Isolated Left Anterior Descending Coronary Artery Disease

Percutaneous Transluminal Coronary Angioplasty Versus Stenting Versus Left Internal Mammary Artery Bypass Grafting

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Background—Single-vessel coronary artery disease is usually treated with PTCA; however, this approach when applied to the left anterior descending coronary artery (LAD) is hampered by high restenosis rates, often approaching 50%. Coronary stenting (STENT) and left internal mammary artery bypass grafting of the LAD (LIMA-LAD) are other options that have been successfully used for single-vessel LAD disease. The optimal mode of revascularization for patients with isolated single-vessel LAD disease is unclear. The purpose of the present study was to examine PTCA versus STENT versus LIMA-LAD with respect to short- and intermediate-term outcomes.

Methods and Results—This was an observational retrospective cohort study comparing in-hospital and intermediate-term outcomes and functional class among patients with isolated single-vessel LAD disease revascularization. Consecutive eligible patients were grouped according to their initial revascularization procedure and systematically followed up. A total of 704 patients qualified for the study: 469 in the PTCA group, 137 in the STENT group, and 98 in the LIMA-LAD group. Follow-up data were complete for 97% of patients and averaged 27±13 months. In-hospital mortality for the PTCA, STENT, and LIMA-LAD groups was 1.1%, 0%, and 0% (P=0.51), respectively. Median hospital stays after the procedure for the respective treatment groups were 1, 1, and 5 days (P<0.001), and occurrences of in-hospital myocardial infarction were 0.9%, 1.5%, and 1.0% (P=NS). Repeat revascularization procedures were performed in 30%, 24%, and 5% of the PTCA, STENT, and LIMA-LAD groups (P=0.011 for PTCA versus STENT). Actuarial 2-year mortality was 3.9%, 2.6%, and 1% in the PTCA, STENT, and LIMA-LAD groups (P=0.33).

Conclusions—Revascularization for isolated LAD disease using PTCA, STENT, or LIMA-LAD results in low in-hospital adverse event rates and good long-term results. Repeat procedures are required less often after LIMA-LAD than after either PTCA or STENT. Long-term mortality was not statistically different, but the trend was for the lowest mortality with LIMA-LAD, a somewhat higher mortality with STENT, and the highest mortality with PTCA. (Circulation. 1999;100[suppl II]:II-114–II-118.)

Key Words: angioplasty ■ stents ■ grafting ■ coronary disease ■ bypass ■ revascularization

The left anterior descending coronary artery (LAD) is almost always the largest of the 3 epicardial coronary arteries. The LAD typically subtends approximately 50% of the left ventricular myocardial mass, or approximately twice as much as either the right or the left circumflex coronary arteries.1,2 Patients with significant LAD disease, particularly when the proximal vessel is involved, have been noted to have an adverse cardiac prognosis compared with patients with coronary artery disease that does not involve the LAD.3–5 Although PTCA, coronary stenting (STENT), and left internal mammary artery bypass grafting (LIMA-LAD) are all used frequently for this high-risk lesion, the optimal approach remains unclear. No prior study has compared the outcomes of patients with isolated LAD disease treated with PTCA versus STENT versus LIMA-LAD surgery.

The purpose of the present study was to compare short- and intermediate-term outcomes of patients with isolated LAD disease who received PTCA versus STENT versus LIMA-LAD surgery.

Methods

Overview

This was an observational retrospective cohort study comparing in-hospital and intermediate-term morbidity and mortality rates as well as functional status among patients with isolated single-vessel LAD revascularization who received PTCA or STENT or LIMA-LAD.

Identification of Eligible Patients

Patients were retrospectively identified for inclusion in the study from the PTCA and coronary artery bypass surgery databases at the
TABLE 1. Baseline Demographics

<table>
<thead>
<tr>
<th></th>
<th>PTCA (n=469)</th>
<th>STENT (n=137)</th>
<th>LIMA-LAD (n=98)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt;80 y</td>
<td>37 (8%)</td>
<td>10 (7%)</td>
<td>3 (3%)</td>
<td>0.24</td>
</tr>
<tr>
<td>Creatinine &gt;1.5 mg/dL</td>
<td>32 (7%)</td>
<td>8 (6%)</td>
<td>5 (5%)</td>
<td>0.78</td>
</tr>
<tr>
<td>Male</td>
<td>307 (66%)</td>
<td>86 (63%)</td>
<td>72 (74%)</td>
<td>0.21</td>
</tr>
<tr>
<td>Prior infarction</td>
<td>202 (43%)</td>
<td>49 (36%)</td>
<td>33 (34%)</td>
<td>0.11</td>
</tr>
<tr>
<td>Prior PTCA</td>
<td>157 (34%)</td>
<td>47 (34%)</td>
<td>41 (42%)</td>
<td>0.29</td>
</tr>
<tr>
<td>Ejection fraction &lt;35%</td>
<td>52 (11%)</td>
<td>9 (7%)</td>
<td>12 (12%)</td>
<td>0.25</td>
</tr>
<tr>
<td>Diabetes</td>
<td>72 (15%)</td>
<td>23 (17%)</td>
<td>20 (20%)</td>
<td>0.46</td>
</tr>
<tr>
<td>Proximal LAD disease</td>
<td>281 (60%)</td>
<td>85 (62%)</td>
<td>81 (83%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Urgent procedure</td>
<td>30 (6%)</td>
<td>3 (2%)</td>
<td>6 (6%)</td>
<td>0.16</td>
</tr>
</tbody>
</table>

Data are number of patients, with percentage of specified patient population in parentheses.

Mid America Heart Institute, Kansas City, Mo. Patients were eligible for inclusion if they underwent their procedure between the dates of July 1, 1993, and October 31, 1997. Patients with angiographically documented, isolated single-vessel LAD revascularization with a ≥70% luminal diameter stenosis (usually estimated by ≥1 of a core group of 5 experienced invasive cardiologists) in the proximal or midvessel location were candidates for the study. The decision as to which, if any, revascularization procedure to use for each specific patient was made by the clinical physicians managing the case, often in consultation between cardiologists and surgical colleagues and the patient. Systematic guidelines about when to use the different modalities for revascularization of the LAD were not used. Only patients who received LIMA-LAD were included in the surgical group. Any patient with prior coronary stenting or any type of prior cardiac surgery was excluded as well as any patient presenting with an evolving acute myocardial infarction. All patients who underwent any concomitant surgery, such as valve replacement or repair, or carotid surgery were excluded from the surgical group.

If the patient underwent a subsequent procedure after the initial index revascularization procedure, the results were analyzed by the "intention to treat" principle. For example, patients who initially underwent PTCA of the LAD but required stenting of the vessel at a separate procedure remote from the initial coronary angioplasty procedure were analyzed as PTCA patients.

By use of these parameters, a total of 704 consecutive patients with isolated proximal or mid-LAD disease who underwent a revascularization procedure were identified. This group included 469 PTCA patients, 137 STENT patients, and 98 LIMA-LAD patients.

Baseline Data
The patient groups were very similar with respect to baseline demographic and anatomic variables. Details are outlined in Table 1. The mean ages were similar (62±13, 60±12, and 61±11 years) as were the mean ejection fractions (49±10, 52±10, and 52±10) in the PTCA, STENT and LIMA-LAD groups, respectively. The incidence of unstable angina at baseline was significantly higher in the LIMA-LAD group. Patients in the PTCA group underwent coronary angioplasty alone or in conjunction with directional atherectomy in 5.6% of cases and rotational atherectomy in 16%. In patients who received stent implantation, 5.8% of patients had rotational atherectomy and 1.5% had directional atherectomy. Values were P=0.003 (rotational atherectomy) and P=0.05 (directional atherectomy) when the STENT and PTCA patients were compared. All patients in the STENT group underwent PTCA with stenting. Patients who received an intracoronary stent were discharged on ticlopidine and aspirin. High-pressure balloon inflation was used, and stent underexpansion was avoided; in some cases, intravascular ultrasound was used as a guide. Angiography revealed coronary obstructions in non-LAD vessels in a small number of the PTCA, STENT, and CABG groups (≥70% stenosis in the right coronary artery: 1.2%, 1.4%, and 5.6%, respectively; in the circumflex artery: 2.5%, 1.4%, and 14.0%, respectively). Note that CABG patients had a higher incidence of totally obstructed non-LAD vessels in the right coronary and left circumflex arteries (PTCA patients: 0.3% and 0.7%, respectively; STENT patients: 5.6% and 0.8%, respectively; and CABG patients: 0.7% and 2.8%, respectively). Previous PTCA had been performed in 33.5%, 34.3%, and 41.8% (P=0.29) of PTCA, STENT, and CABG patients, respectively. Previous LAD PTCA had been performed in 22%, 25.5%, and 28.6% of the PTCA, STENT, and CABG patients, respectively (P=0.34). Proximal LAD disease was present more often in the LIMA-LAD group than the other 2 groups (Table 1). Other major baseline characteristics of the 3 groups were similar; these characteristics included the sex of the patient, baseline creatinine, and diabetes.

Follow-Up
Follow-up was complete in 97% of patients and was performed between November 1997 and February 1998. A comprehensive follow-up survey used both mail and telephone questionnaires. In addition to the follow-up survey, subsequent hospital and outpatient records were reviewed on all patients who reported any major events.

Statistical Analysis
Kaplan–Meier survival analyses were performed to evaluate differences in intermediate outcome among the 3 groups. Event-free survival was defined as freedom from death, myocardial infarction, and repeat revascularization procedures. Procedural myocardial infarction was defined as the presence of new Q waves that were 0.03 seconds in width and/or one third of the QRS complex in ≥2 contiguous leads. A multivariable analysis was carried out evaluating independent predictors of subsequent revascularization procedures. Repeat revascularization was modeled by using the Cox proportional hazards regression model. The treatment group (PTCA versus STENT versus LIMA-LAD) was forced into the model, and stepwise variable selection was used to identify further significant factors. Categorical variables were compared using Student’s t test and χ² methods.

Results
In-hospital events were rare among all 3 groups (Table 2). In-hospital death occurred in 5 (1.1%) of the 469 PTCA patients; no patient died in hospital in the STENT or LIMA-LAD group (P=NS). The median length of stay after the procedure was only 1 day for both the PTCA and STENT groups; this was significantly shorter than the median stay of 5 days in the LIMA-LAD group (P<0.001). In-hospital transient ischemic attack without permanent neurological sequelae occurred in 2 patients in the LIMA-LAD group; no patient suffered a postprocedural neurological complication in the PTCA or STENT group (P=NS).

Intermediate-term follow-up was obtained in 97% of patients, with a mean follow-up of 27±13 months. The frequency of repeat revascularization procedures was significantly higher in both the PTCA and STENT groups compared with the LIMA-LAD group (Figure 1). The need for a subsequent revascularization procedure in the STENT group (24%) was marginally lower than in the PTCA group (30%, P=0.11). Frequency of myocardial infarction was low in all groups, without any meaningful differences between them. The 2-year actuarial mortality trended lowest (1.1%) in the LIMA-LAD group compared with 2.6% in the STENT group and 3.9% in the PTCA group, although the differences did not meet statistical significance (P=0.33) (Figure 2). The survival advantage of LIMA-LAD over PTCA was exaggerated in patients who had proximal LAD rather than mid-LAD
disease. Patients with proximal LAD disease that underwent PTCA had a 2-year mortality of \( \approx 5\% \).

By use of multivariable analysis modeling, the only resulting significant baseline factors predicting need for subsequent procedures were PTCA (odds ratio, 4.7 versus LIMA-LAD), STENT (odds ratio, 3.3 versus LIMA-LAD), and diabetes (odds ratio, 1.45 versus nondiabetics) (Table 3).

Total event-free survival, calculated using actuarial (Kaplan-Meier) methodology, was substantially better in the LIMA-LAD group than in the PTCA or STENT group (Figure 3).

**Discussion**

The present study showed that revascularization for isolated LAD disease using PTCA, STENT, or LIMA-LAD resulted in low in-hospital morbidity and mortality rates and good intermediate-term results. Repeat revascularization was required significantly more often after both PTCA and STENT than after LIMA-LAD, and event-free survival was superior in the LIMA-LAD group. Intermediate-term mortality was not significantly different, but consistent trends were noted, with the lowest mortality in the LIMA-LAD group, a slightly higher mortality rate in the STENT group, and the highest mortality after PTCA.

In general, patients with single-vessel coronary artery disease are treated with medical therapy or PTCA. In a study comparing angioplasty with medicine,6 69 of the 212 patients with single-vessel disease who were randomly assigned to PTCA or medical therapy had a significant stenosis in the proximal LAD. At follow-up after 6 months, the PTCA patients had superior exercise tolerance and improved anginal status compared with the medically treated patients. However, PTCA of the LAD is limited by the frequent occurrence of restenosis.7,8 Compared with PTCA of the proximal LAD, STENT has been documented to result in a significantly decreased risk of restenosis.9–11 A trial involving 120 patients with symptomatic isolated LAD stenosis randomized patients to STENT or PTCA.9 The restenosis rates at 12 months were 19% for the stented group versus 40% for the PTCA group (\( P = 0.02 \)). Additionally, 12-month rates of event-free survival were 87% after stenting versus 70% after angioplasty (\( P = 0.04 \)).

CABG surgery using LIMA-LAD has been documented to be an effective treatment strategy for isolated stenosis of the proximal LAD.12 Studies have been performed comparing LIMA-LAD with PTCA of the LAD. One study showed

### Table 2. In-Hospital Events

<table>
<thead>
<tr>
<th>Event</th>
<th>PTCA</th>
<th>STENT</th>
<th>LIMA-LAD</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital stay from procedure to discharge, median (range), d</td>
<td>1 (0–34)</td>
<td>1 (0–12)</td>
<td>5 (2–47)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Death</td>
<td>5 (1.1%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>NS</td>
</tr>
<tr>
<td>Urgent/redo CABG</td>
<td>2 (0.4%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>NS</td>
</tr>
<tr>
<td>Transient ischemic attack</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>2 (2.0%)</td>
<td>0.019</td>
</tr>
<tr>
<td>Stroke</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>NS</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Q and Q wave</td>
<td>4 (0.9%)</td>
<td>2 (1.5%)</td>
<td>1 (1.0%)</td>
<td>NS</td>
</tr>
<tr>
<td>Q wave only</td>
<td>3 (0.6%)</td>
<td>1 (0.7%)</td>
<td>1 (1.0%)</td>
<td>NS</td>
</tr>
</tbody>
</table>

Data are number of patients, with percentage of specified patient population in parentheses, except where indicated otherwise.

**Figure 1.** Incidence of repeat revascularization procedures (PTCA or CABG) during follow-up. Compared with the LIMA-LAD (LIMA) group, both the STENT group (\( P<0.001 \)) and the PTCA (balloon) group (\( P<0.001 \)) experienced higher rates of revascularization procedures. The STENT group fared marginally better than did the PTCA group (\( P=0.11 \)).

**Figure 2.** Twenty-four month all-cause mortality. Although death rate during follow-up trended lowest in the LIMA-LAD group compared with the STENT and PTCA groups, differences did not meet statistical significance (\( P=0.33 \)).
similar long-term survival rates in these 2 groups, with a greater need for repeat revascularization procedures in the PTCA group and a lower incidence of overall cardiac events in the patients who underwent LIMA-LAD. Another study in which patients were randomly assigned to bypass surgery, PTCA, or medical therapy indicated that patients who underwent surgery that included LIMA-LAD had a significantly lower incidence of cardiac events during follow-up than did patients assigned to PTCA or medical therapy. In 2 large database studies, hazard-analysis risk adjustment revealed that patients with LAD disease, especially in the proximal segment, had superior intermediate-term outcomes after CABG surgery than after PTCA. In single-or double-vessel disease not involving the LAD, outcomes were similar after bypass surgery or PTCA. Follow-up studies extending for 17 years indicate that people with single-vessel LAD disease have long-term survival rates after LIMA-LAD that are as good or better than the rates in an age-matched population without coronary disease at baseline.

The present study shows, as do prior studies, that STENT is superior to PTCA with respect to need for repeat revascularization procedures. However, in the present study, 24% of patients still required another procedure after STENT. On the other hand, repeat procedures after LIMA-LAD were quite uncommon and occurred significantly less often than after either PTCA or stenting.

CABG surgery does entail substantially higher early morbidity rates than do percutaneous approaches. The median postprocedure length of stay was 5 days after LIMA-LAD versus only 1 day for either PTCA or STENT. The in-hospital mortality rates, however, were similar in the 3 groups. Although a decreased length of stay has been shown to carry initial cost and patient comfort advantages, the need for repeat revascularization procedures during follow-up at least partially offsets these early benefits of the less invasive approach.

Study Limitations

The present study is not a randomized trial; thus, baseline differences between the groups may have accounted for some of the observed differences. However, the findings were very consistent with other recent reports concerning these procedures. Technique and technology continue to improve rapidly in the field of coronary revascularization. For instance, coronary stents continue to evolve with improved designs and potential for adjunctive therapy, such as intracoronary radiation, that may reduce rates of restenosis. Minimally invasive CABG surgery without using cardiopulmonary bypass is being explored as a less traumatic option for LIMA-LAD. These changes when incorporated into clinical practice may alter the relative outcomes in patients with isolated LAD disease.

The present study confirms that the patient with isolated LAD disease has 3 effective revascularization options. Additional studies will be important in evaluating the effectiveness of aggressive medical therapy (eg, lipid-lowering drugs, antiplatelet therapy, and β-blockers) as either an alternative to or adjunctive therapy for coronary revascularization in patients with isolated LAD disease.

References


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