comparison is the important methodological differences between the 2 studies. In BARI, films were elevated by clinical sites that used computer-assisted caliper measurements backed up by an independent angiographic core laboratory, whereas in the Dynamic Registry, only clinical site visual estimates were used. This difference in methodology may have contributed to the marked improvements in angiographic success rates (from 72% to 91% in the Dynamic Registry), because absolute differences of 10% to 20% are expected between Core Laboratory and clinical site readings.7 The different angiographic measurement methodologies may also explain the observed differences in reference vessel size and preprocedural percent stenosis between the 2 groups,8 while precluding use of reference vessel size or posttreatment lumen diameter—important predictors of subsequent restenosis—in multivariable models of repeat revascularization.

Although it is understandable that natural history markers such as late mortality and myocardial infarction rates after PCI have not been reduced substantially over the past decade, it is surprising that the frequency of periprocedural myocardial infarction has remained unchanged. Proponents of GP IIb/IIIa inhibitors might argue that the frequency of use of GP IIb/IIIa inhibitors in the Dynamic Registry was insufficient (26%), to fully realize the benefits of these agents in reducing MI, compared with the current 50% to 60% use of GP IIb/IIIa blockers in this country. But another reason could be a change in the definition of MI. In the BARI trial, the conservative World Health Association criteria (CK >2× normal) was used, whereas current criteria have become more sensitive measures of CK-PK-MB fractions or troponin.8 A net beneficial effect on reduction of MI in parallel with the reduction in emergency surgery may have been masked by the increased sensitivity of MI detection in more recent series.

Where Do We Go From Here?
The most dramatic demonstration of benefit shown in this study was the 50% reduction in repeat revascularization (PCI or CABG at one year falling from 40.7% to 19.4% in the Dynamic Registry), which is a robust measure of treatment durability. Much of this benefit is what would be expected from the use of stents rather than POBA, and similar results were seen in the Arterial Revascularization Therapy Study (ARTS) in which multivessel stenting (average 2.4 lesions per patient) was compared with bypass surgery.10 This should thus be seen as real progress. But still newer therapies that may further improve the late clinical outcomes in patients undergoing multivessel PCI—such as drug-eluting stents—are already on the horizon.11,12 Additional studies (ARTS-II, Freedom) are thus planned to examine the benefits of drug-eluting stents compared with coronary bypass surgery in patients with multivessel disease.

Issues Relating to Diabetes and Progressive Atherosclerosis
Although the application of new PCI technology has led to continuous improvement in the frequency of restenosis at the treated site, there has been no substantial impact on the underlying atherosclerosis process or the manifest risk of spontaneous myocardial infarction. This risk varies from 1% to 2% per year for nondiabetic patients with single-vessel disease to up to 10% to 15% per year for diabetic patients with 3-vessel disease.13 Roughly 20% of the patients in the Randomized BARI and multivessel Dynamic Registry cohorts had diabetes mellitus, and although BARI showed no mortality benefit of bypass surgery over PCI overall, the diabetic cohort showed a large mortality benefit for CABG. Although the higher incidence of restenosis in the patients with diabetes after PCI may have contributed,14 most of the benefit derived from the substantial reduction in the 5-year incidence of MI for patients with diabetes randomized to CABG compared with PCI. Moreover, the BARI investigators recently reported that the 5-year mortality rate from late Q-wave MI was reduced by 90% in patients with diabetes assigned to CABG compared with those assigned to PCI.15 We must therefore be mindful that CABG offers a unique long-term MI protective effect by replacing a proximal native vessel laden with vulnerable plaque with a less vulnerable graft, helping to minimize new infarctions originating from plaque rupture outside the site of original PCI site.16 This notion has been confirmed by the ARTS trial, which showed a suggestive (but not statistically significant) 50% higher 1-year mortality rate for patients with diabetes assigned to multivessel stenting rather than CABG.17

With the introduction of promising drug-eluting stents that may nearly eliminate restenosis, the weakest link for PCI might shift from restenosis to its inability to prevent future spontaneous myocardial infarction. At the very least, this underscores the need for aggressive risk-factor modification in all patients undergoing intervention. It may also drive the development of modalities to detect and localize nonobstructive (but vulnerable) plaques and evaluation of treatments (including possibly drug-eluting stents) to stabilize the highest risk lesions, in an effort to prevent MI in those patients felt to be at high risk.

A Decade’s Progress Report
As an interventional community, we should take pride in the major strides we have made in the success, safety, and durability of PCI over the past decade. During that time we have acquired significant understanding of the importance of obtaining an excellent acute mechanical result, the technique of stent delivery and deployment, how to design optimal pharmacology for the prevention of subacute stent thrombosis, and how to use brachytherapy to reduce the chance for an additional recurrence of in-stent restenosis. On the other hand—and despite high initial expectations, positive randomized trials,18 and approval by the Food and Drug Administration—other technologies such as directional, rotational, and...
laser atherectomy have been reduced to niche applications that together account for <10% of current interventional volume. Still newer technologies—drug-eluting stents, distal embolic protection, and devices for crossing chronic total occlusions, among others—are now on the horizon. Although each new technology will make its way into clinical practice via the results of controlled, randomized trials performed in carefully chosen, homogeneous patient and lesion subsets, well-run registries can continue to serve important roles in the initial evaluation of device indications and technique and in hypothesis generation, as was done by the New Approaches to Coronary Intervention (NACI) registry at the onset of the new device era. Even in the postapproval phase, each new device invariably finds clinical use beyond that studied in a randomized trial. “Real-world” registries, such as the Dynamic Registry, may then provide important feedback to validate that the improved outcomes predicted on the basis of the homogeneous populations in pivotal randomized studies are actually obtained in our most broadly constituted patient population.

References


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A Decade of Improvement in the Clinical Outcomes of Percutaneous Coronary Intervention for Multivessel Coronary Artery Disease
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