Heart Sci J 2022; 3(3): 25-32

Contents list available at www.heartscience.ub.ac.id

Heart Science Journal

Journal Homepage : www.heartscience.ub.ac.id

Original Article

The Impact of Successful Percutaneous Coronary Intervention on the Reduction of Major Adverse Cardiovascular Events in Patients with Chronic Total Coronary Occlusion

Ratna Pancasari[1*], Mohammad Saifur Rohman[2], Ardian Rizal[2], Novi Kurnianingsih[2], Anna Fuji Rahimah[2]

[1] *Brawijaya Cardiovascular Research Center, Department of Cardiology and Vascular Medicine, Faculty of Medicine, Universitas Brawijaya, Malang, Indonesia.*
[2] *Department of Cardiology and Vascular Medicine, Faculty of Medicine, Universitas Brawijaya, Malang, Indonesia.*

ARTICLE INFO

Keywords:
Chronic Coronary Total Occlusion;
MACE;
Percutaneous Coronary Intervention;
Revascularization

ABSTRACT

Background: Chronic total coronary occlusion (CTOs) is associated with an increased risk of adverse clinical outcomes. The benefits of percutaneous coronary intervention (PCI) in CTO are still being debated due to the limited data available. This study aimed to determine the relationship between the revascularization of CTO and the reduction of major adverse cardiovascular events (MACE).

Methods: We conducted a retrospective cohort analytic observational study. Around 578 individuals with at least one CTO were detected among a total of 2165 patients who had angiography at Dr. Saiful Anwar Hospital in Malang from August 2017 to September 2020. This study included 510 participants after excluding 68 individuals. They were separated into two groups: the revascularized CTO (n = 141) and the non-revascularized CTO (n = 369) groups. The outcome of this study was MACE, which included cardiac mortality, all-cause mortality, and rehospitalization.

Result: Patients with revascularized CTO compared to those with non-revascularized CTO had a higher history of heart failure, involvement of LM disease, multivessel disease, and three vessel disease (41.2% vs 18.4%, p = 0.041; 16.5% vs 1.8%, p < 0.001; 69.4% vs 22.7%, p < 0.001; 56.5% vs 14.1%, p < 0.001) with a lower mean LVEF (0.49 ± 0.06 vs 0.51 ± 0.07, p=0.045) and older age (60±9 vs 57±8 years; p=0.007). At a 12-month follow-up, in the revascularized CTO group had a better prognosis than the non-revascularized CTO group in terms of MACE (19.9% vs 33.1% Log-rank p= 0.002). These results were consistent for all-cause mortality (5.5% vs 20.6%, Log-rank p=0.027), cardiac mortality (3.7% vs 20.6%, Log-rank p< 0.001) and rehospitalization. (7.5% vs 32.2%, Log-rank p= 0.001).

Conclusion: Successful revascularization of CTO by PCI may provide clinical benefits in patients with CTO including MACE reduction.

1. Introduction

Chronic total coronary occlusion (CTO) is defined as a total coronary artery occlusion in which no blood flow is obtained through the lesion with thrombolysis in myocardial infarction (TIMI) flow of 0 and for a minimum duration of 3 months.[1] CTO is often found in patients with coronary artery disease (CAD) who underwent angiography. The prevalence of CTO in CAD patients is estimated to be around 20–30% of all CAD patients undergoing angiography.2 CTO has an adverse impact on patient quality of life and prognosis. Currently, the management of patients with CTO is mainly with optimal medical treatment, and only a small number of patients are treated with surgery (22-26%) or percutaneous revascularization (10-22%).[3,4] The choice of medical therapy in patients with CTO is considered because of concerns about the clinical benefits of revascularization. The patient's prognosis is still debated because of the complexity of CTO-PCI with a relatively high complication rate, the need for a high amount of contrast, and the increased use of radiation; there are doubts about the myocardium viability in the CTO territory. However, the availability of CTO-PCI experts and equipment has grown as percutaneous revascularization techniques and operator expertise has progressed. This has resulted in an increase in the success rate of percutaneous revascularization in CTO from 50–70% to 80–90%, even higher by operators with higher volumes of procedures. Therefore, CTO PCI has emerged as a viable and essential therapeutic option to consider.

Compared to failed revascularization, successful CTO revascularization has been related to decreased symptoms.[5,6,7] improved left ventricular function, reduced need for coronary artery bypass graft (CABG)[7,8] and increased long-term survival.[9,10,11,12] However, other research has shown inconsistent results concerning the potential benefit of successful CTO-PCI on survival, even though many of these researches were performed before the widespread use of

*Corresponding author at: Brawijaya Cardiovascular Research Center, Department of Cardiology and Vascular Medicine, Faculty of Medicine, Universitas Brawijaya, Malang, Indonesia.
E-mail address: ratnapacasari@gmail.com (R. Pancasari).

https://doi.org/10.21776/ub.hsj.2022.003.03.5
Received 9 March 2022; Received in revised form 30 April 2022; Accepted 15 June 2022
Available online 30 July 2022

current techniques, medical equipment, and management standards.[13, 14, 15] Along with improving procedural techniques, operator expertise, and optimal medical therapy in CAD, it is essential to re-evaluate the success or failure of CTO-PCI. This study aimed to assess the difference in the success of CTO-PCI on MACE in patients with revascularized CTO compared with those who did not or failed to revascularize CTO.

2. Materials and Method

2.1 Study Design and Population

This study is an analytic observational study with a retrospective cohort design. From August 2017 to September 2020, medical record data were used to identify patients who underwent angiography with the results of at least 1 CTO. The outcome of this study was MACE, which included cardiac mortality, all-cause mortality, and rehospitalization. The target population in this study were all patients who underwent coronary angiography at dr. Saiful Anwar Hospital, Malang. The affordable population in this study were patients who underwent coronary angiography with a minimum of 1 CTO. The data were taken consecutively according to the sample selection criteria. Inclusion criteria included age >18 years and subjects who underwent coronary angiography with a minimum of 1 CTO. Exclusion criteria were patients who underwent CABG after being diagnosed with CTO, incomplete medical record data, patients who could not be followed up, and patients not taking regular medication. This study was approved by the Ethical Committee of dr. Saiful Anwar Hospital and conformed with the principles outlined in the Declaration of Helsinki.

2.2 Statistical Analysis

The data were analyzed by the Statistical Package for the Social Science (SPSS) ver 25 software to determine the differences between variables. Baseline characteristics were presented by means and standard deviation or median and interquartile range (IQR) for continuous variables and compared with the T-test, Mann-Whitney, or Wilcoxon test. Categorical variables were shown as frequencies and percentages and compared with Chi-square or Fisher's tests. The Kolmogorov-Smirnov test was used to assess the normality of the data distribution. Survival curves were performed using the Kaplan–Meier estimate and compared with the log-rank test. To estimate the effect of the independent variables on the risk of adverse clinical events, the revascularized CTO group and the non-revascularized CTO group were carried out with multivariate analysis using the logistic regression method.

3. Result

Of a total of 2165 patients who underwent angiography at Saiful Anwar Hospital, Malang, for the period August 2017–September 2020, consecutively, 578 (26.7%) patients with lesions of at least one CTO were found. Sixty-eight patients were excluded, so 510 patients were analyzed. They were divided into 2 groups, revascularized CTO group (n = 141) and non-revascularized CTO group (n = 369). Subjects included in the CTO, not revascularized group were those who failed PCI (n = 135) and those who did not do PCI (n = 234). The success rate of CTO-PCI in this study was 51% of the total CTO-PCI tried to do (141 successful out of 276 subjects). Periprocedural complications in this study, perforation of coronary artery occurred in 5 patients, dissection of femoral artery occurred in 1 patient, and non-sustained VT during surgery in 4 patients.

3.1 Baseline characteristic

The baseline clinical characteristics of subjects in the successfully revascularized CTO and non-revascularized CTO groups in this study are shown in table 1 below. It was found that 441 (86.47%) subjects were male, and 69 (13.53%) subjects were female, with the mean age of the study population being 59.2±9.2 years, where the age range was 34 – 83 years. Anthropometric data showed a mean body weight of 61.98 ± 7.47 kg, a mean height of 159.29 ± 4.87 cm, and a BMI of 24.36 ± 2.13. It appears that patients with CTO who were not revascularized compared to patients who were revascularized had a higher prevalence of history of heart failure, LM disease, multivessel disease, and three-vessel disease (41.2% vs. 19.2%, p=0.012; 15.3% vs. 3.1%, p=0.009; 69.4% vs 22.7%, p < 0.001; 56.5% vs 14.1%, p < 0.001), with a lower mean LVEF (0.49±0.06 vs 0.51±0.07, p=0.008). Additionally, age in the non-revascularized CTO group was significantly older than in the revascularized CTO group (60±9 vs. 57±8 years; p=0.007). From the angiographic data, CTO lesions were found in LAD: 151 (29.6%), LCx: 89 (17.5%), RCA: 198 (38.8%) and ≥2 vessels: 72 (14.1%). The proportion of CTO-PCI success in LAD is the highest compared to other CTO lesion sites. CTO lesions with well-developed collateral were less likely to undergo revascularization (56.1% vs. 16.3%). It also appears that of all the dominant CTO lesions with well-developed collaterals (74.5%), For the other variables, no significant difference existed between the two groups.

3.2 Follow-up of Clinical Outcomes

Follow-up of clinical outcomes in this study was carried out up to 1 year after PCI. The clinical outcomes observed in this study were MACE, including all-cause mortality, cardiac mortality, or rehospitalization (table 2). Kaplan Meier analysis was carried out to see the difference in the success of CTO revascularization to MACE, all-cause mortality, cardiac mortality, or rehospitalization, as depicted in Figure 1. The data showed that there was a significant difference between successfully revascularized CTO and non-revascularized CTO in terms of MACE (Log-rank p= 0.002) and all-cause mortality (Log-rank p= 0.027), and cardiac mortality (Log-rank p= 0.027). < 0.001) and rehospitalization (Log-rank p= 0.001).

Variables were significantly different in the baseline characteristics of subjects in the revascularized CTO group compared to those not revascularized, including age (p = 0.007), HF (p = 0.041), LM disease (p < 0.001), multivessel disease (p < 0.001), three vessel disease (p < 0.001), LVEF (p = 0.045), CTO location (p < 0.001), rentrop (p = 0.016) and collateral category (p=0.016). A multivariate analysis was conducted to determine the effect of these variables on the clinical outcome of MACE, all-cause mortality, cardiac mortality and rehospitalization (table 2).

The final result of the multivariate analysis (Table 3) showed that successful revascularization of CTO was associated with a decrease in MACE, cardiac mortality, and rehospitalization. It was a protective predictor of MACE (HR: 0.518, 95% CI 0.339–0.790, p = 0.002), cardiac mortality (HR: 0.416, 95% CI 0.243–0.712, p= 0.001), and rehospitalization (HR: 0.543, 95% CI 0.350–0.843, p= 0.006). Meanwhile, a low LVEF (LVEF 50%) in patients with CTO is a harmful predictor of MACE, all-cause mortality, cardiac mortality, and rehospitalization. In addition, the involvement of multivessel disease in patients with CTO is also a predictor of an increased incidence of rehospitalization.

Although the history of heart failure, three-vessel disease, location of CTO, and the collateral category was significantly different between the CTO groups that were successfully revascularized and the CTO groups that were not revascularized, these variables had no impact on the clinical outcome of MACE; all-cause mortality, cardiac mortality, or rehospitalization.

Table 1. Baseline characteristics of the study population.

Variable	Non-revascularized CTO	Revascularized CTO	P
Age	60±9	57±9	0.007
Gender			0.483
Male	322 (63.1)	119 (23.3)	
Female	47(9.2)	22 (4.3)	
Body weight	65 (40-89)	65 (44-100)	0.315
Height	160 (150-173)	160 (151-177)	0.610
BMI	25 (16-35)	25.39 (17-32)	0.449
Smoke	272 (53.3)	104(20.4)	1.000
Drink	23 (4.5)	6(1.2)	0.516
History of ACS	238 (46.1)	88 (17.3)	0.869
HF	210 (41.2)	94 (18.4)	0.041
Hypertension	284 (55.7)	106 (20.8)	0.757
DM	130 (25.5)	45 (8.8)	0.548
Dislipidemia	52 (10.2)	27 (5.3)	0.202
CKD	3 (0.6)	2 (0.4)	0.906
Stroke	27 (5.3)	7 (1.4)	0.451
LM disease	84 (16.5)	9 (1.8)	<0.001
Multivessel disease	354 (69.4)	116 (22.7)	<0.001
Three vessel disease	288 (56.5)	72(14.1)	<0.001
RBS	112 (74-396)	108 (78-522)	0.097
Ureum	32.0 (11.4-162.6)	29.3 (12-106.2)	0.270
Creatinin	1.07 (0.51-8.2)	1.11 (0.40-2.62)	0.192
eGFR	64.50±19.85	65.09±21.97	0.749
Total Cholesterol	175.00±27.14	189.03±28.59	0.620
TG	133.0 (49-433)	125 (49-409)	0.987
HDL	39.22±9.90	39.03±9.35	0.841
LDL	117.92±47.17	121.41±47.16	0.401
Hemoglobin	13.78±1.81	13.69±1.69	0.634
Leucocyte	8015 (3390-24390)	8360 (4640-14500)	0.976
Thrombocyte	249000 (66000-705000)	236000(154000-439000)	0.787
LVEF	0.49± 0.06	0.51±0.07	0.045
LVEF group			0.017
≤50	243 (47.6)	76 (14.9	
>50	126 (24.7)	65 (12.7)	
LVIDd	5.4(3.1-7.9)	5.53(3.8-7.1)	0.796
TAPSE	1.98±0.42	1.86±0.44	0.461
CTO location			<0.001
LAD	92 (18.0)	59 (11.6)	
LCx	74 (14.6)	15 (2.9)	
RCA	159 (31.2)	39 (7.6)	
≥ 2 CTO	44 (8.6)	28 (5.5)	
Rentrop			0.016
Rentrop 0	0 (0)	0 (0)	
Rentrop 1	83 (16.3)	47 (9.2)	
Rentrop 2	171 (33.5)	64 (12.5)	
Rentrop 3	115 (22.5)	30 (5.9)	
Collateral category			0.016
Well developed	286 (56.1)	94 (18.4)	
Poorly developed	83 (16.3)	47 (9.2)	

Note. ACS = acute coronary syndrome; BMI = body mass index; CKD = chronic kidney disease; CTO = chronic total occlusion; DM = diabetes mellitus; eGFR = estimated glomerular filtration rate; HDL = high-density lipoprotein cholesterol; HF = heart failure; LAD = left anterior descending; LCX = left circumflex; LDL = low-density lipoprotein cholesterol; LM = left main; LVEF = left ventricular ejection fraction; LVIDd = Left ventricular internal diameter in diastole; RBS = random blood sugar; RCA = right coronary artery; TAPSE tricuspid annular plane systolic excursion; TG = triglycerides.

Table 2. Clinical outcome in all patients with revascularized and non-revascularized CTO

Variable	Non-revascularized CTO (n=369)	Revascularized CTO (n=141)
MACE	169 (33.1)	42 (19.9)
All-cause mortality	105 (20.6)	28 (5.5)
cardiac mortality	105 (20.6)	19 (3.7)
rehospitalization	164 (32.2)	38 (7.5)

Note. CTO = chronic total occlusion; MACE = major adverse cardiovascular events.

Table 3. The results of multivariate analysis of variables associated with clinical outcomes.

	Variabel	P	HR (95% CI)
MACE	HF	0.845	1.040 (0.700 – 1.545)
	Three vessel disease	0.747	1.079 (0.679 – 1.714)
	Multivessel disease	0.144	1.778 (0.822 – 3.845)
	LVEF ≤ 50	<0.001	2.372 (1.612 – 3.491)
	CTO Location	0.760	0.972 (0.813 – 1.163)
	Collateral category	0.341	1.230 (0.803 – 1.882)
	Revascularization	0.002	0.518 (0.339 – 0.790)
All-cause mortality	HF	0.593	0.887 (0.573 – 1.375)
	LM disease	0.389	0.791 (0.464 – 1.348)
	LVEF ≤ 50	0.001	2.112 (1.352 – 3.298)
	Collateral category	0.167	1.410 (0.866 – 2.297)
	Revascularization	0.103	0.672 (0.417 – 1.084)
Cardiac mortality	HF	0.361	0.813 (0.522 – 1.268)
	LM disease	0.228	0.714 (0.413 – 1.235)
	Three vessel disease	0.232	0.712 (0.408 – 1.243)
	Multivessel disease	0.527	1.350 (0.533 – 3.421)
	LVEF ≤ 50	0.006	1.886 (1.196 – 2.975)
	Collateral category	0.235	1.357 (0.820 – 2.247)
	Revascularization	0.001	0.416 (0.243 – 0.712)
Rehospitalization	HF	0.646	1.097 (0.738 – 1.632)
	Three vessel disease	0.901	0.971 (0.611 – 1.542)
	Multivessel disease	0.030	2.597 (1.098 – 6.139)
	LVEF ≤ 50	0.001	1.986 (1.345 – 2.931)
	CTO Location	0.991	0.999 (0.832 – 1.199)
	Collateral category	0.415	1.196 (0.777 – 1.840)
	Revascularization	0.006	0.543 (0.350 – 0.843)

Note. ACS = acute coronary syndrome; CTO = chronic total occlusion; LM = left main; LVEF = left ventricular ejection fraction; MACE = major adverse cardiovascular events.

4. Discussion

According to this study, the prevalence of CTO in all patients undergoing angiography at Dr. Saiful Anwar, Malang, reached 26.7%. In comparison, the global prevalence of CTO ranges between 18 and 52% of all patients undergoing angiography.[3,16,17] The majority of the participants in this study were men (86.47 %), with a mean age of 59 years. In this population, the average BMI was 24.36 ± 2.13 (overweight). These findings are consistent with the results of Lee et al. (2018), who studied CTO populations in five Asian countries (Korea, India, Indonesia, Thailand, and Taiwan). According to Lee et al., men dominated the CTO population (82.5 %), with an average age of 62.5 ±10 years and an average BMI of 25.6 ± 3.5.[18]

Patients with CTO who attempted PCI accounted for 28% of all CTO patients who were obtained. This supports the previous studies, indicating that the CTO-PCI rate is still relatively low, at around 10-15% of all patients with CTO.[3,19,20] This is because CTO lesions themselves are a consideration for operators in making decisions not to perform PCI.[3,17] Additionally, the syntax study demonstrated that the presence of CTO was the strongest independent predictor of incomplete revascularization, owing to a lack of technical experience at the time.[3] Based on the Canadian registry report in 2008-2009, the majority of CTO lesions in patients with CAD who had not previously undergone CABG were not revascularized and only on medical therapy (64% of cases).

CTOs are a frequently observed clinical finding in patients undergoing coronary angiography, accounting for approximately 1 in every four patients with CAD undergoing angiography of coronary.[21] In this study, the prevalence of CTOs reached 26.7%. CTOs are difficult and complex cases to open and are a challenge for interventional cardiology.[22] However, with the development of techniques and equipment as well as operator expertise, the success rate of CTO-PCI is increasing, especially in experienced centers. The success rate of PCI in patients with CTO in this study reached 51%, 141 out of a total of 276 patients with CTO who attempted PCI. This result is lower than the success rate in the study of Lee et al. in the DECISION-CTO study in 2018, which included a population in five countries in Asia and reached 90.6%. The EuroCTO study in Europe in 2018 by Gerald et al.

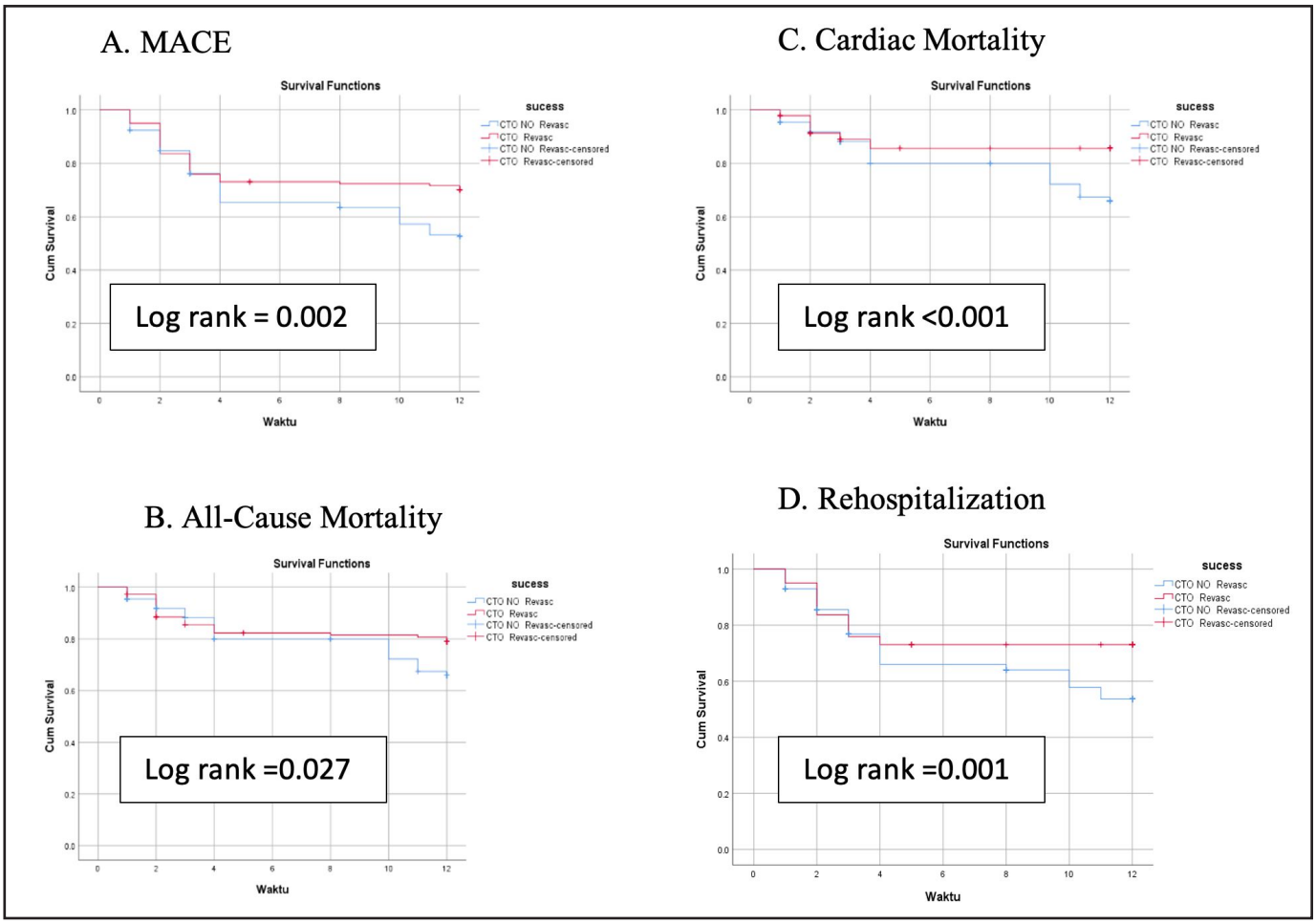

Figure 1. Kaplan Meier analysis of MACE (a), all-cause mortality (b), cardiac mortality (c), and rehospitalization (d) in revascularized (red line) and non-revascularized CTO (blue line). CTO = chronic total occlusion; MACE = major adverse cardiovascular events.

also shows a reasonably high success rate, reaching 86.6%. In the study of Suzuki et al. (2015) from the CTO-PCI registry report by experts in Japan, the success rate reached 89.9%.[23]

In addition, in this study comparing the success rates based on different locations of CTO, The success rate for CTOs in LAD showed a higher procedural success rate (11.6%) followed by RCA (7.6%), ≥ 2 CTOs (5.5%), and LCx (2.9%). However, in a multivariate analysis of clinical outcomes, the location of these CTO lesions did not affect MACE, all-cause mortality, deaths due to cardiac abnormalities, or rehospitalization. Lee et al. also demonstrated that the location of the CTO lesion affected the success of revascularization, with the highest success rate for CTO in the LAD. The LAD is the coronary artery that supplies most of the LV. Its diagonal branches supply blood to the anterior wall, and its septal branches supply blood to the anterior two-thirds of the septum. This will affect overall LV systolic function and decrease LVEF, resulting in heart failure and hypotension.[12] Consequently, clinicians generally consider trying to open CTO in LAD. This could be one of the reasons for the high rate of CTO-PCI in the LAD in the group with revascularized CTOs. CTO-PCI has the lowest success rate in LCx. Numerous studies have confirmed that revascularization is not related to clear clinical benefits.[24]

The prevalence of history of heart failure was significantly higher in the non-revascularized CTO group than in the revascularized CTO group (41.1%) vs. 19.2%, p = 0.041), with a lower mean LVEF (0.49±0.06 vs. 0.51±0.07, p = 0.045). Furthermore, in this study, a history of heart failure had no impact on the clinical outcome of MACE, all-cause mortality, cardiac mortality, or rehospitalization. Meanwhile, low LVEF in CTO patients (LVEF ≤ 50%) in this study population was related to clinical outcomes. Low LVEF (LVEF ≤ 50 %) is associated with an increase in MACE, cardiac mortality, all-cause mortality, and rehospitalization. This study supports the findings of Gong et al., who discovered that low LVEF (LVEF < 50 %) was a predictor of increased MACE (HR: 2,121, 95 % Ci 1.304–3.452, p=0.002) and cardiac mortality (HR: 4,804, 95% CI 1,895–12,177, p=0.001).

In addition, the population of this study also showed that the angiographic characteristics obtained significant differences. Where the involvement of LM disease and multivessel disease and three-vessel disease was higher in the non-revascularized CTO group than in the successfully revascularized group (16.5% vs 1.8%, p < 0.001; 69.4% vs 22.7%, p < 0.001; 56.5% vs 14.1%, p < 0.001). This could be due to operator judgment based on commonly used guidelines, which recommend CABG as the first line of treatment for lesions with multivessel disease. Numerous studies have shown that CABG is superior to PCI in terms of long-term survival in patients with multivessel disease.[25] The findings of this study indicate that the presence of multivessel disease increases the risk of rehospitalization in CTO patients but has no effect on MACE or cardiac mortality and all-cause mortality. For left main disease and three-vessel disease in this study did not affect the clinical outcome.

According to the angiographic data, the most CTO lesions were found in the RCA: 198 (38.8%), followed by LAD: 151 (29.6%), LCx: 89 (17.5%), and two vessels: 72. (14.1 %). This is consistent with

the findings of a 2016 study by McEntegart et al., who followed 481 patients with 519 CTO lesions over four years at six centers in the United Kingdom. The study described that CTO was the most common in RCA (n = 279.53.8%), followed by LAD (n = 153, 29.5%), and LCx (n = 87, 16.8%).26 According to the rentrop category observed in this study population, the proportion of CTO with well-developed collaterals (rentrop ≥ 2) was significantly higher in the non-revascularized CTO group (56.1 vs. 18.4 %, p=0.016). Collateral circulation provides alternative blood flow to obstructed vessels to prevent the risk of myocardial ischemia, resulting in the perception that CTOs with well-developed collateral circulation does not need to be recanalized.[27,28] This may be a consideration for operators to be less likely to revascularize CTO lesions with well-developed collateral circulation (rentrop ≥ 2). However, until now, the functional benefits of collateral circulation are still being debated. Several studies have shown that there is a correlation between the degree of collateral and the FFR., which indicates that even with well-developed collaterals, they are incapable of supplying sufficient blood flow to the occluded segment to prevent ischemia.[29-31]

It was demonstrated in this study that patients with CTO who were successfully revascularized with PCI had a better clinical outcome than non-revascularized CTO patients, with a lower incidence of MACE, cardiac mortality, and all-cause mortality, and rehospitalization (see figs. 5.1 – 5.4). Successful revascularization in CTO was a protective predictor of MACE (HR: 0.518, 95% CI 0.339 – 0.790, p=0.002). This finding contrasts with that of the DECISION–CTO study, which found no significant difference in MACE between CTO-PCI and non-PCI CTOs at a median follow-up of 4 years (22.3 % vs. 22.4 %, HR 1.03; 95 % CI, 0.77-1.37; P=0.86).[18] Other studies have found a positive association between successful revascularization and MACE7,[32–34]. Although the mechanisms of revascularization of CTO are unclear, reducing or eliminating myocardial ischemia may be related to a favorable clinical outcome in patients with CTO.[35] Myocardial viability in areas associated with CTOs will affect LVEF, and successful revascularization of CTO is associated with recovery of the hibernated myocardium and reduced left ventricular remodeling effects. Reduced LVEF is known to increase the risk of MACE, specifically ventricular arrhythmias, the leading cause of cardiac mortality.

Additionally, the results of this study indicated that successful revascularization of CTO affected the reduction of cardiac mortality (HR: 0.416, 95 % CI: 0.243–0.712, p=0.001). This is in contrast to the results of Guo et al. They discovered that successful CTO revascularization did not result in a reduction in the incidence of cardiac death compared to non-revascularized CTO.[33] Meanwhile, the findings of Gong et al. are consistent with those of this study, which demonstrated that revascularized CTO was superior to non-revascularized CTO in terms of cardiac death (HR: 0.239, 95 % confidence interval 0.076–0.751) and MACE (HR: 0.541, 95% CI 0.353–0.83).[12] The results of the meta-analysis of Joyal et al. are in line with the results of this study which showed that successful CTO-PCI was related to lower mortality rates compared to failed CTO-PCI (OR 0.52).[37] Park et al. also found that the CTO-PCI group had a lower rate of cardiac death after a 10-year follow-up than the medical-only group. (10.4% vs 22.3%); HR, 0.44; 95% CI, 0.32–0.59; P0.001).[38]

The success of CTO revascularization was also a protective predictor of rehospitalization (HR: 0.543, 95% CI 0.350 – 0.843, p=0.006). Successful CTO revascularization resulted in a decrease in rehospitalization. However, because the cause of rehospitalization was not differentiated in this study, the results may be biased. Several other cohort studies focused on the outcome of CTO-PCI success versus failure and indicated positive results associated with CTO-PCI success. However, the prognosis for successful CTO revascularization remains unknown, and data on the effect of successful CTO revascularization on long-term cardiovascular survival are scarce.[15,36]

This study has several research limitations, including the following: (i) it is a retrospective cohort study, which provides less evidence than a randomized controlled study. (ii) the viability of the myocardium was not evaluated. (iii), the location of the CTOs was not differentiated between proximal and distal lesions. (iv) for rehospitalization is not differentiated by cause. Thus, unknown confounding factors may still exist. Therefore, the results of this study must be interpreted rationally.

5. Conclusion

In summary, successful revascularization of CTO patients provided more clinical benefits than non-revascularized CTOs, as evidenced by lower rates of MACE, cardiac mortality, all-cause mortality, and rehospitalization during follow-up. Additionally, the presence of LVEF ≤ 0.5 was related to an increased risk of MACE, cardiac mortality, all-cause mortality, and readmission. Successful CTO revascularization was a protective predictor for MACE, cardiac mortality, and readmission. Multivessel disease in patients with CTO was a predictor of an increased risk of rehospitalization. Additional RCTs are required to examine PCI's role in treating patients with CTO.

6. Declarations

6.1. Ethics Approval and Consent to participate
This study was approved by local Institutional Review Board, and all participants have provided written informed consent prior to involvement in the study.

6.2. Consent for publication
Not applicable.

6.3. Availability of data and materials
Data used in our study were presented in the main text.

6.4. Competing interests
Not applicable.

6.5. Funding source
Not applicable.

6.6. Authors contributions
Idea/concept: RP. Design: RP, MSR. Control/supervision: MSR, AR, NK, AF. Literature search: RP, MSR. Data extraction: RP, MSR. Statistical analysis: RP, MSR. Results interpretation: RP, MSR. Critical review/discussion: MSR, AR, NK, AF. Writing the article: RP. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

6.7. Acknowledgements
We thank to Brawijaya Cardiovascular Research Center.

References

1. Di Mario C, Werner GS, Sianos G, Galassi AR, Büttner J, Dudek D, et al. European perspective in the recanalisation of chronic total occlusions (cto): Consensus document from the eurocto club. EuroInterv. 2007; 3: 30-43

2. Werner GS. The role of coronary collaterals in chronic total occlusions. Curr Cardiol Rev. 2014;10(1):57-64. doi:10.2174/1573403x10666140311123814

3. Fefer P, Knudtson ML, Cheema AN, Galbraith PD, Osherov AB, Yalonetsky S, et al. Current perspectives on coronary chronic total occlusions: the Canadian Multicenter Chronic Total Occlusions Registry. J Am Coll Cardiol 2012;59(11):991–7.

4. Ramunddal T, Hoebers LP, Henriques JP, Dworeck C, Angeras O, Odenstedt J, et al. Chronic total occlusions in Sweden—a report from the Swedish Coronary Angiography and Angioplasty Registry (SCAAR). PLoS One 2014;9(8):e103850

5. Grantham JA, Jones PG, Cannon L, Spertus JA. Quantifying the early health status benefits of successful chronic total occlusion recanalization: results from the FlowCardia's Approach to Chronic Total Occlusion Recanalization (FACTOR) Trial. Circ Cardiovasc Qual Outcomes 2010;3:284–90

6. Joyal D, Afilalo J, Rinfret S. Effectiveness of recanalization of chronic total occlusions: a systematic review and meta-analysis. Am Heart J 2010;160:179–87

7. Lee PH, Lee SW, Park HS, Kang SH, Bae BJ, Chang M, Roh JH, et al. Successful Recanalization of Native Coronary Chronic Total Occlusion Is Not Associated With Improved Long-Term Survival. JACC Cardiovasc Interv. 2016 Mar 28;9(6):530-8. doi: 10.1016/j.jcin.2015.11.016.

8. Werner GS, Surber R, Kuethe F, et al. Collaterals and the recovery of left ventricular function after recanalization of a chronic total coronary occlusion. Am Heart J 2005;149:129–37.

9. Tsai TT, Stanislawski MA, Shunk KA, Armstrong EJ, Grunwald GK, Schob AH, Valle JA, Alfonso CE, Nallamothu BK, Ho PM, Rumsfeld JS, Brilakis ES. Contemporary Incidence, Management, and Long-Term Outcomes of Percutaneous Coronary Interventions for Chronic Coronary Artery Total Occlusions: Insights From the VA CART Program. JACC Cardiovasc Interv. 2017 May 8;10(9):866-875. doi: 10.1016/j.jcin.2017.02.044.

10. Werner GS, Martin-Yuste V, Hildick-Smith D, Boudou N, Sianos G, Gelev V, et al. A randomized multicentre trial to compare revascularization with optimal medical therapy for the treatment of chronic total coronary occlusions. Eur Heart J. 2018;39:2484–93.

11. Mashayekhi K, Nührenberg TG, Toma A, Gick M, Ferenc M, Hochholzer W, et al. A randomized trial to assess regional left ventricular function after stent implantation in chronic total occlusion: the REVASC Trial. JACC Cardiovasc Interv. 2018;11:1982–91.

12. Gong X, Zhou L, Ding X, Chen H, Li H. The impact of successful chronic total occlusion percutaneous coronary intervention on long-term clinical outcomes in real world. BMC Cardiovasc Disord. 2021 Apr 15;21(1):182. doi: 10.1186/s12872-021-01976-w.

13. De Labriolle A, Bonello L, Roy P, et al. Comparison of safety, efficacy, and outcome of successful versus unsuccessful percutaneous coronary intervention in "true" chronic total occlusions. Am J Cardiol 2008;102:1175–81

14. Yamamoto E, Natsuaki M, Morimoto T, et al. Long-term outcomes after percutaneous coronary intervention for chronic total occlusion (from the CREDO-Kyoto registry cohort-2). Am J Cardiol 2013;112:767–74.

15. George S, Cockburn J, Clayton TC, et al. Longterm follow-up of elective chronic total coronary occlusion angioplasty: analysis from the U.K. Central Cardiac Audit Database. J Am Coll Cardiol 2014;64:235–43

16. Jeroudi OM, Alomar ME, Michael TT, et al. Prevalence and management of coronary chronic total occlusions in a tertiary veterans affairs hospital: CTO Prevalence and Management. Cathet Cardiovasc Intervent. 2014;84(4):637-643. doi:10.1002/ccd.25264

17. Christofferson RD, Lehmann KG, Martin GV, Every N, Caldwell JH, Kapadia SR. Effect of Chronic Total Coronary Occlusion on Treatment Strategy. The American Journal of Cardiology. 2005;95(9):1088-1091. doi:10.1016/j.amjcard.2004.12.065

18. Lee SW, Lee PH, Ahn JM, et al. Randomized Trial Evaluating Percutaneous Coronary Intervention for the Treatment of Chronic Total Occlusion: The DECISION-CTO Trial. Circulation. 2019;139(14):1674-1683. doi:10.1161/CIRCULATIONAHA.118.031313

19. Key Updates in Cardio-Nephrology from 2018: Springboard to a Bright Future. Rev Cardiovasc Med. 2018;19(1). doi:10.31083/j.rcm.2018.01.906

20. Grantham JA, Marso SP, Spertus J, House J, Holmes DR, Rutherford BD. Chronic Total Occlusion Angioplasty in the United States. JACC: Cardiovascular Interventions. 2009;2(6):479-486. doi:10.1016/j.jcin.2009.02.008

21. Grantham JA. Survival and Chronic Total Occlusion Percutaneous Coronary Intervention. JACC: Cardiovascular Interventions. 2017;10(9):876-878. doi:10.1016/j.jcin.2017.03.010

22. Stone GW, Kandzari DE, Mehran R, et al. Percutaneous Recanalization of Chronically Occluded Coronary Arteries: A Consensus Document: Part I. Circulation. 2005;112(15):2364-2372. doi:10.1161/CIRCULATIONAHA.104.481283

23. Suzuki Y, Tsuchikane E, Katoh O, et al. Outcomes of Percutaneous Coronary Interventions for Chronic Total Occlusion Performed by Highly Experienced Japanese Specialists. JACC: Cardiovascular Interventions. 2017;10(21):2144-2154. doi:10.1016/j.jcin.2017.06.024

24. 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. International Journal of Cardiology. 2017;245:77-82. doi:10.1016/j.ijcard.2017.07.098

25. Habib RH, Dimitrova KR, Badour SA, et al. CABG Versus PCI. Journal of the American College of Cardiology. 2015;66(13):1417-1427. doi:10.1016/j.jacc.2015.07.060

26. McEntegart MB, Badar AA, Ahmad FA, et al. The collateral circulation of coronary chronic total occlusions. EuroIntervention. 2016;11(14):e1596-e1603. doi:10.4244/EIJV11I14A310

27. Jamaiyar A, Juguilon C, Dong F, et al. Cardioprotection during ischemia by coronary collateral growth. American Journal of Physiology-Heart and Circulatory Physiology. 2019;316(1):H1-H9. doi:10.1152/ajpheart.00145.2018

28. Schaper W. Collateral vessels reduce mortality. European Heart Journal. 2012;33(5):564-566. doi:10.1093/eurheartj/ehr385

29. Choo GH. Collateral Circulation in Chronic Total Occlusions – an interventional perspective. CCR. 2015;11(4):277-284. doi:10.2174/1573403X11666150909112548

30. Werner GS, Surber R, Ferrari M, Fritzenwanger M, Figulla HR. The functional reserve of collaterals supplying long-term chronic total coronary occlusions in patients without prior myocardial infarction. European Heart Journal. 2006;27(20):2406-2412. doi:10.1093/eurheartj/ehl270

31. Sachdeva R, Agrawal M, Flynn SE, Werner GS, Uretsky BF. The myocardium supplied by a chronic total occlusion is a persistently ischemic zone: FFR assessment in CTO. Cathet Cardiovasc Intervent. 2014;83(1):9-16. doi:10.1002/ccd.25001

32. Jang WJ, Yang JH, Choi SH, et al. Long-Term Survival Benefit of Revascularization Compared With Medical Therapy in Patients With Coronary Chronic Total Occlusion and Well-Developed Collateral Circulation. JACC: Cardiovascular Interventions. 2015;8(2):271-279. doi:10.1016/j.jcin.2014.10.010

33. Guo L, Zhang X, Lv H, et al. Long-Term Outcomes of Successful Revascularization for Patients With Coronary Chronic Total Occlusions: A Report of 1,655 Patients. Front Cardiovasc Med. 2020;7:116. doi:10.3389/fcvm.2020.00116

34. Yang JH, Kim BS, Jang WJ, et al. Optimal Medical Therapy vs. Percutaneous Coronary Intervention for Patients With Coronary

Chronic Total Occlusion – A Propensity-Matched Analysis –. Circ J. 2016;80(1):211-217. doi:10.1253/circj.CJ-15-0673

35. Shaw LJ, Berman DS, Maron DJ, et al. Optimal Medical Therapy With or Without Percutaneous Coronary Intervention to Reduce Ischemic Burden: Results From the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) Trial Nuclear Substudy. Circulation. 2008;117(10):1283-1291. doi:10.1161/CIRCULATIONAHA.107.743963

36. Jones DA, Weerackody R, Rathod K, et al. Successful Recanalization of Chronic Total Occlusions Is Associated With Improved Long-Term Survival. JACC: Cardiovascular Interventions. 2012;5(4):380-388. doi:10.1016/j.jcin.2012.01.012

37. Joyal D, Afilalo J, Rinfret S. Effectiveness of recanalization of chronic total occlusions: A systematic review and meta-analysis. American Heart Journal. 2010;160(1):179-187. doi:10.1016/j.ahj.2010.04.015

38. Park TK, Lee SH, Choi KH, et al. Late Survival Benefit of Percutaneous Coronary Intervention Compared With Medical Therapy in Patients With Coronary Chronic Total Occlusion: A 10-Year Follow-Up Study. :18.