Dissection and Re-Entry Techniques and Longer-Term Outcomes Following Successful Percutaneous Coronary Intervention of Chronic Total Occlusion

Stéphane Rinfret, MD, SM*, Henrique Barbosa Ribeiro, MD, Can Manh Nguyen, MD, Luis Nombela-Franco, MD, Marina Ureña, MD, and Josep Rodés-Cabau, MD

New techniques involving dissection of the subintimal space and re-entry into the true lumen increase success rates in chronic total occlusion (CTO) percutaneous coronary intervention (PCI). However, their long-term safety and efficacy were unknown. This study included a series of consecutive patients who underwent CTO PCI. All patients who did not present events were contacted 12 to 18 months after their PCI. The combined incidence of cardiac death, myocardial infarction, ischemia-driven target-vessel revascularization (TVR), or reocclusion was assessed as our primary outcome. From January 2010 to January 2013, of 212 CTOs treated in our CTO program, 192 (91%) were successfully opened (in 179 patients). Follow-up data were available for 187 CTOs (97.4%), with 82 (44%) that were opened with dissection re-entry and 105 (56%) with conventional wire escalation techniques. At a median follow-up of 398 days, the primary outcome occurred in 18 of 179 CTOs treated (10.7%), driven by TVR. No patient died from cardiac causes. Eleven CTOs (15.2%) treated with dissection re-entry versus 7 CTOs (7.3%) treated with wire escalation presented with the primary outcome ($p = 0.17$). With multivariate adjustment, dissection re-entry techniques had no significant impact on outcomes. However, treatment of an in-stent occlusion was independently associated with TVR (hazards ratio >6.0, $p < 0.001$). In conclusion, dissection re-entry techniques have minimal impact on long-term outcomes after CTO PCI, which are favorable in most patients. However, treatment of an in-stent occlusion and use of sirolimus-eluting stent were predictors of subsequent adverse outcomes. **(Am J Cardiol 2014;114:1354–1360)**

Better outcomes have been associated with successful versus failed recanalization of chronic total occlusion (CTO) in observational studies[1] and with drug-eluting stent (DES) compared with bare-metal stent implantation,[2] especially with newer-generation DESs versus the first generation[3] when used for CTOs. However, the impact of the technique used to open the CTO on longer-term outcomes after successful recanalization and DES implantation is largely unknown. Dissection and re-entry techniques (DARTs), performed either from the retrograde[4] or the anterograde approach, with wires or with novel devices such as the CrossBoss and Stingray (Boston Scientific) catheters,[5] improve technical success while maintaining low complication rates.[6–9] Such novel techniques invariably result in subintimal DES implantation. To date, only 2 studies specifically assessed long-term outcomes of DESs implanted in the subintimal space.[10,11] Both studies reported mitigated results, which raises questions on the safety of subintimal re-entry techniques. No study has to date evaluated outcomes including anterograde and retrograde DART, both resulting in subintimal or subadventitial stenting. The purpose of the study was therefore to examine the longer-term outcomes of patients who underwent successful CTO percutaneous coronary intervention (PCI) in our program, compare the effect of DART on outcomes, and assess predictors of long-term events.

Methods

A total of 248 consecutive CTO PCI procedures were performed by 1 operator (SR) from January 2010 to January 2013 inclusively. Of these, 36 procedures were performed outside our institution and were excluded of follow-up (FU) analysis. Baseline, procedural, and hospitalization data were prospectively collected and entered into a dedicated database. Data collection was approved by our institutional review committee as part of the Recherche Évaluative en Cardiologie InTervenionnelle registry, and subjects provided signed informed consent for long-term telephone FU. Events such as cardiac death, myocardial infarction (MI), target-vessel revascularization (TVR), or target-vessel reocclusion were collected when patients were readmitted in our institution. If not, they were systematically contacted 12 to 18 months after their PCI by 1 trained research assistant who was not aware of procedural data. During those telephone calls, need for repeat revascularization in another hospital, need for emergency department visit for angina, clinical status as defined by the Canadian Cardiovascular Society class, use of nitroglycerin (none, daily, weekly, or less than weekly), and frequency of angina (none, daily, weekly, or less than weekly) within the last 4 weeks were assessed.

Multidisciplinary Department of Cardiology, Institut universitaire de cardiologie et de pneumologie de Québec (Quebec Heart & Lung Institute), Laval University, Quebec City, Quebec, Canada. Manuscript received June 5, 2014; revised manuscript received and accepted July 18, 2014.

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*Corresponding author: Tel: (418) 656-8711; fax: (418) 656-4544.
E-mail address: stephane.rinfret@criucpq.ulaval.ca (S. Rinfret).

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The techniques and algorithm we use to perform CTO PCI in our program have been published elsewhere and is based on CTO anatomy.[8,9,12,13] It is a combination of conventional anterograde wire escalation (WE), anterograde DART, retrograde WE, and retrograde DART, the so-called hybrid procedure, rapidly switching from one approach to another when the initial strategy attempted is failing. An anterograde approach was initially attempted for short lesions (<20 mm) with clear proximal cap location and good distal vessel target using a WE strategy. Anterograde DART using dedicated devices (CrossBoss and Stingray catheters) was, however, preferred for longer lesions with an optimal distal re-entry zone, without significant side branches that could be occluded by the technique, or when an initial WE strategy failed. Wire-based anterograde DART was also used successfully when an initial attempt at crossing from a "true-to-true" approach failed. Such a strategy involves the use of a microcatheter delivered on a knuckled polymer-jacketed wire advanced into the subintimal dissection plane, with subsequent re-entry into the true distal lumen using a stiff tapered guidewire or a knuckled guidewire. Other complex lesions with unclear location of the proximal cap or with poor distal target were initially attempted by the retrograde approach. In those cases, after positioning of a microcatheter at the distal CTO cap, a true-to-true retrograde lumen crossing technique was first attempted for shorter lesions (<20 mm). When entering in the subintimal space or with longer lesions, knuckled wires were used to reach the proximal cap, followed most often by reverse-controlled anterograde and retrograde re-entry techniques. The occluded segment was stented with DESs (if no contraindication for prolonged dual antiplatelet therapy) and postdilation performed to optimize stent expansion and apposition as needed.[12] For this analysis, we considered only the final successful crossing strategy leading to subsequent placement of DES, as recorded into the database. For the main analysis, we considered that the lesion was crossed with DART when (1) a wire-based anterograde dissection was performed followed by re-entry into the true distal lumen with a straight or knuckled wire, (2) a Stingray system was used to cross from the false lumen to the true lumen, and (3) when a reverse-controlled anterograde and retrograde re-entry technique was used to cross the CTO segment. Other CTO crossing techniques were considered "intraplaque," "true-to-true," or WE techniques.

A CTO was defined as a total obstruction of a coronary artery with anterograde Thrombolysis In Myocardial Infarction (TIMI) flow grade 0 that was confirmed or presumed to be at least 3 months old.[14] The duration of the CTO was estimated by clinical information or the results of previous angiography. Successful angiographic recanalization was defined as a restoration of TIMI flow grade 3 and residual stenosis <30% in the occluded artery.[14] The Japanese-CTO (J-CTO) score was calculated in all the patients to assess case complexity. This score was derived from the J-CTO registry from the analysis of nearly 500 native CTO lesions[15] and was recently validated in this cohort of patients.[13] The score ranges from 0 to 5.

The combined incidence of cardiac death, hospitalization for MI, ischemia- or symptoms-driven TVR, or reocclusion was assessed as our primary outcome of interest. Hospitalization for MI was considered if the patient presented with a typical acute coronary syndrome associated with an increase in serum troponin levels. A TVR was defined as any procedure (PCI or coronary artery bypass grafting) performed in the vessel in which the CTO was present, either in the previously occluded segment or somewhere else in the same vessel. It was considered to be attributable to ischemia if a functional test documented inducible ischemia or if the patient presented with an acute coronary syndrome and acute electrocardiographic changes. Symptoms considered as potential triggers for TVR were recurrence of chest pain or dyspnea. Given varying FU durations, a time-to-event analysis was performed, and patients were censored at the time of the last FU if they did not present any of those events. A second analysis combined cardiac death, MI, ischemia-driven TVR, or reocclusion and any residual angina as an end point. Residual angina was defined as any angina of Canadian Cardiovascular Society class $\geq$1, use of nitroglycerin, occurrence of any angina during the last 4 weeks at clinical assessment.

Binary variables are expressed as percentages and continuous variables as mean values and standard deviation. When assessing factors in the 2 groups that could contribute to outcomes, categorical variables were compared using Fisher's exact test, multiple category variables with the chi-square, and continuous variables with the Kruskal-Wallis test. We first compared baseline characteristics of patients treated with DART with those treated with an intraplaque or true-to-true crossing. As exploratory analyses, we tested the univariate impact of a retrograde procedure versus anterograde, antegrade dissection re-entry (ADR) (with the CrossBoss and Stingray devices or using knuckled wires) versus other techniques, and finally treatment of an in-stent occlusion versus no previous stenting of the target CTO segment. Time-to-event analysis and the unadjusted log-rank test were performed to assess the crude impact of DART (and the other 3 exploratory analysis variables) on the primary and secondary outcomes. Then, after confirmation of the proportional hazard assumption, several Cox proportional hazards models were derived to assess the adjusted impact of DART over several other factors that were also associated, alone, with adverse events. Model 1 was the less parsimonious, controlling for all factors simultaneously. Model 2 first selected the most potent predictors using backward selection, keeping variables associated with a $p < 0.1$, and then controlled for the effect of those factors on the hazards ratio (HR) of DART. Model 3 was built based on the individual effect of covariates, keeping in the final model only variables that varied the HR of DART by >10%. All analyses were conducted using the statistical package SAS (version 9.3; SAS Institute Inc., Cary, North Carolina) considering significant results with p values <0.05.

Results

Of the 212 CTOs treated in our institution program, 192 (91%) were successfully reopened in 179 patients. Therefore, 13 patients had either >1 CTO treated (10 patients) or underwent >1 successful PCI for the same CTO (3 patients: 2 who presented 1 in-stent reocclusion of the CTO segment and 1 who presented 2 subsequent episodes of in-stent reocclusion) during the same period. Given that no patient presented cardiac death during FU, all 192 CTOs were