EuroSCORE as a Predictor of Death and Myocardial Infarction After Unprotected Left Main Coronary Stenting

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This study aimed to identify the independent predictors of death and myocardial infarction (MI) after unprotected left main coronary artery stenting with bare metal (n = 148) or sirolimus-eluting (n = 176) stents between January 2000 and March 2005. To identify independent predictors of death and nonfatal MI, all available parameters were evaluated. Systemic surgical risk stratification systems such as the EuroSCORE and Parsonnet score were included in the analysis. Clinical information at 9 months was available in 98% of patients (median follow-up 26.3 months). During this period, death/MI occurred in 42 patients (13%). Of the 5 deaths, 4 were related to cardiac and 1 to noncardiac causes. By multivariate Cox regression analysis, a high EuroSCORE (≥6; hazard ratio 3.4, 95% confidence interval 1.2 to 9.6, p = 0.023), number of stents used (hazard ratio 1.8, 95% confidence interval 1.0 to 3.1, p = 0.042), and treatment with a glycoprotein IIb/IIIa inhibitor (hazard ratio 8.6, 95% confidence interval 2.7 to 27.4, p <0.001) were independent predictors of death/MI. Areas under the receiver-operating characteristic curve of EuroSCORE and number of stents were 0.61 (95% confidence interval 0.52 to 0.70, p = 0.023) and 0.61 (95% confidence interval 0.51 to 0.70, p = 0.028), respectively. In conclusion, high surgical risk estimated by systemic risk stratification of the EuroSCORE appears to be associated with unfavorable outcomes of unprotected left main coronary artery stenting. **(Am J Cardiol 2006;98:1567–1570)**

To identify the predictive factors of serious adverse clinical events after elective unprotected left main coronary artery (LMCA) stenting, we analyzed the association of survival without myocardial infarction (MI) with various clinical, angiographic, and procedural characteristics and systemic risk evaluation systems in a relatively large cohort of patients.

Methods and Results

This study included 324 consecutive patients who underwent elective coronary stenting for the treatment of unprotected LMCA stenoses between January 2000 and March 2005. Inclusion criteria were symptomatic or documented myocardial ischemia and significant stenosis (≥50% stenosis by visual estimate) of the unprotected LMCA suitable for stent placement. Patients who had ST-elevation MI at the unprotected LMCA and underwent emergency percutaneous coronary intervention (PCI) within 24 hours of symptom onset were excluded. LMCA was considered unprotected if there were no patent coronary artery bypass grafts to the left anterior descending or left circumflex arteries. Informed written consent was obtained from all patients in accordance with the Declaration of Helsinki.

The stenting technique at the unprotected LMCA has been previously described.[1,2] Bare metal stents were used in 148 patients and sirolimus-eluting stents in 176 patients. Intra-aortic balloon pumps were used prophylactically or therapeutically in selected unstable patients for hemodynamic support. Glycoprotein IIb/IIIa inhibitors were administered to patients who had very complex lesions or impaired distal coronary flow. Aspirin was administered to all patients indefinitely. Clopidogrel (75 mg/day) or ticlopidine (250 mg 2 times a day) was administered for 1 month after bare metal stent implantation or for ≥6 months after sirolimus-eluting stent implantation. In addition, cilostazol (100 mg 2 times a day) was administered to patients who received sirolimus-eluting stents.[3] A loading dose of ticlopidine (500 mg or 250 mg 2 times a day), clopidogrel (300 mg), and cilostazol (200 mg) was administered ≥24 hours before the procedure. Total creatine kinase and creatine kinase-MB fraction levels were routinely measured at 4, 12, and 24 hours after the procedure.

Before the procedure, serum concentrations of C-reactive protein, lipoprotein(a), and total L-homocysteine were measured in 287 patients (89%) without acute or chronic infectious disease or inflammatory states. C-reactive protein was measured using a high-sensitivity turbidimetric assay (Cobas Integra, Roche Diagnostics, Basel, Switzerland) and a threshold of detection of 0.0064 mg/dl.[4] Lipoprotein(a) was measured with a 1-step sandwich enzyme-linked immunosorbent assay using 2 monospecific polyclonal antiapolipoprotein(a) antibodies (ImmunoGMBH, Saarbroeken, Ger-

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Table 1
Clinical and angiographic characteristics in relation to occurrence of death and myocardial infarction

Variable	Death/MI		p Value
	Yes (n = 42)	No (n = 282)	
Age (yrs)	60.6 ± 11.4	58.5 ± 12.0	0.309
Men	30 (71.4%)	194 (68.8%)	0.730
Diabetes mellitus	8 (19.0%)	72 (25.5%)	0.363
Total cholesterol >200 mg/dl	11 (26.2%)	61 (21.6%)	0.507
Smoker	15 (35.7%)	85 (30.1%)	0.466
Hypertension	15 (35.7%)	123 (43.6%)	0.334
Previous PCI	5 (11.9%)	44 (15.6%)	0.649
Left ventricular ejection fraction (%)	62.0 (55.0–66.0)	62.0 (59.0–66.0)	0.456
Acute coronary syndrome	26 (61.9%)	133 (47.2%)	0.075
Renal failure	0 (0%)	4 (1.4%)	1.000
EuroSCORE	3.0 (2.0–6.0)	2.0 (1.0–4.0)	0.022
Parsonnet score	7.0 (6.0–13.0)	7.0 (6.0–8.3)	0.175
C-reactive protein (mg/dl)	2.4 (1.1–3.9)	2.0 (0.9–4.0)	0.736
Lipoprotein(a) (mg/L)	20.9 (12.1–35.4)	21.5 (9.4–37.2)	0.888
Homocysteine (μmol/L)	12.7 (9.9–15.0)	12.4 (10.2–15.1)	0.778
Bifurcation involvement	29 (69.0%)	157 (55.7%)	0.102
Multivessel coronary (≥2) involvement except for left main coronary artery	29 (69.0%)	137 (48.6%)	0.013
Reference diameter (mm)	3.56 ± 0.80	3.69 ± 0.70	0.314
Minimal lumen diameter before procedure (mm)	1.28 ± 0.61	1.48 ± 0.66	0.066
Minimal lumen diameter after procedure (mm)	3.52 ± 0.65	3.72 ± 0.64	0.069
Lesion length (mm)	12.1 (9.1–35.4)	11.8 (8.0–18.4)	0.133

Table 2
Procedural characteristics in relation to occurrence of death and myocardial infarction

Variable	Death/MI		p Value
	Yes (n = 42)	No (n = 282)	
Multivessel PCI	23 (54.8%)	119 (42.2%)	0.126
Bifurcation stenting (stent in side branch)	9 (21.4%)	62 (22.0%)	0.935
Total contiguous stent length (mm)	18.0 (13.0–42.8)	18.0 (12.0–23.0)	0.089
No. of used stents at left main coronary artery	1.0 (1.0–1.3)	1.0 (1.0–1.0)	0.956
No. of total used stents	2.0 (1.0–3.0)	1.0 (1.0–2.0)	0.015
Debulking atherectomy	8 (19.0%)	53 (18.8%)	0.969
Rotablating atherectomy	0 (0%)	4 (1.4%)	1.000
Cutting balloon angioplasty	2 (4.8%)	8 (2.8%)	0.501
Direct stenting	10 (23.8%)	88 (31.2%)	0.330
Maximal device diameter (mm)	4.19 ± 0.52	4.44 ± 0.59	0.120
Intra-aortic balloon pump	8 (19.0%)	16 (5.7%)	0.002
Glycoprotein IIb/IIIa inhibitor	8 (19.0%)	13 (4.6%)	<0.001
Guidance of intravascular ultrasound	30 (71.4%)	202 (71.6%)	0.978
Sirolimus-eluting stent	23 (54.8%)	153 (54.3%)	0.951

many).[5] Total L-homocysteine was measured by polarization immunoassay with an IMX analyzer (Axis Biochemicals ASA, Oslo, Norway).[6] For systemic risk stratification before the procedure, standard EuroSCORE[7] and Parsonnet score[8] were measured for all patients. The 2 scoring methods are composed of groups of weighted patient-related, cardiac-related, and surgery-related risk factors. A high EuroSCORE was defined as ≥6.[7] With a contrast-filled injection catheter as the calibration source, quantitative coronary angiograms were analyzed by 2 experienced angiographers not involved in the stenting procedures who used computerized software (CASS II, Pie Medical, Maastricht, The Netherlands). Minimal lumen diameter was measured before and after intervention from diastolic frames in single, matched views. Diameters of normal segments proximal and distal to the treated area were averaged to determine the reference diameter. In ostial and bifurcation lesions, adjacent normal segments were used as references.

All patients were evaluated clinically by office visits or telephone interviews at 1 month and 3 and 6 months after stenting and then every 4 months. At each visit, evaluation of electrocardiograms was routinely performed. The end point of this study was the composite of all-cause death and MI (death/MI). MI was defined as development of new pathologic Q waves in ≥2 contiguous electrocardiographic leads or an increase in creatine kinase-MB to ≥3 times the upper limit of normal.

Continuous variables are presented as mean ± SD or median (interquartile range) and were compared with Student's *t* test or Mann-Whitney U statistic test. Categorical variables are presented as counts or proportions (percentages) and were compared with chi-square test or Fisher's exact test. To determine the independent predictors of death/MI, Cox regression analysis was performed on all variables, and variables that were predictive at the 0.1 level by univariate analysis were entered into multivariate analysis. The area under the receiver-operating characteristic curve was used to assess the discriminate power of the independent predictors.[9] A p value <0.05 was considered statistically significant.

During hospitalization, periprocedural MI, defined as a creatine kinase-MB increase ≥3 times the normal level, developed in 34 patients (10.5%). However, there were no incidents of death or stent thrombosis. Clinical information at 9 months was available in 98% of patients (median follow-up 26.3 months). After discharge, 5 patients died, 4 from cardiac-related causes and 1 from a noncardiac cause. Nonfatal MI occurred in 4 patients. Angiographic stent thrombosis did not occur in any patient during the follow-up period. Overall, the combined incidence of death/MI after the procedure and at follow-up was 13.0% (42 patients). Repeat revascularization was performed in 36 patients (11.1%), 16 of whom underwent repeat PCI and 20 of whom underwent coronary artery bypass surgery.

Table 1 presents comparisons of clinical, angiographic, and laboratory characteristics between the 2 groups of patients. Eleven patients in the group with death/MI (26.2%) had a high EuroSCORE (≥6), a significantly higher per-

Table 3
Multivariate predictors of death and myocardial infarction

Variable	Hazard Ratio	95% Confidence Interval	p Value
High EuroSCORE (≥6)	3.362	1.181–9.574	0.023
No. of total used stents	1.792	1.021–3.146	0.042
Use of glycoprotein IIb/IIIa inhibitor	8.640	2.722–27.418	<0.001

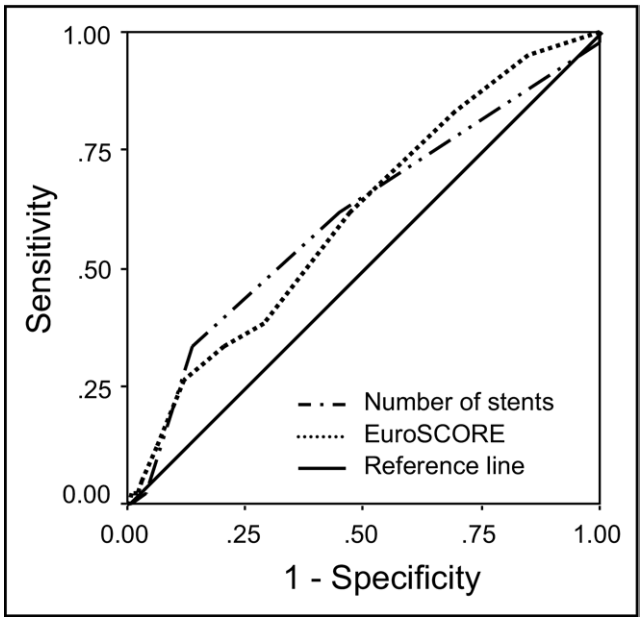

Figure 1. Areas under the receiver-operating characteristic curves for death and MI with respect to EuroSCORE; the number of total used stents was 0.61 (95% confidence interval 0.52 to 0.70, p = 0.023) and 0.61 (95% confidence interval 0.51 to 0.70, p = 0.028), respectively.

centage than in the group without death/MI (34 patients, 12.1%, p = 0.013). Laboratory and angiographic characteristics did not differ significantly between groups. Procedural characteristics of the 2 groups are presented in Table 2. By multivariate analysis, high EuroSCORE (≥6), number of stents used, and treatment with a glycoprotein IIb/IIIa inhibitor were independent predictors of death/MI (Table 3). Figure 1 shows the receiver-operating characteristic curves of EuroSCORE and number of stents used for predicting death/MI. Areas under the receiver-operating characteristic curves for EuroSCORE and number of stents used indicate less discriminatory ability.[9]

Discussion

Unprotected LMCA lesions have been candidates for coronary artery bypass surgery due to the potential risk of serious periprocedural and long-term complications, such as death or MI.[1,2,10–16] Even when drug-eluting stents were used, the incidence of death or MI did not improve significantly.[2,15,16] Therefore, efforts have been made to identify predictors of adverse outcomes after unprotected LMCA stenting. Identification of prognostic markers is valuable in selecting good candidates and modifying the prognosis. Decreased left ventricular function, significant mitral regurgitation, cardiogenic shock, renal failure, multivessel coronary disease, and stent diameter after procedures have been reported to be independent predictors of mortality.[11,12] In addition, it has been recently suggested that the preprocedural level of high-sensitivity C-reactive protein can be used in evaluating the risk of unprotected LMCA stenting.[17] However, these studies had limitations, including small study populations, enrollment of high-risk inoperable patients, and inclusion of emergency procedures. We therefore restricted the study population to those who underwent elective procedures. Due to this selection, the incidence of death/MI after the procedure was relatively low.

The EuroSCORE is an assessment system for the preoperational risk stratification of cardiac surgery.[7] This risk evaluation system has been shown to be useful in predicting the preprocedural risk of PCI in high-risk interventions[15,16] in addition to procedural and long-term outcomes after cardiac surgery.[7,18–21] However, to date, no large cohort study has shown a clear association between EuroSCORE and adverse outcomes of elective unprotected LMCA stenting. The present study associated EuroSCORE with occurrence of death/MI independently of traditional risk factors of unprotected LMCA stenting. This finding suggests that systemic evaluation of a patient's characteristics may be helpful in weighing the risks and benefits of PCI for unprotected LMCA.

Despite the independent association of EuroSCORE and death/MI, the former has limitations to its use in PCI. Because the EuroSCORE was originally designed to assess surgical risk, some of its parameters could not be applied to the evaluation of risk before PCI. This limitation may partly explain why the discriminatory power, estimated by an area under the receiver-operating characteristic curve of 0.61, was less predictive.[9] Thus, no variable was strongly predictive in assessing the risk of death/MI in PCI for LMCA stenting. This finding suggests the need to develop a new systemic risk stratification system that can be applied to PCI.

The limitations of this study should be addressed. It was based on experience in a single center with patients at relatively low surgical risk. For example, 14% of our patients had a high EuroSCORE (≥6), a fraction lower than that in studies including more high-risk patients.[15] In addition, the clinical importance of this study could be challenged because 63% (31 patients) of all events were related to the periprocedural MI. However, because previous studies[22–24] have reported an association between periprocedural MI and long-term clinical outcomes, our study may be clinically relevant and suggest further study to develop and assess a new systemic risk stratification system for a large cohort of patients with unprotected LMCA stenting treated with PCI.

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