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Procedural and longer-term outcomes of wire- versus device-based antegrade dissection and re-entry techniques for the percutaneous revascularization of coronary chronic total occlusions☆

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ABSTRACT

Background: There are few data regarding the procedural and follow-up outcomes of different antegrade dissection/re-entry (ADR) techniques for chronic total occlusion (CTO) percutaneous coronary intervention (PCI).
Methods: We compiled a multicenter registry of consecutive patients undergoing ADR-based CTO PCI at four high-volume specialized institutions. Patients were divided according to the specific ADR technique used: subintimal tracking and re-entry (STAR), limited antegrade subintimal tracking (LAST), or device-based with the CrossBoss/Stingray system (Boston Scientific, Marlborough, MA). Major adverse cardiac events (MACE: cardiac death, target-vessel myocardial infarction and target-vessel revascularization) on follow-up were the main outcome of this study. Independent predictors of MACE were sought with Cox regression analysis.
Results: A total of 223 patients were included (STAR $n = 39$, LAST $n = 68$, CrossBoss/Stingray $n = 116$). Baseline characteristics were similar across groups. Technical and procedural success was lower with STAR (59% and 59%), as compared with LAST (96% and 96%) and CrossBoss/Stingray (89% and 87%; $p < 0.001$ for both). At 24-month follow-up, MACE rates were higher in STAR (15.4%) and LAST (17.5%), as compared with device-based ADR with CrossBoss/Stingray (4.3%, $p = 0.02$), driven by TVR (7.7% vs. 15.5% vs. 3.1%, respectively; $p = 0.02$). Multivariable Cox regression analysis identified wire-based ADR (STAR and LAST) and total stent length as independent predictors of MACE.
Conclusions: In this multicenter cohort of patients undergoing CTO PCI with ADR techniques, STAR had lower success rates, as compared with the CrossBoss/Stingray system and LAST. The CrossBoss/Stingray system was independently associated with lower risk of MACE on follow-up, as compared with wire-based ADR techniques.

1. Introduction

The development and widespread adoption of dissection/re-entry (DR) techniques have promoted a marked increase in success rates of chronic total occlusion (CTO) percutaneous coronary intervention (PCI) [1]. Such techniques allow crossing of long and anatomically-complex occlusions. In particular, antegrade DR (ADR) is the preferred initial crossing strategy for long occlusions, with an unambiguous proximal cap and good-quality distal vessel [2].

Few studies specifically focused on ADR for CTO PCI, reporting similar outcomes as compared with antegrade wire escalation and the retrograde approach [3,4]. However, no comparison of the procedural and follow-up outcomes has been made according to the specific ADR technique used. The aim of the present study is to answer this important clinical question.

2. Methods

2.1. Patient population

This multicenter registry included all consecutive patients who underwent ADR-based CTO PCI at four participating hybrid CTO PCI programs (San Raffaele Hospital,

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Milan, Italy; Quebec Heart and Lung Institute, Quebec City, QC, Canada; VA North Texas Healthcare System, Dallas, TX, USA; Reina Sofia Hospital, Cordoba, Spain) between January 2010 and May 2016. Analyses were performed according to the specific ADR crossing strategy used (see next section). All procedures were indicated according to the presence of symptoms of angina, ischemia or both, and were performed electively after careful planning [1]. Baseline, procedural and hospitalization data were recorded. Follow-up was performed with phone calls, review of hospital records or outpatient visits. Informed consent was obtained from each patient and the study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki, as reflected in a priori approval by the institution's human research committee.

2.2. Definitions

CTO was defined as a 100% stenosis with antegrade Thrombolysis In Myocardial Infarction (TIMI) 0 flow for at least 3 months [5]. The J-CTO score [6] and the PROGRESS-CTO score [7] were calculated for all lesions.

ADR techniques included both wire- and device-based approaches. Wire-based techniques were: 1) subintimal tracking and re-entry (STAR) [8] (including mini-STAR [9] and contrast-guided STAR [10]); and 2) limited antegrade subintimal tracking (LAST) [11]. Device-facilitated techniques were represented by the use of the CrossBoss/Stingray system (Boston Scientific, Marlborough, MA).

DR success was defined as CTO crossing through a subadventitial plane followed by re-entry into the true lumen. Technical success was defined as an antegrade TIMI 3 flow in the CTO target vessel with a residual stenosis <30% [5]. Procedural success was defined as technical success in the absence of in-hospital adverse events (all-cause death, Q-wave myocardial infarction [MI], stroke, recurrent angina requiring target-vessel revascularization [TVR] with PCI or coronary artery bypass graft, tamponade requiring pericardiocentesis or surgery) [5].

Major adverse cardiac events (MACE) on follow-up were defined as the composite of cardiac death, target-vessel MI (Q-wave and non-Q-wave) and ischemia-driven TVR.

2.3. Statistical analysis

Continuous variables are presented as mean ± standard deviation and ANOVA was used for comparisons. Categorical variables are presented as frequency (percentages), and compared using chi-square test.

Procedural outcomes were assessed in all patients undergoing ADR-based CTO PCI during the study period. To avoid confounding in the assessment of outcomes on follow-up, these were assessed only in subjects who underwent successful CTO recanalization, since it is known that patients with unsuccessful revascularization suffer a higher incidence of adverse events [12,13]. Kaplan-Meier curves of survival free from MACE according to the specific ADR technique used were plotted and compared using the log-rank test.

Multivariable Cox regression analysis with backwards-stepwise selection method (p-entry = 0.05, p-exit = 0.05) was used to identify independent predictors of MACE during follow-up. Candidate variables were selected among those showing a $p < 0.10$ in univariate analyses, as well as based on clinical judgment. The results of such analysis are presented as hazard ratios (HR) and 95% confidence intervals (CI).

For all tests, a $p < 0.05$ was considered significant. Statistical analysis was performed using SPSS 24 (IBM Corp., Armonk, NY).

3. Results

3.1. Clinical and angiographic characteristics

A total of 1160 patients underwent CTO PCI at the four participating centers during the study period. Of those, 223 patients (19.2%) were treated with ADR techniques: $n = 116$ (52.0%) with the CrossBoss/Stingray system, $n = 39$ (17.5%) with STAR and $n = 68$ (30.5%) with LAST. Baseline characteristics were balanced across groups (Table 1). In particular, demographics, prevalence of diabetes, and left ventricular and renal function were similar across groups. CrossBoss/Stingray patients had a higher prevalence of dyslipidemia, as compared with the other two groups (95%; $p < 0.001$). The LAST group had a lower proportion of hypertensive patients (66%; $p = 0.03$). Although the most prevalent indication of CTO PCI was angina in all groups (50–77%), silent ischemia was observed more frequently in STAR patients (32%), and acute coronary syndrome in the LAST group (22%; $p = 0.005$).

3.2. Angiographic and procedural characteristics

Angiographic and procedural data are presented in Table 2. LAST patients had the highest burden of coronary artery disease, as compared with CrossBoss/Stingray and STAR (2.0 ± 0.8 vs. 1.8 ± 0.8 vs. 1.6 ± 0.8 diseased vessels, respectively; $p = 0.05$). The right coronary artery (RCA) was the most frequently treated vessel in CrossBoss/Stingray and STAR groups, while in LAST patients the proportions of RCA and circumflex CTO PCI were similar. CrossBoss/Stingray patients had the highest occlusion complexity, as assessed with the J-CTO score, compared with STAR and LAST (2.5 ± 1.2 vs. 2.0 ± 1.2 vs. 2.1 ± 1.2, respectively; $p = 0.03$). Drug-eluting stents were the most frequently implanted stents in all groups; bioresorbable scaffolds were implanted in 16% of LAST cases ($p < 0.001$). Total stent length was highest in the CrossBoss/Stingray group and lowest in STAR ($p = 0.04$). Fluoroscopy and total procedural time were shorter in STAR, as compared with the other groups. There were no differences in the incidence of procedural complications (five perforations with need for intervention and one stroke). However, DR ($p = 0.002$), technical ($p < 0.001$) and procedural ($p < 0.001$) success rates were lower in STAR (77%, 59% and 59%), as compared with CrossBoss/Stingray (94%, 89% and 87%) and LAST (96%, 96% and 96%).

3.3. Clinical outcomes on follow-up

Median follow-up was 388 (interquartile range 234–613) days. Fig. 1 shows clinical outcomes at 24-month follow-up. MACE rates were higher in STAR (15.4%) and LAST (17.5%), as compared with CrossBoss/Stingray (4.3%; $p = 0.02$), driven by TVR (7.7% vs. 15.5% vs. 3.1%, respectively; $p = 0.02$). Accordingly, MACE rates were higher in wire-based ADR techniques as a whole, when compared with CrossBoss/Stingray (16.9% vs. 4.3%, $p = 0.006$), driven by higher TVR (13.1% vs. 3.1%, $p = 0.01$).

Kaplan-Meier curves also indicated that CrossBoss/Stingray was associated with significantly lower risk of MACE, when compared with STAR and LAST (analyzed both separately [$p = 0.03$] or together [$p = 0.02$; Fig. 2]).

3.4. Independent predictors of MACE

Supplementary Tables 1 and 2 show the multivariable analysis for the prediction of MACE. After adjustment with several models, only total stent length (HR ≥ 1.16 for each 10-mm increment, $p \leq 0.004$ for all) and crossing technique remained associated with MACE. In particular, both STAR (HR ≥ 5.31, $p \leq 0.05$ for all) and LAST (HR ≥ 7.76, $p \leq 0.003$ for all) were independent predictors of MACE, as compared with the CrossBoss/Stingray system. When wire-based DR techniques were analyzed together, similar results were obtained.

4. Discussion

The main findings of our study are: 1) in the setting of CTO PCI treated with ADR techniques, STAR has lower success rates, as compared with CrossBoss/Stingray and LAST; and 2) a device-based approach to ADR (CrossBoss/Stingray system) is independently associated with lower risk of MACE on follow-up, as compared with wire-based techniques (STAR and LAST).

Introduced in 2005 by Colombo et al., STAR was the first ADR technique [8]. In STAR, a subadventitial cleavage plane is created by advancing a knuckled polymer-jacketed guidewire to allow a blunt dissection between the anatomical planes of the vessel, with the aim to achieve re-entry into the distal true lumen. It represented a remarkable advance in the field of CTO PCI since it allowed the recanalization of long, tortuous and ambiguous occlusions, which had a low likelihood of success using a conventional wire escalation approach. In contrast-guided STAR [14], contrast injection delineates the vessel contour and also sometimes creates a fenestration towards the true lumen, thus facilitating re-entry. Mini-STAR [9] takes advantage of the higher maneuverability of the Fielder wire family (Asahi Intecc, Nagoya, Japan) to facilitate earlier and easier re-entry. However, both the original STAR technique and its successive iterations showed high rates of restenosis (25–54%) on follow-up [8,9,14]. This can be explained with the poor

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