Arterial properties of ulcerative colitis patients and unaffected controls; a cross-sectional outpatient clinic study.

Published: 20-02-2023
Last updated: 07-02-2025

This study is aimed at understanding status and future cardiovascular disease (CVD) risk in UC outpatients in remission undergoing different anti-inflammatory therapeutic regimens (tofacitinib (a JAK1 - inhibitor), anti-TNF (infliximab or adalimumab...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Gastrointestinal inflammatory conditions
Study type	Observational non invasive

Summary

ID

NL-OMON51814

Source
ToetsingOnline

Brief title
Arterial properties and ulcerative colitis

Condition

- Gastrointestinal inflammatory conditions
- Autoimmune disorders
- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
Ulcerative colitis; inflammatory bowel (colon) disease

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum

Source(s) of monetary or material Support: Pfizer Aspire Grant

Intervention

Keyword: Cardiovascular, Colitis, Ulcerative, Ultrasonography

Outcome measures

Primary outcome

Endothelial function as assessed by brachial artery flow mediated dilatation (FMD).

Statistical analyses.

Brachial Flow mediated dilatation (FMD, %) is the primary endpoint of the study. FMD*s of the UC group and controls will be compared. For normally distributed data an (un)paired Student*s t-test will be used. The Wilcoxon or Mann-Whitney U test will be used for non-normally distributed data. A p-value of < 0.05 is considered statistically significant.

Secondary outcome

Carotid intima media thickness (CIMT)

Blood pressure assessments: RR, Ankle-brachial index (ABI), pulse-pressure (PP) and the brachial-ankle pulse wave velocity (baPWV).

Routine outpatient clinical investigations.

Statistical analyses.

CIMT*s and BP*s/ABI*s between the UC group and controls group will be compared using Student*s unpaired t-test. Multiple comparisons of the vascular endpoints between the UC treatment groups and controls will be assessed using ANOVA. Bonferroni*s correction will be applied if appropriate.

Correlations among clinical index scores, biochemical parameters, ultrasonographic parameters will be analysed using a Pearson correlation coefficient or Spearman rho correlation coefficient when data is normally or not-normally distributed respectively.

To evaluate intra-observer variability of the vascular assessments the mean absolute differences between initial and repeat assessments and kappa-statistics will be used.

Study description

Background summary

Ulcerative colitis (UC) is an inflammatory bowel disease (IBD) characterized by a pattern of relapse and remission. UC and its treatment are associated with inflammation, dyslipidemia and increased cardiovascular disease (CVD) risk.

The status of cardiovascular health can be non-invasively assessed by structural and functional arterial biomarkers, even prior to the occurrence of symptomatic vascular disease. In this study we will therefore do arterial measurements in 90 CU patients and 30 unaffected control subjects. For that

purpose, carotid intima-media thickness (cIMT) using ultrasound, brachial flow mediated dilatation (FMD) to assess endothelial function (EF), and upper arm and ankle blood pressures to assess RR and the ankle-brachial index (ABI) will be assessed.

The results of these studies will create awareness and understanding of the consequences of inflammatory bowel disease in other organsystems outside the gastro-intestinal tract and support decisions on prevention of cardiovascular co-morbidity/mortality in UC patients on top of their IBD.

As safe and efficacious preventive treatments for cardiovascular diseases are available, UC patients may benefit directly by improving their cardiovascular health.

Study objective

This study is aimed at understanding status and future cardiovascular disease (CVD) risk in UC outpatients in remission undergoing different anti-inflammatory therapeutic regimens (tofacitinib (a JAK1 - inhibitor), anti-TNF (infliximab or adalimumab) or mesalamine). as commonly used in clinical UC practice.

Validated non-invasive biomarkers describing long and short term cardiovascular health will be assessed in UC patients and unaffected controls.

The study is of scientific interest and has direct clinical relevance when considering the need for efficacious measures in cardiovascular disease prevention in those with UC.

Study design

A total of 120 subjects will participate in this cross-sectional observational study.

Vascular assessments will be performed in 90 treated UC patients in addition to their routine outpatient clinic visit evaluations and treatments.

Clinically, patients are to be in remission of the disease. Three different anti-inflammatory treatment regimens - tofacitinib (a JAK1 - inhibitor), anti-TNF (infliximab or adalimumab) or mesalamine - in approximately equally sized UC groups of 30 are observed. In addition, 30 unaffected age and gender matched controls will be investigated.

Chronic inflammatory diseases impair arterial structure and function, therefore the following non-invasive and safe biomarkers will be assessed in patients and non-patient controls:.

1. The status of atherosclerosis and long term CVD risk is assessed by means of carotid artery ultrasound intima-media thickness (CIMT) measurements. Progression of early arterial wall thickness changes and atherosclerosis is reflected by CIMT increase. Treatment can inhibit this process and decrease cIMT change. All vascular assessments are completely non-invasive and safe.

2. An automated oscillometric blood pressure measuring device with upper arm and ankle cuffs will be used to assess blood pressures according to RR, the ankle-brachial index (ABI = Systolic ankle blood pressure/ Systolic RR) of subjects, the pulse-pressure (PP) and the brachial ankle pulse wave velocity (baPWV).

3. Functional arterial properties and short term cardiovascular risk will be assessed by means of arterial brachial flow mediated dilatation (FMD), a validated biomarker for endothelial function.

All vascular assessments are completely non-invasive and safe.

Power calculations based on previous endothelial function study observer and clinical data, and under the assumption of an unpaired Student*s t-test with α=0,05, a ß=0.9 (power of 90%) were done. These calculations indicate subgroups of 30 subjects are of sufficient size to detect at least a 1% difference in brachial flow mediated dilatation (FMD, the primary endpoint of the study). Between UC patients and the unaffected (90 versus 30 respectively) an even smaller difference in FMD may be observed.

The overall population size and those of the subpopulations are also of sufficient size to draw relevant conclusions from the secondary endpoints (CIMT and ABI measurements).

Study burden and risks

Vascular assessments will be performed in UC subjects who visit the outpatient clinic routinely anyway.

Routine Outpatient Assessments

The routine UC outpatient clinic check takes 15 minutes on average and entails assessment of:

1. General well being and work/functionality
2. The simple clinical colitis activity Index (SCCAI), e.g.:
- Defecation frequency/day
- Defecation frequency night
- Urge
- Blood in stool
- General well being

- Other symptoms (Uevitis, pyoderma gangrenosum, erythema nodusum, arthritis)

Blood values:
- CRP
- Hb
- Hematocrit
- Platelets
- MCV
- Leukocytes
- Creatinine
- eGFR
- Alat
- Asat
- Alk. Phosphatase
- Iron saturation

Fecal examination: Calprotectin

Blood samples are usually drawn a week prior to outpatient appointments. In patients who use TNF-a inhibitors (infliximab) the values are assessed before they start infliximab treatment

Physical examination or ultrasound scans are done only if clinically indicated (i.e., not at the routine consultations). An ultrasound scan of the bowel is indicated only if no colonoscopy has been done for a longer period of time.

Vascular Assessments (this study)

Potential subjects will have received study and informed consent information and a request to participate in the vascular assessments at least 2 weeks prior to the outpatient clinic visit.

In summary, the vascular assessments entail the following:

Assessments are completely non-invasive, well tolerated and safe.
The overall time investment is approximately 45 minutes.

Participants need to be in the fasting state (required for the endothelial function measurements).
An informed consent and a cardiovascular questionnaire are filled out with the appointed researcher.

All assessments are done in a quiet and temperature-controlled space.
The participant is examined in the reclined position, comfortably at rest on an examination couch.
The blood pressure cuffs will be attached prior to the examinations.

Order of assessments is as follows: carotid ultrasound scans, blood pressure and ABI assessment, endothelial function testing.

Benefits and group relatedness may described as follows:

Inflammatory diseases have major consequences on the cardiovascular system and CVD risk.

The vascular assessments of our studies describe present structural and functional arterial status and allow detection of CVD risk prior to the clinical emergence of coronary and vascular diseases. As efficacious and safe preventive treatments for cardiovascular diseases are available, UC patients may benefit directly by improving their cardiovascular health (e.g. preventing cardiovascular co-morbidity/mortality on top of their inflammatory bowel disease).

Outcomes of the vascular studies are therefore of direct scientific interest and of clinical relevance to patients as such.

Contacts

Public
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105 AZ
NL
Scientific
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105 AZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Ulcerative colitis, clinically in remission
>18 years of age

Exclusion criteria

Age <18 years
Active UC

Study design

Design

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

Primary purpose: Prevention

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	29-01-2024
Enrollment:	120
Type:	Actual

Ethics review

Approved WMO

Date:	20-02-2023
Application type:	First submission
Review commission:	METC Amsterdam UMC

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	NL80597.018.22