

Stenting the Non-Culprit Lesion during Primary Angioplasty of the Infarct-Related Coronary Artery: The Long and Winding Road

Keywords: Primary percutaneous coronary intervention; Non-culprit coronary lesion; Acute myocardial infarction

Abbreviations: PCI: Percutaneous Coronary Intervention; CHD: Coronary Heart Disease; ST-Segment Elevation Myocardial Infarction STEMI; PRAMI: Preventive Angioplasty in Myocardial Infarction; CVLPRIT: Complete Versus Lesion-only Primary PCI

Editorial

The combination of scientific understanding in the adequate utilization of novel pharmacological agents, and the new techniques in percutaneous coronary intervention (PCI) will continue to improve the therapeutic management of the acute coronary syndromes [1-3]. Evidence based medicine provides the convincing proof that primary PCI is the comprehensible treatment of choice for ST-segment elevation myocardial infarction (STEMI) [3]. Considering the fact that patients with multivessel coronary heart disease (CHD) comprise over half of the STEMI population, it is not an uncommon finding to observe a significant non-culprit lesion besides the occluded infarct-related coronary artery during primary PCI. These patients with multivessel disease in this context have a worse prognosis than patients with single vessel disease [4,5]. Now, the problem is what to do with the non-culprit significant stenosis once the infarct-related coronary artery was already treated. Should we proceed and stent the non-culprit lesion turning unstable a coronary plaque that was previously stable and jeopardize another wall in a patient that already has an infarcted territory? It seems logical to think that treating all significant coronary stenosis would provide a better clinical outcome. However, although there is recent data in favor of this therapeutic management, the 2013 ACCF/AHA guidelines for the management of ST-elevation myocardial infarction discouraged this approach due to a significant increase in adverse outcomes for patients undergoing multivessel PCI in the setting of STEMI, and recommended a restrictive approach that discourages treatment of non-culprit lesions during the index PCI, unless the patient is in cardiogenic shock [6]. Moreover, the 2014 ESC/EACTS guidelines on myocardial revascularization are in accordance with the latter approach [7]. They stated that evidence supporting immediate (preventive) intervention in non-infarct-related lesions is a matter of debate [8,9]. On the other hand, patients with extensive CHD in vessels remote from the infarct-related artery have reduced success in reperfusion and an adverse prognosis following primary PCI [8]. They concluded that at present, multivessel PCI during STEMI should be considered in patients with cardiogenic shock in the presence of multiple, critical coronary stenosis, and if there is persistent ischemia after PCI on the supposed culprit lesion [6].

Editorial

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It is well known that patients with stable CHD and multivessel disease benefit from achieving complete revascularization [10-13]. The question is if this assumption also holds true in the setting of STEMI if a more aggressive approach leading to more complete revascularization is performed. This is a controversial subject if we analyze current data based on observational studies and compare them to the results of recent randomized clinical trials in the era of drug eluting stents. In fact, observational data suggested that this approach was not beneficial and might be even harmful, with slightly better outcome depending on the timing of the nonculprit PCI [14,15]. On the other hand, recent evidence obtained from randomized trials documented significant reductions in composite ischemic endpoints by performing multivessel revascularization during STEMI [16,17]. However, there had been some inconsistencies in the analysis of the results. For example, the PRAMI (Preventive Angioplasty in Myocardial Infarction) trial [16], was stopped prematurely due to a much higher than expected treatment efficacy. They found a 65% reduction in ischemic events with complete revascularization during the index PCI in 465 patients. It seems a little surprising to achieve such high statistically significant results with a relatively small number of patients and of clinical events raising concerns of a chance finding magnified by the early termination of the trial. In addition, the CVLPRIT (Complete Versus Lesion-Only Primary PCI) trial [17] did not show reductions in hard endpoints, and the benefit demonstrated in the composite endpoint was obtained by repeat revascularizations. This open-label clinical trial randomized 296 patients in 7 UK centers to either in-hospital complete revascularization (n: 150), or culprit lesion-only revascularization (n: 146). Complete revascularization was performed in the index hospitalization either at the time of primary PCI or before hospital discharge. The primary endpoint of mortality, recurrent myocardial infarction, heart failure, or ischemia-driven revascularization within 12 months occurred in

10% of the complete revascularization group versus 21% in the culprit lesion-only revascularization group (hazard ratio: 0.45; 95% CI: 0.24 to 0.84; $p=0.009$). Although there was no significant reduction in death or myocardial infarction, a non significant reduction in all primary endpoint components was seen. There was no reduction in ischemic burden on myocardial perfusion scintigraphy or in the safety endpoints of major bleeding, contrast-induced nephropathy, or stroke between the groups.

We should take into consideration that multivessel interventions in the setting of STEMI prolong procedural time and contrast exposure, putting the patient at increased risk for procedure-related complications. It is also well known an inclination to overestimate the severity of non culprit lesions, leading to unnecessary stenting [18]. This overestimation of non culprit lesions may be avoided by utilizing intracoronary procedures such as fractional flow reserve (FFR) guidance [19-22] or intravascular ultrasound [13,23-27]. FFR has already become the standard of care for defining flow limiting coronary lesions requiring PCI in patients with stable CHD, and it is under investigation in the setting of STEMI right now. Ongoing studies with FFR will help us to resolve the dilemma of non-culprit lesions in patients undergoing primary PCI. Intravascular ultrasound imaging techniques provide useful information such as plaque volume, lumen area or composition of the vessel wall, but FFR is able to supply a physiological assessment of a coronary stenosis [20-24]. Further randomized trials are ongoing, and the largest study COMPLETE (Complete vs. Culprit-only Revascularization to Treat Multi-vessel Disease After Primary PCI for STEMI) trial [28], (ClinicalTrials.gov #NCT01740479) compares complete revascularization (acute or staged) versus culprit-only with conservative strategy, and is currently enrolling nearly 4 thousand patients in the USA and Canada. This trial will provide a more detailed evaluation of the question of complete versus culprit-only revascularization in the setting of STEMI. Another undergoing prospective, randomized trial is the COMPARE ACUTE (ClinicalTrials.gov #NCT01399736) which is carried out at multiple sites across Europe and Asia [29]. Patients are randomized to receive either an FFR-guided multi-vessel PCI vs. culprit-only PCI in the setting of STEMI. Until the results of these trials are known, we should be cautious and prudent in the evaluation and therapeutical management of multivessel CHD during STEMI. The risk benefit profile for the individual patient in a personalized manner should be carefully analyzed in order to adequately treat and pave the way in this yet long and winding road.

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