

Predictors of successful percutaneous coronary intervention in chronic total coronary occlusions

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Abstract

Introduction: Percutaneous coronary intervention (PCI) of chronic total coronary occlusions (CTOs) is one of the most challenging procedures of interventional cardiology and is associated with increased risk of significant complications. However, debate continues in regard to which factors adversely influence the success rate of PCI and whether the benefits of revascularization of CTO outweigh the risks and challenges.

Aim: To analyze the relationship between lesion characteristics and overall success rates as well as in-hospital outcomes after PCI for CTO.

Material and methods: We retrospectively examined the procedural outcomes of 173 consecutive native coronary artery CTO PCIs performed from February 2012 to March 2013 (78% men; mean age: 60.3 ±12.1 years).

Results: The CTO target vessel was the right coronary artery (53.8%), circumflex (10.4%) and left anterior descending artery (35.8%), respectively. The retrograde approach was used in 13.9% of all procedures. Successful revascularization was achieved in 83.2% of patients. Major complications occurred in 13.3% of patients. In multivariate analysis, bridge collaterals, severe calcification and tortuosity as well as tandem occlusions were independent predictors of procedural failure, whereas existence of micro-channels was the only predictor of procedural success.

Conclusions: Revascularization of coronary CTOs may be performed with high success and low major complication rates. Bridge collaterals, severe calcification and tortuosity, tandem/multiple occlusions and micro-channels were independent predictors of successful CTO revascularization.

Key words: revascularization, coronary chronic total occlusion, lesion characteristics, procedural success.

Introduction

The incidence of coronary chronic total occlusions (CTO) among patients with a clinical indication for diagnostic coronary angiography is nearly 20% [1]. Nonetheless, according to the available data, percutaneous coronary intervention (PCI) rates for CTOs are as low as 10–15% and most of these patients are treated with medical therapy or coronary artery bypass grafting surgery (CABG) [2]. Successful recanalization of CTOs can reduce the ischemic burden and symptoms as well as electrical instability, improves exercise capacity and tends to show a positive effect on left ventricular (LV) remodeling and ejection fraction (LVEF) [3, 4]. Percutaneous coronary intervention for CTO is considered to be one of the most

challenging procedures of interventional cardiology, and in the earlier studies, successful recanalization rates of CTO ranged from 51% to 74% [5]. However, with improved operator experience and the development of novel equipment and techniques, procedural success rates have been increased, which brings an increasing number of CTO into a treatable category [6, 7]. In several previous studies, it has been reported that the appropriate use of both antegrade and retrograde approaches has noticeably improved the overall success without increasing the rate of major complications [8]. Moreover, large studies investigating patients with CTO in different clinical settings have demonstrated short- and long-term survival advantages in patients with successfully revascularized

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when compared with failed procedures and have tried to determine clinical and procedural predictors of the success and outcome [9]. However, debate continues in regard to which factors adversely influence the success rate of PCI and whether the benefits of revascularization of CTO outweigh the risks and challenges.

Aim

The purpose of the present study was to analyze the relationship between lesion characteristics and overall success rates as well as in-hospital outcomes after PCI for CTO.

Material and methods

Study design and patient population

During the period from February 2012 to March 2013, 173 consecutive patients (78% men; mean age 60.3 ± 12.1 years) who underwent PCI for CTO of a native coronary artery were included in this retrospective study. The indication for coronary angiography in all patients and subsequent PCI for CTO was the presence of angina and the demonstration of viable myocardium or silent reversible ischemia in the territory of the occluded artery on myocardial perfusion imaging. Patients with recent myocardial infarction (MI) or unstable hemodynamics, total occlusion of bypass grafts and stents were excluded from the study. After taking detailed medical history and complete physical examination, each participant was questioned for major cardiovascular risk factors such as age, sex, diabetes mellitus (DM), smoking status and hypertension (HT). Estimated glomerular filtration rate (eGFR), calculated by the simplified MDRD equation, was used for the assessment of renal functions [10]. The study was conducted according to the recommendations set forth by the Declaration of Helsinki on Biomedical Research Involving Human Subjects. The Institutional Ethics Committee approved the study protocol and each participant provided written informed consent.

Coronary CTOs were defined as angiographic evidence of a total occlusion with Thrombolysis In Myocardial Infarction (TIMI) grade 0 or 1 and estimated duration of at least 3 months [11]. Estimation of occlusion duration was based on the first onset of angina pectoris, a history of myocardial infarction in the target vessel territory, or comparison with a previous angiogram. Technical success was defined as successful CTO recanalization with achievement of $< 30\%$ residual diameter stenosis within the treated segment and restoration of TIMI grade-3 antegrade flow [12]. In-hospital major adverse cardiac events included any of the following adverse events before hospital discharge: myocardial infarction (both Q-wave and non-Q-wave), recurrent angina requiring urgent repeat target vessel revascularization with PCI or coronary bypass surgery, tamponade requiring pericardiocentesis or surgery, or death from any cause.

Definitions and lesion characteristics

Multi-vessel disease was defined as stenosis of $\geq 70\%$ in more than one major coronary artery. Severe tortuosity was defined as there being one or more bends of 90° or more, or three or more bends of $45\text{--}90^\circ$ proximal of the diseased segment. Presence of calcification was assigned to two categories according to severity. Moderate-severe calcification was accepted as multiple persisting opacifications of the coronary wall visible in at least one projection surrounding the complete lumen of the coronary artery at the site of the lesion, or mild calcification if it did not. The angiographic structure of the occlusion was defined as tapered stump (funnel shape narrowing of the proximal cap with or without a clear microchannel), blunt stump (abrupt occlusion with no microchannel), or stumpless (proximal cap could not be angiographically defined). Intracoronary microchannels at the site of the occlusion were considered to be bridging collateral vessels that established the chronicity of the occlusion. Contralateral injection, performed when retrograde collateral flow was present, was defined as simultaneous dye injection to show the distal portion of the vessel after the occlusion site (filled via collateral vessels) and to estimate the length of the occlusion.

Coronary lesions leading to a diameter stenosis of $\geq 50\%$ in vessels of ≥ 1.5 mm were scored separately and added together to provide the cumulative SYNTAX score, which was prospectively calculated using the SYNTAX score algorithm on the baseline diagnostic angiogram [13]. Moreover, the Multicenter Chronic Total Occlusion Registry of Japan (J-CTO) scoring system was calculated using parameters of lesion complexity such as prior failed attempt, angiographic evidence of heavy calcification, bending within the occluded segment, blunt proximal stump, and occlusion length > 20 mm [14]. Two experienced interventional cardiologists, who were blinded to the clinical characteristics and laboratory results of the patients, examined coronary angiograms, collateral grading, J-CTO score and SYNTAX score. The opinion of a third analyst was obtained and the final judgment was made by consensus in cases of disagreement.

Interventional procedure

Aspirin and loading dose of clopidogrel (600 mg) were given to all patients before the procedure, and dual antiplatelet therapy was prescribed for 12 months after discharge. A bolus of 80–100 U/kg unfractionated heparin was given before the procedure and followed by intravenous infusion to achieve an activated clotting time > 250 s during the procedure. Selection of the wiring techniques and the guidewires was based on the operator's discretion and the patient's coronary anatomy. The antegrade approach was routinely used, and, depending on procedural progress, different strategies and the use of stiffer wires were considered. Retrograde wiring was

defined as a technique that involves manipulating and advancing the guidewire through microcatheters via collaterals into the CTO retrogradely to reach the proximal true lumen and achieve successful recanalization. The distal wire position was confirmed to be in the true lumen by either a coronary angiogram or intravascular ultrasound examination.

Two experienced operators in our institution performed the CTO intervention procedures. The experienced operators met the criteria of “CTO operators” who had specific proctored experience of more than 100 CTOs [15].

Statistical analysis

The analyses were performed using the SPSS software (Statistical Package for the Social Sciences, Version 20.0, SPSS Inc., Chicago, IL, USA). Continuous variables were expressed as mean \pm SD and categorical variables were expressed as percentages. Analysis of normality was performed with the Kolmogorov-Smirnov test. Comparison of categorical variables between the groups was

performed using the chi-square (χ^2) test. Comparisons of continuous variables between the two groups were performed using the independent samples *t*-test. Multivariate, stepwise backward conditional logistic regression analysis was used to determine the independent predictors of successful intervention. All significant parameters in the univariate analysis were selected in the multivariate model. A two-tailed *p*-value of less than 0.05 was considered as significant.

Results

A total of 173 patients (135 men; mean age: 60.3 \pm 12.1 years) underwent PCI for CTO. There were 144 patients (113 men; mean age: 60.6 \pm 12.3 years) in the CTO success group and 29 patients (22 men; mean age: 58.8 \pm 11.4 years) in the CTO failure group. Demographic, clinical and laboratory characteristics of the study population are shown in Table I. More than 1/5 (24.9%) had a family history of coronary artery disease (CAD), 21.4% had diabetes, 60.7% had hypertension and 35.3%

Table I. Demographic, clinical and laboratory characteristics of patients

Parameter	Patients (n = 173)	Technical success (n = 144)	Technical failure (n = 29)	Value of <i>p</i>
Demographic and clinical findings:				
Age [years]	60.3 \pm 12.1	60.6 \pm 12.3	58.8 \pm 11.4	0.473
Gender (male)	135 (78)	113 (78.5)	22 (75.9)	0.462
Diabetes	37 (21.4)	30 (20.8)	7 (24.1)	0.429
Hypertension	105 (60.7)	87 (60.4)	18 (62.1)	0.521
Hyperlipidemia	61 (35.3)	52 (36.1)	9 (31.0)	0.384
Family history	43 (24.9)	34 (23.6)	9 (31.0)	0.266
Smoking	106 (61.3)	89 (61.8)	17 (58.6)	0.451
CABG	22 (12.7)	20 (13.9)	2 (6.9)	0.243
Previous PCI	42 (24.3)	37 (25.7)	5 (17.2)	0.237
Renal failure	14 (8.1)	11 (7.6)	3 (10.3)	0.427
Laboratory findings:				
Total cholesterol [mg/dl]	193.2 \pm 44.3	193.9 \pm 45.6	189.7 \pm 37.6	0.643
Triglyceride [mg/dl]	170.1 \pm 93.6	166.9 \pm 87.9	186.0 \pm 118.1	0.318
HDL cholesterol [mg/dl]	36.3 \pm 8.4	36.7 \pm 8.7	34.0 \pm 6.1	0.110
LDL cholesterol [mg/dl]	126.0 \pm 40.9	127.4 \pm 41.9	119.3 \pm 35.2	0.335
Serum creatinine [mg/dl]	1.07 \pm 0.97	0.97 \pm 0.34	1.57 \pm 2.20	0.002
eGFR [ml/min/1.73 m ²]	88.6 \pm 32.8	88.8 \pm 29.9	85.4 \pm 47.6	0.622
Uric acid [mg/dl]	6.05 \pm 1.86	6.04 \pm 1.88	6.14 \pm 1.80	0.782
Hemoglobin [mg/dl]	12.7 \pm 1.7	12.7 \pm 1.6	12.3 \pm 1.9	0.211
Platelet count, $\times 10^9/l$	240.8 \pm 79.4	242.6 \pm 75.7	231.9 \pm 96.4	0.512

Data are presented as the number (%) of patients or mean value \pm SD. HDL – High-density lipoprotein, LDL – low-density lipoprotein, CABG – coronary artery bypass graft, PCI – percutaneous coronary intervention, eGFR – estimated glomerular filtration rate.

had a history of hyperlipidemia. The clinical and laboratory characteristics were similar between the groups, including eGFR, except for serum creatinine, which was found to be higher in the CTO failure group ($p = 0.002$).

Angiographic and procedural findings

The majority of patients had multivessel disease, and the right coronary artery (RCA) was the target vessel in most of the patients (53.8%). Nine percent of patients had at least 1 previous failed attempt at CTO recanalization. Most PCIs (76%) were performed using an antegrade approach. The overall technical success rate was 83.2%. The average stent length was 60.5 ± 26.2 mm, and drug-eluting stents (DES) were used in all of the patients. Contralateral injection was performed in 154 (89%) patients (Table II).

The incidences of severe calcification, severe tortuosity, absence of tapered stump, existence of bridging collaterals, J-CTO score and tandem occlusions were found to be higher in the CTO failed group ($p < 0.05$, for all), whereas existence of micro-channels and large vessel diameter (> 3 mm) were more frequent in the successful revascularization group ($p < 0.05$, for all) (Table II). In multivariate analysis, bridge collaterals (OR: 0.114, 95% CI: 0.035–0.374, $p < 0.001$), severe calcification (OR: 0.206, 95% CI: 0.058–0.738, $p = 0.015$) and tortuosity (OR: 0.085, 95% CI: 0.013–0.579, $p = 0.012$) as well as tandem occlusions (OR: 7.075, 95% CI: 1.364–36.702, $p = 0.020$) were independently associated with higher technical failure rates. On the other hand, existence of micro-channels (OR: 0.160, 95% CI: 0.040–0.640, $p = 0.010$) was the only independent predictor of technical success (Table III).

A procedural complication occurred in 23 (13.3%) patients (Table IV). One patient died due to intracranial bleeding. Six patients had coronary artery perforation and one of them caused cardiac tamponade that required pericardiocentesis. Sixteen patients had coronary dissection, all of which were treated successfully with stent implantation.

Discussion

The results of the present study suggest that the most powerful predictors of technical failure are bridge collaterals, tandem occlusions, severe calcification and tortuosity. On the other hand, existence of micro-channels is the only predictor of technical success. Moreover, we observed that revascularization is not only an effective but also a safe therapeutic option in adequately selected CTO patients, with a high success rate and low prevalence of complications.

Chronic total occlusive lesions are characterized by heavy atherosclerotic burden, uncertain course of the vessel at the site of occlusion, and longer length of lesions within the artery, which cause a lower success rate in revascularization than that of non-CTOs [16]. The CTOs

are the most complex and challenging coronary lesions for percutaneous revascularization. In several previous studies, the procedural success rates were reported between 58.9% and 75.2% [4, 17]. Recently, the reported success rate of CTO-PCI has reached $> 80\%$ owing to the use of new sophisticated techniques and development of specialized devices [18, 19]. The overall technical success rate of the present study is 83.2% and is similar to those reported in recent large United States and European CTO PCI registries (85.5% to 87.5%) [20]. This is likely because of application of novel crossing strategies (including the retrograde approach and dissection or reentry techniques), novel equipment (microcatheters, guidewires, over the wire balloons (OTWs) and DES) and increasing operator experience [21, 22].

Currently, the most utilized CTO crossing strategies are antegrade wire escalation, antegrade dissection/re-entry, and the retrograde approach [23]. The retrograde approach, introducing a guidewire through a collateral vessel to reach a coronary segment distal to the occlusion, has been reported to significantly increase the procedural success rates of CTO PCI [24, 25]. In the present study, retrograde approach was used in 13.9% of cases. In the J-CTO registry, procedural success rate was 88.6% and retrograde approach was used in 25% of the cases in 528 CTO lesions [26]. Therefore, when compared the success rates of previous CTO PCI studies in which the retrograde approach was not used, we may claim that the retrograde approach improves success especially in complex CTO PCIs.

The morphology of chronic total occlusive plaque is composed of dense, loose and cellular fibrous tissue, as well as calcium, foam cells, and lymphocyte infiltration without foam cells [27]. Therefore, this plaque morphology entail difficulties in crossing a total occlusion with a guidewire, which is the most common reason for failure of CTO revascularization [28]. Thus, it is important to evaluate the probability of success before attempting percutaneous revascularization in CTOs. Although several studies were designed to investigate the influential factors, debate continues in regard to the impact of various clinical and angiographic factors on success, failure of PCI and long-term clinical outcome [29]. It has been reported that several angiographic factors such as absence of tapered stump structure, presence of bridging collateral vessels, and the presence of a side branch at the occlusion site are predictors of technical failure [14, 30]. Severe tortuosity and moderate-to-severe calcification have also been demonstrated to be predictors of technical failure [31]. Moreover, multivessel disease, lesion lengths > 15 mm and subsequent CABG are considered to be associated with less CTO PCI success [29, 32]. Our results support some of the conclusions mentioned above but not others. For instance, absence of tapered stump, multivessel disease, and lesion length

Table II. Angiographic characteristics of study population

Parameter	Patients (n = 173)	Technical success (n = 144)	Technical failure (n = 29)	Value of p
Target vessel:	–	–	–	0.170
LAD	62 (35.8)	52 (36.1)	10 (34.5)	
Cx	18 (10.4)	14 (9.7)	4 (13.7)	
RCA	93 (53.8)	78 (54.2)	15 (51.7)	
Multivessel disease:	–	–	–	0.476
1VD	20 (11.6)	15 (10.4)	5 (17.2)	
2VD	58 (33.5)	54 (37.5)	4 (13.8)	
3VD	95 (54.9)	75 (52.1)	20 (69)	
Previous failed attempt for CTO PCI	16 (9.2)	13 (9)	3 (10.3)	0.524
Syntax score	22.5 ±6.9	22.4 ±6.9	22.7 ±6.9	0.830
Syntax score > 33	20 (11.6)	17 (11.8)	3 (10.3)	0.559
J-CTO score	1.9 ±0.85	1.9 ±0.84	2.3 ±0.81	0.006
Average stent length	60.5 ±26.2	–	–	–
DES	173 (100)	–	–	–
Retrograde approach	24 (13.9)	18 (12.5)	6 (20.7)	0.189
Side branch	71 (41.0)	57 (39.6)	14 (48.3)	0.253
Absence of tapered stump	80 (46.2)	62 (43.1)	18 (62.1)	0.048
Severe tortuosity	18 (10.4)	11 (7.6)	7 (24.1)	0.015
Severe calcification	57 (32.9)	38 (26.4)	19 (65.5)	< 0.001
Lesion length > 20 mm	156 (90.2)	128 (88.9)	28 (96.6)	0.181
Vessel diameter > 3 mm	84 (48.6)	78 (54.2)	6 (20.7)	0.001
Bridging collaterals	38 (22)	20 (13.9)	18 (62.1)	< 0.001
Micro-channels	85 (49.1)	80 (55.6)	5 (17.2)	< 0.001
Tandem occlusions	59 (34.1)	55 (38.2)	4 (13.8)	0.008
Ostial localization	12 (6.9)	8 (5.6)	4 (13.8)	0.120
Poor guiding catheter support	7 (4)	0	7 (24.1)	< 0.001
Contralateral injection	154 (89)	127 (88.2)	27 (93.1)	0.347
Guiding catheter type:	–	–	–	0.209
Judkins	141 (81.5)	115 (79.9)	26 (89.6)	
Extra-support	30 (17.3)	27 (18.8)	3 (10.3)	
Amplatz	2 (1.2)	2 (1.4)	0	
Guiding catheter size:	–	–	–	0.629
6 Fr	73 (42.2)	59 (41)	14 (48.3)	
7 Fr	73 (42.2)	61 (42.4)	12 (41.4)	
8 Fr	27 (15.6)	24 (16.7)	3 (10.3)	
Guidewires:	–	–	–	0.730
Fielder FC	2 (1.2)	1 (0.7)	1 (3.4)	
Fielder XT	55 (31.8)	46 (31.9)	9 (31)	
PT2 MS	74 (42.8)	64 (44.4)	10 (34.5)	
Pilot 150-200	20 (11.6)	17 (11.8)	3 (10.3)	
Miracle series	13 (7.5)	11 (7.6)	2 (6.9)	
Conquest	63 (36.4)	53 (36.8)	10 (34.5)	
PT-Graphix	35 (20.2)	28 (19.4)	7 (24.1)	
Cross-IT	2 (1.2)	1 (0.7)	1 (3.4)	
Penetration technique:	–	–	–	0.478
Deep intubation	19 (11.0)	14 (9.7)	5 (17.2)	
Anchor balloon	25 (14.5)	20 (13.9)	5 (17.2)	
Parallel wire	4 (2.3)	4 (2.8)	0	
Jailed anchor	6 (3.5)	6 (4.2)	0	
Supportive equipment:	–	–	–	0.091
Over the wire balloon	112 (64.7)	95 (66.0)	17 (58.6)	
Micro-catheters	30 (17.3)	22 (15.3)	8 (27.6)	

Data are presented as the number (%) of patients or mean value ± SD. LAD – Left anterior descending artery, Cx – circumflex artery, RCA – right coronary artery, VD – vessel disease, CTO – coronary total occlusion, PCI – percutaneous coronary intervention, DES – drug-eluting stent.

Table III. Independent predictors for failure of CTO revascularization

Variables	Odds ratio	95% CI	Value of <i>p</i>
Bridge collaterals	0.114	0.035–0.374	< 0.001
Severe calcification	0.206	0.058–0.738	0.015
Severe tortuosity	0.085	0.013–0.579	0.012
Tandem occlusions	7.075	1.364–36.702	0.020
Micro-channels	0.160	0.040–0.640	0.010
Vessel diameter > 3 mm	0.550	0.152–1.995	0.363
J-CTO score	1.327	0.318–5.538	0.698
Absence of tapered stump	0.451	0.129–1.572	0.211
Serum creatinine	1.693	0.560–5.118	0.351

CI – Confidence interval, CTO – chronic total occlusion.

Table IV. Complications and in-hospital clinical outcomes

Clinical outcomes	Patients (<i>n</i> = 173)	Technical success (<i>n</i> = 144)	Technical failure (<i>n</i> = 29)	Value of <i>p</i>
Procedural complications:				0.588
Coronary dissection	16 (9.2)	14 (9.7)	2 (6.9)	
Coronary perforation	6 (3.5)	5 (3.5)	1 (3.4)	
Tamponade	1 (0.6)	1 (0.7)	0	
Death	1 (0.6)	1 (0.7)	0	0.676
Myocardial infarction:				0.411
Q wave	0	0	0	
Non-Q wave	4 (2.3)	3 (2.1)	1 (3.4)	
Urgent revascularization	0	0	0	–
Stroke	1 (0.6)	0	1 (3.4)	0.749

Data are presented as the number and percentage of patients.

> 30 mm, identified as negative predictors of success in previous studies, had no predictive value in our study. This conflict might be elucidated by diversity in definitions and durations of chronic occlusion and excluding some important variables such as angiographic structure in previous studies. Moreover, this incongruity might be a consequence of contemporary devices, techniques, and improved operator experience, which reduces the negative impact of lesion length and stump structure of lesion on technical success.

In the present study, the incidence of major adverse events such as death, urgent revascularization, stroke, and MI was similar to previously published large series, as a result of concomitant improvement in the rate of angiographic success [33]. The incidence of coronary dissection (9.2%), which occurs mainly due to subintimal advancement of the guidewires, and coronary perforation (3.5%) in our study agrees with the series reported by Mehran *et al.* (9.4% and 3.5%, respectively) [34]. Another

finding of our study is that when coronary perforation occurred, it only caused tamponade in 1 (0.6%) patient. Therefore, our results suggest that although coronary perforation is one of the most worrying complications of CTO PCI, when only the guidewire enters the pericardial space without introducing a balloon or microcatheter, its possibility to cause a tamponade is very low [35].

In the light of our findings, several factors might have influenced the success rate of CTO PCI in the present study. First of all, although eGFR was similar between the technical success and failure groups, the serum creatinine level was significantly higher in the failure group. In addition, we observed that poor guiding catheter support was more frequently found in the failure group. However, guiding catheters with strong back-up were less frequently used in the failure group. Therefore, limitation of the use of contrast and preferential use of poor back-up guiding catheters by the operators might affect procedural success.

Several limitations of the present study should be mentioned. First, our study is limited by its retrospective and observational design. Second, the number of patients in our failure group was relatively small and was 4 times lower than the number in the success group, which may influence the power of our study and our findings. Likewise, such a problem has been observed in previous studies, which reported success rates of CTO PCI between 60% and 88%. However, in the present study, the frequencies of most variables that were not significantly different between the groups were very similar, and it seems that the results would not change if the sample size were larger. Third, this was a single center experience without a multicenter registry analysis. Fourth, systematic evaluation for certain complications, such as vascular entrance complications, contrast nephropathy, and radiation skin injury, was not performed. Moreover, long-term clinical follow-up was not obtained.

Conclusions

According to the results of our study, we may suggest that the most powerful predictors of technical failure are bridge collaterals, tandem occlusions, severe calcification and tortuosity. On the other hand, presence of micro-channels is the only predictor of technical success. In addition, depending on the novel equipment, contemporary techniques, and careful selection of patients, as well as operator expertise, percutaneous revascularization may be not only an effective but also a safe therapeutic option for CTO patients.

Conflict of interest

The authors declare no conflicts of interest.

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