Familial Paget*s disease of bone: Long-term follow up of index families in the Netherlands

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1. To investigate the presence of PDB in asymptomatic relatives of patients with familial PDB who were investigated for a SQSTM1 mutation 10-15 years previously but had no evidence of PDB .2. To compare the risk of developing the disease between...

Ethical review	Approved WMO
Status	Pending
Health condition type	Other condition
Study type	Observational non invasive

Summary

ID

NL-OMON43197

Source
ToetsingOnline

Brief title
net

Condition

- Other condition

Synonym
osteitis deformans, Paget

Health condition

familiaire botaandoening

Research involving
Human

Sponsors and support

Primary sponsor: Endocrinologie
Source(s) of monetary or material Support: via de Bontiusstichting

Intervention

Keyword: Bone, genetic, long-term, Paget

Outcome measures

Primary outcome

Active PDB is defined as elevated biochemical markers of bone turnover in the form of serum alkaline phosphatase (ALP) activity (in the presence of normal serum γGT), and/or elevated serum P1NP values, in addition to localised increased radioactive isotope uptake on Tc-99m skeletal scintigraphy.

Therefore in all subjects with ALP and or P1NP levels above the upper limit of normal, a skeletal scintigram will be performed and if abnormal X-rays will be performed.

In subjects harbouring the SQSTM1 gene mutations or skeletal complaints or a history of bisphosphonate use without increased bone formation markers radiological assessment will be performed as well to exclude active PDB.

Secondary outcome

Relationship between the presence of a SQSTM1 mutation and the development of clinical, biochemical and scintigraphic features of PDB

In non-carieres new mutation analyses will be performed.

Study description

Background summary

Paget*s disease of bone is a focal disorder of bone remodeling that progresses slowly, leads to changes in the shape and size of affected bones and is associated with to articular and vascular complications. The precise etiology of the disease is unknown and the current view is that the disease is caused by interactions between environmental and genetic factors, the nature of which remains to be determined. In the only epidemiologic study conducted in the Netherlands, which was performed by our group between 2000 and 2003, we demonstrated that first-degree relatives of patients with Paget*s disease of bone have a 10-fold higher risk of being affected by the disease, a risk increase similar to that found in epidemiologic studies conducted in the UK and the USA. In our study, we identified mutations in the SQSTM1 gene in 38.9% of 266 members of 20 families with Paget*s disease(LUMC protocol number P202/98 and P00-088-3). However, the disease was documented in a minority of these subjects, particularly those who were older. It is well established that Paget*s disease of bone seldom presents before the age of 45 years and that the prevalence of the disease increases with age. We, therefore, hypothesize that the identified younger subjects harboring the mutation will be more likely to develop the disease in the course of time than subjects without the mutation. In the present study we propose to test this hypothesis by re-evaluating all subjects for the appearance of PDB 15 years after the initial assessment. Furthermore since 2003 additional mutations have been identified and these mutations will be checked in the subjects in whom no mutation was identified in 2003.

Study objective

1. To investigate the presence of PDB in asymptomatic relatives of patients with familial PDB who were investigated for a SQSTM1 mutation 10-15 years previously but had no evidence of PDB .
2. To compare the risk of developing the disease between members of families with PDB who are carriers versus non-carriers of a SQSTM1 mutation.
3. To asses the genetics of the non cariers with the current mutations known in PDB.

Study design

cohort study

Study burden and risks

This is a follow-up study of previously investigated subjects. The study requires a single visit to the LUMC for medical history taking, clinical examination, filling in of disease-specific questionnaires, laboratory investigations and skeletal scintigraphy and.

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

All members of families with PDB who were previously identified and evaluated, including subjects already diagnosed with PDB, and who are willing to participate in this long-term follow-up study.

Exclusion criteria

not willing to participate

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-05-2016
Enrollment:	100
Type:	Anticipated

Ethics review

Approved WMO

Date:	02-06-2016
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

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	NL56923.058.16