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Percutaneous Coronary Intervention

Percutaneous Coronary Intervention for Left Main Coronary Artery Disease — A Single Hospital Experience without On-Site Cardiac Surgery

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Background: To investigate the safety and outcome of percutaneous coronary intervention for left main coronary artery disease in hospital without on-site cardiac surgery.

Methods: Between January 2007 and December 2010, all patients diagnosed with left main coronary artery disease and refused coronary artery bypass graft surgery in our hospital or a tertiary center, were enrolled. Data including clinical course, angiographic characteristics, and 1- and 3-years outcomes were recorded and analyzed.

Results: Seventy patients (mean age 73.4 ± 10.2 years, 47 male, 23 females) were treated with a mean SYNTAX score of 34.8 ± 12.6 and EuroSCORE of 6.7 ± 3.3. Thirty-two (45.7%) patients had stable angina, 35 (50.0%) had unstable angina/non ST-elevation myocardial infarction, and 3 (4.3%) had ST-elevation Myocardial infarction. Forty-three (61.4%) patients received a single-stent, 26 (37.1%) received two-stents, and 1 (1.4%) received balloon angioplasty. No procedure-related mortalities were noted and no emergency coronary artery bypass graft surgery was required. In the 3-year follow-up period, 2 (2.9%) patients had non-fetal myocardial infarction, 11 (15.7%) had left main target lesion revascularization. The major adverse cardiac and cerebrovascular events rates were 24.3% at 1 year and 37.1% at 3-years. The all-cause mortality rate was 41.4% (29 patients), including 18 (25.7%) cases of septic shock, 7 (10.0%) of sudden cardiac death, 2 (2.8%) of hypovolemic shock due to upper gastrointestinal bleeding, 1 (1.4%) of terminal stage malignancy, and 1 (1.4%) of suffocation at 3 years.

Conclusions: Percutaneous coronary intervention for patients with left main coronary artery disease was found to be a safe and effective strategy in our hospital without on-site cardiac surgery.

Key Words: Incomplete revascularization • Left main coronary artery (LM) • No cardiac surgery • Percutaneous coronary intervention (PCI)

INTRODUCTION

Left main (LM) coronary artery disease, defined as greater than 50 percent lumen narrowing, occurs in around 5~7 percent of all patients who undergoing coronary angiography.[1] Compared with medical therapy, coronary artery bypass graft (CABG) surgery has been reported to confer a survival benefit and is the gold standard therapy in patients with LM disease in guideline.[2] The first case of balloon angioplasty of the LM coronary artery disease was reported in 1979 by Gruntzig, the first series of 129 patients, who received bare-metal stents (BMS) for LM was reported by Hartzler and O'Keefe in 1989, which showed a 10% in-hospital mortality rate and 64% 3-year mortality.[3,4] Due to the poor outcomes and surgical results, the technique was not

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used again till mid-1990s, when the development in stent design, improvement of operator's experience, and major advance of pharmacology such as dual antiplatelet regimes led to LM stenting being considered again as a method of treatment. The ULTIMA experience reported that primary percutaneous coronary intervention (PCI) with stenting was associated with improved outcomes for the patients with acute ST-elevation myocardial infarction (STEMI) with LM coronary artery disease.[5]

The use of BMS for LM has been reported to be associated with high procedural success rates, a 15-34% target lesion revascularization (TLR) rate, and a 6.5-24% mortality rate at 1-2 years.[6-8] The development of drug-eluting stent (DES) was a major breakthrough in PCI for LM coronary artery disease. Compared with BMS, DES were reported to have good efficiency, safety, and significant reduction in restenosis and TLR in several observational, single- and multicenter registries.[9-11] In the ACC/AHA/SCAI 2004 Guideline update for PCI, PCI for LM coronary artery disease was defined as a class IIa indication for unstable angina Canadian Cardiovascular Society (CCS) class III/ non-STEMI and class IIb indication for asymptomatic ischemia, CCS class I or II angina.[12] Furthermore, for concerns about efficient volume of PCI program and realistic strategy to transfer, PCI for LM coronary artery disease is class IIb indication for primary PCI without onsite cardiac surgery, although this is an evolving issue.

Taitung County has an area of 3,515 square kilometers, with an estimated population of 224,989 in Sep 2013. Mackay Memorial hospital, Taitung Branch (TT MMH) has 450 beds, and is located in Taitung City, the only city in Taitung County. The first and only one catheterization laboratory in Taitung was inaugurated in TT MMH at April 30, 2002, however there is no on-site cardiac surgeon in the catheterization laboratory. Elective CABG is performed by a cardiac surgeon from Mackay Memorial Hospital in Taipei, otherwise the patients have to travel 200 km (which takes over 2 hours) to the nearest tertiary center by ground ambulance. We previously reported the safety and efficiency of primary PCI for patients with acute myocardial infarction, which has been available in our hospital at any time of day/week since Sep 2003.[13] There were over 200 cases of PCI performed in 2004, and over 400 cases in 2006. Wennberg et al. reported that high-volume hospitals without on-site cardiac surgery had a comparable mortality rate for patients receiving non-primary/rescue PCI with high volume institutions with cardiac surgery.[14] Therefore, the aim of this study was to investigate the safety and outcomes of PCI for LM coronary artery disease in TT MMH without on-site cardiac surgery.

METHODS

Patients diagnosed as LM coronary artery disease at Mackay Memorial Hospital, Taitung Branch, between January 2007 and December 2010 whose coronary angiography showed a greater than 50% lumen narrowing, and who refused CABG in our hospital or transfer to a tertiary medical center were enrolled into this study. Clinical outcomes were followed-up for at least 3 year by chart review. Baseline characteristics, intervention strategy, emergency CABG, procedural mortality rate, adverse clinical outcomes, and LM TLR were recorded. The EuroSCORE (European System for Cardiac Operative Risk Evaluation) was recorded, and the results were classified as low (0-2), median (3-5), and high ($\geq$ 6) calculated by including age, sex, chronic pulmonary disease, extracardiac arteriopathy, neurological dysfunction, previous cardiac surgery, serum creatinine, active endocarditis, critical preoperative state, unstable angina, left ventricular dysfunction, recent myocardial infarction, pulmonary hypertension, emergency surgery, other surgery than isolated CABG, surgery on the thoracic aorta, and post-infarct septal rupture.[15] The angiographic data were analyzed with SYNTAX (Synergy between PCI with TAXUS™ and Cardiac Surgery) score and classified as low (0-22), intermediate (23-32), and high ($\geq$ 33). This included coronary artery dominance by segment weighting factors, and lesion adverse characteristic scoring by reduction in diameters, total occlusion, bifurcation, trifurcation, aortic ostial stenosis, severe tortuosity, length over 20 mm, heavy calcification, thrombus, diffuse disease and small vessels.[16,17] Procedural-related mortality was defined as any cases of mortality during the procedure of index LM PCI in the catheterization laboratory.

All patients were followed-up clinically. If the patients had no clinical presentation of myocardial ischemia or staged PCI for non-LM lesions, coronary angiography was not performed. LM TLR was defined as any revascularization procedure performed because of restenosis at the site of the treated lesion associated with clinical evidence of myocardial ischemia whether it involved the LM only or the LM crossing the left anterior descending artery (LAD) or left circumflex artery (LCX).

Data collection and statistical analyses

This was a retrospective, observational analysis. Records from the patient's chart regarding LM coronary artery disease and subsequent visits and hospitalizations were obtained for review. All patients were interviewed in person or by telephone within 3 years after the index LM PCI. Comparison for categorical variables were analyzed using Fisher's exact test and continuous variables were compared using the Student's t-test. All statistical tests were two-sided, and a p value of < 0.05 was considered to be significant. All statistical analyses were performed using SPSS 18 (IBM, Armonk, New York, USA).

RESULTS

In total, 70 patients (mean age 73.4 $\pm$ 10.2 years, 47 male, 23 female) were enrolled, of whom 32 (45.7%) had stable angina, 35 (50.0%) had unstable angina/non-STEMI, and 3 (4.3%) had STEMI. The demographic data of all patients and the angiographic and procedural characteristics are listed in Table 1. Of those patients with coronary artery disease in coronary angiography, 4 (5.7%) had LM disease only with no LM distal involvement, 11 (15.7%) had LM disease with single vessel disease, 24 (34.3%) had LM with double vessel disease, and 31 (44.3%) had LM with triple vessel disease (TVD). The mean SYNTAX score of was 34.8 $\pm$ 12.6, including 12 (17.1%) patients with low, 19 (27.1%) with intermediate, and 39 (55.7%) with high scores. The mean EuroSCORE was 6.83 $\pm$ 3.32, including 9 (12.9%) patients with low, 14 (20.0%) with medium, and 47 (67.1%) with high scores.

Forty-three (61.4%) patients received a single stent strategy, including 12 (17.1%) cases of LM only, 27 (38.6%) of LM crossing over LAD, and 6 (8.6%) of LM crossing over LCX. Twenty-six (37.1%) patients received two-stents, including with 19 (27.1%) with culotte stenting, 6 (8.6%) with crush stenting, and 1 (1.4%) with a T-stent. The only patient who underwent balloon angioplasty alone had failed stenting at a severely calcified lesion at the LM to LAD cause by a lack of rotational atherectomy due to economic concern. Nineteen (27.1%) patients underwent intra-vascular ultrasound (IVUS). For the LM only, LM crossing over LAD, and LM crossing over LCX procedures, the stent sizes were 4.07 $\pm$ 0.47 mm, 3.29 $\pm$ 0.39 mm and 3.23 $\pm$ 0.38 mm, and the stent lengths were10.6 $\pm$ 2.6 mm, 26.1 $\pm$ 5.7 mm, and 22.3 $\pm$ 5.8 mm, respectively. Ten (14.3%) patients who underwent PCI with BMS, among whom 9 were deployed at the LM ostium and/or mid-shaft lesion without LM-distal involvement whether it involved LM only or with other vessels, and only 1 was deployed at the near total occluded distal LM with TIMI II flow in patient who had had acute myocardial infarction with profound cardiogenic shock on intra-aortic balloon pump (IABP) support.

Four kinds of DES were deployed including 2 paclitaxel-eluting stents 11 (15.7%) with Taxus Express II, and 12 (17.1%) with Taxus Liberte (Boston Scientific, Marlborough, MA, USA), and 2 zotarolimus-eluting stents 15 (21.4%) with Endeavor, and 18 (25.7%) with Endeavor Resolute (Medtronic Inc., Minneapolis, MN, USA).

There were no cases of procedure-related mortality, and no emergency CABG were required. In the index LM PCI, the procedure time was 1.73 $\pm$ 0.74 hours and the contrast volume was 174.8 $\pm$ 68.6 mL. Seven (9.9%) patients underwent IABP, among whom 3 (4.3%) had acute myocardial infarction Killip IV, 3 (4.3%) had hypotension that developed during PCI, and 1 (1.4%) patient underwent PCI for a LM ostium lesion with chronic total occlusion (CTO) at proximal right coronary artery (RCA). Four (5.7%) patients died in the hospital, one of whom died at day 8 of admission due to refractory ventricular fibrillation in the patient who had acute STEMI with profound cardiogenic shock. IABP support was built-up during the index LM PCI, but no doctor could set up extracorporeal membrane oxygenation in our daily practice in TT MMH without an on-site cardiac surgeon for better support. We contacted the cardiac surgeon in Taipei Mackay Memorial Hospital who took the first plane, which arrived on the following day from Taipei to Taitung because no flight or train as public transportation

Table 1. Clinical demographic data, angiographic and procedural characteristics

Variables	Total N = 70 n (%)
Age y/o Mean ± SD	73.4 ± 10.2
1 year mortality	20 (28.6)
3 year mortality	29 (41.4)
Sex	
Male	47 (67.1)
Female	23 (32.9)
Past history	
Hypertension	65 (92.9)
Diabetes mellitus	30 (42.9)
Hyperlipidemia	41 (58.6)
Uremia	11 (15.7)
Stroke	20 (28.6)
Myocardial infarction	17 (24.3)
Smoking	24 (34.3)
Previous procedure	
Previous PCI	31 (44.3)
Previous CABG	4 (5.7)
Hospitalization diagnosis of index LM PCI	
Angina pectoris	32 (45.7)
Unstable angina & non-STEMI	35 (50.0)
STEMI	3 (4.3)
EuroSCORE Mean ± SD	6.8 ± 3.3
Low (1-2)	9 (12.9)
Intermediate (3-5)	15 (21.4)
High (≥ 6)	46 (65.7)
Access	
Radial artery	27 (38.6)
Brachial artery	11 (15.7)
Femoral artery	32 (45.7)
IABP	7 (9.9)
IVUS	19 (27.1)
LM coronary artery disease Subtype	
LM only	4 (5.7)
LM plus SVD	11 (15.7)
LM plus DVD	24 (34.3)
LM plus TVD	31 (44.3)
SYNTAX score	
High (≥ 33)	39 (55.7)
Intermediate (23-32)	19 (27.2)
Low (0-22)	12 (17.1)
SYNTAX score, Mean,SD	34.8 (12.6)
Strategy of LM PCI	
2-stents	26 (37.1)
0 or 1 stent	44 (62.9)
Stent diameter and length, mm, Mean, SD	
LM only	4.07 (0.47)
	10.6 (2.6)
LM crossing over LAD	3.29 (0.39)
	26.1 (5.7)
LM crossing over LCX	3.23 (0.38)
	22.3 (5.8)
Stent subtype	
Bare-metal stent	10 (14.3)
Taxus Express II	11 (15.7)
Taxus Liberte	12 (17.1)
Endeavor	17 (24.3)
Endeavor resolute	19 (27.1)
Complete/incomplete revasculization within 1 year	
Incomplete revasculization	12 (17.1)
Complete revasculization	58 (82.9)

CABG, coronary artery bypass grafting; DVD, double vessel disease; EuroSCORE, European system for cardiac operative risk evaluation; IABP, intra-aortic balloon pump; IVUS, intravascular ultrasound; LAD, left anterior descending artery; LCX, left circumflex artery; LM, left main coronary artery; PCI, percutaneous coronary intervention; SD, standard deviation; STEMI, ST-elevation myocardial infarction; SVD, single vessel disease; SYNTAX, synergy between PCI with TAXUS and cardiac surgery; TVD, triple vessel disease.

was available at midnight. The other 3 patients died due to sepsis at day 12, 45, and 129, respectively, after the index LM PCI.

Fifty ninth (82.9%) patients had complete revascularization within 1 year after the index LM PCI and 12 patients had residual CTO, including 3 of LAD, 3 of LCX, and 6 of RCA.

Within 1 year of follow-up, 26 (37.1%) patients were hospitalized due to cardiovascular events, including 2 (2.8%) cases of non-fatal myocardial infarction (MI), 18 (25.7%) of unstable angina, 7 (10.0%) of congestive heart failure 7 and 2 (2.9%) of stroke (Table 2). The all-cause mortality rate at 1 year was 28.6% (20 patients), including 12 (17.1%) patients with septic shock, 5 with pneumonia, 5 with intra-abdominal infection and 1 with bacteriemia. Five (7.1%) died due to cardiac events, including 1 who died in hospital and 4 of sudden cardiac death (SCD) at day 17, 89, 122, and 312, respectively. After the index LM PCI, 3 (4.3%) other patients died due to hypovolemic shock due to upper gastrointestinal bleeding, terminal stage of malignancy, and suffocation, respectively, at 1 year.

The LM TLR rate was 11.4% (8 patients) at 1 year. Three (4.3%) patients treated with a single-stent were bailed out by stenting with the culotte method, another single stent, and balloon angioplasty alone, respectively. Another 5 (7.1%) patients treated with two stents were bailed out including 3 with the culotte methods by a single stent, and 2 by balloon angioplasty, and 2 treated by the crush method with a single stent.

Within 3 years of follow-up, 30 (42.9%) patients were hospitalized for cardiovascular events, including 2 (2.8%) with non-fatal MI, 18 (25.7%) with unstable angina, 8 (11.4%) with congestive heart failure, and 4 (5.7%) with stroke (Table 2). The all-cause mortality rate was 41.4% (29 patients) at 3 years. 18 (25.7%) patients

Table 2. The 1 and 3 year results of index LM PCI

Variables	Mortality within 1 year receiving LM PCI (N = 20) n (%)	Living more than 1 year receiving LM PCI (N = 50) n (%)	Mortality within 3 year receiving LM PCI (N = 29) n (%)	Living more than 3 year receiving LM PCI (N = 41) n (%)
Age y/o Mean ± SD	76.9 ± 10.7	72.0 ± 9.7	76.9 ± 10.1	70.9 ± 9.6$^{\#}$
Sex				
Male	13 (65.0)	34 (68.0)	18 (62.1)	29 (70.7)
Female	7 (35.0)	16 (32.0)	11 (37.9)	12 (29.3)
Past history				
Hypertension	19 (95.0)	46 (92.0)	28 (96.6)	37 (90.2)
Diabetes mellitus	11 (55.0)	19 (38.0)	13 (44.8)	17 (41.5)
Hyperlipidemia	13 (65.0)	28 (56.0)	18 (62.1)	23 (56.1)
Uremia	5 (25.0)	6 (12.0)	7 (24.1)	4 (9.8)*
Stroke	10 (50.0)	10 (20.0)*	12 (41.4)	8 (19.5)
Myocardial infarction	4 (20.0)	13 (26.0)	7 (24.1)	10 (24.4)
Smoking	7 (35.0)	17 (34.0)	9 (31.0)	15 (36.6)
Previous procedure				
Previous PCI	7 (35.0)	24 (48.0)	11 (37.9)	20 (48.8)
Previous CABG	1 (5.0)	3 (6.0)	1 (3.4)	3 (7.3)
Hospitalization diagnosis of index LM PCI				
Angina pectoris	9 (45.0)	23 (46.0)	11 (37.9)	21 (51.2)
Unstable angina & non-STEMI	10 (50.0)	25 (50.0)	16 (55.2)	19 (46.3)
STEMI	1 (5.0)	2 (4.0)	2 (6.9)	1 (2.5)
LM subtype				
LM only, LM plus SVD & LM plus DVD	11 (55.0)	28 (56.0)	14 (48.3)	26 (63.4)
LM plus TVD	9 (45.0)	22 (44.0)	15 (51.7)	15 (36.6)
Strategy of LM PCI				
2-Stents	6 (30.0)	20 (40.0)	10 (34.5)	16 (39.0)
SYNTAX score ≥ 33	14 (70.0)	25 (50.0)	20 (69.0)	19 (46.3)
SYNTAX score Mean, SD	40.2 ± 15.6	32.6 ± 10.7	39.9 ± 14.2	31.1 ± 10.1
EuroSCORE ≥ 6	21 (84.0)	29 (64.4)*	20 (80.0)	21 (46.7)*
EuroSCORE Mean ± SD	8.5 ± 3.1	6.0 ± 3.2$^{\#}$	8.5 ± 3.1	5.5 ± 2.9$^{\#}$
Complete/incomplete revascularization				
Incomplete revascularization	7 (35.0)	5 (10.0)*	9 (31.0)	3 (7.3)*
LM TLR	2 (10.0)	6 (12.0)	4 (13.8)	7 (17.1)
MACCE	6 (30.0)	11 (22.0)	12 (41.4)	14 (34.1)

CABG, coronary artery bypass graft; DVD, double vessel disease; EuroSCORE, European system for cardiac operative risk evaluation; LM, left main coronary artery; MACCE, major adverse cardiac and cerebrovascular events; PCL, percutaneous coronary intervention; SD, standard deviation; STEMI, ST-elevation myocardial infarction; SVD, single vessel disease; SYNTAX, synergy between PCI with TAXUS and cardiac surgery; TLR, target lesion revascularization; TVD, triple vessel disease.
* $p < 0.05$ for Fisher's exact test (2-tailed); $^{\#}$ $p < 0.05$ for Student t test for comparing the age between the two groups.

died due to septic shock, which included 9 patients with pneumonia, 5 with intra-abdominal infection, 3 with bacteriemia, and 1 with urinary tract infection. Seven (10.0%) patients died in the hospital, and 6 due to SCD at day 17, 89, 122, 312, 30 and 31 months after the index of LM PCI, respectively. Another patient died of hypovolemic shock due to upper gastrointestinal bleeding at 3 years. The LM TLR rate was 15.7% (11 patients), including 1 (7.7%), 2 (10.5%), and 8 (20.5%), with low, intermediate, and high SYNTAX score at 3 years, respectively. Compared with patients who underwent LM TLR at 1 year, 3 more patient underwent LM TLR. The major adverse cardiac and cerebrovascular events (MACCE) rate, which were defined as cardiac mortality, acute MI, stroke, and any revascularization, were 24.3% at 1 year and 37.1% at 3 years.

In univariate analysis listed in Table 3, all-cause mortality was associated with a high EuroSCORE (≥ 6), high SYNTAX score (≥ 33) and incomplete revascularization at 1 and 3 years, history of stroke at 1 year, and history of uremia at 3 years. The older patients were not significantly associated with mortality at 1 year (p = 0.66), however this reached a level of significance at 3 years (p < 0.05). In multivariate analysis, all-cause mortality was associated with history of stroke at 1 year [odds ratio (OR) 3.92, 95% confidence interval (CI) 1.15~13.42, p < 0.05] and history of uremia at 3 years (OR 6.46, 95% CI 1.06~39.19, p < 0.05). Age (OR 1.05, 95% CI 0.96~1.13 at 3 year), high EuroSCORE (≥ 6) (OR 2.67, 95%CI 0.50~ 14.38 at 1 year; OR 3.85, 95% CI 0.77~19.65 at 3 year) and incomplete revascularization (OR 2.32, 95% CI 0.47~ 11.42 at 1 year; OR 1.78, 95%CI 0.35~8.99 at 3 year) was not significantly associated with mortality (Table 3).

DISCUSSION

Non-primary PCI in a hospital with no on-site cardiac surgery needs to take into consideration PCI volume, experienced operators and technicians, nursing staff, clear plans and agreements for the rapid transport of patients to a facility with CABG surgery. In a review of 308,161 cases submitted to the American College of Cardiology (ACC) National Cardiovascular Data Registry between 2004 and 2006, Kutcher and colleagues found that the overall incidence of emergency CABG was 0.37%, and they found no significant differences in risk-adjusted mortality between centers with and without surgery on site, in either primary or non-primary PCI patients.[18] In addition, when emergency CABG was necessary, the mortality rate was similarly high between off- (13.6%) and on-site (12.8%) facilities. The Cardiovascular Patient Outcomes Research Team (CPORT) Non-Primary PCI (CPORT-E) trial reported that outcomes of PCI performed at hospitals without on-site cardiac surgery were not worse than at hospitals with on-site cardiac surgery with respect to mortality at 6 weeks and major adverse cardiac events at 9 months.[19] Cardiac surgery was not available at our hospital from 2007 to 2010, during which the annual rate of PCI for LM coronary artery disease was 13 in 447 (2.9%), 13 in 513 (2.5%), 20 in 448 (4.5%) and 24 in 469 (5.1%) cases, respectively. The lack of emergent CABG in this study may be due to our performance, which is a high-volume institution.

A large amount of data from observational registries to clinical randomized trials supports the feasibility, efficacy and safety of stenting compared with CABG for the treatment of LM coronary artery disease.[20-27] A meta-

Table 3. Logistic regression model for the patients within or without mortality in 1 and 3 years

Variable	Crude OR (95% CI)		Adj. OR (95% CI)	
	1 year	3 year	1 year	3 year
Age		1.06 (1.00~1.11)		1.05 (0.96~1.13)
Uremia		4.83 (1.15~20.16)		6.46 (1.06~39.19)*
Stroke	4.00 (1.31~12.23)		3.92 (1.15~13.42)*	
Euroscore ≥ 6	4.01 (1.06~15.83)	5.95 (1.76~20.17)	2.67 (0.50~14.38)	3.85 (0.77~19.65)
SYNTAX Score ≥ 33	1.05 (1.00~1.10)	1.07 (1.02~1.12)	1.04 (0.98~1.10)	1.05 (0.99~1.12)
Incomplete revasculization	3.95 (1.13~13.83)	4.16 (1.14~15.23)	2.32 (0.47~11.42)	1.78 (0.35~8.99)

Cl, confidence interval; OR, odds ratio; SYNTAX, synergy between PCI with TAXUS and cardiac surgery.
* p < 0.05after adjusted odds ratio; # Controlled by variables p < 0.05 in univariate analysis.

analysis of DES versus CABG by Athappan et al. demonstrated that there were no significant differences in the incidence of all-cause mortality, cardiac mortality and MACCE at 1 to 5 years.[28] Furthermore, there were significantly fewer cases of stroke in the PCI patients at 1 to 5 years, with a statistically significant trend towards a higher incidence of non-fetal MI in the PCI patients at 1 to 3 years, but similar at 4 and 5 years. In addition, the need for target vessel revascularization was significantly higher in the PCI patients at 1 to 5 years. Therefore, PCI for patients with LM disease is another option for the patients who are not eligible for or refused CABG.

Although CABG remains the standard therapy for LM coronary artery disease, several studies in Taiwan have demonstrated the clinical outcomes of LM revascularization (Tables 4 and 5).[29-34,36,37,39,44-48] Hsu et al. demonstrated that Chinese patients with unprotected LM coronary artery disease who underwent CABG had a higher MACCE rate than those who underwent PCI at 1 year, and that there were significant differences in in-hospital MACCE and 1-year MACCE between the elective CABG group and elective PCI group; however there was no significant differences between the emergent CABG and emergent PCI groups.[30] Huang et al. demonstrated a significantly higher risk of cardiovascular death in patients receiving conservative medical therapy, and similar long-term cardiovascular survival with either PCI or CABG at 6 years of follow-up.[33]

Yip et al. reported that acute LM obstructive disease in patients who had acute myocardial infarction and generally presented with pulmonary edema, cardiogenic shock or sudden death could survive especially when they had the combined coexistence of intercoronary collaterals, a dominant RCA and an incompletely occluded LM.[34] Three (4.3%) patients with STEMI underwent primary PCI in our study, among whom 2 had cardiogenic shock including one patient who died in the hospital. It has been reported that the recanalization and procedure time of PCI is shorter than that of CABG, although only limited data are available. A study in Switzerland on acute myocardial infarction reported that LM patients had higher rates of cardiogenic shock compared with either isolated or concomitant PCI for other vessel segments to non-LM vessel segments only (12.2% vs. 3.5%, $p < 0.001$).[35]

In this study, a history of stroke was significantly associated with all-cause mortality at 1 year, but was not significant at 3 years, whereas a history of uremia was not significant with all-cause mortality at 1 year, but it reached significance at 3 years. Lee et al. reported that a history of stroke could predict cardiovascular mortality and that a low left ventricular ejection fraction could predict all-cause mortality.[36] Wu et al. reported that hyperlipidemia and LM bifurcation involvement were independent predictors for MACCE in patients undergoing PCI.[37] In the current study, older age was not significantly associated with all-cause mortality at the 1 year interval ($p = 0.66$) and then reached significance at 3 years ($p < 0.05$) in univariate analysis. However it was not significant in multivariate analysis which may be due to the small sample size and shorter following period.

The application for EuroSCORE is easy to use and can provide some degree of operative risk prediction.[15] At 1 and 3 years follow-up, Rodes-Cabau et al. demonstrated that cardiac death, MI and MACCE-free survival were similar in patients undergoing PCI and CABG, however a higher EuroSCORE value was an independent predictor of MACCE regardless of the type of revascularization in octogenarians.[38] In addition, Jou et al. demonstrated that EuroSCORE and clinical SYNTAX Score may be independent predictors for 30-day and 1-year all-cause mortality and MACCE.[39] In this study, the mean EuroSCORE was 6.83 ± 3.32, including 9 (12.9%) patients with low, 14 (20.0%) with median, and 47 (67.1%) with high scores. We also found that a high EuroSCORE (≥ 6) was significant associated with all-cause mortality at 1 and 3 years in univariate analysis but it was not significant in multivariate analysis. We considered that larger sample size and longer following-up period may be needed.

The MACCE rates in patients with low, intermediate and high SYNTAX score were 15.4%, 10.5% and 33.3%, respectively, at 1 year, and 23.1%, 21.1%, and 48.7%, respectively, at 3 years in this study. These rates were similar to a SYNTAX trial in which the MACCE rate was similar between patients with low and intermediate SYNTAX scores (7.7%, 12.6% at 1 year, and 18%, 23.4% at 3 years in those undergoing PCI) but significantly higher those with high scores (25.3% at 1 year, $p = 0.008$, and 37.3% at 3 year, $p = 0.003$).[25] In the current study, compared to low and intermediate SYNTAX scores, a high SYNTAX scorewas not significantly associated with

Table 4. Clinical demographic data from registries of left main revasculization in Taiwanese population

Study	Time	Duration, months Mean, SD	n	Revasculization (%)	Age, years Mean, SD	EuroSCORE Mean, SD	LM plus TVD (%)	IVUS (%)	IABP (%)	Single stent strategy (%)	Stenting across LM bifurcation (%)
Yip et al.[34]	May 1993~	44 (14)	18	Balloon (44.4)	67 (12)				94.4		
KH CGMH	Jul 2000			BMS (55.6)							
Lee et al.[46]	Dec 1997~	18 (3)	13	BMS	57 (4)				15.4	100	
SKWHSMH	Jun 2000										
Lee et al.[36]	Aug 1997~	40 (26)	76	BMS (93)	68 (10)						
SKWHSMH	July 2005			DES (7)							
Hu et al.[45]	Aug 1997~	45 (35)	122	BMS (75)	70 (10)		17			85.2	68.9
SKWHSMH	Dec 2008			DES (25)							
Cheng et al.[47]	Oct 2002~	20.2	17	BMS (64.7)	80.8		47.1		11.8		
TSGH	Mar 2005			DES (23.5)							
				Balloon (11.8)							
Hsu et al.[31]	Sep 2003~	12	20	BMS (50)	66.6 (12.2)	5.6 (2.8)	35.0		10.0		
CY CGMH	Jun 2005			DES (50)							
			39	CABG	66.9 (10.9)	6.3 (3.7)	53.8		2.6		
Cheng et al.[44]	Jun 2000~	16.5 (6.8)	49	DES	67.1 (10.0)	7.8 (3.7)	63.3	63.3	10.2	69.4	95.9
KH CGMH	Oct 2005	17.6 (9.3)	29	BMS	69.1 (7.9)	8.9 (3.8)	65.5	24.1	6.9	89.7	79.3
		19.8 (9.3)	11	DCA + BMS	60.5 (12.9)	4.8 (2.4)	54.5	100	9.1	81.8	63.3
Hsueh et al.[30]	Dec 2000~	6	116	Transradial	67.4 (10.4)	7.3 (3.7)	61.2	51.7	5.2	70.6	78.4
KH CGMH	Oct 2006			BMS (31.0)							
				DES (69.0)							
			15	Transfemoral	65.5 (10.6)	8.7 (5.1)	53.3	66.7	20.0	93.3	53.3
				BMS (80.0)							
				DES (20.0)							
Cheng et al.[48]	Jan 2000~	26.7 (22.2)	216	CABG	66.6 (8.8)	6.4 (3.3)	75.9		19		
KH CGMH	Mar 2007	15.8 (10.3)	94	DES	67.6 (10.2)	6.9 (3.5)	60.6	60.6	6.4	62.7	83.0
		29.1 (21.7)	53	BMS	68.7 (10.7)	8.4 (4.2)	54.7	41.5	9.4	92.4	67.9
Huang et al.[33]	Jan 1996~	1587 (1136)	136	Medication	68 (9)		17.6				
NTUH	Jun 2006	days	148	BMS (43)	66 (11)		15.5				
				DES (57)							
			336	CABG	66 (10)		41.3				
Wu et al.[37]	Jan 2003~	867 (410)	55	BMS (25.5)	66.4 (11.0)	3.7 (2.7)	58.2	1.8	0	29.1[b]	
NTUH	Feb 2007	days		DES (72.7)							
				Both (1.8)							
Wang et al.[32]	Mar 2003~		34	BMS (17.7)	67.6 (11.3)	5.4 (2.9)	52.9	14.7	2.9	41.2	82.3
TC TCGH	Oct 2008			DES (85.3)							
			87	CABG	65.7 (8.9)	4.4 (2.4)	59.8		0		
Jou et al.[39]	Jan 2000~	31.8	198	BMS (49.0%)	71.5 (10.7)	6	44.7	11.6	16.2	70.7	80.7
TP VGH	Dec 2009			DES (51.0%)							
Cheng et al.	Jan 2007~	36	70	BMS (14.3)	73.4 (10.2)	6.8 (3.3)	44.3	27.1	9.9	61.4	82.9
TT MMH	Dec 2010			DES (84.3)							
				Balloon (1.4)							

BMS, bare metal stent; CY CGMH, Chayi Chang Gung Memorial Hospital; DCA, debulking strategy with directional atherectomy; DES, drug eluting stent; EuroSCORE, European system for cardiac operative risk evaluation; IABP, intra-aortic balloon pump; IVUS, intravascular ultrasound; SD, standard deviation; KH CGMH, Chang Gung Memorial Hospital-Kaohsiung Medical Center; LM, left main coronary artery; NTUH, National Taiwan University Hospital; SKWHSMH, Shin Kong Wu Ho-Su Memorial Hospital; TC TCGH, Taichung Buddhist Tzi-Chi Genernal Hospital; TP VGH, Taipei Veterans Genernal Hospital; TSGH, Tri-Service Genernal Hospital; TT MMH, Taitung Mackay Memorial Hospital; TVD, triple vessel disease.

[a] 3 patitents received elective CABG; [b] 50 patients underwent bifurcation stenting.

Table 5. Revasculization strategy and clinical outcome from registries of left main revasculization in Taiwanese population

	Final kissing balloon	CR (%)	All-cause mortality (%)			Cardiac mortality (%)			TLR (%)		MACCE (%)		Stroke (%)	
Yip et al., KH CGMH[34]			In-hospital						28.6					
			33.3	44.4										
Lee et al., SKWHSMH[46]			8						23					
Lee et al., SKWHSMH[36]			9			7			25[a]		32			
Hu et al., SKWHSMH[45]	50.8		25			20			28[b]					
Cheng et al., TSGH[47]	35.3		In-hospital			In-hospital			0		47.1		5.8	
			11.8	11.8		0	5.8							
Hsu et al., CY CGMH[31]			In-hospital	1y					0		In-hospital		In-hospital	1y
			5.0	5.0							5.0	5.0	0	0
			20.5	20.5					10.3		25.6	33.3	2.6	2.6
Cheng et al., KH CGMH[44]	85.7					In-hospital			19.3[d]				In-hospital	
						0[d]	4.1[d]						2.0	0
	44.8					6.9[d]	6.9[d]		25.4[d]				0	0
	81.8					9.1[d]	9.1[d]		49.5[d]				0	0
Hsueh et al., KH CGMH[30]	62.9		In-hospital	6m		In-hospital	6m		3.5		8.9		In-hospital	
			0.9	3.6		0.9	2.7						0	0.9
	66.7		13.3	7.7		13.3	7.7		15.4		23.1		0	0
Cheng et al., KH CGMH[48]			In-hospital	3y	6y	In-hospital	3y	6y	3y	6y	3y	6y		
			10.2	21.1	34.1	5.6	10.9	18.5	6.1	12.9	25.4	50.0		
		56.4	0	12.2		0	12.2		42.7		37.3			
		37.7	5.7	17.9	17.9	5.7	9.4	12.0	47.0	64.6	43.7	51.8		
Huang et al., NTUH[33]			56			46								
			18			20								
			29			24								
Wu et al., NTUH[37]	100f		5.5			3.6	21.8				29			
Wang et al., TC TCGH[32]	82.1		In-hospital				In-hospital						In-hospital	
			0	5.9[d]		5.9[d]	0	29.4[d]			32.4[d]		0	0
			8.1[d]	10.0[e]		2.5[e]	1.2d	8.8[e]			15[e]		2.3[d]	3.8[e]
Jou et al., TP VGH[39]	36.9		1y		1y		1y				MACE[c]			
			15.7	25.3	13.6	19.2	8.6	12.6			37.9			
Cheng et al., TT MMH	57.1	82.9	1y	3y	1y	3y	1y	3y	1y		3y		1y	3y
			30.0	42.9	7.1	10.0	11.4	15.7	22.9		37.1		2.9	5.7

CY CGMH, Chayi Chang Gung Memorial Hospital; CR, complete revasculization; DCA, debulking strategy with directional atherectomy; DES, drug eluting stent; KH CGMH, Chang Gung Memorial Hospital-Kaohsiung Medical Center; m, month; MACCE, major adverse cardiac and cerebrovascular events; NTUH, National Taiwan University Hospital; SKWHSMH, Shin Kong Wu Ho-Su Memorial Hospital; TC TCGH, Taichung Buddhist Tzi-Chi Gevernal Hospital; TLR, target lesion revascularization; TP VGH, Taipei Veterans Genernal Hospital; TSGH, Tri-Service Genernal Hospital; TT MMH, Taitung Mackay Memorial Hospital; y, year.
[a] including PCI 18, CABG 5, both PCI and CABG 1; [b] including PCI 16, CABG 10, both PCI and CABG 2; [c] MACE including all-cause death, nonfetal MI; clinical-driven TLR; [d] cumulative; [e] excluded in-hospital mortality 7 patients; [f] kissing balloon all done in 50 pateints who had bifurcation lesion.

cardiac death, all-cause mortality, or MACCE rate. However 26 (37.1%) patients had both high SYNTAX and high EuroSCORE scores. Excluding 1 case of in-hospital mortality and 1 patient with SCD at day 17 owing to a lack of medication after discharge from index LM PCI, the other 5 patients who had SCD and both had high SYNTAX and high EuroSCORE scores died of cardiac events.

For LM PCI, the stenting strategies and techniques depended upon whether or not the lumen anatomy involves distal LM, the operator's experience, and the cost.[40] This is especially true for LM distal lesions. There were no significant differences between a single- and 2-stent strategy for PCI in each year in this study. We observed that LM TLR decreased from 3 (23.1%) of 13 patients in 2007, 3 (23.1%) of 13 patients in 2008, 3 (15.0%) of 20 patients in 2009 to 2 (8.3%) of 24 patients in 2010. There are several possible reasons for this. First, 19 (27%) patients underwent IVUS during LM PCI, including 6 (46.2%) in 2007, 5 (38.5%) in 2008, 3 (15.0%) in 2009 and 5 (20.8%) in 2010. Subgroup analysis in the MAIN-COMPARE study reported that IVUS guidance seemed to be associated with an improvement in 3-year mortality rate compared with a conventional angiography-guided procedures.[41] IVUS is not routinely performed in our hospital due to its high cost and the limited support from the National Health Insurance Bureau during the study period. Second, improvement in the operator's experience and knowledge over time suggests that the learning curve is the major factor in decreasing LM TLR.

Only a few studies have compared first generation DES with second generation DES in LM PCI. In a randomized trial of intracoronary stenting and angiographic results comparing PCI with sirolimus-eluting stents versus paclitaxel-eluting stents, no significant differences were found with regards to death, MI, or TLR at 12 months followed-up.[42] On the other hand, the PRECOMBAT 2 study compared second generation everolimus-eluting stents to first-generation sirolimus-eluting stents, and found that the rate of clinical driven target vessel revascularization was 3.1% versus 6% over 18 months.[43] Therefore, with the increasing use of second generation DES, a drop in TLR should be expected in future trials. There were no significant differences in clinical outcome between the DES in our study because of the limited sample size.

Numerous studies have discussed a single or 2-stent strategy and different techniques to treat LM distal lesions.[40] The outcomes seem to depend on LM anatomy and technique, the operator's experience, and cost. Cheng et al. demonstrated that a debulking strategy with directional atherectomy from the LAD to LM before BMS implantation did not achieve better clinical outcomes than a non-debulking strategy with either DES or BMS.[44] Calcified lesions still require rotational atherectomy in certain condition, however DES and rotational atherectomy are expensive with partial or no reimbursement from NHI program in Taiwan. Hu et al. demonstrated that young age and BMS implantation could predict repeated PCI and/or CABG.[45]

The LM coronary artery supplies 75% of the left ventricle in RCA dominant status, and 100% in left side dominant status. Cheng et al. reported a higher TLR rate in patient undergoing PCI with either DES or BMS with no significant difference in cardiac death between PCI and CABG, and that advanced age and diffuse atherosclerosis may increase the risk of cardiac death following revascularization.[47] The arterial revascularization therapies study revealed a lower incidence of death, MI, and stroke in patients with complete revascularization by CABG than in patients undergoing incomplete revascularization by PCI.[49] The patients with a low possibility of complete revascularization with CABG had a better prognosis after initial diagnostic coronary angiography. Huang et al. also reported that CABG provides better survival outcomes in high-risk subgroups, including those with ventricular dysfunction (left ventricular ejection fraction < 40%), older age (age > 65 years), and chronic kidney disease (creatinine clearance < 60 mL/min).[33] Although incomplete revascularization in our study was significantly associated with all-cause mortality in univariate analysis ($p < 0.05$), it was insignificant in multivariate analysis. The patients with incomplete revascularization within 1 year had CTO without successful recanalization by PCI, including 3 of the LAD, 3 if the LCX, and 6 of the RCA. Within 1 and 3 years of follow-up, 9 patients with residual CTO were died, including 3 of the LAD, 3 of the LCX, and 3 of the RCA. Therefore, a lot of research has focused on CTO PCI with the aim of improving clinical outcomes and the devices and techniques are still in development.[50]

Limited data are available about LM PCI in hospitals with no on-site cardiac surgery except for primary PCI for patients with STEMI.[5] The randomized trial by Jacobs et al. demonstrated that non-emergency PCI procedures performed at hospitals in Massachusetts without on-site surgical services were not worse than procedures performed at hospitals with on-site surgical services with respect to the 30-day and 1-year rates of clinical events.[51] Andrea et al. reported PCI in patients with acute coronary syndrome with LM disease including 88.5% distal LM lesions in an institution with more than 700 annual

PCI procedures without on-site surgery backup.[52] Between January 2003 and January 2010, in 200 consecutive patients 16% had overall pre-procedural cardiogenic shock, 22% had peri-procedural cardiogenic shock, 3.5% had cardiac arrest during procedure, and 9% underwent orotracheal intubation during the procedure 9%, with an in-hospital mortality of 11%, cardiac death of 16%, MI rate of 7%, and TLR rate of 10.5% in 26 months of follow-up. Elevated EuroSCORE and pre-procedural hemodynamic instability were the strongest predictors of target lesion failure which was defined as cardiac death, MI and TLR. This study by Andrea et al. demonstrated PCI as feasible revasculization strategy without onsite cardiothoracic support.

According to the outcomes in the studies including Taiwanese patients listed in Table 5, the MACCE, cardiac mortality and TLR rate were 15-47%, 5.8-19.2%, and 6.1-29.4%, respectively at 2-3 years of follow-up, compared to 24.3%, 7.1%, and 11.4% at 1 year, respectively, and 37.1%, 10.0%, and 15.7% at 3 years, respectively, in the current study. Neither emergency CABG nor PCI switched to CABG surgery was needed in our patients. These results are similar to cohort studies with regards to the safety and efficacy for patients with LM disease in Taiwan. However the all-cause mortality rates were high at 30.0% at 1 year and 40.9% at 3 years, the majority of which were caused by sepsis, including 12 patients (60%) at 1 year, and 18 patients (62.1%) at 3 years. In 2011, the average life expectancy of people in Taitung County was 74.36 years (70.64 for males, 79.05 for females), compared with 79.15 years in Taiwan (75.96 for males and 82.63 for females). This study was not designed to examine this complex issue, and further studies on the relationship between sepsis, mortality, LM PCI, social-economic status and long-term care system, are required.

CONCLUSIONS

Patients with a history of previous stroke at 1 year and a history of uremia at 3 years were associated with all-cause mortality in multivariate analysis. This demonstrated that high-risk patients in pre-procedure evaluation still have a relatively higher mortality rate during LM PCI. Our clinical outcomes demonstrate that PCI for patients with LM coronary artery disease is a safe and effective strategy in a high-volume hospital with around-the-clock ability to perform primary PCI for patients with STEMI without on-site cardiac surgery. Sepsis was the major cause of mortality in our study, however, and further studies are needed to elucidate this complex issue.

Study limitations

First, this study was an observational study and a lack of discussion with surgical team in urgent cases may have forced the selection of PCI treatment at the discretion of the physician or the patient. Moreover, the context of LM PCI had a limited revascularization strategy (angiographic or IVUS guided), device selection (rotational atherectomy), stent choice (BMS or DES), which largely depended on the cost beyond our health insurance reimbursement during the study period, and this may have affected the procedural outcomes. Although we used propensity analysis to enable a rigorous adjustment for selection bias and confounders, there is no way to eliminate bias caused by the influence of unmeasured confounders, or the presence of patients deemed to be so. Second, the patients who were diagnosed with LM coronary artery disease and received CABG in our hospital or were transferred to other medical centers were excluded because of the small number of cases. Third, this study contained a relatively small sample size and the findings should not be generalized to other subgroups. Further large scale randomized trials to confirm the best revascularization strategy for patients with significant LM stenosis in hospitals with or without onsite cardiac surgery are needed.

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