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ORIGINAL CONTRIBUTION

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# Randomized Comparison of a Gladius First vs Standard Antegrade Wiring Strategy for Crossing Coronary Chronic Total Occlusions: The Gladius First Trial

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## Abstract

**Objectives.** Antegrade wiring (AW) is the most common coronary chronic total occlusion (CTO) crossing strategy and usually relies on stepwise guidewire escalation starting from the low tip-load polymer-jacketed wire (standard guidewire escalation). The authors aimed to investigate whether the upfront use of intermediate tip-load polymer-jacketed guidewire translates into improved procedural outcomes of CTO percutaneous coronary intervention (PCI).

**Methods.** The Gladius First trial was a single-center, investigator-initiated, randomized, prospective trial. The primary endpoint was the time of AW strategy, while the secondary endpoints included CTO crossing success, procedural success, contrast volume, radiation dose, total procedural time, safety parameters, equipment use, and cost.

**Results.** Between 2021 and 2023, 69 patients with 70 CTO lesions (J-CTO score ≥ 1) were randomized to either upfront Gladius EX (Asahi Intecc) AW (n = 33) or standard guidewire escalation AW (n = 37). The clinical and angiographic characteristics of 2 groups were similar. Overall, CTO crossing and procedural success were 92.9% and 90%, respectively, and similar between groups. Although the AW time was significantly shorter in the Gladius AW group (10 minutes; IQR: 4-16 minutes) than in the standard AW group (21 minutes; IQR: 11-28 minutes, *P* = .001), the total procedural time, procedural success, safety parameters, resource use, and equipment cost were similar between groups.

**Conclusions.** Compared with standard guidewire escalation, the upfront use of the Gladius guidewire was associated with a shorter AW time but similar total procedural time, procedural success, safety, and cost.

## Introduction

Coronary chronic total occlusions (CTO) are increasingly encountered during invasive and non-invasive coronary angiography, and remain the most challenging lesions for percutaneous revascularization in patients with coronary artery disease.[1-3] Percutaneous coronary intervention (PCI) improves quality of life and may have positive effects on prognosis in patients with CTO.[4,5] While the application of a systematic algorithm comprising swift changes of CTO-PCI strategies and techniques (the so-called “hybrid approach”) is currently widely employed to cross the occlusion in a time-efficient and safe manner,[6] antegrade wiring (AW) is still the most common primary CTO recanalization strategy.[7,8] Specifically, it usually relies upon stepwise guidewire escalation starting from the low tip-load polymer-jacketed guidewire (the so-called standard guidewire escalation strategy) with subsequent exchange to stiffer wires if necessary.[9]

Recently, a new intermediate tip-load polymer-jacketed guidewire – the Gladius EX (Asahi Intecc) – was introduced for enhanced guidewire trackability in CTO lesions. In addition, there is emerging data that the exclusive use of polymer-jacketed guidewires is associated with higher technical success and lower perforation risk as compared with cases where at least 1 non-polymer-jacketed guidewire was used.[10] It is unknown whether the initial and systematic use of the intermediate tip-load polymer-jacketed guidewire within the AW strategy could translate into improved procedural outcomes as compared with the standard AW escalation strategy. We therefore performed a 2-arm randomized controlled trial to compare the time, efficacy, and safety outcomes between an AW strategy using a first-choice intermediate tip-load polymer-jacketed guidewire vs an AW strategy using the standard guidewire escalation strategy.

## Methods

### Study design and population

The Gladius First trial was a single-center, investigator-initiated, unblinded, randomized, prospective trial (www.clinicaltrials.gov identifier, NCT04691778). The trial was funded solely by the National Institute of Cardiology in Warsaw, Poland. Between January 2021 and December 2023, consecutive patients referred to CTO PCI based on clinical grounds were screened for inclusion. Eligible patients were those who were able to give informed consent and were scheduled for CTO PCI of a major coronary artery with an at least intermediate (≥ 1) Multicenter CTO Registry in Japan (J-CTO) score[11] and a planned AW strategy. Patients were excluded if they had a CTO with a J-CTO score of 0, in-stent CTO, severe chronic kidney disease (defined as an estimated glomerular filtration rate ≤ 30 mL/min/$m^2$), or if the operator planned to use a primary retrograde approach or antegrade dissection and reentry strategy for CTO crossing. The study was approved by the institutional ethics committee and complied with the Declaration of Helsinki, and all patients provided written informed consent. The study ended once all participants were recruited.

### Randomization and PCI procedure

Patients were randomly assigned in a 1:1 ratio to AW using the standard guidewire escalation or AW starting with the Gladius EX guidewire. Data collection and randomization was performed by study investigators (M.P.O and A.Z.) via an online electronic case report forms website (Castor EDC) using a validated variable block size randomization method and was stratified by the J-CTO score (cutoff value ≥ 2 points) and by age (> 65 years). To exclude randomization failure, randomization was performed in the catheterization laboratory directly after dual catheter injection in patients with a definitive decision on CTO PCI.

All interventional procedures were performed on an Artis Zee monoplane cardiovascular x-ray system (Siemens) by 2 experienced hybrid CTO-PCI operators (M.P.O. and A.D.) using all crossing strategies (AW, antegrade dissection and re-entry, retrograde wiring, and retrograde dissection and re-entry). In the standard AW group, the operator attempted CTO crossing using a low-penetration-force polymer-jacketed guidewire (Fielder XT-A or Fielder XT-R; Asahi Intecc); in the Gladius group, AW was initiated using the Gladius EX guidewire. All subsequent choices of guidewires in the AW-strategy group, as well as the selection of microcatheters and subsequent CTO crossing strategies, were left to the operators' discretion, as was the decision to stop the intervention in case of failure.

### Definitions and study endpoints

Coronary CTO was defined as a luminal occlusion on invasive coronary angiography with a Thrombolysis In Myocardial Infarction (TIMI) flow grade of 0 for an estimated duration of at least 3 months. Each CTO lesion was graded using the J-CTO score and the Prospective Global Registry for the Study of Chronic Total Occlusion Intervention (PROGRESS-CTO) score as previously described.[11,12] In addition, preprocedural angiograms were analyzed offline using a 2-dimensional quantitative coronary angiography software tool (CAAS II; Pie Medical) by an experienced reader (W.S.) who was blinded to all other test results.

CTO crossing success was defined as angiographic confirmation of guidewire placement in the true lumen beyond the occluded segment according to the coronary CTO Academic Research Consortium.[13] Technical success was defined as achievement of a TIMI grade 3 antegrade flow with less than 30% residual stenosis of the target CTO lesion, while procedural success was defined as achievement of technical success with the absence of an in-hospital major adverse cardiovascular event (MACE) (death, myocardial infarction [MI], or clinically driven target vessel revascularization).[13] MI was defined using the fourth universal definition of MI.[14] Total procedural time was defined as the time interval between obtaining arterial access and removal of the arterial sheaths.

The primary endpoint was duration of AW strategy, defined as the time from advancement of the first wire into the proximal cap to either the time of successful AW through the lesion or the time of cessation of AW and changing CTO PCI strategy according to the hybrid algorithm. This was decided based upon the common utility of AW strategy among all CTO operators,

and inverse correlation of the guidewire manipulation time with the CTO crossing success rate in the prior large J-CTO registry.[15] The secondary endpoints included CTO crossing success using the AW strategy, contrast volume and radiation dose related to the AW strategy, CTO crossing success using any strategy, technical success, procedural success, total procedural time, total contrast volume, total radiation dose, incidence of periprocedural complications, equipment use, and equipment cost.

### Statistical analysis

Data are presented as mean ± SD or median with IQR for continuous variables and frequency (percentage) for categorical variables. The distribution of the data was assessed using the Shapiro-Wilk normality test. Continuous variables were compared using the Student's t-test or non-parametric Mann-Whitney U-test. Categorical variables were analyzed with the Fisher's exact test. Due to the lack of prior data on time of AW strategy, the sample size was hypothetically estimated to be 35 patients per group. A *P*-value of less than 0.05 was considered statistically significant. Analyses were performed using SPSS software, version 20.0 software (IBM Corp.).

## Results

### Study population

From a total of 225 patients undergoing CTO PCI between January 2021 and December 2023, we excluded patients with a J-CTO score of 0 (n = 40), patients with in-stent CTO (n = 35), patients with severe chronic kidney disease (n = 11), and patients with a planned primary retrograde strategy or primary antegrade dissection and re-entry strategy for CTO crossing (n = 18). Of the remaining potentially eligible 121 patients, we excluded patients who declined informed consent (n = 37) and patients with screening failure (n = 15), resulting in a final study sample of 69 individuals with 70 CTO lesions who were randomized to AW using a first-choice Gladius wire (n = 33) or standard AW strategy (n = 37). The patient flowchart is shown in the **Figure**. The median age was 66.5 years (range, 39-83 years), 89% of patients were men, 26% had diabetes mellitus, and 13% had prior coronary artery bypass graft surgery. Approximately half of the target CTO lesions (53%) were located in the right coronary artery. The median occlusion length was 15.05 mm (IQR: 10.2-20.1 mm), while calcification and bending greater than 45˚ within the CTO segment were present in 47% and 36% of lesions, respectively. The mean J-CTO and PROGRESS-CTO scores were 1.89 ± 0.93 and 0.89 ± 0.77, respectively. The clinical and angiographic characteristics of the study groups were well balanced except for the significantly larger proximal reference diameter of the CTO vessel in the Gladius AW group than in the standard AW group (3.0 [IQR: 2.5-3.1] vs 2.8 [IQR: 2.4-3.0], *P* = .019) **(Tables 1 and 2)**.

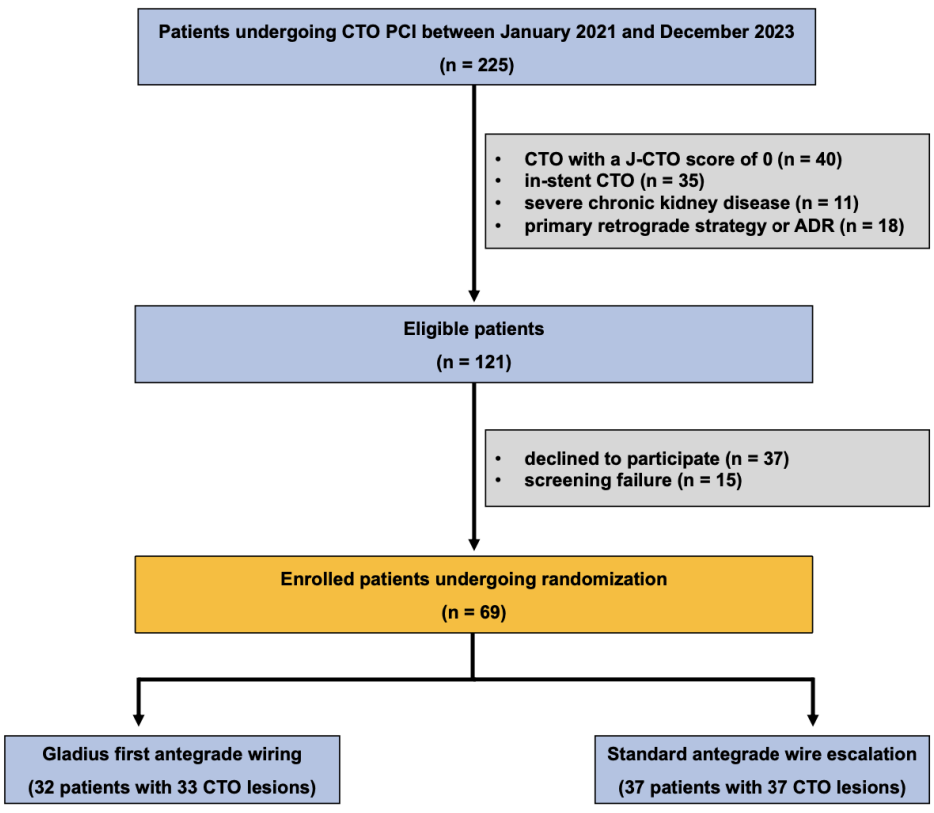


**Figure.** Study flow chart. *CTO = chronic total occlusion; J-CTO = Multicenter CTO Registry in Japan; PCI = percutaneous coronary intervention.*

**TABLE 1.** BASELINE CLINICAL CHARACTERISTICS

| | Standard AW (n = 37) | Gladius-first AW (n = 32) | *P*-value |
|---|---|---|---|
| Age, yrs | 66 (60-69) | 67 (60.8-70.2) | 0.451 |
| Male | 33 (89.2%) | 28 (87.5%) | 1.000 |
| Body mass index, kg/m$^2$ | 28.7 (26.7-29.4) | 28.2 (27.3-31) | 0.866 |
| Diabetes mellitus | 9 (24.3%) | 9 (28.1%) | 0.787 |
| Family history of coronary artery disease | 15 (40.5%) | 16 (50%) | 0.474 |
| Hypertension | 34 (91.9%) | 29 (90.6%) | 1.000 |
| Dyslipidemia | 35 (94.6%) | 30 (93.7%) | 1.000 |
| Current smoking | 7 (18.9%) | 6 (18.7%) | 1.000 |
| Prior percutaneous coronary intervention | 28 (75.7%) | 24 (75%) | 1.000 |
| Prior coronary artery bypass grafting | 5 (13.5%) | 4 (12.5%) | 1.000 |
| Prior myocardial infarction | 16 (43.2%) | 16 (50%) | 0.633 |
| Heart failure | 12 (32.4%) | 5 (15.6%) | 0.161 |
| Peripheral artery disease | 4 (10.8%) | 4 (12.5%) | 1.000 |
| Hemoglobin, mg/dL | 13.8 (12.7-15.5) | 14.2 (13.3-14.7) | 0.938 |
| Creatinine, mg/dL | 1.0 (0.8-1.2) | 0.9 (0.8-1.1) | 0.125 |
| Total cholesterol, mg/dL | 131 (114-150) | 130.5 (104-145.2) | 0.489 |
| LDL, mg/dL | 67 (55-84) | 60.5 (49.2-77.2) | 0.301 |
| Clinical presentation | | | |
| Chest pain | 28 (75.7%) | 26 (81.2%) | 0.771 |
| CCS class | 2.0 (2.0-3.0) | 2.0 (2.0-3.0) | 0.706 |
| Dyspnea on exertion | 27 (73%) | 19 (59.4%) | 0.307 |
| NYHA Class | 2.0 (2.0-2.0) | 2.0 (2.0-3.0) | 0.248 |
| Medication | | | |
| Aspirin | 31 (83.8%) | 28 (87.5%) | 0.742 |
| P2Y12 inhibitor | 20 (54%) | 19 (59.4%) | 0.808 |
| Beta-blocker | 33 (89.2%) | 27 (84.4%) | 0.723 |
| Calcium channel blocker | 13 (35.1%) | 14 (43.7%) | 0.621 |
| ACE-inhibitor/angiotensin receptor blocker | 33 (89.2%) | 31 (96.9%) | 0.363 |
| Nitrates | 8 (21.6%) | 7 (21.9%) | 1.000 |
| Statins | 36 (97.3%) | 32 (100%) | 1.000 |

Per-patient analysis. Data are presented as the number of patients (percentage) or as median (interquartile range). *ACE = angiotensin converting enzyme; AW = antegrade wiring; CCS = Canadian cardiovascular society; LDL = low-density lipoprotein; NYHA = New York Heart Association.*

**TABLE 2.** ANGIOGRAPHIC CHARACTERISTICS

| | Standard AW (n = 37) | Gladius-first AW (n = 33) | *P*-value |
|---|---|---|---|
| Number of diseased vessels | | | |
| Single vessel | 6 (16.2%) | 8 (25%) | 0.388 |
| Two vessel | 9 (24.3%) | 8 (25%) | 1.000 |
| Three vessel | 22 (59.5%) | 16 (50%) | 0.474 |
| CTO target vessel | | | |
| Right coronary artery | 19 (51.3%) | 18 (54.55%) | 0.815 |
| Left anterior descending artery | 14 (37.8%) | 13 (39.4%) | 1.000 |
| Left circumflex artery | 4 (10.8%) | 2 (6.1%) | 0.677 |
| Lesion length, mm | 15 (9.2-20.2) | 15.1 (12.0-20.1) | 0.837 |
| Proximal reference diameter, mm | 2.8 (2.4-3.0) | 3.0 (2.5-3.1) | 0.019 |
| Distal reference diameter, mm | 1.8 (1.5-2.0) | 1.9 (1.6-2.5) | 0.245 |
| Blunt proximal cap | 22 (59.5%) | 14 (42.4%) | 0.231 |
| Proximal cap ambiguity | 14 (37.8%) | 12 (36.4%) | 1.000 |
| Bifurcation involvement | 31 (83.8%) | 27 (81.8%) | 1.000 |
| Calcification | 16 (43.2%) | 17 (51.5%) | 0.632 |
| Bending > 45° | 14 (37.8%) | 11 (33.3%) | 0.804 |
| Occlusion length ≥ 20 mm | 10 (27%) | 9 (27.3%) | 1.000 |
| Poor distal target | 21 (56.8%) | 20 (60.6%) | 0.811 |
| Prior failed attempt at CTO | 10 (27%) | 9 (27.3%) | 1.000 |
| Absence of interventional collaterals | 8 (21.6%) | 13 (39.4%) | 0.124 |
| J-CTO score | 1.95 ± 1.03 | 1.82 ± 0.81 | 0.797 |
| PROGRESS score | 0.89 ± 0.84 | 0.88 ± 0.70 | 0.919 |

Per-lesion and per-patient analyses. Data are presented as the number of lesions or patients (percentage), median (interquartile range) or mean ± SD. *AW = antegrade wiring; CTO = chronic total occlusion; J-CTO = Multicenter CTO Registry in Japan; PROGRESS = Prospective Global Registry for the Study of Chronic Total Occlusion Intervention.*

## CTO-PCI techniques and outcomes

The procedural techniques, cost analysis, and in-hospital outcomes are presented in **Table 3**. Overall, crossing success, technical success, and procedural success were 92.9%, 90% and 90%, respectively, and did not differ between the studied groups. The primary AW was applied in all cases and was successful in 39 lesions (55.7%). The most common final successful crossing strategy was AW (60%), followed by the retrograde approach (19%) and antegrade dissection and re-entry (14%), while in 5 lesions (7%), no successful CTO recanalization was achieved. The distribution of the final and applied CTO-PCI strategies and techniques was comparable between groups.

**TABLE 3.** PROCEDURAL CHARACTERISTICS

| | Standard AW (n = 37) | Gladius-first AW (n = 33) | *P*-value |
|---|---|---|---|
| Crossing success | 33 (89.2%) | 32 (97%) | 0.361 |
| Technical success | 32 (86.5%) | 31 (93.9%) | 0.434 |
| Procedural success | 32 (86.5%) | 31 (93.9%) | 0.434 |
| Successful crossing strategy | | | |
| AW | 25 (67.6%) | 17 (51.5%) | 0.224 |
| Retrograde | 4 (10.8%) | 9 (27.3%) | 0.123 |
| Antegrade dissection and re-entry | 4 (10.8%) | 6 (18.2%) | 0.499 |
| None | 4 (10.8%) | 1 (3%) | 0.361 |
| Attempted strategies and techniques | | | |
| AW | 37 (100%) | 33 (100%) | 1.000 |
| Retrograde | 12 (32.4%) | 10 (30.3%) | 1.000 |
| Antegrade dissection and re-entry | 9 (24.3%) | 10 (30.3%) | 0.601 |
| Antegrade dissection and re-entry following AW | 6 (16.2%) | 10 (30.3%) | 0.254 |
| Stingray (Boston Scientific) and/or Crossboss (Boston Scientific) | 3 (8.1%) | 4 (12.1%) | 0.699 |
| Limited Antegrade Subintimal Tracking | 3 (8.1%) | 3 (9.1%) | 1.000 |
| Subintimal tracking and reentry | 3 (8.1%) | 2 (6.1%) | 1.000 |
| Number of strategies used | 1.0 (1.0-2.0) | 1.0 (1.0-2.0) | 0.313 |
| Crossing success related to initial AW | 23 (62.2%) | 16 (48.5%) | 0.336 |
| Time of AW, min | 21 (11-28) | 10 (4-16) | 0.001 |
| Time of successful AW, min | 15 (9-24) | 4 (3-8) | 0.001 |
| Time to change of strategy from AW, min | 26.5 (18-30) | 11.5 (10-16.8) | 0.004 |
| Fluoroscopy time related to AW, min | 11.3 (4.9-15.6) | 3.4 (1.5-7.5) | <0.001 |
| Absorbed dose related to AW, mGy | 230 (102.5-474.5) | 120.5 (38.8-241.5) | 0.009 |
| Contrast volume related to AW, mL | 23.5 (15.8-36.8) | 15 (8-26) | 0.005 |
| CTO guidewires number used during AW | 3.0 (2.0-4.0) | 2.0 (1.0-3.0) | <0.001 |
| Time of lesion preparation and stenting, min | 54 (44-62) | 78.5 (54.2-106) | 0.003 |
| Total procedural time, min | 124 (101-168) | 156 (111-203) | 0.141 |
| Total fluoroscopy time, min | 52.4 (21.4-83.3) | 60.5 (27.7-93.3) | 0.291 |
| Total absorbed dose, mGy | 1338 (836.4-1801) | 1592 (917.5-2688) | 0.39 |
| Total contrast volume, mL | 130 (115-145) | 139 (120-161) | 0.38 |
| CTO guidewires number | 3.0 (2.0-5.0) | 2.0 (1.0-4.0) | 0.018 |
| Microcatheters number | 1.0 (1.0-2.0) | 2.0 (1.0-2.0) | 0.101 |
| Stents number | 2.0 (1.0-3.0) | 3.0 (2.0-4.0) | 0.099 |
| Stent implantation | 29 (78.4%) | 27 (81.8%) | 0.772 |
| Stent total length | 64 (47-89) | 88 (58-103) | 0.117 |
| Maximal stent diameter | 3.5 (3.0-3.5) | 3.5 (3.5-4.0) | 0.066 |
| Minimal stent diameter | 2.8 (2.5-3.0) | 2.8 (2.5-3.0) | 0.824 |
| Drug-coated balloon use | 13 (35.1%) | 16 (48.5%) | 0.333 |
| Intravascular ultrasound use | 33 (89.2%) | 31 (93.9%) | 0.677 |
| Mechanical atherectomy | 0 (0%) | 2 (6.1%) | 0.219 |
| Overall equipment cost, PLN | 13 070 (10 744-17 538) | 14 470 (13 349-18 955) | 0.112 |
| CTO guidewires cost | 1 401 (891-2 285) | 1 465 (416-2 776) | 0.434 |
| Non-CTO guidewires cost | 874 (670-1 021) | 855 (704-1 163) | 0.540 |
| Microcatheter cost | 3 456 (3 002-5 130) | 3 456 (3 240-5 400) | 0.217 |
| Stingray (Boston Scientific) and/or Crossboss (Boston Scientific) cost | 0 (0-0) | 0 (0-0) | 0.869 |
| Guide extension cost | 0 (0-1 239) | 0 (0-1 404) | 0.242 |
| Balloon cost | 1 132 (797-1 708) | 1 325 (979-1 541) | 0.202 |
| Stent cost | 1 253 (518-2 160) | 1 755 (1 102-2 624) | 0.215 |
| Drug-coated balloon cost | 0 (0-1 457) | 1280 (0-1 944) | 0.077 |
| Intravascular ultrasound cost | 2 592 (2 592-2 754) | 2 592 (2 592-2 754) | 0.549 |
| Other costs | 983 (704-1 154) | 935 (755-1 108) | 0.426 |
| Major adverse cardiovascular events | 0 (0%) | 0 (0%) | 1.000 |
| Minor adverse cardiovascular events | 2 (5.4%) | 4 (12.1%) | 0.411 |
| Arrhythmia requiring treatment | 0 (0%) | 1 (3%) | 0.471 |
| Vascular access site haematoma | 1 (2.7%) | 2 (6.1%) | 1.000 |
| Femoral aneurysm | 1 (2.7%) | 1 (3%) | 1.000 |

Per-lesion analyses. Data are presented as the number of lesions (percentage) or as median (IQR). *AW = antegrade wiring, CTO = chronic total occlusion, PLN = Polish zloty.*

The primary endpoint (time to cross the CTO or change the initial AW strategy) was significantly shorter in the Gladius AW group than in the standard AW group (10 minutes [IQR: 4-16 minutes] vs 21 minutes [IQR: 11-28 minutes], *P* = .001) **(Supplemental Figure)**. The standardized mean difference (Cohen's d) was 0.676. In addition, the upfront use of the Gladius EX guidewire was associated with a significantly shorter AW fluoroscopy time and significantly lower AW absorbed dose and contrast volume, as well as a significantly lower number of CTO guidewires during the AW strategy. This, however, did not translate into lower values of total procedural time, total absorbed dose, and total contrast volume, which were comparable between both groups. There were no MACE, and the incidence of in-hospital minor adverse events was similar in the Gladius First AW and standard AW groups (12.1% vs 5.4%, *P* = .411). There was no significant difference in the equipment use and the equipment cost between groups **(Table 3)**.

Subgroup analyses showed that upfront use of the Gladius EX guidewire was associated with shorter AW time than standard-guidewire-escalation AW among lesions with blunt proximal cap, bending greater than 45°, longer lesions (≥ 20 mm), and lesions with a J-CTO score of at least 2, but there was no difference in lesions with calcification within the

occlusion site **(Supplemental Tables 1-5)**. In the standard-guidewire-escalation group, lesions with a successful initial AW strategy had significantly less proximal cap ambiguity and moderate or severe tortuosity, as well as significantly lower J-CTO and PROGRESS CTO scores; however, none of the CTO characteristics differentiated between successful vs failed initial AW in the Gladius-first group **(Table 4)**. Upon multivariable analysis, only ambiguous proximal cap (OR: 0.09; 95% CI, 0.01-0.72; *P* = .022) was an independent predictor of successful initial AW in the standard-guidewire-escalation group.

**TABLE 4.** RELATIONSHIP BETWEEN CTO CHARACTERISTICS AND PRESENCE OR ABSENCE OF SUCCESSFUL INITIAL AW STRATEGY

| **Standard-guidewire-escalation group** | | | |
|---|---|---|---|
| | **Successful AW (n = 23)** | **Failed AW (n = 14)** | ***P*-value** |
| Blunt proximal cap | 12 (52.2%) | 10 (71.4%) | 0.314 |
| Bifurcation involvement | 19 (82.6%) | 12 (85.7%) | 1.000 |
| Calcification | 8 (34.8%) | 8 (57.1%) | 0.305 |
| Bending > 45° | 6 (26.1%) | 8 (57.1%) | 0.085 |
| Occlusion length ≥ 20 mm | 4 (17.4%) | 6 (42.9%) | 0.132 |
| Poor distal target | 13 (56.5%) | 8 (57.1%) | 1.000 |
| Prior failed attempt at CTO | 5 (21.7%) | 5 (35.7%) | 0.454 |
| J-CTO score | 1.0 (1.0-2.0) | 3.0 (2.0-3.0) | 0.002 |
| Proximal cap ambiguity | 4 (17.4%) | 10 (71.4%) | 0.002 |
| Moderate/severe tortuosity | 1 (4.3%) | 6 (42.9%) | 0.007 |
| PROGRESS-CTO score | 0 (0-1.0) | 1.0 (1.0-2.0) | 0.005 |
| **Gladius-first group** | | | |
| | **Successful AW (n = 16)** | **Failed AW (n = 17)** | ***P*-value** |
| Blunt proximal cap | 6 (37.5%) | 8 (47.1%) | 0.728 |
| Bifurcation involvement | 14 (87.5%) | 13 (76.5%) | 0.656 |
| Calcification | 7 (43.7%) | 10 (58.8%) | 0.494 |
| Bending > 45° | 5 (31.2%) | 6 (35.3%) | 1.000 |
| Occlusion length ≥ 20 mm | 6 (37.5%) | 3 (17.6%) | 0.259 |
| Poor distal target | 12 (75%) | 8 (47.1%) | 0.157 |
| Prior failed attempt at CTO | 3 (18.7%) | 6 (35.3%) | 0.438 |
| J-CTO score | 1.5 (1.0-2.0) | 2.0 (1.0-3.0) | 0.438 |
| Proximal cap ambiguity | 4 (25%) | 8 (47.1%) | 0.282 |
| Moderate/severe tortuosity | 0 (0%) | 2 (11.8%) | 0.485 |
| PROGRESS-CTO score | 1.0 (0-1.0) | 1 (1.0-1.0) | 0.595 |

Per-lesion analysis. Data are presented as the number of patients or lesions (percentage) or as median (interquartile range). *AW = antegrade wiring, CTO = chronic total occlusion, J-CTO = Multicenter CTO Registry in Japan, PROGRESS = Prospective Global Registry for the Study of Chronic Total Occlusion Intervention.*

## Discussion

The Gladius First study is the first randomized trial designed to compare 2 common approaches to AW, namely, standard guidewire escalation starting with the soft polymer-jacketed guidewire or AW with a direct use of the intermediate tip-load polymer-jacketed guidewire, as the initial CTO-PCI strategy. Our study demonstrated that although upfront use of the Gladius EX wire among lesions with a J-CTO score greater than 1 resulted in a significantly shorter AW and consequently lower AW-related contrast and radiation use, the total procedural time, final crossing and technical success, equipment cost and use, and procedural complications were similar as compared with the standard antegrade wire escalation. Notably, our results were consistent across more complex CTO lesion subsets, including a J-CTO score greater than 2. Finally, the success of the initial AW strategy was predictable in the standard guidewire escalation technique but not in the Gladius-first group based on preprocedural angiographic analysis.

Due to its widespread availability and simplicity, AW is currently the most common primary CTO recanalization strategy (up to 84% of cases),[7,8] resulting in final crossing success in approximately 50% of CTO lesions.[16] This strategy usually starts with gentle manipulation of a low-penetration-force polymer-jacketed guidewire with potential escalation to intermediate- and/or high-penetration-force guidewires;[9] alternatively, the upfront use of intermediate tip load polymer-jacketed guidewires has been implemented by some expert hybrid-CTO operators. The potential advantages of the latter approach might include higher time efficiency of AW with swifter change to antegrade dissection and re-entry and/or the retrograde approach in case of extraplaque guidewire position, and, consequently, a shorter total duration of CTO PCI. Moreover, the exclusive use of polymer-jacketed guidewires (potentially less often applied in the standard-guidewire-escalation AW) was independently associated with a higher technical success rate and lower perforation risk in a prior observational study.[10] Another potential benefit of the upfront use of an intermediate tip-load polymer-jacketed guidewire is a higher rate of successful crossing in longer lesions with tortuosity and/or poor distal target. We therefore performed a 2-arm randomized trial comparing the time, efficacy, and safety between the upfront use of an intermediate tip-load polymer-jacketed guidewire (Gladius EX) vs standard guidewire escalation for antegrade crossing of CTO.

As expected, we found a significantly shorter duration of AW as well as lower AW-related radiation exposure and contrast volume in the Gladius-first group as compared with the standard-guidewire-escalation group, substantiating the higher time efficiency of AW when omitting the low tip-load guidewire. Of note, the shorter AW time in the Gladius-first group was a result of both a shorter successful AW crossing time as well as a shorter time to change strategy in cases of AW failure. This,

however, did not translate into a shorter total procedural time (including total radiation and contrast exposure), as the total times were similar between groups. The explanation for this observation might lie in the numerically higher initial AW crossing rates in the standard-guidewire-escalation group, thus potentially favoring longer CTO recanalization attempts using non-AW secondary strategies in the Gladius-first approach. In addition, a longer lesion preparation and stenting time in the Gladius group than in the standard-guidewire-escalation group could further constrain the contribution of the AW time to the total procedural time in the former. Nonetheless, the results on shorter AW time following upfront use of the Gladius guidewire were retained in more complex CTO lesion subsets, including blunt proximal cap, bending greater than 45°, longer lesions of at least 20 mm, and lesions with a J-CTO score of at least 2. Future large-scale trials powered for the assessment of clinical outcomes should provide further insights into the benefits of shortening the AW time.

Of particular interest, there were no significant differences between the groups regarding the initial AW crossing success or technical and procedural success, highlighting similar procedural efficacy irrespective of the type of the first guidewire selected for AW. Likewise, the distribution of applied and final successful CTO-PCI strategies was similar, and no preference on higher use of antegrade dissection and re-entry in the Gladius-first group could be confirmed. Notably, although the number of guidewires used (both AW-related and the total number) was significantly lower in the Gladius-first group, the total cost of CTO equipment was comparable between groups, suggesting a negligible cost component of CTO guidewires as compared with other devices (microcatheters, guide extensions, stents, and balloons, etc).

The ability to predict successful guidewire crossing using initial AW should be instructive for choosing a primary AW strategy.[11,17] To this end, our results demonstrating the differing CTO angiographic characteristics in lesions with vs without successful AW crossing in the standard-guidewire-escalation group but not in the Gladius-first group suggest a higher predictability of initial AW in the former. Moreover, while an ambiguous proximal cap was a negative independent predictor of successful initial AW in the standard-guidewire-escalation group, the presence of proximal cap ambiguity on baseline angiogram should guide the interventionalist against AW starting with a low tip-load polymer-jacketed guidewire.

### Limitations

First, this was a single center study with a relatively small number of patients. Indeed, due to the lack of prior data on the time efficiency of AW strategy, the sample size was hypothetically estimated at 70 and might be underpowered to detect between group differences. Second, although the procedures were performed by experienced hybrid-CTO operators, the results may not be replicated by interventionalists with less experience and/or different approaches to CTO PCI. Third, the cost-analysis might be hampered by the usage of different types of devices (specifically microcatheters and drug-eluting stents) throughout the study period. Finally, due to prespecified study inclusion and exclusion criteria, most of our CTO lesions had an intermediate difficulty level. Thus, our results should be viewed with caution and need external validation in more difficult CTO subsets.

## Conclusions

AW strategy with the upfront use of an intermediate tip-load polymer-jacketed guidewire for crossing coronary CTO translates into a higher time efficiency of AW, without significant effects on the total procedural time, procedural success, and total resource use as compared with standard-guidewire-escalation AW starting with the low tip-load polymer-jacketed guidewire. The presence of proximal cap ambiguity should guide the interventionalist against AW with a low tip-load polymer-jacketed guidewire.

## Affiliations and Disclosures

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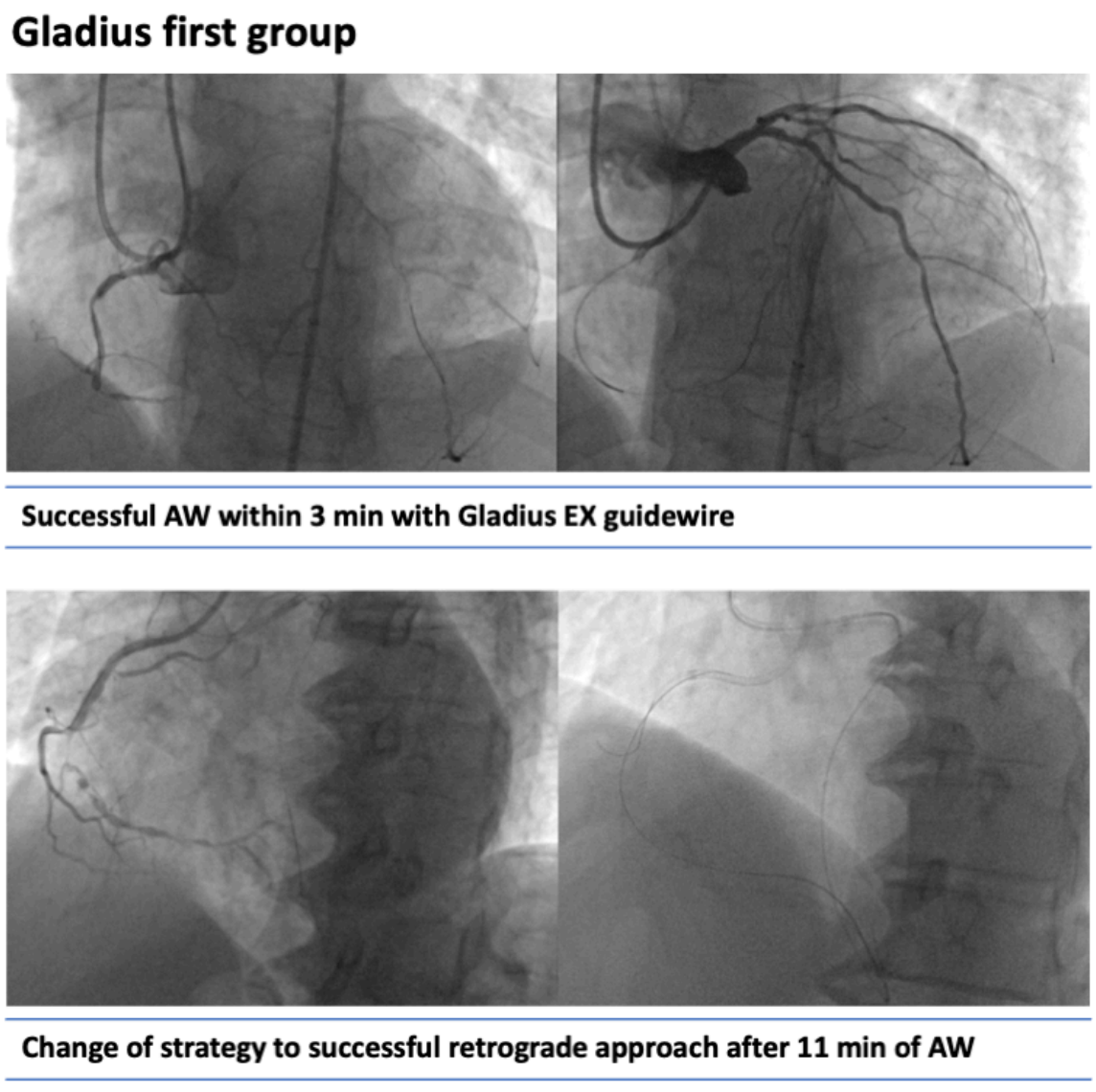
## Supplemental Material




**Supplemental Figure.** Illustrative examples of the time of antegrade wiring in 2 patients assigned to Gladius-first group. *AW = antegrade wiring.*

**SUPPLEMENTAL TABLE 1.** PROCEDURAL CHARACTERISTICS IN LESIONS WITH BLUNT PROXIMAL CAP

| | Standard AW (n = 22) | Gladius-first AW (n = 14) | *P*-value |
|---|---|---|---|
| Crossing success | 19 (86.4%) | 14 (100%) | 0.267 |
| Technical success | 19 (86.4%) | 14 (100%) | 0.267 |
| Procedural success | 19 (86.4%) | 14 (100%) | 0.267 |
| Successful crossing strategy | | | |
| AW | 14 (63.6%) | 6 (42.9%) | 0.307 |
| Retrograde | 3 (13.6%) | 4 (28.6%) | 0.394 |
| Antegrade dissection and re-entry | 2 (9.1%) | 4 (28.6%) | 0.181 |
| None | 3 (13.6%) | 0 (0%) | 0.267 |
| Attempted strategies and techniques | | | |
| AW | 22 (100%) | 14 (100%) | 1.000 |
| Retrograde | 9 (40.9%) | 4 (28.6%) | 0.501 |
| Antegrade dissection and re-entry | 6 (27.3%) | 6 (42.9%) | 0.471 |
| Antegrade dissection and re-entry following AW | 3.0 (13.6%) | 6.0 (42.9%) | 0.111 |
| Stingray (Boston Scientific) and/or Crossboss (Boston Scientific) | 1 (4.5%) | 2 (14.3%) | 0.547 |
| Limited Antegrade Subintimal Tracking | 2 (9.1%) | 1 (7.1%) | 1.000 |
| Subintimal tracking and reentry | 2 (9.1%) | 2 (14.3%) | 0.634 |
| Number of strategies used | 1.0 (1.0-3.0) | 2.0 (1.0-2.0) | 0.53 |
| Crossing success related to initial AW | 12 (54.5%) | 6 (42.9%) | 0.733 |
| Time of AW, min | 23.5 (15.2-27.8) | 11.0 (5.0-17.8) | 0.014 |
| Time of successful AW, min | 22.5 (12.2-27) | 5 (4.2-18.5) | 0.116 |
| Time to change of strategy from AW, min | 25 (18-27.8) | 12 (9.2-15.2) | 0.058 |
| Fluoroscopy time related to AW, min | 12 (5.9-15.1) | 6 (1.6-10.1) | 0.045 |
| Absorbed dose related to AW, mGy | 349 (191-539) | 164 (75-255) | 0.023 |
| Contrast volume related to AW, ml | 30.5 (20-42) | 16.5 (10-32.5) | 0.049 |
| Guidewires used during AW | 3.0 (3.0-4.0) | 2.0 (1.0-3.0) | 0.009 |
| Total procedural time, min | 143 (105-178.5) | 133.5 (111.5-171.8) | 0.948 |
| Total fluoroscopy time, min | 52.9 (28.5-77.3) | 49.8 (26.4-73.3) | 0.710 |
| Total absorbed dose, mGy | 1437.5 (960.5-2291) | 1330.5 (931.1-1712.2) | 0.446 |
| Total contrast volume, mL | 130.5 (125-145) | 144.5 (120.2-158.8) | 0.733 |
| CTO guidewires number | 3.5 (3.0-5.0) | 3.0 (1.2-4.0) | 0.136 |
| Microcatheters number | 1.0 (1.0-2.0) | 1.0 (1.0-2.0) | 0.839 |
| Stents number | 2.0 (1.0-3.0) | 3.0 (2.5-4.0) | 0.046 |
| Stent implantation | 17 (77.3%) | 11 (78.6%) | 1.000 |
| Stent total length | 64 (50-89) | 94 (70-113) | 0.066 |
| Maximal stent diameter | 3.5 (3.0-4.0) | 3.5 (3.2-4.0) | 0.589 |
| Minimal stent diameter | 2.8 (2.5-3.0) | 3.0 (2.4-3.0) | 0.714 |
| Drug-coated balloon use | 7 (31.8%) | 9 (64.3%) | 0.087 |
| Intravascular ultrasound use | 20 (90.9%) | 14 (100%) | 0.511 |
| Major adverse cardiovascular events | 0 (0%) | 0 (0%) | 1.000 |
| Minor adverse cardiovascular events | 1 (4.5%) | 2 (14.3%) | 0.547 |
| Arrhythmia requiring treatment | 0 (0%) | 0 (0%) | 1.000 |
| Vascular access site haematoma | 0 (0%) | 1 (7.1%) | 1.000 |
| Femoral aneurysm | 1 (4.5%) | 1 (7.1%) | 1.000 |

*AW = antegrade wiring.*

**SUPPLEMENTAL TABLE 2.** PROCEDURAL CHARACTERISTICS IN LESIONS WITH CALCIFICATION WITHIN OCCLUSION SITE

| | Standard AW (n = 16) | Gladius-first AW (n = 17) | *P*-value |
|---|---|---|---|
| Crossing success | 13 (81.2%) | 16 (94.1%) | 0.335 |
| Technical success | 12 (75%) | 15 (88.2%) | 0.398 |
| Procedural success | 12 (75%) | 15 (88.2%) | 0.398 |
| Successful crossing strategy | | | |
| AW | 9 (56.2%) | 8 (47.1%) | 0.732 |
| Retrograde | 1 (6.2%) | 4 (23.5%) | 0.335 |
| Antegrade dissection and re-entry | 3 (18.7%) | 4 (23.5%) | 1.000 |
| None | 3 (18.7%) | 1 (5.9%) | 0.335 |
| Attempted strategies and techniques | | | |
| AW | 16 (100%) | 17 (100%) | 1.000 |
| Retrograde | 8 (50%) | 5 (29.4%) | 0.296 |
| Antegrade dissection and re-entry | 6 (37.5%) | 6 (35.3%) | 1.000 |
| Antegrade dissection and re-entry following AW | 3.0 (18.7%) | 6.0 (35.3%) | 0.438 |
| Stingray (Boston Scientific) and/or Crossboss (Boston Scientific) | 2 (12.5%) | 2 (11.8%) | 1.000 |
| Limited Antegrade Subintimal Tracking | 3 (18.75%) | 2 (11.8%) | 0.656 |
| Subintimal tracking and reentry | 2 (12.5%) | 2 (11.8%) | 1.000 |
| Number of strategies used | 1.0 (1.0-3.0) | 2.0 (1.0-2.0) | 1.000 |
| Crossing success related to initial AW | 8 (50%) | 7 (41.2%) | 0.732 |
| Time of AW, min | 14 (11-30.5) | 11 (5-18) | 0.112 |
| Time of successful AW, min | 11 (8-32) | 4.5 (3.5-19.2) | 0.176 |
| Time to change of strategy from AW, min | 24.0 (13-30) | 11 (10-16) | 0.135 |
| Fluoroscopy time related to AW, min | 9.2 (4.9-16.8) | 4.7 (1.8-7.8) | 0.044 |
| Absorbed dose related to AW, mGy | 224.0 (83.0-379) | 140.0 (52.0-333) | 0.264 |
| Contrast volume related to AW, mL | 21.5 (15.2-32) | 15.0 (8.0-26) | 0.279 |
| Guidewires used during AW | 3.0 (2.0-4.0) | 2.0 (1.0-3.0) | 0.012 |
| Total procedural time, min | 154.0 (119.5-199.2) | 161.0 (136.0-198) | 0.746 |
| Total fluoroscopy time, min | 63.3 (26.7-99.8) | 63.5 (29.9-97.2) | 0.983 |
| Total absorbed dose, mGy | 1372.0 (989.9-2555) | 1697.0 (972.0-2910) | 0.528 |
| Total contrast volume, mL | 128.0 (115.0-150.0) | 135.0 (95.0-155) | 0.814 |

| | | | |
|---|---|---|---|
| CTO guidewires number | 3.0 (2.8-5.0) | 2.0 (1.0-3.0) | 0.072 |
| Microcatheters number | 2.0 (1.0-2.0) | 2.0 (1.0-2.0) | 0.905 |
| Stents number | 3.0 (2.0-5.0) | 3.0 (3.0-4.0) | 0.784 |
| Stent implantation | 9 (56.2%) | 13 (76.5%) | 0.282 |
| Stent total length | 76 (47-129) | 93 (48-104) | 0.841 |
| Maximal stent diameter | 3.5 (3.5-4.0) | 3.5 (3.5-4.0) | 0.743 |
| Minimal stent diameter | 2.5 (2.5-2.8) | 2.5 (2.5-3.0) | 0.369 |
| Drug-coated balloon use | 8 (50%) | 5 (29.4%) | 0.296 |
| Intravascular ultrasound use | 12 (75%) | 15 (88.2%) | 0.398 |
| Major adverse cardiovascular events | 0 (0%) | 0 (0%) | 1.000 |
| Minor adverse cardiovascular events | 1 (6.2%) | 2 (11.8%) | 1.000 |
| Arrhythmia requiring treatment | 0 (0%) | 1 (5.9%) | 1.000 |
| Vascular access site haematoma | 1 (6.2%) | 1 (5.9%) | 1.000 |
| Femoral aneurysm | 0 (0%) | 0 (0%) | 1.000 |

*AW = antegrade wiring.*

**SUPPLEMENTAL TABLE 3.** PROCEDURAL CHARACTERISTICS IN LESIONS WITH OCCLUSION LENGTH GREATER THAN OR EQUAL TO 20 MM

| | Standard AW (n = 10) | Gladius-first AW (n = 9) | p Value |
|---|---|---|---|
| Crossing success | 8 (80%) | 9 (100%) | 0.474 |
| Technical success | 8 (80%) | 9 (100%) | 0.474 |
| Procedural success | 8 (80%) | 9 (100%) | 0.474 |
| Successful crossing strategy | | | |
| AW | 5 (50%) | 6 (66.7%) | 0.65 |
| Retrograde | 2 (20%) | 3 (33.3%) | 0.628 |
| Antegrade dissection and re-entry | 1 (10%) | 0 (0%) | 1.000 |
| None | 2 (20%) | 0 (0%) | 0.474 |
| Attempted strategies and techniques | | | |
| AW | 10 (100%) | 9 (100%) | 1.000 |
| Retrograde | 5 (50%) | 3 (33.3%) | 0.65 |
| Antegrade dissection and re-entry | 3 (30%) | 1 (11.1%) | 0.582 |
| Antegrade dissection and re-entry following AW | 2 (20%) | 1 (11.1%) | 1.000 |
| Stingray (Boston Scientific) and/or Crossboss (Boston Scientific) | 0 (0%) | 1 (11.1%) | 0.474 |
| Limited Antegrade Subintimal Tracking | 1 (10%) | 0 (0%) | 1.000 |
| Subintimal tracking and reentry | 2 (20%) | 0 (0%) | 0.474 |
| Number of strategies used | 1.5 (1.0-3.0) | 1.0 (1.0-3.0) | 0.646 |
| Crossing success related to initial AW | 4 (40%) | 6 (66.67%) | 0.37 |
| Time of AW, min | 22.5 (16.0-29) | 5 (2-8) | 0.001 |
| Time of successful AW, min | 21 (15-24) | 3.5 (2-5) | 0.008 |
| Time to change of strategy from AW, min | 26 (19-30) | 10 (8.5-14.5) | 0.099 |
| Fluoroscopy time related to AW, min | 11.3 (7.4-14.9) | 2.4 (1.3-4.7) | 0.004 |
| Absorbed dose related to AW, mGy | 558.5 (194.8-2028.8) | 52 (22-626) | 0.277 |
| Contrast volume related to AW, mL | 22.5 (16.2-33.8) | 10 (8-20) | 0.037 |
| Guidewires used during AW | 3.0 (3.0-4.0) | 1.0 (1.0-2.0) | 0.003 |
| Total procedural time, min | 166 (115.2-215.8) | 178 (111-248) | 0.775 |
| Total fluoroscopy time, min | 64 (33.8-94.2) | 69.4 (26-112.8) | 0.752 |
| Total absorbed dose, mGy | 1758.5 (1129.2-2753.8) | 1697.0 (667.5-2915) | 1.000 |
| Total contrast volume, mL | 137.5 (118.8-153.5) | 125 (110-161) | 0.806 |
| CTO guidewires number | 4.5 (3.0-5.8) | 1.0 (1.0-3.0) | 0.071 |
| Microcatheters number | 1.0 (1.0-2.0) | 2.0 (1.0-2.0) | 0.339 |
| Stents number | 3.0 (2.5-3.0) | 3.0 (2.0-4.0) | 0.780 |
| Stent implantation | 7 (70%) | 9 (100%) | 0.211 |
| Stent total length | 83 (65.5-88.5) | 99 (48-120) | 0.832 |
| Maximal stent diameter | 3.5 (3.5-3.8) | 3.5 (3.5-4.0) | 1.000 |
| Minimal stent diameter | 2.8 (2.5-2.9) | 2.5 (2.5-3.0) | 0.736 |
| Drug-coated balloon use | 2 (20%) | 3 (33.3%) | 0.628 |
| Intravascular ultrasound use | 9 (90%) | 9 (100%) | 1.000 |
| Major adverse cardiovascular events | 0 (0%) | 0 (0%) | 1.000 |
| Minor adverse cardiovascular events | 1 (10%) | 0 (0%) | 1.000 |
| Arrhythmia requiring treatment | 0 (0%) | 0 (0%) | 1.000 |
| Vascular access site haematoma | 1 (10%) | 0 (0%) | 1.000 |
| Femoral aneurysm | 0 (0%) | 0 (0%) | 1.000 |

*AW = antegrade wiring; CTO = chronic total occlusion.*

**SUPPLEMENTAL TABLE 4.** PROCEDURAL CHARACTERISTICS IN LESIONS WITH BENDING GREATER THAN 45°

| | Standard AW (n = 14) | Gladius-first AW (n = 11) | *P*-value |
|---|---|---|---|
| Crossing success | 11 (78.6%) | 11 (100%) | 0.23 |
| Technical success | 10 (71.4%) | 11 (100%) | 0.105 |
| Procedural success | 10 (71.4%) | 11 (100%) | 0.105 |
| Successful crossing strategy | | | |
| AW | 6 (42.9%) | 5 (45.4%) | 1.000 |
| Retrograde | 3 (21.4%) | 4 (36.4%) | 0.656 |
| Antegrade dissection and re-entry | 2 (14.3%) | 2 (18.2%) | 1.000 |
| None | 3 (21.4%) | 0 (0%) | 0.23 |
| Attempted strategies and techniques | | | |
| AW | 14 (100%) | 11 (100%) | 1.000 |
| Retrograde | 6 (42.9%) | 4 (36.4%) | 1.000 |
| Antegrade dissection and re-entry | 5 (35.7%) | 4 (36.4%) | 1.000 |
| Antegrade dissection and re-entry following AW | 4.0 (28.6%) | 4.0 (36.4%) | 1.000 |
| Stingray (Boston Scientific) and/or Crossboss (Boston Scientific) | 2 (14.3%) | 3 (27.3%) | 0.623 |
| Limited Antegrade Subintimal Tracking | 1 (7.1%) | 0 (0%) | 1.000 |
| Subintimal tracking and reentry | 3 (21.4%) | 0 (0%) | 0.23 |
| Number of strategies used | 2.0 (1.0-3.0) | 2.0 (1.0-2.5) | 0.885 |
| Crossing success related to initial AW | 6 (42.86%) | 5 (45.45%) | 1.000 |
| Time of AW, min | 25 (16-30.8) | 7 (3-10) | 0.001 |
| Time of successful AW, min | 19 (10.5-29.8) | 3 (2-3) | 0.013 |
| Time to change of strategy from AW, min | 26.5 (22.8-30.2) | 10 (7.8-10.8) | 0.005 |
| Fluoroscopy time related to AW, min | 12.8 (7.4-16.8) | 2.5 (1.6-4.4) | 0.002 |
| Absorbed dose related to AW, mGy | 339.5 (136.5-451) | 92.0 (26.5-171.5) | 0.009 |
| Contrast volume related to AW, mL | 25 (20-43) | 9 (6.5-19) | 0.012 |
| Guidewires used during AW | 3.0 (3.0-4.0) | 1.0 (1.0-2.0) | 0.002 |
| Total procedural time, min | 157.5 (115.2-223.2) | 178.0 (130.5-235) | 0.547 |
| Total fluoroscopy time, min | 59.8 (29.9-89.6) | 67.6 (33.9-101.4) | 0.542 |
| Total absorbed dose, mGy | 1372 (1098.5-2320) | 1715 (1130.9-2646.5) | 0.681 |
| Total contrast volume, mL | 144.5 (127.5-165) | 145 (130-168) | 0.826 |
| CTO guidewires number | 3.5 (3.0-5.8) | 2.0 (1.0-4.0) | 0.112 |
| Microcatheters number | 1.0 (1.0-2.0) | 2.0 (1.5-2.0) | 0.141 |
| Stents number | 3.0 (2.2-3.0) | 3.0 (2.0-3.8) | 0.906 |
| Stent implantation | 10 (71.4%) | 10 (90.9%) | 0.341 |
| Stent total length | 73.5 (50.5-88.8) | 93.5 (65.5-102.8) | 0.307 |
| Maximal stent diameter | 3.5 (3.1-3.9) | 3.8 (3.5-4.0) | 0.447 |
| Minimal stent diameter | 2.6 (2.5-3.0) | 2.9 (2.5-3.0) | 0.552 |
| Drug-coated balloon use | 4 (28.6%) | 6 (54.5%) | 0.241 |
| Intravascular ultrasound use | 11 (78.6%) | 11 (100%) | 0.23 |
| Major adverse cardiovascular events | 0 (0%) | 0 (0%) | 1.000 |
| Minor adverse cardiovascular events | 1 (7.1%) | 1 (9.1%) | 1.000 |
| Arrhythmia requiring treatment | 0 (0%) | 0 (0%) | 1.000 |
| Vascular access site haematoma | 1 (7.1%) | 0 (0%) | 1.000 |
| Femoral aneurysm | 0 (0%) | 1 (9.1%) | 0.440 |

*AW = antegrade wiring; CTO = chronic total occlusion.*

**SUPPLEMENTAL TABLE 5.** PROCEDURAL CHARACTERISTICS IN LESIONS WITH A J-CTO SCORE OF GREATER THAN OR EQUAL TO 2

| | Standard AW (n = 22) | Gladius-first AW (n = 19) | *P*-value |
|---|---|---|---|
| Crossing success | 18.0 (81.8%) | 19.0 (100%) | 0.111 |
| Technical success | 17 (77.3%) | 18 (94.7%) | 0.191 |
| Procedural success | 17 (77.3%) | 18 (94.7%) | 0.191 |
| Successful crossing strategy | | | |
| AW | 12 (54.5%) | 9 (47.4%) | 0.758 |
| Retrograde | 3 (13.6%) | 5 (26.3%) | 0.436 |
| Antegrade dissection and re-entry | 3 (13.6%) | 5 (26.3%) | 0.436 |
| None | 4.0 (18.2%) | 0 (0%) | 0.111 |
| Attempted strategies and techniques | | | |
| AW | 22 (100%) | 19 (100%) | 1.000 |
| Retrograde | 10 (45.4%) | 6 (31.6%) | 0.522 |
| Antegrade dissection and re-entry | 7 (31.8%) | 7 (36.8%) | 0.754 |
| Antegrade dissection and re-entry following AW | 4 (18.2%) | 7 (36.8%) | 0.290 |
| Stingray (Boston Scientific) and/or Crossboss (Boston Scientific) | 2 (9.1%) | 3 (15.8%) | 0.649 |
| Limited Antegrade Subintimal Tracking | 3 (13.6%) | 1 (5.3%) | 0.610 |
| Subintimal tracking and reentry | 3 (13.6%) | 2 (10.5%) | 1.000 |
| Number of strategies used | 1.0 (1.0-3.0) | 2.0 (1.0-2.0) | 0.989 |
| Crossing success related to initial AW | 11 (50%) | 8 (42.1%) | 0.756 |
| Time of AW, min | 22.5 (12-30) | 10 (5-15.5) | 0.003 |
| Time of successful AW, min | 21.5 (10.5-26) | 5 (2-8) | 0.021 |
| Time to change of strategy from AW, min | 25 (16-30) | 11 (10-17.2) | 0.033 |
| Fluoroscopy time related to AW, min | 11.7 (6.2-15.8) | 3.4 (1.5-7.5) | 0.001 |
| Absorbed dose related to AW, mGy | 330 (149-440) | 122 (45.5-223.5) | 0.023 |
| Contrast volume related to AW, mL | 21.5 (16.2-35.8) | 11 (8.5-26) | 0.042 |
| Guidewires used during AW | 3.0 (3.0-4.0) | 2.0 (1.0-3.0) | 0.002 |
| Total procedural time, min | 154 (109-215.8) | 178 (131.5-220.5) | 0.472 |
| Total fluoroscopy time, min | 62.9 (28.4-97.5) | 65.9 (31.3-100.6) | 0.785 |
| Total absorbed dose, mGy | 1437.5 (1038-2679) | 1704 (1136.5-2254) | 0.784 |

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|---|---|---|---|
| Total contrast volume, mL | 135.0 (125-153.5) | 135 (115-160.5) | 1.000 |
| CTO guidewires number | 4.0 (3.0-5.0) | 3.0 (1.0-4.0) | 0.033 |
| Microcatheters number | 1.5 (1.0-2.0) | 2.0 (1.0-2.0) | 0.217 |
| Stents number | 3 (2.0-3.5) | 3 (2.5-4.0) | 0.429 |
| Stent implantation | 15 (68.2%) | 15 (78.9%) | 0.499 |
| Stent total length | 70 (53-92) | 94 (66-107) | 0.299 |
| Maximal stent diameter | 3.5 (3.2-4.0) | 3.5 (3.5-4.0) | 0.658 |
| Minimal stent diameter | 2.8 (2.5-3.0) | 2.5 (2.5-3.0) | 0.584 |
| Drug-coated balloon use | 8 (36.4%) | 9 (47.4%) | 0.537 |
| Intravascular ultrasound use | 18 (81.8%) | 18 (94.7%) | 0.350 |
| Major adverse cardiovascular events | 0 (0%) | 0 (0%) | 1.000 |
| Minor adverse cardiovascular events | 1 (4.5%) | 1 (5.3%) | 1.000 |
| Arrhythmia requiring treatment | 0 (0%) | 0 (0%) | 1.000 |
| Vascular access site haematoma | 1 (4.5%) | 0 (0%) | 1.000 |
| Femoral aneurysm | 0 (0%) | 1 (5.3%) | 0.463 |

*AW = antegrade wiring; CTO = chronic total occlusion; J-CTO = Multicenter CTO Registry in Japan.*

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