

Template research PROTOCOL
For non-WMO-applicable research

19-01-2023, versie 2

Full Title of protocol	Metabolic Risk Factors and Impact of GLP-1 on Perioperative Outcomes after Major Hepatectomy, an international multicenter retrospective cohort study
Short Title	Meta-Risk Hepatectomy
Protocol ID	PaNaMaID: 15410 OZBSA2.26112 MEC-2026-0420
Registration	CCMO NL-012279 10aug2026 Clinical trial NCT
Version	1.0
Date	17 April 2026
Coordinating investigator / Project leader	**PRIMARY CENTER** ***Erasmus MC***
Principle Investigator **Erasmus MC**	
Research team Erasmus MC	
Sponsor	Erasmus MC Department of Anesthesiology
Subsidizing party	Undetermined

Name	**Signature**	**Date**
Sponsor **Head of Department**		

Coordinating Investigator / Project Leader / Principal Investigator		

Table of Content

List of Abbreviations 4

Abstract 5

Protocol Summary 5

1. **Introduction and rational** 7
2. **Objectives** 8
3. **Study Type** 8
4. **Study population** 9
5. **Methods** 10
6. **Incidental findings** 10
7. **Statistical analysis** 10
8. **Ethical considerations** 13
9. **Handling and storage of data / images / sound recordings / photos / film recordings** 14
10. **Handling and storage of human material** 15
11. **Exchange, sharing or transfer of data and/or human material and/or Images** 16
12. **Amendments** 16
13. **End of Study report** 16
14. **Publication** 17
15. **References** 17
16. **Attachments** 18

List of Abbreviations

AI	Artificial Intelligence
ASA	The American Society of Anesthesiologists
BMI	Body Mass Index
CBO	Kwaliteitsinstituut voor de Gezondheidszorg
CT	Computer Tomografie
DRE	Digital Research Environment
EMC	Erasmus Medisch Centrum
GLP-1	glucagon-like peptide-1
Hb	Hemoglobine
ICU	Intensive Care Unit
non-WMO	niet-Wet medisch-wetenschappelijk onderzoek met mensen-plichtig
NWTC	Niet WMO Toetsingscommissie
PHI	Personal Health Information
R	R Foundation for Statistical Computing, Vienna, Austria
SPSS	Statistical Packages for Social Sciences
WMO	Wet medisch-wetenschappelijk onderzoek met mensen

Protocol Summary

Full Title

Metabolic Risk Factors and Impact of GLP-1 on Perioperative Outcomes after Major Hepatectomy, an international multicenter retrospective cohort study.

Short Title

Meta-Risk Hepatectomy

Sample Size

~ 10,000 patients

Study Population

All adult patients undergoing major hepatectomy (3 or more segments).

Study Design

International Multicenter Retrospective Cohort Study

Study Data Period

Patients are included from the 1st of January, 2015 to the 30th of June 2026, with a minimum of 1 month of follow-up. The planned start of the study is the first of July 2026 until 31st of December 2028.

Objectives

1) To determine the effect of GLP-1 exposure on postoperative severe complications including post-hepatectomy liver failure.
   - To determine a (potential) dose dependent effect.
   - To determine optimal timing of cessation.
2) To identify patients at high risk for severe postoperative complications.
3) To evaluate the risk of aspiration and pulmonary complications and GLP-1 exposure.
4) To evaluate anesthesia techniques and perioperative outcomes, specifically in patients with metabolic risk factors and GLP-1 exposure.
5) To evaluate if metabolic risk factors or GLP-1 exposure are associated with post hepatectomy chronic pain.
6) To develop a prediction tool for severe postoperative complications prior to hepatectomy.
7) To identify potential prehabilitation strategies for preoperative optimization prior to hepatectomy, including GLP-1 strategies.

Main study parameters/endpoints

The occurrence of the composite of severe complications (Clavien-Dindo ≥3); Post-hepatectomy liver failure defined according to the ILGLS criteria (1); Aspiration; Transfusion details; Patient and Surgical characteristics; Health system outcomes (mortality, length of hospital and ICU stay, costs).

Burden and risks

There is no direct benefit for individual patients. Because this study is retrospective, no direct risks are expected for study participants as the data being used in the study already exists. Results of this study will not impact the patient care already delivered, and the results do not include any identifying variables. The provision of past or current clinical care of the patient's data who is used in this study will not be affected by this study.

Recruitment and Consent

All patients who underwent major hepatectomy during the study period will be retrospectively included. We will not seek informed consent from patients as the study aims to include >10,000 patients in an international multicenter setting, therefore obtaining individual patient consent cannot reasonably be required. Additionally, it involves no more than minimal risk to patients in the study with its retrospective design, as data has already been collected within existing databases. This research will be performed under the exception consent.

1.0 Introduction and Rationale

Major liver resection remains a cornerstone treatment for both primary and secondary hepatic malignancies and benign conditions with -severe- clinical consequences. Advances in surgical technique, perioperative care, and patient selection have improved outcomes over the past decades. However, post-hepatectomy liver failure (PHLF) remains the most important cause of postoperative mortality following major hepatectomy. The regenerative capacity of the liver determines the ability of the remnant liver to maintain metabolic homeostasis after resection, and impaired regeneration is a critical determinant of adverse outcomes (2). Liver regeneration is a complex and highly coordinated process involving metabolic reprogramming, inflammatory signaling, and cellular proliferation. Among the metabolic pathways involved, lipid metabolism plays a central role in supporting regeneration. Experimental studies have demonstrated that hepatic regeneration requires rapid mobilization and redistribution of lipids, which provide energy through β-oxidation and structural components required for membrane synthesis during hepatocyte proliferation. Disruption of intrahepatic lipid accumulation has been shown to impair regeneration (3).

In recent years, incretin hormones such as glucagon-like peptide-1 (GLP-1) have emerged as important regulators of metabolic homeostasis. GLP-1 is an enteroendocrine hormone secreted by intestinal L-cells in response to nutrient intake and plays a central role in glucose regulation, appetite suppression, and insulin secretion. Pharmacologic GLP-1 receptor agonists are widely used in the treatment of type 2 diabetes mellitus and obesity, and their use has expanded rapidly due to additional cardiovascular and metabolic benefits (4). Beyond its endocrine effects, GLP-1 has increasingly been implicated in hepatic metabolic regulation and liver disease. GLP-1 receptor agonists have demonstrated beneficial effects in non-alcoholic fatty liver disease (NAFLD) and metabolic dysfunction-associated steatotic liver disease (MASLD), including reductions in hepatic steatosis, inflammation, and hepatocellular injury (5). Experimental models show that GLP-1 receptor agonists can reduce intrahepatic triglyceride accumulation and improve markers of hepatic inflammation and metabolic dysfunction (3, 6). Similar effects can be achieved via DPP-4 inhibitors which bind to the enzyme dipeptidyl peptidase-4, preventing it from degrading GLP-1, resulting in an increase in GLP-1 levels.

However, the role of GLP-1 signaling during liver regeneration after hepatic resection remains incompletely understood. Animal studies suggest a complex relationship between GLP-1 signaling and hepatic regenerative responses. In murine models of partial hepatectomy, GLP-1 receptor agonist therapy has been associated with improvements in liver injury and survival in models of steatohepatitis but did not enhance restoration of liver mass and may alter inflammatory and stellate cell activation pathways

involved in regeneration (3). Human data on the relationship between GLP-1 and hepatic regeneration are limited. Observational studies evaluating perioperative hormone dynamics during liver resection have demonstrated significant alterations in circulating GLP-1 and GLP-2 levels during the regenerative process (6). Notably, GLP-1 concentrations appear to decline early after surgery while GLP-2 levels increase, suggesting reciprocal regulation of incretin signaling during hepatic regeneration. Furthermore, patients who develop PHLF exhibit distinct perioperative GLP-1 dynamics, including higher preoperative levels and pronounced postoperative changes (7). These findings suggest that incretin signaling may be closely linked to metabolic adaptation during liver regeneration and may represent a potential biomarker and modifiable pathway influencing postoperative outcomes. Furthermore, lipid homeostasis and metabolism is essential for liver regeneration and elevated GLP-1 levels might intervene in this process.

Therefore, the widespread use of GLP-1 receptor agonists for diabetes and obesity raises important clinical questions for patients undergoing major surgery. Moreover, the metabolic effects of GLP-1 signaling on hepatic lipid metabolism and regeneration raise the possibility that GLP-1 therapy could influence postoperative liver function after hepatectomy. Despite these plausible mechanisms, the clinical impact of GLP-1 analogue use on outcomes after major liver resection remains unknown. Large-scale clinical studies assessing the association between GLP-1 analogue use and postoperative liver failure, liver regeneration, and surgical outcomes are lacking. Given the rapidly increasing global use of GLP-1 receptor agonists and the rising prevalence of metabolic liver disease among patients undergoing hepatic surgery, understanding the potential impact of these agents on postoperative outcomes is of increasing clinical importance.

Therefore, the aims of the study are to assess GLP-1 analogue/DPP-4 inhibitor use and outcomes following major hepatic resection in a large international multicenter cohort. Specifically, we will evaluate whether perioperative GLP-1 exposure is associated with the occurrence of post-hepatectomy liver failure and severe postoperative complications. In addition, we aim to explore dose-dependent effects of GLP-1 therapy, assess perioperative complications, options for prehabilitation, and evaluate broader health system outcomes such as length of stay, ICU admission, and mortality.

2.0 Study Objectives

Primary Objective

To determine if preoperative GLP-1 exposure is associated with risk of PHLF following major hepatectomy.

Directionality to be tested:

- Plausible for harm via impaired lipid mobilization/regenerative energetics.
- Plausible for benefit via improved steatotic liver phenotype.

Secondary Objectives:

- To determine the incidence of severe complications (Clavien-Dindo 3-5) after major hepatectomy in association with GLP-1 exposure.
- To determine if there is a dose–response relationship between GLP-1 exposure (agent, dose, duration, and recency) and risk of PHLF and severe complications.
- To determine if GLP-1 exposure is associated with differences in liver regeneration (radiologic/volumetric regeneration when available; surrogate postoperative functional recovery trajectories when not; subgroup analysis in the patient population who underwent vena porta embolization prior to surgery).
- To determine if GLP-1 exposure is associated with peri-anesthetic aspiration/regurgitation events and related pulmonary complications.
- To determine if anesthesia techniques are associated with perioperative outcomes after hepatectomy, specifically in patients with metabolic risk factors and GLP-1 exposure.
- To determine if metabolic risk factors or GLP-1 exposure are associated with post hepatectomy chronic pain.
- To determine if metabolic risk factors or GLP-1 exposure is associated with health system outcomes (LOS, ICU admission, costs) mediated through postoperative complication burden.
- To identify patients at high risk for severe postoperative complications and to develop a preoperative prediction tool.
- To identify potential prehabilitation strategies for preoperative optimization prior to hepatectomy, including GLP-1 strategies.

3.0 Study Design

3.1 Study Design

Retrospective cohort study

3.2 Single/Multicenter

International multicenter study

3.3 Check all the applicable boxes

x Medical records (re-use of data from healthcare, including AI)

☐ Case report

☐ Re-use data from research

X Evaluations of quality of healthcare (retrospective)

☐ Research with additional use of residual material from regular healthcare

☐ Research with re-use of human material from research or existing biobank

☐ De novo biobank

☐ Phase IV research

☐ Healthcare evaluation research (prospective)

☐ Research with medical devices

☐ Research with In Vitro Diagnostic Tests

☐ Other research, describe

4.0 Study Population

4.1 Study population

X Adults (18 years and older)

☐ Minors (younger than 16 years)

☐ Incapacitated adults (16 years and older)

☐ Incapacitated minors (younger than 16 years)

4.2 Population base

Adult patients undergoing major hepatectomy between 1st of January, 2015 to the 30th of June 2026 in multiple centers in Europe, Canada, US, and India. We anticipate approximately 10,000-15,000 eligible patients during that time period.

4.3 Inclusion criteria

- Adult patients ≥ 18 years undergoing major hepatectomy (3 or more segments)

4.4 Exclusion Criteria

- Patients who objected against the use or re-use of their data for research purposes.

4.5 Sample size calculation

We expect a sample size of 10,000-15,000 patients. Assuming an incidence of 8% PHLF (based on a general hepatectomy cohort (9, 10)), we expect >800 events.

Secondary risk-factor analyses are constrained by the expected number of events; with 800 events we will use logistic regression with a limited number of predictors of 80, or alternatively consider a nested case–control approach if additional covariates are required. For patient level analysis only the first procedure during the study duration is included.

5.0 Methods

5.1 Research methods

The data for this study will be obtained in collaboration with the data stewards according to Erasmus protocol. In participating centers, the data will be obtained from -electronic-patient databases, according to local protocol and after REB approval. Data will be entered in a CASTOR database.

5.2 Standard clinical versus extra for research

All data already exists and is part of standard clinical care, therefore, no tests or visits are extra for research purposes.

5.3 Burden and risks

Because this study is retrospective, no direct risks are expected for study participants as the data being used in the study already exists. Results of the study will not impact the patient care already delivered, and the results do not include any identifying variables. The provision of past or current clinical care of the patient's data who is used in this study will not be affected by this study.

5.4 Medical device(s) / In vitro diagnostic tests

Not applicable

6.0 Incidental findings

6.1 Chance of incidental findings

Is there a chance of incidental findings?

☐ Yes

X No

6.2 Procedures

Not applicable

7.0 Statistical analysis

Exposure:

GLP-1 analogue

The half-life of GLP-1 analogues is 7 days. Generally, no effects of the drug remains after 5 times the half-life of a drug (36> days or 5 weeks). No clinically relevant effects are expected after GLP-1 analogues have been stopped for 4 weeks or more. Therefore, patients who stopped 28<days (4 weeks) prior to hepatectomy are included in the NON-GLP-1 analogue group. Sub analyses per stop date will be performed (3-4 weeks; 2-3 weeks; 1-2 weeks; 1 week; continued use).

DPP-4 inhibitor

These drugs are usually continued or held the morning of surgery, with clinical effects still expected (half life ±20h for the long acting alogliptin and linagliptin).

For the sake of readability, the protocol will use 'GLP-1 exposure' for GLP-1 analogue use and or DPP-4 inhibitor use.

7.1 Main study parameters / endpoints

Post-hepatectomy liver failure defined according to the ILGLS criteria (1): POD 5: INR>1.7, bilirubin > 3mg/dL (or peak>7mg/dL).

7.2 Secondary study parameters / endpoints

Outcomes:

Grading of PHLF:

- Grade A: no change in patient management (laboratory deviations only).
- Grade B: deviation from the normal clinical course, but invasive treatment.

- Grade C: requires invasive, high-dependency care (renal replacement therapy, intubation vasopressors, or emergency re-resection/take back).

Composite of severe complications (defined as Clavien-Dindo 3-5) (11)
Cause of severe complication
Aspiration
Transfusion
Chronic Pain (at 3 months)
Health system outcomes (hospital length of stay, ICU admissions, ICU length of stay, 90-day and in hospital mortality, and total health system costs)

Patient and Procedure Level Variables:
Age, BMI, comorbidities (charlson comorbidity index, diabetes, OSAS, hypertension, hypercholesterolemia, metabolic syndrome, liver steatosis (grading), GERD, diagnosis/underlying etiology for hepatectomy, ASA classification, chemotherapy). Previous bariatric surgery (highest BMI before bariatric surgery, BMI before hepatectomy).

Laparoscopic, robotic, or open procedure. Length of surgery. Pringle and times. Center level and number of procedures per year.

Anesthesia (tiva, inhalation anesthetics). Phlebotomy, if yes in mL. Intraoperative NTG or nitroprusside use. Transfusion details (PC, plasma, platelets, fibrinogen, factor concentrates, albumin).

Analgesia (acetaminophen, NSAIDs, opioids, ketamine, gabapentin, dexmeditomidin, clonidin, neuroaxial, locoregional, other). Analgesia use at 3 months. Chronic Pain, or consultation pain specialist at 3 months.

Covariates:
Laboratory values (Hb, platelets, coagulation, kidney function and electrolytes, liver panel, infection parameters, hba1c, troponin, NT pro-bnp, blood gas).
Imaging results (Xray, CT imaging, ultrasound results, Fibroscan/transient elastography/MRE).
Pathology results (steatosis (grade / %), fibrosis (F0-F4), MASH (yes/no). Cirrhosis (grade).
Medication use, other than GLP-1 analogues (e.g., statins, anticoagulation, oral DM medication, insulin).

7.3 Analysis

Statistical analyses will be performed using R (R Foundation for Statistical Computing, Vienna, Austria) and/or SPSS ((IBM Corp., Armonk, NY, USA).

All consecutive hepatectomies between the 1st of January, 2015 to the 30th of June 2026will be included in the dataset. Variables will first be inspected graphically for distributional characteristics, outliers, and completeness using histograms, Q–Q plots, and box plots. Descriptive statistics will summarize patient, procedural, and pharmacologic characteristics as mean ± standard deviation or median (interquartile range) for continuous variables, and as counts (%) for categorical variables.

Primary analysis

The primary objective is to determine whether preoperative GLP-1 exposure is associated with the risk of PHLF. As GLP-1 exposure is not randomly assigned but likely influenced by patient-, disease-, and center-level characteristics, treated and untreated patients are likely to differ in their baseline characteristics. These differences may confound the relationship between treatment and outcome, limiting the validity of crude comparisons. To address this, statistical techniques are required to adjust for measured confounders and enable a more balanced comparison between groups. Therefore, a causal inference framework using inverse probability weighting (IPW) is proposed.

A propensity score (PS) for GLP-1 exposure will be estimated for each patient, incorporating predefined covariates that are considered clinically relevant confounders (i.e., variables associated with both GLP-1 exposure and risk of PHLF, mapped by creating direct acyclic graphs (DAGs)). These will include variables such as patient characteristics, comorbidities, liver function parameters, surgical factors, and center.

Based on the estimated propensity scores, stabilized inverse probability weights will be calculated to create a pseudo-population in which measured baseline covariates are balanced between patients with and without GLP-1 exposure. The distribution of weights will be assessed, and if necessary, truncation of extreme weights will be applied to improve stability. Covariate balance before and after weighting will be evaluated to ensure adequate balance.

The association between GLP-1 exposure and PHLF will be estimated using a weighted logistic regression model, applying the IPW weights. In addition to the exposure (GLP-1/DPP-4), the model will include key prognostic covariates, including center, to further adjust for residual confounding. This combined approach (propensity score weighting together with covariate adjustment in the outcome model) constitutes a doubly robust estimation strategy. Effect estimates will be reported as odds ratios (ORs) with corresponding 95% confidence intervals (CIs).

Sensitivity analysis

To assess the robustness of the primary findings, several sensitivity analyses will be performed:

1. Multivariable Regression

A multivariable logistic regression model will be fitted including GLP-1 exposure and all prespecified confounders.

2. Center-Specific Analyses

IPW analyses will be repeated in separate per (main) center to evaluate consistency of the association across institutions and to assess the impact of center-level heterogeneity.

Secondary objectives

The association between GLP-1 exposure and the incidence of severe postoperative complications (Clavien–Dindo grade III–V) will be assessed using similar approaches as described for the primary outcome, including regression-based methods with adjustment for relevant confounders and, where appropriate, propensity score based techniques.

To evaluate potential dose–response relationships, GLP-1 exposure will be further characterized according to agent type, dose, duration of use, and timing of discontinuation prior to surgery.

Liver regeneration will be assessed using available radiologic or volumetric data. In the absence of direct measurements, surrogate markers of postoperative functional recovery will be explored. Subgroup analyses will be performed in patients undergoing preoperative portal vein embolization to assess potential differences in regenerative capacity associated with GLP-1 exposure.

The occurrence of peri-anesthetic aspiration or regurgitation events and related pulmonary complications will be evaluated descriptively and, where feasible, using regression-based methods adjusted for relevant risk factors.

Health system–related outcomes, including length of hospital stay, ICU admission, and costs, will be analyzed in relation to GLP-1 exposure. Where appropriate, exploratory analyses will assess whether these associations are mediated by postoperative complication burden.

In addition, predictive modeling techniques will be used to identify patients at increased risk for severe postoperative complications. A multivariable prediction model will be developed using a priori selected, clinically relevant preoperative variables, based on existing literature and expert consensus. To reduce the risk of overfitting, the number of candidate predictors included in the model will be restricted according to the number of observed outcome events, adhering to a minimum of approximately 10 events per variable (EPV). Missing data will be handled using multiple imputation under the missing-

at-random (MAR) assumption, employing multiple imputation by chained equations (MICE). Model development will be performed across imputed datasets with appropriate pooling of estimates. Internal validation will be conducted using bootstrapping, to assess model performance and to account for potential optimism in model estimates. Model performance will be described in terms of discrimination (c-statistic) and calibration (O:E ratio, calibration plots). If the sample size permits, an additional validation strategy may be applied by reserving a subset of patients for validation purposes.

8.0 Ethical considerations

8.1 Regulation statement

The study will be conducted according to the principles of the Declaration of Helsinki (version 2024, see for the most recent version: www.wma.net), Gedragscode Gezondheidsonderzoek 2022 and in accordance with other guidelines, regulations and Acts.

8.2 Informed consent

Will the subjects be asked for informed consent?

☐ Yes (Upload Participant Information Letter and Informed Consent)

☐ No, consent already given in previous study (Upload Participant Information Letter and Informed Consent previous study)

X No, this research will be performed under the exception consent (Upload form Care for data Template, in Dutch: Formulier uitzondering toestemming)

☐ Other (e.g. partly, indirectly) Please describe the situation.

8.3 Recruitment and informed consent procedures

Not applicable

8.4 Exception consent

In this study, data will be extracted from existing patient databases according to local ethics protocols without obtaining individual informed consent. In the Erasmus MC this will be performed in collaboration with the data stewards. As described previously, the large cohort size and the retrospective nature of the study makes that we will not seek

informed consent from patients as obtaining individual patient consent cannot reasonably be required. Additionally, it involves no more than minimal risk to patients in the study with its retrospective design, as data has already been collected within existing databases. This research will be performed under the exception consent. Patients who have objected to the use of their data in research will be excluded. Please find the Form "Care for Data" as an attachment to this protocol (Erasmus MC only).

9.0 Handling and storage of data / images / sound recordings / photos / film recordings

9.1 Data / images / sound recordings / photos / film recordings

The data for this study will be obtained from the various participating medical centers and will be used to provide the following data for this study: baseline characteristics, comorbidities, intraoperative variables, procedural information, laboratory, pathology, and radiology reports, and clinical post-procedural outcomes. This data already exists and was gathered as part of standard clinical care. No additional data will be gathered for this study for research purposes.
Data will be stored in a CASTOR database.
Data will be shared according to predefined DTA's with the Erasmus as primary center.

9.2 Privacy protection

The privacy of the participants is protected by using the study number as identifiable reference, with the decoding file kept within the Erasmus MC servers, which is password protected, and only accessible for the investigators within the Erasmus MC research team. The handling of personal data is in compliance with the EU General Data Protection Regulation and the Dutch Act on Implementation of the General Data Protection Regulation (in Dutch: Algemene Verordening Gegevensbescherming en Uitvoeringswet Algemene Verordening Gegevensbescherming).
Data from participating centers will be coded and the files that identify the individual patient will be kept at that particular medical center. Data will only be shared based on a DTA in close collaboration with the Legal Departments of participating medical centers and the Erasmus MC. The DTA per center will be uploaded in PaNaMa once approved by the respective legal departments.

9.3 Handling and storage of data

All study information including any potential Personal Health Information (PHI) will be maintained within the Erasmus MC network. Data will be presented in aggregate and the

risk of re-identification of any patients is minimal. We will use primarily CASTOR as database, when possible also for international collaborations, or Excel. Study data from this study will be retained on Erasmus MC networks for 10 years after retrieval which is in line with the Erasmus MC guidelines.

According to guidelines within the Erasmus MC storage will be organized on Erasmus MC servers and in a Digital Research Environment (DRE) for larger data files.

The individuals who will have direct access to the study data will be those who are listed investigators at the primary research site and as part of the research group at the Erasmus MC. External authors will not have access to raw data and will only have access to the final tables/figures and manuscript.

9.4 handling and storage of images / sound recordings / photos / film recordings
Not applicable

9.5 Approval of access to data / images / sound recordings / photos / film recordings
The Principle Investigator will grant participating members of the research team approval for access to the data for this study. Logbooks of data retrieval and handling will be kept.

10.0 Handling and storage of human material

10.1 Human material
Not applicable

10.2 Check all the boxes which are applicable to the human material origin:

☐ Residual material from regular healthcare

☐ Research (material acquired from a previous study).

Add the reference of the study i.e., MEC-number Erasmus MC.

☐ Re-use of human material from existing biobank

Describe whether the human material originates from research into the same disease.

☐ Other, please specify

10.3 Handling and storage of human material

☐ Anonymous, i.e. the material can never be traced back to an individual subject

☐ Pseudonymized/Coded

☐ Identifiable

10.4 Biobank
Not applicable

10.5 Approval of access to human material
Not applicable

11 Exchange, sharing or transfer of data and/or human material and/or images

Applicable

All study information including any potential Personal Health Information (PHI) will be maintained within the Erasmus MC network. Data will be presented in aggregate and the risk of re-identification of any patients is minimal. We will use primarily CASTOR as database, when possible also for international collaborations, or Excel.

The individuals who will have direct access to the study data will be those who are listed investigators at the primary research site and as part of the research group at the Erasmus MC. External authors will not have access to raw data and will only have access to the final tables/figures and manuscript. All Data Exchange will be from participating centers to the Erasmus and no raw data will go from the Erasmus to participating centers. These data transfers will be covered by Data Transfer Agreements drawn up in close collaboration with the Legal Department at the Erasmus MC and participating centers.

We have ongoing sponsor applications with whom no data will be shared when approved and the results of the studies will not be altered or influenced.

12 Amendments

Amendments are changes made to the research after a favorable opinion by the NWTC has been given. All amendments will be submitted to the NWTC that gave the favorable opinion. Substantial amendments must be approved by the Niet WMO Toetsingscommissie before they can be implemented.

13 End of study report

Within one year after the end of the study a final study report will be submitted with the results of the study, including any publications/abstracts of the study. In case the final study report will not be available within one year, another term will be defined including the reasons.

14 Publication

Do you have the intention to submit the study results in a manuscript for publication in a journal:

X Yes

☐ No, please motivate

The final study report with the results of the study will be submitted once the analyses and evaluation of the results have taken place.

15 References

1. Ray S, Mehta NN, Golhar A, Nundy S. Post hepatectomy liver failure - A comprehensive review of current concepts and controversies. Ann Med Surg (Lond). 2018;34:4-10.
2. Murtha-Lemekhova A, Fuchs J, Ghamarnejad O, Nikdad M, Probst P, Hoffmann K. Influence of cytokines, circulating markers and growth factors on liver regeneration and post-hepatectomy liver failure: a systematic review and meta-analysis. Sci Rep. 2021;11(1):13739.
3. Valdecantos MP, Ruiz L, Pardo V, Castro-Sanchez L, Garcia-Monzon C, Lanzon B, et al. Differential Effects of a Glucagon-Like Peptide 1 Receptor Agonist in Non-Alcoholic Fatty Liver Disease and in Response to Hepatectomy. Sci Rep. 2018;8(1):16461.
4. Barzgar H, Darmadi D, Nafisa J, Narkulov S, Sviridova MB. Peptide drugs for obesity and type 2 diabetes mellitus: an overview of clinical trials. Clin Chim Acta. 2026;581:120772.
5. Deng M, Wen Y, Yan J, Fan Y, Wang Z, Zhang R, et al. Comparative effectiveness of multiple different treatment regimens for nonalcoholic fatty liver disease with type 2 diabetes mellitus: a systematic review and Bayesian network meta-analysis of randomised controlled trials. BMC Med. 2023;21(1):447.
6. Ammann M, Santol J, Pereyra D, Kalchbrenner T, Wuerger T, Laengle J, et al. Glucagon-like peptide-1 and glucagon-like peptide-2 regulation during human liver regeneration. Sci Rep. 2023;13(1):15980.

7. Ammann M, Jonas JP, Pereyra D, Santol J, Hackl H, Kalchbrenner T, et al. Plasma GLP-1 and metabolic dynamics during human liver regeneration and their association with posthepatectomy liver failure. Hepatobiliary Surg Nutr. 2025;14(1):49-65.
8. Hang LW, Chen CF, Wang CB, Wu TN, Liang WM, Chou TC. The association between continuous positive airway pressure therapy and liver disease development in obstructive sleep apnea/hypopnea syndrome patients: a nationwide population-based cohort study in Taiwan. Sleep Breath. 2017;21(2):461-7.
9. Kauffmann R, Fong Y. Post-hepatectomy liver failure. Hepatobiliary Surg Nutr. 2014;3(5):238-46.
10. Vibert E, Pittau G, Gelli M, Cunha AS, Jamot L, Faivre J, et al. Actual incidence and long-term consequences of posthepatectomy liver failure after hepatectomy for colorectal liver metastases. Surgery. 2014;155(1):94-105.
11. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg. 2004;240(2):205-13.

16 Attachments

☐ Participant information letter and Informed consent document

X Care for data Template – Formulier uitzondering toestemming

☐ Questionnaires

☐ Data Management Plan

☐ Data Transfer Agreement

☐ Material Transfer Agreement

☐ Clinical Trial (Site) Agreement

☐ Other, please describe