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Ischemic heart disease with damage of the left main coronary artery

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Abstract: It is known and proven that the degree of damage to the left main coronary artery (LMCA), along with the indicators of the left ventricle (LV) myocardium's contractile function, are the main factors determining the survival of patients with coronary artery disease (CAD). Therefore, the effectiveness of the chosen management strategy for such patients determines not only the quality of life, i.e relief from angina symptoms, but also long-term prognosis [1,2].

Keywords: Contractile function, survival of patients.

Introduction: It is known and proven that the degree of damage to the left main coronary artery (LMCA), along with the indicators of the left ventricle (LV) myocardium's contractile function, are the main factors determining the survival of patients with coronary artery disease (CAD). Therefore, the effectiveness of the chosen management strategy for such patients determines not only the quality of life, i.e relief from angina symptoms, but also long-term prognosis [1,2].

More than 100 years have passed since the first description by American physician J. Negis of the case of a death of a 55-year-old patient with large anterior myocardial infarction (MI), complicated by cardiogenic shock, the cause of which, according to the occlusion of the left main coronary artery (LMCA) [2,3]. It was only 50 years ago that the issue of treating such patients became the subject of intense research attention [4]. However, this issue still remains a topic of discussion and debate. One of the most debated questions is the choice of treatment strategy for patients with hemodynamically significant left main coronary artery

(LMCA) disease.

The left main coronary artery (LMCA) is the proximal segment of the left coronary artery, starting from the left sinus Valsalva and extending to the bifurcation into the left anterior descending (LAD) and circumflex (Cx) coronary arteries [5]. This type of bifurcation is found in two-thirds of cases, while in about one-third of patients, the trunk ends in trifurcation, with the third branch referred to as the intermediate branch. Cases of more than three branches are extremely rare. There are also reports of complete absence of the LMCA trunk, where the LAD and Cx arise from separate orifices. This variant occurs in less than 1% of patients [6,7].

In the right coronary circulation type, approximately 75% of the blood supplying the myocardium passes through the LMCA, while in the left type, nearly 100% does. Due to this, patients with hemodynamically significant LMCA disease have a high risk of mortality [2,5].

Anatomically, the left main coronary artery (LMCA) is divided into the ostium, the middle portion, and the distal segment. The average diameter of a healthy LMCA, as measured by angiography, is $4,5 \pm 0,5$ mm in men and $3,9 \pm 0,4$ mm in women [8]. However, there have been reports of autopsy findings where the diameter of the LMCA in individuals with healthy hearts reached 10 mm. The length of the LMCA trunk is highly variable. In one study analyzing 106 hearts based on autopsy data, the length of the LMCA ranged from 2 to 44 mm. A short LMCA is notably associated with the presence of a bicuspid aortic valve [9,10]. However, most studies indicate a weak correlation between the size of the LMCA and the patient's anthropometric data [11]. The LMCA, compared to other coronary arteries, contains a large number of elastic smooth muscle fibers, which contributes to rapid re-narrowing of the vessel (recall - effect) and makes isolated balloon angioplasty without stenting ineffective, due to the development of the "elastic recoil" phenomenon [12].

European and American experts are unanimous in their opinion that a hemodynamically significant stenosis is a narrowing of the LMCA greater than 50% [1]. It is well known that atherosclerotic plaques tend to form in specific areas of the coronary network, characterized by low levels of vascular wall shear stress [13]. In the most cases, the plaque in the trunk is located in the distal segment, with further involvement of the middle portion and the ostium. In the bifurcation area, atherosclerotic lesions typically begin on the lateral walls, where the shear stress of the vascular wall is lower than at the point where the blood flow splits into

the LAD and Cx. The arterial wall at the blood flow division point is usually unaffected. This patterns of lesion distribution is found in 80% of patients with stenosis of the trunk [2,11].

Lesions of the LMCA, as assessed by coronary angiography (CAG), occur in 4-8% of patients with coronary artery disease (CAD) [14–16]. In one of the first large registries, the CASS (Coronary Artery Surgery Study), which included 24,958 patients with angiographic evaluations conducted at 14 centers in the United States and Canada between 1974 and 1979, due to the presence of or suspicion of CAD, LMCA lesions with stenosis of 50% or more were found in 1,484 (5,9%) patients [17]. Isolated LMCA lesions are more the exception than the rule. Most patients with LMCA disease have multi-vessel involvement. According to various registries and studies, the incidence of isolated LMCA lesions ranges from 1,5% to 13% [18–20]. The results of the CASS registry show that isolated LMCA lesions were identified in 7% of patients, combined with one additional artery lesion in 13%, two in 27%, and three in 52%. Total occlusion of the LMCA, as assessed by CAG, is rare, occurring in 0,01-0,7% of cases [21, 22].

When assessing the severity of coronary artery disease using the SYNTAX score, LMCA lesions are considered the most prognostically dangerous, increasing the score by 5 to 6 points, depending on the type of myocardial perfusion [23].

The portrait of patient with LMCA stenosis was first described by R. Favaloro: severe disease symptoms, including low exercise tolerance, high functional class (FC) of angina and heart failure, and the development of life – threatening arrhythmias [24]. On the electrocardiogram (ECG), recorded during a stress-induced angina episode, deep depression of the ST segment is seen in the leads corresponding to the anterior wall of the left ventricle, as well as a prolonged recovery period after the termination of physical load [25].

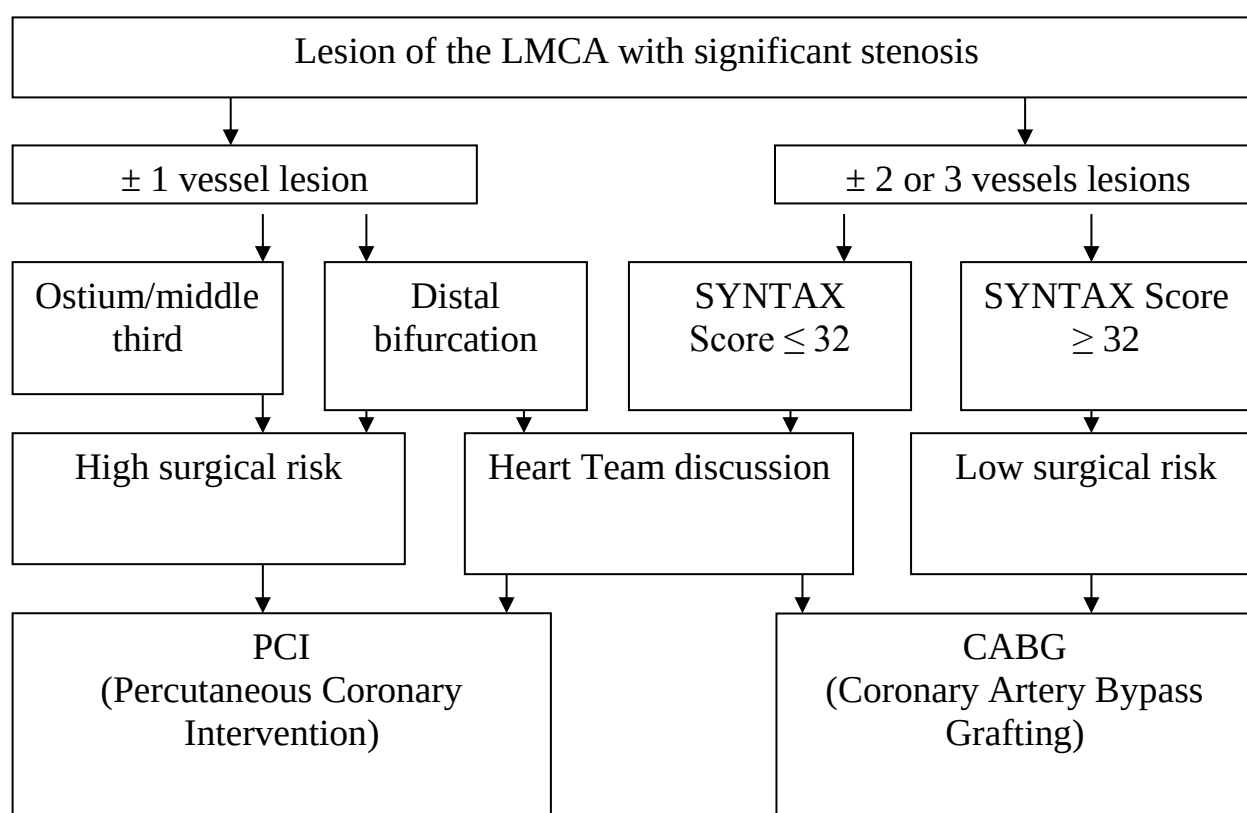
A LMCA stenosis of more than 50% places patients in a high-risk category for sudden death. Sudden death occurs 3-4 times more frequently in patients with LMCA stenosis compared to those with coronary artery lesions in other locations [25].

M.S. Gotsman referred to the LMCA as the "artery of sudden death" [26]. Consequently, several authors equate patients with LMCA stenosis to those with acute coronary syndrome, regardless of the severity of their clinical condition [27].

In later studies, a detailed description of the clinical and functional characteristics of patients with LMCA stenosis was provided. Monitoring of 6,436 patients with coronary artery disease (CAD) allowed D.B. Pryor

and colleagues [28] to identify 11 key predictors of “three vessel coronary artery disease or LMCA stenosis. These characteristics included the typicality of clinical manifestations of myocardial ischemia (angina), patient age and gender, disease duration, and the presence of cardiovascular risk factors such as hypertension, diabetes, dyslipidemia, and smoking. Another distinctive feature for this group of patients is the presence of multifocal atherosclerosis (MFA). In patients without carotid stenosis, LMCA stenosis is detected in 5% of cases, while in patients with MFA (those with carotid artery involvement), it occurs in

40% of cases [29]. The presence of high functional class (FC) angina and signs of impaired myocardial contractility determines the need for invasive coronary angiography (CAG) as a first diagnostic step. Subsequently the strategy for intervention should be determined and the correct method must be chosen. For patients with LMCA stenosis, the decision-making algorithm, according to the latest European guidelines for the management of stable angina, requires discussion by a team of cardiologists and cardiac surgeons – “Heart Team” – to determine the most effective and safe revascularization strategy.



The role of the cardiologist in this discussion cannot be overestimated! The choice of revascularization method is based on the degree of coronary artery involvement, the assessment of disease severity and the presence of comorbidities, which are crucial factors when dealing with patients with left main coronary artery (LMCA) disease [30,31].

Coronary artery bypass grafting (CABG) is considered the “gold standard” in the treatment of unprotected LMCA disease. The technique of CABG has been well-established and proven in the treatment of coronary artery disease (CAD) since the 1970s. In a review by D. Taggart et al., published in 2008 y., the in-hospital mortality rate after CABG for LMCA disease was

reported to be 2-3%, with a 5 – year mortality rate of 5-6% [32].

According to the guidelines of the American Heart Association (AHA) and the American College of Cardiology (ACC), coronary artery bypass grafting (CABG) is recommended for left main coronary artery (LMCA) stenosis more than 50% in patients with stable angina or silent myocardial ischemia. In a study W. Rogers, the 4-year survival rate for patients with hemodynamically significant LMCA disease on medical therapy was 63%, while for those who underwent CABG, was 88% [33].

According to A. Dacosta, the 30- month survival rate for patients with hemodynamically significant LMCA

disease on medical therapy was 64%, compared to 80% for those who underwent CABG [34].

E. Caracciolo et al. reported data on 1484 patients with hemodynamically significant LMCA stenosis. One group of patients received only medical therapy, while the other group underwent CABG. The average survival in the first group was 6,6 years, while in the second group it was 13,3 years [35].

The assessment of the complexity of atherosclerotic coronary artery disease (CAD) has long been one of the primary concerns of non-interventional cardiologists, not only for predicting potential peri-procedural complications during percutaneous coronary interventions (PCI), but also for determining the risk-benefit of various myocardial revascularization methods. Several randomized clinical trials (RCTs) and registries have shown that in patients with left main coronary artery (LCA) stenosis and/or multi-vessel coronary artery disease (CAD), myocardial revascularization with coronary artery bypass grafting (CABG) is preferable and more effective [36–39]. One of the largest RCTs comparing two myocardial revascularization strategies, CABG and PCI, in patients with multi-vessel atherosclerotic CAD with a SYNTAX Score of 33 or higher, is the SYNTAX trial [40,41].

The SYNTAX score holds a central position in the ESC/EACTS 2014 guidelines, with a class I level of evidence, and serves as a long-term predictor of serious adverse cardiovascular and cerebrovascular events in patients following PCI.

The SYNTAX Score is divided into three tiers: low-risk PCI– 0–22, intermediate-risk– 23–32, and high-risk greater than 33). Higher scores indicate greater complexity in performing PCI and represent the greatest risk for patients undergoing PCI, with a worse prognosis for revascularization compared to CABG. Intermediate SYNTAX scores allow for a choice between PCI and CABG, while lower scores favor PCI.

The 5-year follow-up results of this RCT demonstrated that, in patients with high SYNTAX score (33 or higher), CABG was associated with lower mortality compared to PCI (14,1% vs. 20,9%, $p=0,11$) and reduced need for repeat revascularization (11,6% vs. 34,1%, $p=0,001$), however, an increased frequency of stroke was noted in the CABG group (4,9% vs. 1,6, $p=0,13$). The findings of this RCT became the cornerstone of the European myocardial revascularization guidelines of 2014 [42], which emphasize the priority of CABG for patients with left main coronary artery stenosis and/or multi-vessel CAD with a SYNTAX score of 33 or higher.

Researchers such as W.E. Boden and G.B. Mancini have shown that despite the findings of the SYNTAX trial,

many cardiologists and therapists continue to recommend PCI for patients with severe multi-vessel coronary artery disease (CAD) [43]. Aggregate data on myocardial revascularization in the USA indicate that more than half of patients who are candidates for CABG undergo endovascular interventions [44–46].

It is also important to mention a large meta-analysis published in 2016, which summarized the results of several RCTs comparing two revascularization strategies for unprotected left main coronary artery (LMCA) disease in 4594 patients (CABG vs. PCI using drug eluting stents) [47]. The analysis included the following RCTs: PRECOMBAT (Premier of Randomized Comparison of Bypass Surgery versus Angioplasty Using Sirolimus-Eluting Stent in Patients with Left Main Coronary Artery Disease) (with 60 months of follow-up) [48], SYNTAX (with 60 months of follow-up) [49], NOBLE (Coronary Artery Bypass Grafting Vs Drug Eluting Stent Percutaneous Coronary Angioplasty in the Treatment of Unprotected Left Main Stenosis) (with 60 months of follow-up) [50], EXCEL (with 36 months of follow-up) [51] and one study with 12 months of clinical follow-up [52].

The results of the meta-analysis indicate that there were no difference between PCI and CABG in terms of the overall mortality rate (OR 1,03; 95% CI 0,78–1,35; $p=0,61$), myocardial infarction (OR 1,46; 95% CI 0,88–2,45; $p=0,08$) and stroke (OR 0,88; 95% CI 0,39–1,97; $p=0,53$). However, PCI was associated with a higher frequency of repeat revascularization (OR 1,85; 95% CI 1,53–2,23; $p<0,001$). It is important to note that only the SYNTAX trial, among other RCTs, included patients with severe coronary artery disease (CAD) defined by a SYNTAX Score of 33 or higher. In all other RCTs comparing the two revascularization strategies, either patients with a SYNTAX Score below 32 were included, or the group with a SYNTAX Score of 33 or more was small. This fact is more likely to have contributed to the absence of differences in cardiac mortality and the development of myocardial infarction between the study groups in the meta-analysis mentioned above. The study by Y. Cho and colleagues in 2016 published 10-year follow-up data on patients after CABG with varying severity of CAD based on the SYNTAX Score [53].

This study demonstrated that the increased incidence of “major” adverse cardiovascular and cerebrovascular events correlates with higher SYNTAX Score (log-rank $p=0,0012$) and is associated with a significant increase in the frequency of repeat revascularization in patients with a high SYNTAX Score (log-rank $p=0,0032$). The cumulative rate of repeat revascularization over 10 years in patients with low, moderate, and high SYNTAX Score was 4,6, 15,7 and 16,8% respectively (log-rank $p=0,0032$); The composite endpoint (all-cause mortality,

stroke, myocardial infarction) over 10 years showed no statistically significant differences between the three groups – 22,3, 25,0 and 38,4% respectively (log-rank $p=0,063$).

Currently, according to the latest recommendations on myocardial revascularization, PCI is not indicated for patients with stable CAD and left main coronary artery (LMCA) stenosis and/or multivessel coronary artery disease (SYNTAX Score of 33 or higher). However, in patients with high surgical risk, some researchers consider endovascular interventions to be justified.

In 2016, I. Sanchez-Perez et al. published 10-year follow-up data on patients with left main coronary artery (LMCA) stenosis and high SYNTAX Score, who underwent myocardial revascularization with PCI [54]. The incidence of “major” adverse cardiac events over the 10-year follow-up period was 16,1% (10,3% cardiac death, 0,9% nonfatal myocardial infarction, 4,9% repeat revascularization and 0% stent thrombosis). The authors of this study conclude that revascularization of the left main coronary artery with a high SYNTAX Score using PCI is an effective and safe procedure. The success of endovascular treatment for patients with CAD and complex coronary lesions can be attributed to the evolution of stents and the emergence of a new class of antithrombotic drugs, which have played a revolutionary role in reducing stent thrombosis and restenosis.

Currently, the number of endovascular interventions in patients with CAD significantly exceeds the number of open-heart surgeries. Undoubtedly, PCI is a minimally invasive method for treating CAD, but when choosing between CABG or PCI, a careful approach must be taken for each individual patient, based on European and American guidelines for myocardial revascularization, which are derived from the results of large randomized trials and the assessment of long-term quality of life and the development of adverse cardiac and non-cardiac events. The decision of CABG, PCI or to continue with optimal medical therapy should be made by a multidisciplinary team, including cardiologists, interventional cardiologists and cardiac surgeons. This decision must be based on risk stratification, discussed collaboratively with the patient, and take into account the experience of the interventional cardiologists and cardiac surgeon involved.

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