Hypothermic oxygenated perfusion (HOPE) of human liver grafts before transplantation - A multicenter, randomized controlled trial

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The purpose of this study is, in a phase II randomized trial, to test a newly developed machine perfusion technique of human liver allografts before transplantation.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Gastrointestinal conditions NEC
Study type	Interventional

Summary

ID

NL-OMON47605

Source
ToetsingOnline

Brief title
Hypothermic Oxygenated Perfusion (HOPE) of Human Liver Grafts

Condition

- Gastrointestinal conditions NEC
- Hepatic and hepatobiliary disorders
- Hepatobiliary therapeutic procedures

Synonym
End-stage liver disease

Research involving
Human

Sponsors and support

Primary sponsor: UniversitätsSpital Zürich
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: hypothermic machine liver perfusion, liver reperfusion injury, liver transplantation, machine liver perfusion

Outcome measures

Primary outcome

Major postoperative complications (Clavien Grade III or higher), using the established Clavien classification supported by a recently developed comprehensive complication index by Slankamenac et al.. Based on the Clavien complication grading (I-V, 36), the CCI considers the total number of complications, occurring during the first three and six months after liver transplantation.

Secondary outcome

Plasma AST and ALT, reflecting hepatic injury in humans, will be measured 6 and 12 hours after OLT, and at day 1-7 postoperatively. The area under the curve will be determined. In addition, we will assess:

- Liver samples taken at the end of cold storage (quantification of steatosis)

- Postoperative liver function measured by INR and factor V (plasma, day 1-7).

- Intra- and extrahepatic biliary complications within the first year after liver transplantation, assessed by serum cholestasis parameter (Bilirubin, Gammaglutamyltransferase, Alkaline Phosphatase) every three month and liver MRI including an MCRP 12 months after liver transplantation.

- Length of hospital and ICU stay,

- One-year patient and graft survival

Study description

Background summary

Ischemia-reperfusion injury is universal in organ transplantation and leads to varying degrees of graft dysfunction. Despite this fact, the preservation method in organ transplantation has been left unchanged for many years and remains simple static cold storage. Given the scarce donor supply, an increasing number of so called marginal or extended criteria donor organs have been used for liver transplantation, grafts which were previously rarely considered. In addition, allocation policy has changed in Switzerland, as in many other countries, and livers are now distributed by the severity of the recipient*s disease. In this context, the MELD system (Model for end stage liver disease) is frequently used for allocation of livers. As a result, transplant candidates present sicker, with higher MELD scores, at the time of transplant and the risk of graft dysfunction or even failure due to reperfusion injury is high after the use of marginal livers in sick recipients.
Machine liver perfusion techniques have been improved during the past decade to decrease reperfusion injury, and a number of promising results show beneficial effects in various animal transplant models by either normothermic or hypothermic oxygenated continuous liver perfusion. These techniques generally require machine liver perfusion immediately after organ procurement. Hence continuous perfusion has several drawbacks, including major logistic efforts and risk of organ damage during perfusion and transport.
Our group, therefore, focused on the practicability of machine liver perfusion. We developed an endischemic hypothermic oxygenated perfusion (HOPE) concept. This technique can be easily applied in the operation room shortly before transplantation of the recipient, thus after organ transport and back table preparation.
Recently, the beneficial effect of such approach has been confirmed in human liver grafts by a phase I non randomized trial. These results prove feasibility and safety of an endischemic hypothermic machine perfusion approach and warrant further randomized studies.

We therefore plan to test now HOPE in standard human grafts from brain death donors by a multicenter prospective randomized trial.

Study objective

The purpose of this study is, in a phase II randomized trial, to test a newly developed machine perfusion technique of human liver allografts before

transplantation.

Study design

An international, multicenter, prospective, randomized, interventional, clincal study with two parallel groups (intervention and control).

Intervention

In the intervention group liver grafts will be subjected to two hours of hypothermic, oxygenated perfusion(HOPE) at the end of SCS and before implantation. In the control group donor liver grafts will be preserved in accordance to standard practice by SCS only, without any further intervention.

Study burden and risks

Patients participating in this trial will experience minimal burden. There are only two differences compared with the routine practice: half of the livers will undergo HOPE and patients will undergo a MRCP at twelve months after transplantation. The intervention, HOPE, is associated with a non-significant risk of injury of the isolated liver due to perfusion pressure or perfusion failure. The perfusion pressures in this protocol are very low and are reported to cause no harm to the organ. In case of perfusion failure, the liver can easily and quickly (within minutes) be brought to the same conditions as in the control group. There is a burden but there are no risks related to MRCP, which is planned during a routine hospital visit. When the intervention is effective in reducing post operative morbidity and mortality, the patients participating in this trial benefit substantially when they are randomized to the intervention group. This study can only be permored in these patients because they undergo liver tranpslantation.

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

-Adult (>=18 years) patients with acute liver failure or liver cirrhosis (CHILD A, B or C) and/ or malignant liver tumors requiring liver transplantation
-Whole liver graft
-Signed informed consent

Exclusion criteria

- Split graft,
- Living donor liver transplantation
- Grafts donated after cardiac arrest (DCD grafts)
- Domino transplantation
- Combined liver transplant
- Cold storage > 15h
- acute and unexpected medical contraindication

Study design

Design

Study phase:	3
Study type:	Interventional

Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	28-09-2017
Enrollment:	35
Type:	Actual

Medical products/devices used

Generic name:	Liver Machine Perfusion with Liver Assist
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	08-06-2017
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	18-10-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	03-09-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	17-12-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO	

Date:	24-01-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
ClinicalTrials.gov	NCT01317342
CCMO	NL60969.042.17