Trial Description

Title

Perioperative assessment of the remnant liver functional capacity with the 13C methacetin breath test

Trial Acronym

ReLiF study

URL of the trial

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Brief Summary in Lay Language

Background:
The measurement of the remaining liver volume (remnant liver) with the aid of computed tomography or magnetic resonance tomography and the evaluation of the liver function with the 13- C-methacetin breath test are two modern ways to assess before a major liver resection whether a sufficient and functional liver volume will still be available after the operation.
For the planning of major liver resections (≥3 liver segments), these two procedures are part of our clinical routine. The postoperative measurement of actual residual liver function with the 13C methacetin breath test is also performed regularly.
An intraoperative "real-time" measurement of liver function is not yet available, but would be very helpful for the liver surgeon. For example, the effect of vascular injury could be weighed, or the function of the remaining liver evaluated immediately before the final resection.

Aim of the study:
The aim of this study is the intraoperative evaluation of the 13C methacetin breath test.
We hope that the assessment of the study data could indicate that this test can provide an intraoperative monitoring of liver function. In that way a further decision-supporting tool for choosing the optimal surgical strategy will be available to the liver surgeon. This could ultimately reduce the frequency of the life-threatening postoperative liver failure.

Possible study participants:
All adult patients (> 18 years of age) able to give consent, who will undergo a major liver resection (3 or more liver segments) at the Department of General and Visceral Surgery of the Asklepios Klinik Barmbek within one year of the study beginning.

Examination's course:
Perioperative: Measurement of liver function with the 13 C methacetin test before and after each liver resection

Intraoperative: An examination of the exhalation air will be performed during the operation via the normal ventilator at different times, at least once after the incision and once before the abdominal wall closure. Surgeons are not going to

see the intraoperative outcomes of the study and are therefore not influenced by the results.

The peri- and intraoperative measurements will be compared, statistically evaluated and correlated to postoperative complications.

Brief Summary in Scientific Language

The aim of this pilot study is the evaluation of the intraoperative, "real-time" measurement of liver functional capacity using the 13C-methacetin breath test during liver operations in an exploratory, hypothesis-generating intention. Therefore the intraoperative metabolism of the liver-specific 13C-methacetin will be evaluated and correlated to the liver volume loss.

Hypothesis: The intraoperative values of the 13C methacetin breath test before and after the resection correspond to the respective pre- and postoperative values.

Secondary hypotheses:
1. The reduction of 13C-methacetin breath test values post resectionem corresponds to the reduction of the liver volume by the resection.
2. Segmental vessel occlusion is similar to resection of occluded liver segments to 13C methacetin breath test values.

Do you plan to share individual participant data with other researchers?

[---]*

Description IPD sharing plan

[---]*

Organizational Data

- DRKS-ID: **DRKS00016795**
- Date of Registration in DRKS: **2019/02/21**
- Date of Registration in Partner Registry or other Primary Registry: **[---]***
- Investigator Sponsored/Initiated Trial (IST/IIT): **yes**
- Ethics Approval/Approval of the Ethics Committee: **Approved**
- (leading) Ethics Committee Nr.: **PV5948 , Ethik-Kommission der Ärztekammer Hamburg**

Secondary IDs

- Universal Trial Number (UTN): **U1111-1218-6114**

Health condition or Problem studied

- Free text: **Liver resection of 3 or more liver segments (according to Couinaud classification) and its effect on liver functional capacity**
- ICD10: **C22 - Malignant neoplasm of liver and intrahepatic bile ducts**
- ICD10: **C78.7 - Secondary malignant neoplasm of liver and intrahepatic bile duct**
- ICD10: **C24 - Malignant neoplasm of other and unspecified parts of biliary tract**
- ICD10: **D37.6 - Neoplasm of uncertain or unknown behaviour: Liver, gallbladder and bile ducts**
- ICD10: **D13.4 - Benign neoplasm: Liver**

Interventions/Observational Groups

- Arm 1: **In this single-centre, prospective study will be enrolled all patients who will undergo a liver resection of three or more liver segments according to Couinaud classification at the Clinic for General and Visceral Surgery of the Asklepios Clinic Barmbek for one year from the start of the study.**
  The 13C methacetin breath test is performed once preoperative and once on the first postoperative day, something that belongs to the clinical practice in our centre. The test is based on the liver-specific metabolization of 13C-methacetin by the cytochrome P450 1A2 (CYP1A2) to 13CO2 and paracetamol. After intravenous administration of 13C-methacetin, the ratio of 13CO2 to 12CO2 is measured from the expired air.
  By the intraoperative measurements, which have not previously been clinically evaluated, the test will be performed once after skin incision and during abdominal exploration and once before abdominal closure in the hemostasis and final control phase.
  The corresponding breath test measurements are carried out with the aid of a portable measuring device by the anesthesiological team with the help of one of the cooperation partners and stored electronically as a PDF file. In order to rule out any influence of the intraoperative results on the surgical decision-making, the surgical team will be blinded.
  Perioperatively, the liver volume to be removed and the remaining liver volume are radiologically measured. The volume of resection specimen is measured by water displacement immediately after resection.
  The pre-, peri- and postoperative patient data, namely the demographic patient data (gender, age, height, weight, BMI), the comorbidities, the type of surgery, the duration of the operation, the laboratory values and the perioperative complications in a follow-up period of 90 days are recorded from the electronic patient record. The patient data documentation concludes with the medical contact and if necessary examination of the patients (in domo or by the family doctor) from the 90th postoperative day on.

Characteristics

- Study Type: **Interventional**
- Study Type Non-Interventional: **[---]***
- Allocation: **Single arm study**
- Blinding: **[---]***
- Who is blinded: **investigator/therapist**
- Control: **Uncontrolled/Single arm**

Study Type: **Interventional**

Study Type Non-Interventional: **[---]***

Allocation: **Single arm study**

Blinding: **[---]***

Who is blinded: **investigator/therapist**

Control: **Uncontrolled/Single arm**

- Purpose: **Prevention**
- Assignment: **Single (group)**
- Phase: **N/A**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **N/A**

Primary Outcome

The LiMAx (maximum liver function capacity) value

Secondary Outcome

1. The "delta over baseline" (DOB) values at representative times and the DOB curve.
2. Postoperative complications in a 90-day "follow-up" according to the Clavien-Dindo classification and 30- and 90-day mortality correlated with the above-mentioned measurements.
3. The postoperative liver failure (PHLF) as defined by the "50-50 criteria", the "peak bilirubin" value, the International Study Group of Liver Surgery (ISGLS) definition and the "Hyder et al. Risk Score".

Countries of recruitment

- DE **Germany**

Locations of Recruitment

- Medical Center **Allgemein- und Viszeralchirurgie, Asklepios Klinik Barmbek, Hamburg**

Recruitment

- Planned/Actual: **Actual**
- (Anticipated or Actual) Date of First Enrollment: **2019/02/25**
- Target Sample Size: **30**

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(Anticipated or Actual) Date of First Enrollment: **2019/02/25**

Target Sample Size: **30**

- Monocenter/Multicenter trial: **Monocenter trial**
- National/International: **National**

Inclusion Criteria

- Gender: **Both, male and female**
- Minimum Age: **18 Years**
- Maximum Age: **no maximum age**

Additional Inclusion Criteria

All adult patients (> 18 years of age) able to give consent, who will undergo a liver resection of 3 or more liver segments according to Couinaud classification at the Department of General and Visceral Surgery of the Asklepios Klinik Barmbek within one year of the study beginning.

Exclusion criteria

1. Patients with an allergy to acetaminophen or methacetin.

2. Patients who have received a strong CYP1A2 agonist (e.g., ciprofloxacin, fluvoxamine, enoxacin, verapamil) within the half-life of these substances

Addresses

- **Primary Sponsor**

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Sources of Monetary or Material Support

■ **Institutional budget, no external funding (budget of sponsor/PI)**

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Status

- Recruitment Status: **Recruiting complete, follow-up continuing**
- Study Closing (LPLV): **[---]***

Trial Publications, Results and other documents

- Approval of ethics comm. (mandatory for transfer to Studybox) **Ethikvotum**
- trial protocol (mandatory for transfer to Studybox) **Prüfprotokoll**

** This entry means the parameter is not applicable or has not been set.*

**** This entry means that data is not displayed due to insufficient data privacy clearing.*