

# Functional and biochemical assessment of liver regeneration after major hepatectomy - FLASH study

No registrations found.

<b>Ethical review</b>	Positive opinion
<b>Status</b>	Recruiting
<b>Health condition type</b>	-
<b>Study type</b>	Observational non invasive

## Summary

### ID

NL-OMON22009

### Source

NTR

### Brief title

FLASH

### Health condition

Liver regeneration after major liver resection

## Sponsors and support

**Primary sponsor:** Academic Medical Center, University of Amsterdam

**Source(s) of monetary or material Support:** .

## Intervention

## Outcome measures

### Primary outcome

The correlations between the changes in liver function (as measured with hepatobiliary scintigraphy) at day of admission versus postoperative day 5 and the concomitant changes in circulating regeneration biomarkers (such as bile acids and FGF19)

## Secondary outcome

- Assessment of the variation of hepatobiliary scintigraphy measurements within a patient in order to establish the critical differences for this parameter.
- Assessment of the correlation between postoperative changes in liver stiffness and changes in liver function (as measured with hepatobiliary scintigraphy) at day of admission versus postoperative day 5.

## Study description

### Background summary

Posthepatectomy liver failure (PHLF) is the most severe complication that can occur after major liver resection with an incidence between 7% in patients with healthy parenchyma and 30% in patients with liver cirrhosis. The current management is mostly supportive whereas the mortality rate of PHLF is over 80%.

After hepatectomy, the remaining hepatocytes undergo regeneration which is a crucial step for the liver to uphold its function. When this is insufficient, due to decreased functional mass, PHLF develops.

Liver regeneration involves well-coordinated regulatory pathways aimed at inducing cell proliferation and maturation. Cytokines, growth factors and bile salts play important roles in these processes. Immediately after resection, hemodynamic changes and inflammation cause exposure to pro-regeneration signaling molecules that activate the regeneration process. Subsequently, growth factors produced by several cell types and organs induce cellular proliferation, maturation and survival.

Recently, bile acids have been recognized as important regulators of liver regeneration. The liver maintains a bile acid hemostasis. After resection, bile acids act on several nuclear receptors that are involved in liver regeneration. A disturbance in this hemostasis can impair liver regeneration. The circulating biomarkers involved in liver regeneration can be measured in blood plasma and represent the regeneration activity.

In order to minimize the risk of PHLF, pre-operative assessment of liver function is undertaken with the use of a liver function test. Technecium-99 (99Tc)-mebrofenin hepatobiliary scintigraphy (HBS) is a validated liver function test that is able to calculate the global and regional liver function. Here, the hepatic mebrofenin uptake rate (MUR, %/min) represents liver function. This assessment is traditionally performed using CT-volumetry, with which the percentage of the liver volume that remains after the resection is calculated. However, liver function does not correlate with liver volume.

Another tool to assess the quality of liver parenchyma is liver stiffness measurement (LSM). Transient elastography (TE) and shear wave elastography (SWE) are both ultrasound-based methods that measure the speed of shear wave propagation through liver tissue. The velocity of the shear wave is related to tissue stiffness. Liver elasticity is correlated with grade of fibrosis, parenchymal inflammation and bile outflow obstruction.

So far, no studies have been conducted that assess the postoperative changes in measured liver function in relation to liver regeneration.

Evaluating the role of biomarkers in postoperative liver function can provide new insights in the regeneration physiology, potentially leading to new monitoring tools or therapeutic strategies aimed at preventing or treating PHLF. Furthermore, there is a lack of information regarding the normal variation of liver function within a single patient; this information is crucial for patients undergoing serial HBS. Lastly, the change in liver stiffness after liver resection and its correlation with regeneration, inflammation and other complications remains unanswered. Perioperative measurements of liver stiffness could provide useful means for assessing the physiology of liver regeneration and might provide an easy accessible, cheap and non-invasive bed-side tool for monitoring postoperative patients. This study aims to provide new insights that influence selection of candidates for liver resection, their postoperative monitoring and their management.

## **Study objective**

After resection, the increase in liver function will correlate with the concentrations of circulating biomarkers. These functional changes, measured at day 5 postoperatively, will better correlate with the biomarkers than the volumetric changes. Patients with a diminished increase in postoperative liver function will show impaired liver regeneration which is reflected by the concentration of circulating biomarkers.

## **Study design**

Day of admission, 1, 2 and 5 postoperatively and 6 weeks postoperatively

## **Intervention**

Patients will undergo three extra liver function scans (HBS) and liver stiffness measurements (TE and SWE) at day of admittance, postoperative day 5 and 6 weeks postoperatively. Furthermore, at 5 time-points during regular blood drawings, extra blood samples are taken (day of admittance, day 1, 2 and 5 postoperatively and 6 weeks postoperatively) for measurements of circulating liver regeneration biomarkers.

## **Contacts**

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## Eligibility criteria

### Inclusion criteria

- > 18 years old
- Scheduled for major liver resection (3 or more Couinaud segments), including hemihepatectomy or extended hemihepatectomy
- Colorectal liver metastasis or perihilar cholangiocarcinoma
- Written informed consent

### Exclusion criteria

- Bilirubin > 50  $\mu\text{mol/L}$
- History of chronic liver disease, including hepatitis, fibrosis, cirrhosis or hepatocellular carcinoma.
- Patients with allergies to mebrofenin
- Preoperative PVE
- Staged procedures, including two-staged resections and ALPPS
- Pregnancy

## Study design

### Design

Study type: Observational non invasive  
Intervention model: Other  
Allocation: Non controlled trial

**Control:** N/A , unknown

### Recruitment

NL  
Recruitment status: Recruiting  
Start date (anticipated): 16-02-2018  
Enrollment: 33  
Type: Anticipated

## Ethics review

Positive opinion  
Date: 01-03-2018  
Application type: First submission

## Study registrations

### Followed up by the following (possibly more current) registration

ID: 46514  
Bron: ToetsingOnline  
Titel:

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

No registrations found.

## In other registers

Register	ID
NTR-new	NL6885
NTR-old	NTR7063
CCMO	NL63868.018.17
OMON	NL-OMON46514

## Study results