Clinical and angiographic results of angioplasty with a paclitaxel-eluting stent for unprotected left main coronary artery disease (a study of 101 consecutive patients)

Résultats cliniques et angiographiques de l’angioplastie avec stent au paclitaxel des sténoses du tronc commun coronaire gauche (à propos de 101 patients consécutifs)

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Summary

Background. — After coronary stenting with drug eluting stents, long-term clinical outcome of unprotected left main coronary artery disease is unknown, even large scale registries or randomised trials with coronary artery bypass graft are ongoing.

Aims. — To report clinical and angiographic results of paclitaxel-eluting stent implantation for left main coronary artery stenosis (a series of 101 consecutive patients).

Methods. — This report is a prospective study performed to evaluate the immediate and mid-term clinical and angiographic outcomes of patients undergoing paclitaxel-eluting stent (PES) implantation for unprotected left main coronary artery (LMCA) stenosis. From January 2004 to December 2005, 101 consecutive patients were stented with paclitaxel-eluting stents (the provisional T stenting technique followed by Kissing balloon for distal left main vessel disease).

Results. — Mean age was 68.9±11.07 years. 73.3% of patients were male. Acute coronary syndrome was present in 65% of patients, of whom 22.8% had ST elevation. Distal left main trunk lesions were present in 87.1% of cases. Three-vessel disease represented 7% of cases. Angiographic success was obtained in 97.03% of patients with an acute gain of 2.18±0.53mm. GPIIb/IIIa inhibitors were used in only 8.9% of cases. Hospital stay was 7.6 ± 3.7 days. In-hospital complications were present in 7.9%, with a hospital mortality rate of 2%.

At six month follow-up, the rate of target lesion revascularization (TLR) was 3%, and the rate for major adverse cardiac events (MACE) was 8.9%. Angiographic control was performed in 88.1% and a late loss of 0.1mm (0.04-0.2mm) was noted. Re-stenosis occurred in 4 patients (4.5% of cases). 4 patients (4%) died, including 2 from cardiac causes.

KEYWORDS

Left main; Angioplasty; Drug-eluting stent; Re-stenosis.

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Conclusion. — Paclitaxel-eluting stent implantation for unprotected left main coronary disease appears to be safe with high procedural success rate and a low re-stenosis rate at six month-follow-up.

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Résumé
Justification. — L’histoire naturelle des dilatations avec stents des lésions du tronc commun de la coronaire gauche reste mal connue, en l’absence d’étude à large échelle et de comparaison randomisée à la chirurgie.

Objectifs. — Cette étude prospective rapporte les résultats immédiats et à moyen terme de l’angioplastie avec stent au Paclitaxel du tronc commun coronaire gauche (TCG).


Résultats. — L’âge moyen est de 68.9 ± 11.07 ans avec une prédominance masculine (73.3%). Un tableau de syndrome coronarien aigu est présent dans 65% des cas dont 22.8% avec élévation du segment ST. Les lésions de bifurcation du TCG distal sont présentes dans 87.1% des cas. L’atteinte tritronculaire représente 7% des cas. Le succès angiographique est obtenu dans 97% des cas avec un gain précoce de 2.18±0.53mm. Le recours aux anti-Gp IIb-IIIa a été nécessaire dans 8.9% des cas. La durée d’hospitalisation est de 7.6±3.7 jours. Les complications hospitalières sont présentes dans 7.9% dont 4% d’origine cardio-vasculaire. Le taux de mortalité hospitalière est de 2%. A 6 mois, le taux de revascularisation de la lésion cible est de 3% et celui des événements cardio-vasculaires majeurs est de 8.9%. Le contrôle angiographique (88.1%) retrouve une perte tardive de 0.1 (0.04-0.2) mm avec 4 cas de resténose soit 4.5%. 4 décès (4%) surviennent dont 2 d’origine cardiaque.

Conclusion. — L’angioplastie avec stent actif au paclitaxel du TCG paraît une technique fiable avec un taux de succès initial important et un faible taux de resténose à 6 mois.

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Materials and methods
Patients

From January 2004 to December 2005, 101 consecutive patients with unprotected LMCA stenosis underwent percu-
taneous dilatation with implantation of a paclitaxel-eluting stent, representing 2.5% of overall activity. The LMCA was considered to be unprotected when there was no coronary bypass supplying the LAD or circumflex artery (CX).

The inclusion criteria were symptomatic lesions or angiographic stenoses > 50% with documented myocardial ischemia. The decision to perform percutaneous angioplasty was taken if the coronary anatomy was favourable and the patient or referring physician requested it, in the absence of surgical contraindications or significant comorbidity. Patients with a contraindication to platelet anti-aggregant treatment were excluded. In keeping with the Helsinki principles, this study was approved by the local ethics committee, and clear written consent was obtained for each patient.

**Procedure**

All of the patients received 160mg aspirin daily for life, and a loading dose of clopidogrel 300mg 12 hours before the procedure if they had not already received it, followed by 75mg a day for 6 months in the absence of any instability. In cases of acute coronary syndrome this double anti-aggregation therapy was continued for a year. Anticoagulation with a bolus of 55 U/kg of unfractionated heparin was administered during the procedure, keeping the ACT > 250 seconds. The use of GPIIbIIIa inhibitors was left to the discretion of the individual operators.

The various angioplasty techniques used were carefully noted (pre-dilatation of the stenosis with a balloon, or rotablator, followed by stenting; direct stenting; provisional T stenting with kissing balloon). In the case of LMCA bifurcation angioplasty, provisional T stenting was performed as follows: angioplasty with positioning of the stent in the distal LMCA and the ostium of one of the two coronaries (LADO or CXO), known as the mother branch (MB); the ostium of the other coronary or daughter branch (DB) was then dilated with a kissing balloon across the stent mesh after having changed the guides between the two arteries. In cases where the result was incomplete, a second endoprosthesis was positioned, either at the distal LMCA and the ostium of the second branch (Y stent), or solely at the ostium of the second branch (T stent); the procedure was finished with a final kissing balloon, with the balloons of both stents being inflated simultaneously.

**Quantitative coronary angiography**

The coronary angiography acquisition and analysis was performed using a digital system (MEDICAL QCA/CMS MEDIS Imaging System). After administration of 1mg of molsidomine, the images were recorded and then transferred to CD-ROM. The stented coronary segment was then analysed. For angioplasty of the LMCA-LADO-CXO bifurcation, the stented segment of the MB (LMCA-LADO or LMCA-CXO) was analysed as well as the ostium of the non-stented daughter branch.

Quantification of the segments in two orthogonal projections was performed whenever possible, before and after angioplasty, and also during angiographic control at 6 months. The measurements taken were the minimum luminal diameter (MLD), reference vessel diameter (RVD), stenosis diameter percentage (SD%), and stenosis length (SL). After angioplasty, quantification was carried out for the residual stenosis percentage (post-dilatation SD%), post-dilatation MLD, and the acute gain (AG), defined as post-dilatation MLD less pre-dilatation MLD. A stenosis percentage less than 30% following dilatation was used to define primary success. At 6 months, quantification was carried out for SD%, MLD and late loss (LL), defined as the difference between post-dilatation MLD at month 0 and month 6. A reduction in luminal diameter greater than or equal to 50% (including complete obstruction) at six months was considered as significant re-stenosis.

**Modes of follow-up**

All of the patients were evaluated clinically at 1 and 3 month consultations, and again in hospital at 6 months, or by telephone for the patients who were followed up for more than 8 months. A check angiography was carried out systematically during hospitalisation or earlier in the presence of clinical symptoms or evidence of myocardial ischemia.

**Definitions**

Angiographic success was defined as grade 3 TIMI flow, a degree of residual stenosis determined by quantitative angiographic analysis < 30% and the absence of major adverse cardiac events (MACE). Myocardial infarction was defined as an elevation of creatinine kinase more than twice normal with elevation of the CK-MB fraction. Angiographic re-stenosis was defined as more than 50% stenosis in the mother or daughter branch at angiographic control after 6 months.

**Statistical analysis**

The results are presented as a mean and standard deviation of the mean for quantitative variables. Qualitative variables are expressed as a percentage. For continuous variables the data are presented as mean deviation and inter-quartile range. Statistical analysis was performed using SAS statistical software (SAS/STAT user’s guide, release 6.12; SAS Institute Inc).

**Results**

**Patients’ clinical characteristics**

The baseline clinical and angiographic data are summarized in Table 1. A total of 101 patients, predominantly male (73.3%) underwent LMCA dilatation. The mean age was 68 ± 11.07 years, ranging from 34 to 87 years. Diabetes was present in 23.8% of our patients. 20% had already had a revascularization procedure, either CABG or angioplasty. 65% underwent an emergency procedure in the context of acute coronary syndrome (ACS), of whom 22.8% had ACS with ST elevation. 73.7% of our patients had a medium or increased Euroscore risk. The left ventricular ejection fraction was reduced (<40%) in 28.2% of cases. The mean hospital stay was 7.6 ± 3.7 days. In-hospital complications occurred in 7.9%, including 4% which were of cardiovascular origin. The hospital mortality rate was 2%.

**Patients’ angiographic characteristics : Table 2**

A radial approach was used in 9.9% of cases, and a femoral approach in 88.1%. The LMCA lesions were mostly distal at the bifurcation (87.1%). Ostial lesions represented only
11.9% and median lesions 1% of cases. The distal lesions usually encompassed the ostium of the left anterior descending artery (LADO) either alone (57.3%) or in conjunction with the ostium of the circumflex artery (CXO) (19.1%). In 2.3% of cases the stenosis involved the trifurcation of the distal LMCA. Coronary involvement was diffuse in 25% of cases (two-vessel disease: 18%, three-vessel disease: 7%).

**Procedural results**

The procedural characteristics are summarized in Table 3. In 79.2% of cases dilatation was performed by direct sten-
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Pre-dilatation for tight stenoses or a very calcified angiographic appearance was only necessary in 20.8% of cases. The endoprosthesis was positioned on the LADO in 78.6% of patients. Among the patients with bifurcation lesions, a final kissing balloon was carried out in 83.5% and a double kissing balloon (simultaneous inflation of 3 balloons) was necessary in 5.9% of patients. The technique of 2 stents implanted in the form of a Y was carried out in 2% of cases. The mean diameter of the stents was 3.45 ± 0.44mm and the mean inflation pressure was 15 atm. GPIIbIIIa inhibitors were only required in 9% of cases.

The overall success rate was 97%. Three failed angioplasties (3%) were recorded (1 stent thrombosis, 1 dissection, 1 no-reflow). Two in-hospital deaths occurred (1 stent thrombosis, and 1 retroperitoneal hematoma). GPIIbIIIa inhibitors were only required in 9% of cases.

The mean diameter of the vessels increased after angioplasty from 1.2 ± 0.48 to 3.37 ± 0.45mm; and the stenosis percentage decreased from 62.4 ± 8.2 to 11 ± 10.2%. The acute gain was 2.18 ± 0.53mm.

### Six-month results

Angiographic control at 6-months was performed in 89 patients (88.1%). 12 patients were not checked (4 deaths, 1 lost to follow-up, 7 due to refusal or co-morbidity). Quantitative angiographic analysis is presented in Table 4. The degree of stenosis was 14.3 ± 8.5% and the late loss was 0.1mm (0.04 - 0.2mm). 4 cases of re-stenosis occurred in the daughter branches in 3 patients, and was diffuse in a fourth.

### 9-month results

The mean duration of follow-up was 12.15 ± 3.18 months, and the clinical follow-up rate was 99.0% (1 patient lost to follow-up). A total of four patients died (two from cardiac causes): in addition to the two in-hospital deaths, there was one sudden death at 6 months, and one death from septic shock associated with HIV infection at 5 months. The cumulative rate of major adverse cardiac events (Table 6), including death from all causes, myocardial infarction, heart failure, target lesion revascularization was 8.9%, with a revascularization rate of 3%. The overall mortality rate was 4%.

### Characteristics of patients with re-stenosis

Among the four patients with re-stenosis, three were asymptomatic. The LMCA lesion was distal in all four cases, with three-vessel disease in two cases. A T-stenting angioplasty had been performed in three cases, with direct stenting in all three. Three patients underwent revascularization (1 CABG and 2 angioplasties).

### Table 4 Baseline and post-procedure angiographic data

<table>
<thead>
<tr>
<th></th>
<th>MB</th>
<th>DB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reference vessel diameter (mm)</td>
<td>3.39 ± 0.42</td>
<td>3.10 ± 0.54</td>
</tr>
<tr>
<td>Lesion length</td>
<td>7.4 ± 2.8</td>
<td>6.8 ± 2.14</td>
</tr>
<tr>
<td>Minimum luminal diameter (mm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Basal</td>
<td>1.2 ± 0.48</td>
<td>2.33 ± 0.39</td>
</tr>
<tr>
<td>Final</td>
<td>3.37 ± 0.45</td>
<td>3.05 ± 0.57</td>
</tr>
<tr>
<td>Degree of stenosis (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Basal</td>
<td>62.4 ± 8.2</td>
<td>24.73 ± 23.8</td>
</tr>
<tr>
<td>Final</td>
<td>11.05 ± 10.2</td>
<td>7.4 ± 8.5</td>
</tr>
<tr>
<td>Acute gain (mm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MB</td>
<td>2.18 ± 0.53</td>
<td></td>
</tr>
<tr>
<td>DB</td>
<td>0.72 ± 0.79</td>
<td></td>
</tr>
</tbody>
</table>

MB : mother branch  
DB : daughter branch

### Table 5 9-month follow-up

<table>
<thead>
<tr>
<th></th>
<th>To</th>
<th>T&gt;6 months(cumul)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deaths</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Cardiac</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Non-cardiac</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Heart failure</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Target lesion revascularization</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Others</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stent thrombosis</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Stroke</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Acute renal failure</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Major hemorrhage</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Rhythm disorder</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Major cardiovascular adverse events</td>
<td>4 (4.0 %)</td>
<td>9 (8.9%)</td>
</tr>
<tr>
<td>Total mortality</td>
<td>2 (1.98%)</td>
<td>4 (3.96%)</td>
</tr>
</tbody>
</table>

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Discussion

The first studies concerning angioplasty of the left main coronary artery disease without stent implantation often reported unsatisfactory mid- and long-term results (13, 14), restricting this procedure to inoperable patients, those with protected left main trunks (15) and cases of myocardial infarction with acute occlusion of the left main trunk (16, 17).

The recent development of coronary endoprosthesis together with advances in implantation techniques and peri-procedural anti-thrombotics have spectacularly reduced thrombotic and hemorrhagic complications following endoprosthesis implantation. However, intra-stent re-stenosis is the principal factor limiting long term efficacy (12) and is probably associated with an surplus of late mortality for LMCA angioplasties (12, 20, 21).

In a recent series reported by the authors (12), 57 patients underwent coronary dilatation with implantation of bare-metal stents for unprotected LMCA stenoses. At 8 month follow-up, the rate for myocardial infarction was 5.1% and 22.8% for revascularization. The rate of angiographic re-stenosis was 29.8%.

The advent of drug-eluting stents has resulted in a reduction in re-stenosis in several series (21, 22, 23). A recent report from the T-SEARCH registry suggested that implantation of a paclitaxel-eluting stent for LMCA stenoses has a favourable effect on reducing re-stenosis (11). Despite these encouraging results, angioplasty of the main trunk remains a complicated procedure with very high risks. Angioplasty of the bifurcation of the distal LMCA is an additional problem in the treatment of LMCA lesions, because it combines the risks of LMCA dilatation with the technical difficulties inherent at the bifurcation. Several techniques have been described for treating bifurcation lesions (provisional T stenting, Crush stenting…) with the recent introduction of bifurcation-dedicated stents (data insufficient at present).

Very few studies have evaluated the results of LMCA angioplasty using drug-eluting stents. Valgimigli et al in the RESEARCH and T-SEARCH study of 110 patients undergoing LMCA angioplasty with a drug-eluting stent (sirolimus and paclitaxel), reported a lower distal stenosis rate (76%) than in our series. Their dilatation procedure included a higher pre-dilatation rate (60%) and a kissing balloon technique in only 20%. The acute gain was lower with a higher late loss. Re-stenosis in the paclitaxel group was 13% and the rate of major adverse cardiac events was 29% (11). In another study, Chieffo et al revealed a MACE rate of 20% and a mortality of 3.5% (10). In a comparison with coronary artery bypass surgery, a recent study on 123 patients showed a higher MACE rate in the CABGs group (3).

Our series is distinguished by the patients’ elevated mean age (68.9 ± 11.07 years), the inclusion of high-risk individuals (increased Euroscore risk in 23.7%), and a significant rate of left ventricular dysfunction (28.2%). However, we recorded a MACE rate of just 8.9%, a mortality rate of 4%, and a re-stenosis rate of 4.5%, all of which are relatively low compared to the rates reported in the literature.

In the various reported studies, mortality varies between 0% and 12%. In our work it was only 4%, despite the presence of high-risk patients and a surplus of LMCA bifurcation lesions. Although our rate of angiographic control was not totally exhaustive, we recommend systematic coronary angiographic control between 6 and 12 months, in view of the serious and complex nature of main trunk lesions. This would seem to be more specific and more sensitive than a stress test or coronary CT. In our study we have attempted to determine the predictive factors for major adverse cardiac events. However, no significant relationship was shown between the different parameters due to our low complication rate.

### Table 6 Angiographic data at 6 months (n=89; 88.1%)

<table>
<thead>
<tr>
<th></th>
<th>Minimum luminal diameter (mm)</th>
<th>Degree of stenosis (%)</th>
<th>Late loss (mm)</th>
<th>Angiographic re-stenosis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MB</td>
<td>3.16 ± 0.54</td>
<td>14.34 ± 8.5</td>
<td>0.1 (0.04-0.2)</td>
</tr>
<tr>
<td></td>
<td>DB</td>
<td>2.85 ± 0.77</td>
<td>10 ± 12.5</td>
<td>0.03 (0-0.16)</td>
</tr>
<tr>
<td>MB : mother branch</td>
<td>DB : daughter branch</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Table 7 Characteristics of patients with re-stenosis

<table>
<thead>
<tr>
<th>Age and sex</th>
<th>Dilatation strategy</th>
<th>LMCA stenosis site</th>
<th>Clinical state</th>
<th>Re-stenosis site</th>
<th>TLR</th>
</tr>
</thead>
<tbody>
<tr>
<td>M, 54 years</td>
<td>Provisional T stenting</td>
<td>Distal</td>
<td>Asymptomatic</td>
<td>DB</td>
<td>None</td>
</tr>
<tr>
<td>M, 84 years</td>
<td>T stenting</td>
<td>Distal</td>
<td>Asymptomatic</td>
<td>DB</td>
<td>PCA</td>
</tr>
<tr>
<td>M, 58 years</td>
<td>T stenting</td>
<td>Distal</td>
<td>Angina</td>
<td>Diffuse</td>
<td>CABG</td>
</tr>
<tr>
<td>M, 73 years</td>
<td>T stenting</td>
<td>Distal</td>
<td>Asymptomatic</td>
<td>DB</td>
<td>PCA</td>
</tr>
</tbody>
</table>

TLR : target lesion revascularization  
MB : mother branch  
DB : daughter branch  
PCA : Percutaneous coronary angioplasty  
CABG : Coronary artery bypass graft
Limits of this study

Our work concerns a limited number of patients and our results cannot be generalised to all LMCA lesions. In addition, the angiographic data were not analysed by a central laboratory, and the evaluation of the procedure’s final result was not confirmed by endocoronary echography. Lastly, the data could have been biased by the individual experience of the different LMCA angioplasty operators, and should not be generalised to all interventional centres.

Conclusion

Coronary artery bypass remains the treatment of reference for lesions of the unprotected left main coronary artery. However, data from recent studies showing that drug-eluting stents reduce mortality and intra-stent re-stenosis will probably improve the therapeutic management of these lesions. Multicenter and randomised trials are required to compare surgery with drug-eluting stent angioplasty in the management of these complex left main trunk lesions.

References