The Impact of Successful Chronic Total Occlusion Percutaneous Coronary Intervention on Long-Term Clinical Outcomes in Real World

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Research

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Abstract

Backgroud: Chronic total occlusions (CTOs) are an important and increasingly recognized subgroup of coronary lesions; the optimal treatment strategy for CTO has not been well established. We sought to examine the impact of CTO percutaneous coronary intervention (PCI) on long-term clinical outcome in the real world.

Methods: A total of 592 consecutive patients with CTO in Beijing Friendship Hospital from June 2017 to December 2019 were enrolled. 29 patients were excluded due to Coronary artery bypass grafting (CABG), 301 patients were revascularized by PCI (CTO-R group) and 262 were not revascularized (CTO-NR group). The primary endpoint was cardiac death; Secondary endpoint was major adverse cardiac and cerebrovascular events (MACCE), a composite of all-cause death, cardiac death, recurrent myocardial infarction, target lesion revascularization, re-hospitalization, heart failure, and stroke.

Results: Percent of Diabetes mellitus (53.4% vs 39.5), Chronic kidney disease (8.8% vs 3.7%), CABG history (7.6% vs 1%), three vessel disease(96.2% vs 90%) and LM disease(25.2% vs 13.6%) was significantly higher in the CTO-NR group than in success PCI group (all P<0.05). Moreover, the CTO-NR group has lower EF (0.58±0.11 vs 0.61±0.1, p=0.002) and FS (0.32±0.07 vs 0.33±0.07, p=0.003). At a median follow-up of 12 months, CTO-R was superior to CTO-NR in terms of cardiac death (adjusted hazard ratio [HR]: 0.32, 95% conference interval [CI] 0.11-0.94). The superiority of CTO-R was consistent for MACCE (HR: 0.57, 95% CI 0.37-0.87). At multivariable Cox hazards regression analysis, CTO-R remains one of the independent predictors of lower risk of cardiac death and MACCE.

Conclusions: Successful revascularization by PCI offered CTO patients more clinical benefits. The presence of LVEF≤0.5 and LM-disease was associated with an incidence of cardiac death; CTO revascularised was a protected predictor of cardiac death.

1. Introduction

Coronary chronic total occlusions (CTOs) are common and have been associated with adverse clinical outcomes. With the development of devices and technologies, percutaneous coronary intervention (PCI) of CTO is increasingly pursued, and the success rate of CTO is getting higher and higher. However, its beneficial effect remains debatable. Some observational studies comparing successful versus failed PCI have demonstrated better outcomes associated with PCI, while a few randomized controlled trials (RCTs) 's conclusions did not consistently support the benefit of CTO PCI, moreover, this benefit is only the improvement of clinical symptoms[1, 2]. Overall, whether CTO-PCI actually translates into a significant improvement in long-term survival of CTO patients is still unclear. Therefore, by using the Cardiovascular Center Beijing Friendship Hospital Database Bank, we attempted to determine whether successful revascularization offers a clinical benefit in the CTO patients. This study focused on the major adverse cardiac and cerebrovascular events (MACCE), the MACCE includes all-cause death, cardiac death, recurrent myocardial infarction, heart failure, target lesion revascularization, re-hospitalization, and stroke.

2. Methods

Study design and population

The present study was based on the Cardiovascular Center Beijing Friendship Hospital Database Bank (CBD Bank). Briefly, this is a single center study. From June 2017 to October 2019, a total of 592 consecutive patients with CTO were enrolled in this study. The local institutional review board at our hospital approved the study protocol, and this study was in accord with the Declaration of Helsinki.

The inclusion criteria were as follows: (1) consecutive patients 18 years of age or older (2) patients with CTO that was diagnosed by angiography. We excluded those patients with (1) infectious diseases (tuberculosis, active infective endocarditis), rheumatic disease (systemic lupus erythematosus, rheumatoid arthritis, vasculitis), (2) Patients treated by CABG (within 3 months after the CTO diagnosis). Finally, a total of 563 patients were included in the final analysis. All patients included in the study were prospectively followed and a minimum of 6-month follow-up was warranted in order to be included in the present survival analysis. The patient flow of the study is shown in Fig. 1.

Definitions of variables and clinical endpoints

The hospital medical records were detailed and intact. Most of the data was extracted from the medical records including demographic data (age and sex), history of past illness (hypertension, coronary heart disease, diabetes, hyperlipemia and other diseases), conditions of smoking and drinking. Body mass index (BMI) was calculated by dividing weight in kilograms by height in meters squared (kg/m^2). The estimated glomerular filtration rate (eGFR) was calculated by standard calculations (GFR based on levels of creatinine [GFR(epi)]) [3].

For the angiogram data, experienced, interventional physicians rescanned the cine angiograms by using standard definitions in order to reduce bias. The definition of CTO was a TIMI flow grade of 0 and an estimated duration of at least 3 months. CTO revascularization (CTO-R) was defined as final residual stenosis less than 20%, with TIMI grade ≥ 2 flow on visual assessment [4]. CTO no- revascularization (CTO-NR) included patients who not PCI and failed PCI.

The primary endpoint was cardiac death, defined as death within 7 days after myocardial infarction, unexpected death presumed to be due to ischemic cardiovascular disease or arrhythmia occurring within 24 hours after the onset of symptoms, without clinical or postmortem evidence of another cause. The secondary endpoint was major adverse cardiac and cerebrovascular events (MACCE), a composite of all-cause death, cardiac death, recurrent myocardial infarction, target lesion revascularization, re-hospitalization, heart failure, and stroke.

All the information was recorded by physicians collecting data from new hospitalizations or by telephone calls and/or ambulatory visits performed 6 months after PCI and at least one time per year. Clinical follow-up was censored at the date of last follow-up or at 2 years, whichever came first.

STATISTICAL ANALYSIS

Demographic and clinical factors were compared between cohorts of patients depending on the result of CTO revascularization and the different coronary artery CTO lesions. Baseline characteristics are described with mean ± SD (or medians and first and third IQRs) for continuous variables and compared with Student's t test or Mann–Whitney or Wilcoxon tests, based on the normality of the data. Categorical variables are expressed as frequencies and percentages, and were compared by Chisquare or Fisher's extract statistics.

Survival curves were conducted using Kaplan–Meier estimates and compared with the log-rank test. Cox proportional hazards methods were used to estimate the independent effect of multiple independent variables on the risk of adverse clinical events in both CTO-R and CTO-NR patients. All factors showing significance in the univariate analysis ($p < 0.05$) were then examined by a multivariate analysis. The results are reported as adjusted hazard ratios (HR) with associated 95% Confidence Intervals (CI). All statistical tests were two-tailed, with statistical significance defined as a p value of < 0.05. All analyses were performed by using SPSS 25 ((SPSS Inc, Chicago, IL, USA) and Metaninf function in Stata 12.0; Kaplan–Meier survival curves were generated with the use of GraphPad Prism software (version 5; GraphPad, Inc, San Diego, CA).

3. Results

From June 2017 to December 2019, a total of 592 CTO patients were consecutively enrolled in the present study (Fig. 1). Of these patients, 29 (4.9%) patients were excluded due to CABG, 301 (50.8%) were managed by successful PCI revascularization (CTO-R group) and 262 (44.3%) were not revascularized (CTO- NR group). The CTO-NR group included patients who initial CTO-no PCI (n = 171) and failed CTO-PCI (n = 91).

Baseline characteristics

The baseline clinical characteristics of different coronary artery CTO lesions are reported in Table 1. LAD-CTO 164 cases (28%), LCX-CTO 148 cases (25%), RCA- CTO 218 cases (36%), ≥ 2 vessel CTO 61 cases (11%). Previous history of CABG, the probability of choosing CABG treatment after CTO and successful PCI to open the vessel were different. Four groups of baseline comparison the history of CABG and the proportion of choosing CABG treatment after CTO in ≥ 2 vessel CTO group compared LAD-CTO, LCX-CTO and RCA-CTO group were high, and the proportion of successful PCI in LAD group was the highest.

Table 1
Baseline characteristics of the study population grouped by the different coronary artery CTO lesions

Variable	LAD (n = 164)	LCX (n = 147)	RCA (n = 216)	≥ 2 vessel (n = 65)	P
Age(years)	64.89 ± 10.14	64.2 ± 10.04	64.66 ± 10.7	64.25 ± 11.67	0.937
Male	137(83.5)	118(80.3)	172(79.6)	52(80)	0.793
Days	7(5,8.75)	6(5,8)	7(5,9)	7(5,10.5)	0.275
BMI(kg/m^2)	25.83 ± 3.29	26.26 ± 3.34	25.94 ± 3.37	26.16 ± 4.16	0.706
AC(cm)	93.07 ± 9.71	94.14 ± 10.07	93.32 ± 9.44	93.29 ± 12.11	0.812
Smoke	102(62.2)	94(63.9)	153(70.8)	42(64.6)	0.303
Drink	31(18.9)	20(13.6)	54(25)	14(21.5)	0.062
HT	114(69.5)	111(75.5)	162(75)	47(72.3)	0.589
DM	78(47.6)	72(49)	87(40.3)	37(56.9)	0.085
Hyperlipemia	92(56.1)	91(61.9)	118(54.6)	35(53.8)	0.346
CHD	94(57.3)	88(59.9)	140(64.8)	40(61.5)	0.505
OMI	32(19.5)	29(19.7)	56(25.9)	16(24.6)	0.375
HF	2(1.2)	1(0.7)	3(1.4)	2(3.1)	0.578
CKD	8(4.9)	10(6.8)	13(6)	3(4.6)	0.87
PAD	10(6.1)	12(8.2)	20(9.3)	4(6.2)	0.665
Stroke	36(22)	38(25.9)	42(19.4)	12(18.5)	0.467
History of PCI	50(30.5)	47(32)	64(29.6)	19(29.2)	0.965
History of CABG	**3(1.8)**	**2(1.4)**	**8(3.7)**	**10(15.4)**	**0.000**
ISR	15(9.1)	5(3.4)	17(7.9)	2(3.1)	0.109
PCI open	**108(68.4)**	**58(40.8)**	**111(53.9)**	**24(42.1)**	**0.000**
CABG	**6(3.7)**	**5(3.4)**	**10(4.6)**	**8(12.3)**	**0.03**

Data are presented as absolute numbers and percentages (for categorical variables) or mean value ± SD (for continuous variables) unless otherwise specified. BMI, body mass index; AC, Abdominal circumference; HT, hypertension; DM, diabetes mellitus; HF, heart failure; CHD, coronary heart disease; OMI, old myocardial infarction; CKD, Chronic kidney disease; PAD, Peripheral arterial disease; CABG, coronary artery bypass grafting; CTO, coronary chronic total occlusion; PCI, percutaneous coronary intervention; ISR, In stent restenosis.

Differences in terms of clinical characteristics with CTO-R group and CTO-NR group are reported in Table 2. Compared to CTO revascularized patients, those not revascularized had a higher prevalence of diabetes, chronic kidney disease, prior CABG, three-vessel disease and LM disease, moreover, these patients were significantly older (67 ± 11 vs 63 ± 10 years; p = 0.000), with lower mean ejection fraction (0.58 ± 0.11 vs 0.61 ± 0.1; p = 0.002) and fraction shortening (0.32 ± 0.07 vs 0.33 ± 0.07; p = 0.003), the level of CHOL and LDL-C were also lower. Whereas the peak concentration of NT-proBNP was higher (482 vs 280, p = 0.002) in the CTO-NR group. For the other variables, there were no significant differences between the groups.

Table 2
Baseline characteristics of patients stratified for CTO lesion Revascularized or Not.

Variable	CTO-R group (n = 301)	CTO-NR group (n = 262)	P
Age	63 ± 10	67 ± 11	0.000
Male	249(82.7)	207(79)	0.262
Days	7(5,9)	6(5,8)	0.678
BMI(kg/m^2)	26.19 ± 3.59	25.85 ± 3.21	0.249
AC(cm)	93.33 ± 9.96	93.72 ± 9.76	0.647
Smoke	200(66.4)	171(65.3)	0.769
Drink	63(20.9)	50(19.1)	0.585
HT	221(73.4)	192(73.3)	0.97
DM	**119(39.5)**	**140(53.4)**	**0.001**
Hyperlipemia	163(54.2)	156(59.5)	0.198
CHD	177(58.8)	167(63.7)	0.231
OMI	58(19.3)	68(26)	0.058
HF	4(1.3)	4(1.5)	0.843
CKD	**11(3.7)**	**23(8.8)**	**0.011**
PAD	22(7.3)	20(7.6)	0.884
Stroke	63(20.9)	58(22.1)	0.728
History of PCI	89(29.6)	87(33.2)	0.353
History of CABG	**3(1)**	**20(7.6)**	**0.000**
CHOL(mmol/L)	4.12 ± 1.09	3.91 ± 1.01	**0.016**
LDL-C(mmol/L)	2.34 ± 0.76	2.21 ± 0.73	**0.043**
eGFR(ml/min)	**86.12 ± 20.65**	**80.27 ± 23.33**	**0.002**
NT-proBNPmax(Pg/ml)	280(81.9,1076)	482(144,2171.25)	**0.002**
LVEDD	5.24 ± 0.64	5.27 ± 0.59	0.426

Values are n (%), mean ± SD or median with interquartile range. CHOL, cholesterol; LDL-c, low-density lipoprotein cholesterol; NT-proBNP, N-terminal pro-brain natriuretic peptide, eGFR, estimated glomerular filtration rate; LVEDD, left ventricular end-diastolic dimension, LVEF, left ventricular ejection fraction; FS, fraction shortening, LM disease, Left main disease.

Variable	CTO-R group (n = 301)	CTO-NR group (n = 262)	P
LVEF	**0.61 ± 0.1**	**0.58 ± 0.11**	**0.002**
FS	**0.33 ± 0.07**	**0.32 ± 0.07**	**0.003**
ISR	25(8.3)	12(4.6)	0.075
three vessel disease	**271(90)**	**252(96.2)**	**0.005**
LM disease	**41(13.6)**	**66(25.2)**	**0.000**

Values are n (%), mean ± SD or median with interquartile range. CHOL, cholesterol; LDL-c, low-density lipoprotein cholesterol; NT-proBNP, N-terminal pro-brain natriuretic peptide, eGFR, estimated glomerular filtration rate; LVEDD, left ventricular end-diastolic dimension, LVEF, left ventricular ejection fraction; FS, fraction shortening, LM disease, Left main disease.

Significant correlates of CTO revascularized in multivariable analysis are shown in Fig. 2. Compared with CTO-R group, no revascularized patients were more likely to be older (age ≥ 65 years), and the proportion of diabetes, three-vessel disease and LM disease is higher. Also, the CTO-R group was more likely to be in-stent (IS) CTO.

Clinical follow-up

Up to 2-year follow-up (median 1 years, IQR 6–12 months), compared with CTO-R patients, those with CTO-NR had significantly higher rate of cardiac death (5.7% vs 1.7%; $P_{log-rank}$=0.013) and of MACCE (21.8% vs 12.3%; $P_{log-rank}$=0.004) (Fig. 3A, B respectively). Re-hospitalization tended to occur more frequently in CTO-NR patients than in CTO-R patients (17.6% vs 11.3%, p = 0.034). Moreover, no revascularized CTO patients suffered more often from target vessel revascularization (2.3% vs 0.3%, p = 0.037), and have therefore a higher MACCE rate (p = 0.003). Other clinical events are reported in Table 3.

Table 3
Comparison of clinical outcome between CTO-R group and CTO-NR group

Event, n (%)	CTO-R group (n = 301)	CTO-NR group (n = 263)	P
MACCE	37(12.3)	57(21.8)	0.003
All–cause death	8(2.7)	16(6.1)	0.043
Cardiac death	5(1.7)	15(5.7)	0.009
Re-hospitalization	34(11.3)	46(17.6)	0.034
Heart failure	8(2.7)	4(1.5)	0.354
Target vessel revascularization	1(0.3)	6(2.3)	0.037
Recurrent myocardial infarction	6(2)	5(1.9)	0.942
Stroke	1(0.3)	3(1.1)	0.252

Predictors of survival

Considering all CTO patients, a multivariable Cox regression analysis (Table 4) was used to identify clinical and angiographic independent predictors of cardiac death and MACCE. For MACCE, the final multivariable mode included LVEF≤0.5 and CTO-R. For cardiac death, the final multivariable mode included LVEF≤0.5, CTO-R and LM disease.

Table 4
Multivariate Cox regression analysis in the overall CTO patients

	Predictor variable	HR (95% CI)	P
MACCE	Age ≥ 65 years	0.93(0.585–1.479)	0.759
	Male	0.665(0.399–1.109)	0.118
	HT	0.952(0.593–1.53)	0.839
	DM	0.824(0.537–1.262)	0.373
	HP	0.893(0.591–1.351)	0.593
	OMI	0.853(0.509–1.427)	0.544
	PAD	1.316(0.673–2.573)	0.423
	Stroke	1.026(0.631–1.67)	0.917
	eGFR□90	0.999(0.639–1.561)	0.997
	LVEF□0.5	**2.124(1.305–3.456)**	**0.002**
	CTO-R	**0.567(0.37–0.868)**	**0.009**
	LM disease	1.215(0.736–2.008)	0.447
Cardiac death	Age ≥ 65 years	0.529(0.182–1.533)	0.24
	Male	0.437(0.149–1.28)	0.131
	HT	1.516(0.494–4.654)	0.468
	DM	0.796(0.301–2.106)	0.646
	HP	0.968(0.376–2.495)	0.946
	OMI	0.557(0.175–1.772)	0.322
	PAD	2.246(0.713–7.076)	0.167
	Stroke	0.904(0.305–2.683)	0.856
	eGFR□90	1.388(0.494–3.904)	0.534
	LVEF□0.5	**4.8(1.893–12.172)**	**0.001**
	CTO-R	**0.324(0.112–0.941)**	**0.038**
	LM disease	**3.877(1.543–9.745)**	**0.004**

By multivariate analysis (Fig. 4), CTO-R was a protected predictor of cardiac death (HR: 0.32, 95% CI 0.11–0.94) and MACCE (HR: 0.57, 95% CI 0.37–0.87). Additionally, lower LVEF (LVEF□0.5, HR: 4.8, 95% CI

1.89–12.17) and LM disease (HR: 3.88, 95% CI 1.54–9.75) predicted a worse probability for cardiac death.

Effects of different CTO lesion vessels (LAD, LCX and RCA) on MACCE

In Fig. 5, the effect of different CTO vessels (LAD, LCX and RCA) revascularization on MACCE was studied, there was no difference in the effect of different CTO lesion vessels revascularization on MACCE (p = 0.4488). Although there was no statistical difference, the cumulative survival rate of LCX-CTO revascularization is still the lowest.

4. Discussion

The present study showed patients with CTO not revascularised by PCI had worse outcomes compared with those with CTO revascularised, with higher incidence of cardiac death and MACCE. The presence of LVEF≤0.5, LM-disease was associated with an incidence of cardiac death, CTO revascularised was a protected predictor of cardiac death.

In our study population, the proportion of older (age≥65 years), diabetes, LM disease and three-vessel disease was higher in the no-revascularised CTO patients. This suggests that CTO with the above characteristics is more difficult to open. More importantly, previous studies have shown that age is an independent risk factor for cardiovascular mortality [5]. Elderly patients with decreased body function are more likely to have hypertension and diabetes, which promote atherosclerosis. In addition, the treatment strategy of CTO will also take into account the age factor; older patient tend to choose conservative treatment rather than PCI intervention. Meanwhile, there were more patients with in-stent restenosis (ISR) CTO in the revascularised group, which is also consistent with clinical practice; the ISR-CTO is easier to open because of the contour of the stent.

Evaluation of cardiac function in patients with CTO is of great significance for their prognosis. Serum NTproBNP is an important biomarker in our clinical practice. Abnormal elevation of NTproBNP can accurately reflect the degree of heart failure[6], and its combination with LVEF can comprehensively reflect the state of cardiac function. In our study, the peak of NTproBNP was higher and the LVEF was lower in the no-revascularised CTO patient. Moreover, low-LVEF was a harmful predictor of cardiac death, we found that the presence of LVEF≤0.5 was associated with an incidence of cardiac death at least 4 times higher than those with LVEF ≥ 0.5. Overall, cardiac dysfunction is more unfavorable to the clinical prognosis of CTO patients, which can significantly increase the incidence of major adverse cardiovascular events.

CTO are a common clinical finding among patients undergoing coronary angiography, approximately 1 in 4 patients with obstructive coronary artery disease on coronary angiography had CTOs [7]. CTO have been referred to as the “final frontier” in interventional cardiology, which are complex and difficult to open [8]. Although overall success rates remain low, with improvement in equipment and techniques, high success rates can be achieved at experienced centers; PCI for CTOs has been rapidly evolving during recent years.

Our study compared the opening rates of different CTO sites, the results showed that the opening rates of LAD, LCX, RCA, and > 2 vessels were 68.4%, 40.8%, 53.9% and 42.1%, respectively. There were significant differences in the opening rate of different CTO vessels (p = 0.000).

We can found that the opening rate of LAD-CTO is the highest, the LAD coronary artery supplies a major portion of the left ventricle, its diagonal branches perfuse the entire anterior wall, and its septal branches supply the anterior 2/3 of the septum. Especially a proximal LAD-CTO will affect the entire anterior and anteroseptal wall from base to apex. Typically such a lesion, if not revascularized, will compromise overall LV systolic function and reduces the overall LVEF to at least 35–40%; which will lead to hypotension and heart failure[9]. Therefore, clinicians are more willing to try to open LAD-CTO. This may be one of the reasons for the high opening rate of LAD-CTO. Nevertheless, the success rate of CTO with more than 2 vessels was low, and the probability of choosing CABG treatment is higher (p = 0.03). This result is also consistent with the clinical practice; CABG is the first choice for multi-vessel coronary artery disease. Many studies have suggested a long-term survival advantage for CABG compared with PCI in patients with multi-vessel coronary artery disease [10]. Moreover, the success rate of LCX-CTO was the lowest; many studies have confirmed that the successful opening of LCX-CTO has not seen obvious clinical benefits [11], and LCX-CTO is more difficult to open, one of the diagnostic criteria of the PROGRESS-CTO score is LCX-CTO [12].

Although the successful opening of CTO lesion vessels was significantly associated with the decrease of MACCE, in the CTO-R group, different target vessel lesions (LAD, LCX and RCA) revascularization did not affect MACCE. It can be seen from Fig. 5 that successfully opened the LCX-CTO has the least effect on prognosis and the lowest cumulative survival rate. This confirmed the limited clinical significance of opening the LCX-CTO.

Our result showed that successful CTO PCI is associated with a statistically significant improvement in cardiac death and MACCE, CTO revascularised was a protected predictor of cardiac death (HR: 0.32, 95% CI 0.11–0.94) and MACCE (HR: 0.57, 95% CI 0.37–0.87). It may be that the successful opening of CTO can improve cardiac function and ultimately improve the clinical outcome. A previous meta-analysis of 34 studies with 2735 patients on the impact of CTO PCI on LV function was performed in 2018 by Michael Megaly et al and showed a statistically significant increase in LVEF (3.8%, 95% CI 3.0-4.7, P < 0.0001) as compared with baseline[13]. Additionally, in our study, lower LVEF (LVEF≤0.5) and LM disease predicted a worse probability for cardiac death. In summary, the predictive risk factors of cardiac death in CTO patients include vascular not revascularised, LM lesions and low LVEF.

Limitations

The following limitations were present in this study. (1) This study was a retrospective cohort study. The evidence grade is lower than that of a randomized controlled trial. (2) The signs of a viable myocardium were not evaluated in our study. (3) Although we used multivariate Cox regression analysis to adjust for differences in baseline characteristics, there may still be unknown confounding factors, therefore, the

research results should be reasonably interpreted. Moreover, the randomized clinical trials should be conducted to verify the results in the future.

Conclusions

In summary, compared with CTO not revascularised, successful revascularization offered patients more clinical benefits, manifested by lower incidence of cardiac death and MACCE during follow-up. Moreover, the presence of LVEF≤0.5 and LM-disease was associated with an incidence of cardiac death; CTO revascularised was a protected predictor of cardiac death. Further RCTs are needed to investigate the role of PCI for management of patients with CTO.

Abbreviations

CTO
chronic total occlusion; PCI:percutaneous transluminal coronary intervention; ISR:in-stent restenosis; MACCE:major adverse cardiac and cerebrovascular events; MI:myocardial infarction; TVR:target vessel revascularization; LAD:left anterior descending coronary artery; LCX:left circumflex artery; RCA:right coronary artery; CHD:coronary heart disease; CKD:chronic kidney disease; LVEF:left ventricular ejection fraction; BMI:body mass index; CHOL:cholesterol; LDL-C:low-density lipoproteine-cholesterol;HR:hazard ratio; CI:conference interval; RCTs:randomized controlled trials.

Declarations

Ethics approval and consent to participate

This study was approved by the Institutional Review Board of Beijing Friendship Hospital. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Consent for publication

Consent to publish from the participant to report individual patient data: not applicable (no patient identifier or personalized data shown).

Availability of data and materials

The data and materials can be found from the first author and corresponding author.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

LH and CH designed the protocol, DX and ZL participated in the clinical data collection, GX drafted the manuscript. All authors read and approved the final manuscript.

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References

1. WERNER GS, MARTIN-YUSTE V, HILDICK-SMITH D, et al. A randomized multicentre trial to compare revascularization with optimal medical therapy for the treatment of chronic total coronary occlusions [J]. European heart journal, 2018, 39(26): 2484 – 93.10.1093/eurheartj/ehy220.
2. MASHAYEKHI K, N HRENBERG T G, TOMA A, et al. A Randomized Trial to Assess Regional Left Ventricular Function After Stent Implantation in Chronic Total Occlusion: The REVASC Trial [J]. JACC Cardiovascular interventions, 2018, 11(19): 1982 – 91.10.1016/j.jcin.2018.05.041.
3. LAMBRINOUDAKI I, TOURLAKIS D, ARMENI E, et al. Variations in glomerular filtration rate are associated with subclinical atherosclerosis in healthy postmenopausal women [J]. Menopause (New York, NY), 2015, 22(3): 317 – 24.10.1097/gme.0000000000000302.
4. GODINO C, BASSANELLI G, ECONOMOU F I, et al. Predictors of cardiac death in patients with coronary chronic total occlusion not revascularized by PCI [J]. International journal of cardiology, 2013, 168(2): 1402 – 9.10.1016/j.ijcard.2012.12.044.
5. MARSHALL RJ, MILNE R J, LYNN R, et al. Quantifying the effect of age on short-term and long-term case fatality in 14,000 patients with incident cases of cardiovascular disease [J]. European journal of cardiovascular prevention and rehabilitation: official journal of the European Society of Cardiology, Working Groups on Epidemiology & Prevention and Cardiac Rehabilitation and Exercise Physiology, 2008, 15(2): 179 – 84.10.1097/HJR.0b013e3282f14a7f.
6. SANTAGUIDA PL, DON-WAUCHOPE A C, OREMUS M, et al. BNP and NT-proBNP as prognostic markers in persons with acute decompensated heart failure: a systematic review [J]. Heart failure reviews, 2014, 19(4): 453 – 70.10.1007/s10741-014-9442-y.
7. Chronic Total Occlusion Percutaneous Coronary Intervention
GRANTHAM JA, Survival. and Chronic Total Occlusion Percutaneous Coronary Intervention: The Never-Ending Debate Continues [J]. JACC Cardiovascular interventions, 2017, 10(9): 876 – 8.10.1016/j.jcin.2017.03.010.

8. STONE G W, KANDZARI D E, MEHRAN R, et al. Percutaneous recanalization of chronically occluded coronary arteries: a consensus document: part I [J]. Circulation, 2005, 112(15): 2364 – 72.10.1161/circulationaha.104.481283.
9. WU JC. 18 - Acute Myocardial Infarction,Essential Echocardiography A Companion to Braunwald's Heart Disease [M]. 2019.
10. EFIRD JT, O'NEAL W T, DAVIES S W, et al. Long-Term Mortality of 306,868 Patients with Multi-Vessel Coronary Artery Disease: CABG versus PCI [J]. British journal of medicine and medical research, 2013, 3(4): 1248 – 57.10.9734/bjmmr/2013/3380.
11. MITOMO S, NAGANUMA T, JABBOUR RJ, et al. Impact of target vessel on long-term cardiac mortality after successful chronic total occlusion percutaneous coronary intervention: Insights from a Japanese multicenter registry [J]. International journal of cardiology, 2017, 245(77-82.10.1016/j.ijcard.2017.07.098.
12. FOROUZANDEH F, SUH J, STAHL E, et al. Performance of J-CTO and PROGRESS CTO Scores in Predicting Angiographic Success and Long-term Outcomes of Percutaneous Coronary Interventions for Chronic Total Occlusions [J]. The American journal of cardiology, 2018, 121(1): 14-20.10.1016/j.amjcard.2017.09.013.
13. MEGALY M, SAAD M, TAJTI P, et al. Meta-analysis of the impact of successful chronic total occlusion percutaneous coronary intervention on left ventricular systolic function and reverse remodeling [J]. Journal of interventional cardiology, 2018, 31(5): 562 – 71.10.1111/joic.12538.

Figures

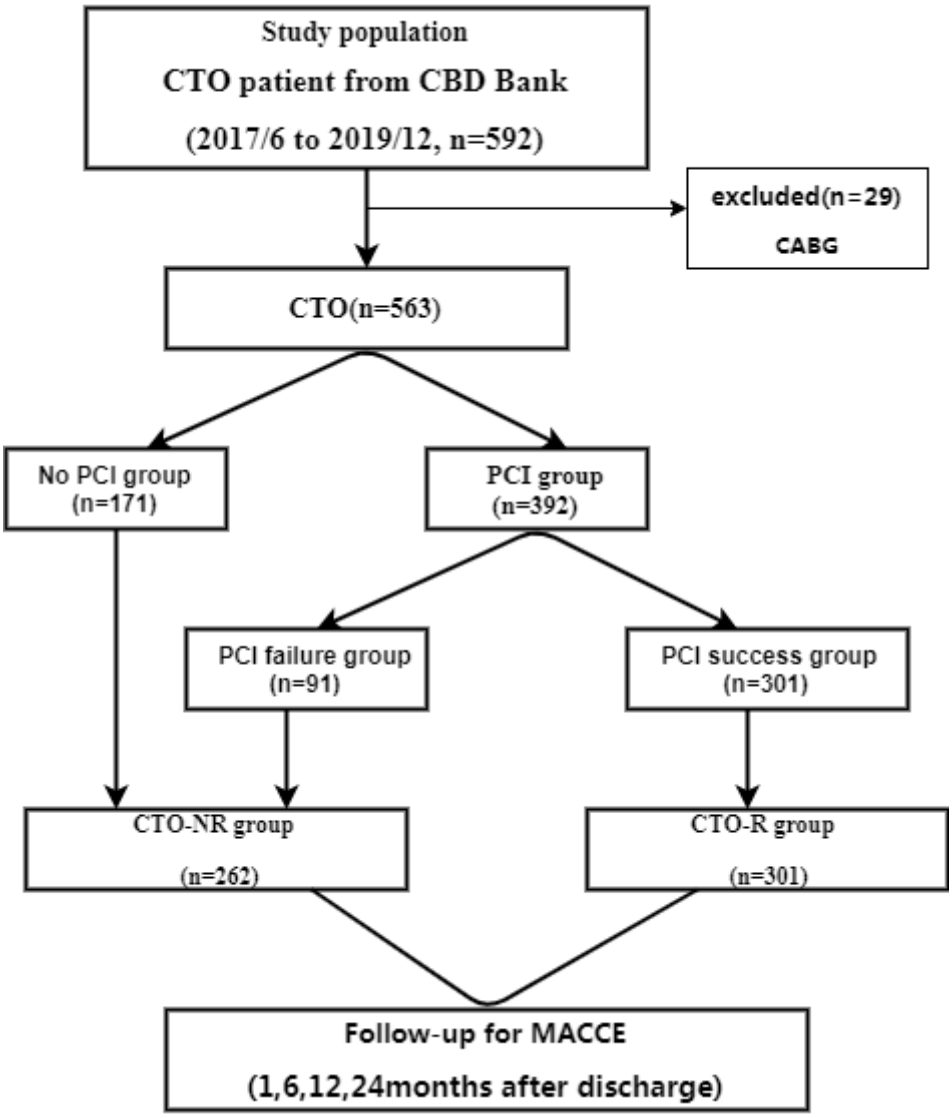

Figure 1

Flow chart of patient enrollment, MACCE: major adverse cardiac and cerebrovascular events, CTO-R: CTO revascularized. CABG: Coronary artery bypass grafting.

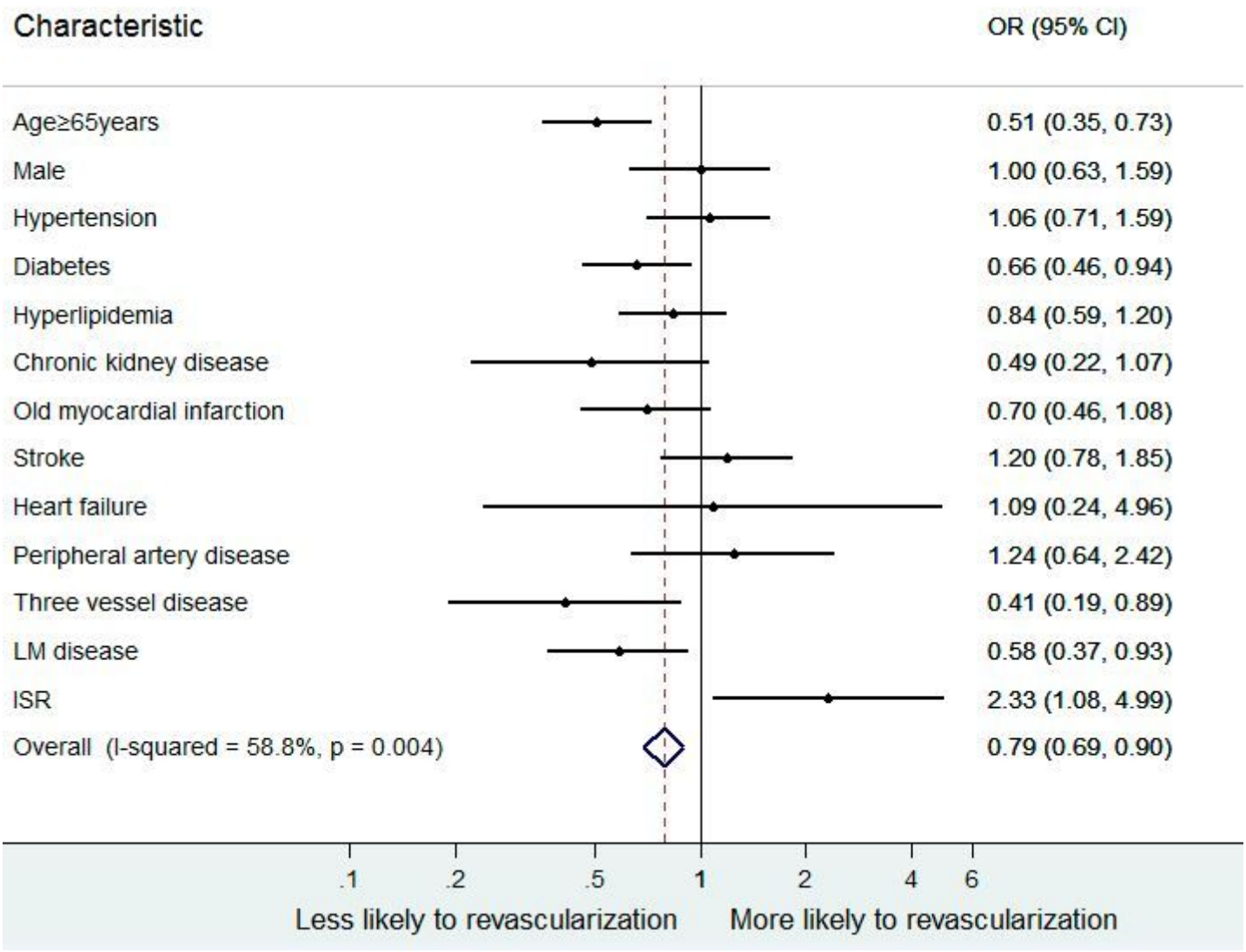

Figure 2

Factors associated with CTO revascularization in multivariable analysis. Variables associated with CTO revascularization are shown along the vertical axis. The strength of effect is shown along the horizontal axis with the vertical line demarcating an odds ratio (OR) of 1 (i.e., no association); estimates to the right (i.e., > 1) are associated with a greater likelihood of CTO revascularization, whereas those to the left (i.e., < 1) indicate a reduced likelihood of CTO revascularization. Each dot represents the point estimate of the effect of that variable in the model, whereas the line shows the 95% confidence interval (CI).

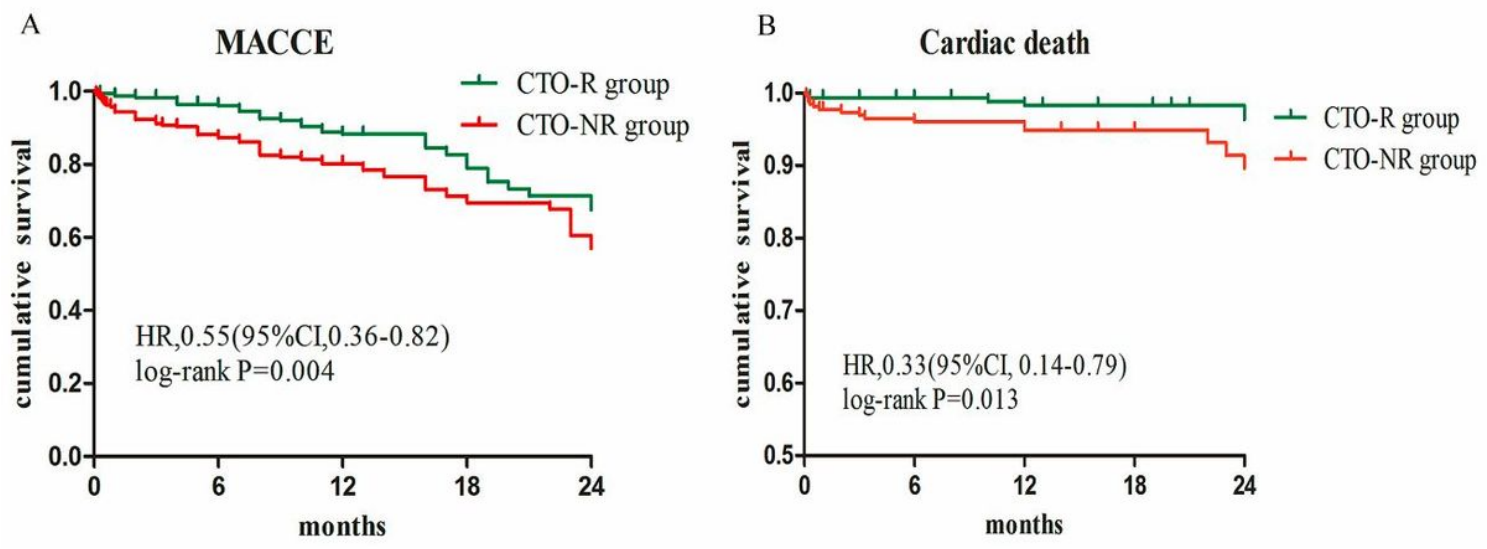

Figure 3

Kaplan-Meier analysis of MACCE (secondary endpoint, panel A) and cardiac death (panel B) for overall patients stratified for CTO revascularised (R: green continuous line) and not revascularised (NR: red dotted line).

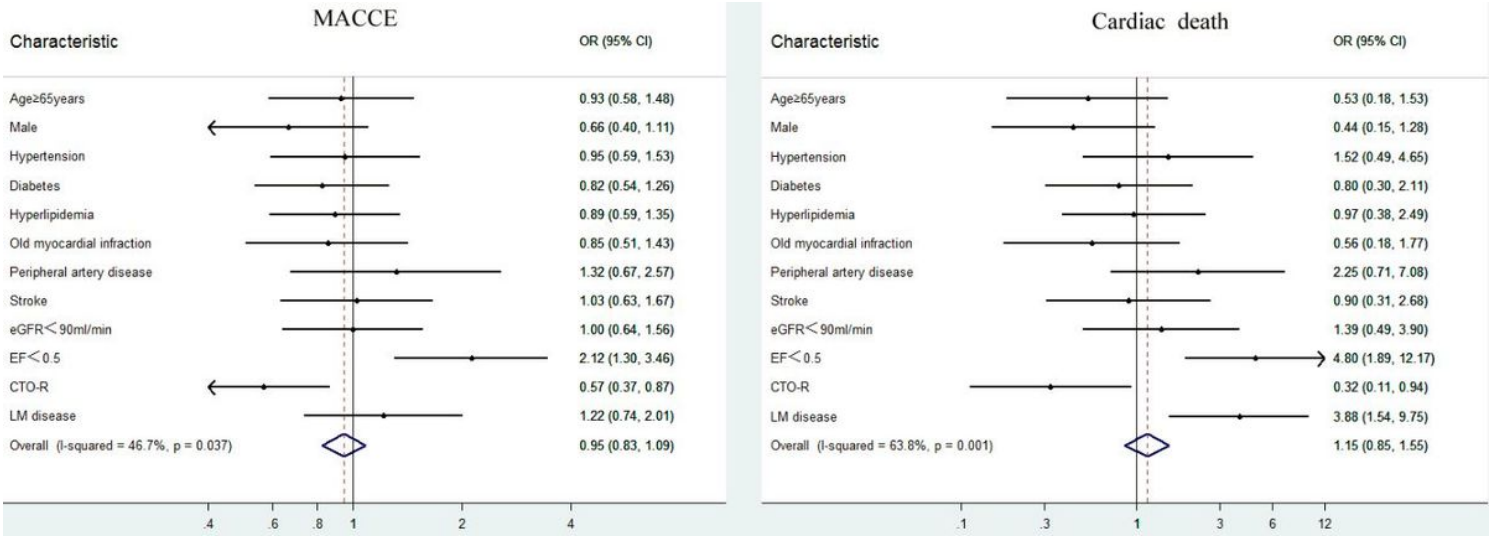

Figure 4

Predictors of cardiac death and MACCE in all CTO patients. CTO-R was a protected predictor of cardiac death and MACCE. Additionally, LVEF□0.5 and LM disease predicted a worse probability for cardiac death.

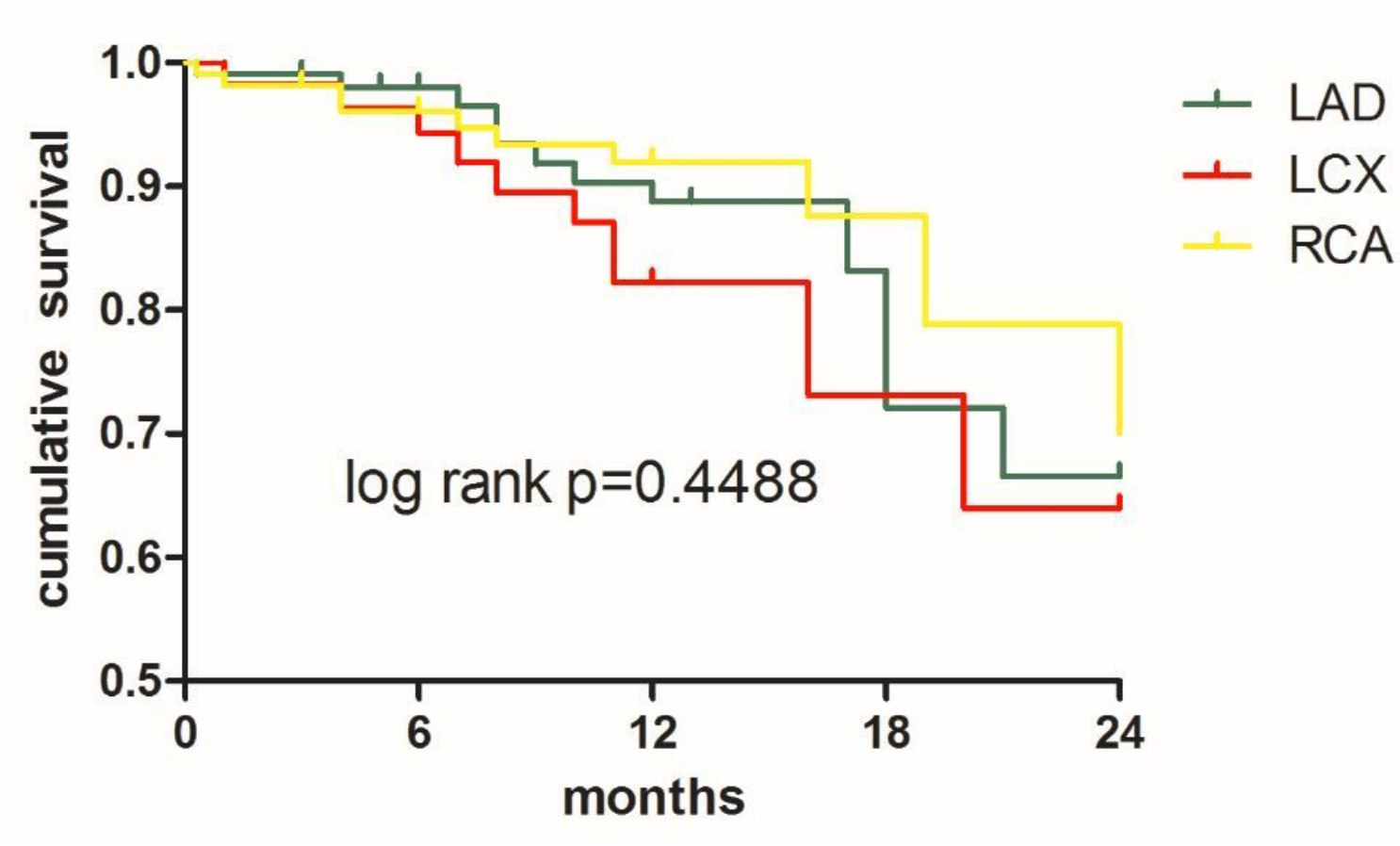

Figure 5

Comparison of Kaplan meire survival curves of different CTO target vessels revascularization.