Are patients with a nonunion after a femoral neck fracture more osteoporotic than others? BMD measurement before the choice of treatment?

A pilot study of hip BMD and biochemical bone markers in patients with femoral neck fractures

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ABSTRACT The incidence of nonunion is high after a femoral neck fracture. If reliable predictors were available, fractures that heal well could be subjected to internal fixation while fractures that do not could undergo an arthroplasty. In this pilot study of 28 patients, those with a low hip BMD on admission had a higher risk of developing non-union.

About 50% of hip fractures involve the femoral neck and run the risk complications—e.g., nonunion or segmental collapse. Because of the difficulty in predicting the outcome of internal fixation of femoral neck fractures, many authors advocate primary prosthetic replacement. If one could predict the high-risk fractures in which either complication was likely to occur, it would be easier to choose between internal fixation and prosthetic replacement (Parker 2000).

I evaluated in this pilot study, whether hip bone mineral density (BMD) and biochemical bone markers could predict the occurrence of nonunion after a displaced femoral neck fracture.

Patients and methods

Women over 65 years of age, living independently in their own homes were included. Patients who had been treated with bone active drugs during the past year or had any metabolic disease that might affect BMD were excluded, as also were current smokers and those who had previously sustained a fracture in the contralateral hip or a cerebrovascular lesion that affected the legs. The study was approved by the Committee for Medical Ethics of Karolinska Hospital.

Study protocol

28 women with a displaced (Garden III–IV) femoral neck fracture were recruited consecutively from January 1995 to February 1997. They were operated on with two parallel screws (Olmed, DePuy, Uppsala, Sweden) within 30 hours of admission to hospital. All patients were mobilized on the day after the operation with full weight-bearing on the operated leg. Patients were followed with a review at 3, 6 and 12 months. 1 patient was excluded after 4 months because of poor health. We found no differences between the groups as regards s-calcium, s-phosphates or serum creatinine (Table 1).

Bone densitometry was done 2–3 days after surgery. Area BMD, expressed as "area density" (g/cm^2) of the unoperated hip, was determined by dual energy X-ray absorptiometry (DXA) using DPX-L (Lunar Corp. Madison, WI, USA). The DPX-L equipment given findings in 3 regions of interest: the neck, Ward's triangle and the trochanter region. The standard deviation of BMD in hip fracture patients, as compared to the mean BMD in young adults and age-matched normal

Table 1. Laboratory values on admission. Mean (SD)

Variables	Nonunion	Healed fracture
S-Calcium (mmol/L)	2.3 (0.1)	2.2 (0.1)
S-Phosphate (mmol/L)	1.1 (0.09)	1.0 (0.04)
S-Albumin (g/L)	37 (4.6)	37 (3.8)
S-Creatinine (mmol/L)	96 (27)	82 (14)

subjects, was expressed as the T and Z scores, respectively. The precision error of the method was 2% for the femoral neck measurements in this group of patients, which is similar to those reported elsewhere (Lees and Stevenson 1992).

Assays

We measured the following biochemical bone markers on admission: the formation markers—i.e., serum-osteocalcin (NovoCalcin), C-terminal propeptide of type I collagen (PICP, Prolagen-C), bone-specific alkaline phosphatase (S-bALP, Alkphase-B) and resorption markers urine—i.e., deoxypyridinoline crosslinks (U-Dpd, Pyrilinks-D). All measurements were done with ELISA kit methods from Metra Biosystems Inc., USA (Novatek Healthcare AB, Södertälje, Sweden). Serum C-terminal telopeptide of collagen type I (I-CTP) was measured with a 125-I RIA kit from Orion Diagnostica (Espoo, Finland).

Samples were run in duplicate. The controls included in kits were run together with an independent control sample from a healthy donor to check reproducibility. They were taken in the morning (6–10 a.m.), within 18 hours of the hip fracture. The first voided urine samples were used for measurements of U-Dpd. Aliquots dispensed in polypropylene tubes were preserved at –70 °C for up to 12 months. The reference ranges given by the manufacturer for premenopausal women are shown in Table 2. The analytical imprecision (% CV) was found to be 3.6, 4.7, 5.1, 5.3, and 3.2, respectively. The cross-reactivity of the anti-bALP monoclonal antibody for the liver isoenzyme was 3–8%, according to the manufacturer.

Statistics

The Student's t-test was used for parametric independent groups, and the Wilcoxon rank sum test for nonparametric tests to compare the groups of patients. A logistic regression analysis was done to estimate the effect of bone markers, age and BMD on nonunion/union. A p-value less than 0.05 was considered statistically significant. Two-sided tests were employed. The statistical software JMP 3.1 was used.

Results

7/28 developed nonunion during the first year and they were subjected to a hip arthroplasty. 2 other patients were operated on for a segmental collapse. Those who developed a nonunion had lower BMD in the contralateral hip in all 3 regions of interests on admission (Table 3). The median hip BMD values (ranges) in all patients was 0,7 g/cm^2 (0.51–0.92) in the neck region, 0.64 (0.35–0.84) in the trochanter region and 0.56 (0.34–0.83) in the ward region. The bone resorption markers U-DPD and s-ICTP were higher on admission in those who developed nonunion (Table 2).

For every 0.1 g/cm^2 lower BMD in the hip regions, an odds ratio (OR) of about 10 was calculated for nonunion (Table 4). When an adjustment was made for age, the observed effect of BMD in the trochanter and Ward regions on nonunion/

Table 2. Biochemical serum and urine bone markers on admission

	Reference range	Nonunion (mean)	Healed fracture (mean)	Diff. between groups and 95%CI
S-osteocalcin (ng/mL)	3.7–10.0	12	8.6	3.3 (–0.47–7)
S-bALP (U/L)	11.6–30.6	21	18	3.0 (–3.1–9.4)
S-PICP (ng/mL)	69–147	79	75	4.0 (–41–49)
S-ICTP (ug/L)	1.8–5.0	11	4.7	6.3 (1.9–10.7)
U-DPD (nM/mM creatinine)	3.0–7.4	10	6.6	3.4 (1.2–5.6)

Table 3. Differences in bone density on admission between the patients whose fractures healed and those who developed nonunion

	Nonunion during the following year (n 7)	Healed fracture group (n 21)	Differences between groups and 95%CI for the differences
Age (years, median and range)	85 (80–91)	80 (65–90)	
DXA g/cm^2 (unoperated hip)			
Neck	0.60 (0.08)	0.72 (0.09)	–0.12 (–0.2 to –0.04)
Ward	0.44 (0.09)	0.61 (0.11)	–0.17 (–0.3 to –0.08)
Trochanter	0.49 (0.08)	0.67 (0.09)	–0.18 (–0.3 to –0.09)
Neck T-score	–3.1 (0.7)	–2.1 (0.8)	–1.1 (–1.7 to –0.04)
Ward T-score	–3.6 (0.7)	–2.3 (0.8)	–1.3 (–2.0 to –0.57)
Troch T-score	–2.7 (0.8)	–1.1 (0.9)	–1.6 (–2.4 to –0.87)
Neck Z-score	–0.9 (0.6)	–0.2 (0.7)	–0.6 (–1.3 to 0.05)
Ward Z-score	–1.0 (0.7)	–0.1 (0.8)	–0.9 (–1.7 to –0.17)
Troch Z-score	–1.4 (0.8)	–0.03 (0.8)	–1.3 (–2.1 to –0.52)

Table 4. Risk for nonunion expressed as odds ratios with 95% confidence intervals for every 0.1 g/cm^2 reduction in BMD values

	Odds ratio	CI
Ward BMD	8.9	1.6–52
Neck BMD	7.4	1.5–37
Troch BMD	12	1.5–100

union was the same. The associated odds ratios (OR) for s-ICTP and u-DPD were not statistically significant when adjusted for age.

Discussion

This pilot study showed a considerable increase in the risk of nonunion after a displaced femoral neck fracture in patients with a low BMD the hip region on admission. The bone resorption markers were higher, a sign of increased bone turnover, in those who developed nonunion, but when adjusted for age, the associated odds ratio was not statistically significant.

The holding power of screws in cortical bone in relation to bone mineral has been studied by Stromsoe et al. (1993), who found high correlations between the QCT mass, the DXA density and the holding power of the screws. The relation between poor bone quality—i.e., osteoporosis and nonunion after a femoral neck fracture—has been evaluated with the previously used Singh index as a measure of osteoporosis (Singh et al. 1970). However, it was of no clinical value in predicting nonunion in these studies (Parker 1994). Only a few studies have reported data on biochemical bone markers or assessed DXA measurements in relation to the risk of developing nonunion after a femoral neck fracture. DXA is a quantitative method, unlike the Singh method which is a morphologic-qualitative method used to estimate the degree of osteoporosis.

More studies are needed to assess the diagnostic value of BMD measurements preoperatively to predict failure after a femoral neck fracture. If reliable criteria were available, one could choose the right fractures for osteosynthesis versus endoprosthesis, and the arthroplasty operation and/or reoperation rate could be reduced to a minimum.

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