Orthop Muscular Syst 2016, 5:3(Suppl)
http://dx.doi.org/10.4172/2161-0533.C1.030

Low bone mineral density and fat-free mass in younger patients with a femoral neck fracture

Amer Al-Ani, Tommy Cederholm, Maria Saaf, Gustaf Neander, D Richard Blomfeldt, Wilhelmina Ekstrom and **Margareta Hedstrom**
Karolinska Institute, Sweden

Background: Reduced bone mineral density (BMD) together with muscle wasting and dysfunction, i.e. sarcopenia, emerge as risk factors for hip fracture. The aim of this study was to examine body composition, BMD and their relationship to trauma mechanisms in young and middle-aged patients with femoral neck fracture.

Materials & Methods: In this study 185 patients with femoral neck fracture aged 20-69 were included. BMD, body composition, including fat-free mass index (FFMI) were determined by dual-X-ray absorptiometry (DXA) and trauma mechanisms were registered.

Results: 90% of the whole study population had a femoral neck BMD below the mean age. In the young patients (<50 years) 27% had a Z-score of BMD ≤ -2 SD. More than half of the middle-aged patients (50-69 years) had osteopenia, i.e. T-score -1 to -2.5, and 35% had osteoporosis, i.e. T-score<-2.5, at the femoral neck. Patients with low-energy trauma, sport injury or high-energy trauma had a median standardized BMD of 0.702, 0.740 vs. 0.803 g/cm2 (P=0.03), and a median FFMI 15.9, 17.7 vs. 17.5 kg/m2 (P<0.001), respectively. FFMI<10th percentile of an age- and gender matched reference population was observed in one third.

Conclusions: A majority had low BMD at the femoral neck and one third had reduced FFMI (i.e. sarcopenia). Patients with fracture following low-energy trauma had significantly lower femoral neck BMD and FFMI than patients with other trauma mechanisms. DXA examination of both BMD and body composition could be of value especially in those with low energy trauma.

amer.al-ani@ptj.se

The skeletal phenotype in neurofibromatosis type 1-structural defects, molecular mechanisms and therapeutic approaches

Jirko Kühnisch
[1]Charité - University Medicine Berlin, Germany
[2]Experimental and Clinical Research Center, Germany
[3]Max-Delbrück-Centrum for Molecular Medicine, Germany

Patients with Neurofibromatosis Type 1 (NF1) develop subcutaneous benign tumors and dysfunction of multiple organs. About 30% of NF1 patients are affected by skeletal signs such as osteopenia, kyphoscoliosis, tibia bowing, or pseudarthrosis of the tibia. NF1 is caused by autosomal dominant mutation of the NF1 gene encoding the protein neurofibromin a regulator of the MAPK/ERK pathway. During the last decade we and others elucidated for the NF1 associated skeletal phenotype the molecular mechanisms, structural defects and explored therapeutic approaches by using tissue specific knockout mice and patient samples. In Nf1-Prx1 and Nf1-Col1 mice we demonstrated that loss of neurofibromin leads to multiscale defects in cortical bone i) increased marco-porosity, ii) increased micro-porosity (osteocyte lacunae), iii) diminished mineralization, and iv) reduced organic matrix maturation. This overall weakens the mechanical strength of bone tissue in long bones significantly. In NF1 patients this may result in fractures and pseudarthrosis. Inhibition of the MAPK/ERK pathway with Lovastatin, Trametinib, PD0325901 and Selumetinib normalized bone healing in neurofibromin knockout mouse models. Downregulation of the MAPK/ERK pathway restored normal osteoblast differentiation/function and sufficiently prevented accumulation of fibroblasts within the bone fracture site. In a recent breakthrough study, Asfotase-α replacing alkaline phosphatase (ALP) function specifically in bone tissue, was used to restore normal bone mass in Nf1-Osx1 knock-out mice. In summary, neurofibromin controls development of the skeletal system by regulating the MAPK/ERK pathway in chondrocytes, pre-osteoblasts, osteoblasts, and osteocytes. Therapeutic approaches normalizing MAPK/ERK and ALP activity promise future therapeutic inventions for NF1 patients.

jirko.kuehnisch@gmx.de