

Periarticular bone in rheumatoid arthritis versus arthrosis

Histomorphometry in 103 hip biopsies

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Histomorphologic differences of the periarticular bone in rheumatoid arthritis (RA) and osteoarthritis (OA) may be of importance for long-term prosthetic fixation. We have evaluated bone specimens, obtained during total hip replacement from an acetabular and a femoral biopsy site, in 42 RA-hips and 61 OA-hips. In both groups the bone turnover was increased in the acetabulum compared to that in the femur. In the acetabulums the total trabecular bone

volume was equal, but osteoid volume, osteoid surface, resorptive surface, and the appositional rate were increased in RA. On the femoral side, only the osteoid volume was higher in RA.

The increased bone turnover with a greater amount of unmineralized tissue, as well as resorptive activity in the acetabulum, may be of importance for the higher rate of acetabular component migration and loosening after total hip replacement in RA.

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Submitted 93-05-20. Accepted 93-10-30

A generalized osteoporosis has been recognized in patients with rheumatoid arthritis (RA) (Sambrook and Reeve 1988), whereas an increased bone mineral content has been described in arthrosis (OA) (Roh et al. 1974). A more specific localized periarticular osteopenia has also been attributed to RA (Larsen et al. 1977, Magaro et al. 1991). Impairment of the bone quality is also a well-known peroperative finding in RA hips, perhaps associated with increased frequency of migration and loosening of the acetabular component in RA compared to OA (Carlsson et al. 1986, Önsten et al. 1993). Such differences have not been found for the femoral component.

The underlying morphology possibly responsible for this discrepancy have not been fully studied. Thus, our aim has been to histomorphometrically evaluate the periarticular bone quality of the acetabulum and proximal femur in patients with RA and OA undergoing total hip replacement.

Material and methods

The study comprised bone biopsies acquired peroperatively during total hip replacement at our hospital, 1990-1991. Samples were obtained in 35 consecutive patients with RA, 28 women and 7 men, with a mean age of 65 (range 44-80) years. Similar samples were obtained from 54 OA patients, 28 women and 26 men, mean age 63 (range 46-80) years, consecutively oper-

ated on by one of the authors. This represents 42 RA-hips and 61 OA-hips, as 4 RA- and 7 OA-patients had simultaneous bilateral total hip replacement. In 3 RA-cases, the contralateral side was operated on within a year and a half.

The diagnosis of RA in all cases was established by an experienced rheumatologist. At the time of surgery, 25/35 rheumatoid patients were seropositive, 9/35 were on corticosteroid medication. Virtually all RA- and OA- patients had been using NSAID.

All patients underwent a Charnley total hip replacement following our standard procedure, using a lateral incision and a trochanteric osteotomy. Peroperatively, a bone specimen was taken from a standardized site in the upper, loaded part of the acetabulum by means of a Bordier trephine. The biopsy from the proximal femur was taken after the trochanteric and the femoral neck osteotomies were made. The biopsy was taken from the edge of the osteotomy angle and in downward direction. From the acetabular site, the subchondral and trabecular bone were included in the sample. From the femoral site, only trabecular bone was obtained.

Prior to biopsy, tetracycline double-labeling was done following a 2-10-2 day regimen with demethylchlorotetracycline 600 mg daily in 26 hips including 12 RA-hips and 14 OA-hips.

The cylindrical bone specimens were fixated in 70% ethanol and dehydrated in ascending concentrations of ethanol, defatted in xylol and subsequently embedded undecalcified in methylmethacrylate. Sec-

Table 1. Histomorphometric evaluation of the acetabular subchondral trabecular bone and femoral trabecular bone in patients undergoing total hip replacement for rheumatoid arthritis (RA) or arthrosis (OA). Median (range)

Acetabulum	RA	P-value RA Acetab. vs femur	OA	P-value OA Acetab. vs femur	P-value RA vs OA
<i>Acetabulum</i>					
Trabecular bone volume (TBV) %	31.9 (10.8-55.8)	<0.001	27.0 (8.3-55.5)	<0.001	NS
Osteoid volume (OV) %	0.9 (0-3.1)	<0.001	0.3 (0-2.5)	<0.001	<0.001
Osteoid surface (OS) %	17.8 (2.1-45.7)	<0.001	6.8 (0-34.9)	<0.001	<0.001
Resorption surface (RS) %	1.0 (0-7.0)	<0.001	0.6 (0-5.8)	<0.01	<0.05
Appositional rate $\mu\text{m}/\text{day}$	1.3 (0.7-1.7)	<0.02	0.8 (0.4-1.2)	NS	<0.01
<i>Femur</i>					
Trabecular bone volume (TBV) %	11.5 (5.7-35.4)		11.7 (6.0-33.6)		NS
Osteoid volume (OV) %	0.1 (0-1.2)		0.0 (0-0.9)		NS
Osteoid surface (OS) %	3.1 (0-23.8)		1.9 (0-15.4)		<0.05
Resorption surface (RS) %	0.0 (0-1.9)		0.0 (0-3.2)		NS
Appositional rate $\mu\text{m}/\text{day}$	0.6 (0.5-0.8)		0.7 (0.3-1.2)		NS

tions 5 μm thick were cut with a Jung hard-sectioning microtome and stained according to Goldner (Schenk 1965). Histomorphometric evaluation was performed with a microscope equipped with a Merz grid (Merz and Schenk 1970). The following variables were calculated for both groups of patients and for the 2 biopsy sites: trabecular bone volume (TBV)—the percentage of the section surface covered by mineralized or unmineralized trabecular bone; osteoid volume (OV)—the percentage of the trabecular bone volume consisting of osteoid; the osteoid surface (OS)—the percentage of all trabecular surfaces covered by osteoid; resorption surface (RS)—the percentage of all trabecular surfaces covered by resorption lacunae with osteoclasts.

In addition, 20 μm sections were cut and mounted unstained for analysis of tetracycline fluorescence. The appositional rate was calculated as the mean width between the middle of the lines in the double-labeled zones divided by the interval of days between the given doses of tetracycline. All specimens were evaluated blindly by one observer.

Histomorphometric evaluation was not done in 5 acetabular specimens and 6 femoral specimens because of poor specimen quality. The appositional rate could not be calculated in 8 of the femoral specimens.

For statistical evaluation, the StatView® 1.04 program was used on the Macintosh system. The Mann-Whitney *U*-test and the Spearman rank correlation test were used.

Results (Table 1)

Within each diagnostic group there was no consistent difference attributable to sex, thus allowing for the comparison between the OA- and RA-hips as groups. None of the variables was found to correlate with age in either group.

At the acetabular site, TBV was equal in RA and OA. The OV, OS and RS and the apposition rate were all increased in RA. In the femur, only OS was increased in RA.

All 4 static variables were higher in the acetabulum than in the femur in both RA- and OA-cases.

Discussion

Bone quality and bone turnover are routinely described after histomorphometric evaluation of iliac crest bone biopsies. However, the findings are only valid for the specific biopsy site and conclusions do not with certainty comprise the morphology of the entire skeleton and even less the periarticular region of a diseased hip. The TBV distinguishes between a normal amount of bone and osteopenia, while the other variables may identify abnormalities in bone turnover.

A TBV-value of about 20 percent for the iliac crest is normal, according to Chavassieux et al. (1985), but, as pointed out by de Vernejoul et al. (1981), this value may have an individual variation of about 20 percent, depending on the exact biopsy location. An equal variation in the other variables has been reported. These estimations may, however, also be influenced by the staining and analytical techniques applied by each laboratory.

The juxtaarticular bone of the hip and other weight-bearing joints is subjected to completely different loading properties as well as possible influences from permeating synovial mediators, which may lead to a different morphologic response. In patients undergoing total hip replacement because of RA or OA, these factors may be of importance for the long-term surgical success.

In the acetabulum, the biopsy site was standardized and chosen to represent the area of maximum stress in relation to loading, which also represents the crucial area for the prosthetic anchorage. Stereophotogrammetric studies have confirmed this proximal direction as the direction of increased socket migration (Önsten et al. 1993). It was somewhat surprising to find that the acetabular TBV was similar in the RA- and OA-patients, challenging a relatively immediate periarticular osteoporosis in the RA-hips. The values were also higher than the above-mentioned normative data for the iliac crest.

This is contrary to findings from iliac crest biopsies with a decreased TBV in RA (Stulberg et al. 1989, Rico et al. 1990) and to the findings in studies of bone mineral content, in which patients with OA of the hip have a greater bone mass (Roh et al. 1974, Carlsson et al. 1979, Gotfredsen et al. 1990). However, this discrepancy should be explained by the fact that, even with an equal TBV, the total bone mineral content may be decreased, as the amount of unmineralized osteoid tissue was relatively increased in the RA-patients.

From smaller and heterogeneous data, mainly using the knee joint, metabolic hyperactivity of the bone has previously been described in RA compared to OA (Havdrup et al. 1976, Shimizu et al. 1985). These findings, together with the present results, may reflect that the subchondral alterations in both RA- and OA-hips occur in response to the special loading situation within a joint but also in response to the disease, including an influence from synovial mediators. In the RA-cases, a relatively increased bone turnover was associated with higher bone formative and resorptive indices. The enhancement of the bone turnover was further verified by using tetracycline labeling and in the acetabulum an increased appositional rate was found in the RA-patients. The appositional rate was also increased when compared to normative data from the literature concerning iliac crest biopsies, where the mean rate is $0.65 \pm 0.10 \mu\text{m/day}$ (Melsen and Mosekilde 1978).

On the femoral side there was an increase in the OS only in the RA-patients, while all other variables were equal in the 2 groups. An expected decrease in TBV compared to the acetabular side was found. In an earlier study, biopsies were taken from a juxtapositioned

region of the trabecular bone in the proximal femur in patients with OA (Obrant 1984). The present figures for the OA-patients were almost identical with those obtained in that study regarding TBV and the 2 osteoid variables. In that case, the OA-patients differed from controls with higher osteoid variables but not regarding TBV. This may indicate that the RA-patients in our study differ even more from the normal.

Acknowledgements

Financial support was obtained from the Swedish Medical Research Council, grant no. B92-17X-09906-01A, Lund University funds, and the Kock and Österlund Foundations.

References

- Carlsson Å, Nilsson B E, Westlin N E. Bone mass in primary coxarthrosis. *Acta Orthop Scand* 1979; 50 (2): 187-9.
- Carlsson Å S, Gentz C F, Sanzén L. Socket loosening after hip arthroplasty. Radiographic observations in 241 cases up to 15 years. *Acta Orthop Scand* 1986; 57 (2): 97-100.
- Chavassieux P M, Arlot M E, Meunier P J. Intersample variation in bone histomorphometry: comparison between parameter values measured on two contiguous transiliac bone biopsies. *Calcif Tissue Int* 1985; 37 (4): 345-50.
- Gotfredsen A, Riis B J, Christiansen C, Rødbro P. Does a single local absorptiometric bone measurement indicate the overall skeletal status? Implications for osteoporosis and osteoarthritis of the hip. *Clin Rheumatol* 1990; 9 (2): 193-203.
- Havdrup T, Hulth A, Telhag H. The subchondral bone in osteoarthritis and rheumatoid arthritis of the knee. A histological and microradiographical study. *Acta Orthop Scand* 1976; 47 (3): 345-50.
- Larsen A, Dale K, Eek M. Radiographic evaluation of rheumatoid arthritis and related conditions by standard reference films. *Acta Radiol (Diagn) (Stockh)* 1977; 18 (4): 481-91.
- Magaro M, Tricerri A, Piane D, Zoli A, Serra F, Altomonte L, Mirone L. Generalized osteoporosis in non-steroid treated rheumatoid arthritis. *Rheumatol Int* 1991; 11 (2): 73-6.
- Melsen F, Mosekilde L. Tetracycline double-labeling of iliac trabecular bone in 41 normal adults. *Calcif Tissue Res* 1978; 26 (2): 99-102.
- Merz W A, Schenk R K. Quantitative structural analysis of human cancellous bone. *Acta Anat (Basel)* 1970; 75 (1): 54-66.
- Obrant K J. Trabecular bone changes in the greater trochanter after fracture of the femoral neck. *Acta Orthop Scand* 1984; 55 (1): 78-82.
- Rico H, Hernandez E R, Gomez Castresana F, Yague M, Cabranes J A, Valor R. Osteopenia in rheumatoid arthritis: a biochemical, hormonal and histomorphometric study. *Clin Rheumatol* 1990; 9 (1): 63-8.

- Roh Y S, Dequeker J, Mulier J C. Bone mass in osteoarthritis, measured in vivo by photon absorption. *J Bone Joint Surg (Am)* 1974; 56 (3): 587-91.
- Sambrook P N, Reeve J. Bone disease in rheumatoid arthritis. *Clin Sci* 1988; 74 (3): 225-30.
- Schenk R K. Zur histologischen Verarbeitung von unentkalkten Knochen. *Acta Anat* 1965; 60: 3-19.
- Shimizu S, Shiozawa S, Shiozawa K, Imura S, Fujita T. Quantitative histologic studies on the pathogenesis of periarticular osteoporosis in rheumatoid arthritis. *Arthritis Rheum* 1985; 28 (1): 25-31.
- Stulberg B N, Bauer T W, Watson J T, Richmond B. Bone quality. Roentgenographic versus histologic assessment of hip bone structure. *Clin Orthop* 1989; 240: 200-5.
- de Vernejoul M C, Kuntz D, Miravet L, Goutallier D, Ryckewaert A. Bone histomorphometric reproducibility in normal patients. *Calcif Tissue Int* 1981; 33 (4): 369-74.
- Önsten I, Bengnér U, Besjakov J. Increased socket migration in rheumatoid arthritis. A roentgen stereophotogrammetric study of the low-friction arthroplasty. *J Bone Joint Surg (Br)* 1993. Accepted for publication.