

# **Bone and fat tissue in children and adolescents: studies with focus on osteocalcin**

Akademisk avhandling

som för avläggande av Medicine doktorsexamen vid Sahlgrenska akademien, Göteborgs universitet kommer att offentligen försvaras i föreläsningssal Tallen, Drottning Silvias barn- och ungdomssjukhus, fredagen den 7:e oktober, klockan 13:00

av

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Leg. läkare

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**Avhandlingen baseras på följande delarbeten**

- I. Tubić B, Magnusson P, Swolin-Eide D, Mårild S; IDEFICS Consortium. Relation between bone mineral density, biological markers and anthropometric measures in 4-year-old children: a pilot study within the IDEFICS study. *International Journal of Obesity (London)* 2011; 35(Suppl 1): S119-124.
- II. Tubić B, Magnusson P, Mårild S, Leu M, Schwetz V, Sioen I, Herrmann D, Obermayer-Pietsch B, Lissner L, Swolin-Eide D; IDEFICS consortium. Different osteocalcin forms, markers of metabolic syndrome and anthropometric measures in children within the IDEFICS cohort. *Bone* 2016; 84: 230-236.
- III. Tubić B, Pettersson C, Svedlund A, Bertéus Forslund H, Magnusson P, Swolin-Eide D. Increased bone mineral content during rapid weight gain therapy in anorexia nervosa. E-published. *Hormone and Metabolic Research*, DOI: 10.1055/s-0042-115304.
- IV. Tubić B, Zeijlon R, Wennergren G, Obermayer-Pietsch B, Mårild S, Dahlgren J, Magnusson P, Swolin-Eide D. Whole body vibration intervention: a randomized, prospective, controlled study in children with obesity. Manuscript submitted.

**SAHLGRENKA AKADEMIN**



# Bone and fat tissue in children and adolescents: studies with focus on osteocalcin

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## Abstract

The general **aim** was to investigate the possible interplay between bone and fat tissue through clinical studies of children and adolescents. Osteocalcin (OC), a bone formation marker, has been proposed to act as a link between bone and energy metabolism in mice, but human data are inconclusive. The specific aims of this thesis were: (i) to clarify the role of OC in relation to weight, with focus on undercarboxylated OC (ucOC) and carboxylated OC (cOC); (ii) to gain insight on how obesity and underweight affect bone and fat tissue in children and adolescents and; (iii) to study the effect of whole body vibration (WBV) on parameters of metabolic syndrome, bone metabolism and body composition in children with obesity. **Methodology:** Children and adolescents aged 2-24 years were included in the four studies. Study I and II were cross-sectional (case-control), and study III and IV were interventional with a 12-week follow-up, of which study IV was a randomized case-control study. Biochemical parameters were examined in all four studies. Bone mass and body composition were assessed by dual-energy X-ray absorptiometry (DXA), peripheral quantitative computed tomography, heel DXA and laser. Methods of intervention were high-energy diet in patients with anorexia nervosa (AN) and WBV in patients with obesity. **Results:** Total OC and ucOC did not differ between normal-weight and overweight subjects; however, overweight subjects had lower cOC levels, and the measured OC forms did not correlate with insulin and glucose. Overweight children had increased bone mineral content (BMC) and bone mineral density (BMD) in comparison with normal-weight children, and there was a positive correlation between BMC, BMD and body mass index standard deviation score. Adiponectin was inversely correlated with BMC and BMD, and was an independent determinant of BMC and BMD. Patients with AN gained in weight and levels of all three forms of OC and BMC increased. The WBV did not result in any anthropometric changes; however, a reduction of sclerostin implies that WBV therapy has direct effects on bone mechanotransduction.

**Conclusions:** This thesis could not confirm the hypothesis that OC has a positive effect on glucose and insulin homeostasis, although cOC was lower in obese subjects than in normal-weight subjects. The home-based WBV intervention study in young children with obesity did not result in any effect on weight, metabolic parameters or calcaneal bone mass.

**Keywords:** Osteocalcin, obesity, adiponectin, carboxylation, anorexia nervosa, paediatric, bone turnover markers, bone mass, whole body vibration, muscle