

WHeezing Illnesses Study Leidsche Rijn / Childhood adiposity and Arterial Disease Onset 2

Published: 25-08-2010

Last updated: 02-05-2024

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON43961

Source

ToetsingOnline

Brief title

WHISTLER/Cardio 2

Condition

- Other condition

Synonym

Cardiovascular diseases and overweight

Health condition

cardiovasculaire aandoeningen en overgewicht

Research involving

Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: adipokines, arterial wall properties, cardiovascular diseases, dysfunctional adipose tissue

Outcome measures

Primary outcome

To study the association between fat distribution and the adipokine profile in childhood, the main study parameters consist of anthropometric parameters, namely weight, quetelet index, waist circumference, and the main outcome parameters are the adipokine concentrations and clusters of adipocytokines. Moreover, to determine the effect of adipocytokines on the vascular system, the adipokine profile is used as determinant and the main outcome parameters are the carotid IMT and vascular stiffness.

In the second part of the study the main study parameters are changes in fat distribution between the age of 5 and 8 years. The main outcome parameters are the changes in Z-score IMT and distension at the age of 8 years.

Secondary outcome

Since the abdominal fat will be measured ultrasonographically as well, secondary study parameters will be the intra-abdominal fat and subcutaneous fat as determinants of adipokine concentration and of IMT and vascular stiffness.

Study description

Background summary

Cardiovascular diseases (CVD) belong to the major causes of morbidity and mortality in adults. Since the process of atherosclerosis is known to begin in early childhood, CVDs become a major threat for children's health.

Overweight and obese subjects more often develop dyslipidemia, insulin resistance leading to diabetes mellitus, and atherosclerosis. One of the causes of this association is thought to be dysfunctional adipose tissue, which leads to secretion of hormones, so called adipokines, and pro-inflammatory cytokines. In adults, adipocytokines are associated with hypertension, insulin resistance and thereby increased cardiovascular risk. However, in children it remains unclear whether these adipocytokines are associated with fat distribution. Moreover, the exact impact of adipocytokines on the cardiovascular system in childhood remains uncertain.

Besides the role of dysfunctional adipose tissue on early atherosclerotic changes, other determinants of early atherosclerosis are of interest. In the ongoing WHISTLER study and in the follow-up at the age of 5 year, the WHISTLER/Cardio study, relationships between both smoking and overweight and early functional and structural changes of the carotid arterial wall were already detected at the age of 5 year. However, the effect of changes in fat distribution on the vascular properties remains unknown. Moreover, the persistence of changes of the arterial wall to later childhood is unknown.

Study objective

This research theme consists of two related studies with the primary aim to investigate determinants of the pathogenesis of atherosclerosis in early childhood. The first part is performed to determine the association of adipocytokines with fat distribution and the arterial wall in children.

Although adipocytokines are produced by adipose tissue, it is not known whether weight itself is associated to the adipokine profile, or if the secretion of adipocytokines is more dependent on the distribution of fat, for example the waist circumference. Furthermore, dysfunctional adipose tissue, and therefore a changed adipokine profile, might be present in non-obese children. One of the research questions in this first study will therefore be *Are adipocytokines related to anthropometric parameters in childhood?* The second research question is conducted to learn about the effect of different adipocytokines and the adipocytokine profile on the arterial wall, since arterial wall properties like IMT and vascular stiffness are known to change in the early stages of atherosclerosis. This will be studied by the following research question: *Are adipocytokines related to properties of the arterial walls, namely the carotid IMT and vascular stiffness, in childhood?*

The second part of this study is performed to investigate the effect of growth and relative weight changes on the vascular system in childhood. It is unknown whether changes in the vascular system present at the age of 5 year persist over time. Moreover, the effects of growth and changes in weight, blood

pressure and other cardiovascular risk factors on the persistence of vascular changes from the age of 5 years to the age of 7-9 years are unknown. Research questions belonging to this objective are: Do vascular changes in IMT and stiffness persist over time in childhood? To what extent is the vascular system influenced by the process of growth in childhood?

Study design

The WHISTLER study is a cohort study. This study is a follow-up measurement of children who participated in WHISTLER, an ongoing birth cohort study, and who already were followed at the age of 5 years (WHISTLER/Cardio).

Due to a different nature of the different research questions, this study contains a cross-sectional and a longitudinal component. The relation between adipocytokines and both anthropometrics and vascular properties will be studied cross-sectionally, at the age of approximately eight years. In the cross-sectional part of this study, the relation between the adipocytokine profile and the vascular system, the assessment of the determinant and outcome will not per se be performed on the same day, since the adipocytokine profile has to be assessed in the morning, after an overnight fasting period. However, we do not consider both outcome measurements as highly changeable variables and therefore it is very unlikely that this small period between the two visits will have consequences for the validity of this study.

By (re)measurement of the carotid IMT and distension at the age of 8 years, longitudinal data on ultrasonographic measures of the carotid artery will be obtained. In this longitudinal component, the persistence of vascular changes over time and the effect of growth and differences in fat distribution over time on the vascular system can be studied.

Study burden and risks

Since the pathogenesis of CVDs is known to start early in life and symptoms of cardiovascular disease become present later in life, early factors associated with the pathogenesis of CVDs have to be studied in children and is therefore group-related.

Subjects will have no benefit from participating to this study. The risks associated with participating to this study are very small and the possible complications non-severe. The only procedure in this study which implies a health risk, although it is a very small risk, is the venous puncture. There are no risks associated with the other measurements in this study.

The risks associated with the venous puncture include the sensation of pain for a short period during and after the venous puncture and the risk on a vasovagal collapse. Moreover, there is a risk on the development of a haematoma after the venous puncture. These risks have a short duration and are non-severe. The study related burden for the subjects will be minimized by using local anaesthetics before the venous puncture will be conducted and by using a small needle. Moreover, the venous puncture will be only performed once. If after one

venous puncture, the blood sample is not collected, only if the subject and the parents agree a second venous puncture will be performed.

Contacts

Public

Universitair Medisch Centrum Utrecht

Lundlaan 6
Utrecht 3508 AB
NL

Scientific

Universitair Medisch Centrum Utrecht

Lundlaan 6
Utrecht 3508 AB
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Inclusion criteria

children who reached the age of 8 years and who already participated to the WHISTLER and WHISTLER/Cardio study, and who's parents are willing to give informed consent to participate to this study.

Exclusion criteria

There are no exclusion criteria. In case of current or recent (last week) infections, the second visit to obtain the blood sample will be rescheduled. (this is not applicable after may 2012, as the venipuncture has stopped).

Study design

Design

Study type: Observational invasive

Masking: Open (masking not used)

Control: Uncontrolled

Primary purpose: Basic science

Recruitment

NL

Recruitment status: Recruitment stopped

Start date (anticipated): 27-10-2010

Enrollment: 1000

Type: Actual

Medical products/devices used

Registration: No

Ethics review

Approved WMO

Date: 25-08-2010

Application type: First submission

Review commission: METC NedMec

Approved WMO

Date: 30-03-2011

Application type: Amendment

Review commission: METC NedMec

Approved WMO

Date: 17-10-2011

Application type: Amendment

Review commission: METC NedMec

Approved WMO

Date: 07-06-2012

Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	03-10-2012
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	03-11-2014
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	07-01-2015
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	30-11-2016
Application type:	Amendment
Review commission:	METC NedMec

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	NL31013.041.10