The Clock thickens: Morning or evening training for the treatment of NAFLD?

Published: 12-06-2023
Last updated: 07-04-2024

The aim of the study is to identify the effect of exercise timing on NAFLD. Additionally, we aim to increase the understanding of the exercise-related modulation of the metabolic and inflammatory processes causing NAFLD, including insulin resistance...

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

Summary

ID

NL-OMON53691

Source
ToetsingOnline

Brief title
TikTac study

Condition

- Hepatic and hepatobiliary disorders
- Lipid metabolism disorders

Synonym
fatty liver disease, hepatic steatosis

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Maag Lever Darm Stichting;project number

ZP 21-10 (73.600¤)

Intervention

Keyword: Circadian rhythm, Exercise, Non-alcoholic fatty liver disease

Outcome measures

Primary outcome

The primary endpoint of the study is the reduction of liver fat levels and

other markers of NAFLD after 12 weeks of morning or evening exercise.

Secondary outcome

Secondary endpoints include the improvement of insulin resistance, circulating

levels of liver enzymes, fitness, and gut microbiota composition in response to

morning or evening exercise.

Study description

Background summary

Non-alcoholic fatty liver disease (NAFLD) is a disease of alarmingly increasing prevalence that can progress from simple steatosis to non-alcoholic steatohepatitis (NASH) with hepatic fibrosis and, ultimately, to cirrhosis and hepatocellular carcinoma (HCC). Not only increases NAFLD liver-related morbidity and mortality, patients with NAFLD are at high risk for developing type 2 diabetes (T2DM) and cardiovascular diseases. Since NAFLD is mainly associated with obesity and increasingly common as a result of the *Western lifestyle* (i.e. high-caloric diet, physical inactivity and poor physical fitness), the cornerstone of the treatment of NAFLD consists of lifestyle adjustments such as exercise training. Many of the processes that are dysregulated in NAFLD and modulated by exercise, including energy metabolism, whole-body inflammation and the interplay with the gut microbiota, are under control of the internal circadian clock. However, it is unknown at what time of day the circadian control aligns best with exercise training and, therefore, what the *ideal* training time is to maximize the impact on NAFLD.

Study objective

The aim of the study is to identify the effect of exercise timing on NAFLD. Additionally, we aim to increase the understanding of the exercise-related modulation of the metabolic and inflammatory processes causing NAFLD, including insulin resistance and the gut microbiota.

Study design

Forty obese patients with NAFLD will be enrolled by randomization to participate in an exercise training program over 12 weeks, either in the morning (n=20) or evening (n=20). Blood and stool samples will be collected before, during and after the intervention to monitor diagnostic markers such as liver enzymes (AST, ALT, GGT, etc.) and changes of the gut microbiota with exercise, respectively. Moreover, mixed meal tolerance tests will be performed before and after the intervention and hepatic fat content and cardiovascular parameters (e.g. arterial stiffness) will be monitored via MRI. Throughout the study, physical fitness will be assessed and monitored using the steep ramp test.

Study burden and risks

The research can cause discomfort/adverse effects. Dangerous side effects are not to be expected. Although the training program is adapted to the physical capabilities, the participants may initially feel muscle pain after the training sessions. It is expected that participating in this study will improve the physical condition of the participants, it is also possible that they will lose weight and their blood pressure will be lowered, but this is not certain.

Contacts

Public
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2333ZA
NL
Scientific
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2333ZA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Age >= 45 years and <= 75
- Obese (BMI > 27 kg/m2)
- Males and postmenopausal females
- Caucasian
- Hepatic steatosis defined as increased hyperechogenicity of the liver on abdominal ultrasound, CAP score on Fibroscan > 280, and/or histological signs of steatosis
- Sedentary lifestyle (maximum of 20*minutes of moderate-to-vigorous physical activity per day on less than three days per week)
- Written informed consent

Exclusion criteria

- Exclusion criteria for MRI (claustrophobia, pacemaker, metal implants, etc.)
- Any other liver disease than NAFLD/NASH
- Present excessive alcohol use defined as > 2 units/day
- Recent use (< 3 months) of antibiotics
- Recent changes in dosages of regular medication (< 3 months)
- Recent (< 3 months) weight change (>5%)
- Recent (< 3 months) substantial diet changes
- Cardiovascular co-morbidity defined as heart failure, coronary insufficiency and hypertension in past history
- Comorbidity that contraindicates exercise training and exercise testing or that affects exercise response and exercise capacity
- Ongoing or recent use of glucocorticoids, oral/transdermal hormonal substitution, paclitaxel, theofyllin, amiodarone, myelosuppresive agents
- A psychiatric, addictive or any other disorder that compromises the subjects

ability to understand the study content and to give written informed consent for participation in the study
- Working night or alternating shifts, known sleeping disorders such as narcolepsy or insomnia

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-08-2023
Enrollment:	40
Type:	Anticipated

Ethics review

Approved WMO

Date:	12-06-2023
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	NL83431.058.22