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Optimising the cardiovascular system following liver transplantation surgery

Submission date	**Recruitment status**	[_] Prospectively registered
21/03/2016	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
04/04/2016	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
19/05/2023	Digestive System	

Plain English summary of protocol

Background and study aims
Cirrhosis is a serious complication of liver disease, which involves widespread scarring of the liver. The damage to the liver caused by cirrhosis means that eventually the liver is unable to fulfil its normal functions, ultimately leading to liver failure. Cirrhosis develops gradually, however the damage to the liver is irreversible, and gets worse over time. When cirrhosis is so advanced that the liver is unable to function, a liver transplant is the only treatment option. Liver transplantation is currently the mainstay of treatment for liver failure and more than 800 liver transplants are performed each year in UK. Although a lifesaving treatment, liver transplantation is linked with a high risk of postoperative complications, and nearly two thirds of patients develop serious complications such as failure of the heart and lungs, loss of kidney function, infection, blood clots, or bleeding. Complications such as these can increase a patient's length of hospital stay, decrease their quality and length of life and result in failure of the transplanted organ, or even death. Following other types of major surgery goal directed fluid therapy (GDFT) is used in order to determine the amount of intravenous (through a drip) fluid needed by the patient. GDFT has been shown to markedly reduce the occurrence of postoperative complications. It is not known whether this method of treating patients is beneficial or harmful following liver transplantation because the fact that these patients have liver cirrhosis means that their bodies process things differently. The aim of this study is to assess the practicability and safety of GDFT following liver transplantation.

Who can participate?
Adults with liver cirrhosis who have been selected to have a liver transplant

What does the study involve?
Participants are randomly allocated to one of two groups. Participants in the first group receive GDFT for 12 hours after their transplant surgery. This involves using a device to measure the volume of blood ejected by the heart at each beat (stroke volume), which is used to determine whether IV fluid should be given to the patient, according to a commonly used method for surgical patients. Participants in the second group are treated using the standard current management of IV fluids (drips) for the first 12 hours after surgery. Participants in both groups

are followed up after six months to find out if the new liver is working properly and there have been any complications after the transplant, as well as their quality of life and length of stay in hospital after the surgery.

What are the possible benefits and risks of participating?
There are no direct benefits for participants taking part in this study. In most studies, goal directed fluid therapy has been shown to be of benefit to patients undergoing surgery. Goal directed fluid therapy has never been evaluated in patients following liver transplantation, and we shall closely assess its safety in this setting. There are no notable risks involved with participating in this study.

Where is the study run from?
Royal Free Hospital (UK)

When is the study starting and how long is it expected to run for?
May 2014 to October 2018

Who is funding the study?
National Institute for Health Research (UK)

Who is the main contact?
Dr Daniel Martin

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
A feasibility study of Cardiac Output optimisation following Liver Transplantation (COLT trial)

Acronym
COLT

Study objectives
Managing IV fluid requirements using a cardiac output monitor according to a GDFT protocol following transplantation for liver cirrhosis will be both feasible and safe. In addition, surgical outcomes can be improved in this patient group through the use of GDFT, however, the feasibility of this approach must be thoroughly explored prior to a definitive large-scale trial.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Bloomsbury Research Ethics Committee, 05/01/2016

Study design
Single-centre randomised controlled feasibility trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Prevention

Participant information sheet
See additional files

Health condition(s) or problem(s) studied
Liver transplantation for liver cirrhosis

Interventions
Participants immediately post liver transplant will be randomised on admission to the intensive care unit to one of two treatment groups for the first 12 hours.

Intervention group: Participants undergo goal directed fluid therapy (GDFT) for 12 hours post-operatively. This involves the used of a FloTrac cardiac output monitor (EV1000 Clinical Platform, Edwards Lifesciences, Irvine, USA) to measure stroke volume, which will be used to

determine IV fluid administration. The Edwards EV1000 cardiac output monitor is a non-invasive pulse wave contour analysis device that calculates cardiac output and stroke volume. Electronic information from the indwelling arterial catheter that all of these patients have inserted as part of their routine treatment is sent to the EV1000 to calculate cardiac output and stroke volume.

Control group: Participants are treated using the standard current management of IV fluids for 12 hours post-operatively.

Participants in both study arms are followed up after six months

Intervention Type
Device

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
FloTrac cardiac output monitor (EV1000 Clinical Platform, Edwards Lifesciences, Irvine, USA)

Primary outcome measure
Feasibility is determined at the end of the study period as the:
1. Ability to recruit patients at the site: A recruitment rate of greater than 40% of patients fulfilling the criteria for this study will be deemed as successful
2. Rate of withdrawal from GDFT protocol: A withdrawal rate of less than 10% will be deemed as successful
3. Reasons for withdrawal from GDFT protocol: Qualitatively assessed
4. Ability to adhere to the GDFT protocol for the 12 hour intervention period: Less than 10% of patients with a deviation from the protocol will indicate success

Secondary outcome measures
1. Quality of life is measured using Eq5D pre-transplant, 3 and 6 months
2. Postoperative complications are measured using the Clavien-Dindo Classification of surgical complications at 6 months
3. Hospital length of stay is measured using hospital computer system in days
4. ICU length of stay is measured using using hospital computer system in days
5. Graft (liver) function and survival is measured at 6 months by monitoring postoperative complications specifically related to liver transplantation surgery, occurring within 180 days of liver transplantation, defined as any of the following:
5.1. Two or more episodes of graft rejection (biopsy proven and treated)
5.2. Vascular thrombotic episodes
5.3. Bleeding requiring intervention
5.4. Acute kidney injury requiring renal replacement therapy
5.5. Biliary leak requiring intervention
5.6. Biliary stricture requiring intervention
5.7. Cytomegalovirus, fungal or bacterial infection at any site confirmed by culture
6. Patient survival is measured using hospital information system at 6 months

Overall study start date
28/05/2014

Completion date

01/10/2018

Eligibility

Key inclusion criteria
1. Aged between 18 and 80 years
2. Liver cirrhosis
3. Selected to undergo liver transplantation
4. Competent to give consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
50

Total final enrolment
60

Key exclusion criteria
1. Non-cirrhotic liver disease
2. Pregnancy
3. Age less than 18 years or over 80 years
4. Body weight less than 40 kg
5. Re-transplantation for primary graft non-function
6. Fulminant hepatic failure
7. Emergency surgery
8. Known learning disabilities or previously lacking capacity to consent for themselves
9. Prisoners
10. Patients already enrolled in an interventional study
11. Refusal or inability to consent

Date of first enrolment
01/04/2016

Date of final enrolment
31/08/2017

Locations

Countries of recruitment

England

United Kingdom

Study participating centre
Royal Free Hospital
Royal Free London NHS Foundation Trust
Pond Street
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NW3 2QG

Sponsor information

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University College London

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Sponsor type
University/education

ROR
https://ror.org/02jx3x895

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

Results and Publications

Publication and dissemination plan
Publication in a high impact peer-reviewed journal

Intention to publish date
01/10/2019

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version V2	13/04/2016	02/06/2016	No	Yes
Protocol article	protocol	07/03/2018		Yes	No
Results article	results	01/08/2020	16/07/2020	Yes	No
Abstract results		01/12/2018	19/05/2023	No	No