

Twelve month clinical and angiographic outcome after stenting of unprotected left main coronary artery stenosis with paclitaxel-eluting stents – results of the multicentre FRIEND registry

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KEYWORDS

Paclitaxel eluting stent,
unprotected left main coronary artery,
percutaneous coronary intervention,
multicentre registry

Abstract

Aims: To evaluate the angiographic and clinical outcome of patients undergoing paclitaxel-eluting stent (PES) implantation for unprotected left main coronary artery (ULMCA) stenosis in a multicentre, prospective registry. The overall event rate for PCI of ULMCA disease remains higher than in on-label use making additional outcome data and risk-stratification tools for the ULMCA population desirable.

Methods and results: A prospective registry included all patients with a significant (>50%) stenosis in ULMCA disease. In 151 of these patients the target lesion involved the distal bifurcation in 100 patients (66%), which was treated by predominantly using a "provisional T stenting" strategy. In distal ULMCA disease group, 72% had only one stent implantation while 28% had multiple (either 2 or 3) stents implanted. At a median follow-up of 472±75 days, cardiac death occurred in 3 patients (2%) and major adverse cardiac and cerebrovascular events (MACCE) in 16 patients (10.6%).

Conclusions: In the drug-eluting stent era, paclitaxel eluting stent implantation of ULMCA stenosis provided excellent immediate and mid-term results in this selected population, suggesting that it may be considered as a safe and effective alternative to CABG for selected patients with ULMCA who are treated in institutions performing large numbers of PCI procedures.

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Abbreviations and acronyms

BMS	bare metal stent
CABG	coronary artery bypass graft
CAD	coronary artery disease
DES	drug eluting stent
DLMD	distal left main disease
FRIEND	French multicentre registry for stenting of unprotected LMCA stenosis
IVUS	intravascular ultrasound
LAD	left anterior descending artery
LCX	left circumflex artery
LMCA	left main coronary artery
MACE	major adverse cardiac event
MACCE	major adverse cardiac and cerebrovascular event
MI	myocardial infarction
MLD	mimimal luminal diameter
MSCT	multislice computer tomography
PES	paclitaxel eluting stent
PCI	percutaneous coronary intervention
PTCA	percutaneous transluminal coronary angioplasty
QCA	quantitative coronary angiography
RCA	right coronary artery
RVD	reference vessel diameter
SES	sirolimus eluting stent
STEMI	ST elevation myocardial infarction
TIMI	thrombolysis in myocardial infarction
TLR	target lesion revascularisation
TVR	target vessel revascularisation
ULMCA	unprotected left main coronary artery

Introduction

Left main coronary artery (LMCA) disease has remained a challenge for percutaneous coronary intervention (PCI) throughout the last 25 years. In the bare metal stent (BMS) era, early results were very promising, but the long-term results showed too many restenotic events for PCI to compete with coronary artery bypass graft (CABG). The marked decrease in restenosis rates observed with drug-eluting stents has prompted explorations of their use in unprotected left-main coronary artery (ULMCA) disease. Preliminary data, mainly retrospective and single centre studies, suggest that sirolimus-eluting stents (SES) and paclitaxel-eluting stents (PES) implantation are each associated with better six-months results than bare-metal stents in ULMCA disease¹⁻⁴ although target-vessel revascularisation (TVR) rates remain somewhat higher in many series for distal left main bifurcation lesions, particularly when multiple stent techniques (T, Kissing, or crush) are used^{5,6}. By and large, however, the effectiveness of DES in ULMCA has still not been good enough to

replace CABG in LMCA revascularisation of patients who are good surgical candidates. The aim of the present study was to evaluate the angiographic outcome of ULMCA stenosis percutaneous intervention using the TAXUS Express-2 PES Stent System (Boston Scientific, Natick, MA, USA) in a prospective multicentre registry.

Methods

Patient selection and study population

FRIEND – the French multicentre Registry for stenting of unprotected LMCA Stenosis – included 23 clinical centres and a coordinating centre. The participating hospitals were selected on the basis of recognised experience with PCI of unprotected LMCA stenoses. To be eligible for the registry, patients had to have angiographic evidence of $\geq 50\%$ diameter stenosis of the LMCA suitable for stent placement, with either anginal symptoms or documented myocardial ischaemia. Exclusion criteria consisted of contraindications to antiplatelet or anticoagulation therapy, emergency situations such as acute ST-elevation myocardial infarction (STEMI) or cardiogenic shock, serum creatinine > 1.8 mg/dl, reference vessel diameter < 2.5 mm or > 4.5 mm, in-lesion restenosis, severe obstructive pulmonary disease, pregnancy women, and life expectancy less than three years to underlying medical conditions. Between December 2005 and July 2006, a total of 600 patients with ULMCA disease were screened; 445 patients (74%) did not comply with the clinical or angiographic requirements for inclusion, or refused to give informed consent. Of these, 45.4% had CABG treatment, 36% PCI treatment. For the remaining patients (18.7%) the coronary features were unsuitable for CABG or PCI and were treated by medical therapy. One hundred and fifty-five consecutive patients (26%), who underwent PES placement in an unprotected LMCA stenosis, were enrolled in the prospective registry (Figure 1).

Angioplasty procedure

PCI technique, including the selection of arterial access or predilation devices, IIb/IIIa inhibitors, prophylactic intra-aortic balloon pump use, and intravascular ultrasound (IVUS) guidance, was left to the discretion of the operator. However, the use of a “provisional T stenting” strategy was strongly recommended in the treatment of distal left main lesions, in which a single PES was implanted from left main, preferentially through the left anterior

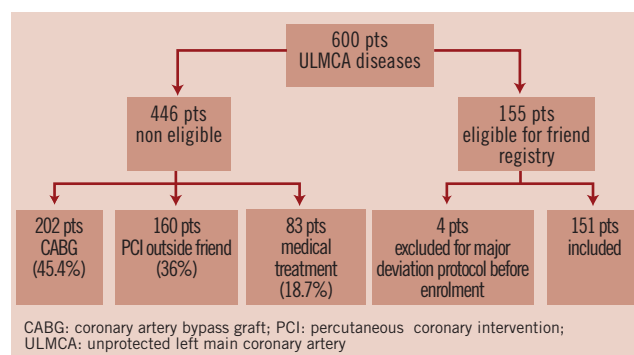


Figure 1. Selection of study population.

descending artery (LAD). A second stent was implanted in proximal circumflex only if there was a residual moderate to severe dissection or significant residual stenosis after final kissing-balloon inflation. All elective patients were pretreated with aspirin and clopidogrel beginning at least 3 days before angioplasty. Unfractionated heparin, 50-70 U/kg (with a goal activated clotting time of ≥ 250 s), or bivalirudin, was administered during the procedure. All patients were instructed to take daily aspirin 160 mg indefinitely and clopidogrel 75 mg for at least 12 months. Cardiac enzymes were determined routinely after percutaneous coronary procedures, at 8 hour intervals during the first 24 hours, or until discharge. At least one post-procedural 12-lead electrocardiogram was obtained and compared with pre-intervention tracings.

Angiographic methods

Quantitative coronary angiography was performed by an off-site, independent core laboratory (Corisis system) using a validated edge-detection program. The projection showing the maximal degree of stenosis was selected at baseline and was used for systematic angiographic control. For purposes of bifurcation analysis, the LMCA of each patient was divided into the parent vessel and side branch. By convention, the parent vessel was defined as the LMCA and proximal LAD, and the side branch as the LCX. The target lesion was defined as involving the distal LMCA if it was within 3 mm of the circumflex ostium. For the parent vessel and side branch, the reference vessel diameter (RVD), minimal luminal diameter (MLD), acute luminal gain (MLD immediately after the procedure minus the MLD before the procedure), binary restenosis (diameter stenosis of $\geq 50\%$ relative to the angiographically uninvolved left main lumen), percent diameter stenosis, and late luminal loss (MLD immediately after the procedure minus the MLD at follow-up) were measured separately. In-stent restenosis was defined angiographic restenosis anywhere inside or within 5 mm of the stented segment.

Endpoints and definitions

The primary endpoint was the occurrence of in-stent restenosis at 9-months follow-up. The secondary endpoints were the rate of major adverse cardiac and cerebrovascular events (MACCE) at one, 12, 18 and 36 months. The LMCA was defined as "unprotected" if there was no history of CABG. Non-Q-wave myocardial infarction (MI) was defined as creatine kinase greater than two times the upper limit of normal with an abnormal CK-MB in the absence of pathological Q waves. Stent thrombosis was defined as any of the following angiographic demonstration of stent closure or intrastent filling defect, unexplained sudden death, or MI without concomitant documentation of a patent stent. Acute stent thrombosis was defined as thrombosis occurring within 24 hours, subacute thrombosis between 24 hours and 30 days, and late thrombosis more than 30 days after the index procedure. Target lesion revascularisation (TLR) was defined as any repeat intervention (surgical or percutaneous) to treat a stenosis anywhere within the LMCA or within 10 mm distal to the LAD and LCX ostia. Target lesion revascularisation was further characterised as "ischaemia-driven" if signs or symptoms of ischaemia were present. MACCE were defined

as any MI, any TLR, thrombosis, stroke, or death. Technical success was defined as a final diameter stenosis $\leq 30\%$ and Thrombolysis in Myocardial Infarction (TIMI) flow grade 3.

The European system for cardiac operative risk evaluation (EuroSCORE) which is based on patient, cardiac and operation related factors, was used to stratify the risk of death at 30 days^{7,8}. According to this scoring system, the patients were stratified as risk patients if the logistic EuroSCORE was ≥ 6 (see <http://www.euroscore.org/calc.html>).

Data collection and follow-up

The study protocol was approved by the FRIEND Review Board, the French Society of Cardiology, and was conducted in accordance with the Declaration of Helsinki. All patients signed informed consents before elective procedures, and data were reported using a standard case report form, and then forwarded to the coordinating centre. Clinical information about death, myocardial infarction, repeated revascularisation, bypass surgery, and stroke was obtained during clinic visits or telephone interviews and was evaluated by a Clinical Event Committee which was independent of the operators. All the patients were followed up for at least 36 months.

Statistical analysis

The size of the cohort of patients was based on being able to show a 50% relative reduction in in-stent restenosis compared to the literature rate of 30% for BMS⁹⁻¹², with alpha and beta errors of 5% (i.e., $p < 0.05$) and 20% (i.e. 80% power), respectively. One hundred and thirty-one patients were required. With the estimated attrition due to death, or lost for angiographic follow-up, the total number of inclusion was a maximum of 150 patients. Categorical variables were expressed as counts and percentages and continuous variables as mean \pm SD. Angiographic characteristics and coronary angiography measurements were presented according to distal or non-distal ULMCA disease. Results were compared using Student's t-test for continuous variables, Chi-square test or Fisher's exact test for categorical variables. Logistic regression analyses were used to determine risk factors influencing 9-month in-stent restenosis and MACCE rates. The considered covariates were: age, diabetes mellitus, EuroSCORE, vessel reference diameter, distal ULMCA disease, baseline angulation between LAD and LCx ($<$ or $> 70^\circ$), use of single vs multiple stents and final post PCI MLD.

Cumulative probability of survival free from cardiac death, total death and MACCE were drawn for the whole population, and for distal versus non-distal ULMCA disease as sub-groups. Survival free from MACCE was also drawn in distal LMCA disease for patients with one stent versus 2-3 stents in distal left main lesion. All p values were 2-tailed, with statistical significance set at a level of < 0.05 . Confidence intervals were calculated at the 95% level. All analyses were performed using SAS software version 8.2 (SAS Institute Inc, Cary, NC, USA).

Results

Baseline characteristics

Concerning intention to treat, 155 patients were enrolled in this trial. However, four patients were excluded at the beginning of enrolment for major protocol deviation (one death before coronary stenting,

one acute coronary syndrome < 12 hours, one patient with a contra-indication to antiplatelet therapy and one PCI involving only balloon angioplasty). Thus, 151 patients were included in this prospective registry after percutaneous intervention of the ULMCA using one or more PES. Clinical, procedural and angiographic characteristics are summarised respectively in Tables 1, 2 and 3. The procedure was elective for stable angina or silent ischaemia in 89 patients (59%), with no emergency revascularisation procedures for ST-elevation myocardial infarction or cardiogenic shock. Diabetes mellitus was

Table 1. Clinical characteristics of the study population (n=151).

Variables	n
Age, years mean±SD	68.3±10.8 (40 - 91)
Female gender n (%)	27 (17.4%)
Hypertension n (%)	97 (62.6%)
Hypercholesterolaemia n (%)	105 (67.7%)
Smoking n (%)	27 (17.9%)
Diabetes mellitus n (%)	5 (3.3%)
Family history of coronary artery disease n (%)	38 (25.2%)
Renal failure 1.3 to 1.8 mg/dl (%)	11 (7.3%)
Clinical presentation	
Stable angina n (%)	67 (43.2%)
Unstable angina/NSTEMI n (%)	62 (41.1%)
STEMI	0
Previous CABG	0
Previous PCI	0
EuroSCORE (mean±SD)	4.13±2.85
EuroSCORE ≥ 6 n (%)	41 (27.2%)
Disease in RCA n (%)	55 (36.4%)
Treatment in RCA n (%)	34 (22.5%)
LVEF,% mean ±SD	59.5±10.1

NSTEMI: non ST elevation myocardial infarction; STEMI: ST elevation myocardial infarction; CABG: coronary artery bypass graft; PCI: percutaneous coronary intervention; LVEF: left ventricular ejection fraction

Table 3. Angiographic characteristics of the study population (n=151).

Variables	Distal LMCA disease (n=100 pts, 131 stents)	Non distal LMCA disease (n=51 pts, 53 stents)	p value
Pure LMCA disease (%)	18 (18.0%)	17 (33.3%)	
LMCA plus 1-vessel disease (%)	25 (25.0%)	13 (25.5%)	0.1081 (1)
LMCA plus 2-vessel disease (%)	33 (33.0%)	11 (21.6%)	
LMCA plus 3-vessel disease (%)	24 (24.0%)	10 (19.6%)	
Bifurcation lesion classification (%)			
Isolate distal LMCA stenosis	28 (28.0%)		
Distal LMCA plus ostial LAD or LCx	46 (46.0%)		
Distal LMCA plus both LAD/LCx ostia	26 (26.0%)		
Number of implanted stents			
Main branch/ bifurcation stenting (%)			
1 stent	72 (72.0%)	49 (96.1)	
2 stents	25 (25.0%)	2 (3.9)	0.0005 (2)
3 stents	3 (3.0%)	0	
Nominal stent diameter (184 stents)	3.59±0.49	3.81±0.45	0.0056 (3)
Total stent length per patient (mm)	22.12±8.52	13.33±5.47	<0.0001 (3)

(1) Chi-square test; (2) Fisher's exact test; (3) Student's t test; LCx: left circumflex artery, LAD: left anterior descending artery

Table 2. Procedural characteristics of patients treated with DES implantation (n=151).

Variables	n (%)
Trans radial approach	32 (21.2%)
6 French guiding - catheter	103 (68.2%)
IABP	2 (1.3%)
IIb - IIIa inhibitors	
before PCI	6 (3.97%)
during PCI	17 (11.4%)
Bivalirudin	
before PCI	1 (0.7%)
during PCI	13 (8.6%)
IVUS guidance	10 (6.6%)
Other lesions treated	137
Predilation strategy (balloon or other techniques)	71 (47.0%)
Direct stenting	80 (53.0%)
Cutting-balloon	1 (0.7%)
Rotablator	2 (1.3%)
Location	
Non Distal (Ostial / Proximal or mid)	51 (33.8%)
Distal	100 (66.2%)
Bifurcation	92 (92.0%)
Trifurcation	8 (8.0%)
T-provisional technique	95 (95.0%)
Other techniques	5 (5%)
Two stents used	27 (17.9%)
Three stents used	3 (2.0%)
Final kissing-balloon	90 (92.8%)

IABP: intra-aortic balloon pump; IVUS: intravascular ultrasound

only present in five patients (3.3%) and renal failure in 11 patients (7.3%), but 55 patients (36.4%) had additional disease in the RCA, 34 of which were treated during the index procedure. Twenty-seven percent of patients had an estimated EuroSCORE operative mortality > 5%.

One-hundred (66%) patients had distal LMCA stenosis: 92 were bifurcations and 8 were trifurcations. For this group, T-provisional technique was performed in 95% of cases, with 72% of patients receiving only 1-stent, and 28% receiving 2 or 3 stents. Final kissing-balloon dilation was performed in 93% of case, and 20 patients (13%) received glycoprotein IIb/IIIa inhibitors before or during the procedure. Technical success was achieved in all patients.

In-hospital and long-term MACCE

In-hospital and 12-month clinical outcome are illustrated in Table 4. Three patients (2%) with high-risk EuroSCORE died of acute stent thrombosis during hospitalisation. One patient underwent TLR for residual dissection of LCx outside the previously stented segment. The combined endpoint of MACCE including death, stroke, any MI, TLR, or thrombosis thus occurred in six patients (4%), before hospital discharge. MACCE between hospital discharge and 12-month follow-up occurred in another 10 patients, so the cumulative incidence MACCE occurred in 16 patients (8%) by 12-months. Kaplan-Meier MACCE free of survival is shown in Figure 2. There was no significant difference in clinical outcome between patients with vs. without distal left main disease, although there was a non-significant statistical trend towards lower MACCE in non-distal (i.e., proximal or mid) lesions as shown in Figure 3 (hazard ratio [HR] 0.82, 95% confidence interval [CI] 0.27 to 2.51; $p=0.73$). For distal lesions, the MACCE rate through 12-month follow-up remained slightly lower for patients receiving a single stent versus multiple (2 or 3) stents, but this difference did not reach statistical significant differences (HR 1.09, 95% CI 0.29 to 4.1; $p=0.89$). (Figure 4)

Quantitative coronary angiography

Overall, follow-up angiography was performed in 133 patients. Angiography was not performed in 18 patients because of death before the scheduled angiography (4 patients), patient refusal (8 patients), age > 80 or serious comorbidities (6 patients) and the absence of clinical symptoms of cardiac ischaemia. Baseline and follow-up angiographic results are shown in Table 5. As shown,

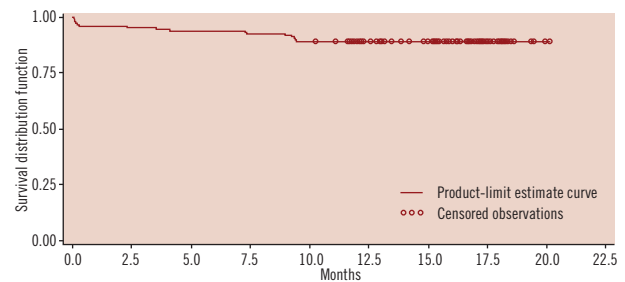


Figure 2. Actuarial rate of event free survival.

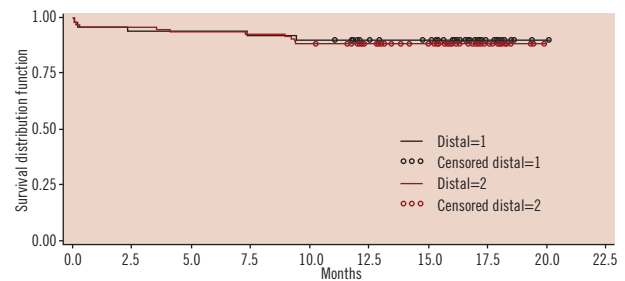


Figure 3. Actuarial rate of event free survival between non-distal and distal left main disease.

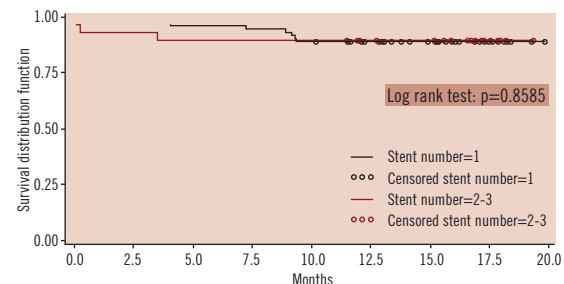


Figure 4. Actuarial rate of event free survival between one and two or three stents implantation in distal left main disease.

Table 4. MACE at hospitalisation and at 12-month clinical follow-up.

	In-hospital	Hospital to follow-up 472.56±75.65	Cumulative events
Total death n (%)	3 (2.0%)	3 (2%)	6 (4%)
Cardiac death, n (%)	3 (2.0%)	0	3 (2.0%)
Cardiac death in high-risk pts (EuroSCORE ≥6) n (%)	3 (2.0%)	0	3 (2.0%)
Cardiac death in low risk-pts (EuroSCORE < 6)	0	0	0
Q-wave MI n (%)	1 (0.7%)	2 (1.4%)	3 (1.3%)
Stable angina	0	2 (1.3%)	2 (1.3%)
Non Q-wave MI n (%)	2 (1.3%)	1 (0.7%)	3 (2.0%)
Repeat PCI	1 (0.7%)	0	1 (0.7%)
CABG	1 (0.7%)	1 (0.7%)	2 (1.4%)
TLR n (%)	1 (0.7%)	2 (1.3%)	3 (2.0%)
TVR n (%)	0	2 (1.3%)	2 (1.3%)
MACE n (%)	6 (3.9%)	10 (6.6%)	16 (10.6%)

despite a similar LMCA reference vessel diameter, patients with distal lesion location tended to have a longer lesion length and a slightly greater MLD. In-stent acute luminal gain was similar in both

Table 5. Quantitative coronary angiography measurements.

Variables	Distal LMCA disease (n=89)	Non distal LMCA disease (n=44)	Total population (n=133)	p value
Baseline				
RVD (mm)	3.94±0.67	3.87±0.72	3.92±0.69	0.5483
MLD (mm)	1.70±0.74	1.67±0.68	1.69±0.72	0.8614
Diameter stenosis (%)	56±19	56±17	56±18	0.9951
Lesion length (mm)	9.80±4.82	6.69±5.09	8.79±5.10	0.0010
After procedure				
In-stent				
RVD (mm)	4.32±0.65	4.17±0.54	4.27±0.62	0.1964
MLD (mm)	3.64±0.70	3.41±0.64	3.56±0.69	0.0741
Acute luminal gain (mm)*	1.94±0.85	1.73±0.69	1.87±0.80	0.1646
Diameter stenosis (%)	15±11	18±12	16±12	0.2217
9-month follow-up				
In-stent				
RVD (mm)	3.94±0.50	3.89±0.54	3.92±0.51	0.6359
MLD (mm)	3.21±0.55	3.15±0.63	3.19±0.58	0.5240
Diameter stenosis (%)	18±12	19±13	18±12	0.7419
Late loss (mm)**	0.48±0.78	0.26±0.68	0.40±0.75	0.1210
Net luminal gain (mm)***	-1.52±0.84	-1.47±0.70	-1.50±0.79	0.7620
Binary restenosis (%)	1 (1.1%)	2 (4.5%)	3 (2.3%)	0.5032

*Difference between MLD after procedure and MLD before procedure; **Difference between MLD at follow-up and MLD after procedure; ***Difference between MLD at follow-up and MLD before the procedure; LMCA: left main coronary artery; MLD: minimal luminal diameter; RVD: reference vessel diameter

groups, but late loss in the distal ULMCA disease was almost double that of proximal or mid-lesions (0.48±0.78 mm vs. 0.26±0.68 mm, $p=0.12$). Binary restenosis occurred only in three of the 133 patients studied (2.3%), including two (4.5%) of 44 patients with ostial or mid-shaft LMCA stenosis and in one (1.1%) of 89 patients with bifurcation involvement.

Discussion

The percutaneous treatment of LMCA disease has remained a challenging task, with historically unacceptably high long-term adverse event rates⁹⁻¹². However, the outcomes associated with percutaneous coronary intervention have improved dramatically with the introduction of stents, high-pressure balloon dilation, and glycoprotein IIb/IIIa inhibitors¹³.

Procedural safety

Many studies of unprotected LMCA PCI have been published. Most have involved the Cypher sirolimus-eluting stent (Cordis, Miami Lakes, FL, USA) or both SES and PES^{1-6,14}. The largest such series to date includes 220 patients, and the smallest only 50 patients. Procedural success (diameter stenosis <30% in the absence of MACE) was high (90-100%) in each series, with a low rate of in-hospital death (0.8-2.0%). All studies had low (2.3-3.1%) use of debulking devices prior to stent placement, compared with the higher rates of debulking used in the pre-DES era. The present study is similar to these other DES series of ULMCA in showing a favourable (2%), 30-day mortality after stenting of unprotected LMCA stenosis in elective treatment, supporting consideration of this therapy as an alternative to bypass surgery in selected patients.

Nine month angiographic and 12-month clinical outcome

The advent of BMS offered only slight improvement in the percutaneous treatment of unprotected left main lesions^{15,16} due to the continued frequent occurrence of in-stent restenosis (some of which was fatal in presentation)^{9,10}. Recently, the liberal use of DES to treat LMCA has been shown to favourably affect restenosis compared to that with BMS²⁻⁴, but the rate of major cardiovascular events still remains high in the first series of patients in the DES era^{3,4}. Several studies have shown better medium-term prognosis when unprotected LMCA stenting is confined to low-risk groups (i.e., excluding acute myocardial infarction, poor left ventricular function, or cardiogenic shock), with good clinical stability through six months after revascularisation^{15,16}. In the current study of a similarly restricted population, the primary endpoint of angiographic in-stent restenosis rate at 9-months was only 2.3% and was statistically significantly lower than the benchmark comparison of 30% in-stent restenosis rate for BMS. This was associated with a low incidence of clinical events through 12-months. These results in the future could change our practice with maybe a systematic control of ULMCA stenting not by QCA but by MSCT.

These extremely favourable short- and long-term outcomes in the current study, with no major events during the follow-up period have several potential explanations. First, this population as opposed to other trials^{11,17}, had a low percentage (3.3%) of diabetic patients, good left ventricular ejection fraction, good renal function, mean age of 68.3±10.8 years, and a large reference vessel diameter of 3.92±0.69 mm. Second, this prospective multicentre registry of 23

participating centres is the first to systematically study the provisional T-stenting approach for distal left main disease (DLMD) rather than the double stent techniques used in many prior studies. The earlier literature has consistently shown significantly worse long-term outcomes in patients undergoing percutaneous treatment of distal compared to proximal or mid-vessel LMCA lesions. Valgimigli et al⁵ showed that distal LMCA disease carried independent negative prognostic implications that should be considered when selecting the most appropriate patients for LMCA intervention. With our use of provisional T stenting (and mostly (72%) single stent technique and final kissing-balloon in 93%), however, the procedural success and short-term (30 days) outcome was remarkably similar between proximal mid and distal lesions. Although there was still a weak trend towards slightly higher rate of events at 12-month follow-up, driven mainly by a higher rate of TVR in the DLMD group, the avoidance of more complex multi-stent techniques such as crush, V, culotte or kissing stenting in the current series may well account for our excellent mid-term results. We cannot, however, prove this benefit here given the small number of such multiple stent patients in our series. At the same time, DES implantation in non-bifurcation left main coronary artery lesions showed an excellent (0.9%) long-term restenosis rate, with a favourable (7.4%) rate of any major adverse clinical event, compared to prior studies¹⁹. Unlike the left main Taxus pilot study¹⁸, we didn't find any impact of bifurcation angle between LAD and LCx (< or >70°) at 12-month clinical outcome. In our registry, even luminal late loss is greater in DLMD than in non DLMD (0.48±0.78 mm vs 0.26±0.68 mm), there is no difference and no predictive factors in terms of in-stent restenosis.

PCI with DES vs CABG

Even though current guidelines still recommend surgical revascularisation for LMCA stenosis, it is clear that the PCI approach using DES offer an increasingly excellent alternative in selected patients. Some retrospective studies evaluating surgical treatment for left main stenosis have reported higher in-hospital mortality (1.7% to 7.0%) and 1-year mortality (6% to 14%) than seen in our study, although these surgical series were not limited to the lower risk settings studied here^{20,21}. Three other non-randomised trials²²⁻²⁴ comparing CABG vs PCI, however, similarly failed to detect any difference in either mortality or the combined occurrence of MACE and major adverse cerebrovascular events at the one or two year outcomes. But none of the studies thus far has compared the safety and efficiency of DES to that of CABG in patients with LMCA stenosis in an appropriately sized randomised trial. Such randomised studies comparing CABG vs DES are now in progress, including PRE-COMBAT (Premiere of Randomised Comparison of Bypass Surgery versus Angioplasty using Sirolimus-Eluting stent in Patients with left main coronary artery disease), FREEDOM (Future revascularisation evaluation in patients with Diabetes mellitus: optimal management of multivessel disease) and SYNTAX (Synergy between percutaneous coronary intervention with Taxus and cardiac surgery study), which recently (April 2007) completed enrolment of 1,800 randomised left main and 3 vessel disease patients including 710 patients with left main disease. These

studies, will hopefully more closely evaluate the benefits of DES in the treatment of selected patients with LMCA disease.

Study limitations

First, our findings in carefully selected patients may not be able to be generalised to the entire range of unprotected LMCA stenosis. Second, the data does not necessarily apply to interventional cardiologists with less prior experience with LMCA stenting. Third, the results of our study are very encouraging, but they cannot be conclusive until the conclusion of pending studies with larger sample sizes and more prolonged clinical follow-up; all of which is clearly needed to confirm our findings and extend our capability to risk-stratify this challenging subset of patients^{24,25}.

Conclusions

The event rate after percutaneous treatment of ULMCA disease in the FRIEND multicentre registry seems to be remarkably low, with an excellent short and long-term prognosis in a low surgical risk population. Our current findings extend the previous knowledge about risk stratification and technical approach and may be helpful in identifying the most appropriate LMCA patients in whom catheter-based intervention perhaps offers the best alternative to bypass surgery. Additional data from large scale randomised trials like SYNTAX, will be forthcoming to shed further light on this important subgroup of patients.

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