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ORIGINAL ARTICLE

Efficacy of Primary Retrograde Approach in Complex Chronic Total Occlusions With Unfavorable Antegrade Characteristics and Feasible Interventional Collaterals

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Background: The retrograde approach improves the procedural success rate of chronic total occlusion percutaneous coronary interventions (CTO-PCIs). However, it remains unclear whether the primary retrograde approach (PRA) offers benefits in terms of procedural success and burden/resource use in challenging cases. Therefore, we compared efficacy between the primary antegrade approach (PAA) and PRA in complex CTO-PCIs.

Methods and Results: This single-center retrospective cohort study included all patients undergoing coronary CTO-PCI attempted by experienced high-volume operators between January 2016 and July 2023. The difficulty of the antegrade approach was determined using the Japanese CTO score, and the feasibility of interventional collaterals was determined using the collateral channel score. In 698 patients undergoing CTO-PCI, the overall technical and initial guidewire success rates were 91.4% and 83.8%, respectively. Of 380 patients with a Japanese CTO score ≥3 and a collateral channel score ≥2, PAA and PRA were performed in 161 (42.4%) and 219 (57.6%) patients, respectively. Initial guidewire success was higher with PRA than PAA (88.1% vs. 78.9%; P=0.01), and bail-out success was higher for a retrograde than antegrade approach (91.2% vs. 56%; P=0.0019). PRA was associated with longer guidewire crossing time, longer fluoroscopy time, and greater contrast use.

Conclusions: In patients with challenging CTO, poor antegrade conditions, and feasible interventional collaterals, PRA achieved higher initial guidewire success at the expense of higher procedural burden/resource use.

Key Words: Chronic total occlusion percutaneous coronary intervention (CTO-PCI); Complex chronic total occlusion (CTO); Primary retrograde approach

Evidence supports the role of chronic total occlusion percutaneous coronary intervention (CTO-PCI) in improving health status.[1,2] However, CTO-PCI remains one of the most technically challenging procedures in interventional cardiology, requiring careful patient selection due to its procedural complexity and associated risks.[3] Nevertheless, advances in operator expertise and device technology have substantially improved procedural success rates in the contemporary era.[4]

Despite the prevailing use of the antegrade approach, the retrograde approach remains essential for achieving a high success rate. The use of the retrograde approach, particularly for complex lesions, has led to a 90% success rate for CTO-PCI when performed by experienced operators worldwide.[5] According to the global chronic total occlusion (CTO) algorithm, the retrograde approach is advocated as the first option when there is an ambiguous proximal cap, poor distal opacification, or aorto-ostial occlusion.[6] However, the retrograde approach is associated with higher periprocedural complications and higher procedural burden/resource use.[7] Based on the Prospective Global Registry for the Study of Chronic Total Occlusion Intervention (PROGRESS-CTO) registry, Allana et al.[8] revealed that the retrograde approach had an increased risk of in-hospital

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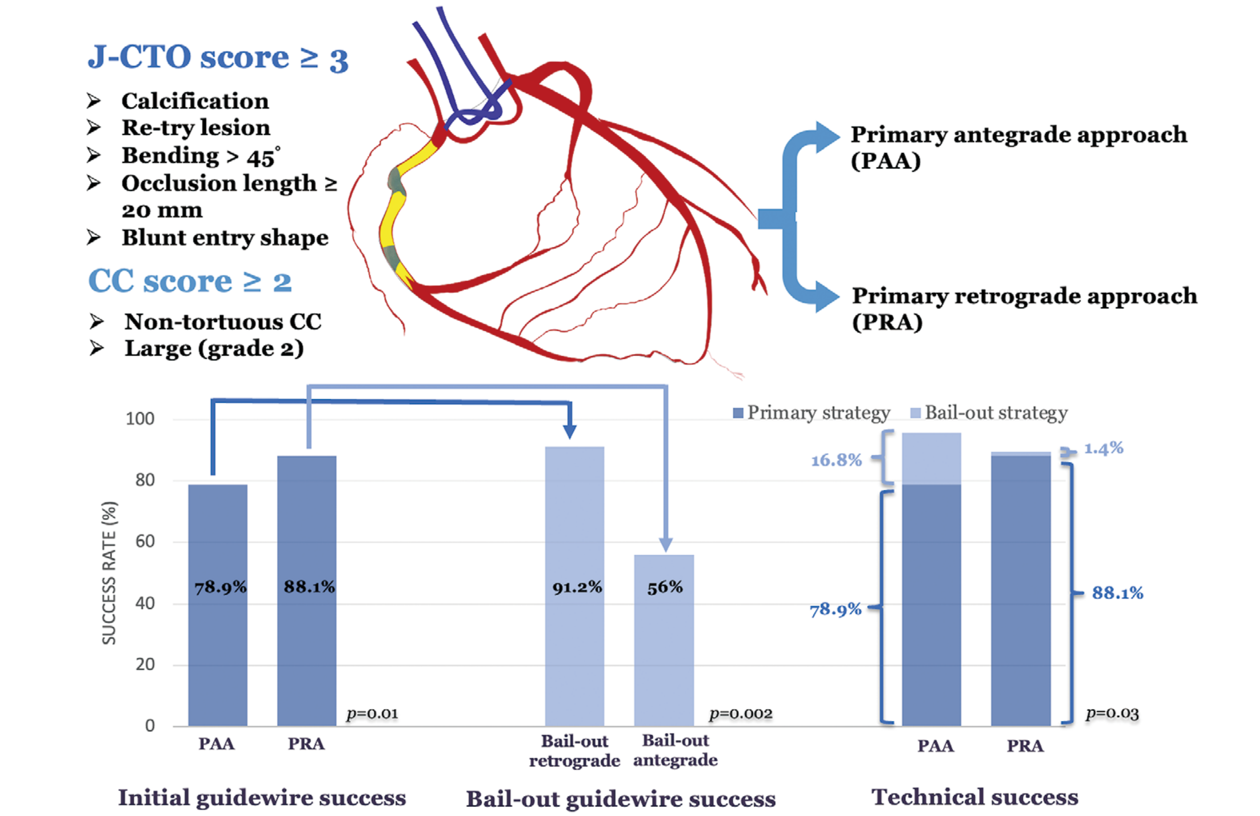

Central Figure. Comparison of efficacy between primary antegrade approach (PAA) and primary retrograde approach (PRA) in patients with a Japanese chronic total occlusion (J-CTO) score ≥3 and collateral channel (CC) score ≥2. PRA resulted in a significantly higher initial guidewire success rate than PAA (88.1% vs. 78.9%; P=0.01). The bail-out success rate was higher for the retrograde than antegrade approach (91.2% vs. 56%; P=0.0019). The overall technical success rate was higher for the PAA than PRA treatment group (95.7% vs. 89.5%; P=0.03).

major adverse cardiovascular events, and bailout antegrade crossing was needed in half the patients in whom a primary retrograde approach (PRA) was used. These results challenge the efficacy of the retrograde approach and the scenarios in which a PRA is appropriate.

The definition of complex CTO-PCI varies among operators. According to the widely used Japanese chronic total occlusion (J-CTO) score,[9] antegrade wire crossing is considered very difficult in patients with a J-CTO score ≥3. For a strategy involving the retrograde approach, thorough evaluation of collateral channels (CCs) is necessary, and successful CC crossing is the most critical predictor of retrograde procedural success.[8] Huang et al. subsequently developed and validated the first scoring system specifically designed to predict CC trackability and retrograde success.[10,11]

Several studies have shown that the PRA is superior to the retrograde rescue approach for complex CTO-PCI. A report from the Japanese CTO-PCI expert registry showed that the PRA led to a shorter guidewire manipulation time, despite the presence of more complex lesions, compared with the rescue retrograde approach.[12] In a multicenter registry, retrograde CTO-PCI as the primary crossing strategy demonstrated higher technical and procedural success with comparable safety to the secondary retrograde approach.[13] However, the benefits of the PRA in patients with highly complex CTO morphologies and the presence of feasible interventional collaterals have not been reported. Therefore, the aim of the present study was to explore the efficacy and efficiency of the retrograde approach for recanalizing complex CTOs.

Methods

Study Population

We conducted a single-center retrospective cohort study and reviewed 805 CTO-PCI procedures performed between January 2016 and July 2023 by experienced operators at the National Taiwan University Hospital, a tertiary center. Patients for whom J-CTO or CC scores were not available were excluded from the study. Based on the global crossing algorithm for CTO-PCI,[6] we divided patients into those undergoing a primary antegrade approach (PAA) or PRA according to the initial treatment strategy. PAA was defined as starting the procedure from the proximal cap using antegrade wire-based techniques; PRA was defined as starting the procedure with CC crossing to approach the CTO segment from the distal vessel. The primary strategy was at the operator's discretion, and was determined based on angiographic characteristics and procedural considerations.

This study was approved by Research Ethics Committee

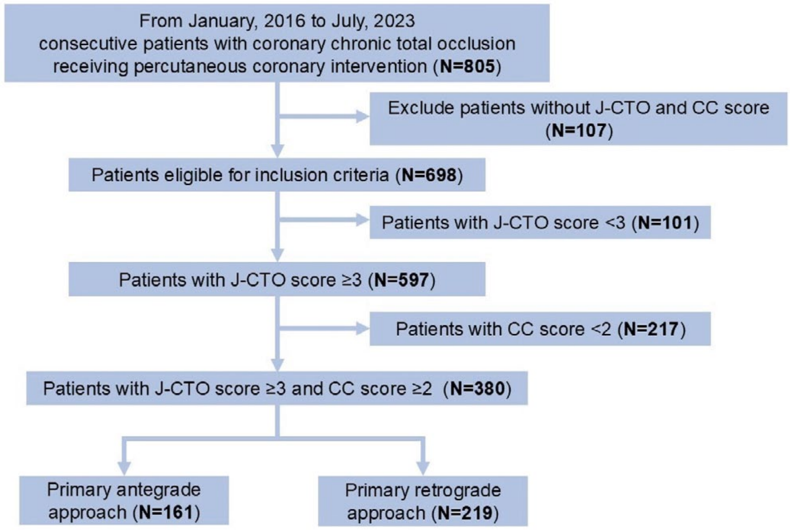

Figure 1. Flowchart of study population groups. After excluding patients without Japanese chronic total occlusion (J-CTO) or collateral channel (CC) scores, 698 patients were included in the final analysis. Of the 380 patients with a J-CTO score ≥3 and a CC score ≥2, 161 (42.4%) underwent a primary antegrade approach and 219 (57.6%) underwent a primary retrograde approach.

A of the National Taiwan University Hospital (Reference no. NTUH-REC No.201612048RINA). The requirement for patient consent was waived owing to study design. This study used data exclusively from the National Taiwan University Hospital. Co-authors from Assiut University, Egypt, contributed to study conception and manuscript revision, but did not provide patient data.

Definition and Study Endpoints

We calculated the most widely used antegrade scoring system, namely the J-CTO score,[9] along with the CC score[11] by collecting data on individual components of each score after reviewing all angiograms. The components of the J-CTO score were any degree of lesion calcification, bending >45° in the CTO segment or at entry, blunt proximal cap, length of the occluded segment >20 mm, and a previously failed recanalization attempt, with 1 point assigned for each parameter if present.[9] The components of the CC score were CC size and tortuosity. CC size was assessed by the grading system proposed by Werner et al.[14] A tortuous CC was defined as the presence of more than one high-frequency curve (within 2 mm) in the non-septal channels or at least one high-frequency curve that failed to uncoil in diastole in the septal channels.[15] A high-frequency curve was defined as a curve >180° occurring within a segment length <3 times the diameter of the CC.[15] A score of 2 points was assigned if the CC was not tortuous, and a score of 1 point was assigned if the CC size was large (grade 2, artery-like). The CC score was obtained by summing these scores.[11]

Previous studies stated that a J-CTO score ≥3 indicates that antegrade wire crossing is very difficult, whereas retrograde collateral crossing is likely if the CC score is ≥2.[9,11] Therefore, we focused on analyzing patients deemed suitable for the retrograde approach (CC score ≥2) but poor candidates for the antegrade approach (J-CTO score ≥3) to investigate whether PRA would benefit these patients.

The study endpoints included a mechanistic procedural endpoint, namely guidewire success, and technical success, based on final clinical outcomes (see below). Initial guidewire success was defined as successful guidewire crossing of the CTO body using the primary strategy. Bail-out guidewire success was defined as successful guidewire crossing achieved using a secondary strategy after failure of the initial approach, without requiring wire externalization. Guidewire crossing was defined as the passage of the guidewire into the distal true lumen in antegrade procedures or into the proximal true lumen in retrograde procedures. The technical success of CTO-PCI was defined as successful CTO revascularization with <30% residual diameter stenosis within the treated segment and restoration of Thrombolysis in Myocardial Infarction (TIMI) Grade 3 antegrade flow.[16] Guidewire manipulation time, fluoroscopy times, and contrast doses were used as indices of procedural burden/resource use. Other procedural definitions and endpoint classifications in this study were aligned with the CTO Academic Research Consortium consensus definitions.[16]

Statistical Analyses

Continuous variables are presented as the mean±SD, whereas categorical variables are presented as numbers and percentages. Comparisons between groups were performed using t-tests for continuous variables and Chi-squared tests for categorical variables. Propensity score matching (PSM) was performed to adjust for potential confounding between the PAA and PRA groups. Propensity scores were estimated using a logistic regression model in which treatment status was used as the dependent variable and baseline covariates were included as independent variables. Covariates included in PSM were selected a priori based on their known or plausible associations with both strategy selection and procedural outcomes. One-to-one nearest-neighbor greedy matching without replacement was performed using a caliper width of 0.2× the SD of the logit of the propensity score. Covariate balance before and after matching was assessed using absolute standardized mean differences (SMDs) for the logit of the propensity score and all included baseline covariates, with an absolute SMD <0.10 considered indicative of adequate balance. After one-to-one matching, binary outcomes were evaluated using the McNemar test, and continuous variables were analyzed using paired t-tests. All statistical analyses were

Table 1. Clinical Characteristics of Patients With a J-CTO Score ≥3 and a CC Score ≥2

	PAA (n=161)	PRA (n=219)	P value
Age, years	64.61±11.74	61.50±11.62	0.01
Sex			0.39
Male	147 (91.30)	194 (88.58)	
Female	14 (8.70)	25 (11.42)	
Body mass index (kg/m²)	26.42±4.11	26.81±3.69	0.32
Current smoker	74 (45.96)	114 (52.05)	0.24
Comorbidities			
Hypertension	122 (75.78)	160 (73.06)	0.55
Diabetes	61 (37.89)	91 (41.55)	0.47
Peripheral artery disease	19 (11.80)	13 (5.94)	0.04
Hyperlipidemia	117 (72.67)	131 (59.82)	<0.01
Chronic kidney disease	80 (49.69)	118 (53.88)	0.58
Left main disease	31 (19.25)	20 (9.13)	<0.01
No. diseased vessels			0.89
1	21 (13.21)	27 (12.39)	
2	44 (27.67)	65 (29.82)	
3	94 (59.12)	126 (57.80)	
History of CABG	19 (11.80)	20 (9.13)	0.40
History of PCI	49 (30.43)	119 (54.34)	<0.01
Family history of CAD	28 (17.39)	33 (15.07)	0.54
LVEF (%)	58.74±12.27	56.13±11.29	0.04
eGFR (mL/min/1.73 m²)	60.66±23.02	58.73±19.80	0.39

Unless indicated otherwise, data are given as the mean±SD or n (%). Chi-squared tests were used to examine associations between 2 categorical variables; independent t-tests were used to compares mean values between 2 groups. CABG, coronary artery bypass graft; CAD, coronary artery disease; CC, collateral channel; eGFR, estimated glomerular filtration ratio; J-CTO, Japanese chronic total occlusion; LVEF, left ventricular ejection fraction; PAA, primary antegrade approach; PCI, percutaneous coronary intervention; PRA, primary retrograde approach.

performed using SAS version 9.4 (SAS Institute, Cary, NC, USA). Statistical significance was set at two-tailed P<0.05.

Results

After excluding patients without J-CTO or CC scores, 698 patients were included in the final analysis (**Figure 1**). In the entire cohort, 398 (57%) patients underwent PAA and 300 (43%) underwent PRA. The baseline characteristics of the entire cohort are presented in **Supplementary Table 1**. The overall technical success rate was 91.4%. The procedure-related complication rate was 2.4%, including one periprocedural myocardial infarction requiring emergency coronary bypass surgery, one acute stent thrombosis, 2 coronary embolisms, 4 coronary perforations complicated by cardiac tamponade requiring pericardiocentesis, and 5 puncture-site complications necessitating additional endovascular or surgical intervention. Retrograde-related complications included one case of CC perforation resulting in cardiac tamponade, and another CC perforation causing an intraventricular septal hematoma with dry tamponade. In addition, there was one case of donor vessel occlusion, leading to periprocedural myocardial infarction.

Patient and Lesion Characteristics

Of the 380 patients with a J-CTO score ≥3 and a CC score ≥2, 161 (42.4%) underwent PAA and 219 (57.6%) underwent PRA (**Figure 1**). Compared with the PRA group, patients in the PAA group were significantly older (64.6±11.7 vs. 61.5±11.6 years; P=0.01), had higher a prevalence of peripheral arterial disease (11.8% vs. 5.94%; P=0.04), hyperlipidemia (72.7% vs. 59.8%; P<0.01), and left-main disease (19.2% vs. 9.1%; P<0.01), a lower rate of previous PCI (30.4% vs. 54.3%; P<0.01), and slightly, albeit significantly, better left ventricular ejection fraction (58.7±12.3% vs. 56.1±11.3%; P=0.04; **Table 1**). In terms of lesion complexity, J-CTO scores were lower in the PAA than PRA group (3.52±0.65 vs. 4.00±0.69; P<0.01). The PRA group had significantly more right coronary artery CTOs, fewer in-stent CTOs, more ambiguous CTO entry and exit shapes, higher degrees of calcification and bending in the CTO segments, and longer occlusion lengths than PAA group. Regarding CC characteristics, there were more contralateral CCs in the PRA group, but no statistically significant differences between the 2 groups in terms of collateral type, CC grade, collateral tortuosity, or CC score (**Table 2**).

Procedural Outcomes

PRA resulted in a significantly higher initial guidewire success rate than PAA (88.1% vs. 78.9%; P=0.01). Among patients in the PAA group, 34 experienced failure of the initial guidewire attempt and were subsequently converted to a retrograde approach. Failure was primarily attributed to an inability to cross the CTO segment or persistent subintimal tracking without successful distal re-entry. Of these 34 patients, guidewire success was achieved in 31 after crossover to a bail-out retrograde strategy. In the PRA group, 26 patients experienced failure of the initial guide-

Table 2. Angiographic Characteristics of Patients With a J-CTO Score ≥3 and a CC Score ≥2

	PAA (n=161)	PRA (n=219)	P value
Syntax score	24.55±9.50	23.72±7.26	0.37
CC score	2.82±0.39	2.76±0.43	0.18
J-CTO score	3.52±0.65	4.00±0.69	<0.01
In-stent CTO	31 (19.25)	9 (4.11)	<0.01
Exit shape of CTO			0.01
Diffuse narrowing	27 (16.77)	24 (10.96)	
Taper	61 (37.89)	89 (40.64)	
Blunt	35 (21.74)	29 (13.24)	
No stump	38 (23.60)	77 (35.16)	
Distal opacification of CTO			0.18
Good	155 (96.27)	216 (98.63)	
Uncertain	6 (3.73)	3 (1.37)	
Length of CTO segment occlusion			<0.01
<20 mm	60 (37.27)	39 (17.81)	
≥20 mm	101 (62.73)	180 (82.19)	
Calcification in CTO segment			0.01
None	2 (1.24)	2 (0.91)	
Mild	36 (22.36)	23 (10.50)	
Moderate	103 (63.98)	166 (75.80)	
Severe	20 (12.42)	28 (12.79)	
Bending of CTO segment			<0.01
Straight	0 (0.00)	0 (0.00)	
Mild	114 (70.81)	86 (39.27)	
Moderate	36 (22.36)	103 (47.03)	
Severe	11 (6.83)	29 (13.24)	
Not identified	0 (0.00)	1 (0.46)	
Entry shape of CTO			0.05
Taper	62 (38.51)	76 (34.70)	
Blunt	47 (29.19)	50 (22.83)	
No stump	50 (31.06)	93 (42.47)	
Not identified	2 (1.24)	0 (0.00)	
Origin of collateral channels			0.01
Ipsilateral	23 (14.29)	17 (7.76)	
Contralateral	101 (62.73)	167 (76.26)	
Contralateral and ipsilateral	37 (22.98)	35 (15.98)	
CTO target			0.04
RCA	78 (48.45)	136 (62.10)	
LAD	63 (39.13)	59 (26.94)	
LCX	18 (11.18)	24 (10.96)	
Left main	1 (0.62)	0 (0.00)	
Graft	1 (0.62)	0 (0.00)	
Collateral type			0.43
Not identified	2 (1.24)	0 (0.00)	
Epicardial	52 (32.30)	73 (33.33)	
Septal	102 (63.35)	139 (63.47)	
Graft	5 (3.11)	7 (3.20)	
CC grade			0.23
Non-connected (0)	1 (0.62)	0 (0.00)	
Thread like (1)	28 (17.39)	50 (22.83)	
Artery like (2)	132 (81.99)	169 (77.17)	
Collateral tortuosity			1.00
Tortuous	0 (0.00)	0 (0.00)	
None	161 (100.00)	219 (100.00)	

Unless indicated otherwise, data are given as the mean±SD or n (%). Chi-squared tests were used to examine associations between 2 categorical variables; independent t-tests were used to compares mean values between 2 groups. CTO, chronic total occlusion; LAD, left anterior descending artery; LCX, left circumflex artery; RCA, right coronary artery. Other abbreviations as in Table 1.

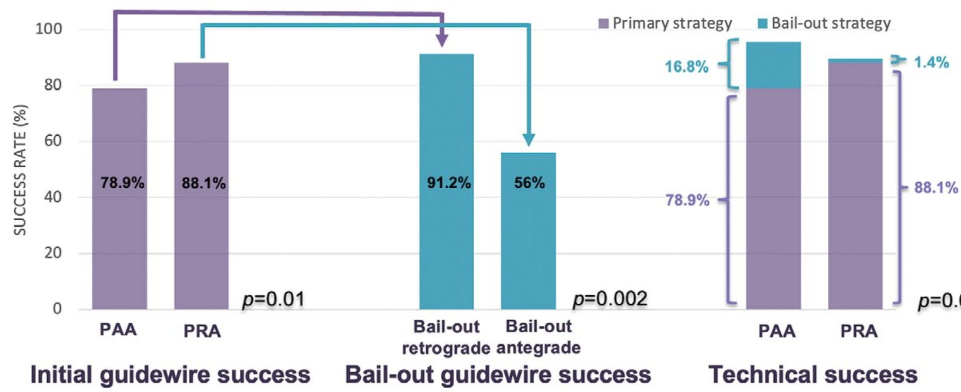

Figure 2. Procedural outcomes in patients with a Japanese chronic total occlusion (J-CTO) score ≥3 and collateral channel (CC) score ≥2. The primary retrograde approach (PRA) resulted in a significantly higher initial guidewire success rate than the primary antegrade approach (PAA). The bail-out success rate was higher for the retrograde than antegrade approach. The overall technical success rate, combining the success of the initial and bail-out procedures, was higher for the group treated with the PAA than PRA.

Table 3. Procedural Outcomes in Patients With a J-CTO Score ≥3 and a CC Score ≥2

	All participants (n=380)	PAA (n=161)	PRA (n=219)	P value
Initial guidewire success	320 (84.21)	127 (78.88)	193 (88.13)	0.01
Bail-out guidewire success[A]	45 (76.27)	31 (91.20)	14 (56.00)	<0.01
Technical success	350 (92.11)	154 (95.65)	196 (89.50)	0.03
Procedural complication	8 (2.10)	3 (1.86)	5 (2.28)	0.73
Acute stent thrombosis (n)	1	1	0	
Coronary distal embolization (n)	1	1	0	
Coronary perforation (n)	3	1	2	
Puncture site bleeding (n)	3	0	3	
Procedural burden/resource use				
CTO wire crossing time (min)	46.89±35.05	31.14±29.95	58.47±34.05	<0.01
Fluoroscopy time (min)	51.27±29.69	37.18±24.47	61.72±28.93	<0.01
Procedure time (min)	265.81±128.42	239.55±119.54	285.11±131.53	<0.01

Unless indicated otherwise, data are given as the mean±SD or n (%). [A]n=59 for all participants; n=34 for the PAA; n=25 for the PRA. Chi-squared tests were used to examine associations between 2 categorical variables; independent t-tests were used to compares mean values between the PAA and PRA groups. Abbreviations as in Tables 1,2.

wire attempt. One procedure was aborted due to vessel perforation. The remaining 25 patients (unsuccessful CC crossing in 16 patients, failure to cross the CTO segment in 9) were converted to an antegrade approach. Among these 25 patients, guidewire success was achieved in 14 after crossover to a bail-out antegrade strategy. This yielded a higher bail-out success rate for the retrograde than antegrade approach (91.2% vs. 56%; P=0.0019). The overall technical success rate, defined as a combination of the success of the initial and bail-out strategies, was higher in the group treated with PAA than PRA (95.7% vs. 89.5%; P=0.03; **Figure 2**; **Table 3**). With regard to indicators of procedural burden/resource use, PRA led to markedly longer guidewire crossing time (58.5±34.1 vs. 31.1±30.0 min), longer fluoroscopy time (61.7±28.9 vs. 37.2±24.5 min), and higher contrast volume (285.1±131.5 vs. 239.6±119.5 mL; all P<0.01; **Figure 3**; **Table 3**). In subgroup comparisons, patients who achieved guidewire success with a bail-out retrograde approach had numerically longer CTO-wire crossing time, fluoroscopy duration, and contrast volume than those with successful PRA (**Supplementary Table 2**).

There was no significant differences in procedural complications between the PAA and PRA groups (1.86% vs 2.28%, respectively; **Table 3**; P=0.73). In the PAA group, complications included one stent thrombosis, one coronary distal embolization, and one coronary perforation (**Table 3**). In the PRA group, 2 coronary perforations and 3 cases of puncture site bleeding were reported (**Table 3**).

PSM Between the PAA and PRA Groups

Given the greater complexity of CTO lesions in the PRA group among patients with a J-CTO score ≥3 and CC score ≥2, PSM was performed to adjust for potential confounding between the PAA and PRA groups. The covariates used for PSM included sex, hypertension, diabetes, hyperlipidemia, left main disease, prior PCI, in-stent CTO, exit shape of the CTO, occlusion length, calcification, and bending of the CTO segment. There were no missing data among the

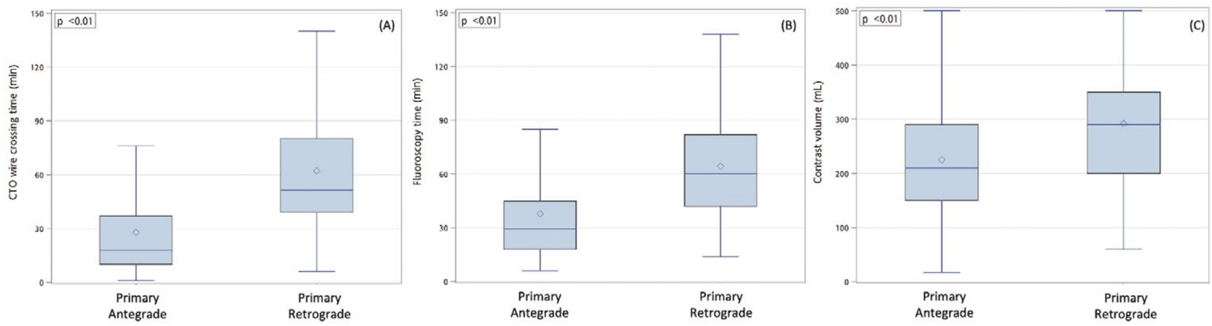

Figure 3. Procedural burden/resource use in patients with a Japanese chronic total occlusion (J-CTO) score ≥3 and collateral channel (CC) score ≥2: (**A**) chronic total occlusion (CTO) wire crossing time; (**B**) fluoroscopy time, and (**C**) contrast volume. The primary retrograde approach led to markedly higher procedural burden/resource use in terms of guidewire crossing time, fluoroscopy time, and contrast volume. The boxes show the interquartile range, with the median value indicated by the horizontal line; whiskers show the range.

Table 4. Procedural Outcomes After Propensity Score Matching Between PAA and PRA in Patients With a J-CTO Score ≥3 and a CC Score ≥2

	PAA (n=104)	PRA (n=104)	P value
Initial guidewire success	75 (72.12)	91 (87.50)	<0.01
Bail-out guidewire success[A]	28 (96.55)	9 (69.23)	<0.01
Technical success	101 (97.12)	94 (90.38)	0.052
Procedural burden/resource use			
CTO wire crossing time (min)	35.79±30.60	57.00±36.73	<0.01
Fluoroscopy time (min)	42.34±26.31	55.84±25.45	<0.01
Procedure time (min)	84.88±46.92	111.36±45.64	<0.01

Unless indicated otherwise, data are given as the mean±SD or n (%). [A]n=29 for the PAA; n=13 for the PRA. Binary outcomes were evaluated using the McNemar test; continuous variables were analyzed using paired t-tests. Abbreviations as in Tables 1,2.

included covariates except for 2 patients, who were excluded from the matching process. The results before and after matching are presented in **Supplementary Table 3**. After PSM, the difference in overall technical success between the PAA and PRA groups was not statistically significant (97.12% vs. 90.38%, respectively; P=0.052; **Table 4**). In contrast, the initial guidewire success rate remained significantly higher in the PRA than PAA group (87.5% vs. 72.1%, respectively; P<0.01; **Table 4**). In both matched groups, after initial guidewire failure, a bail-out strategy was attempted in all patients. Consequently, guidewire success was achieved in 28 of 29 patients in the PAA group with a bail-out retrograde strategy, and in 9 of 13 patients in the PRA group with a bail-out antegrade approach. Accordingly, bail-out guidewire success was significantly higher in the PAA than PRA group (96.6% vs. 69.2%, respectively; P<0.01; **Table 4**). Procedural burden/resource use remained significantly higher in the PRA than PAA group (**Table 4**).

Multivariable Logistic Regression for Initial Guidewire Success and Technical Success

To further evaluate the robustness of the findings, multivariable logistic regression analyses were performed in both cohorts before and after PSM. Both crude and adjusted models were analyzed. In the original cohort, PRA was associated with a higher likelihood of initial guidewire success compared with PAA (adjusted odds ratio [OR] 0.26; 95% confidence interval [CI] 0.12–0.51; P=0.0001 for PAA vs. PRA). In contrast, no significant difference in technical success was observed after adjustment (adjusted OR 2.54; 95% CI 0.82–7.89; P=0.106). Similar findings were observed after PSM: PRA remained associated with higher initial guidewire success (adjusted OR 0.34; 95% CI 0.16–0.74; P=0.007), whereas technical success did not differ significantly between strategies (adjusted OR 3.82; 95% CI 0.76–19.25; P=0.105; **Supplementary Table 4**).

Discussion

In this single-center retrospective study, with most procedure performed by extremely experienced operators, PRA demonstrated superior initial guidewire success than PAA in challenging CTO-PCI with poor antegrade conditions but suitable interventional collaterals. Furthermore, after the failure of the initial strategy, the bail-out retrograde approach resulted in a higher guidewire success rate than the bail-out antegrade approach. This led to a higher overall technical success rate in the PAA group (**Central Figure**).

In the modern era of CTO-PCI, advances in equipment and techniques continue to enhance the success and safety of the retrograde approach. However, the optimal timing for the use of PRA remains controversial. The latest Asia Pacific Chronic Total Occlusion algorithm emphasizes the antegrade approach and recommends the use of PRA only in patients with proximal cap ambiguity, poor distal vessel opacification, or bifurcation in the distal cap in whom a retrograde option is feasible.[17] Nevertheless, the retrograde approach warrants greater emphasis, because contemporary experienced operators can achieve high success rates (approaching 90%) with retrograde procedures.[18] Ochiumi et al. reported that the use of the PRA in short-segment CTOs (<20 mm) was associated with patients with high J-CTO scores, poor distal run-off, ostial lesions, and grade 2 collaterals.[19] Furthermore, factors such as hemodialysis, the presence of calcification, and CTO lesion tortuosity, were independently associated with unsuccessful antegrade guidewire crossing.[19] Indeed, in our cohort, with a high proportion of patients undergoing PRA (43%) and more challenging CTO lesions (mean J-CTO score 3.55±0.98), a strategy of "retrograde first" in patients with both high J-CTO and CC scores was found to be superior in terms of initial guidewire success despite higher CTO complexity. In addition, after the failure of the initial approach in the case of PAA, switching to a bail-out retrograde approach resulted in significantly higher success rate, which implied that these patients may have been more suitable for treatment with PRA as the initial strategy. Conversely, among patients in whom PRA failed, a bail-out antegrade strategy achieved guidewire success in only 56%. This likely reflects an intrinsically more complex lesion subset with a limited probability of success regardless of crossing strategy. In addition, extensive resource utilization and operator fatigue developing during prolonged retrograde attempts may further diminish the feasibility of subsequent antegrade reattempts. Collectively, these findings indicate that proficiency in retrograde techniques is essential for contemporary CTO-PCI; however, they also underscore that a retrograde strategy should be used selectively rather than indiscriminately.

The favorable success rate of the bail-out retrograde approach observed in the present study contrasts with prior registry data, most notably that reported by Suzuki et al.,[20] in which the success rate of rescue retrograde PCI after failed antegrade attempts was approximately 78%. This difference is likely attributable to variations in patient selection and anatomical feasibility rather than procedural technique alone. Although the mean J-CTO score in the registry study of Suzuki et al. was substantially lower than in the present study, detailed information regarding CC characteristics was not reported by Suzuki et al.[20] In contrast, our analysis was deliberately restricted to lesions with well-developed and trackable CCs (CC score ≥2), thereby increasing the subgroup anatomically favorable for retrograde options. This strategy-driven selection likely contributed to the high bail-out retrograde success rate observed in our study and underscores the importance of systematic CC assessment in procedural planning for CTO-PCI. Furthermore, our study reflects contemporary practice (2016–2023), whereas the registry study by Suzuki et al.[20] enrolled patients from an earlier era (2014–2015). Advances in devices, techniques, and operator experience over the past decade may have further enhanced retrograde success rates. Collectively, these factors highlight that the effectiveness of a retrograde strategy depends on both CC suitability and contemporary procedural context.

An alternative interpretation of the high success rate of the bail-out retrograde approach following antegrade failure in our study is that the initial antegrade attempt may have facilitated subsequent retrograde crossing in a subset of patients with complex CTO. Although antegrade crossing did not always result in immediate success, limited antegrade manipulation may have facilitated plaque modification, microchannel formation, and subintimal space creation, thereby promoting subsequent retrograde crossing. In addition, an antegrade wire may serve as an anatomical reference for subsequent retrograde wiring, potentially aiding techniques such as reverse controlled antegrade and retrograde tracking or the kissing-wire technique, and improving procedural burden/resource use. Notably, the relatively short antegrade crossing time observed in our cohort suggests that antegrade attempts were brief and followed by early conversion to a retrograde strategy once antegrade progress was deemed unlikely. This approach allows operators to derive procedural benefit from initial antegrade engagement while minimizing excessive manipulation or inefficiency.

Our findings are in agreement with those from a study in South Korea, which compared the efficiency of CTO-PCI using primary vs. rescue (bailout) retrograde approach in complex CTO (mean J-CTO scores 2.62±1.07 vs. 2.38±1.06) and found that PRA had lower procedural burden/resource use with comparable safety.[21] In addition, in a multicenter registry including over 2700 patients, Kostantinis et al. reported that the success rate was higher for PRA than the retrograde approach following unsuccessful antegrade crossing (81.4% vs. 77.3%; P=0.01), with more advanced lesion complexity in the PRA than antegrade group (mean J-CTO scores 3.31 vs 2.99).[13] Accordingly, PRA may be appropriate in certain clinical scenarios, indicating that a universal antegrade-first strategy may warrant reconsideration.

In our study, in the unadjusted analysis, the overall technical success rate was higher in the PAA than PRA group. However, this finding should not be interpreted as the effect of the initial strategy itself, given the substantially greater lesion complexity in the PRA group. To further explore this issue, PSM was performed to adjust for baseline differences in lesion characteristics. After matching, the difference in technical success between the 2 strategies was attenuated and no longer statistically significant, supporting the interpretation that the observed difference in technical success may be more strongly related to lesion complexity than to the initial crossing strategy per se. In the study using Outcomes, Patient Health Status, and Efficiency in Chronic Total Occlusion Hybrid Procedures (OPENCTO) registry data, a retrograde approach was used in 51% of patients and was found to be associated with a lower success rate than an antegrade-only approach (82.4% vs. 94.2%; P≤0.001).[22] Yet, as in the present study, in OPENCTO, patients who underwent the retrograde approach were more medically complex, with higher J-CTO scores than those who underwent the antegrade approach (2.7 vs. 1.9). Furthermore, that study did not account for the quality of the CC.[22] The present study included a careful evaluation of CC, and we found that consideration of the presence of good interventional CCs should be included when planning the initial approach.

Notably, the initial antegrade guidewire success rate in the PAA group (78.9%) was higher than previously reported for lesions with high J-CTO scores,[9] likely reflecting contemporary advances in CTO equipment, techniques, and operator expertise. In our cohort, when antegrade advancement was deemed ineffective (e.g., persistent subintimal tracking without distal re-entry, inability to cross heavily calcified or tortuous segments, or lack of meaningful progress within a reasonable timeframe) the procedure was promptly converted to a bail-out retrograde strategy, provided suitable collaterals had been identified. Although time spent on each strategy during hybrid procedures was not systematically recorded, antegrade attempts were conducted by experienced operators according to predefined, efficiency-oriented CTO algorithms that favored early conversion rather than prolonged persistence.

CTO recanalization remains the ultimate challenge for every PCI operator, but procedural safety and burden/resource use should always be balanced against success rate. Although no significant difference in procedural complication rates was observed between the PAA and PRA groups in the present study, this finding should be interpreted with caution because all procedures were performed by highly experienced CTO operators. In routine practice, retrograde techniques are generally associated with higher procedural risk than antegrade-only strategies, particularly in less experienced hands. Our previous study demonstrated that the retrograde approach is associated with higher resource usage.[7] Similarly, in the present study, PRA was inferior to PAA in terms of contrast volume, fluoroscopy time, and guidewire manipulation time. However, our subgroup analysis showed numerically less procedural burden/resource use with a standalone PRA than a PAA strategy that required bail-out retrograde attempts. Accordingly, although an antegrade-first strategy with early conversion remains appropriate in many cases, a carefully selected PRA may represent a rational and efficient option for highly complex CTO lesions with confirmed retrograde feasibility.

Study Limitations

This study has some limitations. First, this was an observational retrospective study conducted at a single center without clinical event adjudication, core laboratory evaluation of the study angiograms, or long-term follow-up. Second, because the procedures were performed by knowledgeable and experienced operators, the same outcomes may not be achievable by less-experienced operators. The high proportion of complex CTOs in our cohort (mean J-CTO score 3.55±0.98) reflects the role of the National Taiwan University Hospital as a tertiary referral center for reattempts and challenging cases; therefore, the outcomes should be interpreted with caution when being extrapolated to general hospitals. Third, a selection bias could not be excluded because the procedural strategy was at the operator's discretion. Despite adjustment using PSM, residual confounding related to unmeasured anatomical factors cannot be excluded. Fourth, in the present study, the PAA strategy consisted exclusively of antegrade wire-based techniques. This reflects the practice pattern at the National Taiwan University Hospital and may limit the generalizability of comparisons with studies incorporating approaches based on intentional antegrade dissection/re-entry techniques. Fifth, temporal changes and the impact of the COVID-19 pandemic may have influenced patient outcomes over the study period among patients undergoing PCI, as reported previously.[23] In addition, operator clustering may have affected strategy selection and clinical success. Further prospective randomized controlled trials are warranted to confirm our findings and to identify specific CTO subtypes that may benefit more from PRA.

Conclusions

In the present study of patients with a J-CTO score ≥3 and a CC score ≥2, PRA was associated with higher initial guidewire success but at the cost of increased procedural burden and resource use, without a clear advantage in terms of final technical success. These findings suggest that, in select patients with markedly unfavorable antegrade anatomy and well-developed, trackable collaterals, a retrograde-first strategy may be a reasonable option, whereas an antegrade-first approach with timely conversion to a retrograde approach remains appropriate in many patients. Overall, the results underscore the importance of individualized, anatomy-driven decision-making, the appropriate use of retrograde techniques, and balancing procedural efficiency with resource utilization in contemporary CTO-PCI practice.

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Disclosures

The authors have no conflicts of interest to declare.

IRB Information

This study was approved by Research Ethics Committee A of the National Taiwan University Hospital (Reference no. NTUH-REC No.201612048RINA).

Data Availability

The deidentified individual participant data, including data dictionaries and all datasets underlying the findings of this study (including raw data from the retrospective cohort), will be made available upon reasonable request to the corresponding author. No additional related documents (e.g., study protocol or statistical analysis plan) are available. Data will become available 3 months after publication and will be available for 1 year. Access will be granted to qualified researchers whose proposed use of the data is scientifically and ethically appropriate, subject to approval by the corresponding author and, where applicable, institutional review board or ethics committee oversight. Requestors may be required to provide a methodologically sound research proposal and to sign a data use agreement to ensure compliance with institutional policies and data protection regulations. Data will be shared in a secure electronic format (e.g., password-protected files via email or secure transfer platform).

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Supplementary Files

Please find supplementary file(s);
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