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Bahadir Simsek

Spyridon Kostantinis

Judit Karacsonyi

Khaldoon Alaswad
Henry Ford Health, kalaswa1@hfhs.org

Dimitri Karmpaliotis

See next page for additional authors

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Authors

Bahadir Simsek, Spyridon Kostantinis, Judit Karacsonyi, Khaldoon Alaswad, Dimitri Karmpaliotis, Amirali Masoumi, Farouc A. Jaffer, Darshan Doshi, Jaikirshan Khatri, Paul Poommipanit, Sevket Gorgulu, Nidal Abi Rafeh, Omer Goktekin, Oleg Krestyaninov, Rhian Davies, Ahmed ElGuindy, Elias V. Haddad, Jimmy Kerrigan, Mitul Patel, Raj H. Chandwaney, Olga C. Mastrodemos, Salman Allana, Bavana V. Rangan, and Emmanouil S. Brilakis

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Predictors of success in primary retrograde strategy in chronic total occlusion percutaneous coronary intervention: insights from the PROGRESS-chronic total occlusion registry

Bahadir Simsek MD[1] | Spyridon Kostantinis MD[1] | Judit Karacsonyi MD, PhD[1] | Khaldoon Alaswad MD[2] | Dimitri Karmpaliotis MD, PhD[3] | Amirali Masoumi MD[3] | Farouc A. Jaffer MD, PhD[4] | Darshan Doshi MD[4] | Jaikirshan Khatri MD[5] | Paul Poommipanit MD[6] | Sevket Gorgulu MD[7] | Nidal Abi Rafeh MD[8] | Omer Goktekin MD[9] | Oleg Krestyaninov MD[10] | Rhian Davies MD[11] | Ahmed ElGuindy MD[12] | Elias V. Haddad MD[13] | Jimmy Kerrigan MD[13] | Mitul Patel MD[14] | Raj H. Chandwaney MD[15] | Olga C. Mastrodemos BA[1] | Salman Allana MD[1] | Bavana V. Rangan BDS, MPH[1] | Emmanouil S. Brilakis MD, PhD[1]

[1]Center for Coronary Artery Disease, Minneapolis Heart Institute and Minneapolis Heart Institute Foundation, Minneapolis, Minnesota, USA

[2]Division of Cardiology, Henry Ford Hospital, Detroit, Michigan, USA

[3]Gagnon Cardiovascular Institute, Morristown Medical Center, Morristown, New Jersey, USA

[4]Division of Cardiology, Massachusetts General Hospital, Harvard University, Boston, Massachusetts, USA

[5]Division of Cardiology, Cleveland Clinic Foundation, Cleveland, Ohio, USA

[6]Division of Cardiology, University Hospitals, Case Western Reserve University, Cleveland, Ohio, USA

[7]Department of Cardiology, Acibadem Kocaeli Hospital, Kocaeli, Turkey

[8]Depatment of Cardiology, North Oaks Healthcare System, Hammond, Louisiana, USA

[9]Department of Cardiology, Bahcelievler Memorial Hospital, Istanbul, Turkey

[10]Department of Invasive Cardiology, Meshalkin National Medical Research Center, Ministry of Health of the Russian Federation, Novosibirsk, Russia

[11]Department of Cardiology, Wellspan York Hospital, York, Pennsylvania, USA

[12]Department of Cardiology, Aswan Heart Centre, Aswan, Egypt

[13]Department of Cardiology, Ascension Saint Thomas Heart, Nashville, Tennessee, USA

[14]Division of Cardiovascular Medicine, UCSD Medical Center, La Jolla, California, USA

[15]Department of Cardiology, Oklahoma Heart Institute, Tulsa, Oklahoma, USA

Correspondence

Emmanouil S. Brilakis, MD, PhD, Minneapolis Heart Institute, Chairman of the Center for Coronary Artery Disease at the Minneapolis Heart Institute Foundation, 920 E 28th St #300, Minneapolis, MN 55407, USA.
Email: esbrilakis@gmail.com

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Abstract

Background: An upfront (primary) retrograde strategy is often used in complex chronic total occlusion (CTO) percutaneous coronary intervention (PCI).

Methods: We examined the clinical, angiographic characteristics, and procedural outcomes of CTO PCIs that were approached with a primary retrograde strategy in the Prospective Global Registry for the Study of CTO Intervention (PROGRESS-CTO, NCT02061436).

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Results: Of 10,286 CTO PCIs performed between 2012 and 2022, a primary retrograde strategy was used in 1329 (13%) with an initial technical success of 66%, and a final success of 83%. Patients who underwent successful versus unsuccessful primary retrograde cases had similar characteristics: age (65 ± 10 vs. 65 ± 9, years, $p = 0.203$), men (83% vs. 87%, $p = 0.066$), prior PCI (71% vs. 71%, $p = 0.809$), and prior coronary artery bypass graft surgery (52% vs. 53%, $p = 0.682$). The PROGRESS-CTO score (1.3 ± 0.9 vs. 1.6 ± 0.9, $p < 0.001$), air kerma radiation (3.9 ± 2.8 vs. 3.4 ± 2.6, gray, $p = 0.013$), and contrast use (294 ± 148 ml vs. 248 ± 128, ml, $p < 0.001$) were higher in the unsuccessful group, whereas the presence of interventional collaterals (95% vs. 72%, $p < 0.001$) and Werner collateral connection grade 2 (43% vs. 31%, $p < 0.001$) were higher in the successful group. On multivariable logistic regression analysis, the only variable associated with a successful primary retrograde strategy was the presence of interventional collaterals: odds ratio: 6.52 (95% confidence intervals; 3.5–12.1, $p < 0.001$).

Conclusion: Presence of interventional collaterals is independently associated with higher success rates with a primary retrograde strategy in CTO PCI.

KEYWORDS

chronic total occlusion, percutaneous coronary intervention, predictors of success, primary retrograde strategy, technical success

1 | INTRODUCTION

The retrograde approach is used in 20%–50% of chronic total occlusion (CTO) percutaneous coronary interventions (PCI).[1] While retrograde crossing has been associated with higher risk of complications, it has also significantly improved CTO PCI success rates.[2] In most cases, the retrograde approach is used after failure of antegrade crossing attempts, but in some cases, it can be used upfront (primary retrograde), such as in lesions with proximal cap ambiguity, a bifurcation at the distal cap, and/or a poor quality distal vessel.[2,3] We examined the clinical and angiographic characteristics and outcomes of patients who underwent CTO PCI using a primary retrograde approach.

2 | METHODS

We examined clinical and angiographic characteristics and in-hospital outcomes of primary retrograde CTO PCI cases in the Prospective Global Registry for the Study of Chronic Total Occlusion Intervention (PROGRESS-CTO, NCT02061436). PROGRESS-CTO includes patient level data for CTO PCI procedures performed between 2012 and 2022 at experienced CTO PCI centers from the United States, Canada, Greece, Turkey, Egypt, Russia, and Lebanon. We compared the outcomes of technically successful versus unsuccessful procedures using a primary retrograde strategy.

2.1 | Definitions

CTOs were defined as total occlusion of a coronary artery with the absence of antegrade flow through the lesion with a presumed or documented duration of ≥3 months, according to the definitions of the CTO Academic Research Consortium.[4]

Technical success was defined as the successful recanalization of the CTO vessel with <30% residual stenosis and final Thrombolysis in Myocardial Infarction (TIMI) 3 flow.[4]

Procedural success was defined as technical success in the absence of in-hospital major adverse cardiovascular events (MACE).

Use of a primary retrograde strategy was defined as an attempt to cross CTO lesions with a guidewire in a retrograde manner as the first strategy. Successful primary retrograde strategy was defined as technically successful CTO PCI with the primary retrograde strategy. Unsuccessful primary retrograde cases were defined as technically unsuccessful primary retrograde crossing attempt(s), regardless of whether nonretrograde crossing strategies were then attempted, and regardless of the final outcome.

MACE were defined as the composite of in-hospital all-cause mortality, myocardial infarction (MI), stroke, urgent repeat revascularization (re-PCI or surgery), or pericardiocentesis.

Interventional collaterals were defined as collaterals with continuous connection to CTO target vessel that appeared suitable for retrograde CTO PCI.

Werner classification was used to assess the size of collaterals as previously described.[5]

The study was approved by the institutional review board of each site.

2.2 | Statistical analysis

Continuous variables are presented as mean ± standard deviation and median (interquartile range) and were compared using the independent *t*-test or Mann–Whitney *U*-test, as appropriate. Categorical variables are presented as absolute numbers and percentages and were compared using chi-square or Fisher's exact test, as appropriate. Univariable logistic regression analysis was performed to identify variables that might be different between the successful versus unsuccessful groups, and variables that had $p < 0.10$ and were deemed clinically/angiographically significant were included in the multivariable analysis.

Statistical analyses were performed using Stata v17.0 (StataCorp).

3 | RESULTS

After excluding centers with <40 case entries to the registry and cases with missing information (e.g., unknown technical success, primary or successful crossing strategy), the analysis included 1329 CTO PCI procedures (13% of the cohort) in which a primary retrograde strategy was used. Mean patient age was 65 ± 10 years, and 85% of the patients were men with a high prevalence of hypertension (92%), diabetes mellitus (45%), dyslipidemia (89%), prior coronary artery bypass graft surgery (CABG) (52%), prior PCI (71%), current smoking (27%), and prior MI (50%).

3.1 | Clinical, angiographic characteristics, and procedural outcomes

Of 10,286 CTO PCIs performed between 2012 and 2022, a primary retrograde strategy was used in 1329 (13%). Initial technical success was achieved in 878 cases (66%). Following the unsuccessful primary retrograde attempt, the most common second crossing strategy was antegrade wiring (AW) (61%), followed by antegrade dissection and re-entry (ADR) (19%). The final successful strategy for these cases was AW (27%) and ADR (23%), with a final technical success rate of 83% (Figure 1).

The clinical characteristics of patients in whom a primary retrograde strategy was successful versus unsuccessful were comparable (Table 1); however, atrial fibrillation and diabetes mellitus were more prevalent in patients who had a successful CTO PCI with a primary retrograde strategy. These patients were also more likely to have lower left ventricular ejection fraction (LVEF) and anemia (Table 1).

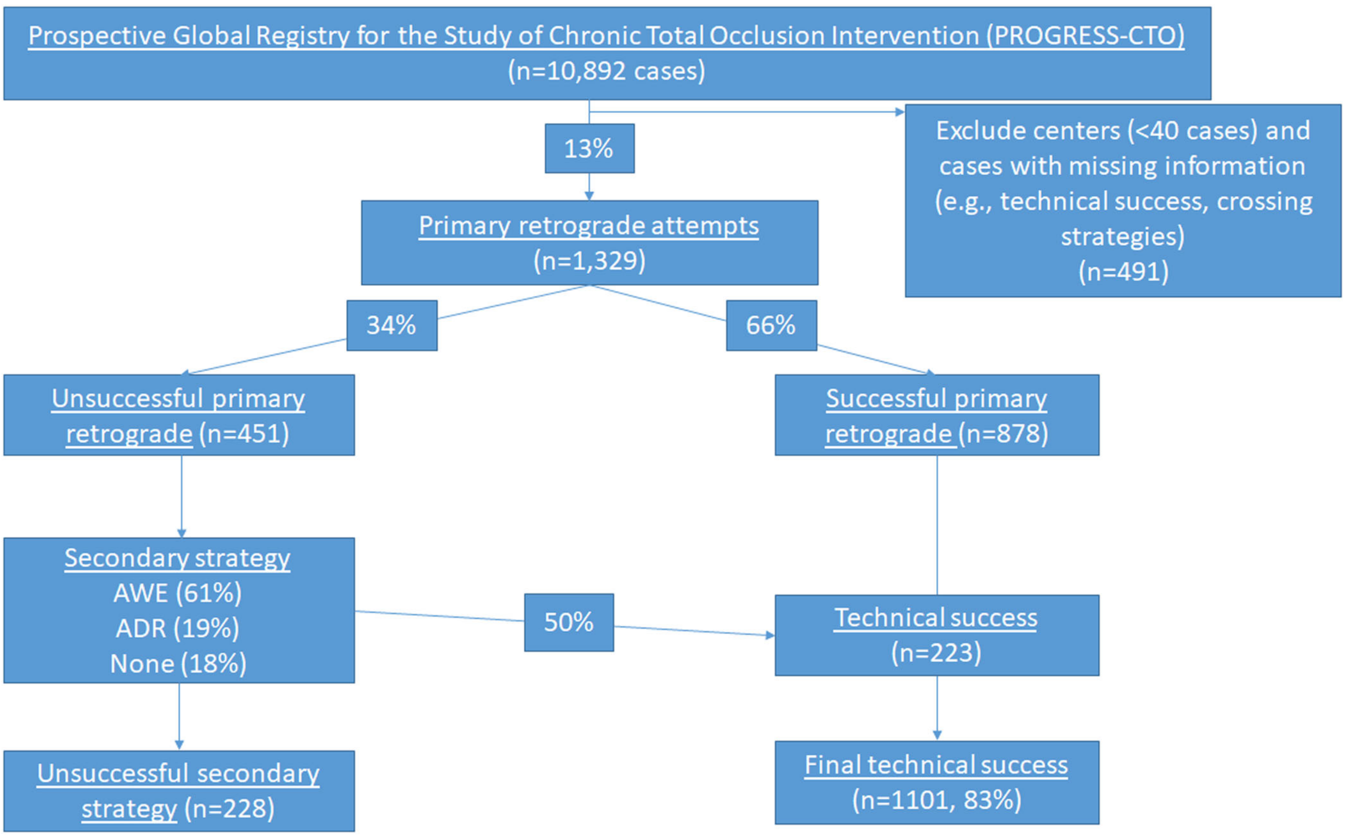


FIGURE 1 Flowchart describing the study design and technical success rate. [Color figure can be viewed at wileyonlinelibrary.com]

Patients who had successful primary retrograde CTO PCI were more likely to have a lower PROGRESS-CTO score (1.3 ± 0.9 vs. 1.6 ± 0.9, $p < 0.001$), have contralateral collateral filling the CTO vessel (67% vs. 58% $p = 0.007$), distal opacification more commonly defined as good, right coronary artery (RCA) CTOs (72% vs. 67%, $p = 0.048$), and Werner collateral connection (CC) grade 2 (43% vs. 31%, $p = 0.001$).[2] While procedure time and fluoroscopy time were similar between the groups, contrast volume and air kerma (AK) fluoroscopy dose were higher in the unsuccessful group (Table 2).

In-hospital outcomes including death (1.25% vs. 0.89%, $p = 0.550$), MACE (3.76% vs. 3.55%, $p = 0.847$), acute MI, stroke, re-PCI, emergency CABG, tamponade, pericardiocentesis, and vascular access complications were similar between the successful versus unsuccessful group, with a trend towards higher perforation rates in the unsuccessful group (7.7% vs. 10.6%, $p = 0.076$) (Table 3).

3.2 | Univariable/multivariable logistic regression model

On univariable logistic regression analysis using successful primary retrograde CTO PCI as the outcome, gender (women), atrial

TABLE 1 Clinical characteristics of patients who had successful primary retrograde versus unsuccessful primary retrograde CTO PCI.

Clinical characteristics	Successful primary retrograde (*n* = 878)	Failed primary retrograde (*n* = 451)	*p*-value
Age in years, mean ± SD (*n*)	64.6 ± 10 (751)	65.4 ± 9 (387)	0.203
Men, *n* (%)	636 (83)	342 (87)	0.066
BMI, mean ± SD (*n*)	30.6 ± 6.0 (660)	31.0 ± 8.8 (360)	0.438
Race (White/Caucasian), *n* (%)	592 (85)	312 (85)	0.785
Smoking status, *n* (%)			0.783
Current/Recent (within 1 year)	195 (27)	103 (27)	
Past (>1 year ago)	297 (41)	165 (43)	
Never	224 (31)	112 (29)	
Hypertension, *n* (%)	697 (93)	350 (91)	0.259
Dyslipidemia, *n* (%)	478 (74)	255 (3)	0.757
Atrial fibrillation, *n* (%)	72 (16)	28 (11)	0.041
CKD on dialysis, *n* (%)	17 (2.3)	8 (2.1)	0.802
Chronic lung disease, *n* (%)	118 (16)	59 (16)	0.810
Sleep apnea, *n* (%)	19 (15)	14 (13)	0.623
Dyspnea, *n* (%)	478 (74)	255 (73)	0.757
Fatigue, *n* (%)	310 (52)	167 (52)	0.951
Diabetes mellitus, *n* (%)	345 (47)	156 (41)	0.033
Peripheral arterial disease, *n* (%)	144 (20)	73 (19)	0.846
Family history of premature coronary artery disease, *n* (%)	209 (36)	110 (35)	0.728
Prior myocardial infarction, *n* (%)	356 (50)	188 (50)	0.967
Prior heart failure, *n* (%)	231 (32)	99 (26)	0.052
Prior percutaneous coronary intervention, *n* (%)	561 (71)	291 (71)	0.809
Prior coronary artery bypass graft surgery, *n* (%)	416 (52)	222 (53)	0.682
LVEF, mean ± SD (*n*)	49 ± 13 (674)	50 ± 13 (343)	0.045
Creatinine, mean ± SD (*n*)	1.2 ± 0.8 (649)	1.2 ± 0.9 (344)	0.621
Anemia, *n* (%)	124 (26)	49 (18)	0.009
CCS class (III and IV), *n* (%)	447 (70)	208 (65)	0.091

Abbreviations: BMI, body mass index; CCS, Canadian Cardiovascular Society; CKD, chronic kidney disease; CTO, chronic total occlusion; LVEF, left ventricular ejection fraction; SD, standard deviation.

TABLE 2 Angiographic and procedural characteristics and outcomes of patients who had successful primary retrograde versus unsuccessful primary retrograde CTO PCI.

Characteristic/procedural outcomes	Successful primary retrograde (*n* = 878)	Unsuccessful primary retrograde (*n* = 451)	*p*-value
Use of MCS, *n* (%)	65 (9.0)	28 (7.7)	0.454
Dual injection, *n* (%)	621 (85)	338 (89)	0.072
J-CTO score, mean ± SD (*n*)	3.2 ± 1.0 (841)	3.3 ± 1.0 (422)	0.163
PROGRESS-CTO score, mean ± SD (*n*)	1.3 ± 0.9 (593)	1.6 ± 0.9 (318)	<0.001
PROGRESS-CTO complications score, mean ± SD (*n*)	4.1 ± 1.7 (530)	4.1 ± 1.7 (288)	0.735
CTO length in mm, mean ± SD (*n*)	46 ± 26 (783)	44 ± 27 (392)	0.132
Ad hoc procedure, *n* (%)	19 (2.9)	7 (2.0)	0.397
Interventional collateral, *n* (%)	558 (95)	230 (72)	<0.001
Total number of collaterals used, mean ± SD (*n*)	1.3 ± 0.6 (585)	1.7 ± 0.8 (302)	<0.001
J-channel septal score, mean ± SD (*n*)	1.8 ± 1.2 (156)	2.0 ± 1.3 (88)	0.161
Werner collateral connection			<0.001
CC 0	32 (6.2)	37 (13)	
CC 1	260 (50)	155 (55)	
CC 2	223 (43)	88 (31)	
Mod-sev. prox tortuosity, *n* (%)	358 (43)	177 (42)	0.716
Mod-sev. calcification, *n* (%)	484 (58)	269 (63)	0.065
Proximal cap ambiguity, *n* (%)	480 (65)	256 (69)	0.243
Side branch at proximal cap, *n* (%)	454 (63)	248 (67)	0.185
Stump, *n* (%)			0.212
Blunt	341 (46)	187 (48)	
Tapered	147 (20)	60 (15)	
No	261 (35)	143 (37)	
Distal opacification, *n* (%)			0.002
Good	240 (33)	99 (27)	
Faint	408 (57)	206 (56)	
Not visible	72 (10)	62 (17)	
Distal cap at bifurcation, *n* (%)	347 (48)	183 (51)	0.438
Good distal landing zone, *n* (%)	342 (48)	195 (53)	0.068
Collateral filling, *n* (%)			
Contralateral	479 (67)	214 (58)	0.007
Ipsilateral	91 (10)	56 (15)	0.239
Ipsilateral + Contralateral	136 (19)	88 (24)	0.052
Previously treated ISR, *n* (%)	89 (11)	54 (13)	0.241
Overall target vessel, *n* (%)			
Left anterior descending	97 (11)	57 (13)	0.381
Left circumflex	126 (15)	69 (16)	0.630
Left main	5 (0.6)	6 (1.4)	0.146
Right coronary artery	611 (72)	290 (67)	0.048
Use of collaterals, *n* (%)			
Septal	542 (62)	282 (63)	0.777
Contralateral Epicardial	188 (21)	101 (22)	0.681
Bypass-SVG	180 (21)	94 (21)	0.884

TABLE 2 (Continued)

Characteristic/procedural outcomes	Successful primary retrograde (*n* = 878)	Unsuccessful primary retrograde (*n* = 451)	*p*-value
Bypass-LIMA	8 (0.9)	8 (1.8)	0.172
Ipsilateral Epicardial	25 (2.9)	23 (5)	0.037
IVUS/OCT use, *n* (%)	438 (63)	133 (44)	<0.001
Contrast volume (ml), mean ± SD (*n*)	248 ± 128 (793)	294 ± 148 (410)	<0.001
Procedure time (min), mean ± SD (*n*)	181 ± 82 (667)	185 ± 96 (343)	0.490
Fluoroscopy Time (min), mean ± SD (*n*)	78 ± 35 (801)	77 ± 31 (404)	0.642
AK Fluoroscopy Dose (Gray), mean ± SD (*n*)	3.4 ± 2.6 (675)	3.9 ± 2.8 (335)	0.013
Second crossing strategy, (%)	N/A	AW (61) ADR (19) None (18)	N/A
Successful crossing strategy, (%)	Retrograde (100)	AW (27) ADR (23) None (50)	N/A

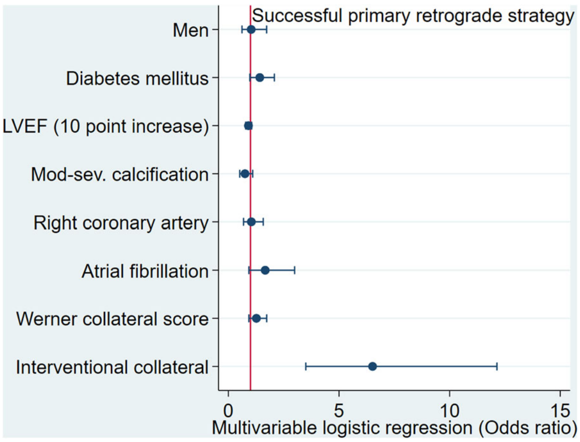
Abbreviations: ADR, antegrade dissection and re-entry; AK, Air Kerma; AW, antegrade wiring; CC, collateral connection; CTO, chronic total occlusion; ISR, in-stent restenosis; IVUS/OCT, intravascular ultrasound/optical coherence tomography; LIMA, left internal mammary artery; MCS, mechanical circulatory support; PCI, percutaneous coronary intervention; SVG, saphenous vein graft.

TABLE 3 In-hospital clinical outcomes of patients who had successful primary retrograde versus unsuccessful primary retrograde CTO PCI.

In-hospital events	Successful primary retrograde (*n* = 878)	Unsuccessful primary retrograde (*n* = 451)	*p*-value
Death, *n* (%)	11 (1.2)	4 (0.9)	0.550
MACE, *n* (%)	33 (3.8)	16 (3.5)	0.847
Acute MI, *n* (%)	14 (1.6)	9 (2.0)	0.596
Stroke, *n* (%)	2 (0.2)	2 (0.4)	0.497
Repeat PCI, *n* (%)	4 (0.5)	1 (0.2)	0.510
Emergency CABG, *n* (%)	1 (0.1)	0 (0.0)	0.473
Tamponade, *n* (%)	5 (0.6)	3 (0.7)	0.831
Perforation, *n* (%)	68 (7.7)	48 (11)	0.076
Pericardiocentesis, *n* (%)	6 (0.7)	2 (0.4)	0.592
Vascular access complications, *n* (%)	13 (1.5)	5 (1.1)	0.579
Dissection/Thrombus of donor artery, *n* (%)	11 (1.3)	9 (2.0)	0.292
Bleeding, *n* (%)	13 (1.5)	3 (0.7)	0.197
Aortocoronary dissection, *n* (%)	3 (0.3)	2 (0.4)	0.774

Abbreviations: CABG, coronary artery bypass graft surgery; CTO, chronic total occlusion; MACE, major adverse cardiovascular events; MI, myocardial infarction; PCI, percutaneous coronary intervention.

fibrillation, diabetes mellitus, heart failure, lower LVEF, anemia, Werner collateral classification, the presence of interventional collaterals, lack of moderate–severe calcification, and a CTO of the RCA were associated with technical success. On multivariable logistic regression analysis, the presence of interventional collaterals (odds ratio: 6.52, 95% confidence interval, 3.50–12.1, $p < 0.001$) was the only variable that was significantly associated with the success of a primary retrograde strategy (Central Illustration 1).



CENTRAL ILLUSTRATION 1 Multiple logistic regression analysis to predict variables associated with a successful primary retrograde strategy. [Color figure can be viewed at wileyonlinelibrary.com]

4 | DISCUSSION

The main findings of our study are as follows: (a) a primary retrograde strategy w used in 13% of the cases in our registry with an initial 66% technical success and 83% final technical success, (b) the baseline clinical and angiographic characteristics were comparable between patients who had successful versus unsuccessful primary retrograde attempts, and (c) the presence of interventional collaterals was independently associated with higher success when using a primary retrograde approach.

4.1 | Prevalence, comorbidities, and angiographic risk factors

A primary retrograde strategy was used in 13% of our patients, which is similar to other studies from the United States (13.3%),[6] and Europe (13%–17%),[1,7,8] but is lower when compared with publications from Asia–Japan (16%–30%).[9,10] The retrograde approach has been shown to improve success rates from ~70% to ~90%, and the success rate of the retrograde strategy itself has been increasing over the last two decades.[3,11–13] Given higher complexity and procedural risk, the retrograde approach is often reserved for cases in which AW fails or when the angiographic characteristics are not favorable for AW (e.g., proximal cap ambiguity, presence of a bifurcation at distal cap, and/or poor distal vessel visualization). This is consistent with the choices made by operators in our registry where patients who underwent primary retrograde CTO PCI had more comorbidities and more unfavorable angiographic characteristics with higher J-CTO (3.2 ± 1.0 vs. 2.2 ± 1.3, $p < 0.001$) and PROGRESS-CTO scores (1.4 ± 0.9 vs. 1.2 ± 1.0, $p < 0.001$), higher prevalence of moderate-severe calcification (90% vs. 83%, $p < 0.001$), presence of the distal cap at a bifurcation (91% vs. 82%, $p < 0.001$), and proximal cap ambiguity (66% vs. 31%, $p < 0.001$) compared with patients in whom other crossing strategies (AW-ADR) were first attempted. This is similar to previous studies where the prevalence of patient comorbidities and unfavorable angiographic characteristics were higher in cases treated with a primary retrograde approach.[9,14]

In our study, use of IVUS/OCT was more common in successful primary retrograde cases versus unsuccessful primary retrograde attempts (63% vs. 44%, $p < 0.001$). While IVUS can be useful in CTO crossing (for identification of proximal cap ambiguity, determination of guidewire position, determination of balloon size in reverse controlled antegrade and retrograde subintimal tracking [CART]), IVUS should be performed after guidewire crossing for stent optimization. OCT is usually not used until after successful lesion crossing due to need for contrast injections. We did not include IVUS/OCT in the multiple logistic regression analysis to predict successful retrograde crossing attempts because their use is dependent on successful CTO crossing.

A study that investigated the potential predictors of retrograde CTO PCI failure after successful collateral crossing found that lesion calcification was independently associated with unsuccessful retrograde CTO PCI.[15] In our study, the presence of interventional collaterals was the only parameter associated with success of the primary retrograde approach after adjusting for sex, atrial fibrillation, diabetes mellitus, LVEF, presence of interventional collaterals, Werner classification, and presence of an RCA CTO. There are several differences between the aforementioned study and ours that could explain the differences: (1) whereas in our study, we compared successful primary retrograde versus unsuccessful primary retrograde cases (irrespective of any other subsequent strategies), the aforementioned study included cases only if a collateral channel was successfully crossed (primary or not), (2) the definitions of technical success and procedural success in the aforementioned study were different from those developed by the CTO-ARC,[4] and (3) operator preference regarding the use of retrograde strategy likely differs geographically given the differences in the prevalence of primary retrograde strategy utilization, which could explain differences in comorbidities and angiographic characteristics.[15]

Our findings are comparable to a study that enrolled 211 patients who underwent primary retrograde CTO PCI. In that study, operators achieved an initial technical success of 54.5%, followed by an additional 21.8% through the use of adjunctive crossing strategies, resulting in a final technical success of 76.3%.[16] In that study, the most common reason (50%) for retrograde failure was inability to cross the collateral channels with a guidewire, highlighting the importance of having interventional collaterals. Moreover, an association was observed between lack of prior PCI and higher technical failure.[16]

In a study of 285 patients who underwent retrograde CTO PCI between 2004 and 2016 in China, the authors showed that procedural failure was associated with a higher number of diseased vessels and unfavorable collateral circulation.[17] In the Asia-Pacific Chronic Total Occlusion Club (APCTO Club) registry, wherein 497 patients (149 [30%] primary retrograde) underwent CTO PCI, advanced age and moderate/severe tortuosity were associated with technical failure on multivariable analysis.[18]

Given that (1) complication rates are higher with the retrograde approach compared with AW, (2) uncertainty on the success of AW until after it is tried, and (3) with the need for antegrade preparation even if retrograde crossing is eventually required, AW should be the initial crossing strategy in most cases, unless the lesion characteristics are unfavorable (such as flush aorto-ostial occlusions or proximal cap ambiguity).

In summary, while patients treated with a primary retrograde crossing strategy have a higher prevalence of comorbidities and more unfavorable angiographic characteristics, predictors of retrograde success/failure vary between studies, likely due to (1) the way the groups are defined for analysis (e.g., primary retrograde vs. overall retrograde attempts, after successful collateral crossing vs. including all steps of the procedure) and (2) varied utilization of primary retrograde crossing (13%–30%).

4.2 | Limitations

Our study has important limitations. First, the PROGRESS-CTO registry is observational, and while consecutive case entry is recommended, cases entered into the registry might be subject to selection bias. Second, clinical events were not adjudicated by an independent clinical events adjudication committee. Third, PROGRESS-CTO operators are highly experienced in CTO PCI, which could limit external validity.

5 | CONCLUSIONS

In our data set, a primary retrograde strategy was used in 13% of CTO interventions with an initial technical success of 50% and a final technical success of 83%. The presence of interventional collaterals is associated with higher technical success of a primary retrograde strategy, even after adjusting for comorbidities and angiographic characteristics.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

Research data are not shared.

ORCID

Bahadir Simsek http://orcid.org/0000-0001-6198-8006
Spyridon Kostantinis http://orcid.org/0000-0003-1099-681X
Khaldoon Alaswad http://orcid.org/0000-0003-1368-5320
Farouc A. Jaffer http://orcid.org/0000-0001-7980-384X
Jaikirshan Khatri http://orcid.org/0000-0002-0315-3219
Jimmy Kerrigan http://orcid.org/0000-0001-6769-5087
Salman Allana http://orcid.org/0000-0003-1069-2437
Emmanouil S. Brilakis http://orcid.org/0000-0001-9416-9701

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AUTHOR BIOGRAPHIES

Dr. Alaswad: Consultant and speaker for Boston Scientific, Abbott Cardiovascular, Teleflex, and CSI.

Dr. Karmpaliotis: Honoraria: Boston Scientific, Abbot Vascular; Equity: Saranas, Soundbite, Traverse Vascular.

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