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ORIGINAL STUDIES

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EDITORIAL COMMENT: Expert Article Analysis for:
Retrograde approach for chronic total occlusion angioplasty: At your own risk

Outcomes with retrograde versus antegrade chronic total occlusion revascularization

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Abstract

Objectives: The aim of the study was to evaluate the outcomes of retrograde versus antegrade approach in chronic total occlusion (CTO) percutaneous coronary intervention (PCI).

Background: The retrograde approach has increased the success rate of CTO PCI but has been associated with a higher risk for complications.

Methods: We conducted a meta-analysis of studies published between 2000 and August 2019 comparing the in-hospital and long-term outcomes with retrograde versus antegrade CTO PCI.

Results: Twelve observational studies (10,240 patients) met our inclusion criteria (retrograde approach 2,789 patients, antegrade approach 7,451 patients). Lesions treated with the retrograde approach had higher J-CTO score (2.8 vs. 1.9, $p < .001$). Retrograde CTO PCI was associated with a lower success rate (80.9% vs. 87.4%, $p < .001$). Both approaches had similar in-hospital mortality, urgent revascularization, and cerebrovascular events. Retrograde CTO PCI was associated with higher risk of in-hospital myocardial infarction (MI; odds ratio [OR] 2.37, 95% confidence intervals [CI] 1.7, 3.32, $p < .001$), urgent pericardiocentesis (OR 2.53, 95% CI 1.41–4.51, $p = .002$), and contrast-induced nephropathy (OR 2.12, 95% CI 1.47–3.08; $p < .001$). During a mean follow-up of 48 ± 31 months retrograde crossing had similar mortality (OR 1.79, 95% CI 0.84–3.81, $p = .13$), but a higher incidence of MI (OR 2.07, 95% CI 1.1–3.88, $p = .02$), target vessel revascularization (OR 1.92, 95% CI 1.49–2.46, $p < .001$), and target lesion revascularization (OR 2.08, 95% CI 1.33–3.28, $p = .001$).

Conclusions: Compared with antegrade CTO PCI, retrograde CTO PCI is performed in more complex lesions and is associated with a higher risk for acute and long-term adverse events.

KEYWORDS
antegrade, chronic total occlusion, outcomes, percutaneous coronary intervention, retrograde

1 | INTRODUCTION

Coronary chronic total occlusion (CTO) percutaneous coronary interventions (PCI) can be challenging with failure to cross being the main cause of failure. The introduction of retrograde CTO crossing techniques was instrumental in increasing CTO PCI success rates from <70%[1,2] to nearly 90%.[3–5] Some, but not all,[6,7] studies have reported that the retrograde approach is associated with longer procedural time, increased use of contrast and fluoroscopy, and higher incidence of periprocedural and possibly long-term adverse cardiac events.[4,8–17] We performed a systematic review and a meta-analysis of in-hospital and long-term outcomes with retrograde as compared with antegrade CTO PCI.

2 | METHODS

2.1 | Literature search

The current meta-analysis was conducted and reported according to the proposal for conducting and reporting Meta-analyses of observational studies (MOOSE)[18] and is registered with the International Prospective Register for Systematic Reviews (PROSPERO: CRD42019124763). We performed a systematic computerized search of the EMBASE, Cochrane, and MEDLINE databases from 2000 to August 2019 using the following search terms separately and in combination; "chronic total occlusion," "CTO," "CTO PCI," "retrograde," "antegrade," and "revascularization." We screened the bibliographies of the retrieved studies for relevant studies not retrieved through the initial search. Our search was limited to the English language. Abstracts and review papers were not included in this study.

2.2 | Study selection

We included published studies that compared the outcomes with retrograde versus antegrade approaches in CTO PCI. If more than one study reported outcomes of the same cohort of patients, we included the most recent or most comprehensive publication. For long-term outcomes, we included studies with a minimum of 12 months follow-up.

2.3 | Data extraction and quality assessment

The data were abstracted by two independent investigators (AA, MS) and adjudicated by a third investigator (MM); all the investigators are physicians. Discrepancies were settled by consensus. The risk of bias of the included studies was assessed using the Newcastle-Ottawa Scale for observational studies.[19]

2.4 | Study end-points

Primary endpoints were in-hospital mortality, myocardial infarction (MI), need for urgent revascularization, need for urgent pericardiocentesis, contrast-induced nephropathy, procedural success, procedural time, fluoroscopy time, and contrast volume. Secondary endpoints included long-term outcomes: all-cause mortality, MI, target lesion revascularization (TLR), and target vessel revascularization (TVR). The definitions of outcomes, according to each included study are described in Table S1. Long-term outcomes were reported at the longest follow-up time available. For this analysis, the total number of lesions was utilized for procedural success while the total number of patients was used for clinical outcomes. One study reported baseline characteristics and outcomes according to the total number of lesions, and this number was used for our analysis.[12] Lesion complexity was reported using the J-CTO score.[20]

2.5 | Data synthesis and statistical analysis

Statistical analysis was conducted using the Review Manager Software (Version 5.3.5. Copenhagen: The Nordic Cochrane Centre, the Cochrane Collaboration, 2014). Categorical variables were described as percentages while continuous variables were described as means with SD. Categorical variables were compared using Fisher's exact test or chi-square test, while continuous variables were compared using the two-sample *t* test. Tests were two-tailed, and a p value ≤.05 was considered statistically significant.

Odds ratios (ORs), and mean difference (MD) with 95% confidence intervals (CIs) are presented as summary statistics. CIs were calculated at 95% level for overall estimates effect. Statistical heterogeneity was assessed by I^2 statistics; I^2 statistic >50% was considered substantial, and $I^2 > 75\%$ was considered considerable.[21] As a high degree of clinical and methodological heterogeneity was anticipated, we used the Der-Simonian and Laird random-effects and random-effects generic inverse variance methods to calculate OR and MD, respectively.[22] Baseline characteristics, follow-up periods, and event rates were weighted according to sample size. Potential publication bias was assessed using the Egger's test through visual examination of the funnel plots.[23]

A subgroup test for statistical interaction was performed to assess whether the association between retrograde (vs. antegrade) procedures and outcomes differed when retrograde was used as a primary strategy (retrograde approach was the primary approach used in >95% of the patients) versus only after failure of the antegrade approach. Sensitivity analysis was performed excluding lower quality studies as assessed by the Newcastle–Ottawa Scale.[10]

3 | RESULTS

3.1 | Characteristics of the included studies and quality assessment

The study selection process is described in Figure S1. Twelve observational studies with a total of 10,240 patients (10,363 lesions) met our inclusion criteria.[4,8,10–17,24,25] The characteristics of the included studies are described in Table 1. Patients were enrolled from 2005 to 2016. Three studies reported patients from North America,[4,8,11] four from Europe,[10,12,16,17] and five from Asia.[13–15,24,25] The retrograde approach was used as the primary approach in two studies[17,24]; after the failure of antegrade approach in two studies[10,16]; and as a mix of both in the rest of the studies.[4,8,11–15,25] The retrograde arm included 2,789 patients (2,816 lesions), while the antegrade arm included 7,451 patients (7,547 lesions).

Long-term outcomes were reported in four studies, including 2,269 patients who completed follow-up.[8,13,15,17] The weighted mean follow-up duration was 48 ± 31 months. All studies met the inclusion criteria. Publication bias, as assessed by the Egger's test funnel plots is illustrated in Figures S2–S11. Bias assessment as per the Newcastle–Ottawa Scale for observational studies is shown in Table S2.

3.2 | Baseline characteristics of the included cohort

The baseline clinical and angiographic characteristics for lesions and patients undergoing CTO PCI using the retrograde versus an

TABLE 1 Baseline characteristics of the included studies

Study	Study type	Country, number of centers	Enrollment dates	Number of patients/lesions	Retrograde grade approach (primary or after antegrade approach failure)
Galassi et al. 2011	Observational	Europe, 16	2008–2009	1983/1983	97.2% primary
Michael et al. 2014	Observational	USA, 1	2008–2011	193/193	34% primary
Werner et al. 2014	Observational	Germany, 1	2006–2011	392/492	After failure of antegrade
Bijuklic et al. 2016	Observational	Germany, 1	2008–2012	369/369	After failure of antegrade
Dautov et al. 2016	Observational	Canada, 1	2010–2015	175/175	Both
Karmpaliotis et al. 2016	Observational	USA, 11	2012–2015	1276/1301	46% primary
Lee et al. 2017	Observational	Taiwan,1	2012–2013	321/321	40.2% primary
Suzuki et al. 2017	Observational	Japan, multi-center	2014–2015	2596/2596	100% primary
Zivelonghi et al. 2018	Observational	Belgium & Netherlands, 8	2012–2015	330/330	100% primary
Tanaka et al. 2018	Observational	Japan, 1	2005–2009	842/928	Not reported
Kwon et al. 2018	Observational	Korea,1	2007–2015	1151/1151	58% primary
Wu et al. 2019	Observational	Asian pacific registry	2016	485/497	65% primary

antegrade-only approach are summarized in Table S3. Patients in the retrograde arm had more prior MIs (43% vs. 35.2%, $p < .001$), prior PCIs (69.7% vs. 41.7%, $p < .001$), and prior failed attempts (43.7% vs. 19.9%, $p < .001$). Lesions treated with the retrograde approach were more likely to be in the right coronary artery (RCA) (62.8% vs. 47.3%, $p < .001$), were longer (35.2 ± 13.6 vs. 21.9 ± 9 mm, $p < .001$) and had higher mean J-CTO score (2.8 ± 1.2 vs. 1.9 ± 1.2, $p < .001$).

3.3 | Study endpoints

3.3.1 | In-hospital adverse events

The retrograde and antegrade-only CTO PCI had similar in-hospital mortality (0.5% vs. 0.21%; OR 2.01, 95% CI 0.91–4.43; $p = .08$, $I^2 = 0\%$). Use of the retrograde approach was associated with higher incidence of MI (3.07% vs. 1.27%; OR 2.37, 95% CI 1.7–3.32, $p < .001$; $I^2 = 0\%$), need for urgent pericardiocentesis (1.07% vs. 0.42%; OR 2.53, 95% CI 1.41–4.51, $p = .002$, $I^2 = 0\%$), and contrast-induced nephropathy (3.38% vs. 1.57%; OR 2.12, 95% CI 1.47–3.08; $p < .001$, $I^2 = 0\%$). There was no difference in the need for urgent revascularization (0.21% vs. 0.34%; OR 0.82, 95% CI 0.30–2.25, $p = .70$; $I^2 = 0\%$) or cerebrovascular events (0.44% vs. 0.19%; OR 1.95, 95% CI 0.87–4.38; $p = .11$, $I^2 = 0\%$) (Figures S12 and S13).

3.3.2 | Procedural characteristics

Compared with antegrade CTO PCI, retrograde CTO PCI was associated with lower procedure success rate (80.9% vs. 87.4%; OR for procedural failure 2.16, 95% CI 1.71–2.73, $p < .001$, $I^2 = 63\%$), longer duration (mean difference 61.52 min, 95% CI 50.57–72.48 min), $p < .001$, $I^2 = 97\%$), longer fluoroscopy time (mean difference 32.33 min, 95% CI 23.45–41.22 min; $p < .001$, $I^2 = 99\%$), and higher contrast volume (mean difference 76.73 mL; 95% CI 50.9–96.55 mL, $p < .001$, $I^2 = 95\%$), (Figure S14).

3.3.3 | Long-term outcomes

During a mean follow-up duration of 48 ± 31 months, there was no difference in long-term mortality with retrograde versus antegrade procedures (13% vs. 8.8%; OR 1.79, 95% CI 0.84–3.81, $p = .13$, $I^2 = 74\%$). The retrograde approach, however, was associated with higher risk of MI (5.6% vs. 2.6%; OR 2.07, 95% CI: 1.10–3.88, $p = .02$, $I^2 = 0\%$), TVR (32.3% vs. 17.3%; OR 1.92, 95% CI: 1.49–2.46, $p < .001$, $I^2 = 0\%$), and TLR (12.9% vs. 7.2%; OR 2.08, 95% CI: 1.33–3.25, $p = .001$, $I^2 = 0\%$; Figure S15).

3.4 | Subgroup and sensitivity analyses

On subgroup analysis, the association between retrograde PCI and outcomes was not significantly different based on whether retrograde was performed as the primary approach versus after a failed antegrade crossing attempt: in-hospital mortality (p interaction = .28), procedural success (p interaction = .68), or the need for urgent pericardiocentesis (p interaction = .30; p interaction = .28); Figure S16). With the exclusion of one lower quality study,[10] there was no difference in the outcomes after both approaches.

The summary of the study results is illustrated in Figure 1.

4 | DISCUSSION

To the best of our knowledge, this is the first meta-analysis of both in-hospital and long-term outcomes with retrograde versus antegrade-only crossing techniques in CTO PCI. The main findings can be summarized as follows: (a) patients who underwent retrograde CTO PCI had more technically complex lesions, a higher prevalence of prior PCI and CABG, and more comorbidities; as a result, the retrograde procedures were longer requiring more contrast and fluoroscopy; (b) the retrograde approach was associated with higher in-hospital MI, urgent pericardiocentesis, and contrast-induced nephropathy compared with the antegrade approach, but no difference in in-hospital mortality, urgent revascularization, or cerebrovascular events; and (c) the retrograde approach was associated with higher long-term incidence of MI, TLR, and TVR but not mortality.

Several observational studies[26–31] and two RCTs[32,33] have reported that successful CTO PCI is associated with improvement in the quality of life, reduced need for CABG, improved left ventricular (LV) function, and LV reverse remodeling compared with failed revascularization. The retrograde approach is currently an essential tool for achieving high success rates, especially in complex lesions where the antegrade approach is not technically feasible or fails.[34] According to the hybrid algorithm, proximal cap ambiguity, poor-quality distal vessel and the presence of interventional collaterals favor the use of the retrograde approach.[35] In a multicenter CTO PCI registry, overall technical success was 86%, and the retrograde approach was used in 34.9% of the successful cases.[5] The higher success rate with the retrograde approach is likely related to the histopathological features of the distal CTO cap which is more likely to be tapered and less fibrocalcific and therefore less resistant to guidewire advancement.[36,37]

In our analysis, the retrograde procedures were longer requiring more contrast and fluoroscopy and were associated with more in-hospital adverse events. Coronary perforation (Ellis classification grade III) with subsequent need for pericardiocentesis has been associated with high rates of long-term major adverse cardiac events.[38] Peri-procedural MI, which is more likely to occur with the retrograde approach, likely due to the prolonged obstruction of collateral channels by the retrograde wire and microcatheters, has also been associated with worse long-term outcomes and higher mortality in some but not all studies.[16,39,40] Most of these CTOs, however, could not have been revascularized by an antegrade-only approach and some of the complications attributed to the retrograde approach may have occurred during antegrade crossing attempts. Moreover, some studies in our analysis included patients from 2005, which was early in the learning curve of the retrograde technique.

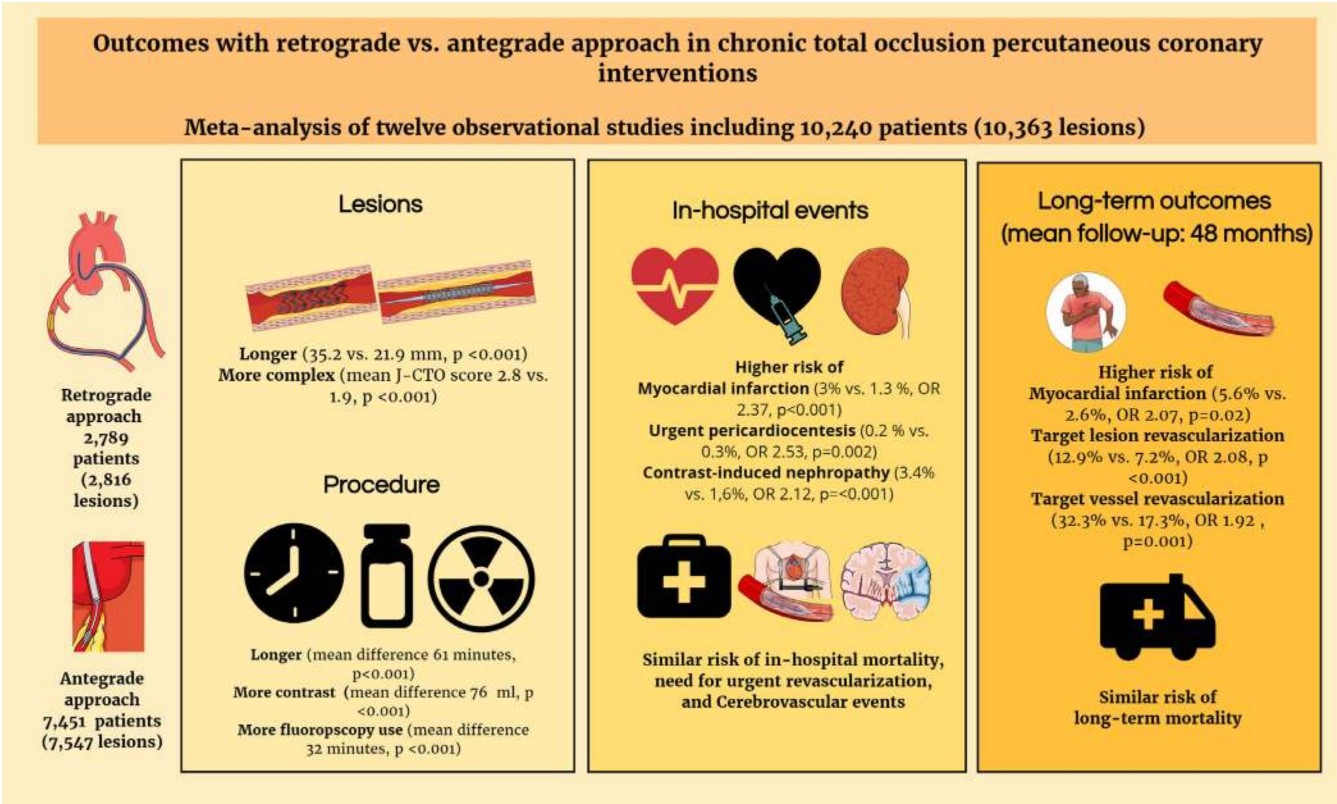

FIGURE 1 Summary of the study results [Color figure can be viewed at wileyonlinelibrary.com]

Similar to previous reports[7,41] in our study retrograde CTO PCI was associated with more TLR, TVR, and MI as compared with antegrade-only CTO PCI during a mean follow-up of 4 years. Retrograde PCI is usually performed in more complex anatomy and might lead to implantation of longer and smaller-caliber stents, which in turn is associated with a higher risk of restenosis.[42] Moreover, dissection and re-entry techniques, which are frequently used in the retrograde approach, may increase restenosis rates.[43,44]

The majority of patients in the retrograde group might have failed revascularization leading to subsequent worse outcomes, and a higher number of lesions in the retrograde group had already failed prior attempts rendering the retrograde approach the final option for successful revascularization. It possible that the worse outcomes with the retrograde approach are related to higher patient and lesion complexity and not the crossing strategy per se. Nevertheless, the retrograde approach should only be used when the perceived benefits outweigh the potential risks. Performance of retrograde CTO PCI by experienced operators who can identify and treat complications early and are attentive to the need for stent optimization,[45] as well as using approaches that help reduce complications like the radial approach,[46] could improve the outcomes of retrograde CTO PCI.

4.1 | Limitations

Our study has limitations. First, only observational studies compared antegrade and retrograde CTO PCIs, which are subject to selection bias. Second, there was a high degree of heterogeneity between the studies (e.g., in the definition of success and periprocedural MI). Third, the details of the crossing techniques and the collaterals used for retrograde approach were not consistently reported in all studies and could not be used for further analysis. Fourth, the differential outcomes based on J-CTO components (e.g., calcification, occlusion length) were not consistently reported and, therefore, could not be reported. Finally, the included studies did not report the adjusted odds ratios. Thus, despite being the optimal statistical method, we could not use the pooled adjusted OR to confirm our results.

5 | CONCLUSION

Compared with antegrade CTO PCI, the retrograde approach is attempted in more complex lesions and is associated with a higher risk for acute and long-term complications. Judicious and skillful application of the retrograde approach remains a pillar of contemporary CTO PCI.

DISCLOSURE OF INTERESTS

Michael Megaly, Abdelrahman Ali, Marwan Saad, Mohamed Omer, Iosif Xenogiannis, Juan J. Russo, Masahisa Yamane, Roberto Garbo, Andrea Gagnor, Imre Ungi, Ashish Pershad, Jaroslaw Wojcik, Georgios Sianos, Alfredo R. Galassi: nothing to disclose. Gerald Werner: speaker honoraria for Asahi Intecc, Abbott Vascular, Biosensors, and Terumo;

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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