Application of the Hybrid Approach to Chronic Total Coronary Occlusion Percutaneous Coronary Intervention

Ph.D. Thesis

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LIST OF PUBLICATIONS

This doctoral thesis is based on the following publications:

I. **Tajti P**, Karmpaliotis D, Alaswad K, Jaffer FA, Yeh RW, Patel M, Mahmud E, Choi JW, Burke MN, Doing AH, Dattilo P, Toma C, Smith AJC, Uretsky B, Holper E, Wyman RM, Kandzari DE, Garcia S, Krestyaninov O, Khelimskii D, Koutouzis M, Tsiafoutis I, Moses JW, Lembo NJ, Parikh M, Kirtane AJ, Ali ZA, Doshi D, Rangan BV, Ungi I, Banerjee S, Brilakis ES. The Hybrid Approach to Chronic Total Occlusion Percutaneous Coronary Intervention: Update from the PROGRESS-CTO (PROspective Global REgiStry for the Study of Chronic Total Occlusion Intervention) International Registry. JACC Cardiovasc Interv. 2018 Jul 23;11(14):1325-1335. *IF: 9.881*

II. **Tajti P**, Ungi I. Az anterográd technikák szerepe a krónikus teljes koszorúér-elzáródás perkután revaszkularizációjában. Cardiologia Hungarica 2018 November; 48(5):330-339.

III. **Tajti P**, Abu-Fanne R, Ungi I, Katona A, Sasi V, Nagy FT. Kettős lumenű mikrokatéterek alkalmazása krónikus teljes koronária okklúzió katéteres revaszkularizációjában - egy komplex beavatkozás tanulságai. Cardiologia Hungarica 2019 September; [In Press].

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INTRODUCTION

Coronary chronic total occlusions (CTOs) are defined as 100% occlusions with TIMI 0 flow with at least 3 month duration. Treatment options for patients with coronary CTOs include lifestyle changes, medications (as is appropriate for all patients with coronary artery disease) and coronary revascularization with either percutaneous coronary intervention (PCI) or coronary bypass graft surgery (CABG). Chronic total occlusion (CTO) percutaneous coronary intervention (PCI) is a rapidly evolving area of interventional cardiology that has undergone a remarkable technical improvement over the past two decades.

Treatment of CTO with PCI currently remains less preferred in clinical practice possibly due to the limited operator expertise, high procedural cost, limited cardiac catheterization laboratory time availability, high risk for procedural complications and the ongoing controversy regarding its clinical benefits. However, various randomized controlled and observational studies indicates that CTO PCI improves patient symptoms and quality of life, whereas there is limited, retrospective data on whether it can impact the subsequent incidence of death, myocardial infarction and arrhythmias. Accordingly, the key indication for offering and performing CTO PCI should be the alleviation of symptoms and CTO PCI should be performed when the anticipated benefits (which depend on the patient's baseline clinical condition and the likelihood of success) exceed the potential short- and long-term risks.

Achieving clinical benefit with CTO PCI requires the procedure to be successful. The hybrid approach (**Figure 1**) to chronic total occlusion (CTO) percutaneous coronary intervention (PCI) advocates dual coronary injection, careful and structured review of the angiogram, and flexibility. Use of all crossing strategies (antegrade wire escalation, antegrade dissection reentry and the retrograde approach) is encouraged, with initial and subsequent choices influenced by the CTO anatomic characteristics and the outcomes of the originally selected approach.

With contemporary equipment and techniques (such as the hybrid algorithm), high success rates (85-90%) are achieved at experienced centers. However, success rates in unselected populations remain low: 61% in the New York State PCI Registry and 59% in the National Cardiovascular Data Registry in the US. Therefore, there is a gap between what is achieved at dedicated CTO PCI centers and the outcomes at less experienced centers.

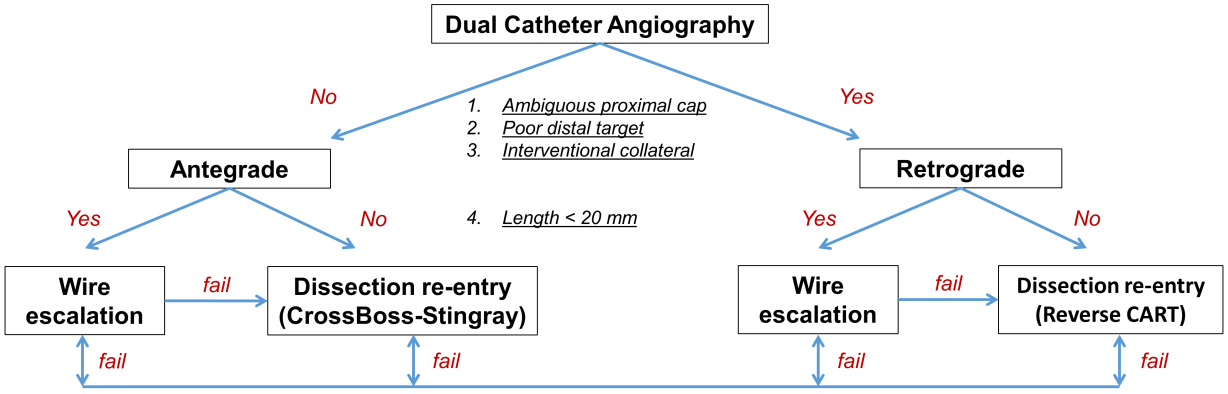

Figure 1 *Hybrid algorithm for CTO PCI.*

Dual angiography is performed and 4 parameters are assessed: based on them the initial crossing strategy is selected, followed by early change in case of failure to achieve progress with any other strategy.

CART: controlled antegrade and retrograde subintimal tracking.

AIMS

(i) We sought to examine a contemporary, multicenter CTO PCI registry to determine the techniques and outcomes of CTO PCI.

(ii) Our goal was to validate the hybrid algorithm in a diverse group of patients and operators in two continents.

(iii) We aimed to identify areas in need for improvement in the field of CTO PCI.

MATERIAL AND METHODS

We analyzed the clinical, angiographic, and procedural characteristics of 3,122 CTO PCIs performed in 3,055 patients enrolled in the PROGRESS-CTO (Prospective Global Registry for the Study of Chronic Total Occlusion Intervention, NCT02061436) registry between January 2012 and November 2017 at eighteen US, one European, and one Russian centers. All statistical analyses were performed with JMP 13.0 (SAS Institute, Cary, North Carolina). A two-sided p value of 0.05 was considered statistically significant.

RESULTS

Clinical characteristics

As compared with patients in whom CTO PCI failed, patient in whom CTO PCI was successful were younger and less likely to be men, and to have hypertension. They were also less likely to have had a myocardial infarction, congestive heart failure, prior coronary artery bypass graft surgery, and prior PCI along with higher left ventricular ejection fraction. Most patients (89%) were symptomatic having at least Class 2 Canadian Cardiovascular Society (CCS) Angina Classification level (CCS 2: 25%; CCS 3: 54%; CCS 4: 10%), and mostly had stable (64%) or unstable (18%) angina.

Angiographic characteristics

The CTO target lesions were located in the right coronary artery (55%), left anterior descending artery (24%) and left circumflex artery (20%). Failed CTO PCI was associated with longer lesion length (37.8±24.0 mm vs. 33.4±24.1 mm, p=0.0030), proximal cap ambiguity (54% vs. 32%, p<0.0001), moderate to severe calcification (73% vs. 52%, p<0.0001) and tortuosity (45% vs. 33%, p<0.0001), or previously failed recanalization attempt (27% vs. 19%, p=0.0005).

Procedural outcomes of the hybrid approach

Overall technical and procedural success was 87% and 85% respectively and the in-hospital major complications rate was 3.0%. Antegrade wire escalation was the most commonly used initial approach (in 75%), especially in lower complexity CTOs (J-CTO score: 2.28±1.29, PROGRESS-CTO score: 1.35±1.05), while antegrade dissection/reentry (8%; J-CTO score: 2.86±1.16, PROGRESS-CTO score: 1.50±1.07) and the retrograde approach (16%; J-CTO score: 3.12±1.07, PROGRESS-CTO score: 1.33±0.96) were used in more complex lesions (p<0.0001). The initial approach was successful in 55% of the cases, while 41% of the cases underwent further attempts that were technically successful in 79%.

The final successful crossing strategy was antegrade wire escalation (46%), antegrade dissection reentry (19%), and the retrograde approach (24%). The success of antegrade wire escalation decreased with lesion complexity, as classified with the J-CTO score (easy [J-CTO 0]:

88%; intermediate [J-CTO 1]: 72%; difficult [J-CTO 2]: 51% and very difficult [J-CTO ≥3]: 32% to 17%; p<0.0001), and the PROGRESS-CTO score (55%, 43%, 42%, 39% and 43%, respectively for scores of 0, 1, 2, 3, and 4; p<0.0001).

Dual injection was used in 70% of all cases, and was more frequent in failed interventions (76% vs. 70%, p=0.026) and in complex lesions with high J-CTO scores (48% vs. 78%, p<0.0001). Radial access was used in 37% overall, with biradial approach in 14%, and in combination with femoral approach in 20% of the cases. Use of radial access was lower with increasing lesion complexity (easy: 50%, intermediate: 39%, difficult: 36%, very difficult: 38%, p=0.003), whereas the frequency of femoral (63%, 78%, 83%, 84%, p<0.0001) and bifemoral approach (28%, 43%, 51%, 57%, p<0.0001) increased with increasing lesion complexity. Median contrast volume, air kerma radiation dose, procedure and fluoroscopy time were 270 (200-360) ml, 2.9 (1.7-4.7) Gray, 123 (81-188) and 47.0 (28.6-77.0) minutes, respectively, and were higher in more complex lesions.

Higher median annually performed CTO PCI per center was associated with higher procedural success on both univariable and multivariable analysis but not in-hospital MACE (major adverse cardiac event). The incidence of in-hospital MACE was 3.04% [death (0.85%), acute myocardial infarction (1.08%), stroke (0.26%), emergency CABG (0.16%), urgent re-PCI (0.36%), and pericardial tamponade (0.85%)], and increased with increasing lesion complexity. The prevalence of in-hospital MACE were higher in failed procedures (7.54% vs. 2.37%, p<0.0001) and with more complex crossing techniques: antegrade wire escalation, antegrade dissection reentry or retrograde crossing (1.09% vs. 2.96% vs. 5.61%, p<0.0001). Use of the retrograde approach was associated with higher incidence of complications. Median length of hospital stay was significantly higher in patients with vs. without in-hospital MACE (6 [2-9] days vs. 1 [1-2] days), p<0.0001).

DISCUSSION

To the best of our knowledge this is the largest study reported to date on CTO PCI using the hybrid approach, demonstrating high technical success rates (87%) with acceptable major complication rate (3.04%). These outcomes were achieved despite high lesion complexity and relatively low success of the initially selected CTO crossing strategy (55%).

In the present study we found that technical and procedural success remained high with reasonably low complication rates despite expansion of the registry in recent years. Antegrade wire escalation was more commonly applied as the initial crossing approach (74%) in less complex lesions (J-CTO score: 2.24±1.24, PROGRESS-CTO score: 1.32±0.87) and was the most common final crossing strategy (in approximately half the cases). Antegrade dissection reentry and retrograde techniques were more likely to be used as initial strategy in cases with complex anatomy (J-CTO score 2.78±1.21 and 3.32±0.98, respectively; PROGRESS-CTO score 1.38±0.93 and 2.00±0.89, respectively), and were the final successful strategy in 22% and 28% of all cases.

Failure to cross with a guidewire was the most common reason for CTO PCI failure (in 86%). In 13% the procedure failed despite successful guidewire crossing due to balloon undilatable lesions (3.9%), inability to deliver stents (2.3%), final TIMI flow <3 (1.3%), residual stenosis >30% (1.0%), and procedure-related complications (0.8%, 1 patient with donor vessel thrombosis, 1 patient with aortocoronary dissection, and 1 procedure related death due to pericardial tamponade and subsequent cardiogenic shock). The presence of balloon uncrossable (29% vs. 10%, p<0.0001), and undilatable lesions (22% vs. 11, p=0.0109) was higher in the failed CTO PCI group, highlighting the need for CTO PCI operators to have experience in treating these and other complex lesions, such as severe calcification and bifurcations.

As shown in prior studies higher annual CTO PCI volume was independently associated with higher success rates, reflecting the importance of center and operator experience in optimizing outcomes, even among complex lesion and patient subgroups. Our study confirms that annual CTO PCI volume significantly improves procedural success amongst various operators and lesion subsets (1.21 OR, CI 95%, 1.13 to 1.29, p<0.0001). Attempting 2 or more CTO PCI during the same procedure (0.38 OR, CI 95% 0.18 to 0.77, p=0.0074) lowers the likelihood of procedural

success, that is currently not recommended due to high potential risk for compromising larger myocardial territory that may result in higher procedure-related in-hospital mortality.

Based upon both univariate and multivariate analysis, several anatomic parameters were found to have significant impact on decreasing procedural success (calcification, tortuosity, proximal cap ambiguity) that have been linked with CTO PCI failure in prior studies, and also were implemented into various scores. Nevertheless, distal occlusion anatomy also determines procedural outcomes which is well represented in our study: bifurcation at distal cap decreases [0.62 OR, CI 95% 0.46 to 0.82, p=0.0011], and conversely, appropriate distal vessel landing zone increases the likelihood of success (1.40 OR, CI 95% 1.03 to 1.91, p=0.0340).

The overall complication rate was 3.04%, and occurred less frequently in technically successful procedures (2.37% vs. 7.54%, p<0.0001). The risk for complications was higher in more complex lesions (easy [J-CTO score 0] 1.36% vs. very difficult [J-CTO score 3≤] 3.11%, p=0.01) and with use of advanced crossing techniques (which were more commonly used in more complex lesions). This highlights the importance of weighing the risks and benefits of the procedure, both during discussions with patients and family (to determine whether CTO PCI should be done), but also during the procedure itself: implementing more complex CTO crossing strategies (such as retrograde crossing via epicardial collaterals) may predispose to increased risk for complications, which may be justified in some patients due to significant potential benefit, but not in some others. Accordingly, adjustment and improvement of advanced CTO crossing techniques – such as antegrade dissection re-entry and retrograde approach – may further improve procedural outcomes in more challenging patient populations and complex lesion subsets.

Despite the encouraging findings from our study and other contemporary registries, the success rates of CTO interventions in unselected patient cohorts remain low. Hence, CTO PCI should be performed by experienced operators at dedicated centers in order to achieve optimal results. The CTO PCI success rates in all comer registries (54%-80%) are significantly lower than those achieved at experienced centers (85%-90%).

Given the complexity of CTO PCI, becoming a successful CTO operator requires appropriate training and continued practice. Optimal training for CTO PCI remains controversial, as there are only few dedicated fellowship programs. Most operators learn CTO PCI after being in

practice for a few years through participation in courses and proctoring. Developing experience in CTO PCI is important, both for achieving high success rates but also for minimizing the risk for complications and efficiently managing them if they occur.

Bridging the gap will likely require development of novel equipment and techniques as well as development of comprehensive, high-volume CTO PCI programs and continued education through live case demonstrations, online educational contents, CTO PCI workshops and proctorships. CTO PCI is one of the key components of the growing complex, high-risk, PCI programs.

CONCLUSIONS

(i) Application of the hybrid approach resulted in high technical success rates (87%) and acceptable rate of major in-hospital complications (3%) across a large number of sites and operators in the US, Europe, and Russia.

(ii) Changing crossing strategy was required in 41% of cases with the final success strategy being antegrade wire escalation in 52%, retrograde in 27%, and antegrade dissection reentry in 21%.

(iii) Bridging the gap between what is currently achieved (50-60%) and what can be achieved (85-90%) in chronic total occlusion intervention should be a major focus of upcoming research and education efforts.

(iv) CTO PCI can currently be achieved with high success and acceptable complication rates among various operators and patient populations in the US and Europe, highlighting the need for developing more CTO PCI centers of excellence in order to achieve the best possible clinical outcomes in this challenging patient and lesion group.

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