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REVIEW ARTICLES

Morphological Aspects and Treatment Strategies for Chronic Total Occlusions of the Coronary Arteries

Albi Fagu[1], Ormir Shurdha[2], Nevila Caushi[1], Ketjon Menkshi[1], Dervish Hasi[1], Meriton Siqeca[3]

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Abstract

Coronary total occlusions are routinely found in patients suffering from chronic coronary artery disease. Their prevalence is between 20-50% and is higher in patients with prior coronary artery bypass surgery. Patients with CTOs have a higher risk profile, higher Syntax scores and in approximately 80% of the cases, a multi-vessel disease. Advances in technology that supports CTO-PCI and the increasing operator experience in high volume centers has raised important questions about the revascularization strategy. In the majority of cases, the treatment strategy for this group of patients should aim at achieving full revascularization. In this context CABG should be considered the first choice and percutaneous coronary intervention can be considered for patients with less advanced disease. It is not clear, whether successful CTO revascularization (CABG or PCI) have an impact on long-term outcomes. For these reasons, the treatment of patients in the presence of CTOs should be based on the current evidence on the treatment of multivessel coronary disease.

Keywords: Chronic total occlusions, Coronary artery disease, CTO, CABG, CTO-PCI.

Abrevviations

CTO - Chronic total occlusions; CAD - Coronary Artery Disease; RCA - Right Coronary Artery; LAD - Left Anterior Descending; LCX - Left Circumflex Artery; PCI - Percutaneous Coronary Intervention; CABG - Coronary Artery Bypass Grafting; LV - Left Ventricle

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* ***Corresponding author:***
Albi Fagu MD
albifagu@yahoo.com

1 Cardiac Surgery Clinic, University Hospital "Shefqet Ndroqi", Tirana, ALBANIA
2 Department of Cardiovascular Diseases, University Hospital "Mother Theresa" Tirana, ALBANIA
3 Cardiology Clinic, University Hospital "Shefqet Ndroqi", Tirana, ALBANIA

Introduction

Coronary artery disease (CAD), as a major cause of mortality and disability, is the most addressed pathology by cardiologists and cardiac surgeons worldwide.[1, 2] Coronary artery total occlusions (CTO) are considered to be the highest grade of atherosclerotic involvement of a coronary artery and are considered chronic if older than three months.[3, 4]

Since this process occurs gradually, it gives time to the collateral system to develop and therefore it is consistently found in stable patients with or without symptoms. Occasionally these patients become symptomatic because of the generalized CAD and the CTO is an incidental finding without clear information about the timing of the occlusion event.[5–7]

Large registries or single center series show that the overall prevalence of CTOs in the CAD population ranges between 20-50% and is higher among patients with prior coronary artery bypass surgery (CABG) (Table 1). They affect more often the right coronary artery (RCA) and involve more than one coronary artery in around 17% of cases.[8–10]

According to the 2018 ESC/EACTS Guidelines on myocardial revascularization, the treatment of patients with coronary disease in the presence of a CTO, may be based on the same principles as those without a CTO. The limited number of randomized controlled trials that analyze the effect of the revascularization of these lesions and the conflicting results, does not allow for more specific recommendations.[11] The majority of patients with CTOs have a higher risk profile, higher Syntax Scores and in approximately 80% of the cases, a multi-vessel disease.[12, 13] In this context, CABG should be considered as the primary treatment strategy and percutaneous coronary intervention (PCI) may be considered in patients with a less extensive CAD (single vessel) or in high-risk patients such as in redo surgery [8, 14, 15].

Current technological and device innovations that facilitate PCI, as well as the increasing operator experience, have generated higher success rates of CTO-PCI. These rates are dependent on center volume, operator skills and specific equipment and vary from 60-90%. [16–18]

The incrementing use of PCI to recanalize CTOs is not based on strong evidence and the success rates reported are only exclusive to high-volume centers. Both revascularization strategies have specific advantages that must be taken into consideration in order to offer an individualized treatment for the patients with CTO.

In this review, we aim to describe the anatomic variability of CTOs, the impact it has in the treatment success and to summarize the existing evidence regarding treatment strategies for this group of patients.

Morphological aspects and their impact on outcomes

CTOs are a common finding in patients undergoing coronary angiographic examinations for stable CAD.[8, 10] The prevalence of CTOs shows a high level of variability in different reports (Table 1) and is higher in patients with advanced disease involving all 3 coronary vessels. The Canadian multicenter CTO registry found that solitary CTOs (not in context of multivessel disease) are found in only 10% of patients and the rest was identified in patients suffering from left main, or multivessel CAD.[10]

CTOs are localized in the RCA in 40-60% of cases and affect the left anterior descendent artery (LAD) and the circumflex artery (LCX) almost equally (Table 1).

The occlusions are mostly located in the proximal or middle segment of the artery, but also in the distal portion in the case of LCX (Fig.1).[22] This has important implications in the treatment strategy when choosing between CABG or PCI. In fact, CABG addresses the distal segments of the diseased coronaries, and the localization of the CTO plays a minor role in the revascularization strategy. In the case of CTO-PCI, the revascularization of distal occlusions is avoided and considered not amenable to PCI. In the DECISION-CTO trial, Euro-CTO trial and EXPERT-CTO trial, different inclusion criteria like: "target coronary diameter ≥2.5 mm", or "CTO localized in segments 1-3 for RCA, 6-7 for LAD, 11-12 for LCX are used to exclude the more distal CTO localizations.[23–25] The occluded vessel is almost always perfused by either the ipsilateral or the contralateral coronary artery and the length between the 2 occlusion extremities is considered the CTO length (Fig. 2B). CTOs of the RCA tend to be longer and more angulated than those located in the LAD and LCX. This can be explained by the fact that RCA-CTOs are mostly located at the marginal part of the artery and from this segment originate only small branches that do not influence the progression of the occlusive process. Occlusion length together with other morphological characteristics of the CTO lesion are

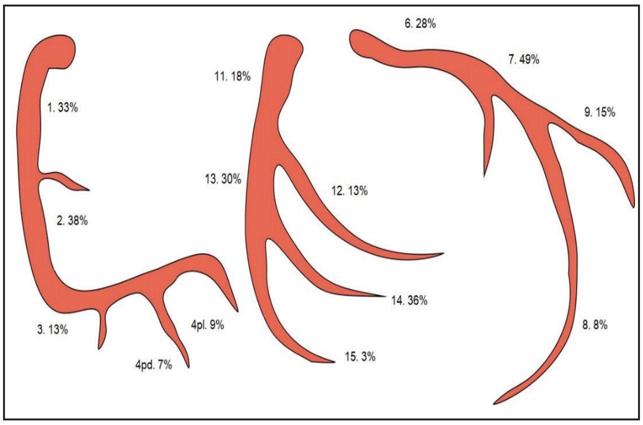

Figure 1 Localisation of CTOs according to the coronary segments (Own unpublished data)

Table 1 Prevalence and localization of CTO in the literature

Chronic total occlusion prevalence and location in different studies					
Reference	Study population	CTO prevalence	RCA	LAD	LCX
Kahn et al 1993(19)	333	35%	58%	18%	24%
Toma et al 2017(20) 2002	-	47%	28%	25%	
Tsai et al 2017(21)	111273	26.4%	42.9%	28.1%	29.4%
Christofferson et al 2005 (8)	3087	52%	49.4%	22%	28.6%
Jeroudi et al 2013 (9)	1015	31.3%	-	-	-
Fefer et al (10)	14439	18.2%	46.9%	19.86%	15.43%

CTO:Chronic Total Occlusion; RCA:Right Coronary Artery; LAD: Left Anterior Descending; LCX: Left Circumflex important predictive factors for the procedural success of CTO-PCI.

In fact, occlusion length of more than 20 mm is related to worse procedural outcomes.[22, 26]

The collateral system

Despite being responsible for the blood perfusion of separate areas of the heart muscle, the coronary arteries "communicate" with an intricate system of inter-arterial anastomoses. In patients with coronary disease, hypertrophy and other diseases that affect the myocardial perfusion, the presence of a collateral system is described in more than 50% of the cases [27, 28]. Collateral arteries can be epicardial or intramuscular and create ipsilateral or contralateral communication between coronary arteries. Ipsilateral collaterals are mostly found when the CTO is localized in the LCX position. In the case of LAD-CTOs and RCA-CTOs they show a higher tendency towards contralateral collateral formation (Fig.2).[22]

There are visible, functioning collaterals (>0,5 mm) and potentially recruitable collaterals (<100 µm). The latter are almost invisible in the absence of occlusion and develop into important collaterals when coronary occlusion is present [29]

The collateralization of the occluded coronaries helps in preventing myocardial infarction and in preserving the left ventricular function in as much as 50% of cases. Only 17-20% of the cases present with a severely reduced left ventricular function [5, 8, 10].

On the other hand, despite a well-developed collateralization and almost normal contractility, this area of myocardium is under perfused and ischemic. Because of the reduced functional reserve of the collateral system these patients become often symptomatic during activity. The presence of a good functioning collateral system is not a guarantee for a preserved viability. It is found both in patients with large dysfunctional areas and in patients with preserved left ventricular function [30, 31].

Cardiovascular profile of patients with CTO

Patients with chronic occluded arteries differ considerably

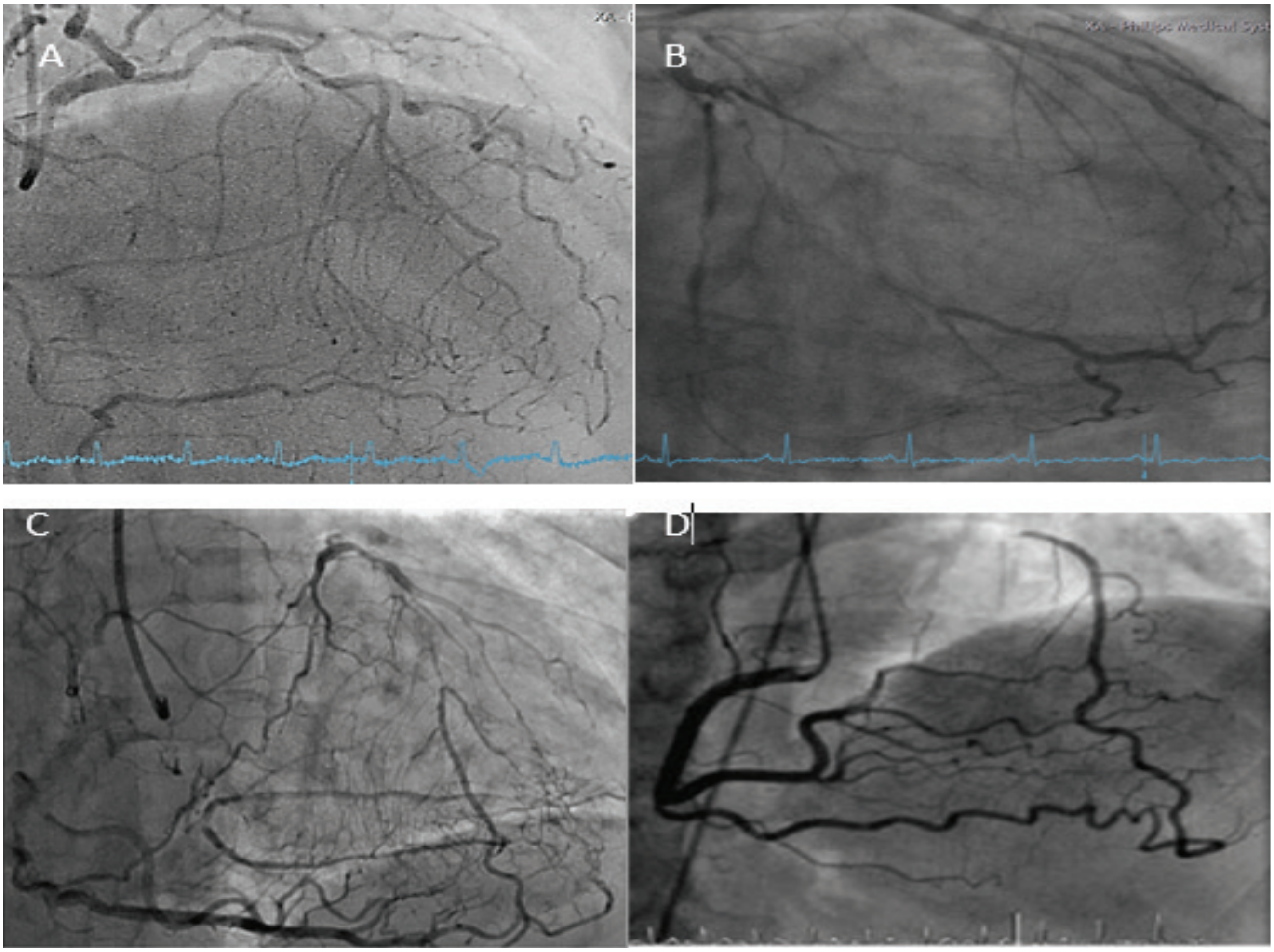

Figure 2 Collateralization of CTOs; A: CTO of the right coronary artery, septal and apical collaterals; B: CTO of the posterolateral branch of the circumflex artery, epicardial, lateral wall collaterals; C: multiple CTOs; D: CTO of the left anterior descending, apical and septal collaterals. (Own database)

from other CAD patients. They are generally older and have higher SYNTAX Scores. Approximately 80% of these patients have a multivessel disease and in 7-10% the left main artery is involved, generally with severe calcification of the coronaries. The LV function may be preserved in as much as 50% of patients, but the rest presents with extensive LV scarring and with different grades of residual viability in the infarcted area.[32] They also have more often other comorbidities such as hypertension, diabetes, and peripheral vascular disease. CTO patients are more often smokers, overweight and have dyslipidemia [8, 10, 14].

Viability assessment

There is conflicting e vidence r egarding t he v alue of preprocedural and preoperative viability assessment. In a meta-analysis, Allman et al.[33] showed improvement in outcomes after revascularization in patients with LV disfunction and viable myocardium, but not in the absence of viability. A randomized trial from Beanlands et al. (PARR-2), failed to support the importance of viability testing in patients with severe LV disfunction.[34]

There is a general consent that the assessment of myocardial viability is a prerequisite for the revascularization of patients with severely reduced LV Function. The recommendation to objectify the viability of the "collateralized" area of the CTO makes more sense in the case of the CTO-PCI. The recanalization of a CTO with PCI is a complex procedure associated with longer procedural times, increased risk of complications and adverse outcomes [13, 17, 35]. On the other hand, the treatment of CTOs with CABG does not require specific techniques to be performed and achieves comparable results with respect to other CAD patients. [36, 37] The majority of patients with a CTO that are treated with CABG have a 3-vessel disease, and the decision to bypass the occluded artery does not have an impact on the complexity of the procedure.

CABG for the treatment of CTOs

The recommendation for surgical treatment of patients with advanced CAD is based on the results of different randomized trials.[12, 38] Patients with multivessel disease and in the presence of CTOs are preferably assigned to CABG. The SYNTAX Trial demonstrated that the surgical revascularization of patients with multivessel disease, left main disease and those with CTOs is associated with better outcomes when compared with PCI. The difference in outcomes was more significant in patients with higher SYNTAX scores including those with CTOs. [12] The use of arterial grafts and the tendency towards complete revascularization has a positive impact on the results achieved by CABG.

Techniques of bypassing CTO vessels do not differ from CABG of other coronary lesions. However, in our experience it is sometimes mandatory to anastomose the vessel in its most distal part, especially in the case of long CTO lesions. Coronary endarterectomy for the treatment of the occluded vessel is rarely needed and does not offer good long-term results [39–41]

The mortality and morbidity of CABG have decreased substantially over time. Mortality rates of 1-3% and stroke rates 0.5-1.5% show that CABG can be considered a low-risk procedure. [42, 43] For the abovementioned reasons, CABG should be the first therapeutic choice for patients presenting with advanced CAD and particularly in the presence of a CTO.

PCI for the treatment of CTOs

CTO-PCI is being increasingly used in dedicated centers and there is a tendency to replace CABG for this purpose. Advances in technology that supports CTO-PCI and the increasing operator experience in high volume centers has resulted in increasing recanalization success rates.[16, 44] The actual evidence is mostly based on observational studies and no RCTs have confirmed its efficacy compared to surgery. The Euro-CTO trial compared CTO-PCI plus medical treatment vs medical treatment alone for patients with CTOs. The principal findings were improved angina frequency scores and quality of life scores for the PCI group. Cardiovascular death and myocardial infarction events were similar after 3 years but MACCEs were significantly lower in the PCI group.[25] The Decision-CTO trial compared outcomes between 2 treatment strategies for patient being treated with PCI when CTOs were present: recanalization of the CTO vs no recanalization of the CTO. This trial showed no differences in the incidence of major cardiovascular events and in the quality of life.[23]

A meta-analysis of patients with stable obstructive coronary artery disease treated either with PCI and medical treatment or medical treatment alone showed no differences regarding death, MI, need for repeat revascularization, or angina.[45]

Also, angiographic evidence of the patency of recanalized CTO vessels is scarce. Different reports show that re-occlusions or restenosis after successful CTO-PCI can occur in as much as 50% of cases, thus raising important questions regarding the efficacy of the procedure.[46, 47]

CTO-PCI is a complicated and very invasive procedure associated with increased exposure times, increased use of contrast and increased incidence of renal failure.[48] Other factors that should be considered when choosing this treatment strategy are: increased risk for coronary perforation and the resulting tamponade, coronary dissections, distal coronary micro embolism that can occlude an otherwise functioning collateralized vessel and the increased procedural mortality in comparison with normal PCI.

Revascularization rates

Revascularization rates of the CTOs vary considerably depending on the treatment strategy and local expertise. In the case of CTO-PCI, this variability is more pronounced because of the increased complexity of the procedure in comparison to routine PCI procedures and in this case operator experience and center volume play an important role. Jones et al, investigated the impact successful revascularization had on mortality and described revascularization rates of 69.6%. The multivariate analysis demonstrated that failed revascularization was predictive of worse outcomes.[49] In a meta-analysis from Patel et al. that included 18061 patients, successful revascularization of CTOs was achieved in 77% of cases and the failed CTO-PCI was associated with worse outcomes. Publications comparing successful with non-successful CTO-PCI and their impact on outcomes should be interpreted cautiously. The fact that failed CTO-PCI is related to worse outcomes does not necessarily mean that successful CTO recanalization have a positive impact. In fact, attempted and failed CTO recanalization imply an increased level of invasiveness compared to successful CTO-PCI, with coronary dissections, bleeding complications and urgent surgery being the typical complications.[50]

From the other side, the treatment of CTOs with CABG does not require additional technical efforts and technology and from a certain point is less influenced by operator experience and center volume. In a study from Banerjee et al. the authors were able to demonstrate that CABG achieves high CTO revascularization rates (100% for LAD CTOs, 92% for LCX and RCA).[51]

Fefer et al, reported similar revascularization rates in a report of 405 patients, with 100% successful revascularization in the case of LAD-CTO.[52] No clear evidence exists regarding the impact of CTO revascularization in the results of patients being treated with CABG. In fact, the rationale for the surgical CTO revascularization is based on the intention to achieve full revascularization and the confirmed impact it has on outcomes.[53, 54]

Conclusion

It is not clear, whether successful CTO revascularization (CABG or PCI) have an impact on long-term outcomes of patients being treated for CAD. For these reasons, the treatment of patients in the presence of CTOs should be based on the current evidence on the treatment of multivessel coronary disease. Evidence comparing different treatment strategies for the treatment of CTOs and evaluating their impact on long-term outcomes is scarce and does not allow for specific recommendations. Comparing outcomes between successful and not successful CTO-PCI and using high revascularization rates as a measure to compare CTO-PCI with CABG, cannot provide clear evidence about treatment options. There is an increasing need for a randomized controlled trial comparing CTO-PCI with CABG or evaluating the impact CTO revascularization has on outcomes.

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