

# CHRONIC TOTAL CORONARY ARTERY OCCLUSION RECANALISATION WITH PERCUTANEOUS CORONARY INTERVENTION — SINGLE CENTRE 10-YEAR EXPERIENCE

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*Coronary artery chronic total occlusions (CTO) are common — approximately one-third of patients with significant coronary artery disease on angiography have at least 1 CTO. Invasive treatment of these lesions still remain a major challenge for interventional cardiology due to their complexity. Historically, success rates have improved to about 60–70% by using only the traditional antegrade approach. The results have dramatically improved during the last decade after more widespread application of new retrograde techniques. The aim of our study was to review and analyse single hospital experience in CTO invasive treatment and to evaluate the long-term results. A total of 519 patients undergoing percutaneous coronary interventions (PCI) for CTO at a single tertiary PCI centre (Rīga East University Hospital), were included in the study. The median age was 64 years (38–88), and 80% were male. The retrograde approach (RA) was used for 167 (32.2%) of the CTO PCI patients. The overall patient success rate was 81.3% and it increased from 73.9% in 2007 to 95.2% in 2015 ( $p < 0.001$ ). Mean patient observation time was five years. Overall survival was found significantly better in patients group after successful CTO PCI procedures (Long-rank test,  $p = 0.013$ ).*

**Key words:** *invasive treatment, chronic total occlusions, antegrade and retrograde approach.*

## INTRODUCTION

Despite developments in interventional cardiology during the last decade, chronic total occlusions (CTO) still remain as one of the unresolved problems in percutaneous coronary interventions (PCI) (Prasad *et al.*, 2007). CTO prevalence is high; approximately one-third of patients with significant coronary artery disease on angiography has at least 1 CTO, but only less than 10% of percutaneous revascularisations are CTO interventions (Werner *et al.*, 2009). CTO PCI is performed infrequently, likely due to historically low procedural success rates, technical complexity, high equipment use and the potential for major procedural complications (Shah, 2011). Although several studies have shown that successful recanalisation of chronic total occlusion (CTO) of the coronary arteries has been associated with improved survival, improved left ventricular systolic function, reduced angina, avoidance of coronary artery bypass grafting, and increased exercise capacity, the overall benefit of recanalisation of CTO is still limited by the deficiency of pro-

spective randomised trials, properly powered for hard clinical endpoints, comparing contemporary optimal medical therapy with contemporary state of the art CTO recanalisation (Hoye *et al.*, 2005).

The retrograde approach is a relatively novel technique of PCI for CTO, which allows the advancement of a guide wire in a coronary segment distal to occlusion through collateral vessels. In 1990, the first report of a retrograde approach for CTO was published, in which the retrograde wire crossing technique was applied via a degenerated saphenous vein graft (SVG) (Kahn *et al.*, 1990). Later septal collaterals were considered to provide potential access for the retrograde approach. In 2005, Katoh and colleagues opened a new era of retrograde CTO recanalisation with the Controlled Antegrade and Retrograde subintimal Tracking (CART) technique (Surmely *et al.*, 2006). Different kinds of retrograde techniques were introduced in the last years. Novel techniques hold promise in the field of percutaneous coronary intervention for CTO (Saito *et al.*, 2008).

The first successful retrograde PCI of CTO in Riga East University Hospital was conducted in January 2007.

The aim of our study was to review 10-year data from a single hospital on CTO PCI experience and compare CTO PCI procedural parameters and treatment results using antegrade and/or retrograde approaches.

## MATERIALS AND METHODS

The study included all patients undergoing PCI for CTO at a single tertiary PCI centre during 10 years — between January 2007 and January 2016. A total of 9564 PCI procedures were conducted in this period in our institution. 591 (6.17%) of them were CTO PCI, which was applied for 519 patients. Ten patients had 2 coronary arteries CTOs, for 49 patients more than one CTO PCI attempt was made. The retrograde approach was used for 167 (32.2%) of all CTO PCI patients.

A CTO lesion was defined as an obstruction of a coronary artery with Thrombolysis in Myocardial Infarction (TIMI) flow grade 0 with an estimated duration of at least three months. The duration of the occlusion was determined by the interval from the last episode of acute coronary syndrome consistent with the location of the occlusion or proven by previous angiography.

Indications for performing CTO PCI were at least one of the following: symptoms (angina), positive exercise test, ischemia. PCI was also performed for asymptomatic CTO patients after myocardial infarction in the non CTO area with normal ECG and normal echo findings at CTO related area.

The J-CTO score was used for CTO complexity assessment. This score is the sum of anatomical findings and previous attempt results — predictors of procedure failure: blunt stump, CTO length > 20 mm, presence of severe calcification, proximal segment tortuosity, and previous attempt failure.

An attempt of using the retrograde approach was defined as the introduction of a guide wire into the collateral channels (CCs), which was connecting to the target CTO vessel distal to the lesion. Length of the CTO was measured following bilateral simultaneous coronary injections by visualising the filling of both proximal and distal occluded artery.

Procedural success was defined as a successful guide wire and balloon crossing with residual stenosis < 10% and Thrombolysis in Myocardial Infarction grade 3 flow.

All patients were pretreated with aspirin and clopidogrel. 5000 units of Heparin was used at the beginning of every procedure. Additional 2500 units of Heparin were injected every hour. Activated clotting time (ACT) was not measured. No GP 2B3A receptor blockers used. Both femoral punctures with 6–8 French (Fr) guiding catheter were used commonly. In some cases a radial route was performed to-

gether with femoral approach. Only guiding catheters with side holes were used.

The decision and technique used to perform a retrograde attempt was based on operators discretion. If CTO lesion morphology was unfavourable (i.e., blunt stump, ostial location, side branch located exactly at the proximal cap of CTO), with expected low success rate of an antegrade approach, or in a case of unsuccessful antegrade attempt(s) to recanalise a CTO with connecting collaterals filling of the distal part of the target vessel, the retrograde approach was considered as a treatment option. The retrograde approach technique evolved over time with growing operator experience and emergence of dedicated devices.

Patients were separated according to year when PCI was performed, approach (antegrade or retrograde) and PCI results (successful or unsuccessful). Demographic and procedural data were collected at the time of intervention. In-hospital MACE (myocardial infarction, urgent revascularisation, stroke or death) was documented at discharge. Post discharge data was obtained by telephone follow up.

Statistical analysis was performed using IBM SPSS Statistics for Windows, version 22.0. Continuous variables were summarised as mean value  $\pm$  standard deviation (SD) if normally distributed or as median value and interquartile range (IQR) if data distribution was skewed. Unpaired two-sided t-test and Mann-Whitney U tests were used to compare subgroups. Categorical variables were presented as proportions and subgroups compared by a chi-square test (or chi-square test for trends if applicable). Significance of differences in overall survival between subgroups was tested by Kaplan-Meier method and log-rank test. A Cox proportional hazard model was used to adjust for potential confounders such as age and sex; the results of the model were presented as hazard ratio (HR) with 95% confidence intervals (CI). A *p* value less than 0.05 was set to indicate statistically significant differences.

## RESULTS

A total of 519 patients undergoing PCI for CTO were included. The median (IQR) age was 64 yrs (38–88), and 80% (415) were male. A retrograde approach (RA) was used for 167 (32.2%) patients. Use of a retrograde approach (RA) increased from 13% in 2007 to 51.3% in 2013 and decreased to 40.5% in 2015 (Fig. 1, Table 1). The overall patient success rate was 81.3% and it increased from 73.9% in 2007 to 95.2% in 2015 (*p* < 0.001) (Fig. 2).

Table 2 shows baseline demographic and angiographic characteristics of CTO patients.

The target artery with CTO lesions included the left main (two cases, 0.4%) right coronary artery (305 cases, 58.8%), the left anterior descending artery (167 cases, 32.17%), and the left circumflex artery (45 cases, 8.7%). A retrograde approach was used in 36.9% (*n* = 111) of RCA, 25.9% (*n* = 43) of LAD and 26.7% (*n* = 12) of LCX cases.

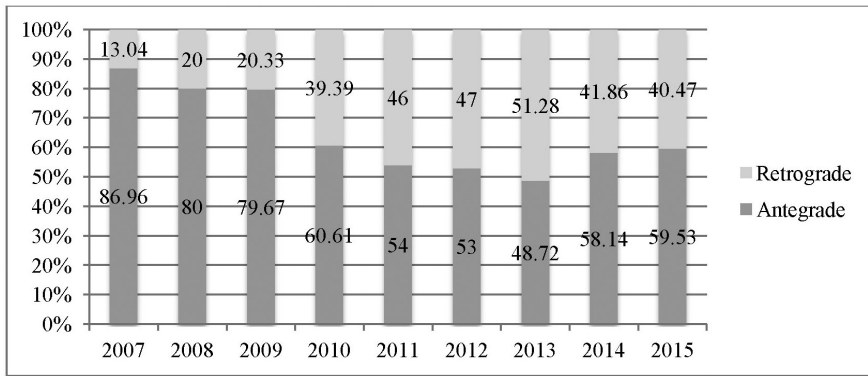


Fig. 1. Antegrade and retrograde approach usage in CTO PCI cases 2007–2015. CTO, chronic total occlusions; PCI, percutaneous coronary interventions

Table 1

NUMBER OF TOTAL AND RETROGRADE CTO PCI 2007–2015

Year	Overall CTO PCI	Retrograde CTO PCI	Retrograde CTO %
2007	69	9	13.0
2008	100	20	20.0
2009	59	12	20.3
2010	66	26	39.4
2011	50	23	46.0
2012	51	24	47.0
2013	39	20	51.3
2014	43	18	41.9
2015	42	17	40.5
Total	519	167	32.2

CTO, chronic total occlusions; PCI, percutaneous coronary interventions

Follow up started on the date of procedure, ended at the day of death or 1 June 2016. Mean patient observation time was 58.7 months (median 60.1 month).

We did not find significant differences in patient clinical characteristics undergoing antegrade and retrograde, successful and unsuccessful procedures, except regarding prior coronary artery bypass grafting (CABG). In the retrograde approach patient group, 23 (13.6%) had previous CABG, compared to 21 (6.0%) of patients in the antegrade group ( $p = 0.004$ ). Median (IQR) CTO duration was similar in both retrograde and antegrade groups — 12 (3–60) and 12 (5–36) months, respectively.

Patients with diabetes (insulin dependent and non-insulin dependent) were 21.1% ( $n = 74$ ) in the antegrade approach

group and 15.4% ( $n = 26$ ) in the retrograde approach group ( $p = NS$ ).

The J-CTO score was calculated for all patients: 215 (41.4%) had J CTO score 0 and 263 (50.7%) had score 2–3, and 41 (7.9%) of patients had score 4–5. A retrograde approach was used more frequently in complex cases. For less complex CTO lesions (J-CTO score 0–1), a retrograde approach was used in 7.7% and 19.7% of cases, respectively, for intermediate complex lesions (J-CTO score 2 and 3) in 30.3% and 52.9%, respectively, for very complex lesions (J-CTO score 4) in 70.1% of cases ( $p < 0.001$ ).

Septal collaterals were more frequently used as the retrograde access route (85.3%), but during the last two years use of epicardial channels has increased.

The main reasons for failure in both groups (antegrade and retrograde) was inability to cross the occlusion with a wire (68.7% of all unsuccessful cases).

The total complication rate was 6.5%: 5.9% in the antegrade patients group and 7.2% ( $p = 0.630$ ) in the retrograde group.

Kaplan-Meier curves showed better overall survival in the successful procedure group compared to the unsuccessful group (Long-rank test,  $p = 0.013$ ) (Fig. 3), but the method used (antegrade or retrograde) did not have any effect on survival (Fig. 4). In the retrograde procedure group, survival was significantly better ( $p = 0.019$ ) if the procedure was successful. Similarly, there was a tendency of better survival in the case of success also among patients who underwent an antegrade procedure, albeit it was not statistically significant ( $p = 0.118$ ) (Figs. 5–6).

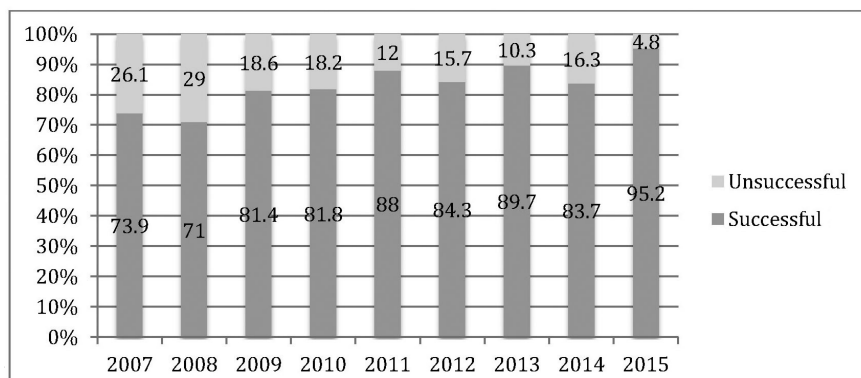


Fig. 2. Overall CTO PCI success rates 2007–2015. CTO, chronic total occlusions; PCI, percutaneous coronary interventions

CTO PCI PATIENT CHARACTERISTICS ACCORDING TO PROCEDURAL SUCCESS

	Total (n = 519)	Successful (n = 422)	Unsuccessful (n = 97)	<i>p</i>
Mean age ( $\pm$ SD)	63.4 (10.5)	63.3 (10.7)	64.1 (10.0)	0.501
Male, n (%)	415 (80.0%)	338 (80.1%)	77 (79.4%)	0.874
Smokers :				
-never	292 (56.3%)	231 (54.7%)	61 (61.9%)	0.336
-ex	160 (30.8%)	134 (31.8%)	26 (26.8%)	
-current	67 (12.9%)	57 (13.5%)	10 (10.3%)	
Hypertension	434 (83.6%)	356 (84.4%)	78 (80.4%)	0.343
Dislipidemia	358 (69.0%)	298 (70.6%)	60 (61.9%)	0.093
Diabetes	100 (19.3%)	86 (20.4%)	14 (14.4%)	0.181
Prior MI	380 (73.2%)	303 (71.8%)	77 (79.4%)	0.128
Prior CABG	44 (8.5%)	34 (8.1%)	10 (10.3%)	0.473
Prior PCI	266 (51.3%)	205 (48.6%)	61 (62.9%)	0.011

CTO, chronic total occlusions; PCI, percutaneous coronary interventions; MI, myocardial infarction; CABG, coronary artery bypass grafting

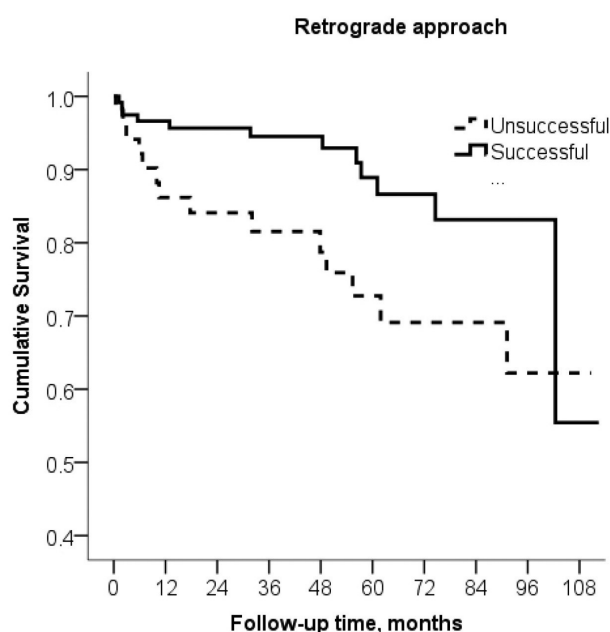


Fig. 3. Survival after successful and unsuccessful CTO PCI retrograde cases. CTO, chronic total occlusions; PCI, percutaneous coronary interventions

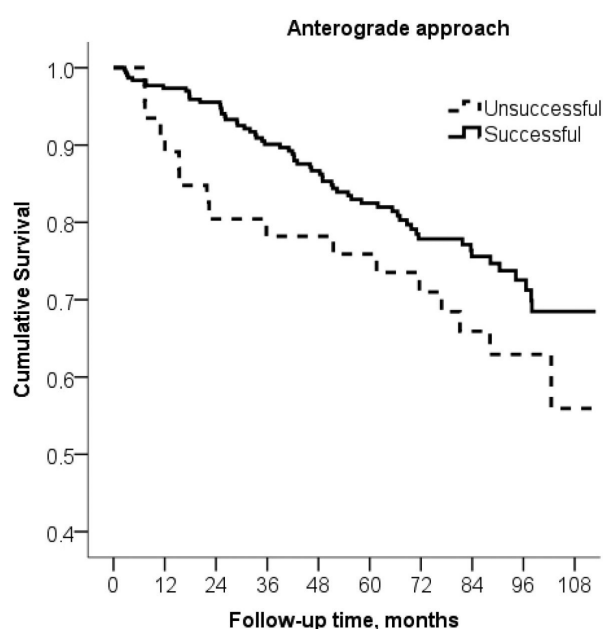


Fig. 4. Survival after successful and unsuccessful CTO PCI antegrade cases. CTO, chronic total occlusions; PCI, percutaneous coronary interventions

Success was associated with lower mortality (Cox regression: HR 0.59 (95%CI 0.39–0.90;  $p = 0.014$ ). The success of the procedure remained significant also after adjustment for patient age, sex and method: HR 0.58 (95%CI 0.38–0.89;  $p = 0.012$ ).

## DISCUSSION

The true prevalence of a CTO in the general population is unknown and not well studied. In a few older studies the prevalence of CTO in patients undergoing coronary angiography ranged between 10% and 52% depending on the clinical profile of the patient being examined. Among patients who underwent coronary angiography because of sus-

pected coronary artery disease, CTO prevalence was 18%, but in patients with angiographically significant coronary artery disease it was 30% (Christofferson, 2005). CTO prevalence was observed to be higher (54%) among patients with a history of aortocoronary bypass graft (CABG) surgery and lower (10%) among patients with acute coronary syndrome undergoing primary PCI (Fefer, 2012).

Data from registries reveal striking variability between different centres and countries. For example, in Japanese centres CTO incidence was 19% and 61.2% of these cases were treated percutaneously (Yamamoto *et al.*, 2013), however in North America, where CTOs are more frequent (29–33%), only between 6% and 9% of patients were treated percutaneously (Srinivas *et al.*, 2002).

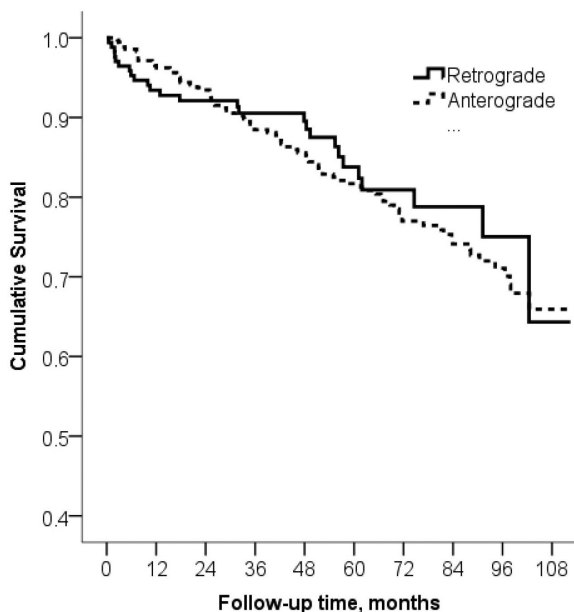


Fig. 5. Overall survival after CTO PCI antegrade and retrograde cases. CTO, chronic total occlusions; PCI, percutaneous coronary interventions

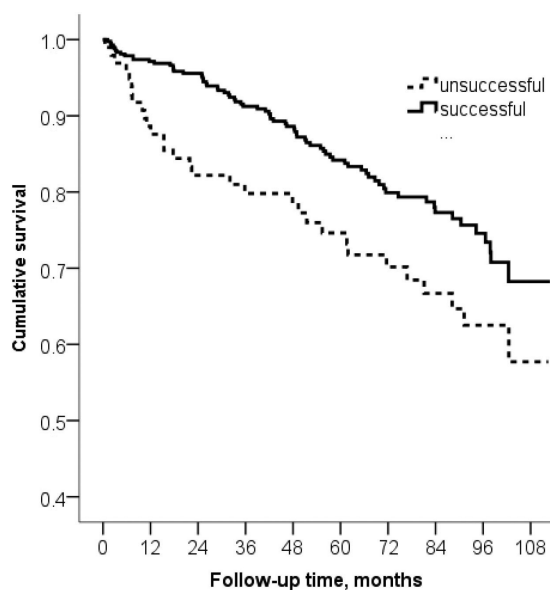


Fig. 6. Overall survival after successful and unsuccessful CTO PCI cases. CTO, chronic total occlusions; PCI, percutaneous coronary interventions

In our study the percentage of CTO PCI procedures was low — only 6.2% of all PCI. The number of CTO PCI procedures has decreased during the last years, mainly due to more careful patient selection.

According to definition, CTOs are at least three month old lesions. They are therefore always found in stable chronic patients, with varying levels of symptoms. Patients with acute coronary syndrome occasionally also have a CTO in another, non culprit artery, and is therefore considered a CTO.

Several studies showed that CTO patients are a high-risk population with more traditional cardiovascular risk factors,

multivessel disease, history of MI and PCI (Fefer *et al.*, 2012; Grantham *et al.*, 2009).

There is no doubt that treatment of CTO affecting an ischemic myocardial area that causes symptoms, such as angina, should improve patient symptoms by providing a greater perfusion flow than that provided by collateral circulation, as a consequence of opening the occluded artery (Werner *et al.*, 2006). In the FACTOR Trial (Flow Cardia Approach to CTO Recanalization), 125 patients completed the Seattle Angina Questionnaire at baseline and one month after percutaneous coronary intervention (Grantham *et al.*, 2010). Successful CTO treatment in this trial was associated with an improvement in the frequency of angina, physical capacity and quality of life. However, this improvement was only observed in previously symptomatic patients but not in asymptomatic patients.

If a patient has angina (and therefore ischemia), the benefit of CTO treatment is symptom relief. For patients without angina, but with ischemia, the benefit is not symptomatic and can be evaluated only in prognostic terms (Aziz *et al.*, 2007). There is not much evidence about the benefit of CTO invasive treatment for non symptomatic patients. The SWISSI II trial conducted in the late 1990s included asymptomatic CTO patients with 1 or 2 coronary artery disease after myocardial infarction and inducible ischemia in an imaging test. The results showed significant reduction of coronary events in the successful CTO PCI group during long-term follow up (Erne *et al.*, 2007).

The recent Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial, which compared PCI with optimal medical therapy in stable coronary disease, did not show a significant difference in mortality or myocardial infarction between the two treatment options. However, CTOs were not included in the COURAGE trial (Boden *et al.*, 2007).

Some older registries have reported that patients with complete revascularisation have a better prognosis than those with incomplete revascularisation, including the presence of an untreated CTO (Hannan *et al.*, 2006, Valenti *et al.*, 2008). The SCAAR (Swedish Coronary Angiography and Angioplasty) Registry includes data from 2006 and 2010 on 23 342 patients with multivessel disease. Incomplete revascularisation (IR) was defined as any non-treated significant (60%) stenosis in a coronary artery supplying 10% of the myocardium. IR at the time of hospital discharge in patients with multivessel disease undergoing PCI was associated with a high risk of recurrent 1-year adverse cardiac events (Hambraeus *et al.*, 2016).

Although CTO patients are common in clinical work, the evidence for the current guidelines and clinical practice is limited. According to the current European Society of Cardiology (ESC) Revascularisation guidelines, CTO percutaneous revascularisation is considered in patients with myocardial ischemia given myocardial segment and / or symptoms associated with angina (II A, Class B level rec-

Table 3

## CTO ANGIOGRAPHIC CHARACTERISTICS

	Total (n = 519)	Successful (n = 22)	Unsuccessful (n = 97)	p
CTO location:				
-LAD	166 (32.0%)	138 (83.1%)	28 (16.9%)	0.507
-LCX	45 (8.7%)	36 (80.0%)	9 (20.0%)	
-RCA	301 (58.0%)	241 (80.1%)	60 (19.9%)	
-other	7 (1.3%)	7 (100%)	0 (0%)	
Coronary artery disease				
-1	174 (33.5%)	145 (83.3%)	29 (16.7%)	0.042
-2	210 (40.5%)	177 (84.3%)	33 (15.7%)	
-3	135 (26.0%)	100 (74.1%)	35 (25.9%)	
Median CTO length (IQR), mm				
	20 (15–25)	20 (15–25)	20 (15–30)	0.017
Median CTO vessel diameter (IQR), mm				
	3.0 (3.0–3.5)	3.0 (3.0–3.5)	3.0 (3.0–3.5)	0.111
Average Mean J-CTO score (±SD)				
	1.8 (1.2)	1.7 (1.2)	2.5 (1.0)	< 0.001
Average Median J-CTO score (IQR)				
	2 (1–3)	2 (1–3)	3 (2–3)	< 0.001
Previous CTO PCI attempt				
	114 (22.0%)	74 (64.9%)	40 (35.1%)	< 0.001
Calcinosi				
	269 (51.8%)	212 (50.2%)	57 (58.8%)	0.130
J-CTO score				
				< 0.001
0	78	94.9	5.1	
1	137	91.2	8.8	
2	142	80.3	19.7	
3	121	66.9	33.3	
4 and 5	40	67.5	32.5	

CTO, chronic total occlusions; PCI, percutaneous coronary interventions; IQR, interquartile range;

ommendation) (Kolh *et al.*, 2014). A Retrograde approach is recommended as a class IIb recommendation level C, after an unsuccessful antegrade approach or as a starting method for selected patients, without describing this patient group (Kolh *et al.*, 2014).

In our study indication for CTO PCI was at least one of the following: symptoms (angina), positive exercise test, ischemia. We also performed PCI for asymptomatic CTO patients after myocardial infarction in a non-CTO area with normal ECG and normal echo findings in the CTO-related area. Of course, this does not fully comply with modern understanding about myocardial viability and ischemia, but for several reasons modern myocardial viability examinations in our hospital were not available until 2013 and the main examination given for these patients was an exercise test. Due to better patient selection the number of CTO PCI procedures in our hospital has decreased.

Until 2005, the success rates of operators experienced in conventional CTO percutaneous coronary intervention (PCI) techniques has remained unchanged (60–70%), which is considerably lower than the success rates in non-occlusive coronary artery disease (Ivanhoe *et al.*, 1992). Many techniques and devices (wires, microcatheters) have

Table 4

## COMPLICATIONS IN ANTEGRADE AND RETROGRADE CTO PCI PATIENTS

	Total (n = 519)	Antegrade (n = 352)	Retrograde (n = 167)	p
Complications	34 (6.5%)	21 (5.9%)	12 (7.2%)	0.630

Table 5

## COMPLICATIONS IN SUCCESSFUL AND UNSUCCESSFUL CTO PCI PATIENTS

	Total (n = 519)	Successful (n = 422)	Unsuccessful (n = 97)	p
Complications	34 (6.5%)	23 (5.4%)	10 (10.3%)	0.077

CTO, chronic total occlusions; PCI, percutaneous coronary interventions

been introduced into clinical practice to improve the effectiveness of CTO revascularisation (Sumitsuji *et al.*, 2011). One of the most important and popular techniques is the retrograde approach, nowadays widely used, and first described in 1990 by Kahn and Hartzler (1990). The first report of retrograde crossing via septal collaterals was published in 2006, starting the modern era, rapidly evolving with the introduction of specialised equipment (Surmely *et al.*, 2006).

Vast experience in CTO invasive treatment has been gained in Japan. According to data from the Japan Retrograde Summit registry (Yoshikawa *et al.*, 2013), use of the retrograde method was 26.6% of all PCI CTO and rate of success has reached 84.8%.

Slightly lower success rates appear in the Euro CTO Club register, which is world's largest. According to the data from this register, during the period from year 2008 to 2012, a retrograde method was used in 16.5% of successful procedures and the success rate reached 75% (Gallassi *et al.*, 2015).

In our study a retrograde approach was used in 32.2% of cases with success rate 71%, which is comparable with data from Euro CTO Club registry. Use of a retrograde approach has decreased during the last two years, likely due to operator skill improvement and introduction of new technologies for antegrade CTO crossing.

The goal of CTO PCI has always been to make life easier for patients by reducing symptoms and improving prognosis by reducing the number of major cardiovascular events. Multi-register data shows that successfully undergone CTO PCI improves patient prognosis (Mehran, 2011; Joyal, 2010). In our study, unfortunately, symptom evaluation of patients was not carried out, but, comparing survival after successful and unsuccessful CTO PCI, significantly better results were observed in the successful patient group (Fig. 3). These results coincide with data obtained in our hospital in 2013 in a shorter observation period (Kalnins *et al.*, 2013).

## CONCLUSIONS

The main finding of this study was increased survival in patients with successful CTO opening for symptomatic and/or ischemic patients and patients with CTO, but without previous myocardial infarction. Long-term outcome and survival after CTO PCI not only depends on the approach (antegrade or retrograde), but depends on results of the procedure.

The authors declare that there is no conflict of interests regarding the publication of this paper.

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## HRONISKU TOTĀLU KORONĀRO ARTĒRIJU OKLŪZIJU REKANALIZĀCIJA, PIELIETOJOT PERKUTĀNO KORONĀRO INTERVENCI — VIENA CENTRA 10 GADU PIEREDZE

Hroniskas totālas koronāro artēriju oklūzijas (HTO) sastopamas vienai trešdaļai pacientu ar nozīmīgu koronāro sirds slimību. HTO invazīva ārstēšana ir apgrūtināta tās sarežģītības dēļ. Pielietojot tradicionālo anterogrādo metodi, sekmīgo procedūru skaits nepārsniedz 60–70%. Rezultātus iespējams ievērojami uzlabot, lietojot jaunākās retrogrādās HTO rekanalizācijas metodes. Pētījuma mērķis bija izanalizēt vienas terciārā līmeņa slimnīcas desmit gadu pieredzi HTO invazīvā ārstēšanā un izvērtēt ilgtermiņa rezultātus. Pētījumā tika iekļauti 519 pacienti. To vidējais vecums bija 64 gadi, un 80% no tiem bija vīrieši. Retrogrādā rekanalizācijas metode tika pielietota 167 (32,2%) pacientiem. Sekmīgo procedūru skaits pieaudzis no 73,9% 2007. gadā līdz 95,2% 2015. gadā. Vidējais pacientu novērošanas laiks bija 4,5 gadi. Statistiski labāka dzīvildze tika novērota sekmīgi veikto procedūru pacientu grupā (*Long-rank test*,  $p = 0,013$ ).