Chapter 9

Summary

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In this thesis several aspects of bone quality in patients at risk for secondary osteoporosis are studied. In chapter 2 an overview of osteoporosis and fracture risk is given. The subsequent chapters involve studies on clinical risk factors and measurements of bone mineral density, bone turnover and prevalent vertebral fractures in patients with thyroid carcinoma, sarcoidosis or inflammatory bowel disease (IBD).

In chapter 3 a study is described in which we investigated the influence of a suppressive dose of levothyroxin on bone in patients with differentiated thyroid carcinoma. Z-scores of bone mineral density (BMD) were not different from the reference population, even after long-term (>10 years) suppression therapy. Patients with a BMD in the lowest and highest quartile showed significant differences in the presence of known clinical risk factors. The bone turnover parameter carboxy-terminal cross-linked telopeptide of type I collagen (ICTP, a marker of bone resorption) was higher than in age-matched controls. In addition, we found in 7% of patients a vertebral deformity, suggestive of fracture. As data on vertebral fractures in healthy young patients are lacking, the best comparison we have is the EVOS study, comprising a very large cross-sectional population based study on the prevalence of vertebral deformities in European men and women. In this study, in a group of 15570 males and females aged 50-79 years, a prevalent vertebral deformity was observed in 12% (range 6-21%). We therefore had no indication that the prevalence of vertebral fractures in this particular patient group is higher than in a European reference population. In all studies published thus far on this subject, a significant bone loss was observed in patients using a 30-50% higher dose of levothyroxin than in our study. We therefore concluded that patients with well-differentiated thyroid carcinoma are not at increased risk of developing low bone mass nor have a higher prevalence of vertebral fracture, at least when treated with levothyroxin with doses not higher than necessary to suppress TSH.

Chapter 4 involves a study on the prevalence of vertebral deformities in IBD patients and their relation with BMD and bone turnover. Vertebral deformities were found in 25% of patients either with Crohn's disease (CD) or ulcerative colitis (UC). Comparing patients with and without vertebral deformities, no significant difference was found between Z- and T-scores of BMD, or levels of ICTP and serum procollagen type I amino-terminal propeptide (PINP). Neither disease activity, bone turnover markers, clinical risk factors, nor BMD were predictive for the presence of vertebral deformities. The determinants for having more than one vertebral deformity were age and glucocorticoid use.

This may imply that in addition to screening for low BMD, morphometric assessment of vertebral deformities is warranted in CD and UC to identify patients with decreased bone quality and consequently an increased fracture risk.

Sarcoidosis is a chronic inflammatory T-cell-driven disease that can also affect bone. In **chapter 5**, a study is summarized regarding bone remodelling, BMD and prevalent vertebral deformities in patients with sarcoidosis and their dependency of disease-related and treatment-related factors. We found that hip BMD was normal in patients with sarcoidosis, despite an increased bone turnover. As the increased bone resorption was found to be related to angiotensin converting enzyme (ACE) and soluble IL-2 receptor (sIL-2R), we concluded that this is - at least partly - the result of disease activity. In addition, vertebral deformities suggestive of fracture were found in a significant number of patients (21%). This implies that in sarcoidosis increased bone turnover affects bone quality rather than bone density.

As we found a high incidence of morphometric vertebral deformities suggestive of fractures in this patient group, the aim of the subsequent follow-up study was to determine the incidence of new and/or progressive vertebral deformities and the evolution of BMD during the course of sarcoidosis (**chapter 6**). The BMD of the total group appeared unchanged after follow-up, even in the groups with current or previous glucocorticoid use. The prevalence of vertebral deformities, however, appeared increased from 20 to 32% in the total group, and in 26% of subjects one or more new or progressive vertebral deformities were diagnosed. We found that the combination of a low normal BMD and a family history of fragility fractures confers an increased risk of the incidence of these deformities.

The last years there has been increasing interest for Quantitative Ultrasound (QUS) methods for refined assessment of bone strength. We hypothesized that in these populations (IBD and sarcoidosis) with decreased bone strength as reflected by the presence of vertebral deformities but with preservation of BMD, QUS measurements might have additional value to BMD measured with DXA to predict the presence of morphometric vertebral fractures. This is the subject of **chapter 7**. In addition to measurement of QUS vertebral fracture assessment and BMD measurement with DXA was done to determine whether or not QUS could be used to identify subjects with an inflammatory disease at risk for fracture. It appeared that, in contrast to DXA, decrease of bone density parameters of calcaneal QUS measurements was not associated with prevalent vertebral deformities and is hence not a useful clinical tool to identify patients at risk for fracture.

The studies described in this thesis imply that in subjects with inflammatory diseases who are at risk for secondary osteoporosis both DXA BMD measurements and assessment of vertebral deformities are warranted to identify individuals with reduced bone strength.