JACC: CARDIOVASCULAR INTERVENTIONS
VOL. 7, NO. 1, 2014

ISSN 1936-8798/$36.00
PUBLISHED BY ELSEVIER INC.
http://dx.doi.org/10.1016/j.jcin.2013.08.013

Impact of Coronary Anatomy and Stenting Technique on Long-Term Outcome After Drug-Eluting Stent Implantation for Unprotected Left Main Coronary Artery Disease

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Objectives This study sought to evaluate the impact of anatomic and procedural variables on the outcome of the unprotected left main coronary artery (uLMCA) itself after drug-eluting stent (DES) implantation.

Background There is a controversial debate regarding when and how to perform percutaneous coronary intervention (PCI) for an uLMCA stenosis.

Methods This analysis is based on a randomized study of 607 patients undergoing PCI for uLMCA, randomized 1:1 to receive paclitaxel- or sirolimus-eluting stents. We evaluated the impact of the SYNTAX score, uLMCA anatomy, and stenting technique on in-stent restenosis (ISR), target lesion revascularization (TLR), and the 3-year outcomes.

Results The 3-year cardiac mortality rate was 5.8%; 235 (39%) patients had a true bifurcation lesion (TBL), and the median SYNTAX score was 27. TBL was associated with a higher need for multiple stents (72% vs. 37%, $p < 0.001$). TBL was a significant predictor of ISR (23% vs. 14%, $p = 0.008$) and for TLR (18% vs. 9%, $p < 0.001$). The need for multiple stents was a predictor of ISR (22% vs. 13%, $p = 0.005$) and for TLR (16% vs. 9%, $p = 0.005$). Culotte stenting showed better results compared with T-stenting for ISR (21% vs. 56%, $p = 0.02$) and for TLR (15% vs. 56%, $p < 0.001$). We observed a significant association between uLMCA-TLR and SYNTAX scores (9.2% for scores $\leq$22, 14.9% for scores 23 to 32, and 13.0% for scores $\geq$33, $p = 0.008$).

Conclusions PCI of uLMCA lesions with DES is safe and effective out to 3 years. TBL and multiple stents were independent predictors for ISR. In the multivariate analysis, independent predictors for TLR were TBL, age, and EuroSCORE (European System for Cardiac Operative Risk Evaluation). (Drug-Eluting-Stents for Unprotected Left Main Stem Disease [ISAR-LEFT-MAIN]; NCT00133237) (J Am Coll Cardiol Intv 2014;7:29–36) © 2014 by the American College of Cardiology Foundation

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Manuscript received May 14, 2013; revised manuscript received August 16, 2013, accepted August 30, 2013.

JACC: CARDIOVASCULAR INTERVENTIONS, VOL. 7, NO. 1, 2014
JANUARY 2014:29–36

Significant left main disease is observed with increasing incidence, given the progressively older patients with higher prevalence of cardiovascular risk factors (1). Left main disease has a significant impact on the symptomatic and prognostic outcome, with a controversial debate regarding the optimal treatment (1–3). Early studies using bare-metal stents have shown high restenosis rates, especially in the presence of left main bifurcation lesions, declaring elective left main percutaneous interventions to be almost a taboo or a palliative approach (1,2). Large randomized trials showed a reduction of restenosis rates in non-left main lesions by 60% to 80% using drug-eluting stents (DES) compared with bare-metal stents, reaching low single-digit rates with different DES (2–9).

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Abbreviations and Acronyms

CABG = coronary artery bypass graft surgery
DES = drug-eluting stent(s)
ISR = in-stent restenosis
LCX = left circumflex coronary artery
LMCA = left main coronary artery
MACE = major adverse cardiac event(s)
MI = myocardial infarction
PCI = percutaneous coronary intervention
TBL = true bifurcation lesion
TLR = target lesion revascularization
uLMCA = unprotected left main coronary artery

In the last few years, different randomized and nonrandomized studies have addressed the percutaneous coronary intervention (PCI) of the unprotected left main coronary artery (uLMCA) with DES and compared it with aorto-coronary artery bypass graft surgery (CABG) (3,10–12). The largest trial to date, the SYNTAX (Synergy Between PCI With TAXUS and Cardiac Surgery) trial, randomized 1,800 patients with 3-vessel disease and/or left main lesions into 2 equally large groups, comparing PCI using the first-generation Taxus DES with CABG (3). In the overall population, major adverse cardiac or cerebrovascular events at 1 year were higher in the PCI group because of an increased rate of repeat revascularization; the hard safety endpoint, including death and myocardial infarction (MI), was similar between the 2 groups, whereas stroke occurred significantly more often after CABG (3). Interestingly, within the subgroup of the 705 patients with left main stenosis, the primary endpoint major adverse cardiac or cerebrovascular events was not different between PCI and CABG ($p = 0.44$), with a better outcome after PCI in the left main subgroup compared with the other patients (13). Despite these results, the worldwide proportion of patients treated with PCI compared with CABG is still higher for patients with 3-vessel disease compared with patients with left main disease, who are often still sent to CABG (14). This might be related to the frequent involvement of the challenging uLMCA bifurcation and concerns of restenosis requiring complex re-interventions, whereas restenosis in the rest of the coronary tree is felt to be treated safely nowadays. But there is no systematic analysis on the basis of an adequate number of left main lesions treated with DES implantation regarding the impact of coronary anatomy, stenting technique, full DES coverage, need for final kissing balloon dilation, and overall coronary disease burden regarding the outcome of the important left main site. To our knowledge, this is the first analysis to systematically address these issues.

Methods

Patient population and analyzed variables. This analysis is based on the previously published randomized ISAR-LEFT MAIN (Drug-Eluting-Stents for Unprotected Left Main Stem Disease) study including 607 symptomatic patients with uLMCA disease undergoing PCI (10); 302 patients were assigned to receive a paclitaxel-eluting stent (Taxus, Boston Scientific, Natick, Massachusetts) and 305 assigned to receive a sirolimus-eluting stent (Cypher, Cordis, East Bridgewater, New Jersey) (10). The primary trial focused on the comparison of the 2 different stent platforms and showed no significant difference in the outcome between paclitaxel-eluting stents and sirolimus-eluting stents, with an overall low MACE (major adverse cardiac events) rate, comparable to the SYNTAX trial (3,10). Given the similar outcome of the 2 stent platforms, this current analysis evaluated the prognostic impact of the overall coronary anatomy (reflected by the SYNTAX score), the left main anatomy, and the stenting technique on the angiographic restenosis rate (in-stent restenosis [ISR]) and target lesion revascularization (TLR) for the left main itself, independent of the DES used.

The methods of the randomized ISAR-Left Main trial have been published in detail (10). Written informed consent for participation in this trial has been obtained from all subjects (or their guardians). The study was conducted in accordance with the provisions of the Declaration of Helsinki and with the International Conference on Harmonisation's Good Clinical Practices, and protocol approval was obtained from the medical ethics committee for both participating centers, the Deutsches Herzzentrum and Medizinische Klinik I, Klinikum Rechts der Isar, Munich, Germany (10).

We assessed the Parsonnet score and EuroSCORE (European System for Cardiac Operative Risk Evaluation) to evaluate possible differences between the subgroups (15–17). Baseline, procedural, and follow-up coronary angiograms were digitally recorded and assessed off-line in the quantitative angiographic core laboratory (ISAR Center, Munich) with an automated edge-detection system (CMS version 7.1, Medis Medical Imaging Systems, Leiden, the Netherlands) by 2 independent experienced operators unaware of the treatment allocation and clinical characteristics. Quantitative analysis was performed on the left main area, which was considered the anatomic coronary region