

# Percutaneous Intervention of CTO Lesion and Non-CTO Lesion in Patients with Coronary Chronic Total Occlusion

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## Abstract

**Background:** With the improved lifestyle of people, the incidence of coronary artery disease is gradually increasing. Approximately 15% - 20% of patients undergoing diagnostic catheterization had one or more chronically occluded coronary arteries. **Method:** The patients who were diagnosed with chronic total occlusion (CTO) in our hospital within one year period have been included. They were initially divided into two groups based on angiographic reports: single vessel disease (SVD) and non-single vessel disease (non-SVD) group, then into optimal medical therapy (OMT) group, percutaneous coronary intervention (PCI) group and coronary artery bypass graft (CABG) group. Finally, PCI group is further divided into PCI of CTO lesion (CTO PCI group) and PCI of non-CTO lesion (non-CTO PCI group). **Results:** A total of 261 patients were enrolled as CTO patients, mean age was 62.83 years, 70.1% were male patients. The incidence rate of common risk factors was hypertension (64.4%), followed by smoking (48.3%), diabetes (34.5%) and hyperlipidaemia (27.2%). SVD, DVD and TVD were present in 39 patients (14.94%), 81 patients (31.03%) and 141 patients (54.02%) respectively. Comparing the long term efficacy, the rates of MACE and non-target vessel revascularization were higher in CTO PCI than non-CTO PCI group, and were statistically significant ( $p < 0.05$ ). The rates of target vessel revascularization, CABG and all cause death were also lower in CTO PCI group, but were not statistically significant ( $p > 0.05$ ). **Conclusion:** The rates of MACE, non-target vessel revascularization, CABG and all cause death are lower if PCI is successfully performed in CTO patients. CTO PCI success also improves quality of life, decreases myocardial ischemia induced angina, and overall improves long term efficacy.

## Keywords

Chronic Total Occlusion, Percutaneous Coronary Intervention, Clinical

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Efficacy

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## 1. Introduction

Coronary artery disease is the most common form of heart diseases. Among the patients undergoing diagnostic catheterization, the CTO is found in approximately 15% - 20% of patients, the prevalence is much higher among individuals with history of coronary artery disease [1] [2] [3] [4]. Pathologically, CTO is the result of atherosclerotic changes in coronary artery causing increased plaque burden leading to complete occlusion of the artery with time. It is also defined as 100% stenosis of coronary artery diagnosed by coronary angiography with TIMI flow grade 0 [5] [6] [7]. The duration of occlusion should be more than 3 months, which can be estimated via initial onset of symptoms, or increased frequency of angina or previous history of myocardial infarction or total occlusion revealed by coronary angiography. The chronic total occlusion is basically a slow process. Long term ischemia promotes collateral circulation. The relatively patent collateral is like 90% of stenosis [8]. However, myocardial ischemia can occur when the oxygen demand is more, and patient can feel angina or clinical manifestations of cardiac insufficiency. Long term myocardial ischemia leads to myocardial necrosis, myocardial remodelling and cardiac dysfunction which can affect the quality of life and prognosis. Early management is important in improving these symptoms. The treatment of CTO includes medical therapy, PCI and CABG. Recently, with improvements in PCI related tools and techniques, especially the use of drug eluting stents and increased operator's experience, CTO PCI success rate is increasing, while, complication rate is decreasing. CTO revascularization by PCI improves patient's quality of life [9] [10] [11], myocardial function [12]-[17], and decreases need for CABG and mortality [18] [19] [20] [21]. Several factors influence CTO PCI. They include CTO duration, length of occlusion, proximal end morphology, calcification, and collateral circulation. Many scoring systems have been established to assess CTO PCI success. The most commonly used is J-CTO score [22]. In this study, we have evaluated the procedural and clinical efficacy after PCI of CTO lesion and non-CTO lesion in patients with coronary chronic total occlusion. Similarly, the baseline clinical characteristics, angiographic characteristics and procedural characteristic of CTO patients were also discussed.

## 2. Method

We have conducted an observational analysis of consecutive patients with chronic total occlusion of at least one native coronary artery CTO diagnosed by coronary angiography performed by interventional experts of cardiology department of the First Hospital of Jilin university from Jan 2016 to Dec 2016. The inclusion criteria were patients requiring non-emergency PCI to treat a 100%

occlusion of a coronary artery, defined as CTO by CAG showing total occlusion of one vessel, TIMI grade 0, and diameter of occluded vessel > 2.5 cm. The evidence of myocardial ischemia of >3 months duration obtained from angina onset or previous ECG testing or previous coronary angiography. The exclusion criteria were CAG showing TIMI  $\geq 1$  coronary flow or with occlusions known to be of less than three months duration, previous history of stroke for 6 months, severe renal insufficiency, haemorrhage, coagulation disorder, previous CABG history, allergy to contrast, aspirin or clopidogrel. Non-CTO lesion was defined as  $\geq 70\%$  stenosis of major vessels. CTO PCI success is defined as residual stenosis < 50% after PTCA of target lesion, and <30% stenosis after stenting with TIMI 3 and without any complications. Major adverse cardiovascular events (MACE) included cardiac death, STEMI, non-STEMI, cardiac tamponade, recurrent symptoms requiring urgent repeat target vessel revascularization (either PCI or CABG). Peri-procedure MI was defined as elevation of serum troponin level by more than five times the 99<sup>th</sup> percentile of the upper limit of normal in patients with normal baseline values, or rise in troponin level of >20%, if the baseline values were elevated. All these patients initially divided into two groups based on angiographic report: single vessel disease (SVD) group and non-single vessel disease (non-SVD) group. Then, they were divided into optimal medical therapy (OMT) group, PCI group and CABG group. PCI group further divided into PCI of CTO lesion (CTO PCI group) and PCI of non-CTO lesion (non-CTO PCI group). CTO PCI group has PCI success group and PCI failure group. PCI success group was treated by either PTCA or stenting. Optimal medical therapy included antiplatelet medications, beta-blocker, renin-angiotensin system blockers, nitrates, calcium channel blocker, and aggressive lipid lowering therapy. The medication regimens of all patients were considered optimal, with doses as allowed by heart rate, blood pressure, and symptoms in the absence of justifiable relative contraindications. Decision to perform bilateral injection and a retrograde approach, in addition to the type of wire, microcatheter, and use of intravascular ultrasound and glycoprotein IIb/IIIa receptor inhibitor, were all left to physician discretion. Drug eluting stents were used in all patients. Study variables were divided into baseline clinical characteristics, angiographic characteristics, procedural details, procedural complications and long term clinical outcomes. Each patient was followed up at 12 months and 24 months. Follow up methods included outpatient follow up, messaging or telephone follow up. Follow up included primary study endpoints. Primary study endpoints were MACE, target vessel revascularization, non-target vessel revascularization, CABG and all cause death. Secondary endpoints were post-procedure MI, coronary perforation, in-stent thrombosis, bleeding, access site complications, and contrast nephropathy. Finally, data were analysed using SPSS 20.0 software and applying t test and chi square test.  $p < 0.05$  was considered as statistically significant.

### 3. Result

A total of 261 patients enrolled as CTO patients, mean age was 62.83 years,

70.1% were male patients. The common risk factors were hypertension (64.4%), followed by smoking (48.3%), diabetes (34.5%) and hyperlipidaemia (27.2%). Baseline clinical characteristics of all CTO patients were included in **Table 1**. The mean LVEF of CTO patients was  $55.34 \pm 8.96$ . The lipid profile included TC, TG, LDL-C, and HDL-C and were  $6.35 \pm 29.63$ ,  $2.18 \pm 1.64$ ,  $2.80 \pm 1.12$ , and  $1.04 \pm 0.23$  respectively. Based on angiographic findings, all CTO patients were divided into two groups: single vessel disease (SVD) group and non-single vessel disease (non-SVD) group. The non-SVD group included double vessel disease (DVD) and triple vessel disease (TVD). SVD group further divided into medical therapy group (4 patients) and PCI group (35 patients). The most commonly chronically occluded lesion was seen in right coronary artery 111 (42.5%), followed by LAD 91 (34%), and LCX 59 (22.6%). Two coronary arteries were found to have occluded in 16 (6.13%) patients. Right radial approach was the most common approach for coronary angiography (**Table 2** shows the angiographic characteristics of all CTO patients). J-CTO score was done for each patient and found score of 1 was most common that accounted 42.14%. The J-CTO score was determined by assigning 1 point to each independent predictor of revascularization difficulty. These predictors included blunt stump, calcification, bending, occlusion length > 20 mm and previously failed attempt.

**Table 1.** Baseline clinical characteristics of all CTO patients.

<b>Age</b>	62.83 $\pm$ 9.149
<b>Male</b>	183 (70.1%)
<b>HTN</b>	164 (64.4%)
<b>DM</b>	90 (34.5%)
<b>Hyperlipidaemia</b>	71 (27.2%)
<b>Smoking</b>	126 (48.3%)
<b>Cerebrovascular disease</b>	34 (13%)
<b>Old MI</b>	97 (37.2%)
<b>Hb</b>	141.05 $\pm$ 15.67
<b>FBS</b>	6.99 $\pm$ 2.99
<b>Cr</b>	77.94 $\pm$ 21.22
<b>Urea</b>	5.92 $\pm$ 1.84
<b>ALT</b>	29.92 $\pm$ 40.77
<b>AST</b>	26.01 $\pm$ 18.70
<b>TC</b>	6.35 $\pm$ 29.63
<b>TG</b>	2.18 $\pm$ 1.64
<b>LDL-C</b>	2.80 $\pm$ 1.12
<b>HDL-C</b>	1.04 $\pm$ 0.23
<b>LVEF</b>	55.34 $\pm$ 8.96
<b>LVEDD</b>	50.19 $\pm$ 5.79

**Table 2.** Angiographic characteristics of all CTO patients (261).

<b>CTO lesion</b>	
LAD	91 (34%)
LCX	59 (22.6%)
RCA	111 (42.5%)
<b>2 CTO lesion</b>	16 (6.13%)
<b>LM disease</b>	20 (7.66%)
SVD	39 (14.94%)
DVD	81 (31.03%)
TVD	141 (54.02%)
<b>Previous PCI</b>	79 (30.26%)
<b>Collateral</b>	171 (65.51%)
<b>Dominance</b>	
Right	198 (75.86%)
Left	36 (13.79%)
Co-dominance	27 (10.34%)
<b>Approach</b>	
Right radial	241 (92.33%)
Right femoral	17 (6.51%)
Left radial	3 (1.14%)
<b>J-CTO score</b>	
0	44 (16.84%)
1	110 (42.14%)
2	89 (34.09%)
≥3	18 (6.89%)

A total of 222 patients was diagnosed either double vessel disease (DVD) or triple vessel disease (TVD). Information of 15 patients was missing or incomplete. 48 patients were managed with medical therapy, 22 patients advised for surgical consultation. Finally, 152 patients were planned for PCI management. Non-CTO lesion was intervened in 44 patients, while CTO lesion was intervened in 108 patients. All patients in non-CTO lesion group were successfully managed by PTCA. While, first attempt failed in 16 patients in CTO lesion group. Primary success achieved in 92 patients with PTCA in 4 patients and stenting in 88 patients. The right radial approach was still the commonest approach used in our centre both for CTO lesion and non-CTO lesion. The comparison between procedural characteristics of non-CTO lesion PCI and CTO lesion PCI was illustrated in **Table 3**. There was no statistical significance between these groups regarding arterial approach, number of stent used, diameter of stent, and length of stent. In CTO lesion group, the number of guidewires and microcatheter per procedure used was significantly higher. In hospital outcomes were considered as short term outcomes and these outcomes included lesion success,

**Table 3.** Comparison of Procedural characteristics of between CTO lesion group and non-CTO lesion PCI group.

	CTO lesion group (88)	Non-CTO lesion group (44)	p value
<b>Approach</b>			
Right radial	83 (94.32%)	43 (97.7%)	0.495
Right femoral	1 (1.14%)	1 (2.3%)	0.36
Dual access	4 (4.5%)	0 (0%)	0.145
Total no of guidewires/per procedure	1.75 (1.75 ± 0.81)	1.25 (1.25 ± 0.44)	0.001
Microcatheter use	34 (38.64%)	2 (4.5%)	0.001
No of stent used	1.6 (1.6 ± 0.72)	1.43 (1.43 ± 0.66)	0.137
<b>Types of stents</b>			
Firebird	21 (47.73%)	5 (11.36%)	0.057
Tivoli	5 (5.68%)	7 (15.9%)	0.033
Excel	17 (19.32%)	9 (20.45%)	0.957
Partner	14 (15.91%)	11 (25%)	0.552
Endeavour	23 (26.13%)	7 (15.9%)	0.159
Xience	5 (5.68%)	3 (6.82%)	0.825
Diameter of stent	2.87 (2.87 ± 0.37)	3.03 (3.03 ± 0.39)	0.019
Length of stent	28.27 (28.27 ± 5.51)	26.56 (26.56 ± 6.07)	0.107
Maximus pressure used	13.90 (13.90 ± 2.45)	13.53 (13.53 ± 2.42)	0.418
Post dilatation	41 (46.59%)	21 (47.73%)	0.161

procedural success, peri-procedural MI, coronary perforation, stent thrombosis, bleeding requiring transfusion, access site vascular complications and contrast induced nephropathy. Common vascular access complications included radial artery spasm, forearm hematoma, compartment syndrome, and development of pseudo-aneurysm, arteriovenous fistula and retroperitoneal hematoma. The comparison of in-hospital outcomes between CTO lesion group and non-CTO lesion group in non-SVD patients was included in **Table 4**, which showed complications were higher in CTO lesion PCI success group with maximal complications being access site vascular complication which was found in 7 (7.97%) patients.

Patients were evaluated at 1 year and at 2 years of their procedure. The enquiry was done on the occurrence of major adverse cardiac events, target vessel revascularization, non-target vessel revascularization, CABG and all cause death. MACEs included cardiac death, STEMI, non-STEMI, cardiac tamponade, recurrent symptoms requiring urgent repeat target vessel revascularization (either PCI or CABG). Target lesion revascularization indicated repeat percutaneous intervention of the treated lesion. Target vessel revascularization indicated repeat percutaneous intervention of the treated blood vessel. Restenosis was defined as narrowing to a diameter stenosis > 50% either within the stent or within 5 mm proximal or distal to the stent margin. The results were shown in **Table 5**.

**Table 4.** Comparison of in-hospital outcomes between CTO lesion group and non-CTO lesion group in non-SVD patients.

Variables	CTO lesion PCI success group (88)	Non-CTO lesion PCI success group (44)	p value
Access site vascular complication	7 (7.97%)	3 (6.81)	0.816
Coronary dissection	3 (3.4%)	0	0.215
Death	1 (1.13%)	0	0.478
Peri-procedural MI	1 (1.13%)	1 (2.3%)	0.614
Stent thrombosis	0	0	
Bleeding requiring perfusion	0	0	
Contrast induced nephropathy	1 (1.13%)	0	0.478

**Table 5.** 2-year follow up results of CTO and non-CTO patients.

	CTO lesion group (88)	Non-CTO lesion group (44)	p value
<b>Follow up at 1 years</b>			
MACE	4 (4.5%)	7 (15.9%)	0.026
Target vessel revascularization	0 (0 %)	1 (2.3 %)	0.156
Non-target vessel revascularization	7 (7.9 %)	9 (20.4%)	0.038
CABG	0 (0 %)	1 (2.3 %)	0.156
All cause death	0 (0 %)	1 (2.3 %)	0.156
<b>Follow up at 2 years</b>			
MACE	7 (7.9 %)	10 (22.7 %)	0.017
Target vessel revascularization	3 (6.8 %)	2 (4.5 %)	0.474
Non-target vessel revascularization	10 (11.3 %)	12 (27.3 %)	0.021
CABG	1 (1.13 %)	2 (4.54 %)	0.215
All cause death	2 (2.3 %)	3 (6.8 %)	0.197

Based on follow up results, the rate of MACE, target vessel revascularization, non-target vessel revascularization higher in non-CTO group. The all cause death and need for CABG were also found be higher in non-CTO group. That mean revascularization of CTO lesion has more beneficial effect on quality of life, myocardial function, long term survival, tolerance of future coronary events.

#### 4. Discussion

With the advancement in PCI related techniques and increased operator's experience, success rate of CTO PCI has increased [23] [24]. CTO PCI success improves patients' quality of life, decreases myocardial ischemia induced angina, improves heart function, prevents cardiac arrhythmias, and decreases need of anti-anginal medications and mortality [25]-[30]. This study showed long term prognosis of CTO PCI success patients was better. Four patients in OMT group expired and MACE rate was higher in this group. This is due to refusal of PCI treatment by the patient although they were indicated to PCI treatment or due to

poor patient financial condition. Literatures reported only 1/3 of patients with CTO was intervened to their CTO lesion [2], but, we have managed to almost 2/3 of patients by PCI except those with CTO PCI failure. DECISION-CTO trial [31] randomized 834 patients and divided into CTO PCI + OMT group and OMT group, follow up for 3.1 years and reported similar clinical efficacy and quality of life between these groups. According ACC/AHA appropriate use criteria, if patients had better symptomatic relief, better functional and quality of life, they were indicated to revascularization [32]. In recent years, tremendous progress in CTO PCI techniques experts has achieved high rates of procedural success [33] [34]. If there are high risk, complex procedure, high cost, high radiation, less symptomatic relief, those patients can be recommended medical therapy. Before undergoing CTO PCI, following things should be considered: 1) whether the patient had myocardial ischemia induced angina; 2) rate of CTO PCI success; 3) risk and complications of CTO PCI. Neither medical therapy nor percutaneous intervention is feasible in certain groups of patients with chronic total occlusion. Factors that favor surgical revascularization include multiple vessel involvement, poor LV function, total occlusions of native coronary arteries, and the availability of arterial conduits [35]. According to updated ACC guideline, class I indications for CABG include left main stenosis > 50%, stenosis of proximal LAD and proximal circumflex > 70%, triple vessel disease, double vessel disease with large area of viable myocardium in high risk area, disabling angina, ongoing ischemia in the setting of a non-ST segment elevation myocardial infarction that is unresponsive to medical therapy [36]. In this study, we referred for surgical consultation to 22 patients who had triple vessel disease with one or more than one chronic total occlusion.

The main reason for failure of CTO revascularization is inability to cross the occlusion with guidewire [37]. Success of wire crossing mostly depends on operator's skills and experience. However, in some cases, a balloon cannot cross the lesion after successful guidewire crossing and confirmation of guidewire placement into distal true lumen. Complex CTO PCI increases the risk of coronary artery perforation, higher radiation exposure, collateral vessel loss and contrast induced nephropathy recently [38]. In order to minimize the risk of contrast induced nephropathy, hydration protocol should be followed. Proper planning should be done to get higher CTO PCI success rate. The assisted modalities can be used in certain cases. These modalities include intravascular ultrasonography (IVUS), rotational atherectomy (RA), and excimer laser coronary atherectomy (ELCA) [39] [40].

This study has certain limitation: the sample size is less, single-centered, short follow up duration. The possibility of selection bias inherent to the observational design of our analyses could not be avoided. In addition, two years of follow up were not sufficient to draw conclusions regarding the long term performances of CTO PCI. The selection of treatment strategy was influenced by patient characteristics and by patient and doctor preferences. The radiation exposure dose,



operational duration and contrast dose were also not calculated, which could have significant impact on clinical and procedural outcomes of the patients.

## 5. Conclusion

The rate of MACE, non-target vessel revascularization, CABG and all cause death are lower if PCI is successfully performed in CTO patients. CTO PCI success also improves quality of life, decreases myocardial ischemia induced angina, and overall improves long term efficacy. If the patients improve with symptoms, functional ability and quality of life, revascularization of CTO can be considered. Optimal medical therapy can be considered if there is high procedural risk, complex procedure, high cost, increased radiation, and improved angina symptoms, proper planning should be considered before undergoing CTO PCI and assisted examinations (such as IVUS, RA and laser therapy) should be performed in selected cases, which will increase success rate and decrease complication rate.

## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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