Boneloss following immobilization in diabetes mellitus, an inventory using an ultrasound method (BINDEX).

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The purpose of the study is to investigate the effect of (repeated) cast immobilization on the bone strength of the lower leg in patients with diabetes mellitus. In this study, bone strength is examined by cortex thickness in millimeters and density…

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Diabetic complications
Study type	Observational non invasive

Summary

ID

NL-OMON44529

Source
ToetsingOnline

Brief title
Bone loss following immobilization in diabetic patients

Condition

- Diabetic complications
- Bone disorders (excl congenital and fractures)
- Peripheral neuropathies

Synonym
diabetes, Diabetes mellitus

Research involving
Human

Sponsors and support

Primary sponsor: Reinier de Graaf Groep

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Bone loss, Diabetes, Immobilization, Neuropathy

Outcome measures

Primary outcome

Primary outcome measures are Density Index (g / cm 2) and cortex thickness (mm) in both legs, difference in mean density index between paired legs, difference in mean cortex thickness between paired legs, difference in medians of density index between paired legs, Difference in medians of cortex thickness between paired legs.

Secondary outcome

To extract from patient records:

Secondary: Number of cast treatments, total duration of cast treatments, average HbA1c, number of years suffering from diabetes.

Other: Medication use, Type of Diabetes, EGFR, Degree of Neuropathy: Monofilament, Vibration. , Degree of vasculopathy: EAI, pulsations, toe pressure. Side of dominant leg.

Study description

Background summary

Diabetes mellitus leads to an increased risk of bone fractures for a not completely known reason, which is not reflected in bone density measurement. On

average, a patient with diabetes mellitus has a normal to increased bone density. Presumably, the cause of the increased fracture risk is multifactorial and is based on a greater chance of falling through vaso-lability and neuropathy and adverse effects of high blood sugar on the bone mineral properties of the bone mineral. It is known that diabetes mellitus gives a decrease in bone turnover and an accumulation of AGEs: Advances Glycation End products. This results in reduced bone strength. Also, diabetic neuropathy is thought to lead to a decrease in bone strength.

Bone loss by immobilization is a known clinical phenomenon presumably partly caused by a decreased load on the osteocytes . This cell type is an osteogenic cell derived from osteoblasts. In fact they are differentiated osteoblasts which are arranged in a network in the bone. Applied pressure on this network causes an osteocytic fluid flow, which causes less sclerostin to be produced. This is a bone producing-inhibiting peptide. This reduction of sclerostine results in more bone production. Conversely, bone breakdown occurs if there is no pressure. From previous studies in space, a decrease in BMD was found to be 1 to 2 percent per month. The tibia cortex thickness decreased by 4% in 4-6 months. [6-7] However, in a case report on a patient with diabetic neuropathy, a 20% decrease in bone density was found after 6 weeks immobilization using calcaneal ultrasound.

Diabetes mellitus results in neurogenic and vascular complications. Known complications are the diabetic footulcers and the charcot-foot. Both complications are, among other things, treated by total cast immobilization of the lower leg. This immobilization may last for many months and several periods of immobilization may be necessary. Based on current literature one would expect that this extensive immobilization would result in a decrease in bone strength. Considering the already increased fracture risk, this is a very undesirable effect. To our knowledge there are no studies on this phenomenon and the extent of this effect is still unknown.

Research regarding the effect of bone loss on bone strength has shown that the cortex contributes significantly to bone strength. A decreased cortex thickness is a predictor for decreased bone strength. Evaluation of the cortex can be done by ultrasound assessment (Speed **of Sound (SOS) and Broadband Attenuation (BUA)). The Reinier de Graaf Gasthuis has gained considerable experience with ultrasound of the lower leg using Bindex®. Bindex® is a Class I medical device with a CE mark. The system used has been developed in Finland and is well applicable in acute situations, either directly after a trauma or immediately prior to the application of plaster. This method measures the cortex thickness in millimeters and estimates the femoral neck density index in g / cm2 based on patient characteristics and the measured cortex thickness of the tibia.

References:

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Study objective

The purpose of the study is to investigate the effect of (repeated) cast immobilization on the bone strength of the lower leg in patients with diabetes mellitus. In this study, bone strength is examined by cortex thickness in millimeters and density index in grams per cm 2. The following questions will be answered:

1. What is the effect of cast immobilization of the lower leg on the difference in cortex thickness between both legs of diabetes mellitus patients, measured with Bindex?

2. What is the effect of cast immobilization of the lower leg on the difference in density index between both legs of diabetes mellitus patients, measured with Bindex?

3. What is the difference in effect of cast immobilization between patients with diabetes studied in a tertial care institute, HGC, compared to patients with diabetes at the Reinier de Graaf Hospital?

4. What is an average difference in density index and cortex thickness between both legs, measured in healthy subjects with Bindex?

Secondarily, the impact of the following factors will be assessed by analysis:

- Number of cast treatments
- Duration of cast treatments
- Number of years known with diabetes mellitus
- Average HbA1c

Study design

It is an inventory study.

Study burden and risks

During their already planned visit to the plaster room for assessment by the special multidisciplinary 'feettteam', the plaster will first be removed. Then, patients are waiting for their physicians to come to them. At the time they are usually waiting, both lower legs will be measured by using ultrasound to measure the cortex thickness and the estimated bone density. This takes about 5 minutes, the measurment is not painful and patients do not have to change their position. It does not affect normal treatment. This happens every time they visit the plaster room again during the study period.

There are no changes in treatment due to participation in the research. There are no risks known for ultrasound.
Both the pressure on the patient and the risk are therefore very minimal.

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

For patients: Men and women aged > 18 years, suffering from diabetes with an indication for cast immobilization of the lower leg due to neuropathic or vascular complications.;For controls: Non-diabetic men and woman aged >18 years

Exclusion criteria

For patients: Chronic immobilization (wheelchair-dependent), not ADL-independent, metastasized cancer, not-Dutch speaking, use of bisphosphonates <1 year before inclusion. Cast immobilization of the contralateral leg < 6 months before inclusion.;For controls: Cast immobilization of a lower leg < 6 months before inclusion. Use of bisphosphonates <1 year before inclusion

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other

Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	18-09-2017
Enrollment:	150
Type:	Actual

Medical products/devices used

Generic name:	Bindex
Registration:	Yes - CE intended use

Ethics review

Approved WMO

Date:	05-09-2017
Application type:	First submission
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	NL62748.098.17