P-ISSN 2586-9000
E-ISSN 2586-9027
Homepage : https://tci-thaijo.org/index.php/SciTechAsia
Science & Technology Asia
Vol.27 No.4 October - December 2022
Page: [86-94]
Original research article

Cardiovascular Risk Factors Predicted MACE Outcomes in Chronic Total Occlusion Patients Undergoing Percutaneous Coronary Intervention at Thammasat University Hospital

Kan Witoonchart*, Pisit Hutayanon

Department of Cardiology, Faculty of Medicine, Thammasat University Hospital, Pathum Thani 12120, Thailand

Received 20 June 2022; Received in revised form 4 December 2022;
Accepted 7 December 2022; Available online 31 December 2022

ABSTRACT

Revascularization of chronic total occlusion (CTO) lesions by percutaneous coronary intervention (PCI) has high difficulty and associated morbidity and mortality. The benefits of successful CTO-PCI and what factors confer poor outcomes are not well studied. There have been some large-scale studies on the efficacy of recanalising CTO lesions but most were not done in Thailand. This study aimed to find cardiovascular risk factors and their characteristics which predict major adverse cardiovascular and cerebral event (MACE) outcomes in relation to PCI of CTO lesions and investigate whether successful CTO-PCI can affect MACE outcomes. In total, 84 patients were consecutively enrolled. The majority of the study population was male (64.3%) with a mean age of 65.3±10.8 years old. Eighty-five percent had multivessel disease (syntax score 23.8± 7.6) and most of the CTO lesions were complex (CTO J-score 2.7 ± 0.8). There were 60 cases (71.4%) of successful CTO-PCI. The overall MACE rate was 32.1%. After a 1-year follow-up, the successful CTO-PCI group showed a lower rate of MACE outcomes than the failed PCI group on all parameters. From this, it is concluded that CTO-PCI success is a predictor of lower MACE outcome rates. Predictors of MACE outcomes were reduced LVEF < 40%, CTO of left anterior descending artery, previous stroke and a CTO J-score of more than 3.

Keywords: Chronic total occlusion; CTO; MACE; Percutaneous coronary intervention; PCI

***Corresponding author:** dr.kanwit@gmail.com

1. Introduction

Chronic total occlusion (CTO) is defined as the total occlusion of coronary blood flow on angiography (Thrombolysis in Myocardial Infarction, TIMI 0) which persists for more than 3 months [1]. Its incidence varies depending on registry but is generally reported to be up to about 25% of all patients undergoing angiography [2]. Generally, CTO lesions are difficult, expensive and time-consuming to attempt recanalization via percutaneous coronary intervention (PCI). The most current set of guidelines on recanalization of CTO lesions by PCI was published in the European Society of Cardiology (ESC) 2018 guidelines on myocardial revascularization, which gave a class IIa recommendation that CTO-PCI should be considered in patients with angina resistant to medical therapy or who have a large area of ischemia in the territory of the occluded vessel [3].

With recent advancements of stent technology, medications and techniques in interventional cardiology, attempts to recanalise CTO lesions are more common with varying degrees of success and outcomes. However, there has not been a lot of strong evidence to support the long-term benefits of CTO-PCI yet, as there are not many large prospective modern trials investigating these issues directly. Most of the data are from aggregate findings of smaller observational studies and these often found equivocal outcomes on major adverse cardiovascular and cerebral event (MACE) endpoints. Therefore, the interactions between successful CTO-PCI, MACE and cardiovascular risk factors are not well established.

There is no large multi-center CTO registry in Thailand and CTO-PCI outcomes have never been investigated before at Thammasat University Hospital (TUH). The aim of this study was to find cardiovascular risk factors and their characteristics which predict MACE outcomes in relation to PCI of CTO lesions as well as to investigate whether a successful CTO-PCI can affect MACE outcomes.

2. Materials and Methods

2.1 Study population

This study was a single center, non-randomized retrospective cohort study. All patients who met the criteria undergoing PCI to CTO lesions at TUH from January1st, 2014 to December 31st, 2016 were consecutively enrolled into this study. Most of the data were collected from the TUH cardiac catheterization laboratory (cath lab) database using a pre-existing CTO patient database from 2015. For data prior to 2015, we searched for equipment commonly used in CTO-PCI procedures such as Asahi Gaia® wire which generated a list of patients and these patients were then verified for true CTO and assessed according to our inclusion/exclusion criteria. Patient inclusion criteria were age over 18 years old and received a coronary angiogram at the TUH cath lab. Patients must have had at least 1 CTO lesion detected via coronary angiogram, with clear documentation or records kept on the angiographic cine electronic system (Xcelera, Philips Healthcare). PCI must have been attempted on the CTO lesion, all successful and unsuccessful procedures were included in this study. The decision to proceed with PCI was decided by the operators at the time of the procedure. The patients must also have had accessible medical files, whether electronic or physical, and must have had a follow-up in the outpatient clinic at least once within a one-year period following the procedure. Patients were excluded if they did not receive PCI to the CTO lesions or if they received operations such as a coronary artery bypass graft to correct CTO lesions during the follow-up period.

2.2 Definitions and endpoints

A successful CTO-PCI was defined as a CTO lesion corrected by a PCI procedure with a final angiographic result of TIMI 3. A

failed CTO-PCI was defined as when the PCI procedure was abandoned, and the lesions were not corrected. Complete revascularization was defined as when all the significant coronary artery lesions were revascularized by PCI. MACE outcomes included all-cause mortality, congestive heart failure (CHF), cardiovascular death (death from any cardiac-related cause such as arrhythmia, CHF, or myocardial infarction), myocardial infarction and stroke/transient ischemic attack (TIA). CTO J-score is a validated scoring tool which is used to predict the success of CTO-PCI procedures based on difficulty and complexity of the lesion: entry shape, calcification, bending and occlusion length [4, 5]. Contrast-induced nephropathy (CIN) was defined as a 25% increase in serum creatinine from baseline or a 0.5 mg/dL (44 μmol/L) increase in absolute value within 72 hours after the index procedure. Its incidence was collected in view of CTO-PCI procedures often requiring a large amount of contrast; however, this parameter was not part of the main MACE categorization and its data was designed to be used as a possible marker of complicated PCI. Clinical follow-up data was collected from outpatient files and an electronic data record system. The follow-up period was 1 year from the date of the procedure.

2.3 Statistical analysis

Categorical variables are expressed as frequency and percentage; continuous variables are expressed as mean and standard deviation. Univariable and multivariable Cox regression analysis were used to determine independent predictors of MACE outcomes. Kaplan-Meier survival curve analysis of MACE was used to compare successful and failed PCI groups. *P*-values of less than 0.05 were considered statistically significant. Data were analysed using STATA software.

3. Results and Discussion

3.1 Patient and procedural characteristics

A total of 84 patients met the criteria and were included in this study. The majority of patients were male (64.3%) with a mean age of 65.3±10.8 years and a BMI of 25±0.5 (overweight). About half of the population had previous myocardial infarction (50%) and diabetes mellitus (47.6%), and most had dyslipidemia (71.4%). The population had a mildly reduced left ventricular ejection fraction (LVEF 49.7%±15.2) and were not at the ESC 2019 recommended target LDL cholesterol level of less than 70 mg/dL for the high-risk group, or less than 55 mg/Dl for the very-high-risk group of (95.9 ± 33.1) [6] (Table 1). Multivessel disease was found in 85% of all cases (syntax score 23.8±7.6). Most of the CTO lesions in our study were difficult to very-difficult lesions (CTO J-score 2.7 ± 0.8). There were 60 cases (71.4%) of successful CTO-PCI procedures. Antegrade approach was the main technique used (85.7%) and the average stent length was 46.8 ± 34.3 mm (Table 2).

3.2 Clinical follow up

The overall MACE rate was 32.1%. In the successful CTO-PCI group, MACE outcome prevalence was lower than in the failed PCI group (23.3% vs. 54.2% respectively, $p = 0.007$) (Table 3). There was 1 incident of new myocardial infarction in the failed PCI group. There were no new incidences of stroke in either group.

When the data was stratified into complete and incomplete revascularization, MACE occurrence was also higher in the incomplete revascularized group (17.2% vs 40% respectively, $p = 0.49$) (Table 4). After adjusting for univariate and multivariate Cox regression analysis, significant predictors of MACE outcomes were a reduced LVEF of less than 40% ($p = 0.003$), previous history of myocardial infarction ($p = 0.017$), previous stroke ($p = 0.003$) and a CTO J-score of more than 3 ($p = 0.005$) (Fig 5). Kaplan-Meier survival curve analysis of

MACE outcomes and death between successful PCI and failed PCI groups showed that most of the MACE events occurred early on after the index procedure and the successful PCI group had a higher survival rate and were less likely to have MACE outcomes (Fig. 1).

Table 1. Baseline characteristics. Data are presented as number of patients, percentages are shown in brackets (%), mean ± SD.

	All CTO (n = 84)	Successful PCI (n = 60)	Failed PCI (n = 24)	p-value
Clinical characteristic				
Age	65.3 ± 10.8	64.9 ± 10.2	66.1 ± 12.4	0.64
Male gender	54 (64.3)	41 (68.3)	13 (54.2)	0.31
BMI	25 ± 0.5	25.7 ± 0.6	25.3 ± 0.9	0.74
Hypertension	58 (69)	39 (65)	19 (79.2)	0.3
Diabetes mellitus	40 (47.6)	29 (48.3)	11 (45.8)	0.81
Dyslipidemia	60 (71.4)	44 (73.3)	15 (65.2)	
Total cholesterol, mean ± SD	166.6 ± 40.2	167.3 ± 40.5	164.9 ± 40.3	0.8
LDL, mean ± SD	95.9 ± 33.1	96.9 ± 34.1	93.6 ± 31.2	0.68
HDL, mean ± SD	44.6 ± 11.3	43.6 ± 11	47 ± 12	0.22
LVEF , mean ± SD	49.7 ± 15.2	49.8 ± 15.4	49.5 ± 15	0.93
GFR	61 ± 29.6	64 ± 30	54 ± 27.8	0.16
Previous MI	42 (50)	30 (50)	12 (50)	1
Previous stroke	10 (12)	7 (11.7)	3 (12.5)	1
Previous CABG	2 (2.4)	0	2 (8.3)	0.08

Table 2. Angiographic and Procedural data. Percentages are shown in brackets (%).

	All CTO (n = 84)	Successful PCI (n = 60)	Failed PCI (n = 24)	p-value
Angiographic characteristics				
Triple vessel disease	54 (64.3)	39 (65)	15 (62.5)	1
Double vessesl disease	18 (21.4)	14 (23.3)	4 (16.7)	0.57
Single vessel disease	12 (14.3)	7 (11.7)	5 (20.8)	0.31
CTO LAD	21 (25)	14 (23.3)	7 (29.2)	0.59
CTO LCX	14 (16.7)	10 (16.7)	4 (16.7)	1
CTO RCA	47 (56)	35 (58.3)	12 (50)	0.63
CTO J-Score	2.7± 0.8	2.5 ± 0.9	3 ± 0.7	0.03
Syntax Score	23.8 ± 7.6	23 ± 6.2	26 ± 10.1	0.09
Antegrade approach	72 (85.7)	52 (86.7)	20 (83.3)	0.73
No. of stent	1.7 ± 1.1	2.2 ± 0.7		0.73
Total stent length	46.8 ± 34.3	60.2 ± 26.5		
Procedual characteristics				
Procedural time	154.6 ± 72.6	156.2 ± 68.2	150.6 ± 83.8	0.75
Fluoroscopic time	60.6 ± 37.7	57.5 ± 33.2	68.5 ± 47.1	0.23
Total contrast usage (ml)	187 ± 84.6	190.4 ± 84.2	178.8 ± 86.7	0.57
Complete revascularization	26 (33.8)	29 (48.3)		
Successful CTO	54 (70.1)			

Table 3. MACE outcomes. Percentages are shown in brackets (%).

	All CTO (n = 84)	Successful PCI (n = 60)	Failed PCI (n = 24)	p-value
Outcome				
MACE Incident	27 (32.1)	14 (23.3)	13 (54.2)	0.007
All-Cause mortality	10 (11.9)	6 (10)	4 (16.7)	0.38
Cardiac Death	3 (3.6)	2 (3.3)	1 (4.2)	0.68
CHF	17 (20.2)	8 (13.3)	9 (37.5)	0.02
Cerebrovascular Death	0	0	0	
Stroke/TIA	2 (2.4)	1 (1.7)	1 (4.2)	0.49
CIN	4 (4.8)	3 (5)	1 (4.2)	0.66

Table 4. MACE outcomes by complete and incomplete revascularization. Data are presented as number of patients (%).

Outcome		Complete Revascularised n = 29	Incomplete Revascularised n = 55	p-value
MACE Incident		5 (17.2)	22 (40)	0.49
All-Cause mortality		3 (10.3)	7 (12.7)	0.14
Cardiac Death		0	3 (5.5)	N/A
CHF		2 (6.9)	15 (27.3)	0.5
MI		0	1 (1.8)	N/A
Cerebrovascular death		0	0	N/A
Stroke/TIA		0	2 (3.6)	N/A
CIN		0	4 (7.3)	N/A

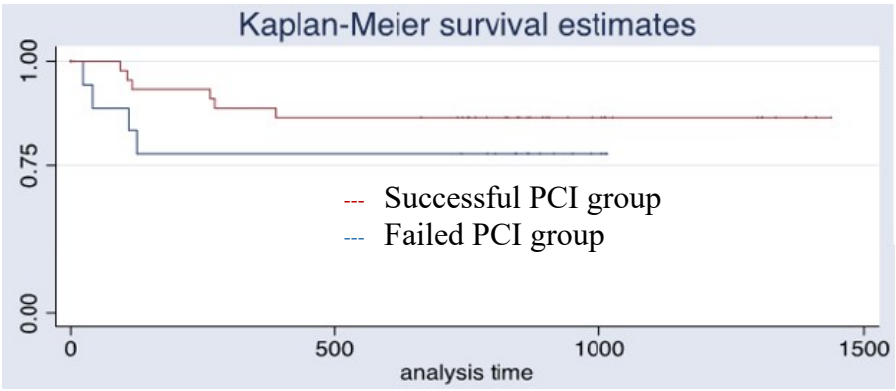

Fig.1. Kaplan-Meier survival analysis for death.

Table 5. Multivariable Cox regression analysis hazard ratio of MACE by risk factors. mHR for multivariate hazard ratio. CI for confidence interval.

Risks		mHR	95% CI of Hazard Ratio	p-value
Gender	Male	1.24	0.04-3.79	0.71
BMI	<20	0.32	0.04- 2.77	0.3
	20-25	1		
	>25	0.73	0.24- 2.21	0.58
LVEF	<40	4.88	1.70-13.99	0.003
	>=40	1		
DM	Yes	1.91	0.60-6.04	0.27
	No	1	-	
HT	Yes	0.85	0.25-2.94	0.87
	No	1	-	
DLP	Yes	0.27	0.08-0.88	0.03
	No	1	-	
Previous MI	Yes	5.04	1.34-18.93	0.017
	No	1	-	
Stroke	Yes	8.1	1.99-32.98	0.003
	No	1	-	
CABG	Yes	2.36	0.21-7.12	0.49
	No	1	-	
Vessel	SVD	1	-	
	DVD	1.96	0.34-11.22	0.45
	TVD	0.82	0.15- 4.58	0.82
CTO site	RCA	1	-	
	LAD	2.77	0.59-12.86	0.19
	LCx	1.42	0.25-7.99	0.69
Jscore	<2	1	-	
	>=3	10.65	2.05-55.25	0.005
Syntax	0-22	1	-	
	23-32	0.56	0.11 -2.94	0.49
	>32	1.16	0.13-10.61	0.89
Approach	Antegrade	1		
	Retrograde	0.43	0.94-1.98	0.281

3.4 Discussion

The patients in our cohort were considered to be a high-risk population due to a high prevalence of cardiovascular co-morbidities with complex CTO lesions based on CTO J-Scores. Our overall success rate of complex CTO-PCI lesions was 71.4%. MACE outcomes were higher in the failed PCI group for all MACE parameters. This was largely driven by CHF in both groups. For all-cause mortality, the main causes of death were from sepsis and cancer, which can be difficult or, in some instances, impossible to avoid. However, this parameter was still relatively higher in the failed PCI group, which may be related to prolonged or more frequent hospitalization which led to an increase in hospital-acquired infection. When we stratified our data by the completeness of revascularization, the complete revascularization group (which included successful PCI patients) showed fewer MACE outcomes than the incomplete group. However, due to the small number of incidences, these results were not statistically significant and will require further study to confirm the significance of this relationship. Despite the statistical outcomes, it was interesting to see that most of the MACE subcategories such as cardiac death, myocardial infarction, stroke and CIN did not occur at all in the complete revascularization group. Perhaps this showed a possible benefit of complete revascularization in this patient group - better perfused organs were less likely to develop complications. For example, increased renal perfusion led to better contrast filtration from the body and well perfused myocardium were less likely to develop ischemia, CHF and cardiac death.

Due to the difficulty, high morbidity and mortality of CTO-PCI, these lesions are often attempted only if there are strong indications such as symptomatic patients and viable myocardium as suggested by recent revascularization guidelines [3]. Our results may be used as an additional tool to risk stratify and weigh the risks and benefits for patients before proceeding with the procedure. This study found that significant independent predictors of MACE outcomes for CTO-PCI procedures were a LVEF of less than 40%, previous myocardial infarction, previous stroke/TIA and a CTO J-Score of more than 3. Most of these predictors such as previous myocardial infarction, stroke and a high CTO J-score are not modifiable by interventions. They can be seen as markers of high risk and high disease burden and therefore, can indicate a higher likelihood of MACE outcomes. However, for a low LVEF, guideline directed optimal medical therapy (GDMT) and revascularization of diseased vessels (with viable myocardium) have been extensively

studied in patients with heart failure of various causes, including ischemia, and are known to be able to improve CHF outcomes [7, 9] and LVEF [10-12]. Therefore, GDMT and revascularization of other diseased coronary arteries should be done to improve LVEF prior to CTO-PCI, in order to minimize the risk of MACE outcomes.

There have been many large PCI studies that have done CTO subgroup analysis but not many studies that specifically looked at CTO and its outcome predictors. Most of these were observational studies focusing on the success of revascularization of CTO as a good outcome predictor. Joyal et al. (2010) [13] conducted one of the first large meta-analyses of CTO-PCI, containing clinical data from the 1980s to 2006. Their main focus was on the outcome of CTO recanalization when compared to medical therapy. In this meta-analysis, the overall PCI success rate was 69% and the successful CTO-PCI group had a 44% mortality reduction but no difference in MACE outcomes. More recently, Christakopoulos et al. (2015) [14] carried out one of the largest meta-analyses to date, which included in it more recent studies which used modern stents and PCI techniques. This meta-analysis, which included 28,486 patients, found that the overall procedure success rate was 71% and successful CTO-PCI was associated with a significantly lower mortality rate and fewer MACE outcomes. These findings are also very similar to what was found in our study. Our procedural success rate was 71.4% with a significant reduction in MACE outcomes in the successful CTO-PCI group.

Other studies have looked at certain aspects of cardiovascular risk factors as predictors of CTO-PCI survival. Godino et al. (2013) [15] carried out a study on predictors of cardiac death in CTO cases without revascularization or failed revascularization. They found that the mortality rate was significantly higher in the non-revascularized group; significant independent predictors for cardiac death were a low LVEF (less than 35%), chronic renal failure, insulin-dependent DM and triple vessel disease. Our study also found that low a LVEF of less than 40% is a significant MACE predictor. However, there are some studies that contrast with the results we found, such as a Swedish Coronary Angiography and Angioplasty Registry (SCAAR) study [16]. When subgroup analysis for CTO was done, they found that CTO is a prognostic marker for cardiovascular events and increased mortality; however, diabetes did not have further adverse effects on outcomes. SYNTAX score was also found to be an independent predictor of MACE outcomes in CTO-PCI [17], however, this factor was not statistically significant in our study.

DECISION-CTO is the latest, largest prospective, randomized controlled CTO-PCI trial which compared optimal medical therapy to CTO-PCI [18]. The study found that CTO-PCI was feasible with a very high success rate of up to 90.6%. However, there was no significant difference in the incidence of MACE outcomes in the CTO-PCI group versus the no CTO-PCI group (medical therapy group).

There were some similarities between our population and the population in DECISION-CTO, such as similar SYNTAX scores (20.8 vs 23.8±7.6 in our study) and CTO J-scores (2.1 vs 2.7±0.8 respectively). However, our population was considered to be at a higher risk with a lower LVEF (49.7%±15.2 vs 57.2±9.8% respectively), and had a much higher prevalence of previous myocardial infarction (50% vs 10.9%, respectively). Therefore, the findings from DECISION-CTO may not be directly applicable to our group and our findings may be more applicable to higher risk populations.

From the findings of our study and those gathered from similar studies, we could surmise that in many cases, it may be better to revascularize CTO lesions by PCI and the

MACE outcome rate may improve if the procedures are successful. However, most of these studies were observational and retrospective, such as in our case, which could not provide strong enough evidence to conclusively recommend PCI for all CTO cases.

It is clear that there are still conflicting data on the benefits of CTO-PCI as it is still a developing field of PCI and large studies are still ongoing. Currently, there are not many studies available on specific cardiovascular risk factors as predictors of CTO-PCI outcome. Furthermore, patient populations with CTO are often heterogeneous, with varying degrees of complexity of CTO lesions and multiple interacting cardiovascular risks, which made the analysis on the effects of CTO-PCI not as straight forward as other coronary lesions.

Our study contribution to this field is that certain cardiovascular risk factors and patient characteristics can significantly contribute to MACE outcomes and successful CTO-PCI can reduce the risk of developing MACE outcomes.

3.5 Limitations

This was a small, single-center retrospective study, therefore, it is possible that there may have been confounding factors and biases affecting the results. Our adverse event rates were low and as such, we included CV death and all-cause mortality in our MACE outcomes. However, it is worth noting that our findings were similar to many of the larger studies, as well as several large meta-analyses. For this first stage, retrospective studies such as this one are suitable for the purpose of investigating the current state of CTO-PCI in Thailand. It can be considered as a pilot study since no similar study has been done before at our institution or in Thailand. However, future studies will need to incorporate larger cohorts, prospective data collection and longer follow-up periods. With these changes, other risk factors and procedural characteristics may become statistically significant, or the opposite may occur. Thus, it is vital to conduct further research in order to confirm our findings and gain more knowledge on CTO-PCI and its outcomes.

4. Conclusions

CTO lesions are complicated and can lead to many adverse cardiovascular outcomes. Cardiovascular risk factors and predictors of MACE outcomes were having a LVEF of less than 40%, CTO of LAD, previous stroke/TIA and a CTO J-Score of over 3. Successful CTO-PCI can reduce the risk of developing MACE outcomes within a 1-year post-procedure time period.

References

[1] Di Mario C, Werner GS, Sianos G, Galassi AR, Buttner J, Dudek D, et al. European perspective in the recanalisation of Chronic Total Occlusions (CTO): consensus document from the EuroCTO Club. EuroIntervention. 2007;3:30-43.

[2] Christofferson RD, Lehmann KG, Martin GV, Every N, Caldwell JH, Kapadia SR. Effect of chronic total coronary occlusion on treatment strategy. Am J Cardiol. 2005;95:1088-91.

[3] Neumann FJ, Sousa-Uva M, Ahlsson A, Alfonso F, Banning AP, Benedetto U, et al. 2018 ESC/EACTS Guidelines on myocardial revascularization. Eur Heart J. 2019;40:87-165.

[4] Christopoulos G, Wyman RM, Alaswad K, Karmpaliotis D, Lombardi W, Grantham JA, et al. Clinical Utility of the Japan-Chronic Total Occlusion Score in Coronary Chronic Total Occlusion Interventions: Results from a Multicenter Registry. Circ Cardiovasc Interv. 2015;8:e002171.

[5] Fujino A, Otsuji S, Hasegawa K, Arita T, Takiuchi S, Fujii K, et al. Accuracy of J-CTO Score Derived From Computed Tomography Versus Angiography to

Predict Successful Percutaneous Coronary Intervention. JACC Cardiovasc Imaging. 2018;11:209-17.

[6] 2019 ESC/EAS guidelines for the management of dyslipidaemias: Lipid modification to reduce cardiovascular risk. Atherosclerosis. 2019;290:140-205.

[7] Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JG, Coats AJ, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. Eur J Heart Fail. 2016;18:891-975.

[8] StephanWindecker, Kolh P, Alfonso F, Collet JP, Cremer J, Falk V, et al. 2014 ESC/EACTS guidelines on myocardial revascularization. Rev Esp Cardiol (Engl Ed). 2015;68:144.

[9] Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE, Jr., Colvin MM, et al. 2017 ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. Circulation. 2017;136:e137-e61.

[10] Cleland JGF, Bunting KV, Flather MD, Altman DG, Holmes J, Coats AJS, et al. Beta-blockers for heart failure with reduced, mid-range, and preserved ejection fraction: an individual patient-level analysis of double-blind randomized trials. Eur Heart J. 2018;39:26-35.

[11] Lee YH, Chiou WR, Hsu CY, Lin PL, Liang HW, Chung FP, et al. Different left ventricular remodeling patterns and clinical outcomes between non-ischemic and ischemic etiologies in heart failure patients receiving sacubitril/valsartan treatment. Eur Heart J Cardiovasc Pharmacother. 2020.

[12] Peng D, Liu JH. Improvement of LVEF in patients with HFrEF with coronary heart disease after revascularization-A real-world study. J Interv Cardiol. 2018;31:731-6.

[13] Joyal D, Afilalo J, Rinfret S. Effectiveness of recanalization of chronic total occlusions: a systematic review and meta-analysis. Am Heart J. 2010;160:17987.

[14] Christakopoulos GE, Christopoulos G, Carlino M, Jeroudi OM, Roesle M, Rangan BV, et al. Meta-analysis of clinical outcomes of patients who underwent percutaneous coronary interventions for chronic total occlusions. Am J Cardiol. 2015;115:1367-75.

[15] Godino C, Bassanelli G, Economou FI, Takagi K, Ancona M, Galaverna S, et al. Predictors of cardiac death in patients with coronary chronic total occlusion not revascularized by PCI. International Journal of Cardiology. 2013;168:1402-9.

[16] Råmunddal T, Hoebers L, Henriques JPS, Dworeck C, Angerås 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.

[17] Nagashima Y, Iijima R, Nakamura M, Sugi K. Utility of the SYNTAX score in predicting outcomes after coronary intervention for chronic total occlusion. Herz. 2015;40:1090-6.

[18] Lee SW, Lee PH, Ahn JM, Park DW, Yun SC, Han S, et al. Randomized Trial Evaluating Percutaneous Coronary Intervention for the Treatment of Chronic Total Occlusion. Circulation. 2019;139:1674-83.