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Efficient distal tip size of primary guidewire for antegrade percutaneous coronary intervention in chronic total occlusion: The G-FORCE study

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ABSTRACT

Background: Although several new techniques have been introduced for CTO such as the retrograde approach, the fundamental question of what type of guidewire is the most appropriate as a primary guidewire in the antegrade approach has not been answered.
Methods: The G-FORCE study was designed as a prospective multicenter randomized controlled trial to determine the efficient primary guidewire in antegrade approach for chronic total occlusion (CTO). The first guidewire was randomly assigned to a regular size distal tip group (0.014 in. size) or tapered tip group (0.010 in. or less). The primary endpoint was defined as successful lesion penetration by the first guidewire into distal true lumen. This study was registered at ClinicalTrials.gov with identifier NCT00987610.
Results: A total of 260 patients were enrolled, with an average age of 66 ± 11 years and 16% were female. The average J-CTO score was 1.8 ± 1.1. The primary endpoint was achieved in 38% and 32% of patients using tapered and regular distal tip guidewires, respectively ($P = 0.80$). The final PCI success rate was 81% vs. 85%, respectively ($P = 0.57$). Easy CTO lesions with a J-CTO score = 0 exhibited a primary endpoint significantly different between tapered and regular distal tip primary guidewires (79% vs. 40%; $P = 0.046$). Guidewire distal coating or distal tip load did not relate with primary guidewire success rate.
Conclusion: Tapered and regular distal tip guidewires are equivalent as a first choice for CTO. Tapered guidewires are superior for CTO lesions with a J-CTO score = 0.

1. Introduction

Although percutaneous coronary intervention (PCI) for chronic total occlusion (CTO) is technically challenging, prognoses and left ventricular function have improved in successful cases [1] and long-term results enhanced with the use of second generation drug-eluting stents [2]. A great challenge is the passage of the guidewire [3] even with a variety of new methods, including new types of guidewires, a parallel wire technique and a retrograde approach. However, the fundamental question of what type of guidewire is the most appropriate as a primary guidewire has not been answered. Tapered guidewires and 0.010 in., slender guidewires have recently been reported to be useful for CTO lesions [4,5]. A small distal tip may also be advantageous for microchannel tracking inside a CTO lesion. In this study, patients were prospectively randomized into groups using either tapered (0.010 in. or less) or

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standard (0.014 in.) distal tip guidewires in order to determine the most appropriate first-choice guidewire size for CTO PCI.

2. Methods

2.1. Study design

The G-FORCE study was a prospective multicenter randomized controlled trial to determine the most efficient distal tip size for first-choice guidewires in CTO PCI. The first guidewire was randomly assigned to a regular (distal tip size 0.014 in.) or tapered tip group (distal tip size 0.010 in. or less). A computer-generated 1:1 randomization was performed without stratification. The primary guidewire passage was performed using an antegrade approach. The study was registered at ClinicalTrials.gov with identifier NCT00987610.

2.2. Patient inclusion and exclusion criteria

Inclusion criteria for patients were: 21 years or older, de novo CTO lesion in a native coronary artery, and an elective PCI procedure. The definition of a CTO was an angiographic occlusion with thrombolysis in myocardial infarction (TIMI) zero blood flow for three months or more. Exclusion criteria were as follows: no indication of a PCI, a prior failed lesion, a restenotic or in-stent restenotic lesion, vein or arterial grafts, pregnancy, or informed consent not given. The existence of bridging collaterals was not a factor for exclusion.

2.3. PCI procedure

Operators were required to use the assigned distal tip size guidewire for CTO treatment using an antegrade approach. As the randomization was only with regards to the size of the distal tip, the coating or stiffness of the guidewire was at the operator's discretion. The timing of the first guidewire manipulation was also at the discretion of the operator. The approach site, shape or size of the guiding catheter was not restricted. If the first guidewire was unsuccessful, any CTO PCI procedure following the first wire was also at the discretion of the operator, including a parallel wire or retrograde approach. PCI operators were required to have a thorough knowledge of CTO PCI and were also required to have participated in at least 50 CTO PCI cases within the last two years.

2.4. Primary endpoint and statistical methods

The primary endpoint was a successful lesion penetration rate of the first guidewire. All the cineangiograms were received by staff at an independent core laboratory (TCAL, Kanagawa, Japan) who were unaware of the assignments. Primary endpoint was assessed at the core laboratory. The PIKACHU registry indicates a 0.010 guidewire passes through a lesion with a success rate of 60%. Assuming the penetration rate of a 0.014 guidewire is 40%, the necessary number of patients required would be 260 for a two-sided test with 90% power and a significance level of 0.05. We assumed the dropout rate as high as 10% since the core laboratory strictly excluded lesions not having CTO by baseline angiography. Thus, target sample size was set around 290 patients. But enrollment was finished at 283 cases since the valid case number reached 260.

All analyses were performed according to the intention-to-treat principle. Categorical variables were presented as frequency values and were compared using the chi-square test. Continuous variables were expressed as mean ± SD and were compared by using Student's *t* test. Logistic regression was performed for the analysis of predictors for the primary endpoint. Statistical analysis was performed with SAS version 9.2, (SAS Institute, Inc., Cary, NC, USA).

3. Results

3.1. Study flow and patient backgrounds

A total of 283 patients gave informed consent. Since 23 patients were excluded according to the study protocol as shown in Fig. 1, 260 patients were enrolled in this study. The patient number met the criteria for the power calculation. According to 1:1 randomization, patients were divided into two groups: regular distal tip ($n = 130$) or tapered distal tip ($n = 130$). For the regular distal tip group, a tapered distal tip guidewire was mistakenly used in one case. For the tapered distal tip group, a regular guidewire was mistakenly used in five cases. The actual guidewire list is shown in a Supplemental Table 1. However, further analysis was performed according to the intention-to-treat principle.

Patient characteristics are shown in Table 1. The average patient age was 66 ± 11 years and females made up 16% of patients. Patients were well randomized, except for age. Angiographic characteristics are shown in Table 2. The frequency of single vessel disease was 36% and that of an unprotected left main coronary artery stenosis was 3%. CTO lesion morphology was 62% of the tapered type, 15% showed a short lesion length < 10 mm, 76% displayed CTO lesion bending at <45 degrees and 62% of CTO lesions showed no or mild calcification. The average multicenter CTO registry Japan (J-CTO) score was 1.8 ± 1.1. Angiographic backgrounds were also well randomized.

3.2. PCI procedure and primary endpoint

The characteristics of PCI procedures are shown in Table 3. Soft distal tip load of guidewire with 1 g or less was 98% in the tapered group but 56% in the regular group ($P < 0.001$). Distal coating with silicone or uncoated was 2% in the tapered group but 33% in the regular guidewire group ($p < 0.001$). A femoral approach was used for antegrade wiring in 65% of cases. The average guiding catheter size was 6.8 ± 0.9 Fr. Retrograde access was performed in 55% of procedures, either for diagnostic angiography (35%) or retrograde wiring (20%). The PCI procedure was also well randomized. As shown in Fig. 2 and Table 3, for the primary endpoint, the first guidewire success rate was 38% of patients for the tapered distal tip and 32% for the regular distal tip group (Fig. 3), with no significant difference observed ($P = 0.80$). A parallel wire technique, retrograde approach and intravascular ultrasound (IVUS)- or computed tomography (CT)-guided techniques were performed in 24%, 20%, 27% and 22% of total PCI procedures, respectively. The final PCI success rates were 81% vs. 85% for the tapered and regular distal tip groups, respectively, which did not show a significant difference ($P = 0.57$).

3.3. Clinical outcomes

Table 4 lists 30-day clinical outcomes and complications for the catheterization laboratory. All-cause mortality, myocardial infarction and stroke rates were 0%, 0.4% and 0.4%, respectively. Puncture site bleeding was observed in 5% of cases, contrast-induced nephropathy was seen in 1.5%, and radiation dermatitis in 0.4%, of cases. Coronary perforation was reported in 5% of cases, but the rate of cardiac tamponade was 0.4%. Retrograde approach-related complications occurred at a rate of 1.5% of cases.

3.4. Analysis of factors relating with primary endpoint

In Table 5, factors relating with the primary endpoint were demonstrated. There was no difference in guidewire success in terms of distal tip load (35% success in 1 g or less vs. 37% success in >1 g) or distal tip coating (40% success in hydrophilic coating, 34% in plastic coating or 33% in silicone or uncoated). Only the J-CTO scores significantly related with the primary endpoint. In Fig. 4, the first guidewire success (primary endpoint) rate was stratified according to J-CTO scores. The graph indicates that wire selection significantly influenced the success rate when J-CTO = 0 or over. Ad hoc regression analysis, including an interaction term between the treatment group and J-CTO score, revealed that the interaction was marginally significant at the level of $P = 0.0702$, suggesting that stratified analysis by J-CTO scores is relevant. In the J-CTO = 0 subsample, the tapered distal tip group exhibited a significantly higher success rate compared to the control group ($P = 0.046$).

4. Discussion

This study tested the superiority of using a tapered distal tip guidewire as a first choice for PCI of CTO lesions. However, results revealed guidewire distal tip sizes, distal tip load or distal tip coating did not show any significant difference in primary outcomes. In lesions with J-CTO score = 0, tapered distal tip guidewire had better primary outcomes.