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**Ren-Jen Lee · Ko-Nien Shih · Shih-Huang Lee
Kou-Gi Shyu · Chiung-Zuan Chiu · Shen-Chang Lin
Huei-Fong Hung · Jer-Young Liou · Jun-Jack Cheng
Peiliang Kuan**

Predictors of long-term outcomes in patients after elective stent implantation for unprotected left main coronary artery disease

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Abstract The purpose of this study was to investigate the predictor of long-term outcomes in patients after stent implantation for unprotected left main coronary artery (LMCA) disease. Coronary stenting has recently been advocated as an alternative procedure for LMCA disease. Information on the predictors of long-term outcomes in patients after stent implantation for unprotected LMCA disease is not clear. Seventy six patients (51 men and 25 women, age 68 ± 10 years) with medically refractory angina received coronary stenting for unprotected LMCA disease. During a follow-up period of 40 ± 26 months, 7 patients (9%) died because of cardiovascular disease in 5 (7%) and noncardiovascular disease in 2 (3%). In the other 69 patients, 19 patients (25%) needed repeated percutaneous coronary intervention (PCI) and/or coronary artery bypass grafting (CABG). In a univariate analysis, only female sex was related to the repeated PCI and/or CABG ($P = 0.04$). A history of cerebral vascular attack (CVA) ($P = 0.005$), anemia ($P = 0.03$) and lower left ventricular ejection fraction (LVEF) ($P = 0.008$) were related to the cardiovascular mortality. A history of myocardial infarction ($P = 0.03$), a history of CVA ($P = 0.02$), anemia ($P = 0.02$), and lower LVEF ($P = 0.002$) were related to the total mortality. In a multivariate analysis, female sex ($P = 0.007$; odds ratio 5.29, 95% confidence interval [CI] 1.57–17.80) and young age ($P = 0.025$; odds ratio 3.92, 95% CI 1.19–12.98) could predict the repeated PCI and/or CABG. Only a history of CVA could predict the cardiovascular mortality ($P = 0.027$; odds ratio 34.18, 95% CI 1.49–783) and only lower LVEF could predict the total mortality ($P = 0.027$; odds ratio 13.26, 95% CI 1.34–131). Female sex and young age could predict the repeated PCI and/or CABG in patients after stent implantation for unprotected LMCA disease. Furthermore, a history of CVA could predict the cardiovascular mortality and lower LVEF could predict the total mortality.

Key words Left main coronary artery · Stent · Coronary artery disease · Unprotected

R.-J. Lee · K.-N. Shih · S.-H. Lee[1] (✉) · K.-G. Shyu · C.-Z. Chiu · S.-C. Lin · H.-F. Hung · J.-Y. Liou · J.-J. Cheng · P. Kuan
Yuanpei Institute of Science and Technology, Fu Jen Catholic University and Shin Kong Wu Ho-Su Memorial Hospital, Taipei, Taiwan

Correspondence address:
[1]Division of Cardiology, Shin Kong Wu Ho-Su Memorial Hospital, 95 Wen Chang Road, Shih Lin, Taipei, Taiwan
Tel. +886-2-2833-2211 ext. 2091; Fax +886-2-2834-8910
e-mail: shlee@aptg.net

Introduction

Left main coronary artery (LMCA) disease is now uniformly treated with coronary artery bypass grafting (CABG).[1–4] Percutaneous transluminal coronary angioplasty (PTCA) is a potential revascularization procedure for LMCA disease in critically ill patients with prohibitive operative risk. However, the risk of irreversible hemodynamic collapse after acute LMCA closure and a relatively high risk of late sudden death after PTCA in patients with unprotected LMCA disease have been reported.[5,6] Coronary stenting has recently been advocated as an alternative procedure for LMCA disease, but target-lesion revascularization and mortality may occur in some patients after stent implantation for unprotected LMCA disease.[7–12] Previous studies have evaluated the predictors of long-term outcomes after stent implantation for unprotected LMCA disease.[7–12] However, the predictors of long-term outcomes in patients after stent implantation for unprotected LMCA disease have not been well concluded. Therefore, the purpose of the study was to investigate the predictors of long-term outcomes in patients after stent implantation for unprotected LMCA disease.

Methods

From August 1997 to July 2005, 76 patients (51 men and 25 women, age 68 ± 10 years) with medically refractory angina

received coronary stenting for unprotected LMCA disease in this institute. Elective LMCA stenting was performed in 26 patients (34%) for prohibitive surgical risk. The main reasons for percutaneous instead of surgical revascularization are sepsis ($n = 1$), cerebrovascular disease ($n = 4$), severe obstructive pulmonary disease ($n = 4$), neoplasia with limited life expectancy ($n = 1$), unstable hemodynamic status ($n = 7$) and old age (≥80 years) ($n = 9$). The remaining 54 patients (66%) had refused CABG. In the present study, we excluded patients in whom emergent stent implantation was performed for an acute myocardial infarction.

Stent implantation

After fully informed consent, the percutaneous transfemoral approach using an angioplasty sheath and standard angioplasty technology were used in these patients.[8] Each patient received intravenous heparin (10000 units) and, if necessary, an additional bolus of heparin was administered to maintain activated clotting time >300 s. Quantitative angiographic analysis was performed to demonstrate the stenosis in its most severe and nonforeshortened projection. With use of the contrast-filled guiding catheter as the calibration standard, reference and lesion minimal lumen diameter were determined. Successful immediate outcome of stent implantation for LMCA disease was defined as a <30% residual stenosis. Myocardial infarction was diagnosed by a rise in the creative kinase level to more than twice the upper normal limit with an increased creative kinase-MB fraction. Poststent regimens included aspirin (100 mg/day) and clopidogrel (75 mg/day).[13] Therapy was continued for 3–9 months and aspirin was continued indefinitely. Clinical follow-up was obtained by clinic visits, telephone conversation and chart review.

Predictors of long-term cardiovascular outcomes

The analyzed variables included age (≥65 or <65 years), sex, a history of prior myocardial infarction, a history of prior percutaneous coronary intervention (PCI), a history of prior cerebral vascular attack (CVA), smoking, diabetes mellitus, hypertension, anemia (hemoglobin <13 mg/dl in men, hemoglobin <11 mg/dl in women), chronic renal insufficiency (serum creatinine ≥2 mg/dl), hypercholesterolemia (low-density lipoprotein ≥130 mg/dl), left ventricular ejection fraction (LVEF) (>35% or ≤35%), position of LMCA stenosis (proximal, middle, or distal), and stent size (≥4.0 or <4.0 mm).

Statistical analysis

Quantitative data are expressed as mean ± SD. The chi-square test with Yates' correction or Fisher's exact test was used to analyze the nonparametric data. Multivariate analysis was performed with logistic regression to determine the independent predictors of the long-term outcomes. Variables selected to be tested in the multivariate analysis were those with a $P < 0.1$ in the univariate model. A significant odds ratio was obtained if the 95% confidence interval (CI) exceeded 1 and the P value was less than 0.05. $P < 0.05$ was considered statistically significant.

Results

Immediate and long-term outcomes of stent implantation

The LMCA lesions were treated with either bare metal stent (93%) or drug eluting stent (7%). The mean stent size was 3.4 ± 0.4 mm and the mean stent length was 16 ± 6 mm. Distal LMCA bifurcation stenting was performed in 9 patients (12%). Sixty-two patients (82%) underwent PTCA with or without stent implantation at other coronary arteries at the time of LMCA stenting. Immediate success was achieved in all of the patients without major complications.

During a follow-up period of 40 ± 26 months (range 2–94 months), 7 patients (9%) died because of cardiovascular disease in 5 (7%) and noncardiovascular disease in 2 (3%). In the other 69 patients, 19 patients (25%) underwent repeated coronary intervention for recurrent angina; 14 (18%) received PCI, 4 (5%) received CABG and 1 (1%) received both PCI and CABG for restenosis of LMCA. In the 4 deaths within 3 months after LMCA stenting, three patients died because of acute myocardial infarction and two of them received second PCI. The other one patient died because of congestive heart failure after CABG for unstable angina (Table 1).

Predictor of repeated PCI and/or CABG

Comparisons between the patients with repeated PCI and/or CABG ($n = 23$) and those without repeated PCI and/or CABG ($n = 53$) are shown in Table 2. Univariate analysis revealed that female sex was related to the repeated PCI and/or CABG ($P = 0.04$) (Table 3). Multivariate analysis showed that female sex and young age could predict the presence of repeated PCI and/or CABG.

Predictor of cardiovascular mortality

Comparisons between the patients with cardiovascular mortality ($n = 5$) and those without cardiovascular mortality ($n = 71$) are shown in Table 2. Univariate analysis revealed that a history of CVA ($P = 0.005$), anemia ($P = 0.03$) and lower LVEF ($P = 0.008$) were related to the cardiovascular mortality (Table 3). Multivariate analysis showed that only a history of CVA could predict the presence of cardiovascular mortality.

Predictor of total mortality

Comparisons between the patients with mortality ($n = 7$) and those without mortality ($n = 71$) are shown in Table 2.

Table 1. Clinical data of patients with mortality

Patient no.	Repeated PCI	CABG	Mortality reasons	Follow-up (days)
1	–	+	Sepsis	540
2	+	–	Acute myocardial infarction	21
3	–	–	Acute myocardial infarction	27
4	+	–	Acute myocardial infarction	58
5	–	+	Congestive heart failure	89
6	–	–	Congestive heart failure	358
7	–	–	Colon carcinoma	553

CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention

Table 2. Patient characteristics

Variables	Repeated PCI and/or CABG		Cardiovascular mortality		Total mortality	
	Yes (n = 23)	No (n = 53)	Yes (n = 5)	No (n = 71)	Yes (n = 7)	No (n = 69)
Age (years)	65 ± 9	70 ± 10	77 ± 8	68 ± 10	73 ± 10	68 ± 10
Female sex	52%	24%	40%	33%	43%	32%
Prior MI	26%	19%	60%	18%	57%	17%
Prior PCI	52%	42%	40%	45%	29%	46%
Prior CVA	13%	8%	60%	6%	43%	6%
Smoking	30%	42%	40%	38%	43%	38%
Diabetes mellitus	48%	43%	20%	47%	29%	46%
Hypertension	74%	77%	80%	76%	71%	77%
Anemia	26%	32%	80%	27%	71%	26%
Chronic renal insufficiency	13%	11%	20%	11%	14%	12%
Hypercholesterolemia	44%	42%	20%	44%	29%	44%
LVEF (%)	60 ± 18	60 ± 17	44 ± 21	61 ± 20	43 ± 18	62 ± 17
Position of LMCA stenosis						
Proximal	13%	17%	0%	17%	14%	16%
Middle	0%	13%	0%	10%	0%	10%
Distal	87%	70%	100%	73%	86%	74%
Small stent size	100%	83%	100%	87%	100%	87%

Data are presented as mean ± SD or %
CABG, coronary artery bypass grafting; CVA, cerebral vascular attack; LMCA, left main coronary artery; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PCI, percutaneous coronary intervention

Univariate analysis revealed that a history of myocardial infarction ($P = 0.03$), a history of CVA ($P = 0.02$), anemia ($P = 0.02$), and lower LVEF ($P = 0.002$) were related to the total mortality (Table 3). Multivariate analysis showed that only lower LVEF could predict the presence of total mortality.

Discussion

Major findings

The present study showed that female sex and young age could predict the repeated PCI and/or CABG in patients after stent implantation for unprotected LMCA disease. Furthermore, a history of CVA could predict the cardiovascular mortality and lower LVEF could predict the total mortality.

Comparisons with previous studies

Previous studies demonstrated that in-hospital mortality was 0%–4% after stent implantation in the patients with unprotected LMCA disease.[7,11,12,14] In the present study, none of the patients had in-hospital mortality after stenting of unprotected LMCA stenosis. However, 4 of 5 cardiovascular deaths in the present study occurred within the first 3 months after stent implantation; this finding suggested that restenosis of LMCA after stent implantation might play an important role in the early cardiovascular mortality and other therapeutic strategies such as drug-eluting stent and CABG might prevent some of these early deaths.[15,16]

Previous studies showed that the incidence of restenosis after stenting of unprotected LMCA stenosis was about 17%–31%.[7,9,12] The present study showed similar results. The incidence of long-term major cardiovascular events after stent implantation for unprotected LMCA disease was 32% in the present study. These findings suggested that CABG should be the first choice for the patients with unprotected LMCA disease, and PCI is an alternative choice in selected circumstances; those presenting highly symptomatic but inoperable and those refusing CABG.

Predictor of repeated PCI and/or CABG

The present study demonstrated that female sex and young age could predict repeated PCI and/or CABG after stent implantation for unprotected LMCA disease. Cameron

Table 3. Univariate and multivariate analysis for repeated PCI and/or CABG, cardiovascular mortality and total mortality

Variables	Repeated PCI and/or CABG				Cardiovascular mortality				Total mortality			
	Univariate	Multivariate			Univariate	Multivariate			Univariate	Multivariate		
	P value	*P* value	Odds ratio	95% CI	*P* value	*P* value	Odds ratio	95% CI	*P* value	*P* value	Odds ratio	95% CI
Young age (years)	0.06	0.025	3.92	1.19–12.98	0.16	–	–	–	0.41	–	–	–
Female sex	0.04	0.007	5.29	1.57–17.80	1.0	–	–	–	0.68	–	–	–
Prior myocardial infarction	0.55	–	–	–	0.06	0.17	–	–	0.03	0.08	–	–
Prior PCI	0.54	–	–	–	1.0	–	–	–	0.45	–	–	–
Prior CVA	0.43	–	–	–	0.005	0.027	34.18	1.49–783	0.02	0.07	–	–
Smoking	0.51	–	–	–	1.0	–	–	–	1.0	–	–	–
Diabetes mellitus	0.92	–	–	–	0.37	–	–	–	0.45	–	–	–
Hypertension	0.98	–	–	–	1.0	–	–	–	0.67	–	–	–
Anemia	0.80	–	–	–	0.03	0.27	–	–	0.02	0.22	–	–
Chronic renal insufficiency	1.0	–	–	–	0.48	–	–	–	1.0	–	–	–
Hypercholesterolemia	1.0	–	–	–	0.39	–	–	–	0.69	–	–	–
Lower LVEF	0.69	–	–	–	0.008	0.11	–	–	0.002	0.027	13.26	1.34–131
Position of LMCA stenosis	0.16	–	–	–	0.74	–	–	–	1.0	–	–	–
Small stent size	0.05	0.79	–	–	1.0	–	–	–	0.59	–	–	–

CABG, coronary artery bypass grafting; CVA, cerebral vascular attack; LMCA, left main coronary artery; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention; CI, confidence interval

et al. reported that female sex and young age were the predictors of recurrent angina within 1 year of CABG for coronary artery disease.[17] Previous studies also showed that the need for CABG after PCI for coronary artery disease was higher in women than in men.[18,19] Furthermore, Park et al. showed that reference vessel diameter was the only predictor of angiographic restenosis in patients after stent implantation for unprotected LMCA disease.[9] These findings suggested that small vessel size might explain the higher incidence of restenosis after stent implantation for unprotected LMCA disease in women. The present study showed that the patients who needed repeated PCI and/or CABG tended to have small stent size ($P = 0.05$); however, the stent size was not a predictor of repeated PCI and/or CABG.

Predictor of cardiovascular mortality

Takagi et al. reported that lower LVEF could predict the cardiovascular mortality after PCI for unprotected LMCA disease.[12] Black et al. also showed that the final stent lumen diameter and post-stent stenosis were predictive of cardiovascular mortality after stent implantation for unprotected LMCA disease.[11] To our knowledge, the present study is the first to show that a history of CVA could predict the cardiovascular mortality after stent implantation for unprotected LMCA disease. Previous studies did not provide the data of prior CVA in their patient groups.[7,9–12]

Predictor of total mortality

Silvestri et al. reported that high-risk groups had a higher mortality rate after stent implantation for unprotected LMCA disease compared with low-risk groups; high-risk group was defined to be >75 years, with prior CABG, LVEF <35%, renal failure, poor coronary runoff, or severe respiratory failure.[7] Tan et al. demonstrated that both lower LVEF and chronic renal insufficiency could predict the total mortality after stent implantation for unprotected LMCA disease.[10] The present study showed that lower LVEF but not chronic renal insufficiency could predict the total mortality after stent implantation for unprotected LMCA disease.

Clinical implications

The present study showed that female sex and young age could predict repeated PCI and/or CABG after stent implantation for unprotected LMCA. Thus, doctors and patients should be aware of this information before stent implantation for unprotected LMCA disease. Furthermore, this study showed that a history of CVA could predict the cardiovascular mortality and lower LVEF could predict the total mortality. Thus, other therapeutic strategies such as drug-eluting stent and CABG should be considered in those patients with a history of CVA and lower LVEF.

Study limitations

First, the number of patients and total number of deaths were small in the present study. Second, most patients in the cohort received bare metal stent implantation for unprotected LMCA disease. Previous studies have shown that the use of drug-eluting stent as a strategy to treat unprotected LMCA disease was associated with a significant reduction in adverse cardiovascular events compared with bare metal stent.[15,16] However, doctors cannot routinely implant a drug-eluting stent for unprotected LMCA disease in some countries because they are too expensive. Third, because we obtained angiographic follow-up only in those patients who returned with unstable angina, we could not assess the actual restenosis rate of LMCA stenting.[20,21] Fourth, it is still possible that CABG is necessary for the long-term survival of some patients.[22]

Conclusions

The present study showed that female sex and young age could predict repeated PCI and/or CABG in patients after stent implantation for unprotected LMCA disease. Furthermore, a history of CVA could predict the cardiovascular mortality and lower LVEF could predict the total mortality.

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