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Goal-directed therapy: to determine a systematic approach in reducing complications after a cardiac surgery

Submission date
12/06/2013

Recruitment status
No longer recruiting

Registration date
25/11/2013

Overall study status
Completed

Last Edited
06/11/2014

Condition category
Circulatory System

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Over 30,000 cardiac surgery operations are performed every year. For the first day or two following surgery, the care provided by the medical and nursing team involves close monitoring of bodily functions and prompt management of any disturbances. Ensuring that the heart and circulation are functioning adequately is important to prevent organs, including kidneys, from failing. The clinical team frequently uses intravenous fluids (fluid injected directly into the vein) to compensate for any fluid losses during and after surgery. Previous studies on patients following major non-cardiac surgery have shown a benefit from increasing the amount of blood pumped around the body by giving intravenous fluids targeted at specific therapeutic goals. This process is called haemodynamic goal-directed therapy (GDT). There have been a smaller number of studies on patients following cardiac surgery and the positive results were similar. We have recently evaluated GDT following cardiac surgery and it was shown to be safe and associated with better kidney function. The aim is to follow this up by looking at a direct link between GDT and reduction in kidney dysfunction. Specifically kidney dysfunction that requires the use of renal replacement therapy.

Who can participate?
Patients over 18 years of age and admitted to intensive care post surgery, who are having coronary artery bypass grafting and/or aortic valve replacements.

What does the study involve?
Participants will be randomly allocated to either GDT or the standard therapy that is currently provided is many centres across the UK. Both groups of patients will be monitored closely in the intensive care unit and will have the same level of care. The difference will be in the methods used to guide the administration of intravenous fluids. The standard therapy group will have fluids directed by the clinical team, indicated in accordance with current practice. Patients allocated to the GDT group will have an extra monitoring (cardiac output monitor) to guide the timing and the amount of intravenous fluids administered. The results of this monitor will be concealed from the clinical team but can be revealed if there is any question about patient safety. This process will last for 6 hours from admission to the intensive care unit. We are

planning to collect information about kidney function and the amount of time spent in intensive care and hospital. We will have a record of all complications following surgery to help us understand the role of GDT in this group of patients and to ensure safety. A committee composed of specialist doctors independent from the research team, a nurse representative, a statistician and a patient representative will have full access to the information we collect from the study patients. This committee have the authority to stop the study if patients are coming to harm. We would also like to follow up the patient after a year from surgery to assess the study patients long-term outcome.

What are the possible benefits and risks of participating?
If the planned intervention shows an improvement in renal outcome with a positive impact on overall patient experience then a plan to implement GDT is warranted in all future cardiac surgery patients. By participating in this study, patients will contribute to future advances in healthcare.

Where is the study run?
The study is being conducted by St Georges NHS Trust, London in the Cardiothoracic Intensive Care Unit. Up to 10 participating centres will join this large multicenter randomized controlled trial.

When is the study starting and how long is it expected to run for?
The study will be expected to start within the next 12 months.

Who is funding the study?
The funding application is in process.

Who is the main contact?
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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
N/A

Study information

Scientific Title
Randomised controlled trial of post-operative goal-directed haemodynamic therapy following a cardiac surgery and the effects on acute kidney injury

Study objectives
Maximising stroke volume for 6 hours post cardiac surgery reduces acute kidney injury by increasing renal perfusion.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Study design
Multi-centre double-blinded randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Prevention

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
Complications following cardiac surgery, specifically acute kidney injury and renal function

Interventions
Current interventions as of 14/10/2014:
Patients in the control group will have routine post-operative care with the standard

haemodynamic targets of:
1. Systolic blood pressure within 20% of baseline
2. Urine output greater than 0.5 ml/kg/hour
3. Lactate less than 2.0 mmol/L.
IV fluid administration will be guided by the clinical team. Cardiac output monitoring will be used but concealed to understand the mechanisms behind the success or failure of GDT. The clinical team can request disclosure of the cardiac output measurements to decide on further management of the patient, should the patient show signs of shock (predefined within the protocol).

The intervention group: the protocol will start on admission to intensive care and continue for 6 hours. The main therapeutic goal is to achieve stroke volume maximisation (SVmax) using a cardiac output monitor concealed from the clinical team. A fluid challenge of 250 ml Ringers lactate solution will be administered. Fluid responsiveness is defined by an increase in stroke volume (SV) by equal to or greater than 10%. The fluid challenge will be repeated until the patient is no longer fluid responsive, in order to maintain a perfusion pressure after SVmax, noradrenaline will be used to maintain a mean arterial pressure >65 mmHg. A further fluid challenge will be given if the stroke volume decreases by 10%. It is difficult to maintain SVmax in the cardiac surgery patient due to the re-warming phase post-operatively and the changes in sedation/analgesia, which ultimately affect stroke volume by changing systemic vascular resistance. Patients also receive cardioplegia intra-operatively and the myocardium slowly recovers affecting the stroke volume, therefore other indicators for fluid challenges have to be considered. If the lactate rises by 1.0 mmol or more, urine output is less than 0.5 ml/kg/hour or systolic arterial pressure drops below 90 mmHg then one further fluid challenge can be given to assess stroke volume, providing no fluid has be administered within the past 30 minutes. If unresponsive, further fluid should not be given and this will trigger the research nurse to seek a medical review if the symptoms persist.

Previous interventions:
Patients in the control group will have routine post-operative care with the standard haemodynamic targets of: systolic blood pressure within 20% of baseline, urine output greater than 0.5 ml/kg/hour and lactate less than 2.0 mmol/L. IV fluid administration will be guided by the clinical team. Cardiac output monitoring will be used to allow comparison of results in the analysis but will be concealed unless the clinical team request disclosure to decide on further management of the patient.

The intervention group: the protocol will start on admission to intensive care and continue for 6 hours. The main therapeutic goal is to achieve stroke volume maximisation (SVmax) using a cardiac output monitor concealed from the clinical team. A fluid challenge of 250 ml Ringers lactate solution will be administered. Fluid responsiveness is defined by an increase in stroke volume (SV) by equal to or greater than 10%. The fluid challenge will be repeated until the patient is no longer fluid responsive. A further fluid challenge will be given if the stroke volume decreases by 10%. It is difficult to maintain SVmax in the cardiac surgery patient due to the re-warming phase post-operatively and the changes in sedation/analgesia which ultimately affect stroke volume by changing systemic vascular resistance. Patients also receive cardioplegia intra-operatively and the myocardium slowly recovers affecting the stroke volume, therefore other indicators for fluid challenges had to be considered. If the lactate rises by 1.0 mmol or more, urine output is less than 0.5 ml/kg/hour or systolic arterial pressure drops below 90 mmHg then one further fluid challenge can be given to assess stroke volume. If unresponsive, further fluid should not be given and will trigger the nurse to seek a medical review if the symptoms persist.

Intervention Type

Other

Phase
Not Applicable

Primary outcome measure
Current primary outcome measures as of 14/10/2014:
The primary outcome variable for this study is Acute Kidney Injury (AKI) that requires renal replacement therapy within 7 days following cardiac surgery. Death before day 7 is a competing risk and will be treated in the analysis accordingly. One approach would consist of a multinomial logit model, which deals with unordered multichotomous dependent variables, i.e. both death and AKI.

Previous primary outcome measures:
The primary outcome variable for this study is Acute Kidney Injury (AKI) stage 1 or above as defined by the AKIN criteria. Day 3 creatinine, compared to the most recent pre-operative value, will be used. Day of surgery is considered day 0. Death before day 3 is a competing risk and will be treated in the analysis accordingly. One approach would consist of a multinomial logit model, which deals with unordered multichotomous dependent variables, i.e. both death and AKI.

Secondary outcome measures
Current secondary outcome measures as of 14/10/2014:
1. AKIN and RIFLE criteria for AKI
2. The incidence of renal replacement therapy within the same hospital admission. This is defined as haemofiltration, haemodialfiltration within intensive care and haemodialysis on the renal dialysis unit
3. Re-admission to intensive care within 30 days of surgery
4. Time to readiness for discharge from intensive care as per unit guidelines
5. Time to medically fit for discharge from hospital as decided by the clinical team. Transfer to another hospital will be considered additional stay in acute care unless transferred for social reasons only
6. Time to actual discharge from hospital
7. Respiratory, infectious, renal, gastrointestinal, cardiovascular, haematological, biochemical and wound infections as predefined in the protocol
8. Morbidity and organ failure scores as defined by Sequential Organ Failure Assessment (SOFA)
9. Morbidity scores for ward patients using cardiac postoperative morbidity score (C-POMS) at day 1, day 3, day 5 and day 8
10. In-hospital mortality
11. Mortality at day 30, 6 months and 1 year
12. Health survey at 30 days and 1 year

Previous secondary outcome measures:
1. RIFLE criteria: the incidence of renal replacement therapy within the same hospital admission. This is defined as haemofiltration, haemodialfiltration within intensive care and haemodialysis on the renal dialysis unit.
2. Re-admission to intensive care within 30 days of surgery
3. Time to readiness for discharge from intensive care as per unit guidelines
4. Time to medically fit for discharge from hospital as decided by the clinical team. Transfer to another hospital will be considered additional stay in acute care unless transferred for social reasons only.
5. Time to actual discharge from hospital

6. Respiratory, infectious, renal, gastrointestinal, cardiovascular, haematological, biochemical and wound infections
7. Morbidity and organ failure scores as defined by Sequential Organ Failure Assessment (SOFA)
8. Morbidity scores for ward patients using cardiac postoperative morbidity score (C-POMS) at day 1, day 3, day 5 and day 8
9. In-hospital mortality
10. Mortality at day 30, day 90, 180 and 360 days following surgery

Overall study start date
01/01/2016

Completion date
01/07/2018

Eligibility

Key inclusion criteria
1. Coronary artery bypass grafts (CABG), aortic valve replacement (AVR) or combined CABG and AVR
2. Informed consent
3. Admission to intensive care from theatre
4. Patients over 18 years of age

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Approximately 4,000-6,000 (to be confirmed)

Key exclusion criteria
1. Myocardial infarction (MI) less than 48 hours prior to surgery
2. Infective endocarditis
3. Chronic Kidney Disease Stage 5 (end stage renal failure)
4. Cardiogenic shock requiring intra-aortic balloon pump
5. Pulmonary hypertension WHO-FC III/IV
6. Known right ventricular failure
7. Diagnosis of congenital heart disease

Added 14/10/2014:
8. Renal replacement therapy prior to surgery within 30 days

Date of first enrolment
01/01/2016

Date of final enrolment
01/07/2018

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Cardiac Intensive Care
London
United Kingdom
SW17 0QT

Sponsor information

Organisation
St George's Healthcare NHS Trust (UK)

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+44 (0)20 8672 1255
lparker@sgul.ac.uk

Sponsor type
Hospital/treatment centre

Website
https://www.stgeorges.nhs.uk/

ROR
https://ror.org/039zedc16

Funder(s)

Funder type
Other

Funder Name
Funding application - awaiting approval

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