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Can warming and supplying oxygen to a donor liver before transplantation improve the success of liver transplants?

Submission date
31/10/2018

Recruitment status
No longer recruiting

Registration date
05/11/2018

Overall study status
Completed

Last Edited
19/10/2022

Condition category
Surgery

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

Plain English summary of protocol

Background and study aims
End-stage liver disease is where the liver cannot function properly because of long-term damage, for example from heavy alcohol use or hepatitis virus infection. Liver transplantation is the current most effective treatment for end-stage liver disease. The donor liver is usually stored on ice during transportation to the recipient patient. This is to reduce damage to the organ while it is out of the body and has no oxygen supply. However, when the liver is connected to the recipient's blood supply, there can be damage to the liver cells (reperfusion injury) caused by the sudden restarting of normal processes, including the sudden change from no oxygen to normal oxygen levels. This study aims to investigate whether the reperfusion injury can be reduced by gently warming the liver and flushing it through with liquid containing oxygen in a machine perfusion apparatus before transplantation.

Who can participate?
Adults on the list for liver transplantation at the University Hospital Essen who consent to participating in the study.

What does the study involve?
Participants will be randomly allocated to one of two groups. In both groups the recipient preparation and transplant surgery will be carried out as usual. In the control group, the donor liver will be prepared as usual. In the study group, the donor liver will be attached to a machine that pumps liquid containing oxygen through it via the artery and vein that circulate blood through it normally. The liquid will be gradually warmed up so that by the time the liver has been receiving the liquid for 60 minutes, the temperature will be 20°C. The total time that the liver is receiving the liquid before it is transplanted into the recipient will be at least 90 minutes.

What are the possible benefits and risks of participating?
This procedure has been tested in animals and in an initial study in humans and is thought to be safe. The study group might benefit from reduced reperfusion injury to the transplanted liver, which might mean that it regains full function more quickly.

Where is the study run from?
University Hospital Essen

When is the study starting and how long is it expected to run for?
August 2016 to November 2021

Who is funding the study?
The Else Kröner Fresenius Foundation

Who is the main contact?
Professor Thomas Minor, thomas.minor@uk-essen.de

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
Nil known

Study information

Scientific Title
Controlled Oxygenated Rewarming as Novel Endischemic Therapy for cold stored liver grafts (CORNET): a prospective randomized controlled trial

Acronym
CORNET

Study objectives
1. Controlled oxygenated rewarming of the cold preserved liver graft prior to warm reperfusion will mitigate rewarming/reperfusion injury upon liver transplantation.
2. Functional data obtained during ex-situ machine perfusion will help to evaluate graft integrity prior to transplantation

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics Committee, Medical Faculty, University of Duisburg-Essen [Ethik Kommission der Medizinischen Fakultät der Universität Duisburg-Essen], 29/11/2016 (amended 27/09/2018), 16-7110 BO

Study design
Single-center randomized controlled parallel-arm pilot study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

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

Health condition(s) or problem(s) studied
Preservation and transplantation of liver grafts

Interventions
Randomisation: 1:1 block randomisation. The donor liver is randomised by our study design. Only patients who had given informed consent to participate in the study will be included in the randomisation and the study.
Control study arm: Procedure according to usual clinical standards without any experimental treatment.
Experimental study arm: Livers will be put on a CE-certified organ perfusion machine (Liver Assist®, Fa. Organ Assist, The Netherlands) and machine perfusion started via the hepatic artery and hepatic portal vein in a closed circuit with Belzer machine perfusion solution. Perfusate will be oxygenated to a pO2 >500mmHg via two oxygenators included in the arterial and portal circuits. The temperature of the perfusate will be increased slowly over time to reach a steady state of 20°C after 60 min. Total perfusion time will be 90 min or slightly longer, if the recipient

preparation time exceeds the minimum perfusion time of 90 min (for further details see: Hoyer DP et al. Controlled Oxygenated Rewarming of Cold Stored Livers Prior to Transplantation: First Clinical Application of a New Concept. Transplantation. 2016;100:147-52).

Intervention Type
Procedure/Surgery

Primary outcome measure
Serum peak value of aspartate aminotransferase (AST) during the first 3 days after transplantation

Secondary outcome measures
1. Death assessed using patient medical records from admission until 3 months after transplantation
2. Early Allograft Dysfunction (EAD) according to Olthoff (bilirubin >10 mg/dl or INR >1.6 at POD 7, or peak-AST >2000 U/l during first week after transplantation, based on patient medical records from admission until 1 week after transplantation
3. Re-transplantation assessed using patient medical records from admission until 3 months after transplantation
4. Duration of stay in intensive care unit assessed using patient medical records
5. Ischemia reperfusion injury based on laboratory tests assessed using patient medical records from admission until 1 week after transplantation
6. Liver maximum function capacity assessed using LiMAx® test 1 day after transplantation
7. Evaluation of correlation of machine perfusion parameters (obtained during ex vivo machine perfusion) with ulterior graft function after transplantation as assessed using patient medical records from admission until 3 month after transplantation
All patients are observed for 7 days following transplantation on a daily basis. Follow up includes additional observations on the day of discharge and 3 months after transplantation. Patients are followed until 3 months after the last patient is randomised for this trial and are asked to attend clinical routine follow up subsequent to termination of the study.

Overall study start date
20/08/2016

Completion date
30/11/2021

Eligibility

Key inclusion criteria
Inclusion criteria for the recipient:
1. Aged ≥18 years
2. Indication for liver transplantation
3. Listed as 'transplantable' at Eurotransplant
4. Resident in Germany
5. Provided informed consent

Inclusion criteria for donor liver:
1. Expanded criteria donor
2. Donor liver offered to the Transplantation Clinic Essen
3. Requiring one of the following criteria:

3.1. Age of donor >65 years
3.2. Intensive care including ventilation of the donor for >7 days
3.3. Obesity in the donor, i.e. BMI >30 kg/m2
3.4. Serum sodium >165 Mol/l,
3.5. Aspartate aminotransferase (AST/GOT) or alanine aminotransferase (ALT/GPT) >3 x normal
3.6. Serum bilirubin >3 mg/dl (last value prior to donor listing)
3.7. Liver steatosis (histologically confirmed) >40%

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
40

Total final enrolment
40

Key exclusion criteria
1. High Urgency (HU) listing
2. Re-transplantation
3. Simultaneous participation in another preservation trial
4. Severe allergic diathesis
5. HIV-positive

Date of first enrolment
02/01/2019

Date of final enrolment
30/04/2021

Locations

Countries of recruitment
Germany

Study participating centre
University Hospital Essen
Hufelandstr. 55
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Essen
Germany
45147

Sponsor information

Organisation
University Hospital Duisberg-Essen

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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/02na8dn90

Funder(s)

Funder type
Charity

Funder Name
Else Kröner-Fresenius-Stiftung

Alternative Name(s)
Else Kroener-Fresenius-Stiftung, Else Kröner Fresenius-Stiftung, Else Kroner-Fresenius Foundation, EKFS

Funding Body Type
Private sector organisation

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

Location
Germany

Results and Publications

Publication and dissemination plan
Dissemination of the results is planned by publication in a high-impact peer reviewed journal.

Intention to publish date
31/12/2022

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		17/10/2022	19/10/2022	Yes	No