Debate: Chronic total coronary occlusions. The clinician perspective

A debate: Oclusión coronaria total crónica. Perspectiva del clínico

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QUESTION: Is there enough evidence to be able to say that the coronary recanalization of a chronic total coronary occlusion (CTO) improves the prognosis of patients?

ANSWER: No, there is not. However, many cardiologists believe so based on observational studies that report that patients with CTO who are successfully treated have better prognosis compared to those who undergo failed procedures. In many of these registries, the baseline characteristics, risk factors, ventricular function, and coronary anatomy are substantially different between patients treated successfully and those treated with failed procedures. When the outcomes are adjusted by these confounding variables, success in treatment does not condition the prognosis anymore.

One less biased way to know the effect this has on the prognosis of patients undergoing percutaneous treatment of their CTO is to compare them to those who receive medical treatment. In this sense, several registries have been published with different results. For instance, in a study of patients with CTO treated percutaneously versus patients treated medically (using propensity-score matching), Ladwiniec et al., showed a lower rate for the composite endpoint of death or myocardial infarction at 5 years, but not death as the single event that was favorable to those patients treated percutaneously. However, Yang et al., with a similar matching of patients, did not show any benefits derived from treating the CTO. This shows that dozens of registries on CTO still cannot replace the need for randomized clinical trials.

Very few studies randomizing patients to having their CTO treated or not have been published so far, and not all of them have had the assessment of cardiovascular events as their primary endpoint. The EXPLORe trial included 304 patients with a CTO as the non-culprit artery in individuals with ST-segment elevation myocardial infarction treated with primary angioplasty. At 4 months no differences were seen in the ejection fraction, the left ventricular end-diastolic volume (the primary endpoint) or cardiovascular events analyzed through cardiovascular magnetic resonance. By the way, the result of this study had somehow already been anticipated in a Spanish registry. The REVASC clinical trial randomized 205 patients with stable chronic coronary artery disease to treat or not to treat a CTO. At 6 months, no differences were seen in the global or segmental left ventricular function (the primary endpoint) or cardiovascular events analyzed through cardiovascular magnetic resonance between the 2 groups. The EuroCTO trial randomized 396 patients (2:1) to treat or not to treat a CTO. At the 12-month follow-up, no differences were seen in the rate of cardiovascular or cerebrovascular events reported in the arm where the CTO was treated. It should be mentioned that this study anticipated including 1200 patients but had to be interrupted prematurely due to its low inclusion rate. The IMPACTOR-CTO clinical trial randomized 96 patients with a CTO in their right coronary artery to receive percutaneous treatment or not. This study conducted in a single Russian center showed a reduction of ischemia and improved 6-minute walk test results without any changes in cardiovascular events.

Finally, the DECISION-CTO clinical trial has been the most important study published so far with 834 randomized patients. During a mean 4-year follow-up, the incidence of the composite endpoint of death, myocardial infarction or stroke was similar in both arms.

Therefore, to this day no randomized clinical trial or meta-analysis of all randomized clinical trials published so far has been able to prove that treating a CTO changes the prognosis of patients.

Q.: In what subgroups of patients or situations should we expect to see greater prognostic benefits?

A.: There is something clear: the CTO is a common lesion in patients with ischemic heart disease and its presence is associated with poor prognosis. Therefore, the issue is to be able to identify those patients whose prognosis may change with a percutaneous coronary intervention. The revascularization of a CTO that causes significant ischemia (> 10% quantified using imaging...
modalities) may improve long-term prognosis as a clinical trial is trying to prove: the ISCHEMIA-CTO (Nordic and Spanish Randomized Trial on the Effect of Revascularization or Optimal Medical Therapy in Chronic Total Coronary Occlusions with Myocardial Ischemia; NCT03563417). But before the ISCHEMIA-CTO findings become available, we will probably have the results of the ISCHEMIA (International Study of Comparative Health Effectiveness with Medical and Invasive Approaches, NCT01471522) clinical trial first. This study has been trying to prove something similar in patients who do not necessarily have a CTO. If the ISCHEMIA trial is positive, the hypothesis of revascularizing a CTO based on the presence of significant myocardial ischemia will be much more attractive.

Q.: And what about symptom and functional improvement?
A.: There are at least 2 studies that indicate that symptomatic patients can improve once their CTO has been treated. The FACTOR is a non-randomized clinical trial that showed improved quality of life test results in symptomatic patients. This is a small study of 125 non-randomized patients in whom the quality of life test is analyzed 1 month after the procedure. Also, it compares patients successfully treated versus patients with failed procedures. The benefit derived from successful treatment was greater in symptomatic patients and significant with respect to physical activity and quality of life according to the Seattle Angina Questionnaire. However, the most significant evidence of symptom improvement after treating a CTO comes from the EuroCTO clinical trial that showed modest symptomatic benefits in the quality of life test results after percutaneous treatment. However, the premature interruption of the study and its low inclusion rate make the results questionable.

Regarding functional improvement, there is also evidence that the treatment of a CTO modestly reduces the ischemic region in patients with at least mild to moderate ischemia and barely improves ventricular function, although we still do not know how these aspects may impact the patient’s clinical signs.

Q.: What clinical indications does the percutaneous revascularization of a CTO have?
A.: Today, the main indication for treating a CTO should be to improve symptoms in patients who remain symptomatic despite the optimal medical treatment. In order to achieve this, the occluded artery needs to be recalculated effectively, which totally depends on its angiographic characteristics and the experience of the interventional cardiologist in charge.

The current clinical guidelines of the European Society of Cardiology contemplate 1 indication only for the management of a CTO: patients with angina refractory to treatment and a significant ischemic region as seen on the imaging modalities. This is a class IIa indication with a B-level of evidence. As long as we don’t have any other evidence, we encourage all Spanish interventional cardiologists experienced in the management of CTO, who are actually many and with very good results, to include patients in the current ISCHEMIA-CTO randomized clinical trial. This clinical trial is essential and will shed light on many of the issues we have discussed here.

CONFLICTS OF INTEREST
None declared.

REFERENCES