TRANSITIONS IN GOUT RESEARCH STUDY

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The aim of this study is to figure out which factors can predict the development of gout, in addition to hyperuricemia.

Ethical review	Approved WMO
Status	Will not start
Health condition type	Joint disorders
Study type	Observational invasive

Summary

ID

NL-OMON51151

Source
ToetsingOnline

Brief title
TIGER study

Condition

- Joint disorders

Synonym
Gout

Research involving
Human

Sponsors and support

Primary sponsor: Sint Maartenskliniek
Source(s) of monetary or material Support: unrestricted grants

Intervention

Keyword: crystal depositions, Gout, hyperuricemia, uric acid

Outcome measures

Primary outcome

ROLE OF MSU CRYSTAL DEPOSITION IN TRANSITION FROM HYPERURICEMIA TO GOUT

- To determine whether ultrasound imaging evidence of MSU crystal deposition predicts development of symptomatic gout (according to the 2015 ACR/EULAR criteria [3]) over 5 years, in people who already have a high risk of gout due to elevated serum urate concentrations (>=8 mg/dL).

- To describe the time-course for the development of gout over 5 years in people at risk of gout with and without MSU deposition on ultrasound.

Secondary outcome

TRANSITION FROM HYPERURICEMIA TO DE NOVO MSU CRYSTAL DEPOSITION

- To determine factors that are associated with a higher risk of developing de novo MSU crystal deposition on ultrasound over 5 years, in people who have serum urate >=8 mg/dL.

TRANSITION TO SYMPTOMATIC GOUT AND ASSOCIATED COMORBIDITIES

- To identify risk factors (including clinical, genetic and biological) for the development of gout in people who are at high risk of gout with serum urate >=8 mg/dL.

- To determine whether ultrasound evidence of MSU crystal deposition predicts development of medical comorbidities including cardiovascular disease and

kidney disease

Baseline variables collected:

- demographic information as well as a physical exam including assessment of body mass index, blood pressure and the presence of tenderness and swelling using the 66/68 Tender Swollen Joint Count [5] and assessment for the absence of subcutaneous tophi.
- Assessment of clinical risk factors, including exercise habits, consumption of sugar-sweetened beverages, fruit and alcohol, smoking history and family history of gout. I
- In addition, medications and comorbidities (including those required for the gout-modified-Rheumatic Diseases Comorbidity Index (mRDCI) [6, 7]) will also be collected.
- Health related quality of life (using the EuroQoL questionnaire [8]), hyperuricemia-related illness perception (using the Brief Hyperuricemia Perceptions Questionnaire (BIPQ) [9], beliefs about medicines (using the Beliefs about Medicines Questionnaire) [10]
- body pain and foot pain over the past week using a 100 mm pain visual analogue scales (VAS), activity limitation using the Health Assessment Questionnaire - II (HAQ-II) [11] and foot-related pain and disability using the Manchester Foot Pain and Disability Index (MFPDI) [12] will be assessed.
- Laboratory tests: creatinine and C-reactive protein (CRP), serum urate, IL-1β.

- For those participants who agree to genetic testing, candidate gene analysis

for the progression from asymptomatic hyperuricemia to gout will include ABCG2,

TLR4, IL1B and PPARGC1B.

Study description

Background summary

From cross-sectional studies it is known that 17% to 86% of people with apparently asymptomatic hyperuricemia have ultrasound imaging evidence of monosodium urate (MSU) crystal deposition. These observations suggests that this deposition constitutes the first stage of the clinical syndrome of gout, which has led to a revised model of disease progression and staging. This models proposes a linear progression from asymptomatic hyperuricaemia without deposition, to asymptomatic hyperuricaemia with deposition, to symptomatic disease. However, no longitudinal studies have been undertaken to establish whether such imaging findings are necessary preconditions for the development of gout nor what pathological mechanisms are responsible for the transition from asymptomatic crystal deposition to gout, nor what mechanisms are involved in the transition from hyperuricemia to de novo crystal deposition. Only a prospective cohort study of persons at risk with careful, regular evaluation can answer such questions.

Study objective

The aim of this study is to figure out which factors can predict the development of gout, in addition to hyperuricemia.

Study design

This is a 5 year prospective cohort study of people with hyperuricemia but no clinical symptoms of gout

Study burden and risks

Nature and extent of the burden associated with participation
Participants will be asked to attend a study visit at the Sint Maartenskliniek Nijmegen. The study visit will take up to 2 hours. A second longer visit will take place 5 years later, or sooner, if a participant develops gout. At each study visit we will ask to complete some questions about health, assess the height and weight, examine the joints for tenderness and swelling, assess walking, and ask participants to provide a urine sample and blood samples to

test the urate levels, creatinine (kidney function) and CRP (marker of inflammation).
We will also ask participants to provide blood tests to be stored. It is up to the participants whether they also agree to the blood samples being used to look at DNA, the genetic code material found inside the blood. It has been known for a long time that high urate levels and the development of gout are partly genetic because of certain genes that we inherit from our parents. We want to find out what these genes are, and how they cause the disease. If they wish to participate in the genetic study we will ask to also complete a separate Genetics Testing Consent Form.
At the study visits we will also perform ultrasound scans of the feet and knees to check for any urate crystals. At the first visit we will also take an x-ray of the feet to check the health of the bones and joints in the feet.
Over the 5 years between the two study visits we will regularly contact participants by phone, text, mail or email to check with whether participants have developed any new joint pain or swelling. If so, we may schedule them in for a second longer study visit earlier, to assess whether or not this pain or swelling is due to gout.
As part of this study, we will ask participants whether they agree to providing us with the contact details of a family member and/or close friend(s) that we can contact if they cannot be reached.
With their consent we also may contact the family doctor.

Risks and benefits associated with participation
This study will involve the sampling of blood. A blood sample taken may hurt a little, and some people get a small bruise where the needle goes in. Occasionally the needle hole can become infected, but this is very rare. Most people have no problems.
This study involves radiation exposure from a foot x-ray which will take place at the first of the two longer study visits. As part of everyday living, everyone is exposed to a small amount of background radiation that comes from soil, rocks, outer space and within the body itself. The radiation dose participants will receive in this study is about the amount that people receive over 1 day from background radiation. This radiation exposure is necessary for us to obtain information about the health of the bones and joints. The risk from this dose is small.
The ultrasound scans involve no radiation exposure. Ultrasound scanning is safe and painless. Sound waves are used to obtain images of the joints. This technology is the same as that used to scan a pregnant woman and has no known side effects.

Contacts

Public

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• Current serum urate level of >=8 mg/dl
• No current or previous clinical symptoms of gout (including flares or clinically apparent tophi)
• Aged between 18 and 80 years
• Able to provide informed consent, according to requirements of local IRB/ethics committee

Exclusion criteria

• eGFR < 30 mL/min/1.73 m² or on renal replacement therapy
• Serious illness with poor prognosis less than 5 years
• Auto-immune inflammatory arthritis
• Plans to shift out of area in the next 5 years
• Previous synovial fluid analysis showing MSU crystals
• The presence of subcutaneous tophi

• Taking urate lowering therapy (e.g. allopurinol, probenecid, benzbromarone, febuxostat), canakinumab, or colchicine.
• Elevated serum urate documented only at the time of an acute medical illness

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	25
Type:	Anticipated

Ethics review

Approved WMO

Date:	26-07-2021
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL75260.091.20