The late open artery hypothesis: the case and the artery remain closed

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This editorial refers to ‘Lack of benefit from percutaneous intervention of persistently occluded infarct arteries after the acute phase of myocardial infarction is time independent: insights from the Occluded Artery Trial’ by V. Menon et al. on page 183

The OAT trial1 was a key investigation, contributing to contemporary practice in the treatment of acute myocardial infarction (AMI). It unexpectedly demonstrated that for patients undergoing angiography between 3 and 28 days after AMI with poor or absent flow in a major infarct-related artery (IRA), re-establishing flow by percutaneous coronary intervention (PCI) provided no benefit, with indeed the suggestion of harm. There were some caveats to this statement, based on the specific population studied: the patients were a high-risk group, in that the lesion had to be in a proximal vessel, or there had to be an ejection fraction (EF) of <50%. The patients were also those about which little information was previously available regarding optimum treatment: the subtended myocardium had to be either dyskinetic or akinetic, or, if the myocardium was hypokinetic or normal, then mild or moderate (but not severe) ischaemia had to be present.

This lack of benefit was despite sustained patency of the IRA (83% vs. 25% for medical therapy alone) and similar EF at 1 year in an angiographic substudy, and almost universal use of aspirin plus thienopyridine for the successfully treated PCI group (97%) compared with 26% for medical therapy alone.

A number of arguments exist to explain this lack of effect. The observations of periprocedural macro- and microembolization and an attenuation of rapidly recruitable collateral vessels following PCI2,3 have received particular attention, as contributors to worse early and late outcomes, respectively. Yet the wealth of data supporting the early open artery hypothesis which provided the rationale for the OAT study, and the broad time frame (3–28 days post-AMI) for patient inclusion, might contribute to the suspicion that perhaps a benefit in those patients in OAT undergoing angiography and PCI somewhat earlier rather than later might have been obscured. The subgroup analysis of patients undergoing angiography and PCI at ≤3 days by Menon et al.4 suggests that this suspicion is unfounded.

The authors compared outcomes in patients treated by PCI vs. a medically treated group, according to whether randomization was ≤3 days or ≤7 days post-AMI. Because randomization was done on the basis of calendar days, some patients were randomized as early as 24 h post-AMI. Although the ≤3 day data were included in the original OAT ≤7 day data showing no interaction with the overall result,1 the absolute numbers of patients are clearly diminished by this subgroup analysis (total patients ≤3 days = 331 from a total of 2201 in the original study), the present lack of knowledge about patients with ‘somewhat early’ late artery opening makes these analyses of interest.

In keeping with the original study, and despite significantly higher absolute risk for patients randomized at ≤3 days, PCI again failed to show benefit over medical therapy in patients treated within this time frame. In addition, there was a suggestion of harm in those patients treated later than 3 days, with a trend toward higher rates of myocardial infarction, both fatal and total (non-fatal + fatal infarction). It is therefore possible that a small benefit of relatively early late reperfusion from late salvage of ischaemic myocardium was obscured by a small hazard of later opening of the artery. It could be argued that reductions in collateral formation might be of less importance in this ‘somewhat early’ late group, but, conversely, thrombotic microembolisation might be expected to be increased. Further pathophysiological insights will have to await other studies.

Since the publication of the OAT trial, two principal developments in PCI in AMI have occurred. First, the use of the Export aspiration catheter has been shown to be an effective therapy for microembolization, improving outcomes in the acute setting in AMI.5 Even if this approach is considered in future trials of late reopening of the IRA, it may be expected to influence mainly periprocedural outcomes. Secondly, there is the question of whether any differences in outcomes could be achieved by using drug-eluting stents, used infrequently in OAT and increasingly advocated by some in AMI.6 This question would seem a distraction from the as yet unresolved pathophysiological issues raised...
by the OAT study and the new subgroup analysis. The relatively disappointing results in this analysis by Menon et al. underscore once again the importance of achieving early reperfusion in ST-segment elevation myocardial infarction (STEMI), and support continued efforts to reduce the large numbers of patients who still fail to achieve this.

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References

Giant calcified cardiomegaly

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A 65-year-old male, ex-smoker, with previous extensive anterior myocardial infarction 18 years ago and NYHA functional class III, presented to the emergency room with diarrhoea and vomiting associated with epigastric pain and acute renal failure. Myocardial enzymes were markedly elevated with an ECG evidence of an old anterior myocardial infarction. Chest X-ray showed an enlarged and calcified cardiac silhouette (Panel A). Transthoracic echocardiogram revealed a large ventricular anteroapical aneurysm occupied by a huge mural thrombus (Panel B). Coronary angiography showed an occluded proximal left anterior descending artery without any evidence of collateral circulation (Panel C). Left ventriculogram demonstrated a large calcified ventricular aneurysm (Panel D) and cardiac magnetic resonance (Panel E and F) revealed left ventricular end-diastolic and end-systolic volumes of 875 and 821 mL, respectively. The left ventricular ejection fraction was only 6%. The patient was rejected for cardiac resynchronization, therefore underwent cardiac defibrillator implantation and was referred for consideration of cardiac transplantation.

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