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Single-stent strategy for left coronary artery bifurcation lesions in patients with chronic ischemic heart disease: protocol of a randomized trial

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Aim. This study aims to compare the intraoperative, immediate postoperative and long-term postoperative results of stenting followed by final kissing balloon angioplasty (FKB) and without FKB for left coronary artery (LCA) bifurcation lesions in patients with chronic ischemic heart disease.

Material and methods. We plan to perform an open-label, prospective, randomized, single-center, cohort trial that will include 40 patients with left main coronary artery bifurcation lesion, who will undergo stenting procedure followed by FKB or without FKB, using the second-generation drug-eluting stents. Randomization into two groups will be done after performing coronary angiography, confirming the inclusion criteria and the absence of non-inclusion criteria and signing a written consent in 2 copies. Group 1 — stenting followed by FKB. Group 2 — stenting without FKB. The total follow-up period is 24 weeks. It is planned to contact by phone on 30th and 180th day (±7 days) of postoperative period to obtain the information about patient condition, general survival rate, the events of combined controlled points and drug therapy. During 2nd phone contact, on 180th day (±7 days), a patient will be invited to undergo multispiral computed tomography of the coronary arteries.

The primary combined end-point: cardiac death, nonfatal myocardial infarction, acute cerebrovascular accident and the repeat target vessel revascularization.

The secondary combined end-point: thrombosis and stent restenosis.

Conclusion. Our study will optimize the approach to the choice of stenting strategy (with or without FRB) for left main coronary artery bifurcation lesions in patients with chronic ischemic heart disease.

Keywords: stenting of left main coronary artery, final kissing balloon angioplasty, true bifurcation lesion, false bifurcation lesion.

Relationships and Activities: none.

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Key messages

- The type of left main coronary artery bifurcation lesion may influence the choice of optimal single-stenting technique to treat left main coronary artery bifurcation lesions in patients with chronic ischemic heart disease.
- The stenting without final kissing balloon angioplasty may be used in false bifurcation lesion with the main coronary artery caliber Ø⩾4 mm and regardless of the angle of the lateral branch origin.

Hemodynamically significant bifurcation lesion of left main coronary artery (LMCA) in patients with chronic ischemic heart disease (IHD) is the absolute indication for surgical intervention [1]. The choice of the optimal interventional treatment method is still under discussion in professional communities [2]. It is recommended to use this or that approach to percutaneous coronary intervention (PCI) depending on the type of LMCA bifurcation lesion [3]. The single-stent strategy (provisional-stenting) is recommended in case of true or false lesion, while the double-stent approach is justified for a complex case determined according to the criteria of the DEFINITION II research [4, 5]. The stenting algorithm is presented in the final 16th document of European Bifurcation Club, published in 2022, which once again raises the question of the need of the routine final kissing balloon angioplasty (FKB) in single-stent strategy [6].

The study aims to compare the immediate and long-term results of LMCA bifurcation lesion stenting followed by FKB and without FKB in patients with chronic IHD.

Material and methods

Study design. We plan to perform an open-label, prospective, randomized, single-center, cohort trial that will include 40 patients with LMCA bifurcation lesion, who will undergo stenting procedure (followed by FKB or without FKB), using the second-generation drug-eluting stents. Randomization will be done after performing coronary angiography (CA), confirming the inclusion criteria and the absence of non-inclusion criteria. Group 1 — stenting followed by FKB. Group 2 — stenting without FKB. The timing for PCI will be determined individually by a multidisciplinary team according to international relevant recommendations.

The study meets the standards of Good Clinical Practice and ethical aspects of Helsinki Declaration created by the World Medical Association, paragraph 15 of Article 37 of Federal Law № 323-FZ of November 21, 2011 "On the basics of Public Health protection in the Russian Federation". The Local Bioethics Committee has examined the objectives and plan of the study conduction and has given its positive opinion about the study. We will obtain written informed consent from all participants prior to inclusion into the study.

Criteria of inclusion. Gender (any); age ⩾18 years old; chronic IHD (stable exertional angina pectoris, painless form of ishemia) with proven myocardial ischemia according to non-invasive and/or invasive (determination of fractional flow reserve (FFR) and/or instant flow reserve (IFR)) methods of functional assessment of blood flow; presence or absence of myocardial infarction (MI) in the anamnesis; left ventricular ejection fraction >35%; "unprotected" LCA trunk — the absence of working aortocoronary shunts; the presence of true or false bifurcation lesion; technical possibility and good anatomical conditions for the PCI conduction; informed patient consent to participate in the study.

Criteria of non-inclusion. The diagnosis of acute coronary syndrome (ST-segment elevation MI, MI without ST-segment elevation, early postinfarctional angina pectoris, unstable angina pectoris); left ventricular ejection fraction ⩽35%; "protected" LCA trunk; local lesion of the ostium, proximal or middle third, not affecting the bifurcation and requiring PCI within the limits of LCA trunk; multivascular lesion in the coronary bed with SYNTAX Score >32; patients with diabetes mellitus and multivascular lesion in the coronary bed with SYNTAX Score >22; impossibility to receive double antithrombotic or double/triple antithrombotic therapy (antiplatelet + anticoagulant) in case of atrial fibrillation and/or valvular prosthesis in the anamnesis; severe chronic obstructive pulmonary disease: III-IV stage; acute heart failure II-IV (Killip); mental disorders; oncological diseases that limit life expectancy; pregnancy and lactation.

Inclusion into the study. At admission, the standard drug therapy in accordance with the clinical recommendations will be prescribed to a potential study participant, all necessary examinations will be conducted, and after confirming the non-invasive inclusion criteria and the absence of the non-inclusion criteria with suspected the left main coronary artery bifurcation lesion, a patient will undergo CA. After performing CA, in case of confirmation of the invasive inclusion criteria and the absence of the non-inclusion criteria, a patient will receive full information about the study, and he will be asked to sign the informed consent in 2 copies (one of them will be given to him). The information of each study participant will be recorded to specially designed individual registration patient cards.

Randomization. Randomization will be carried out by the envelope method in 1:1 ratio intraoperatively, after performing CA and confirming all inclusion criteria and the absence of non-inclusion criteria, into two groups, with 20 patients in each. Group 1 — stenting followed by FKB. Group 2 — stenting without FKB. The surgical approach to perform PCI will be determined by a radiosurgeon. Drug-eluting stents used in routine practice will be implanted. Predilation of the target lesion is at the discretion of an operating surgeon. Proximal optimization with noncompliant balloon is mandatory step. It is mandatory to protect the lateral branch (LB) with the second coronary conductor. If in group 1 LB is com-

	During hospital period		Observation after discharge from hospital	
	Before CA, after CA conduction	After PCI	Phone contact on 30th day	Phone contact on 180th day and face-to-face visit
Informed consent, inclusion/non-inclusion criteria	✓			
Anamnesis, clinical status	✓	✓	✓	✓
Laboratory methods	✓	✓		
ECG	✓	✓		
EchoCG	✓	✓		
MSCT				✓
Load testing	✓			✓
Drug therapy	✓	✓	✓	✓
Evaluation of intraoperative results		✓		
Evaluation of combined control points		✓	✓	✓

Figure 1. Research flowchart.

Abbreviations: CA — coronary angiography, MSCT — multispiral computed tomography, PCI — percutaneous coronary intervention, ECG — electrocardiography, EchoCG — echocardiography.

promised according to QCA (Qualitative comparative analysis) angiographic data and the results of invasive functional examination methods (FFR and IFR), it needs to pass to forced stenting with FKB. At the end of the operation, the category of angiographic result of PCI will be given, based on the designed method for determination of postoperative management tactics of patients with IHD according to classification of PCI angiographic results. Double antiplatelet therapy will be prescribed for 6 months.

Telephone contact and face-to-face visit. The total follow-up period will be 24 weeks (Figure 1). The research personnel will contact the patients on 30th and 180th (±7 days) day after the operation. The information about patient condition, general survival rate, the events of combined controlled points and drug therapy will be collected. On the 6th month after operation a patient will be invited to undergo multispiral computed tomography of the coronary arteries. If the participants inform that an event has occurred, it is recorded in special event reporting form with the source documents collected by the research personnel.

End-points. The intraoperative results and combined points will be assessed. The primary combined end-point was determined as MACEs: cardiac death, nonfatal myocardial infarction, acute cerebrovascular accident and the repeat target vessel revascularization. The secondary combined end-point: thrombosis and hemodynamically significant stent restenosis.

Statistical analysis. It is supposed to evaluate the comparable results of the two methods (non-inferiority). Statistical processing of the obtained data will be carried out using a software package Statsoft Statistica 8 (USA). Quantitative variables will be described by the number of the patients, mean ± standard deviation and the median (95% confidence interval (CI)). Qualitative variables will be presented in the form of absolute and relative (percentage) frequencies. To study the relationship between categorical variables, the Fisher exact test will be used, and the reliability of differences between quantitative indicators will be evaluated using non-parametric Mann-Whitney and Wald-Wolfowitz criterion. In all statistical analysis procedures, the achieved significance level (p) will be calculated, and the critical significance level will be assumed to be <0,05. The log-rank test will be used to compare before-event time. Freedom from events will be estimated by constructing a curve using the Kaplan-Meier method.

Current study status. Currently, patients are being recruited into the study.

Discussion

The improvement of PCI techniques and the introduction of modern drug-eluting stents allowed endovascular surgery to occupy its niche in operative treatment of LMCA bifurcation lesion along with aortocoronary shunting in patients with chronic IHD [7]. By now, the LCA trunk stenting has shown its safety and efficacy in patients without diabetes mellitus and with the SYNTAX Score value ⩽32 [8]. A number of clinical studies aimed to compare the different stenting methods have been conducted and showed that the choice of the strategy and technique in stable patients largely depends on the type of bifurcation lesion [3, 4, 6, 9]. European

Bifurcation Club as the main vector of bifurcation stenting development recommends routine use of provisional stenting which is the simplest from the technical point of view and does not limit a surgeon in implanting the second stent if necessary, in true and false lesions [4, 6]. However, the issue of application of FKB which is classic technique aimed to optimization of bifurcation stent and carina, remains relevant. Various studies dedicated to this problem were conducted, the largest of them are RAIN-CARDIOGROUP VII (n=2742) and the analysis of the study database EXEL (n=948), which show the comparable results of the two stenting methods (with FKB and without FKB) [10, 11]. Based on the world tendency, in 2022 European Bifurcation Club came to conclusion that it is not mandatory to perform FKB in case of the optimal angiographic result achieved by stent implantation into the main branch (the most hemodynamically significant branch of the bifurcation — the anterior interventricular branch or the circumflex artery in case of the bifurcation of the LCA trunk), and regardless of the angle of the LB origin [6]. It should be noted that this is primarily referring to the bifurcation lesions that do not affect the LCA trunk therefore, the issue of routine FKB in the immediate bifurcation lesion of the LCA trunk itself remains poorly studied and relevant.

In our study, we propose a hypothesis that the two single-stenting strategy methods (with FKB and without FKB) of LMCA bifurcation lesions in patients with chronic IHD will have comparable immediate and long-term results by the control points. The stenting without routine FKB which reduces the amount of the necessary consumable material and instruments, and reliably reduce the surgical operative duration according to a previously performed retrospective analysis, can be recommended in false bifurcation lesion with the LCA trunk caliber Ø⩾4 mm and regardless of the angle of the LB origin upon condition of the absence of LB compromise confirmed by QCA angiographic data and by the results of invasive functional examination methods (FFR and IFR). But FKB must remain mandatory in case of true LMCA bifurcation lesions regardless of the angle of the LB origin due to the high risk of the LB compromise development.

As you can see from the above, such a hypothesis of single-stent strategy envelopes true and false LMCA bifurcation lesions only. Other lesions in stable patients, which can be referred to the criteria of complex cases according to DEFINITION II research [5], may require the applying double-stent strategy [4] or are recommended to revascularization by aortocoronary shunting method.

Limitations of the study. The main limitations will be single-center study type and small patient sampling, and the factors of diversity in structure of cells of the stents from different manufactures will not be taken into account, that is the important predictor of possible LB compromise.

Conclusion

The planned study will optimize and systematize the approach to routine performance of FKP in single-stent strategy depending on the type of LMCA bifurcation lesion in patients with chronic IHD.

Relationships and Activities: none.

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