In the modern era of percutaneous coronary interventions (PCI), drug-eluting stents are commonly used to reduce the risk of restenosis. With the development of second-generation drug-eluting stents, there has been a significant reduction in the incidence of restenosis with rates ranging from 6% to 10% in most clinical trials, with emerging evidence for a reduction in late myocardial infarction (MI). Numerically, the rate of clinical restenosis is now close to the rate of MI, 1 to 2 years after a PCI. However, among patients with multivessel coronary artery disease (CAD) there remains uncertainty regarding the risk of restenosis, stent thrombosis (ST), and possible late MI. Interventional cardiologists are, therefore, faced with a dilemma in trading off the various risks of adverse events (such as the need for repeat revascularization and periprocedural MI) during decision-making for the most appropriate use of PCI.

In this issue of Circulation: Cardiovascular Interventions, Stolker and colleagues report on the use and need for repeat revascularization in a large contemporary registry. The EVENT Registry was a prospective observational registry designed to study PCI in clinical practice in 55 US centers. A total of 10,144 patients were included; ≈5%, ST-segment-elevation myocardial infarction (STEMI); 40% other acute coronary syndromes; and 49% with stable CAD. Analysis of 4 main outcomes was undertaken: ST, target lesion revascularization (TLR), target vessel revascularization, or other vessel revascularization. TLR was defined as repeat PCI or bypass graft placement for restenosis at the lesion treated during index PCI, or occurring within 5 mm of the PCI site (edge effect) as determined clinically by the investigator at each site. Target vessel revascularization was defined as unplanned repeat PCI or bypass graft placement for a stenosis in another part of the vessel treated at the index PCI (ie, exclusive of TLR events). Other vessel revascularization was defined as unplanned repeat revascularization of a coronary artery or bypass graft other than the vessel treated at index PCI. Unfortunately, there is no information on the rate of periprocedural MI, or on later MI that did not lead to repeat revascularizations. Thus, the global risk with PCI still cannot be inferred from this article. For instance, the risk of ST was 0.6% at 1 year, but it represented 7.1% of all repeat procedures, presumably all with a presenting MI, suggesting that some patients had MI or sudden death that was not accounted for. In addition, using a hierarchical type of analysis, late ST after a repeat procedure was not included in the analysis. Despite these caveats, this study offers other very important findings that will likely shape the future of PCI.

In the registry, during the 1-year follow-up period, 11.9% required repeat procedures, of which TLR and target vessel revascularization represented 62%, thus yielding an overall clinical restenosis rate of 6.2% (including ST), a remarkably low rate in a mixed case population that includes multivessel PCI and ST-elevation MI. The registry also showed that the remaining burden of repeat procedures lies among patients with multivessel PCI, as nontarget vessel revascularization represented 38% of repeat procedures. Among the 1687 patients who had multivessel PCI, the majority had it during the index hospitalization, whereas 19% underwent staged procedures with remarkable heterogeneity in practice (0% in some hospitals, up to >40% in others).

What can explain this variance in practice? There are remarkably few randomized trials that have explored the practice of multivessel PCI and whether to stage the procedure or not. In many cases it is based on the perceived risk of late ST when multiple coronary beds are treated, the emergence of a complication, or the risk of overexposure to angiographic dye. Although some of this is to be expected, it cannot explain the variance seen. The use of fractional flow reserve (FFR) has moved us from an anatomical approach in multivessel coronary artery disease to one of functional importance, with improved clinical outcomes as a consequence. In the first fractional flow reserve versus angiography for multivessel evaluation study, there was a 28% reduction in clinical events at 1 year, with a consistent reduction in death, MI, and repeat revascularization when FFR was applied routinely compared with angiography alone. When FFR was applied, some 37% of lesions had an FFR >0.8, thus suggesting that many of the patients who were destined for staged procedures in the EVENT registry may not have required it. These findings have now been extended to evaluating the culprit lesion. In the fractional flow reserve versus angiography for multivessel evaluation-2 trial, 888 patients were randomized to optimal medical therapy versus optimal medical therapy and FFR of the vessel thought to be most likely giving rise to ischemia (with PCI performed if FFR<0.8). The trial was stopped early because of a significant reduction in the need for urgent revascularization (1.6% versus 11.1%; P<0.001) among

The opinions expressed in this article are not necessarily those of the editors or of the American Heart Association.

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patients assigned to FFR+optimal medical therapy. These 2 trials combined highlight the importance of moving toward a functional assessment of lesion evaluation in the current era of PCI.7 Unfortunately, the use of FFR was not recorded in the EVENT registry, making it hard to assess the impact this may have had on the staged procedures.

It is important to recognize that many patients destined for staged procedures are those who receive primary PCI in the early setting of their MI. This is highlighted in the registry, as there was a significant difference in STEMI among those with staged or initial index multivessel PCI (18% versus 4%, P<0.01). In STEMI patients, the American College of Cardiology/American Heart Association practice guidelines have recommended against (Class III, level C) performing multivessel PCI outside the culprit lesion,8 whereas it is performed routinely in other forms of acute and elective PCI. In general, complete revascularization has been associated with better outcomes in stable CAD patients.7 Furthermore, a recent meta-analysis of STEMI multivessel PCI has suggested that long-term outcomes are comparable from evaluation of registries as there are few randomized trials in this setting.8 It is also unclear at this point whether one can safely perform FFR in the nonculprit vessel in STEMI, and what the optimal FFR would be. These findings suggest that we need randomized trials in the setting of MI that can inform us whether we should perform acute multivessel PCI, in-hospital staged PCI, or deferred PCI in multivessel CAD. The EVENT registry already informs us that multivessel CAD is an independent predictor (hazard ratio 1.19; 95% CI: 1.06–1.35) of the need for late nontarget revascularization; what we need to understand is the best timing.

The EVENT registry also defines the area of opportunity to further reduce the rate of clinical restenosis. It is remarkable that many of the lesion characteristics that lead to restenosis are similar to those that existed in the early phase of PCI.10 Although drug-eluting stents use has had a profound effect with a lower need for TLR, and diabetes is no longer an important factor, we have yet to solve the recurrence rate of TLR in left main or saphenous vein graft PCI.

Carefully conducted registries, like the EVENT registries, are crucial for further development of PCI in an optimal way. With these observations on repeat revascularization procedures, we have seen that to some extent we have re-invented the wheel, trying to define the right timing of additional PCI procedures in MI, but with a move toward functional assessment of lesions. The Achilles’ heel of clinical restenosis is still exposed, albeit to a lesser extent, with certain lesion characteristics that elude what we have accomplished for most. Continued reappraisal of our PCI practice in the current era is as much needed now as it was in the 1990s and needs to be continuously built upon randomized trials and registries.

**Disclosures**

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**References**


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