Recanalization of a chronic total occlusion in ST-segment elevation myocardial infarction patients: why and when?

Current guidelines recommend that primary percutaneous coronary intervention should be limited to the infarct-related artery in patients with acute myocardial infarction and multivessel disease. However, patients with acute myocardial infarction and concomitant multivessel coronary artery disease have a worse prognosis, mainly due to the presence of a chronic total occlusion (CTO) in a nonculprit lesion. Few studies have addressed the specific issue of CTO treatment in the setting of acute myocardial infarction. We review the currently available literature regarding coronary revascularization of the nonculprit CTO in ST-segment elevation myocardial infarction patients, starting with a clinical case of an infero–postero–lateral ST-segment elevation myocardial infarction in a multivessel coronary artery disease patient with concurrent left anterior descending CTO complicated by hemodynamic instability.

KEYWORDS: chronic total occlusion  multivessel disease  primary percutaneous coronary intervention  ST-elevation myocardial infarction

Primary percutaneous coronary intervention (PCI) in patients with ST-segment elevation myocardial infarction (STEMI) aims at early and sustained restoration of anterograde flow in the infarct-related artery (IRA) [1,2]. The strategy of the mechanical reopening of an acutely occluded coronary artery allows the reperfusion of ischemic myocardium, thus limiting infarct size and reducing hemodynamic and arrhythmic complications [3]. However, coronary angiography during primary PCI often shows that the atherosclerotic process can extend over the IRA. Of note, the finding of multivessel coronary artery disease (MVD) in the setting of STEMI is associated with higher morbidity and mortality, even after reperfusion therapy [4–6]. At present, multivessel PCI in the setting of acute myocardial infarction (AMI) is discouraged since it does not appear to confer a net beneficial effect on clinical end points [7]. Conversely, it has recently been shown that in patients with AMI and concomitant MVD, the higher mortality rate is mainly due to the presence of a chronic total occlusion (CTO) in a non-IRA rather than the mere presence of MVD [8]. However, current guidelines with regard to multivessel PCI in the setting of primary PCI are based on only a few clinical evidences and do not even address the specific issue of CTO treatment. Consequently, in this particular setting in which clear evidence from randomized controlled trials is still lacking, the usual strategy is mainly based on clinical judgment.

We review the currently available literature regarding coronary revascularization of nonculprit CTO in STEMI patients starting with a clinical case of an infero–postero–lateral STEMI in a MVD with concurrent CTO in a non-IRA complicated by hemodynamic instability. In particular, we aim to assess whether a revascularization of the nonculprit CTO has to be attempted and when it should be performed.

Clinical case

A 64-year-old man was admitted to our emergency department owing to acute onset of chest pain and dyspnea in the last 2 h. He had a history of hypertension and smoking habit without previous cardiovascular events. Recent laboratory tests revealed normal renal function. On admission, physical examination revealed tachypnea and cyanosis with pulmonary rales in the absence of significant heart murmurs. Blood pressure was 100/60 mmHg and a 12-lead ECG showed a sinus tachycardia at 125 beats per min, an ST-segment elevation in inferior leads and poor anterior R-wave progression from V2 to V5 (Figure 1). The patient was treated with aspirin and clopidogrel and immediately transferred to our catheterization laboratory to undergo primary PCI. Upon arrival in the catheterization laboratory, the patient had persistent chest pain with Killip class III requiring mechanical ventilation. A femoral access (7 Fr) was chosen to eventually switch to intra-aortic balloon pump (IABP) counter-pulsation if clinically needed during the...
procedure. Coronary angiography revealed a diffuse coronary artery disease (CAD) with acute thrombotic occlusion of the posterior descending artery (PDA) of the right coronary artery (RCA) and a CTO of the proximal left anterior descending (LAD) previously supported by septal collaterals from the PDA. Left ventricular (LV) function appeared significantly impaired. Anterograde flow in the IRA was restored by multiple manual thrombus aspirations with Invatec (Italy) Diver CE Max. Next, the culprit lesion was stented with a Chrono Carbostent 3 × 16 mm at 18 atm, obtaining a final thrombolysis in myocardial infarction (TIMI)-3 flow and myocardial blush grade 2 (Figure 2). Nevertheless, the patient continued to be hemodynamically unstable. Thus, considering the low dose of contrast used and the short duration of the recanalization of the culprit vessel, LAD was engaged with a Cordis Extra Back Up guiding catheter and LAD CTO was crossed with an intermediate wire (ACS, Abbott Vascular) supported by an over-the-wire 2.0 × 20 mm balloon in a relatively easy manner. The procedure was completed by implanting a carbostent & implantable device: chrono Carbostent 3.5 × 25 mm postdilated with a non-compliant balloon 3.5 × 20 mm at 26 atm with an optimal angiographic result (Figure 3). The patient was sent to a coronary care unit without the need for an intra-aortic balloon pump and discharged after 6 days with a moderately impaired LV function. No major adverse coronary events (MACEs) were recorded at the 6-month clinical follow-up.

The present case represents a situation occurring with an increasing frequency in interventional cardiology, consisting of a patient with an AMI and MVD further complicated by the concurrent presence of a CTO in the non-IRA. Nevertheless, despite the relatively high frequency of this scenario, clear evidence from randomized clinical trials that can guide the strategy of the interventional cardiologist is lacking. Consequently, the correct clinical management of similar cases can be inferred only indirectly from the literature.

**Negative prognostic role of multivessel coronary artery disease & noninfarct-related artery CTO in the setting of acute myocardial infarction**

Multivessel CAD in the setting of primary PCI represents a frequent finding, ranging from 40 to 65% of STEMI patients undergoing urgent coronary angiography [4,5]. The presence of MVD is associated with a significant increase in the rate of early recurrence of MACEs, especially reinfarction and need for revascularization [4,9,10].

More importantly, the presence of MVD has been shown to be an independent predictor of 1-year mortality after mechanical reperfusion of the culprit vessel [10].

The presence of MVD can adversely affect survival through several mechanisms. Notably, patients with MVD have a greater incidence of comorbidities such as older age and a higher rate of cardiovascular risk factors, possibly contributing to an adverse prognosis. However, MVD has been shown to be an independent predictor of mortality even after adjustment for all these risk factors [10]. A reduced reperfusion success may play a relevant role. Indeed, Sorajja et al. have demonstrated that in patients with single-, double- and triple-vessel disease, despite similar rates of epicardial TIMI-3 flow, successful myocardial reperfusion – as assessed by
ST-segment resolution – is impaired in patients with significant disease remote from the infarct artery, proportional to the extent of CAD [11]. Accordingly, a lower successful myocardial perfusion, as assessed by myocardial blush grade or ST-segment resolution, results in a lower survival rate despite the restoration of normal epicardial blood flow in the culprit vessel [12,13].

Importantly, several studies have recently shown that the higher mortality rate observed in patients with AMI and MVD is mainly determined by the presence of a CTO in a non-IRA and not by the mere presence of MVD. The finding of a CTO in non-IRA in the setting of primary PCI is not so uncommon, as randomized trials and registries indicate that it represents almost a third of all cases with MVD and 12–13% of all patients with STEMI [8,9].

Moreno et al., while assessing the event-free survival rate among 630 patients with AMI treated with PCI within 12 h after symptom onset according to the presence of single vessel disease, MVD without CTO and MVD with CTO, demonstrated that the group of patients with MVD and CTO had the worst outcome [9]. In accordance with these results, in a larger population, Van der Schaaf et al. demonstrated that STEMI patients with MVD had a higher mortality at 1-year follow-up compared with patients with single vessel disease and that this increased risk profile in MVD patients is mainly due to CTO of non-IRA (odds ratio [OR]: 3.8; 95% CI: 2.5–5.8) [8]. In a recently published paper, the same group, while confirming that CTO rather than the mere presence of MVD is a strong predictor of mortality during the first 30 days after PCI (OR: 3.6; 95% CI: 2.6–4.7; p < 0.01), have also shown that the negative prognostic value of CTO is maintained up to a 5-year follow-up, even excluding patients who died within 30 days of the acute event (OR: 1.9; 95% CI: 0.8–1.6; p < 0.01) [14]. Interestingly, the presence of a CTO, but not of MVD alone, was strongly associated with a decrease in LV ejection fraction (OR: 3.5; 95% CI: 1.6–7.8; p < 0.01) suggesting that a possible explanation for this worse outcome might reside in the fact that STEMI patients with a non-IRA CTO undergo a more pronounced postinfarction worsening of LV function and an unfavorable LV remodeling process.

Importance of CTO revascularization in multivessel coronary artery disease

While the aforementioned findings highlight the prognostic relevance of a CTO in MVD in the setting of AMI, the long-term benefit of a CTO recanalization is limited to patients with MVD only. In fact, Valenti et al., testing the efficacy of a modern percutaneous approach to CTO treatment using drug-eluting stents in a series of 486 consecutive patients with at least one CTO, found that PCI success (in almost three out of four patients) conferred a long-term survival benefit compared with a failed recanalization only in patients with MVD [15]. Of note, this survival benefit was restricted to MVD patients receiving a complete revascularization, while patients with incomplete revascularization showed a worse prognosis.

The site of the occlusion influences the prognostic impact of a CTO, as well as the clinical relevance of its recanalization. In a large cohort of stable patients, Safley et al. demonstrated that the benefit of reopening a CTO was evident in the recanalization of a chronically occluded LAD since its success was associated with reduced long-term mortality (hazard ratio [HR]: 0.61; 95% CI: 0.42–0.80), while this was not the case for the left circumflex artery or for RCA (HR: 0.84; 95% CI: 0.53–1.32 and HR: 0.95; 95% CI: 0.63–1.44, respectively) [16]. Nevertheless, a clinical benefit in the reopening of non-LAD CTO can be predicted when a large area of myocardial vitality is subtended by a CTO. Consequently, in order to decide whether to obtain a revascularization of a CTO lesion, either percutaneous or surgical, a careful evaluation of myocardial viability in the territory of the occluded vessel, using nuclear imaging, MRI or stress echo, is generally warranted. However, when these techniques are not available, the simple 12-leads resting ECG has a strong prognostic relevance since, while
in the presence of Q-waves myocardial viability has been demonstrated in more than half of cases [17], their absence represents an absolutely reliable marker of myocardial viability and of functional recovery in the territory of the occluded vessel [18].

When to attempt a complete revascularization in STEMI patients with multivessel coronary artery disease: evidence from literature

Taken together, all these data suggest that a patient with an AMI and MVD presenting a concurrent CTO of the LAD and with evidence of myocardial viability in the territory of CTO should undergo CTO recanalization. However, as previously mentioned, current guidelines recommend a staged ischemia-driven strategy of treating nonculprit lesion in patients with AMI and MVD. This suggested approach is referred to a single study by Corpus et al. demonstrating not only a lack of benefit of treatment of nonculprit lesions, but also a higher rates of reinfarction, target vessel revascularization and MACEs among patients undergoing multivessel PCI [19]. Moreover, in this study, the proportion of patients undergoing multivessel PCI within the same procedure was only 5% (26 out of 506) of all patients showing MVD. Finally, the higher rate of mortality among patients with multivessel PCI during the same procedure occurred within the hospitalization and it was mainly driven by the presence of cardiogenic shock at admission, a situation in which the same guidelines recommend a complete revascularization, as discussed below.

More recently, other studies have demonstrated that simultaneous nonculprit vessel PCI in the setting of AMI is feasible and safe [20–24], while the benefit of this more aggressive approach remained unclear. In the Hepacoat for Culprit or Multivessel Stenting for Acute Myocardial Infarction (HELP AMI) trial, Di Mario et al. demonstrated that the 1-year incidence of repeat revascularization was similar among patients randomized to IRA treatment only or to complete multivessel treatment [22]. By contrast, in a retrospective analysis of more than 3500 patients treated with primary PCI, Hannan et al. demonstrated that PCI limited to IRA was associated with significantly lower inhospital mortality than multivessel PCI, while patients undergoing staged PCI of nonculprit vessels within 60 days had a significantly lower 12-month mortality rate than patients undergoing culprit vessel PCI only [23]. Moreover, Ochala et al., testing the hypothesis that an aggressive multivessel revascularization strategy would have beneficial effects on LV function and on clinical outcomes, found that despite a trend towards an improvement in LV ejection fraction at 6 months, no significant difference in the incidence of MACEs during follow-up was present [24]. Several reasons might explain the uncertain benefit of multivessel PCI in the setting of AMI. First, it is well known that myocardial infarction is associated with an enhanced thrombotic and inflammatory state. Thus, in the acute setting and in the immediate short term after AMI, an unfavorable thrombotic and inflammatory milieu compounded by multiple areas of vascular injury induced by multivessel intervention might create a high-risk situation for recurrent ischemic events and restenosis. Moreover, the prolonging of the procedure and the consequent increase in contrast media utilization exposes the patient to a higher risk for contrast-induced nephropathy, a complication known to adversely impact the prognosis of STEMI patients [25]. Finally, it has been shown that degree of stenosis in moderately obstructive nonculprit lesions may be overestimated during primary PCI owing to the widespread vasoconstriction of the entire coronary tree and to the change in reference segment observed at angiographic follow-up [26]. This observation has important implications for decision-making on complete revascularization strategy in patients with MVD, possibly leading to the unnecessary and eventually harmful treatment of nonsignificant coronary stenosis.

However, all the studies that have tested the potential benefit of the aggressive strategy of multivessel revascularization during primary PCI have important limitations. First, the sample size is always small. Second, most of the evidence is based on retrospective observations. Last, and more importantly, the prognostic relevance of non-IRA CTO in the setting of AMI is not addressed at all.

Hemodynamic instability: the relevant role of a non-IRA CTO

An exception to the general rule of limiting PCI to the IRA in patients with AMI and MVD is represented by cardiogenic shock. In fact, given the notion that the restoration of blood flow is the major predictor of survival in these patients and based on the results of the Should We Emergetely Revascularize Occluded Coronaries for Cardiogenic Shock? (SHOCK)
of the PDA branch of the right coronary artery. Moreover, the successful recanalization of the CTO promptly allowed the patient to hemodynamically stabilize.

**Conclusion**

The available data indicate that MVD has a tremendous deleterious effect on prognosis of STEMI patients and that this mainly depends on the presence of a CTO in a non-IRA. While the treatment of MVD in patients with STEMI represents a controversial issue in contemporary interventional cardiology, the prognostic impact of a non-IRA CTO and its management are not adequately taken into account by current guidelines. This is not a secondary issue, especially considering the relatively high incidence of a CTO in the context of an urgent coronary angiography in patients with STEMI and its strong predictivity of cardiogenic shock. In general, in the absence of acute decompensation of shock, an ischemia-driven staged procedure might be of first choice in case of non-IRA CTO, since it might have more risks than advantages. However, starting from a paradigmatic clinical case and analyzing the available literature, we believe that in particular conditions, such as in case of hemodynamic or electrical instability, in the presence of ECG findings suggesting myocardial viability in the territory of occluded vessel, in a patient with preserved renal function and when the procedure can be completed in a short time with a reasonable amount of contrast medium, PCI of the CTO might be attempted within the same procedure.

**Future perspective**

Definitive data should come from specifically designed randomized clinical trials. However, these are unlikely to be performed for practical reasons. Consequently, clinical judgment, based on the available data and on the specific characteristics of the patient, has to be applied in this particular situation.

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Impact of multivessel disease on long-term outcome

Papers of special note have been highlighted as:

**REVIEW**

In case of hemodynamic instability, percutaneous coronary intervention of a non-IRA-related CTO might be attempted within the same procedure.

- Demonstrates that negative long-term prognostic patient with acute myocardial infarction and multivessel disease is related to the presence of a non-IRA related artery (IRA) chronic total occlusion (CTO).
- Demonstrates that the concurrent presence of a non-IRA CTO in STEMI patients is associated with an unfavorable left ventricular remodeling.

**Bibliography**

* of interest
** of considerable interest


Recanalization of a CTO in ST-segment elevation myocardial infarction patients


* Demonstrates that in the presence of a CTO, collateral branches do not provide a sufficient functional supply to the occluded vessel.