COVID-ASTER Obesity and COVID-19: AdipoSe TissuE Responses to SARS-CoV-2 infection

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Objective: To investigate the adipose tissue response upon ex vivo SARS-CoV-2 infection, more specifically to answer the following questions:1. Is adipose tissue permissive to direct SARS-CoV-2 infection? 2. Are adipose tissue-derived factors...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Viral infectious disorders
Study type	Observational invasive

Summary

ID

NL-OMON51186

Source
ToetsingOnline

Brief title
COVID-ASTER

Condition

- Viral infectious disorders

Synonym
COVID-19, SARS-CoV-2

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: ZonMw

Intervention

Keyword: Adipose tissue, COVID-19, Obesity, SARS-CoV-2

Outcome measures

Primary outcome

Main study parameters/endpoints :

1. To determine if adipose tissue is permissive to infection by plaque assay

and qPCR of viral RNA.

2. To determine the mRNA and protein expression of SARS-CoV-2 receptors such as

ACE2 and to perform blocking experiments to elucidate the entry receptor.

3. To determine if there is an exaggerated inflammatory response upon

SARS-CoV-2 infection by examining the mRNA levels of inflammatory mediators and

adipokines. As well as the protein levels of adipose-tissue derived factors and

inflammatory mediators released upon SARS-CoV-2 infection in culture medium by

Luminex analysis.

Secondary outcome

NA

Study description

Background summary

We hypothesize that obesity is a major amplifier of organ inflammation and injury accounting for the severe respiratory failure and death in SARS-CoV-2 infected patients. The rationale for this hypothesis is based on our clinical observations that most of the SARS-CoV-2 infected patients admitted to the ICU with respiratory failure had central obesity, extensive visceral fat and a Body Mass Index (BMI) of 25 kg/m2 or higher (mean 30 kg/m2). Recent findings from the UK, in the largest cohort study to date, confirm that the likelihood of hospital death due to SARS-CoV-2 is associated with obesity severity1.

Circulating adipose tissue (AT)-derived mediators including leptin are known to be associated with BMI and are known to have immunomodulating properties which may prime obese individuals to infection resulting in an exaggerated response. We therefore postulate that excess adipose tissue, its distribution and secreted mediators play an important role in the type of immune response and subsequently in the progression towards respiratory insufficiency in patients with SARS-CoV-2.

Study objective

Objective: To investigate the adipose tissue response upon ex vivo SARS-CoV-2 infection, more specifically to answer the following questions:
1. Is adipose tissue permissive to direct SARS-CoV-2 infection?
2. Are adipose tissue-derived factors released in response to SARS-CoV-2 infection?
3. What is the response of adipose tissue-derived factors on endothelial and epithelial cell behaviour?

Study design

Study design: Small visceral and subcutaneous adipose tissue samples collected from obese (BMI 40 and higher, intervention group) and lean (BMI 25 or lower, control group) patients undergoing surgery will be infected with SARS-CoV-2 virus ex vivo.

Intervention

Patients who have given informed consent for participation in this study will undergo surgery. The bariatric surgery procedure will be performed normally, no modifications are necessary. After introduction of the laparoscopic instruments, a small piece of omental fat of 2 cm3 will be collected by diathermia and taken out of the patient by one of the trocarts. After this, the bariatric procedure will be continued and performed as it normally would. At the end of the operation, the location in the omentum where the fat tissue was harvested will be checked for bleeding complications. In patients undergoing abdominal surgery (Control group), after the abdomen is opened by laparotomy or the instruments are placed in laparoscopic procedure a piece of omental fat of 2 cm3 will be collected by diathermia and taken out of the patient by one of the trocarts or the laparotomy. After the omental fat is taken out of the patient it will be immediately placed into Dulbecco*s modified Eagle*s medium (DMEM) containing 10% fetal bovine serum and antibiotics. Samples will then immediately be transferred to the UMCG BSL3 laboratory for subsequent SARS-CoV-2 infection experiments.

Study burden and risks

Collection of visceral and subcutaneous fat tissue:. This can induce bleeding which can be resolved immediately during the operation. In the worst-case scenario, bleeding can occur post-operatively and patients have to be reoperated by laparoscopy. The chance of bleeding after finishing the operation is very small.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Intervention group (Obese)
Healthy participants who give informed consent to participate in this study that are male and female, between aged between 18 and 65 years old with a BMI above 40.

Control group (Lean)

The control group will consist of participants that give informed consent to participate in this study, male and female aged between 18 and 65 years old, without comorbidities, no cancer and a BMI of 25 or less.

Exclusion criteria

For both groups: Diabetes mellitus, hypertension, metabolic syndrome, asthma, immune disease such as Crohn colitis, rheumatic disease, cancer, use of soft/hard drugs or smoking. Previous COVID-19 infection.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	04-10-2021
Enrollment:	36
Type:	Actual

Ethics review

Approved WMO

Date:	16-08-2021
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NL76208.042.21
Other	NL9141