Current diagnosis and management of left main coronary disease

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Summary

Left main coronary artery (LMCA) disease remains an important risk factor for increased mortality and morbidity at all stages of diagnosis and treatment of coronary artery disease. Left main stem pathology is often silent, with unpredictable presentation: as such it poses diagnostic and management challenges. This article reviews the anatomy, epidemiology and diagnosis of left main stem disease, as well as advances in multidisciplinary concepts of diagnosis and management, and summarises the outcomes of recent prospective studies comparing percutaneous and surgical revascularisation in LMCA disease.

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1. Introduction

Left main coronary artery (LMCA) disease remains an important risk factor for increased mortality and morbidity at all stages of diagnosis and treatment of coronary artery disease. Left main stem pathology is often silent, with unpredictable presentation: as such it poses diagnostic and management challenges. With the advent of drug-eluting stents, improvements in percutaneous intervention and aggressive interventional centres, the management of left main coronary disease is no longer purely surgical. This article reviews the anatomy, epidemiology and diagnosis of left main stem disease, as well as recent advances in multidisciplinary concepts of diagnosis and management.

1.1. Search strategy

The medical literature was searched to identify articles relevant to LMCA pathology, as well as the epidemiology, diagnosis and treatment of left main stem disease. Searches were conducted via the following databases covering the period from their commencement to March 2009: MEDLINE, EMBASE, Cochrane library and Science Citation index. The Internet and major textbooks were also searched. No language restrictions were applied.

2. Anatomical and morphological considerations

2.1. Normal anatomy

The LMCA runs from its origin in the aorta to its bifurcation into the left anterior descending and circumflex coronary arteries. The average diameter of a non-diseased LMCA measured angiographically is $4.5 \pm 0.5$ mm in men, and $3.9 \pm 0.4$ mm in women [1], although diameters up to 10 mm have been recorded in post-mortem studies of non-diseased hearts [2]. The length of the LMCA is highly variable: in one study of 106 hearts at autopsy the length ranged from 2 to 40 mm [2]. A short LMCA has been associated with bicuspid aortic valve [3]. Most studies show little correlation between the length of the LMCA and heart size, or patient height.

The LMCA is divided into three parts [1]: the origin of the LMCA from just above the left sinus of Valsalva (the ostium), a mid portion (body) and a distal portion or bifurcation. The ostium has a greater proportion of smooth muscle and elastic tissue than the rest of the coronary vessels [4]. The course of the LMCA is normally leftward, posterior and superior, running at about 90° from the ostium, and travelling 2–4 mm through the aortic wall. It emerges posterior to the pulmonary trunk, and then travels in the left atrioventricular groove, dividing before the base of the left atrial appendage.

2.2. Anatomical variants and anomalies

There are several important anatomical variants and anomalies in origin, course and termination of the LMCA. In
two-thirds of cases the distal portion divides into two major branches: the left anterior descending and circumflex coronary arteries. In about one-third of cases the distal portion ends as a trifurcation [5]: the third branch is known as the intermediate coronary artery. More than three branches have been reported in 2.4% of cases [5].

There may be no LMCA: the left anterior descending and circumflex arteries arise from a common ostium, or separate ostia, in less than 1% of adult patients [5,6]. This is the most common congenital coronary anomaly, and may be associated with a higher incidence of aortic valve disease [3,6]. The second most common anomaly is origin of either the left anterior descending or the circumflex coronary artery, either as a separate branch from the right or non-coronary sinus of Valsalva, or as a branch from the right coronary artery [6]. A right sinus origin is associated with sudden death, particularly when the LMCA runs between the aorta and pulmonary trunk. Non-coronary sinus origin is usually benign. 'High take-off' occurs in 0.013% of patients [6]. In these cases the LMCA ostia is high on the aorta, some way distal to the left sinus of Valsalva.

2.3. Classification and definitions of left main stem disease

LMCA disease may be classified by aetiology (Table 1). As a guide to treatment options and prognosis, the most useful classifications indicate severity and morphology of obstructive disease. Most trials of treatment and treatment guidelines define significant LMCA stenosis as a greater than 50% diameter stenosis, and left main equivalent disease is as severe (greater than or equal to 70%) diameter stenosis of the proximal left anterior descending and proximal left circumflex as judged by contrast angiography [7]. Obstructive LMCA disease, which is most commonly atherosclerotic, may be further classified according to morphology: most recently the Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery (SYNTAX) trial score, which was developed to prospectively characterise coronary vasculature with respect to the number of lesions and their location, complexity and functional impact, has been shown to predict a higher incidence of major adverse cardiac and cerebrovascular events following percutaneous coronary intervention (PCI), with greater accuracy than the modified lesion classification scheme of the American College of Cardiology/American Heart Association (ACC/AHA) [8]. When only patients with left main stem disease were analysed (as opposed to the SYNTAX trial which included patients with three-vessel disease), a higher SYNTAX score was also found to predict adverse events after coronary artery bypass grafting (CABG) [9].

2.4. Morphological characteristics

Compensatory enlargement of the LMCA occurs before atherosclerosis encroaches on the lumen (the Glagov phenomenon): luminal flow is not compromised until plaque area exceeds 40% of the total vessel cross-sectional area [10]. In one retrospective analysis of 384 patients who underwent surgical revascularisation for significant LMCA obstruction, a bifurcation stenosis, present in 40% of patients, was the most frequent finding [11]. Bifurcation stenoses were more likely to be severe than other types of lesions. Circular stenoses had an incidence of 25% and were the most frequently calcified lesions. Mid-shaft stenoses had an incidence of 24% and were the least frequently calcified lesions. Isolated LMCA disease was found to be unusual: stenotic disease of the other coronary arteries was observed in more than 80% of patients. An isolated ostial stenosis is present in less than 1% of patients, who tended to be younger females, and less likely to have risk factors for atherosclerosis [12].

3. Clinical features

3.1. Incidence and epidemiology

By far the most common aetiology of LMCA disease is atherosclerosis. The prevalence of significant LMCA atherosclerotic disease at angiography in men over 65 years of age presenting with New York Heart Association (NYHA) class II angina in one report was 11%, NYHA class III angina was 13% and NYHA class IV angina was 9%. These percentages were 0, 7 and 12, respectively, for females [13].

Non-atherosclerotic causes of LMCA lesions are rare. Tertiary syphilis, the presentation of which includes aortitis, has an incidence of five cases per 100 000: in one study of 100 patients with syphilitic aortitis, 26 were found to have ostial coronary stenosis [14]. Takayasu’s arteritis has an incidence of two to three cases per million: the incidence of coronary arterial lesions (which are confined to the proximal and ostial segments in 80% of these cases), on the basis of post-mortem
examinations, was found to be 10% [15]. Spontaneous dissection of the LMCA is rare: there are 150 reports in the literature. It occurs most commonly in young women during the peri-partum or early post-partum period [16].

Iatrogenic ostial and LMCA lesions are more common. Of the 68 cases of coronary artery disease attributed to radiotherapy identified in one literature review, 11 involved ostial stenosis of right, left or both coronary ostia [17]. The incidence of LMCA ostial stenosis as a result of trauma from direct intubation for antegrade cardioplegia delivery has been reported to be around 1% postoperatively [18], similar to the incidence of LMCA stenosis following percutaneous intubation which ranges from 0.2% to 1.7% [19]. However, when measurable LMCA stenosis is already present prior to percutaneous transluminal coronary angioplasty, the risk of subsequent disease progression is increased, with a reported incidence of 17% at 6 months [20]. The strut of an aortic valve bioprosthesis, if incorrectly positioned, may also result in ostial obstruction.

3.2. Clinical associations

Several studies have examined the value of clinical variables for identifying the presence of LMCA disease. In an analysis of 6435 patients, Pryor et al. identified 11 clinical characteristics that predicted three-vessel or LMCA stem disease including typical angina, previous myocardial infarction, age, gender, duration of anginal symptoms, risk factors (e.g., hypertension, diabetes, hyperlipidaemia, smoking), carotid bruit and chest pain frequency [21]. A predictive model was constructed using logistic regression based on these variables, and validated in an independent sample of 2342 patients: of the 37% of patients referred for non-invasive testing who were classified as ‘low risk’ by their scale, fewer than 1% had LMCA disease, compared with almost 70% of patients identified by the model as ‘high risk’. The validity of the model was also extended to large series from other institutions: the reported prevalence of severe disease in the Coronary Artery Surgery study correlated well with the probabilities predicted by the model for men and women of various age and angina strata, although this model has not been independently validated.

There is a strong association between LMCA disease and carotid artery stenosis. Carotid artery disease is present in almost 40% of patients undergoing angiography for evaluation of angina, with significant left main stem disease, compared with just 5% with single-vessel disease [22]. The AHA guidelines recommend screening all patients undergoing bypass surgery for left main stem disease to identify carotid artery disease [23].

3.3. Natural life history

The median survival was 6.6 years in medically treated patients with significant atherosclerotic left main stem disease, and 6.2 years for medically treated patients with severe left main stem equivalent disease in the Coronary Artery Surgery study [24]. These patients were not, however, a homogeneous group. Patients with LMCA disease enrolled in the Veterans Administration cooperative study of CAGB versus medical management of coronary artery disease were stratified into high and low risk based on the presence of LMCA stenosis >75% and presence of left ventricular dysfunction [25]. At 42 months, over 90% of low-risk patients managed medically were alive, whereas this figure was under 50% in the high-risk patient group.

In general, the severity and distribution of coronary artery stenoses increase with time, but the rate and pattern of progress are highly variable. After CAGB, majority of significant native vessel coronary stenoses proximal to a bypass graft become more severe within 5 years of surgery: significant lesions have a strong tendency to obstruct, but the rate of progression of lesser lesions is uncertain [26]. In a series of 30 patients requiring repeat revascularisation more than 3 years after primary CABG, a fifth of patients had developed new left main stem stenosis [27]. The progression of atheromatous disease distal to the graft anastomosis is of particular relevance, and has been reported in approximately 20% of grafts, a significantly lower rate than that of progression proximal to a bypass graft, which has been reported to occur in 96% of grafts [26]. The routine use of anti-platelet and antihypertensive therapy, and cholesterol-lowering agents which was much less widespread at the time of studies of this era, is likely to slow progression significantly.

4. Diagnostic modalities

4.1. Coronary angiography

Coronary angiography remains the gold standard diagnostic modality in diagnosis of clinically important LMCA lesions. There are, however, several important limitations, which lead to a small but significant number of false-positive and false-negative results, as well as significant inter-observer variability [28]. In order to avoid precipitating myocardial ischaemia in patients with severe LMCA disease, operators try to limit the number of angiographic shots, as well as keep dye injections to a minimum: this may have an impact on diagnostic accuracy of less experienced operators.

Ostial LMCA stenosis is not well shown angiographically, diagnosis relies on detection of pressure damping on engagement of the ostia with the catheter tip and the absence of reflux of dye into the coronary sinus on injection. Detecting and quantifying stenosis of the LMCA and bifurcation rely on a normal segment for comparison: the severity of concentric stenoses of the entire LMCA may therefore be underestimated. Angiography is also poor at assessing lesion calcification. This is important firstly because where visual assessment is inaccurate it is often because of the presence of calcification, and secondly because the presence of calcification is an important risk factor for dissection following PCI.

Several studies comparing conventional angiography with adjunctive imaging modalities have shown LMCA lesions considered angiographically indeterminate to, in fact, be severely stenosed [29]. Adjunctive technology, which is used to increase diagnostic accuracy and facilitate decision making, includes intravascular ultrasound imaging (IVUS), fractional flow reserve (FFR) and coronary vasodilatory reserve (CVR).
4.2. Intravascular ultrasound imaging

IVUS provides a tomographic 360° sagittal scan of the vessel from the lumen through the media to the vessel wall. Intravascular ultrasound measurements of arterial dimensions (minimal and maximal diameters, cross-sectional area and plaque area) provide important additional information compared with angiography alone. IVUS detects calcification twice as often as angiography and is more sensitive at detecting significant LMCA stenosis than angiography alone [29]. IVUS has been successfully used as an adjunct to stent implantation, but a systematic literature review found that although there was some evidence for a reduction in restenosis rates, there was not sufficient evidence at present for routine use of IVUS as a tool for improving outcome in PCI [30]. IVUS may have a role in the assessment of high-risk patients and in deciding whether patients with angiographically indeterminate LMCA lesions should undergo PCI or surgery [29].

4.3. Fractional flow reserve

FFR is the ratio of distal coronary pressure to aortic pressure measured during maximal hyperaemia. It is a relatively simple technique that gives a representation of the fraction of normal blood flow through a stenotic artery. The normal FFR for all vessels under all haemodynamic conditions, regardless of the status of the microcirculation, is 1.0. FFR values <0.75 are associated with abnormal stress tests. Lesions that are responsible for reversible ischaemia have FFRs <0.75. FFR may have a role in deciding whether patients with angiographically mild or moderate LMCA disease should undergo revascularisation: 56% of patients with FFR <0.75 in one study had significant LMCA stenoses [31]. CABG was performed in this group, whereas a medical approach was selected in patients with LMCA FFR >0.75: the 100% survival in the medical group and 97% survival in the surgical group at 3 years was taken by the authors to demonstrate the efficacy of FFR as a predictor of risk.

4.4. Coronary vasodilatory reserve

CVR is the ratio of hyperaemic to basal flow and reflects flow resistance through the epicardial artery and the corresponding myocardial bed. Unlike FFR, the value is affected by the coronary microcirculation and haemodynamic conditions. Although of use in the further assessment of angiographically indeterminate lesions, no studies have specifically addressed the use of this diagnostic adjunct in assessment of LMCA disease.

4.5. Cross-sectional imaging

There are case reports of LMCA stenotic and aneurysmal lesions diagnosed by multi-slice computerised tomography (CT), but surgical intervention was invariably preceded by conventional angiography. Compared with conventional coronary angiography, the sensitivity and specificity of multi-slice CT for detecting significant lesions (defined as >50% stenosis) were 95% and 98%, respectively [32]. Magnetic resonance imaging (MRI) offers good views of the first few centimetres of the coronary tree, but resource limitations mean that even with continued improvement in image resolution, MRI is unlikely to become the investigation of choice in delineating LMCA anatomy on a routine basis in the near future.

In summary, adjunctive imaging modalities such as FFR and intravenous ultrasound can be used to improve assessment of indeterminate lesions, as well as helping to decide which patients will benefit from early revascularisation. With further refinements in technology, multi-slice CT may offer an alternative less invasive means of imaging the LMCA within the next decade.

5. Treatment

5.1. Guidelines for treatment

The AHA/ACC guidelines state that ‘The benefit of surgery over medical treatment for patients with significant left main stenosis is little argued.’ [23]. In the 2004 update of the AHA/ACC guidelines, CABG is recommended over PCI for any patient with stable angina, unstable angina, mild or asymptomatic disease and significant left main or left main equivalent coronary stenosis; as well as for patients with poor left ventricular function, acute myocardial infarction (MI) or life-threatening ventricular arrhythmias and significant LMCA or left main equivalent disease.

5.2. Percutaneous coronary intervention

The results outlined above of medically managed LMCA disease mean that this is not an acceptable alternative in operable patients, and the risks of PCI in LMCA stenosis already described have meant that until relatively recently these patients were excluded from most trials of PCI. Historically, LMCA stenosis has been treated percutaneously in three circumstances: electively when the LMCA is already ‘protected’ by a patent bypass graft; as an emergency for acute closure caused by diagnostic catheterisation; or in the setting of acute MI. This limited experience encouraged some groups to attempt LMCA PCI in broader patient categories. Over 20 studies of elective and emergency LMCA PCI in over 3000 patients have been published to date. Although initial experience was discouraging: in-hospital mortality in elective patients ranged from 9% to 36%, increasing to over 80% in emergency patients [33]; in-hospital mortality rates were lower in subsequent studies. For example, Silvestri et al. reported an in-hospital mortality of 3% in 140 patients [34]. Tan et al. reported 1-year mortality from all causes of 24% and from cardiac causes of 20% in 278 unselected patients; however, even in relatively low risk, elective patients, 1-year event-free survival was poor at around 70% [35]. In-stent restenosis after bare-metal stent (BMS) is the most important reason for bypass surgery being the first choice of treatment. Further, in-stent restenosis in patients with BMS makes repeat intervention sufficiently complex such that surgery is often required. Bifurcation and ostial lesions appear to be at higher risk of restenosis than stented lesions in the body of the LMCA.

More recently, several observational studies reported high procedural success and improvements in event-free survival
at 1 year using drug-eluting stents in LMCA stenosis. Park et al. conducted a study comparing clinical and angiographic outcomes of sirolimus-eluting stent (SES) and BMS for elective unprotected LMCA stenosis [36]. Elective SES was performed in 102 patients compared with 121 patients with BMS. Procedural success rate was 100% for both groups with no incidents of death, stent thrombosis, Q-wave MI or emergent bypass surgery during hospitalisation. SES patients showed a lower rate of lumen loss and had a lower 6-month angiographic restenosis rate (7.0% vs 30.3%, p < 0.001) than the BMS patients. At 12 months, the rate of freedom from death, MI and target lesion revascularisation was 98.0 ± 1.4% in the SES group and 81.4 ± 3.7% in the BMS group (p = 0.0003). This was despite the fact that SES patients had more complex baseline characteristics with more multivessel disease, more bifurcation lesions and longer lesion lengths. Price et al. followed 50 patients after unprotected LMCA intervention with SES and found in-lesion restenosis in 42% of patients, with 82% involving the branch of the LMCA. These studies show differences in outcomes of this study were reproduced, their outcomes of 97.2% freedom from death or re-intervention at 1 year, and ‘coronary artery disease’-related annual mortality of 1% would merit a review of the current guidelines of indications for CABG. Other patient characteristics have also been found to yield prognostic information. The Unprotected Left Main Trunk Investigation Multicenter Assessment (ULTIMA) registry of 279 consecutive patients undergoing LMCA PCI at 25 centres between 1993 and 1998 identified several patient characteristics that were independent correlates of all-cause mortality, including left ventricular ejection fraction <30%, mitral regurgitation grade 3 or 4+, presentation with MI or shock, creatinine >200 mg l⁻¹ and severe lesion calcification [35].

Several observational studies as well as three randomised studies (Table 2) have compared CABG to DES in the treatment of LMCA. Methodological problems limiting interpretation of these results include the facts that majority of these studies were underpowered to detect key outcome differences between groups; the unmatched observational studies had significant variation in baseline characteristics between groups with higher-risk patients undergoing CABG (reflected by unusually high operative mortality in these studies); and two of the three randomised studies had strict inclusion criteria effectively biasing the results heavily towards PCI. In a study of 105 patients with unprotected left main stenosis, Buszman et al. randomised 52 patients to receive PCI and 53 to undergo CABG [40]. There was a small increase in left ventricular ejection fraction after 12 months in the PCI group (3.3 ± 6.7% after PCI vs 0.5 ± 0.8% after CABG; p = 0.047). PCI was also associated with a lower 30-day major adverse event rate and major adverse cardiac and cerebrovascular event rate. At 1 year, total major adverse cardiac and cerebrovascular events were not significantly different between the two groups. LMCA in-stent restenosis occurred in five patients (9.6%), of whom four underwent repeat stenting and one required CABG.

### Table 2

<table>
<thead>
<tr>
<th>Study</th>
<th>n PCI/CABG</th>
<th>Duration</th>
<th>MI %</th>
<th>RR %</th>
<th>MACCE %</th>
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<td></td>
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<tr>
<td>SYNTAX [41]</td>
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<td>1</td>
<td>4.2/4.4</td>
<td>11.8/6.5</td>
<td>15.8/13.7</td>
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<td>0/0</td>
<td>6.2/0.0</td>
<td>7.7/7.9</td>
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<td>1.9/7.5</td>
<td>0.0/3.8</td>
<td>30.8/24.5</td>
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<td>Observational studies</td>
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<td>2.8/6.4</td>
<td>15.8/3.6</td>
<td>10.4/11.4</td>
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<td>13.0/5.0</td>
<td>17.0/25.0</td>
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<td>2</td>
<td>18.0/5.9</td>
<td>27.4/5.9</td>
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</table>

Only studies with at least 50 patients in each arm were included. PCI: percutaneous coronary intervention, CABG: coronary artery bypass grafting, MI: myocardial infarction, RR: repeat revascularisation, CVA: cerebrovascular accident, MACCE: major adverse cardiac and cerebrovascular events. Bold indicates difference reached statistical significance (p < 0.05).
In the Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery (SYNTAX) trial, 1800 patients with three-vessel or left main disease were randomised to undergo CABG or PCI with DES [41]. This trial was not powered for analysing data from the subgroup of patients with LMCA disease, and conclusions about long-term outcomes are currently limited by the 12-month follow-up. In both the overall study and in the group of patients with left main disease, the difference in the combined trial endpoint of death from any cause, stroke, MI or repeat revascularisation was driven primarily by increased repeat revascularisation in the PCI group. In LMCA patients, there was a similar rate of major adverse cardiac and cerebrovascular events in CABG and PCI arms (13.7% and 15.8%, respectively; \( p = 0.44 \)). Rate of revascularisation was higher in the PCI arm (11.8% vs 6.5% in the CABG group; \( p = 0.02 \)). There were significantly higher rates of stroke in the CABG subgroup with LMCA disease (2.7%, vs 0.3% in PCI; \( p = 0.01 \)); 16% of the 19 strokes in the overall CABG arm (\( n = 3 \)) occurred preoperatively.

The trial is particularly noteworthy for its ‘all-comers’ design that included more complex disease anatomy than has previously been the case in randomised trials of this nature, as well as for the detailed description of diagnostic angiograms, which were scored using the SYNTAX score algorithm. More than 80% of lesions were at bifurcations or trifurcations, over 60% were multivessel, more than 25% were in diabetics, 20% of lesions were longer than 20 mm and over 25% were totally occluded: all of which are known predictors for restenosis. Routine angiographic assessment at 12 months was not part of the study protocol and, as in other studies of this nature, it is not completely clear how much of the higher rate of repeat angiography in the PCI arm (151 patients compared with 56 patients in the CABG group) was driven by clinicians’ individual bias towards repeat angiography in post-PCI patients rather than clinical presentation. It is also difficult to quantify the impact of the differences in the percentages of patients on aspirin, statins, beta-blockers and angiotensin-converting enzyme (ACE) inhibitors between the PCI and CABG arms at discharge, 6 and 12 months after randomisation, all of which were significantly lower in the CABG arm.

Further randomised controlled trials comparing CABG and PCI are under way. In the Bypass Surgery Versus Angioplasty Using Sirolimus-Eluting Stent in Patients With Left Main Coronary Artery Disease (PRECOMBAT) trial, Park et al. will compare CABG to PCI with SES in patients with LMCA disease looking at the primary outcome of major cardiac and cerebrovascular event (MACCE): the composite of death, MI, stroke and ischaemia-driven target-vessel revascularisation after 12 months.

Given the available data, who should undergo PCI of left main stem disease? Symptomatic patients with relative contraindications to surgery such as major co-morbidity or debilitation, or a strong personal preference for a percutaneous approach may benefit from PCI, particularly if they do not possess risk factors for procedural mortality, which include emergency presentation and reduced ejection fraction. A high SYNTAX score and ostial disease, short left main stems, bifurcation and calcific disease are predictive of adverse clinical outcomes after PCI, which should be probably be avoided in such patients.

6. Surgery

6.1. Prioritisation of patients

The incidence of sudden death in patients with critical LMCA disease means that these patients are accorded priority on surgical waiting lists. The presence of significant LMCA disease in the setting of acute MI or life-threatening ventricular arrhythmias is an indication for emergency CABG [23]. Maziak et al. looked at waiting-list mortality in 281 patients with critical LMCA disease who waited an average of 38 days (range 0—84) [42]. Patients were triaged to a waiting list on the basis of urgency of symptoms and anatomy, giving priority to the symptomatic state of the patient over the patient’s coronary anatomy. They divided patients into an early group who underwent revascularisation within 10 days of angiography, and a late group that underwent revascularisation after 10 days. The early group was more likely to have NYHA class IV symptoms, unstable angina or recent preoperative MI, but postoperative mortality and morbidity did not differ significantly between groups. Analysis of the impact of other significant coronary artery stenoses was limited to that of concomitant right coronary artery stenosis, which did not influence time to revascularisation. The authors concluded that carefully selected patients with significant LMCA stenosis, and without unstable angina or recent MI, can safely wait for up to 5 weeks for elective surgery with a low risk of complications.

6.2. Myocardial protection

The optimum strategy for myocardial protection in severe LMCA disease remains unclear. Advanced coronary disease results in an uneven distribution of cardioplegia, slow diastolic arrest and delayed functional recovery. Studies have shown that although retrograde cardioplegia results in better distribution, myocardial cooling and more complete functional recovery of myocardium distal to coronary artery stenoses, the presence of veno-venous shunts and thebesian channels means that distribution of retrograde cardioplegia may not effectively protect the right ventricle and posterior septum [43]. A combined approach where diastolic arrest is achieved with antegrade blood cardioplegia and maintained with continuous retrograde blood cardioplegia has been shown to result in reduced postoperative serum troponin I levels and rates of atrial fibrillation, compared with approaches using solely antegrade cardioplegia in patients with significant LMCA disease [44].

6.3. Off-pump surgery

The presence of critical left LMCA disease was, until recently, considered a relative contraindication to the use of off-pump techniques. However, haemodynamic disturbances during displacement of the heart have been minimised, thanks to improvements in stabiliser technology, use of intracoronary shunts and greater surgical and, perhaps most importantly, anaesthetic experience. A meta-analysis of nine studies comparing outcomes of on- and off-pump surgery in patients with severe LMCA disease in 4411 patients showed a statistically significant reduction in the rates of post-
operative stroke in the off-pump groups than in on-pump groups [45]. Despite greater preoperative co-morbidity, including a higher incidence of poor left ventricular function in the off-pump groups than in the on-pump groups, these studies consistently showed equivalent or improved outcomes in patients treated with off-pump surgery. Perioperative mortality ranged from 0.0% to 1.9% in the off-pump group compared with 2.2% to 6% with conventional CABG. Although in three of these studies off-pump patients received significantly fewer grafts, it is difficult to assess whether this was due to clinical or technical reasons as none of the studies was randomised.

6.4. Choice of conduit

The left internal mammary artery is the conduit of choice for revascularisation of the left anterior descending distal to an LMCA lesion, as it affords superior short- and long-term patency and clinical outcomes to alternative conduits. Although arterial conduits such as the radial artery have been shown to offer superior long-term patency to saphenous vein grafts, the risk of arterial graft spasm in the immediate postoperative period has discouraged some surgeons from total arterial revascularisation of LMCA lesions. Few studies have addressed this question directly. Tatoulis et al. who analysed 8420 patients, including 849 with significant LMCA disease, did not report adverse sequelae attributable to graft spasm in patients with LMCA disease who underwent total arterial grafting [46]. This may reflect more appropriate use of adjuncts including topical application of papaverine, a no-touch handling technique, avoidance of electrocautery for internal thoracic artery harvest, postoperative calcium channel blockers and avoidance of potent vasoconstrictors in the immediate postoperative period.

6.5. Surgical angioplasty

Surgical repair of the LMCA, or angioplasty, is not a commonly employed surgical technique: there are less than 150 cases described in the medical literature, the largest series containing 47 patients [47]. LMCA lesions treated by surgical angioplasty include occlusive disease due to atherosclerosis, radiotherapy, post-surgical and aneurysmal disease and acute Stanford type A dissection extending into the LMCA. Autologous pericardium, saphenous vein or internal thoracic artery patches have all been used to reconstruct the LMCA, which may be approached anteriorly via the pulmonary trunk or posteriorly. Theoretical advantages of surgical angioplasty over CABG include restitution of normal blood flow through the LMCA providing antegrade perfusion to the entire coronary vasculature, avoiding competitive flow, saving conduits in young patients for future use and ensuring the left main stem remains patent facilitating later PCI [47]. Complications reported include a rate of early technical failure of close to 10%, mid-term failure of about 5% and patency rates at 7 months of 87% [47]. An effective left internal mammary to left anterior descending coronary artery bypass reproducibly provides excellent long-term outcomes and, as most surgeons have more experience with bypass grafting, this approach is widely favoured over surgical angioplasty of the LMCA for isolated left main stem disease. Improvements in surgical technique mean left main angioplasty may provide reasonable results in patients with isolated, non-calcified lesions, confined to the proximal half of the coronary trunk.

6.6. Adjuncts to surgery

In the Beauford et al. retrospective review of 654 patients with significant LMCA stenosis undergoing CABG, 11% of patients undergoing on-pump surgery required perioperative intra-aortic balloon counterpulsation, compared with only 1% of off-pump cases [48]. In off-pump cases, coronary shunts were occasionally used for grafting large dominant right coronary systems. Postoperatively, a strategy of aggressive lipid lowering has been shown to result in significantly less progression of obstructive lesions in LMCA disease, as well as in saphenous vein grafts, than conventional dosing [49]. Warfarin had no effect on LMCA disease progression in this study.

6.7. Results of surgery

Significant LMCA stenosis is a consistent predictor of morbidity and mortality after CABG. Low cardiac output states are significantly more common post-CABG in patients with significant LMCA disease [50]. The Society of Thoracic Surgeons database shows a relative risk of perioperative mortality of 1.3 for patients with significant LMCA stenosis, compared with patients without LMCA disease [51]. At 5 years post-CABG, the mortality in patients with three-vessel disease is 10.7%, compared with 15.8% in patients with LMCA disease.

Risk factors associated with increased operative mortality post-CABG for severe LMCA disease are slightly different than those identified for CABG for all atherosclerotic disease [52]. In addition to female sex, older age and left ventricular impairment, studies have identified additional specific risk factors for operative mortality in CABG for LMS, including Canadian Cardiovascular Society anginal scores III—IV, duration of anginal symptoms, left dominant coronary artery anatomy, increased duration of cardiopulmonary bypass time, fewer grafts [52], significant right coronary artery stenosis and absence of collaterals [53].

7. Conclusion

LMCA disease is an important independent risk factor for increased mortality and morbidity at all stages of diagnosis and treatment of coronary artery disease. Although there have been advances in the percutaneous treatment of LMCA stenosis resulting in indications for PCI in clearly defined patient groups with LMCA disease, CABG confers a significant event-free survival benefit over percutaneous and medical treatment in high- and low-risk patient subsets, that persists over 15 years postoperatively. Off-pump surgery offers equivalent outcomes to on-pump surgery in patients undergoing CABG for LMCA disease. Despite advances in the diagnosis and management of these patients, LMCA disease remains a poor prognostic factor.


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**Editorial comment**

Is there enough evidence that proves clinical equipoise between stenting and coronary surgery for patients with left main coronary artery disease?

**Keywords:** Coronary artery disease; Angioplasty; Coronary artery bypass surgery

1. **Introduction**

The current issue of the *European Journal of Cardio-thoracic Surgery* publishes a review article on the current diagnosis and management of left main coronary disease [1]. The main stem of the coronary tree is of vital importance to supply blood to the myocardium. Obstructive left main disease is best treated with coronary artery