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Editorial Comment

Understanding the CAVEAT Paradox*

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Directional coronary atherectomy was first developed by Simpson in 1984 to overcome the limitations of balloon angioplasty—abrupt vessel closure and restenosis. On the basis of encouraging results from an uncontrolled registry of consecutively treated patients, the Food and Drug Administration (FDA) approved directional atherectomy in 1990 for general use, and it gradually became accepted in the early 1990s by the interventional cardiology community as an alternative to balloon angioplasty.

In 1993 the reports of the first Coronary Angioplasty Versus Excisional Atherectomy Trial (CAVEAT-I) and the Canadian Coronary Atherectomy Trial (CCAT) were published together in the *New England Journal of Medicine* (1,2). These randomized trials showed that directional coronary atherectomy caused more myocardial infarctions than did balloon angioplasty, was more expensive, and failed to significantly lower the rate of restenosis. Despite concerns about directional atherectomy (3), Omoigui et al. (4) report in this issue of the Journal that the 35 clinical sites participating in CAVEAT-I increased their use of directional atherectomy during the year after publication of the study from 10.7% of all interventional cases in 1993 to 14.1% 1 year later. During the same time period, the use of balloon angioplasty decreased from 83.8% to 68.5%. What explains the increase in directional atherectomy procedures performed by well informed investigators after publication of two negative trials?

Randomized trials and clinical practice. Several factors that determine how randomized trials influence clinical practice, including the timing of the studies, direction of the findings (positive or negative), analysis of the end points and counterforces that emerge when unexpected results are obtained (5). Some of these factors may help us understand the CAVEAT paradox.

Timing. Meinert and Tonascia (5) write that the optimal time to perform a randomized trial is before a treatment is accepted or rejected in clinical practice. A trial carried out after a treatment has already been accepted will have a smaller effect than one that is carried out before a treatment is established. By the time the randomized trials were reported in 1993, directional atherectomy had been in general, noninvestigational use for almost 3 years. Its growing acceptance was based on the attractive concept that removing tissue with atherectomy was superior to compressing it with balloons. This concept was supported by several studies published at the time suggesting that the strongest predictor of restenosis was the size of lumen achieved at the time of the procedure, and that directional atherectomy produced consistently larger lumens than conventional balloon angioplasty (6,7).

Negative results. The randomized trials of directional atherectomy not only failed to show that this treatment could significantly reduce the rate of restenosis, but they raised serious questions about the safety of the technique. These negative results contradicted the prevailing notions about directional atherectomy. However, it is a basic rule of clinical trial research that studies with positive results are easier to accept and translate into clinical practice than those with negative findings (5).

Counterforces. A company whose product is threatened by the results of a negative trial can be expected to provide alternative explanations (5). Several investigators quickly pointed out that directional atherectomy resulted in better angiographic outcomes than did balloon angioplasty. In CAVEAT-I, directional atherectomy produced a greater increase in the diameter of the coronary artery than did balloon angioplasty (1.05-mm vs. 0.86-mm increase) and produced a favorable trend in the rate of restenosis (50% vs. 57%, $p = 0.06$) (1). In CCAT, directional atherectomy enlarged the lumen diameter more than did balloon angioplasty (1.45-mm vs. 1.16-mm increase), but restenosis was identical in the two treatment groups (46% vs. 43%) (2).

The impact of a randomized trial on clinical practice depends on the number of persons in the medical community who believe that a treatment is useful (5). Many investigators believed that the benefits of tissue removal were intuitive, but they were concerned that the extent of tissue removal in the randomized trials was inadequate. The use of small atherectomy devices in the majority of cases, retrieval of scant tissue and lack of adjunctive balloon angioplasty for further lumen enlargement were identified as factors responsible for the "underwhelming" posttreatment diameter stenoses of 29% in CAVEAT-I (1) and 26% in CCAT (2). These immediate posttreatment results were thought to be responsible for the inability of directional atherectomy to significantly lower the rates of restenosis or to produce clinical benefits. Several investigators were convinced that "optimal" atherectomy techniques could consistently achieve <10% diameter stenosis without increasing the risk of myocardial infarction, a goal that was later demonstrated in the Optimal Atherectomy Restenosis Study (8).

No alternative techniques available. Randomized trials such as CAVEAT-I and CCAT establish only broad therapeutic principles, not the precise details of a regimen (5). Although it was recognized that directional atherectomy should not substitute for balloon angioplasty for the broad range of low

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Abbreviations and Acronyms

CAVEAT = Coronary Angioplasty Versus Excisional Atherectomy Trial
CCAT = Canadian Coronary Atherectomy Trial
FDA = Food and Drug Administration

risk and moderately complex lesions studied in CAVEAT-I and CCAT, it was believed that atherectomy could be used for complex coronary lesions judged to be unsuitable for balloon angioplasty. Directional atherectomy prevailed at a time when no other advanced technique was available to overcome the limitations of balloon angioplasty. The selective use of atherectomy was justifiable for complex lesions in the era before approval of coronary artery stenting, especially for situations in which balloon angioplasty would have led to unsuccessful outcomes or would have been complicated by emergency bypass surgery.

Epilogue. Since 1994 several additional studies have evaluated the performance of directional atherectomy against balloon angioplasty. In CAVEAT-II, 305 patients with lesions in saphenous vein grafts were randomly assigned to treatment with directional atherectomy or balloon angioplasty (9). Although the initial lumen gain was greater with atherectomy (1.45-mm vs. 1.12-mm increase), distal embolization was significantly increased, and the rates of restenosis were similar at 6 months (46% for atherectomy vs. 51% for angioplasty). In the Balloon Versus Optimal Atherectomy Trial (10), the aggressive use of directional atherectomy resulted in larger lumen diameters than balloon angioplasty (2.82 mm vs. 2.33 mm). However, a significant increase in the incidence of postprocedural elevations of creatine kinase was seen (34.4% vs. 14.4%), and similar rates of target vessel revascularization at 1 year were reported (17.1% vs. 19.7%). Thus, the more recent atherectomy studies replicated the findings of CAVEAT-I and CCAT, as well as those of the recent randomized studies of excimer laser and rotational atherectomy (11,12), demonstrating that the ablative therapies could produce larger lumens without achieving durable clinical benefit. In the overall investigation of new devices for coronary intervention, the goal of tissue removal to reduce restenosis has slowly lost favor and in retrospect may have been another example of an attractive theory becoming an accepted fact if it gets published often enough.

What has happened to the use of directional atherectomy since 1994? In their analysis, Omoigui et al. (4) evaluated the use of directional atherectomy during two 1-week periods at the 35 CAVEAT study sites. At the same time, financial analysts have tracked the worldwide sales of various interventional devices. The global sales of directional atherectomy devices remained flat between 1993 and 1994 but fell off 33% during 1995 and dropped another 58% in 1996 (13). It is too simplistic to attribute these striking changes to the results of randomized clinical trials or to what everybody claims to have known about atherectomy all along. It is more realistic to attribute the ultimate decrease in sales of directional atherectomy devices to the landmark decision of the FDA to approve coronary stenting (14). Since 1995, the use of coronary stenting revolutionized the field of interventional cardiology because this treatment successfully achieved the dual goals of producing better clinical and angiographic results than balloon angioplasty for many lesion types. If coronary stenting had not been approved by the FDA or was unsuccessful in overcoming the limitations of balloon angioplasty, the use of directional atherectomy would have been refined and prevailed at moderate levels in the progressive field of interventional cardiology until better alternatives did become available.

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References

1. Topol EJ, Leya F, Pinkerton CA, et al. A comparison of balloon angioplasty with directional atherectomy in patients with coronary artery disease. N Engl J Med 1993;329:221–7.
2. Adelman AG, Cohen EA, Kimball BP, et al. A comparison of coronary atherectomy with coronary angioplasty for lesions of the proximal left anterior descending coronary artery. N Engl J Med 1993;329:228–33.
3. Bittl JA. Directional atherectomy versus balloon angioplasty [editorial]. N Engl J Med 1993;329:273–4.
4. Omoigui NA, Silver MA, Rybicki LA, et al. Influence of a randomized clinical trial on practice by participating investigators: lessons from the coronary angioplasty versus excisional atherectomy trial (CAVEAT). J Am Coll Cardiol 1997;31:264–71.
5. Meinert CL, Tonascia S. Clinical Trials: Design, Conduct, and Analysis. New York: Oxford University Press, 1986:49–62.
6. Kuntz RE, Safian RD, Levine MJ, Reis GJ, Diver DJ, Baim DS. Novel approach to the analysis of restenosis after the use of three new coronary devices. J Am Coll Cardiol 1992;19:1493–9.
7. Kuntz RE, Gibson CM, Nobuyoshi M, Baim DS. A generalized model of restenosis following conventional balloon angioplasty, stenting, and directional atherectomy. J Am Coll Cardiol 1993;21:15–25.
8. Baim DS, Simonton CA, Popma JJ, et al. Mechanism of lumen enlargement by optimal atherectomy—IVUS insights from the OARS study [abstract]. J Am Coll Cardiol 1996;27 Suppl A:291A.
9. Holmes DR Jr, Topol EJ, Califf RM, et al., for the CAVEAT-II Investigators. A multicenter, randomized trial of coronary angioplasty versus directional atherectomy for patients with saphenous vein bypass graft lesions. Circulation 1995;91:1966–74.
10. Baim DS, Cutlip DE, Sharma SK, et al. Final results of the Balloon vs. Optimal Atherectomy Trial (BOAT). Circulation. In press.
11. Reifart N, Vandormael M, Krajcar M, et al. Randomized comparison of angioplasty of complex coronary lesions at a single center: Excimer Laser Rotational Atherectomy and Balloon Angioplasty Comparison (ERBAC) Study. Circulation 1997;96:91–8.
12. Appelman YEA, Piek JJ, Strikwerda S, et al. Randomised trial of excimer laser versus balloon angioplasty for treatment of obstructive coronary artery disease. Lancet 1996;347:79–84.
13. Lemaitre DT, Barber AP, Mullen MG. Interventional cardiology. The Cowen Report, March 6, 1996;1–32.
14. Bittl JA. Medical progress: clinical trials of coronary angioplasty. N Engl J Med 1996;335:1290–302.