Determinants of liver fat composition in overweight and obese humans

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The primary objective of this study is to determine the association between DNL and hepatic %SFA in overweight/obese subjects differing in liver fat content. The secondary objectives are to determine the association between adipose tissue fat...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Hepatic and hepatobiliary disorders
Study type	Observational invasive

Summary

ID

NL-OMON45290

Source
ToetsingOnline

Brief title
Determinants of liver fat composition

Condition

- Hepatic and hepatobiliary disorders
- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
fatty liver, Non-alcoholic fatty liver (NAFL)

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht
Source(s) of monetary or material Support: TKI,Unilever

Intervention

Keyword: Adipose tissue fat composition, De Novo Lipogenesis, Insulin sensitivity, Liver fat composition

Outcome measures

Primary outcome

- %SFA expressed as relative amount of SFA to the total amount of fatty

acids.

- DNL expressed as percentage of palmitate in very-low-density-lipoprotein

(VLDL)-TG originating from DNL

Secondary outcome

- Liver fat composition expressed as relative amount of MUFA and PUFA to the

total amount of fatty acids, in addition to %SFA

- Adipose tissue fat composition expressed as relative amount of SFA, MUFA and

PUFA to the total amount of fatty acids

- Adipose tissue fat composition expressed as relative amount of linoleic acid,

docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) to the total amount

of fatty acids.

- Hepatic, peripheral and whole body insulin sensitivity expressed as %

suppression of endogenous glucose production (EGP), rate of disappearance (Rd)

in *mol/kg/min and glucose infusion rate (GIR) in *mol/kg/min.

- Muscle insulin sensitivity expressed as determinants/markers for muscle

insulin sensitivity in muscle biopsy (oxphos, GLUT4, intramyocellular lipids

(IMCL).

Study description

Background summary

Excessive fat in the liver, in absence of high alcohol consumption, is diagnosed as non-alcoholic fatty liver (NAFL). NAFL prevalence is as high as 50-70% in obese people and is associated with impairments in metabolic health, e.g. insulin resistance. Not only the amount, but also the composition of the fat stored in the liver appears to be linked to health outcome measures, such as insulin resistance, but this evidence comes mainly from animal studies. Since fat composition has been linked to health outcome measures, it is important to understand what determines the fatty acid composition of liver fat. De novo lipogenesis (DNL) and adipose tissue fat composition are factors that could determine liver fat composition. Since the end product of DNL are saturated fatty acids and as the majority of fatty acids in the liver originate from adipose tissue, both may influence hepatic fatty acid composition profoundly. Up to now, relations between hepatic fatty acid composition, DNL and adipose tissue fatty acid composition have never been determined in the same study.

Study objective

The primary objective of this study is to determine the association between DNL and hepatic %SFA in overweight/obese subjects differing in liver fat content. The secondary objectives are to determine the association between adipose tissue fat composition and liver fat composition and the association between liver fat composition and liver, muscle and whole body insulin sensitivity.

Study design

This is a cross-sectional observational study.
Twenty-two volunteers, 8 with liver fat content <5% and 14 with liver content >5%, will take part in the total study. MRS measurements will be performed on approximately 31 subjects to determine amongst others liver fat content, based on liver fat content it will be determined whether subjects can take part in the rest of the study.
In this study liver fat content and composition (MRS), adipose tissue composition (MRS and biopsy), de novo lipogenesis (D2O in VLDL-TG), liver, muscle and whole body insulin sensitivity (2 step hyperinsulinemic euglycemic clamp and biopsy) and body composition (BodPod) will be measured.

Study burden and risks

Results of this study will provide insight in the relation between factors that influence liver fat and liver fat composition and in the clinical relevance of

liver fat composition in humans. The risks of the performed measurements and the physical discomfort are low; risks related to the clamp, adipose tissue biopsy, muscle biopsy, DNL measurement and MRS measurements are low because of clear exclusion criteria aimed at reducing risks and the well-experienced researchers performing these tests and isotopically-labelled water ingestion is entirely safe and non-toxic with body water enrichment up to 20 mol%.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Signed informed consent
Caucasian (people will be excluded when having a 50% or more then 50% racial African/Asian background)
Male or postmenopausal female

Aged 45-70 years at start of the study
Body mass index (BMI) 27 * 35 kg/m2
Stable dietary habits (no weight loss or gain >3kg in the past 3 months)
Sedentary lifestyle (not more than 2 hours of sports per week)

Exclusion criteria

Type 2 diabetes
Active diseases (cardiovascular, diabetes, liver, kidney, cancer or other)
Contra-indication for MRI
Alcohol consumption of >2 servings per day
Smoking >5 cigarettes per day
Use of anti-coagulants

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	15-08-2017
Enrollment:	31
Type:	Actual

Ethics review

Approved WMO

Date:	18-05-2017

Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	26-07-2017
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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
CCMO	NL60263.068.16

Study results

Date completed:	17-05-2018
Actual enrolment:	19