Review Article

Interventional Cardiology

A review on percutaneous coronary intervention of chronic total occlusion in the non-ST elevation myocardial infarction cohort

Sunil Thambi[1], Vinoda Sharma[2*]

[1]Department of Cardiology, Birmingham City Hospital, Birmingham, United Kingdom;

[2]Department of Medicine, University Hospitals Birmingham, United Kingdom

*Author for correspondence:
Vinoda Sharma, Department of Cardiology, Birmingham City Hospital, Birmingham, United Kingdom, E-mail: vinodasharma@nhs.net

Received date: 29-Apr-2024, Manuscript No. FMIC-24-133466;
Editor assigned: 01-May-2024, PreQC No. FMIC-24-133466 (PQ);
Reviewed date: 17-May-2024, QC No. FMIC-24-133466;
Revised date: 24-May-2024, Manuscript No. FMIC-24-133466 (R);
Published date: 31-May-2024, DOI: 10.37532/1755-5310.2024.16(3).874

Abstract

A Chronic Total Occlusion or (CTO), is defined as a 100 percent stenosis of a coronary artery with Thrombolysis in Myocardial Infarction (TIMI) 0 flow for more than three months. There is published data on the management of CTOs in an elective setting or with ST Elevation Myocardial Infarction (STEMI). However, the evidence is more conflicting when it comes to a CTO in the Non-ST Elevation Myocardial Infarction (NSTEMI) cohort. A recent six centre observational, retrospective study attempts to delineate the characteristics and outcomes of patients with CTO and NSTEMI. Patients in their cohort were older men with cardiovascular risk factors and worse in-hospital and long term outcomes. We review the existing literature on CTO in a NSTEMI cohort with specific reference to the above study.

Keywords: Cardiac arrest • Myocardial Infarction • Thrombolysis

Abbreviations: CASTLE-SCORE: Coronary Artery Bypass Graft History; RECHARGE SCORE: Retrograde Entry Calcification History Anatomy Resistance Graft Endpoint; DECISION-CTO: Does Endovascular Chronic Intervention save Impaired Open Narrowings-Chronic Total Occlusion; REVASC: Revascularization

Introduction

A Chronic Total Occlusion or CTO, is defined as a 100 percent stenosis of a coronary artery with Thrombolysis In Myocardial Infarction (TIMI) 0 flow for more than three months (based on angiography and symptoms) [1]. Functional CTOs have a perceivable channel through the occlusion with visibility of contrast beyond the occlusion. A CTO is seen in approximately 18%-30% of patients undergoing angiograms [2,3]. Notably, about one-third of patients who are resuscitated because of a cardiac arrest have a CTO [4]. In the ERCTO [European Registry of Chronic Total Occlusion] registry published in 2024, the Right Coronary Artery (RCA) was the most commonly intervened vessel followed by the Left Anterior Descending (LAD) [5].

Literature Review

The volume of CTO work has increased exponentially, exposing gaps in knowledge especially in patients with Non-ST Elevation Myocardial Infarction (NSTEMI). The characteristics, revascularization strategies, and outcomes of patients with CTO in the NSTEMI cohort are not well studied or very well understood.

In this review, we focus on CTO PCI in an NSTEMI cohort referring to a recently published study by Sharma, et al., who analyzed patients with an NSTEMI admitted to six United Kingdom (UK) cardiac centers.

Traditionally, coronary CTOs were conservatively managed or treated surgically if the rest of the coronary tree mandated surgical revascularization [6]. In the initial years of CTO Percutaneous Coronary Intervention (PCI), the main goal was relieving anginal symptoms. However, with compelling data emerging in recent years that there may also be better long-term outcomes, including mortality benefit, we have seen an increasing number of CTO PCI performed across the globe. The risk of CTO PCI compared to PCI on a non-occlusive vessel is much higher, and the success rates average about 70% in comparison to 98% in non-occlusive vessel PCI unless it is a functional CTO in which it is technically less challenging [7,8]. To help with case selection and to predict success various operative scores have been used including the most popular J-CTO score [9], the others being PROGRESS CTO (Prospective Global Registry for the Study of Chronic Total Occlusion Intervention) [10], CASTLE-SCORE [11], and RECHARGE SCORE [12]. All of these scores predominantly looked into the presence of an ambiguous entry point, length of CTO, calcification, tortuosity, age of the patient and landing zone of the distal coronary vessel to predict success. Although no large randomized controlled trials are looking at the clinical outcomes of CTO PCI versus optimal medical therapy, smaller trials such as the DECISION-CTO study [13,14], and the REVASC trial [15], have not shown the benefit of CTO PCI. These studies were limited by small numbers and were not powered for clinical endpoints. An observational study of 13,443 patients with long-term follow-up of elective CTO angioplasty analysis from the United Kingdom (UK) central cardiac audit database showed successful CTO PCI in elective patients was associated with lower mortality. Mortality was lower in patients with complete revascularization compared to those with partial revascularization or those with failed elective CTO PCI [16]. The improvement in survival was demonstrable after multivariate analysis, suggesting this was independent of confounding factors.

Sharma, et al., [2], analyzed patients with an NSTEMI admitted to six United Kingdom (UK) cardiac centres (Morrison Hospital, Swansea; University Hospital Wales, Cardiff; Trent Cardiac Centre, Nottingham; Birmingham City Hospital, Birmingham; Essex Cardiothoracic Centre, Essex; and Royal Stoke University Hospital, Stoke-on-Trent) between 2015 and 2020. Anonymized British Cardiovascular Intervention Society (BCIS) data from the six centers was analyzed. A total of 17,355 patients with NSTEMI underwent PCI in these 6 centers between 2015 and 2020. 10.4% of patients had a CTO. There was a significantly higher prevalence of CTO in males and a higher prevalence of cardiovascular risk factors in CTO patients. In addition, these CTO patients were found to be more likely to have Left Ventricle (LV) dysfunction [moderate to severe LVSD: 20.4% vs non-CTO 7.1%, p<0.0001]. A third of all CTOs were LAD CTOs. In the hospital, Major Adverse Cardiovascular Events (MACE) were higher in the CTO cohort [CTO 1.4% vs no CTO 0.8%], as were the procedural complication rates [CTO 2.5% vs no CTO 1.6%, p<0001]. Surprisingly, the mean time for revascularization in this study was quite quick at 13.4 days. There was no difference in the success rate of early revascularization [defined as<7 days] versus late revascularization. Details of ischemia testing (if any) were not available. The proportion of patients on optimal medical therapy before PCI was also not evident. Patients who underwent successful CTO PCI were younger (66.4 [± 11.7] vs 68.4 [± 11.4]) with less comorbidity. This may potentially have a bearing on with them having better long-term outcomes. The absence of the core lab also meant not being able to evaluate the residual SYNTAX score (rSS) [17]. In the context of an ST-Elevation Myocardial Infarction (STEMI), the presence of a non-culprit CTO has clearly shown worse outcomes [18]. Intuitively, one would expect the same in the NSTEMI population and this paper demonstrates that fairly certainly. There was no core lab or data available to evaluate if the operator felt the CTO was the culprit or a bystander lesion. Interestingly, there was a considerable variation in practice across the 6 centers, with attempts at CTO PCI varying from 16% to 100% and also significant variation in success rates from 65% to 100%, which raises the possibility that recently occlusive vessels or functional CTOs were counted as CTOs in some centres and not others. This is also likely a reflection of the absence of clear guidelines on the management of CTO patients in any cohort and varying operator comfort and experience in different centres. A recent Japanese CTO-PCI registry analysis has demonstrated CTO PCI success rates of over 85% [19,20], perhaps indicating a more homogenous method of practice and/or guidelines.

A similar observational study from Korea by Hsin-I Teng, et al. looking at the outcomes of CTO PCI in their centre in the NSTEMI cohort showed that after a mean of 2.5-year follow-up, the long-term cardiac death was still significantly lower in the successful CTO PCI group (16.9% vs 42.3%, P<0.001) [21]. Theirs was a small study with CTO patients forming 11% (n=106) of the total NSTEMI cohort. Similarly, another Korean study, data collected prospectively from 26 cardiac centres (the Korean multicenter chronic total occlusion registry) demonstrated that successful CTO-PCI in patients with an MI was associated with improved 1-year survival. They also demonstrated that failed CTO PCI in the NSTEMI cohort was associated with increased incidence of total death at 1 year [22]. Cox-proportional analysis showed that successful CTO-PCI was beneficial in NSTEMI patients in preventing mortality.

One common theme amongst all these studies, in addition to the observational nature, is the lack of data on patients who underwent functional studies before CTO intervention hence it could not be ascertained whether the procedures were appropriate

or underutilized.

Even if CTO PCI in the NSTEMI population has shown survival benefits, as seen in the observational studies mentioned, the question remains unanswered due to multiple confounding factors. Patients, who underwent PCI in the CTO cohort, rather than being medically managed, perhaps acknowledged their cardiovascular status and adhered to secondary prevention and cardiac rehabilitation in comparison to the ones that were "medically treated" reflecting the difference in outcomes. A lack of data/comparison on patients treated medically in some of these observational studies can be considered a huge confounding factor.

The European Society of Cardiology (ESC) Association of Percutaneous Cardiovascular Interventions (EAPCI), the ESC Association of Cardiovascular Imaging (EACVI), as well as the ESC Working Group on Cardiovascular Surgery, advocate CTO PCI for symptom improvement in patients who are already on optimum medical therapy and maintains that currently no compelling evidence for CTO PCI for prognostic benefits [23]. In the case of LVSD then cardiac MRI was suggested as the favoured choice of investigation over stress ECHO or nuclear tests [24,25].

Larger, multicenter prospective RCT trials with CTO PCI in the NSTEMI population with a core lab are required to show survival benefits. In published data, few randomized clinical trials have provided information on CTO PCI compared with patients not undergoing CTO PCI. In the largest of these trials, Lee, et al., in the DECISION-CTO Trial, randomly assigned 834 patients to CTO or non-CTO PCI.

The success rate of CTO PCI was high at 90.6% but interestingly did not show any difference in the incidence of MACE at the 2 and 4 year follow up. The significant cross-over from non-CTO PCI to CTO PCI was noteworthy in this study. Few other small RCTs have shown an improvement in quality of life with no improvement in MACE. In another small study, Werner, et al., [26], randomly assigned 396 patients (2:1) to CTO PCI versus non-CTO PCI. At 12 months, patients randomly assigned to the CTO PCI group had improvement in the angina frequency and no difference in the incidence of MACE. The EXPLORE trial (Evaluating Xience and Left Ventricular Function in Percutaneous Coronary Intervention on Occlusions After ST-Elevation Myocardial Infarction) trial in 304 patients evaluated if patients with STEMI and concurrent CTO in a non-infarct-related artery would a benefit from Percutaneous Coronary Intervention (PCI) of CTO within a week after primary PCI. 14 centres across Europe and Canada were involved. There was no difference at 4 months in the Left Ventricular Ejection Fraction (LVEF) or MACE [27]. The REVASC study that evaluated Segmental Wall Thickening (SWT) and LV function at 12 months, showed no differences between patients undergoing CTO PCI versus non-CTO PCI. The study demonstrated the clinical benefit of CTO PCI by a reduction in major coronary event rate at 12 months mainly driven by repeat revascularisation procedures.

Two larger ongoing clinical studies, NOBLE-CTO (Nordic-Baltic Randomized Coronary Occlusion; Registry Study for Evaluation of PCI in Chronic Total Occlusion; ClinicalTrials.gov ID NCT03392415) and ISCHEMIA-CTO (Nordic and Spanish Randomized Trial on the Effect of Revascularization or Optimal Medical Therapy of Chronic Total Coronary Occlusions With Myocardial Ischemia; NCT03564317) are likely to provide more information on the efficacy and safety of CTO PCI in the future.

The NOBLE-CTO study is looking at Quality of life measures, procedural data, echo and CMRI findings before and after CTO PCI. The ISCHEMIA-CTO study involves establishing patients on optimal medical therapy for 3 months. They are then divided into two cohorts: Asymptomatic or symptomatic. Primary endpoints in the asymptomatic cohort are MACE, hospitalization and malignant arrhythmias. The primary endpoint in the symptomatic group is improvement in QoL. The results of these two trials are likely to shape future guidelines on CTO PCI.

Conclusion

The trials and literature discussed have not shown any concrete evidence for advantage of CTO PCI in terms of improvement in left ventricular function and have provided disparate results when it comes to improving quality of life. Patients with NSTEMI also require immediate treatment of the culprit artery, with the added challenge of ruling out the CTO as the cause of or contributor to the acute event. Attempting to identify if the CTO vessel is the culprit and offering PCI to the CTO in that cohort may be more fruitful. Admission troponin essays and variability, absence of obvious other culprit lesions [with ± imaging modalities], could strongly suggest culprit CTO lesions. Preferentially targeting CTO PCI in this cohort would be interesting. Case selection for CTO PCI in the NSTEMI population remains an area without clear guidelines. Potentially, a large cohort of the population could benefit once clear, demonstrable evidence is shown in this group of patients, in whom most of the benefit would be. CTO PCI remains one of the most challenging arenas in PCI. Targeting and channeling resources towards the cohort with the most benefit may shape this area in the future as would the future CTO trials mentioned above.

References

1. Stone GW, Kandzari DE, Mehran R, et al. Percutaneous recanalization of chronically occluded coronary arteries: A consensus document: Part I. Circulation.112(15):2364-2372 (2005).

2. Sharma V, Jadhav ST, Harcombe AA, et al. Impact of proctoring on success rates for percutaneous revascularisation of coronary chronic total occlusions. Open Heart.2(1):e000228 (2015).

3. Sharma V, Choudhury A, Basavarajaiah S, et al. Chronic total occlusion in non-ST elevation myocardial infarction-A multi-centre observational study. Cardiovasc Revasc Med.(2024).

4. van der Graaf M, Jewbali LS, Lemkes JS, et al. Infarct-related chronic total coronary occlusion and the risk of ventricular tachyarrhythmic events in out-of-hospital cardiac arrest survivors. Neth Heart J.29(10):500-505 (2021).

5. Vadalà G, Galassi AR, Werner GS, et al. Contemporary outcomes of chronic total occlusion percutaneous coronary intervention in Europe: The ERCTO registry. EuroIntervention.20(3):e185-e197 (2024).

6. Delacrétaz E, Meier B. Therapeutic strategy with total coronary artery occlusions. J Am Coll Cardiol. 79(2):185-187 (1997).

7. Fefer P, Knudtson ML, Cheema AN, et al. Current perspectives on coronary chronic total occlusions: The canadian multicenter chronic total occlusions registry. J Am Coll Cardiol.59(11):991-997 (2012) .

8. Rathore S, Matsuo H, Terashima M, et al. Procedural and in-hospital outcomes after percutaneous coronary intervention for chronic total occlusions of coronary arteries 2002 to 2008: Impact of novel guidewire techniques. JACC Cardiovasc Interv.2(6):489-497 (2009).

9. Morino Y, Abe M, Morimoto 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.4(2):213-221 (2011).

10. Christopoulos G, Kandzari DE, Yeh RW, et al. Development and validation of a novel scoring system for predicting technical success of chronic total occlusion percutaneous coronary interventions: The PROGRESS CTO (Prospective Global Registry for the Study of Chronic Total Occlusion Intervention) score. JACC Cardiovasc Interv.9(1):1-9 (2016) .

11. Szijgyarto Z, Rampat R, Werner GS, et al. Derivation and validation of a chronic total coronary occlusion intervention procedural success score from the 20,000-patient EuroCTO registry: The EuroCTO (CASTLE) score. JACC Cardiovasc Interv.2(4):335-342 (2019).

12. Maeremans J, Spratt JC, Knaapen P, et al. Towards a contemporary, comprehensive scoring system for determining technical outcomes of hybrid percutaneous chronic total occlusion treatment: The RECHARGE score. Catheter Cardiovasc Interv.91(2):192-202 (2018).

13. Brilakis ES, Mashayekhi K, Burke MN, et al. How DECISION-CTO can help guide the decision to perform chronic total occlusion percutaneous coronary intervention. Circulation.139(14):1684-1687 (2019).

14. 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.139(14):1674-1683 (2019).

15. Mashayekhi K, Nührenberg TG, Toma A, et al. A randomized trial to assess regional left ventricular function after stent implantation in chronic total occlusion: The REVASC trial. JACC Cardiovasc Interv.11(19):1982-1991 (2018).

16. George S, Cockburn J, Clayton TC, et al. Long-term follow-up of elective chronic total coronary occlusion angioplasty: Analysis from the UK central cardiac audit database. J Am Coll Cardiol. 64(3):235-243 (2014).

17. Généreux P, Palmerini T, Caixeta A, et al. Quantification and impact of untreated coronary artery disease after percutaneous coronary intervention: The residual SYNTAX (Synergy between PCI with Taxus and Cardiac Surgery) score. J Am Coll Cardiol.59(24):2165-2174 (2012).

18. Généreux P, Palmerini T, Caixeta A, et al. Quantification and impact of untreated coronary artery disease after percutaneous coronary intervention: The residual SYNTAX (Synergy between PCI with Taxus and Cardiac Surgery) score. J Am Coll Cardiol.59(24):2165-2174 (2012).

19. Tanaka H, Morino Y, Abe M, et al. Impact of J-CTO score on procedural outcome and target lesion revascularisation after percutaneous coronary intervention for chronic total occlusion: A substudy of the J-CTO Registry (Multicentre CTO Registry in Japan). EuroIntervention.11(9):981-988 (2016).

20. Mohandes M, Moreno C, Rojas S, et al. J-chronic total occlusion score predictive capacity for percutaneous coronary intervention success of chronic total occlusion: Results from a European single centre cohort with progressive experience over time. Cardiology J.30(1):59-67 (2023).

21. Teng HI, Sung SH, Huang SS, et al. The impact of successful revascularization of coronary chronic total occlusions on long-term clinical outcomes in patients with non-ST-segment elevation myocardial infarction. J Interv Cardiol.31(3):302-309 (2018).

22. Park JY, Choi BG, Rha SW, et al. Chronic total occlusion intervention of the non-infarct-related artery in acute myocardial infarction patients: The Korean multicenter chronic total occlusion registry. Coron Artery Dis.29(6):495-501 (2018).

23. Galassi AR, Vadalà G, Werner GS, et al. Evaluation and management of patients with coronary chronic total occlusions considered for revascularisation. A clinical consensus statement of the European Association of Percutaneous Cardiovascular Interventions (EAPCI) of the ESC, the European Association of Cardiovascular Imaging (EACVI) of the ESC, and the ESC Working Group on Cardiovascular Surgery. EuroIntervention.20(3):e174-e184 (2024).

24. Neumann FJ, Sousa-Uva M, Ahlsson A, et al. 2018 ESC/EACTS Guidelines on myocardial revascularization. Eur Heart J.40(2):87-165 (2019).

25. Windecker S, Kolh P, Alfonso F, et al. 2014 ESC/EACTS Guidelines on myocardial revascularization. Eur Heart J.72(12):1253-1379 (2014).

26. Werner GS, Martin-Yuste V, Hildick-Smith D, et al. A randomized multicentre trial to compare revascularization with optimal medical therapy for the treatment of chronic total coronary occlusions. Eur Heart J.39(26):2484-2493 (2018).

27. Henriques JP, Hoebers LP, Råmunddal T, et al. Percutaneous intervention for concurrent chronic total occlusions in patients with STEMI: The EXPLORE trial. J Am Coll Cardiol.68(15):1622-1632 (2016).