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Use of the Limited Antegrade Subintimal Tracking Technique in Chronic Total Occlusion Percutaneous Coronary Intervention



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ABSTRACT

BACKGROUND There are limited data on the limited antegrade subintimal tracking (LAST) technique for chronic total occlusion (CTO) percutaneous coronary intervention (PCI).

OBJECTIVES The aim of this study was to analyze the frequency of use and outcomes of the LAST technique for CTO PCI.

METHODS We analyzed 2,177 CTO PCIs performed using antegrade dissection and re-entry (ADR) in the PROGRESS-CTO (Prospective Global Registry for the Study of Chronic Total Occlusion Intervention) registry between 2012 and January 2022 at 39 centers. ADR was attempted in 1,465 cases (67.3%).

RESULTS Among antegrade re-entry cases, LAST was used in 163 (11.1%) (primary LAST in 127 [8.7%] and secondary LAST [LAST after other ADR approaches failed] in 36 [2.5%]), the Stingray system (Boston Scientific) in 980 (66.9%), subintimal tracking and re-entry in 387 (26.4%), and contrast-guided subintimal tracking and re-entry in 29 (2.0%). The mean patient age was 65.2 ± 10 years, and 85.8% were men. There was no significant difference in technical (71.8% vs 77.8%; P = 0.080) and procedural (69.9% vs 75.3%; P = 0.127) success and major cardiac adverse events (1.84% vs 3.53%; P = 0.254) between LAST and non-LAST cases. However, on multivariable analysis, the use of LAST was associated with lower procedural success (OR: 0.61; 95% Cl: 0.41-0.91). Primary LAST was associated with higher technical (76.4% vs 55.6%; P = 0.014) and procedural (75.6% vs 50.0%; P = 0.003) success and similar major adverse cardiac event (1.57% vs 2.78%; P = 0.636) rates compared with secondary LAST.

CONCLUSIONS LAST was used in 11.1% of antegrade re-entry CTO PCI cases and was associated with lower procedural success on multivariable analysis, suggesting a limited role of LAST in contemporary CTO PCI.

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ntegrade dissection and re-entry (ADR) is often used in chronic total occlusion (CTO) percutaneous coronary intervention (PCI)1-4 and can be achieved using guidewires (wire-based reentry) or a dedicated device, such as the CrossBoss catheter (Boston Scientific) and the Stingray re-entry balloon (Boston Scientific).^{4,5} Wire based re-entry can be achieved using polymer-jacketed guidewires (subintimal tracking and re-entry [STAR]6 and mini-STAR⁷) or high tip stiffness, non-polymer-jacketed wires (limited antegrade subintimal tracking [LAST]). The following CTO lesion characteristics favor the use of dissection/re-entry: a well-defined proximal cap, a large-caliber distal vessel, no large branches within the CTO or at the proximal or distal cap, lack of good interventional collateral channels, and a longer occlusion length.8 The LAST technique was developed to limit the length of dissection by re-entering immediately distal to the distal cap (Central Illustration C). There are limited published data on the outcomes of the LAST technique, which was the focus of the present study.

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METHODS

We analyzed the baseline clinical and angiographic characteristics and procedural outcomes of 2,177 CTO PCIs performed using antegrade dissection re-entry in the PROGRESS-CTO (Prospective Global Registry for the Study of Chronic Total Occlusion Intervention) registry between 2012 and January 2022 at 39 centers. Data collection was performed in a dedicated online database (Prospective Global Registry for the Study of Chronic Total Occlusion Intervention [PROGRESS-CTO]; NCT02061436). Study data were collected and managed using REDCap (Vanderbilt University) electronic data capture tools hosted at the Minneapolis Heart Institute Foundation. 9,10 The study was approved by the Institutional Review Board of each site.

Coronary CTOs were defined as coronary lesions with Thrombolysis In Myocardial Infarction (TIMI) flow grade 0 of at least a 3-month duration. Estimation of the duration of occlusion was clinical based on the first onset of angina, prior history of myocardial infarction (MI) in the target vessel territory, or comparison with a prior angiogram. Calcification was assessed by angiography as mild (spots), moderate (involving \leq 50% of the reference lesion diameter), or severe (involving >50% of the reference lesion diameter). Moderate proximal vessel tortuosity was defined as the presence of at least 2 bends >70° or 1 bend >90° and severe tortuosity as 2 bends >90° or

1 bend >120° in the CTO vessel. A retrograde procedure was an attempt to cross the lesion through a collateral vessel or bypass graft supplying the target vessel distal to the lesion; otherwise, the intervention was classified as an antegrade-only procedure. ADR was defined as antegrade PCI during which a guidewire was intentionally introduced into the extraplaque space proximal to the lesion, or re-entry into the distal true lumen was attempted after intentional or inadvertent extraplaque guidewire crossing. Technical success was defined as successful CTO revascularization with achievement of <30% residual diameter stenosis within the treated segment and restoration of TIMI grade 3 antegrade flow.4 Procedural success was defined as the achievement of technical success without any in-hospital major adverse cardiac event (MACE), which was defined as

any of the following events before hospital discharge: death, MI, recurrent symptoms requiring urgent repeat target vessel revascularization with PCI or coronary artery bypass graft (CABG) surgery, tamponade requiring either pericardiocentesis or surgery, or stroke. MI was defined using the Third Universal Definition of Myocardial Infarction (type 4a MI). The Japanese chronic total occlusion (J-CTO) score was calculated as described by Morino et al and the PROGRESS-CTO score as described by Christopoulos et al. Primary LAST was defined as cases in which the LAST technique was applied first, whereas secondary LAST was defined as cases in which other ADR techniques were applied before LAST.

Categoric variables were expressed as percentages and compared using the Pearson's chi-square test. Continuous variables were presented as mean \pm SD or median (IQR) unless otherwise specified and were compared using the Student's t-test for normally distributed variables and the Kruskal-Wallis test for nonparametric variables as appropriate. The association of LAST with procedural success was examined using univariable logistic regression; variables exhibiting significant univariable association (P < 0.10) were entered in a multivariable model. All statistical analyses were performed using JMP version 13.0 (SAS Institute). Two-sided P values <0.05 were considered statistically significant.

RESULTS

During the study period, 10,344 patients were enrolled in the registry, and ADR was used in 2,177 cases (21%); antegrade dissection only was used in 712

ABBREVIATIONS AND ACRONYMS

Karacsonyi et al

ADR = antegrade dissection and re-entry

AFR = antegrade fenestration and re-entry

CABG = coronary artery bypass graft

CTO = chronic total occlusion

J-CTO = Japanese chronic total

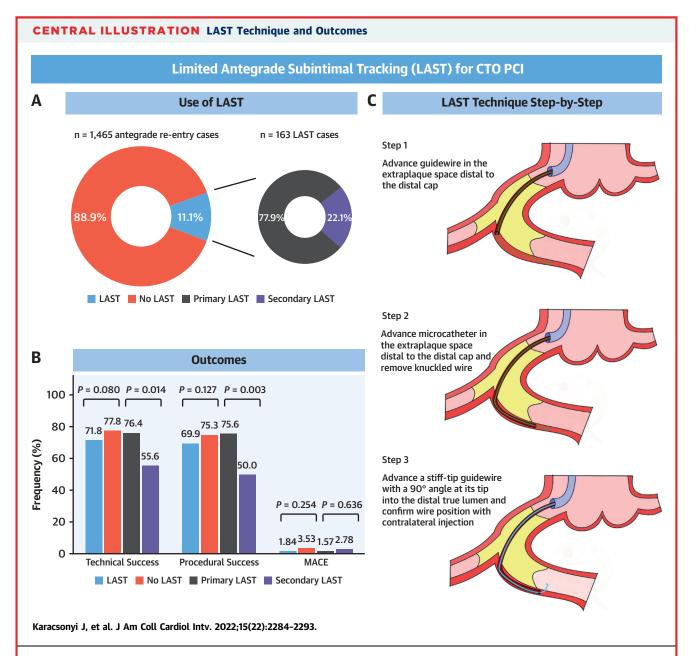
LAST = limited antegrade subintimal tracking

MACE = major adverse cardiac event(s)

MI = myocardial infarction

PCI = percutaneous coronary intervention

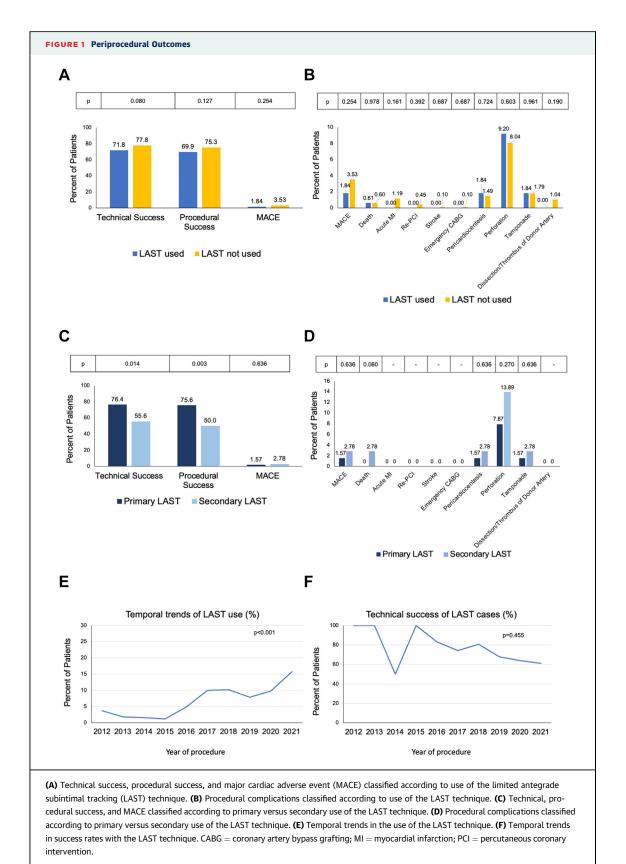
STAR = subintimal tracking and re-entry



(A) Frequency of use of the limited antegrade subintimal tracking (LAST) technique. (B) Technical, procedural success, and major cardiac adverse event (MACE) classified according to use or not of the LAST technique and according to primary versus secondary LAST technique. (C) The LAST technique step by step. Step 1: extraplaque guidewire advancement distal to the distal cap. Step 2: a microcatheter is advanced in the extraplaque space distal to the distal cap, and the knuckled guidewire is removed. Step 3: a stiff tip guidewire with a 90° angle at its tip is advanced into the distal true lumen, which is usually confirmed with contralateral contrast injection. CTO PCI = chronic total occlusion percutaneous coronary intervention.

cases, and antegrade re-entry (with or without antegrade dissection) was used in 1,465 cases (Central Illustration A). The reason for not attempting reentry in 712 cases was failure to reach the vicinity of the distal true lumen in 71% and direct true lumen crossing in 29%. Among antegrade re-entry cases, LAST was used in 163 (11.1%: primary LAST in 127)

[8.7%] and secondary LAST [LAST after other ADR approaches failed] in 36 [2.5%]), the Stingray system in 980 (66.9%), STAR in 387 (26.4%), and contrast-guided STAR in 29 (2.0%). The use of LAST increased over time (Figures 1E and 1F). The distribution of LAST cases by study center is shown in Supplemental Table 1.



of MACE (1.84% vs 3.53%; P = 0.254) between LAST and non-LAST cases (Figure 1, Table 3); however, on multivariable analysis, LAST was associated with lower procedural success rates (Figure 2). Among primary LAST cases (n = 127), LAST was the successful re-entry strategy in 87 (68.5%) cases. A secondary LAST technique was used in 36 cases: after Stingray failure in 18 cases, after contrast-guided STAR in 3 cases, and after STAR in 15 cases. Among secondary LAST cases, LAST was the successful re-entry strategy in 7 cases (19.4%). Primary LAST cases were less complex with lower J-CTO scores compared with secondary LAST cases (2.47 \pm 1.40 vs. 3.31 \pm 0.96; P <

0.001). A primary LAST technique was associated with higher technical (76.4% vs 55.6%; P = 0.014) and procedural (75.6% vs 50.0%; P = 0.003) success rates, similar MACE rates (1.57% vs 2.78%, P = 0.636), and similar complication rates compared with secondary LAST (Figure 1, Central Illustration B).

LAST cases required shorter procedure (124 [IQR: 84-170] minutes vs 158 [IQR: 112-213] minutes; P < 0.001) and fluoroscopy (52 [IQR: 34-75] vs 62 [IQR: 41-88] minutes; P = 0.001) times (Figure 3). The use of LAST increased over time without significant change in success rates (Figures 1E and 1F).

Follow-up was available in 629 cases (28.9%), with a median follow-up time of 70 days (IQR: 20-362 days). Follow-up acute coronary syndrome rates (7.1% vs 4.3%; P = 0.381) and target lesion revascularization rates (4.76% vs 5.28%; P = 0.884) were similar in LAST and non-LAST cases (Supplemental Figure 1).

TABLE 1 Baseline Clinical Characteristics of Study Patients Classified According to Use of the Crossing Technique

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	LAST Used	LAST Not Used				
	(n = 163)	(n = 2,014)	P Value			
Age, y	63.8 ± 9	65.3 ± 10	0.037			
Men	138 (85.2)	1603 (85.8)	0.826			
BMI, kg/m ²	30.1 ± 6	30.5 ± 6	0.414			
Diabetes mellitus	66 (41.0)	763 (42.1)	0.784			
Hypertension	148 (91.9)	1654 (90.7)	0.614			
Dyslipidemia	128 (79.5)	1708 (93.3)	< 0.001			
Smoking (current)	47 (28.8)	467 (23.2)	0.103			
LVEF, %	50 ± 11	50 ± 13	0.863			
Family history of CAD	39 (25.8)	496 (35.5)	0.017			
Congestive heart failure	42 (26.4)	508 (28.5)	0.569			
Prior myocardial infarction	90 (57.3)	783 (45.1)	0.003			
Prior CABG	35 (21.9)	683 (36.0)	< 0.001			
Prior CVD	14 (8.8)	176 (9.8)	0.658			
Prior PVD	22 (13.8)	282 (15.8)	0.525			
Clinical presentation						
Stable angina	109 (68.6)	1194 (69.5)	0.010			
Unstable angina	12 (7.6)	273 (15.9)				
NSTEMI	15 (9.4)	106 (6.2)				
STEMI	3 (1.9)	16 (0.9)				
Nonischemic symptoms	5 (3.1)	35 (2.0)				
No symptoms	15 (9.4)	95 (5.5)				
Baseline creatinine (mg/dL)	1.0 (0.9-1.1)	1.0 (0.9-1.2)	0.112			

Values are mean \pm SD, n (%), or median (IQR).

BMI = body mass index; CABG = coronary artery bypass graft surgery; $\mathsf{CAD} = \mathsf{coronary} \ \mathsf{artery} \ \mathsf{disease}; \ \mathsf{CVD} = \mathsf{cerebrovascular} \ \mathsf{disease}; \ \mathsf{LAST} = \mathsf{limited}$ antegrade subintimal tracking; LVEF = left ventricular ejection fraction; PVD = peripheral vascular disease.

The baseline clinical and angiographic characteristics of the study patients classified according to use of the LAST technique are shown in Tables 1 and 2. The mean patient age was 65.2 \pm 10 years, and 85.8% were men; 42% had a history of diabetes mellitus, and 35% had prior CABG surgery. LAST patients were younger (mean age: 63.8 \pm 9 years vs 65.3 \pm 10 years; P = 0.037). Prior MI was more common in LAST patients (57% vs 45%; P = 0.003), whereas prior CABG was less common (22% vs 36%; P < 0.001).

CTOs approached with LAST had a lower J-CTO score (2.65 \pm 1.36 vs 2.93 \pm 1.11; P = 0.014), were less likely to have moderate/severe calcification (42% vs 53%; P = 0.009) and tortuosity (26% vs 35%; P = 0.015), and underwent implantation of a similar number of stents (2.8 \pm 1.1 vs 2.8 \pm 1.1; P = 0.488) compared with non-LAST cases The distribution of guidewires that were used with the LAST technique is shown in Supplemental Table 2.

There was no significant difference in technical success (71.8% vs 77.8%; P = 0.080) or procedural success (69.9% vs 75.3%; P = 0.127) and the incidence

DISCUSSION

The main findings of our study are that LAST was used in 11.1% of antegrade re-entry CTO PCI cases and in less complex lesions and was associated with lower procedural success on multivariable analysis compared with non-LAST cases.

ADR is an important CTO PCI technique. The first form of ADR (STAR) was developed by Dr Antonio Colombo and involved advancing a knuckled guidewire until it spontaneously re-entered into the distal true lumen, usually at a bifurcation.⁶ The classic STAR technique is rarely used as a primary crossing strategy currently because it often results in side branch loss and requires long stent length with high restenosis and reocclusion rates.14 STAR without stenting is currently used as a bailout strategy (investment procedure). 15 An evolution of STAR was contrast-guided STAR in which a large contrast volume (3-4 mL) is injected in the subintimal/extraplaque space to allow hydraulic recanalization of the

vessel, but crossing was unpredictable with poor long-term outcomes. This technique later evolved into what is currently known as the "Carlino technique" in which a minimal volume of contrast (<0.5 mL) is gently injected inside the occlusion, with the goal of modifying plaque compliance to facilitate guidewire and microcatheter advancement through fibrocalcific plaque.¹⁶ Another variation of the STAR technique was the "mini-STAR" in which a soft, polymer-jacketed wire is used to achieve a more proximal wire re-entry after the occlusion. Compared with the initial STAR technique, newer guidewires such as Fielder XT (Asahi Intecc) were used in mini-STAR; however, the acute and long-term results were similar with the original STAR, with high rates of restenosis/reocclusion. 7,17 The Stingray system revolutionized ADR by increasing the success and reliability of re-entry. The Stingray LP balloon has a flat shape with 2 side exit ports. Upon low-pressure (4 atm) inflation, it orients 1 exit port automatically toward the true lumen, facilitating targeted re-entry.18 A more recent antegrade re-entry technique is antegrade fenestration and re-entry (AFR). In AFR, after achieving extraplaque wire position at the distal cap, a second guidewire is placed close to the first guidewire. A balloon is advanced to the distal cap, after verifying that the position of both guidewires is roughly in the same part of the extraplaque space. The balloon is inflated to fenestrate the intima, creating a route for the first guidewire to enter in the true lumen. 19,20 In contrast to STAR where re-entry is unpredictable, AFR allows more predictable re-entry in the area of balloon inflation.

LAST is a wire-based ADR technique that was developed to minimize vessel disruption and stent length by re-entering immediately distal to the distal cap using a stiff tip guidewire, such as the Confianza Pro 12 (Asahi Intecc), MiracleBros 3-12 (Asahi Intecc), Gaia and Gaia Next (Asahi Intecc), Hornet 14 (Boston Scientific), or Warrior (Teleflex), with a 90° angle at its tip. If successful, LAST can minimize the extent of dissection and stent length but may also cause extraplaque hematoma that could hinder re-entry. ^{3,21}

In our study, the LAST technique was used in 11.1% of antegrade re-entry attempts. In a study of 4 high-volume institutions, Azzalini et al 3 reported the use of LAST in 30.5% (n = 68) of ADR cases, whereas the CrossBoss/Stingray system was used in 52.0% (n = 116) and STAR in 17.5% (n = 39). In another study by the same group comparing old (STAR, mini-STAR, contrast-guided STAR, LAST, and controlled antegrade and retrograde tracking) versus modern (Stingray, CrossBoss, and reverse controlled

TABLE 2 Baseline Angiographic and Technical Characteristics of Study Patients
Classified According to Use of the LAST Crossing Technique

	LAST Used $(n = 163)$	LAST Not Used $(n=2,014)$	P Value
CTO target vessel			
RCA	109 (66.9)	1,181 (60.7)	0.180
LAD	29 (17.8)	420 (21.6)	
LCX	25 (15.3)	319 (16.4)	
LM	0 (0)	6 (0.3)	
Other	0 (0)	20 (1.0)	
Successful crossing strategy			
Antegrade wiring	5 (3.1)	149 (7.4)	< 0.001
Retrograde	9 (5.5)	329 (16.4)	
ADR	106 (65.0)	1,165 (58.0)	
None	43 (26.4)	365 (18.2)	
First crossing strategy			
Antegrade wiring	134 (82.2)	1,413 (70.3)	0.015
Retrograde	10 (6.1)	203 (10.1)	
ADR	19 (11.7)	393 (19.6)	
Retrograde crossing strategy	53 (32.5)	940 (46.7)	< 0.001
J-CTO score	2.65 ± 1.36	2.93 ± 1.11	0.014
PROGRESS-CTO score	1.28 ± 1.00	1.28 ± 1.07	0.950
Calcification (moderate/severe)	69 (42.3)	1068 (53.0)	0.009
Proximal vessel tortuosity (moderate/severe)	42 (25.8)	708 (35.2)	0.015
Proximal cap ambiguity	73 (45.9)	743 (44.2)	0.673
In-stent restenosis	24 (14.9)	256 (13.4)	0.631
Side branch at the proximal cap	98 (61.6)	953 (57.4)	0.299
Blunt/no stump, %	101 (62.0)	1,411 (70.1)	0.031
Vessel diameter, mm	2.8 (2.5-3.0)	3.0 (2.5-3.0)	0.013
Occlusion length, mm	30 (17-50)	30 (20-50)	0.032
Number of stents used	2.8 ± 1.1	2.8 ± 1.1	0.488

Values are n (%), mean \pm SD, or median (IQR).

CTO = chronic total occlusion; J-CTO = Japan chronic total occlusion score; LAD = left anterior descending artery; LAST = limited antegrade subintimal tracking; LCX = left circumflex coronary artery; LM = left main coronary artery; PROGRESS-CTO score: Prospective Global Registry for the Study of Chronic Total Occlusion Intervention score; SVG = saphenous vein graft.

antegrade and retrograde tracking) dissection/reentry techniques versus true-to-true lumen crossing, LAST was used in 62 cases (6.7% of the successful CTO cases).22 The lower utilization of LAST in our study may be related to more contemporary data and more extensive use of the Stingray system. Azzalini et al³ also reported that STAR had lower technical and procedural success rates (technical success: 59%, procedural success: 59%) compared with CrossBoss/ Stingray (technical success: 89%, procedural success: 87%) and LAST (technical success: 96%, procedural success: 96%; P < 0.001). The complication rates were similar in all 3 groups (STAR: 2.6% vs CrossBoss/ Stingray: 5.1% vs LAST: 1.5%; P = 0.53). The Stingray system and LAST both aim to limit the extent of dissection, but the Stingray system is often preferred because it is more reproducible and does not require highly refined wiring skills. In our study, LAST had

TABLE 3 Procedural Characteristics and Outcomes of Study Patients Classified According to Use of the LAST Crossing Technique

	LAST Used	LAST Not Used	
	(n = 163)	(n = 2,014)	P Value
Technical success	117 (71.8)	1,566 (77.8)	0.080
Procedural success	114 (69.9)	1,517 (75.3)	0.127
Procedural time, min	124 (84-170)	158 (112-213)	< 0.001
Fluoroscopy time, min	52 (34-75)	62 (41-88)	0.001
Air kerma radiation dose, Gy	2.63 (1.80-3.99)	2.85 (1.70-4.57)	0.390
Contrast volume	280 (200-380)	265 (195-360)	0.367
MACE	3 (1.84)	71 (3.53)	0.254
Death	1 (0.61)	12 (0.60)	0.978
Acute MI	0 (0)	24 (1.19)	0.161
Re-PCI	0 (0)	9 (0.45)	0.392
Stroke	0 (0)	2 (0.10)	0.687
Emergency CABG	0 (0)	2 (0.10)	0.687
Pericardiocentesis	3 (1.84)	30 (1.49)	0.724
Perforation	15 (9.20)	162 (8.04)	0.603
Tamponade	3 (1.84)	36 (1.79)	0.961
Dissection/thrombus of donor artery	0 (0)	21 (1.04)	0.190

Values are n (%) or median (IQR)

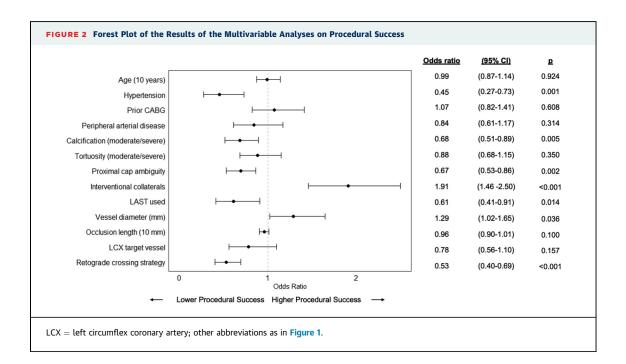
MACE = major cardiac adverse event(s): MI = myocardial infarction: PCI = percutaneous coronary intervention: other abbreviations as in Table 1.

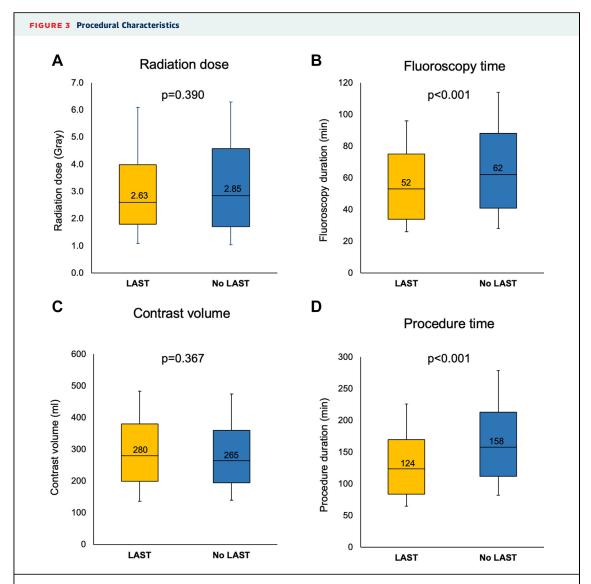
> similar technical and procedural success and major complication rates as other antegrade re-entry strategies; however, patients in the LAST group were younger with a lower prevalence of CABG and less complex angiographic characteristics, such as

moderate/severe calcification and a lower J-CTO score. On multivariable analysis, LAST was associated with lower procedural success, which is similar to the findings of Azzalini et al.3 Primary LAST was associated with higher technical and procedural success rates, similar MACE rates, and similar complication rates compared with secondary LAST. The higher technical and procedural success rates observed with primary LAST were likely related to the treatment of less complex lesions (lower J-CTO score) as well as less vessel trauma and less extraplaque hematoma caused by prior failed crossing attempts.

Azzalini et al³ reported a higher adjusted risk of MACE during follow-up with STAR and LAST, which is possibly caused by more aggressive manipulation of the extraplaque space and more distal re-entry, compared with the CrossBoss/Stingray system. Our study had limited follow-up and hence cannot provide reliable assessment of the impact of LAST on long-term outcomes.

What should the role of LAST be in contemporary CTO PCI? According to a global consensus document on CTO PCI, "subintimal (extraplaque) guidewire advancement distal to the distal cap should be avoided because it can lead to hematoma formation, causing luminal compression and reducing the likelihood of success."23 Similar to STAR and mini-STAR, our study suggests that LAST should not be the first choice for antegrade re-entry given the lower success rates and the risk of extraplaque hematoma formation. Device-based re-entry using the Stingray balloon





The boxplots represent the **(A)** median radiation dose, **(B)** median fluoroscopy time, **(C)** median contrast volume, and **(D)** median procedure time classified according to the use of the limited antegrade subintimal tracking (LAST) technique, showing **(from top to bottom)** maximum, Q3, median, Q1, and minimum.

remains the preferred antegrade re-entry strategy with the ReCross catheter (Biotronik) (dual lumen microcatheter with 2 over-the-wire lumens) emerging as another favorable option. AFR could be applied as a bailout strategy in case of significant vessel disruption after the wire-based ADR techniques. Another solution is intravascular ultrasound-guided antegrade re-entry, but this approach requires significant expertise and may be hindered by limited wire maneuverability in the presence of the extraplaque imaging catheter. Use of the retrograde approach, if feasible, is another highly effective way for achieving CTO crossing when ADR fails and may

be the only feasible option in case of extensive extraplaque hematoma formation.

STUDY LIMITATIONS. The limitations of our study include the observational design, the lack of clinical event adjudication, the limited use of IVUS to verify extraplaque wire position in LAST cases, no core laboratory adjudication, and the performance of all procedures at high-volume, experienced PCI centers, limiting the generalizability of our findings to centers with limited CTO PCI expertise. Finally, follow-up was only available in 29% of the cases and was limited to a median follow-up time of 70 days (IQR: 20-362 days).

CONCLUSIONS

In summary, LAST was used in 11.1% of antegrade re-entry CTO PCI cases and was associated with lower procedural success on multivariable analysis, suggesting that it should not be a first-choice strategy for antegrade re-entry.

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PERSPECTIVES

WHAT IS KNOWN? There are limited data on the LAST technique for CTO PCI.

WHAT IS NEW? In a contemporary, multicenter CTO PCI registry, LAST was used in 11.1% of antegrade reentry CTO PCI cases. On multivariable analysis, LAST was associated with lower procedural success compared with ADR cases that did not use LAST.

WHAT IS NEXT? Further studies are needed to examine optimal application and outcomes of LAST in CTO PCI.

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KEY WORDS chronic total occlusion, limited antegrade subintimal tracking, percutaneous coronary intervention

APPENDIX For supplemental tables and a figure, please see the online version of this