

# A prospective cohort study on bone formation and bone loss in ankylosing spondylitis

Akademisk avhandling

Som för avläggande av medicine doktorexamen vid Sahlgrenska akademien, Göteborgs universitet kommer att offentligen försvaras i föreläsningssalen våning 3, Guldhedsgatan 10A, Göteborg, fredagen den 25 oktober, klockan 9.00

av **Anna Deminger**

Fakultetsopponent:

**Professor Glenn Haugeberg**

Norges teknisk-naturvitenskapelige universitet, Norge

## Avhandlingen baseras på följande delarbeten

- I. Deminger A, Klingberg E, Lorentzon M, Geijer M, Göthlin J, Hedberg M, Rehnberg E, Carlsten H, Jacobsson LT, Forsblad-d'Elia H. Which measuring site in ankylosing spondylitis is best to detect bone loss and what predicts the decline: results from a 5-year prospective study. *Arthritis Research & Therapy*, (2017) 19:273
- II. Deminger A, Klingberg E, Geijer M, Göthlin J, Hedberg M, Rehnberg E, Carlsten H, Jacobsson LT, Forsblad-d'Elia H. A five-year prospective study of spinal radiographic progression and its predictors in men and women with ankylosing spondylitis. *Arthritis Research & Therapy*, (2018) 20:162
- III. Deminger A, Klingberg E, Lorentzon M, Hedberg M, Carlsten H, Jacobsson LT, Forsblad-d'Elia H. Factors associated with changes in volumetric bone mineral density and cortical area in men with ankylosing spondylitis. A five-year prospective study using HRpQCT. *Submitted*.
- IV. Deminger A, Klingberg E, Nurkkala M, Geijer M, Carlsten H, Jacobsson LT, Forsblad-d'Elia H. Elevated serum level of hepatocyte growth factor predicts development of new syndesmophytes in men with ankylosing spondylitis. Results from a five-year prospective study. *Manuscript*.

# A prospective cohort study on bone formation and bone loss in ankylosing spondylitis

Anna Deminger

Avdelningen för reumatologi och inflammationsforskning, Institutionen för medicin,  
Sahlgrenska akademien, Göteborgs universitet, Sverige, 2019.

## ABSTRACT

**Background and objectives:** Patients with ankylosing spondylitis (AS) have an increased risk of bone loss with development of osteoporosis and vertebral fractures (VFs) but also spinal new bone formation with growth of bony spurs (syndesmophytes) between the vertebrae. Measurements of spinal bone mineral density (BMD) by the routine method dual-energy x-ray absorptiometry (DXA) in anteroposterior (AP) projection can be difficult to interpret due to the spinal new bone formation. The general aims of this thesis were to study the development of bone loss and new bone formation over 5 years in patients with AS and to assess factors associated with the changes.

**Methods:** The studies included in this thesis are based on a cohort of patients with AS according to the modified New York criteria recruited from three rheumatology clinics in western Sweden. Patients completed the same protocol at baseline and at the 5-year follow-up with assessment of BMD with DXA at the hip (femoral neck, total hip), the spine (AP, lateral) and total radius and spinal radiographs for grading of AS related spinal alterations and VFs. A group of men were randomized in an age-adjusted algorithm to undergo high-resolution peripheral quantitative computed tomography (HRpQCT) at the ultra-distal radius and tibia for assessment of volumetric BMD (vBMD), cortical area and microarchitecture. Serum hepatocyte growth factor (s-HGF) was analyzed with enzyme-linked immunosorbent assay (ELISA) in the total cohort.

**Results:** Over 5 years, there were significant decreases in femoral neck BMD and tibia vBMD. Decreases were associated with signs of inflammation. In contrast, BMD at the total hip and the spine AP and lateral projections increased. Use of bisphosphonates was associated with increases in BMD at all measured sites except tibia. Use of tumor necrosis factor inhibitors (TNFi) was associated with increases in BMD at AP spine and tibia. Only three patients developed new VFs. AS related spinal alterations increased significantly with higher increases in men compared to women. New predictors identified for spinal radiographic progression were obesity in both sexes and use of bisphosphonates and impaired mobility in women. Among previously known predictors, baseline AS related spinal alterations was shared by sexes, whereas baseline elevated CRP and smoking were predictors in men. The biomarker s-HGF was identified as a novel independent predictor of spinal radiographic progression in men.

**Conclusion:** The studies in this thesis suggest that the best site to assess bone loss in patients with longstanding AS is at the femoral neck and that inflammation has a negative impact on bone loss and development of AS related spinal alterations and thus is an important treatment target. The studies give further reasons to counsel the patients to stop smoking and to encourage obese patients to weight loss. Treatments with bisphosphonates and TNFi had a positive impact on BMD. Further studies are suggested regarding the role of bisphosphonates in relation to spinal radiographic progression and whether s-HGF can be useful as a predictor for spinal radiographic progression.

**Keywords:** Ankylosing spondylitis, bone mineral density, spinal new bone formation, longitudinal cohort study

ISBN: 978-91-7833-540-4 (PRINT)

<http://hdl.handle.net/2077/60782>

ISBN: 978-91-7833-541-1 (PDF)