Influence of Pre-PTCA Strategy and Initial PTCA Result in Patients With Multivessel Disease

The Bypass Angioplasty Revascularization Investigation (BARI)

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Background—In PTCA patients with multivessel coronary artery disease, incomplete revascularization (IR) is the result of both pre-PTCA strategy and initial lesion outcome. The unique contribution of these components on long-term patient outcome is uncertain.

Methods and Results—From the Bypass Angioplasty Revascularization Investigation (BARI), 2047 patients who underwent first-time PTCA were evaluated. Before enrollment, all significant lesions were assessed by the PTCA operator for clinical importance and intention to dilate. Complete revascularization (CR) was defined as successful dilatation of all clinically relevant lesions. Planned CR was indicated in 65% of all patients. More lesions were intended for PTCA in these patients compared with those with planned IR (2.8 versus 2.1). Successful dilatation of all intended lesions occurred in 45% of patients with planned CR versus 56% with planned IR ($P<0.001$). In multivariable analysis, planned IR (versus planned CR), initial lesions attempted (not all versus all intended lesions attempted), and initial lesion outcome (not all versus all attempted lesions successful) were unrelated to 5-year risk of cardiac death or death/myocardial infarction but were all independently related to risk of CABG.

Conclusions—Overall, a pre-PTCA strategy of IR in BARI-like patients appears comparable to a strategy of CR except for a higher need for CABG. Whether the use of new devices may attenuate the elevated risk of CABG in patients with multivessel disease and planned IR remains to be determined. 

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Key Words: angioplasty ■ coronary disease ■ revascularization

The effect of incomplete revascularization (IR) on clinical outcome in patients with multivessel coronary artery disease (CAD) treated with PTCA remains unclear. Early reports suggest higher rates of CABG and angina in patients incompletely versus completely revascularized with PTCA, whereas others, including those with adjustment for differences in pretreatment clinical profiles, report modest or no adverse effect associated with IR. Small patient cohorts and different analytic techniques and definitions of complete revascularization (CR) have contributed to the uncertainty.

Anatomic IR in patients with multivessel CAD can occur for several reasons, including untreated chronic total occlusions considered not amenable to PTCA; untreated, less-severe coronary narrowings (ie, 50% to 69%); untreated lesions supplying akinetic or dyskinetic left ventricular segments; and less frequently, unsuccessful lesion dilation. Thus, both pre-PTCA treatment strategy and initial outcome of treated lesions determine the patient’s anatomic completeness of revascularization. Conceptually, when revascularization is anatomically incomplete, it can be subdivided by functional adequacy or inadequacy (ie, revascularization of all versus not all stenoses in arteries supplying viable myocardium), and this distinction appears to have prognostic significance. Hence, investigation of the effect of IR on clinical outcome requires consideration of pre-PTCA strategy, initial dilatation success, and functional significance of the myocardial territory revascularized.

Here, we evaluate the relative contributions of pre-PTCA strategy (planned CR versus planned IR), initial lesions attempted (whether or not all planned lesions were attempt-

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been described elsewhere.14–16 Briefly, eligibility required clinically entry (Figure 1). Recruitment and selection criteria of BARI have tional registry and received initial PTCA within 3 months of study in the randomized trial but consented to be followed in an observa-

were 1147 of 1189 eligible patients who did not agree to participate ed), and initial lesion outcome on short- and long-term

clinical outcome in patients with multivessel disease.

Methods

Patient Population

A total of 2047 patients who underwent first-time PTCA were considered. This included 900 of 904 patients who were assigned to and received PTCA in the Bypass Angioplasty Revascularization Investigation (BARI) randomized trial, a randomized study of 1829 patients comparing initial PTCA versus CABG.14,15 Also included were 1147 of 1189 eligible patients who did not agree to participate in the randomized trial but consented to be followed in an observa-

tional registry and received initial PTCA within 3 months of study entry (Figure 1). Recruitment and selection criteria of BARI have been described elsewhere.14–16 Briefly, eligibility required clinically severe angina or objective evidence of ischemia requiring revascular-

ization, multivessel CAD suitable for both PTCA and CABG, and informed consent. Ability to achieve CR was not required, although the protocol required anticipated successful relief of the major areas of ischemia. Patients were enrolled in 18 centers across North America between August 1988 and August 1991.

Forty-six patients who received initial PTCA were excluded (4 randomized and 42 registry patients) because of incomplete angiographic data. A central radiological laboratory interpreted angiograms from patients in the randomized trial; however, the same mechanism was not used in the observational registry. Therefore, clinical site readings were used for all patients.

Angiographic Definitions

Angiographically significant lesions were defined as ≥50% stenoses in a vessel ≥1.5 mm, as measured by electronic calipers.17 The number of diseased vessels was determined from the 3 major coronary perfusion territories (anterior, lateral, and inferoposterior) supplied by a vessel with a significant lesion. Lesion complexity was classified by use of American Heart Association/American College of Cardiology consensus panel criteria.18 Flow distal to each stenosis was defined by TIMI flow criteria.19 A reduction in stenosis of ≥20% with residual stenosis of <50% and TIMI grade 3 flow defined successful lesion dilation.

Determination of Pre-PTCA Strategy and Initial Completeness of Revascularization

Before patients entered the study, their angiograms were reviewed by the PTCA operator to assess the clinical importance of each significant lesion and its suitability for PTCA.20 Angiographically significant lesions were judged as culprit (responsible, entirely or partially, for the patient’s clinical syndrome), important (contributed to patient’s ischemic syndrome), borderline (considered for revascular-

ization incidental to treatment of culprit/imimportant lesions), or unimportant (territory too small or nonviable myocardium—ie, on the basis of evidence of transmural infarction). For lesions considered culprit, important, or borderline, the intention (yes versus no) to perform PTCA was indicated. About 4% of all significant lesions were not rated for clinical importance or intention. These lesions were generally characterized as class C, excessively long or diffuse, and were assumed to be unintended for PTCA.

CR was considered planned when all lesions deemed culprit, important, or borderline were designated by the PTCA operator as intended for revascularization. Otherwise, the patient had a pre-

PTCA strategy of IR. Thus, the definition of planned CR refers to functionally adequate revascularization. When CR was planned and all intended lesions were successfully dilated, the patient was considered to be completely revascularized.

Data Collection

Details of the initial PTCA and follow-up clinical events, including procedural and long-term mortality, recurrence of angina, and repeated revascularization, were recorded on standardized forms. Resting ECGs were collected at study entry, before and after coronary revascularization procedures, at scheduled follow-up, and for suspected myocardial infarction (MI) events. A central ECG laboratory coded all Q-wave events. According to protocol, cardiac enzymes were not used to define MI within 96 hours of revascular-

ization.14,21 Cause of death was classified by an independent Mor-

tality and Morbidity Classification Committee.

Statistical Analysis

The patient population was analyzed by a 3 × 2 design. The 3 group components were determined from initial lesion outcome: (1) all intended lesions were attempted and successful, (2) all intended lesions were attempted but not all were successful, and (3) not all intended lesions were attempted. Within these groups, patients were dichotomized by pre-PTCA strategy (planned CR versus planned IR) (Figure 2).

Initially, baseline clinical and angiographic characteristics were compared separately within the 3 and 2 group components. Subse-
quent, in-hospital characteristics and complications were compared by planned strategy (CR versus IR) within the 3 initial outcome groups (from the above 3 × 2 design). Proportions were compared by chi-2 analysis; mean differences in continuous variables were assessed by Student’s t tests.

The Kaplan-Meier method was used to estimate 5-year clinical event rates. Additionally, a subset of 1830 patients (89.4% of total cohort) who did not experience in-hospital death, MI, or CABG at the initial PTCA were analyzed separately. At the data freeze, 95% of surviving patients had ≥4 years of follow-up; 67% had ≥5 full years. Patients with <5 years were censored at the last follow-up date. Similarly, for estimates of cardiac mortality, deaths classified as noncardiac were censored. Within the 3 initial outcome groups (groups 1 through 3), the log-rank statistic was used to compare hazard curves between patients with planned CR and those with planned IR. Cox regression analysis22 was used to estimate the independent contribution of planned IR (versus planned CR), lesions attempted (not all versus all intended lesions attempted), and lesion outcome (not all versus all attempted lesions successfully dilated) on
5-year clinical outcome. A stepwise algorithm was used to adjust for baseline clinical and angiographic variables associated with 5-year clinical outcome. When the planned strategy and initial lesion outcome variables did not step into the model, they were forced in at the last stage of model development.

**Results**

**Baseline Clinical Characteristics and Completeness of Revascularization**

Among the 3 columns of patients with planned CR (Figure 2), 595 (45%) had all intended lesions successfully dilated. This compared with 399 patients (56%) with planned IR ($P<0.001$). At baseline, patients with planned IR had a worse clinical profile than patients with planned CR (data not shown). This included older mean age (62.2 versus 60.9 years, $P=0.006$) and history of MI (56% versus 50%, $P=0.01$), congestive heart failure (9% versus 5%, $P=0.002$), treated diabetes (20% versus 15%, $P=0.004$), and peripheral vascular disease (9% versus 6%, $P=0.02$).

**Baseline Angiographic Characteristics and Completeness of Revascularization**

Characteristics associated with planned IR included triple-vessel disease, $\geq 4$ significant lesions, diffuse lesions, presence of total occlusions or class C lesions, and poor ejection fraction (Table 1, left). Most of these same factors were also associated with failure to successfully dilate all intended lesions (Table 1, right).

**Initial Procedural Outcome**

Overall, the mean numbers of intended and attempted lesions were higher in patients with planned CR compared with those with planned IR (2.8 versus 2.1 and 2.2 versus 1.8, respectively; Table 2). Among patients with all intended lesions successfully dilated (Table 2, left), in-hospital death/Q-wave MI and repeated revascularization were infrequent and were attributed to postdilatation complications, including out-of-laboratory abrupt closure.

Among patients without all intended lesions successfully dilated (Table 2, middle and right columns), in-laboratory...
abrupt closure occurred ≥10% in each group but not differ by whether or not CR was planned. Therefore, the reason that not all intended lesions were attempted in some patients (Table 2, right) was not attributed predominantly to acute vessel occlusion.

Finally, among patients with all intended lesions attempted but not all successful (Table 2, middle), those with planned CR had a lower incidence of in-hospital CABG than those with planned IR (9.9% versus 18.7%). In contrast, the incidence of in-hospital CABG among patients without all intended lesions attempted (Table 2, right) did not differ by pre-PTCA strategy but was frequent (∼17%).

**Long-Term Clinical Outcome**

Among patients with all intended lesions successfully dilated (Table 3, left), the 5-year incidence of death, cardiac death, and death/MI was similar regardless of whether or not CR was planned. However, the prevalence of angina at 5 years was higher in patients with planned IR (20.0% versus 14.8%, P=0.002). A similar trend was observed in these same patients for cardiac mortality (7.8% versus 3.9%, P=0.001).

Finally, as shown in Table 3 and Figure 4A, 5-year incidence of CABG was markedly higher in patients with planned IR. This excess risk occurred regardless of whether or not all intended lesions were attempted and successful and held true among patients free of initial in-hospital death/MI/CABG (Figure 4B). Most CABGs were performed in the first year of follow-up, with the excess risk associated with planned IR observed within the first 2 years. Roughly 70% of patients who underwent CABG had unstable angina and/or an urgent or emergent revascularization priority (regardless of whether CR was planned and among both randomized and registry patients).

**Multivariable Analysis**

Pre-PTCA strategy (planned IR versus planned CR), lesions attempted (not all versus all intended lesions attempted), and lesion outcome (not all versus all attempted lesions successful) were not independently associated with 5-year risk of cardiac death or death/Q-wave MI (Figure 5). However, the point estimate for planned IR and risk of death approached significance (relative risk [RR], 1.36; 95% CI, 1.00 to 1.84; P=0.05). In contrast, 5-year risk of CABG was independently associated with planned IR (RR, 1.27; 95% CI, 1.01 to 1.60; P=0.04), not attempting all intended lesions (RR, 1.50; 95% CI, 1.22 to 1.85; P=0.0001), and unsuccessful dilatation of all attempted lesions (RR, 1.48; 95% CI, 1.20 to 1.84; P=0.0003).

**Discussion**

In patients with multivessel CAD treated with PTCA, IR occurs frequently and is the result of both pre-PTCA strategy and initial lesion outcome. These components, coupled with varying definitions and the distinction between anatomic
versus functional CR, have led to numerous yet equivocal reports on the influence of CR on clinical outcome.\textsuperscript{1–4,7} Among >2000 BARI patients treated with first-time PTCA during 1988 through 1991, we evaluated the relative contribution of pre-PTCA strategy (planned CR versus planned IR) and initial lesion outcome on clinical outcome. We considered a functional rather than anatomic definition of planned CR.

### Initial PTCA Outcome

Overall, about one third of all patients had a planned strategy of IR, and not unexpectedly, these patients had a higher prevalence of triple-vessel disease and more significant stenoses. Patients with planned CR were less likely to have all intended lesions successfully diluted than patients with planned IR. This lower rate of total angiographic success was probably the result of 2 factors. First, patients with planned CR had, on average, more lesions intended for PTCA. Thus, there was additional opportunity for failure of ≥1 lesion. Second, although patients with planned CR had overall less extensive CAD than patients with planned IR, more lesions were intended and attempted in this group. This suggests a more aggressive approach, perhaps including lesions difficult to treat with conventional PTCA. The fact that about one fourth of all patients with planned CR had ≥1 class C lesion supports this contention. Previous studies have reported the difficulty in achieving CR in attempts to revascularize chronic total occlusions.\textsuperscript{6,23}

When all planned lesions were not attempted or successfully diluted, the incidence of abrupt closure and Q-wave MI was similar by pre-PTCA strategy. Thus, incident abrupt closure, which precipitated a substantial proportion of the major in-hospital complications, was not influenced by whether or not CR was planned. Moreover, abrupt closure alone was not the primary reason why not all intended lesions were attempted. Thus, other factors, such as suboptimal result (but not acute occlusion) and poor patient tolerance of PTCA, may be important contributors to the reason that less revascularization is attempted compared with what is initially intended.

### Long-Term Clinical Outcome

In unadjusted analyses, planned IR (versus planned CR) was associated with higher mortality and a trend toward higher cardiac mortality in patients in whom all intended lesions were not attempted and/or successfully diluted. However, after statistical adjustment, 5-year risk of cardiac death and death/MI was similar in patients by pre-PTCA strategy. These results are consistent with reports suggesting comparable mid-term survival with and without CR after PTCA.\textsuperscript{4,5,7} Our data suggest that clinically appropriate use of planned IR by experienced angioplasty operators is a reasonable strategy in patients with multivessel disease.

### Table 3. Kaplan-Meier 5-Year Event Rates by Initial Lesion Outcome and Pre-PTCA Strategy

<table>
<thead>
<tr>
<th>5-Year Clinical Event</th>
<th>All Intended Lesions Attempted</th>
<th>Not All Intended Lesions Attempted</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Planned CR (n=595)</td>
<td>Planned IR (n=399)</td>
</tr>
<tr>
<td>Death</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All patients*</td>
<td>9.2</td>
<td>11.9</td>
</tr>
<tr>
<td>Patients without in-hospital death/MI/CABG†</td>
<td>9.0</td>
<td>12.2</td>
</tr>
<tr>
<td>Cardiac death</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All patients</td>
<td>5.3</td>
<td>5.6</td>
</tr>
<tr>
<td>Patients without in-hospital death/MI/CABG</td>
<td>5.1</td>
<td>5.8</td>
</tr>
<tr>
<td>Death/Q-wave MI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All patients</td>
<td>14.8</td>
<td>16.9</td>
</tr>
<tr>
<td>Patients without in-hospital death/MI/CABG</td>
<td>13.5</td>
<td>16.3</td>
</tr>
<tr>
<td>Angina‡</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All patients§</td>
<td>14.8</td>
<td>20.0</td>
</tr>
<tr>
<td>Patients without in-hospital death/MI/CABG</td>
<td>14.8</td>
<td>19.5</td>
</tr>
<tr>
<td>CABG</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All patients§¶</td>
<td>17.8</td>
<td>23.3</td>
</tr>
<tr>
<td>Patients without in-hospital death/MI/CABG‡</td>
<td>16.5</td>
<td>21.7</td>
</tr>
<tr>
<td>Repeat PTCA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All patients*</td>
<td>37.3</td>
<td>36.1</td>
</tr>
<tr>
<td>Patients without in-hospital death/MI/CABG</td>
<td>36.6</td>
<td>35.9</td>
</tr>
</tbody>
</table>

For “all successful” comparison (planned CR vs planned IR), §P<0.05.
For “not all successful” comparison (planned CR vs planned IR), ¶P<0.01.
For “not all attempted” comparison (planned CR vs planned IR), †P<0.01, *P<0.05.
‡Crude rate rather than Kaplan-Meier estimate.
suboptimal result. These findings support previous reports and the contention that IR, whether by intention or suboptimal PTCA result, is associated with higher risk of CABG. These findings persist even among patients initially free of major in-hospital complications and are particularly prominent in the first year after PTCA. In essence, among patients with multivessel CAD not suitable for CR via PTCA, the angioplasty operator may ultimately be more inclined to “give up” and triage to CABG those patients with subsequent need for repeated revascularization.

Study Limitations
All PTCA procedures were performed in 1988 through 1991 without the use of new devices, including stents. The excess risk of CABG observed in relation to both pre-PTCA strategy and suboptimal result with conventional PTCA might have been attenuated had stents been used and similarly may be less prominent today.

Our definition of CR is study specific and based on angiographic criteria and PTCA operator judgments of the importance and suitability of significant stenoses for PTCA. Possibly, a more physiologically relevant definition of CR, such as successful treatment of lesions >70% stenosis (as opposed to >50%), could have been used. Similarly, quantitative evaluation of patient atherosclerotic burden was not derived from a core laboratory. There may have been site variability in determining which patients were intended to undergo and those who achieved CR. With random variation within centers assumed, the misclassification of planned and achieved CR would likely be nondifferential and would tend to bias study results toward the null.

Finally, although patients from the randomized trial and observational registry met the same clinical eligibility criteria, differences exist between the cohorts. Specifically, registry patients were more often white; were more educated with a higher self-rated quality of life; and had a less frequent history of MI, diabetes, and smoking. These differences, however, do not appear to be influential here because, remarkably, the percentages of patients with planned CR (65%) and those with actual CR achieved (29%) were identical between the 2 cohorts. This suggests that PTCA operators were equally motivated to achieve CR in both populations.

Conclusions
Among >2000 patients with multivessel CAD treated with first-time PTCA, about one third had a pre-PTCA strategy of functional IR, ≈50% had all intended lesions attempted and successfully dilated, and only 29% were completely revascularized. Triple-vessel disease, ≥4 significant lesions, and difficult lesions for conventional PTCA (ie, class C lesions) were associated with planned IR and suboptimal PTCA. Abrupt closure strongly precipitated major in-hospital com-

Figure 3. Plots of 5-year death/Q-wave MI by lesion outcome and pre-PTCA strategy for all patients (A) and for patients free of initial in-hospital death, MI, or CABG (B).
applications but was unrelated to whether or not CR was planned. In multivariable analysis, planned IR and failure to successfully dilate all intended lesions were unrelated to long-term risk of cardiac death or cardiac death/MI. However, risk of CABG, particularly within the first year following PTCA, was higher in patients with planned IR and among those with a suboptimal initial result.

Overall, a pre-PTCA strategy of IR in BARI-like patients appears comparable to a strategy of CR, except for a higher need for CABG. Whether or not the use of new devices may

Figure 4. Plots of 5-year CABG by lesion outcome and pre-PTCA strategy for all patients (A) and for patients free of in-hospital death, MI, or CABG (B).

Figure 5. Plot of 5-year adjusted relative risks of pre-PTCA strategy and lesion outcome variables on clinical outcomes (patients free of initial in-hospital death, MI, or CABG). Bullets depict relative risks; dashed lines, 95% CIs. Q-MI indicates Q-wave MI.
attenuate this elevated risk of CABG in similar patients remains to be determined.

References
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