Osteoporosis and Psoriatic Arthritis

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Osteoporosis and Psoriatic Arthritis

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ABSTRACT. Osteoporosis (OP) is a skeletal disorder characterized by compromised bone strength that predisposes to an increased risk of fracture. The prevalence of OP in the general population is very high as established in several studies, and OP represents one of the possible aspects of bone involvement in arthritis. In psoriatic arthritis this involvement is particularly complex because it affects not only mechanisms of bone loss but also of bone formation. We will discuss these aspects and the available epidemiological data. (J Rheumatol 2012;39 Suppl 89:36–38; doi:10.3899/jrheum.120240)

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Osteoporosis (OP) is one possible aspect of bone involvement in arthritis. However, while this is the case for rheumatoid arthritis (RA), in which we observe OP at a systemic level and bone erosion locally as expression of bone loss manifestations, the situation is not so clear in psoriatic arthritis (PsA). In this disease the involvement of bone is more complex because it affects not only mechanisms of bone loss but also of bone formation (ankylosis, periostitis, syndesmophytes).

OP is classically defined as a condition characterized by reduced bone mass, microarchitectural damage, and increased fragility of bone. Diagnosis is made using dual energy x-ray absorptiometry (DEXA). The examination is usually performed at 2 sites: lumbar and proximal femur. The first site is potentially more affected by bone formation, which should be taken into account in data evaluation. The variables generated are bone mineral density (BMD), expressed in gm/cm² and 2 relative numbers: t-score and z-score, both expressed in SD. The first value is age-dependent and is used for diagnosis of OP below a threshold of –2.5 SD.

The prevalence of OP in the general population has been established in several populations. We performed an epidemiological study aimed at defining prevalence and risk factors for OP in a population of healthy, active, noninstitutionalized women¹. Sample size was representative of the general population and adequately powered. Completion rate of recruitment was very high. The data showed a prevalence of OP of 40.6% among women aged 50 years or more, compared to twice as many controls². No difference was found among women, while among men, patients with psoriasis showed a prevalence higher than controls (3.1% vs 1.7%; multivariate OR: 1.7; p < 0.001). No data were provided on the presence of arthritis.

Unfortunately, the studies that identify patients with arthritis deal with sample smaller sizes. Borman, et al reported on 47 patients with psoriasis, some with and some without arthropathy³. The only differences in bone density variables involved z-score, which was lower among patients with PsA both at lumbar and femoral sites. In another study comparing subjects with psoriasis with and without arthritis, the prevalence of OP was greater among patients with PsA as established in several studies, and OP represents one of the possible aspects of bone involvement in arthritis. In psoriatic arthritis this involvement is particularly complex because it affects not only mechanisms of bone loss but also of bone formation (ankylosis, periostitis, syndesmophytes).

In a preliminary study, Dreher, et al analyzed the prevalence of OP in a large database of patients with psoriasis (close to 8000 subjects), compared to twice as many controls². No difference was found among women, while among men, patients with psoriasis showed a prevalence higher than controls (3.1% vs 1.7%; multivariate OR: 1.7; p < 0.001). No data were provided on the presence of arthritis.

In another study, patients with arthritis are categorized by sex and menopausal status. BMD was significantly lower in PsA cases than in control in all categories and at both sites. Prevalence of OP was measured around 45% in PsA menopausal women, but comparison with healthy controls was not reported.

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according to the presence of articular erosions\textsuperscript{7}. Those with erosions have lower t-scores only at lumbar spine.

The last 2 studies compare patients with PsA to patients with RA and with ankylosing spondylitis (AS). In the first case, a very large database was used and patients were matched for all major confounding factors\textsuperscript{8}. The variable used was t-score, which did not show any difference between the 2 groups. Similarly, no difference in OP prevalence was found in a study of 120 patients with PsA and 76 with AS\textsuperscript{9}.

Therefore, available data seem to indicate that OP is a very likely finding in PsA. However, the likelihood is affected by site of measurement and arthritic subset. It is very important to have studies with larger samples and adequate healthy control groups, which may allow better definition of these aspects and better control for confounding factors.

However, at this point it is crucial to determine why we are concerned about OP. The answer opens a wider perspective that is worth exploring. The reason for the general concern for OP stems from its main complication: fragility fractures. OP is associated with increased risk of vertebral and nonvertebral fractures. Among the latter group we include also hip fracture, the most serious complication of OP. Fractures cause significant clinical, social, and economic burden. More than 40\% of women who fracture a hip will never be able to walk again without assistance and fewer than 20\% will recover to their prefracture competence in activities. Recent literature has also highlighted another field of concern linked to fractures: not only hip but also vertebral fractures are associated with a significant increase in mortality, in both sexes.

Unfortunately, awareness of these aspects is lacking. For example, data show that most women do not receive treatment during the year following an OP-related fracture. Following a low-trauma fracture, only 42\% of women with a hip fracture undergo treatment and < 20\% of women who have a non-hip fracture.

Another indication of this lack of awareness is the substantial absence of data on fracture in patients with PsA. Only 1 recent article reports, as an ancillary finding, data on the prevalence of low-trauma fractures in postmenopausal women with PsA (Pedreira, et al)\textsuperscript{10}. Data refer to a sample of 45 patients with PsA, 52 subjects with psoriasis, and 98 healthy controls. Pedreira, et al describe a 33.3\% prevalence of fragility fractures among patients with PsA, significantly greater than the finding (28.8\%) among patients with psoriasis. Both prevalence rates are reported as significantly greater compared to controls, but prevalence of fractures in controls is not described. Interestingly, in this study BMD data of lumbar spine and proximal femur are not significantly different in the 3 groups.

This finding raises another consideration. BMD is clearly important, but it is not the only risk factor for fractures. Several other significant risk factors have a relative risk dimension absolutely comparable with that of BMD. The new definition of OP, in fact, takes into account this evidence. The focus of the definition is no longer “bone mass;” instead, OP is defined as a skeletal disorder characterized by compromised “bone strength.” A reduced “bone strength” predisposes to an increased risk of fracture. The concept of bone strength encompasses both bone density and bone quality.

A major factor determining bone quality is bone turnover, or expression of the cycle of coupling. That is the basic expression of bone metabolism and is characterized by the combined action of the 2 cellular types working together in the bone: osteoclasts (the cells that reabsorb bone) and osteoblasts/osteocytes (the cells forming new bone). The rate and the balance of the coupling cycle determine bone metabolism, and this cycle may be considered the key point that links systemic and local bone involvement.

Arthritis affects both rate and balance of the coupling cycle, generating the conditions for the features we have discussed as patterns of bone involvement in arthritic diseases. At a systemic level are osteoporosis, microarchitectural damage, and fractures. At a local level are focal erosions and/or bone formation phenomena. The coupling cycle is also the crucial point where the differences between various kinds of arthritis may be expressed, determining, for example, the diverse bone involvement in RA and PsA. At this level the differences in the control systems of the coupling cycle may represent distinctive characteristics between the 2 diseases.

An interesting example of this comes from recent data on a factor, Dickkopf-1 (DKK-1), an inhibitor of the wingless pathway and an important means of activation of osteoblast precursors\textsuperscript{11,12,13}. Unopposed DKK-1 causes an increase in the number of osteoclasts (because of reduced production of osteoprotegerin by osteoblasts) and a decrease in new bone formation. This could be a condition similar to what happens in RA; in fact this is the result of unopposed DKK-1 in a mouse model of RA\textsuperscript{14}. In this model, when adding increasing concentrations of anti-DKK-1, represented by antibodies, a progressive reduction is observed in the number of active osteoclasts and an increase in the capacity of osteophyte (new bone) formation, as an expression of osteoblast action. This may closely resemble what happens in PsA. Therefore the difference in bone involvement between PsA and RA could be largely determined by a different balance and expression of the factors controlling the coupling cycle.

Our agenda concerning bone involvement in PsA is extensive. We will continue studies on BMD distribution and OP prevalence in patients with PsA that better define questions relative to disease subgroups and confounding factors involved. We need fracture studies that can define the risk of such an important complication, which may depend largely on factors other than BMD alone. We should continue to investigate cellular mechanisms causing bone...
involvement in PsA and to determine the different effects in different kinds of arthritis. However, the critical point is that we should not forget bone in our daily clinical practice.

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