Long-Term Analysis of Conventional Coronary Balloon Angioplasty and an Initial “Stent-like” Result

The NHLBI PTCA Registry

DAVID R. HOLMES, JR., MD, FACC,* KEVIN E. KIP, MSPH,† WANLIN YEH, MS,‡ SHERYL F. KELSEY, PhD,† KATHERINE M. DETRE, MD, DrPH, FACC,† DAVID O. WILLIAMS, FACC,‡ FOR THE INVESTIGATORS OF THE NHLBI PTCA Registry

Rochester, Minnesota, Pittsburgh, Pennsylvania and Providence, Rhode Island

Objectives. We examined the influence of an initial “stent-like” result on long-term outcome in patients in the 1985–86 NHLBI PTCA Registry.

Background. Stent use in selected patients is associated with improved angiographic and short-term clinical outcome; however, due to potential for in-stent restenosis and high costs of stents, there is interest in a strategy of more optimal dilatation to achieve a “stent-like” result without a stent. The long-term outcome of patients with a “stent-like” percutaneous transluminal coronary angioplasty (PTCA) remains unknown.

Methods. Ten-year outcome was compared between 225 successfully treated patients with and 1,764 successfully treated patients without an initial “stent-like” result (>21 lesion dilated to <210% stenosis). The sample had 75% and 80% power, respectively, to detect an absolute difference of 8% in the 10-year rate of death and myocardial infarction (MI) between the two groups.

Results. Ten-year rates of death and MI were similar between the stent-like and non–stent-like groups (22.3% vs. 22.2%, 17.6% vs. 17.9%), however, there was less target lesion revascularization in the stent-like group (30.2% vs. 36.8%). In subgroup analysis of patients with multivessel disease, those with a stent-like result had less follow-up bypass surgery (25.2% vs. 32.7%), yet more repeat PTCA (53.8% vs. 42.7%). These findings were unaffected by adjustment for differences in baseline characteristics between the two patient groups.

Conclusions. Achievement of an initial stent-like result via balloon angioplasty alone may not appreciably reduce the long-term risk of death or MI, nor confer equivalent clinical benefit as achieving a stent-like result with a stent.

(J Am Coll Cardiol 1998;32:590–5)

©1998 by the American College of Cardiology

Compared with conventional balloon angioplasty, coronary stenting reduces the immediate need for bypass surgery following abrupt vessel closure (1–3) and reduces the short-term requirement for repeat revascularization (4–7) by achieving a stable, large lumen (8). Stent implantation does not prevent neo-intimal hyperplasia, and indeed, probably exaggerates it, but it is better tolerated because of the large initial gain and lack of acute recoil (9). Because of the potential for in-stent restenosis and the high costs of stents, there have been attempts to optimize conventional coronary angioplasty and achieve a “stent-like” result without the stent. Early data (10,11) suggest this results in better outcome compared with the result of less optimal coronary angioplasty. The long-term outcome of patients with a “stent-like” result without use of a stent remains unknown. The purpose of this study is to compare 10-year outcome in patients with successful dilatation in the 1985–86 NHLBI PTCA Registry on the basis of whether or not an initial “stent-like” result was achieved with conventional coronary angioplasty.

Methods

Patient population. Of 2,431 patients from 16 participating NHLBI PTCA Registry sites, a subset of 1,989 patients who achieved an initially successful result were considered. An initially successful coronary angioplasty was defined as at least one lesion successfully dilated (<50% residual stenosis and ≥20% improvement in lumen diameter) and no in-hospital death, myocardial infarction (MI), or emergency bypass surgery. Eligibility criteria for the Registry and patient characteristics have been described (12–15). Briefly, consecutive patients at participating sites were entered at the time of first-time coronary angioplasty. All patients gave written informed consent to be contacted annually after the initial procedure to report health status and intercurrent clinical events. The study protocol was approved by the Institutional Review Board for

From the *Mayo Clinic, Rochester, Minnesota; †Department of Epidemiology, University of Pittsburgh, Pittsburgh, Pennsylvania; and ‡Brown University/Rhode Island Hospital, Providence, Rhode Island. This study was supported by National Institutes of Health Grant HL-33292.

Manuscript received January 15, 1998; revised manuscript received April 27, 1998, accepted May 8, 1998.

Address for correspondence: Kevin E. Kip, University of Pittsburgh, Graduate School of Public Health, Epidemiology Data Coordinating Center, 127 Parran Hall, 130 DeSoto Street, Pittsburgh, Pennsylvania. E-mail: kip@cdc.gphp.pitt.edu.

©1998 by the American College of Cardiology
Published by Elsevier Science Inc.
Abbreviations and Acronyms

CABG = coronary artery bypass graft surgery
ECG = electrocardiogram
MI = myocardial infarction
MVD = multivessel disease
NHBLI = National Heart, Lung, and Blood Institute
NSL = non–stent-like result
PTCA = percutaneous transluminal coronary angioplasty
SL = stent-like result
SVD = single vessel disease
TLR = target lesion revascularization

Biomedical Research at the University of Pittsburgh, Coordinating Center for the Registry. Patient confidentiality was ensured by the use of alphanumeric codes rather than names. In this cohort, outcome following successful coronary angioplasty was studied on the basis of whether or not an initial “stent-like” result was achieved.

Definitions. Patients were considered to have achieved a stent-like result if at least one lesion was successfully dilated to $\leq 10\%$ diameter stenosis, as determined by visual assessment of multiple orthogonal views by the coronary angioplasty operator. A non–stent-like result was defined as at least one lesion dilated to $\leq 50\%$ stenosis with $\geq 20\%$ improvement in lumen diameter, but with no lesions dilated to $\leq 10\%$ stenosis. No routine method of visual reading was required, but at most clinical centers caliper reading was used to define the percent stenosis. Approximately 25% of the registry patients had pre- and post-PTCA angiographic readings centrally reviewed by use of quantitative coronary angiography (University of Maryland) (16); however, to maintain consistency, only visual assessments were used in the analysis. A review of 294 lesions with both visual and core laboratory readings revealed that, on average, the percent stenosis after coronary angioplasty was about 10% lower in the visual readings than by quantitative coronary angiography. Our stringent definition of $\leq 10\%$ stenosis for a stent-like result, as derived from visual readings, was selected because of the potential overestimation of lumen gain from visual readings. Coronary artery lesions were classified by arterial segments in accordance with definitions in the Coronary Artery Surgery Study (17).

MI was documented by at least two of the following: clinical symptoms, ECG evidence (Q-wave criteria of a definite MI according to the Minnesota Code) (18), and enzyme changes (more than double the upper normal limits of creatine kinase and/or the presence of creatine kinase-MB). Infarctions after hospitalization for initial coronary angioplasty were recorded whether they occurred alone, during a repeated coronary angioplasty, or during subsequent coronary artery bypass graft surgery (CABG). Hospital records were examined to verify that ECG findings, enzyme test results, and clinical symptoms were consistent with the Registry definition of MI.

Repeat angioplasty was defined as a procedure performed during a subsequent hospitalization after the initial coronary angioplasty. For all lesions attempted at the initial procedure, target lesion revascularization (TLR) during follow-up was defined as either repeat coronary angioplasty on the same lesion, or a graft placed on the native vessel downstream from the treated lesion. The time at which TLR occurred was defined as the first time the index lesion was retreated, either by coronary angioplasty or CABG.

Follow-up. At each participating site, annual telephone interviews of the patients were conducted by the site coordinator. Information on hospitalizations for MI or repeated revascularization, angina, and cardiac catheterizations was collected. At year 10 of follow-up, 1,850 (93.0%) of the baseline cohort of 1,989 patients were still providing follow-up information or were known to have died. Of the 139 patients, 93 (4.7%) were lost to follow-up, and 46 (2.3%) refused to be followed.

Statistical analysis. Patients were grouped by initial coronary angioplasty result (stent-like versus non–stent-like), as previously defined. Comparisons of long-term patient outcome were made between the two patient groups, including freedom from all-cause death (e.g., cardiac and noncardiac mortality combined), MI, TLR, and repeat revascularization, which includes recurrent revascularization for both initially treated and untreated lesions. The total sample had 75% and 80% power, respectively (at $\alpha = 0.05$), to detect an absolute difference of 8% (relative difference $\approx 40\%$) in the 10-year rate of death or MI between the two groups. Assuming 10-year death and MI rates of 22% and 18%, respectively, in the reference group (patients with a stent-like result), the absolute difference of 8% corresponds to a clinically meaningful excess of each event (death or MI) of nearly 1% for each year of follow-up.

Stent-like versus non–stent-like comparisons were also performed in subgroups of patients with single or multivessel disease. These subgroups were selected because $>80\%$ of patients with single vessel disease were completely revascularized, whereas consistent with earlier reports (19,20), $<40\%$ of patients with multivessel disease were completely revascularized (irrespective of whether or not a stent-like result was achieved). Hence, we postulated that if a treatment difference existed between the stent-like and non–stent-like groups (e.g., as a result of the difference in initial lumen gain), it might be pronounced in patients with single vessel disease.

Differences in mean baseline and angiographic characteristics were analyzed by Student’s $t$ tests when continuous variables were normally distributed, and by the Wilcoxon rank-sum test when nonnormality was present. Differences in proportions of categorical variables were assessed by chi-square tests. Life table analysis by the method of Kaplan-Meier (21) was used to compare short- and long-term clinical event rates between the stent-like and non–stent-like groups. Cox regression analysis (22) was used to assess the relative risk of an initial stent-like versus non–stent-like result on the occurrence of clinical events at 10 years of follow-up. The covariates age, gender, multivessel disease, and initial procedural result (stent-like versus non–stent-like) were forced to remain in each model, with stepwise selection performed on other baseline
factors univariately associated (at p < 0.05) with the clinical event of interest.

### Results

#### Baseline medical history and initial procedural results.
Overall, 225 of the 1,989 successfully treated patients (11.3%) achieved an initial stent-like result, with 12.3% of single vessel disease patients and 10.3% of multivessel disease patients achieving a stent-like result in at least one coronary vessel (Table 1). Multiple stent-like results occurred in only 1% of all patients. Patients who had an MI within 10 d prior to the initial procedure were less likely to achieve a stent-like result (7.4% vs. 11.8%, p = 0.046) compared with those without acute MI. Patients with single vessel disease and a history of hypercholesterolemia were less likely to achieve a stent-like result (4.7% vs. 14.4%, p < 0.0001) than those without hypercholesterolemia, however, among multivessel disease patients, a reverse result was seen (7.7% in patients without and 12.7% in patients with a history of hypercholesterolemia, p = 0.017).

When multi-lesion coronary angioplasty was performed, whether within the same or multiple vessels, a stent-like result occurred more frequently (Table 1). Similarly, completeness of revascularization was significantly related to whether or not an initial stent-like result was achieved. Fourteen percent of patients with complete revascularization had a stent-like result, whereas only 9% of patients with incomplete revascularization had an initial stent-like result (Table 1).

#### Lesion characteristics and initial lesion results.
Per lesion analysis revealed that a stent-like result occurred in 249 of 3,176 attempted lesions (7.8%) and was more frequently achieved in diffuse lesions (11.2% vs. 7.4%, p = 0.03), while less frequently observed in lesions in the right coronary artery (6.1% vs. 8.5%, p = 0.02). Although the number of inflations and maximum balloon inflation pressure applied during the initial procedure were unrelated to achievement of a stent-like result, a higher median time of the longest single inflation was associated with greater likelihood of achieving a stent-like result (Table 2). The incidence of intimal tear with or without coronary dissection, as well as severe coronary dissection that, by definition, raised a portion of the vessel layer and caused an obstruction or a cessation of blood flow, was unrelated to whether or not an initial stent-like result was achieved.

#### Need for target lesion revascularization (TLR).
Of 3,176 initially treated lesions, 979 (30.8%) underwent TLR (with coronary angioplasty and/or CABG) at some time during 10 years of follow-up. Lesions with an initial stent-like result had a significantly lower incidence of TLR than non–stent-like result lesions (Fig. 1). The majority of this difference in need for repeat revascularization occurred within the first 2 years of follow-up. Overall, 923 of 2,927 (31.5%) non–stent-like result lesions underwent TLR compared with 56 of 249 (22.5%) stent-like result lesions (p = 0.003). These crude rates of TLR were similar, yet slightly lower than corresponding Kaplan-Meier estimates of TLR at 10 years of follow-up, which account for censoring of patients with <10 years of follow-up (TLR for non–stent-like lesions = 34.8%; stent-like result = 25.0%, p = 0.004). At a patient rather than lesion level, 649 of 1,764 patients without an initial stent-like result (36.8%) compared with 68 of 225 patients with an initial stent-like result (30.2%) underwent TLR at some time during follow-up (p = 0.06).

#### Mortality and MI.
Table 3 presents Kaplan Meier untoward event rates stratified by stent-like versus non–stent-like status, and baseline vessel disease. At both short- and long-term follow-up intervals, the incidence of death, MI, or the combined end point death/MI was similar between the two groups.
patient groups. These findings were consistent in both single and multivessel disease patients (Fig. 2, Table 3).

Repeat revascularization (by coronary angioplasty or CABG). The 10-year incidence of any revascularization (by coronary angioplasty or CABG), which includes re-treatment of initial attempted lesions (TLR) and first-time treatment of initially untreated lesions, is presented in Table 3. There was a nonsignificant trend for patients with multivessel disease and an initial stent-like result to require less CABG than multivessel disease patients without an initial stent-like result (25.2% vs. 32.7%, p = 0.09). However, a reverse trend was apparent in these same patients for the incidence of intercurrent coronary angioplasty (53.8% vs. 42.7%, p = 0.07). In patients with single-vessel disease, the incidence of CABG and intercurrent coronary angioplasty was similar between patients with and without an initial stent-like result.

Multivariable analysis. In Cox regression analysis, the 10-year risk of death, death/MI, or repeat coronary angioplasty

Table 3. Kaplan Meier Untoward Event Rates

<table>
<thead>
<tr>
<th>Untoward Event</th>
<th>6 months</th>
<th>1 year</th>
<th>5 years</th>
<th>10 years</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with SVD (n = 973)</td>
<td>0.8</td>
<td>0.9</td>
<td>1.5</td>
<td>0.9</td>
<td>7.0</td>
</tr>
<tr>
<td>Patients with MVD (n = 1,016)</td>
<td>1.2</td>
<td>0.0</td>
<td>2.6</td>
<td>1.9</td>
<td>11.1</td>
</tr>
<tr>
<td>All Patients (n = 1,989)</td>
<td>1.0</td>
<td>0.5</td>
<td>2.1</td>
<td>1.4</td>
<td>9.1</td>
</tr>
<tr>
<td>MI</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with SVD</td>
<td>1.3</td>
<td>1.7</td>
<td>2.1</td>
<td>3.4</td>
<td>7.2</td>
</tr>
<tr>
<td>Patients with MVD</td>
<td>1.8</td>
<td>0.0</td>
<td>3.2</td>
<td>2.0</td>
<td>11.4</td>
</tr>
<tr>
<td>All Patients</td>
<td>1.5</td>
<td>0.9</td>
<td>2.7</td>
<td>2.8</td>
<td>9.4</td>
</tr>
<tr>
<td>Death/MI</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with SVD</td>
<td>2.0</td>
<td>2.6</td>
<td>3.4</td>
<td>4.3</td>
<td>13.0</td>
</tr>
<tr>
<td>Patients with MVD</td>
<td>2.9</td>
<td>0.0</td>
<td>5.2</td>
<td>3.9</td>
<td>19.9</td>
</tr>
<tr>
<td>All Patients</td>
<td>2.5</td>
<td>1.4</td>
<td>4.3</td>
<td>4.1</td>
<td>16.5</td>
</tr>
<tr>
<td>CABG</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with SVD</td>
<td>3.5</td>
<td>4.3</td>
<td>4.9</td>
<td>6.9</td>
<td>9.4</td>
</tr>
<tr>
<td>Patients with MVD</td>
<td>6.3</td>
<td>1.9</td>
<td>9.2</td>
<td>2.9</td>
<td>19.7</td>
</tr>
<tr>
<td>All Patients</td>
<td>5.0</td>
<td>3.2</td>
<td>7.1</td>
<td>5.0</td>
<td>14.2</td>
</tr>
<tr>
<td>Repeat coronary angioplasty</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with SVD</td>
<td>16.2</td>
<td>12.0</td>
<td>21.0</td>
<td>15.5</td>
<td>28.4</td>
</tr>
<tr>
<td>Patients with MVD</td>
<td>15.1</td>
<td>15.5</td>
<td>20.8</td>
<td>25.4</td>
<td>32.3</td>
</tr>
<tr>
<td>All Patients</td>
<td>15.6</td>
<td>13.7</td>
<td>20.9</td>
<td>20.1</td>
<td>30.4</td>
</tr>
<tr>
<td>CABG/Repeat coronary angioplasty</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with SVD</td>
<td>18.2</td>
<td>12.9</td>
<td>23.7</td>
<td>17.2</td>
<td>33.4</td>
</tr>
<tr>
<td>Patients with MVD</td>
<td>20.2</td>
<td>17.5</td>
<td>27.3</td>
<td>27.3</td>
<td>44.9</td>
</tr>
<tr>
<td>All Patients</td>
<td>19.2</td>
<td>15.1</td>
<td>25.5</td>
<td>21.9</td>
<td>39.3</td>
</tr>
</tbody>
</table>

MVD = multi-vessel disease; NSL = initial non–stent-like result; SL = initial stent-like result; SVD = single-vessel disease; p value is for log-rank test over 10 years of follow-up.
was unrelated to whether or not a stent-like result was achieved at the initial coronary angioplasty. After adjustment for age, gender, vessel disease, and other significant baseline factors, there was a nonsignificant trend for patients with an initial stent-like result to be at lower risk of 10-year CABG (relative risk = 0.77, 95% confidence interval = 0.55, 1.08, p = 0.13) and 10-year TLR (relative risk = 0.79, 95% confidence interval = 0.60, 1.05, p = 0.11).

**Discussion**

We compared the long-term outcome of patients with successful conventional dilatation on the basis of whether or not an initial “stent-like” result was achieved. Overall, patients with an initial stent-like result were more completely revascularized (irrespective of baseline vessel disease) than non–stent-like result patients. Although a stent-like result occurred more often in diffuse lesions, we suspect this may relate to the selection of proximal and distal segments (averaged) to determine reference (“normal”) diameter. If either (or both) of the reference segments included diseased areas, then the reference lumen would be reduced, thereby making a stent-like result more probable.

**Repeat revascularization.** In per-lesion analysis, the larger gain in lumen achieved in lesions with an initial stent-like result corresponded to a markedly lower incidence of TLR, particularly in the first 2 years of follow-up. This finding is consistent with results from the BENESTENT (4) and STRESS (5) trials, where the incidence of lesion restenosis was significantly lower after coronary stenting than after coronary angioplasty. Similarly, on a patient level, the group of patients with a stent-like result had a better long-term outcome in terms of repeat revascularization. This included less need for TLR and a decreased incidence of CABG. In these patients if repeat revascularization was required, repeat dilatation was more frequently performed.

The importance of achieving an initial excellent angiographic result has been emphasized (8). Following treatment, the development of neo-intimal hyperplasia and arterial contraction is better tolerated if the initial gain in lumen is large. Stents have been proven to be the most reliable technique to achieve an initial excellent result with a residual stenosis <10%. However, the use of stents has not solved all the problems. Indeed, stents increase the amount of neo-intimal hyperplasia even though they do decrease TLR. Effective treatments for diffuse in-stent restenosis have not been identified. In addition, stents are costly, particularly when multiple stents are required in the setting of multivessel disease. For these reasons, there is a rebirth of interest in optimizing conventional coronary angioplasty. In the OCBAS trial (23), the rate of restenosis and target vessel revascularization at 7.6 months was similar between stented patients and those with an optimal result obtained with conventional coronary angioplasty. The approach of optimizing the initial results and only placing the stent if the initial result is not optimal is called “provisional stenting.” There are limited long-term data on patients with a stent-like result with conventional coronary angioplasty. In the 1985–86 NHLBI PTCA Registry, a stent-like result was achieved in only 11% of successfully treated patients, as determined by visual assessment. Nonetheless, there was a definite relationship between achieving a stent-like result and multi-lesion dilatation. This probably was a result of the fact that the operators were encouraged to continue sequentially during a procedure when the results were ideal.

**Death and MI.** Despite the more complete revascularization and lower incidence of TLR in patients with an initial stent-like result, the long-term risk of MI or death was unaffected by whether or not an initial stent-like result was achieved. One factor that may contribute to this apparent lack of difference stems from the fact that stability of atherosclerotic lesions and potential for rupture and subsequent infarction may be unrelated to the severity of lesion stenosis (24,25). In both the stent-like and non–stent-like patient groups, not all significant lesions were dilated at the initial coronary angioplasty, and further, virtually all lesions <50% stenosis were not dilated. Therefore, there was a substantial pool of initially untreated lesions, varying in degree of stenoses, in both the stent-like and non–stent-like patient groups. It is possible that a similar proportion of the untreated lesions within each group (stent-like vs. non–stent-like) had the potential for rupture and subsequent MI and/or sudden cardiac death. Our findings of
comparable long-term mortality and incidence of MI between the stent-like and non–stent-like patient groups are consistent with shorter term (6 month to 1 year) randomized trial comparisons of mortality and MI rates between patients assigned to conventional coronary angioplasty and those receiving stents (4–7).

Limitations. Patients in the Registry were treated in 1985–86 prior to recent technical refinements in balloon catheters. We cannot speculate as to whether similar results would be seen from patients being treated today. In addition, the assessment of postdilatation stenosis was determined by visual assessment. Quantitative coronary angiography is known to be more reliable than visual interpretation of coronary angiograms (26), although visual assessment is the method most commonly used in clinical practice. The use of visual assessment in this study may have resulted in some misclassification in terms of patients who did, or did not, achieve an initial stent-like result. We purposely selected a stringent definition of a stent-like result (≤10% stenosis) to maximize the likelihood that patients deemed to have had a stent-like result, by visual assessment, truly did achieve an optimal result. In the registry, 7.8% of all attempted lesions were considered to have achieved a stent-like result (Table 2). This compares with 8.5% of de novo lesions treated with conventional coronary angioplasty, and assessed by a core angiographic laboratory (Stanford University), in 904 randomized patients (2,252 lesions) in the Bypass Angioplasty Revascularization Investigation (K. Kip, personal communications). The similarity between these two studies would suggest reasonable visual assessment reliability in the PTCA Registry determination of an initial optimal (stent-like) result.

Conclusions. In this study of 1,989 patients who underwent de novo coronary angioplasty in 1985–86, an initial stent-like result achieved with coronary angioplasty alone did not influence the long-term risk of death or MI. However, a stent-like result was associated with less TLR, particularly within the first 2 years of follow-up. Among patients with multivessel disease, those with an initial stent-like result (vs. those without) were less likely to undergo CABG, yet more likely to undergo repeat coronary angioplasty when repeat revascularization was required. Achieving a stent-like result with balloon angioplasty alone may not confer equivalent clinical benefit as achieving a stent-like result with a stent. Whether or not “provisional stenting” (e.g., in cases of suboptimal dilatation) rather than primary intracoronary stenting should be recommended remains to be determined.

References