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Predictors of unsuccessful endovascular recanalization of coronary chronic total occlusion

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The prevalence of endovascular interventions for coronary chronic total occlusion (CTO) remains small worldwide. This is due to the complexity of procedure and the risk of intraoperative complications. In this regard, the search for predictors of unsuccessful endovascular intervention in CTO plays a special role. This will allow for a careful selection of patients with the most favorable expectation effect of the operation.

Aim. To identify predictors of unsuccessful endovascular recanalization of CTO.

Material and methods. This retrospective study included 180 patients with chronic coronary artery disease (CAD) in the period from November 2017 to June 2019, who had multivessel lesion in combination with CTO. In all patients, an attempt was made to achieve complete myocardial revascularization. Depending on the success of procedure, the patients were divided into two groups: complete and incomplete myocardial revascularization. The follow-up period was 12 months.

Results. All baseline characteristics of patients in the compared groups were similar. The successful recanalization rate of occlusion was 79,5%. Multivariate regression analysis showed that calcified CTO (p<0,001), baseline SYNTAX (Synergy between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery) score >32 (p=0,006), CTO length >30 mm (p=0,046) and CTO of circumflex artery (p<0,01) are significant predictors of unsuccessful endovascular recanalization of CTO. To assess the predictive value of the model, a ROC analysis was carried out, and the area under the curve (AUC) was calculated. The AUC was 0,87, which indicates a high predictive quality of the model. The sensitivity and specificity of the model were 78 and 81%, respectively.

Conclusion. The study showed that the presence of calcified CTO, SYNTAX score >32 points, CTO length >30 mm, and CTO of circumflex artery are significant predictors of unsuccessful CTO recanalization.

Keywords: percutaneous coronary intervention, coronary chronic total occlusion, coronary artery disease, coronary artery bypass grafting.

Relationships and Activities: none.

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Introduction

Cardiovascular diseases remain the leading cause of death both in Russia and throughout the world [1-3]. Coronary chronic total occlusion (CTO) are diagnosed in 18-52% of cases with coronary angiography (CA) in patients with coronary artery disease (CAD) [4, 5]. With CTO, there is a slow growth of atherosclerotic plaque followed by complete coronary artery obstruction. This triggers a compensatory mechanism for collateral circulation from adjacent vascular systems. The formation of collateral blood flow ensures the myocardial function. Nevertheless, the CTO is associated with adverse coronary events, despite the pronounced collateral network and the absence of myocardial scarring [6]. According to data from two randomized clinical trials, endovascular recanalization in CTO does not improve long-term clinical outcomes [7, 8]. This fact is reflected in the low grade of recommendation for percutaneous coronary interventions (PCI) in CTO [9]. Previously, several studies have shown that successful endovascular CTO recanalization reduces angina symptoms, improves left ventricular function and patient survival compared with unsuccessful CTOA recanalization [10, 11]. According to a meta-analysis by Wang N, et al. [12], the successful CTO recanalization rate is 77%. However, endovascular intervention in CTO is performed only in 4% of cases. This low level is due to the high complexity of CTO PCI and the risk of intraoperative complications.

In this regard, the search for predictors of successful and unsuccessful endovascular intervention in CTO plays a special role. This will allow risk stratification for unsuccessful PCI in CTO and careful selection of patients for intervention.

The aim was to identify predictors of unsuccessful endovascular CTO recanalization.

Material and methods

Based at the National Medical Research Center for Therapy and Preventive Medicine, a retrospective study

Table 1

Clinical and demographic parameters in the groups of complete and incomplete myocardial revascularization

Parameter	Group of complete myocardial revascularization, n=143	Group of incomplete myocardial revascularization, n=37	p-value
Age, years	63,8±8,3	63,6±8,8	0,765
Male sex, % (n)	74,8 (107)	86,5 (32)	0,186
Smoking, % (n)	18,8 (27)	18,9 (7)	0,343
Positive family history of CVD, % (n)	35 (50)	35,1 (13)	1
Angina class			
Class I, % (n)	0,7 (1)	0 (0)	
Class II, % (n)	49,6 (71)	43,2 (16)	
Class III, % (n)	49,6 (71)	56,76 (21)	0,666
HF:			
Yes, % (n)	49,6 (71)	48,6 (18)	
No, % (n)	50,3 (72)	51,3 (19)	1
NYHA HF class			
Class I, % (n)	4,2 (6)	8,1 (3)	
Class II, % (n)	27,2 (39)	32,4 (12)	
Class III, % (n)	18,2 (26)	8,1 (3)	0,257
Atrial fibrillation, % (n)	22,4 (32)	18,9 (7)	0,799
Conduction disorders, % (n)	41,4 (59)	27 (10)	0,191
Cancer, % (n)	5,1 (7)	2,7 (1)	1
COPD/asthma, % (n)	3,5 (5)	2,7 (1)	1
HTN, % (n)	100 (143)	100 (37)	
Old myocardial infarction, % (n)	76,9 (110)	75,7 (28)	0,831
Multifocal atherosclerosis (⩾2 vascular systems), % (n)	74,1 (106)	75,7 (28)	1
Diabetes, % (n)	25,9 (37)	27 (10)	1
CKD, % (n)	13 (18)	10,8 (4)	1
LVEF (%)	46,8	50,3	0,207
LV EDD (cm)	5,5±0,8	5,5±0,7	0,862
LV ESD (cm)	3,9±0,9	3,8±0,9	0,589
LV EDV (ml)	149,7±46,3	145,6±40,7	0,776
LV ESV (ml)	70,4±41,3	68,2±35,1	0,922
LV stroke volume (ml)	74±17	73,4±15,9	0,756

Note: HTN — hypertension, LV — left ventricle, EDV — end-diastolic volume, EDD — end-diastolic dimension, ESV — end-systolic volume, ESD — end–systolic dimension, CVD — cardiovascular diseases, LVEF — left ventricular ejection fraction, CKD — chronic kidney disease, COPD — chronic obstructive pulmonary disease, HF — heart failure, NYHA — New York Heart Association. The p-value was calculated using Student's t-test for continuous variables and Fisher's test for discrete variables.

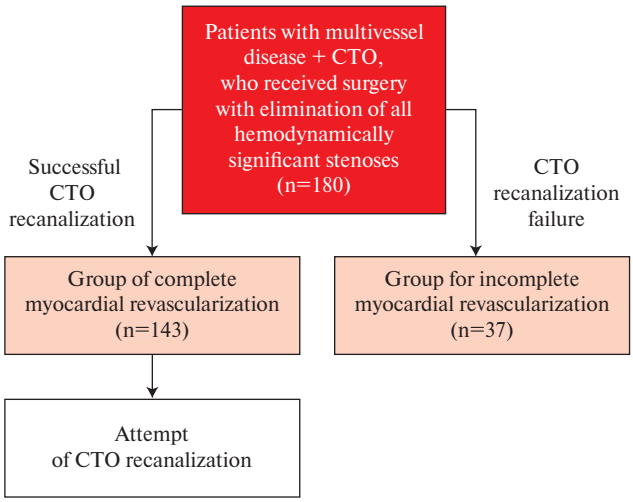

Figure 1 Study design.

was conducted, which included 180 patients in the period from November 2017 to June 2019. The study included patients with chronic CAD who, according to CA data, had multivessel coronary disease with CTO. General characteristics of patients are shown in Table 1. The mean age in the group of complete myocardial revascularization was 63,8±8,3 years, and in the group of incomplete myocardial revascularization — 63,6±8,78 years; 74% of the were male. All patients underwent endovascular treatment in combination with an attempt of CTO recanalization. Depending on the success of CTO recanalization, the patients were divided into a group of complete revascularization (n=143) and a group of incomplete revascularization (n=37) (Figure 1). CTO was defined as the absence of any antegrade blood flow (TIMI grade 0) for at least 3 months. [13]. The CTO duration was assessed by clinical picture or the time of myocardial infarction (MI) in the CTO area. The severity of coronary lesions was assessed using the Synergy between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery (SYNTAX)

Table 2

Characteristics of involved coronary system

Parameter	Group of complete myocardial revascularization, n=143	Group of incomplete myocardial revascularization, n=37	p-value
CTO location			
LAD, % (n)	44,8 (64)	51,3 (19)	
Cx, % (n)	18,2 (26)	21,6 (8)	
RKA, % (n)	37 (53)	27 (10)	0,510
CTO length (mm)	30,24±4	30,59±4,6	0,977
Bridging collaterals, % (n)	18,8 (27)	18,9 (7)	1
Calcification, % (n)	5,6 (8)	64,8 (24)	<0,0001
CTO diameter (mm)	3±0,2	3±0,3	0,595

Note: the p-value was calculated using Student's t-test for continuous variables and Fisher's test for discrete variables.

Table 3

Characteristics of endovascular CTO intervention

Parameter	Group of complete myocardial revascularization, n=143	Group of incomplete myocardial revascularization, n=37	p-value
Recanalization technique type:			
Antegrade, % (n)	90,2 (129)	83,8 (31)	
Retrograde, % (n)	9,8 (14)	16,2 (6)	0,263
Mean SYNTAX score before PCI	26,7	25,5	0,068
Residual SYNTAX score	6,2	9,7	<0,0001

Note: the p-value was calculated using Student's t-test for continuous variables and Fisher's test for discrete variables.

score (https://rnoik.ru/syntax/syntaxscore/frameset.htm) with following grades: mild (⩽22 points), moderate (23-32 points) and severe (⩾33 points) [14]. Ultrasound investigations were performed using iE-33 system (Philips, Netherlands). Endovascular interventions were performed using cardiovascular imaging systems GE Innova 3100 (General Electric, USA) and Philips Allura (Philips, Netherlands). Stenting was performed with following drug-eluting stents: Resolute Integrity (Medtronic, USA), Promus Premier (Boston Scientific, USA), Promus Element (Boston Scientific, USA), and Xience Xpedition (Abbott, USA).

The choice of CTO revascularization strategy using antegrade or retrograde approaches, the choice of guidewires, microcatheters and other equipment was at the discretion of the operator. CTO recanalization with TIMI grade 3 blood flow and a residual stenosis <20% was considered a successful intervention. Unsuccessful CTO recanalization was considered to be the impossibility of guidewire insertion through the occluded segment. Intraoperative complications included MI, cardiac tamponade, stent thrombosis, and coronary artery perforation. Death, emergency coronary artery bypass grafting (CABG), emergency PCI, bleeding, contrast-induced nephropathy, and stroke were reported as hospital complications.

There were following inclusion criteria:

- Age >18 years.
- Presence of high operative risk — Society of Thoracic Surgeons (STS) score (assessment of surgical risk in CABG; http://riskcalc.sts.org/stswebriskcalc/calculate) ⩾8, and contraindications to CABG.
- Patients with stable CAD.
- Severe coronary lesions (SYNTAX Score >22 points), including the CTO.
- Clinical indications (verified myocardial ischemia according to functional tests) for endovascular CTO revascularization.
- Viable myocardium in the CTO area (no akinesia).

There were following exclusion criteria:

- Acute inflammatory diseases.
- Hematological diseases.
- Mental illness.
- Refusal of the patient from surgery.
- Impossibility of dual antiplatelet therapy.
- Contrast agent intolerance.

Statistical analysis. For comparison of categorical variables, Fisher's exact test was used. The normality of distribution of continuous variables was assessed using the Kolmogorov-Smirnov test. To equalize the initial difference in group parameters, the indirect sex and age standardization was used. To compare continuous variables, the following methods were used: for normally distributed values — Student's t-test (for equal variances) and Welch's t-test (for unequal variances); for lognormal distribution, a logarithmic transformation was applied, after which the variables become normally distributed; for variables with unknown distribution and the same variance — Mann-Whitney U-test; for frequencies — Yates's chi-squared test. For analysis of changes before and one year after the intervention, the paired Student's t-test was used. The differences were considered significant at $p<0,05$. To search for clinical, morphological, and demographic predictors of an unfavorable clinical outcome of endovascular treatment in CAD patients with CTO, univariate analysis and a logistic multivariate regression model were chosen as statistical methods. The following logistic regression model was considered:

$f(Y)=1/(1+exp(-Y))$,

Table 4

Intraoperative and in-hospital complications in the groups of successful and unsuccessful PCI

Clinical outcomes	Total	Group of complete myocardial revascularization	Group of incomplete myocardial revascularization
In-hospital death	0	0	0
Bleeding	7	5	2
MI	0	0	0
Perforation and cardiac tamponade	2	0	2
Stent thrombosis	0	0	0
Emergency CABG	0	0	0
Emergency PCI	0	0	0
CIN	3	1	2
Stroke	0	0	0

Note: CIN — contrast-induced nephropathy.

Table 5

Predictors of percutaneous coronary intervention failure in endovascular CTO recanalization

Clinical and morphological characteristics	OR	95% CI		p-value
		Lower	Upper	
Age	1	0,94	1,07	0,974
Sex (F)	0,26	0,03	1,26	0,139
SYNTAX Score >32	1,61	1,13	4,27	0,006
CTO calcification	31,15	12,18	88,15	<0,001
CTO length >30 mm	1,17	1,03	3,89	0,046
CTO location in Cx	3,06	1,96	9,58	0,01

Note: the p-value was calculated using Student's t-test for continuous variables and Fisher's test for discrete variables.

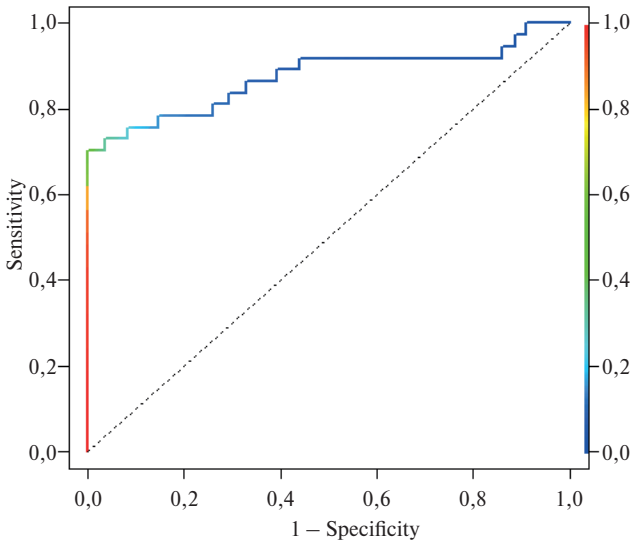

Figure 2 ROC analysis of predictors for endovascular CTO recanalization failure.

where $Y=b_0+b_1X_1+b_2X_2+\ldots+b_mX_m$, which shows the probability of a certain event with X_1, X_2, ..., X_m predictors. To assign a patient to the unsuccessful CTO recanalization risk group, the logit function f(Y) must exceed the value of 0,436 obtained by Youden's index maximization. Data analysis was carried out using the R 3.6.1 statistical software environment (R Foundation for Statistical Computing, Vienna, Austria). To assess the predictive value of the model, a ROC analysis was performed.

Results

The characteristics of the affected coronary arteries and CTO PCI are presented in Table 2. The CTO was more common in the left anterior descending artery (LAD), less often in the right coronary artery (RCA) and circumflex artery (Cx). The intraoperative data are shown in Table 3. The success rate for CTO recanalization was 79,5%. Table 4 shows intraoperative and in-hospital complications in the compared groups. In total, complications occurred in 12 patients. Most often, the antegrade CTO recanalization was used. In the group of complete revascularization, the antegrade method was used in 90,2% of cases, while in the group of incomplete revascularization — in 83,8% of cases. The retrograde recanalization was performed in the groups of complete and incomplete revascularization in 9,8 and 16,2% of cases, respectively. After PCI, the residual SYNTAX score was significantly higher in the group of incomplete revascularization and amounted to 9,7. In the group of complete revascularization, SYNTAX score was 6,2 (p<0,0001). The average length of stay was 5,1±3 bed-days.

The logistic multivariate regression was used to search for predictors of unsuccessful CTO PCI. The model included the factors leading to largest area under the curve (AUC). Variable factors were sex, age, CTO length >30 mm, SYNTAX Score >32, CTO calcification, and CTO localization (LAD + RCA

group and Cx group). The analysis showed that CTO calcification (odds ratio (OR), 31,15; 95% confidence interval (CI): 12,18-88,15, p<0,001), baseline SYNTAX Score >32 (OR,1,61; 95% CI: 1,13-4,27, p=0,006), CTO length >30 mm (OR, 1,17; 95% CI: 1,03-3,89, p=0,046) and CTO in Cx (OR, 3,06; 95% CI: 1,96-9,58, p<0,01) are significant predictors of unsuccessful endovascular CTO recanalization (Table 5). The AUC was 0,87, which indicates a high predictive quality of the model (Figure 2). The sensitivity and specificity were 78 and 81%, respectively.

Discussion

Previous studies have shown convincingly that successful CTO recanalization leads to angina symptoms relief, improved left ventricular ejection fraction, and increased life expectancy [15-19]. Given the current lack of a unified approach to CTO treatment and the highly variable rates of successful CTO PCI (60 to 90%), it is important that clinicians have a tool to stratify the risk of successful intervention [20-22].

Some studies have been devoted to identifying demographic and angiographic predictors of unsuccessful CTO recanalization. The Japan-Chronic Total Occlusion (J-CTO) register revealed the following predictors of CTO recanalization failure: abrupt CTO entry, calcification, bending, and occlusion length [23]. The Progress CTO register revealed additional negative predictor: proximal cap ambiguity and Cx CTO [24]. The *Institut Cardiovasculaire Paris Sud* found the following independent predictors of surgery failure: previous MI, previous CABG, non-LAD CTO location, blunt stump morphology, bending, and CTO length >20 mm [25].

According to a study conducted at the National Medical Research Center for Therapy and Preventive Medicine, the demographic data of patients did not significantly affect the outcome. At the same time, it was shown that the presence of pronounced CTO calcification, severe multivessel disease (SYNTAX Score >32 points), CTO length >30 mm, and CTO location in Cx are predictors of unsuccessful CTO recanalization.

The presence of vascular calcification and severe multivessel disease usually cause technical difficulties in endovascular interventions [26]. This is due to the complexity of instrumentation and adequate dilatation of the vessel during predilatation, stent implantation, and postdilatation. Severe CTO calcification also causes complications of the intervention. The denser and calcified CTO, the more difficult it is to pass the guidewire through it. In such cases, a specialized line of guidewires for CTO recanalization is used. These guidewires have a stiffer tip that allows easier passage through the occluded segment.

In most studies, including and in this case, it has been shown that Cx location of CTO is a predictor of unsuccessful intervention [27-29]. There is an anatomical explanation for this fact. The left main coronary artery is divided into LAD and Cx. In this case, the LAD is a natural continuation of left main coronary artery, and the Cx departs at a right angle. This can explain the difficulties in recanalization of Cx CTO. It is necessary to overcome the angle of 90° with the guidewire and recanalize the CTO. The presence of additional bends in front of CTO decrease the successful recanalization rate for Cx CTO.

The CTO length also influences the successful CTO recanalization rate. The longer the lesion, the lower the success rate. The presented data are consistent with other studies and show that CTO length >30 mm is a predictor of unsuccessful CTO PCI [30, 31]. In the case of long CTO, it is more often necessary to resort to retrograde recanalization through the system of collateral branches. For successful recanalization, it is also necessary to use a microcatheter, which allows replacing the coronary guidewires without losing the achieved result and successfully recanalizing the CTO.

Conclusion

The study showed that the presence of calcified CTO, SYNTAX score >32 points, CTO length >30 mm, and CTO of circumflex artery are significant predictors of unsuccessful CTO recanalization. Thus, an accurate assessment of predictors of successful CTO recanalization will optimize the selection of patients for endovascular CTO treatment.

Relationships and Activities: none.

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