Therapeutic Choices in the Patient With Coronary Artery Disease and Left Ventricular Dysfunction

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In this issue of Circulation, Holmes and colleagues report the National Heart, Lung, and Blood Institute percutaneous transluminal coronary angioplasty (PTCA) results for patients with depressed left ventricular function. The report describes the experience of 15 collaborating centers that enrolled patients in the registry during a 9-month period in 1985 and 1986. The clinical investigators should be congratulated for providing a snapshot of their clinical experience. The report contributes some important pieces to the clinician’s puzzle of how to manage patients with coronary artery disease and left ventricular dysfunction. A number of pieces of the puzzle, however, remain missing.

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Holmes and his colleagues have shown that PTCA can be performed in a number of centers with excellent short-term results, even in patients at increased risk because of depressed left ventricular function. Short-term complication rates were very similar to those observed in registry patients with normal left ventricular function. Long-term results were also impressive (an 87% 4-year survival rate) and better than reported in other series. This difference, however, may reflect, at least in part, different patient populations as suggested by the lower mean ejection fractions of the other reported series. A strong gradation in survival in PTCA patients based on left ventricular function was shown in the National Heart, Lung, and Blood Institute PTCA registry (4-year survival rates of 93%, 92%, 78%, and 45%, respectively for patients with ejection fractions >45%, 36–45%, 25–35%, and <25%).

Much more information is needed by the clinician and the patient with coronary artery disease and left ventricular dysfunction to make wise decisions about when to use revascularization and which procedure to choose. Perhaps the most glaring deficit is the lack of randomized clinical trial results comparing medical therapy alone, coronary artery bypass graft surgery, and PTCA. Randomized trials help to ensure that different treatment groups are equal with respect to both known and unknown baseline characteristics. Consequently, they are the best approach for comparing the efficacy of different treatment strategies. The Veterans Affairs Angioplasty Compared to Medicine (ACME) trial in the treatment of one-vessel disease showed improved angina relief, better treadmill performance, and enhanced overall psychological well-being at 6 months with angioplasty but at a higher cost and complication rate. Mean ejection fraction of patients enrolled in ACME was 65%. No randomized trials comparing PTCA with alternative therapies for patients with depressed left ventricular function have been reported. In fact, no large-scale prospective comparative studies (that use statistical techniques to adjust for known baseline inequalities even though not randomized) have been published.

The place of the report in the hierarchy of clinical evidence deserves consideration. In evaluating the degree to which the findings of a clinical outcome study should impact practice, the reader of observational studies should include an assessment of the validity and the generalizability of the results. The realm of observational studies includes a spectrum from the small case series at one end of the spectrum to large observational studies that include careful adjustment for baseline characteristics with prospective validation in multiple populations at the other end. Within a single center, careful data collection and increasing sample size can lead to important observations, but the generalizability can be questioned. Multicenter studies can provide a more generalizable answer, but they may sacrifice data quality. When comparisons with other treatment options are made, specific attention must be focused on the rigorous use of multivariable statistical methods to adjust for differences in baseline characteristics. In the National Heart, Lung, and Blood Institute PTCA registry study, the population of patients at the reporting institutions undergoing medical or surgical therapy is not described; thus, the reader should avoid any conclusion about the merits of angioplasty relative to alternative therapies. The excellent survival of these patients undergoing angioplasty may reflect their underlying risk as well as the impact of the procedure.

From previous studies with medical or surgical therapy, we have learned that patients with depressed left ventricular function are at increased risk when treated medically. Both observational analyses and randomized trial results have documented the benefits of bypass surgery compared with medical therapy alone for im-

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proving life expectancy in patients with decreased left ventricular function, particularly in the setting of multivessel disease.\textsuperscript{7,8} The benefits of bypass surgery are proportional to the underlying medical risk (due to decreased left ventricular function or other characteristics such as advanced age or severe angina), and surgical revascularization is particularly effective as a function of worsening extent of anatomic disease. We do not know where PTCA fits in. Results of the Bypass and Angioplasty Investigation (BARI) and other ongoing trials [ACME (two vessel), EAST, RITA, GABI, and CABRI] will substantially improve this understanding. The importance of the ongoing randomized trials cannot be overemphasized. Unfortunately, even knowledge of these trial results will leave some missing pieces of the puzzle.

One such piece will be concern about the generalizability of the trial results. Trials tend to focus on limited populations and enroll only limited subsets of these populations in the trials.\textsuperscript{9} In the ACME trial,\textsuperscript{4} only 4\% of screened patients satisfied the entry criteria, of whom 57\% were enrolled. Observational studies suggest that populations of patients selected for surgery or angioplasty in routine clinical practice differ substantially from each other,\textsuperscript{10} highlighting this concern.

Revascularization technologies are evolving. Almost certainly, coronary artery bypass graft surgery has improved over time, extending the range of patients likely to benefit from the procedure.\textsuperscript{11} Similarly, angioplasty and other catheter-based techniques are an evolving technology. The National Heart, Lung, and Blood Institute registry has reported improved outcomes in the hospital and at 1 year for the 1985–1986 cohort compared with the 1977–1981 cohort.\textsuperscript{12,13} Holmes and colleagues\textsuperscript{1} allude to intra-aortic balloon counterpulsation, coronary sinus retroperfusion, cardiopulmonary bypass, and partial left heart bypass. Stents, lasers, catherecomy devices, and medical approaches to prevent restenosis may all impact on the efficacy of angioplasty.

Improved results over time also may occur with improved patient selection. As more experience is gained with the therapies, physicians may become better at selecting patients most likely to benefit from a specific therapy. Adjunctive medical therapies and risk factor modification also may improve the outcomes of patients managed with a specific therapy. The improved survival benefits observed in patients undergoing bypass surgery represent not only improved surgical survival but also improved long-term survival.\textsuperscript{11}

Improvements in technique, patient selection, and adjunctive therapy are expected in the evolution of a therapeutic technology. Similarly, the diffusion of the technology (and its improvements) more broadly in the medical community typically follows an S-shaped curve. The curve reflects early adoption in relatively few centers, followed by more generalized use, and gradual tapering off to resistant practitioners slow to adopt the innovation.\textsuperscript{14} As one might expect, typically there are differences in the performance of the technology from one center to the next, particularly for new or more rapidly evolving technologies. The difference between clinical performance in ideal settings (efficacy) and that observed more generally (effectiveness) may have significant implications regarding treatment decisions for a specific patient in a specific center or in health policy recommendations (particularly regarding regionalization and cost-effectiveness). Not surprisingly, differences between efficacy and effectiveness for PTCA (a newer therapy) appear larger than differences observed for bypass graft surgery,\textsuperscript{10} at least in the 1985 Medicare experience.

Difficulties in therapeutic decision-making are an inevitable clinical conundrum bred from improvements in clinical care. Evaluation methods that couple randomized clinical trial snapshots with large, representative, observational experiences are now possible given the advances in information processing. As the process of clinical care becomes routinely retrievable, recorded in a standardized fashion across centers, and coupled with outcomes, it should be possible to target randomized trials and better understand how best to apply therapeutic technologies. The development of large, multicenter, carefully collected prospective clinical experiences in fields with developing technologies should be pursued with the same zeal as the advances in the technologies themselves. Access to such an information resource would provide answers to many of the missing pieces in the clinical decision-making puzzle.

Our understanding of how best to manage the coronary patient with left ventricular dysfunction will be substantially improved when trial results become available. Presently, high-risk patients should be considered for revascularization. Coronary bypass graft surgery is a proven technology. Percutaneous catheter-based revascularization techniques can be performed safely in the short term and offer great potential. Current decision making should incorporate patient preferences and should recognize the uncertainty present in the decision about the choice of revascularization strategy. Minimizing future uncertainty will depend on the continued evolution of new strategies combining prospective data bases with clinical trials for the routine evaluation of developing technologies.

\textbf{References}


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