OUTCOME OF CONCOMITANT TREATMENT OF NON-CHRONIC TOTAL OCCLUSION LESION AT THE TIME OF CHRONIC TOTAL OCCLUSION INTERVENTION

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ABSTRACT

Objective: To study the outcome of concomitant treatment of a non-chronic total occlusion lesion at the time of chronic total occlusion intervention at AFIC-NIHD.

Study Design: Observational study.

Place and Duration of Study: Armed Forces Institute of Cardiology/National Institute of Heart Diseases Rawalpindi, from Nov 2020 to Apr 2021.

Methodology: A total of 171 patients presenting with chronic total coronary occlusion lesions were enrolled in study. Patients were randomized into two groups, group one with chronic total coronary occlusion only group and group two with combined group (chronic total coronary occlusion with non- chronic total coronary occlusion lesion) after coronary angiogram. The primary end-point assessed was angiographic (<30% residual diameter stenosis), clinical and procedural outcomes (TIMI grade flow, major adverse cardiac events (MACE) including death, stent thrombosis (ST), MI, repeated symptoms requiring repeat target vessel revascularization (TVR) either PCI or CABG, pericardial tamponade requiring pericardiocentesis or surgery and stroke) in patients with only chronic total coronary occlusion PCI group and combined group (chronic total coronary occlusion with non- chronic total coronary occlusion).

Results: A total of 171 patients with chronic total coronary occlusion lesions were enrolled in the study. The mean age was 60.61 ± 9.68. There was no significant difference in perihospital complications, MACE in the two groups. However, there was increased contrast volume and radiation used in the combined group.

Conclusion: Combined chronic total coronary occlusion and non- chronic total coronary occlusion lesion PCI can be done in a single procedural setting with acceptable complications and high success rate.

Keywords: Concomitant treatment, Chronic total occlusion, Intervention, Lesion, PCI.

INTRODUCTION

Chronic total coronary occlusion (CTO) percutaneous coronary intervention (PCI) remains a major technical challenge for interventional cardiologists. Someolder CTOs have traditionally been associated with lower CTO PCI success rates due to longer lesion length[1], and higher degree of calcification[2,3]. However with recent advancements made in techniques that safely and more predictably overcome this essential challenge[4]. CTO PCIs are time consuming, requires large volume of contrast and radiation dose[5,6], and experienced operators with advanced CTO specific equipments in high volume PCI centers.

Sometimes patients with CTO lesions may present with acute coronary syndrome (ACS). During primary percutaneous coronary intervention (PPCI), a concurrent CTO in a non-infarct-related artery is (accidentally) found in about 10-15% of patients with ST-segment elevation myocardial infarction (STEMI)[7]. The presence of this concurrent CTO is a strong predictor for both short-term and long-term mortality[8]. The adverse impact of a CTO in patients with STEMI is present in an early phase after PPCI and remains consistently even after excluding the early deaths[9]. In elective setting, long-term benefits of CTO-PCI have been suggested: improved survival, reduced need for CABG and a lower incidence of future MI[10]. Sometimes if patients characteristics allow then CTO lesion is also treated in the same PPCI setting to improve long-term survival.

CTO-PCI is a complex and always a challenging procedure, needs proper treatment plan and strategy, trained catheterization laboratory staff. Recent advancements in guidewire technology have improved the technical success of approaching difficult CTOs, such as occlusions that are calcified, long, and/or old. Performing CTO-PCI depends on the patient's clinical presentation and risk benefit ratio and not the patient's anatomy. Also on lesion characteristics: duration that the vessel has been closed, lesion length, presence or absence of antegrade flow, presence or absence of a stump, presence or absence of bridging collaterals.

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CTO-PCI success also depends on operators expertise in CTOs. Experienced operators using contemporary CTO PCI techniques can be expected to be successful in the great majority of patients (80-90%), even among the most complex CTO lesions. Successful CTO PCI can provide numerous benefits: improve symptoms, such as angina and dyspnea[11], decrease the need for CABG surgery, decrease the need for antianginal medications, reduce mortality[12], (compared to patients with failed CTO PCI), improve left ventricular function and improve tolerance of ACS that may occur in the future.

Many patients with CTO lesions have non-CTO lesions that requires treatment too. Weather these lesions are treatedin staged procedure or concomitant with CTO PCI in the same procedural setting remains controversal[13]. Mostly non-CTO lesions are treated as staged procedureto prevent contrast and radiation induced complications and fatigue of the operator. But sometimes non-CTO lesion is treated before attempting CTO PCI to prevent donor vessel ischemia, for example in retrograde PCI and dual injection CTO procedures. Performing non-CTO PCI before CTO PCI in a symptomatic patient, enables the treating physician to assess clinical response and the need for further intervention of the more complex lesions. Performing combined CTO lesion with non-CTO lesion has many effects: reduces number of procedures, reduces repeated hospital admissionsand ameliorates psychological effects of multiple procedures, economic benefits of doing combined procedure and reduced risk of complications with multiple procedures. We studied the clinical, angiographic and periprocedural outcomes of performing combined non-CTO lesion with CTO lesion intervention at AFIC/NIHD Rawalpindi.

METHODOLOGY

A total 171 patients enrolled in study between November 2020 and April 2021 admitted in tertiary care hospital, Armed Forces Institute of Cardiology/ National Institute of Heart Diseases Rawalpindi (AFIC/NIHD RWP).

Data collected from the designed questionnaire/ proforma. All participants satisfying inclusion criteria were recruited in the study group.It is an observational study, baseline demographics, risk factors and procedural details collected for all patients who underwent CTO-PCI either combined CTO with non-CTO lesion PCI or CTO only PCI, during the study duration. For all patients clinical characteristics recorded were, age, gender, pre and post procedure serum creatinine and clinical risk factors including diabetes mellitus, hypertension and smoking. Angiographic details including TIMI grade flow and residual stenosis collected for all patients. Procedural outcomes including MACE also calculated for all enrolled patients.

The outcomes assessed in this study included angiographic (<30% residual diameter stenosis, thrombolysis in Myocardial Infarction (TIMI) grade flow >3), clinical characteristics (age, gender, risk factors, comorbid conditions, clinical presentation either ACS or CCS, baseline labs, type of procedure weather ad hoc or planned elective PCI) and procedural outcomes (major adverse cardiac events (MACE) including death, stent thrombosis (ST), myocardial infarction (MI) repeated symptoms requiring repeat target vessel revascularization (TVR) either PCI or CABG, pericardial tamponade requiring pericardiocentesis or surgery and stroke) for both the enrolled groups. Conditions in which non-CTO PCI done with CTO intervention included 1) donor vessel ischemiaespecially in retrograde procedures 2) donor vessel complications and 3) for the purpose of complete revascularization, 4) cost effectiveness of single procedure versus multiple staged procedures, 5) to decrease risks with repeated multiple procedures.

Coronary CTO is defined as a 100 percent occlusion of a coronary artery with TIMI-0 flow for more than three months (based on angiography or onset of symptoms, history of MI in target vessel territory)[14]. Procedural success was defined as successful CTO revascularization with achievement of <30% residual diameter stenosis within the treated segment and restoration of TIMI grade 3 flow and without any in-hospital major adverse cardiac events (MACE) including death, ST, MI, repeated symptoms requiring TVR either PCI or CABG, pericardial tamponade requiring pericardiocentesis or surgery and stroke. CTO lesion complexity assessed using Japan-chronic-total-occlusion (J-CTO)score[15] to predict the likelihood of successful guidewire crossing within 30 min. Angiographic predictors of failure (each given 1 point) that made up the J-CTO score included prior failed attempt, angiographic evidence of heavy calcification, bending ≥45° within the occluded segment, blunt proximal stump, and occlusion length >20 mm. CTO lesions were then graded as easy, intermediate, difficult, and very difficult (J-CTO scores of 0, 1, 2, and ≥3 respectively). Another scoring system used was, PROGRESS-CTO score[16], a prediction model for estimating technical success and consisted of four angiographic variables a) proximal cap ambiguity [1 point], b) moderate/severe tortuosity

[1 point], c) circumflex artery CTO [1 point], and absence of "interventional" collaterals [1 point]. MI was defined using fourth universal definition of MI[17] (Type-4a).

Statistical analysis was performed using SPSS-23). Categorical data was expressed as percentages and continuous variables as mean + SD or median as appropriate. For comparison of normally distributed variables, t-test applied. All values reported as mean ± SD and *p*-value of <0.05 considered statistically significant.

RESULTS

A total of 171 patients fulfilling the inclusion criteria were enrolled in the study. The mean age of the study population was 60.61 ± 9.68. Among which 148 (86.5%) were males while 23 (13.5%) were females, 53 (31%) patients were diabetic, 65 (38%) were active smokers among the enrolled population. The study population was divided into two groups, Group one with only CTO while group two was combined (CTO and non-CTO lesion) group. Medical history for any previous cardiac procedure was asked from patients 36(21.1%) had elective PCI, 30 (17.5%) had primary PCI, 7 (4.1%) had CABG and 98 (57.3%) had diagnostic coronary angiography done previously described in table-I.

Table-I: Demographic characteristics of patient population.

Variable	Mean ± SD / n(%)
Age	60.61 ± 9.68
Gender	
Male	148 (86.5%)
Female	23 (13.5%)
Diabetes	
Yes	53 (31%)
No	118 (69%)
Smoking	
Yes	65 (38%)
No	106 (62%)
Creatinine at admission	1.03 ± 0.28
Creatinine at discharge	1.21 ± 0.48
Previous Procedure	
Elective PCI	36 (21.1%)
PPCI	30 (17.5%)
CABG	7 (4.1%)
Coronary Angiography	98 (57.3%)

Creatinine levels were determined at the time of admission and at discharge time and are expressed in mean respectively 01 ± 0.20, 1.16 ± 0.30 for group one. While for group two the mean serum creatinine levels at time of admission and discharge respectively were 1.06 ± 0.33, 1.25 ± 0.61. In group one, 45 (52.3%) patients had 01 vessel involved (SVCAD), followed by 17 (19.8%) patients who had 2 vessels (DVCAD) involved while 24 (27.9%) had 3 vessels involved (TVCAD). Whereas in group two 60 (69.8%) patients had two vessels involved followed by 25 (29.1%) patients who had 3 vessels involve. In CTO only group 37 (43%) had LAD involved as CTO vessel while 28 (32.6%) had RCA involved followed by 20 (23.3%) patients having LCX involved while only 1 (1.2%) patient had trifurcation as the CTO vessel involved. In group two 36 (41.9%) patients had LAD as CTO vessel involved while 27 (31.4%) patients had RCA involved followed by 22 (25.6%) patients who had LCX involved and only 1 (1.2%) had trifurcation involved. Among group one study population 23 (26.7%) patients had LAD as non-CTO vessel involved followed by 14 (16.3%) patients who had RCA involved whereas among group two 32 (37.2%) patients had LAD involved as non-CTO vessel followed by 19 (22.1%) having RCA involved. The mean duration of hospital stay in group 1 was 2.17 ± 1.54 while in group two the duration was 2.34 ± 1.77. In group one the procedure was successful among 81 (94.2%) patients while in group two 80 (93%) patients had successful procedure. Clinical characteristics are represented in tables-II & III.

Table-II: Clinical characteristics of patient population in group one (CTO only).

No. of Vessels Involved	
1	24 (27.9%)
2	45 (52.3%)
3	17 (19.8%)
CTO Vessel Involved	
LAD	37 (43%)
LCX	20 (23.3%)
RCA	28 (32.6%)
Trifurcation	1 (1.2%)
Non-CTO Vessel Involved	
LAD	23 (26.7%)
LCX	23 (26.7%)
RCA	14 (16.3%)
Trifurcation	1 (1.2%)
None	25 (29.1%)
Duration of hospital stay	2.34 ± 1.77
Procedure	
Successful	80 (93%)
unsuccessful	6 (7%)

DISCUSSION

Coronary CTOs are common. Among patients with CTO lesions Left ventricular systolic function is normal in >50% of patients. Kahn reported a CTO

Table-III: Table of association between creatinine at discharge and procedure outcome (Group CTO).

Creatinine at discharge	Procedure outcome		*p*-value
	Successful	Unsuccessful	
1.25 ± 0.61	80 (93%)	6 (7%)	0.002

p-value 0.002 shows statistically significant association between creatinine at discharge and procedure outcome in group A (CTO only).

Table-IV: Clinical characteristics of patient population in group two (Combined).

No. of Vessels Involved	
2	60 (69.8%)
3	25 (29.1%)
CTO Vessel Involved	
LAD	36 (41.9%)
LCX	22 (25.6%)
RCA	27 (31.4%)
Trifurcation	1 (1.2%)
Non-CTO Vessel involved	
LAD	32 (37.2%)
LCX	32 (37.2%)
RCA	19 (22.1%)
Trifurcation	2 (2.3%)
Duration of hospital stay	2.17 ± 1.54
Procedure	
Successful	81 (94.2%)
unsuccessful	5 (5.8%)

prevalence of 35%, while Werner *et al*, demonstrated a prevalence of 33% among patients with CAD presenting with stable angina[18]. With the advancements in the field of interventional cardiology CTO-PCI is now chosen as preferred procedure among patients presenting with multi-vessel CAD with CTO lesions. In this study we shared our experience of performing combined CTO lesion with non-CTO lesion in the same procedural setting at AFIC/NIHD RWP. We enrolled a total of 171 patients with CTO presented in our set up. We assessed angiographic, clinical and procedural outcomes of patients treated for CTO-PCI and also the major in-hospital cardiovascular events.

In this study both femoral and radial access site used depending on procedural complexity and the size of guide catheter used. But radial access favored in feasible patients and is recommended as per new recommendations and the recent trials on the access site; RIVAL and MATRIX[19]. In most patients dual injection technique for double stick used to visualize cross-filling and collaterals. We used unfractionated heparin (UFH) according to body weight as preferred anticoagulant as per new recommendations UFH remains the standard anticoagulant for elective PCI and proven by various trials[20]. All patients were preloaded with aspirin 300mg and clopidogrel[21], 600mg, and also ticagrelor in some selected patients with high ischemic and low bleeding risks.

Guiding catheter selection was case based and chosen according to the vessel anatomical origin, but guiding catheters with good support were used. Variety of micro-catheters used including finecross, turnpike, corsair or crusade used. Choice of Guidewire was lesion dependent but wire used in most cases were pilot-50, pilot-200, gaia family or fielder FC, conquest wire used in few selected complex cases. In all cases we used antegrade wire escalation strategy. Guide extension used only when there was difficulty in passing the stents or other gadgetry to the target lesion.

It has been more than two decades that drug-eluting stents (DES) are being used. Early-generation DES technology used sirolimus or paclitaxel from a permanent polymer matrix coating on a relatively thick-strut (120–140 mm) stainless steel backbone. These stents reduced angiographic and clinical ISR by approximately 50-70%, but increased the risk of very late stent thrombosis compared with BMS[22]. These are now replaced with newer generations of DES with thin struts (50–100 mm). Newer generation DES have higher efficacy and safety in comparison with both early-generation DES and BMS. Moreover, the risk of very late stent thrombosis is at least comparable to that of BMS and lower than that of early-generation DES[23]. So in all patients with successful 161 (94.2%) CTO-PCI, DES were implanted.

In our study patients demographics included mean age 60 ± 9.7 years. Among which 53 (31%) patients were diabetics, 65 (38%) were active smokers. We measured creatinine level before and after the procedurefor both groups. In our study, most commonCTO vessel involved in group one was LAD 37 (43%), followed by 28 (32.6%) RCA involved and 20 (23.3%) patients having LCX involved while only 1 (1.2%) patient had trifurcation. In group two 36 (41.9%) patients had LAD as CTO vessel involved while RCA involved in 27 (31.4%) patients, followed by LCX in 22 (25.6%) patients and ramus in only 1 (1.2%) patient. Procedural success was 81 (94.2%) in group one while 80 (93%) in group two. In a study of Xenogiannis *et al*[24], procedure success rate was 86%. In our study unsuccessful CTO was 5.8% group two patients, while 7% in group one patents and was due to inability of wire crossing in all cases, with 0% mortality among attempted patients.

Procedural outcomes comparing CTO only PCI with combined group (CTO ± non-CTO lesion) PCI included; 1) increased procedural timein combined

group compared with CTO only group, 2) radiation dose was higher in combined group compared with CTO only group, 3) no difference in MACE in both groups, 4) serious access site complications like compartment syndrome or retroperitoneal hematoma not seen in anygroup, 5) intra-procedural complications like heart blocks, coronary perforation, stroke, pericardial effusion requiring pericardiocentesis did not occur in both groups, but coronary no-flow phenomenon seen in 2 (2.9%) patientsin combined group-6) Stent thrombosis (type-4a MI as per 4th universal definition of MI)[25] requiring repeat PCI or CABG didn't occur in any case, 8) contrast-induced nephropathy requiring dialysis not seen in any case but post-procedure creatinine was slightly higher in combined group (1.16 ± 0.30 vs 1.25 ± 0.61) for group one and two respectively.

CONCLUSION

This study shows that during CTO-PCI procedure if a patient has a non-CTO lesion in any other coronary artery territory then it can be proceeded safely in the same setting. This combined procedure has high success rate with acceptable complication. In order to further improve outcomes, our goal should be to decrease procedure and fluoroscopy time and contrast volume in combined group to minimize the risk of contrast-induced nephropathy and radiation induced injury.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

REFERENCES

1. Morino Y, Abe M, Morimoto T, Kimura T, Hayashi Y, Muramatsu T, et al. Predicting successful guidewire crossing through chronic total occlusion of native coronary lesions within 30 minutes. JACC: Cardiovascul Intervent 2011; 4(2): 213-221.
2. Irving J. CTO Pathophysiology: How does this affect management?. Current Cardiol Rev 2014; 10(2): 99-107.
3. Sakakura K, Nakano M, Otsuka F, Yahagi K, Kutys R, Ladich E, et al. Comparison of pathology of chronic total occlusion with and without coronary artery bypass graft. Europ Heart J 2013; 35(25): 1683-1693.
4. Brilakis E, Grantham J, Rinfret S, Wyman R, Burke M, Karmpaliotis D, et al. A percutaneous treatment algorithm for crossing coronary chronic total occlusions. JACC: Cardiovascul Intervent 2012; 5(4): 367-379.
5. Christakopoulos G, Christopoulos G, Karmpaliotis D, Alaswad K, Yeh R, Jaffer F, et al. Predictors of excess patient radiation exposure during chronic total occlusion coronary intervention: insights from a contemporary multicentre registry. Canad J Cardiol 2017; 33(4): 478-484.
6. Vemmou E, Alaswad K, Khatri J, Nikolakopoulos I, Karacsonyi J, Xenogiannis I, et al. Patient radiation dose during chronic total occlusion percutaneous coronary intervention. Circulation: Cardiovasc Interv 2020; 13(10): 1-5.
7. Ramunddal T, Hoebers L, Henriques J, 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(8): e103850.
8. Claessen B, van der Schaaf R, Verouden N, Stegenga N, Engstrom A, Sjauw K, et al. Evaluation of the effect of a concurrent chronic total occlusion on long-term mortality and left ventricular function in patients after primary percutaneous coronary intervention. JACC Cardiovascul Intervent 2009; 2(11): 1128-34.
9. Watanabe H, Morimoto T, Shiomi H, Furukawa Y, Nakagawa Y, Ando K. Chronic total occlusion in a non-infarct-related artery is closely associated with increased five-year mortality in patients with ST-segment elevation acute myocardial infarction undergoing primary percutaneous coronary intervention (from the CREDO-Kyoto AMI registry). Euro Inter 2017; 12(15): e1874-82.
10. Christakopoulos G, Christopoulos G, Carlino M, Jeroudi O, Roesle M, Rangan B. Meta-analysis of clinical outcomes of patients who underwent percutaneous coronary interventions for chronic total occlusions. Amer J Cardiol 2015; 115(10): 1367-1375.
11. Werner G, Ferrari M, Heinke S, Kuethe F, Surber R, Richartz B, et al. Angiographic assessment of collateral connections in comparison with invasively determined collateral function in chronic coronary occlusions. Circulat 2003; 107(15): 1972-77.
12. Yamamoto E, Natsuaki M, Morimoto T, Furukawa Y, Nakagawa Y, Ono K, et al. Long-term outcomes after percutaneous coronary intervention for chronic total occlusion (from the CREDO-Kyoto Registry Cohort-2). Amer J Cardiol 2013; 112(6): 767-774.
13. Farooq V, Serruys P, Garcia-Garcia H, Zhang Y, Bourantas C, Holmes D, et al. The negative impact of incomplete angiographic revascularization on clinical outcomes and its association with total occlusions. J Amer Coll Cardiol 2013; 61(3): 282-294.
14. The Thrombolysis in Myocardial Infarction (TIMI) Trial. New Eng J Med 1985; 312(14): 932-36.
15. Morino Y, Abe M, Morimoto T, Kimura T, Hayashi Y, Muramatsu T, et al. Predicting successful guidewire crossing through chronic total occlusion of native coronary lesions within 30 minutes. JACC: Cardiovascul Intervent 2011; 4(2): 213-221.
16. Christopoulos G, Kandzari D, Yeh R, Jaffer F, Karmpaliotis D, Wyman M, et al. Development and validation of a novel scoring system for predicting technical success of chronic total occlusion percutaneous coronary interventions. JACC: Cardiovascul Interv 2016; 9(1): 1-9.
17. Thygesen K, Alpert J, Jaffe A, Chaitman B, Bax J, Morrow D, et al. Fourth universal definition of myocardial infarction. Circulat 2018; 138(20): 1-5.
18. Werner G, Gitt A, Zeymer U, Juenger C, Towae F, Wienbergen H, et al. Chronic total coronary occlusions in patients with stable angina pectoris: impact on therapy and outcome in present day clinical practice. Clin Res Cardiol 2009; 98(7): 435-41.
19. Valgimigli M, Gagnor A, Calabró P, Frigoli E, Leonardi S, Zaro T, et al. Radial versus femoral access in patients with acute coronary syndromes undergoing invasive management: a randomised multicentre trial. Lancet 2015; 385(9986): 2465-76.
20. Montalescot G, White H, Gallo R, Cohen M, Steg P, Aylward P, et al. Enoxaparin versus unfractionated heparin in elective percutaneous coronary intervention. New Eng J Med 2006; 355-(10): 1006-17.
21. Bellemain-Appaix A, O'Connor S, Silvain J, Cucherat M, Beygui F, Barthélémy O, et al. Association of clopidogrel pretreatment with mortality, cardiovascular events, and major bleeding among patients undergoing percutaneous coronary intervention. J Am Med Assoc 2012; 308(23): 2507-10.
22. Räber L, Magro M, Stefanini G, Kalesan B, van Domburg R, Onuma Y, et al. Very late coronary stent thrombosis of a newer-generation everolimuseluting stent compared with early-generation drug-eluting stents. Circul 2012; 125(9): 1110-21.

23. Palmerini T, Benedetto U, Biondi-Zoccai G, Della Riva D, Bacchi-Reggiani L, Smits P. Long-term safety of drug-eluting and bare-metal stents. J Amer Coll Cardiol 2015; 65(23): 2496-2507.
24. Xenogiannis I, Karmpaliotis D, Alaswad K, Jaffer F, Yeh R, Patel M, et al. Impact of concomitant treatment of non-chronic total occlusion lesions at the time of chronic total occlusion intervention. Inter J Cardiol 2020; 299(2): 75-80.
25. Hartikainen T, Sorensen N, Haller P, Gobling A, Lehmacher J, Zeller T, et al. Clinical application of the 4th universal definition of myocardial infarction. Eur Heart J 2020; 41(23): 2209-2216.