INTRODUCTION

Left main (LM) coronary artery disease is defined as significant if the stenosis diameter is ≥ 50% on angiography [1]. Advances in angioplasty technique, stent design and adjunctive pharmacology have led to the use of percutaneous coronary intervention (PCI) as an alternative to coronary artery bypass graft (CABG) surgery in this high-risk group.

While there are no randomized comparisons of medical treatment versus CABG, observational studies have shown a clear-cut survival benefit for myocardial revascularization.

The functional SYNTAX score was developed to guide the need for stenting when multiple lesions are present and counts only the ischemia-producing lesions (Fractional flow Reserve (FFR) ≤ 0.80). It has resulted in reclassification of high-risk patients to lower-risk categories, and more accurately assesses risk in multivessel disease [2]. The prognostic value of calculating the SYNTAX revascularization index and functional SS in conjunction with FFR-guided PCI has shown equivalent outcomes with 'functionally' complete, rather than angiographically complete revascularization [3]. There are certain considerations regarding FFR measurement in LM lesions. In patients with prior infarction and scarring in the territory of the left coronary artery, the FFR measurement may be higher. Conversely, the FFR values may be lower in patients with severely diseased right coronary arteries with contralateral collateral flow to that vessel. In tandem lesions, in the LM and proximal LAD, FFR measurement can be overestimated and it can difficult to assess the individual contribution of the single plaques. These are situations where IVUS measurement can be particularly helpful.

Aim of the Work

Is coronary artery bypass surgery superior over percutaneous for management and treatment of patients with left main coronary artery dieases as postoperative mortality, myocardial infarction, stroke and repeated revascularization ?!

REVIEW OF LITERATURE

1. Anatomical aspects of LMCA

The LMCA emerges from the aorta within the sinus of Valsalva through the ostia of the left aortic cusp. It passes between the pulmonary trunk and the left atrial appendage and just under the appendage; the artery divides into the left anterior descending (LAD) and the left circumflex coronary arteries (LCx). In one third of the patients, LMCA bifurcates into LAD, LCx and ramus intermedius branches [(4)]. The LMCA is responsible for supplying about 75% of the left ventricular (LV) cardiac mass in patients with right dominant type and 100% in the case of left dominant type, and as a result, severe LMCA disease will significantly reduce blood flow to a large portion of the myocardium and place the patient at high risk for life-threatening events, such as LV dysfunction and arrhythmias [(5)].

Significant LMCA disease is defined as greater than 50% angiographic narrowing of the artery and was shown to be present in about 4–6% of all patients who underwent coronary angiography [(6)]. Besides, patients with unprotected LMCA (ULMCA) disease treated medically have a 3-year mortality rate of about 50% [(7)].

The LMCA is anatomically divided into three portions: origin of LMCA from the aorta (ostium), mid portion and the distal portion.

The LMCA is different from the other coronary arteries because it has relatively greater elastic tissue content; this feature explains the elastic recoil and its high restenosis rate, following balloon angioplasty procedures [8]. Since one-third of patients have trifurcated LMCA, this anatomical feature is important because in distal LMCA stenosis, PCI is much more difficult in trifurcated lesions than the bifurcated ones [9]. In 1% of the population, the LMCA is absent, and the LAD and LCx arteries originate directly from the aorta via separate ostia.

As with other coronary artery disease, the most common cause of LMCA disease is atherosclerosis. Non-atherosclerotic causes of LMCA lesions are rare. Other reasons may be either obstructive or nonobstructive [10]. Since it is originated directly from the aorta, any disease affecting the ascending aorta can also cause LMCA obstruction such as aortic dissection, external compression resulting from aortic aneurysm or tumor, iatrogenic injury resulting from coronary interventions or vasospasm, irradiation, syphilitic aortitis, Takayasu's arteritis, rheumatoid arthritis, aortic valve disease including malposition of prosthesis, aneurismal dilatations such as Kawasaki disease and atherosclerotic aneurysms [10].

There is a relationship between the length of LMCA and the LMCA segment that is diseased. In short LMCAs (<10 mm), the stenosis is more frequently localized at the ostium and then at the distal bifurcation (55 vs. 38%), in contrast to long LMCA that develops stenosis more frequently near the distal bifurcation compared to near the ostium (77 vs. 18%). The mid segment of LMS is rarely affected (5–7% of patients). Ostial LMCA stenoses are more common in women (44 vs. 20%) [11].

3. Diagnosis of LMCA disease

Most patients with LMCA disease are symptomatic. Since occlusion of this vessel compromises about 75% of blood flow to the LV, patients are at high risk of major cardiovascular events unless protected by a collateral flow. The diagnosis of LMCA disease is usually made by coronary angiography [12]. The use of noninvasive imaging studies does not specifically distinguish LMCA from other types of coronary artery disease. Certain findings on exercise testing or, in patients with acute coronary syndromes on the electrocardiogram (ECG), are suggestive of LMCA disease. These include diffuse and severe ST-segment deviation or significant ventricular arrhythmias on ECG monitoring or hypotension during exercise [13].

Coronary angiography remains the gold standard diagnostic technique for the diagnosis of clinically important LMCA disease, although small but significant number of false-positive and false-negative results is present with inter-observer variabilities. In order to avoid precipitating myocardial ischemia 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; the 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 (11). Coronary angiographic views of some patients with diagnosis of LMCA disease is shown in **Figure 1**.

In some cases, additional studies including intravascular ultrasound imaging (IVUS), fractional flow reserve (FFR) and coronary vasodilatory reserve (CVR) may be helpful for increasing diagnostic accuracy and decision-making.

IVUS is an intracoronary imaging modality that facilitates the anatomic visualization of the vessel lumen and characterizes plaques. It provides a 360° sagittal scan of the vessel from the lumen through the media to the vessel wall. It provides additional information such as minimal and maximal diameters, cross-sectional area and plaque area compared with coronary angiography alone (14). IVUS detects calcification twice as often as angiography and is more sensitive at detecting significant LMCA stenosis than angiography alone. 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 [15]. Since IVUS is an effective method to examine the coronary architecture and extent of atherosclerotic plaque with changes in vessel dimensions, it should be considered in angiographically borderline lesions as a complimentary method [16].

FFR is the ratio of distal coronary pressure to aortic pressure measured during maximal hyperemia which represents fraction of normal blood flow through a stenotic artery. The normal FFR for all vessels under all hemodynamic conditions, regardless of the status of the microcirculation, is 1.0. FFR values <0.75 are associated with abnormal stress tests. FFR may have a role in deciding whether patients with angiographically mild or moderate LMCA disease should undergo revascularization: 56% of patients with FFR <0.75 in one study had significant LMCA stenoses [17].

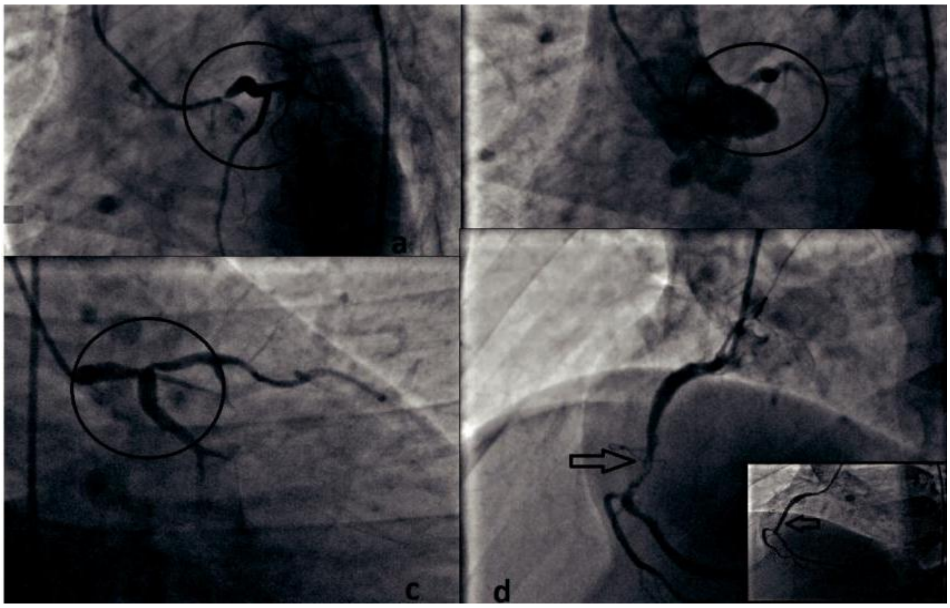

Figure (1): (a–b) Proximal LMCA stenosis at the level of aorto-ostial junction (in circles). (c–d) Acute MI patient withdistal LMCA stenosis at the level of bifurcation and proximal part of LAD (in circle) and thrombosis of the RCA (arrow). (e) After thrombolytic infusion and balloon angioplasty flow in RCA is restored, patient is operated in elective conditions for left main disease [18].

A LM pattern on exercise nuclear testing is characterized by perfusion defects in the LAD and LCx territories (i.e., reduced nuclear tracer uptake in the septal, anterior and lateral walls) [19]. It may also be associated with a picture of “balanced” ischemia where there is uniform diminution of tracer uptake with stress, often indicative of LM with three-vessel disease. This may be accompanied by transient ischemic dilation (TID), which is considered present when the image of the left ventricular cavity appears to be significantly greater after stress as compared with that at rest [20].

More recently, cardiac CT and MRI have been shown to have a high correlation with angiography for the diagnosis of LM disease. This may be particularly useful in surveillance imaging after revascularization of the LM often performed after stenting [(19)]. Multislice computed tomography (MSCT), also called multidetector coronary angiography, has rapidly gained in popularity and applicability. MSCT has a good diagnostic accuracy for detecting more than 50% luminal stenosis with a sensitivity of 97% (CI: 94–98%) and specificity of 86% (CI: 78–90%) compared with quantitative conventional coronary angiography [(21), (22)].

Cardiovascular magnetic resonance imaging (CMRI) has some advantages and limitations compared with cardiac CT imaging. Advantages of CMRI include the absence of ionizing radiation and contrast media, as well as no requirement for heart rate control with b-blockers Detection of coronary lesions in heavily calcified coronary segments by CMRI can be more reliable than by cardiac CT [(23)].

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. The AHA guidelines recommend screening all patients undergoing bypass surgery for left main stem disease to identify carotid artery disease [(24)].

4. Preventive and medical therapies

There are three options for treating LMCA disease: optimal medical therapy, PCI, or surgical revascularization (CABG) [25]. All patients with LMCA disease should receive preventive therapies to decrease the risk of subsequent cardiovascular events. Preventive therapies include smoking cessation, exercise, lipid lowering therapy with stains, management of diabetes mellitus with proper oral antidiabetics or insulin and achievement of target blood pressure goals with suitable antihypertensive medications [18]. In the 1970s and 1980s, three randomized controlled trials (the Veterans Affairs Cooperative Study [26], European Coronary Surgery Study [27], and CASS (Coronary Artery Surgery Study) [5] established the survival benefit of CABG compared with contemporaneous medical therapy without revascularization in certain subjects with stable angina. They reported a survival rate of 80–88% for CABG and 63–68% for medical treatment only. Subsequently, a 1994 meta-analysis of 7 studies that randomized a total of 2649 patient to medical therapy for CABG showed that CABG offered a survival advantage over medical therapy for patients with LMCA disease or three-vessel coronary artery disease (CAD) [28]. The studies also established that CABG is more effective than medical therapy at relieving anginal symptoms.

5. Treatment of significant LMCA disease

As stated above, CABG offers a survival advantage over medical therapy for significant LMCA disease since medical therapy alone has been associated with poor outcomes. CABG surgery has been accepted as the standard revascularization method for LMCA disease for several decades. Recently, several randomized controlled trials and meta-analyses have shown favorable results for PCI with drug-eluting stents (DES) compared with CABG [29], [30]. In this part of the review, scoring systems for decision making and treatment strategies for LMCA disease will be discussed, mainly focusing on the surgical treatment of LMCA disease.

Compared with the early days, contemporary bypass surgery has been greatly refined. Cardio-preservation techniques have improved and nearly all patients with LMCA disease receive an internal mammary artery (IMA) graft. In addition, patients undergoing surgery are more aggressively treated medically. The outcomes are excellent. When comparing the results of CABG with PCI, the coronary stents must perform at least as well as surgery in terms of outcomes [31].

A percutaneous approach for revascularization in LMCA disease has both attractive and undesirable features. Surgery needs a long recovery period with significant potential morbidities including postsurgical atrial fibrillation, pleural effusions, infections, delayed wound healing, anemia and depression which have negative effects on patient's quality of life [12]. A percutaneous approach is clearly more palatable to patients than surgery. For the physician, LM stem is large and easily accessible for PCI techniques. However, especially for the patients with absent collateral vasculature, balloon inflation may lead to cardiovascular collapse with ischemia. Abrupt vessel closure or subsequent stent thrombosis involving the LM stem may be a fatal event. All of these factors must be taken into account and their effect clearly understood when comparing the two revascularization methods [31].

6. Scoring systems for decision-making in LMCA disease

The assessment of patients with LMCA disease both as a candidate for surgery or PCI is often a complex procedure and best achieved by the "Heart Team" approach. When one method of revascularization is preferred over the other for improved survival, this consideration takes precedence over improved symptoms. ACCF/AHA guideline suggests that a Heart Team approach to revascularization is recommended in patients with unprotected LM or complex CAD (Class I recommendation, Level of evidence; C) [24].

Several risk stratification scores, based on either angiographic or clinical parameters, have been developed to evaluate outcomes in patients with LMCA disease who undergo bypass surgery. Despite the use of various objective scoring systems derived from hundreds of thousands of patients, an experienced surgeon who spends time evaluating the coronary angiogram, taking a detailed history and examining the patient may provide the most accurate assessment of operative risk [31].

The Synergy between PCI with TAXUS and Cardiac Surgery (SYNTAX) score includes factors of coronary angiographic complexity rather than clinical factors. Although the limitations of using the SYNTAX score for certain revascularization recommendations are recognized, the SYNTAX score is a reasonable surrogate for the extent of CAD and its complexity and serves as important information that should be considered when making revascularization decisions. Recommendations that refer to SYNTAX scores use them as surrogates for the extent and complexity of CAD [24].

ACCF/AHA guideline suggests that calculation of the SYNTAX and STS (The Society of Thoracic Surgeons) scores is reasonable in patients with unprotected LM and complex CAD (Class IIa recommendation, level of evidence; B). Variables which contribute to the determination of the score include dominance of the coronary artery system, number of lesions, segment involved per lesions and presence of chronic total occlusions, trifurcation, bifurcation, aorto-ostial lesions, tortuosity, calcification, thrombi, long lesions and/or diffuse disease. By the highlights of these variables, a separate number is calculated for each lesion. Then, these values are summed up to generate the total SYNTAX score. An online tool for easy calculation of the score may be found online at

http://www.syntaxscore.com. Some of the steps illustrating the scoring are shown in Figure 2.

SYNTAX trial is the largest, single published study to date, comparing the outcome of PCI vs. CABG in patients with 3-vessel coronary disease and LMCA disease [(32)]. The higher the score, the greater is the extent and the complexity of the disease. The SYNTAX trial stratified the entire randomized population (i.e., both patients with 3-vessel and patients with left main coronary artery disease) by tercile of SYNTAX score and found that the patients in the lowest tercile (score:0–22) fared just as well with PCI as surgery, whereas those in the highest tercile (score ≥ 33) clearly did better with surgery [(33)]. Capodanno et al. applied the SYNTAX score to a registry of 819 patients undergoing LM PCI or surgery and found that the outcomes of patients with SYNTAX score ≥ 34 was better with surgery as compared with PCI but patients with SYNTAX score < 34 had similar outcomes with surgery or PCI in terms of 2-year mortality rates [(34)]. They concluded that a SYNTAX score threshold of 34 may usefully identify a cohort of patients with LMCA disease who benefit most from surgical revascularization in terms of mortality.

The SYNTAX study included a subset of 705 patients with LM stem disease and their 5-year outcomes have been published [(35),(36)]. For the overall group with LMCA disease, there was no significant difference in the rate of major adverse cardiac and cardiovascular events (MACCE), MI, or death at 5