Original Research Article

CLINICAL CHARACTERISTICS AND OUTCOME OF PATIENTS WITH CORONARY CHRONIC TOTAL OCCLUSION: SINGLE CENTRE STUDY

ABSTRACT

BACKGROUND: There is a significant gap in knowledge regarding clinical presentation, treatment decisions, and clinical follow-up for patients diagnosed with coronary chronic total occlusions (CTOs) in India.

METHODS: All individuals >18 years diagnosed with CTO involving any vessel on coronary angiography at our institute were prospectively studied. Demographic details, treatment decisions, and 1-year follow-up were documented. The primary outcome variable was major adverse cardiovascular events at 1 year. Secondary outcome measures included symptom alleviation and the requirement of antianginal agents during follow-up. We also compared the outcomes of patients with and without revascularization.

RESULTS: One hundred and fourteen consecutive patients (90.4% male, mean age of 59.5±9.8 years, and mean SYNTAX score of 28.3±11.1) with coronary CTO were studied. Angina (74.3%) was the predominant symptom. Seventy-six (66.7%) patients underwent successful coronary revascularization (PCI- 25.4%, CABG- 41.3%). At 1-year follow-up, there was no significant difference in mortality (p=0.07) and myocardial infarction (p=0.08) between the patients who underwent revascularization and who did not. Most patients

(86.8%) showed symptomatic improvement, and 13.2% required additional antianginal agents for symptom alleviation.

CONCLUSION: Regardless of the status of revascularization, major adverse cardiovascular events and symptom alleviation did not differ significantly in patients with CTO.

KEYWORDS: Coronary Angiogram, Chronic Total Occlusion, Percutaneous Coronary Intervention

INTRODUCTION

Coronary chronic total occlusion (CTO) is defined as complete occlusion of a coronary artery for at least 3 months with TIMI (thrombolysis in myocardial infarction) grade 0 flow.Approximately one-fourth of individuals with coronary artery disease (CAD) who undergo coronary angiography have coronary CTO (1). It has a diverse clinical presentation. Management strategies for CTO include medical therapy, percutaneous coronary intervention (PCI), and coronary artery bypass graft (CABG). CABG is the preferred choice for patients with multi-vessel disease. Despite optimal medical therapy, refractory angina is an indication of revascularization (2). Complete coronary revascularization is associated with a better prognosis regarding enhanced survival and decreased major adverse cardiovascular events(MACE). Surgical revascularization is currently the standard method to achieve complete revascularization in patients with multi-vessel CAD and CTO (4). Recently, PCI has been gaining popularity with success rates of approximately 90% and minimal complications (5); this could be attributed to meticulous pre-procedural lesion assessment and advanced techniques and materials used at dedicated centresThere are many studies on Coronary CTO in western literature, but very few have been done from India on the subject.

In this study, we aimed to evaluate the clinical features, angiographic profile, management options, major adverse cardiac events ~~(MACE)~~, and symptom relief at 1 year in patients diagnosed with CTO.

MATERIALS AND METHODS

This prospective observational study was conducted at Apollo Main Hospital, Chennai, from July 2021 to July 2022. A convenient sample size was taken. All patients >18 years with coronary artery disease(CAD) diagnosed with Coronary chronic total occlusion (CTO) following coronary angiography were included.CTO is defined as complete occlusion of a coronary artery for at least 3 months with TIMI (thrombolysis in myocardial infarction) grade 0 flow (7). Patients with a history of CABG were excluded. Demographic details were recorded. The extent of CAD was measured by the SYNTAX SCORE I(Synergy Between percutaneous coronary intervention (PCI) With Taxus and coronary artery bypass surgery (CABG)).The SYNTAX Score I takes into account various factors related to the anatomical complexity of coronary lesions, such as the number of lesions, their location, and their severity. SYNTAX score Iwas generated by adding the individual scores for each distinct lesion, which was defined as vessels with diameter of > 1. 50mm and 50% or more luminal obstruction. All patients' SYNTAX scores were computed using specialized software (available at http://www.syntaxscore.com/calc/start.htm).Angiographic analyses included the number, location, severity, vessel tortuosity, calcification, length of the occlusion, and vessel tortuosity. The Japanese Chronic Total Occlusion (J-CTO) score was used to evaluate the technical complexity of the lesion. Management decisions taken subsequently were documented.Medical therapy, percutaneous intervention (PCI) and coronary artery bypass graft (CABG) surgery were the management strategies in our study population.Management decisions were taken solely by the treating physician as per the recent myocardial revascularisation guidelines(2). At 1-year follow-up, MACE (myocardial

infarction, stroke, and death), symptomatic improvement (angina/dyspnoea), and the requirement of additional antianginal agents were recorded. The study was approved by our Institutional Review Board, and written informed consent was obtained from all patients (AMH-DNB-069/07-21).

STATISTICAL ANALYSIS

Statistical analysis was performed using SPSS (IBM, version 28.0). The normality of continuous variables was tested using the Shapiro-Wilk test. Continuous variables were presented as either mean ± standard deviation or median with range. Categorical variables were presented as percentages and frequencies. Student's t-test/Mann Whitney U test was used to determine the significant changes in the continuous factor between CTO and non-CTO vascularization. The chi-square/Fisher's exact test was used to determine the association between two independent categorical factors. *P-value* <0.05 was considered significant.

RESULTS

The majority of the study population had multi-vessel disease (79.8%) with a high SYNTAX score (>23). Angina was the most common symptom. Table 1 represents the baseline characteristics of the study population.The mean syntax score was 28.3 ± 11.1, and the mean J CTO score in the CTO artery was 2.1 ± 0.,7 which denoted technically difficult lesions.

Table 1-Baseline characteristics and clinical features of the study population(n=114)

Parameters	**n (%)**
Age (in years) Mean ± SD	 59.5 ± 9.8
Gender Male Female	 103(90.4) 11(9.6)
Chest Pain	83(72.8)
Dyspnoea	42(36.8)
Hypertension	69(60.5)

Diabetes	58(50.9)
Past Acute Coronary Syndrome	34(29.8)
Prior PCI Yes Attempted and failed	 8(7.0) 1 (0.9)
Dyslipidaemia	27(23.7)
Chronic Kidney Disease	3(2.6)
SYNTAX 1 score Mean ± SD Grouping <23 23-33 >33	 28.3 ± 11.1 38(33.3) 42(36.8) 34(29.8)
J-CTO score Mean	 2 ± 0.7

J-CTO*: Japanese Chronic Total Occlusion score, PCI*: Percutaneous Coronary Intervention, SD*: Standard deviation, SYNTAX*: Synergy Between percutaneous coronary intervention (PCI) With Taxus and coronary artery bypass surgery (CABG)

Table 2: Angiographic profile in the study population

Parameters	**n (%)**
Angiographic Diagnosis TVD DVD SVD	 60 (52.6) 31 (27.2) 23 (20.2)
Total no of CTO lesions	144
CTO Artery LAD LCX RCA	 34 (29.8) 34 (29.8) 76 (66.7)
CTO in 2 Arteries LAD & LCX LAD & RCA LCX & RCA	 8 (7.0) 11 (9.6) 19 (16.7)
CTO in 3 Arteries LAD, LCX & RCA	 3 (2.6)

DVD*-Double vessel disease, SVD*-Single Vessel Disease, TVD*-Triple vessel disease, LCX*-Left circumflex artery, LAD*-Left Anterior Descending Artery, RCA*-Right Coronary Artery

Table 2 represents the angiographic findings of the patients.Two-thirds of the study population had CTOs involving the right coronary artery. Half of the study population had triple vessel disease.

Management strategies in the study population:

Forty-nine (43%) patients underwent CABG, and 36 (31.6%) individuals were managed medically. Among those who underwent CABG, a bypass graft was placed in the artery with a CTO for 47 (95.9%) patients. PCI was attempted in 31.5% of patients, with a success rate of 80.6%. Thirteen (11.4%) patients underwent PCI to the non-CTO artery. Figure 1 demonstrates an overview of the management strategies for the CTO. Table 3 represents the outcomes of management strategies.

Figure 1:Management strategies in the study population

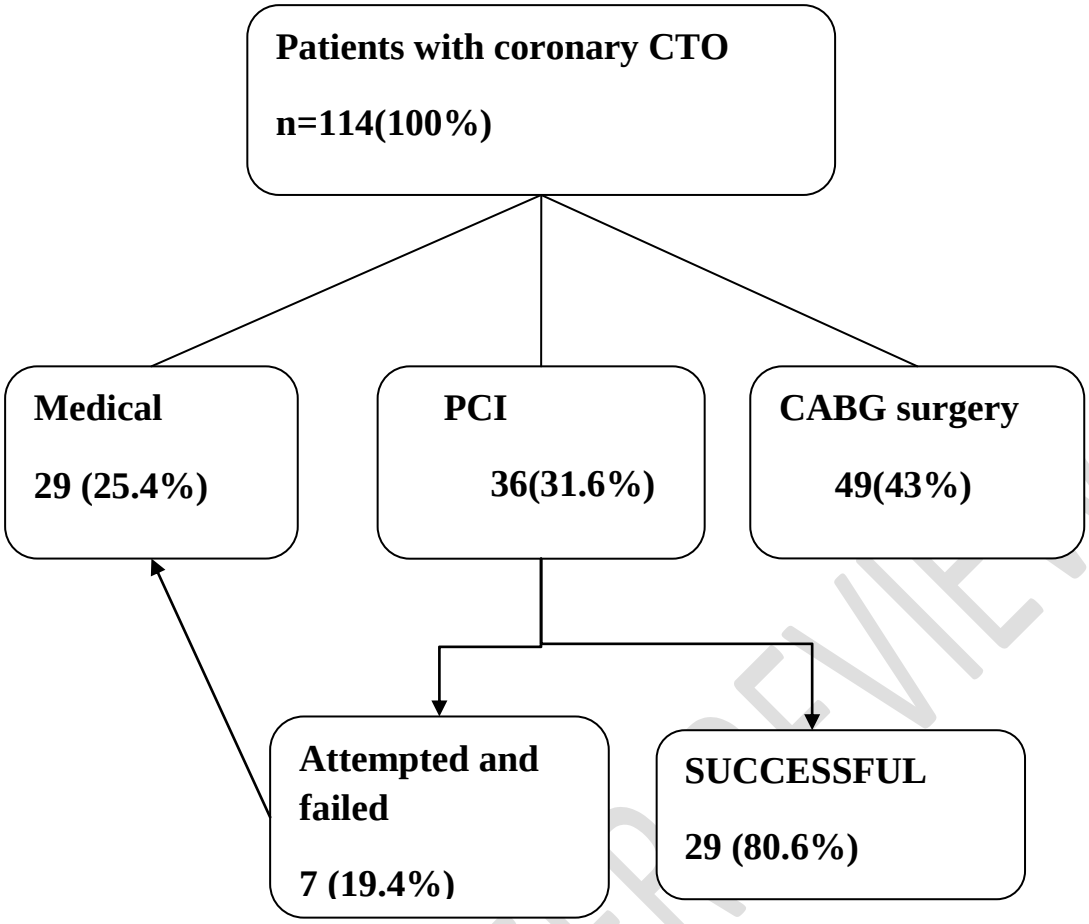

Table 3: Outcomes of various management strategies adopted for CTO

Parameters	**n (%)**
CABG **CABG CTO artery revascularization** -Yes No	49 47 (95.9) 2 (4.1)
PCI to non-CTO artery	13(11.4)
MACE Death MI	 5 (4.4) 2 (1.8)
Antianginals added Yes	 15 (13.2)
Symptomatic Improvement Yes No N/A(Death)	 99 (86.8) 10 (8.8) 5 (4.4)

PRIMARY AND SECONDARY ENDPOINTS OF THE STUDY POPULATION

During the course of twelve months of follow-up, the majority of patients (93.8%) did not experience any MACE. Eight patients required antianginal agents for symptom relief.

SUB-GROUP ANALYSIS BASED ON REVASCULARISATION OF CTO ARTERY

A subgroup analysis was performed depending on whether the artery having CTO was re-vascularized or not. Table 4 indicates that the baseline characteristics in both the sub-groups were comparable.

Table 4: Baseline characteristics and clinical features of the study population categorized based on whether revascularization was performed or not

Parameters	CTO revascularization (n=76)	No CTO revascularization, (n=38)	Overall, (n=114)	P-value
Age (In years)				
Mean ± SD	59.4 ± 9.4	59.9 ± 10.9	59.5 ± 9.8	0.785#
Range	36 – 85	36 – 84	36 – 85	
Gender				
Male	68(89.5)	35(92.1)	103 (90.4)	>0.99*
Female	8 (10.5)	3 (7.9)	11 (9.6)	
Chest Pain	60(78.9)	23 (60.5)	83 (72.8)	0.071*
Dyspnea	27(35.5)	15(41.7)	42 (36.8)	0.533*
Hypertension	47 (61.8)	22 (57.8)	69 (60.5)	0.538*
Diabetes	38 (50.0)	20 (52.6)	58 (50.9)	0.842*
Past ACS	22 (28.9)	12 (26.3)	34 (29.8)	0.661*
Prior PCI				
Yes	5 (6.6)	3 (7.9)	8 (7.0)	0.744*
Attempted & Fail	1 (1.3)	-	1 (0.9)	
Dyslipidemia	16 (21.1)	11 (28.9)	27 (23.7)	0.487*
CKD	3 (3.9)	-	3 (2.6)	0.550*
Diagnosis				
TVD	45 (59.2)	15 (39.5)	60 (52.6)	**0.041***
DVD	21 (27.6)	10 (26.3)	31 (27.2)	

SVD	10 (13.2)	13 (34.2)	23 (20.2)	
Syntax 1 score Mean ± SD Range	 29.1 ± 10.9 6 – 65	 26.5 ± 11.4 8 – 49.5	 28.3 ± 11.1 6 – 65	0.196#
J-CTO score Mean ± SD Range	 2.1 ± 0.7 1 – 4	 1.9 ± 0.7 1 – 4	 2.1 ± 0.7 1 – 4	0.228#
Syntax grouping <23 23 to 33 >33	 21 (27.6) 32 (42.1) 23 (30.3)	 17 (44.7) 10 (26.3) 11(29)	 38 (33.3) 42 (36.8) 34 (29.8)	0.202*

ACS-Acute Coronary syndrome, CKD-Chronic Kidney disease DVD-Double vessel disease, SVD-Single Vessel Disease, TVD-Triple vessel disease #- Student's t-test/Mann Whitney U test; *- Chi-square/Fisher's exact test

Table 5 represents a comparison of outcomes between the subgroups. MACEoccurred at a lower rate amongst patients who underwent CTO revascularization than those who did not (2.6% vs. 13.1%, p=0.066), but the result was not statistically significant.Symptomatic relief from angina was better in the group having re-vascularization (89.5% vs. 81.6%, p=0.077). A small proportion of patients required antianginal agents during follow-up.

TABLE 5: Primary and secondary endpoint in the subgroups

Parameters	**CTO revascularization, (n=76)**	**No CTO revascularization, (n=38)**	**Overall, (n=114)**	**P-value***
MACE Death MI	 1 (1.3) 1 (1.3)	 4 (10.5) 1 (2.6)	 5 (4.4) 2 (1.8)	 0.066 0.078
Symptomatic Improvement Yes	68 (89.5)	31(81.6)	99 (86.8)	0.077
Antianginals Added Yes	8 (10.5)	7 (18.4)	15(13.2)	0.189

DISCUSSION:

It is widely known that, compared to the West, CAD affects the South Asian population more frequently and at a younger age. The mean age of the participants in our study was lower, and gender predominance was similar to that found in studies conducted in the West (8) (9) (10). Similar to previous reports, angina was the most common symptom in our study (10) (8) (11) (12). The prevalence of CAD risk factors was greater in patients with CTO. There was no appreciable difference in terms of comorbidities, including diabetes, hypertension, and dyslipidemia, between patients who received revascularization and those who did not, which was consistent with findings from the Canadian CTO registry (16).

The RCA was most frequently affected. This finding is in line with the results of several previous studies (13), (14), (15), and data from the CTO registries of Canada and Japan (16) (9). The majority of our patients had multi-vessel disease with a high SYNTAX score (>23) and J CTO score, confirming that coronary CTOs are indeed technically challenging lesions (8, 45, 9). In accordance with established standards for revascularization, several patients underwent CABG or PCI (17). The success rate of PCI was 80.5%, which is lower than that reported by the OPEN CTO registry (21) and the RECHARGE registry (5).

The DECISION CTO trial (22) compared patients with ACS and CTO who underwent PCI with those who did not regarding all-cause mortality, myocardial infarction, stroke, and vessel revascularization. There was no difference in the evaluated endpoints at 3-year follow-up patients. Results of the Euro CTO trial involving 96 patients with stable angina randomized to receive PCI versus medical therapy showed no significant difference in major adverse cardiovascular and cerebrovascular events between the two groups (23). According to data from the Canadian multicenter CTO registry (16), patients with CTO arteries revascularized had a significantly lower 10-year mortality rate.

PCI significantly improves health status compared to medical therapy alone in patients with stable angina (2). Our 12-month follow-up showed greater improvement in NYHA symptom class among patients receiving revascularization.

STUDY LIMITATIONS:

The main drawback of our study was that the patients with CTOs were not randomly assigned to one of two therapy allocation groups. Additionally, using standard questionnaires like the Seattle Angina Questionnaire (SAQ) to assess the overall health status would have added benefit to the findings. Large multicenter randomized trials are necessary to determine the validity of our results.

CONCLUSIONS:

Most patients with CTO had multi-vessel disease with a high SYNTAX score. Regardless of the status of revascularization, major adverse cardiovascular events and symptom alleviation did not differ significantly in CTO patients.

REFERENCES:

1. Tsai TT, Stanislawski MA, Shunk KA, Armstrong EJ, Grunwald GK, Schob AH, et al. 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):866–75.

2. Mares A, Mukherjee D. Management of Chronic Total Occlusion of Coronary Artery. Int J Angiol , 2021 Mar 1;30(1):48.

3. Sousa-Uva M, Ahlsson A, Alfonso F, Banning AP, Benedetto U, Byrne RA, et al. 2018 ESC/EACTS Guidelines on myocardial revascularization The Task Force on myocardial revascularization of the European Society of Cardiology (ESC) and European Association for Cardio-Thoracic Surgery (EACTS)

4. Muraca I, Carrabba N, Virgili G, Bruscoli F, Migliorini A, Pennesi M, et al. Chronic total occlusion revascularization: A complex piece to "complete" the puzzle. World J Cardiol. 2022 Jan 1;14(1):13.

5. Maeremans J, Walsh S, Knaapen P, Spratt JC, Avran A, Hanratty CG, et al. The Hybrid Algorithm for Treating Chronic Total Occlusions in Europe: The RECHARGE Registry. J Am Coll Cardiol. 2016 Nov 1;68(18):1958–70.

6. Sapontis J, Salisbury AC, Yeh RW, Cohen DJ, Hirai T, Lombardi W, et al. Early Procedural and Health Status Outcomes After Chronic Total Occlusion Angioplasty: A Report From the OPEN-CTO Registry (Outcomes, Patient Health Status, and Efficiency in Chronic Total Occlusion Hybrid Procedures). JACC Cardiovasc Interv. 2017 Aug 14;10(15):1523–34.

7. Brilakis ES, Mashayekhi K, Tsuchikane E, Abi Rafeh N, Alaswad K, Araya M, et al. Guiding Principles for Chronic Total Occlusion Percutaneous Coronary Intervention: A Global Expert Consensus Document. Vol. 140, Circulation. Lippincott Williams and Wilkins; 2019 [cited 2021 Apr 30]. p. 420–33.

8. 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 Mar 13;59(11):991–7.

9. Morino Y, Kimura T, Hayashi Y, Muramatsu T, Ochiai M, Noguchi Y, et al. In-Hospital Outcomes of Contemporary Percutaneous Coronary Intervention in Patients With Chronic Total Occlusion: Insights From the J-CTO Registry (Multicenter CTO Registry in Japan). JACC Cardiovasc Interv. 2010 Feb 1;3(2):143–51.

10. Tomasello SD, Boukhris M, Giubilato S, Marza F, Garbo R, Contegiacomo G, et al. Management strategies in patients affected by chronic total occlusions: results from the Italian Registry of Chronic Total Occlusions. Eur Heart J,2015 Dec 1;36(45):3189–98.

11. Stone GW, Kandzari DE, Mehran R, Colombo A, Schwartz RS, Bailey S, et al. Percutaneous Recanalization of Chronically Occluded Coronary Arteries. Circulation. 2005 Oct 11;112(15):2364–72. A

12. Olivari Z, Rubartelli P, Piscione F, Ettori F, Fontanelli A, Salemme L, et al. Immediate results and one-year clinical outcome after percutaneous coronary interventions in chronic total occlusions: data from a multicenter, prospective, observational study (TOAST-GISE). J Am Coll Cardiol. 2003 May 21;41(10):1672–8.

13. Christofferson RD, Lehmann KG, Martin G V., Every N, Caldwell JH, Kapadia SR. Effect of chronic total coronary occlusion on treatment strategy. Am J Cardiol 2005

May 1;95(9):1088–91.

14. Cohen HA, Williams DO, Holmes DR, Selzer F, Kip KE, Johnston JM, et al. Impact of age on procedural and 1-year outcome in percutaneous transluminal coronary angioplasty: a report from the NHLBI dynamic registry. Am Heart J. 2003 Sep 1;146(3):513–9.

15. Anderson HV, Shaw RE, Brindis RG, Hewitt K, Krone RJ, Block PC, et al. A contemporary overview of percutaneous coronary interventions: The American College of Cardiology–National Cardiovascular Data Registry (ACC–NCDR). J Am Coll Cardiol. 2002 Apr 3;39(7):1096–103.

16. Strauss BH, Knudtson ML, Cheema AN, Galbraith PD, Elbaz-Greener G, Abuzeid W, et al. Canadian Multicenter Chronic Total Occlusion Registry: Ten-Year Follow-Up Results of Chronic Total Occlusion Revascularization. Circ Cardiovasc Interv. 2021 Dec 1;14(12):E010546.

17. Lawton JS, Tamis-Holland JE, Bangalore S, Bates ER, Beckie TM, Bischoff JM, et al. 2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2022 Jan 18;145(3):E18–114.

18. Stone GW, Reifart NJ, Moussa I, Hoye A, Cox DA, Colombo A, et al. Percutaneous Recanalization of Chronically Occluded Coronary Arteries. Circulation ,2005 Oct 18;112(16):2530–7.

19. Prasad A, Rihal CS, Lennon RJ, Wiste HJ, Singh M, Holmes DR. Trends in Outcomes After Percutaneous Coronary Intervention for Chronic Total Occlusions: A 25-Year Experience From the Mayo Clinic. J Am Coll Cardiol. 2007 Apr 17;49(15):1611–8.

20. 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: The J-CTO (Multicenter CTO Registry in Japan) Score as a Difficulty Grading and Time Assessment Tool. JACC Cardiovasc Interv. 2011 Feb 1;4(2):213–21.

21. Sapontis J, Salisbury AC, Yeh RW, Cohen DJ, Hirai T, Lombardi W, et al. Early Procedural and Health Status Outcomes After Chronic Total Occlusion Angioplasty: A Report From the OPEN-CTO Registry (Outcomes, Patient Health Status, and Efficiency in Chronic Total Occlusion Hybrid Procedures). JACC Cardiovasc Interv. 2017 Aug 14;10(15):1523–34.

22. 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 Apr 2;139(14):1674–83.

23. 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 tratment of chronic total coronary occlusions. Eur Heart J. 2018 Jul 7;39(26):2484–93.