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9-28-2021

### **Safety and efficacy of dedicated guidewire, microcatheter, and guide catheter extension technologies for chronic total coronary occlusion revascularization: Primary results of the Teleflex Chronic Total Occlusion Study**

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#### **Recommended Citation**

Kandzari DE, Alaswad K, Jaffer FA, Brilakis E, Croce K, Kearney K, Spaedy A, Yeh R, Thompson C, Nicholson W, Wyman RM, Riley R, Lansky A, Buller C, and Karpalotis D. Safety and efficacy of dedicated guidewire, microcatheter, and guide catheter extension technologies for chronic total coronary occlusion revascularization: Primary results of the Teleflex Chronic Total Occlusion Study. *Catheter Cardiovasc Interv* 2021.

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## ORIGINAL STUDIES

WILEY

# Safety and efficacy of dedicated guidewire, microcatheter, and guide catheter extension technologies for chronic total coronary occlusion revascularization: Primary results of the Teleflex Chronic Total Occlusion Study

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## Abstract

**Background:** Description of procedural outcomes using contemporary techniques that apply specialized coronary guidewires, microcatheters, and guide catheter extensions designed for chronic total occlusion (CTO) percutaneous revascularization is limited.

**Methods:** A prospective, multicenter, single-arm study was conducted to evaluate procedural and in-hospital outcomes among 150 patients undergoing attempted CTO revascularization utilizing specialized guidewires, microcatheters and guide extensions. The primary endpoint was defined as successful guidewire recanalization and absence of in-hospital cardiac death, myocardial infarction (MI), or repeat target lesion revascularization (major adverse cardiac events, MACE).

**Results:** The prevalence of diabetes was 32.7%; prior MI, 48.0%; and previous bypass surgery, 32.7%. Average (mean  $\pm$  standard deviation) CTO length was  $46.9 \pm 20.5$  mm, and mean J-CTO score was  $1.9 \pm 0.9$ . Combined radial and femoral arterial access was performed in 50.0% of cases. Device utilization included: support microcatheter, 100%; guide catheter extension, 64.0%; and mean number of study guidewires/procedure was  $4.8 \pm 2.6$ . Overall, procedural success was achieved in 75.3% of patients. The rate of successful guidewire recanalization was 94.7%, and in-hospital MACE was 19.3%. Achievement of TIMI grade 2 or 3 flow was observed in 93.3% of patients. Crossing strategies included antegrade (54.0%), retrograde (1.3%) and combined antegrade/retrograde techniques (44.7%). Clinically significant perforation resulting in hemodynamic instability and/or requiring intervention occurred in 16 (10.7%) patients.

**Abbreviations:** CTO, chronic total occlusion; MACE, major adverse cardiac event; MI, myocardial infarction; PCI, percutaneous coronary intervention; TIMI, Thrombolysis in Myocardial Infarction; TLR, target lesion revascularization.

Clinical Trial Registration: NCT03988166

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**Conclusions:** In a multicenter, prospective registration study, favorable procedural success was achieved despite high lesion complexity using antegrade and retrograde guidewire maneuvers and with acceptable safety, yet with comparably higher risk than conventional non-CTO PCI.

#### KEYWORDS

chronic total occlusion, guide catheter extensions, guidewires, microcatheters, percutaneous coronary intervention

## 1 | INTRODUCTION

Against the background of increasing complexity in percutaneous coronary intervention (PCI) and paralleled by advancement in procedural technique, chronic total occlusion (CTO) revascularization persists among lesion complexities with the highest rates of procedural failure. Despite a marked escalation in attempted CTO PCI over recent years, rates of procedural success have only modestly improved, and procedural-related safety has at best plateaued, if not worsened.<sup>1–5</sup>

Aside from predictive models to inform procedural outcome, factors commonly associated with improvements in CTO success include operator experience<sup>5,6</sup> and the application of enabling strategies that incorporate not only advanced technique but also device technologies that include purpose-built guidewires, microcatheters and guide catheter extensions.<sup>2,7</sup> Unlike conventional coronary guidewires, for example, contemporary development of CTO-specific guidewire design enables penetration of fibrous and calcified proximal cap disease, navigation through microchannels or subintimal planes and luminal re-entry. Similarly, specialized microcatheters are constructed to permit guidewire crossing penetrability, permit guidewire exchange or traverse collateral channels. Guide catheter extensions provide not only advanced support for guidewire crossing but also enable device delivery and exchange, and in some instances facilitate retrograde guidewire recanalization.

Despite their common use in CTO PCI, relatively few studies have detailed procedural outcomes and technique related to CTO-specific guidewires, microcatheters and guide catheter extensions among patients undergoing attempted revascularization.<sup>7,8</sup> Further, many of these commonly used devices do not have formal regulatory approval for this specific clinical indication. We performed a prospective, multicenter registration study to evaluate procedural and in-hospital outcomes among patients undergoing attempted CTO PCI using specialized coronary guidewires, microcatheters and guide catheter extensions to inform CTO procedural technique and strategy.

## 2 | METHODS

### 2.1 | Study design and population

The Teleflex Chronic Total Occlusion Study (Vascular Solutions/Teleflex, Inc., Minneapolis, MN; clinicaltrials.gov identifier NCT03988166) was a prospective, single-arm, multicenter study examining procedural

and in-hospital outcomes among patients undergoing attempted CTO PCI at 13 investigational centers in the United States (US). The study was designed with guidance from the US Food and Drug administration (FDA) and was intended to support US device approval. Eligible patients provided written informed consent prior to the interventional procedure. Eligible patients were aged 18 years or older with symptomatic ischemic heart disease undergoing elective, clinically indicated percutaneous recanalization of a de novo occlusive coronary lesion exhibiting Thrombolysis in Myocardial Infarction (TIMI) grade 0 or 1 flow and estimated to be at least 3 months duration by clinical history and/or comparison with a prior angiogram or electrocardiography. Consented patients were considered enrolled upon advancement of a study device within the guide catheter. Angiographic exclusion criteria were in-stent total occlusions, proximal disease (> 75% stenosis) that cannot be treated with a stent that also is intended for the target CTO lesion, and extensive lesion-related thrombus. Principal clinical exclusion criteria were recent (< 72 h) myocardial infarction (MI), prior interventional procedure of any kind within 30 days of the index procedure or any general contraindication to the revascularization procedure and routine pharmacologic therapies. There were no restrictions regarding ejection fraction, lesion length, or treatment strategy (e.g., antegrade, retrograde, wire escalation, or dissection re-entry technique). The study was approved by the institutional review board at each site.

### 2.2 | Device description and interventional procedure

The investigational devices used in this study included guidewires, microcatheters, and guide catheter extensions. Per protocol, use of at least one study guidewire and microcatheter was mandated, and utilization of a guide extension catheter was permitted according to operator discretion. Study guidewires included Spectre (nitinol and stainless steel), Raider (stainless steel, polymer jacket), Warrior (stainless steel, 0.009 inch diameter tapered distal tip), Bandit (stainless steel, polymer jacket, 0.008 inch diameter tapered distal tip), and R350 (externalization guidewire). The investigational microcatheters were Turnpike, Turnpike LP, Turnpike Spiral, and Turnpike Gold. Details regarding guidewire dimensions, construction and tip load and microcatheter design are provided in the Appendix. Rapid-exchange guide extensions evaluated in the study were the GuideLiner and

TrapLiner catheters (Appendix). The TrapLiner catheter incorporates a trapping balloon on the distal end of the pushrod to facilitate device exchange over a guidewire. The intended purposes of the study guidewires, microcatheters and guide catheter extensions are summarized in Table 1.

Procedural methods and technique were performed according to the investigator's discretion. Specifically, there were no protocol criteria related to procedural methods other than exclusion of planned target lesion treatment with a device other than balloon angioplasty and stent placement after successful guidewire crossing (i.e., planned use of atherectomy was excluded). Prior to PCI, all patients received treatment with aspirin (100–325 mg) and either clopidogrel, ticagrelor, or prasugrel per investigator discretion. For patients not receiving chronic P<sub>2</sub>Y<sub>12</sub> receptor or ADP receptor antagonist therapy, a loading dose was administered according to individual product labeling. Dual anti-platelet therapy was prescribed per investigator discretion. Procedural anticoagulation with unfractionated heparin was recommended to achieve an activated clotting time >250 s, and treatment with a glycoprotein IIb/IIIa inhibitor was discouraged. All lesions were treated with commercially available drug-eluting stents.

### 2.3 | Study endpoints and definitions

The primary endpoint was procedural success, defined as angiographic confirmation of CTO crossing and guidewire placement in the target vessel true lumen and absence of in-hospital cardiac death, MI or repeat target lesion revascularization (major adverse cardiac events, MACE) among patients undergoing attempted CTO revascularization. As a primary analysis, the primary endpoint was compared with a performance goal established from pooled analysis of five studies reporting procedural success in CTO PCI.<sup>7–11</sup> Although an investigational guidewire and microcatheter must have been used during attempted crossing of the CTO, use of additional guidewires were permitted.

Additional secondary endpoints included the individual components of the composite clinical endpoint through hospital discharge in addition to technical success (i.e., successful guidewire recanalization), procedural success according to crossing technique and measures of resource utilization. Clinical events were assessed during hospital stay until discharge. Cardiac death was considered as any fatal event not attributable to a non-cardiac cause. Myocardial infarction was determined per Academic Research Consortium definition criteria<sup>12</sup> and consistent with a predicate CTO registration study.<sup>7</sup> Peri-procedural myocardial infarction was defined as an increase in creatine kinase MB fraction ≥ 3 times upper normal limit within 48 h of the index procedure. Clinically significant coronary perforation was defined as any perforation requiring intervention (e.g., prolonged balloon occlusion, pericardiocentesis, stent graft, or comparable therapy) and/or resulting in hemodynamic compromise. An independent clinical events committee adjudicated all adverse events, and study conduct was supervised by an independent data safety monitoring committee. All baseline and any additional follow-up angiograms during the study

**TABLE 1** Study devices and general purpose

| Study device    | Category        | Purpose  |
|-----------------|-----------------|--|
| GuideLiner      | Guide extension | Use in conjunction with guide catheters to facilitate deliverability and placement of interventional devices; provide device/catheter support; facilitate retrograde wire re-entry   |
| TrapLiner       | Guide extension | Same purposes as GuideLiner but has an inflatable balloon on the distal shaft to facilitate the exchange of interventional devices while maintaining the position of a guidewire within the vasculature  |
| Turnpike        | Microcatheter   | Used to access discrete regions of the coronary artery anatomy; increase guidewire crossing penetrability; traverse collateral channels; facilitate placement and exchange of guidewires; and infuse/deliver diagnostic and therapeutic agents |
| Turnpike LP     | Microcatheter   | Same purposes as Turnpike but has a lower profile and increased flexibility  |
| Turnpike Spiral | Microcatheter   | Same purposes as Turnpike but has an added outer coil on the distal shaft for additional rotational advancement  |
| Turnpike Gold   | Microcatheter   | Same purposes as Turnpike but with an added outer coil on the distal shaft and a gold-plated stainless steel, threaded distal tip for additional rotational advancement in resistant lesions   |
| Spectre         | Guidewire       | 0.014" all-purpose, workhorse guidewire  |
| Raider          | Guidewire       | 0.014" polymer-jacketed guidewire to facilitate penetration of fibrous and calcified proximal cap disease, navigation through microchannels or subintimal planes and luminal re-entry; tip load 4 gm   |
| Warrior         | Guidewire       | 0.014" guidewire with 0.009" diameter tapered distal tip with hydrophilic coating; penetration guidewire with 14 gm tip load   |
| Bandit          | Guidewire       | 0.014" with a 0.008" diameter tapered distal tip; polymer jacketed guidewire with 0.8 gm tip load; first escalation guidewire or knuckle wire subintimal tracking  |
| R350            | Guidewire       | 350 cm 0.013" externalization guidewire for retrograde procedures  |

period were reviewed by an independent angiographic core laboratory.

## 2.4 | Statistical methods

All primary and secondary efficacy and safety endpoints were performed in the intention-to-treat population. Baseline characteristics of study patients were summarized in terms of frequencies and percentages for categorical variables and by means with standard deviations (SD) for continuous variables. Categorical variables were compared by Chi-Square or Fisher's exact test.

The primary endpoint was tested using a performance goal for procedure success, defined as successful guidewire recanalization and the absence of in-hospital MACE. The estimate of 73.2% for the procedure success endpoint is derived from five historical trials.<sup>7–11</sup> Incorporating a 10% statistical delta for hypothesis testing purposes, the performance goal for the primary endpoint was therefore 63.2%. With a one-sided type I error rate of 0.05% and 80% statistical power, a sample size of 135 evaluable patients was required to assess the performance goal. Secondary efficacy and safety variables were summarized in terms of frequencies and percentages for categorical variables and by means with standard deviations for continuous variables.

All analyses were performed with SAS software (version 9.4, SAS Institute, Cary, NC), R (version 3.2) or other widely accepted statistical or graphical software.

## 3 | RESULTS

### 3.1 | Patient enrollment and characteristics

Baseline clinical and angiographic characteristics are summarized in Table 2. Among 150 enrolled patients, the prevalence of diabetes was 32.7%; prior MI was documented in 48.0% of patients; and more than half of patients were characterized as class III/IV angina. Most patients underwent previous coronary revascularization (prior coronary artery bypass surgery, 32.7%; prior PCI, 51.3%). The average (mean  $\pm$  SD) occlusion length was  $46.9 \pm 20.5$  mm, and average Japan CTO (J-CTO) score was  $1.9 \pm 0.9$ . More than half of the target lesions (56.7%) were located in the right coronary artery, and moderate/severe calcification was identified in nearly all cases (94.7%).

### 3.2 | Procedural and clinical outcomes

Technical success was observed in 94.7% (142/150) of cases, and in-hospital MACE occurred in 19.3% (29/150) of patients (Tables 3 and 4). Procedure success was therefore achieved in 75.3% (113/150) of patients. Final TIMI grade III and II flow was achieved in 89.3% and 4.0% of cases, respectively. Final TIMI grade III flow and a percent residual stenosis  $< 30\%$  was observed in 80.0% of cases (120/150). Compared with the guidewire performance goal endpoint of 63.2%

**TABLE 2** Baseline patient clinical and angiographic characteristics

|                                      | N = 150         |
|--------------------------------------|-----------------|
| <b>Clinical characteristics</b>      |                 |
| Age (years)                          | $65.4 \pm 10.8$ |
| Male gender                          | 84.7 (127)      |
| Diabetes mellitus                    | 32.7 (49)       |
| Hypertension                         | 91.3 (137)      |
| Hyperlipidemia                       | 96.7 (145)      |
| Prior myocardial infarction          | 48.0 (72)       |
| Angina class III/IV                  | 56.0 (84)       |
| Heart failure class III/IV           | 8.0 (12)        |
| Prior percutaneous revascularization | 51.3 (77)       |
| Prior coronary bypass surgery        | 32.7 (49)       |
| Prior stroke/TIA                     | 4.7 (7)         |
| <b>Angiographic characteristics</b>  |                 |
| Target vessel                        |                 |
| Left main                            | 1.3 (2)         |
| Left anterior descending artery      | 22.7 (34)       |
| Right coronary artery                | 63.2            |
| Left circumflex artery               | 19.3 (29)       |
| TIMI 0 flow                          | 99.3 (149)      |
| Moderate/severe calcification        | 94.7 (142)      |
| Side branch involvement              | 36.0 (54)       |
| Reference vessel diameter (mm)       | $2.99 \pm 0.56$ |
| Occlusion length (mm)                | $46.9 \pm 20.5$ |
| J CTO Score                          | $1.9 \pm 0.9$   |
| J CTO Score $\geq 3$                 | 24.0 (36)       |
| <b>Collateral circulation</b>        |                 |
| Ipsilateral                          | 24.0 (36)       |
| Contralateral                        | 62.0 (93)       |
| Bridging                             | 14.0 (21)       |

Note: Values expressed as mean  $\pm$  SD or percent (N). Angina and heart failure severity according to Canadian Cardiovascular Society and New York Heart Association classification, respectively. TIMI denotes Thrombolysis in Myocardial Infarction; J CTO, Japanese Chronic Total Occlusion; TIA, transient ischemic attack.

for procedural success, the study primary endpoint was met (lower one-sided 95% confidence interval [CI] boundary 68.9%,  $P = 0.001$ ). Among patients with in-hospital adverse events, cardiac death occurred in 1 patient (0.7%), and rates of MI and target lesion revascularization were 18.0% and 0.7%, respectively (Table 4). All MI events were peri-procedural (i.e., no spontaneous events), and MI defined as CK MB  $> 10$  times upper normal limit occurred in 6.0% of patients. As a prespecified analysis by this modified MI definition, in-hospital MACE and procedural success rates were 7.3% and 87.3%, respectively. No major adverse events were reported from hospital discharge through 30 days.

Coronary perforation was characterized according to both angiographic criteria<sup>13</sup> and protocol definition. Among 21 angiographically

**TABLE 3** Procedural results

|   | N = 150      |
|---|--------------|
| Vascular access                                 |              |
| Femoral   | 41.3 (62)    |
| Radial  | 8.7 (13)     |
| Femoral and radial                              | 50.0 (75)    |
| Stent length (mm)                               | 61.7 ± 23.6  |
| Final TIMI 3 flow                               | 89.3 (134)   |
| Clinically significant perforation <sup>a</sup> | 10.7 (16)    |
| Procedure time (minutes)                        | 149.0 ± 90.9 |
| Contrast volume (mL)                            | 205.2 ± 94.8 |
| Radiation dose (mGy)                            | 2220 ± 1608  |
| Procedural success                              | 75.3 (113)   |
| Technical success                               | 94.7 (142)   |
| Procedural success by crossing strategy         |              |
| Antegrade                                       | 85.2 (69/81) |
| Retrograde                                      | 50.0 (1/2)   |
| Combined antegrade and retrograde               | 64.2 (43/67) |

Note: Values expressed as percent (N) or mean ± SD.

<sup>a</sup>Clinically significant perforation defined as any perforation resulting in hemodynamic instability and/or requiring intervention.

**TABLE 4** In-hospital clinical outcomes

|                                 | N = 150   |
|---------------------------------|-----------|
| Death                           | 0.7 (1)   |
| Cardiac Death                   | 0.7 (1)   |
| MI                              |           |
| CK MB ≥3X ULN                   | 18.0 (27) |
| CK MB ≥10X ULN                  | 6.0 (9)   |
| Target lesion revascularization | 0.7 (1)   |
| MACE <sup>a</sup>               |           |
| Using CK MB ≥3X ULN             | 19.3 (29) |
| Using CK MB ≥10X ULN            | 7.3 (11)  |

Note: Values expressed as percent (N).

<sup>a</sup>Major adverse cardiac events (MACE) included myocardial infarction (MI) defined as creatine kinase myocardial band (CK MB) ≥3X upper limit of normal (ULN) as the primary analysis.

determined perforations, 10 and 8 events were classified as type II and III, respectively. Clinically significant coronary perforation occurred in 16 (10.7%) patients (Table 2). Among these cases, 10 events were adjudicated as unrelated to a study device. Covered stent implantation and/or pericardiocentesis was performed in eight cases, and the remaining cases were resolved with prolonged balloon occlusion and one instance of vessel branch embolization. Despite the occurrence of perforation, technical success was achieved in 12/16 (75.0%) cases, yet procedural success was reported for 5/16 (31.3%) patients. For the one episode of cardiac death, coronary perforation occurred followed by covered stent placement and subacute stent thrombosis.

A total of 1022 guidewires were reported to facilitate or cross the CTO: 566 study guidewires (55.4%) and 456 non-study guidewires (44.6%). The mean number of  $4.8 \pm 2.8$  study guidewires were used per subject, and a mean number of  $5.1 \pm 3.3$  all guidewires (study devices and non-study devices) were used per subject. Reasons for non-study guidewires cited were crossing difficulty and physician preference. Overall, Spectre was used in 86.0% of patients; Raider guidewire, 68.0%; Bandit guidewire, 45.3%; Warrior guidewire, 23.3%; and R350 guidewire 26.0%. Study guidewires were the final crossing guidewire in 60 subjects (40%), most commonly using the Raider guidewire in 18% of subjects.

A Turnpike microcatheter was used in all cases (Turnpike standard, 22.0%; Turnpike LP, 56.7%; Spiral, 62.7%; Gold, 0.7%), and the GuideLiner and TrapLiner guide extensions were utilized in 16.0% and 55.3% of cases, respectively.

Regarding procedural method, 54.0% of procedures employed antegrade only crossing techniques; 44.7% applied combined antegrade and retrograde techniques; and 1.3% involved retrograde crossing only. Reverse controlled antegrade-retrograde subintimal tracking (CART) represented 14.0% of procedures, and antegrade dissection/re-entry with StingRay catheters occurred in 11.3% of cases. Among retrograde cases, an antegrade guide catheter extension was used in 12 subjects. Procedural success by method is listed in Table 3. Technical success for antegrade only methods was 95.1% (77/81 cases); for retrograde only methods, 100.0% (2/2 cases); and for combined antegrade/retrograde methods, 94.0% (63/67 cases). Major adverse cardiac events during hospitalization were more common among procedures involving a retrograde strategy compared with antegrade-only procedures (30.4% [21/69] versus 9.9% [8/81],  $P = 0.002$ ), a difference driven by protocol-defined MI (retrograde 29.0% [20/69], versus antegrade 86% [7/81],  $P = 0.0014$ ). Using a modified definition of MI defined as CK MB >10 times upper normal limit, no significant differences were observed between antegrade and retrograde procedures (retrograde 8.7% [6/69], versus antegrade 3.7% [3/81],  $P = 0.30$ ).

The mean total procedure time was  $149 \pm 91$  min. The average contrast volume per procedure was  $205 \pm 95$  mL, and the mean radiation dose was  $2220 \pm 1608$  mGy.

## 4 | DISCUSSION

In a registration study evaluating specialized guidewires, microcatheters and guide catheter extensions for CTO PCI, successful guidewire recanalization was achieved in 94.7% of patients, and overall procedural success per protocol definition was 73.5%, achieving statistical significance compared with a prespecified performance goal established from pooled analysis of prior studies reporting procedural success in CTO PCI. Despite a high coronary perforation rate similar to other contemporary CTO studies,<sup>7,14,15</sup> in-hospital major adverse events were principally related to periprocedural biomarker elevation. Altogether, these results inform both CTO procedural strategy applying contemporary technique and devices but also the opportunity for advancement of procedural safety.



Despite remarkable progress in complex percutaneous revascularization, chronically occluded coronary arteries represent a persistent challenge regarding patient selection, interventional technique and likelihood of procedural success. For more than a decade—and despite increasing performance of attempted CTO PCI—advances in procedural success have been limited, and measurable improvement in safety has been offset by increasing case complexity. In part highlighting the variability in operator experience, case selection and availability of advanced device technology, procedural success rates have ranged from 60% to more than 90%<sup>1,16–18</sup> among contemporary series. In the present study with limited clinical and angiographic exclusion criteria, PCI employing advanced guidewire technique and procedural strategy resulted in a guidewire crossing rate that exceeds historical standards. Equally remarkable is the use of procedural strategies in which these CTO-specific technologies were applied, including a very high prevalence of retrograde procedures representing approximately one-half of cases. The favorable success rates achieved despite extensive lesion length, severe calcification and a high prevalence of prior coronary bypass surgery challenge historical perception that successful guidewire crossing is inversely related to lesion complexity.

Reflecting the complexity of both anatomy and procedural strategy, performance of CTO PCI defines the need for an “interventional toolbox” that features an array of enabling device technologies. Because coronary guidewires vary in numerous ways that affect device performance and procedural outcomes, the dedicated purpose of a CTO-specific guidewire may be to penetrate the proximal cap occlusion, navigate collateral channels, facilitate subintimal tracking, or enable true lumen re-entry (Table 1). Representative of both the technical complexity and intended design, an average ( $\pm$ SD) of  $4.8 \pm 2.8$  study guidewires were used per case in the present study. As an additional enabling technology, at least one microcatheter was utilized in all study procedures, and similar to guidewires, the microcatheter designs have been further modified to match a specific objective such as navigation through tortuous or small caliber collateral channels or crossing through calcified, resistant occlusive plaque (Table 1). Guide catheter extensions provide not only advanced support for guidewire crossing but also enable device delivery and exchange, and in some instances facilitate retrograde guidewire recanalization (Table 1).<sup>19</sup> As a unique guide extension design, the TrapLiner device also enables device exchange over a 180–190 cm guidewire without the need for guidewire exchange, guidewire extension or introduction of an additional trapping angioplasty balloon within the guiding catheter.

Despite a high rate of technical success in the present study, the lower procedural success rate was principally driven by the incidence of protocol-defined peri-procedural MI. In previous reports, rates of procedural-related MI have ranged from 8.6% to 18.3% when applying similar criteria.<sup>7,20–22</sup> However, comparison of MI rates (and therefore also procedural success) with most CTO observational studies should be done with caution given the absence of protocol-mandated, systematic biomarker ascertainment, and subsequent underreporting of procedural-related events. Importantly, all MI events in the current study were related to peri-procedural

biomarker elevation and were not associated with clinically manifest events from discharge through 30-day follow-up. The MI rate may also have been influenced by a high prevalence of retrograde procedures that have been associated with increased procedural-related adverse events.<sup>16,20,23,24</sup> Criteria for MI in CTO trials have been proposed,<sup>25,26</sup> and protocol-specific definitions of MI may substantially influence event rates, as in this trial example. As a prespecified analysis, when measured by an alternative Society of Coronary Angiography and Interventions definition of peri-procedural MI,<sup>27</sup> the in-hospital MACE and procedural success rates were 7.3% and 87.3%, respectively.

The incidence of coronary perforation is representative of CTO lesion complexity, high-risk procedural technique and the specialized design of guidewires. By similar criteria, clinically significant coronary perforation was reported in 8.0%, 5.2%, and 4.3% of procedures in the Asahi CTO, PERSPECTIVE, and OPEN CTO studies, respectively.<sup>7,14,15</sup> In the present study, among 16 (10.7%) clinically significant perforations that required intervention and/or resulted in hemodynamic instability, eight cases required covered stent implantation and/or pericardiocentesis, and one event death occurred following covered stent thrombosis. Although successful guidewire crossing of the CTO was successful in 75.0% of these cases, the occurrence of procedural success was considerably lower compared to cases without significant perforation (31.3% vs. 80.0%,  $P = 0.0003$ ) related to a higher incidence of major adverse events. These observations underscore the need not only for operator proficiency in achieving vessel patency but also regarding skillsets for complication management. The persistently high rate of coronary perforation and its association with both early and late adverse outcome<sup>28,29</sup> temper the advancement of technical and procedural success and inform the need to refine strategies that promote procedural safety.

A limitation of this study is that as a non-randomized design, measured, or unmeasured confounders may have influenced the comparison of outcomes with a performance goal derived from a pooled analysis of prior CTO trials reporting procedural outcomes. In addition, the systematic ascertainment of peri-procedural biomarkers for all patients and a more conservative definition of MI applied in this study limits comparison with historical studies but would be expected to bias against the present study results. As a registration trial with FDA oversight, this definition was required to maintain comparability with previous studies evaluating CTO-specific technologies.<sup>7,8</sup> Also, as a study intended to evaluate the utility and effectiveness of guidewire and catheter technologies, clinical follow-up was also limited to 30 days, thereby limiting insight to late-term outcomes that may be related to early procedural failure or complications.<sup>29,30</sup> Finally, these results were observed among centers identified with expertise in CTO PCI and therefore may not be generalizable to a broader, less selected group of interventional operators.

## 5 | CONCLUSION

Complementing the evolution of procedural technique and strategy in CTO PCI, the advancement of dedicated guidewire and catheter



technologies enable the highest observed success rates compared with historical studies. In a prospective, multicenter registration study, a high level of technical and procedural success was achieved despite considerable lesion complexity through application of antegrade and retrograde guidewire maneuvers and with acceptable safety, yet with comparably higher risk than conventional non-CTO PCI. Altogether, these results inform procedural technique and strategy using CTO-specific guidewires, extension catheters and microcatheters with applied contemporary methods.

### CONFLICT OF INTEREST

Dr. Kandzari reports institutional research and educational grant support from Abbott Vascular, Biotronik, Boston Scientific, Cardiovascular Systems, Inc., Medtronic CardioVascular, Orbus Neich, and Teleflex; personal consulting honoraria from Cardiovascular Systems and Medtronic; and equity, Traverse Vascular. Dr. Alaswad reports institutional research and educational grant support from Boston Scientific, and Abiomed, and personal consulting honoraria from Cardiovascular Systems, Inc., Boston Scientific, Livanova, and Teleflex; Dr. Jaffer reports sponsored research from Canon, Siemens, Teleflex, Shockwave, and Boston Scientific; consultant for Boston Scientific, Abbott Vascular, Siemens, Magenta Medical, Asahi Intecc and IMDS; equity in Intravascular Imaging, Inc. and DurVena.; Dr. Brilakis reports consulting/speaker honoraria from Abbott Vascular, American Heart Association (associate editor *Circulation*), Amgen, Asahi Intecc, Biotronik, Boston Scientific, Cardiovascular Innovations Foundation (Board of Directors), ControlRad, CSI, Elsevier, GE Healthcare, IMDS, InfraRedx, Medtronic, Medtronic, Opsens, Siemens, and Teleflex; owner, Hippocrates LLC; equity, MHI Ventures, Cleerly Health; Dr. Croce reports grant/research support from Abbott, Takeda, Teleflex, CSI; consulting honoraria from Abbott, BSCI, Biotronik, Philips, Abiomed, CSI, Takada, Cordis; equity, Dyad Medical; Dr. Kearney reports Consulting/Advisory board/honoraria from Abbott, Abiomed, Boston Scientific, CSI, Medtronic and Teleflex; Dr. Spaedy reports clinical research support from Teleflex and Abbott Vascular; consulting honoraria from Abbott Vascular, Boston Scientific, and Medtronic; Dr. Yeh reports institutional research grant support from Abbott Vascular, AstraZeneca, BD Bard, Boston Scientific, Cook Medical, Medtronic and Philips Medical, and personal consulting honoraria from Abbott Vascular, AstraZeneca, Boston Scientific, Elixir Medical, Medtronic, Shockwave Medical and Zoll; Dr. Thompson reports no related conflicts of interest; Dr. Nicholson reports consulting and proctoring honoraria from Boston Scientific, Medtronic, Abbott Vascular, Rampart; intellectual property/founder, Traverse Vascular; Dr. Wyman reports consulting honoraria from Boston Scientific, Abbott Vascular, Asahi. Dr. Riley reports honoraria from Boston Scientific, Shockwave Medical, Medtronic, and Asahi Intecc.; Dr. Lansky reports no related conflicts of interest; Dr. Buller is an employee of Teleflex, Inc.; Dr. Karpaliotis reports honoraria from Boston Scientific, Abbott Vascular; equity, Saranas, Soundbite and Traverse Vascular.

### ACKNOWLEDGEMENT

Study support provided by Vascular Solutions LLC, a subsidiary of Teleflex, Inc., Minneapolis, MN.

### DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from Vascular Solutions LLC, a subsidiary of Teleflex, Inc. Restrictions apply to the availability of these data, which were used under license for this study. Data are available with the permission of Vascular Solutions, LLC.

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## SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

**How to cite this article:** Kandzari DE, Alaswad K, Jaffer FA, Brilakis E, Croce K, Kearney K, et al. Safety and efficacy of dedicated guidewire, microcatheter, and guide catheter extension technologies for chronic total coronary occlusion revascularization: Primary results of the Teleflex Chronic Total Occlusion Study. *Catheter Cardiovasc Interv*. 2021;1-8. <https://doi.org/10.1002/ccd.29962>