New Aspects in Percutaneous Coronary Intervention of Chronic Total Occlusions

Ph.D. Dissertation

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Publications directly related to the subject of the dissertation

I. **Karacsonyi J**, Karatasakis A, Karmpaliotis D, Alaswad K, Yeh RW, Jaffer FA, Wyman MR, Lombardi WL, Grantham JA, Kandzari DE, Lembo N, Moses JW, Kirtane AJ, Parikh MA, Green P, Finn M, Garcia S, Doing A, Patel M, Bahadorani J, Parachini JRM, Resendes E, Rangan BV, Ungi I, Thompson CA, Banerjee S, Brilakis ES. Effect of Previous Failure on Subsequent Procedural Outcomes of Chronic Total Occlusion Percutaneous Coronary Intervention (from a Contemporary Multicenter Registry) AMERICAN JOURNAL OF CARDIOLOGY 117:(8) pp. 1267-1271. (2016) IF: 3.398

II. **Karacsonyi J**, Alaswad K, Jaffer FA, Yeh RW, Patel M, Bahadorani J, Karatasakis A, Danek BA, Doing A, Grantham JA, Karmpaliotis D, Moses JW, Kirtane A, Parikh M, Ali Z, Lombardi WL, Kandzari DE, Lembo N, Garcia S, Wyman MR, Alame A, Nguyen-Trong PKJ, Resendes E, Kalsaria P, Rangan BV, Ungi I, Thompson CA, Banerjee S, Brilakis ES. Use of Intravascular Imaging During Chronic Total Occlusion Percutaneous Coronary Intervention: Insights From a Contemporary Multicenter Registry JOURNAL OF THE AMERICAN HEART ASSOCIATION 5:(8) Paper e003890. 13 p. (2016) IF: 4.425

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IV. **Karácsonyi Judit** , Nagy Ferenc , Sasi Viktor , Katona András , Ungi Imre. Use of rotational atherectomy in chronic total occlusion percutaneous revascularization: Rotációs aterectomia alkalmazása krónikus teljes koronária-okklúzió katéteres revaszkularizációjában. CARDIOLOGIA HUNGARICA 48: pp. 40-43. (2018)

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1. INTRODUCTION

Chronic total occlusions (CTOs) are defined as 100% occlusion with thrombolysis in myocardial infarction (TIMI) 0 flow in a coronary artery of at least 3 months of duration. CTOs are common, the data vary in literature regarding the prevalence of such lesions between 16% to 31% of the cases in patients with coronary artery disease (CAD) without prior coronary artery bypass surgery (CABG).

Treatment of CTOs should include optimal medical therapy complemented if indicated and possible with revascularization with either CABG or percutaneous coronary intervention (PCI). Revascularization is indicated in patients with angina or other symptoms resulting from ischemia such as dyspnea in spite of optimal medical therapy, and in those with ischemia on non-invasive testing or left ventricular dysfunction. The clinical decision on whether to perform CTO PCI depends on two things, estimated risk and anticipated benefit resulting from the procedure.

Prior CTO PCI failure has been associated with lower procedural success rates and is part of the Japanese Chronic Total Occlusion (J-CTO) score that was developed to predict the likelihood of successful guidewire crossing within 30 minutes. However, prior CTO PCI failure can be due to multiple factors, such as patient instability, limited local experience, or early cessation of recanalization efforts without exploring alternative CTO crossing options.

Balloon uncrossable lesions are lesions that cannot be crossed with a balloon after successful advancement of the guidewire distal to the lesion. CTOs are often balloon uncrossable and they can be challenging to treat often requiring multiple techniques focusing on either plaque modification or increasing guide catheter support.

Use of IVUS for stent optimization during CTO PCI has been shown to improve long-term outcomes, yet its impact on crossing has received limited study. Intravascular imaging can help resolve proximal cap ambiguity by identifying the position of the main branch and clarify guidewire position during both antegrade and retrograde CTO crossing attempts. Moreover, intravascular imaging can facilitate sizing of balloons and stents and optimize stent expansion and stent strut apposition.

2. AIMS

1. To examine the impact of prior failure on the outcomes of CTO PCI.

2. To determine the prevalence of balloon uncrossable lesions associated treatments and outcomes in a multicenter CTO PCI registry.

3. To determine the frequency of intravascular imaging use during CTO PCI and the associated procedural outcomes.

3. METHODS

We examined the baseline and angiographic characteristics, and clinical outcomes of consecutive CTO PCIs between 2012 and 2016. Data collection was performed both prospectively and retrospectively and was recorded in a dedicated online database (PROGRESS CTO: Prospective Global Registry for the Study of Chronic Total Occlusion Intervention, Clinicaltrials.gov Identifier: NCT02061436). All statistical analyses were performed with JMP 11.0 (SAS Institute; Cary, North Carolina). Two-sided p-values <0.05 were considered statistically significant.

4. RESULTS

4.1 Effect of prior failure on outcomes of CTO PCI

In the first section we sought to examine the impact of prior failure on the outcomes of CTO PCI. During the study period 1,213 consecutive patients underwent 1,232 CTO PCI. Mean age was 65.5 ± 10 years, 84.8% of the patients were men and 44.2% had diabetes. Nearly one third of the study population had congestive heart failure (28%) and family history of coronary artery disease (30%), 34% had prior CABG, and 42% had a prior myocardial infarction.

The most common CTO PCI target vessel was the right coronary artery (59%). Antegrade wire escalation was the most common successful crossing strategy (41%), followed by retrograde (27%) and antegrade dissection and re-entry (24%). The overall technical and procedural success were 90% and 89%, respectively.

As compared with patients without prior CTO PCI failure, those with prior failed attempts were more likely to have in-stent restenosis, larger target vessel diameter, and were more likely to undergo CTO crossing using the retrograde approach.

Technical and procedural success were similarly high among patients with and without prior failed CTO PCI attempts, whereas the incidence of MACE was numerically higher among prior failed cases (4.2% vs. 2.1%, $p = 0.067$). Mean procedure duration was significantly longer in the group with prior failed CTO PCI attempts, as was mean fluoroscopy time, whereas mean air kerma radiation dose and mean contrast volume were similar in the two study groups.

4.2 Balloon uncrossable lesions

Overall, technical and procedural rates were 97.6% and 95.9% respectively (only cases with successful guidewire crossing were included in this analysis).

Balloon uncrossable lesions were encountered in 63 (9%) of the CTO PCI procedures and were more likely to have moderate or severe calcification, moderate or severe tortuosity and higher J-CTO score.

Balloon uncrossable lesions were associated with significantly lower technical (90.5% vs. 98.3%, $p<0.0001$) and procedural (88.9% vs. 96.6%, $p=0.004$) success rates, but similar incidence of MACE (1.6% vs. 2.2 %, $p=0.751$). These lesions were associated with longer procedure and fluoroscopy time, and air kerma radiation dose but similar contrast volume.

Several techniques were used to treat balloon uncrossable lesions. The most commonly used techniques were grenadoplasty (23%), laser (18%) and rotational atherectomy (16%), followed by use of various microcatheters. Laser atherectomy and grenadoplasty had the highest technical and procedural success rates. In the University of Szeged we applied rotational atherectomy in 2.9% of the CTO PCIs.

4.3 Intravascular imaging

In the third part of the analyses a total of 619 CTO PCI procedures performed in 606 patients were included. Intravascular imaging was used in 38% of the procedures, as follows: IVUS in 36%, optical coherence tomography (OCT) in 3%, and both in 1.45%. The indications for intravascular imaging were to facilitate CTO crossing (overall 35.7%) and stent sizing (26.3%) or optimization (38.0%).

4.3.1 Intravascular imaging for crossing

Overall technical and procedural rates were 90.1% and 88.6%, respectively. Intravascular imaging for crossing was used more commonly in lesions with proximal cap ambiguity, side branch at the proximal cap, and longer occlusion length and higher J-CTO and Progress CTO score. Technical and procedural success were similar in cases in which intravascular imaging was used for crossing (92.8% vs. 89.6%, $p=0.302$ and 90.1% vs. 88.3%, $p=0.588$, respectively), whereas the incidence of major adverse events was similarly low in both groups (2.7% vs. 3.2%, $p=0.772$). Mean procedure duration was significantly longer among procedures in which intravascular imaging was used for crossing as was median fluoroscopy time, mean air kerma radiation dose, as compared with cases in which intravascular imaging was not used.

4.3.2 Intravascular imaging for stent sizing and/or optimization

Among CTOs successfully crossed with a guidewire, cases in which imaging was used for stent sizing and optimization were more complex and had higher J-CTO and

Progress CTO scores. Use of intravascular imaging was associated with similar technical (97.7% vs. 97.5%, p= 0.854) and procedural (97.1% vs. 95.4%, p= 0.347) success rates and similarly low MACE rates (2.3% vs. 3.1%, p= 0.622). There was a trend toward larger number of stents in procedures where intravascular imaging was used for stent sizing/and/or optimization.

5. DISCUSSION

5.1 Effect of prior failure

In the first section of our study the main finding is that a prior failed CTO PCI attempt is associated with higher angiographic complexity, longer procedural duration and fluoroscopy time, but not with the success and complication rates of subsequent CTO PCI attempts.

Few studies have examined the impact of prior failed CTO PCI attempt on subsequent procedural outcomes. Our findings support a limited role of prior failure in predicting subsequent CTO PCI success. Indeed, prior failure was not included in the recently developed Progress-CTO risk score that is associated with technical success and includes four variables (proximal cap ambiguity, presence of interventional collaterals, moderate/severe tortuosity, and circumflex target vessel).

There are multiple potential explanations for the lack of impact of prior failure on CTO PCI outcomes. First, initial failure could be related to limited experience and expertise or lack of equipment at the treating center. Second, it could have been due to a complication. Third, at times a failure can predispose to subsequent success by allowing recanalization of the occlusion after angioplasty of a subintimal dissection plane (investment procedure).

5.2 Balloon uncrossable lesions

In the second section of our study examining the balloon uncrossable CTOs the main findings are that (a) balloon uncrossable lesions are common in CTO PCI, being encountered in approximately 9% of occlusions that are successfully crossed with a guidewire; (b) often require use of multiple treatment modalities; and (c) are associated with lower technical and procedural success rates.

As anticipated, balloon uncrossable lesions were more likely to have complex angiographic characteristics, that can hinder advancement of equipment through the occlusion. Moreover, failure to cross with a balloon tended to be more common when crossing was achieved using antegrade wire escalation. This is not surprising given that the subintimal space provides less resistance as compared with intimal planes, and highlights a potential advantage of dissection/re-entry strategies in those lesions.

Several techniques are currently available to treat balloon uncrossable lesions, both simple and more advanced. Those techniques can be categorized into those that modify the lesion and those that increase guide catheter support. Simpler techniques are attempted first, such as using a new, small (1.2 to 1.5 mm) balloon, that can sometimes be ruptured intentionally to modify the plaque. Alternatively, various microcatheters can be used. Another advanced lesion modification technique is the “see-saw balloon-wire cutting technique”: the lesion is crossed by two guidewires over which two short and low profile balloons are alternatively advanced and inflated at high pressure producing a cutting effect to crush the proximal fibrous cap in multiple positions.

Enhanced support can be achieved by using guide catheter extensions or anchoring techniques. More advanced treatment strategies for balloon uncrossable lesions include laser and rotational atherectomy, that were among the most successful techniques in our analysis. Laser is particularly well suited for treating such lesions as it can be used over any standard 0.014-inch guidewire, but has limited availability. Rotational atherectomy is highly effective for facilitating lesion crossing, but requires exchange of the guidewire for a specialized guidewire, possibly resulting in failure to re-cross the lesion.

If all else fails, subintimal strategies can be used for balloon uncrossable lesions, by advancing a knuckled guidewire or a CrossBoss catheter through the subintimal space across the occlusion. Given the high prevalence and significant impact of balloon uncrossable lesions in reducing procedural success, having a clear understanding and local availability of equipment and techniques to treat balloon uncrossable lesions is critical.

5.3 Intravascular imaging in CTO PCI

The main findings of the third section of our study are that intravascular imaging is frequently performed during CTO PCI both for crossing and for stent selection/optimization. Intravascular imaging was used in more complex occlusions and was associated with similarly high success rates, but longer procedure time and higher radiation dose.

In our study intravascular imaging was used in 38% of CTO PCI cases, which is similar to 39% utilization in the Multicenter Korean CTO Registry but it is in contrast to the European Registry of Chronic Total Occlusion (2.9% overall and 9.2% in retrograde cases), suggesting that imaging use may be low even among experienced operators and centers. IVUS guidance for antegrade crossing require high operator skill and experience.

IVUS was the intravascular imaging modality used in most CTO PCIs, as in contrast to OCT, does not require flushing of the blood column within the arterial lumen and has higher penetration depth. OCT however offers superior resolution compared to IVUS and has been used in CTO PCI to determine guidewire position and stent optimization after deployment.

Intravascular imaging can assist CTO crossing by: (a) identifying the proximal cap in cases with proximal cap ambiguity, for example by imaging through a side branch adjacent to the occlusion; (b) confirming whether the antegrade guidewire has engaged the occlusion and navigating the antegrade guidewire to the true lumen in case of dissection; (c) confirming that the retrograde guidewire has entered the proximal true lumen before externalization; and (d) determining the appropriate balloon size for the CART and reverse CART techniques. Moreover, use of IVUS could assist re-entry into the distal true lumen after subintimal crossing and reduce the need for fluoroscopy and contrast injection. IVUS may be particularly useful for the retrograde approach to CTO crossing, as retrograde cases are often more complex than antegrade-only cases due to difficulties crossing the collateral and/or crossing the occlusion and externalizing the guidewire.

Intravascular imaging can assist with optimizing stent diameter and length selection, and further ensure that optimal expansion has occurred. Stent underexpansion is an important risk factor for both restenosis and stent thrombosis. Use of intravascular imaging may be of particular importance in long and calcified CTOs. This could be related to higher lesion complexity among imaged lesions, but could also indicate increased detection of dissection flaps, gaps between stents, or untreated residual coronary disease that might have not been apparent during diagnostic angiography.

6. CONCLUSIONS

1. Prior failed CTO PCI attempt is associated with higher angiographic complexity, longer procedural duration and fluoroscopy time, but not with the lower success and higher complication rates of subsequent CTO PCI attempts.

2. Balloon uncrossable lesions: (a) are commonly encountered during CTO PCI, especially in more complex occlusions; (b) often require advanced treatment strategies; and (c) are associated with lower technical success rate, emphasizing the importance of advanced training in order to develop expertise in treating these challenging lesions.

3. Intravascular imaging is frequently performed during CTO PCI both for crossing and for stent selection/optimization. Even though intravascular imaging was used in more complex lesions, it was associated with similar rates of technical and procedural success, but higher use of radiation and longer procedure time.

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