

# Systematic Review/Meta-analysis

## Overview of Contemporary Chronic Total Occlusion Percutaneous Coronary Intervention Techniques: A Narrative Systematic Review

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### ABSTRACT

**Background:** Despite the abundance of coronary chronic total occlusions (CTO) percutaneous coronary intervention (PCI) studies, the literature is not easy to digest for both general PCI operators and CTO PCI specialists because of the many varied terms used for approaches and inconsistency in terminology. This inconsistency makes it challenging to understand the advantages and disadvantages of these different approaches and, most importantly, their downstream clinical outcomes. Accordingly, we conducted a systematic review of all published studies on CTO PCI to describe techniques and algorithms used in the last decade to provide an overview on the efficacy and safety of contemporary CTO PCI techniques.

**Methods:** We performed a comprehensive search of the PubMed, EMBASE, and the Cochrane library databases for manuscripts about PCI of CTOs. We included studies published between the years 2005 and 2019. We categorized studies into those using a single approach (antegrade, retrograde) and those with a prespecified algorithm (ie, hybrid approach).

Chronic total occlusions (CTOs) are defined as 100% occlusions with thrombolysis in myocardial infarction (TIMI) grade 0 flow within the index segment, with a proven or estimated duration of at least 3 months.<sup>1,2</sup> CTOs are commonly

### RÉSUMÉ

**Contexte :** Malgré l'abondance d'études sur l'intervention coronarienne percutanée (ICP) en cas d'occlusion totale chronique (OTC), la littérature n'est pas facile à assimiler, tant pour les opérateurs généraux qui effectuent des ICP que pour les spécialistes des ICP en cas d'OTC, en raison des nombreux termes utilisés pour les approches et de l'incohérence sur le plan de la terminologie. Cette incohérence rend difficile la compréhension des avantages et des inconvénients de ces différentes approches et, surtout, de leurs résultats cliniques en aval. Nous avons donc procédé à une revue systématique de toutes les études publiées sur l'ICP en cas d'OTC afin de décrire les techniques et les algorithmes utilisés au cours de la dernière décennie et de donner un aperçu de l'efficacité et de l'innocuité des techniques contemporaines d'ICP en cas d'OTC.

**Méthodologie :** Nous avons effectué une recherche exhaustive dans les bases de données PubMed, EMBASE et Cochrane Library pour trouver des articles sur l'ICP en cas d'OTC. Nous avons retenu les études publiées entre 2005 et 2019. Nous avons classé ces études en deux catégories : celles qui utilisent une seule approche (antérograde,

found in patients undergoing coronary angiography, with a prevalence of 18%–52%.<sup>3–5</sup> Successful CTO PCI have been associated with improvement in angina and overall quality of life. Observational studies have also found improvement in left ventricular function, a decreased need for coronary artery bypass grafting, and potentially improved survival in patients with successful CTO PCI recanalization compared with those in whom CTO PCI has failed.<sup>6,7</sup> Historically, the Achilles heel of CTO PCI was the low success rate and a perception of unacceptably high complication rates with the use of conventional PCI approaches and equipment; this finding has led to a general reluctance in practice to perform PCI to a CTO.<sup>8</sup>

Received for publication April 17, 2021. Accepted May 31, 2021.

**Ethics Statement:** The research reported has adhered to the relevant ethical guidelines.

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See page 1278 for disclosure information.

**Results:** Fifty-five observational studies including 28,907 patients who underwent CTO were included in this review. CTO PCI generally carries low risk of major procedural complications, with angiographic success rates being higher in studies that used an algorithmic vs single technical approach.

**Conclusions:** This systematic review highlights the wide variation in definitions and practices in CTO PCI and calls for standardization in terminology and practice.

In the last decade, tremendous improvement in PCI devices and equipment, increased operator experience, and development of novel crossing strategies as well as codified and effective technical algorithms, have helped overcome previous challenges and have led to predictably higher procedural success rates.<sup>9</sup> Indeed, data suggest that CTO PCI success rates improve,<sup>10</sup> and complication rates decrease with operator experience, even among challenging patients and lesion subgroups.<sup>11,12</sup> As a result, the impetus for percutaneous recanalization of CTO lesion continues to grow.<sup>13</sup>

A limitation of the CTO PCI literature is the overwhelming number of varied terms used to describe technical approaches and an inconsistency in outcome terminology between studies. This inconsistency makes it challenging to understand or compare the advantages and disadvantages of the various approaches or their clinical outcomes. Accordingly, we conducted a systematic review of all published studies on CTO PCI to address these gaps in knowledge. Our intent was to examine approaches used in the last decade, broadly categorizing them as single strategy versus algorithmic approaches, to provide an overview on the efficacy and safety of these 2 broad contemporary CTO PCI approaches. By this simple categorization, we hope to make this literature more accessible to the broad audience of general PCI operators, as well as CTO PCI specialists.

## Methods

### Protocol and registration

Our systematic review was conducted and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines<sup>14</sup> and was registered with the International Prospective Register for Systematic Reviews (PROSPERO: CRD42019127312).

### Study design and search strategy

Search strategy was developed and performed in collaboration with an experienced clinical research librarian. We performed a comprehensive search of the PubMed, EMBASE, and the Cochrane library databases for manuscripts about PCI of CTOs. The search strategy included the following keywords: “chronic total occlusion,” “percutaneous coronary intervention,” “angioplasty,” “stent,” and “drug-eluting stents.” Details of the search strategy are provided in Supplemental Table S1. In addition, we manually searched

rétrograde) et celles qui utilisent un algorithme prédéfini (approche hybride).

**Résultats :** Cette revue portait sur 55 études observationnelles, pour un total de 28 907 patients présentant des OTC. L'ICP en cas d'OTC comporte généralement un faible risque de complications importantes liées aux interventions, les taux de réussite angiographique étant plus élevés pour les études où une approche algorithmique était utilisée que pour celles où l'on recourait à une approche technique unique.

**Conclusions :** Cette revue systématique souligne la grande variation des définitions et des pratiques en matière d'ICP en cas d'OTC, ainsi que le besoin d'une normalisation de la terminologie et de la pratique.

references of retrieved articles and related articles on PubMed's related article feature to identify additional studies. The full text of all relevant studies was analyzed to determine whether they met the study selection criteria noted subsequently. We used the Covidence software in screening articles.<sup>15</sup>

### Eligibility

Human studies in English published between the 2005 and 2019 were included if they reported on 1 or more CTO PCI approaches as well as procedural success and any of the following procedural complications during CTO PCI: death, major adverse cardiovascular events (MACE), myocardial infarction (MI), stroke, emergent or urgent coronary artery bypass graft (CABG), target vessel revascularization (TVR), perforation, tamponade, stent thrombosis, major vascular complications, major bleeding, and contrast nephropathy. Major adverse cardiovascular events are defined as the composite of death, emergent CABG, stroke, and MI. Technical success of CTO PCI was defined as successful CTO revascularization with achievement of < 30% residual diameter stenosis within the treated segment and restoration of TIMI grade 3 antegrade flow. Procedural success was defined as achievement of technical success with no in-hospital MACE. We excluded case series of less than 10 patients, case reports, editorials, and reviews. A list of the included studies is shown in Supplemental Table S2.

### Study selection

Two authors (A.K. or K.G. and T.A. or G.E.-G) simultaneously screened titles and abstracts using the eligibility criteria. After applying exclusions, remaining articles were reviewed using the full text by 2 authors (T.A. and G.E.-G.), and controversies were resolved by consensus.

### Data extraction

Data from included studies were extracted by 2 authors (A.K. and K.G.) using a standardized data collection form. Extracted data included the first author's surname, year of publication, country, publication year, study design, sample size, characteristics of the subjects (age, gender, smoking status, and comorbidities, such as hypertension, hyperlipidemia, diabetes mellitus, and prior PCI or CABG), CTO technique, procedural characteristics and outcomes, in-hospital complications, and the incidence of adverse clinical events during

follow-up. Lesion severity was captured by the Japanese Chronic Total Occlusion (JCTO) score. Where there were duplicate data in 2 publications, only the first published study was included.

### Classification of studies

The included studies were classified according to the crossing technique used. Studies that used a single strategy approach were classified to 1 of the 3 broad categories of CTO crossing techniques currently utilized<sup>16</sup>: antegrade wire escalation (AWE),<sup>17</sup> antegrade dissection/reentry (ADR),<sup>18,19</sup> or retrograde.<sup>20,21</sup> AWE was defined as the use of antegrade wiring to penetrate the proximal cap and cross the lesion into the true lumen distally while remaining intraplaque within the CTO segment. ADR was defined as subintimal crossing of the CTO with subsequent reentry into the distal true lumen. Retrograde approach was defined as retrograde CTO crossing either with retrograde wiring or using retrograde dissection/reentry techniques.

Because contemporary CTO practice is typically not limited to a single approach, we provide the details of these approaches in [Supplemental Appendix S1](#). Studies that used multiple strategy approaches were classified based on the pre-specification of a defined algorithm. Studies that used a standard hybrid approach,<sup>22</sup> based on 4 key angiographic characteristics (proximal cap location and morphology, lesion length, target coronary vessels beyond the distal cap, and presence of collaterals), were classified in the hybrid category. Studies that used a clear Asian-Pacific algorithm<sup>23</sup> were classified in the Asian-Pacific category. Studies that varied between techniques with no clear pre-specified algorithm, were classified in the unclassified hybrid category.

In studies that report data on 2 different techniques, all data related to each technique were combined and accounted for in the relevant technique category. Studies that report data on 1 technique, but the technique was initiated after a failure of a primary technique or secondary attempts were made using different strategy, were classified in the unclassified category. If no technique was specified, the study was excluded.

### Risk of bias/quality assessment

Included articles were evaluated for potential biases using Cochrane risk of bias assessment tool (**Risk of Bias in Non-randomised Studies - of Interventions** [ROBINS-I]), which was performed independently by 2 authors (T.A. and G.E.-G.), and controversies were resolved by consensus. As shown in [Supplemental Table S3](#), most of these studies showed a moderate degree of bias.

### Statistical analysis

Absolute number of events was extracted for the outcomes when available or calculated from the pertinent statistical measures. The estimated incidence rates were expressed as a percentage. Because of significant study design heterogeneity between the included studies, a meta-analysis was not performed.

## Results

### Study selection

A total of 6708 articles were identified through literature search, all written in the English language. A total of 2189 duplicate publications were identified and removed. After an initial screening, 565 studies were eligible for full-text assessment. Finally, 55 studies fulfilled the eligibility criteria and were included in the systematic review.<sup>24-78</sup> The detailed PRISMA flow diagram is presented in [Figure 1](#).

### Study characteristics

All studies included in the review were observational and were published between 2005 and 2019. We did identify 3 randomized controlled trials over the period<sup>79-81</sup>; however, all 3 were excluded because the crossing technique was not specified, and outcomes were not available by approach. In total, 28,907 patients with CTO were included in this analysis with sample sizes for each study varying between 18 and 3055 patients. The follow-up duration ranged from 30 days to 36 months.

Patients in the studies were predominantly male (70%-100%) with mean age ranging from 55.4 to 67 years. Of the 55 studies, 47 were single arm studies: 3 AWE studies, 13 retrograde studies, 2 ADR studies, 1 Asian-Pacific study, 21 hybrid studies, and 7 unclassified hybrid studies. We identified 8 double-arm studies: 6 studies compared the AWE and retrograde techniques, 1 study compared AWE with unclassified hybrid, and 1 study compared ADR with non-ADR techniques. All studies defined CTO similarly as 100% vessel occlusion with TIMI 0 flow for more than 3 months. Primary and secondary endpoints slightly varied from study to study ([Supplemental Table S2](#)) but were mainly focused on procedural success rate and individual or composite of major adverse cardiovascular events such as cardiac death and MI.

### Procedure success rate and outcomes

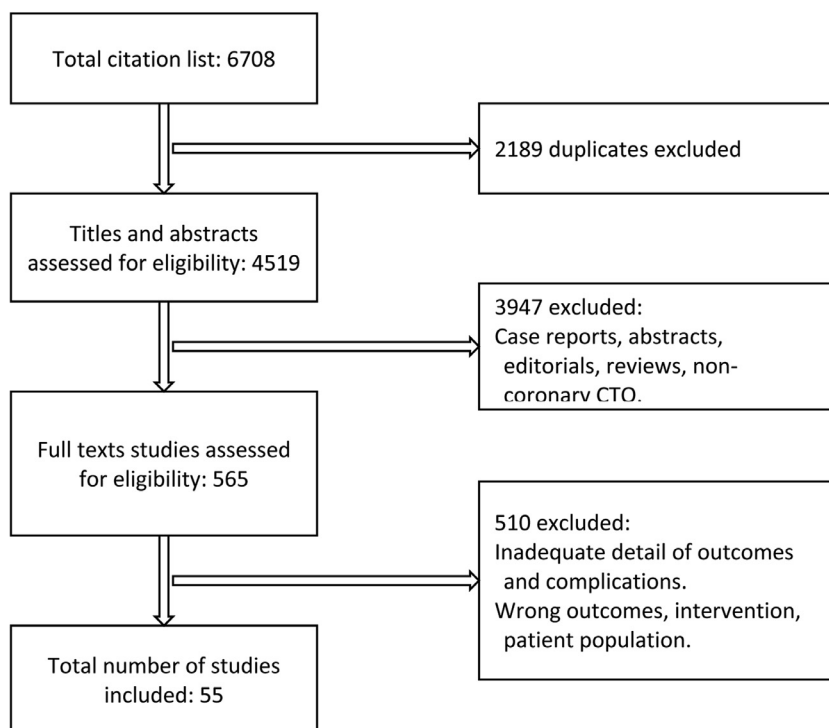
The summary of CTO approaches outcomes presented in [Table 1](#). In general, lesion complexity as measured by JCTO score was substantially higher for the non-AWE approaches.

### Single-arm studies

The details of the single techniques (AWE, retrograde, and ADR) are found in the [Supplemental Appendix S1](#). A comparison of overall outcomes is shown in [Table 1](#). Broadly, there was greater technical and procedural success with algorithmic approaches vs AWE or retrograde. Although ADR had high procedural success, this was at the cost of higher complications. A detailed evaluation of the algorithmic approaches follows below.

### Asian-Pacific algorithm

Only 1 study was included in this group comprising 485 patients.<sup>42</sup> Patient demographics, clinical characteristics, and outcomes are reported in [Supplemental Table S4](#). The mean JCTO score was 2.9. Rates of procedural and technical success were 89.9% and 93.8%, respectively. Incidence of all-cause mortality was 0.2%. Incidence of MACE was 3.8%. The



**Figure 1.** Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram of study selection. CTO, chronic total occlusion.

incidence for MI was 3.4%, and 0.2% for stroke, stent thrombosis, and tamponade.

### Hybrid algorithm

Twenty-one studies using the hybrid technique for CTO PCI published between 2014 and 2018 were included.<sup>43-63</sup> The 21 studies included 13,012 patients and 13,466 CTO lesions (Supplemental Table S4). In 16 studies, where JCTO scores were reported, the average JCTO score was 2.51. The average procedural duration was 115 minutes. The procedural success rate was included in 12 of the studies, and the mean success rate was 87.5%. The mean technical success rate was 88.77%. The incidence of periprocedural all-cause mortality was 0.60%. Periprocedural cardiac death, reported in 1 study by Maeremans et al.,<sup>61</sup> was 0.24%. The incidence of periprocedural MACE, MI, and stroke was 3.33%, 1.27% and 0.21%, respectively. The incidence of periprocedural target

vessel revascularization was 0.20%. Rates of coronary artery perforation and tamponade were 4.24% and 0.79%, respectively.

### Unclassified approach

Seven studies were categorized into the unclassified technique.<sup>64-70</sup> They included 3028 patients and 3222 CTO lesions (Supplemental Table S4). In 2 studies in which JCTO scores were reported, the average JCTO score was 2.74. The average procedural duration was 188 minutes. The procedural success rate was included in 5 of the studies, and the mean success rate was 82.61%. The mean technical success rate was 87.74%. The incidence of periprocedural all-cause mortality was 0.56%. The periprocedural cardiac death, reported in 2 studies, was 0.26%. The incidence of periprocedural MACE, MI, and stroke was 1.71%, 1.72% and 0.20%, respectively. The incidence of periprocedural target lesion revascularization

**Table 1.** Summary of outcomes for each CTO approach

CTO Approach	J-CTO score, mean	Procedural success (%)	Technical success (%)	All cause death (%)	MACE (%)
Single approach					
Antegrade	1.74	65	90	0.3 (in-hospital) 1.2 (long term)	0 (in-hospital)
Retrograde	2.95	77	80.5	0.3 (in-hospital) 5 (long term)	4 (in-hospital) 14 (long term)
Dissection re-entry	3.3	91.7	98.8	1.6 (in-hospital) 3.2 (long term)	6.4 (in-hospital) 0 (long term)
Algorithm approach					
Hybrid	2.51	87.5	88.7	0.6 (in-hospital) 1.7 (long term)	3.3 (in-hospital) 4.2 (long term)
Asian-Pacific	2.9	89.9	93.8	0.2 (in-hospital)	3.8 (in-hospital)
Unclassified	2.74	82.6	87.7	0.56 (in-hospital) 2.1 (long term)	1.7 (in-hospital) 2.1 (long term)

CTO, chronic total occlusion; JCTO, Japanese chronic total occlusion; MACE, major adverse cardiovascular events.

was 0.09%. The incidence of coronary artery perforation and tamponade was 6.02% and 0.80%, respectively.

### Double-arm studies

**Antegrade vs retrograde approach.** Six studies compared antegrade approach with retrograde approach.<sup>71-76</sup> The largest study included 2596 patients.<sup>76</sup> It compared outcomes for 1872 patients who underwent antegrade approach with 724 patients treated with retrograde approach. Use of the antegrade approach was associated with higher technical (91% vs 87%;  $P = 0.006$ ) and procedural (90% vs 85%;  $P \leq 0.0001$ ) success. Lesions attempted with retrograde approach had higher JCTO score (1.9 vs 2.4;  $P \leq 0.0001$ ). Incidence of MI, coronary perforation, and contrast-induced nephropathy was higher in the retrograde group. There were no significant differences between 2 groups in rates of death, stroke, or acute stent thrombosis. Similar findings were seen in the other studies (Supplemental Table S5). However, in Galassi et al.<sup>71</sup> coronary perforation was higher in the retrograde group, but there was no significant difference in the rates of death, MI, stroke, TVR, or stent thrombosis. Karpaliotis et al.<sup>74</sup> also found that in-hospital MACEs were more common among retrograde cases (4.3% vs 1.1%;  $P < 0.001$ ) mostly because of higher incidence of MI (2.1% vs 0.3%;  $P < 0.003$ ). Coronary perforation (5.5 vs 1.9;  $P < 0.001$ ) and emergency pericardiocentesis (1.3 vs 0.3;  $P = 0.039$ ) were also more common in the retrograde group.

**Antegrade vs unclassified approach.** We identified only 1 double-arm study comparing antegrade approach with combined antegrade and retrograde approach (unclassified approach).<sup>77</sup> This study compared outcomes for 59 patients who underwent antegrade approach and compared them with 49 patients treated with unclassified approach. Follow-up duration was 6 months. There was no significant difference between the groups in technical (94% vs 86%;  $P = 0.127$ ) or procedural (90% vs 80%;  $P = 0.129$ ) success. There were no significant differences between the 2 groups in rates of death (0% vs 0%;  $P$  value not significant), MI (4.3% vs 6%;  $P = 0.684$ ), stroke (0% vs 0%;  $P$  value not significant), coronary dissection (7.2% vs 6%;  $P = 0.789$ ), coronary perforation (7.2% vs 14%;  $P = 0.227$ ), and TVR (16.7% vs 27.3%;  $P = 0.333$ ) (Supplemental Table S5).

**ADR vs non-ADR.** We identified 1 double-arm study comparing ADR approach with non-ADR approaches (AWE and retrograde).<sup>78</sup> This study compared outcomes for 452 patients who underwent ADR approach with 836 patients who underwent non-ADR approach. Use of ADR was associated with lower technical (86.9% vs 91.8%;  $P \leq 0.005$ ) and procedural (85% vs 90.7%;  $P = 0.002$ ) success and longer procedural time. Lesions attempted with ADR were more likely to have a higher JCTO score (2.8 vs 2.4;  $P \leq 0.001$ ). There were no significant differences between the 2 groups in terms of death (0.4% vs 0.4%;  $P = 0.88$ ), MACE (2.9% vs 2.2%;  $P = 0.42$ ), MI (0.9% vs 1.1%;  $P = 0.74$ ), and stroke (0% vs 0.5%;  $P = 0.14$ ). Notably, the rate of tamponade requiring emergency pericardiocentesis was higher in the ADR group (1.8% vs 0.1%;  $P \leq 0.001$ ).

After excluding cases that used retrograde approach, ADR cases were compared with AWE-only cases. ADR cases were associated with longer procedure time and higher JCTO score (2.5 vs 1.9;  $P \leq 0.001$ ). However, there was no significant difference between technical success, procedural success, or MACE between the ADR and AWE-only cases (Supplemental Table S5).

### Discussion

This systematic review included cohort studies that examined the efficacy and safety of contemporary CTO PCI techniques. The main findings are (1) in general, CTO PCI is performed with high success rates; (2) CTO PCI carries low risk of major complications; and (3) compared with studies with single CTO approach, technical and procedural success rates were higher in studies that used a CTO algorithm approach, whereas adverse events were lower. This finding reinforces the need for modern CTO PCI practice to include expertise in multiple procedural approaches and a systematic approach to switch from one to another to maximize procedural success while minimizing complications and ensuring efficiency.

Despite the abundance of CTO PCI studies in the literature, the literature is not easy to digest for both general PCI operators and CTO PCI specialists in part because of the overwhelming number of varied terms used for approaches and inconsistency in terminology among studies. This inconsistency makes it challenging to understand the advantages and disadvantages of these different approaches and, most importantly, their downstream clinical outcomes. In addition, there is wide variation in practice of CTO PCI worldwide. Despite the excellent results with use of the hybrid algorithm in North America and Europe, there has been infrequent adoption of this paradigm in the Asia-Pacific region where most of the world's population resides. This infrequent adoption is caused, in part, by the preference of parallel wire technique over ADR that is prevalent in this region, possibly driven by limited access to the CrossBoss and Stingray system (Boston Scientific, Marlborough, MA). Other factors, such as lower rates of coronary artery bypass grafting,<sup>82</sup> have also likely contributed to the differences in CTO PCI approaches seen in the Asia-Pacific region.

In our study, we observed that excellent outcomes can be achieved with both the hybrid and Asian-Pacific algorithms. Both hybrid and Asian-Pacific algorithms were associated with higher procedural success rates (87.5% and 89.9%, respectively) with lower risks of major complications. These favorable outcomes are likely multifactorial, reflecting the importance of dual injections for CTO PCI angiography, the adoption of a standardized anatomic approach for angiogram evaluation, the use of angiographic characteristics to guide strategy selection, and rapid/early conversion to an alternative crossing strategy if the initial crossing strategy failed. The unclassified approach had a longer procedure time than the other hybrid approaches. This finding suggests that a more rigorous and algorithmic approach to switching strategies translates to improved procedural efficiency.

The tremendous improvement in PCI devices and equipment, increased operator experience, and development of new crossing techniques and treatment algorithms have helped

overcome technical complexities leading to improved procedural success rates. This finding will likely make CTO PCI expand in the future. Furthermore, a recent systematic review found that there was an improvement in quality-of-life metrics in patients with CTO who undergo revascularization.<sup>83</sup>

As such, there is a need for terminology standardization in the CTO PCI field. Standardized definitions of data elements and clinical endpoints of CTO PCI will allow effective communication among all relevant stakeholders, including patients. Such standardization would serve both clinical, research, and regulatory purposes as well as facilitate training and future equipment development.

The **Chronic Total Occlusion Academic Research Consortium (CTO-ARC)** project was recently published to standardize the field.<sup>84</sup> CTO-ARC has provided uniform definitions for endpoints specific to CTO interventions and recommends a consensus framework for the design of clinical trials and registries, including the procedural data collected during CTO-PCI. CTO-ARC is a first step toward improved comparability and interpretability of study results, supplying an increasingly growing body of CTO percutaneous coronary intervention evidence.

### Limitations

Our study must be interpreted in the context of several limitations that merit discussion. First, all included studies were observational in nature; thus, the available data are subject to potential biases, such as selection bias, publication bias, and confounding. Only 3 randomized studies were found in our search, and all were excluded as the crossing technique was not specified, which reinforces the need for standardization of trial reporting. Second, because of significant clinical heterogeneity, we did not meta-analyze our data across included publications. We believe that the heterogeneity of the populations and outcome metrics precludes the ability to synthesize our findings into a single summary statistic. As such, we would argue that a qualitative systematic review is more appropriate.

### Conclusion

This systematic review found better technical and procedural success with CTO algorithmic approaches compared with single technique approaches. However, there was wide variation in definitions and practices in CTO PCI. This call for standardization in terminology in modern CTO PCI practice is a requisite first step to evaluate new algorithms to maximize effectiveness and safety.

### Funding Sources

There are no funding sources to report.

### Disclosures

Dr Sanjog Kalra is a proctor, preceptor, speaker's bureau, advisory board member, and new product tester for Abiomed Inc, Boston Scientific, Philips Healthcare, Translumina Therapeutics, Cardiovascular Systems Inc, Abbott Vascular, and Asahi Intecc. The other authors have no conflicts of interest to declare.

### References

1. Carlino M, Magri CJ, Uretsky BF, et al. Treatment of the chronic total occlusion: a call to action for the interventional community. *Catheter Cardiovasc Interv* 2015;85:771–8.
2. Sianos G, Werner GS, Galassi AR, et al. Recanalisation of chronic total coronary occlusions: 2012 consensus document from the EuroCTO club. *EuroIntervention* 2012;8:139–45.
3. Christofferson RD, Lehmann KG, Martin GV, et al. Effect of chronic total coronary occlusion on treatment strategy. *Am J Cardiol* 2005;95:1088–91.
4. 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* 2012;59:991–7.
5. Jeroudi OM, Alomar ME, Michael TT, et al. Prevalence and management of coronary chronic total occlusions in a tertiary Veterans Affairs hospital. *Catheter Cardiovasc Interv* 2014;84:637–43.
6. Grantham JA, Marso SP, Spertus J, House J, Holmes Jr DR, Rutherford BD. Chronic total occlusion angioplasty in the United States. *J Am Coll Cardiol* 2009;2:479–86.
7. Joyal D, Afilalo J, Rinfret S. Effectiveness of recanalization of chronic total occlusions: a systematic review and meta-analysis. *Am Heart J* 2010;160:179–87.
8. Shuvy M, Qiu M, Chee-A-Tow A, et al. Management of chronic total coronary occlusion in stable ischemic heart disease by percutaneous coronary intervention versus coronary artery bypass grafting versus medical therapy. *Am J Cardiol* 2017;120:759–64.
9. Galassi AR, Tomasello SD, Reifart N, et al. In-hospital outcomes of percutaneous coronary intervention in patients with chronic total occlusion: insights from the ERCTO (European Registry of Chronic Total Occlusion) registry. *EuroIntervention* 2011;7:472–9.
10. Christopoulos G, Menon RV, Karpaliotis D, et al. The efficacy and safety of the “hybrid” approach to coronary chronic total Occlusions: Insights from a contemporary multicenter US registry and comparison with prior studies. *J Invasive Cardiol* 2014;26:427e432.
11. Christopoulos G, Menon RV, Karpaliotis D, et al. Application of the “hybrid approach” to chronic total occlusions in patients with previous coronary artery bypass graft surgery (from a Contemporary Multicenter US registry). *Am J Cardiol* 2014;113:1990e-4.
12. Christopoulos G, Karpaliotis D, Alaswad K, et al. The efficacy of “hybrid” percutaneous coronary intervention in chronic total occlusions caused by in-stent restenosis: insights from a US multicenter registry. *Catheter Cardiovasc Interv* 2014;84:646e-1.
13. Patel Vishal G, Kimberly M, Brayton MD, et al. Angiographic success and procedural complications in patients undergoing percutaneous coronary chronic total occlusion interventions: a weighted meta-analysis of 18,061 patients from 65 studies. *JACC* 2013;128–36.
14. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. *BMJ* 2009;339:b2700.
15. Covidence systematic review software, Veritas Health Innovation, Melbourne, Australia. Available at: [www.covidence.org](http://www.covidence.org). Accessed October 16, 2021.
16. Galassi A, Grantham JA, Kandzari D, et al. Percutaneous treatment of coronary chronic total occlusion. Part 2: technical approach. *Interv Cardiol Rev* 2014;9:201–7.
17. Rinfret S, Joyal D, Spratt JC, Buller CE. Chronic total occlusion percutaneous coronary intervention case selection and techniques for the ante-grade-only operator. *Catheter Cardiovasc Interv* 2015;85:408–15.

18. Michael TT, Papayannis AC, Banerjee S, Brilakis ES. Subintimal dissection/reentry strategies in coronary chronic total occlusion interventions. *Circ Cardiovasc Interv* 2012;5:729–38.
19. Colombo A, Mikhail GW, Michev I, et al. Treating chronic total occlusions using subintimal tracking and reentry: the STAR technique. *Catheter Cardiovasc Interv* 2005;64:407–11.
20. Brilakis ES, Grantham JA, Thompson CA, et al. The retrograde approach to coronary artery chronic total occlusions: a practical approach. *Catheter Cardiovasc Interv* 2012;79:3–19.
21. Joyal D, Thompson CA, Grantham JA, Buller CE, Rinfret S. The retrograde technique for recanalization of chronic total occlusions: a step-by-step approach. *JACC Cardiovasc Interv* 2012;5:1–11.
22. Christopoulos G, Karpaliotis D, Alaswad K, et al. Application and outcomes of a hybrid approach to chronic total occlusion percutaneous coronary intervention in a contemporary multicenter US registry. *Int J Cardiol* 2015;198:222–8.
23. Scott Harding, Wu E, Lo S, et al. A new algorithm for crossing chronic total occlusions from the Asia Pacific Chronic Total Occlusion Club. *J Am Coll Cardiol Interv* 2017;10:2135–43.
24. BoganaShanmugam V, Psaltis P, Wong DT, et al. Chronic total occlusion—percutaneous coronary intervention (CTO-PCI) experience in a single, multi-operator Australian centre: need for dedicated CTO-PCI programs. *Heart, Lung & Circ* 2016;25:676–82.
25. Ks G, Iype M, Viswanathan S, et al. Angiographic predictors of success in antegrade approach of chronic total occlusion interventions in a South Indian population in the contemporary era. *Indian Heart J* 2018;70:15–9.
26. Akinseye OA, Haji SA, Koshy SKG, et al. Outcomes of percutaneous antegrade intraluminal coronary intervention of chronic total occlusion with remote surgical backup. *Curr Prob Cardiol* 2019;44:100390.
27. Sheiban I, Moretti C, Omede P, et al. The retrograde coronary approach for chronic total occlusions: mid-term results and technical tips & tricks. *J Intervent Cardiol* 2007;20(6):466–73.
28. Sianos G, Barlis P, Di Mario C, et al. European experience with the retrograde approach for the recanalisation of coronary artery chronic total occlusions. A report on behalf of the euroCTO club. *Eurointervention* 2008;4:84–92.
29. Suk HC, Moo HK, Long HY, et al. Initial experience of retrograde wire approach in coronary chronic total occlusion intervention. *Korean Circ J* 2009;39:228–35.
30. Rathore S, Katoh O, Matsuo H, et al. Retrograde percutaneous recanalization of chronic total occlusion of the coronary arteries: procedural outcomes and predictors of success in contemporary practice. *Circ Cardiovasc Interv* 2009;2:124–32.
31. Ge L, Qian JY, Liu XB, et al. Retrograde approach for the recanalization of coronary chronic total occlusion: preliminary experience of a single center. *Chinese Med J* 2010;123:857–63.
32. Lee NH, Seo HS, Choi JH, et al. Recanalization strategy of retrograde angioplasty in patients with coronary chronic total occlusion—analysis of 24 cases, focusing on technical aspects and complications. *Int J Cardiol* 2010;144:219–29.
33. Karpaliotis D, Michael TT, Brilakis ES, et al. Retrograde coronary chronic total occlusion revascularization: procedural and in-hospital outcomes from a multicenter registry in the United States. *JACC: Cardiovasc Interv* 2012;5:1273–9.
34. Stojkovic S, Sianos G, Katoh O, et al. Efficiency, safety, and long-term follow-up of retrograde approach for CTO recanalization: initial (Belgrade) experience with international proctorship. *J Interv Cardiol* 2012;25:540–8.
35. Muramatsu T, Tsukahara R, Ito Y, et al. Changing strategies of the retrograde approach for chronic total occlusion during the past 7 years. *Catheter Cardiovasc Interv* 2013;81:E178–85.
36. Ma JY, Qian JY, Ge L, et al. Retrograde approach for the recanalization of coronary chronic total occlusion: collateral selection and collateral related complication. *Chinese Med J* 2013;126:1086–91.
37. Tsuchikane E, Yamane M, Mutoh M, et al. Japanese multicenter registry evaluating the retrograde approach for chronic coronary total occlusion. *Catheter Cardiovasc Interv* 2013;82:E654–61.
38. Galassi AR, Siano G, Werner GS, et al. Retrograde recanalization of chronic total occlusions in Europe: procedural, in-hospital, and long-term outcomes from the multicenter ERCTO registry. *J Am Coll Cardiol* 2015;65:2388–400.
39. Azzalini L, Agostoni P, Benincasa S, et al. Retrograde chronic total occlusion percutaneous coronary intervention through ipsilateral collateral channels: a multicenter registry. *JACC: Cardiovasc Interv* 2017;10:1489–97.
40. Colombo A, Mikhail GW, Michev I, et al. Treating chronic total occlusions using subintimal tracking and reentry: the STAR technique. *Catheter Cardiovasc Interv* 2005;64:407–11.
41. Xenogiannic I, Karpaliotis D, Alaswad K, et al. Comparison between traditional and guide-catheter extension reverse controlled antegrade dissection and retrograde tracking: insights from the PROGRESS-CTO Registry. *J Invas Cardiol* 2019;31:27–34.
42. Chan CY, Wu EB, Yan BP, et al. Procedure failure of chronic total occlusion percutaneous coronary intervention in an algorithm driven contemporary Asia-Pacific Chronic Total Occlusion Club (APCTO Club) multicenter registry. *Catheter Cardiovasc Interv* 2019;93:1033–8.
43. Menon RV, Alaswad K, Lombardi W, et al. The safety and efficacy of the "hybrid approach" to chronic total occlusions: Insights from a contemporary multicenter us registry. *J Am Coll Cardiol* 2013;1:B119.
44. Christopoulos G, Menon RV, Karpaliotis D, et al. Application of the "hybrid approach" to chronic total occlusions in patients with previous coronary artery bypass graft surgery (from a contemporary multicenter US registry). *Am J Cardiol* 2014;113:1990e–94.
45. Christopoulos G, Menon RV, Karpaliotis D, et al. The efficacy and safety of the "hybrid" approach to coronary chronic total occlusions: insights from a contemporary multicenter US registry and comparison with prior studies. *J Invas Cardiol* 2014;26:427–32.
46. Christopoulos G, Karpaliotis D, Alaswad K, et al. The efficacy of "hybrid" percutaneous coronary intervention in chronic total occlusions caused by in-stent restenosis: insights from a US multicenter registry. *Catheter Cardiovasc Interv* 2014;84:646–51.
47. Michael TT, Mogabgab O, Fuh E, et al. Application of the "hybrid approach" to chronic total occlusion interventions: a detailed procedural analysis. *J Interv Cardiol* 2014;27:36–43.
48. Rinfret S, Ribeiro HB, Nguyen CM, et al. Dissection and re-entry techniques and longer-term outcomes following successful percutaneous coronary intervention of chronic total occlusion. *Am J Cardiol* 2014;114:1354–60.
49. Christopoulos G, Karpaliotis D, Alaswad K, et al. Application and outcomes of a hybrid approach to chronic total occlusion percutaneous coronary intervention in a contemporary multicenter us registry. *Int J Cardiol* 2015;198:222–8.
50. Saponis J, Christopoulos G, Grantham JA, et al. Procedural failure of chronic total occlusion percutaneous coronary intervention: insights

- from a multicenter US registry. *Catheter Cardiovasc Interv* 2015;85:1115–22.
51. Vo MN, McCabe JM, Lombardi WL, et al. Adoption of the hybrid CTO approach by a single non-CTO operator: procedural and clinical outcomes. *J Invas Cardiol* 2015;27:139–44.
  52. Amsavelu S, Christakopoulos GE, Karatasakis A, et al. Impact of crossing strategy on intermediate-term outcomes after chronic total occlusion percutaneous coronary intervention. *Can J Cardiol* 2016;32:1239.e1–e7.
  53. Wilson WM, Walsh SJ, Yan AT, et al. Hybrid approach improves success of chronic total occlusion angioplasty. *Heart* 2016;102:1486–93.
  54. Basir MB, Karatasakis A, Alqarqaz M, et al. Further validation of the hybrid algorithm for CTO PCI; difficult lesions, same success. *Cardiovasc Revasc Med* 2017;18:328–31.
  55. Benincasa S, Azzalini L, Carlino M, et al. Outcomes of the retrograde approach through epicardial versus non-epicardial collaterals in chronic total occlusion percutaneous coronary intervention. *Cardiovasc Revasc Med* 2017;18:393–8.
  56. Daniels DV, Banerjee S, Alaswad K, et al. Safety and efficacy of the hybrid approach in coronary chronic total occlusion percutaneous coronary intervention: The Hybrid Video Registry. *Catheter Cardiovasc Interv* 2018;91:175–9.
  57. Lee CK, Chen YH, Lin MS, et al. Retrograde approach is as effective and safe as antegrade approach in contemporary percutaneous coronary intervention for chronic total occlusion: a Taiwan single-center registry study. *Acta Cardiologica Sinica* 2017;33:20–7.
  58. Sapontis J, Salisbury AC, Yeh RW, 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;10:1523–34.
  59. Sapontis J, Marso SP, Cohen DJ, et al. The Outcomes, Patient Health Status, and Efficiency IN Chronic Total Occlusion Hybrid Procedures registry: rationale and design. *Coronary Artery Dis* 2017;28:110–9.
  60. Wilson WM, Walsh SJ, Bagnall A, et al. One-year outcomes after successful chronic total occlusion percutaneous coronary intervention. *Catheter Cardiovasc Interv* 2017;90:703–12.
  61. Maeremans J, Kayaert P, Bataille Y, et al. Assessing the landscape of percutaneous coronary chronic total occlusion treatment in Belgium and Luxembourg: the Belgian Working Group on Chronic Total Occlusions (BWGCTO) registry. *Acta Cardiologica* 2018;73:427–36.
  62. Maeremans J, Avran A, Walsh S, et al. One-year clinical outcomes of the hybrid CTO revascularization strategy after hospital discharge: a subanalysis of the multicenter RECHARGE registry. *J Invas Cardiol* 2018;30:62–70.
  63. Tajti P, Karpaliotis D, Alaswad K, et al. The hybrid approach to chronic total occlusion percutaneous coronary intervention: update from the PROGRESS CTO Registry. *JACC: Cardiovasc Interv* 2018;11:1325–35.
  64. Surmely JF, Katoh O, Tsuchikane E, et al. Coronary septal collaterals as an access for the retrograde approach in the percutaneous treatment of coronary chronic total occlusions. *Catheter Cardiovasc Interv* 2007;69:826–32.
  65. 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* 2009;2:489–97.
  66. Nombela-Franco L, Urena M, Jerez-Valero M, et al. Validation of the J-chronic total occlusion score for chronic total occlusion percutaneous coronary intervention in an independent contemporary cohort. *Circulation: Cardiovasc Interv* 2013;6:635–43.
  67. Galassi AR, Boukhris M, Tomasello SD, et al. Long-term clinical and angiographic outcomes of the mini-STAR technique as a bailout strategy for percutaneous coronary intervention of chronic total occlusion. *Can J Cardiol* 2014;30:1400–6.
  68. Okamura A, Yamane M, Muto M, et al. Complications during retrograde approach for chronic coronary total occlusion: sub-analysis of Japanese multicenter registry. *Catheter Cardiovasc Interv* 2016;88(1):7–14.
  69. Chai WL, Agyekum F, Zhang B, et al. Clinical prediction score for successful retrograde procedure in chronic total occlusion percutaneous coronary intervention. *Cardiology (Switzerland)* 2016;134:331–9.
  70. Kirk Christensen M, Freeman PF, Rasmussen JG, et al. Chronic total coronary occlusion: treatment results. *Scand Cardiovasc J* 2017;51:197–201.
  71. Galassi AR, Tomasello SD, Reifart N, et al. In-hospital outcomes of percutaneous coronary intervention in patients with chronic total occlusion: insights from the ERCTO (European Registry of Chronic Total Occlusion) registry. *Eurointervention* 2011;7:472–9.
  72. Michael TT, Mogabgab O, Alomar M, et al. Long-Term outcomes of successful chronic total occlusion percutaneous coronary interventions using the antegrade and retrograde approach. *J Interv Cardiol* 2014;27:465–71.
  73. Bijklic K, Schwencke C, Schofer J. Long-term major adverse cardiac and cerebrovascular events (MACCE) rate: comparison of retrograde and antegrade recanalization of chronic total coronary occlusions. *Wiener Klinische Wochenschrift* 2017;129:243–50.
  74. Karpaliotis D, Karatasakis A, Alaswad K, et al. Outcomes with the use of the retrograde approach for coronary chronic total occlusion interventions in a contemporary multicenter US registry. *Circulation: Cardiovasc Interv* 2016;9:6.
  75. Stetler J, Karatasakis A, Christakopoulos GE, et al. Impact of crossing technique on the incidence of periprocedural myocardial infarction during chronic total occlusion percutaneous coronary intervention. *Catheter Cardiovasc Interv* 2016;88:1–6.
  76. Suzuki Y, Tsuchikane E, Katoh O, et al. Outcomes of percutaneous coronary interventions for chronic total occlusion performed by highly experienced Japanese specialists: the first report from the Japanese CTO-PCI Expert Registry. *JACC: Cardiovasc Interv* 2017;10:2144–54.
  77. Hsu JT, Tamai H, Kyo E, et al. Traditional antegrade approach versus combined antegrade and retrograde approach in the percutaneous treatment of coronary chronic total occlusions. *Catheter Cardiovasc Interv* 2009;74:555–63.
  78. Danek BA, Karatasakis A, Karpaliotis D, et al. Use of antegrade dissection re-entry in coronary chronic total occlusion percutaneous coronary intervention in a contemporary multicenter registry. *Int J Cardiol* 2016;214:428–37.
  79. Henriques JP, Hoebbers LP, Råmunddal T, et al. Percutaneous intervention for concurrent chronic total occlusions in patients with STEMI: The EXPLORE Trial. *J Am Coll Cardiol* 2016;68:1622–32.
  80. 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* 2018;39:2484–93.



81. Lee SW, Lee PH, Ahn JM, et al. Randomized trial evaluating percutaneous coronary intervention for the treatment of chronic total occlusion. *Circulation* 2019;139:1674–83.
82. Kim BK, Shin S, Shin DH, et al. Clinical outcome of successful percutaneous coronary intervention for chronic total occlusion: results from the Multicenter Korean Chronic Total Occlusion (KCTO) Registry. *J Invasive Cardiol* 2014;26:255–9.
83. Abuzaid W, Zivkovic N, Elbaz-Greener G, et al. Association between revascularization and quality of life in patients with coronary chronic total occlusions: a systematic review. *Cardiovasc Revasc Med* 2020; S1553-8389:30653–9.
84. Ybarra LF, Rinfret S, Brilakis ES, et al. Definitions and clinical trial design principles for coronary artery chronic total occlusion therapies. CTO-ARC consensus recommendations. *Circulation* 2021;143:479–500.

### **Supplementary Material**

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