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Review Article

Treatment Strategies of the Left Mean Coronary Artery Lesions

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Abstracts

Left main coronary artery (LMCA) disease is the highest-risk lesion subset of ischemic heart disease and has traditionally been an indication for coronary artery bypass grafting (CABG). Recent evidence suggests comparable clinical outcomes between a percutaneous coronary intervention (PCI) and CABG for LMCA disease, with similar rates of mortality and severe composite issues, a higher percentage of stroke with CABG, and a higher rate of repeat revascularization with PCI. In this Review, we describe the pathophysiology of unprotected left primary coronary artery disease, discuss diagnostic approaches in light of new noninvasive and invasive imaging techniques, and detail risk stratification models to aid the Heart Team in the decision- making process for determining the best revascularization strategy for these patients.

Introduction

Significant left main (LM) disease is observed in only 5% of patients referred for a coronary angiogram, involving the distal bifurcation in the majority of cases [1] with a significant prognostic impact [2]. Significant left main coronary artery (LMCA) disease is the highest-risk lesion subset and is associated with poorer clinical outcomes compared with none-LMCA CAD. Medical treatment has yielded unacceptable results with a mortality of around 50% at three years [2] and surgery, considered the gold standard strategy, has shown its superiority over medical therapy on death for decades [3]. With the remarkable improvements in medical device technology, procedural techniques, antithrombotic agents, and background medical therapy during the last two decades, PCI with stenting for LMCA disease has become technically feasible. It shows favourable clinical outcomes [4]. Two randomized clinical trials published in 2016, EXCEL and NOBLE, demonstrated the safety and efficacy of PCI compared with CABG surgery in selected patients with unprotected left main coronary artery disease, showing similar survival with CABG surgery and PCI at midterm follow- up [5,6]. Although studies with long- term follow- up are warranted, PCI might be considered an alternative revascularization strategy for selected patients with unprotected left main coronary artery disease.

Anatomy and Pathophysiology

The left main coronary artery arises from the left aortic sinus, below the sinotubular junction, and ends by bifurcating into the left anterior descending artery and left circumflex artery and, in one- third of the patients, by trifurcating with an intermediate ramus. The left main coronary artery has an average length of 10mm (2-23mm), with a mean diameter of 3.9 ± 0.4mm in women and 4.5 ± 0.5mm in men [7], and is divided into three parts: ostium, shaft, and a distal segment. The lesion may be underestimated, and mathematical models should be used to determine the correct diameter of the proximal MV according to the distal MV and SB diameters [8]. The simplified law of Finet can be used in Daily practice (Proximal LM diameter=0.678 (left anterior descending artery (LAD)+circumflex diameters)) [9].

The development of atherosclerosis in the left main coronary artery has been linked to flow haemodynamics, with atherosclerotic plaques described at areas of low endothelial shear stress in the lateral wall of the bifurcation (Figure 1), opposite to the carina [10].

Conversely, the carina is often free from disease, probably owing to the protective effect of high shear stress against plaque formation (Figure 1); [11]. The length of the left main coronary artery also influences stenosis location and morphology. In short left main coronary arteries (<10mm), lesions develop more frequently near the ostium than in the bifurcation (55% versus 38%). In contrast, in long arteries, lesions develop predominantly near the bifurcation (ostium 18% versus bifurcation 77%) [12,13]. Moreover, the PCI strategy for LM treatment should be anticipated by a thorough examination of the anatomy of the bifurcation lesion using tools such as the Medina classification [14], and difficulties should be assessed utilizing the SYNTAX score allowing a risk stratification of the procedure into low, intermediate or high-risk [15].

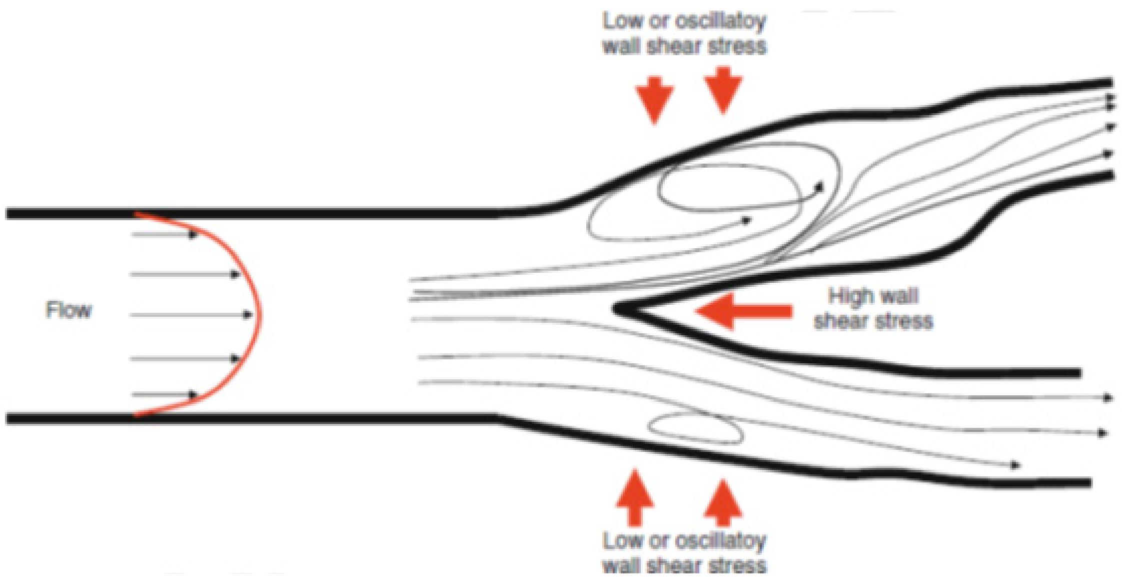

Figure 1: Role of endothelial shear stress in atherosclerotic plaque formation in the left main coronary bifurcation. Endothelial shear stress is the tangential force derived from the friction of the flowing blood on the endothelial surface and is the product of the shear rate at the wall and the blood viscosity. In arterial regions with disturbed laminar flow, low endothelial shear stress shifts the endothelial function and structure towards an atherosclerotic phenotype, thereby promoting atherogenesis, atherosclerotic plaque formation and progression, and vascular remodelling. In contrast, the carina is exposed to high shear stress [13].

Use of Intracoronary Imaging

IVUS can provide an estimate of the ischemic burden of the LM lesion, and its use following LM PCI improves clinical outcomes [16]. In the multicenter prospective LITRO study [17] of intermediate LM stenosis between 25% and 60%, deferring revascularization of LM lesions with minimal luminal area (MLA) of ≥6 mm2 (53% of lesions) was safe and associated with favourable outcomes at two years of follow-up (cardiac death-free survival of 97.7%). Although IVUS is good at describing the anatomical extent of disease, the LM-MLA cutoff for determining a functionally significant lesion differs between populations. Thus these values need to be interpreted with caution. The other benefit of IVUS is to ensure stent optimization of LM PCI. IVUS can ensure adequate expansion and apposition of stents after LM PCI, which improves clinical outcomes following LM PCI, particularly in patients with distal LM lesions and those treated with a 2- stent strategy [16].

In a Korean study, the MLA cutoff for FFR <0.80 was 4.5mm^2 with a sensitivity of 77% and a negative predictive value of 75%,[18] whereas another US study yielded a cutoff value of 5.9mm^2 with a sensitivity and specificity of 93% and 94%, respectively, for an FFR<0.75 [19]. Optical coherence tomography is another intracoronary imaging modality that is often employed for lesion characterization and PCI guidance in non-LMCAD, particularly given its higher resolution imaging. Another drawback of optical coherence tomography use in LM imaging is its limited penetration depth (2-3mm) as compared with IVUS (4-8mm), given that the average LMCA diameter is 3.5 to 4.5mm. Finally, literature regarding clinical outcomes or correlation with physiology for optical coherence tomography in LMCAD is lacking.

Treatment

A meta-analysis of the early studies showed that patients with unprotected left main coronary artery disease had the highest survival benefit with surgical revascularization (OR 0.32, 95% CI 0.15-0.70, P = 0.0004), establishing CABG surgery as the treatment of choice for these patients [3]. Surgical myocardial revascularization techniques have evolved with developments in off-pump and clampless procedures, periaortic ultrasonography, conduit selection for total arterial revascularization, intraoperative graft assessment, and minimally invasive procedures [20].

The development of drug-eluting stents (DESs) has markedly improved the prognosis after PCI in patients with unprotected left main coronary artery disease, with randomized trials demonstrating a similar survival with PCI and CABG surgery at midterm follow- up. In the SYNTAX randomized trial, LM PCI with first-generation DES as compared to CABG in a subgroup of patients. In patients with a SYNTAX score <33, significant adverse events and mortality were similar at five years, albeit with an increased risk of target lesion revascularization in the PCI group (23%) [21].A recent meta-analysis of the four randomized trials comparing the first-generation DES to CABG in LM disease confirmed the non-inferiority of PCI concerning mortality and MACE [22]. This meta-analysis highlighted a higher risk of stroke at one year in the surgery group and established a higher risk of target vessel revascularization in the PCI group. The EXCEL study reported an initial benefit of PCI within the first month concerning the primary endpoint [23]. However, a reversal of results was observed between 30 days and three years with a higher target vessel revascularization in the PCI group. Nevertheless, the non-inferiority of PCI for the primary endpoint was reached at three years.

In the NOBLE study, PCI was inferior to CABG at 5-years' follow-up due to a higher rate of non-procedural myocardial infarction in the PCI group with an unusual trend towards a higher rate of stroke in the PCI group [24]. In both these recent trials with new-generation DES, target vessel revascularization was comparable to, and nearly twice as low as the TLR reported in the SYNTAX study, suggesting improved outcomes with new-generation devices. Moreover, these two studies provide consistent data suggesting the safety of both strategies with a long-term benefit associated with surgery despite a primary benefit of PCI in the EXCEL trial. Four consecutive randomized clinical trials (RCTs) comparing early-generation DES and CABG reported similar results [25,26]. Overall, the rates of death or MI were identical between the two groups; however, stroke was more familiar with CABG, and repeat revascularization was more common with PCI. Subsequently, several meta-analyses have confirmed these findings [27,28].

Contemporary standards of PCI for unprotected left main coronary artery disease include pre-procedural imaging and functional assessment, procedural planning based on clinical and anatomical characteristics with the use of new- generation DES with thin struts and bioresorbable or biocompatible polymer, lesion preparation and stenting with proximal optimization with or without kissing balloon inflation based on the chosen technique, post-procedural imaging and functional assessment with further optimization as necessary and potent dual antiplatelet therapy after the procedure [29]. The provisional stenting strategy begins with implantation of a single stent and allows SB stenting only in cases of incomplete results. The provisional stent has, consequently, become the default strategy in bifurcation lesions and is considered the most appropriate option for LM PCI. The literature shows that a high rate of single-stent plan can be achieved when provisional stenting is performed, with a trend towards a lower incidence of significant events and target lesion revascularization in registries [30,31], but with a probable bias regarding the flat rate of "true bifurcation" (Medina 111) in these studies.

A two-stent strategy is implemented in a limited number of cases and may be needed in the presence of ≥2.50mm SB diameter and >50% diameter stenosis as well as in lesions difficult to wire or in cases of extensive disease >5-10mm according to criteria from the European bifurcation club II trial [32]. Recently, the randomized DKCRUSH-V study challenged results from registries with less target lesion failure in patients treated for "true bifurcation" LM disease with a DK-crush two-stent strategy compared to those with a provisional stenting strategy [33]. The outcomes of the two-stent strategies for the LM do not differ in the literature between T-stent and crush techniques [34]. Still, the incidence of MACE was reduced with the DK-crush method in comparison to the culotte technique in a recent trial [35].The European Bifurcation Club recommends the KISSS principle (Keep it simple, swift and safe) [34]. The T-stent technique is the most appropriate option for distal LM PCI as the angle between the LAD, and the circumflex is approximately 90° and is associated with good outcomes [36]. An optimal view should be selected to avoid missing the SB ostium during deployment of the second stent (Figure 1). The TAP technique with minimal stent overlap is also appropriate for distal LM bifurcation. This technique should be avoided in narrow angles because of a risk of late endothelialization associated with the potential presence of a long metallic carina.

The culotte technique may be appropriate for distal LM if the angle between the LAD and the circumflex is inferior to 60° and if both branches have similar diameters. The culotte technique has been studied in clinical trials with favourable results [32]. The first stent is deployed from the LM to the most angulated branch, which is frequently the circumflex. Short stent overlap in the proximal MV and rewiring of the MV near the carina are recommended. The V-stent technique, whereby two stents are positioned at the ostium of the LAD and the the ostium of the circumflex is only used in the presence of Medina 0, 1, 1 distal LM disease. The mini-crush technique is a variation of the standard crush technique allowing minimal overlapping of stent struts. The first stent is usually deployed in the circumflex with minimal protrusion into the LM and with simultaneous positioning of the second stent from the LM to the LAD. The second stent is subsequently deployed by crushing the proximal part of the circumflex stent. The circumflex is then rewired through a proximal strut, and the struts are opened. The DK-crush technique may also be implemented in the presence of distal LM stenosis (Figure 2). The SB is stented first. A balloon is crushed in place from the LM to the LAD. The first kissing balloon inflation is carried out before deployment of the second stent from the LM to the LAD. The second kissing balloon inflation is performed once the two stents are deployed [35].

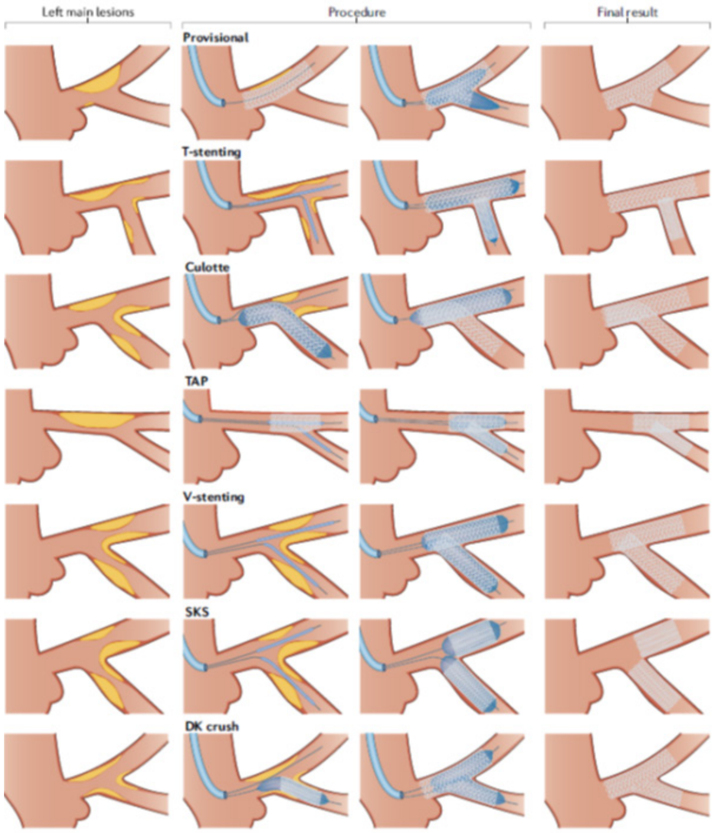

Figure 2: PCI bifurcation techniques for patients with unprotected left main coronary artery disease.

The percutaneous coronary intervention (PCI) provisional one-stent technique is the recommended approach for the Majority of bifurcation lesions. After stent implantation in the main branch, proximal optimizing method (POT) allows for the reconstruction of the initial anatomy of the bifurcation and facilitates wire exchange. After POT, a final kissing balloon dilatation (that is, simultaneous inflation of two coronary balloons in the main and side branch) can be performed. For approximately 15% of bifurcation lesions, a two- stent technique is required. The choice is left to the operator, but technique selection might also depend on the bifurcation angulation. T- stenting is preferred for T- shape angulation, whereas T and protrusion (TAP) stenting or culotte stenting is preferred for Y- shape angulation. In all two- stent cases, high- pressure side branch and main vessel dilatation is mandatory to achieve full stent expansion. A final re- POT should be considered to correct for proximal main vessel stent distortion if overlapping of the two balloons occurred proximal to the polygon of confluence. V- stenting and simultaneous kissing stenting (SKS) are less commonly used and can be considered in cases involving only the left anterior descending artery or the circumflex artery. The double- kissing (DK) crush technique has been proposed for unprotected left main coronary artery disease treatment. In DK crush stenting, one balloon is introduced into the main vessel and a stent deployed at the side branch. The balloon in the main vessel is then inflated to crush the side branch stent after its deployment. After rewiring the side branch proximally, first kissing is performed, followed by stenting of the main vessel. Final kissing balloon inflation is conducted after rewiring the side branch from the proximal main vessel stent cell. After stenting both the main vessel and the side branch, POT should be performed to improve main vessel stent strut apposition [37].

Conclusion

Patients with significant unprotected left main coronary artery disease should undergo prompt revascularization. Noninvasive and invasive diagnostic imaging with the use of adjunct methods is often required to assess the need for revascularization. Both PCI and CABG have proven to be therapeutic options for LM disease revascularization with comparable short-term safety in patients with low to intermediate SYNTAX score. Developments in the field of percutaneous revascularization including refinements in patient selection, improvements in device technology, implantation techniques, and medical therapy have made PCI a feasible, safe, and effective alternative to CABG surgery for unprotected left main coronary artery disease. The results of the EXCEL and NOBLE trials may reposition the therapeutic role and change the recommendation for PCI relative to CABG for patients with LMCA disease.

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