Long-term outcomes of PCI vs. CABG for ostial/midshaft lesions in unprotected left main coronary artery

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Abstract

Background There are limited data on long-term (> 5 years) outcomes of drug-eluting stent (DES) implantation compared with coronary artery bypass grafting (CABG) for ostial/midshaft left main coronary artery (LMCA) lesions. Methods Of the 259 consecutive patients in Beijing Anzhen Hospital with ostial/midshaft LMCA lesions, 149 were treated with percutaneous coronary intervention (PCI) with DES and 110 were with CABG. The endpoints of the study were death, repeat revascularization, myocardial infarction (MI), stroke, the composite of cardiac death, and major adverse cardiac and cerebrovascular events (MACCE, the composite of cardiac death, MI, stroke or repeat revascularization). The duration of follow-up is 7.1 years (interquartile range 5.3 to 8.2 years). Results There is no significant difference between the PCI and CABG group during the median follow-up of 7.1 years (interquartile range 5.3 to 8.2 years) in the occurrence of death (HR: 0.727, 95% CI: 0.335–1.578; \( P = 0.421 \)), the composite endpoint of cardiac death, MI or stroke (HR: 0.730, 95% CI: 0.375–1.421; \( P = 0.354 \)), MACCE (HR: 1.066, 95% CI: 0.648–1.753; \( P = 0.801 \)), MI (HR: 1.112, 95% CI: 0.414–2.987; \( P = 0.833 \)), stroke (HR: 1.875, 95% CI: 0.528–6.659; \( P = 0.331 \)), and repeat revascularization (HR: 1.590, 95% CI: 0.800–3.161; \( P = 0.186 \)). These results remained after multivariable adjusting. Conclusion During a follow-up up to 8.2 years, we found that DES implantation had similar endpoint outcomes compared with CABG.

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Keywords: Coronary artery bypass graft; Drug-eluting stent; Percutaneous coronary intervention

1 Introduction

Coronary artery bypass grafting (CABG) has been the gold standard in the treatment of unprotected left main coronary artery (ULMCA) disease.¹ ¹ ² Previous studies have reported that percutaneous coronary intervention (PCI) with drug-eluting stents (DES) for ULMCA disease is associated with similar 5-year survival compared with CABG, and PCI has been an acceptable treatment for ULMCA disease besides CABG.³ ⁶ The left main coronary artery can be divided into three segments: ostial, midshaft, and bifurcation. Ostial/midshaft lesions undergoing PCI in ULMCA are associated with better clinical outcomes than bifurcation lesions undergoing PCI because PCI for bifurcation lesions have more complicated operation procedures in conjunction with higher risks along with poorer prognosis compared with PCI for ostial/midshaft lesions.⁷ ⁹ Therefore, it is important to consider the segments of left main coronary arteries when the patients with ULMCA disease select the way of revascularization. Thus far, there are few reports on comparing the long-term outcomes of patients with ostial/midshaft lesions of ULMCA between PCI and CABG. Our study aimed at comparing the longer-term clinical outcomes of consecutive all comers with ostial/midshaft lesions of ULMCA having undergone PCI with DES and CABG.

2 Methods

2.1 Study population

Of a total 922 enrolled patients with ULMCA disease who underwent DES implantation or CABG between January 2003 and July 2009 in Beijing Anzhen Hospital, 259
patients with isolated ostial/midshaft lesions were analyzed (PCI, \( n = 149 \); CABG, \( n = 110 \)). Patients with prior stents implanted at the left main coronary artery were excluded. Patients with prior CABG, concomitant valvular or aortic surgery, or cardiogenic shock were excluded. Those ST-elevation myocardial infarction (STEMI)/non-STEMI patients who were treated with primary PCI or urgent CABG were excluded. Patients with age > 80 years old were also excluded.

### 2.2 Revascularization procedures

The decision to perform PCI or CABG depended on the patient’s co-morbidities and physician’s choice, and/or patient preference. Coronary angioplasty and stent implantation was performed according to the operator’s criteria following the Center’s usual practice, and the choice of sirolimus-, paclitaxel-, or zotarolimus-eluting stents was at the discretion of the physician (zotarolimus-eluting stents became available for clinical use in our Center in September 2006). Before stent implantation, all patients received aspirin (100 mg/d) and either clopidogrel 75 mg/d for three days before the procedure, or a preprocedural loading dose of clopidogrel \( \geq 300 \text{ mg/d} \), and patients were continued on clopidogrel for at least 12 months (75 mg/d) as well as aspirin indefinitely (100 mg/d) after the procedure. CABG was performed using standard bypass techniques.\(^{10}\) Patients received aspirin indefinitely (100 mg/d) after CABG.

### 2.3 ULMCA study outcomes and follow-up

ULMCA disease was defined as left main coronary artery stenosis \( \geq 50\% \) and no bypass grafts to the left anterior descending or left circumflex coronary artery. The endpoints of the study were death, repeat revascularization, myocardial infarction (MI), stroke, the composite of cardiac death, MI, stroke or repeat revascularization (MACCE, the composite of cardiac death, MI, stroke or repeat revascularization). Any death due to proximate cardiac cause (e.g., MI, low-output failure, and fatal arrhythmia), unwitnessed death and death of unknown cause, and all procedure-related deaths, including those related to concomitant treatment, were classified as cardiac death.\(^{11}\) Death was defined as death from any cause. Periprocedural MI (\(< 7 \text{ days after intervention}\)) was defined as elevated serum creatinine kinase-MB isoenzyme five times the upper limit of normal after CABG and three times the upper limit of normal after PCI.\(^{11}\) MI after the periprocedural period was defined as any typical increase and decrease of biochemical markers of myocardial necrosis with one of the following: cardiac symptoms, development of Q waves on electrocardiography, or electrocardiographic changes indicative of ischemia. Stroke, as indicated by neurologic deficits, was confirmed by a neurologist based on imaging studies.

Clinical follow-up was performed at one month, six months, one year, and then annually thereafter. All follow-up data were collected by outpatient or telephone interview and angiographic follow-up. Angiographic follow-up was recommended in the DES group from 8 to 12 months after the procedure or whenever clinically indicated. For patients who underwent CABG, angiographic follow-up was recommended if there were ischemic symptoms or signs during follow-up. Angiographic follow-up was not mandatory. All outcomes of interest were confirmed by source documentation and were adjudicated by the local events committee at Beijing Anzhen Hospital, Capital Medical University.

### 2.4 Statistical analysis

Continuous variables were presented as a mean ± SD or median [interquartile range (IQR)] compared between the study group with independent sample Student’s \( t \)-test or Mann-Whitney \( U \)-test, dependent on if the data followed a normal distribution. Categorical variables were reported as counts and percentages, and differences between the two groups were assessed by means of the Chi-square test. Cumulative event curves were generated with the Kaplan-Meier method and the log-rank test was applied to compare the incidence of the endpoints between patients treated with PCI and CABG. Cox proportional hazards models were used to compare risks of adverse events between patients having undergone PCI with DES as well as CABG and for multivariate adjusting. Cox proportional hazard models were tested with CABG as the reference category. All statistical analyses were performed with the Statistical Package for Social Sciences version 22.0 system for Windows (SPSS Inc., USA). A \( P \) value < 0.05 was considered statistically significant.

### 3 Results

A total of 259 patients were analyzed: 149 underwent PCI with DES and 110 underwent CABG. The flow chart is presented in Figure 1. Baseline clinical characteristics are summarized in Table 1 and demonstrate that the PCI group has prominently lower proportions of prior stroke, left main coronary artery plus triple-vessel disease and chronic total occlusion compared to the CABG group. The left ventricular ejection fraction (LVEF) in the CABG group is lower
compared with the PCI group. Propensity score adjusted baseline clinical characteristics are presented in Table 2. In propensity-matching methods, there was no significant difference in all baseline clinical characteristics, including prior stroke, left main coronary artery plus triple-vessel disease, chronic total occlusion and LVEF of the two groups. The median follow-up was 7.1 years (IQR: 5.3–8.2 years) in the overall patients. Complete follow-up was acquired in 92.7% of the total cohort (93.3% for the PCI group, and 91.8% for the CABG group). During overall follow-up, 30 patients (11.6%) died, of whom 18 (7.0%) died of a cardiovascular cause. A total of 11 (4.2%) suffered a stroke, and 17 (6.6%) suffered a MI. Repeat revascularization was performed in 39 (15.1%).

The crude relative risks are presented in Figure 2 and Table 3. There is no significant difference between PCI and CABG in the occurrence of death (HR: 0.540, 95% CI: 0.259–1.129, P = 0.096), the composite endpoint of cardiac death, MI or stroke (HR: 0.670, 95% CI: 0.349–1.284, P = 0.224), MACCE (HR: 0.983, 95% CI: 0.604–1.602, P = 0.946), MI (HR: 0.908, 95% CI: 0.347–2.374, P = 0.844), stroke (HR: 1.077, 95% CI: 0.323–3.589, P = 0.904), and repeat revascularization (HR: 1.488, 95% CI: 0.770–2.876, P = 0.234).

The multivariable adjusted results are presented in Figure 3 and Table 3. There were also no significant between-group differences in the occurrence of death (HR: 0.727, 95% CI: 0.335–1.578, P = 0.421), the composite endpoint of cardiac death, MI or stroke (HR: 0.730, 95% CI: 0.375–1.421, P = 0.354), MACCE (HR: 1.066, 95% CI: 0.648–1.753, P = 0.801), MI (HR: 1.112, 95% CI: 0.414–2.987, P = 0.833), stroke (HR: 1.875, 95% CI: 0.528–6.659, P = 0.331), and repeat revascularization (HR: 1.590, 95% CI: 0.800–3.161, P = 0.186).

4 Discussion
The main finding of the follow-up study is that PCI for
ostial/midshaft lesions with DES appears to be associated with clinical outcomes comparable to those seen with CABG at long-term follow-up. Event rates for MACCE, the composite endpoint of death, MI, stroke, and target lesion revascularization (TVR) at five-year follow-up.[13] In the MAIN COMPARE substudy (n = 123 in PCI group vs. n = 140 in CABG group), PCI for ostial lesions demonstrated event rates similar to those subjected to CABG for the composite endpoint of death, MI, stroke, and target vessel revascularization (TVR) at five-year follow-up.[13] In the DELTA substudy,[14] a total of 856 patients were included: 482 treated with PCI and 374 with CABG. At a median follow-up period of 1293 days, there was no significant difference in the composite endpoint of all-cause death, MI, and cerebrovascular accident (CVA), all-cause death, the composite endpoint of death and MI, and MACCE between the PCI and the CABG group. Only a higher TVR (HR: 1.94, 95% CI: 1.03–3.64; \( P = 0.039 \)) was observed in the PCI group compared with the CABG group, but target lesion revascularization (\( P = 0.090 \)) had no significant difference in the two groups.

Repeat revascularization rate was higher in PCI with DES compared with CABG in most of the previous studies for patients with ULMCA disease.[3–6] This study shows for ostial/midshaft ULMCA lesions were unknown. Therefore, this study aimed at comparing the long-term outcomes of consecutive patients with ostial/midshaft ULMCA disease having undergone PCI with DES and CABG.

Our study demonstrates that there is no significant difference between PCI and CABG group during the median follow-up of 7.1 years in the event rates for MACCE. At present, there are only two studies comparing PCI and CABG in the treatment of ostial/midshaft ULMCA disease.

As ostial/midshaft lesions in ULMCA are associated with better clinical outcomes than bifurcation lesions by PCI,[3–6] PCI for ostial/midshaft ULMCA lesions receives a Class IIa recommendation compared with Class IIb for bifurcation ULMCA lesions in the guidelines. Considering PCI has several advantages for ostial/midshaft ULMCA lesions, including large lumena diameter and no concerns about plaque shift and subsequent stenosis after stenting, whether CABG was still a standard therapy for ostial/midshaft ULMCA lesions was unknown. Therefore, this study aimed at comparing the long-term outcomes of consecutive patients with ostial/midshaft ULMCA disease having undergone PCI with DES and CABG.

Table 2. Propensity score adjusted baseline clinical and procedural characteristics.

| Variables                          | PCI (n = 90) | CABG (n = 90) | \( p \) |
|------------------------------------|-------------|--------------|--------|
| Age, yrs                           | 61.9 ± 9.7  | 61.0 ± 9.4   | 0.560  |
| Male                               | 66 (73.33%) | 68 (75.56%)  | 0.733  |
| Diabetes mellitus                  | 25 (27.8%)  | 28 (31.1%)   | 0.624  |
| Smoking history                    | 39 (43.3%)  | 42 (46.7%)   | 0.653  |
| Hypertension                       | 51 (56.7%)  | 49 (54.4%)   | 0.764  |
| Family history                     | 10 (11.1%)  | 8 (8.9%)     | 0.619  |
| Dyslipidemia                       | 41 (45.6%)  | 35 (38.9%)   | 0.365  |
| Prior stroke                       | 3 (3.3%)    | 6 (6.7%)     | 0.305  |
| Prior myocardial infarction        | 18 (20.0%)  | 22 (24.4%)   | 0.473  |
| Prior PVD                          | 5 (5.6%)    | 5 (5.6%)     | 1.000  |
| Prior PCI                          | 16 (17.8%)  | 13 (14.4%)   | 0.543  |
| EuroSCORE                          | 4.7 (2.6–6.8)| 4.6 (2.4–6.8)| 0.913  |
| LVEF, %                            | 63%         | 61%          | 0.156  |
| Serum creatinine, μmol/L           | 77.7 (67.3–90.8) | 80.7 (70.5–92.0) | 0.838  |

| Indications for revascularization  | 0.117       |
|-----------------------------------|-------------|
| NSTEMI                             | 1 (1.1%)    | 2 (2.2%)    |        |
| STEMI                              | 5 (5.6%)    | 5 (5.6%)    |        |
| Stable angina                      | 9 (10.0%)   | 19 (21.1%)  |        |
| Unstable angina                    | 72 (80%)    | 64 (71.1%)  |        |
| Silent ischemia                    | 3 (3.3%)    | 0 (0.0)     |        |
| Extent of diseased vessel          | 0.266       |
| LM only                            | 9 (10.0%)   | 7 (7.8%)    |        |
| LM plus single-vessel disease      | 23 (25.6%)  | 17 (18.9%)  |        |
| LM plus double-vessel disease      | 28 (31.1%)  | 23 (25.6%)  |        |
| LM plus triple-vessel disease      | 30 (33.3%)  | 43 (47.8%)  |        |
| Chronic total occlusion            | 19 (21.1%)  | 30 (33.3%)  | 0.065  |
| Complete revascularization         | 56 (62.2%)  | 56 (62.2%)  | 1.000  |

Data were presented as n (%), mean ± SD or median (interquartile range). Complete revascularization: all lesions occupying > 50% diameter of a segment with a reference diameter of ≥ 1.50 mm were treated. CABG: coronary artery bypass grafting; EuroSCORE: European System for Cardiac Operative Risk Evaluation; LM: left main coronary artery; LVEF: left ventricular ejection fraction; NSTEMI: non-ST-elevation myocardial infarction; PCI: percutaneous coronary intervention; PVD: peripheral vascular disease; STEMI: ST-elevation myocardial infarction.
Figure 2. Kaplan-Meier survival curves of clinical outcome in patients with unprotected left main coronary artery disease underwent PCI with drug-eluting stents and CABG. (A): MACCE; (B): cardiac death, MI and stroke; (C): death; (D): MI; (E): stroke; (F): repeat revascularization. CABG: coronary artery bypass grafting; MACCE: major adverse cardiac and cerebrovascular events; MI: myocardial infarction; PCI: percutaneous coronary intervention.

Table 3. Clinical outcomes of patients with unprotected left coronary artery disease having undergone revascularization.

| Outcomes                      | Unadjusted | Multivariate *adjusted |
|-------------------------------|------------|------------------------|
|                               | Unadjusted | Multivariate adjusted  |
|                               | PCI n (%)  | CABG n (%)  | P   | HR (95% CI)  | PCI (%)  | CABG (%)  | P   | HR (95% CI)  |
| MACCE                         | 36 (37.5%) | 30 (34.2%) | 0.946 | 0.983 (0.604–1.602) | 35.8 | 34 | 0.801* | 1.066 (0.648–1.753) |
| Cardiac death/MI/stroke       | 17 (18.9%) | 20 (20.3%) | 0.224 | 0.670 (0.349–1.284) | 13.7 | 18.2 | 0.354§ | 0.730 (0.375–1.421) |
| Death                         | 12 (12.7%) | 18 (29.7%) | 0.096 | 0.540 (0.259–1.129) | 18.6 | 24.6 | 0.421* | 0.727 (0.335–1.578) |
| MI                            | 9 (14.8%)  | 8 (8.5%)  | 0.844 | 0.908 (0.347–2.374) | 8.7 | 7.8 | 0.833* | 1.112 (0.414–2.987) |
| Stroke                        | 6 (9.3%)   | 5 (6.3%)  | 0.904 | 1.077 (0.323–3.589) | 6.5 | 3.5 | 0.331* | 1.875 (0.528–6.659) |
| Repeat revascularization      | 25 (26.8%) | 14 (19.0%) | 0.234 | 1.488 (0.770–2.876) | 25 | 16.5 | 0.186* | 1.590 (0.800–3.161) |

Adjusted factors: *LVEF, prior peripheral vascular disease diabetes mellitus; §LVEF, prior peripheral vascular disease, EuroSCORE; sex, LVEF, serum creatine; age, LVEF, EuroSCORE; LVEF, prior peripheral vascular disease, prior stroke; age, extent of diseased vessel. CABG: coronary artery bypass grafting; EuroSCORE: European System for Cardiac Operative Risk Evaluation; LVEF: left ventricular ejection fraction; MACCE: major adverse cardiac and cerebrovascular events; MI: myocardial infarction; PCI: percutaneous coronary intervention.

Effective as CABG. The DELTA substudy had a relatively short follow-up so that it might fail to detect a higher vein graft occlusion rate over time in the CABG group. Moreover, the occurrence of target lesion revascularization was similar between PCI and CABG in DELTA substudy, indicating other vascular lesions but not ostial/midshaft lesions were responsible for the increase of repeat revascularization.

Recently, there have been two prospective, randomized, open-label studies (EXCEL study and NOBLE study) reporting their outcomes of comparing PCI and CABG in the treatment of ULMCA disease. In the EXCEL study involving patients (n=948 in PCI group vs. n=957 in CABG group) with left main coronary artery disease and low or intermediate SYNTAX scores, PCI with everolimus-eluting stents was non-inferior to CABG with respect to the primary composite endpoint of death, stroke, or myocardial infarction at three years. In the NOBLE study, 1201 patients were randomly assigned, 598 to PCI and 603 to CABG. At a follow-up period of five years, CABG was significantly better than PCI in the rates of MACCE (P = 0.0066).
non-procedural myocardial infarction \(P = 0.0040\) and any revascularization \(P = 0.032\). Whereas there was no significant difference in the rates of all-cause mortality \(P = 0.77\) and stroke \(P = 0.073\). And according to the subgroup analysis of SYNTAX score, whether it is less than 32 or more than 33 of the patients, the PCI group had a higher risk of MACCE than CABG.

As to which is the better revascularization strategy in PCI or CABG for the patients with left main coronary artery disease and low or intermediate SYNTAX scores, EXCEL study and NOBLE study have reached different conclusions. However, it is worth noting that the inclusion criteria of patients, the primary endpoint, follow-up duration and the type of DES are different, so the results of the two studies should not be compared directly. In the NOBLE study, treatment for left main coronary artery disease involved the bifurcation in 508 (88%) of 579 patients in the PCI group, which is significantly different compared with our study. Ostial/midshaft lesions in ULMCA are associated with better clinical outcomes than bifurcation lesions undergoing PCI in previous studies,\(^{[4–6]}\) that is why our study has different clinical outcomes compared with the NOBLE study.

This study still has some limitations. Firstly, a major limitation is that our study is a non-randomized and observational study. Although propensity score analyses are known to be a valuable method for taking into account the potential confounding factors attributable to between-groups imbalances, it is not possible to control all variables. Secondly, there is a lack of subgroup analysis according to SYNTAX score. Finally, so far, although the study has the longest follow-up time than similar studies, the rate of loss to follow-up has increased, which may have some impact on the analysis of the results of the study. And the sample size was relatively small in our study, thus our analysis was underpowered to detect clinically significant differences in repeat revascularization and composite outcomes.

In conclusion, this study demonstrates that PCI with DES for ostial/midshaft lesions of ULMCA disease is as safe and effective as CABG during the median follow-up of 7.1 years.

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