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Emergency Management for Critical Left Main Coronary Artery Stenosis

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ABSTRACT

Background: Increased experience and improvements in technology seem to have encouraged the use of percutaneous interventions for left main coronary artery (LMCA) occlusions. There is no consensus, however, and the data are inadequate on whether surgery or percutaneous procedures should be the intervention of choice for critical occlusions.

Methods: From January 2002 to December 2006, 108 patients with unprotected LMCA stenosis >80% were treated at our center. Eighty-three patients (77%) underwent bypass grafting and 20 (18%) underwent percutaneous intervention for the purpose of myocardial revascularization. We analyzed parameters demonstrated as risk factors for myocardial revascularization and their predicted effects on outcome.

Results: Five patients (5%) died following emergency cardiopulmonary resuscitation before any intervention was performed. The early survival rate was 84.1% in the coronary bypass group and 63% in the percutaneous intervention group. The mean (±SD) survival time was 55.7 ± 2.6 months in the bypass group and 7.6 ± 1.3 months in the percutaneous group. The late-survival rate was also significantly higher in the bypass group. The mean late-survival time was 44.5 ± 3.6 months in the bypass group and 2.3 ± 0.8 months in the percutaneous group.

Conclusion: Although emergency percutaneous interventions are lifesaving in some cases, these results clearly demonstrate that coronary bypass grafting should be the intervention of choice for myocardial revascularization in patients with critical LMCA occlusion.

INTRODUCTION

Critical left main coronary artery (LMCA) stenosis >80% remains a strong indication for early coronary artery bypass grafting (CABG). Recent improvements in percutaneous coronary interventions (PCI) have increased interest in treatment with stenting. Although the use of bare-metal stents (BMS) has been limited by restenosis and sudden cardiac death [Tan 2001; Takagi 2002], favorable medium-term outcomes with drug-eluting stents (DES) have been reported [Chieffo 2005].

Despite the crucial anatomic location of the occlusion and its severe interference with left ventricular function, the clinical presentation may vary considerably. Patients with critical LMCA occlusion usually present with serious myocardial

Table 1. Demographic and Clinical Data of the Patients*

	Management		
	Surgery (n = 83), n (%)	Stent (n = 20), n (%)	*P*†
Age ≥65 y	35 (42.2)	5 (25)	.008‡
Sex			
Female	15 (18.1)	6 (30)	.235
Male	68 (81.9)	14 (70)	
Diabetes mellitus	55 (66.3)	11 (55)	.346
Hypertension	55 (66.3)	15 (75)	.452
EF (≤40%: increased risk)	47 (56.6)	19 (95)	.001‡
Inotropic support	37 (44.6)	13 (65)	.101
IABP	9 (10.8)	6 (30)	.029§
ACS	75 (90.4)	16 (80)	.195
Lung edema	6 (7.2)	4 (20)	.083
VF	1 (1.2)	—	1.000
ACS + lung edema	1 (1.2)	—	1.000
Resuscitation	2 (2.4)	7 (35)	.001‡
Early mortality	13 (15.7)	7 (35)	.050§
Overall mortality	24 (28.9)	19 (95)	.001‡

*EF indicates ejection fraction; IABP, intra-aortic balloon pump; ACS, acute coronary syndrome; VF, ventricular fibrillation.

†Chi-square test, Fisher exact test.

‡$P < .01$.

§$P < .05$.

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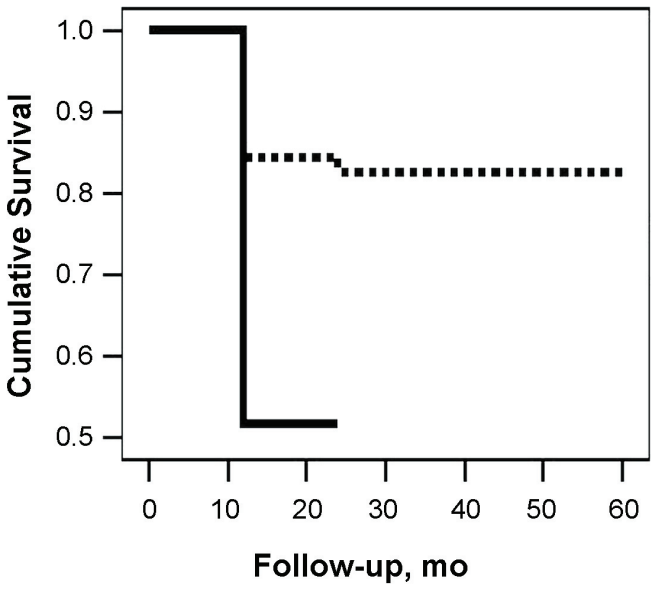

Figure 1. Survival analysis for early mortality. Dotted line, coronary artery bypass grafting; solid line, percutaneous coronary intervention.

infarction, and patients may die before seeking medical attention [Hsu 2000; Yip 2001].

The purpose of this study was to delineate the survival rates of patients with critical LMCA stenosis who underwent percutaneous or surgical myocardial revascularization and to ascertain the impact of the initial revascularization method on survival rates.

MATERIALS AND METHODS

Patient Selection

From January 2002 to December 2006, 108 patients with unprotected critical left main stenosis (in which none of the distal arteries are protected by a graft or good collaterals) were treated in our institution. Critical left main occlusion was defined as stenosis >80%. All surgical or percutaneous interventions were performed according to institutional policy. The standard therapy for LMCA stenosis in our institution is CABG. Patients who are in cardiogenic shock and cannot be transferred for emergency surgery are treated with PCI. Preoperative clinical and demographic variables were collected retrospectively from the institutional database to investigate the predictors of outcome and risk-adjusted survival rates for the patients with critical occlusion of the LMCA who underwent CABG and PCI.

Demographic and clinical parameters previously demonstrated as risk factors for myocardial revascularization were obtained from the database, and their predictive effects on outcome were analyzed (Table 1).

The mean (SD) patient age was 63.9 ± 11.4 years (range, 32-86 years). Twenty-one patients (20%) were female, and 82 (80%) were male. Diabetes mellitus was present in 66 patients (64%), and 70 patients (68%) had hypertension. Ninety-one (88%) of the patients were admitted to our emergency unit with acute coronary syndrome.

Table 2. Risk Factors for Early Mortality*

	Early Mortality		
	Yes (n = 23), n (%)	No (n = 85), n (%)	*P*†
Age ≥65 y	18 (78.3)	35 (41.2)	.002‡
Female sex	7 (30.4)	14 (16.5)	.133
Diabetes mellitus	18 (78.3)	52 (61.2)	.128
Hypertension	17 (73.9)	57 (67.1)	.530
EF (≤40%: increased risk)	23 (100)	47 (55.3)	.001‡
Emergency stenting	7 (35)	13 (15.7)	.050§
Inotropic support	20 (87)	32 (37.6)	.001‡
IABP	8 (34.8)	7 (8.2)	.001‡
ACS	13 (56.5)	81 (95.3)	.001‡
Lung edema	7 (30.4)	3 (3.5)	.001‡
VF	—	1 (1.2)	1.000
ACS + lung edema	3 (13)	0	.009‡
Resuscitation	10 (43.8)	0	.001‡

*EF indicates ejection fraction; IABP, intra-aortic balloon pump; ACS, acute coronary syndrome; VF, ventricular fibrillation.

†Chi-square test, Fisher exact test.

‡$P < .01$.

§$P < .05$.

Statistical Analysis

Data for numerical parameters were described as the mean ± SD, whereas the distributions of categorical measurements were expressed as frequencies and percentages. The chi-square test was used in univariate assessments of numerical data. Odds ratios (OR) were calculated by estimating risk.

Parameters found to be nearly statistically significant in a univariate analysis were evaluated with logistic regression analysis, and independent risk factors for early and late mortality were determined.

Analysis of survival free of major adverse cardiac events was performed according to the Kaplan-Meier method. The log-rank test was used for survival analysis of treatment options. The 95% confidence intervals (CI) were assessed, and a *P* value of .05 was established as the level of statistical significance. Statistical analysis was performed with SPSS 10.0 for Windows (SPSS, Chicago, IL, USA).

RESULTS

Five patients (5%) who underwent cardiopulmonary resuscitation died before a percutaneous or surgical intervention could be performed. These patients underwent coronary arteriography and received a diagnosis of critical left main stenosis, but they did not have a chance to undergo a treatment option (either CABG or PCI). Eighty-three patients (77%) underwent CABG, and 20 patients (18%) underwent a PCI for the purpose of myocardial revascularization. The demographic and clinical characteristics of

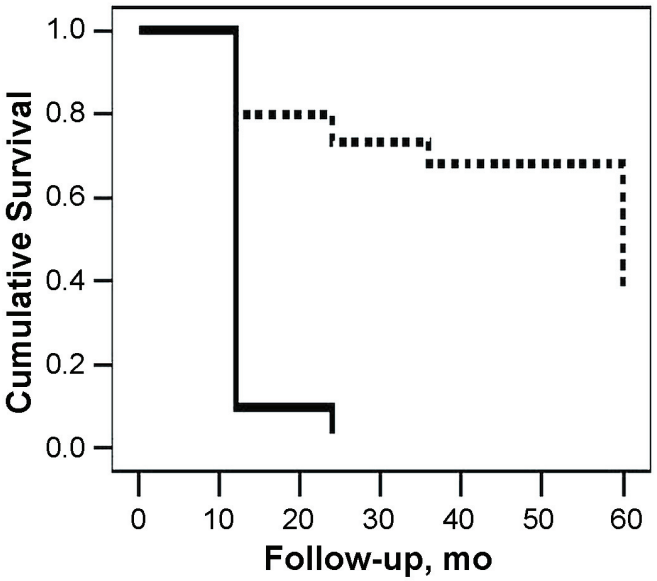

Figure 2. Survival analysis for late mortality. Dotted line, coronary artery bypass grafting; solid line, percutaneous coronary intervention.

Table 3. Risk Factors for Early Mortality Determined with Univariate Analysis and Logistic Regression*

	Univariate		Multivariate (Logistic Regression)	
	OR	95% CI	OR	95% CI
Age ≥65 y	5.143	1.74-15.15	12.22	2.31-64.6
Female sex	2.219	0.77-6.38		
Diabetes mellitus	2.317	0.77-6.74		
Hypertension	1.392	0.49-3.91		
Stenting	2.899	0.97-8.65		
Inotropic support	11.042	3.03-40.12	5.601	1.23-25.32
IABP	5.943	1.87-18.86	3.391	0.77-14.80
ACS	0.064	0.01-0.23	0.051	0.009-0.301
Lung edema	11.95	2.79-51.22		

*OR indicates odds ratio; CI, confidence interval; IABP, intra-aortic balloon pump; ACS, acute coronary syndrome.

the patients are summarized in Table 1. The mean patient age was 63.9 ± 11.4 years. Twenty-one patients (20%) were female, and 82 (80%) were male. Diabetes mellitus was present in 66 patients (64%), and 70 patients (68%) had hypertension. Ninety-one (88%) of the patients were admitted to our emergency unit with acute coronary syndrome, and lung edema was present in 10 patients (9.7%). Only 1 patient, who was in the surgery group, experienced ventricular fibrillation.

No significant differences were detected between the 2 groups with respect to sex, diabetes mellitus, hypertension, and the use of inotropic agents. The 2 groups also did not differ in the rates of acute coronary syndrome, acute lung edema, acute coronary syndrome plus acute lung edema, and ventricular fibrillation.

The number of patients ≥65 years of age was higher in the CABG group, whereas an ejection fraction (EF) <40% and use of an intra-aortic balloon pump (IABP) were predominant in the PCI group. These differences were statistically significant. The rate of cardiopulmonary resuscitation and the rates of early and late mortality were also significantly higher in the PCI group.

The early-survival rate was 84.1% in the CABG group and 63% in the PCI group (log-rank, 5.55; P = .018; Figure 1). The mean survival time was 55.7 ± 2.6 months in the CABG group and 7.6 ± 1.3 months in the PCI group. The late-survival rate was also significantly higher in the CABG group (41%) than in the PCI group (5%) (log-rank, 52.15; P = .001) (Figure 2). The mean late-survival time was 44.5 ± 3.6 months in the CABG group and 2.3 ± 0.8 months in the PCI group.

A comparison of early-mortality rates indicated that sex, a history of diabetes mellitus, hypertension, and ventricular fibrillation were not significant risk factors for patients with critical LMCA occlusion; however, an age ≥65 years, LMCA stenting (marginal statistical significance, P = .05), an EF ≤40%, use of inotropic agents, use of an IABP, presence of pulmonary hypertension, and a history of resuscitation were significant risk factors (Table 2).

Risk factors for early mortality were evaluated by univariate analysis. The risk of early mortality was increased in patients with an age ≥65 years, diabetes mellitus, hypertension, pulmonary edema, and revascularization by PCI stenting. The early-mortality rate was strongly increased in patients who were supported with inotropic agents and an IABP (Table 3).

Logistic regression analysis of significant risk factors demonstrated the model to be highly significant (P < .001). The Negelkerke R^2 value for the model was 0.527, with an explanatory coefficient of 85.7%. The mortality risk was increased with an age ≥65 years (OR, 12.22; 95% CI, 2.31-64.6), inotropic support (OR, 5.601; 95% CI, 1.23-25.32), and use of an IABP (OR, 3.391; 95% CI, 0.77-14.8).

The early-survival rate was 78.7%. The cumulative survival rate was 78.1%, with a mean survival time of 51.6 ± 2.6 months (Figure 3).

Rates of overall mortality were also analyzed. Sex, history of diabetes mellitus, hypertension, ventricular fibrillation, and acute coronary syndrome with lung edema were not found to be risk factors for mortality in patients with critical LMCA occlusion (Table 4), whereas an age ≥65 years, coronary artery stenting, an EF ≤40%, inotropic support, use of an IABP, presence of pulmonary hypertension, presence of acute coronary syndrome, and an experience of cardiopulmonary resuscitation were significantly higher in the patients who died after revascularization. In addition, the overall mortality rate was significantly lower in the patients with acute coronary syndrome (Table 5).

Univariate analysis showed that an age ≥65 years, female sex, diabetes mellitus, hypertension, LMCA stenting, an EF ≤40%, inotropic support, use of an IABP, and lung edema

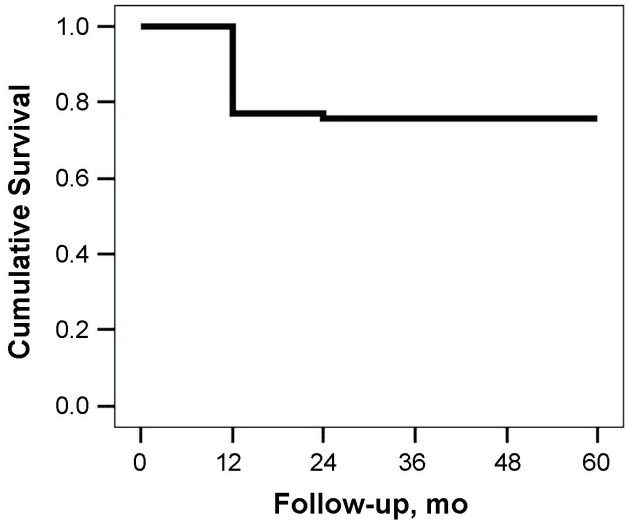

Figure 3. Cumulative survival curve for early mortality.

Table 4. Risk Factors Determined for Overall Mortality*

	Overall Mortality		
	Yes, n (%)	No, n (%)	P†
Age ≥65 y	33 (70.2)	20 (32.8)	.001‡
Female sex	13 (27.7)	8 (13.1)	.058
Diabetes mellitus	31 (66)	39 (63.9)	.827
Hypertension	35 (74.5)	39 (63.9)	.243
EF (≤40%: increased risk)	43 (89.4)	28 (45.9)	.001‡
Stenting	19 (44.2)	1 (1.7)	.001‡
Inotropic support	31 (66)	21 (34.4)	.001‡
IABP	11 (23.4)	4 (6.6)	.012§
ACS	34 (72.3)	60 (98.4)	.001‡
Lung edema	9 (19.1)	1 (1.6)	.002§
VF	1 (2.1)	0	.435
ACS + lung edema	3 (6.4)	0	.079
Resuscitation	10 (21.3)	0	.001‡

*EF indicates ejection fraction; IABP, intra-aortic balloon pump; ACS, acute coronary syndrome; VF, ventricular fibrillation.

†Chi-square test, Fisher exact test.

‡$P < .01$.

§$P < .05$.

increased overall mortality. When these factors were evaluated with a stepwise logistic regression analysis, the model was found to be highly significant ($P < .005$), with a Negelkerke R^2 value of 0.579 for the model and an explanatory coefficient of 81.6%. The risk of mortality was increased with LMCA stenting (OR, 27.57; 95% CI, 3.23-235.2), an age ≥65 years (OR, 4.135; 95% CI, 1.34-12.70), and a low EF (ie, ≤40%) (OR, 3.36; 95% CI, 0.970-11.68).

Analysis of overall survival revealed a survival rate of 56.5%. The cumulative survival rate was 33.2% at a mean survival time of 35.6 ± 3.3 months (Figure 4).

DISCUSSION

Critical stenosis of the LMCA is a life-threatening condition, usually with hemodynamic instability. The extent of the jeopardized myocardium and concomitant coronary artery disease makes critical LMCA stenosis the most important coronary lesion. Although some patients are known to survive several years without CABG [Topaz 1991], current practice guidelines state the standard recommended treatment for LMCA stenosis to be CABG [Smith 2001]. In our series, we found that the rates for early, mean, and late survival were higher in the CABG group than in the PCI group. This finding is important because the interest in the use of PCI for treating LMCA stenosis has grown in recent years, and our results have shown once again that CABG is the treatment of choice in patients with critical LMCA stenosis.

Treatment options for LMCA stenosis include balloon pumping, intracoronary thrombolysis, PCI, and surgery [Valle 1979]. American Heart Association guidelines state that PCI is not recommended for LMCA stenosis and that surgical revascularization is preferred [Smith 2001]. PCI can be a treatment option for high-risk patients who are not suitable candidates for surgery [Edwards 1994; Charitos 1997]. The safety and efficacy of interventional procedures for critical LMCA stenosis are still controversial. The Coronary Artery Surgery Study found a 7-fold increase in the risk of death in the presence of LMCA stenosis, and LMCA disease was diagnosed in 46% to 75% of cardiac catheterization–related deaths [Zimmern 1982].

In recent years, there has been a growing interest and experience in the use of PCI for critical LMCA stenosis. The APPROACH study showed that CABG was associated with better long-term (5 years) survival than PCI in patients with critical LMCA stenosis [Dzavik 2001]. Recent studies that compared CABG with the use of DES revealed similar outcomes. Lee et al [2006] reported that the 2 groups were not significantly different with respect to the rate of survival free of major adverse cardiac and cerebrovascular events (MACCE) and freedom from target vessel revascularization at 1 year. The 1-year results of the SYNTAX trial for 1800 patients with 3-vessel or LMCA disease suggested that the 2 groups were similar with respect to death rates (3.5% for CABG versus 4.4% for PCI) but that the rates of repeat revascularization were higher in the PCI group (5.9% versus 13.5%). Stroke was less likely to occur with DES (2.2% versus 0.6%) [Serruys 2009].

Revascularization by PCI is generally performed as an alternative to CABG in selected patients with critical LMCA stenosis. The patient's medical condition and the angiographic findings are considered for procedural preferences. High-risk patients with a high EuroSCORE or Parsonnet score and hemodynamically unstable patients are candidates for PCI treatment. The patients in our study who underwent PCI were in cardiogenic shock, and there was insufficient

Table 5. Risk Factors for Overall Mortality Determined by Univariate Analysis and Logistic Regression*

	Univariate		Multivariate (Logistic Regression)	
	OR	95% CI	OR	95% CI
Age >65 y	4.832	2.12-10.99	4.135	1.34-12.70
Female sex	2.533	0.95-6.75		
Diabetes mellitus	1.093	0.49-2.42		
Hypertension	1.645	0.71-3.80		
EF (≤40%: increased risk)	9.900	3.44-28.43	3.36	0.970-11.68
Stenting	46.70	5.91-368.7	27.57	3.23-235.22
Inotropic support	3.690	1.65-8.22		
IABP	4.354	1.28-14.72		
ACS	0.044	0.005-0.34	0.053	0.05-0.520
Lung edema	14.21	1.73-116.6		

*OR indicates odds ratio; CI, confidence interval; EF, ejection fraction; IABP, intra-aortic balloon pump; ACS, acute coronary syndrome.

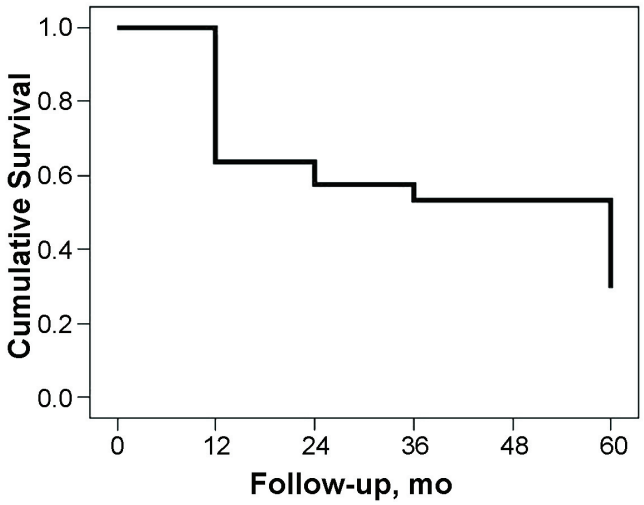

Figure 4. Survival analysis concerning overall mortality.

time to perform surgery. Although the procedure is technically feasible and the medium-term mortality rates for PCI and CABG are comparable [Shimizu 2010], the incidences of major adverse cardiac and cerebrovascular events (MACCE) and repeat revascularization (repeat PCI or CABG) are still high [Javaid 2007; Park 2008]. Therefore, it seems unlikely that PCI can replace CABG for the treatment of unprotected LMCA disease. The restenosis rate for either elective or primary LMCA stenting may remain high, and the clinical impact of restenosis after LMCA stenting may present additional serious complications, such as acute pulmonary edema, malignant arrhythmia, or sudden death. Yip and colleagues reported rates of up to 22% for subsequent CABG following PCI, 33% for in-hospital deaths, 11% for deaths after discharge, and 55% for long-term survival in cases of total or subtotal LMCA occlusion [Yip 2001].

We believe that critical LMCA occlusion is a surgical emergency requiring immediate intervention and should not be delayed. CABG is an excellent treatment of LMCA stenosis but with some potential limitations, such as complete graft-dependent perfusion because of progressive occlusion of the LMCA and the risk of arteriosclerotic changes in or occlusion of the grafts [Hsu 2000]. Although patients might maintain hemodynamic stability in cases of right coronary artery collateral and/or retrograde blood supply, sudden deterioration could ensue, and IABP assistance and high inotropic support might be mandatory. Cardioprotection during the operation plays a key role for such critical patients; thus, coronary venous retroperfusion should be administered [Svedjeholm 2001]. Administration of antegrade cardioplegia via the aortic root may not protect the myocardium effectively in the presence of a critical LMCA stenosis. Isolated retrograde or combined antegrade and retrograde perfusion of the myocardium with the cardioplegic solution seems to be a better option for myocardial protection. An alternative technique for revascularization is off-pump CABG. Shimizu and colleagues performed off-pump surgery in >90% of their patients with acceptable good results with respect to medium-term mortality rates [Shimizu 2010]. Although off-pump coronary artery surgery has lower complication rates than conventional CABG [Puskas 2008], a major disadvantage of off-pump surgery is repeat or incomplete revascularization, which can be related to the learning curve or modifications in surgical strategies (hybrid treatment with PCI) for a calcified aorta.

Coronary artery surgery has been regarded as the treatment of choice for chronic LMCA stenosis; nevertheless, some investigators have suggested that poor visualization of the distal left coronary arteries due to poor dye opacity during coronary arteriography is a potential problem [Zimmern 1982]. Recently, chronic total occlusion of the coronary artery has been recognized as a target for coronary intervention. Some investigators have attempted to perform PCI for total LMCA occlusion when the left coronary arteries were protected by CABG or good collaterals [Spiecker 1994] or even when they were unprotected [Dzavik 2001]. Although PCI to the LMCA may be effective alone for some patients with cardiogenic shock, subsequent CABG is almost always necessary to achieve complete revascularization and improve survival. Today, it is generally accepted that the most common cause of LMCA stenosis is arteriosclerosis, which accounts for the majority of the LMCA stenosis, particularly that affecting the mid portion and the distal bifurcation. Such stenosis is mostly associated with 2- or 3-vessel coronary artery disease. Isolated stenosis of the ostium and the first third of the LMCA has a prevalence of only 1% [Brueren 2004].

The cost-effectiveness of the procedure is another source of debate regarding the treatment of critical LMCA disease. A comparison of DES and BMS has indicated that DES is feasible when a high risk of restenosis is present [Brunner-La Rocca 2007]. A comparison with CABG revealed that PCI

with a BMS might be less costly in high-risk patients over a 5-year period than CABG [Stroupe 2006]. Shimizu et al [2010] stated that when the overall survival rate and MACCE-free survival rate are considered, PCI with DES is more costly than CABG surgery, especially when an off-pump technique is used for revascularization.

These results show that CABG is still the treatment of choice for myocardial revascularization in patients with critical LMCA stenosis. Emergency CABG can be lifesaving, enable myocardial salvage, and improve functional status. PCI for LMCA stenosis is recommended forn patients with hemodynamic instability and for patients who do not have good collaterals from the right coronary artery that can be used as a bridge to operation. We believe that an immediate initial evaluation of these patients followed by quick transfer to the operating room significantly reduces mortality and morbidity.

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