

# Long-Term Outcome of Percutaneous Coronary Intervention of a Persistent Total Occlusion in the Infarct-Related Coronary Artery

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## Editorial

Primary percutaneous coronary intervention (PCI) is the gold standard treatment in patients with acute myocardial infarction (AMI). Early coronary reperfusion with PCI reduces long-term mortality in patients who present with ST-segment elevation AMI [1-4]. Patients with failed thrombolysis or those with late-presenting AMI may still benefit from PCI by mechanisms independent of myocardial salvage. There are several possible mechanisms of benefit from late PCI outside the time window of myocardial salvage. These may include reduction of ventricular remodeling, decreased ventricular instability with the resulting diminished incidence of ventricular arrhythmias, and provision of collateral vessels to other territories in the event of further coronary artery occlusion [5-10]. In addition to promoting an acute inflammatory response and local edema, reperfusion of IRA with an adequate blood flow at a proper arterial perfusion pressure increases tissue turgor, which may have a scaffolding effect on the vulnerable infarcted territory increasing tissue stiffness to possibly resist infarct expansion [6]. All of these changes in the compromised zone should have a beneficial influence on the remodeling process by altering the properties of the scar tissue and by diminishing the ischemic burden in the non-infarcted myocardium at the border zone [5-7]. All of these plausible mechanisms should be tested in clinical situation to properly evaluate clinical outcomes. However, caution must be exercised when interpreting the results of studies examining this open artery hypothesis. This hypothesis can be tested in its purest sense in experimental animal models, a setting where almost all the variables are known and controlled. However, the clinical situation is much more complex depending on the extension of damaged, ischemic/necrotic territory. Patients may have acute-on-chronic coronary artery occlusion in the presence of multivessel disease and well-developed collateral channels. The pattern of necrosis may also be different with areas of necrosis separated by islands of ischemic, stunned, hibernating, or normal cells [11-13]. The random combination of these different variables could have diverse impact on clinical outcomes and events.

The role of late opening of the totally occluded infarct-related coronary artery (IRA) after AMI has been controversial. Although there is a large body of experimental and clinical evidence supporting the concept of late PCI for AMI, the mechanism responsible for the observed benefits remain speculative [14-18]. There are observational data suggesting a lower incidence of clinical events, and experimental studies reporting a reduction in adverse left ventricular remodeling after late PCI of a totally

occluded IRA. In order to properly test the open artery hypothesis, vessel patency should be assessed days to weeks after AMI and a demonstrable beneficial effect should be independent of early left ventricular (LV) function. This approach will diminish the influence of spontaneous closure of the vessels that were open early post AMI or the spontaneous opening of the vessels that were closed early. White H et al. [19], examined infarct vessel patency and LV function in their patients one month after the first AMI. These two parameters, vessel patency and LV function, were found independently predictive of survival over 3 years of follow-up on multivariate analysis. They observed that the beneficial effect of a patent vessel was greatest when the IRA supplied more than 25% of the myocardium and the ejection fraction was less than 50%. However, it is very important to state that serial assessment of left ventricular function was not performed. Therefore, the mechanism for the benefit is unclear. In a similar study [20] done in a cohort of 58 patients, infarct-related vessel patency was assessed 7 to 10 days after AMI. In the first week of AMI, left ventricular function was similar in patients with a patent or an occluded vessel. However, over the subsequent year those with an occluded IRA developed the most ventricular dilatation and the greatest decrease in ejection fraction. They observed an intermediate effect when the IRA was patent but possessed a minimal luminal diameter of less than 1.5 mm. Hence, it seems that there is a dose response inverse relationship between the degree of stenosis and the quantity of remodeling, suggesting an important beneficial effect of late PCI in opening occluded vessels or severe stenotic arteries. The independent effect of a patent IRA on survival and the importance of the quality of perfusion are

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further reinforced by other reported studies [21-25]. These latter investigations demonstrated that late patency of an IRA seems to have a positive influence on remodeling and survival and that this effect is independent of any acute reduction of infarct size secondary to reperfusion during the acute phase of an evolving AMI.

Nevertheless, despite these favorable observational and experimental clinical findings, the Occluded Artery Trial (OAT) failed to confirm these observations in a large prospective randomized clinical study [26].

The OAT investigation demonstrated that PCI did not reduce the occurrence of death, reinfarction, or heart failure, and that there was a trend toward excess reinfarction during 4 years of follow-up in stable patients with occlusion of the IRA 3 to 28 days after AMI. There was no interaction between treatment effect and any subgroup variable, namely, age, sex, race or ethnic group, infarct-related artery, ejection fraction, diabetes, Killip class, and the time from myocardial infarction to randomization [26]. Surprisingly, the OAT did not confirm the hypothesis that late PCI after AMI in stable patients with a totally occluded IRA would reduce the occurrence of death, reinfarction, or hospitalization compared with optimal medical therapy alone. However, there are interesting aspects in the design of the trial, the type of stents utilized, and the duration of medical treatment that need to be mentioned. The large majority of stents placed during protocol PCI were bare metal stents, only 8% of PCI patients received drug eluting stents. Considering the medical management in this trial, in most OAT patients clopidogrel was stopped by the 4-month visit. Prolonged treatment with thienopyridines was not required. Therefore, it was used only in 15% of the patients. In addition, a relatively large number of patients were not studied due to rigid exclusion criteria, a fact that might have precluded clinical benefit of late PCI in certain subgroup of patients. Indeed, there was an early significant benefit of assignment to PCI on the prevalence of angina. Dyspnea and angina were less common in the PCI arm through 24 months. These results suggest that revascularization should be used selectively for the management of angina in patients with persistent total occlusion of the IRA. Despite the conclusive clinical findings of the OAT there still remain additional experimental mechanisms of benefit in late reperfusion therapy. However, there is a robust long-term follow-up data which confirms that there is no benefit on cardiovascular events and clinical outcomes associated with a routine strategy of late PCI in stable AMI patients with persistent total occlusion of the IRA. The selective utilization of PCI in the revascularization of ischemic myocardium for the management of angina in patients with persistent total occlusion of the IRA definitely provides clinical benefit in this subgroup of patients.

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