Results and Long-Term Predictors of Adverse Clinical Events After Elective Percutaneous Interventions on Unprotected Left Main Coronary Artery

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Background—The safety and efficacy of percutaneous coronary intervention of de novo lesions in unprotected left main coronary arteries remains an unresolved issue.

Methods and Results—We analyzed 67 consecutive patients treated with the following devices: 39 with stents, 12 with rotational atherectomy plus stents, 13 with directional coronary atherectomy plus stents (a total of 64 patients were treated with stents), and 3 patients with directional coronary atherectomy only. The reference vessel size was $3.78 \pm 0.73$ mm and lesion length was $6.6 \pm 3.0$ mm. In-hospital complications were 2 coronary artery bypass grafts (CABGs) (3.0%), 2 Q-wave myocardial infarctions (MIs) (3.0%), and 3 non–Q-wave MIs (4.5%); there were no deaths. The estimated cardiac survival at 3 years was 91%. The cardiac mortality rate was higher in patients with Parsonnet score $\geq 15$ versus $<15$ (21.4% versus 4.2%, $P=0.02$) at 3 years. The independent covariate of cardiac death was preserved left ventricular ejection fraction; for combined cardiac events (cardiac death, MI, repeat revascularization) it was large reference vessel size. Follow-up angiography at 5±2 months in 85% of eligible patients revealed 31.4% restenosis. Extending the follow-up to 31±23 months (19 patients with follow-up beyond 3 years) the cumulative event rates were 11 deaths (16.4%), 8 of them cardiac (11.9%), 2 (3.0%) MI, and 16 (23.9%) repeat revascularizations (CABG in 5 patients).

Conclusions—Elective percutaneous coronary intervention of de novo lesions in left main coronary arteries is feasible, with low procedural risk. The long-term follow-up revealed a high rate of angiographic restenosis and repeat revascularization, with a relatively high incidence of cardiac death. Reference vessel size and left ventricular function are the most important predictors of favorable follow-up. (Circulation. 2002;106:698-702.)

Key Words: angioplasty ■ coronary disease ■ revascularization ■ stents ■ survival

The application of percutaneous coronary interventions (PCI) has expanded beyond standard indications in recent years as the result of the wide availability and use of stents.1,2 Lesions in the left main coronary artery (LM) are considered a standard indication for surgical revascularization, on the basis of the results of randomized studies.3 Several recent reports using coronary stenting for unprotected LM lesion showed encouraging follow-up clinical results with this technique. The first published multicenter experience in 107 patients (ULTIMA Registry: Unprotected Left Main Trunk Investigation Multicenter Assessment) including both elective and emergent treatment4 showed an in-hospital mortality rate of 12% and a cumulative 1-year mortality rate of 29%, whereas recent studies in patients with elective treatment reported very low hospital complications and a 1-year survival rate of 97% or higher.5 However, an updated report from the ULTIMA Registry continued to show a high in-hospital and follow-up mortality rates.6

One major problem is that many series include elective and emergency interventions, making the results difficult to use when recommending this procedure to a specific patient. With the intent to provide further data in this controversial field, we examined and report our complete experience with elective percutaneous treatment of lesions involving unprotected LM.

Methods

Patients and PCI

From April 1993 to June 2001, 67 consecutive patients with de novo unprotected LM stenosis were electively treated in our institution. Every patient had $\geq 50\%$ diameter stenosis by visual estimate. The decision to perform PCI versus surgery was considered when one of
the two conditions was present: (1) suitable anatomy and lesion characteristics for stenting and preference by the patient and by the referring physician for a percutaneous approach, both of them being aware of the procedural risks; (2) suitable anatomy and lesion characteristics for stenting and contraindication to surgery on the basis of the presence of comorbidity evaluated by a cardiac surgeon. The Parsonnet surgical risk score was calculated for each patient, and patients were stratified in high- and low-surgical risk groups. Lesions underwent balloon predilation, rotational atherectomy, directional atherectomy, or intravascular ultrasound evaluation, according to the operator’s decision. Final stent implantation was encouraged in most of the lesions.

Stents were deployed to achieve the best possible final lumen diameter. Preprocedural and postprocedural therapy consisted of ticlopidine and aspirin.

A clinical and angiographic follow-up was scheduled for all patients. Clinical follow-up was performed at 1, 3, and 6 months and at the latest follow-up time by clinic visits or by telephone interview with the patient’s physician. Angiographic follow-up was scheduled at 6 months after successful procedure or earlier if noninvasive evaluation or clinical presentation suggested the presence of ischemia.

Definitions

Procedural success was defined as revascularization in the target lesion within 30% residual stenosis according to angiography and with the patient leaving hospital free from any of the following events: death, Q-wave or non-Q-wave myocardial infarction (MI), or coronary artery bypass graft (CABG). Non-Q wave MI was defined as elevation of total CK 2 times above the upper limit of normal with a positive MB fraction, in the absence of pathological Q waves. The events analyzed for follow-up in this study were cardiac death, CABG, MI (Q-wave and non-Q-wave), restenosis, and target vessel revascularization (TVR), including ostium of left anterior descending artery (LAD) and circumflex artery (LCx). Deaths were classified as either cardiac or noncardiac. Deaths that could not be classified were considered to be cardiac related.

Restenosis was defined as ≥50% luminal narrowing at the target site or ostium of the LAD and/or LCx demonstrated at the follow-up angiography, irrespective of clinical symptoms of the patient. Parsonnet score is a numeric scoring system used to stratify the risk of death at 30 days in patients undergoing open heart surgery.

The score is calculated as the sum of predefined numerical values assigned to 15 different clinical risk factors (example: 1 for morbid obesity and 20 for a second or subsequent reoperation). A score value >15 was chosen to express a risk >4%.

Quantitative Coronary Angiography

The reference diameter, the stenosis length, and the minimal luminal diameter were determined with the use of a validated edge-detection program (CMS version 4.0, MEDIS) at baseline, after procedure, and at follow-up. The luminal indexes (eg, acute gain, late loss, loss index, and so forth) were calculated according to the standard criteria.

Statistical Analysis

Data were analyzed with commercial statistical programs (StatView 5, SAS Institute Inc). Continuous data are expressed as mean±SD. For the analysis of continuous data, the Student’s t test was used to assess differences between groups with and without clinical events. Categorical data were compared with the use of χ2 or Fisher’s exact tests. Cox proportional hazards model with the use of the stepwise procedure was used to assess the correlates of events among multiple clinical, procedural, and angiographic variables. Event-free survival during follow-up at 3 years (72% of patients) was evaluated according to the Kaplan-Meier method. A comparison of cardiac survival between low- and high-surgical risk groups was performed by means of the log-rank test.
patients died: 8 of these patients had cardiac death (8 of 67; 11.9%). The characteristics of these patients and the time of occurrence of death are presented in Table 4. The total event rate at the end of the follow-up period, comprising cardiac death, MI, and any revascularization, was 34.3%.

Angiographic follow-up was performed in 51 patients of 60 eligible (angiographic follow-up rate 85%) after 5±2 months. Angiographic restenosis was found in 16 patients (31%). The specific location of the restenotic lesions according to the LM segment originally involved are presented in Table 2.

TVR was performed in 16 patients (11 repeat PCI and 5 CABG). Among these patients, 3 late (average, 16.7 months) TVR were observed, all at the ostium of LAD or LCx. Figure 1 shows the Kaplan-Meier curve for freedom from major adverse cardiac events.

Cardiac Deaths
In total, there were 11 deaths (16.4%), 8 of which were cardiac related. Six cardiac deaths occurred within 6 months after the procedure. The other two patients died >3 years after hospital discharge.

### Follow-Up Cardiac Events
After hospital discharge, patients completed a mean clinical follow-up of 31±23 months (range, 5 to 94.7). Table 3 shows cardiac events during the follow-up period. A total of 11 patients died: 8 of these patients had cardiac death (8 of 67; 11.9%). The characteristics of these patients and the time of occurrence of death are presented in Table 4. The total event rate at the end of the follow-up period, comprising cardiac death, MI, and any revascularization, was 34.3%.

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after procedure, and both had low left ventricular ejection fraction (LVEF) (≤0.35). Three noncardiac deaths were due to cancer. The estimated cardiac survival rates at 1 and 3 years were 91% and 91%, respectively (Figure 2). By multivariate analysis, the covariate of cardiac death was LVEF ≤0.40 (hazard ratio, 8.6; \( P = 0.003; 95\% \text{ CI, 2.2 to 34.8} \)).

Cardiac mortality rate was higher in the patients with high Parsonnet score (95.8% freedom from cardiac death at 3 years in the low-risk group versus 78.6% in the high-risk group, \( P = 0.021 \)) (Figure 3).

### Directional Atherectomy and Stenting for Bifurcation Lesions

Forty patients had lesions involving the bifurcation of the left main. Debubling with atherectomy was performed in 15, and in 12 a stent was implanted. The angiographic restenosis rate in these patients was 35.7% (5 of 14) and was not different from patients who had stenting without debulking (47.1%, 8 of 17, \( P = 0.7 \)). When we consider only the branch of the bifurcation that underwent debulking, the restenosis rate was 23.5% (4 of 17).

### Discussion

The major findings in this study are (1) PCI with stenting of lesions located in the LM is feasible in a variety of lesions with high immediate clinical success; (2) at an average follow-up time of 31 months there is an incidence of cardiac death of 11.9% and of a need of TVR of 24.6%; (3) patients with a high surgical risk by Parsonnet score have a 21.4% 3-year cardiac mortality rate compared with 4.2% in patients with a low surgical risk; and (4) the most important predictor of major adverse cardiac events during follow-up is the reference vessel size of the LM, whereas LVEF ≤0.40 is the only covariate of cardiac death.

Results of clinical follow-up of PCI performed on the LM are inferior to the ones obtained after PCI in other locations. An analysis of 4 recently published studies\(^5,12-14\) addressing elective LM interventions with stenting in most of the lesions shows an incidence of in-hospital mortality rates ranging from 0% to 4% for elective procedures, but cardiac mortality rate increases to 13.7% when emergency PCIs are included.\(^6\)

The long-term outcome in the same studies with a follow-up time ranging from 7.3 to 25.5 months shows a cardiac mortality rate between 0.7% to 5.7%, an incidence of MI between 0% to 2.6%, and a need for revascularization from 6.8% to 16.4%.

In these studies, the predictors of freedom from cardiac events, including the need for revascularization, were angiographic reference vessel size of the LM for the incidence of restenosis\(^5\) and final lumen diameter for death.\(^14\) Our results emphasize one important aspect of this type of procedure: The hospital outcome is favorable, but the follow-up is affected by a relatively high incidence of events such as cardiac death, MI, and the need for reintervention. The fact that 6 of 8 cardiac deaths occurred in the first 6 months highlights the dramatic way restenosis could manifest when PCI is performed on the LM and stresses that only a clear improvement in this area will justify a wider application of the PCI approach to LM disease. It could be argued that a surgical approach could have avoided some of these early deaths. Despite these valid concerns, we should consider that LM disease carried a 15% mortality rate 5 years after surgical revascularization in the Coronary Artery Surgery Study (CASS).\(^3\) On the other side, we cannot dismiss that there are improvements in surgical mortality rate, and it is difficult to exactly estimate the surgical risk of this small cohort.

Along with the other investigators, we found favorable outcome in patients with a low surgical risk. In our series, patients (72% of total population) with a Parsonnet score <15 had 3-year cardiac mortality rate of 4.2%.

Despite these encouraging results in the group with unprotected LM disease and low surgical risk, it is important to consider that only a prospective study with a predefined characterization of the low risk group will support this preliminary finding.

The fact that there were predictors of long-term success may help the selection of the most appropriate patient for this type of procedure. The size of the reference vessel, a low surgical risk, and a preserved left ventricular function\(^5,14\) are the most important parameters to be considered.
Unfortunately, the finding that patients with LM disease and a high Parsonnet score or a low LVEF have the worst prognosis undermines the value of PCI as an alternative to surgery in these patients.

Another way to look at the practice of PCI of unprotected LM is that in our series only 2 cardiac deaths occurred from surgery in these patients.

With regard to the value of atherectomy debulking before stenting, we cannot draw any conclusion from our study, most probably because of the small number of patients treated with this approach, the tendency of the operator to use atherectomy in the most complex bifurcations, and some limitations in the ability to perform effective debulking in both branches, especially with the old devices used in the early time of this experience. It is interesting to notice that the lowest numeric restenosis (4 of 17, 23.5%) was found in the branch of a bifurcation in which debulking was performed before stenting.

On the basis of these data, we conclude that while awaiting a solution to the problem of restenosis, elective PCI on unprotected LM has good long-term results in patients with low surgical risk and large reference vessel diameter.

**Limitations**

The most important limitation of this study is that this series represents a selected group of patients with LM disease. The fact that the procedures were performed over a long time period introduces variables related to the evolution of devices (more friendly stents) and operator experience. With regard to the use of atherectomy, we need to take into account that this approach was mostly used in bifurcations, making a comparison with simple stenting difficult. The wide difference in cardiac mortality rates among patients with low versus high Parsonnet scores could be partially accounted for by chance, as the result of our small sample size.

The fact that this study was not randomized versus surgery is in our view a minor limitation because PCI of the LM is still an approach in evolution and not yet ready for randomization versus an established technique such as CABG.

**References**

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