Skeletal phenotyping of patients with Osteogenesis Imperfecta

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

Summary

ID

NL-OMON51155

Source
ToetsingOnline

Brief title
SkeDOI

Condition

- Musculoskeletal and connective tissue disorders congenital

Synonym
Brittle Bone Disease, Osteogenesis Imperfecta

Research involving
Human

Sponsors and support

Primary sponsor: Isala Klinieken
Source(s) of monetary or material Support: Wetenschapsfonds VieCuri Medisch Centrum

Intervention

Keyword: Bone deformities, HrpQCT, Osteogenesis Imperfecta

Outcome measures

Primary outcome

The main outcome parameter is bone strength at the standard scan region, obtained with HR-pQCT-based micro-finite element (µFE-) analysis, in terms of bone stiffness and failure load. Additionally, volumetric bone and tissue mineral density and cortical and trabecular microarchitecture will be assessed with HR-pQCT. More specifically, density parameters include total, cortical, and trabecular volumetric bone and tissue mineral density. Microarchitecture parameters include trabecular bone volume fraction, number, thickness, and separation, and cortical thickness and porosity.

Secondary outcome

-

Study description

Background summary

Osteogenesis imperfecta (OI) is a rare hereditary connective tissue disorder characterized by increased bone fragility and skeletal deformity. Various causative genes are known, resulting in a diversity of phenotypic manifestations and severity of OI. Previous studies on skeletal phenotypes among different types of OI were mainly limited to measurements of areal bone mineral density (BMD), whereas bone quality is also determined by bone microarchitecture. High-resolution peripheral quantitative computed tomography (HR-pQCT) allows detailed assessment of microarchitecture and strength of the distal radius and tibia. Currently, the specific microarchitectural properties of the different OI phenotypes are not well defined and due to the short stature of patients with some OI-types, it is not known whether the standard

protocol for HR-pQCT imaging is sufficient to assess microarchitecture in OI.

Study objective

- to compare the skeletal phenotypes of each OI-type obtained at the standard scan region (i.e. using the fixed offset distance) with a recently published sex- and site-specific normative dataset of a general adult population, obtained with the same generation HR-pQCT scanner and at the same region, and to determine whether deviations from this dataset differ between OI-types
- to compare skeletal phenotypes obtained at the standard scan region with the genotypes of teh OI-patients with known genotype categorised as a defect COL1A1 or COL1A2
- to explore whether there is a difference in skeletal phenotypes for each OI-type between the standard scan region and a lenght-dependent scan region.

Study design

In this cross-sectional study, patients with known OI, diagnosed and treated at the Center of Expertise of the Isala Clinic in Zwolle, will visit VieCuri Medical Center once. During this visit, four HR-pQCT scans will be performed; two of the distal radius and two of the distal tibia. The first set of scans (distal radius and distal tibia) will be acquired using the standard HR-pQCT imaging protocol with a fixed offset distance. The second set of scans (distal radius and distal tibia) will be acquired with a HR-pQCT imaging with a relative offset distance depending on the length of the lower arm and leg. Depending on the mobility of a patient, it is possible that a patient is not able to position properly and comfortably before the gantry of the scanner, in which case the scan will not be acquired. All scans will be analysed to quantify volumetric bone mineral density, cortical and trabecular microarchitecture, and bone strength.
The bone strength obtained at the standard scan region parameters will be compared between the different OI-types. For each OI-type separately, bone strength will also be compared with the recently published normative dataset of a general adult population, and it will be compared whether deviations from this dataset differ between the OI-types. Additionally, bone strength will be compared among genotypes of the OI-patients with a known genotype already available as part or regular care at the Center of Expertise of the Isala Clinic in Zwolle. Finally, the bone parameters will be compared between the standard scan region and the length-dependent scan region, for each OI-type separately.

Study burden and risks

Patients do not have any direct benefits from participation in this study, but participation may provide new insights into the disease that could lead to more optimal treatment strategies for themselves and other patients with OI. The

risk of study participation is limited to the relatively low radiation exposure. If a patient*s mobility allows proper and comfortable positioning for scan acquisition, four HR-pQCT scans of one stack each will be taken: two scans of the distal radius and two of the distal tibia. Each HR-pQCT scan has an effective radiation dose of 5 µSv, which brings the total radiation dose of study participation to 20 µSv (i.e. two radius and two tibia scans). The scans will be graded according to a clinically used grading system using a five-grade scale. In case motion artefacts necessitate a repeated HR-pQCT scan, a patient is exposed to a maximum radiation dose of 40 µSv when all four scans have to be repeated. This amounts to approximately 0.69% (four scans acquired; no repeated scans) to 1.38% (four scans acquired and all repeated once) of the average annual effective background radiation dose per capita in the Netherlands (2.9 mSv). The time to perform the HR-pQCT scans is approximately 2 minutes per scan, and total visit duration will be approximately 60 minutes.

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

- Patients with Osteogenesis Imperfecta
- Adult (>18 years)
- Recent DEXA-scan (< 3 years)

Exclusion criteria

- Patients whose mobility does not allow proper and comfortable positioning for scan acquisition due to extreme bowing of the extremities. Pre-screening on the basis of already performed radiographs.
- Patients who have had a fracture at recent medical history (<2 years) at both distal radii and tibiae.
- Patients who have had a malignancy at recent medical history (<2 years), who have been treated with glucocorticoids less than 3 months ago, who have severe kidney disease (eGFR <30 ml/min) or who suffer from other metabolic diseases affecting bone.
- Female patients who are pregnant.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	25-06-2021
Enrollment:	120
Type:	Actual

Ethics review

Approved WMO
Date: 02-03-2021

Application type: First submission

Review commission: METC Isala Klinieken (Zwolle)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 23070
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL76107.075.21
Other	NL9134
OMON	NL-OMON23070

Study results

Date completed: 08-07-2022

Results posted: 27-06-2023

First publication
27-06-2023