Pegem Journal of Education and Instruction, Vol. 14, No. 3, 2024 (pp. 1091-1100)

RESEARCH ARTICLE **WWW.PEGEGOG.NET**

Precision Revascularization in Distal Left Main Coronary Artery Disease: Integration of Coronary Physiology, Imaging, and Contemporary PCI

Ahmed Saed Eldamanhoury [1], Mohammed Hossam El-Din Elshaer [1], Mohammed Abdelnaby Elsayed Mohammed Emara [2], Alaa Elsayed Salama [1]

1 Department of Cardiology, Faculty of Medicine, Zagazig University
2 Cardiovascular Specialist - National Heart Institute

Corresponding author: Mohammed Abdelnaby Elsayed Mohammed Emara

Abstract

***Background*:** Distal left main coronary artery disease (LMCAD) represents one of the most anatomically complex and prognostically significant subsets of coronary artery disease because of the extensive myocardial territory supplied by the left main coronary artery and the frequent involvement of complex bifurcation anatomy. Although coronary artery bypass grafting (CABG) has historically remained the standard revascularization strategy for significant left main disease, major advances in percutaneous coronary intervention (PCI) technologies, coronary physiology, intracoronary imaging, and bifurcation stenting techniques have transformed the contemporary management of distal LMCAD. The emergence of precision-based coronary revascularization has enabled more individualized therapeutic decision-making through the integration of functional lesion assessment, advanced imaging modalities, and optimized PCI strategies.

Coronary physiological assessment using fractional flow reserve (FFR) and instantaneous wave-free ratio (iFR) has significantly improved the identification of hemodynamically significant lesions beyond conventional angiographic assessment alone. In particular, iFR has emerged as an effective adenosine-free physiological modality with validated clinical outcomes comparable to FFR while improving procedural efficiency and patient comfort. Simultaneously, intracoronary imaging modalities including intravascular ultrasound (IVUS) and optical coherence tomography (OCT) have become essential tools for lesion characterization, plaque morphology assessment, calcium evaluation, stent optimization, and procedural guidance during complex distal left main interventions.

Contemporary PCI techniques for distal left main bifurcation disease, including provisional stenting, DK-crush, culotte, and hybrid bifurcation approaches, have demonstrated improved procedural success and long-term clinical outcomes when combined with physiology- and imaging-guided optimization. Emerging technologies such as quantitative flow ratio (QFR), computational physiology, artificial intelligence-assisted imaging, and calcium modification devices further support the evolving concept of precision revascularization in complex coronary disease.

This review discusses the integration of coronary physiology, intracoronary imaging, and contemporary PCI strategies in the management of distal left main coronary artery disease. Particular emphasis is placed on the evolving role of iFR and FFR, imaging-guided intervention, bifurcation stenting optimization, major clinical evidence, and future innovations in precision coronary revascularization. Current evidence supports a multidisciplinary and individualized approach that combines physiological and anatomical assessment to improve procedural safety, optimize revascularization strategies, and enhance long-term clinical outcomes in patients with distal left main coronary artery disease.

Keywords: Distal Left Main Disease; Coronary Physiology; Precision PCI

INTRODUCTION

Distal left main coronary artery disease (LMCAD) remains one of the most clinically challenging and prognostically significant forms of coronary artery disease because the left main coronary artery supplies a substantial proportion of the left ventricular myocardium. Significant stenosis involving the distal left main bifurcation can compromise blood flow to both the left anterior descending (LAD) and left circumflex (LCx) arteries, resulting in extensive myocardial ischemia, impaired ventricular function, heart failure, malignant arrhythmias, and sudden cardiac death. Historically, coronary artery bypass grafting (CABG) has been considered the standard revascularization strategy for complex left main disease because of its established long-term durability and survival benefit. However, rapid technological advancements in percutaneous coronary intervention (PCI) have substantially transformed the therapeutic landscape of distal left main revascularization [1,2].

Contemporary PCI for distal left main disease has evolved beyond conventional angiography-guided intervention toward a more individualized precision-based approach integrating coronary physiology, intracoronary imaging, lesion preparation technologies, and advanced bifurcation stenting techniques. This paradigm shift reflects the recognition that angiographic severity alone may not accurately represent the hemodynamic significance or morphological complexity of left main lesions. Distal left main bifurcation disease is particularly difficult to evaluate using angiography because of vessel overlap, foreshortening, eccentric plaque distribution, diffuse atherosclerosis, and side-branch involvement. Consequently, functional and anatomical lesion assessment has become increasingly important in optimizing patient selection and procedural outcomes [3].

Coronary physiology now plays a central role in the evaluation and management of left main disease. Fractional flow reserve (FFR) has historically been considered the gold standard physiological index for determining lesion-specific ischemia. More recently, instantaneous wave-free ratio (iFR) has emerged as a validated adenosine-independent physiological modality capable of accurately assessing coronary lesion significance while improving patient comfort and procedural efficiency. Major randomized studies demonstrated the noninferiority of iFR compared with FFR in guiding coronary revascularization decisions, supporting its growing role in complex PCI and precision coronary intervention [4,5].

Intracoronary imaging has similarly revolutionized left main PCI. Intravascular ultrasound (IVUS) and optical coherence tomography (OCT) provide detailed assessment of vessel size, plaque morphology, calcium distribution, lesion length, stent expansion, and procedural optimization beyond what can be achieved with angiography alone. Multiple studies have demonstrated that imaging-guided left main PCI significantly improves stent expansion, reduces restenosis, minimizes stent thrombosis, and lowers major adverse cardiovascular events. Consequently, IVUS-guided PCI is now strongly recommended during left main interventions by contemporary international guidelines [6].

Distal left main bifurcation lesions remain among the most technically demanding lesions in interventional cardiology because of their complex anatomy and high risk of side-branch compromise. Contemporary bifurcation PCI strategies now incorporate physiology-guided lesion assessment, imaging-guided stent optimization, proximal optimization technique (POT), and advanced two-stent techniques such as DK-crush, culotte, and TAP stenting. The integration of these technologies and procedural concepts has substantially improved PCI outcomes in patients with low-to-intermediate anatomical complexity [7].

The emergence of precision revascularization reflects a broader transition toward personalized cardiovascular medicine. Rather than relying solely on anatomical stenosis severity, contemporary left main intervention increasingly incorporates physiological significance, plaque characterization, calcium burden assessment, patient-specific clinical risk, and procedural feasibility into individualized treatment planning. Emerging technologies including quantitative flow ratio (QFR), artificial intelligence-assisted imaging analysis, computational coronary physiology, and advanced calcium-modification devices are expected to further refine decision-making and procedural optimization in distal left main disease [8].

Despite remarkable progress, several unresolved challenges remain in contemporary distal left main revascularization. Questions persist regarding the optimal integration of physiology and imaging, the most effective bifurcation strategy for complex lesions, long-term durability of PCI compared with CABG, and the role of precision-guided intervention in diabetic patients and heavily calcified disease. Additionally, the expanding use of physiology-guided PCI requires careful interpretation in left main lesions because downstream disease and microvascular dysfunction may influence pressure-derived measurements [9].

Accordingly, this review aims to discuss the contemporary concept of precision revascularization in distal left main coronary artery disease through the integration of coronary physiology, intracoronary imaging, and advanced PCI strategies. Particular emphasis is placed on the evolving role of iFR and FFR, imaging-guided PCI optimization, complex bifurcation intervention, emerging technologies, and future directions in precision coronary revascularization.

Coronary Physiology in Distal Left Main Coronary Artery Disease

Accurate physiological assessment of distal left main coronary artery disease is essential because angiographic evaluation alone often fails to reflect the true hemodynamic significance of intermediate or complex lesions. Distal left main bifurcation disease presents unique diagnostic challenges due to vessel overlap, diffuse plaque distribution, eccentric stenosis, foreshortening, and involvement of both the left anterior descending (LAD) and left circumflex (LCx) arteries. Consequently, visual angiographic estimation may lead to substantial overestimation or underestimation of lesion severity, potentially resulting in inappropriate revascularization decisions. The growing integration of coronary physiology into contemporary PCI reflects the transition toward more individualized and evidence-based revascularization strategies [10,11].

Fractional flow reserve (FFR) was the first extensively validated invasive physiological index used to determine the ischemic significance of coronary stenoses. FFR is calculated as the ratio of distal coronary pressure to aortic pressure during maximal hyperemia induced by pharmacological vasodilation, typically using adenosine. An FFR value ≤0.80 is generally considered indicative of functionally significant myocardial ischemia warranting revascularization. Multiple landmark studies demonstrated that FFR-guided PCI improves clinical outcomes, reduces unnecessary stent implantation, lowers healthcare costs, and decreases adverse cardiovascular events compared with angiography-guided intervention alone [12].

Despite its established role, FFR assessment in distal left main disease presents important technical and physiological limitations. Significant downstream disease involving the LAD or LCx may artificially increase FFR values and underestimate the true severity of left main stenosis. Similarly, diffuse atherosclerosis, serial lesions, microvascular dysfunction, and acute coronary syndromes may influence hyperemic flow dynamics and affect measurement accuracy. These limitations are particularly relevant in distal bifurcation lesions where lesion interaction between daughter vessels complicates physiological interpretation [13].

Instantaneous wave-free ratio (iFR) has emerged as a major advancement in coronary physiological assessment because it eliminates the need for pharmacologically induced hyperemia. iFR measures the pressure gradient across a coronary lesion during a specific diastolic wave-free period characterized by naturally minimized and stable microvascular resistance. This approach allows accurate physiological assessment while avoiding adenosine-related adverse effects such as chest discomfort, dyspnea, atrioventricular block, hypotension, and prolonged procedural duration. An iFR value ≤0.89 is generally considered hemodynamically significant [14].

The DEFINE-FLAIR and iFR SWEDEHEART randomized trials fundamentally established the clinical validity of iFR-guided coronary intervention. Both studies demonstrated that iFR-guided revascularization was noninferior to FFR-guided strategies regarding major adverse cardiovascular events, including death, myocardial infarction, and unplanned revascularization. Importantly, iFR significantly improved procedural efficiency and patient tolerance because hyperemic agents were not required. Extended follow-up analyses confirmed sustained long-term safety and comparable mortality outcomes between iFR- and FFR-guided intervention strategies [15,16].

The application of iFR in distal left main disease is particularly attractive because of the complexity and variability of bifurcation anatomy. Physiological assessment may help differentiate lesions requiring intervention from angiographically intermediate but functionally insignificant stenoses. This distinction is clinically important because unnecessary left main stenting may expose patients to procedural complications, prolonged dual antiplatelet therapy, restenosis, and stent thrombosis without clear ischemic benefit. Physiology-guided decision-making therefore contributes substantially to precision revascularization [17].

Coronary physiology also plays an important role during and after bifurcation PCI. Following crossover stenting from the left main artery into the LAD, angiographic compromise of the jailed LCx branch is common; however, angiographic narrowing does not always correlate with functional ischemia. Studies evaluating FFR in jailed side branches demonstrated significant discrepancies between angiographic appearance and physiological significance. Similar principles support the growing role of iFR in post-PCI physiological assessment to identify side branches requiring additional intervention while avoiding unnecessary complex two-stent procedures [18].

Physiological pullback assessment represents another important innovation in complex left main disease. iFR pullback allows mapping of pressure gradients along diffuse coronary disease and may identify the precise segments contributing most significantly to ischemia. This technique enables virtual PCI planning by predicting the physiological impact of intervention before stent deployment. Such physiology-guided procedural planning may optimize lesion selection, minimize stent length, and improve overall procedural efficiency in diffuse or serial coronary disease [19].

The integration of coronary physiology with intracoronary imaging has become increasingly important in contemporary distal left main intervention. Physiological assessment provides information regarding ischemic significance, whereas imaging modalities such as intravascular ultrasound (IVUS) and optical coherence tomography (OCT) provide detailed anatomical characterization including plaque morphology, calcium burden, vessel sizing, lesion length, and stent optimization. Combining physiological and imaging data enables a more comprehensive precision-guided approach to left main PCI [20].

Emerging technologies continue to expand the field of coronary physiology. Quantitative flow ratio (QFR), angiography-derived FFR, computational fluid dynamics, and artificial intelligence-assisted physiological modeling now offer less invasive alternatives for lesion assessment. These technologies may further simplify physiological evaluation, improve workflow efficiency, and reduce procedural complexity during left main intervention. As precision cardiology continues to evolve, the integration of physiology, imaging, and computational technologies is expected to become central to future management strategies for distal left main coronary artery disease [21].

Intravascular Ultrasound and Optical Coherence Tomography in Distal Left Main PCI

Intracoronary imaging has become a cornerstone of contemporary distal left main percutaneous coronary intervention because angiography alone frequently underestimates lesion complexity, plaque burden, vessel dimensions, and stent-related complications. Distal left main bifurcation disease presents unique anatomical challenges involving large vessel caliber, extensive plaque distribution, severe calcification, and side-branch involvement that may not be adequately visualized with conventional angiography. Consequently, intravascular ultrasound (IVUS) and optical coherence tomography (OCT) have assumed increasingly important roles in lesion characterization, procedural planning, stent optimization, and long-term outcome improvement during left main PCI [22,23].

Among available imaging modalities, IVUS remains the most extensively studied and widely recommended tool for left main intervention. IVUS provides high-quality cross-sectional imaging with excellent tissue penetration, enabling accurate assessment of vessel size, plaque burden, calcium distribution, lesion length, and reference vessel dimensions. This information is particularly valuable in distal left main disease because angiography frequently underestimates the true vessel diameter and plaque extent. Accurate vessel sizing is critical to avoid stent underexpansion, malapposition, edge dissection, and restenosis, all of which are associated with adverse cardiovascular outcomes [24].

One of the major advantages of IVUS in left main disease is its ability to determine minimal lumen area (MLA), which serves as an important anatomical surrogate of lesion significance. Several studies demonstrated correlations between IVUS-derived MLA measurements and physiological ischemia assessed by FFR. Although physiological assessment remains the preferred strategy for determining ischemic significance, IVUS-derived MLA thresholds may provide additional diagnostic support in intermediate left main lesions, particularly when physiological assessment is technically challenging or inconclusive [25].

IVUS also plays a critical role during procedural optimization. Contemporary left main PCI increasingly incorporates predefined IVUS criteria for optimal stent expansion and apposition. Adequate minimal stent area within the left main artery, proximal LAD, and LCx ostium has been strongly associated with lower rates of restenosis, target lesion failure, and stent thrombosis. Furthermore, IVUS allows early identification of edge dissections, tissue prolapse, geographic miss, and incomplete lesion coverage that may not be apparent angiographically [26].

Multiple observational studies and meta-analyses demonstrated superior outcomes with IVUS-guided compared with angiography-guided left main PCI. IVUS guidance has consistently been associated with lower mortality, reduced target vessel revascularization, improved stent expansion, and decreased stent thrombosis rates. Consequently, contemporary international guidelines strongly recommend IVUS-guided PCI for left main interventions whenever feasible. The benefit of IVUS appears particularly pronounced in distal bifurcation lesions, heavily calcified disease, and complex two-stent procedures [27].

Optical coherence tomography (OCT) represents another highly valuable intracoronary imaging modality characterized by extremely high spatial resolution. OCT provides detailed visualization of plaque morphology, calcium thickness, stent strut apposition, tissue prolapse, thrombus formation, and microstructural vessel characteristics. This high-resolution imaging capability makes OCT particularly useful for identifying subtle procedural complications and optimizing stent deployment in complex bifurcation interventions [28].

Despite its advantages, OCT has several limitations in left main disease. The large caliber of the left main artery may exceed the imaging field of OCT, potentially limiting complete vessel visualization. In addition, OCT requires transient blood clearance using contrast injection, which may increase contrast volume and procedural complexity, especially in patients with renal dysfunction or hemodynamic instability. Consequently, IVUS generally remains the preferred imaging modality for large proximal vessels such as the left main artery, whereas OCT may provide complementary information in selected cases [29].

Intracoronary imaging is especially important during distal left main bifurcation PCI because complex anatomy frequently necessitates advanced procedural strategies. Imaging guidance facilitates accurate wire positioning, assessment of side-branch ostial disease, proximal optimization technique (POT), evaluation of stent expansion after kissing balloon inflation, and detection of carinal shift or side-branch compromise. Imaging-guided optimization is particularly critical in DK-crush and other two-stent techniques where procedural precision strongly influences long-term outcomes [30].

Calcium assessment represents another major application of intracoronary imaging in distal left main disease. Severe calcification impairs stent expansion and increases the risks of restenosis, stent thrombosis, and target lesion failure. IVUS and OCT allow detailed characterization of calcium arc, thickness, depth, and longitudinal distribution, helping operators determine the need for calcium-modification techniques such as rotational atherectomy, orbital atherectomy, or intravascular lithotripsy before stent implantation [31].

The integration of intracoronary imaging with coronary physiology reflects the broader concept of precision revascularization. Physiological assessment using iFR or FFR identifies lesions responsible for ischemia, while IVUS and OCT provide detailed anatomical information necessary for procedural optimization. This combined physiology-imaging strategy enables more individualized treatment planning, minimizes unnecessary intervention, improves procedural safety, and enhances long-term clinical outcomes in patients with distal left main coronary artery disease [32].

Contemporary PCI Strategies for Distal Left Main Bifurcation Disease

Distal left main bifurcation lesions remain among the most technically demanding subsets of coronary intervention because of their large myocardial territory, complex anatomy, high plaque burden, and risk of side-branch compromise. Successful PCI in these lesions requires meticulous procedural planning, individualized bifurcation strategy selection, optimal lesion preparation, intracoronary imaging guidance, and physiological assessment. Contemporary distal left main PCI has evolved from simple angiography-guided stenting toward a precision-based approach integrating coronary physiology, intravascular imaging, and advanced bifurcation techniques to improve procedural safety and long-term outcomes [33,34].

The provisional one-stent strategy is currently considered the preferred default approach for most distal left main bifurcation lesions because of its relative simplicity, lower procedural complexity, reduced metal burden, and favorable clinical outcomes. In this technique, a stent is implanted from the left main artery into the main branch, typically the left anterior descending artery, while maintaining side-branch access through the stent struts. Additional side-branch intervention is reserved for cases with significant residual stenosis, impaired coronary flow, dissection, or physiological ischemia after main-vessel stenting. Numerous studies demonstrated that provisional stenting is associated with lower rates of procedural complications and similar long-term outcomes compared with routine two-stent strategies in appropriately selected lesions [35].

Despite the widespread use of provisional stenting, many distal left main bifurcation lesions exhibit anatomical characteristics that favor an upfront two-stent approach. These features include Medina 1,1,1 lesions, long side-branch disease extending beyond 10 mm, severe calcification, large side-branch diameter, diffuse ostial involvement, unfavorable bifurcation angles, and anticipated side-branch compromise. In such anatomically complex lesions, planned two-stent strategies may improve side-branch scaffolding, reduce residual ischemia, and decrease the risk of restenosis or repeat revascularization [36].

Among contemporary two-stent techniques, double-kissing (DK) crush has emerged as one of the most extensively studied and clinically validated approaches for complex distal left main bifurcation disease. The DK-crush technique incorporates sequential side-branch stenting, crushing of the side-branch stent, rewiring, and repeated kissing balloon inflation to optimize bifurcation scaffolding and minimize stent distortion. Randomized trials demonstrated that DK-crush significantly reduces target lesion failure, myocardial infarction, stent thrombosis, and repeat revascularization compared with provisional stenting in complex left main bifurcation lesions [37].

The DKCRUSH-V trial represented a major milestone in bifurcation PCI and demonstrated superior outcomes with DK-crush compared with provisional stenting in true distal left main bifurcation disease. Patients treated with DK-crush experienced significantly lower rates of target lesion failure and stent thrombosis during long-term follow-up. These findings substantially influenced contemporary bifurcation guidelines and reinforced the importance of lesion complexity assessment when selecting bifurcation strategies [38].

Other two-stent techniques including culotte stenting, T-and-protrusion (TAP), mini-crush, and nano-crush continue to play important roles in selected anatomical scenarios. Culotte stenting may provide excellent coverage in bifurcations with similar daughter-vessel diameters, whereas TAP stenting is often useful for bailout side-branch treatment following provisional crossover stenting. The choice of bifurcation technique depends on vessel anatomy, bifurcation angle, plaque distribution, side-branch size, operator experience, and imaging findings [39].

The proximal optimization technique (POT) has become a fundamental component of modern bifurcation PCI. POT involves balloon dilation within the proximal segment of the stent using a balloon appropriately sized to the proximal reference vessel diameter. This maneuver improves stent apposition, restores stent geometry, facilitates side-branch rewiring, reduces stent malapposition, and improves final kissing balloon results. POT is particularly important in distal left main intervention because of the marked diameter discrepancy between the large proximal left main artery and the daughter vessels [40].

Coronary physiology increasingly influences bifurcation PCI strategy selection and optimization. Physiological assessment using iFR or FFR may help identify functionally significant side-branch disease before intervention and determine the need for additional side-branch treatment after crossover stenting. Importantly, angiographic narrowing of the jailed side branch frequently overestimates true ischemic significance. Physiology-guided side-branch assessment may therefore reduce unnecessary two-stent procedures and minimize procedural complexity without compromising clinical outcomes [41].

Intracoronary imaging is equally essential during contemporary distal left main bifurcation PCI. IVUS-guided assessment allows accurate vessel sizing, lesion characterization, calcium evaluation, stent expansion optimization, and identification of edge dissections or malapposition. OCT may provide additional high-resolution visualization of stent strut apposition and bifurcation architecture. Imaging-guided PCI consistently demonstrates superior procedural outcomes and lower adverse cardiovascular events compared with angiography-guided intervention alone [42].

The management of heavily calcified distal left main lesions remains particularly challenging during bifurcation PCI. Severe calcium may impair balloon expansion, prevent adequate stent deployment, and increase the risks of restenosis and stent thrombosis. Contemporary calcium-modification techniques including rotational atherectomy, orbital atherectomy, intravascular lithotripsy, and cutting balloons are increasingly used to optimize lesion preparation before stent implantation. Adequate calcium modification is essential for achieving optimal stent expansion and durable long-term results in complex distal left main bifurcation intervention [43].

Emerging Technologies and Future Directions in Precision Left Main Revascularization

The concept of precision revascularization in distal left main coronary artery disease continues to evolve rapidly with the integration of advanced physiological assessment, computational technologies, intracoronary imaging, artificial intelligence (AI), and novel PCI devices. Contemporary management increasingly emphasizes individualized treatment strategies tailored to lesion morphology, physiological significance, plaque composition, calcium burden, and patient-specific clinical risk. These technological advances aim to optimize procedural planning, improve stent deployment, minimize complications, and enhance long-term cardiovascular outcomes in one of the most complex subsets of coronary intervention [44,45].

Quantitative flow ratio (QFR) has emerged as an important nonhyperemic physiological modality capable of estimating coronary lesion significance using standard angiographic images without pressure wires or pharmacologically induced hyperemia. QFR utilizes computational fluid dynamics and three-dimensional coronary reconstruction to estimate pressure gradients across coronary stenoses. Several studies demonstrated good correlation between QFR and invasive FFR measurements, supporting its potential role in rapid functional lesion assessment during coronary angiography. In distal left main disease, QFR may simplify physiological evaluation and reduce procedural complexity while maintaining diagnostic accuracy [46].

Angiography-derived physiological indices represent a major advancement in functional coronary assessment because they avoid the need for pressure-wire manipulation in complex bifurcation anatomy. These technologies may be particularly useful in distal left main intervention where wiring both daughter vessels and interpreting physiological measurements can be technically challenging. Ongoing studies continue to evaluate the accuracy, reproducibility, and prognostic value of computational physiology-guided PCI in complex coronary disease [47].

Artificial intelligence is increasingly being integrated into coronary imaging and physiological analysis. AI-assisted algorithms can now support automated plaque characterization, calcium quantification, vessel sizing, bifurcation anatomy reconstruction, and prediction of procedural outcomes. Machine-learning models may also help identify patients most likely to benefit from PCI versus CABG based on combined anatomical, physiological, and clinical datasets. Such technologies have the potential to enhance procedural planning, reduce operator variability, and support precision-based revascularization strategies [48].

Advanced intracoronary imaging technologies are also expanding the capabilities of precision PCI. Contemporary OCT systems provide ultra-high-resolution imaging capable of detecting microcalcifications, plaque erosion, thin-cap fibroatheroma, stent malapposition, and subtle procedural complications. Hybrid imaging systems integrating IVUS and OCT are under investigation to combine the superior penetration of IVUS with the high spatial resolution of OCT. These innovations may further improve lesion characterization and procedural optimization during distal left main intervention [49].

Calcium-modification technologies continue to play an increasingly important role in complex left main PCI. Severe calcification remains a major predictor of stent underexpansion, restenosis, and adverse cardiovascular events. Contemporary techniques including rotational atherectomy, orbital atherectomy, excimer laser atherectomy, cutting balloons, scoring balloons, and intravascular lithotripsy have improved the ability to modify calcified lesions safely before stent implantation. Intravascular lithotripsy is particularly promising because it enables circumferential calcium fracture with relatively low risk of vessel perforation or distal embolization [50].

Robotic-assisted PCI represents another emerging innovation in complex coronary intervention. Robotic systems allow precise device manipulation, reduce operator radiation exposure, and potentially improve stent positioning accuracy during bifurcation PCI. Although current experience in distal left main intervention remains limited, robotic technology may become increasingly relevant as procedural complexity and precision requirements continue to increase [51].

Hybrid coronary revascularization strategies are also attracting growing interest in selected patients with distal left main disease. Hybrid approaches combine minimally invasive surgical left internal mammary artery grafting to the LAD with PCI of non-LAD lesions, aiming to integrate the durability of surgical grafting with the minimally invasive advantages of PCI. Such strategies may provide an individualized alternative for selected patients with complex anatomy or elevated surgical risk [52].

The future of distal left main intervention will likely involve increasing integration of multimodality assessment. Combining coronary physiology, intracoronary imaging, computational modeling, AI-guided procedural planning, and advanced bifurcation techniques may facilitate more accurate lesion selection and individualized treatment optimization. The growing emphasis on precision cardiology reflects the broader transition from anatomy-driven intervention toward physiology- and patient-centered revascularization [53].

Despite substantial progress, several important knowledge gaps remain. Long-term comparative data regarding physiology-guided PCI versus CABG in distal left main disease are still limited, particularly beyond 10 years of follow-up. Additional randomized trials focusing specifically on iFR-guided left main PCI, imaging-guided bifurcation optimization, computational physiology, and AI-assisted intervention are needed to establish standardized precision-revascularization algorithms. As technology continues to evolve, future management of distal left main coronary artery disease will increasingly depend on multidisciplinary collaboration integrating physiology, imaging, engineering, and computational medicine to optimize patient-specific outcomes [54].

How to cite this article: Ahmed Saed Eldamanhoury, Mohammed Hossam El-Din Elshaer, Mohammed Abdelnaby Elsayed Mohammed Emara, Alaa Elsayed Salama (2024). Precision Revascularization in Distal Left Main Coronary Artery Disease: Integration of Coronary Physiology, Imaging, and Contemporary PCI. Vol. 14, No. 3, 2024,1091--1100.

Source of support: None.

Conflict of interest: Nil.

Accepted: 26.03.2024 **Received** 03.03.2024

REFERENCES

1. Collet C, Capodanno D, Onuma Y, et al. Left main coronary artery disease: pathophysiology, diagnosis, and treatment. Nat Rev Cardiol. 2018;15(6):321-331.
2. Davidson LJ, Cleveland JC Jr, Welt FG, et al. A Practical Approach to Left Main Coronary Artery Disease: JACC State-of-the-Art Review. J Am Coll Cardiol. 2022;80(22):2119-2134.
3. Dąbrowski EJ, Kożuch M, Dobrzycki S. Left Main Coronary Artery Disease-Current Management and Future Perspectives. J Clin Med. 2022;11(21):6515.
4. Götberg M, Christiansen EH, Gudmundsdottir IJ, et al. Instantaneous Wave-free Ratio versus Fractional Flow Reserve to Guide PCI. N Engl J Med. 2017;376(19):1813-1823.
5. Eftekhari A, Holck EN, Westra J, et al. Instantaneous wave free ratio vs fractional flow reserve and 5-year mortality: iFR SWEDEHEART and DEFINE FLAIR. Eur Heart J. 2023;44(42):4376-4384.
6. Apostolos A, Gerakaris A, Tsoni E, et al. Imaging of Left Main Coronary Artery; Untangling the Gordian Knot. Rev Cardiovasc Med. 2023;24(1):26.
7. Burzotta F, Lassen JF, Louvard Y, et al. European Bifurcation Club white paper on stenting techniques for patients with bifurcated coronary artery lesions. Catheter Cardiovasc Interv. 2020;96(5):1067-1079.
8. Dai J, Guan C, Xu X, et al. Angiographic Quantitative Flow Ratio-Guided Treatment of Patients With Physiologically Intermediate Coronary Lesions. J Am Heart Assoc. 2025;14:e035756.
9. Kayaert P, Coeman M, Gevaert S, De Pauw M, Haine S. Physiology-Based Revascularization of Left Main Coronary Artery Disease. J Interv Cardiol. 2021;2021:4218769.
10. Modi BN, van de Hoef TP, Piek JJ, Perera D. Physiological assessment of left main coronary artery disease. EuroIntervention. 2017;13(7):820-827.
11. Johnson NP, Tóth GG, Lai D, et al. Prognostic value of fractional flow reserve: linking physiologic severity to clinical outcomes. J Am Coll Cardiol. 2014;64(16):1641-1654.
12. Escaned J, Petraco R, Fearon WF. Coronary Physiology to Guide Percutaneous Coronary Intervention: Why, When, and How. JSCAI. 2024;3(2):102198.
13. De Waard GA, Di Mario C, Lerman A, Serruys PW, Van Royen N. Instantaneous wave-free ratio to guide coronary revascularisation: physiological framework, validation and differences from fractional flow reserve. EuroIntervention. 2017;13(7):820-827.
14. Lee CH, Choi SW, Hwang J, et al. 5-Year Outcomes According to FFR of Left Circumflex Coronary Artery After Left Main Crossover Stenting. JACC Cardiovasc Interv. 2019;12(9):847-855.
15. Nijjer SS, Sen S, Petraco R, et al. Pre-angioplasty instantaneous wave-free ratio pullback provides virtual intervention and predicts hemodynamic outcome for serial lesions and diffuse coronary artery disease. JACC Cardiovasc Interv. 2014;7(12):1386-1396.
16. Li Kam Wa ME, Ezad SM, Modi B, et al. Randomized Comparison of Fractional Flow Reserve and Instantaneous Wave Free Ratio in Serial Disease. JACC Cardiovasc Interv. 2025;18(13):1617-1627.
17. Hwang D, Jeon KH, Lee JM, et al. Diagnostic Performance of Resting and Hyperemic Invasive Physiological Indices to Define Myocardial Ischemia. JACC Cardiovasc Interv. 2017;10(8):751-760.
18. Berry C, van 't Veer M, Witt N, et al. VERIFY (VERification of Instantaneous Wave-Free Ratio and Fractional Flow Reserve for the Assessment of Coronary Artery Stenosis Severity in EverydaY Practice): a multicenter study in consecutive patients. J Am Coll Cardiol. 2013;61(13):1421-1427.
19. Jeremias A, Maehara A, Généreux P, et al. Multicenter core laboratory comparison of the instantaneous wave-free ratio and resting Pd/Pa with fractional flow reserve: the RESOLVE study. J Am Coll Cardiol. 2014;63(13):1253-1261.
20. Räber L, Mintz GS, Koskinas KC, et al. Clinical use of intracoronary imaging. Part 1: guidance and optimization of coronary interventions. Eur Heart J. 2018;39(35):3281-3300.
21. Rubinshtein R, Ota T, Waksman R. Imaging of the left main coronary artery: current state of the art. Catheter Cardiovasc Interv. 2015;86(4):662-672.
22. Li L, Dash D, Gai LY, et al. Intravascular Ultrasound Classification of Plaque in Angiographic True Bifurcation Lesions of the Left Main Coronary Artery. Chin Med J (Engl). 2016;129(13):1538-1543.

23. Jasti V, Ivan E, Yalamanchili V, Wongpraparut N, Leesar MA. Correlations between FFR and intravascular ultrasound in patients with ambiguous left main coronary artery stenosis. Circulation. 2004;110(18):2831-2836.
24. Kang SJ, Mintz GS, Kim WJ, et al. Preintervention angiographic and intravascular ultrasound predictors for side branch compromise after a single-stent crossover technique. Am J Cardiol. 2011;107(12):1787-1793.
25. Park SJ, Kim YH, Park DW, et al. Impact of intravascular ultrasound guidance on long-term mortality in stenting for unprotected left main coronary artery stenosis. Circ Cardiovasc Interv. 2009;2(3):167-177.
26. Tearney GJ, Regar E, Akasaka T, et al. Consensus standards for acquisition, measurement, and reporting of intravascular optical coherence tomography studies. J Am Coll Cardiol. 2012;59(12):1058-1072.
27. Fujino A, Mintz GS, Matsumura M, et al. A new optical coherence tomography-based calcium scoring system to predict stent underexpansion. EuroIntervention. 2018;13(18):e2182-e2189.
28. Riley RF, Don CW, Aldea GS, et al. Contemporary Management of Left Main Coronary Artery Disease. JACC Cardiovasc Interv. 2021;14(22):2446-2457.
29. Lassen JF, Albiero R, Johnson TW, et al. Treatment of coronary bifurcation lesions, part II: implanting two stents. EuroIntervention. 2022;18(6):457-470.
30. Chen SL, Sheiban I, Xu B, et al. Impact of the complexity of bifurcation lesions treated with drug-eluting stents: the DEFINITION study. JACC Cardiovasc Interv. 2014;7(11):1266-1276.
31. Zhang JJ, Chen SL, Ye F, et al. DK crush versus provisional stenting for left main bifurcation lesions: subgroup analysis of the DKCRUSH-V randomized trial. JACC Cardiovasc Interv. 2020;13(6):718-728.
32. Chen SL, Zhang JJ, Han Y, et al. Double Kissing Crush Versus Provisional Stenting for Left Main Distal Bifurcation Lesions: DKCRUSH-V Randomized Trial. J Am Coll Cardiol. 2017;70(21):2605-2617.
33. Loh PH, Lassen JF, Jepson N, et al. Asia Pacific consensus document on coronary bifurcation interventions. EuroIntervention. 2020;16(9):e706-e714.
34. Burzotta F, Finet G, Trani C, et al. Proximal optimization technique in bifurcation stenting: the POT concept revisited. EuroIntervention. 2022;18(5):e366-e375.
35. Milzi A, Dettori R, Lubberich RK, et al. Quantitative Flow Ratio Is Related to Anatomic Left Main Stem Lesion Parameters as Assessed by Intravascular Imaging. J Clin Med. 2022;11(3):707.
36. Bennett J, Chandrasekhar S, Woods E, et al. Contemporary Functional Coronary Angiography: An Update. Future Cardiol. 2024;20(10):755-778.
37. Weisz G, Metzger DC, Caputo RP, et al. Safety and feasibility of robotic percutaneous coronary intervention: PRECISE (Percutaneous Robotically-Enhanced Coronary Intervention) Study. J Am Coll Cardiol. 2013;61(15):1596-1600.
38. Harskamp RE, Brennan JM, Xian Y, et al. Practice patterns and clinical outcomes after hybrid coronary revascularization in the United States. Circulation. 2014;130(11):872-879.
39. Higuchi S, Yamaji N, Noma H, et al. Physiology- versus angiography-guided percutaneous coronary intervention for people with coronary artery disease. Cochrane Database Syst Rev. 2026;1:CD016318.
40. Collet C, Capodanno D, Onuma Y, et al. Left main coronary artery disease: pathophysiology, diagnosis, and treatment. Nat Rev Cardiol. 2018;15(6):321-331.
41. Davidson LJ, Cleveland JC Jr, Welt FG, et al. A Practical Approach to Left Main Coronary Artery Disease: JACC State-of-the-Art Review. J Am Coll Cardiol. 2022;80(22):2119-2134.
42. Dąbrowski EJ, Kożuch M, Dobrzycki S. Left Main Coronary Artery Disease-Current Management and Future Perspectives. J Clin Med. 2022;11(21):6515.
43. Götberg M, Christiansen EH, Gudmundsdottir IJ, et al. Instantaneous Wave-free Ratio versus Fractional Flow Reserve to Guide PCI. N Engl J Med. 2017;376(19):1813-1823.
44. Eftekhari A, Holck EN, Westra J, et al. Instantaneous wave free ratio vs fractional flow reserve and 5-year mortality: iFR SWEDEHEART and DEFINE FLAIR. Eur Heart J. 2023;44(42):4376-4384.
45. Apostolos A, Gerakaris A, Tsoni E, et al. Imaging of Left Main Coronary Artery; Untangling the Gordian Knot. Rev Cardiovasc Med. 2023;24(1):26.
46. Burzotta F, Lassen JF, Louvard Y, et al. European Bifurcation Club white paper on stenting techniques for patients with bifurcated coronary artery lesions. Catheter Cardiovasc Interv. 2020;96(5):1067-1079.
47. Dai J, Guan C, Xu X, et al. Angiographic Quantitative Flow Ratio-Guided Treatment of Patients With Physiologically Intermediate Coronary Lesions. J Am Heart Assoc. 2025;14:e035756.
48. Kayaert P, Coeman M, Gevaert S, De Pauw M, Haine S. Physiology-Based Revascularization of Left Main Coronary Artery Disease. J Interv Cardiol. 2021;2021:4218769.
49. Modi BN, van de Hoef TP, Piek JJ, Perera D. Physiological assessment of left main coronary artery disease.

EuroIntervention. 2017;13(7):820-827.
50. Johnson NP, Tóth GG, Lai D, et al. Prognostic value of fractional flow reserve: linking physiologic severity to clinical outcomes. J Am Coll Cardiol. 2014;64(16):1641-1654.
51. Escaned J, Petraco R, Fearon WF. Coronary Physiology to Guide Percutaneous Coronary Intervention: Why, When, and How. JSCAI. 2024;3(2):102198.
52. De Waard GA, Di Mario C, Lerman A, Serruys PW, Van Royen N. Instantaneous wave-free ratio to guide coronary revascularisation: physiological framework, validation and differences from fractional flow reserve. EuroIntervention. 2017;13(7):820-827.
53. Lee CH, Choi SW, Hwang J, et al. 5-Year Outcomes According to FFR of Left Circumflex Coronary Artery After Left Main Crossover Stenting. JACC Cardiovasc Interv. 2019;12(9):847-855.
54. Nijjer SS, Sen S, Petraco R, et al. Pre-angioplasty instantaneous wave-free ratio pullback provides virtual intervention and predicts hemodynamic outcome for serial lesions and diffuse coronary artery disease. JACC Cardiovasc Interv. 2014;7(12):1386-1396.