ISRCTN39653756 https://doi.org/10.1186/ISRCTN39653756

Optimisation of perioperative cardiovascular management to improve surgical outcome II

Submission date
15/11/2016

Recruitment status
No longer recruiting

Registration date
23/11/2016

Overall study status
Completed

Last Edited
04/12/2024

Condition category
Surgery

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

Plain English summary of protocol

Background and study aims
Around 40,000 NHS patients aged 65 years and over undergo major planned gut surgery each year. After surgery, more than 12,000 patients develop an infection while they are in hospital (hospital acquired infection), and 3,600 die within 180 days. Patients who survive complications to leave hospital commonly suffer a loss of mobility, independence and reduced long-term survival. Hospital acquired infections in this patient group cost the NHS more than £80 million each year. Complications after surgery are more likely if patients receive too much or too little fluid through a drip. The use of small doses of drugs that increase heart function (inotropic drugs) is also important. Currently, the type and dose of these drug treatments is decided by a doctor based on opinion-based assessment of the patient. Advanced heart monitoring technologies may provide a more reliable guide to the use of these treatments. However, only one third of eligible patients currently receive this treatment because many doctors are concerned this approach is more aggressive and may therefore harm some patients by causing small heart attacks. Only a large study can resolve this uncertainty, to find out whether giving this treatment to all eligible patients is beneficial, or ineffective or harmful. The aim of this study is to find out the effect of this treatment on the number of patients who develop hospital acquired infection within 30 days after major planned gastrointestinal (gut) surgery.

Who can participate?
Adults over 65 years old who are undergoing planned major gastrointestinal (gut) surgery.

What does the study involve?
Participants are randomly allocated to one of two groups. Both treatments begin at the start of surgery and finish four hours after this has ended. The two treatments involve slightly different ways of deciding the amount of fluid and drugs given through a drip to improve heart function. If participants receive standard care the doctor uses measurements such as heart rate and blood pressure measurements to guide these treatments. If participants receive the new trial treatment doctors also measure the amount of blood the heart pumps each minute using an extra monitor. These extra measurements should help the doctor to decide how much fluid and drugs they should give to improve heart function. After the treatment is over, the study team reviews the participant's medical records and may talk to the doctors to collect information about their recovery. Participants are also contacted by telephone in one month and again in six

months' time to ask some simple questions about their wellbeing. The phone call lasts for around five minutes. With the participant's permission or if it is not possible to contact the participant, the study team may also contact their General Practitioner for further information.

What are the possible benefits and risks of participating?
There are no direct benefits of participating. Previous research suggests that the treatment we are investigating is very safe and should benefit most patients. However, there is a very small risk of a minor heart attack for some patients. For this reason, patients taking part in the study will be closely monitored throughout the trial period and, if necessary, the research team will make adjustments to the treatment to ensure patient safety.

Where is the study run from?
Hospitals in Australia, Canada, Germany, Spain, Sweden, United Kingdom and United States of America.

When is the study starting and how long is it expected to run for?
August 2016 to March 2023

Who is funding the study?
1. National Institute for Health Research (UK)
2. Edwards Lifesciences Corporation (UK)

Who is the main contact?
1. Dr Priyanthi Dias (scientific and public)
p.dias@qmul.ac.uk

Contact information

Type(s)
Scientific

Contact name
Dr Priyanthi Dias

ORCID ID
https://orcid.org/0000-0003-1740-6165

Contact details
Adult Critical Care Research
Room 14 Central Tower
The Royal London Hospital
Whitechapel
London
United Kingdom
E1 1FR
+44 (0)20 3594 0349
p.dias@qmul.ac.uk

Type(s)
Public

Contact name
Dr Priyanthi Dias

Contact details
Adult Critical Care Research
Room 14 Central Tower
The Royal London Hospital
Whitechapel
London
United Kingdom
E1 1FR
+44 (0)20 3594 0349
p.dias@qmul.ac.uk

Type(s)
Public

Contact name
Miss Tasnin Shahid

Contact details
Office 14 Critical Care Research Office
4th Floor
Royal London Hospital
London
United Kingdom
E1 1BB
02035940353
t.shahid@qmul.ac.uk

Additional identifiers

Protocol serial number
011560

Study information

Scientific Title
Open, multi-centre, randomised controlled trial of cardiac output-guided fluid therapy with low dose inotrope infusion compared to usual care in patients undergoing major elective gastrointestinal surgery

Acronym
OPTIMISE II

Study objectives
The aim of the study is to establish whether the use of minimally invasive cardiac output monitoring to guide protocolised administration of intravenous fluid, combined with low dose inotrope infusion for patients undergoing major elective surgery involving the gastrointestinal tract will reduce the incidence of postoperative infection within 30 days of randomisation.

Ethics approval required
Old ethics approval format

Ethics approval(s)
London - Brent Research Ethics Committee, 28/11/2016, ref: 16/LO/2067

Study design
International open multi-centre randomized controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Major elective gastrointestinal surgery

Interventions
Following provision of informed consent, participants will be randomly allocated to one of two groups (1:1) using a computer generated dynamic procedure (minimisation) with a random component. Minimisation will be performed by country and surgical procedure category.

Intervention group: The intervention will commence from the induction of general anaesthesia and continue for four hours following surgery. Cardiac output and stroke volume will be measured by cardiac output monitor. Investigators may only use commercially available cardiac output monitoring equipment provided by Edwards Lifesciences in this trial. No more than 500ml of intra-venous fluid will be administered prior to commencing cardiac output monitoring. In addition to the maintenance fluid and blood products, patients will receive 250ml fluid challenges with a recommended solution as required in order to achieve a maximal value of stroke volume. The absence of fluid responsiveness will be defined as the absence of a sustained rise in stroke volume of at least 10% for 20 minutes or more. In addition, patients will receive a low dose inotrope infusion at a fixed rate which will be commenced after fluid replacement has been initiated. The choice of inotrope will be made at the discretion of the local investigator, according to local preference and availability. The options are dobutamine at a dose/rate of 2.5 µg/kg/min and dopexamine at an equipotent dose/rate of 0.5 µg/kg/min. The infusion rate will be reduced and/or discontinued if the patient develops a tachycardia (heart rate greater than 100bpm) for more than 30 minutes despite adequate anaesthesia and analgesia. Data collection and follow-up for such patients will be performed as normal. All other management decisions will be taken by clinical staff.

Control group: Patients in the control group will be managed by clinical staff according to usual practice. This will include 250ml fluid challenges with a recommended intra-venous fluid administered at the discretion of the clinician guided by pulse rate, arterial pressure, urine output, core-peripheral temperature gradient, serum lactate and base excess. If a specific haemodynamic end-point for fluid challenges is to be used, the most appropriate would usually be a sustained rise in central venous pressure of at least 2 mmHg for 20 minutes or more. Patients should not be randomised if the clinician intends to use cardiac output monitoring regardless of study group allocation; this is considered ‘clinician refusal’ and is a specific exclusion criteria. However, clinical staff are free to request cardiac output monitoring if this is

required to inform the treatment of a patient who becomes critically ill (e.g. because of severe haemorrhage) during the trial intervention period. In this situation a protocol deviation form will be completed.

All participants will be followed for 180 days after randomization.

Intervention Type
Other

Primary outcome(s)
Postoperative infection rate within 30 days of randomisation. This is defined as one or more of the following infections of Clavien-Dindo grade II or greater:
1. Superficial surgical site infection
2. Deep surgical site infection
3. Organ space surgical site infection
4. Pneumonia
5. Urinary tract infection
6. Laboratory confirmed blood stream infection
7. Infection, source uncertain; this is defined as an infection which could be more than one of the above but it is unclear which

The primary outcome will be assessed using information from a patient's medical notes. Patients discharged from hospital before day 30 will be contacted shortly after day 30 to ascertain whether they have received any new treatment since discharge, or if they have been re-admitted to hospital or seen a doctor since discharge. For patients who have received further treatment or seen a health professional since discharge, further details will be collected directly from the hospital/doctor or from the patient's health records.

Key secondary outcome(s))
1. Mortality, assessed by a patient medical record review or data from national databases, within 180 days of randomisation
2. Acute kidney injury of Clavien-Dindo grade II or greater, assessed using a patient medical note review and telephone interview in the same way as primary outcome, within 30 days from randomisation.
3. Acute cardiac event of Clavien-Dindo grade II or greater, assessed by a review of the patient's medical notes, within 24 hours of randomisation
4. Acute cardiac event of Clavien-Dindo grade II or greater, assessed using a patient medical note review and telephone interview in the same way as primary outcome, within 30 days of randomisation.

Process measures:
1. Duration of hospital stay (number of days from randomisation until hospital discharge), assessed by a review of the patient's medical records.
2. Number of critical care free days*, assessed by a review of the patient's medical records, up to 30 days from randomisation.

*A critical care free day is defined as a day in which the patient is alive and is not in a level 2 or level 3 critical care bed.

Completion date
31/03/2023

Eligibility

Key inclusion criteria
1. Age 65 years and over
2. Patients undergoing major elective surgery involving the gastrointestinal tract that is expected to take longer than 90 minutes

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Senior

Lower age limit
65 years

Sex
All

Total final enrolment
2502

Key exclusion criteria
1. Inability or refusal to provide patient consent
2. Clinician refusal (including intention to monitor cardiac output from the start of surgery regardless of study group allocation)
3. American Society of Anesthesiologists (ASA) score of I
4. Patients expected to die within 30 days
5. Acute myocardial ischaemia within 30 days prior to randomisation
6. Acute pulmonary oedema within 30 days prior to randomisation
7. Contra-indication to low-dose inotropic medication
8. Pregnancy at time of enrolment
9. Previous enrolment in the OPTIMISE II trial
10. Current participation in another clinical trial of a treatment with a similar biological mechanism or primary outcome measure

Date of first enrolment
31/12/2016

Date of final enrolment
13/09/2022

Locations

Countries of recruitment
United Kingdom

England

Scotland

Wales

Australia

Canada

Germany

Spain

Sweden

United States of America

Study participating centre
Royal London Hospital
Whitechapel Road
London
United Kingdom
E1 1BB

Study participating centre
Musgrove Park Hospital
Parkfield Drive
Taunton
United Kingdom
TA1 5DA

Study participating centre
Royal Gwent Hospital
Cardiff Road
Newport
United Kingdom
NP20 2UB

Study participating centre
Royal Infirmary of Edinburgh
51 Little France Crescent
Old Dalkeith Road
Edinburgh

United Kingdom
EH16 4SA

Study participating centre
Royal Preston Hospital
Sharoe Green Lane North
Fulwood
Preston
United Kingdom
PR2 9HT

Study participating centre
Warwick Hospital
Lakin Road
Warwick
United Kingdom
CV34 5BW

Study participating centre
The Queen Elizabeth Hospital King's Lynn
Gayton Road
King's Lynn
United Kingdom
PE30 4ET

Study participating centre
Southampton General Hospital
Tremona Road
Southampton
United Kingdom
SO16 6YD

Study participating centre
Austin Hospital
145 Studley Road
PO Box 5555
Heidelberg
Victoria
Melbourne
Australia
3084

Study participating centre
St Vincent's Hospital Melbourne
41 Victoria Parade
Fitzroy
Victoria
Melbourne
Australia
3065

Study participating centre
Westmead Hospital
Cnr Hawkesbury Road and Darcy Road
Westmead
New South Wales
Sydney
Australia
2145

Study participating centre
Toronto General Hospital
200 Elizabeth Street
Toronto
Canada
M5G 2C4

Study participating centre
McMaster Hospital
1200 Main St. West
Hamilton
Canada
L8N 3Z5

Study participating centre
University Hospital Giessen
Baldingerstraße
Marburg
Germany
35043

Study participating centre
University Hospital Bonn
Sigmund-Freud-Straße 25
Bonn
Germany
53127

Study participating centre
Vivantes Hospital Berlin-Friedrichshain
Landsberger Allee 49
Berlin
Germany
10249

Study participating centre
Charité Berlin Campus Virchow and Mitte
Augustenburger Pl. 1
Berlin
Germany
13353

Study participating centre
UKE Hamburg
Martinistraße 52
Hamburg
Germany
20246

Study participating centre
University Hospital Schleswig-Holstein Kiel
Campus Kiel, Schwanenweg 21
Kiel
Germany
24105

Study participating centre
University Hospital Lübeck
Ratzeburger Allee 160

Lübeck
Germany
23538

Study participating centre
University Hospital Oldenburg
Ammerländer Heerstr. 114-118
Oldenburg
Germany
26129

Study participating centre
Hospital Universitario Rio Hortega Valladolid
Calle Dulzaina, 2
Valladolid
Spain
47012

Study participating centre
Hospital Clínico Universitario Valladolid
Av. Ramón y Cajal, 3
Valladolid
Spain
47003

Study participating centre
Hospital Ramon y Cajal de Madrid
Ctra. Colmenar Viejo, km. 9,100
Madrid
Spain
28034

Study participating centre
Hospital Universitario Infanta Leonor Madrid
Av Gran Via del Este, 80
Madrid
Spain
28031

Study participating centre
Hospital Gregorio Marañon Madrid
Calle del Dr. Esquerdo, 46
Madrid
Spain
28007

Study participating centre
Hospital Clinico Universitario Valencia
nº, Av. de Blasco Ibáñez, 17
València
Spain
46010

Study participating centre
Complejo Hospitalario de León
Altos de Navas, s/n
León
Spain
24001

Study participating centre
Hospital Universitario Nuestra Señora de la Candelaria Tenerifa
Ctra. del Rosario, 145
Santa Cruz de Tenerife
Spain
38010

Study participating centre
University Hospital Lund
Getingevägen 4
Lund
Sweden
222 41

Study participating centre
Vanderbilt University Medical Centre
1211 Medical Center Drive
Tennessee

Nashville
United States of America
37232

Study participating centre
Duke University Hospital
2301 Erwin Road
North Carolina
Durham
United States of America
27710

Study participating centre
Ronald Reagan UCLA Medical Centre
757 Westwood Plaza
California
Los Angeles
United States of America
90095

Study participating centre
Stony Brook University Hospital
101 Nicolls Rd
New York
New York
United States of America
11794

Study participating centre
The University of Texas MD Anderson Cancer Centre
1515 Holcombe Blvd
Texas
Houston
United States of America
77030

Study participating centre
University of Virginia Health System
1215 Lee St
Virginia
Charlottesville

United States of America
22903

Sponsor information

Organisation
Queen Mary University of London

ROR
https://ror.org/026zzn846

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
Edwards Lifesciences Corporation

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and analysed during the current study will be available upon request from pctu-data-sharing@qmul.ac.uk. The Pragmatic Clinical Trials Unit (PCTU) shares data via a

data-sharing agreement which is submitted to a panel. Enquiries can be sent to the data sharing email address pctu-data-sharing@qmul.ac.uk. Ideally, the Chief Investigator (CI), Professor Rupert Pearse, should be contacted first with the enquiry at admin@optimiseii.org for CI approval. Data would typically only be available to share at the end of the study. Please see the following page for further details regarding PCTU data sharing: https://www.qmul.ac.uk/pctu/collaborate-with-us/data-sharing.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		03/12/2024	04/12/2024	Yes	No
Protocol article	protocol	15/01/2019	12/02/2020	Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Statistical Analysis Plan	version 3.0	17/01/2023	24/02/2023	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes