





Utility of Coronary Computed Tomography Angiography in Complex Percutaneous Coronary Intervention: A Systematic Review and Meta-Analysis of CTO Studies

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ABSTRACT

Background: Complex percutaneous coronary intervention (PCI) presents technical challenges and elevated procedural risks. Coronary computed tomography angiography (CCTA) is a non-invasive imaging modality that might improve pre-procedural planning and intra-procedural guidance.

Aim: This study evaluates the impact of CCTA-guided PCI compared with standard angiography guidance in complex PCI, with a focus on procedural success, fluoroscopy time, contrast volume, and major adverse cardiac events (MACE).

Study Design: A systematic review and meta-analysis.

Methods: We conducted a systematic search of PubMed/MEDLINE, Embase, Cochrane Library, Scopus, Google Scholar, and ClinicalTrials.gov for studies published between 2014 and 2024. Eligible studies included randomized controlled trials (RCTs) and observational studies comparing CCTA-guided versus angiography-guided PCI in adults. Outcomes were pooled using random-effects meta-analysis. The certainty of evidence was assessed using the GRADE framework.

Results: Five studies (one RCT, four observational; 7,406 participants), all focusing on chronic total occlusion PCI, were included. Meta-analyses revealed no significant differences in procedural success [risk ratio: 0.97, 95% confidence interval (CI): 0.92–1.02], fluoroscopy time [mean difference (MD) +6.0 min, 95% CI: –7.7 to 19.7], or contrast volume (MD –7.0 mL, 95% CI –43.5 to 29.4). MACE rates were also comparable (odds ratio: 1.03, 95% CI: 0.67–1.58). The certainty of evidence was rated as very low due to risk of bias, imprecision, heterogeneity, and limited generalizability.

Conclusion: CCTA-guided PCI is comparable to angiography-guided PCI in terms of procedural success, efficiency, and safety in complex lesions. However, the very low certainty of evidence and reliance on non-randomized studies limit definitive conclusions. High-quality RCTs are required to elucidate the clinical role of CCTA in guiding complex PCI.

Keywords: Cardiovascular, chronic total occlusion (CTO), computed tomography angiography, coronary computed tomography angiography (CCTA), interventional, percutaneous coronary intervention, complex PCI

INTRODUCTION

Despite considerable advances in percutaneous coronary intervention (PCI), complex procedures remain challenging for interventional cardiologists.^{1,2} Lesions such as chronic total occlusions (CTOs), bifurcations, heavily calcified vessels, tortuous anatomies, in-stent restenosis, and post–coronary artery bypass grafting PCI are associated with longer procedural times, higher radiation exposure, increased contrast volume, and greater risk of complications, including vessel perforation, dissection, and no-reflow.^{2,3-6} These factors contribute to adverse clinical outcomes, including elevated morbidity and mortality.

Coronary computed tomography angiography (CCTA) is a non-invasive imaging modality that provides high-resolution, three-dimensional

visualization of coronary anatomy.^{2,5} It allows detailed evaluation of lesion morphology, plaque composition, vessel dimensions, and spatial orientation, thereby improving pre-procedural planning.^{1,2,8} CCTA can aid catheter and device selection, guide procedural strategy, and potentially enhance procedural efficiency and outcomes.^{2,4,5,7,8}

Although evidence suggests potential benefits of CCTA-guided PCI—such as reduced fluoroscopy time, lower contrast volume, and improved procedural success—its use in routine practice remains limited. Barriers include concerns regarding additional radiation exposure, increased contrast load, and the need for specialized equipment and operator expertise.^{1,2,5}

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Objective

This systematic review evaluates the utility of CCTA guidance in complex PCI compared with angiography-guided PCI. The primary outcome assessed was procedural success. Secondary outcomes included fluoroscopy time, contrast volume, and major adverse cardiac events (MACE). Additionally, the certainty of evidence for CCTA-guided PCI in complex coronary interventions was assessed using the GRADE framework.

METHODS

Search Strategy

We conducted a systematic search of PubMed/MEDLINE, Embase, Cochrane Library, Scopus, and ClinicalTrials.gov for studies published between 2014 and 2024, limited to English-language articles. There were no restrictions on geographic location or the number of centers. To ensure comprehensive coverage, reference lists of eligible studies and relevant reviews were screened, and authors of conference abstracts were contacted to identify unpublished or ongoing studies.

To capture grey literature and studies potentially missed by conventional databases, Google Scholar was also searched using the keywords “CCTA,” “complex PCI,” “CTO PCI,” “bifurcation PCI,” and “graft PCI.” For each search, the first 100 results were screened as a pragmatic supplemental approach. We acknowledge that this method might introduce selection bias; therefore, Google Scholar was used solely to complement—not replace—the primary database search strategy.

Study Selection

Two independent reviewers screened titles and abstracts using Covidence, followed by full-text review according to prespecified inclusion criteria. Disagreements were resolved through discussion. Eligible studies included randomized controlled trials (RCTs) and observational studies comparing CCTA-guided PCI with standard angiography-guided PCI in adults undergoing complex PCI. The study selection process is illustrated in the PRISMA flow diagram (Figure 1).

Data Extraction

Two reviewers independently extracted study and patient characteristics, intervention details, and outcomes, including procedural success, fluoroscopy time, contrast volume, and MACE. Data were recorded using piloted extraction forms. Discrepancies were resolved by consensus, and study authors were contacted to obtain missing data when necessary.

Risk of Bias Assessment

Risk of bias was independently evaluated by two reviewers. For RCTs, the Cochrane risk of bias 2 (RoB 2) tool was used to assess bias arising from randomization, deviations from intended interventions, missing outcome data, outcome measurement, and selective reporting. For non-RCTs, the risk of bias in non-randomized studies of interventions (ROBINS-I) tool was applied, considering bias due to confounding, participant selection, intervention classification, deviations from intended interventions, missing data, outcome measurement, and

reporting. Overall risk of bias for each study was determined by the domain with the highest risk.

Measures of Effect

All analyses were performed using Review Manager 5.3. Dichotomous outcomes were summarized as risk ratios (RRs) or odds ratios with 95% confidence intervals (CIs). Continuous outcomes, including fluoroscopy time and contrast volume, were reported as mean differences (MDs) with 95% CIs. When standard deviations were not reported, they were estimated from standard errors or CIs when possible.

Heterogeneity and Reporting Bias

Heterogeneity was evaluated through a visual inspection of forest plots, the chi-square test ($p < 0.10$), and the I^2 statistic. I^2 thresholds followed Cochrane recommendations: unimportant ($< 40\%$), moderate (30–60%), substantial (50–90%), and considerable ($\geq 75\%$). Planned subgroup analyses by complex PCI subtype could not be performed because all included studies focused on CTO PCI. Funnel plot assessment was not feasible due to the small number of studies. To minimize reporting bias, broad search strategies across multiple databases were employed.

Data Synthesis

Random-effects meta-analyses were performed using the inverse variance method. Sensitivity analyses were planned to exclude studies at high-risk of bias; however, their utility was limited by study homogeneity and the small number of included trials.

Certainty of Evidence

The certainty of evidence was assessed using the GRADE approach, considering risk of bias, inconsistency, imprecision, and publication bias. Thresholds for clinical significance were defined as a $\geq 5\%$ difference in procedural success, a ≥ 5 -minute change in fluoroscopy time, a ≥ 10 mL reduction in contrast volume, and any difference in complications. Overall, the certainty of evidence for all outcomes was rated as very low. A Summary of findings table was generated using GRADEpro, with reasons for downgrading provided in footnotes.

RESULTS

Study Selection and Search Results

Literature search was conducted in September 2024 across multiple databases, including Scopus, MEDLINE, Google Scholar, Embase, and PubMed, yielding 201 ($n=132, 25, 17, 15,$ and $12,$ respectively) studies. Additional sources, including citation searches ($n=16$) and grey literature ($n=5$), contributed 21 more studies. After removing 50 duplicates, 172 unique studies were screened.

Following title and abstract screening, 28 studies were retrieved for full-text evaluation. Of these, 24 full-text articles were assessed for eligibility, and 19 were excluded. Full-text evaluation was performed independently by two reviewers, with discrepancies resolved by consensus. Ultimately, five studies met the inclusion criteria and were included in the analyses. The study selection process is summarized in the PRISMA flow diagram (Figure 1).

Study Characteristics

The review included five studies: one RCT and four observational studies (Table 1). Collectively, these studies involved 7,263 patients, with 674 in the CCTA-guided PCI group and 6,589 in the angiography-guided PCI group. The studies were published between 2014 and 2024.

All studies assessed procedural success, fluoroscopy time, contrast volume, and MACE. All included studies focused exclusively on CTO lesions, with no representation of other complex PCI subtypes. Planned subgroup analyses could not be performed due to the lack of studies involving different types of complex PCI.

Excluded Studies

Studies were excluded based on the following criteria: case reports or case series with limited sample size and generalizability; studies

with missing data that could not be retrieved; and studies evaluating outcomes different from those predefined, such as comparisons between CCTA-guided PCI and intracoronary-guided PCI rather than angiography-guided PCI. These criteria ensured that only studies assessing the specified outcomes of procedural success, fluoroscopy time, contrast volume, and MACE in the context of CCTA-guided versus angiography-guided PCI were included in the review.

Risk of Bias in Included Studies

The risk of bias was assessed for all included studies. The single RCT demonstrated a low-risk of bias across all domains (RoB 2), whereas the four observational studies exhibited moderate to high-risk of bias according to ROBINS-I. Table 2 summarizes the risk of bias assessments, and Supplementary 1 provides detailed judgments for each study.

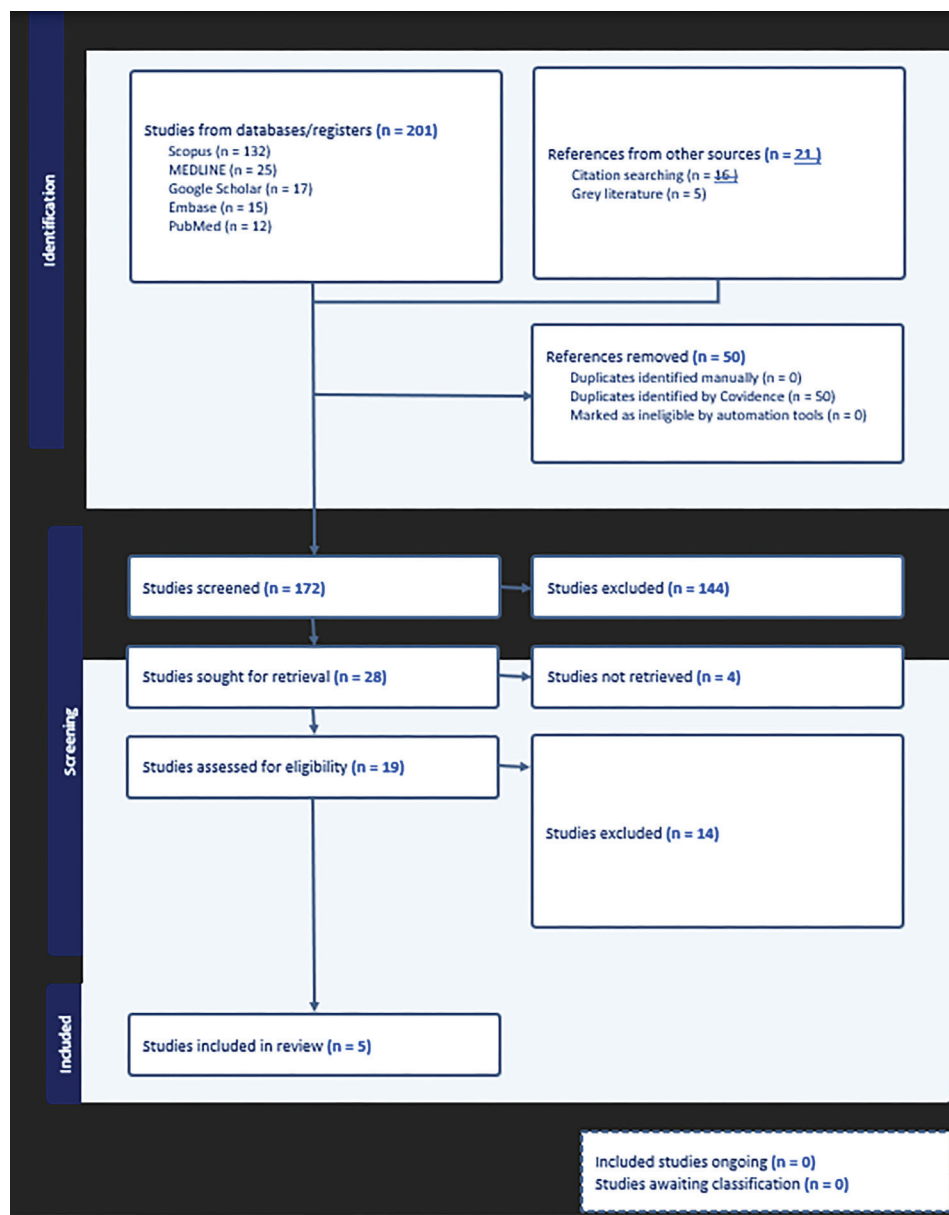


Figure 1. Flow diagram of selecting articles for systematic review

Table 1. Baseline characteristics and outcomes of included studies

Study	Design of the study	Inclusion criteria	Duration	Groups	Patients (n)	Mean age (±SD), years	Main outcomes
Hong et al. ⁵	Multicenter, randomized trial	CTO lesions with typical angina or positive functional test for ischemia	1 year	CTA-guided: n=200 Angiography-guided: n=200	400	62±10 (CTA) 61±11 (Angio)	Higher recanalization success with CTA (94% vs. 84%, p=0.003). Lower antegrade crossing time (44 min vs. 47 min, p=0.042). Benefits primarily in higher J-CTO score cases.
Xenogiannis et al. ⁹	Retrospective observational study	CTO lesions undergoing PCI	2018-2019	CTA Fusion Guidance: n=27 Non-CTA Guidance: n=119	146	66±9 (both groups)	Similar technical success (81% vs. 89%, p=0.279). CTA-guided group had higher lesion complexity (J-CTO score 3.3 vs. 2.7, p=0.009).
Li et al. ¹⁰	Single-center, retrospective observational study	CTO lesions undergoing PCI after CCTA imaging	Retrospective	Success vs. failure outcomes analyzed and compared RECHARGE CCTA score vs. CA based scoring	124 (131 CTO lesions)	54 (IQR: 43–60 years)	Procedural success in 72% of cases. RECHARGE CCTA score as effective as catheter-based scoring for predicting success and wire crossing time.
Yu et al. ¹¹	Multicenter, retrospective observational study	CTO lesions undergoing PCI following CCTA imaging	2007–2015	Single group analyzing procedural success and crossing outcomes Compared CCTA guided scoring system KCCT vs. CA scoring systems for outcomes	643	62 (IQR: 54–70 years)	Procedural success in 74%. KCCT score developed, better prediction than J-CTO or PROGRESS-CTO scores for success and guidewire crossing time.
Simsek et al. ¹²	Multicenter, retrospective observational registry study	CTO lesions with TIMI 0 flow ≥3 months	2012–2022	Preprocedural CCTA: n=375 No-CCTA: n=6659	7,034	64±11 (CCTA) 64±10 (no-CCTA)	Similar procedural success (85% vs. 86%, p=0.329). Higher MACE in CCTA group (3.2% vs. 1.6%, p=0.020). CCTA resolved ambiguity (27%) and identified calcium (18%).

CCTA: Coronary computed tomography angiography, CTO: Chronic total occlusion, PCI: Percutaneous coronary intervention, SD: Standard deviation, IQR: Interquartile range, KCCT: Korea Coronary Calcium Scoring System

Primary Outcome: Procedural Success

Five studies, including one RCT and four observational studies, contributed to this analysis, encompassing a total of 8,311 patients (674 and 6,589 patients in the CCTA-guided and angiography-guided PCI groups, respectively). The forest plot of the meta-analysis (Figure 2) showed a relative risk (RR) of 0.97 (95% CI: 0.92–1.02), indicating no significant difference in procedural success between CCTA-guided and angiography-guided PCI. The risk difference (RD) was –0.03 (95% CI: –0.07 to 0.02), with the CI crossing zero, further suggesting no significant effect.

The minimal important difference (MID) for procedural success was defined as a 5% improvement, a commonly used threshold in PCI studies. The observed difference was below this threshold, and the wide CI crossing 1 indicates uncertainty regarding the direction of effect. Accordingly, the certainty of evidence was downgraded to very low (⊕○○○) due to high-risk of bias, inconsistency, and imprecision.

Using the GRADE framework, the risk of bias was high in the observational studies owing to confounding factors, including lesion complexity, operator expertise, procedural protocols, and variability

Table 2. Summary of risk of bias of included studies

RCTs (RoB 2)								
Study	Sequence generation	Allocation concealment	Blinding of participants, personnel, and outcome assessment	Incomplete outcome data	Selective outcome reporting	Other potential threats to validity		
Hong et al. ⁵	Low	Low	Low	Low	Low	Low		
Non-RCTs (ROBINS-I)								
Study	Confounding	Selection of participants	Classification of interventions	Deviations from intended interventions	Missing data	Measurement of outcomes	Selection of the reported result	Overall judgment
Xenogiannet al. ⁹	High	Low	Low	Low	Moderate	Low	Low	High
Li et al. ¹⁰	Moderate	Low	Low	Low	Moderate	Low	Low	Moderate
Yu et al. ¹¹	Moderate	Low	Low	Low	Moderate	Low	Low	Moderate
Simsek et al. ¹²	High	Low	Low	Low	Moderate	Low	Low	High

in center experience and familiarity with CCTA workflows, as well as missing data. The RCT was judged to have a low-risk of bias because of clear randomization and adequate handling of missing data. Given that the majority of included studies were observational, the overall risk of bias was rated as high.

Heterogeneity was evaluated through visual inspection of the forest plot, which showed overlapping CIs, suggesting potential consistency across studies. Moderate statistical heterogeneity was observed ($I^2=43\%$; $p=0.23$), indicating that variability in study populations and designs had minimal impact on the pooled effect.

Imprecision was assessed by examining the CIs for the RR and RD, which were wide and included the null value, indicating uncertainty about whether the intervention is beneficial or harmful. Because the observed effect did not reach the MID of a 5% increase in procedural success, the evidence was downgraded for imprecision.

Indirectness was not a concern, as the population, intervention, comparison, and outcome (PICO) elements in the included studies were consistent with the review’s objectives. Due to the small number of studies, publication bias could not be formally evaluated using a funnel plot; however, an extensive search across multiple databases and additional sources (including grey literature and citation searching) minimized this risk.

Overall, the certainty of evidence for the effect of CCTA-guided PCI on procedural success was rated as very low, indicating that the true effect is highly uncertain.

Secondary Outcomes

Fluoroscopy Time

Four studies, including one RCT and three observational studies, comprising 6,803 patients, contributed to this analysis. The MD in fluoroscopy time was 6.01 minutes longer for CCTA-guided PCI compared with angiography-guided PCI (95% CI: -7.71 to 19.73). The corresponding forest plot is shown in Figure 3. The MID was defined as a 5-minute change. Although the observed increase exceeded this

threshold, the wide CI crossing zero and high heterogeneity ($I^2=99\%$) indicated substantial uncertainty in the results.

Risk of bias was moderate in the observational studies due to potential confounders, including lesion complexity and variations in procedural protocols. The RCT was judged to have a low-risk of bias owing to clear randomization and blinding procedures.

Heterogeneity was assessed visually and statistically. Visual inspection revealed partial overlap of CIs, but statistical analysis demonstrated substantial inconsistency ($I^2=99\%$; $p<0.001$), likely reflecting differences in study design, populations, and procedural protocols. Consequently, the certainty of evidence was downgraded to very low ($\oplus\circ\circ\circ$) due to heterogeneity.

Imprecision was evaluated based on the wide CIs, which included zero, indicating uncertainty regarding the effect. Although the observed increase slightly exceeded the MID, the CIs suggest the possibility of no effect; therefore, the evidence was further downgraded.

Indirectness was not a concern, as the populations and interventions in the included studies were consistent with the review’s PICO framework. Due to the small number of studies, publication bias was not formally assessed, but comprehensive searching minimized this risk.

Overall, the certainty of evidence for fluoroscopy time was very low, indicating that the true effect of CCTA-guided PCI on fluoroscopy duration remains highly uncertain.

Contrast Volume

Three studies, including one RCT and two observational studies, involving 6,898 patients, were included in this analysis. The pooled MD in contrast volume was -7.05 mL (95% CI: -43.53 to 29.44), suggesting a slight reduction with CCTA-guided PCI (Figure 4). The MID for contrast volume reduction was set at ≥ 10 mL; the observed effect did not reach this threshold. The wide CI crossing zero and the high-risk of bias in some studies contributed to substantial uncertainty, resulting in a very low certainty of evidence ($\oplus\circ\circ\circ$) for imprecision and heterogeneity.

Table 3. Summary of findings: CCTA in complex PCI compared to angiography-guided PCI

Patient or population: Health problem or population Setting: Intervention: CCTA-guided complex PCI Comparison: Angiography-guided complex PCI						
Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with angiography-guided complex PCI	Risk with CCTA guided complex PCI				
Procedure success	859 per 1000	833 per 1000 (790 to 876)	RR 0.97 (0.92 to 1.02)	8311 (5 non-randomised studies)	⊕○○○ Very low ^{a,b,c,d}	CCTA-guided PCI shows a similar likelihood of success compared to angio-guided PCI (RR=0.97, 95% CI: 0.92–1.02) and risk difference: -0.03 (95% CI: -0.07 to 0.02) The evidence is very low certainty about the effect of CCTA in complex PCI on procedure success.
Fluoroscopy time	The mean fluoroscopy Time was 50 minutes	MD 6.01 minutes more (7.71 fewer to 19.73 more)	-	6803 (1 RCT and 1 non-randomised study)	⊕○○○ Very low ^{e,f,g}	Fluoroscopy time increased slightly with CCTA-guided PCI compared to angiography-guided PCI. The increase was small (6.01 minutes on average), but the evidence is uncertain due to inconsistency (high heterogeneity) and imprecision (wide CI crossing zero). Overall, while there is a trend toward longer fluoroscopy times with CCTA, the evidence quality is low.
Contrast volume	The mean contrast volume was 210 mL	MD 7.05 lower (43.53 lower to 29.44 higher)	-	6898 (1 RCT and 2 non-randomised studies)	⊕○○○ Very low ^{h,i,j}	The pooled Mean difference of -7.05 mL suggests a slight decrease in contrast volume with CCTA-guided PCI. However, the evidence is very uncertain due to high-risk of bias, inconsistency, and imprecision.
MACE	15 per 1000	15 per 1000 (10 to 23)	OR 1.03 (0.67 to 1.58)	7236 (4 non-randomised studies)	⊕○○○ Very low ^{k,l,m}	No significant difference in complications between CCTA-guided PCI and angiography-guided PCI. The evidence is very uncertain due to high-risk of bias, inconsistency, and imprecision.

*The risk in the intervention group (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI). CI: Confidence interval, MD: Mean difference, OR: Odds ratio, RR: Risk ratio, CCTA: Coronary computed tomography angiography, PCI: Percutaneous coronary intervention, MACE: Major adverse cardiac events GRADE working group grades of evidence.

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect. Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect. Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

^aMostly non-randomized studies with confounding such as complexity of lesion, operator skills, use of IC imaging. Does not represent other complex lesions, only includes chronic total occlusion (CTO) lesions. ^bVariability in study results, likely due to different populations and procedural protocols, contributed to moderate heterogeneity. ^cFindings primarily apply to CTO PCI and are not generalizable to all types of complex PCI. ^dThe pooled risk difference CI crosses 0, indicating no statistically significant effect. Wide CIs reflect imprecision in the estimate of the effect size. ^eHigh-risk of bias (due to the inclusion of one high-risk study). ^fI²=99%, indicating significant heterogeneity between the studies. Differences in baseline characteristics and study design likely contribute to the inconsistency. High inconsistency. Downgraded: -1. ^gThe CI crosses zero, indicating uncertainty about whether fluoroscopy time increases or decreases with CCTA. The wide CI also reduces confidence in the pooled estimate resulting in imprecise results. ^hTwo of the three studies (Simsek and Xenogiannis) have a high-risk of bias due to imbalances in baseline characteristics, small sample sizes, and no statistical adjustments. Downgraded: -1. ⁱHigh heterogeneity indicates significant variability across studies, driven by differences in study designs and results. Downgraded: -1. ^jThe confidence interval crosses zero, indicating uncertainty about whether contrast volume increases or decreases. Downgraded: -1. ^kModerate to high-risk of bias due to confounding and unadjusted observational data. Downgraded: -1. ^lI²=75%, indicating substantial heterogeneity; Differences in study design (randomized controlled trials vs. observational studies). Variations in baseline characteristics and procedural complexity. Downgraded: -1. ^mCI: 0.67 to 1.58. The CI crosses 1, indicating no significant difference in complications. The wide range of the CI suggests uncertainty. Downgraded: -1

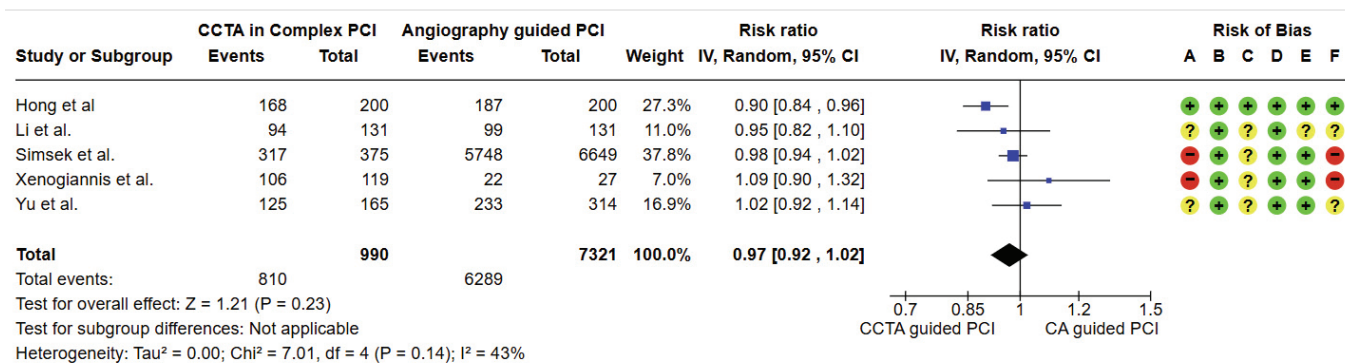


Figure 2. Forest plot for procedure success
 CI: Confidence interval, CCTA: Coronary computed tomography angiography, PCI: Percutaneous coronary intervention

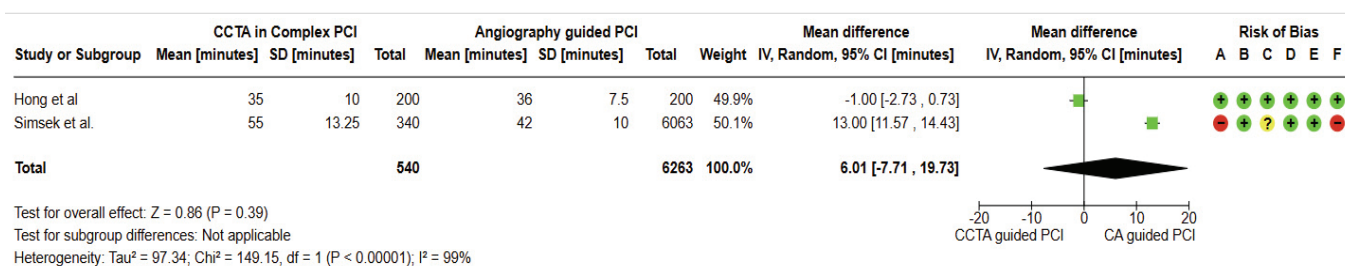


Figure 3. Forest plot for fluoroscopy time
 CI: Confidence interval, CCTA: Coronary computed tomography angiography, PCI: Percutaneous coronary intervention, SD: Standard deviation

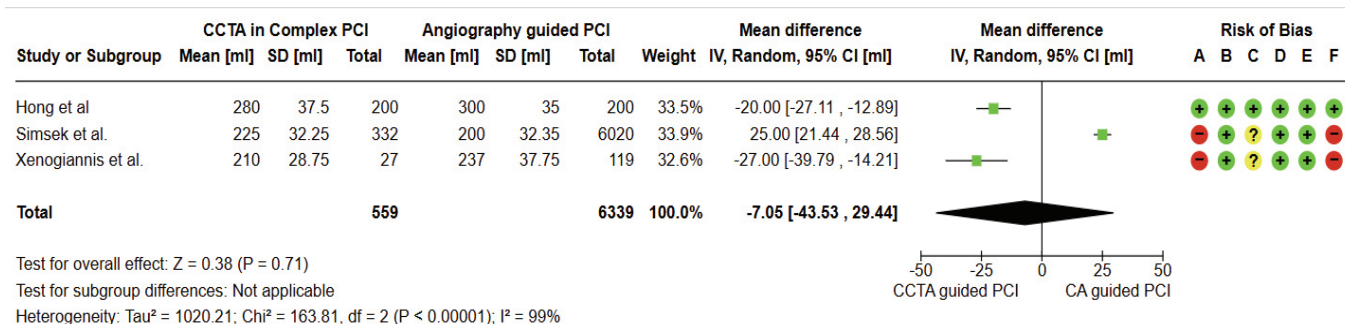


Figure 4. Forest plot for contrast volume
 CI: Confidence interval, CCTA: Coronary computed tomography angiography, PCI: Percutaneous coronary intervention, SD: Standard deviation

Risk of bias was high in the observational studies due to potential confounders, such as baseline differences between groups. The RCT was found to have a low-risk of bias, as it was well-conducted and adhered to standard protocols.

Heterogeneity was moderate (I²=60%; p=0.08), indicating some variability between studies, but not enough to substantially affect the pooled effect. Imprecision remained a concern because the CI included the null value, and the observed effect did not meet the MID.

Indirectness was not a concern, as the PICO elements of the included studies aligned with the review. Publication bias was not formally assessed due to the small number of studies; however, the comprehensive search minimized the risk.

Overall, the certainty of evidence for contrast volume was very low, indicating that the true effect of CCTA-guided PCI on contrast use remains uncertain.

Major Adverse Cardiac Events

Four studies, including one RCT and three observational studies, encompassing 7,236 patients, contributed to this analysis. The pooled OR for MACE was 1.03 (95% CI: 0.67–1.58), indicating no significant difference between CCTA-guided and angiography-guided PCI (Figure 5). The MID for complications was defined as even a single additional event; the observed effect did not reach this threshold.

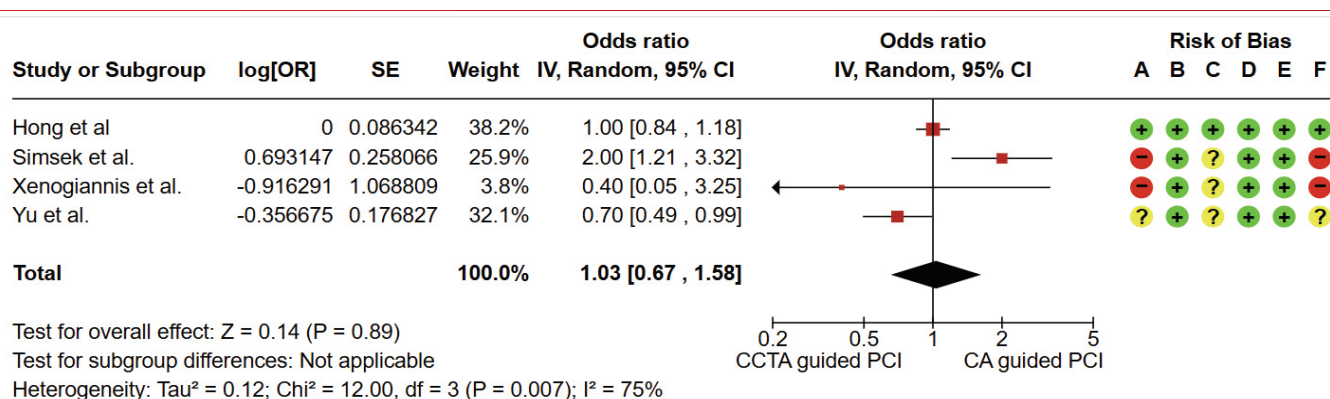


Figure 5. Forest plot for major adverse cardiac events
 CI: Confidence interval, CCTA: Coronary computed tomography angiography, PCI: Percutaneous coronary intervention, OR: Odds ratio

Risk of bias was high in the observational studies due to confounding (e.g., baseline differences in patient characteristics) and incomplete outcome reporting. The RCT demonstrated a low-risk of bias due to proper randomization and accounting for confounders.

Substantial heterogeneity was high (I²=75%; p=0.01), reflecting variability between studies. Wide CIs crossing 1 contributed to uncertainty in the effect estimate. Imprecision and heterogeneity led to downgrading the certainty of evidence to very low (⊕○○○).

Indirectness was not a concern, as populations and interventions were consistent with the review’s PICO. Publication bias was not formally evaluated due to the limited number of studies; nevertheless, the comprehensive search strategy minimized the risk of publication bias.

Overall, the certainty of evidence for MACE was very low, indicating that the true effect of CCTA-guided PCI on MACE was highly uncertain. Table 3 shows the summary of findings for different outcomes.

DISCUSSION

Summary of Results and Certainty of Evidence

This systematic review evaluated the utility of CCTA-guided PCI compared with angiography-guided PCI in CTO lesions. Data from five studies, including one RCT and four observational studies, indicated no clinically meaningful differences between the two strategies with respect to procedural success, fluoroscopy time, contrast volume, and MACE.

Using the GRADE framework, the certainty of evidence for all outcomes was rated as very low, primarily due to high-risk of bias, heterogeneity, and imprecision. For procedural success, the evidence was downgraded due to confounding in observational studies and moderate heterogeneity. For secondary outcomes, wide CIs and substantial heterogeneity (I² ranging from 43–99%) contributed to very low certainty. Similarly, MACE demonstrated no significant difference, with certainty downgraded because of high-risk of bias, heterogeneity, and imprecision.

Overall, while CCTA-guided PCI may offer advantages in procedural planning for CTO lesions, the current evidence remains insufficient

to demonstrate a clear clinical benefit over angiography-guided PCI. High-quality randomized trials are warranted to clarify its role in complex PCI.

Study Limitations

A key limitation of this review is the small number of included studies, resulting in low event rates and imprecision in pooled estimates. The predominance of observational studies, which are susceptible to residual confounding—such as differences in lesion complexity and operator experience—further increased the uncertainty of the evidence.

Heterogeneity across studies, particularly for fluoroscopy time and contrast volume, was another limitation. Variability in patient populations, lesion characteristics, procedural protocols, and real-world differences in operator expertise and familiarity with CCTA workflows likely contributed to this heterogeneity, resulting in imprecision and inconsistency.

Furthermore, although the search strategy encompassed all complex PCI subsets, the included studies focused exclusively on CTO lesions. Consequently, the findings cannot be generalized to other complex PCI types, including multivessel disease, bifurcation lesions, severely calcified lesions requiring atherectomy, or graft interventions, due to insufficient data. Therefore, caution is warranted when extrapolating these results beyond CTO PCI, and further studies are needed to evaluate the utility of CCTA in other complex PCI contexts.

Comparison with Existing Literature

There is a notable gap in systematic reviews specifically evaluating the utility of CCTA in complex PCI procedures compared with angiography-guided PCI across diverse lesion types. Most available studies have focused on CTO procedures, with only one RCT and several observational studies published over the past decade.^{5,9-12} Studies investigating CCTA in bifurcation lesions exist; however, these primarily assess outcomes different from those included in the present review.^{7,8}

Our findings are consistent with the systematic review by Liang et al.,⁴ which examined CCTA-guided PCI in CTOs. They reported that CCTA facilitated pre-procedural planning but had no significant effect on

procedural success or post-procedural MACE. Similarly, Hong et al.⁵ reported that CCTA improved procedural planning in CTO cases but did not influence long-term clinical outcomes, particularly MACE. Several studies have explored emerging applications of CCTA in CTO PCI, and an ongoing randomized trial protocol is expected to provide more insight once completed.¹³⁻¹⁶

In contrast, studies examining CCTA in bifurcation PCI, such as those by Wolny et al.⁷ and Mohamed et al.,⁸ focused on procedural predictors, including side-branch occlusion. While these studies highlight the potential benefits of CCTA in predicting procedural complications, they did not evaluate outcomes such as procedural success or MACE, which were the primary endpoints of our review.

Overall, the current evidence, including our findings and those of Liang et al.,⁴ suggests that CCTA may help optimize pre-procedural planning for CTO PCI. However, its impact on clinical outcomes, including MACE and procedural success, remains uncertain.

CONCLUSION

The current evidence on CCTA-guided PCI in CTO lesions is of very low certainty, leaving the clinical benefits over standard angiography—regarding procedural success, fluoroscopy time, contrast use, and MACE—uncertain. While CCTA may facilitate pre-procedural planning and detailed anatomical assessment, the lack of robust clinical outcome data and high heterogeneity across studies limit its routine application in practice.

Although this review aimed to assess complex PCI broadly, the evidence was confined to CTO populations. Therefore, the conclusions cannot be extended to other complex PCI subsets. High-quality RCTs with larger, more homogeneous cohorts are needed to clarify the role of CCTA in complex PCI. Future studies should evaluate procedural efficiency, clinical outcomes, and cost-effectiveness to provide comprehensive guidance on the utility of CCTA in contemporary interventional practice.

Ethics Committee Approval: Not applicable.

Informed Consent: Not applicable.

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Conflict of Interest: No conflict of interest was declared by the authors.

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Supplementary 1. Detailed risk of bias table of the included studies

Hong et al.⁵ (RCT) - RoB 2 Assessment

Bias domain	Risk level	Support for judgment
Randomization process	Low-risk	The study was well-designed with an effective randomization process, ensuring baseline comparability. Allocation methods were described clearly, and there was no evidence of systematic differences between groups.
Deviations from intended interventions	Low-risk	Although the trial was open-label, the outcomes were objective (e.g., procedural success), minimizing the potential impact of unblinding. The study adhered to its protocol and standardized methods, reducing the risk of bias.
Missing outcome data	Low-risk	The missing data was minimal (2.2%), evenly distributed between groups, and unlikely to bias the results. Complete follow-up data was available for most participants, reducing the risk of bias due to attrition.
Measurement of the outcome	Low-risk	The study used objective outcome measures, such as procedural success and TIMI flow grade. While the study was unblinded, the use of objective measures and careful assessment minimized the potential for bias.
Selection of the reported result	Low-risk	The study followed its pre-specified analysis plan and reported all results as outlined in the protocol. There is no indication of selective reporting, ensuring transparency and accuracy in the findings.
Overall judgment	Low-risk	The study was well-designed and carefully conducted, following proper methods such as randomization, consistent procedures, and objective outcome measurements. These factors minimize the risk of bias, resulting in a low overall risk.

Xenogiannis et al.⁹ (retrospective observational study) - ROBINS-I assessment

Bias domain	Risk level	Support for judgment
Confounding	High-risk	Significant differences between groups (e.g., higher rates of prior failed PCI attempts in the CTA group) were not addressed using statistical adjustments, leading to potential confounding.
Selection of participants	Low-risk	Patients were consecutively selected from the PROGRESS-CTO registry, ensuring comprehensive inclusion.
Classification of interventions	Low-risk	Interventions (CTA fusion-guided vs. non-CTA-guided PCI) were clearly defined and consistently classified.
Deviations from intended interventions	Low-risk	Procedures followed protocol without deviations, and group assignments were inherent to the observational design.
Missing data	Moderate risk	Missing procedural details, such as complete follow-up and patient-level data, may have influenced the analysis.
Measurement of outcomes	Low-risk	Objective outcomes (e.g., procedural success, complications) were reliably measured, minimizing bias.
Selection of the reported result	Low-risk	All pre-specified outcomes were reported transparently without evidence of selective reporting.
Overall judgment	High-risk	The lack of adjustment for baseline imbalances (e.g., prior failed PCI attempts) significantly increases the risk of confounding.

Li et al.¹⁰ (single-center retrospective observational study) - ROBINS-I assessment

Bias domain	Risk level	Support for judgment
Confounding	Moderate risk	Potential confounders, such as operator expertise or lesion characteristics, were not statistically adjusted, which could influence the observed outcomes.
Selection of participants	Low-risk	All consecutive patients undergoing CTO PCI were included, ensuring a representative sample and minimizing selection bias.
Classification of interventions	Low-risk	The interventions and outcomes (CCTA-derived RECHARGE scores and procedural success) were clearly defined and consistently applied.
Deviations from intended interventions	Low-risk	No deviations from the intended interventions were observed, as all procedures followed a consistent protocol.
Missing data	Moderate risk	Missing details on predictors, such as lesion complexity, were not fully described, which may have influenced the results.

Measurement of outcomes	Low-risk	Objective outcomes, such as procedural success and guidewire crossing time, were reliably measured with minimal bias.
Selection of the reported result	Low-risk	All pre-specified outcomes were reported without evidence of selective reporting.
Overall judgment	Moderate risk	Despite some limitations due to confounding and missing data, the study design and objective outcome measures support a moderate overall risk of bias.

Yu et al.¹¹ (multicenter retrospective observational study) - ROBINS-I assessment

Bias domain	Risk level	Support for judgment
Confounding	Moderate risk	Although multivariable analysis was conducted, not all operator-related factors (e.g., expertise) were adjusted for, which could influence the observed outcomes.
Selection of participants	Low-risk	All eligible CTO PCI cases with preprocedural CCTA were included, ensuring a representative sample and minimizing selection bias.
Classification of Interventions	Low-risk	The interventions and outcomes (CCTA-derived predictions and guidewire crossing success) were clearly defined and appropriately classified.
Deviations from intended interventions	Low-risk	No deviations from intended procedures were evident, as all CTO PCI procedures followed planned protocols.
Missing data	Moderate risk	Some missing data on lesion-specific characteristics or operator variability were not fully addressed, potentially influencing subgroup analyses.
Measurement of outcomes	Low-risk	Objective metrics, such as guidewire crossing time and procedural success, were reliably assessed and reported.
Selection of the reported result	Low-risk	All pre-specified outcomes, including the development and validation of the KCCT score, were reported transparently.
Overall judgment	Moderate risk	Despite strengths in the design and outcome measurements, residual confounding and missing data contribute to a moderate overall risk of bias.

Simsek et al.¹² (multicenter retrospective observational registry study) - ROBINS-I assessment

Bias domain	Risk level	Support for judgment
Confounding	High-risk	The study included a disproportionately smaller number of cases with preprocedural CCTA (375 cases, 5.3%) compared to cases without CCTA (6659 cases). This imbalance could amplify confounding effects, as observed differences in outcomes may be driven by the numerical disparity rather than the intervention itself. Although multivariable regression was used to adjust for some factors (e.g., lesion characteristics), residual confounding (e.g., operator expertise or institutional differences) remains likely.
Selection of participants	Low-risk	All eligible CTO PCI cases from the PROGRESS-CTO registry were included without exclusion, minimizing selection bias.
Classification of interventions	Low-risk	The classification of interventions (CCTA vs. non-CCTA) was clear and consistently applied.
Deviations from intended interventions	Low-risk	No deviations from intended procedures were noted, as the observational design naturally assigned interventions based on clinical practice.
Missing data	Moderate risk	Missing details about the decision-making process for using CCTA and other procedural variables could affect interpretability.
Measurement of outcomes	Low-risk	Objective outcomes (e.g., procedural success, MACE) were reliably measured, minimizing the risk of bias.
Selection of the reported result	Low-risk	All pre-specified outcomes were reported transparently without evidence of selective reporting.
Overall judgment	High-risk	The significant numerical imbalance between the groups (375 vs. 6659 cases) and the residual confounding from unmeasured factors contribute to a high risk of bias.

PCI: Percutaneous coronary intervention, CTO: Chronic total occlusion, ROBINS-I: Risk of bias in non-randomized studies of interventions, CCTA: Coronary computed tomography angiography, MACE: Major adverse cardiac events, TIMI: Thrombolysis in myocardial infarction