FOLLOW-UP RESEARCH IN FAMILIAL SYMPTOMATIC OA (FOA) AT MULTIPLE JOINT LOCATIONS

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Musculoskeletal and connective tissue disorders congenital
Study type	Observational invasive

Summary

ID

NL-OMON39803

Source
ToetsingOnline

Brief title
FOA follow up research

Condition

- Musculoskeletal and connective tissue disorders congenital
- Joint disorders

Synonym
degenerative joint disease, Osteoarthritis, wear and tear of the joint

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,Centre of Medical

System Biology and Netherlands Consortium for Healthy Aging both in the framework of the Netherlands Genomics Initiative (NGI).

Intervention

Keyword: Family, Function, Mutation, Osteoarthritis

Outcome measures

Primary outcome

- Clinical OA assessment of familiemembers and thereby obtain the OA phenotype

in the family members and an estimation of the penetrance of the mutation.

- Functional characterization of the detected mutation, providing insight into

how the mutation gives rise to OA in the family

Secondary outcome

In the study we may be able to determine who in the family is carrier of the OA

causing mutation also in young unaffected individuals.

Molecular insight into oa disease mechanism may in the end lead to new disease

modifying druggable targets.

Study description

Background summary

The osteoarthritis (OA) research of Molecular Epidemiology aims to identify determinants conferring OA susceptibility by applying molecular epidemiological approaches to familial OA patients in the GARP study and in early onset OA families (FOA). Up to now little is known about the early molecular processes commencing OA onset, however, such insights are considered crucial for the development of effective disease modifying treatments. Genome wide genetic association studies have identified common DNA variants that associate to OA susceptibility with small effect sizes on disease risk and little biologically relevant information. We then initiated exome sequencing in order to discover rare deleterious mutations with larger effect sizes and more biological meaning. This was performed in a selection of 50 patients with familial OA.

These OA patients originated from the GARP study and from early onset OA families (FOA) collected 20 years ago when the OA research of the Slagboom group started at TNO-Prevention and Health in collaboration with the Rheumatology department of the LUMC. Identification of such mutations may provide important insights into the underlying mechanisms and pathways driving the onset of OA in these families and possibly in the general OA patient population. Once the mutations are identified we perform functional follow up research which provides insights in causal OA pathways in these families, enabling us to make cellular models as a tool to discover agents to prevent and/or cure OA.

Study objective

In one FOA family we have detected a deleterious mutation in a compelling gene which co-segregates with the FOA phenotype in the family. This mutation is, therefore, is likely to be causal to the early onset OA. The objective of the study is:

a) To perform a clinical evaluation (x-rays and physical examination) of family members to assess the penetrance of the mutation in this family.

b)To collect biological speciment (blood urine and a skin biopsy and possibly cartilage) to investigate the mechanism by which the mutation causes OA. The cartilage will be collected in case family members need to undergo a joint replacement surgery as result of their OA

Study design

We will sent the FOA family a newsletter which informs them about; the recent advances in our research, what type of information has now become available in their family and an invitation to participate in follow up research. Family members can express their interest in any of these topics by telephone, regular mail or e-mail. In earlier correspondence, family members indicated their appreciation to be informed on the research progress and were asked permission to be approached again. Only persons who gave permission will be informed and approached.
When FOA family members have responded positively to the newsletter, we will approach the person by telephone to give information about the new results and if applicable refer the patient and/or family members to the clinical geneticist (Prof. Dr. M. Breuning, who has been consulted and informed on the situation). When the patient is willing to participate to the additional follow up research a questionnaire, considering current symptoms, signs and risk factors of OA will be send by post. In this mail correspondence the participants are asked to give informed consent also for a hospital visit. During the hospital visit familymembers will undergo a clinical evaluation and

blood, urine and a skin biopsy will be taken.

Study burden and risks

Participants will be subjected to rontgen radiation (0.9 mSV, category IIa) this means that the research needs to be at least aiming to acquire clinical applied knowledge.

Participants will be asked to give a skin biopsy which may result in a small skar.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Early onset familial symptomatic OA at multiple joint locations

Exclusion criteria

Not member of the family, no consent

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	24-03-2014
Enrollment:	0
Type:	Actual

Ethics review

Approved WMO Date:	05-02-2013
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	03-03-2015

Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	07-10-2015
Application type:	Amendment
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	NL42518.058.12