

Procedures for chronic total occlusion: when are they recommended and when not

Mila Menozzi and Giancarlo Piovaccari*

Cardiology Unit, Infermi Hospital, Rimini

KEYWORDS

Chronic total occlusion (CTO);
Viable myocardium;
Reversible ischaemia;
OMT (optimal medical
treatment)

Coronary chronic total occlusion (CTO) produces an important clinical problem, often treated with medical therapy or coronary artery bypass grafting. Recent clinical studies, both registries and randomized trials, demonstrated that percutaneous coronary interventions (PCI), could provide a valid therapeutic option. Nonetheless, significant reduction in all-cause mortality, cardiac mortality, myocardial infarction, MACE, and MACCE has not been demonstrated in the subgroups analysis of randomized trials. These analyses suggest that PCI for CTO should be reserved for patients with angina or with large areas of the myocardium with reversible ischaemia. Large randomized studies should search for a personalized approach, considering the risks and complexity of PCI in CTO, which should mainly consider the extension of the ischaemia and the viability of the myocardium.

Definition

Chronic coronary occlusion (CTO) is defined as a complete or almost complete obstruction of an epicardial coronary vessel with TIMI 0 or 1 flow, datable for at least 3 months.¹

Prevalence of total chronic occlusions

In the activity of a catheterization laboratory with high volumes of work, the CTOs have a prevalence that varies from 18% of the Canadian Register² to 50%,³ the highest percentage we find in patients with previous coronary artery bypass graft (CABG). However, only a small percentage of these patients, after diagnosis, will undergo percutaneous unclogging (PCI). Furthermore, although there is an increase in the popularity of PCI in CTOs, the vast majority of patients are treated either with medical therapy or CABG. The Guidelines recommend considering PCI in CTOs to improve survival and quality of life but in practice the number of procedures remains low.

Treatment of total chronic occlusions

Percutaneous coronary intervention for CTO should be considered, according to the latest ESC/EACTS Guidelines,⁴ in the same way as a non-PCI CTO. This keeping in mind that

the patient is subjected to an often longer procedure, which requires a higher dose of radiation and a contrast medium and with a higher complication rate.⁵

From the literature data, the potential benefits of PCI for CTO are still controversial due to the small number of randomized trials. There is therefore consensus⁶ that at least one of the following conditions is necessary to proceed with the recanalization of a CTO:

- (1) the presence of angina or dyspnoea limiting daily activities, with the aim of alleviating symptoms as well as increasing exercise capacity.
- (2) in asymptomatic or scarcely symptomatic patients the documentation of myocardial ischaemia through non-invasive imaging tests, with the aim of reducing the extent of ischaemia.
- (3) in patients with depressed left ventricular systolic function, the demonstration of vitality with ecobutamine, myocardial scintigraphy, or magnetic resonance imaging, with the aim of improving dyspnoea or signs of decompensation.
- (4) the presence of multivessel disease with the aim of improving the prognosis.

Symptoms and quality of life

There is evidence from non-randomized, both retrospective and prospective, studies that demonstrate how the recanalization of CTOs improves symptoms.⁷

*Corresponding author. Email: giancarlo.piovaccari@auslromagna.it

In a meta-analysis that assessed the clinical impact on angina in patients undergoing effective vs. ineffective recanalization of a CTO, there is twice the incidence of persistent angina in patients treated unsuccessfully compared to those successfully treated.⁸ It should be emphasized that the symptoms in patients with CTO often have an atypical presentation, also due to the presence of a collateral circulation that can partially reduce ischaemia. Furthermore, the chronic nature of the condition often leads the patient to slowly and progressively reduce the workload so that he rarely complains of reduced exercise capacity. In addition, patients with CTO often report exertion dyspnoea and not angina, a less specific symptom that can be attributed to potential non-cardiac causes.

Despite these diagnostic difficulties, there are comforting and solid data. The EUROCTO randomized trial⁹ evaluated the quality of life in patients with CTO and optimal medical therapy (OMT) and demonstrated a reduction in symptoms with PCI compared to OMT alone. The prospective OPEN CTO study¹⁰ showed that >80% of patients with CTO have dyspnoea and that revascularization of CTO improves dyspnoea in 70% of patients.

Ischaemia

In chronic ischaemic heart disease, an >10% myocardial ischaemic load has been shown to have an unfavourable impact on prognosis.¹¹ The myocardium underlying a CTO, in the absence of previous transmural myocardial infarction, should be considered ischaemic until proven otherwise. The presence of collateral circulation, in fact, protects against necrosis but never completely prevents ischaemia. The point is to quantify the area of myocardial necrosis.¹²

The revascularization of a CTO has a strong rationale in the presence of inducible myocardial ischaemia found with imaging tests. In the case of a large epicardial vessel occluded at the level of a proximal segment in a patient with preserved left ventricular systolic function, the presence of inducible myocardial ischaemia is very likely, therefore revascularization of the CTO could be considered even if not preceded by ischaemia testing.¹³

Viability

The revascularization of a CTO finds another strong indication in patients with reduced systolic function due to alterations of the segmental kinetics of the myocardial segments underlying the chronically occluded vessel.

Recovery is greater the larger the hibernated or stunned but the viable myocardial area is.¹³

Imaging tests such as myocardial scintigraphy, stress echocardiography, and cardiac magnetic resonance imaging (RMC) allow us to evaluate the viability of the myocardial territories with reduced contractility. MRI currently represents the gold standard for the assessment of myocardial viability and the transmural extension of necrosis; the measurement of the infarcted area obtained with RMC is an index that linearly correlates with the favourable remodelling of the left ventricle and the recovery of systolic function, after recanalization of a CTO. In patients with transmural necrosis extension (TNE) <75%, an increase in parietal thickening is observed in the segments

underlying the recanalized CTO, while patients with TNE >75% do not show significant improvements. Therefore, the revascularization of a CTO does not have a rationale if the underlying myocardial segments have a TNE >75% as they are considered non-viable, while the lesser is the extension of transmural necrosis is higher is the benefit of the procedure.

Prognosis

Incomplete revascularization is known to be associated with a higher incidence of adverse events at follow-up, particularly in the presence of a residual CTO. According to the PL-ACS Registry,¹⁴ the CTO is a negative prognostic factor for ACS mortality. In the Horizons-AMI trial,¹⁵ CTO is a negative prognostic factor for mortality in ST-segment elevation myocardial infarction (STEMI). According to some authors in patients with a CTO found in the course of myocardial infarction, the recanalization of the same during a scheduled procedure is associated with lower cardiac mortality and a lower rate of adverse cardiovascular events at 2 years.¹⁶ The data from the Explore trial, on the other hand, do not demonstrate benefits in terms of improving the ejection fraction and reducing the left ventricular volume after scheduled revascularization of a non-culprit CTO in patients with STEMI treated with primary angioplasty.¹⁷

Numerous observational studies have shown a reduction in MACE and an improvement in outcome following revascularization of CTOs in chronic ischaemic heart disease. A systematic review of 25 observational studies showed that CTO angioplasty (CTO PCI) if effective is associated with a favourable 3-year outcome in terms of survival, residual angina, and use of bypass. In a recent study analysing the prognostic impact of CTOs in patients enrolled in the Swedish Coronary Angiography and Angioplasty Registry (SCAAR),¹⁸ the presence of a CTO is an independent mortality factor (hazard ratio 1.29; $P < 0.001$) and among patients undergoing an attempt to recanalization of a CTO, effective procedure is associated with significantly better survival (hazard ratio 0.85; $P < 0.034$). Also in the Italian IRCTO Registry (Drug-Eluting Stent Implantation vs. Optimal Medical Treatment in Patients With Chronic Total Occlusion), with a propensity analysis, patients with CTO treated with PCI show a lower incidence of death (1.5 vs. 4.4%; $P < 0.001$), acute myocardial infarction (1.1 vs. 2.9%; $P = 0.03$), and re-hospitalization (2.3 vs. 4.4% $P = 0.04$) compared to those treated with OMT alone.

While the results of the DECISION CTO trial¹⁹ do not demonstrate superiority of the PCI CTO compared to the OMT, although the numerous limitations of the study are evident: the slow enrolment and the low sample size (fewer patients than those predicted by the sample size); a high cross-over between the two arms; the inclusion of the periprocedural infarction among the endpoint. However, there is a trend towards decreasing mortality in the PCI CTO arm.

Conclusions

Defining the risks and benefits of a recanalization procedure is true in general, even more when it comes to recanalization. The benefit, as we have seen, is in terms of improvement of symptoms in symptomatic patients,

reduction of ischaemic burden, or improvement of ventricular function in asymptomatic patients. It should not be forgotten that the benefit derives from an effective recanalization, which stands at 85-90% in centres of experience, as opposed to 54-80% in the Registers 'all comers'. The risk is around 3% and depends on the age of the patient, the complexity of the lesion, and the recanalization technique used, as well as the experience of the operator. Therefore, training programs for operators and development of specific techniques of CTO PCI, continuous education through courses, live cases, and proctoring, are required.²⁰

Conflict of interest: none declared.

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