Mortality benefits with CTO PCI: moving the goalpost closer

Yaron Arbel and Bradley H. Strauss*

Schulich Heart Centre, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, Canada

Published on behalf of the European Society of Cardiology. All rights reserved. © The Author 2015. For permissions please email: journals.permissions@oup.com.

This editorial refers to ‘Management strategies in patients affected by chronic total occlusions: results from the Italian Registry of Chronic Total Occlusions (IRCTO)’, by S.D. Tomasello et al., on page 3189.

Chronic total occlusions (CTO), defined as a complete arterial occlusion [TIMI (thrombolysis in myocardial infarction) 0 or 1 flow] of at least 3 months duration, occurs in 10–20% of coronary angiographic studies, and 5% of coronary computed tomography angiography (CTA) studies. However, CTO revascularization, whether by percutaneous coronary intervention (PCI) or bypass, remains at relatively low levels, with <40% in most reported studies, compared with 60% of patients with coronary artery disease (CAD) without CTO. CTO revascularization by PCI is particularly infrequent; <10% in the two largest registries. These low rates are due to a number of reasons, including decreased success rates and longer procedure times compared with non-CTO PCI, a pervasive sense amongst clinicians that CTO lesions only rarely cause significant clinical symptoms (especially when well collateralized), and lack of clinical evidence that revascularization results in reduction in hard cardiovascular endpoints. Despite recent improvements in percutaneous techniques, new devices, and new therapeutic approaches, there remains uncertainty regarding which CTOs should be treated by revascularization, and whether this should be done by coronary artery bypass grafting surgery (CABG) or PCI. An unanswered question is whether CTOs are themselves a unique determinant of prognosis, or merely an indication of the extensive plaque burden and severity of coronary disease, since 75% of patients with CTOs have multivessel disease. It is still not clear whether CTOs, either as single vessel disease or part of multivessel disease, should be regarded differently from non-CTO CAD, with respect to prognosis or the benefits of revascularization. This is largely due to the exclusion of patients with CTO from most revascularization trials.

In this issue of the journal, Tomasello and colleagues have brought interesting new insights to these questions with the 1-year follow-up results of 1777 patients from 12 clinical sites consecutively enrolled in the Italian CTO Registry. The patients were divided into three groups according to the specific treatment of the CTO: medical therapy (MT, n = 836), PCI (n = 776), or CABG (n = 175). The PCI success rate for CTOs was 75%, which is certainly achievable in most clinical centres with CTO expertise. At 1 year, patients that underwent PCI had significantly lower rates of cardiac mortality (2.6% compared with 8.2% and 6.9% for MT and CABG, respectively) and major adverse cardiovascular and cerebrovascular events (MACEs). These results are not unexpected since the PCI group had a number of lower risk characteristics, including younger age, less chronic renal failure, fewer Q waves, higher ejection fraction, and more myocardial viability than the CABG or MT groups. However, to adjust for these baseline differences, a propensity-matched analysis of the PCI and MT groups (that included 77% of the patients in these two groups) similarly showed a significant reduction in cardiac mortality, acute myocardial infarction, and re-hospitalization in PCI compared with MT patients.

An extensive number of publications have indicated that CTO patients with successful PCI revascularization have improved intermediate and long-term outcomes compared with a failed PCI attempt. Until recently, there were scant data to evaluate whether revascularization (by either PCI or CABG) improves clinical outcomes compared with optimal medical therapy in patients with CTOs. The first indication of a potential benefit of revascularization was recently reported from Korea. Jang et al. demonstrated reduced cardiac death and MACEs at 42 months in 783 CTO patients with extensive collaterization that underwent revascularization (two-thirds PCI, one-third CABG) compared with medical therapy. These differences also persisted in a propensity-matched analysis. The current study by Tomasello et al. provides additional evidence in support of the beneficial effects of PCI revascularization on hard cardiovascular endpoints, albeit only at 1 year. The major limitations of both registry studies are the higher risk profile of the medical treatments groups, and the possibility of inclusion bias since there is no randomization. Although the propensity-matched analysis tries
to overcome this bias, there may be confounders that have not been accounted for.

There are several features of this study which may not reflect CTO contemporary practice in other countries. The PCI revascularization rates were very high (50% of all the CTO patients), despite a very high percentage of multivessel disease patients, even triple vessel disease patients for whom appropriate use criteria (AUC) would recommend surgical treatment. Current data from the National Cardiovascular Data Registry in the USA show PCI rates of CTOs at <5%. Similar low rates of PCI attempts (<10% of CTOs) were reported in Canada, Poland, and Sweden. Decisions on which patients should be selected for revascularization, and which type (particularly in multivessel disease with high SYNTAX scores) appear to be based on regional and country differences, which probably also reflects the local expertise. Therefore, one must be cautious about generalization of the results.

Secondly, the ‘medical’ therapy group also included patients with non-CTO PCI. Our group has previously shown that treatment of non-CTO lesions lead to quality of life index scores that were intermediate between patients with CTO revascularization and non-revascularized patients that only received medical therapy. In the Canadian CTO registry, two-thirds of patients underwent PCI only to a non-CTO artery and one-third had CTO PCI. The decision to attempt revascularization of a CTO artery in multivessel disease remains a highly relevant clinical question, particularly in ST-segment elevation myocardial infarction (STEMI) patients where the culprit artery is a non-CTO vessel. Due to the complexity of CTOs and lack of demonstrated benefit of CTO revascularization, it remains a common strategy in many centres only to treat the non-CTO artery after diagnostic angiography, in stable and acute coronary syndrome (ACS) patients. Although multiple studies, surgical and angioplasty, have demonstrated the superior clinical outcomes in complete vs. incomplete revascularization, this has generally been in studies that have excluded patients with chronic total occlusions. The current study does not fully address this point since the medical treatment group includes patients with incomplete revascularization (non-CTO only) and non-revascularized patients.

Thirdly, there are differences in the clinical indications for performing PCI for CTOs according to geographic locations. In the current study, 23% of PCI patients were asymptomatic. Only 52% of patients in the PCI group received two antianginal drugs. Current AUC guidelines recommend PCI of CTO only in symptomatic

---

Figure 1  The decision on the type of treatment of a chronic total occlusion (CTO) is dependent on many factors: the severity of symptoms with optimal medical therapy (OMT), the extent of ischaemia (exercise ECG or non-invasive imaging), and the presence of myocardial viability (myocardial function by echo or late gadolinium enhancement by cardiac magnetic resonance) are the main determinants of revascularization. The decision on how to revascularize depends on CTO complexity, local percutaneous coronary intervention (PCI) expertise for complex CTO procedures, and the presence of multivessel disease and co-morbidities that affect PCI and coronary artery bypass (CABG) risks. Evidence that successful revascularization improves cardiac mortality is still preliminary, but may emerge as a potent indication supporting revascularization strategies in patients with CTO. MACE, major adverse cardiovascular and cerebrovascular event.
patients despite two antianginal drugs. The clinical benefit of hard cardiovascular outcomes with revascularization demonstrated in this study, despite a 94% use of two or more antianginal medications in the MT group, suggests that the AUC guidelines may be overly conservative. Additional data from registries and the ongoing randomized trials (EuroCTO and DECISION-CTO) are eagerly awaited.

In the meantime, clinicians still need to make revascularization decisions for CTO patients. These decisions must be guided by a careful evaluation of all of the patient factors, including the severity of the symptoms, adequacy of medical therapy, extent of ischaemia and viability, the patient’s suitability for interventions (percutaneous or bypass surgery), and the local PCI and surgical expertise (Figure 1). Despite the inherent limitations of registry studies, we now have supportive evidence of the benefits of revascularization from two studies that may be factored into these decisions, particularly in borderline cases.

**Conflict of interest:** B.H.S. is the founder of Matrizyme Pharma. Y.A. has no conflict of interest to declare.

**References**


