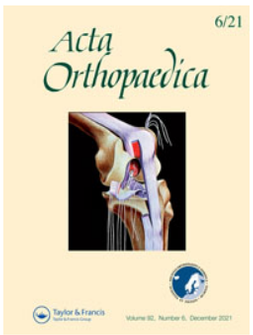

Acta Orthopaedica Scandinavica

ISSN: 0001-6470 (Print) (Online) Journal homepage: informahealthcare.com/journals/iort19

# Vitamin D Metabolism and Osteomalacia in Patients with Fractures of the Proximal Femur

Bjarne Lund, Ole Helmer Sørensen, Birger Lund, Flemming Melsen & Leif Mosekilde

**To cite this article:** Bjarne Lund, Ole Helmer Sørensen, Birger Lund, Flemming Melsen & Leif Mosekilde (1982) Vitamin D Metabolism and Osteomalacia in Patients with Fractures of the Proximal Femur, Acta Orthopaedica Scandinavica, 53:2, 251-254, DOI: 10.3109/17453678208992211

**To link to this article:** https://doi.org/10.3109/17453678208992211

Acta orthop. scand. 53, 251–254, 1982

# VITAMIN D METABOLISM AND OSTEOMALACIA IN PATIENTS WITH FRACTURES OF THE PROXIMAL FEMUR

BJARNE LUND, OLE HELMER SØRENSEN, BIRGER LUND, FLEMMING MELSEN & LEIF MOSEKILDE

Department of Orthopedic Surgery, Frederiksborg County Hospital, Hillerød; Department of Medicine, Sundby Hospital; Department of Medicine E, Frederiksberg University Hospital; and University Institute of Pathology and Department of Medicine III, Århus County Hospital, Århus, Denmark

A high frequency of histological osteomalacia (25 per cent) was seen in patients with fractures of the proximal femur. No correlation was found between the levels of circulating 25-hydroxyvitamin D (25-OHD) or 1,25-dihydroxyvitamin D ($1,25\text{-}(OH)_2D$) and the bone histomorphometric changes.

The serum 25-OHD levels were normal, which excludes a dietary vitamin D deficiency or a reduced hepatic hydroxylation of the vitamin. The mean serum $1,25\text{-}(OH)_2D$ concentration was significantly reduced in the whole patient group, but surprisingly the levels were normal in those with histological osteomalacia, indicating that an impaired conversion of 25-OHD to $1,25\text{-}(OH)_2D$ was not the primary cause of the bone disease. A reduced sensitivity to $1,25\text{-}(OH)_2D$ might be a possible explanation for the osteomalacia.

*Key words:* bone histomorphometry; 1,25-dihydroxyvitamin D; osteomalacia; proximal femoral fractures; vitamin D metabolites

Accepted 18.v.81

A high frequency of osteomalacia has been reported in patients with femoral neck fractures (Aaron et al. 1974). This has been explained by a low dietary intake of vitamin D, low exposure to sunlight and perhaps an impaired conversion of 25-hydroxyvitamin-D (25-OHD) to 1,25-dihydroxyvitamin-D ($1,25\text{-}(OH)_2D$). We have previously found normal serum 25-OHD concentrations in Danish patients with proximal femoral fractures (Lund et al. 1975), but slightly reduced levels of circulating $1,25\text{-}(OH)_2D$ (Lund et al. 1979b). The present study deals with the relationships between the histomorphometric bone changes and the serum levels of 25-OHD and $1,25\text{-}(OH)_2D$ in 20 patients with fractures of the proximal femur.

## PATIENTS AND METHODS

The study comprises 20 patients with fractures of the proximal femur: a man aged 42 and 16 women and 3 men aged 54–90 (mean 74). They all had normal serum creatinine and no signs or symptoms of malabsorption. Orthopaedic surgery was performed within the first 24 hours of admission and transcortical iliac crest biopsies were obtained with a Bordier trepine during the anaesthesia. The control values for bone histomorphometry were selected from our normal series so as to be age- and sex-matched (Melsen et al. 1978). The following parameters were measured on the undecalcified preparations:

Fractional trabecular bone volume [$^{\%}$Vfract (b)], the fraction of a given volume of total trabecular bone (bone + marrow) which is occupied by mineralized and unmineralized bone; fractional bone formation surfaces, [Sfract (f)], the extent of osteoid covered surfaces as a decimal fraction of the total trabecular bone surface; fractional trabecular osteoid volume [$^{\%}$Vfract (O)], the fraction of a given volume of trabecular bone which is occupied of osteoid; mean osteoid seam width ($^{\mu}$Wf),

0001-6470/82/020251-04 $02.50/0

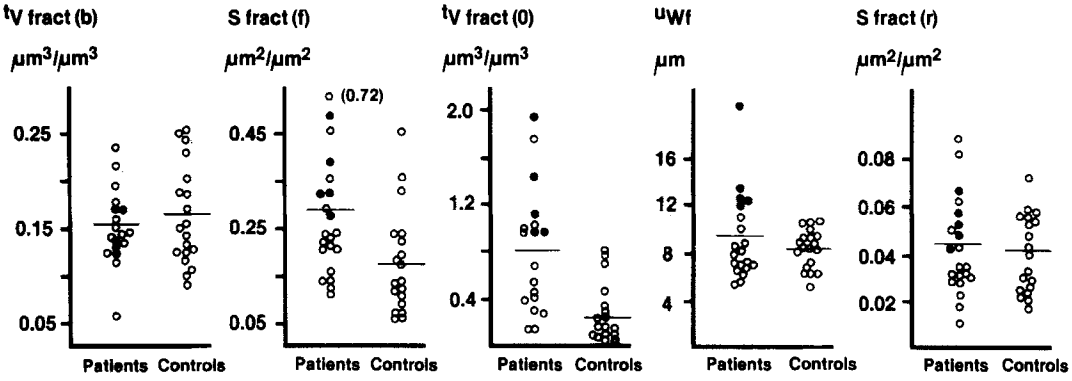


*Figure 1. Histomorphometric values in patients with fractures of the proximal femur and controls.*
*$^{t}$Vfract (b): fractional trabecular bone volume.*
*Sfract (f): fractional bone formation surfaces.*
*$^{t}$Vfract (o): fractional trabecular osteoid volume.*
*$^{u}$Wf: mean osteoid seam width.*
*Sfract (r): fractional trabecular resorption surfaces.*
*Patients with osteomalacia are indicated by closed circles.*

the mean of four extreme, almost equally spaced, measurements on all surfaces covered with osteoid, uncorrected for obliquity of the plane of section; and fractional trabecular resorption surfaces [Sfract (r)], the extent of Howship's lacunae as a decimal fraction of the total trabecular bone surface (Melsen et al. 1978, Melsen & Mosekilde 1978).

Blood samples were taken preoperatively. Serum 25-OHD was measured by a competitive protein-binding assay (Lund & Sørensen 1979). Reference values for the same time of the year (May–June) were obtained from age-matched normal persons. Serum 1,25-$(OH)_2$D was measured by a radioassay using rachitic chick intestinal cytosol as a source of the binding protein (Lund et al. 1979a).

The statistical significance of difference was assessed by the Wilcoxon test for unpaired data. The Spearman rank sum test was used for correlation.

## RESULTS

The histomorphometric values for trabecular bone in 20 patients and in 19 age-matched normal controls are given in Figure 1.

The diagnosis of osteomalacia was defined in this study, in which double labelling with tetracycline was impossible, as an increased osteoid seam width (exceeding the upper range for the control group). By this definition 5 patients or 25 per cent (95 per cent confidence limits: 9–49 per cent) of the material showed osteomalacia. The mean age of the patients with osteomalacia was 77 (range 65–90).

The serum 25-OHD concentrations in the patients were not different from those measured in the controls, whereas the 1,25-$(OH)_2$D levels were reduced ($P < 0.05$) (Figure 2).

The mean values of serum 25-OHD and 1,25-$(OH)_2$D in the 5 patients with osteomalacia

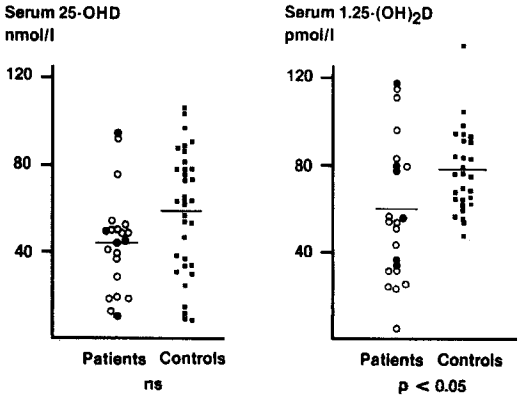


*Figure 2. Serum levels of 25-OHD and 1,25-$(OH)_2$D in patients with fractures of the proximal femur and controls. Patients with osteomalacia are indicated by closed circles.*

were 48.7 ± 30.2 nmol/l and 73.4 ± 30.4 pmol/l, respectively, and not statistically different from the values of 43.0 ± 21.7 nmol/l and 55.1–33.1 pmol/l found in the other 15 patients. Furthermore the 1,25-$(OH)_2$D values in the 5 patients with osteomalacia were not different from the concentrations measured in the control group. No correlation was found between the serum levels of 25-OHD and 1,25-$(OH)_2$D.

## DISCUSSION

It is a well-known fact that osteomalacia will develop in the absence of Vitamin D. Vitamin D is, however, a collective term comprising a group of compounds with antirachitic activity. Reduced serum levels of 25-OHD, 1,25-$(OH)_2$D and 24,25-dihydroxyvitamin D have been reported in a variety of conditions associated with osteomalacia, but it has not been possible so far to ascribe a specific static or dynamic histological feature in osteomalacia to a specific aetiologic factor (Frame & Parfitt 1978). We have earlier reported a lack of correlation between serum 25-OHD levels and bone histomorphometric changes in anticonvulsant osteomalacia, although the mean serum 25-OHD was reduced in the epileptic patients (Mosekilde et al. 1977). Likewise reduced serum concentrations of both 25-OHD and 1,25-$(OH)_2$D were found in patients who had undergone a jejuno-ileal bypass for obesity (Mosekilde et al. 1980), but the presence of osteomalacia was unrelated to the levels of circulating vitamin D metabolites, which is in agreement with the results of Compston et al. (1978). Osteomalacia and osteoporosis frequently coexist but also in this condition we did not find any correlation between the serum concentrations of 25-OHD or 1,25-$(OH)_2$D and the degree of osteomalacia (Sørensen et al. 1979). Attempts to correlate the serum 25-OHD and 1,25-$(OH)_2$D concentrations to bone histology in uraemic bone disease have also been negative (Eastwood et al. 1979).

Baker et al. (1979) recently reported reduced plasma 25-OHD concentrations in patients with fractures of the femoral neck and suggested that a vitamin D deficiency contributes to the high incidence of these fractures in Britain.

We have, however, found normal serum 25-OHD levels in Danish patients (Lund et al. 1975), which is probably due to a high supplementary vitamin D intake in our country (Lester et al. 1980). This shows that factors other than a simple vitamin D deficiency contribute to the development of osteomalacia in patients with proximal femoral fractures. The serum 1,25-$(OH)_2$D levels were not reduced in the patients with osteomalacia, indicating a normal renal conversion of 25-OHD to this hormone. A reduced sensitivity to 1,25-$(OH)_2$D in the target organs might offer an explanation.

## ACKNOWLEDGEMENTS

We are grateful to the Danish Association against Rheumatic Diseases and the Danish Foundation for the Advancement of Medical Science for economic support.

## REFERENCES

Aaron, J. E., Gallagher, J. C., Andersen, J., Stasiak, L., Longton, E. B., Nordin, B. E. C. & Nicholson, M. (1974) Frequency of osteomalacia in fractures of the proximal femur. *Lancet* **i**, 229–233.

Baker, M. R., McDonnell, H., Peacock, M. & Nordin, B. E. C. (1979) Plasma 25-hydroxyvitamin D concentrations in patients with fractures of the femoral neck. *Brit. Med. J.* **1**, 589.

Compston, J. E., Horton, L. W. L., Laker, M. F., Ayers, A. B., Woodhead, J. S., Bull, H. J., Gazet, J.-C. & Pilkington, T. R. E. (1978) Bone disease after jejuno-ileal bypass for obesity. *Lancet* **ii**, 1–4.

Eastwood, J. B., Memmos, D. & Wardener, H. E. (1979) Aetiology of osteomalacia in chronic renal failure and nutritional vitamin D deficiency. In: *Vitamin D. Basic research and its clinical application.* (Ed. Norman, A. W., Schaefer, K., Herrath, D., Grigoleit, H.-G., Coburn, J. W., DeLuca, H. F., Mawer, E. B. & Suda, T.) pp. 1185–1191. Walter de Gruyter, Berlin.

Frame, B. & Parfitt, A. M. (1978) Osteomalacia. Current concepts. *Ann Intern. Med.* **89**, 966–982.

Lester, E., Skinner, R. K., Foo, A. Y., Lund, B. & Sørensen, O. H. (1980) Serum 25-hydroxyvitamin D levels and vitamin D intake in healthy young adults in Britain and Denmark. *Scand. J. Clin. Lab. Invest.* **40**, 145–150.

Lund, B. & Sørensen, O. H. (1979) Measurement of 25-hydroxyvitamin D in serum and its relation to sunshine, age and vitamin D intake in the Danish population. *Scand. J. Clin. Lab. Invest.* **39**, 23–30.

Lund, B., Sørensen, O. H. & Christensen, A. B. (1975) 25-hydroxycholecalciferol and fractures of the proximal femur. *Lancet* **ii**, 300–302.

Lund, Bj., Sørensen, O. H. & Lund, Bi. (1979a) Measurement of circulating 1,25-dihydroxyvitamin D in man. Changes in serum concentrations during treatment with 1-alfa-hydroxycholecalciferol. *Acta Endocrinol. (Kbh.)* **91**, 338–350.

Lund, Bj., Sørensen, O. H. & Lund, Bi. (1979b) Clinical application of the 1,25-$(OH)_2D$ assay. In: *Vitamin D. Basic research and its clinical application.* (Ed. Norman, A. W., Schaefer, K., Herrath, D., Grigoleit, H.-G., Coburn, J. W., DeLuca, H. F., Mawer, E. B. & Suda, T.) pp. 991–997. Walter de Gruyter, Berlin.

Melsen, F., Melsen, B., Mosekilde, L. & Bergmann, S. (1978) Histomorphometric analysis of normal bone from the iliac crest. *Acta Pathol. Microbiol. Scand.* **86**, 70–81.

Melsen, F. & Mosekilde, L. (1978) Tetracycline double-labeling of iliac trabecular bone in 41 normal adults. *Calcif. Tissue Res.* **26**, 99–102.

Mosekilde, L., Christensen, M. S., Lund, B., Sørensen, O. H. & Melsen, F. (1977) The interrelationships between serum 25-hydroxycholecalciferol, serum parathyroid hormone and bone changes in anticonvulsant osteomalacia. *Acta Endocrinol. (Kbh.)* **84**, 559–565.

Mosekilde, L., Melsen, F., Hessov, J., Christensen, M. S., Lund, Bj., Lund, Bi. & Sørensen, O. H. (1980) Low serum levels of 1,25-dihydroxyvitamin D and histomorphometric evidence of osteomalacia after jejuno-ileal bypass for obesity. *Gut* **21**, 624–631.

Sørensen, O. H., Lund, Bi., Lund, Bj., Andersen, R. B., Danneskjold-Samsøe, B., Mosekilde, L., Melsen, F., Saltin, B., Friis, T. & Selnes, A. (1979) Effect of 1-alfa-vitamin D on bone and muscle in senile osteopenia. In: *Molecular endocrinology.* (Ed. MacIntyre, I. & Szelke, M.) pp. 309–318. Elsevier, North Holland.

Correspondence to: Bjarne Lund, M.D., Copenhagen University Hospital, Blegdamsvej 9, 2100 Copenhagen Ø, Denmark.