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Effect of ischemic postconditioning on microvascular obstruction in reperfused myocardial infarction. Results of a randomized study in patients and of an experimental model in swine

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ABSTRACT

Background: Ischemic postconditioning (PCON) appears as a potentially beneficial tool in ST-segment elevation myocardial infarction (STEMI). We evaluated the effect of PCON on microvascular obstruction (MVO) in STEMI patients and in an experimental swine model.
Methods: A prospective randomized study in patients and an experimental study in swine were carried out in two university hospitals in Spain. 101 consecutive STEMI patients were randomized to undergo primary angioplasty followed by PCON or primary angioplasty alone (non-PCON). Using late gadolinium enhancement cardiovascular magnetic resonance, infarct size and MVO were quantified (% of left ventricular mass). In swine, using an angioplasty balloon-induced anterior STEMI model, MVO was defined as the % of area at risk without thioflavin-S staining.
Results: In patients, PCON (n = 49) in comparison with non-PCON (n = 52) did not significantly reduce MVO (0 [0–1.02]% vs. 0 [0–2.1]% p = 0.2) or IS (18 ± 13% vs. 21 ± 14%, p = 0.2). MVO (>1 segment in the 17-segment model) occurred in 12/49 (25%) PCON and in 18/52 (35%) non-PCON patients, p = 0.3. No significant differences were observed between PCON and non-PCON patients in left ventricular volumes, ejection fraction or the extent of hemorrhage. In the swine model, MVO occurred in 4/6 (67%) PCON and in 4/6 (67%) non-PCON pigs, p = 0.9. The extent of MVO (10 ± 7% vs. 10 ± 8%, p = 0.9) and infarct size (23 ± 14% vs. 24 ± 10%, p = 0.8) was not reduced in PCON compared with non-PCON pigs.
Conclusions: Ischemic postconditioning does not significantly reduce microvascular obstruction in ST-segment elevation myocardial infarction.
Clinical Trial Registration
http://www.clinicaltrials.gov. Unique identifier: NCT01898546.

1. Introduction

In ST-segment elevation myocardial infarction (STEMI) timely coronary reperfusion is the primary therapeutic goal to reduce left ventricular infarct size and improve patients' outcome [1]. Unfortunately, despite successful reperfusion of the epicardial blood flow an impairment of microvascular perfusion persists in a significant number of patients, a phenomenon referred to as microvascular obstruction (MVO)

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[2]. In recent years MVO has shown to be a powerful and independent predictor of a poor outcome [3–5].

Availability of cost-effective and easy-to-implement therapies that could reliably reduce MVO and subsequently may optimize the beneficial effects of timely primary percutaneous intervention would be of utmost importance [6,7]. In recent years ischemic postconditioning (PCON) has emerged as a promising option. PCON permits a progressive rather than a brisk restoration of blood flow to the jeopardized myocardium by means of consecutive cycles of inflation and deflation of the angioplasty balloon used to open the acute coronary occlusion [6–8]. Previous experimental evidence [8–11] and preliminary clinical data [12–18] suggest that this simple strategy exerts a number of protective myocardial effects in comparison with the immediate reperfusion achieved by means of a standard primary angioplasty approach. Nevertheless, the effect of PCON on MVO has not been specifically addressed.

In the present study we aimed to analyze the effect of PCON on cardiovascular magnetic resonance-derived MVO in a randomized series of patients with a first STEMI treated with primary angioplasty and on myocardial samples obtained from a highly controlled anterior STEMI swine model. Additionally, the effect of PCON on infarct size was also evaluated in the same scenarios.

2. Methods

2.1. Study group in patients

From October 2011 to July 2012, consecutive patients of age ≥18 years who were admitted to two university hospitals for a first STEMI within the first 12 h of chest pain onset and for whom the clinical decision to treat with percutaneous coronary intervention was made, were considered for inclusion. STEMI diagnosis was established on the basis of current guidelines [19].

The exclusion criteria were as follows: documented history of previous infarction; primary percutaneous revascularization not attempted; severe clinical or hemodynamic deterioration; left main stem disease; thrombolysis in myocardial infarction (TIMI) 2–3 or Rentrop collateral flow grade ≥1; death, re-infarction, cardiac surgery or severe clinical deterioration before cardiovascular magnetic resonance study; patients who denied participation in the registry; any contraindications to cardiovascular magnetic resonance.

The institutional ethics committees of the participating institutions approved the research protocol and written informed consent was obtained from all subjects. The study was conducted in accordance with the Declaration of Helsinki.

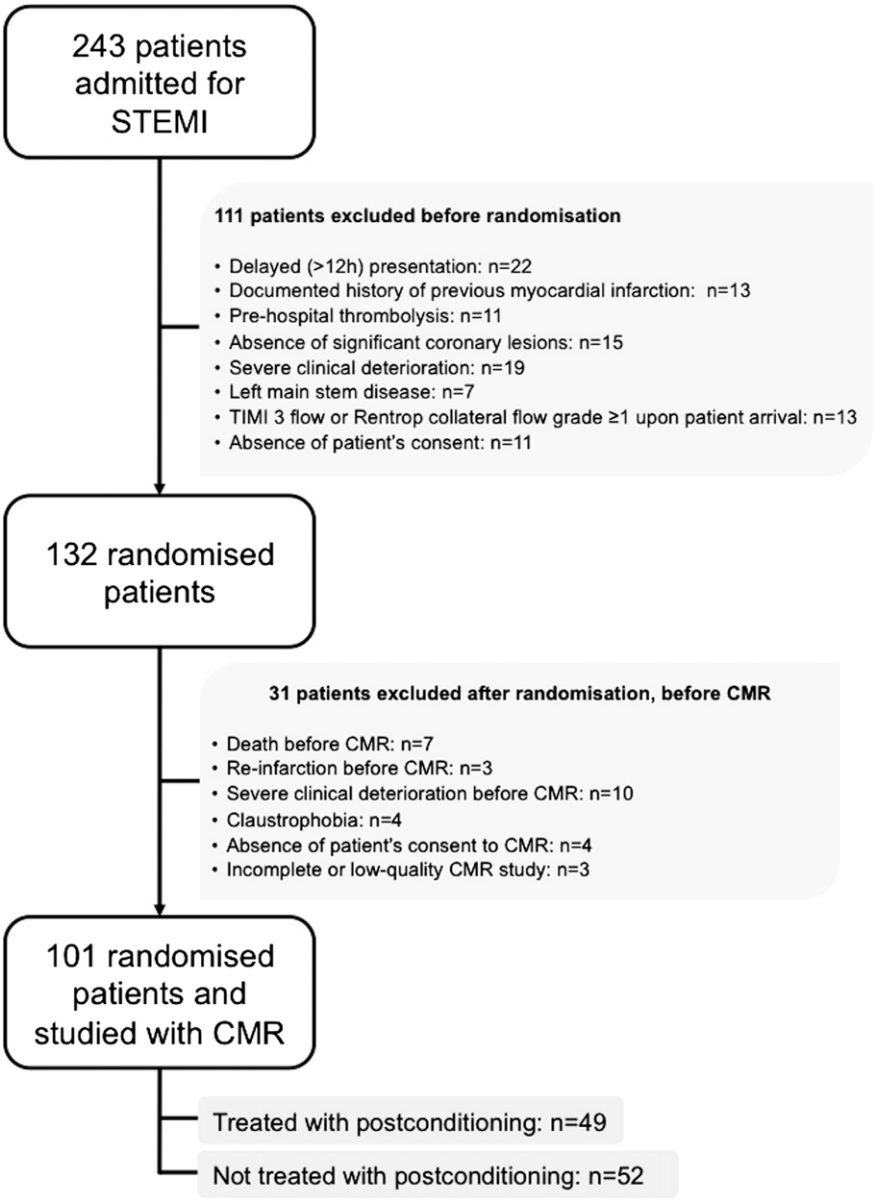

Fig. 1. Flow chart of patients. Reasons for exclusion of patients before randomization and before cardiovascular magnetic resonance are exposed in the flow chart. Abbreviations: CMR = cardiovascular magnetic resonance imaging; STEMI = ST-segment elevation myocardial infarction; TIMI = thrombolysis in myocardial infarction.