Online version at https://www.minervamedica.it

Minerva Cardiology and Angiology 2024 February;72(1):41-55
DOI: 10.23736/S2724-5683.22.06181-6

REVIEW

The role of optical coherence tomography in guiding percutaneous coronary interventions: is left main the final challenge?

Horea-Laurentiu ONEA [1, 2], Florin-Leontin LAZAR [1], Dan-Mircea OLINIC [1, 2], Calin HOMORODEAN [1, 2], Bernardo CORTESE [3] *

[1]Department of Interventional Cardiology, Cluj County Emergency Hospital, Cluj-Napoca, Romania; [2]Medical Clinic Number 1, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania; [3]Fondazione Ricerca e Innovazione Cardiovascolare, Milan, Italy

*Corresponding author: Bernardo Cortese, Fondazione Ricerca e Innovazione Cardiovascolare, Via Gianbattista Vico 2, Milan, Italy. E-mail:bcortese@gmail.com

ABSTRACT

Left main (LM) coronary artery disease is a high-risk lesion subset, with important prognostic implications for the patients. Recent advances in the field of interventional cardiology have narrowed the gap between surgical and percutaneous approach of this complex lesion setting. However, the rate of repeat revascularization remains higher in the case of percutaneous coronary intervention (PCI) on long-term follow-up. As such, the need for better stent optimization strategies has led to the development of intravascular imaging techniques, represented mainly by intravascular ultrasound (IVUS) and optical coherence tomography (OCT). These techniques are both able to provide excellent pre- and post-PCI guidance. While IVUS is an established modality in optimizing LM PCI, and is recommended by international revascularization guidelines, data and experience on the use of OCT are still limited. This review paper deeply analyzes the current role of OCT imaging in the setting of LM disease, particularly focusing on its utility in assessing plaque morphology and distribution, vessel dimensions and proper stent sizing, analyzing mechanisms of stent failure such as malapposition and underexpansion, guiding bifurcation stenting, as well as offering a direct comparison with IVUS in this critical clinical scenario, based on the most recent available data.

(*Cite this article as:* Onea HL, Lazar FL, Olinic DM, Homorodean C, Cortese B. The role of optical coherence tomography in guiding percutaneous coronary interventions: is left main the final challenge? Minerva Cardiol Angiol 2024;72:41-55. DOI: 10.23736/S2724-5683.22.06181-6)

KEY WORDS: Tomography, optical coherence; Percutaneous coronary intervention; Imaging.

Left main (LM) coronary artery disease (CAD) is a high-risk, life-threatening condition, due to the large amount of myocardial territory at risk. The continuous development of strategies and devices in interventional cardiology has changed the paradigm of treatment of LM disease. Coronary artery by-pass graft surgery (CABG) still represents the gold standard in treating LM disease since the beginning of coronary revascularization and even with the development of bare metal stents (BMS) and first-generation drug eluting stents (DES) the results were unsatisfactory with percutaneous coronary interventions (PCI).[1, 2] It was only after the routine use of second-generation DES (2g-DES) when the gap between PCI and CABG has been reduced, with similar long-term survival rates being reported for patients with LM disease and low to intermediate SYNTAX score, with CABG retaining an overall superior clinical benefit over PCI.[3]

As complex lesions (particularly LM stem) have been reported to benefit from intravascular imaging (intravascular ultrasound [IVUS] and optical coherence tomography [OCT]),[4] current European guidelines recommend IVUS (class IIa B indication) to optimize stent results in selected patients. Moreover, IVUS is recommended to assess lesion severity in LM coronary artery disease and to optimize unprotected LM intervention (class IIa B indication).[3] While IVUS has emerged as an important adjuvant tool in enhancing LM PCI, the role of OCT is still unclear and current data is still scarce, but several studies have shown promising results, with ongoing research expected to better clarify the importance of this imaging technique in this complex setting.

LM CAD

LM treatment - PCI *vs.* CABG

The 2018 European Guidelines on Myocardial Revascularization granted percutaneous treatment of LM disease a Class I, IIa and III (level of evidence B) recommendation respectively for low, intermediate and high SYNTAX scores.[3] However, recently the long-term results of two large randomized clinical trials (RCT), NOBLE (Nordic-Baltic-British Left Main Revascularization Study)[5] and EXCEL (Evaluation of XIENCE Versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization)[6] were published and the authors reported contradictory conclusions.

While the EXCEL trial found a similar rate of a composite of death from any cause, stroke, or myocardial infarction (MI) between the two studied groups (PCI using the 2g-DES Xience and CABG) with a higher rate of death from any cause and ischemia-driven revascularization in the PCI group,[6, 7] the NOBLE trial reported at long-term follow-up a more frequent rate of the composite endpoint of death, non-procedural MI, stroke, and repeat revascularization in the PCI arm, with no significant differences between the two groups in terms of mortality.[5, 8] With an important between-study heterogeneity in terms of definition of MI, patient assessment, procedural characteristics, device used and methodology as potential explanations for the opposing results,[9] a series of meta-analyses were conducted, reporting a similar risk for all-cause mortality at five years,[10] but with higher rates of need for repeat revascularization in the PCI arm.[11]

Taking all these information into consideration, PCI represents a viable alternative to CABG for LM disease, with the latest guidelines from the American College of Cardiology/American Heart Association granting different classes of recommendation for LM PCI with respect to lesion location (IIa for isolated ostial or mid-shaft, respectively IIb for distal LM bifurcation lesions or for those associated with complex multivessel disease).[12, 13]

Predictors for long-term adverse outcome in LM PCI

More than a decade ago, the Synergy Between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery (SYNTAX) Trial demonstrated that PCI is an acceptable alternative to CABG for the treatment of multivessel CAD or LM disease with low or intermediate SYNTAX Score.[13] In this trial, the rate of major adverse cardiac and cerebrovascular event rates at one year in LM patients were similar for CABG and PCI (13.7% *vs.* 15.8%; P=0.44), but at the cost of a higher rate of repeat revascularization in the PCI arm, mainly driven by the presence of DM.

A large number of studies managed to identify further poorer prognostic predictors. The GRAVITY Registry found after 15 years of follow-up that old age, number of vessels treated during index PCI and depressed left ventricular ejection fraction increase the risk of all-cause death.[14] Min *et al.* identified advanced age over 75 years old, LM distal bifurcation and acute coronary syndromes (ACS) as independent predictors of target vessel revascularization (TVR). Moreover, in patients with LM disease presenting with an ACS, Homorodean *et al.* recognized cardiogenic shock, TIMI 0/1 flow, old age, baseline SYNTAX Score II, residual SYNTAX Score, SYNTAX Revascularization Index and estimated glomerular filtration rate as independent predictors of mortality at long-term follow-up.[15-17]

While some of these predictors are unmodifiable, intravascular imaging has been shown to have the ability of improving the outcomes when used to guide PCI in complex lesions such as LM disease.

The role of intravascular imaging in guiding PCI

While coronary angiography (CA) has been the main imaging modality used for guiding PCI, it still has several limitations in assessing the vessel wall, plaque composition, atherosclerosis distribution and it is hampered by interobserver variability.[18] Thus, intravascular imaging by IVUS and OCT, providing tomographic sections of the coronary arteries, has been developed in order to better understand atherosclerotic disease, guide the physician in the catheterization laboratory, select the appropriate interventional strategies and optimize PCI.[19]

IVUS

IVUS has been shown to be an important tool in improving the outcome of PCI. In both clinical trials[20, 21] as well as meta-analyses[22] IVUS-guided PCI had a significantly lower rate of major adverse cardiac events (MACE), target vessel failure (TVF) and stent thrombosis (ST) at long-term follow-up.

Current guideline recommendations reflect this data, with a class IIb B indication in using IVUS for guiding PCI from the American College of Cardiology/ American Heart Association[23] and a class IIa B indication respectively from the 2018 ESC/EACTS.[3]

OCT

OCT is an optical imaging modality that uses near-infrared light to offer higher-resolution images (10-20 µm axial resolution) than IVUS, with faster image acquisition but at the cost of lower penetration (up to 3mm).[24] Main features and limitations of each technique in comparison with a functional evaluation are summarized in Table I.[25, 26] Current data on the prognostic benefit of OCT usage in guiding PCI is limited.

Two important RCTs, the DOCTORS and ILUMIEN III trials,[27, 28] found OCT to improve stent underexpansion as well as to lower the number of untreated edge dissections and major malappositions, but there were no significant differences in terms of MACE between OCT-guided PCI and angiography-guided PCI group. Conversely, non-randomized studies[19, 29] found significant improvement in mid- and long-term follow-up outcomes in patients undergoing OCT-guided PCI, by lowering the risk of cardiac death, MI, and all-cause mortality respectively.

Table I.—*Main advantages and disadvantages of OCT, IVUS and FFR.*

OCT	IVUS	FFR
Advantages	Advantages	Advantages
• High spatial resolution (10-20 µm axial, 20-40 µm lateral) • Better tissue characterization (calcium) • Thrombus identification • Assessment of stent edge dissection, strut coverage, malapposition • Better guidance for SB rewiring (of particular interest in distal LM) • Easier to interpret	• Better penetrability • Allows true vessel stent sizing • Allows better quantification of plaque volume • Accurate evaluation of stent area and stent expansion • Extensive clinical experience • Available data that shows better outcome following IVUS-guided PCI, including LM setting • Valuable guide in CTO procedures	• Ability to defer SB stenting in LM bifurcation lesions with seemingly significant residual stenosis • Evaluation of collateral flow
Disadvantages	Disadvantages	Disadvantages
• Limited penetrability (impeding large vessel evaluation, such as LM) • The need for contrast media injection • The need for flushing in order to remove blood (difficulty in evaluating LM ostia) • Limited data on its prognostic benefit in guiding PCI	• Poor tissue characterization • Difficult thrombus identification • Limited assessment capability of strut coverage, strut malapposition • Difficult to interpret	• Difficulty in interpreting LM FFR when paired with significant downstream branch lesion • No information on plaque morphology • Cannot assess plaque vulnerability features • Cannot evaluate stent-related complications

CTO: chronic total occlusion; FFR: fractional flow reserve; IVUS: intravascular ultrasound; LM: left main coronary artery; OCT: optical coherence tomography; PCI: percutaneous coronary intervention; SB: side branch.
Adapted from Raber *et al.*[4] and Longobardo *et al.*[25]).

IVUS *vs.* OCT

So far, several RCTs compared the outcomes of IVUS and OCT when used to guide PCI. The OPINION trial enrolled 829 patients and reported the non-inferiority of OCT-guided PCI with respect to IVUS-guided PCI in terms of TVF at one year[30] as well as similar rates of late lumen loss (LLL), percent diameter stenosis and binary restenosis. Stent diameter was determined by using a lumen-based approach in the OCT group, resulting in significantly smaller final stent sizes as compared to the IVUS group, in which EEL diameter was used as a marker (2.92±0.39 mm *vs.* 2.99±0.39 mm; P=0.005). The ILUMIEN II retrospective study[31] reported similar stent expansion degrees irrespective of the imaging modality used to guide PCI (OCT or IVUS), with an important remark being the fact that IVUS overestimates lumen area by 10%.[32]

ILUMIEN III[28] randomized 450 patients and evaluated a novel OCT stent matching using EEL diameter at the reference segments. Compared to IVUS, OCT was non-inferior in terms of post-PCI minimum stent area (MSA) (5.79 mm^2 *vs.* 5.89 mm^2; P=0.01) and similar in terms of minimum and mean stent expansion. In the OCT group there were significantly fewer major dissections and malappositions compared to the IVUS group, without an impact on MACE.

As all of these studies reported optimistic results regarding the use of OCT in guiding PCI, one important question arose: is OCT efficient enough to guide PCI in LM disease as well? With several small studies trying to answer this question, the available data is still limited, but the initial results are encouraging.

The role of OCT in LM PCI

Plaque assessment (morphology, lesion length, diameter)

Morphology

OCT assessment of plaque characteristics is important for planning the PCI procedure. Plaque individual components, elements of vulnerability, as well as plaque complications can be accurately visualized (Figure 1).

OCT mainly classifies coronary plaques as fibrous, lipid-rich, and calcified based on data from histology studies[33] and correlates well with the latter, as shown by Yabushita *et al.*:[34] sensibility and specificity were 71-79% and 97-98% for fibrous plaque, 90-94% and 90-92% for lipid-rich plaques, and 95-96% and 97% for calcified plaques, with similar results being reported by Kume *et al.*[35]

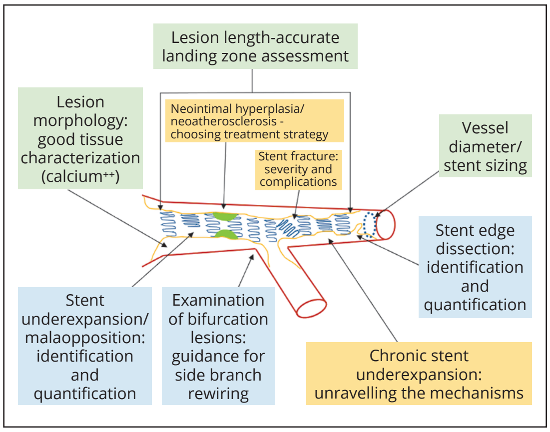

Figure 1.—Use of optical coherence tomography in guiding left main percutaneous coronary interventions: overall features of the advantages of this technology.

Fibrous plaque

Fibrous plaque represents a low-attenuating, signal-rich, relatively homogenous lesion,[36] mainly consisting of collagen fibers, smooth muscle cells, and extra-cellular matrix (proteoglycans). It usually allows the visualization of the EEL, as opposed to lipid/ necrotic core which attenuate light, thus obscuring the EEL.

The use of OCT not only allows the identification of these plaques, but also has the ability to guide long-term pharmaceutical therapy, as Yano *et al.* reported for the first time the effect of proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors in addition to statins on fibrous cap thickness or extension of the atherosclerotic plaque after ACS.[37] In this study, OCT analysis revealed that the use of this approach, even for a short period of time after the onset of an ACS, due to a greater reduction of low-density lipoprotein cholesterol, could be responsible of an incremental growth in fibrous cap thickness and regression of the lipid component.

Lipid-Rich plaque

his type of lesion consists of a high-attenuating, signal-poor region- the lipid-rich necrotic core, covered by a fibrous cap. OCT is best suited to assess fibrous cap thickness due to its high spatial resolution, which is of great importance when defining plaque vulnerability.[33] Macrophages can also be identified as clusters of bright spots along the fibrous cap. A fibrous cap thickness of <65µm defines a thin-cap fibroatheroma, and it is usually correlated with plaque rupture, as shown by Burke *et al.*[38] Also, thin cap rupture was found to be the culprit mechanism in more than two-thirds of ACS.[39]

The clinical implication of identifying these plaques on OCT is the fact that in their management, predilatation with an undersized balloon or direct stenting should be considered and full lesion coverage is preferred, as they are prone to rupture with distal embolization.[40] Several studies have shown that stenting lipid-rich plaques was associated with increased risk of post-procedural MI, distal embolization and no-reflow phenomenon.[41]

Calcific plaque

Calcific plaques are characterized by low-attenuating, signal-poor regions and sharply delineated borders (Figure 2), and are more commonly seen in older patients, with DM or renal failure;[42] the presence of these plaques has been shown to be associated with worse procedural success.[43] Therefore, when tackling moderate to severely calcified plaques, good lesion preparation is mandatory, as severe stent underexpansion is associated with negative outcome, including in-stent restenosis (ISR) and ST.[44] OCT identification of these lesions, especially in the case of LM, should guide the physician into using aggressive debulking strategies, in order to achieve proper stent expansion and apposition.

Rotational atherectomy (RA) is the most commonly used calcium modification strategy. As older studies like the ROTAXUS Trial did not find a benefit in outcomes from using RA when comparing it with standard PCI in moderate to severe calcification (intravascular imaging was not implemented),[45] current guidelines are recommending the use of atherectomy only in case of heavily calcified lesions, with a class IIa C indication.[23]

When comparing orbital atherectomy with RA, Okamota *et al.* found similar MACE, with a slightly higher dissection and perforation rate (1.6% *vs.* 0.3%, P=0.02; 1.6% *vs.* 0.2%, P=0.03) and a trend towards better stent expansion with OA, as assessed by OCT imaging.[46]

Intravascular lithotripsy (IVL) is a relatively novel calcium modification technique useful in both de-novo calcified lesions[47] as well as in stent restenosis with underexpanded stents due to heavy calcifications.[48] In DISRUPT CAD III[49] which prospectively included patients with se-

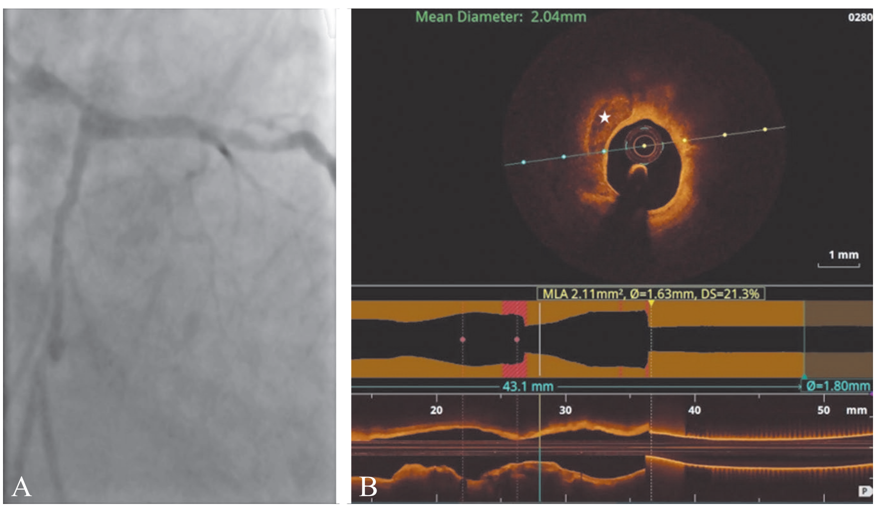

Figure 2.—A) Coronary angiography shows a severe distal left main stenosis (Medina 1-0-0); B) optical coherence tomography reveals two-quadrant, superficial and thick calcification (star).

verely calcified lesions, IVL determined calcium fractures in 67.4% of lesions with a post-PCI stent expansion of 101.7±28.9% and was associated with a procedural success of 92.4% and a freedom from 30-day MACE of 92.2%. Aziz *et al.*[50] reported adequate procedural success and low complication rate when using IVL (99% and 3% respectively) with a MACE rate of 2.6% at long-term follow-up.

OCT not only has the ability to assess the presence of the calcific plaque, but it can also identify several predictors of calcium fracture in case of RA, such as maximum calcium angle of >227° (P<0.001) and calcium thickness of <0.67 mm (P<0.001), with an 86.9% incidence of cracks in these segments.[51] Fujino *et al.*[52] reported the thresholds in case of balloon angioplasty-only lesion preparation, which were much lower regarding calcium thickness (<0.24 mm).

Three main types of calcifications can be identified by OCT:[53] superficial calcium, deep calcium and nodular calcium, important to consider, as each type carries different management. Deep calcification usually requires only balloon-based strategies, such as non-compliant, scoring or cutting balloons, sometimes IVL being necessary. Nodular calcification is best managed using orbital or rotational atherectomy, whereas superficial calcification can be treated with either OA, RA, or IVL.[53]

Another important clinical implication of OCT in heavily calcified lesions is suggested by the data from a retrospective study,[54] in which a high OCT-based calcium scoring system comprising of maximum calcium thickness >0.5 mm, length of calcium >5 mm and maximum arc >180° determined significantly lower stent expansion degrees (median 78%; P<0.01). This indicates the need for additional plaque debulking strategies, although, the study excluded patients with complex calcified lesions, for whom these modalities would have been used.

Lesion length

With the help of L-mode and other features, OCT can be used to accurately measure vessel dimensions, characteristics and structure (Figure 1). The largest lumen with minimal disease either proximal and distal to the lesion is used to define stent landing zones. Accurate choice of stent length is of utmost importance as incomplete lesion coverage is associated with stent failure and MACE.[4]

Landing zones should mainly contain fibrotic tissue, as an OCT retrospective study[55] has shown that the presence of lipid-rich plaque at the stent edges was associated with late stent edge restenosis (SER) (61% in the SER group *vs.* 20% in the non-SER group; P<0.001) and suggested that in case of diffuse disease a lipid arch of <185° could minimize this phenomenon. Kang *et al.*[56] demonstrated that a plaque burden of <55% at the reference segment post-PCI evaluated with IVUS should be associated with a lower SER rate. With respect to calcific plaques, deep calcium with an arc of <180° should determine a more favorable outcome.[57]

Diameter

Stent sizing can be performed using two main strategies- a lumen based and a vessel (EEL) based approach. Using the distal reference is the most common and safest method. IVUS has been long used to evaluate the severity of LM lesions. An MLA value of <6 mm^2 is the established cut-off for LM revascularization, as was demonstrated by a prospective study by de la Torre Hernandez *et al.*[58] At two-year follow-up, the survival rate was 97.7% in the deferred group, compared to 94.5% in the invasive group (P=0.5). This cut-off value has also a strong correlation with a fractional flow reserve (FFR) value of <0.75 with high sensitivity and specificity (93%, 95%).[59] Figure 3 demonstrates how OCT can lead to a change in the decision in case of angiographically nonsignificant lesions.

A smaller study conducted on Asian patients with isolated and mid-shaft angiographically intermediate LM lesions suggested a lower MLA cut-off of <4.5 mm^2.[60] Consequently, race should be taken into account when approaching the LM. It is a known fact that IVUS overestimates lumen dimensions,[32] thus OCT-derived cut-offs must be lower, but are not well established. A retrospective study including patients with LM bifurcation lesions[61] suggests the need for revascularization in case of OCT-measured area stenosis (AS) >75% or MLA ≤4 mm^2 (when AS is between 50% and 75%).

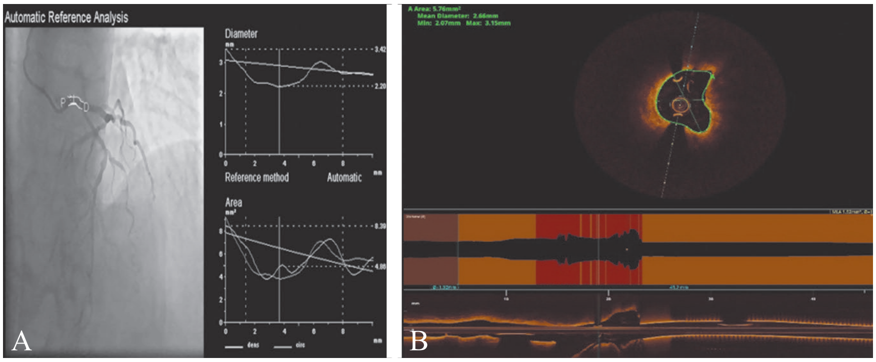

Figure 3.—A) Coronary angiography shows a nonsignificant left main mid-shaft stenosis (42% on quantitative analysis); B) optical coherence tomography reveals a minimum lumen area of 5.76 mm², which led to angioplasty with stent implantation.

Understanding the mechanisms of in-stent restenosis to guide treatment

Based on angiography, ISR is defined as a >50% stenosis in a stent or within 5mm from the proximal and distal edges.[62] As the use of intravascular imaging, especially OCT, has been shown to provide additional information on the mechanisms of ISR (Figure 1),[63] the 2018 ESC/EACTS Guidelines on Myocardial Revascularization[3] recommended the use of OCT for evaluating stent-related mechanical problems leading to restenosis (class IIa C indication). Four main entities have been described:[64] chronic stent underexpansion, stent fracture, neointimal hyperplasia and neoatherosclerosis, each requiring specific therapeutic considerations.

Stent underexpansion

Stent underexpansion as a mechanism of ISR can result from stent undersizing, inadequate balloon deployment or poor lesion preparation, in particular when the calcium burden is high. High-pressure non-compliant balloon is the optimal management, and a balloon/vessel ratio of 1.1 to 1 is generally recommended,[65] with RA[66] or excimer laser coronary angioplasty[67] being safe and effective alternatives in refractory cases.

Neointimal hyperplasia

Neointimal hyperplasia as well as neoatherosclerosis with soft, lipid-rich or fibrotic tissues can also be tackled using high-pressure non-compliant balloons. Conventional balloons carry the risk of migration which can be avoided by using cutting or scoring balloons. The RESCUT Trial[68] which included 428 patients with ISR demonstrated no improvement in the angiographic degree of stenosis or rate of clinical events (16.4% *vs.* 15.4% patients with MACE; P=0.79) at seven-month follow-up when comparing cutting balloon with conventional balloon-angioplasty. The final treatment consists in a prolonged inflation of a drug-coated balloon or in a new DES implantation, as both strategies are granted a class I A recommendation.[3]

Stent fracture

Several risk factors for stent fracture have been described, including abnormal forces placed on the stent, vessel tortuosity (especially in the right coronary artery), vessel calcification, ostial stent location, hinge motion, overlapping stents, increased stent length, smaller stent diameter, coronary aneurysm, and balloon overdilation.[69]

In a large study, Kan *et al.* prospectively studied 6555 patients with 16482 DES implanted, finding a high incidence of stent fracture (12.3%). This complication was associated with higher ISR rates (42.1%), target lesion revascularization (TLR) (24.8%, N.=379), and definite ST (4.6%) compared with stents without fracture (10.7%, 6.6%, and 1.03%; all P<0.001), even though these differences did not translate into higher mortality rates.[70] Lee *et al.* described four types of stent fractures and while most of the type I lesions (single strut fracture) can be identified by CA alone, OCT-guided procedures have been shown to better identify more severe lesions, which require coronary interventions.[71, 72]

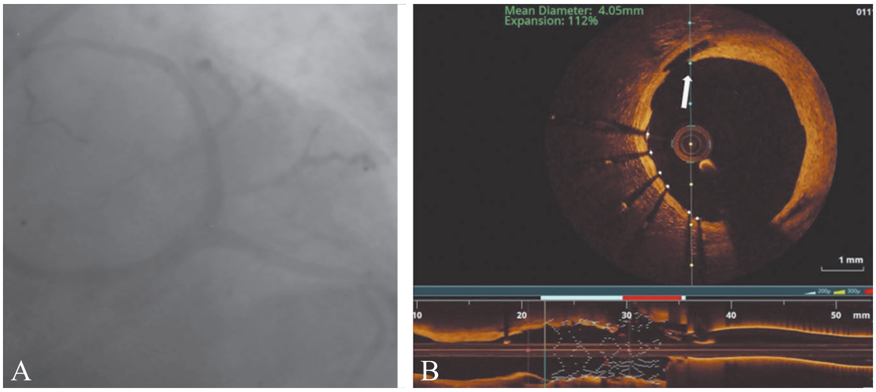

Figure 4.—A) Coronary angiography shows an apparently good result after left main-proximal left anterior descending artery stent implantation; B) optical coherence tomography reveals distal stent edge dissection (arrow).

Stent edge dissection

Stent edge dissection (Figure 4) consists of a tear at the stent-vessel wall interface characterized by a linear rim of tissue with clear separation from the arterial wall.[73] OCT has a high sensibility in detecting even very small, non-flow limiting edge dissections, due to its excellent spatial resolution (Figure 1). It should be noted however that over two-thirds of edge dissections described on OCT have no clinical significance.[40]

The CLI-OPCI II Study[74] retrospectively analyzed 832 patients including those with LM disease and found that a significant dissection (>200 µm width) at the distal stent edge was predictive of MACE (HR: 2.54; P=0.004), which was not the case for a proximal dissection (HR: 0.83; P=0.65). A smaller study[75] has shown that cavity depth at the distal edge (HR: 1.029, 95% CI, 1.012-1.047), reference lumen area at the proximal edge (adjusted HR: 0.63, 95% CI, 0.45-0.87), and overall dissection length (adjusted HR: 1.17, 95% CI, 1.02-1.34) were associated with an increased risk of device-oriented composite end point (cardiac death, target lesion MI, or TLR) at one year.

Stent underexpansion and malapposition

Alongside uncovered stent struts and neoatherosclerosis, stent underexpansion and malapposition (Figure 5) have been identified as the leading mechanisms of ISR and ST. The PRESTIGE registry, the largest available series of patient assessed by OCT for ST, reported stent underexpansion to be highest in patients with early ST, while malapposition was a frequent finding in early ST, but also found in 14% of patients presenting with very late ST.[76] Even if the rates of ST have been decreasing consistently since the

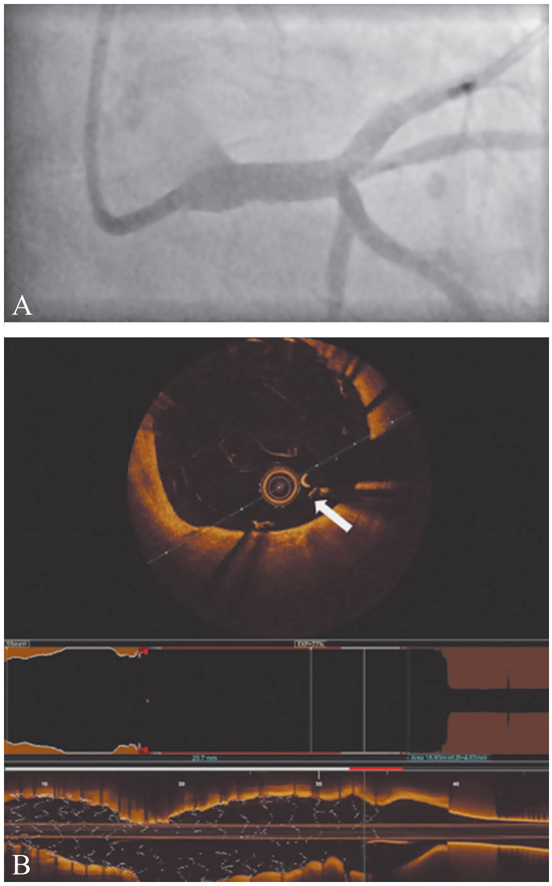

Figure 5.—A) Coronary angiography after left main-proximal left anterior descending artery stent implantation with adequate result; B) optical coherence tomography reveals significant stent malapposition (arrow) of the proximal struts.

introduction of 2 g-DES and tailored antithrombotic regimens, the occurrence of this event in a stent placed in the LM is most likely fatal, although the incidence and mortality from LM ST have not yet been precisely defined.[77] For this reason, the use of available adjuvants in order to minimize the rates of underexpansion and malapposition is mandatory when stenting the LM.

The LEMON Study, a prospective, multicenter trial analyzed the feasibility, safety and impact of OCT-guided mid/distal LM PCI in 70 patients. A combination of residual angiographic stenosis <50%, TIMI 3 flow in all branches and adequate OCT stent expansion was reported in 86% of the patients, while in 26% of the cases the initial strategy was modified by OCT guidance. These results translated into a 98.6% rate of freedom from MACE at one-year follow-up, suggesting the feasibility of OCT-guided LM PCI.[78]

In another study, Agrawal *et al.* reviewed 110 stent implantations (including LM) in 100 consecutive patients, using OCT after the operator considered the stent as optimally deployed based on CA. Surprisingly, strut malapposition was found in 74.5% of the stents, with localized lumen enlargement being the most common mechanism, followed by stent undersizing (46.3%), strut underexpansion (29.3%), stent deployment issue (18.2%) and vessel asymmetry (9.7%).[79]

Taking this data into account, the use of OCT is not only capable of identifying stent malapposition and underexpansion (Figure 1) better than CA alone,[79] but could also guide the physician into choosing the best strategy to overpass them. However, the impact on long-term clinical outcomes is still to be studied.

Bifurcations

Bifurcation lesions in general and distal LM bifurcation disease in particular represent one of the most challenging lesion subsets for PCI. Recently, the results from the EBC MAIN Trial showed how a stepwise provisional strategy resulted in similar primary endpoint rates (a composite of death, MI, and TLR at 12 months) when compared to a systematic dual-stent approach (14.7% *vs.* 17.7%; HR: 0.8, 95% CI, 0.5-1.3; P=0.34) for LM stenting. Thus, the authors recommended the stepwise provisional strategy to remain the default for distal LM bifurcation PCI.[80]

OCT analysis of the distal LM bifurcation can ease the decision regarding the strategy by analyzing four important elements: side branch (SB) ostial stenosis, bifurcation angle, length of the proximal SB disease and the diameter of the distal SB reference segment, as a bifurcation angle <50% and a length from the proximal branching point to the carina tip of <1.70 mm, alongside with high lipid content in the main vessel (MV) lesion and contralateral location of lipid in the bifurcation area have been demonstrated to predict SB stenosis/obstruction after MV stenting, thus requiring a two-stent technique.[25]

In such cases, OCT can also help the interventional cardiologist to plan and conduct the procedure. OCT examination of bifurcation lesions should be performed in both MV and SB with stent size ideally being selected according to the distal MV reference diameter.[81]

Another important application of the OCT guidance in distal LM bifurcation PCI is the side-branch rewiring, which can sometimes be

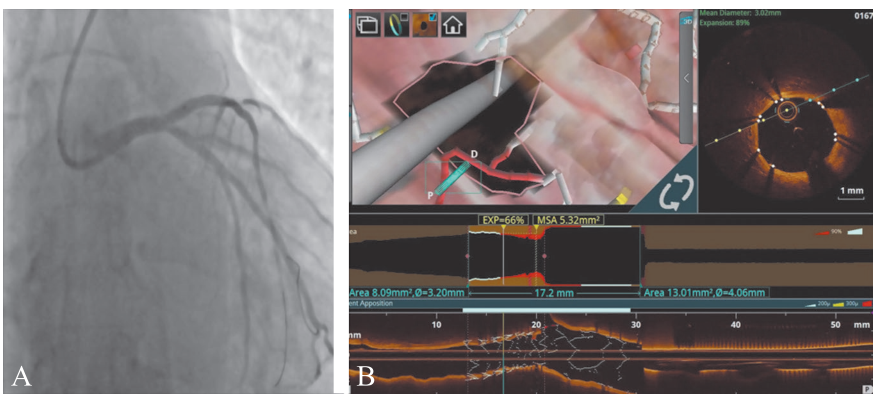

Figure 6.—A) Coronary angiography displays side branch rewiring after main vessel stenting; B) 3D optical coherence tomography facilitates visualization of correct side branch rewiring through the distal stent struts.

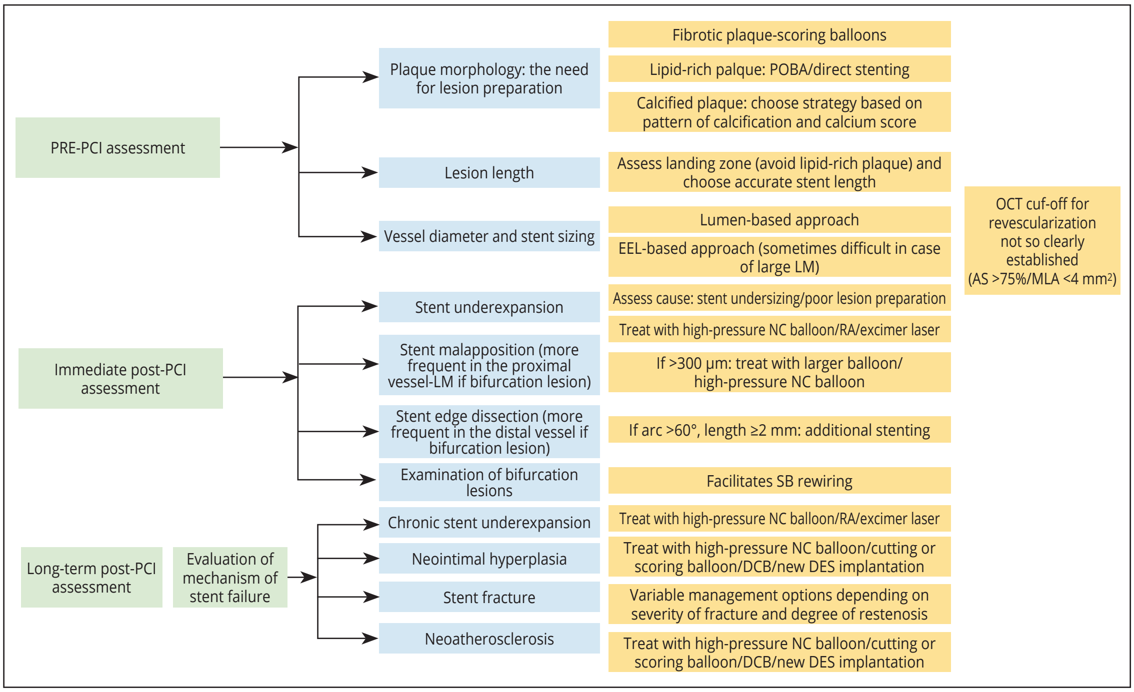

Figure 7.—Stepwise approach for optical coherence tomography guided percutaneous coronary interventions of the left main. AS: area stenosis; DCB: drug-coated balloon; DES: drug-eluting stent; EEL: external elastica lamina; LM: left main coronary artery; MLA: minimum lumen area; NC: non-compliant; OCT: optical coherence tomography; PCI: percutaneous coronary intervention; POBA: plain balloon angioplasty; RA: rotational atherectomy; SB: side branch.

difficult, but even in more “simple” cases the newly developed 3D OCT can help the physician to rewire the SB through the distal stent cell after main branch stenting (Figure 6), as this strategy was shown to optimize the kissing balloon inflation technique and lead to more favorable results.[82]

Nevertheless, after stent(s) implantation, the final result assessment by OCT might identify several factors associated with poor long-term outcomes, such as edge dissection, stent underexpansion and malapposition, in such cases the physician being capable of optimizing the result.

Figure 7 presents a stepwise approach on the use of OCT during and after LM PCI, with all the potential advantages depicted during each step.

OCT *vs.* IVUS in left main PCI

While data on the use of OCT in LM is still limited, a direct comparison between IVUS and OCT in this specific setting is of great interest but also incompletely explored.

Fujino *et al.*[83] conducted a small prospective study comparing these two imaging techniques and found OCT similar to IVUS in terms of mean lumen and stent area (11.24±2.66 mm² *vs.* 10.85±2.47 mm²; P=0.13; 10.44±2.33 mm² *vs.* 10.49±2.32 mm²; P=0.82) with the former being superior in detecting stent malapposition (malapposition area 0.43±0.51 mm² *vs.* 0.12±0.36 mm²; P<0.001) and distal edge dissection (30.3% *vs.* 6.1%; P=0.011). Additionally, it demonstrated that OCT has a similarly high safety profile compared to IVUS in tackling LM coronary disease with no ST-segment changes, dissection, vessel occlusion, coronary spasm or slow flow being documented.

The proof of concept was performed by Cortese *et al.*[84] in the multicenter, retrospective ROCK I study comparing OCT with standard of care stenting (angiography with IVUS adjuvance according to the operator’s preference) in guiding distal LM PCI and showed that at six-month angiographic follow-up the primary endpoint of LLL was lower in the OCT group, not significantly in the proximal stent segment pertaining

LM (0.12±0.41 mm *vs.* 0.26±0.52 mm; P=0.10) and significantly in the distal one- left anterior descending/ circumflex artery (0.03±0.45mm *vs.* 0.24±0.53 mm; P=0.025). What's more, percent diameter stenosis and restenosis rate were also reduced following OCT usage (14±9% *vs.* 19±16%; P=0.05; 3.5% *vs.* 12.9%; P=0.03).

Later, the multicenter, international ROCK II study[85] analyzed 730 patients undergoing distal LM stenting and found no difference between OCT and IVUS in terms of TLF (defined as a composite of cardiac death, target vessel MI and TLR) at one year (P=0.26). Of note, after applying propensity-score matching the rate of TLF was still similar between the groups (7% *vs.* 6%), which was also the case for the individual components of the primary endpoint. As is to be expected, acute stent malapposition and residual edge dissection were more often detected by OCT as compared to IVUS (10% *vs.* 4%; P=0.04; 9.7% *vs.* 5.1%; P=0.04).

In another study[86] including 331 patients the authors reported similar rates of restenosis (15.2% *vs.* 9.4%; P=0.387) and MACE (7.0% *vs.* 7.4%; P=0.98), comprising of cardiac death, MI, and TLR, between the two imaging modalities.

TABLE II.—*Summary of the main studies evaluating the role of OCT in LM PCI.*[61, 74, 78-80, 83-86]

Study	Design	Primary endpoint	Results
CLI-OPCI II[74]	Retrospective	Impact of suboptimal stent deployment on MACE	In-stent MLA<4.5mm2 (HR: 1.64; P=0.040) and dissection>200µm (HR: 2.54; P=0.004) at the distal edge were independent predictors of MACE
Dato *et al.*[61]	Retrospective	TVF at 18 months	Similar survival rates (HR: 0.40, 95% CI, 0.10-1.61; P=0.20) between patients treated conservatively *vs.* invasively based on OCT-measured cut-offs: AS >75% or MLA≤4 mm^2 (when 50%<AS<75%)
Agrawal *et al.*[79]	Retrospective	Evaluation of causes/extent of strut malapposition	Strut malapposition was found in 74.5% of the stents (localized lumen enlargement being the most common mechanism)
LEMON study[78]	Non-RCT	Procedural success comprising of a combination of residual angiographic stenosis <50%, TIMI 3 flow in all branches and adequate OCT stent expansion	86% procedural success and 98.6% rate of freedom from MACE
EBC MAIN[80]	RCT	Composite of all-cause death, MI, and target lesion revascularization at 12 months	A stepwise provisional strategy resulted in similar primary endpoint rates when compared to a systematic dual-stent approach (14.7% *vs.* 17.7%; HR: 0.8, 95% CI, 0.5-1.3; P=0.34)
Fujino *et al.*[83]	Prospective	Safety and feasibility of OCT *vs.* IVUS in LM PCI	OCT was similar to IVUS in assessing lumen/stent dimensions (11.24±2.66 mm2 *vs.* 10.85±2.47 mm2; P=0.13; 10.44±2.33 mm2 *vs.* 10.49±2.32 mm2; P=0.82) as well as in terms of the safety profile (no ST-segment changes, dissection, vessel occlusion, coronary spasm or slow flow were documented)
Rock I[84]	Retrospective	OCT *vs.* angiography-guided PCI (including IVUS) in terms of LLL at six-month follow-up	LLL was lower in the OCT group, not significantly in the proximal stent segment pertaining LM (0.12±0.41 mm *vs.* 0.26±0.52 mm; P=0.10) and significantly in the distal one- LAD/Cx artery (0.03±0.45 mm *vs.* 0.24±0.53 mm; P=0.025)
Rock II[85]	Retrospective	OCT *vs.* IVUS *vs.* angiography-guided PCI in terms of TLF at one year	The composite of cardiac death, target vessel MI and target lesion revascularization was similar between OCT and IVUS at one year (P=0.26)
Miura *et al.*[86]	Retrospective	OCT *vs.* IVUS-guided PCI in terms of eight-month MACE	Similar rates of MACE (7.0% *vs.* 7.4%; P=0.98) and restenosis (15.2% *vs.* 9.4%; P=0.387) between the two modalities
DOCTORS-LM	RCT	OCT *vs.* angiography-guided PCI	Ongoing

AS: area stenosis; Cx: circumflex coronary artery; IVUS: intravascular ultrasound; LAD: left anterior descending coronary artery; LLL: late lumen loss; LM: left main coronary artery; MACE: major adverse cardiac events; MI: myocardial infarction; MLA: minimum lumen area; OCT: optical coherence tomography; PCI: percutaneous coronary intervention; RCT: randomized controlled trial; TIMI: thrombolysis in myocardial infarction; TLF: target lesion failure; TVF: target vessel failure.

With these promising results being published, the need for larger RCTs in order to validate them is imperative, as the use of OCT in LM disease could improve the immediate results and long-term outcomes in this particularly difficult setting.

Table II provides an overview of the main studies focusing on OCT-guided PCI of the LM.[61, 74, 78-80, 83-86]

Ongoing studies

Although IVUS has a more clearly defined role in guiding LM PCI (this is also reflected in the guidelines), it should be noted that most of its value derives from registries or sub-analyses of RCTs. Two ongoing trials, OPTIMAL (NCT04111770) and IVUS CHIP (NCT04854070) (which focuses on complex coronary lesions, including LM) will hopefully fill the gap with more robust data pertaining this modality.

With respect to OCT, DOCTORS-LM (NCT04391413) is the only ongoing RCT at this moment including 188 patients with both ACS or stable CAD and significant non-ostial LM disease. It aims to compare an OCT-guided PCI strategy with angiographic assessment alone by means of post-PCI FFR and promises to provide additional data in support of OCT usage in the critical context of LM disease.

Conclusions

The continuous development of strategies, techniques and devices in the field of interventional cardiology has changed the approach of LM disease over time, with PCI being now indicated for low to intermediate SYNTAX scores. However, LM disease and especially distal LM bifurcation lesions still represent one of the most demanding clinical scenarios. Therefore, the use of intracoronary imaging has materialized as a useful complementary modality in optimizing the results, but while IVUS has a more well-established role, the full extent of the contribution of OCT remains to be determined.

Nevertheless, recent researches reported optimistic results, which outlined the role of OCT in LM interventions, mainly for plaque assessment, identification of ISR mechanisms, edge dissection, guidance in distal LM bifurcation and while several small studies demonstrated the non-inferiority of OCT when compared to IVUS, large RCTs are urgently needed to confirm these results.

Key messages

- Distal LM remains one of the most complex lesion subsets, prompting adequate operator knowledge as well as the need for proper optimization techniques by means of intracoronary imaging.
- There is extensive experience and clinical data that supports the use of IVUS in optimizing LM PCI.
- OCT was proven non-inferior compared to IVUS in guiding LM PCI in several small studies, but large RCTs are still lacking.

References

1. Serruys PW, de Jaegere P, Kiemeneij F, Macaya C, Rutsch W, Heyndrickx G, *et al.*; Benestent Study Group. A comparison of balloon-expandable-stent implantation with balloon angioplasty in patients with coronary artery disease. N Engl J Med 1994;331:489–95.

2. Iqbal J, Gunn J, Serruys PW. Coronary stents: historical development, current status and future directions. Br Med Bull 2013;106:193–211.

3. Neumann FJ, Sousa-Uva M, Ahlsson A, Alfonso F, Banning AP, Benedetto U, *et al.*; ESC Scientific Document Group. 2018 ESC/EACTS Guidelines on myocardial revascularization. Eur Heart J 2019;40:87–165.

4. Räber L, Mintz GS, Koskinas KC, Johnson TW, Holm NR, Onuma Y, *et al.*; ESC Scientific Document Group. Clinical use of intracoronary imaging. Part 1: guidance and optimization of coronary interventions. An expert consensus document of the European Association of Percutaneous Cardiovascular Interventions. Eur Heart J 2018;39:3281–300.

5. Mäkikallio T, Holm NR, Lindsay M, Spence MS, Erglis A, Menown IB, *et al.*; NOBLE study investigators. Percutaneous coronary angioplasty versus coronary artery bypass grafting in treatment of unprotected left main stenosis (NOBLE): a prospective, randomised, open-label, non-inferiority trial. Lancet 2016;388:2743–52.

6. Stone GW, Sabik JF, Serruys PW, Simonton CA, Généreux P, Puskas J, *et al.*; EXCEL Trial Investigators. Everolimus-Eluting Stents or Bypass Surgery for Left Main Coronary Artery Disease. N Engl J Med 2016;375:2223–35.

7. Stone GW, Kappetein AP, Sabik JF, Pocock SJ, Morice MC, Puskas J, *et al.*; EXCEL Trial Investigators. Five-Year Outcomes after PCI or CABG for Left Main Coronary Disease. N Engl J Med 2019;381:1820–30.

8. Holm NR, Mäkikallio T, Lindsay MM, Spence MS, Erglis A, Menown IB, *et al.*; NOBLE investigators. Percutaneous coronary angioplasty versus coronary artery bypass grafting in the treatment of unprotected left main stenosis: updated

5-year outcomes from the randomised, non-inferiority NOBLE trial. Lancet 2020;395:191–9.

9. Park DW, Park SJ. Percutaneous Coronary Intervention of Left Main Disease: Pre- and Post-EXCEL (Evaluation of XIENCE Everolimus Eluting Stent Versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization) and NOBLE (Nordic-Baltic-British Left Main Revascularization Study) Era. Circ Cardiovasc Interv 2017;10:004792.

10. Head SJ, Milojevic M, Daemen J, Ahn JM, Boersma E, Christiansen EH, *et al.* Mortality after coronary artery bypass grafting versus percutaneous coronary intervention with stenting for coronary artery disease: a pooled analysis of individual patient data. Lancet 2018;391:939–48.

11. Nerlekar N, Ha FJ, Verma KP, Bennett MR, Cameron JD, Meredith IT, *et al.* Percutaneous coronary intervention using drug-eluting stents versus coronary artery bypass grafting for unprotected left main coronary artery stenosis: a meta-analysis of randomized trials. Circ Cardiovasc Interv 2016;9:004729.

12. Dregoesc MI, Iancu AC, Homorodean C. The invasive intracoronary imaging assessment of left main coronary artery disease. Med Ultrason 2022;24:218–25.

13. Morice MC, Serruys PW, Kappetein AP, Feldman TE, Ståhle E, Colombo A, *et al.* Outcomes in patients with de novo left main disease treated with either percutaneous coronary intervention using paclitaxel-eluting stents or coronary artery bypass graft treatment in the Synergy Between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery (SYNTAX) trial. Circulation 2010;121:2645–53.

14. D'Ascenzo F, Elia E, Marengo G, Wańha W, González Ferreiro R, Truffa A, *et al.* Long-term (≥15 years) Follow-up of Percutaneous Coronary Intervention of Unprotected Left Main (From the GRAVITY Registry). Am J Cardiol 2021;156:72–8.

15. Min SY, Park DW, Yun SC, Kim YH, Lee JY, Kang SJ, *et al.* Major predictors of long-term clinical outcomes after coronary revascularization in patients with unprotected left main coronary disease: analysis from the MAIN-COMPARE study. Circ Cardiovasc Interv 2010;3:127–33.

16. Homorodean C, Iancu AC, Leucuța D, Bălănescu Ș, Dregoesc IM, Spînu M, *et al.* New Predictors of Early and Late Outcomes after Primary Percutaneous Coronary Intervention in Patients with ST-Segment Elevation Myocardial Infarction and Unprotected Left Main Coronary Artery Culprit Lesion. J Interv Cardiol 2019;2019:8238972.

17. Homorodean C, Iancu AC, Dregoesc IM, Spînu M, Ober MC, Tătaru D, *et al.* Renal Failure Impact on the Outcomes of ST-Segment Elevation Myocardial Infarction Patients Due to a Left Main Coronary Culprit Lesion Treated Using a Primary Percutaneous Coronary Intervention. J Clin Med 2019;8:565.

18. Topol EJ, Nissen SE. Our preoccupation with coronary luminology. The dissociation between clinical and angiographic findings in ischemic heart disease. Circulation 1995;92:2333–42.

19. Prati F, Di Vito L, Biondi-Zoccai G, Occhipinti M, La Manna A, Tamburino C, *et al.* Angiography alone versus angiography plus optical coherence tomography to guide decision-making during percutaneous coronary intervention: the Centro per la Lotta contro l'Infarto-Optimisation of Percutaneous Coronary Intervention (CLI-OPCI) study. EuroIntervention 2012;8:823–9.

20. Hong SJ, Mintz GS, Ahn CM, Kim JS, Kim BK, Ko YG, *et al.*; IVUS-XPL Investigators. Effect of Intravascular Ultrasound-Guided Drug-Eluting Stent Implantation: 5-Year Follow-Up of the IVUS-XPL Randomized Trial. JACC Cardiovasc Interv 2020;13:62–71.

21. Gao XF, Ge Z, Kong XQ, Kan J, Han L, Lu S, *et al.*; ULTIMATE Investigators. 3-Year Outcomes of the ULTIMATE Trial Comparing Intravascular Ultrasound Versus Angiography-Guided Drug-Eluting Stent Implantation. JACC Cardiovasc Interv 2021;14:247–57.

22. Zhang YJ, Pang S, Chen XY, Bourantas CV, Pan DR, Dong SJ, *et al.* Comparison of intravascular ultrasound guided versus angiography guided drug eluting stent implantation: a systematic review and meta-analysis. BMC Cardiovasc Disord 2015;15:153.

23. Levine GN, Bates ER, Blankenship JC, *et al.* 2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Society for Cardiovascular Angiography and Interventions. Circulation 2011;124:574–651.

24. Bezerra HG, Costa MA, Guagliumi G, Rollins AM, Simon DI. Intracoronary optical coherence tomography: a comprehensive review clinical and research applications. JACC Cardiovasc Interv 2009;2:1035–46.

25. Longobardo L, Mattesini A, Valente S, Di Mario C. OCT-guided Percutaneous Coronary Intervention in Bifurcation Lesions. Interv Cardiol 2019;14:5–9.

26. Morice MC, Serruys PW, Kappetein AP, Feldman TE, Ståhle E, Colombo A, *et al.* Five-year outcomes in patients with left main disease treated with either percutaneous coronary intervention or coronary artery bypass grafting in the synergy between percutaneous coronary intervention with taxus and cardiac surgery trial. Circulation 2014;129:2388–94.

27. Meneveau N, Souteyrand G, Motreff P, Caussin C, Amabile N, Ohlmann P, *et al.* Optical coherence tomography to optimize results of percutaneous coronary intervention in patients with non-ST-elevation acute coronary syndrome: results of the multicenter, randomized DOCTORS Study (Does Optical Coherence Tomography Optimize Results of Stenting). Circulation 2016;134:906–17.

28. Ali ZA, Maehara A, Généreux P, Shlofmitz RA, Fabbiocchi F, Nazif TM, *et al.*; ILUMIEN III: OPTIMIZE PCI Investigators. Optical coherence tomography compared with intravascular ultrasound and with angiography to guide coronary stent implantation (ILUMIEN III: OPTIMIZE PCI): a randomised controlled trial. Lancet 2016;388:2618–28.

29. Jones DA, Rathod KS, Koganti S, Hamshere S, Astroulakis Z, Lim P, *et al.* Angiography Alone Versus Angiography Plus Optical Coherence Tomography to Guide Percutaneous Coronary Intervention: Outcomes From the Pan-London PCI Cohort. JACC Cardiovasc Interv 2018;11:1313–21.

30. Kubo T, Shinke T, Okamura T, Hibi K, Nakazawa G, Morino Y, *et al.*; OPINION Investigators. Optical frequency domain imaging vs. intravascular ultrasound in percutaneous coronary intervention (OPINION trial): one-year angiographic and clinical results. Eur Heart J 2017;38:3139–47.

31. Maehara A, Ben-Yehuda O, Ali Z, Wijns W, Bezerra HG, Shite J, *et al.* Comparison of Stent Expansion Guided by Optical Coherence Tomography Versus Intravascular Ultrasound: The ILUMIEN II Study (Observational Study of Optical Coherence Tomography [OCT] in Patients Undergoing Fractional Flow Reserve [FFR] and Percutaneous Coronary Intervention). JACC Cardiovasc Interv 2015;8:1704–14.

32. Kubo T, Akasaka T, Shite J, Suzuki T, Uemura S, Yu B, *et al.* OCT compared with IVUS in a coronary lesion assessment: the OPUS-CLASS study. JACC Cardiovasc Imaging 2013;6:1095–104.

33. Virmani R, Kolodgie FD, Burke AP, Farb A, Schwartz SM. Lessons from sudden coronary death: a comprehensive morphological classification scheme for atherosclerotic lesions. Arterioscler Thromb Vasc Biol 2000;20:1262–75.

34. Yabushita H, Bouma BE, Houser SL, Aretz HT, Jang IK, Schlendorf KH, *et al.* Characterization of human atherosclerosis by optical coherence tomography. Circulation 2002;106:1640–5.

35. Kume T, Akasaka T, Kawamoto T, Watanabe N, Toyota E, Neishi Y, *et al.* Assessment of coronary arterial plaque by optical coherence tomography. Am J Cardiol 2006;97:1172–5.

36. Tearney GJ, Regar E, Akasaka T, Adriaenssens T, Barlis P, Bezerra HG, *et al.*; International Working Group for Intravascular Optical Coherence Tomography (IWG-IVOCT). Consensus standards for acquisition, measurement, and reporting of intravascular optical coherence tomography studies: a report from the International Working Group for Intravascular Optical Coherence Tomography Standardization and Validation. J Am Coll Cardiol 2012;59:1058–72.

37. Yano H, Horinaka S, Ishimitsu T. Effect of evolocumab therapy on coronary fibrous cap thickness assessed by optical coherence tomography in patients with acute coronary syndrome. J Cardiol 2020;75:289–95.

38. Burke AP, Farb A, Malcom GT, Liang YH, Smialek J, Virmani R. Coronary risk factors and plaque morphology in men with coronary disease who died suddenly. N Engl J Med 1997;336:1276–82.

39. Narula J, Nakano M, Virmani R, Kolodgie FD, Petersen R, Newcomb R, *et al.* Histopathologic characteristics of atherosclerotic coronary disease and implications of the findings for the invasive and noninvasive detection of vulnerable plaques. J Am Coll Cardiol 2013;61:1041–51.

40. Chamié D, Bezerra HG, Attizzani GF, Yamamoto H, Kanaya T, Stefano GT, *et al.* Incidence, predictors, morphological characteristics, and clinical outcomes of stent edge dissections detected by optical coherence tomography. JACC Cardiovasc Interv 2013;6:800–13.

41. Tanaka A, Imanishi T, Kitabata H, Kubo T, Takarada S, Tanimoto T, *et al.* Lipid-rich plaque and myocardial perfusion after successful stenting in patients with non-ST-segment elevation acute coronary syndrome: an optical coherence tomography study. Eur Heart J 2009;30:1348–55.

42. Otsuka F, Joner M, Prati F, Virmani R, Narula J. Clinical classification of plaque morphology in coronary disease. Nat Rev Cardiol 2014;11:379–89.

43. Mintz GS. Intravascular imaging of coronary calcification and its clinical implications. JACC Cardiovasc Imaging 2015;8:461–71.

44. Mintz GS. Clinical utility of intravascular imaging and physiology in coronary artery disease. J Am Coll Cardiol 2014;64:207–22.

45. Abdel-Wahab M, Richardt G, Joachim Büttner H, Toelg R, Geist V, Meinertz T, *et al.* High-speed rotational atherectomy before paclitaxel-eluting stent implantation in complex calcified coronary lesions: the randomized ROTAXUS (Rotational Atherectomy Prior to Taxus Stent Treatment for Complex Native Coronary Artery Disease) trial. JACC Cardiovasc Interv 2013;6:10–9.

46. Okamoto N, Ueda H, Bhatheja S, Vengrenyuk Y, Aquino M, Rabiei S, *et al.* Procedural and one-year outcomes of patients treated with orbital and rotational atherectomy with mechanistic insights from optical coherence tomography. EuroIntervention 2019;14:1760–7.

47. Ali ZA, Brinton TJ, Hill JM, Maehara A, Matsumura M, Karimi Galougahi K, *et al.* Optical Coherence Tomography Characterization of Coronary Lithoplasty for Treatment of Calcified Lesions: first Description. JACC Cardiovasc Imaging 2017;10:897–906.

48. Alfonso F, Bastante T, Antuña P, de la Cuerda F, Cuesta J, García-Guimaraes M, *et al.* Coronary lithoplasty for the treatment of undilatable calcified de novo and in-stent restenosis lesions. JACC Cardiovasc Interv 2019;12:497–9.

49. Hill JM, Kereiakes DJ, Shlofmitz RA, Klein AJ, Riley RF, Price MJ, *et al.*; Disrupt CAD III Investigators. Intravascular Lithotripsy for Treatment of Severely Calcified Coronary Artery Disease. J Am Coll Cardiol 2020;76:2635–46.

50. Aziz A, Bhatia G, Pitt M, Choudhury A, Hailan A, Upadhyaya S, *et al.* Intravascular lithotripsy in calcified-coronary lesions: A real-world observational, European multicenter study. Catheter Cardiovasc Interv 2021;98:225–35.

51. Maejima N, Hibi K, Saka K, Akiyama E, Konishi M, Endo M, *et al.* Relationship Between Thickness of Calcium on Optical Coherence Tomography and Crack Formation After Balloon Dilatation in Calcified Plaque Requiring Rotational Atherectomy. Circ J 2016;80:1413–9.

52. Fujino A, Mintz GS, Lee T, Hoshino M, Usui E, Kanaji Y, *et al.* Predictors of Calcium Fracture Derived From Balloon Angioplasty and its Effect on Stent Expansion Assessed by Optical Coherence Tomography. JACC Cardiovasc Interv 2018;11:1015–7.

53. Shlofmitz E, Sosa FA, Ali ZA, *et al.* OCT-Guided Treatment of Calcified Coronary Artery Disease: Breaking the Barrier to Stent Expansion. Curr Cardiovasc Imaging Rep 2019;12.

54. Fujino A, Mintz GS, Matsumura M, Lee T, Kim SY, Hoshino M, *et al.* A new optical coherence tomography-based calcium scoring system to predict stent underexpansion. EuroIntervention 2018;13:e2182–9.

55. Ino Y, Kubo T, Matsuo Y, Yamaguchi T, Shiono Y, Shimamura K, *et al.* Optical Coherence Tomography Predictors for Edge Restenosis After Everolimus-Eluting Stent Implantation. Circ Cardiovasc Interv 2016;9:004231.

56. Kang SJ, Cho YR, Park GM, Ahn JM, Kim WJ, Lee JY, *et al.* Intravascular ultrasound predictors for edge restenosis after newer generation drug-eluting stent implantation. Am J Cardiol 2013;111:1408–14.

57. Shlofmitz E, Ali ZA, Maehara A, Mintz GS, Shlofmitz R, Jeremias A. Intravascular Imaging-Guided Percutaneous Coronary Intervention: A Universal Approach for Optimization of Stent Implantation. Circ Cardiovasc Interv 2020;13:e008686.

58. de la Torre Hernandez JM, Hernández Hernandez F, Alfonso F, Rumoroso JR, Lopez-Palop R, Sadaba M, *et al.*; LITRO Study Group (Spanish Working Group on Interventional Cardiology). Prospective application of pre-defined intravascular ultrasound criteria for assessment of intermediate left main coronary artery lesions results from the multicenter LITRO study. J Am Coll Cardiol 2011;58:351–8.

59. Jasti V, Ivan E, Yalamanchili V, Wongpraparut N, Leesar MA. Correlations between fractional flow reserve and intravascular ultrasound in patients with an ambiguous left main coronary artery stenosis. Circulation 2004;110:2831–6.

60. Park SJ, Ahn JM, Kang SJ, Yoon SH, Koo BK, Lee JY, *et al.* Intravascular ultrasound-derived minimal lumen area criteria for functionally significant left main coronary artery stenosis. JACC Cardiovasc Interv 2014;7:868–74.

61. Dato I, Burzotta F, Trani C, Romano A, Paraggio L, Aurigemma C, *et al.* Optical coherence tomography guidance for the management of angiographically intermediate left main bifurcation lesions: early clinical experience. Int J Cardiol 2017;248:108–13.

62. Pleva L, Kukla P, Hlinomaz O. Treatment of coronary in-stent restenosis: a systematic review. J Geriatr Cardiol 2018;15:173–84.

63. Byrne RA, Joner M, Tada T, Kastrati A. Restenosis in bare metal and drug-eluting stents: distinct mechanistic insights from histopathology and optical intravascular imaging. Minerva Cardioangiol 2012;60:473–89.

64. Solinas E, Dangas G, Kirtane AJ, Lansky AJ, Franklin-Bond T, Boland P, *et al.* Angiographic patterns of drug-eluting stent restenosis and one-year outcomes after treatment with repeated percutaneous coronary intervention. Am J Cardiol 2008;102:311–5.

65. Alfonso F, Byrne RA, Rivero F, Kastrati A. Current treatment of in-stent restenosis. J Am Coll Cardiol 2014;63:2659–73.

66. Ferri LA, Jabbour RJ, Giannini F, Benincasa S, Ancona M, Regazzoli D, *et al.* Safety and efficacy of rotational atherectomy for the treatment of undilatable underexpanded stents implanted in calcific lesions. Catheter Cardiovasc Interv 2017;90:E19–24.

67. Latib A, Takagi K, Chizzola G, Tobis J, Ambrosini V, Niccoli G, *et al.* Excimer Laser LEsion modification to expand non-dilatable stents: the ELLEMENT registry. Cardiovasc Revasc Med 2014;15:8–12.

68. Albiero R, Silber S, Di Mario C, Cernigliaro C, Battaglia S, Reimers B, *et al.*; RESCUT Investigators. Cutting balloon versus conventional balloon angioplasty for the treatment of in-stent restenosis: results of the restenosis cutting balloon evaluation trial (RESCUT). J Am Coll Cardiol 2004;43:943–9.

69. Aung SS, Latt H, Kyaw K, Roongsritong C. An Interesting Case and Literature Review of a Coronary Stent Fracture in a Current Generation Platinum Chromium Everolimus-Eluting Stent. Case Rep Cardiol 2018;2018:4579184.

70. Kan J, Ge Z, Zhang JJ, Liu ZZ, Tian NL, Ye F, *et al.* Incidence and Clinical Outcomes of Stent Fractures on the Basis of 6,555 Patients and 16,482 Drug-Eluting Stents From 4 Centers. JACC Cardiovasc Interv 2016;9:1115–23.

71. Lee SE, Jeong MH, Kim IS, Ko JS, Lee MG, Kang WY, *et al.* Clinical outcomes and optimal treatment for stent fracture after drug-eluting stent implantation. J Cardiol 2009;53:422–8.

72. Lee JH, Kim U. Optical Coherence Tomography-guided Treatment of Multiple Stent Fracture in Patients with Overlapping Drug-eluting Stents. Korean Circ J 2018;48:1030–1.

73. Goldstein JA. Stent edge dissection: depth of injury and adverse outcome. Catheter Cardiovasc Interv 2015;86:247–8.

74. Prati F, Romagnoli E, Burzotta F, Limbruno U, Gatto L, La Manna A, *et al.* Clinical Impact of OCT Findings During PCI: the CLI-OPCI II Study. JACC Cardiovasc Imaging 2015;8:1297–305.

75. van Zandvoort LJ, Tomaniak M, Tovar Forero MN, Masdjedi K, Visseren L, Witberg K, *et al.* Predictors for Clinical Outcome of Untreated Stent Edge Dissections as Detected by Optical Coherence Tomography. Circ Cardiovasc Interv 2020;13:e008685.

76. Mankerious N, Micha J, Kufner S. Malapposed, uncovered, underexpanded-intravascular imaging lessons on coronary stent thrombosis. J Thorac Dis 2018;10:141–4.

77. Pfahl K, Boudoulas KD. Left main coronary artery stent thrombosis: a challenging case. Am J Med 2014;127:e9–10.

78. Amabile N, Rangé G, Souteyrand G, Godin M, Boussaada MM, Meneveau N, *et al.* Optical coherence tomography to guide percutaneous coronary intervention of the left main coronary artery: the LEMON study. EuroIntervention 2021;17:e124–31.

79. Agrawal M, Hakeem A, Ahmed Z, Uretsky BF. Classification of mechanisms of strut malapposition after angiographically optimized stent implantation: an optical coherence tomography study. Catheter Cardiovasc Interv 2017;90:225–32.

80. Hildick-Smith D, Egred M, Banning A, Brunel P, Ferenc M, Hovasse T, *et al.* The European bifurcation club Left Main Coronary Stent study: a randomized comparison of stepwise provisional vs. systematic dual stenting strategies (EBC MAIN). Eur Heart J 2021;42:3829–39.

81. Lassen JF, Holm NR, Banning A, Burzotta F, Lefèvre T, Chieffo A, *et al.* Percutaneous coronary intervention for coronary bifurcation disease: 11th consensus document from the European Bifurcation Club. EuroIntervention 2016;12:38–46.

82. Murasato Y, Iwasaki K, Yamamoto T, Yagi T, Hikichi Y, Suematsu Y, *et al.* Optimal kissing balloon inflation after single-stent deployment in a coronary bifurcation model. EuroIntervention 2014;10:934–41.

83. Fujino Y, Bezerra HG, Attizzani GF, Wang W, Yamamoto H, Chamié D, *et al.* Frequency-domain optical coherence tomography assessment of unprotected left main coronary artery disease-a comparison with intravascular ultrasound. Catheter Cardiovasc Interv 2013;82:E173–83.

84. Cortese B, Burzotta F, Alfonso F, Pellegrini D, Trani C, Aurigemma C, *et al.* Role of optical coherence tomography for distal left main stem angioplasty. Catheter Cardiovasc Interv 2020;96:755–61.

85. Cortese B, de la Torre Hernandez JM, Lanocha M, Ielasi A, Giannini F, Campo G, *et al.* Optical coherence tomography, intravascular ultrasound or angiography guidance for distal left main coronary stenting. The ROCK cohort II study. Catheter Cardiovasc Interv 2022;99:664–73.

86. Miura K, Tada T, Shimada T, Ohya M, Murai R, Kubo S, *et al.* Three-dimensional optical coherence tomography versus intravascular ultrasound in percutaneous coronary intervention for the left main coronary artery. Heart Vessels 2021;36:630–7.

Conflicts of interest
The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Authors' contributions
Horea-Laurentiu Onea and Florin-Leontin Lazar conceived and designed the analysis, collected the data, wrote the paper; Dan-Mircea Olinic, Calin Homorodean and Bernardo Cortese conceived and designed the analysis, collected the data, revised the paper. All authors read and approved the final version of the manuscript.

History
Article first published online: November 2, 2022. - Manuscript accepted: October 14, 2022. - Manuscript revised: September 30, 2022. - Manuscript received: July 18, 2022.