

# Fruitful new data on left main PCI: the LEMON study

Maria D. Radu Juul Jensen<sup>1\*</sup>, MD, PhD; Lorenz Räber<sup>2</sup>, MD, PhD

1. Department of Cardiology, Gentofte University Hospital, Hellerup, Denmark; 2. Department of Cardiology, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland

## Introduction

In patients undergoing percutaneous coronary intervention (PCI), intracoronary imaging provides superior information compared to angiography regarding: 1) lesion pathology and need for lesion preparation; 2) appropriate sizing of devices; 3) choice of stent length for complete lesion coverage; 4) post-PCI results such as insufficient expansion or residual disease at stent edges requiring additional treatment; and 5) mechanisms of acute complications including underexpansion, malapposition, edge dissections and stent deformation. Increasing evidence on the effect of imaging guidance in unprotected left main (LM)-PCI shows consistent benefits in the reduction of target lesion revascularisation and mortality. Accordingly, revascularisation guidelines give a class IIa level B recommendation for intravascular ultrasound (IVUS) guidance<sup>1</sup>. Although the use of optical coherence tomography (OCT) is challenging in ostial LM lesions and vessels >5 mm, the technology surpasses IVUS by more accurately visualising subtle morphological details relevant to PCI procedures and stent failures (as above). Data on the systematic use of OCT to guide LM-PCI are still awaited.

## THE PRESENT STUDY

In the current issue of EuroIntervention, Amabile et al<sup>2</sup> present a pilot study assessing for the first time, prospectively, the feasibility and performance of a standardised protocol for OCT-guided completion and optimisation of mid/distal LM-PCI.

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The LEMON study included 70 patients, from 10 centres throughout France, with stable or non-stable mid/distal LM lesions requiring PCI with a one- (83%) or two-stent (17%) strategy. The standardised protocol prescribed the performance of three OCT runs, which was followed in 100% of cases. The first run was primarily used to guide sizing of stents and proximal optimisation technique (POT) balloons, and choice of landing zones. Runs 2 and 3 were used to evaluate the guidewire recrossing point (optimal in 81%), and stent expansion, apposition and edge dissections, respectively, resulting in a modification of strategy in 26% of cases. The primary endpoint, procedural success (residual angiographic stenosis <50% [100%] + Thrombolysis In Myocardial Infarction [TIMI] 3 flow in all branches [100%] + adequate OCT stent expansion [86%]), was achieved in 86% of patients. The

\*Corresponding author: Department of Cardiology, Gentofte University Hospital, Gentofte Hospitalsvej 1, 2900 Hellerup, Denmark. E-mail: maria\_d\_radu@yahoo.com

study is of great interest to interventional cardiologists as it provides new and timely evidence supporting the feasibility of OCT to guide interventions in the mid/distal LM. The following aspects deserve to be highlighted.

First, the authors should be commended for the challenge of engaging 10 centres at national level, which testifies to the interest and motivation of interventionalists to follow a pre-specified imaging-based treatment protocol and is promising for the implementation of a structured approach in daily routine and for future trials.

Second, the authors state that the proximal stent edge in the LM was visible in all cases, which is reassuring for the feasibility of using OCT in the LM. Still, it is well known that large vessel size may cause “out-of-view” artefacts hindering essential visualisation of the vessel circumference, which, for the LM, may affect automatic lumen measurements in up to 11.4% of frames in the mid portion<sup>3</sup>. Clinically, the ILUMIEN III study that included non-LM lesions and whose device sizing protocol was reused in the LEMON study, reported the visibility of the external elastic membrane (EEM)  $>180^\circ$  of the circumference at either reference segment in 84% of OCT runs, and further that the EEM could be used to decide stent size in 70% and 79% of patients at the proximal and distal reference, respectively<sup>4</sup>. These rates are presumably lower in LM lesions and they would have been valuable to know in the present study, not least since sizing of stents and POT balloons is particularly important in the large LM bifurcation where the use of lumen as opposed to EEM areas may lead to undersizing of devices and thus stent underexpansion.

Third, the LEMON study introduced a new method of calculating relative stent expansion considering the tapering and specific anatomy of the LM bifurcation. Notably, stent expansion is the strongest predictor of future events. According to the LEMON criteria, the stented segment was divided into two parts using the carina instead of the geographic midpoint as division point and comparing the minimal stent area (MSA) of the two obtained segments with the closest (proximal or distal) reference lumen area. Adequate expansion  $\geq 80\%$  was achieved in 86% of cases. When calculated according to the less conservative methods used in the ILUMIEN III and DOCTORS trials (which excluded LM lesions), this was reduced to 37% and 40%, respectively. Interestingly, these rates were lower than the corresponding optimal expansion rates in the two aforementioned non-LM studies (41% and 58%, respectively), supporting the idea that a customised algorithm for the LM bifurcation is needed. Due to the relatively consistent anatomy in the LM, absolute expansion goals can also be applied. The authors assessed the achievement rates for a set of MSA cut-offs (the “8-7-6-5 rule”) previously defined by Kang et al describing IVUS-derived thresholds for the LM, confluence, and ostial left anterior descending (LAD) and left circumflex (LCX) segments that best predict future events<sup>5</sup>. Though these cannot be directly extrapolated to OCT due to the 10% overestimation in area measurements by IVUS<sup>1</sup>, two interesting observations can be made: the MSA achieved in the LM by operators in the LEMON study is comparable to the ones reported

in the IVUS subgroup of the NOBLE trial<sup>6</sup> and larger as compared to the EXCEL subgroup (Maehara A. IVUS-guided left main and non-left main stenting in the EXCEL Trial: Lessons From the EXCEL IVUS Core Laboratory. TCT 2016, Washington, DC, USA) (LEMON OCT: 11.6 mm<sup>2</sup>; NOBLE IVUS: 12.5 mm<sup>2</sup>, EXCEL IVUS: 9.9 mm<sup>2</sup>) and beyond the generally accepted LM-MSA of  $>8$  mm<sup>2</sup>, attesting to optimal procedural outcomes in this study. Additionally, it is interesting that the achievement rates for the classic MSA cut-offs defined by Kang et al were numerically lowest for the ostial LAD and LCX – sites that are known to be problematic in terms of expansion.

Fourth, the study highlights the challenges with guidewire recrossing in bifurcation PCI, where OCT guidance for finding the distal cell is recommended by the European Bifurcation Club<sup>7</sup>. The significant discrepancy in the interpretation of wire position with a disagreement between operators and core lab experts in 27% of cases underscores the importance of training in both image interpretation and handling with 3D-reconstruction software.

Fifth, the study is limited primarily by its small sample size and non-randomised nature which prevents assessment of the clinical impact of OCT guidance. Whether the inability of OCT to evaluate ostial LM lesions is a significant limitation is relevant to discuss: the rate of patients who are ineligible is difficult to estimate since most studies using IVUS for LM-PCI have pooled ostial with shaft/mid lesions; however, it is probably 15-30%. Interestingly, a substudy from EXCEL showed that revascularisation after PCI versus coronary artery bypass grafting (CABG) was similar for isolated ostial/shaft lesions; however, it was greater for lesions in the distal LM bifurcation, which expectedly were treated with a significantly higher number of stents<sup>8</sup>. It is therefore promising that another study has shown that the use of a pre-specified IVUS protocol was an independent predictor of lower risk of events in these lesions<sup>9</sup>. Taken together, the mid/distal compared to the ostial part of the LM appears more relevant to interrogate, and the limitations of OCT in the ostial LM may be outweighed by the potentially superior usefulness in the distal segment.

## REMAINING QUESTIONS

Though the concept of guiding LM-PCI by a standardised protocol is not new<sup>9</sup>, a number of questions remain. The use of an OCT-derived minimum lumen area (MLA) to determine lesion significance in intermediate LM lesions is greatly needed, particularly in situations where fractional flow reserve (FFR) is challenging, e.g., in the presence of concomitant distal disease. Similarly, whether modified IVUS cut-offs for adequate post-procedural MSA in the LM region can be transferred to OCT needs prospective evaluation. It is also important to understand whether OCT imaging can help in identifying specific LM bifurcations that would benefit from a two- rather than a one-stent provisional strategy. Assessment of features associated with a risk of side branch compromise (small MLA, “eyebrow sign”) is already recommended with IVUS guidance<sup>7</sup>, with benefits that should be attainable with OCT as well. Altogether, the correct use of OCT in the evaluation of guidewire

recrossing and more points to the necessity of very prescriptive protocols with detailed definitions to limit “operator discretion”. Although the advantages of an imaging- versus an angiography-guided procedure are obvious, particularly in the LM, randomised data on the efficacy in improving cardiovascular outcomes are greatly needed. The ongoing OCTOBER trial, which includes LM lesions<sup>10</sup>, is therefore awaited with excitement and is expected to contribute to changing the way we perform LM-PCI today.

### Conflict of interest statement

M. Radu Juul Jensen reports speaker fees and advisory board honoraria from Abbott Vascular. L. Räber receives research grants to the institution from Abbott Vascular, Boston Scientific, Biotronik, Sanofi, Regeneron and speaker fees from Abbott Vascular, Amgen, AstraZeneca, Canon, Occlutech, Sanofi, and Vifor.

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