Characteristics and outcomes of patients with percutaneous coronary intervention for unprotected left main coronary artery disease: a Hong Kong experience

KY Lo *, CK Chan

Objective: To evaluate the intermediate-term outcomes of patients with unprotected left main coronary artery stenosis who were treated with percutaneous coronary intervention in Hong Kong.

Design: Historical cohort.

Setting: A regional hospital in Hong Kong.

Patients: Patients with unprotected left main coronary artery disease undergoing stenting with bare-metal stents or drug-eluting stents between January 2008 and September 2011.

Main outcome measures: Incidence of restenosis and major adverse cardiac and cerebrovascular events including cardiac death, non-fatal myocardial infarction, stroke, and target lesion revascularisation.

Results: Of the 111 patients included in the study, 86 received drug-eluting stents and 25 received bare-metal stents. Procedural success was achieved in 98.2% of cases. Angiographic follow-up was available in 83.8% of cases and restenosis rate was significantly lower with drug-eluting stents than with bare-metal stents (14.0% vs 40.0%; P=0.004). After a mean clinical follow-up of 26.1 (standard deviation, 12.6) months, the incidences of cardiac death (5.8% vs 16.0%; P=0.191) and non-fatal myocardial infarction (3.5% vs 8.0%; P=0.262) were similar between drug-eluting stents and bare-metal stents. However, the risks of target lesion revascularisation (9.3% vs 32.0%; P=0.001) and major adverse cardiac and cerebrovascular events (19.8% vs 44.0%; P=0.004) were significantly lower with drug-eluting stents than with bare-metal stents.

Conclusions: Performing percutaneous coronary intervention for unprotected left main coronary artery disease was safe and feasible in selected patients with high procedural success rate. The incidence of major adverse cardiac and cerebrovascular events in patients receiving drug-eluting stents remains low after intermediate-term follow-up. Compared with bare-metal stents, drug-eluting stents were associated with a lower need for repeating revascularisation without increasing the risk of death or myocardial infarction in patients with unprotected left main coronary artery disease.

Introduction

Significant unprotected left main coronary artery (ULMCA) disease occurs in 5% to 7% of patients undergoing coronary angiography. Coronary artery bypass graft (CABG) surgery has been the standard of care for the treatment of ULMCA disease, and percutaneous coronary intervention (PCI) is reserved for patients who are poor surgical...
以香港的經驗來探討冠狀動脈介入治療術應用於無保護左主冠狀動脈疾病患者的特徵和成果

盧家業，陳志堅

目的：探討冠狀動脈介入治療術（PCI）應用於無保護左主冠狀動脈疾病（ULMCA）患者的中期結果。

設計：歷史性隊列研究。

安排：香港一所分區醫院。

患者：曾於2008年1月至2011年9月期間接受置入裸金屬支架（BMS）或滲藥支架（DES）的ULMCA患者。

主要結果測量：血管再狹窄和主要不良心臟及腦血管事件，包括心臟性猝死、非致命性心肌梗塞、中風和病灶再重建的發生率。

結果：參與研究的111名患者中，86人接受了DES，25人接受了BMS。手術成功率為98.2%。血管造影跟進率為83.8%，DES的血管再狹窄率顯著較BMS低（14.0%比40.0%；P=0.004）。在平均26.1（標準差12.6）個月的臨床跟進後，使用DES或BMS的心臟性猝死（5.8%比16.0%；P=0.191）或非致命性心肌梗塞（3.5%比8.0%；P=0.262）的發生率較低。然而，使用DES比BMS的病灶再重建（9.3%比32.0%；P=0.001）和主要不良心臟及腦血管事件（19.8%比44.0%；P=0.004）的風險均顯著下降。

結論：在選擇性ULMCA患者中進行PCI是安全和可行的，手術成功率亦非常高。患者在接受DES後的中期跟進中，主要不良心臟及腦血管事件發生率仍然偏低。ULMCA患者中，在不增加死亡或心肌梗塞的前提下，與BMS相比，DES更能降低目標血管再重建的風險。

Methods

Study population

This was a single-centre retrospective study performed to determine the outcomes of patients who had undergone ULMCA PCI. Between January 2008 and September 2011, 111 patients with ULMCA disease (defined as >50% stenosis) received PCI with either DES or BMS implantation in the United Christian Hospital, Hong Kong. The cohort included unselected consecutive patients who presented with stable angina, acute coronary syndrome, or cardiogenic shock. Therefore, PCI could be performed in an elective or emergency setting (ie an all-comers basis). Moreover, there was no on-site surgical support in our centre.

The decision of performing PCI instead of CABG surgery was based on coronary anatomy, haemodynamic conditions, surgical risks, and patients’ preference. Both interventional cardiologists and cardiac surgeons were involved in making the decision.

Unprotected left main coronary artery PCI was performed using standard techniques. Heparin 70 to 100 units per kg was administered before PCI. Intracoronary balloon pump counterpulsation, intravascular ultrasound (IVUS) or glycoprotein IIb/IIIa inhibitors was used at the discretion of the operators. All patients were pre-treated with 80 to 160 mg aspirin and a loading dose of 300 to 600 mg clopidogrel or 75 mg maintenance dose of clopidogrel at least 7 days before the procedure. After PCI, aspirin 80 to 160 mg daily and clopidogrel 75 mg daily, for 1 month after BMS and 1 year after DES implantation, were prescribed. For ostial and shaft left main stenosis, single stent placement was preferred. Patients with bifurcation stenosis underwent one of the four types of bifurcation stenting techniques (T-stenting, T-stenting and small protrusion technique, Culotte technique, or Crush technique) at the operators’ discretion. Routine surveillance angiography was arranged for all patients 6 to 9 months after the index procedure, except in patients who refused, or with high risk for coronary angiogram. Baseline demographic, procedural, angiographic, and clinical outcome data were collected.

Definitions

Unprotected left main coronary artery stenosis was defined as >50% stenosis without any patent graft to the left anterior descending artery or left circumflex artery. Procedure was defined as successful if revascularisation was achieved in the target lesion with <30% residual stenosis in angiography and patient was discharged from hospital without any of these events: death, Q-wave myocardial infarction (MI), stroke, and target lesion revascularisation (TLR).
Follow-up was completed in June 2012. Endpoints were restenosis and major adverse cardiac and cerebrovascular events (MACCE) including cardiac death, non-fatal MI, stroke, and TLR. Restenosis was defined as >50% luminal narrowing at the left main segment (stent and 5 mm proximal and distal) which was demonstrated at the follow-up angiography, regardless of patient symptoms.

Death was classified as cardiac or non-cardiac. Deaths that could not be classified were considered cardiac. Cardiac death was defined as death from any cardiac cause (eg MI, heart failure, or arrhythmia) or sudden unexplained death without an explanation. Non–Q-wave MI was defined as elevation of total creatine kinase 2 times above the upper normal limit in the absence of pathological Q wave. Target lesion revascularisation was defined as any revascularisation performed on the treated left main segment. Chronic kidney disease was documented if the serum creatinine level was >200 μmol/L or was put on renal replacement therapy. Stent thrombosis was defined as definite and probable according to the Academic Research Consortium.4

**Statistical analyses**

Categorical variables reported as percentages and comparisons between groups were based on the Chi squared test or Fisher’s exact test. Continuous variables were reported as mean ± standard deviation, and differences were assessed with the independent sample t test or Mann-Whitney test.

Cumulative event curves were calculated by the Kaplan-Meier method and compared by the log-rank test. A P value of <0.05 was considered statistically significant. Statistical analyses were performed with the use of the Statistical Package for the Social Sciences (Windows version 15.0; SPSS Inc, Chicago [IL], US).

**Results**

**Patient characteristics**

Baseline clinical, and angiographic and procedural characteristics of the 111 patients are summarised in Table 1 and Table 2, respectively.

Overall, 86 (77.5%) patients were treated with DES, and 25 (22.5%) received BMS. The two groups shared similar clinical and angiographic characteristics. More than 90% of patients had left ventricular ejection fraction of ≥35%. The majority of patients had distal left main disease (81.4% in DES group and 72.0% in BMS group). Only a minority of patients (5.4%) had isolated left main disease, whereas 72.9% had left main and at least two-vessel disease. A high rate of IVUS use was observed in the cohort (84.7%). Final kissing balloon dilatation was performed in >50% of the patients and in all patients with two-stent approach. Other adjuvant PCI devices such as rotational atherectomy were rarely required in this cohort.
Of the 86 patients who received DES at the left main segment, 24 (27.9%) received first-generation DES, 56 (65.1%) received second-generation DES, and six (7.0%) received both types.

Outcomes

Procedural success was achieved in 109/111 (98.2%) cases. There was one death (0.9%) and one stroke (0.9%) but there was no Q-wave MI, stent thrombosis, or urgent repeat revascularisation events during hospitalisation (Table 3).

The mean duration of clinical follow-up was 26.1 ± 12.6 months. Table 4 depicts the incidence of adverse outcomes at the end of follow-up. There was no significant difference between the DES and BMS groups in the cumulative incidences of cardiac death (5.8% for DES vs 16.0% for BMS; P=0.191) or non-fatal MI (3.5% vs 8.0%; P=0.262). Compared with BMS, use of DES was associated with significantly lower risks of TLR (9.3% vs 32.0%; P=0.001) and MACCE (19.8% vs 44.0%; P=0.004) [Fig]. Target lesion revascularisation was ischaemia-driven in 4/16 (25%) patients; in the remaining 12/16 (75%) patients, TLR was driven by restenosis.

### TABLE 2. Angiographic and procedural characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All patients (n=111)</th>
<th>DES (n=86)</th>
<th>BMS (n=25)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intra-aortic balloon pump</td>
<td>6 (5.4)</td>
<td>4 (4.7)</td>
<td>2 (8.0)</td>
<td>0.615</td>
</tr>
<tr>
<td>Glycoprotein IIb/IIIa inhibitors</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0.308</td>
</tr>
<tr>
<td>Lesion type</td>
<td>23 (20.7)</td>
<td>16 (18.6)</td>
<td>7 (28.0)</td>
<td></td>
</tr>
<tr>
<td>Distal</td>
<td>88 (79.3)</td>
<td>70 (81.4)</td>
<td>18 (72.0)</td>
<td></td>
</tr>
<tr>
<td>Two-stent techniques</td>
<td>39 (35.1)</td>
<td>31 (36.0)</td>
<td>8 (32.0)</td>
<td>0.709</td>
</tr>
<tr>
<td>Extent of diseased vessel</td>
<td>63 (56.8)</td>
<td>50 (58.1)</td>
<td>13 (52.0)</td>
<td>0.137</td>
</tr>
<tr>
<td>Left main only</td>
<td>1.3 ± 0.4</td>
<td>1.3</td>
<td>1.2</td>
<td>0.089</td>
</tr>
<tr>
<td>Plus 1-vessel disease</td>
<td>2.0 ± 0.7</td>
<td>2.0 ± 0.7</td>
<td>1.8 ± 0.7</td>
<td>0.219</td>
</tr>
<tr>
<td>Plus 2-vessel disease</td>
<td>3.5 ± 0.4</td>
<td>3.4 ± 0.4</td>
<td>3.7 ± 0.6</td>
<td>0.008</td>
</tr>
<tr>
<td>Plus 3-vessel disease</td>
<td>3.0 ± 0.4</td>
<td>3.0 ± 0.5</td>
<td>2.8 ± 0.3</td>
<td>0.273</td>
</tr>
<tr>
<td>Right coronary artery disease</td>
<td>21.2 ± 7.9</td>
<td>22.6 ± 7.5</td>
<td>16.3 ± 7.4</td>
<td>0.937</td>
</tr>
<tr>
<td>Total No. of stents in left main</td>
<td>17.4 ± 6.0</td>
<td>17.5 ± 6.0</td>
<td>16.3 ± 7.5</td>
<td>0.823</td>
</tr>
<tr>
<td>Stent size at main branch (mm)</td>
<td>3.6 ± 0.6</td>
<td>3.6 ± 0.4</td>
<td>3.9 ± 1.0</td>
<td>0.082</td>
</tr>
<tr>
<td>IVUS use</td>
<td>94 (84.7)</td>
<td>77 (89.5)</td>
<td>17 (68.0)</td>
<td>0.008</td>
</tr>
<tr>
<td>Post-dilatation</td>
<td>94 (84.7)</td>
<td>75 (87.2)</td>
<td>19 (76.0)</td>
<td>0.171</td>
</tr>
<tr>
<td>Kissing balloon</td>
<td>65 (58.6)</td>
<td>51 (59.3)</td>
<td>14 (56.0)</td>
<td>0.768</td>
</tr>
<tr>
<td>Rotablation</td>
<td>3 (2.7)</td>
<td>3 (3.5)</td>
<td>0</td>
<td>0.461</td>
</tr>
</tbody>
</table>

### TABLE 3. Incidence of in-hospital major adverse cardiac and cerebrovascular events

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>1 (0.9%)</td>
</tr>
<tr>
<td>Non-fatal MI</td>
<td>3 (2.7%)</td>
</tr>
<tr>
<td>Stroke</td>
<td>1 (0.9%)</td>
</tr>
<tr>
<td>TLR</td>
<td>0</td>
</tr>
</tbody>
</table>

### TABLE 4. Cumulative incidence of major adverse cardiac and cerebrovascular events at the end of follow-up

<table>
<thead>
<tr>
<th>No. (%) of patients</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>DES (n=86)</td>
<td></td>
</tr>
<tr>
<td>Cardiac death</td>
<td>5 (5.8%)</td>
</tr>
<tr>
<td>Non-fatal MI</td>
<td>3 (3.5%)</td>
</tr>
<tr>
<td>Stroke</td>
<td>2 (2.3%)</td>
</tr>
<tr>
<td>TLR</td>
<td>8 (9.3%)</td>
</tr>
<tr>
<td>MACCE</td>
<td>17 (19.8)</td>
</tr>
<tr>
<td>BMS (n=25)</td>
<td></td>
</tr>
<tr>
<td>Cardiac death</td>
<td>4 (16.0)</td>
</tr>
<tr>
<td>Non-fatal MI</td>
<td>2 (8.0%)</td>
</tr>
<tr>
<td>Stroke</td>
<td>0</td>
</tr>
<tr>
<td>TLR</td>
<td>8 (32.0)</td>
</tr>
<tr>
<td>MACCE</td>
<td>11 (44.0)</td>
</tr>
</tbody>
</table>

Abbreviations: BMS = bare-metal stents; DES = drug-eluting stents; IVUS = intravascular ultrasound

* P values were calculated by the Kaplan-Meier method and compared by the log-rank test.
identified at surveillance angiography after the index procedure. Therefore, the crude rate of ischaemia-driven TLR was only 4/111 (3.6%) in the overall cohort. The mean timing of TLR was 7.6 ± 4.3 months (range, 2-16 months) after the index procedure.

Of 111 cases, 93 (83.8%) underwent routine surveillance angiography 6 to 9 months after PCI; binary restenosis occurred in 22/111 (20%) cases. Restenosis occurred predominantly in patients with distal left main coronary artery disease (19/22 [86%]); and more than half of them (12/22 [55%]) had isolated focal restenosis involving the ostium of the left circumflex artery only. Restenosis occurred less frequently with DES than with BMS (12/86 [14.0%] vs 10/25 [40.0%]; P=0.004).

For stent thrombosis, the event rate was extremely low across the whole cohort. One patient receiving BMS implantation developed subacute stent thrombosis after hospital discharge (which resulted in sudden cardiac death). There was no stent thrombosis of any forms in the DES group.

**Discussion**

The principal findings of the present study were: (1) performing PCI for ULMCA disease was safe and feasible in selected patients with high procedural success rate (98.2%); (2) after an intermediate-term follow-up of 26.1 months, the incidence of MACCE in patients receiving DES implantation was similar

<table>
<thead>
<tr>
<th>FIG. Kaplan-Meier curves for (a) cardiac death, (b) non-fatal MI, (c) TLR, and (d) MACCE, stratified by DES and BMS respectively (P values are for log-rank tests)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Descriptions: BMS = bare-metal stents; DES = drug-eluting stents; MACCE = major adverse cardiac and cerebrovascular events; MI = myocardial infarction; TLR = target lesion revascularisation</td>
</tr>
</tbody>
</table>

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**a)**

Event-free survival against follow-up (months)

- **DES**
- **BMS**

P=0.191

**b)**

Event-free survival against follow-up (months)

P=0.262

**c)**

Event-free survival against follow-up (months)

P=0.001

**d)**

Event-free survival against follow-up (months)

P=0.004
to that reported in recent major international clinical trials including the SYNTAX trial; (3) compared with BMS, the use of DES was associated with a lower risk of restenosis and repeat revascularisation without an increased risk of death or MI.

Historically, CABG has been regarded as the gold standard of treatment for ULMCA disease. Clinical outcomes after PCI for ULMCA stenosis have been shown to vary widely, according to patients’ clinical and angiographic features. The high procedural success rate in our study further confirms the technical feasibility of treating ULMCA lesions with the current PCI techniques in the absence of on-site surgical support.

Promising results were reported from randomised trials comparing first-generation DES versus CABG. In the SYNTAX trial, patients were stratified according to the presence of ULMCA disease and randomised to CABG (n=348) or PCI with paclitaxel-eluting stents (n=357). In the ULMCA subgroups, MACCE at 12 months was comparable between patients treated with PCI and CABG. Moreover, although the rate of repeat revascularisation among patients with ULMCA disease was significantly higher in the PCI subgroup, this result was offset by a significantly higher rate of stroke in the CABG subgroup.

The SYNTAX trial included patients with heterogeneous angiographic characteristics in the left main subgroup (13% with isolated left main coronary artery disease, 20% with left main plus single-vessel disease, 31% with two-vessel disease, and 37% with triple-vessel disease). Although calculation of the SYNTAX score was not incorporated in routine clinical practice at the time of our study, our cohort demonstrated similar heterogeneity and complexity (Table 2).

We report an intermediate-term outcome (mean follow-up of approximately 26 months) for patients with ULMCA PCI, and our results were comparable with those of the SYNTAX trial. At 2 years, the SYNTAX trial reported a MACCE rate of 22.9% in the left main subgroup (including death from any causes, MI, stroke, or repeat revascularisation), which was comparable with the incidence of 19.8% reported in our study.

The incidence of TLR in the subgroup of DES in our registry (9.3%) might be lower than that reported in the SYNTAX trial at 2 years (any revascularisation, 17.3%) and it might be due to inclusion of second-generation DES in two thirds of the patients treated with DES in our registry. The higher rate of IVUS use for optimisation (approximately 90% of cases using DES in our cohort) might also be another reason. One of the main limitations of the SYNTAX trial was thought to be the lack of IVUS use for ULMCA disease in the PCI group. Clinical trials have shown that patients whose coronary interventions are guided by IVUS have larger post-procedure stent areas and significant reductions in TLR than those undergoing angiography-guided PCI only. Registry data have also shown a trend towards reduced mortality in IVUS-guided ULMCA PCI.

It is worth considering that SYNTAX did not have an ‘all-comers’ design, where patients with acute coronary syndrome and cardiogenic shock were excluded. Our registry did have an ‘all-comers’ design, by including patients presenting with stable angina, acute coronary syndrome, ST-elevation and non–ST elevation MI, as well as cardiogenic shock. This might reflect a more ‘real-world’ situation in daily clinical practice. Despite the inclusion of patients with higher clinical risk, the incidence of events remained low in our study during the index hospital admission and upon medium-term follow-up.

In the BMS subgroup, we reported a high incidence of restenosis (40%) and TLR (32%). To date, no randomised controlled trials have been performed using BMS in ULMCA PCI. The longest follow-up available in the literature was from the ASAN-MAIN (ASAN Medical Center–Left MAIN Revascularization) Registry (n=350: BMS, n=100; CABG, n=250), which also reported a high rate of TLR (24.9%) after long-term follow-up. Although the incidence of restenosis and TLR might be over-represented due to the use of routine surveillance angiography in our study, the results suggest that the use of BMS was not favoured.

As mentioned, the situation in Hong Kong is unique in that the public health care system does not cover the cost of using DES in ULMCA disease. Patients with financial difficulty can only choose PCI with BMS or CABG. Because of this restraint, the proportion of patients with ULMCA disease in Hong Kong treated with BMS probably exceeds that in other developed countries. In our opinion, a review of this health care policy is necessary.

In our cohort, the rate of cardiac deaths in the BMS group was relatively high (16.0% in BMS vs 5.8% in DES). While this could be a finding by chance, it could be attributed to a multitude of reasons. Compared with the DES group, a higher proportion of patients presented with acute coronary syndrome including cardiogenic shock in the BMS group (Table 1). Moreover, there was a higher proportion of patients with chronic renal failure or prior stroke in the BMS group (Table 1). Such differences might explain the relatively high cardiac mortality rates in the BMS group. Another postulation is that patients who received BMS implantation may have come from a lower socio-economic class, which might have an impact on their health status and outcome.

The role of routine surveillance angiography remains unclear and controversial. Repeat angiography is suggested because patients with
left main restenosis are considered to be at high risk for adverse events. However, angiography is unable to predict when a patient might be prone to stent thrombosis, and angiography might be associated with a non-negligible risk in patients who have undergone left main stenting.13 Therefore, the 2009 focused update does not recommend routine angiographic follow-up after ULMCA stenting.14 Our result is in line with the guideline as the angiographic restenosis rate in the DES group was low. This would have been even lower had a clinically driven approach been used. Given the low event rate in our cohort, we also recommend that routine surveillance angiography is not necessary and patients can be followed up clinically.

An interesting point is that the risk of stent thrombosis was extremely low (<1%) given the standard prescription of 1-year dual antiplatelet therapy with aspirin and clopidogrel in this group of high-risk patients with multiple complex stenting. No laboratory or genetic assessment was performed on the degree of platelet function inhibition.

The present study had several limitations. Firstly, it was a single-centre non-randomised retrospective study, which might have significantly affected the results due to unmeasured confounders, procedure bias, or detection bias. Secondly, angiographic results were based on visual angiographic or IVUS assessment and a standardised core laboratory anatomical examination was not performed. Thirdly, incomplete angiographic follow-up might underestimate the incidence of restenosis. Finally, this study included high-risk patients with complex coronary anatomy who underwent PCI (including patients who refused bypass surgery); these patients were prone to poor clinical outcomes. Therefore, these results might not be generalised to all populations with ULMCA stenosis, especially those with low-to-intermediate SYNTAX score.

Conclusions
These are the largest available data on ULMCA PCI in Hong Kong. Performing PCI for ULMCA disease was safe and feasible in selected patients with high procedural success. Despite the inclusion of high-risk patients, the incidence of MACCE after intermediate-term follow-up in patients receiving DES implantation was similar to that reported in major clinical trials. Compared with BMS, DES was associated with a reduced need for repeat revascularisation without increasing the risk of death or MI for patients with ULMCA disease. Our result suggest that BMS should not be encouraged due to the high incidence of restenosis and TLR.

Declaration
The authors report no financial relationships or conflicts of interest regarding the content herein.

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References