

Project Title:	Effect of Remote Ischaemic preConditioning on Clinical outcomes in patients undergoing Coronary Artery bypass graft surgery (ERICCA study): A multicentre double-blind randomised controlled clinical trial
Project Ref:	09-100-05
Cost:	£1,511,605 (total cost of research jointly funded by EME and the British Heart Foundation)
Lead Applicant & Institution:	Dr Derek Hausenloy The Hatter Cardiovascular Institute University College London
Start Date:	1 November 2010
Plain English Summary:	<p>Coronary heart disease (CHD) is the leading cause of death in the UK, accounting for 124,000 deaths (2006) and costing the UK economy over £7.9 billion a year. Patients with severe CHD are usually treated by coronary artery bypass graft (CABG) surgery, the risks of which are increasing due to older and sicker patients being operated on. New treatment strategies are therefore required to improve health outcomes in these high-risk patients undergoing CABG surgery with or without valve (CABG±valve) surgery.</p> <p>The objective of this research proposal is to determine whether remote ischaemic preconditioning (RIC), a virtually cost-free, non-pharmacological and simple non-invasive strategy for reducing the damage to the heart muscle at the time of surgery, can improve health outcomes in high-risk patients undergoing CABG±valve surgery.</p> <p>In this research project, 1610 high-risk patients undergoing CABG±valve surgery will be recruited via 9 UK hospitals performing heart surgery. Patients will be randomly allocated to receive either RIC or control. For RIC, a blood pressure cuff will be placed on the upper arm to temporarily deprive it of oxygen and nutrients, an intervention which has been shown in our pilot studies to reduce damage to the heart muscle by up to 40% during CABG±valve surgery. We will determine whether RIC can improve health outcomes in terms of better patient survival, less heart attacks and strokes, shorter hospital stay; less damage to the heart, kidney and brain during surgery; better heart function post-surgery and less chance of developing heart failure; better exercise tolerance and quality of life.</p> <p>This trial will bring together a multi-disciplinary team of investigators each with complementary skills and expertise in the design, running and analysis of the study: heart research scientists, cardiologists, cardiac surgeons, kidney specialists, cardiac anaesthetists, research nurses, clinical trials experts, a database manager, statisticians, and two previous heart bypass surgery patients.</p>

<p>Abstract:</p>	<p><u>Research Design:</u> Multi-centre double-blind randomised controlled clinical trial.</p> <p><u>Study Population:</u> High-risk patients (additive Euro-SCORE of 6 or more) undergoing CABG±valve surgery.</p> <p><u>Planned Interventions:</u> Remote ischaemic preconditioning (RIC) comprising three 5 min cycles of inflation (to 200mmHg) and deflation of a cuff placed on the upper arm. Control will comprise placing an un-inflated cuff on the upper arm for 30 minutes.</p> <p><u>Proposed outcome measures:</u> Primary outcome: Major adverse cardiac and cerebral events at one year (MACCE- death, myocardial infarction, revascularisation, stroke). Secondary outcomes: Peri-operative myocardial and renal injury; Length of ITU/hospital stay and inotrope score; 6 minute walk test; Quality of life analysis and cost-effectiveness analysis. There will be an echo substudy assessing left ventricular ejection fraction.</p> <p><u>Assessment and follow up:</u> Outcome measures will be assessed from the patient GP and medical notes, questionnaires (at 3, 6, 9 months) and 6 week and one year outpatient appointments. Safety will be assessed using a Standard Operating Procedure.</p> <p><u>Proposed sample size:</u> In the SYNTAX study, the MACCE rate was 12.4% at 12 months in CABG patients at lower risk than those proposed for this trial (mean EuroSCORE 3.8)(Serruys et al NEJM 2009;360:961). In a study of high-risk patients with left main stem coronary lesions the MACCE rate at 12 months was 25% (Lee et al JACC 2006;47:864). For our high-risk patients we have estimated a MACCE rate of 20%. Therefore, to detect a 27% relative risk reduction in this primary endpoint (from 20.0% to 14.6%), with a power of 80% and a significance level of 5%, a sample size of 770 patients will be required for each trial arm (1540 in total). A trial of this size would detect an observed relative reduction of 20% (i.e. a risk ratio of 0.8) as statistically significant based on an event rate in the control arm of 20%. To allow for dropouts (4-5% in SYNTAX study) we plan to recruit 1610 patients in total based on 4.5% dropout rate.</p> <p><u>Statistical analysis:</u> Survival analyses will be carried out for the primary MACCE clinical endpoint at one year. MACCE as well as individual components (e.g. mortality); hazard ratios and confidence intervals, together with p-values will be calculated using Cox's proportional hazards modelling. All analyses will be carried out on an intention-to-treat basis.</p> <p><u>Project timetables including recruitment rate:</u> Total duration of study: 48 months. (1) 0-6 months- Study preparation; (2) 6-30 months- Patient recruitment; (3) 18-42 months- One year follow-up; (4) 42-48 months- Data analysis, reporting and dissemination of results. To recruit 1610 high-risk CABG±valve patients over 24 months, each of the 9 recruiting centres will need to recruit on average 2 patients per week (180 patients in total), which is about 25% of the eligible 7-10 patients per week.</p>
<p>ISRCTN: (if applicable)</p>	<p>To follow</p>
<p>Project Protocol:</p>	<p>www.eme.ac.uk/projectfiles/0910005protocol.pdf</p>
<p>Project</p>	<p>To follow</p>

website:	
URL of this Page:	www.eme.ac.uk/projectfiles/0910005info.pdf