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Low Frequency Ventilation during cardiopulmonary bypass for lung protection

Submission date
01/03/2012

Recruitment status
No longer recruiting

Registration date
16/05/2012

Overall study status
Completed

Last Edited
26/02/2016

Condition category
Surgery

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Open-heart surgery is carried out on more than 35,000 UK patients each year. Currently only 3-4% die in the period immediately after surgery. However, the numbers of patients experiencing respiratory complications is much higher and is rising due to the increasing number of high-risk patients having open-heart surgery. Complications after surgery can be life threatening, place an enormous burden on hospital resources and are associated with increased NHS costs.
Conventional open-heart surgery requires the use of the heart-lung machine, also known as cardiopulmonary bypass (CPB), for 1-2 hours or more depending on the complexity of the operation. During this time the heart is stopped and most of the blood supply is diverted from the heart and lungs to allow the operation to proceed in a largely blood-free environment. These steps of diverting the blood supply from the heart and lungs, stopping the heart and artificially deflating the lungs are thought to be associated with injury to the heart and lungs, inflammation and major complications. Over the years, effective techniques have been developed to protect the heart from this injury. These involve feeding the heart with an artificial intermittent supply of blood containing protective chemicals. However, no methods for protecting the lungs have been developed. The lungs are allowed to deflate, and remain deflated with a limited blood supply for the entire period when the heart-lung machine is being used. The aim of this study is to investigate a simple strategy to protect the lungs during cardiac surgery. It involves inflating and deflating the lungs several times a minute for the entire period when the heart-lung machine is being used. We think that this treatment may reduce the risk of an injury to the lungs. This procedure has been tested and validated by our group in large animal experiments and is also being evaluated in a similar trial on safety and feasibility at the Bristol Heart Institute. We propose to compare the strategy of inflating and deflating the lungs when the heart-lung machine is being used with the current standard practice of allowing the lungs to deflate, focusing in particular on the effects of the two strategies on markers of inflammation in the lungs and peripheral blood.

Who can participate?
Patients having elective or urgent coronary artery bypass grafting surgery (CABG) using the heart-lung machine and with the heart stopped.

What does the study involve?
General anaesthesia will be used in the same way for all participants. Patients who give written consent to take part will be assigned by chance (like tossing a coin) to have the operation done in one of two ways: low-frequency ventilation or conventional treatment. In the low-frequency ventilation group, the anaesthetist will inflate and deflate the lungs several times a minute when the heart-lung machine is being used. If the inflated lungs interfere with the surgeons ability to operate on the heart, the lungs will be deflated for as long as is necessary. Then, the anaesthetist starts to inflate and deflate the lungs again. In the conventional treatment group, the anaesthetist will disconnect the lungs from the ventilator. The lungs will be allowed to deflate and remain deflated when the heart-lung machine is being used. Post-operative management will be carried out in the usual way and be the same for all participants, irrespective of the way in which the lungs were treated when the heart-lung machine was being used.

What are the possible benefits and risks of participating?
If we are right in thinking that inflating and deflating the lungs is beneficial, patients treated in this way when the heart-lung machine is being used will be less likely to have a lung injury. However, we do not know that this will happen. It is possible that patients treated conventionally may do better. We can only find out which treatment will benefit patients most by doing the study. We do not expect patients to be at higher risk. In particular, we do not expect patients having the treatment which involves inflating and deflating the lungs to have any additional pain, discomfort, distress or changes to lifestyle compared to patients who have conventional treatment. We will ask all participants to donate some blood while they are in hospital and to do some extra tests to measure how well their lungs are working. Doing these tests may be quite painful because of the chest wound after the operation. However, the tests do not cause any harm and the pain will stop after doing the test.

Where is the study run from?
The study will be run by doctors and researchers at the Hammersmith Hospital where cardiac surgery operations are carried out.

When is the study starting and how long is it expected to run for?
The study is expected to start in June 2012 and it is expected to run for 2 years.

Who is funding the study?
British Heart Foundation (UK)

Who is the main contact?
Professor Gianni Angelini
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Contact information

Type(s)
Scientific

Contact name
Prof Gianni Angelini

Contact details

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
4.0

Study information

Scientific Title
Low Frequency Ventilation during cardiopulmonary bypass for lung protection: a randomised controlled trial

Acronym
LFV

Study objectives
Using low frequency ventilation (LFV) during cardiopulmonary bypass (CPB) will result in reduced inflammatory activation, lung dysfunction, and ischemia/reperfusion injury compared with not ventilating the lungs during CPB.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee London Camden and Islington, 25/04/2012, ref: 12/LO/0458

Study design
Single-centre parallel-group randomised controlled trial

Primary study design
Interventional

Secondary study design

Randomised parallel trial

Study setting(s)
Hospital

Study type(s)
Treatment

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
Open-heart surgery with CPB / coronary artery bypass grafting (CABG)

Interventions
Participants will be randomised to LFV or control group

Low frequency ventilation (Experimental treatment)
In the LFV group, lung ventilation will be maintained for the entire duration of CPB using a respiratory rate of 5 min-1 with oxygen enriched air (FIO2 <0.25) using an unchanged I:E ratio of 1:2 and tidal volume of 6-8 mL/kg. Peak inspiratory pressure will be noted. If the lungs impede surgery then they will be deflated for as long as is necessary then recommenced on low frequency ventilation.

Control
In the control group, the lungs will be disconnected from the ventilator and left collapsed (airways open to the atmosphere) for the entire CPB duration as per usual care.

Intervention Type
Procedure/Surgery

Phase
Not Applicable

Primary outcome measure
NF-kB p65 activation measured in lung biopsies

Secondary outcome measures
1. In the lung biopsies:
1.1. p38 MAPK phosphorylation by Enzyme-linked immunosorbent assay (ELISA) and Western blotting (41-42)
1.2. Expression of TNFa, IL-1b, IL-18, IL-6, IP-10 and IL-8 and IL-10 by real-time polymerase chain reaction (PCR) and ELISA
1.3. Caspase 3 as a marker of apoptosis
2. In peripheral blood samples:
2.1. Reactive oxygen species (ROS) levels
2.2. Phosphorylation of p38 (Thr180/Tyr182) and NF-kB p65 (Ser529)
3. Pulmonary function tests (PFTs)
4. Pulmonary gas exchange
5. Adverse events

Overall study start date
01/06/2012

Completion date
30/06/2015

Eligibility

Key inclusion criteria
A participant may enter the study if ALL of the following apply:
1. Age ≥40 and <85 years
2. Undergoing any elective or urgent coronary artery bypass graft (CABG) with cardiopulmonary bypass (CPB) and cardioplegic arrest (CA)
3. Left ventricular ejection fraction >30%

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
32

Key exclusion criteria
A participant may not enter the study if ANY of the following apply:
1. Previous pulmonary embolism requiring long term warfarin for ≥3 months
2. Previous cardiac surgery
3. Current congestive heart failure (NYHA class IV)/cardiogenic shock
4. Chronic renal failure requiring dialysis
5. Emergency or salvage operation
6. On corticosteroid or immunosuppressive treatment
7. Severe chronic obstructive pulmonary disease (COPD), lung pathology and previous radiotherapy
8. Body mass index (BMI) >35

Date of first enrolment
01/06/2012

Date of final enrolment
30/06/2015

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Hammersmith Hospital
London
United Kingdom
W12 0NN

Sponsor information

Organisation
Imperial College Healthcare NHS Trust (UK)

Sponsor details
c/o Ms Becky Ward
Charing Cross Hospital
Fulham Palace Road
London
England
United Kingdom
W6 8RF

Sponsor type
Hospital/treatment centre

Website
http://www.imperial.nhs.uk/

ROR
https://ror.org/056ffv270

Funder(s)

Funder type
Charity

Funder Name
British Heart Foundation (UK) ref: P41016

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	substudy results	23/02/2016		Yes	No