



Chronic total occlusions in non-infarct-related arteries

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This editorial refers to ‘Prognostic impact of a chronic total occlusion in a non-infarct-related artery in patients with ST-segment elevation myocardial infarction: 3-year results from the HORIZONS-AMI trial’[†], by B.E. Claessen *et al.*, on page 768

Chronic total occlusions (CTOs) are complete obstructions of coronary arteries, described as $\geq 99\%$ stenosis, of >3 months duration, and with poor or no antegrade blood flow, i.e. TIMI flow grade 0–1. Patients with CTOs are frequently encountered in interventional cardiology practice. It has been estimated that one-third of patients with coronary artery disease requiring revascularization have a CTO, and that ~ 10 – 20% of lesions intended for percutaneous revascularization are complete occlusions.¹ In stable coronary artery disease, the negative impact of a CTO has been demonstrated. A New York State survey showed that incomplete percutaneous revascularization leaving untreated CTOs led to higher 3-year mortality.² In the setting of primary percutaneous coronary intervention (pPCI) for ST-segment elevation myocardial infarction (STEMI), previous studies have suggested that the increased mortality observed in patients with multivessel disease (MVD) was mainly driven by the presence of a CTO in a non-infarct-related artery (IRA).^{3,4} Furthermore, STEMI patients with a CTO in a non-IRA were found to have suboptimal reperfusion more frequently, as shown by lower myocardial blush grades and a lesser degree of ST-segment resolution following pPCI.⁵

Claessen *et al.*⁶ have retrospectively evaluated 3283 STEMI patients undergoing pPCI within the HORIZONS-AMI trial and confirmed the worse prognosis of patients with a CTO in a non-IRA ($n = 283$). Accordingly they report impaired markers of reperfusion and increased early (0–30 days), late (30 days–3 years), and cumulative 3-year mortality in this specific group of patients. Patients with MVD but no CTO ($n = 1477$) had increased early but not late mortality. The mechanism related to higher mortality in STEMI patients with a non-IRA CTO is probably multifactorial. In the trial, patients with a non-IRA CTO achieved suboptimal reperfusion following pPCI, as documented by less

frequent complete ST-segment resolution, post-procedural TIMI grade 3 flow, and myocardial blush in the IRA territory. It is also possible that patients with CTO in a non-IRA suffer larger myocardial infarctions following IRA occlusion due to the extension of the infarction beyond the territory normally supplied by the IRA following abrupt cessation or impairment of collateral flow. In the study of Claessen *et al.*, the peak creatine phosphokinase levels tended to be higher in the CTO group, but were not significantly different between patients with and without CTO of a non-IRA, and additional studies are needed to prove the ‘impaired collateral flow’ hypothesis.

The finding that the presence of a CTO in a non-IRA is associated with worse adverse events raises the question of whether revascularization of the CTO would lead to improved outcomes. In stable patients, recanalization of a CTO in the presence of a sizable viable territory has been associated with improvement in symptoms, left ventricular (LV) function, and survival,⁸ but no such data are available in the setting of pPCI for STEMI. While this issue cannot be answered by the study of Claessen *et al.*, there is indeed some evidence that the recanalization of a staged non-IRA CTO may lead to improved outcomes. A retrospective study by Yang *et al.* on 136 patients undergoing staged recanalization of a non-IRA CTO 7–10 days following STEMI suggested a beneficial clinical effect from the procedure.⁷ After adjustment for possible confounders, successful recanalization of the CTO was identified as an independent predictor for lower 2-year cardiac mortality [hazard ratio (HR) = 0.145, 95% confidence interval (CI) 0.047–0.446, $P = 0.001$] and major adverse cardiac events (MACE)-free survival (HR = 0.430, 95% CI 0.220–0.838, $P = 0.013$).⁷

It should be noted that current national guidelines do not recommend non-culprit lesion intervention during pPCI for STEMI without cardiogenic shock or severe haemodynamic compromise.⁹ In fact, prior studies have shown that treatment of non-culprit lesions during pPCI for STEMI in haemodynamically stable patients was associated with increased post-procedural morbidity in the absence of mortality benefit.^{10,11}

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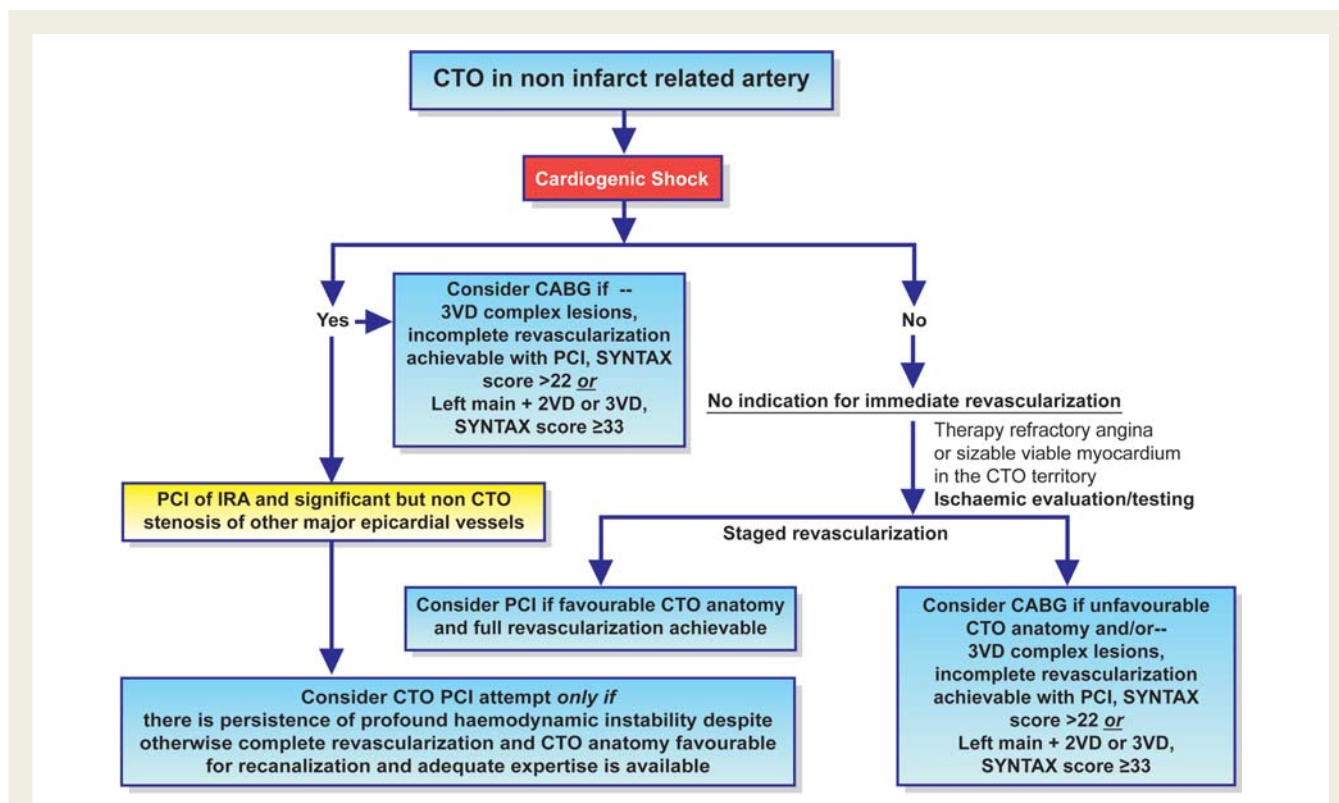


Figure 1 Simplified approach to chronic total occlusions in a non-infarct-related artery in patients presenting with ST-segment elevation myocardial infarction. CTO, chronic total occlusion; PCI, percutaneous coronary intervention; CABG, coronary artery bypass surgery; SYNTAX, Synergy between PCI with Taxus and Cardiac Surgery; VD, vessel disease.

While the study by Yang *et al.*⁷ provides some preliminary evidence for a strategy of staged PCI for a non-IRA CTO, robust randomized trials are indicated to assess this approach objectively. The decision to proceed with revascularization of a non-IRA CTO following STEMI needs to take into account individual patient symptoms, the angiographic complexity of the occlusion, LV function, and myocardial viability, as well as ischaemia in the CTO territory. Clinicians also need to consider the relative merits of coronary artery bypass graft (CABG) and PCI in differing patterns of coronary arterial disease to determine the optimal modality for revascularization. *Figure 1* outlines a simplified approach to patients with CTO in a non-IRA in patients presenting with STEMI.

While complete revascularization should be attempted in patients with cardiogenic shock or severe haemodynamic instability, no data exist on patients with one or more CTOs in this setting. In patients with additional complex multivessel disease, especially if the left main trunk is involved, surgery in the acute phase might be considered.¹² For most patients, pPCI remains the strategy of choice. If patients remain in shock despite revascularization of the IRA and other non-CTO lesions, a limited attempt at revascularization of the CTO may be undertaken if adequate expertise is available. However, several arguments plead against an aggressive CTO revascularization procedure in this setting. First, the clinical benefit is uncertain, because no information on viability or ischaemia in the corresponding territory is available.

Secondly, the armamentarium of techniques and equipment applied is limited by the clinical presentation. Accordingly additional access for contralateral injection is discouraged to reduce the amount of contrast injected and minimize vascular complications in patients that are fully anticoagulated and are frequently treated with glycoprotein IIb/IIIa receptor inhibitors. In addition, the use of 'aggressive' CTO wires may be associated with increased risk of perforation due to the profound antithrombosis. As a consequence, the CTO recanalization rates achieved in this setting are likely to be lower than the 60% reported in a recent multicentre registry.¹³

In the absence of shock, the indication for non-IRA CTO recanalization should be reassessed following the acute phase. Patients with large territory ischaemia or symptoms despite maximal medical therapy should be considered for revascularization. The decision regarding the mode of revascularization should be based on the severity, distribution, and angiographic complexity of the non-IRA coronary artery disease as well as the type of stents implanted in the acute phase (drug-eluting or bare metal stents). A heart team approach including cardiologists and cardiac surgeons is recommended to optimize the revascularization modality for an individual patient.^{14,15} The ongoing Evaluating XIENCE V and LV in PCI on occlusions after STEMI (EXPLORE) trial investigating whether PCI of a CTO in a non-IRA within 1 week after primary PCI has a beneficial effect on LV dimensions and function will provide additional insight into the role of non-IRA CTO

revascularization. Future randomized studies should incorporate residual viability and ischaemia assessment in the decision process and assess clinical endpoints such as survival, myocardial infarction, and freedom from heart failure hospitalization.

Conflict of interest: none declared.

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