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## ***LEFT MAIN STENTING***

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### **EXECUTIVE SUMMARY**

The standard of care for the treatment of unprotected left main coronary artery (ULMCA) disease remains coronary artery bypass surgery. Percutaneous coronary intervention of the ULMCA has been contraindicated because of inferior outcomes after balloon angioplasty and bare metal stenting. However, recent data suggest that drug-eluting stenting of the ULMCA may be an alternative to bypass surgery. The main limitations to drug-eluting stenting of the ULMCA are restenosis, especially in distal bifurcation lesions, and stent thrombosis, which may lead to catastrophic consequences, including sudden death. Ultimately, randomized trials are needed to determine if drug-eluting stenting is a safe and effective alternative to bypass surgery for ULMCA disease.

## Introduction

Significant left main coronary artery disease, which is diagnosed in 5% to 7% of patients undergoing coronary angiography (1), confers a 5-year mortality rate of 42% with medical therapy alone (2). The short- and long-term results of unprotected left main coronary artery (ULMCA) percutaneous transluminal coronary angioplasty (PTCA) also have been disappointing because of the high rate of acute elastic recoil, abrupt vessel closure, acute thrombotic occlusion, early restenosis, and mortality (3). Bare metal stents (BMS) seemed to offer a major advance for the treatment of ULMCA stenosis. In the ULTIMA Registry of 279 consecutive patients having ULMCA intervention, 46% of whom were considered either inoperable or high surgical risk, the in-hospital mortality rate was 13.7% and the 1-year incidence of cardiac mortality was 20.2% (4). Additionally, in the 32% of patients comprising the low-risk subgroup (age <65 years, left ventricular ejection fraction >30%, and absence of cardiogenic shock), there were no periprocedural deaths and the 1-year mortality was 3.4%. For comparison, however, The Cleveland Clinic Foundation reported an overall 2.3% in-hospital mortality rate and an 11.3% 1-year mortality rate for those undergoing coronary artery bypass grafting (CABG) for left main disease (5). Consequently, the American College of Cardiology/American Heart Association/Society for Cardiovascular Angiography and Interventions guidelines currently discourage ULMCA percutaneous coronary intervention (PCI) (6).

## Drug-Eluting Stents

The most important recent advance in ULMCA PCI is the development of drug-eluting stents (DES) (Table 1). At 1-year follow-up, Park et al. reported no deaths, emergent CABG, or myocardial infarction, and a low target lesion revascularization (TLR) rate (2%) in a low-risk cohort with normal left ventricular function using sirolimus-eluting stents (SES); the TLR rate in those receiving BMS was 17.4% ( $p < 0.001$ ) (7). At 6-month follow-up, Chieffo et al. reported a 14.1% TLR rate, a 3.5% mortality rate, and a 20% major adverse cardiac event (MACE) rate in patients receiving DES, the majority of whom had high-risk bifurcation or trifurcation lesions (8). For comparison, the MACE rate in the low-risk BMS recipients reported by Park et al. was 35.9%. The RESEARCH and T-SEARCH registries, which include a proportion of protected left main procedures, also reported a MACE rate that was significantly lower in the DES patients than in the BMS patients, 24% vs. 45%, respectively (hazard ratio (HR): 0.52, 95% confidence interval (CI): 0.31 to 0.88;  $p = 0.01$ ) at a median follow-up of 503 days (9).

Price et al. reported a TLR rate of 38% over a mean follow-up of  $276 \pm 57$  days in those receiving SES which is higher than reported by others (10). The high TLR rate may have been due to a high rate of angiographic follow-up (98%) leading to repeat revascularization that was not ischemia driven, as well as to a 94% involvement of the distal left main with stenting of both limbs of the bifurcation in 84%.

Data from the RESEARCH and T-SEARCH registry shows no difference in angiographic and long-term clinical outcomes between SES and paclitaxel-eluting stents (PES) (11). At a median follow-up of 660 days, the cumulative MACE rate was 25% in the SES group vs. 29% in the PES group (HR: 0.88, 95% CI: 0.43 to 1.82;  $p = 0.74$ ); the frequency of death/myocardial

infarction (16% in the SES group and 18% in the PES group) and TLR (9% in the SES group and 11% in the PES group) were also similar. Stent thrombosis did not occur in the 110 patients who underwent DES PCI of the left main coronary artery.

In a non-randomized study, Lee et al. compared CABG with DES PCI in ULMCA disease (12). No difference in the estimated major adverse cardiac and cerebrovascular event-free survival at 6 months and 1 year was found (83% and 75% in the CABG group vs. 89% and 83% in the PCI group,  $p = 0.20$ ).

In summary, significant variations in the outcomes of death and restenosis were noted in the studies mentioned above, ranging from 0% to 14% mortality and 6% to 44% restenosis, despite the interventions being performed by skilled high-volume operators. The best outcomes were seen in low-risk patients with normal left ventricular function and no distal bifurcation involvement. The data also suggest that outcomes may be worse in diabetic patients (8,12).

### **PCI of Ostial ULMCA**

The ostium of the left main artery can be optimally visualized in the left anterior oblique cranial view. The guiding catheter is disengaged from the ostium of the ULMCA to permit full visualization and expansion of the stent. The proximal portion of the stent can be positioned in between the superior and inferior borders of the ULMCA ostium (Figure 1). Eight millimeter (mm) stents are generally avoided because of the potential for migration and embolization due to poor purchase of the stent in the ULMCA. Rather, a stent that is at least 12 mm is preferred with approximately 1 mm of stent protruding into the ascending aorta. It may be difficult to re-engage the guiding catheter if the stent is placed too far into the aorta. High-pressure inflation at 16 atmospheres (atm) or more for less than 10 seconds is preferred to minimize the duration of ischemia. Post-dilatation with the balloon protruding into the ascending aorta is performed to flare the proximal portion of the stent. Intravascular ultrasound (IVUS) of the ULMCA is crucial to demonstrate that the ostium of the ULMCA is adequately covered and that the stent is fully expanded and apposed to the vessel wall.

### **PCI of Mid-Shaft ULMCA**

If the ULMCA is less than 8 mm long and has a mid-shaft lesion, it may be necessary to extend the stent across the left circumflex artery into the left anterior descending artery. After high-pressure inflation of the stent, post-dilatation is recommended if there remains suboptimal stent apposition on IVUS.

### **PCI of Distal Bifurcation ULCMA**

Stenosis of the ULMCA often involves the distal bifurcation, which is technically more challenging and has the highest rates of restenosis, particularly when a multiple stent approach is used. The majority of the restenosis in bifurcation disease occurs at the level of the ostium of the left circumflex artery (7-10,12). There are four techniques that can be used to treat distal bifurcation lesions, depending on the size of the ULMCA and ostium of the left circumflex artery.

*Cross Over Stenting* is preferred when there is no significant disease in the left circumflex artery ostium, regardless of the size of the ULMCA. If there is subsequent plaque shifting from the ULMCA into the ostium of the left circumflex artery, provisional balloon angioplasty or additional stenting of the left circumflex artery can be performed.

*Simultaneous Kissing Stenting (Double Barrel Technique)* is preferred when there is significant disease in the ostium of the left circumflex artery and the ULMCA is large enough to accommodate two stents. An 8F guiding catheter is used to precisely align two stents juxtaposed to each other at the proximal portion in the left main artery. The stents are inflated simultaneously to create a new carina at the distal bifurcation (Figure 2). Intravascular ultrasound of the ULMCA will show the stents as two semicircles. Repeat PCI for in-stent restenosis may be a particular challenge because of the layer of stent struts in the lumen of the ULMCA.

*Crush Stenting* is preferred when there is significant disease in the ostium of the left circumflex artery but the left main artery is not large enough to accommodate two fully expanded stents (Figures 3-5). Final kissing balloon inflations should be performed to obtain optimal stent apposition and decrease the risk of restenosis.

*T-Stenting* is less commonly used for ULMCA PCI because of higher restenosis rates, especially at the left circumflex artery. Sequential stenting of the ULMCA and then the left circumflex artery is performed. Final kissing balloon inflations may be performed to obtain optimal stent apposition.

### **Intravascular Ultrasound (IVUS)**

The actual size of the left main coronary artery, in particular the ostium, and the severity of the lesion is often difficult to assess by angiography alone. IVUS permits critical assessment of the lesion morphology, sizing of the reference vessel, and verification of complete stent expansion and lesion coverage especially in aorto-ostial lesions. It also can be used to assess the severity of left circumflex artery when the distal bifurcation of the ULMCA is involved. Verifying complete stent expansion is crucial to decrease the risk of stent thrombosis and restenosis. We recommend post-dilatation with a non-compliant balloon to maximal balloon pressure to ensure optimal stent apposition and the largest possible final minimal luminal diameter, as these have been shown to be independent predictors of restenosis of the parent vessel (10).

### **Intra-aortic Balloon Pumps**

Intra-aortic balloon pumps were used in 4.9% of patients who underwent ULMCA PCI with DES in Park et al. (7), 21.2% in Chieffo et al. (8), 15% in Valgimigli et al. (9), and 64% in Lee et al. (12). Intra-aortic balloon pumps are not required in low-risk patients with normal left ventricular function. However, high-risk patients with low ejection fractions may benefit from the hemodynamic support of intra-aortic balloon pump counterpulsation, especially when there is highly complex disease involving the distal bifurcation.

## **Glycoprotein IIb/IIIa Antagonists**

Glycoprotein IIb/IIIa antagonists was used in 7.8% of patients who underwent ULMCA PCI with DES in Park et al. (7), 28.5% in Chieffo et al. (8), 28% in Valgimigli et al (9), and 14% in Lee et al. (12). The impact of glycoprotein IIb/IIIa antagonists, or alternative anticoagulants, on patients undergoing ULMCA PCI is unknown because it has not been studied in randomized clinical trials.

## **Antiplatelet Therapy**

A dreaded complication of ULMCA PCI is stent thrombosis. Stent thrombosis may occur many months after DES implantation if dual antiplatelet therapy is discontinued (13). The studies reviewed here, however, had low stent thrombosis rates (0-1.2%) (Table 1). The two events (4%) that occurred in Price et al. were both non-fatal acute thrombosis. There was no documented out-of-hospital stent thrombosis. The optimal duration of clopidogrel therapy to prevent left main stent thrombosis is unresolved, but a minimum of 6 months therapy is prudent and some would suggest life-long therapy.

## **Follow-up**

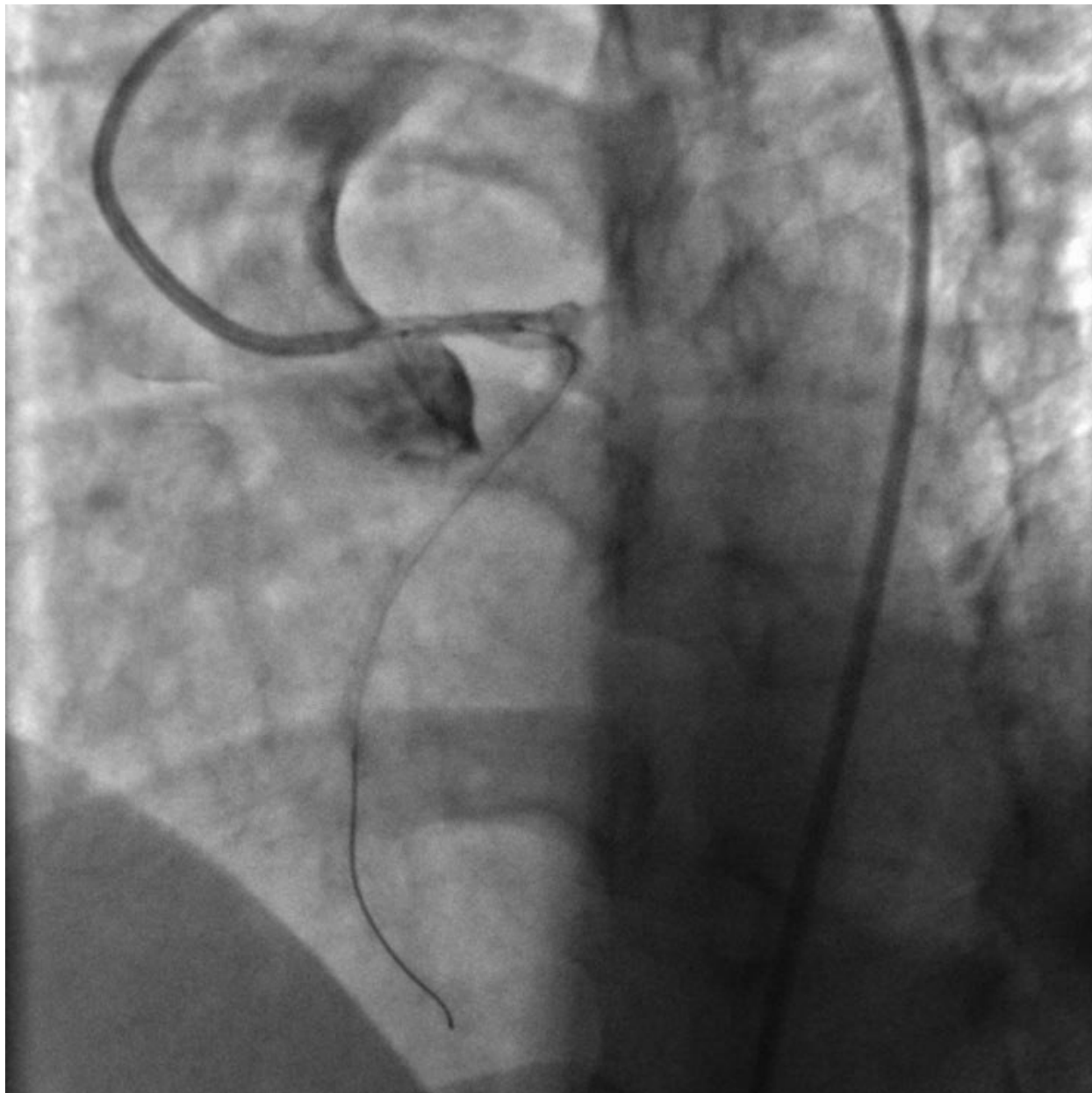
The ideal time for follow-up angiography (3, 6, and/or 9 months) to detect restenosis remains undecided. In addition, the long-term results of ULMCA PCI with DES and the optimal revascularization strategy in patients presenting with restenosis remain unknown.

## **Conclusions**

Percutaneous coronary intervention of the ULMCA has a Class III indication (6). The ultimate proof of the relative value of ULMCA PCI using DES and CABG will clearly depend on the results of multicenter randomized clinical trials, such as the awaited SYNTAX (Synergy between Percutaneous Intervention with Taxus and Cardiac Surgery) and COMBAT (Comparison of Bypass Surgery and Angioplasty using Sirolimus-eluting Stents) trials. Until these trials are performed, judicious selection of appropriate patients will be crucial to define those who are optimal candidates for ULMCA PCI. The available data suggest that PCI using a DES may represent an acceptable alternative therapy for ULMCA in low-risk patients, and that guidelines might reasonably be re-evaluated based on this published and emerging experience. However, we would discourage ad hoc ULMCA PCI except for very unusual circumstances such as emergency conditions. If patients are at high risk due to comorbidities like pulmonary or renal disease, severe left ventricular dysfunction, or advanced age, the decision should be made by careful case evaluation with a surgical consultation.

**Figure Legend**

**Figure 1.** PCI of the Left main Artery Ostium



The guiding catheter is disengaged from the ostium of the left main artery. The ostium of the left main artery can be optimally visualized in the left anterior oblique cranial view. The proximal portion of the stent is positioned in between the superior and inferior borders of the left main coronary artery ostium.

**Figure 2.** Simultaneous Kissing Stenting (or Double Barrel Technique)



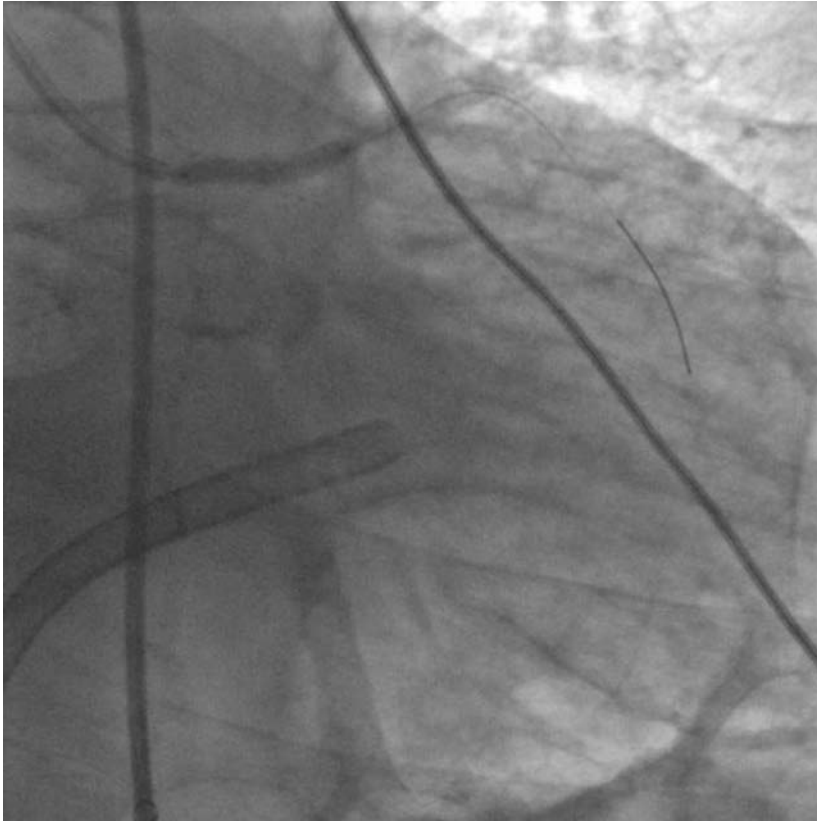
An 8F guiding catheter is used to precisely align two stents juxtaposed to each other at the proximal portion in the left main artery. The stents are inflated simultaneously to create a new carina at the distal bifurcation.

**Figure 3.** Crush Stenting: Positioning and Deployment



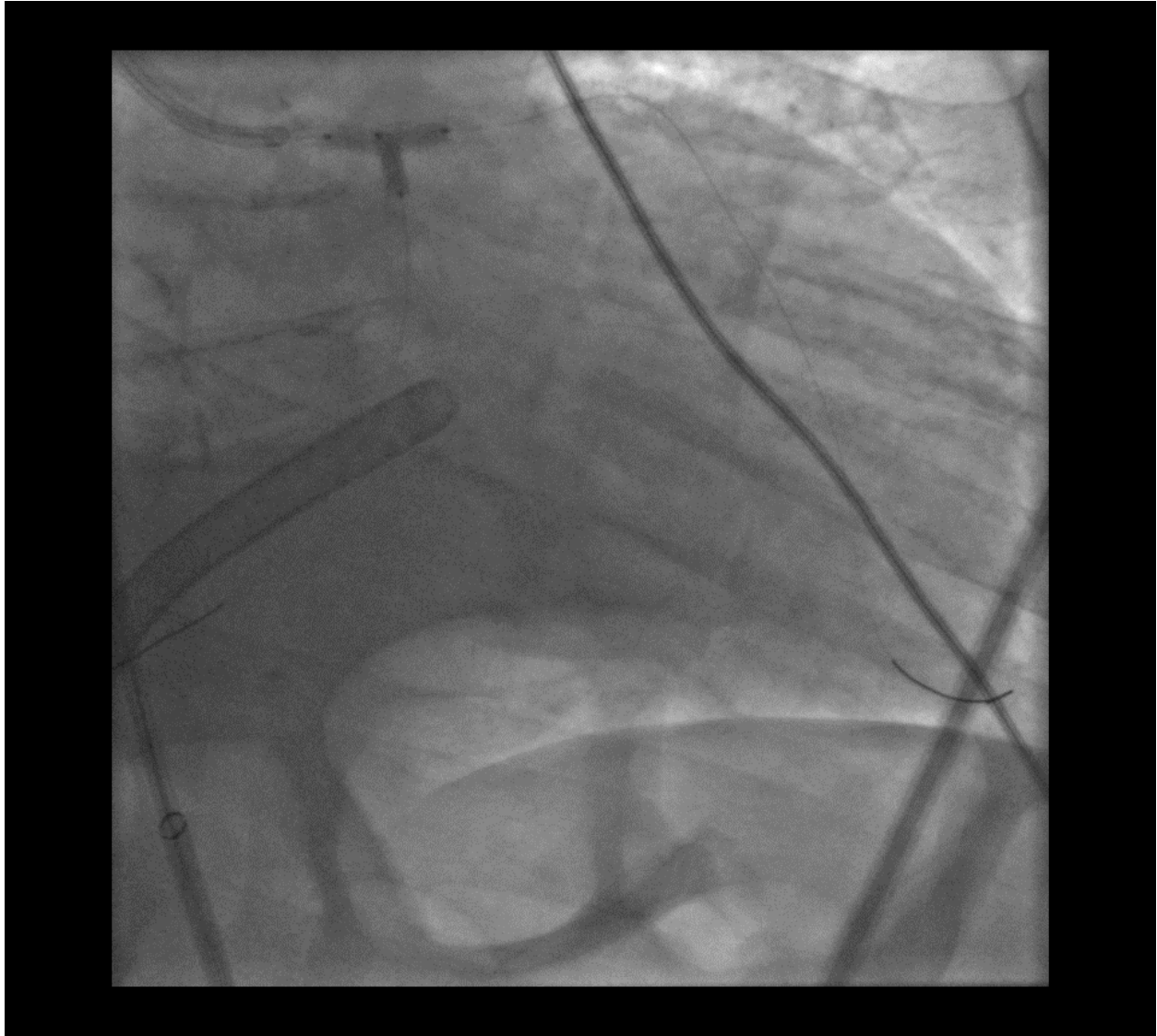
A stent is positioned originating from the left main artery across the left circumflex artery and extending into the left anterior descending artery. The proximal portion of the left circumflex artery stent is positioned inside the left main coronary artery. The left circumflex artery stent is deployed first.

**Figure 4.** Crush Stenting: Crushing



After the left circumflex artery stent is deployed, the balloon catheter and wire are removed. Then, the left main artery stent is deployed, crushing the proximal portion of the left circumflex artery stent.

**Figure 5.** Crush Stenting: Kissing Balloon Inflation



Final kissing balloon inflations are performed after crush stenting to decrease the risk of restenosis.

**Table 1.** Studies of ULMCA PCI with Drug-Eluting Stents

	Dates	# of Centers	# of Patients	% LVEF	% In-hospital Mortality	Mean Follow-up	% Follow-up Mortality	% Distal Location	% Restenosis	% Stent Thrombosis
Park et al. (7)	2003-2004	Single	102	Normal	0	1 year	0	71	7	0
Chieffo et al. (8)	2002-2004	Single	85	51 ± 11	0	6 months	3.5	81	19	1.1
Valgimigli et al. (9)	2001-2003	Multi	95	41 ± 14	11*	503 days	14	65	6	0
Price et al. (10)	2003-2004	Single	50	†	0	276 days	10	94	44	4 (acute)
Lee et al. (12)	2003-2005	Single	50	51 ± 15	2	6 months	4	60	6	0

\* 30-day mortality

†24% of patients with LVEF <40%;

LVEF-left ventricular ejection fraction; m = months; PCI = percutaneous coronary intervention; ULMCA = unprotected left main coronary artery

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