Problems in the Development of New Devices for Coronary Intervention: Possible Role for a Multicenter Registry*

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Information about results and relative benefits is a prerequisite for intelligent choices by payers and consumers as well as by the providers of health care. Inadequately tested technology and insufficient information about outcomes of clinical procedures hamper efforts to improve health care.

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When percutaneous transluminal coronary angioplasty (PTCA) was developed 12 years ago, it was seen as a limited technique applicable to no more than 5% to 10% of the patients undergoing coronary bypass surgery. However, over the last 5 years improvements in angioplasty equipment and technique have allowed balloon angioplasty to expand to the point where more than 200,000 coronary angioplasties were performed in 1988, accounting for more than one half of total coronary revascularization procedures (angioplasty or bypass surgery) (1). At the same time, procedural success has improved (from 65% to 85%) and the need for emergency bypass operations has fallen (from 6% to 2%) (2), even though coronary angioplasty is now being applied in progressively more difficult anatomic and clinical situations. This rapid acceptance of coronary angioplasty by the medical community has been facilitated by the perception that angioplasty is (in selected patients) a less invasive and less costly means of revascularization than the alternative surgical bypass procedure.

Limitations of Conventional Balloon Angioplasty

Despite its current overall success, conventional coronary angioplasty is still troubled by four major problems: 1) difficulty in crossing some lesions (particularly chronic total occlusions) with the guide wire and balloon; 2) difficulty in adequately dilating certain rigid (calcified or fibrotic) or elastic (eccentric) lesions; 3) difficulty in preventing or reversing intimal dissection and resultant abrupt closure, which can lead to emergency bypass surgery; and 4) difficulty in reducing the incidence of proliferative restenosis, which causes return of angiographic narrowing and ischemic symptoms in 25% to 30% of patients within 6 months of initial successful dilation.

Promising New Technologies

Convinced that these problems cannot be solved within the confines of conventional coronary balloon dilation and supported by the venture capital community (itself cognizant of the rapid growth of conventional angioplasty), physician-inventors have devised a variety of alternative approaches to address one or more of these limitations. More than two dozen separate devices are now in or approaching clinical testing, including 1) aggressive mechanical techniques for crossing total occlusions, 2) mechanical atherectomy devices, 3) athero-abrasion and dispersion catheters, 4) intracoronary stents, 5) ablative laser techniques, and 6) thermal techniques ("hot tip" and laser balloon angioplasty).

Two of us (D.S.B. and K.D.) recently performed a survey of interventional cardiologists showing that approximately 1,000 coronary procedures had been performed by the end of 1988 using one of 10 distinct new technology devices. Reports presented at the March 1989 meeting of the American College of Cardiology (3-6) suggest that some of these techniques have early results equal to or better than those of conventional balloon dilation. However, the evaluation of long-term benefit (namely, the restenosis rate) will require ongoing performance of late (4 to 6 month) follow-up angiography. These investigational devices and their concomitant medical therapy are still undergoing refinement, but it is...
already clear that one or more of these new techniques will play an important role in interventional cardiology, although others will offer no proved net advantage over conventional balloon dilation.

**Problems to Be Faced in the Device Approval Process**

If these new techniques can realize their potential, they will allow interventional catheter procedures to be performed with greater success and safety and account for an even larger fraction of revascularization procedures. To be adopted, however, any new procedure must receive approval from three constituencies: 1) the Food and Drug Administration (FDA), 2) the third party payers (led by Medicare), and 3) the medical community. How this approval process unfolds over the next 2 to 3 years will have important consequences for interventional cardiology and, in fact, for the cardiac health of our nation. It is not clear that traditional FDA protocols (even those currently used to evaluate new conventional balloon angioplasty catheters) can deal adequately with the simultaneous clinical investigation of this number of diverse new technologies.

**The Food and Drug Administration**

New devices that entail significant patient risk undergo an evaluation process similar to that required for new drugs (7). On the basis of laboratory and animal testing, a corporate sponsor seeks an Investigational Device Exemption (IDE) to perform clinical testing at a limited number of centers (usually one or two, including that of the physician-inventor). Investigation may begin only after approval of the exemption by both the FDA and the Institutional Review Board at the participating hospital. If the initial results are favorable, the FDA may allow expansion to include more centers while the sponsor continues to collect sufficient clinical experience to establish safety and efficacy in the eyes of the FDA.

Once enough experience has been collected, the company summarizes all preclinical and clinical data in a pre-market approval application. This is reviewed by the FDA itself and by an "FDA Public Advisory Group" composed primarily of physicians. Only after this review (which takes an average of 1 year [7]) is the device granted a Pre-Market Approval allowing general commercial release. Even before Pre-Market Approval is granted, however, companies are allowed to charge participating investigators a "reasonable price" (generally $500 to $1,000) for each device based on manufacturing costs.

Current investigations vary as to what aspects of new device performance are being evaluated (i.e., success, ability to prevent or reverse abrupt closure or ability to prevent restenosis), what comparison standards are used (does a device have to be better than conventional balloon angioplasty or only "as good"?), and how the comparison to conventional balloon angioplasty is made (particularly considering that the population treated with most new devices includes large numbers of patients at "high risk" for an unfavorable outcome with conventional angioplasty and that most early trials do not include a conventional angioplasty arm).

**Third Party Payers**

When conventional balloon angioplasty was in a developmental state (1979 to 1981) similar to that of today's new technology devices, reimbursement was on a "cost" basis. This procedure allowed hospitals performing the still investigational procedure to receive reimbursement for the overall hospitalization (including hospital days and attendant catheterization and angiography), even though the angioplasty procedure itself remained uncovered. By the time the current Medicare system was implemented in 1983, angioplasty devices had already received FDA approval, so that coronary angioplasty became an approved procedure within a Diagnosis Related Group (first DRG 108 and later DRG 112) (8). Private insurance payers (i.e., Blue Cross) have generally provided a similar level of reimbursement, although they do not use a DRG system as such.

*No overall policy has been formulated regarding reimbursement for "new technology" procedures during the years before they are granted a Pre-Market Approval by the FDA. Moreover, FDA approval alone is not sufficient because devices must then undergo independent review by the Health Care Financing Administration (HCFA) (7). Many physicians feel that any percutaneous transluminal procedure that enlarges a coronary artery lumen is an "angioplasty" and is therefore eligible for reimbursement under that code. Thus, new technology procedures might also be reimbursable under DRG 112 in patients who otherwise would be receiving conventional angioplasty as a clinically indicated therapy.*

On the other hand, current Medicare regulations view any procedure that uses an investigational device as "experimental," with potential denial of all hospitalization claims whenever any new technology procedure is performed (alone or in conjunction with conventional angioplasty) (9). If generalized to other payers, this practice would have a chilling effect on current investigation and would bring the development of subsequent devices to a virtual standstill. The cost of hospitalization would then fall on the device sponsor. The companies responsible for new technology angioplasty devices are generally single product firms working on limited venture capitalization. As a result, they are poorly positioned to absorb clinical care expenses (approximately $10,000 per patient) for all procedures performed before FDA approval, in addition to
their substantial engineering, manufacturing and regulatory costs.

The Medical Community

Ideally, the medical community bases its decisions on controlled randomized studies, in this case comparison of each new device with conventional balloon angioplasty (or possibly with other competing devices), examining safety and efficacy against specific problems. Complete studies will ultimately be performed, but experience with balloon angioplasty suggests that they may take 5 to 10 years. By that time, several devices will have already received FDA approval, forcing clinicians to choose among them on the basis of less exhaustive data.

Moreover, interpretation of preliminary results with new devices is difficult because these investigations do not necessarily involve "mainstream" conventional coronary angioplasty candidates. Patient selection is based on anatomic features that favor successful delivery of prototype devices, but it is also skewed strongly toward "high risk" patients referred for new technology procedures as alternative treatment for situations unfavorable to conventional angioplasty (multiple prior restenoses, eccentric lesions, vein graft stenoses). In such patients, accurate interpretation of early results requires careful reporting utilizing standardized definitions of patient subgroups, short- and long-term results and complications. Use of a common definition set is also required if results are to be compared with those expected from conventional balloon angioplasty in similar patients.

A Possible Solution

Although the new technologies for coronary intervention offer substantial potential, they come wrapped in some difficult problems. Failure to solve these problems effectively could lead either to premature release of devices that offer little additional benefit (and possibly greater risk or expense than conventional balloon angioplasty) (10), or to delay in the availability of technologies that have the potential to generate annual savings of over $100 million in surgical costs for the treatment of abrupt closure and over $500 million in subsequent revascularization costs for the treatment of restenosis.

Creation of a registry to collect data on new devices and technology. Broader programs for the assessment of new medical technology are in the planning stage (10), but a possible shorter-term solution entails creation of a registry devoted to the collection of information on new technology coronary angioplasty, analogous to the National Heart, Lung, and Blood Institute-sponsored PTCA Registries I (1979 to 1981) and II (1985 to 1986) (2), which played such an instrumental role in facilitating the understanding and acceptance of conventional balloon angioplasty. Devices would be eligible for inclusion once they had moved to the multicenter level and could continue to participate until receipt of Pre-Market Approval. Baseline clinical and angiographic data, procedural success and complications, and follow-up data would be collected using similar definitions for all participating devices, although the procedure description would be unique to each device. Such a registry would allow easy understanding of results with each device, and would permit comparison with conventional balloon angioplasty in an appropriate group of patients from the prior registries. The results of one device could also be compared with those of another, using similar definitions and carefully selected matched patient subgroups (i.e., mid-graft lesions, more than 1 year postsurgical bypass).

Primary access to registry data could be restricted to the group of physicians (and the corporate sponsor) investigating each device, although data could be submitted to the FDA by the sponsor in parallel. Investigator and sponsor approval would be required before comparisons could be made with conventional angioplasty or other consenting devices.

Although it may be reasonable to ask corporate sponsors to bear part of the cost of initial cases, devices might then be granted provisional third party payer approval for reimbursement at a level equivalent to that of conventional angioplasty, if they could substantiate "angioplasty-equivalent" results after treating specified numbers of patients (i.e., 100, 250 and 500 patients). Devices not meeting these agreed upon performance levels could be placed on probationary funding status until changes in device design or protocol bring results into line. In this way, third party payer expenses would not exceed those of an equivalent number of clinically indicated conventional angioplasty procedures, although the third parties would benefit by participating in the collection of the quality data needed to make intelligent choices among the several potentially beneficial and cost saving new technologies.

Recommendations. We believe that the problems of new technology coronary angioplasty are sufficiently pressing to warrant the creation of a multicenter registry as our best opportunity to perform controlled, high quality investigation of promising new angioplasty technologies at a reasonable pace without jeopardizing either patient safety or health care costs. However, for this approach to be taken, preparations must begin immediately because new technology coronary procedures are now being performed at a rapidly accelerating pace. Once a suitable registry has been created, additional infrastructure (including channels of communication among device sponsors, investigators, the FDA and the HCFA) and a participatory reimbursement scheme (for what already exceeds $10 million in clinical care costs) must be established.
References


