



**A randomised trial of expedited transfer to a cardiac arrest  
centre for non-ST elevation out-of-hospital cardiac arrest  
(ARREST)**

**Summary Protocol Version 4**

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## Introduction

Out-of-hospital cardiac arrest (OHCA) is a global public health issue. There are 60,000 cardiac arrests per year in the UK, of which resuscitation is attempted in just under half. Resuscitation attempts are successful in up to 30%. However, more than two thirds of patients who survive to hospital admission die before discharge. There is wide variation in both regional and inter-hospital survival rates from OHCA; this disparity is also present across London. This variation has been shown to be attributable to hospital infrastructure, resources and personnel rather than patient characteristics. Overall survival therefore remains poor, at 7%.

It is well known that the majority of OHCA are secondary to an acute cardiac ischaemic event. Coronary artery disease is responsible for more than 70% of OHCA of presumed cardiac cause, with acute occlusion demonstrated in 50% of consecutive patients taken for immediate coronary angiography (ICA). Early cardiopulmonary resuscitation (CPR) and defibrillation, with ICA and percutaneous coronary intervention (PCI) in a CAC, prevents re-arrest, preserves myocardial function and has been shown to improve post-arrest outcomes in ST-segment elevation (STE). The management of patients without STE however is controversial, with a delayed approach to intervention. Despite recently published data suggesting PCI in non-STE resulted in a two-fold increase in favourable outcome, randomised data are lacking. Emergent reperfusion therapies come with a weak recommendation from ILCOR, and a Class IIa recommendation by the American Heart Association (AHA) and European Society of Cardiology (ESC), if there is a high suspicion of ongoing infarction.

The European Association of Percutaneous Cardiovascular Interventions (EAPCI) recommends a prior rule-out of non-cardiac cause in the emergency department followed by coronary angiography within 2 hours. It remains unclear if time-critical, definitive hospital based management of the post-arrest patient without STE in a specialist centre improves outcomes, and there has been variable uptake of this strategy both pre-hospital and amongst the interventional cardiology community.

## The need for a randomised controlled trial

There is an urgent need for a randomised controlled trial examining the benefits of early delivery of post-cardiac arrest care in specialist centres, specifically in the absence of STE. Post-arrest care is time-critical, requires a multi-disciplinary approach and may be more optimally delivered in centres with greater provider experience. ILCOR and the EAPCI state that randomised trials are essential in this population to determine if timely delivery by the ambulance services to a CAC with organised post-cardiac arrest care including immediate access to reperfusion therapy improves survival. There are no randomised trials and only indirect evidence that CAC and systems of care may be effective and only two observational studies examining the role of immediate ICA±PCI in the absence of STE. This is an important and topical question as there is a drive to regionalise care for all patients into CACs.

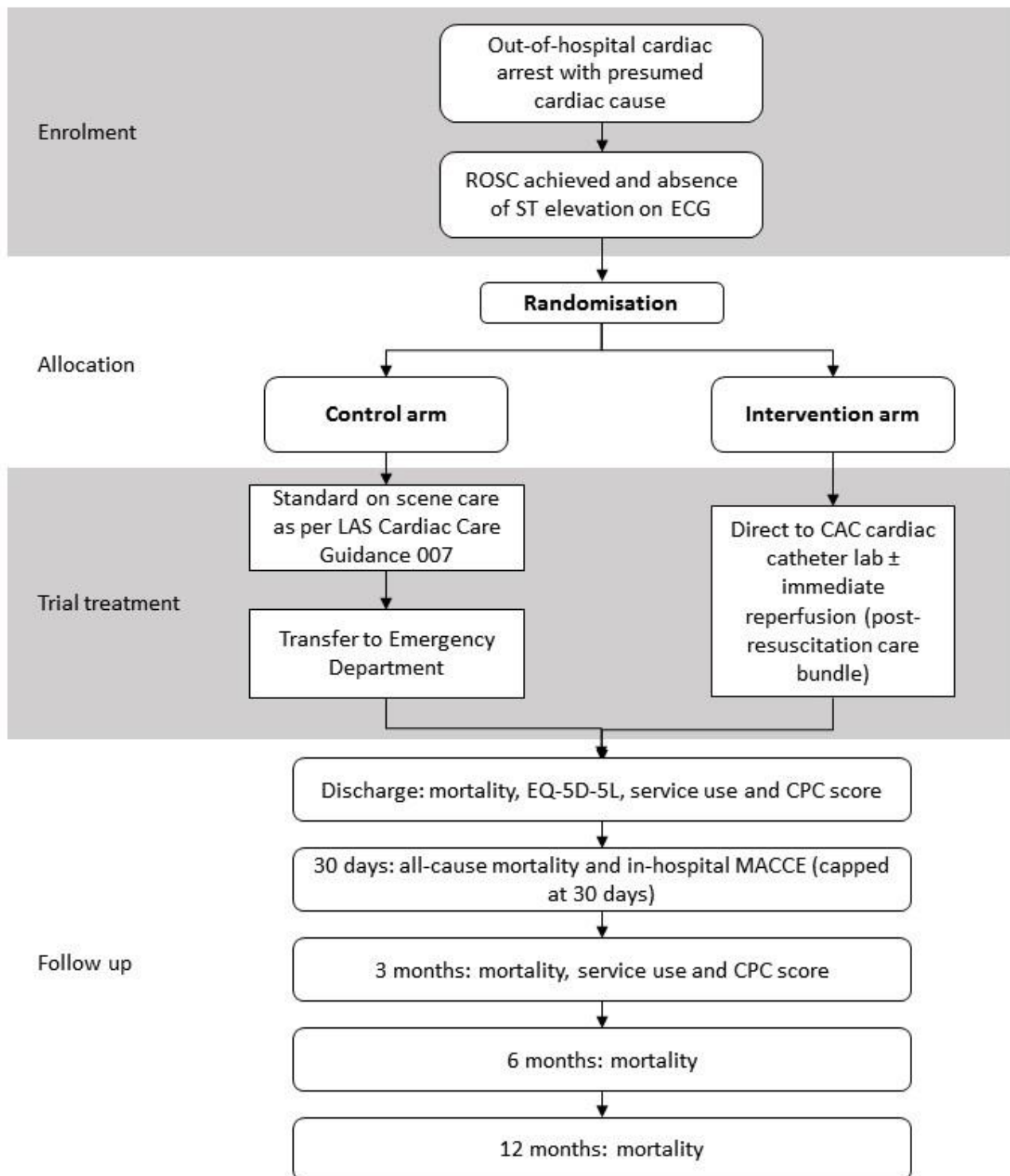
### Aim

The aim is to determine the best post-resuscitation care pathway for patients without STE. We propose that changes to emergency management comprising expedited delivery to a CAC with organised post-cardiac arrest care including immediate access to reperfusion therapy will reduce mortality in patients without STE compared to the current standard of care, which comprises protracted pre-hospital management of the patient without definitive care plan and delivery to geographically closest hospital.

### Trial design and sample size

Randomised controlled interventional trial enrolling 860 OHCA patients with ROSC. Each arm of the trial will include 430 patients.

## Trial Flowchart



### **Inclusion Criteria**

1. Out-of-hospital cardiac arrest (OHCA)
2. Return of spontaneous circulation (ROSC)
3. Age 18 or over (known or presumed)
4. Absence of non-cardiac cause (for example; trauma, drowning, suicide, drug overdose)

### **Exclusion Criteria**

1. Criteria for ST-elevation myocardial infarction on 12-Lead electrocardiogram (ECG)
2. Cardiac arrest suffered after care pathway set and patient en route
3. Do Not Attempt Resuscitation (DNAR) order
4. Suspected pregnancy

### **Primary Endpoint**

All cause mortality at 30 days

### **Secondary Endpoints**

The impact of the intervention on the following outcomes will be assessed.

- Neurological status at discharge and 3 months
- All-cause mortality at 3, 6 and 12 months
- The composite of in-hospital major adverse cardiovascular and cerebrovascular events (MACCE) capped at 30 days
- EQ-5D-5L at discharge

## **Trial Treatment**

The attending paramedics will assess patients for eligibility. If the patient is eligible, randomization will be performed by the advanced paramedic practitioner desk and the allocation will be communicated to the on site paramedic.

### **Intervention Arm: Direct to CAC**

The intervention arm consists of activation of the pre-hospital triaging system currently in place for post-arrest STE patients. This involves pre-alert of the CAC and strategic delivery of the patient to the catheter laboratory (24 hours a day, 7 days a week). Patients will receive definitive post-resuscitation care: intubation and ventilation, where necessary, targeted temperature management, and goal-directed therapies including evaluation and identification of underlying cause of arrest with access to immediate reperfusion if necessary. Prognostication will occur no earlier than 72 hours post-cardiac arrest to prevent premature withdrawal of life-sustaining treatment. Transfer times estimated from the 40-patient pilot are anticipated to be 100 minutes (median; IQR 75 to 113) from time of arrest to the designated centre.

### **Control Arm: Standard of Care**

The control arm comprises the current standard of pre-hospital advanced life support (ALS) care management for patients with ROSC following cardiac arrest of suspected cardiac aetiology. The patient is conveyed to the geographically closest emergency department. Management thereafter will be as per standard hospital protocols however as in the intervention arm, prognostication is to be delayed in trial patients until at least 72 hours post arrest.

Please refer to the full protocol for details of any references mentioned in this summary. The full protocol is available by emailing [arrest@LSHTM.ac.uk](mailto:arrest@LSHTM.ac.uk) to request a copy.