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EDITORIAL COMMENT

Counterintuitive Contributions to the Care of Myocardial Infarction and the Need for Randomized Trials*

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What We Think We See, May Be What We Think We Get, But If We Only Knew

Many practitioners of the fledgling discipline of interventional cardiology may count Charles Dotter, Andreas Gruntzig, Marcus DeWood (and Selinger and Berg), Peter Rentrop, and Geoffrey Hartzler among their heroes. Whatever else each of these individuals did or did not do, for a moment they had the courage to try something for their patients that they believed might help and most authorities of the time "knew" would not (i.e., counterintuitive).

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At the time each of these individuals attempted a new procedure:

- To run a vascular dilator over a wire through the obstructed leg artery of patients tentatively scheduled for lower extremity amputation (1);
- To take acute myocardial infarction (MI) patients to the catheterization laboratory and then to emergency bypass surgery (2,3);
- To inflate a balloon within the lumen of a tight osteal left anterior descending artery of an awake patient, with limiting angina (4);
- To try to open occluded arteries in acutely infarcting patients by using intracoronary nitroglycerin and streptokinase and even a 32/1,000 guide wire (5);
- To take acutely infarcting patients to the catheterization laboratory to combine steps 2 through 4 by ballooning fresh thrombotic occlusion (6).

none of these approaches was considered *reasonable* by most authorities of the time.

Point one: Had they not *dared*, there would have been no subsequent justification for many of the trials that have facilitated a revolution in the care of acute ST elevation MI.

After Dotter, Judkins, Gruntzig, DeWood, Rentrop, Hartzler, and many others, *as well as their courageous patients*, "got away with it" and some of their patients appeared to benefit, it then became possible to consider whether these innovations were real advances, applicable to a broad range of patients, rather than isolated observations. With the concomitant developments in epidemiology, biostatistics, and the growing discipline of randomized clinical trials, it became possible to design, conduct, and analyze trials, ushering in the "reperfusion era" and leading to new debates, such as the intravenous thrombolytic therapy versus primary angioplasty debate and whether patients should be transported for primary angioplasty or have it performed at centers without on-site surgery, among others. We now know that reperfusion therapy is the way to treat acute ST elevation MI, and we know that where an experienced interventional team is available, primary angioplasty confers better results than thrombolytic therapy (7–13).

Point two: Biologic and clinical insights are evolutionary, often requiring revision after new counterintuitive results are obtained in serial randomized clinical trials.

In the meantime, we have also learned from the hard work of countless investigators and hundreds of thousands of brave patients that:

- Stents can treat and prevent occlusive dissection and acute recoil (13);
- Stents can prevent negative remodeling and recoil, thereby reducing restenosis (14,15); and
- Stents are associated with improved short- and long-term outcomes among a variety of subsets, including patients with a heavy thrombus burden, such as acute ST elevation MI (16–24).

By the time the multicenter Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications (CADILLAC) trial was completed, a number of small trials of balloon versus stent in primary angioplasty had been reported, suggesting better outcomes with stents (16–24). Table 23 in the 2001 ACC/AHA PCI Guidelines listed seven trials with a total of nearly 1,000 patients in each arm (13). The CADILLAC trial confirmed that *overall*, stent use was associated with improved outcomes, primarily as a result of decreased repeat revascularization (25). It further clarified the antiplatelet therapy evolution, which has been a parallel and synergistic development. These results have "fit" into the more generalized "stent revolution," which has changed percutaneous intervention more than anything besides the balloon.

Many clinicians and health care planners have questioned the need for routine stenting and have proposed a variety of strategies for "provisional stenting." Essentially, any effort to optimize balloon angioplasty without a stent (such as prolonged inflation or high-pressure inflation) and then document a stent-like result (such as via quantitative angiography or Doppler flow measurements or intracoronary ultrasound measurements), reserving stenting for those patients who fail to achieve the stent-like result, qualifies as "provisional stenting." The primary motivation for provi-

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sional stenting has been economic; however, it is clear that depending upon the method of augmenting simple balloon angioplasty (perfusion balloons, noncompliant balloons) and documenting the stent-like result (ultrasound probes, flow-wires), provisional stenting may entail additional costs, albeit perhaps less than one or more stents.

In addition to economic considerations, many anatomies do not lend themselves to stent delivery (such as diffusely diseased, small-caliber, and heavily calcified lesions) or to adequate stent coverage (such as some bifurcation or sharply angulated segments or transitions from grafts to much smaller native coronary segments) or to as favorable long-term results (bifurcations and small-caliber vessels). When stents were first released, the most counterintuitive setting into which to place them might well have been settings with a heavy thrombus burden. Yet, unstable angina and acute ST elevation MI patients with angiographic thrombus have clearly benefited from this technology.

In this issue of the *Journal*, the CADILLAC trialists (26) focused on the portion of ST elevation MI patients randomly allocated to balloon only, which met rigorous, core lab-adjudicated criteria for a stent-like result. The use of a separate core lab to identify a stent-like angiographic result after the fact is, in a sense, the best-case analysis for provisional stenting. Similarly, if a heavy thrombus burden identifies a particularly unfavorable lesion characteristic for stenting, then the subset of acute ST elevation MI patients who got an optimal result with balloon alone should be one group for which provisional stenting makes the most sense. The finding that even these patients did worse in the long run than their routinely stented brethren joins a list of recent provisional versus routine stenting trials in more favorable (i.e., less acute and less likely to be clot-rich) patient groups (27–31). The concordance of the results across a wide spectrum of pathology is leading many operators to the conclusion that the optimal strategy is to deploy a stent wherever there is a flow-limiting lesion that you can reach and in which you can fully deploy a suitable stent. This may be oversimplified, but for a patient with acute ST elevation MI and a thrombotic occlusion that can be opened, one is likely to get better short- and long-term results with a stent. I am not sure who would have predicted that, when the original stent protocol included dextran, heparin, aspirin, and enough Coumadin to have inpatient hospital stays that rivaled coronary artery bypass grafting, but I do know I wasn't one of them.

Point three: When there is concordance among multiple large, prospective randomized trials testing the same intervention, it is time to incorporate the results into day-to-day practice.

When my children were much younger, we often went to celebrations of our Scottish ancestry called the Highland Games. At these events, Scots and pseudo-Scots participated in many curious forms of behavior that members of earlier generations had devised for their amusement. As we watched a "caber toss," one of my sons inquired, "Daddy, why are these men wearing skirts and throwing a telephone pole?" Before I could formulate a suitable hypothesis, a particularly large Scot turned to my son and bellowed, "Because we donna know any better, laddie." As it happens, that is also why we do randomized clinical trials.

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