Ostial left main coronary artery stenosis as an additional risk factor in off-pump coronary artery bypass grafting

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Background: Our aim was to determine whether general left main coronary artery stenosis (LMS) and ostial LMS pose additional risks after off-pump coronary artery bypass grafting (CABG) relative to non-left main coronary artery stenosis.

Methods: From January 1, 2008, to December 31, 2009, 4366 patients underwent primary isolated off-pump CABG at Beijing Anzhen Hospital. Disease was retrospectively classified as non-left main disease (n = 3523), nonostial LMS (n = 765), and ostial LMS (n = 78). Groups were propensity score matched. Kaplan-Meier freedoms from major adverse cardiac and cerebrovascular events (MACCEs) were calculated.

Results: During the first 30 postoperative days, mortality was significantly higher in the ostial LMS group (6.41%) than in non-left main disease (0.855%, $\chi^2 = 7.78$, $P = .005$) and nonostial LMS (1.28%, $\chi^2 = 4.71$, $P = .03$) groups. Incidence of MACCEs was significantly higher in the ostial LMS group (20.5%) than in non-left main disease (5.98%, $P = .000$) and nonostial LMS (9.62%, $P = .002$) groups. Odds ratio for early MACCEs of ostial LMS versus non-left main disease was 3.74 (95% confidence interval, 1.72–8.17). At mean follow-up 12.8 ± 7.5 months and cumulative follow-up 498.5 patient-years, difference among groups in freedom from MACCEs did not reach statistical significance ($\chi^2 = 2.39$, $P = .303$).

Conclusions: Ostial LMS poses additional early risks of mortality and MACCEs in off-pump CABG. Off-pump CABG for ostial LMS should proceed with greater of intraoperative surveillance and lower threshold for converting to on-pump CABG. (J Thorac Cardiovasc Surg 2012;143:103-10)

Because of improvements in the perioperative and postoperative management of patients undergoing coronary artery bypass grafting (CABG), left main coronary artery stenosis (LMS) no longer is a risk factor for early and late death after CABG.¹ According to current guidelines, CABG remains the treatment of choice for patients with severe coronary artery disease, including those with LMS and those with 3-vessel disease.^{2,3} Even in this era of drug-eluting stent therapy, CABG remains the standard of care for patients with 3-vessel disease or LMS, because the use of CABG, as compared with percutaneous coronary intervention (PCI), has resulted in lower rates of the combined end point of major adverse cardiac and cerebrovascular events (MACCEs).⁴

In our high-volume practice of revascularization procedures, we have believed that significant ostial LMS, although a relatively rare entity, is associated with relatively higher in-hospital and long-term mortalities after off-pump CABG (OPCAB). Although OPCAB has now evolved as routine practice in some cardiac centers, its relative safety and efficacy in ostial LMS relative to coronary artery disease other than LMS (non-left main disease) and to general (nonostial) LMS has never been explored. In this study, we therefore retrospectively evaluated the relative efficacy and safety profiles of OPCAB for patients with non-left main disease, nonostial LMS, and ostial LMS. To correct for the confounding factors and to decrease the potential selection bias, we used propensity scores to match 3 groups, allowing direct comparisons of outcomes during the first 30 days after the procedure and during the midterm follow-up.

MATERIALS AND METHODS

Study Design

From January 1, 2008, through December 31, 2009, a total of 4742 patients underwent CABG at the Beijing Anzhen Hospital. Among these, 4366 (92.1%) with previously untreated coronary artery disease underwent primary isolated OPCAB and 376 (7.9%) underwent on-pump CABG. According to the pathology of the left main coronary artery, the 4366 patients who underwent OPCAB were retrospectively classified as having non-left main disease (n = 3523), nonostial LMS (n = 765), or ostial LMS (n = 78). The non-left main disease group was defined as the group of patients who had coronary artery disease but did not have left main coronary artery

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Abbreviations and Acronyms

CABG	= coronary artery bypass grafting
IABP	= intra-aortic balloon pump
LMS	= left main stenosis
MACCE	= major adverse cardiac and cerebrovascular event
OPCAB	= off-pump coronary artery bypass grafting
PCI	= percutaneous coronary intervention
SYNTAX	= Synergy Between Percutaneous Coronary Intervention With TAXUS and Cardiac Surgery

stenosis. The nonostial LMS group was defined as the group of patients who had left main coronary artery disease in addition to other coronary lesions but did not have ostial left main coronary artery stenosis. Finally, the ostial LMS group was defined as the group of patients who had ostial LMS in addition to other coronary lesions. The 376 patients who underwent on-pump procedures, including primary on-pump CABG ($n = 52$), concomitant valve replacement ($n = 233$), left ventricular aneurysmectomy ($n = 43$), mitral valve repair ($n = 45$), and tricuspid valve repair ($n = 3$), were excluded from this study. Patient ages ranged from 39 to 78 years (mean 62.7 ± 16.3 years). Overall, 1070 patients (24.5%) had Canadian Cardiovascular Society angina class IV symptoms. LMS was defined as at least 50% stenosis in the left main coronary artery, and ostial LMS was defined as stenosis of the proximal left main coronary artery, less than 3 mm from the ostium, of at least 50%. We calculated propensity scores to match similar clinical characteristics among the 3 groups. Logistic regression with backward selection was performed to calculate the propensity score. By matching propensity score, 78 foursomes were successfully matched in a manner of 3 members from the non-left main disease group ($n = 78 \times 3 = 234$) with 1 member from the ostial LMS group ($n = 78$). Moreover, 78 threesomes were successfully matched in a manner of 2 members from the nonostial LMS group ($n = 78 \times 2 = 156$) with 1 member from the ostial LMS group ($n = 78$). We compared the clinical results among these propensity-matched groups. In Table 1, which presents the preoperative demographic characteristics and risk factors of the 3 groups after matching, patients in the 3 groups can be seen to be well balanced with regard to all the baseline demographic and clinical characteristics.

The local ethics committee at Anzhen Hospital and Beijing Institute of Heart, Lung, and Blood Vessel Diseases approved the use of clinical data for this study. Written, informed consent was obtained from each patient for the surgical or interventional procedure, and consent was also obtained from each patient for use of the data in clinical research.

Procedure Indication and Techniques

Six surgical teams affiliated with Anzhen Hospital performed all the CABG procedures. In our center, off-pump CABG had been performed regularly for more than 10 years before the launch of the trial, and each of the 6 participating surgical teams have performed at least 85% of their isolated CABG as off-pump procedures since 2005. The indications for OPCAB in our hospital included all isolated CABG procedures with a reasonable target vessel but without large left ventricular aneurysm, severe mitral valve regurgitation, left ventricular thrombus, severe arrhythmia originating from myocardial infarction, or severe comorbidities making OPCAB impossible. Contraindications to OPCAB included inadequate exposure and aberrant coronary arterial anatomy, such as poorly visualized target vessels on angiography or extremely small, heavily calcified, or

extensively intramyocardial vessels. Preoperative hemodynamic instability was also a contraindication to OPCAB. The indication for on-pump CABG included all CABG procedures with poor target vessel, large left ventricular aneurysm with a volume between 20% and 50% of the left ventricle, severe mitral valve regurgitation, left ventricular thrombus, or severe comorbidities necessitating cardiopulmonary bypass. Large left ventricular aneurysm was defined as a dyskinetic left ventricular wall with a volume greater than 20% of the left ventricle, as assessed through left ventriculography and echocardiography. Severe mitral valve regurgitation was defined as a regurgitation area greater than 9 cm^2 , as assessed through left ventriculography and either transthoracic or transesophageal echocardiography.

The strategy for all isolated CABG procedures in Anzhen Hospital was regularly planned first to proceed as an OPCAB procedure; if the hemodynamic situation was unstable or could not sustain the off-pump manipulation, however, the surgery would be switched to on-pump CABG. All the OPCAB procedures were performed through a median sternotomy approach under conditions of general anesthesia. We used electrocardiography and blood pressure measured through a radial artery catheter to monitor hemodynamic status. In patients with a left ventricular ejection fraction value less than 35%, a Swan-Ganz catheter was also used to monitor continuous cardiac output. There were always bypass setups available in the operating room. All patients were given heparin at 100 IU/kg intravenously to achieve an activated clotting time longer than 300 seconds. An Octopus stabilizer (Medtronic, Inc, Minneapolis, Minn) was used for the distal anastomosis, and a Novare Enclose II manual proximal anastomotic device (Vitalitec International, Inc Plymouth, Mass) was used for the proximal anastomosis. The distal anastomoses were constructed with a continuous running 7-0 polypropylene suture, and the proximal venous or arterial graft anastomosis to the aorta was sutured over a partially occluded area in aorta with a continuous running 6-0 polypropylene suture by means of a Novare Enclose II manual proximal anastomotic device. All patients in the 3 groups were advised to continue lifelong aspirin therapy (100 mg daily).

Study End Points

The primary end point was all-cause mortality within 30 days after the revascularization procedure and during the follow-up. The secondary end point was the incidence of MACCEs within 30 days after the revascularization procedure and during the follow-up. MACCEs were defined to include all-cause death, nonfatal myocardial infarction, stroke, and repeated revascularization. Repeated revascularization was defined as any PCI or CABG performed after the first revascularization procedure. Non-Q-wave myocardial infarction was diagnosed according to World Health Organization criteria, including an increase in total creatine kinase level to at least twice the upper limit of the reference range and an elevated MB isoform level without development of new pathologic Q waves. A Q-wave myocardial infarction was present when, in addition to creatine kinase elevation, a new pathologic Q wave was noted in at least 2 of the electrocardiographic leads.

Data Collection

Among the 468 cases from the 3 propensity-matched groups, there were 460 surgical survivors. One month after discharge, all these surviving patients were assessed at an outpatient clinic for full review by the cardiac surgeon or cardiologist. Canadian Cardiovascular Society angina class, troponin I and cardiac enzymes, transthoracic echocardiography, and electrocardiographic data were recorded. These variables were evaluated at 3-month intervals at the patient's local cardiac center. Long-term clinical outcomes were assessed up to July 2010 by reviewing the medical files of patients' cardiologists, general practitioners, or both as appropriate. Baseline demographic data, procedural data, and perioperative outcomes were recorded. For deaths beyond the first 30 days after the CABG procedure, the medical files were reviewed by a primary investigator (H-L.G., C-S.L., or P-S. W) of this study. The status of the patients was determined by review of hospital records, follow-up questionnaires, or contact with

TABLE 1. Preoperative baseline demographic variables and risk factors in the group with other than left main disease, the group with nonostial left main stenosis, and the group with ostial left main stenosis after matching

Patient data	Non-left main disease (n = 234)	Nonostial LMS (n = 156)	Ostial LMS (n = 78)	P value	F or χ^2
Age (y, mean $\pm$ SD)	59.45 $\pm$ 11.43	58.56 $\pm$ 10.33	58.30 $\pm$ 11.13	.623	0.47
Age >65 y (no.)	96	66	32	.966	0.07
SYNTAX score (mean $\pm$ SD)	28.6 $\pm$ 12.4	28.9 $\pm$ 11.5	29.7 $\pm$ 11.1	.789	0.25
EuroSCORE (mean $\pm$ SD)	6.2 $\pm$ 2.6	6.4 $\pm$ 2.8	6.5 $\pm$ 2.7	.620	0.478
Female (no.)	99	62	30	.791	0.47
All types of diabetes mellitus (no.)	117	74	38	.884	0.25
Type 1 diabetes mellitus (no.)	39	24	10	.718	0.67
HSCRP (mg/L, mean $\pm$ SD)	4.53 $\pm$ 2.06	4.46 $\pm$ 2.17	4.35 $\pm$ 2.14	.803	0.22
Hyperlipidemia (no.)	177	106	57	.247	2.80
Current smoker (no.)	120	80	38	.918	0.17
Renal insufficiency (no.)	21	12	5	.751	0.57
Hypertension (no.)	162	106	51	.817	0.40
Family history of coronary artery disease (no.)	90	60	31	.978	0.05
Previous MI (no.)	114	78	40	.053	5.90
Peripheral vascular disease (no.)	18	12	5	.172	3.52
LV ejection fraction <35% (no.)	30	18	9	.914	0.18
LV ejection fraction (% , mean $\pm$ SD)	53.5 $\pm$ 16.4	54.3 $\pm$ 17.6	55.2 $\pm$ 16.7	.724	0.32
Congestive heart failure (no.)	36	22	10	.842	0.34
Transient ischemic attack (no.)	12	8	3	.892	0.23
Stroke (no.)	9	6	3	.923	0.16
Pulmonary disease (no.)	24	14	6	.778	0.50
CCS angina class IV (no.)	91	62	35	.164	3.61
Periprocedural IABP (no.)	5	4	2	.955	0.09
Aspirin (no.)	234	156	78	>.999	0
β -Blocker (no.)	201	132	64	.711	0.68
Calcium-channel blocker (no.)	108	70	33	.838	0.35
Nitrates (no.)	210	142	72	.778	0.50
Statins (no.)	144	102	50	.732	0.63
Electrocardiographic diagnosis (no.)				.875	1.22
Sinus rhythm	213	144	73		
Atrial fibrillation	15	10	4		
Other rhythm	6	2	1		
Enrollment diagnosis (no.)				.967	1.39
Silent ischemia	12	6	3		
Stable angina*	51	30	14		
Unstable angina†	153	106	54		
Acute MI	18	14	7		
Vessel territory with stenosis (no.)					
RCA	187	124	63	.974	0.05
Total RCA occlusion	17	12	6	.985	0.03
90% Proximal RCA lesion	29	21	10	.953	0.10
LAD	234	156	78	>.999	0
LCX	234	156	78	>.999	0
Small LV aneurysm‡ (no.)	27	14	8	.719	0.66

LMS, Left main stenosis; HSCRP, high-sensitivity C-reactive protein; MI, myocardial infarction; LV, left ventricular; CCS, Canadian Cardiovascular Society; IABP, intra-aortic balloon pump; RCA, right coronary artery; LAD, left anterior descending coronary artery; LCX, left circumflex coronary artery. *Stable angina was defined according to the Canadian Cardiovascular Society system. †Unstable angina was classified according to the Braunwald classification. ‡Small left ventricular aneurysm was defined as left ventricular aneurysm with a volume less than 20% of the left ventricle.

local physicians at an interval of 3 months after the first outpatient visit. Detailed information, including Canadian Cardiovascular Society angina class status, cardiac rhythm, complications and present medications were recorded. At the follow-up, transthoracic echocardiography and electrocardiography were assessed in 458 of the 460 patients surviving hospitalization (99.57%), and the main parameters were collected. Patient

demographic data, preoperative risk factors, and the incidences of adverse postoperative outcomes were retrieved from the Digitalcare database at Beijing Anzhen Hospital. Diagnostic angiograms were scored according to the Synergy Between Percutaneous Coronary Intervention With TAXUS and Cardiac Surgery (SYNTAX) score⁵ and EuroSCORE algorithms by 1 investigator (H-L.G., C-S.L., or P-S. W) of this study.

TABLE 2. Clinical end points within first 30 days after the revascularization and during follow-up for the propensity score-matched cohorts

	Non-left main disease	Nonostial LMS	Ostial LMS	Nonostial LMS vs non-left main disease				Ostial LMS vs non-left main disease			
				OR	95% CI	<i>P</i> value	χ ²	OR	95% CI	<i>P</i> value	χ ²
First 30 days											
No. of patients	234	156	78								
Death	2 (0.86%)	2 (1.28%)	5 (6.41%)	1.51	0.21–10.81	0.682	0.17	7.95	1.51–41.82	0.004	8.23
MI	6 (2.56%)	6 (3.85%)	5 (6.41%)	1.52	0.48–4.80	0.473	0.52	2.60	0.77–8.78	0.111	2.54
Stroke	4 (1.71%)	3 (1.92%)	3 (3.84%)	1.13	0.25–5.11	0.877	0.02	2.30	0.50–10.51	0.270	1.22
Death, MI, or stroke	12 (5.13%)	11 (7.05%)	13 (16.7%)	1.40	0.61–3.27	0.430	0.62	3.36	1.44–7.84	0.001	10.57
Redo CABG*	1 (0.43%)	0 (0%)	1 (1.28%)	0.29	0.002–41.52	0.415	0.66	3.03	0.19–48.96	0.413	0.67
Redo PCI†	1 (0.43%)	2 (1.28%)	2 (2.56%)	3.03	0.27–33.66	0.344	0.90	6.13	0.55–168.57	0.094	2.81
Repeat revascularization‡	2 (0.86%)	2 (1.28%)	3 (3.85%)	1.51	0.21–10.81	0.682	0.17	4.64	0.76–28.30	0.068	3.32
Any MACCEs	14 (5.98%)	15 (9.62%)	16 (20.5%)	1.67	0.78–3.57	0.180	1.79	3.74	1.72–8.17	0.000	13.88
Midterm follow-up											
No. of patients	232	154	73								
Death	2 (0.86%)	2 (1.30%)	1 (1.37%)	1.51	0.21–10.86	0.678	0.17	1.58	0.14–17.63	0.710	0.14
MI	6 (2.59%)	5 (3.25%)	4 (5.5%)	1.26	0.38–4.22	0.702	0.15	2.15	0.59–17.85	0.235	1.41
Stroke	8 (3.45%)	5 (3.25%)	3 (4.1%)	0.94	0.30–2.92	0.219	1.51	1.18	0.301–4.58	0.808	0.06
Death, MI, or stroke	16 (6.90%)	12 (7.79%)	8 (10.9%)	1.14	0.52–2.48	0.740	0.11	1.64	0.67–3.99	0.276	1.19
Redo CABG*	0 (0%)	0 (0%)	0 (0%)	NA		>.999		NA		>.999	
Redo PCI†	2 (0.86%)	2 (1.30%)	3 (4.1%)	1.513	0.21–10.86	0.678	0.17	4.86	0.80–29.67	0.059	3.557
Repeat revascularization‡	2 (0.86%)	2 (1.30%)	3 (4.1%)	1.513	0.21–10.86	0.678	0.17	4.86	0.80–29.66	0.059	3.557
Any MACCEs	18 (7.76%)	14 (9.09%)	11 (15.1%)	1.89	0.57–2.47	0.689	0.16	2.08	0.93–4.62	0.069	3.303

LMS, Left main stenosis; OR, odds ratio; CI, confidence interval; MI, myocardial infarction; CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention; MACCEs, major adverse cardiac and cerebrovascular events; NA, not applicable. *Any coronary artery bypass grafting after the index coronary artery bypass grafting. †Any percutaneous coronary intervention after the index coronary artery bypass grafting. ‡Any coronary artery bypass grafting or percutaneous coronary intervention after the index coronary artery bypass grafting.

Statistical Analysis

All statistical analyses were performed with the statistical software package SPSS 17.0 (SPSS Inc, an IBM Company, Chicago, Ill). Categorical data are summarized as frequencies and percentages. Continuous data are given as mean $\pm$ SD. Cumulative event rates, such as freedom from MACCEs, of the 3 groups were estimated by means of the Kaplan-Meier method. Differences among patients in the 3 groups were analyzed with 1-way analysis of variance, interactive χ^2 test,⁶ Fisher's Exact test, Wilcoxon rank sum test, or log-rank test as appropriate.

RESULTS

Revascularization Data

The results reported here focus on the 3 propensity-matched groups. The average interval between the diagnostic angiogram and the CABG procedure was 4.5 ± 3.7 days. Because of the unstable hemodynamic situation during the intended off-pump manipulation, there were 5 (2.14%), 3 (1.92%), and 8 (10.26%) conversions to on-pump CABG in the non-left main disease group, the nonostial LMS group, and the ostial LMS group, respectively. The rate of conversion to cardiopulmonary bypass in the ostial LMS group was statistically significantly higher than the rates in the non-left main disease group ($\chi^2 = 9.66$, $P = .002$) and the nonostial LMS group ($\chi^2 = 8.06$, $P = .004$). Of the 8 patients with conversion in the ostial LMS group, all had greater than 90% stenosis at the ostial site of the left main coronary artery, whereas of the 70 patients without conversion, only 12 had greater than 90% stenosis at the

ostial site of the left main coronary artery (Fisher's Exact test, $P < .001$).

All patients in the 3 groups used the left internal thoracic artery as a bypass conduit. A second artery conduit, such as the right internal thoracic artery or the radial artery, was also used in the non-left main disease group in 21 patients (7.98%), the nonostial LMS group in 11 patients (7.06%), and the ostial LMS group in 5 patients (6.41%). The difference in multiple arterial conduit use among the 3 groups did not reach statistical significance (χ^2 $P = .237$, $P = .346$). There were 5 (2.14%), 4 (2.56%), and 3 (3.85%) patients in the non-left main disease group, the nonostial LMS group, and the ostial LMS group, respectively, who received intra-aortic balloon pump (IABP) support during the perioperative period. The difference in the rate of IABP use among the 3 groups did not reach statistical significance ($\chi^2 = 0.684$, $P = .710$).

Outcomes During the First 30 Days

As presented in Table 2, the mortality during the first 30 days in the ostial LMS group (6.41%) was significantly higher than the mortalities in the non-left main disease group (0.855%, $\chi^2 = 7.78$, $P = .005$) and the nonostial-LMS group (1.28%, $\chi^2 = 4.71$, $P = .03$). The odds ratio for ostial LMS versus non-left main disease was 7.95 (95% confidence interval, 1.51–41.82; $\chi^2 = 8.23$;

TABLE 3. The reasons for all deaths during the first 30 days and at midterm after off-pump coronary artery bypass grafting procedure in the ostial left main stenosis group

Postoperative interval		Comments
During the first 30 days after off-pump CABG procedure		
1	6 d	Cardiac arrest during the procedure and conversion to on-pump CABG; patient died of low-output syndrome
2	9 d	Tachycardiac arrhythmia and cardiac arrest during the procedure and conversion to on-pump CABG; patient died of low-output syndrome
3	12 d	Cardiac arrest during the procedure and conversion to on-pump CABG; patient died of low-output syndrome and renal failure
4	17 d	Tachycardiac arrhythmia and cardiac arrest during the procedure and conversion to on-pump CABG; patient died of low-output syndrome
5	21 d	Acute myocardial infarction and circulatory collapse
During midterm after off-pump CABG procedure		
6	10 mo	Sudden death from acute myocardial infarction

CABG, Coronary artery bypass grafting.

$P = .004$). The reasons for the deaths during the first 30 days and midterm after off-pump CABG in the ostial LMS group are presented in Table 3. The rate of the composite end point of death, myocardial infarction, and stroke during the first 30 days in the ostial LMS group (15.39%) was significantly higher than the rates in the non-left main disease group (5.13%) and the nonostial LMS group (7.05%, $\chi^2 = 8.955$, $P = .011$). The odds ratio for ostial LMS versus non-left main disease was 3.364 (95% confidence interval 1.443–7.839). The rate of MACCEs during the first 30 days in the ostial LMS group (19.23%) was significantly higher than the rates in the non-left main disease group (5.98%) and the nonostial LMS group (9.62%, $\chi^2 = 12.066$, $P = .002$). The odds ratio for ostial LMS versus non-left main disease was 3.742 (95% confidence interval, 1.715–8.165).

Midterm Clinical Follow-up

Of the 460 survivors from the 3 propensity-matched groups, 3 were unavailable for follow-up. Follow-up was complete for 99.35%. The mean follow-up was (12.8 ± 7.5 months, with a range of 1 to 26 months, and the cumulative follow-up was 498.5 patient-years. As presented in Table 2, the difference in the incidence of MACCEs

during follow-up among the ostial LMS group (13.51%), the non-left main disease group (7.76%), and the nonostial LMS group (9.09%) did not reach statistical significance ($\chi^2 = 3.361$, $P = .186$). The difference in the freedom from MACCEs among the 3 groups, calculated through the Kaplan-Meier method, also did not reach statistical significance ($\chi^2 = 2.39$, $P = .303$; Table 4 and Figure 1).

DISCUSSION

LMS is an important independent risk factor for increased mortality and morbidity at all stages of diagnosis and treatment of coronary artery disease. Although there have been advances in the percutaneous treatment of LMS, resulting in indications for PCI in clearly defined patient groups with LMS, CABG still confers a significant event-free survival benefit relative to percutaneous and medical treatment in both high- and low-risk patient subsets.^{7,8} Thus, as implemented in the commonly accepted guidelines of the American Heart Association (with a level of evidence of A), CABG remains the treatment of choice for patients with LMS.⁹ Even in the era of drug-eluting stent therapy, CABG generally remains the method of choice for patients with LMS.⁵⁻⁷

Until recently, the presence of critical LMS was considered a relative contraindication to the use of off-pump techniques. Such inferences, however, were based on data presented in the 1970s to the first half of this decade, when the techniques of surgery, anesthesia, and medical management were less advanced than they are now. During recent years, there have been major improvements in almost all fields relating to the perioperative management of patients undergoing CABG as a result of better management, with options including more frequent use of arterial grafts, greater use of internal thoracic arteries, and improved techniques in off-pump surgery. Especially, hemodynamic disturbances during displacement of the heart have been minimized, thanks to improvements in stabilizer technology, use of intracoronary shunts, and greater surgical and, perhaps most importantly, anesthetic experience.

OPCAB technique was among the major areas of progress in coronary revascularization, and it has evolved as a regular practice in some cardiac centers. For example, in our cardiac center, we do about 2500 isolated CABG procedures yearly, and more than 85% of the isolated CABG procedures since 2005 in our cardiac center have been completed in off-pump manner. There is a large amount of evidence to prove the safety and efficacy of OPCAB for LMS now. Beauford and colleagues¹⁰ proved that multivessel off-pump revascularization in patients with severe LMS is a safe and effective alternative to conventional CABG and conveys a survival benefit. Yeatman and associates¹¹ also demonstrated that OPCAB is safe and effective in patients with critical LMS in terms of early and late mortality and MACCEs. Suzuki and colleagues¹² have also

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TABLE 4. Freedoms from major adverse cardiac and cerebrovascular events for groups with other than left main disease, nonostial left main stenosis, and ostial left main stenosis after propensity score correction

	Non-left main disease	Nonostial LMS	Ostial LMS
12 mo	93.9% ± 1.8%	94.2% ± 2.2%	89.9% ± 3.9%
18 mo	90.9% ± 2.5%	91.0% ± 3.1%	84.3% ± 5.4%
24 mo	89.5% ± 2.8%	78.8% ± 6.4%	74.4% ± 8.2%

Log-rank test for Kaplan-Meier major adverse cardiac and cerebrovascular event-free curve among non-left main disease, nonostial left main stenosis, and ostial left main stenosis groups, $\chi^2 = 2.39$, $P = .303$ (the P value and χ^2 both refer to overall comparison). LMS, Left main stenosis.

demonstrated the safety of performing OPCAB surgery in all patients, without the need for exclusion criteria. Early and midterm outcomes were acceptable and encouraged continued use of the OPCAB approach for all patients undergoing CABG, including critical LMS. Karic and colleagues¹³ revealed that OPCAB is an effective and safe method for treatment of LMS, and there are certain advantages relative to the classic method in short-term follow-up, with no difference in long-term results. Panesar and colleagues¹⁴ demonstrated that OPCAB could offer a neurologic benefit for patients with significant LMS undergoing CABG. Suzuki and colleagues¹⁵ reported that OPCAB is also feasible and safe for patients with LMS and that LMS, critical or otherwise, is not recognized as a risk factor after OPCAB in either the short or the long term. Emmert and colleagues¹⁶ also reported that a modern OPCAB approach offers low mortality, confers excellent clinical outcomes, and does not come at the price of less complete revascularization in these high-risk patients, such as those with severe LMS. The ROOBY study¹⁷ concluded that at 1 year of follow-up patients in the off-pump group had worse composite outcomes and poorer graft patency than did patients in the on-pump group. In that study, however, the difference in the 30-day composite end point between the off-pump and on-pump groups did not reach statistical significance ($P = .19$), and the difference in the 1-year composite end point was only marginally significant ($P = .04$). This leaves too much room for uncertainty whether OPCAB alone was accountable for the difference. Their conclusion therefore seems unwarranted.

None of these studies, however, explored the effect of the special left main coronary artery lesions, such as ostial LMS, on the early and medium to long-term outcomes after OPCAB procedure. This study was designed to compare the early and midterm clinical outcomes of OPCAB among patients with non-left main disease, nonostial-LMS, and ostial LMS after correction by propensity score. The results of OPCAB in patients with nonostial LMS in our study were comparable with those in other reports with respect to early mortality^{18,19}; however, the early mortality among patients with ostial LMS was much higher than that among patients with non-left main disease or nonostial LMS. Therefore, in

contrast to nonostial LMS, ostial LMS poses additional risk to OPCAB with respect to early mortality and MACCEs after the correction by propensity score.

Two features of OPCAB could lead to hemodynamic instability: transient occlusion of coronary arteries during distal anastomosis construction and displacement of the heart to provide access to distal coronary arteries. It is generally believed that bifurcation lesions carry a worse prognosis than do ostial and midshaft lesions in patients with unprotected LMS treated with PCI²⁰; however, our retrospective study found that for the OPCAB procedure, ostial LMS carries a higher risk than both nonostial LMS and non-left main disease. As all we know, the left main coronary artery could be divided into 3 parts²¹; that is, the origin of the left main coronary artery from just above the left sinus of Valsalva (the ostium), a midportion (the body), and a distal portion or bifurcation. The ostium has a greater proportion of smooth muscle and elastic tissue than the rest of the coronary vessels.²² The smooth muscle and elastic tissue in the ostium of the left main coronary artery, which is always hypertrophied in ostial LMS, is more sensitive to the heart displacement during the procedure than is nonostial LMS. This sensitivity always leads to the spasm of the ostial LMS lesion. The spasms of the ostial LMS lesion during the displacement maneuver often lead to severe ischemia in the left coronary artery territory, and the resulting unstable hemodynamic status often leads to cardiac arrest and emergency conversion to on-pump CABG. In our analysis, a higher incidence of circulatory arrest, which in turn resulted in higher incidence of conversion to on-pump CABG, was the main reason for the higher early mortality and incidence of MACCEs for ostial LMS. In this study, of the 5 early deaths in the ostial LMS group, 4 deaths were related to a sudden circulatory arrest during the procedure and then prompt conversion to on-pump CABG, eventually leading to death (Table 3). The specific pathology in the ostial LMS lesion may be the reason for the higher portion of conversion to on-pump CABG for ostial LMS. We found that within the ostial LMS group, the patients who had conversion had a higher rate of severe stenosis (90%) in the ostial site in the left main coronary artery than did patients not having conversion. Therefore, 90% or greater stenosis might be a marker that could inform the decision of whether to use an IABP during OPCAB or just do it on pump.

We have found no previous reports attempting to correlate ostial LMS with the outcome after CABG. As a special entity of aorto-ostial lesion, ostial LMS should be emphasized in the treatment of coronary artery disease, because ostial LMS accounted for 9.25% of the 843 cases of LMS and for 1.79% of the 4366 cases of isolated OPCAB procedures in our study. Stenosis in the aorto-ostial location is extremely serious because a large myocardial territory is at risk.²³ The location of the ostial lesion may be a marker for more extensive and advanced atherosclerosis. A number

FIGURE 1. The Kaplan-Meier curves of freedom from major adverse cardiac and cerebral events for the non-left main disease (*Non-Mainstem Disease*) group, the nonostial left main stenosis (*Non-Ostial-LMS*) group, and the ostial left main stenosis (*Ostial-LMS*) group. *Cum Survival*, Cumulative survival.

of technical factors could play a role in the relatively poor outcomes after OPCAB in the ostial LMS group. Off-pump manipulation during OPCAB may be challenging, and elastic stenosis may occur, which may lead to cardiovascular collapse.

One further question is whether, on the basis of our analysis, we should suggest that the ostial LMS lesion be treated with an on-pump rather than an off-pump procedure. Without a comparative study between OPCAB and on-pump CABG for ostial LMS, we do not believe that we can now make a firm recommendation that these procedures should all be done on pump, because their mortality and morbidity might well remain high because of the nature of the disease rather than the type of procedure performed. We have demonstrated that this increased mortality was due to intraoperative sudden hemodynamic instability during OPCAB as the predominant problem, resulting in a potential chain of events leading to increased mortality. Around 90% of patients in the ostial LMS group did well with OPCAB in an experienced OPCAB center such as ours. It is therefore warranted to recommend that a higher degree of intraoperative surveillance for the early detection of problems and a lower threshold for converting to an on-pump procedure, rather than a blanket recommendation to do all these procedures on pump. Moreover, to prevent emergency conversion for the patient with a greater than 90% stenosis, prophylactic implantation of an IABP may be a good measure.

The SYNTAX study,²⁴ which compared PCI with drug-eluting stents versus CABG, revealed that a SYNTAX score threshold of 34 might identify patients who would benefit most from surgical revascularization in terms of reducing risk of death.²⁵ Although the SYNTAX study provided

a deep insight into LMS and 3-vessel disease, and it indeed included aorto-ostial lesion in its subjects, it did not provide interventional guidance for such specific lesions as ostial LMS. Our study, by reviewing propensity score-matched patients among the 3 groups, revealed that ostial LMS does pose an additional risk relative to OPCAB procedure in terms of early mortality and MACCEs. Most mortality and MACCEs in the ostial LMS group in the first 30 days after the procedure may be attributable to unstable hemodynamics during the off-pump manipulation, which may stem from the high elastic property of the stenosed ostium of the left main coronary artery. These findings have further expanded the findings of the SYNTAX study.

Because 4 of 5 early deaths in our series were after emergency conversion to on-pump CABG (Table 3), our criteria for conversion to on-pump CABG should be revised. The hemodynamic response seen during lifting of the heart to evaluate targets initially is very important. There are enough data to suggest that mortality is significantly higher when there is emergency conversion to on-pump CABG during an OPCAB procedure. All the patients who have a poor response to initial lifting should have elective conversion to on-pump CABG. If this had been done, the mortality might have been lessened.

In our series, the rate of conversion to cardiopulmonary bypass in the ostial LMS group (10.26%) was significantly higher than in the non-left main disease group (2.14%, $\chi^2 = 9.66$, $P = .06$) and the nonostial LMS group (1.92%, $\chi^2 = 8.06$, $P = .04$). Prophylactic IABP placement can dramatically reduce the instability seen in critical patients and allow a safer OPCAB procedure, but the percentage of patients receiving preoperative IABP support was similar across the 3 groups (Table 1). That may be another reason for the higher incidence of emergency conversion to on-pump CABG during an OPCAB procedure. After checking these data, our surgical strategies for ostial LMS was revised, in that we have adopted prophylactic IABP placement for all patients with ostial LMS, especially for patients with stenosis greater than 90%. Because conversion was significantly frequent among patients with ostial LMS, adequate preparation for pump application is necessary. We expect that this change in the management protocol will decrease the mortality among patients with ostial LMS.

Study Limitations

This study is a retrospective analysis, and some confounding factors may have hidden any clear association between the early and late prognoses of OPCAB and the pathology of LMS. Although we used propensity score matching to balance the 3 nonequivalent groups and reduce any bias for a specific revascularization procedure, prospective, randomized, comparative trials are needed to confirm the findings of this study. In addition, for this special entity of ostial LMS, the relative efficacy of the off-pump CABG

procedure versus the on-pump CABG is yet to be determined through further investigation, especially through randomized, comparative trial. The long-term effects of ostial LMS on OPCAB results still need to be defined further.

CONCLUSIONS

Nonostial LMS does not pose additional early risk after OPCAB, but ostial LMS does, and this difference may stem from the unstable hemodynamic situation during OPCAB. Therefore more caution and attention must be paid to ostial LMS during OPCAB. We suggest that OPCAB procedures for patients with ostial LMS should proceed with a higher degree of intraoperative surveillance for the early detection of problems and a lower threshold for converting to on-pump CABG. IABP support may improve the outcomes of OPCAB for ostial LMS, and because conversion was significantly frequent in patients with ostial LMS, adequate preparation for pump application is necessary.

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