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The Bypass Angioplasty Revascularization Investigation (BARI) trial: implications for clinical practice

For selected patients with multivessel coronary artery disease, balloon angioplasty is a safe alternative to bypass graft surgery. That is the main message from the recently completed Bypass Angioplasty Revascularization Investigation (BARI) trial,[1] in which patients randomized to undergo either treatment had nearly identical survival rates at 5 years.

An exception was patients with diabetes, who fared worse with percutaneous transluminal coronary angioplasty (PTCA) than with coronary artery bypass grafting (CABG).

However, even as the BARI trial answered some questions, it raised new ones. The need for a repeat procedure is much more likely after PTCA than after CABG: 54% of the patients who underwent PTCA in the BARI trial needed repeat procedures during 5 years of follow up, compared with only 8% of patients who underwent CABG.

On the other hand, techniques for both procedures have improved since the BARI trial was designed, making contemporary patients *perhaps* less likely to need repeat procedures.

The upshot? Both PTCA and CABG have their own inherent advantages and disadvantages, which must be weighed in the treatment decision for each patient.

THE RATIONALE FOR BARI: IS PTCA SAFE AND EFFECTIVE FOR MULTIVESSEL DISEASE?

Procedures to restore blood flow to the myocardium fall into two categories: CABG, introduced in 1968 by Cleveland Clinic surgeon Rene Favaloro,[2] and PTCA, introduced in 1977 by Andreas Grüntzig.[3]

In the ensuing years, CABG became the standard of care for patients with symptomatic multivessel coronary artery disease, as randomized trials established that the survival rate was higher in high-risk patients who underwent CABG than in those treated medically.[4–8] (Such high-risk patients were those with left main disease, three-vessel disease and left ventricular dysfunction, and possibly two-vessel disease with proximal left anterior descending coronary artery involvement.)

However, the survival advantage with CABG did not extend to patients with less-extensive disease, even though they had substantially better angina relief with CABG than with medical therapy.

At the same time, the less-invasive PTCA procedure became established as a safe alternative for patients with single-vessel disease. As technique and experience evolved, PTCA was offered to many patients with multivessel coronary disease as well. However, there were no randomized trials to confirm its efficacy and safety in the latter group.

DESIGN AND RESULTS OF THE BARI TRIAL

This lack of data led the National Heart, Lung, and Blood Institute of the National Institutes of Health to fund a multicenter, randomized trial comparing CABG and PTCA—the Bypass Angioplasty Revascularization Investigation (BARI). Eligible patients had symptomatic coronary artery disease or severe ischemia on exercise testing, and angiographically proven stenosis of more than 50% in more than one myocardial territory.

The lower survival rate of diabetic patients treated with PTCA is of concern

We hypothesized that clinical outcomes at 5 years would be no worse with an initial strategy of PTCA than with CABG. Primary outcomes measured were the cumulative rates of survival, Q-wave myocardial infarction, and survival free of Q-wave myocardial infarction; data on in-hospital complications, crossovers, and repeat revascularization procedures were also analyzed. In a subset of patients we also studied costs, quality of life, and angiographic outcomes.

A high-risk patient cohort

Between August 1988 and August 1991, 1829 patients at 18 clinical centers were randomized to undergo either CABG or PTCA.[1] The mean age was 61 years, and one fourth of the cohort were women. More than half of the patients had a history of myocardial infarction, and 9% had a history of treated congestive heart failure. Approximately 20% had diabetes treated with oral agents or insulin; another 5% had untreated diabetes. Two thirds of the patients had unstable angina.

Forty-one percent of patients had triple-vessel disease; more than one third had at least one totally occluded coronary artery. Overall, the mean percentage of myocardium jeopardized by a lesion of at least 50% was 61%. Twenty-two percent of the patients had an ejection fraction less than 50%. None of these baseline characteristics were significantly different between the treatment groups.

More-complete revascularization with CABG than with PTCA

The CABG patients had an average of 3.1 coronary arteries bypassed with a mean of 2.8 grafts. In 82% of patients, at least one internal thoracic artery graft was used.

PTCA was attempted in an average of 2.4 lesions per patient. Therefore, PTCA involved less-complete revascularization by intention of the operator than did CABG. At least one lesion was successfully dilated in 88% of patients. The mean degree of stenosis was 67% before PTCA and 31% afterward.

More hospital days after CABG

The median hospital stay after CABG was 7 days, vs 3 days after PTCA ($P < .01$, Wilcoxon rank-sum test); the median total hospital stay was 12 days with CABG vs 7 days with PTCA.

In-hospital mortality rates similar

The rates of in-hospital mortality were similar in the two treatment groups, 1.3% with CABG and 1.1% with PTCA. However, more patients assigned to CABG had Q-wave myocardial infarctions in the hospital than did patients assigned to PTCA, 4.5% vs 2.1% ($P < .01$, Fisher's exact test). PTCA patients were more likely to need a repeat revascularization procedure in the hospital than were the CABG patients: 6.3% of the PTCA patients underwent emergency CABG vs 1 patient (0.1%) in the CABG group ($P < .001$); and 2.1% underwent emergency PTCA vs no patients in the CABG group ($P < .001$).

Long-term survival rates similar

Over 5 years of follow-up, there were 111 deaths in the CABG group and 131 in the PTCA group; the difference was not statistically significant. The 5-year cumulative survival rate was 89.3% for CABG patients and

86.3% for those assigned to PTCA (**TABLE**). For both groups, the mortality rate was twice as high as expected, probably because the patients were older and had more extensive disease than the patients in earlier studies.

The rates of survival free of Q-wave myocardial infarction were also similar between the two groups: 80.4% in the CABG patients vs 78.7% in the PTCA patients.

More repeat procedures in the PTCA group

The two groups differed substantially in their need for repeat revascularization procedures during the 5 years of follow-up. Eight percent of patients assigned to CABG underwent repeat revascularization (1% CABG; 7% PTCA). In the PTCA group, 54% of patients underwent at least one subsequent procedure. Thirty-one percent of the patients initially treated with PTCA subsequently underwent CABG at some time during the trial; 34% initially treated successfully with PTCA underwent a second PTCA. Most of the repeat revascularization procedures in the PTCA group were clustered during the first year. In all, 60% of PTCA-treated patients avoided bypass surgery by undergoing the initial PTCA or at most one additional procedure.

Diabetic patients fared worse

A striking difference occurred in a group that was not originally marked for subgroup analysis: patients with diabetes severe enough to require drug treatment had a much lower survival rate with either treatment than did patients without diabetes. In addition, this group's survival rate was significantly lower with PTCA than with CABG, 65.5% vs 80.6% (a difference of 15.1 percentage points; 95% CI 1.4% to 28.9%).

Since the original BARI design did not specify patients with treated diabetes as a high-risk subgroup, there has been some controversy as to the importance of this finding. However, the difference was so worrisome that the BARI Data and Safety Monitoring Committee required that it be reported before the final results of the study were released in November 1995.

Further study of CABG and PTCA in patients with diabetes will be needed to clarify this problem. For the remaining BARI patients not treated for diabetes, the rates of survival and event-free survival were nearly identical for the two treatment groups at 5 years.[1]

TABLE

5-YEAR OUTCOMES OF PATIENTS WITH MULTIVESSEL DISEASE TREATED WITH PERCUTANEOUS TRANSLUMINAL CORONARY ANGIOPLASTY (PTCA) OR CORONARY ARTERY BYPASS GRAFTING (CABG)

Outcome	Percent of patients	
	CABG	PTCA
Cumulative survival		
All patients	89.3	86.3
Patients with treated diabetes	80.6	65.5*
All other patients	91.4	91.1
Survival free of Q-wave myocardial infarction	80.4	78.7
Repeat revascularization procedures	8	54

*Statistically significant (see text)

No treatment-related differences in other subgroups

Patients with abnormal left ventricular function, advanced three-vessel disease, total occlusion of at least one vessel, or unstable angina all had equal survival rates whether treated with CABG or PTCA. All of these subgroups were prespecified as high-risk in the treatment protocol, and the study was designed to analyze their risk.

ARE THE BARI RESULTS OBSOLETE ALREADY?

PTCA techniques have evolved since the BARI trial was planned. Second-generation PTCA devices such as stents and ablation catheters, which were not used in the BARI trial, allow more patients to be successfully and safely treated with PTCA today.[9] Further innovations such as glycoprotein IIb/IIIa inhibitors, which profoundly inhibit platelet aggregation, have decreased the acute complication rates with PTCA.[10] Two trials have shown a decrease in restenosis with coronary stenting,[11,12] and patients undergoing PTCA in the future will likely need fewer repeat revascularization procedures than did the BARI patients.

Bypass surgery has also evolved; more patients are receiving multiple arterial grafts than in the BARI trial. Of interest, of the diabetic CABG patients in the BARI trial, only those who received internal thoracic artery grafts had a higher survival rate than did the diabetic PTCA patients. Further increases in the number of arterial grafts performed per

patient will likely lead to increased long-term survival, although this is only speculation.[13] Less-invasive coronary surgery that does not involve bypass is also being developed and may entail fewer acute complications.

FURTHER TRIALS PLANNED

BARI II to study diabetic patients

The lower survival rate of diabetic patients with multivessel disease treated with PTCA compared with CABG is of concern. Diabetic patients in both treatment groups suffered a higher rate of cardiovascular deaths than did nondiabetic patients, although the difference was more impressive in the PTCA group. These excess deaths did not occur during the hospital stays for the initial or subsequent PTCA procedures, but rather at home.

This observation raises the questions of whether a defective warning mechanism ("silent ischemia") may have contributed to sudden cardiac death in the diabetic patients, and whether closer follow-up with more frequent stress testing might improve the survival rate in this group. "BARI II" is being planned specifically to address the optimal treatment strategy for diabetic patients with multivessel disease.

Will stents reduce restenosis?

Even in nondiabetic patients, an initial strategy of CABG led to fewer repeat revascularization procedures than did an initial strategy of PTCA. Coronary stenting should reduce the need for repeat PTCA procedures; two planned trials will compare this strategy with CABG.

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