REVIEWS

Bone mass in osteoarthritis

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Since 1970 a number of studies have noted that osteoarthritis of the hip is uncommon in patients with femoral neck fracture.^{1–4} The negative association between osteoporosis and osteoarthritis has been the subject of a detailed review by Dequeker,⁵ who painted an attractive picture of two very different groups, the osteoporotic, slender with osteopenia and little degenerative joint change, and the osteoarthritic, with above normal bone mass, more fat, greater muscle strength, and fewer fractures, though occasionally both conditions may be present in the same subject.⁶

Although osteoarthritic patients have more bone than osteoporotic patients, controversy still exists as to whether osteoarthritic patients have greater bone mass than normal subjects. Part of the controversy is due to selection of study and control groups. Two different study designs have been used, the 'population based' study and the 'patient based' study. The first method selects a large number of 'normal' subjects and separates them into 'osteoarthritic' or 'non-osteoarthritic', usually on the basis of radiological change in the hands, hips, or spine, and compares the two groups. The second method compares patients with osteoarthritis requiring either medical or surgical treatment with 'normal' people from other sources. The 'normal' group, however, may include people with asymptomatic radiological osteoarthritis.^{7–8} Thus study and control groups are different in the two types of investigation. In addition, bone mass may be measured at a number of sites containing differing amounts of trabecular and cortical bone, and over the past 20 years many different techniques have been used for measurement. These are not the only problems. Bone mass is affected by several factors, including age, weight, sex, menopausal age, and some clinical conditions and drugs. These factors have not always been taken into consideration, particularly in earlier studies. The effect of body weight is complex. Obesity appears to protect against osteoporosis either through the peripheral conversion of androstenedione to oestrone in adipose tissue⁹ or through increased loading, and is also associated with osteoarthritis.^{10–11}

The diagnosis of osteoarthritis is not always easy and there are many clinical variants.¹² The most recent definition of osteoarthritis included the words 'a heterogeneous group of conditions leading to the clinical syndrome of joint symptoms and signs'; and classification criteria are still being perfected.¹³ In general, two osteoarthritic subgroups have been studied: primary generalised osteoarthritis and osteoarthritis of the hip.

Osteoarthritis of the hip

In two of the earliest studies cortical bone mass was measured at the second metacarpal in osteoarthritic men and women and controls by radiographic morphometry.^{4–14} Both studies showed increased bone mass in the osteoarthritic subjects, though one study¹⁴ included tuberculous and psychiatric patients in the normal controls. In both studies large numbers of patients with severe osteoarthritis were studied (100 patients with osteoarthritis undergoing hip surgery,⁴ 75 patients with primary osteoarthritis Kellgren's grade 3–4 at the hip).¹⁴ Neither study took weight or menopausal status into account.

In contrast, another large study of 105 men and women with 'advanced' osteoarthritis of the hip³ showed that these patients had bone mass at the metacarpal similar to that of normal subjects. Although 94% of the osteoarthritic patients were described as endomorphic mesomorphs, direct comparison of body weight was not made with controls. Menopausal age was not discussed, though all subjects were aged 55 or more.

The trabecular pattern in the proximal femur has been classified by the Singh grade,¹⁵ which is related to bone density.^{15–16} Radiographs of 314 men and women over 50 attending for radiology for non-skeletal problems were assessed for osteoarthritis of the hip by Kellgren's grading and bone density by Singh grade.¹⁷ There was a significant negative association between low bone density and osteoarthritis. However, the authors were unable to obtain body weights.

Single photon absorptiometry is a useful technique for measuring bone mass in the appendicular skeleton, most commonly the distal radius comprising mainly trabecular bone, and the mid-radius, a predominantly cortical site, though the precise site on the radius used may vary. Bone mineral content (BMC, g/cm) may be measured or the results adjusted for skeletal size by dividing by bone diameter to give the bone mineral density (BMD, g/cm²); the technique is described in detail by Wahner.¹⁸ Three studies of bone mass by this technique in the forearm of men and women with primary osteoarthritis of the hip gave conflicting results. One group of 53 patients¹⁹ was scheduled for surgery and the other two groups of 31 and 29 patients respectively^{20–21} had osteoarthritis graded as Kellgren's 3 and 4. Women with osteoarthritis were shown to have a higher BMC and BMD at both cortical and trabecular sites in the radius in one study,²⁰ but only the BMC at the predominantly trabecular site of the distal radius was increased in

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women in another study,¹⁹ and the BMD of the cortical site in the radius was actually lower in osteoarthritic women than in controls in the third.²¹ Men had similar bone mass to that of controls in two studies,^{19, 21} and increased BMC but not BMD at the proximal and distal radius and second metacarpal in the third.²⁰ Weight and height in patients and controls were recorded in two of these studies.^{20, 21} In one study²⁰ women with osteoarthritis were taller than controls, but otherwise no significant differences in weight or height were seen. Menopausal age and status were not recorded.

Cortical bone mass at the femoral shaft was examined by single photon absorptiometry in 69 patients with osteoarthritis and rheumatoid arthritis of joints, including the knee,²² and compared with data from 554 normal subjects. Although osteoarthritic subjects were not separately compared with controls, it is of interest that BMC in the mixed group of patients correlated positively with mobility and weight and negatively with the time taken to walk a measured distance and the number of large joints affected. This suggests that function may influence bone mass measurements in osteoarthritic patients, and differences in function might explain some of the variation in study findings. Muscle strength has recently been shown to be a significant predictor of bone mass in the femur and forearm in healthy postmenopausal women.²³

Dual photon absorptiometry is used for measuring regional and total skeletal BMD or BMC, particularly in the spine and hip, which are not accessible by single photon absorptiometry.¹⁸ One study of 17 postmenopausal women with osteoarthritis of the hip referred for surgery showed regional BMD and BMC to be higher than that of 20 postmenopausal controls in head, arms, chest, spine but not legs.²⁴ This was not explained by weight. Reduced activity was suggested as an explanation for the reduction in the amount of bone in the legs.

Iliac crest bone biopsy can be used to assess the quantity of cortical and trabecular bone at that site by histomorphometry, and studies on a heterogeneous group of 22 men and 18 women with osteoarthritis of the hip, knee, or ankle requiring surgery²⁵ showed low trabecular bone volume ('osteoporosis') in 11, though the actual trabecular bone volume defined as osteoporotic was not given. Iliac crest samples were obtained at necropsy from 12 men and eight women who had died suddenly of cardiovascular disease and used as controls. Age ranges were wide in the osteoarthritic subjects (26–78 years) and menopausal status was not taken into account. Men with osteoarthritis were more likely to be osteoporotic than men matched for age who had died suddenly.

Primary generalised osteoarthritis

Patients with osteoarthritis of the hip may be a heterogeneous group, though some of the studies previously discussed attempted to exclude patients with osteoarthritis secondary to congenital or developmental diseases—for

example, Perthes disease, slipped epiphysis, or bone dysplasias,^{19, 20} whereas others specified 'primary' osteoarthritis of the hip without giving further details.^{14, 21} Fewer studies have been performed on bone mass in patients with primary generalised osteoarthritis.

Bone mass in 15 women with primary generalised osteoarthritis fulfilling Kellgren and Moore's criteria²⁶ was assessed by measuring total body calcium by neutron activation analysis, and also by metacarpal morphometry. There was no difference in bone mass between patients and 12 controls matched for age, menopausal status, and skeletal size and no relation was seen between grade of radiological osteoarthritis in the hand and bone mass.²⁷

Quantitative computed tomography has been used to measure trabecular bone at the distal radius and cortical bone at the radius midshaft in women with primary generalised osteoarthritis according to Kellgren and Lawrence's criteria.²⁸ The first study,²⁹ published in abstract form, showed increased trabecular but not cortical bone density in osteoarthritic subjects. The authors followed this up with a second study,³⁰ this time taking weight and height into account, and showed no significant difference between osteoarthritic women and normal values obtained from prediction equations.

Trabecular BMC assessed at the distal radius by single photon absorptiometry in a mixed group of 30 men and women with primary generalised osteoarthritis according to Kellgren and Lawrence's criteria,²⁸ and isolated osteoarthritis of the hip showed increased BMC only in the patients with osteoarthritis of the hip, and as the authors themselves pointed out, weight and skeletal size were not taken into account.³¹

A study on iliac crest biopsy specimens obtained from 38 women aged 60–75 at necropsy found that trabecular bone volume and trabecular width correlated with the grade of osteoarthritis seen radiologically at the hand.³² Subjects with Kellgren's grade 2–4 had more cortical and trabecular bone than those with Kellgren's grade 0.

Two studies, so far published only in abstract form, have measured bone mass in patients with generalised osteoarthritis with dual energy x ray absorptiometry. One population based study compared BMD at the lumbar spine and wrist in 653 women aged 45–65 with and without early radiological osteoarthritis (Kellgren and Lawrence grade 2 or more), at the hands, and knees.³³ The other study measured BMD at the lumbar spine, wrist, and hip in 16 postmenopausal women requiring treatment for primary generalised osteoarthritis and compared the results with BMD for a large number of controls.³⁴ Both studies took body mass index and age into account and both found significantly increased BMD at the spine alone. The presence of osteophytes and degenerative disease at the facet joints, however, might produce artefacts affecting lumbar BMD measurements.¹⁸ A study in 'normal' postmenopausal women showed that the effect of osteophytes was only about 4% of the variance in lumbar BMD.⁷ Interestingly, in that study not only were osteophytes present in most normal postmeno-

pausal women but also lumbar osteophyte score correlated with proximal femoral bone mineral density, suggesting a relation between BMD and osteoarthritis of the spine.

Summary

Present evidence tends to support the hypothesis that bone mass is increased in osteoarthritis of the hip. It is not yet clear whether this is a direct relation or a secondary effect, perhaps due to increased body weight.

Evidence for an increase in bone mass in primary generalised osteoarthritis is more equivocal. If radiographic studies³²⁻³³ are included (although strictly their subjects cannot be labelled as having primary generalised osteoarthritis) then evidence tends to favour an association with an increase in bone mass. The extent of this increase, its distribution throughout the body, its clinical significance, and the roles of obesity and mobility await further investigation.

An increase in bone mass in osteoarthritis independent of obesity, if proved, would lend support to the concept of osteoarthritis as a bone disease resulting in secondary damage to cartilage. Whether osteoarthritis protects against osteoporosis, or osteoporosis and its associated risk factors reduce the risk of osteoarthritis also remains to be determined.

We would like to thank Mrs S P Stewart for helpful discussion of bone mineral measurement techniques.

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