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Ultradian rhythms of cortisol after cardiac surgery

Submission date	Recruitment status	[_] Prospectively registered
12/01/2012	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
05/03/2012	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
08/09/2016	Surgery	

Plain English summary of protocol

Background and study aims

The heart-lung machine (cardiopulmonary bypass) and heart surgery cause massive stress to the body. They can cause a syndrome which leads to multiple organ dysfunction that requires a long stay in the intensive care unit. A critical hormone that protects the body from multiple organ dysfunction is the steroid cortisol. In view of this, some of these patients are treated with steroids. We do not know which patients may be helped and which might be disadvantaged by this treatment. Our group has previously shown that cortisol in normal people is secreted in pulses over short periods of time that form a daily rhythm.

The aim of this study is to establish the different effects of cardiac surgery on or off cardiopulmonary bypass on the regulation of cortisol production. To this end we would like to measure cortisol at 10-minute intervals after people have had coronary bypass surgery and compare what happens when people have surgery using (on-pump) and not using (off-pump) the heart-lung machine. We will compare this to patients who are the same age and sex as the patients having heart surgery, but have medically treated coronary artery disease. Once we know what happens to cortisol levels in the patients having surgery, we can begin to decide which patients will need supplementary steroids.

Who can participate?

Patients approached for this trial will be those having first time, elective coronary artery bypass grafts, aged 18 - 80, and whose operation will be carried out using median sternotomy (i.e., not minimally invasive cardiac surgery).

What does the study involve?

Patients will be randomly allocated to either on- or off-pump surgery. As part of their surgery they have a drip inserted into their neck. We can use this to take small blood samples every 10 minutes and measure the levels of cortisol in their blood. We also will take samples at three points during the surgical process to look at adrenocorticotrophic hormone (one of the stimuli for cortisol) and cortisol binding globulin (the transport molecule for cortisol).

What are the possible benefits and risks of participating?

There are no benefits for the individual taking part in this study. There may be benefits in the

future for patients having cardiac surgery. Potential risks to participating are the possible side effects of taking blood samples after heart surgery. However, patients will typically have this volume of blood taken from them in the first 24 hours following heart surgery for lab tests. They may also typically lose 6-7 times this volume in the 12 hours after the operation and 10 - 12 times this volume in their overall surgical pathway. We are using the absolute minimum volume of blood that can be used to analyse the blood for cortisol.

Where is the study run from?
The Bristol Heart Institute (UK).

When is the study starting and how long is it expected to run for?
Recruitment began in October 2011 and is expected to run for 2 and a half years.

Who is funding the study?
The study is funded by the British Heart Foundation (UK).

Who is the main contact?
Dr Ben Gibbison
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
CS/2010/3614

Study information

Scientific Title
Activation of the hypothalamo-pituitary-adrenal axis during cardiac surgery: the effect of surgical stress and cardiopulmonary bypass

Study objectives
1. Cardiac surgery induces compensatory changes in the pattern of hypothalamo-pituitary-adrenal (HPA) activity and in the levels of free cortisol that maintain optimal HPA function.
2. Conventional coronary artery bypass graft (CABG) with cardiopulmonary bypass (CPB) causes a greater HPA stimulation than Off Pump Coronary Artery Bypass Graft (OPCABG) surgery

Ethics approval required
Old ethics approval format

Ethics approval(s)
South West 5 Research Ethics Committee, 22/02/2011, ref: 11/H0107/9

Study design
Single centre randomised study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Screening

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Coronary artery disease / surgery / endocrinology

Interventions
Patients who are having elective coronary surgery for the first time will either be randomised to the patient having on or off pump coronary surgery and will have 10 minute sampling of cortisol from their existing lines, along with sampling of adrenocorticotropic hormone (ACTH) and Cortisol Binding Globulin (CBG) levels at anaesthetic induction, end of operation and 24 hours post surgery. The methodology is the same for each treatment arm

There is no frequency or administration as patients only have the surgery once. Patients are followed up until they leave hospital.

Intervention Type
Procedure/Surgery

Phase
Not Applicable

Primary outcome measure
Pattern (pulsatility) of cortisol secretion during the peri-operative period, measured using an automated electrochemoluminescent immunoassay (ECLIA)

Secondary outcome measures
Levels of ACTH and CBG measured at three points - anaesthetic induction, end of operation and at 24 hours post surgery

Overall study start date
06/10/2011

Completion date
01/02/2014

Eligibility

Key inclusion criteria
Patients having isolated CABG surgery must fulfil all the following criteria:
1. Patient having first time, elective CABG
2. Aged 18 - 80yrs
3. Operation to be carried out using median sternotomy
4. Written informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
50 participants plus 10 volunteers

Key exclusion criteria
Participant may not enter the study if any of the following apply:
1. Emergency operation
2. Previous sternotomy
3. Myocardial Infarction within the last month
4. Concomitant procedure with CABG
5. Left ventricular ejection fraction <30%
6. Operation to be carried out by other incision than median sternotomy (e.g. left thoracotomy)
7. Contraindication to ONCABG or OPCABG (eg. calcified aorta, intramuscular LAD, calcified

coronaries, small target vessels)
8. Use of exogenous corticosteroids (including inhalers)
9. Past history of adrenal / pitiutary disease
10. Other major co-morbidities

Date of first enrolment
06/10/2011

Date of final enrolment
01/02/2014

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Bristol Royal Infirmary
Bristol
United Kingdom
BS2 8HW

Sponsor information

Organisation
University of Bristol (UK)

Sponsor details
Research and Enterprise Development
3rd Floor
Senate House
Tyndall Avenue
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Sponsor type
University/education

Website

http://www.bris.ac.uk/

ROR
https://ror.org/0524sp257

Funder(s)

Funder type
Charity

Funder Name
British Heart Foundation (UK) ref: PG/11/19/28827

Alternative Name(s)
the_bhf, The British Heart Foundation, BHF

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/04/2015		Yes	No