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PHARMACOTHERAPY

Lack of benefit of cyclosporine to attenuate reperfusion injury after PCI

In the CIRCUS trial presented at the ESC Congress 2015, cyclosporine administered before percutaneous coronary intervention (PCI) for ST-segment elevation myocardial infarction (STEMI) did not prevent left ventricular remodelling or improve clinical outcomes. The quest for an effective therapy to prevent ischaemia–reperfusion injury continues.

In the multicentre, double-blind trial, 970 patients with an acute anterior STEMI and complete occlusion of the culprit artery were randomly assigned to receive an intravenous injection of cyclosporine (2.5 mg/kg body mass) or a matching placebo before recanalization. The primary outcome (a composite of all-cause death, worsening heart failure during initial hospitalization, rehospitalization for heart failure, or ≥15% increase in left ventricular end-diastolic volume at 1 year) occurred in 59.0% of the cyclosporine group and 58.1% of the control group (OR 1.04, $P = 0.77$). No significant differences between the groups occurred in the separate components of the primary end point or in the rate of adverse events.

In an editorial accompanying the trial publication, Derek Hausenloy and Derek Yellon question the use of an increase in left ventricular end-diastolic volume, which is a surrogate marker of adverse left ventricular remodelling, as part of the primary end point. They suggest that the high incidence of this outcome might have masked differences in the other components of the end point. Furthermore, they point out that a new formulation of cyclosporine was used in this study, which might have been "ineffective at preventing myocardial reperfusion injury". Data from the ongoing CYCLE trial are awaited.

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Original article Cung, T.-T. *et al*. Cyclosporine before PCI in patients with acute myocardial infarction. *N. Engl. J. Med.* doi:10.1056/NEJMoa1505489