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Editorial

Sex Effect in Psoriatic Arthritis

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Psoriatic arthritis (PsA) is an inflammatory disease that affects as many as 30% of patients with psoriasis, an immune-mediated inflammatory skin condition. Several domains are recognized in PsA, including peripheral arthritis, axial disease, enthesitis, dactylitis, and skin and nail manifestations.[1] Although PsA affects men and women equally, there may be a sex influence on the development and expression of the disease.[2] In the past few decades, there has been increasing interest in the effect of sex on the manifestations and impact of PsA as well as on the response to therapy. There may be some genetic reasons. For example, a paternal transmission was noted in PsA.[3] The role of female hormones has not been confirmed because although some studies suggested that women with PsA had low pregnancy rates, this was not observed in a recent study.[4,5]

A difference in axial disease expression between men and women was noted in a 1992 study that compared 82 women with 112 men with axial disease and showed that there was more advanced disease in men.[6] Similar observations were reported by Queiro et al, who found that axial disease together with HLA-B27 occurred more commonly among men, whereas women had more severe peripheral disease and functional disability.[7]

Eder et al specifically evaluated gender difference in PsA.[8] The study included 345 men and 245 women followed prospectively. They also found that axial involvement was more common among men, who were also more likely to develop more severe damage in the peripheral joints, demonstrated radiographically, whereas women had more severe functional limitations and worse quality of life (QOL) than men.

Mortality studies in PsA revealed varied results. Initially, the standard mortality ratio was higher in men,[9] but over the decades there was a higher mortality risk in women[10] that has persisted into the current decade.[11]

Buskila et al compared the level of pain in patients with PsA with that of those with rheumatoid arthritis.[12] They found that one could apply significantly more pressure on the most severely affected joints, the fibromyalgia (FM) tender points and the control points, in patients with PsA. When adjusted for sex, the differences were smaller, although still significant, suggesting that female sex was not the main reason for the differences in tenderness.

Polachek et al[13] performed musculoskeletal ultrasound on 115 patients with PsA without FM and 42 patients with FM. Although patients with FM had higher clinical scores than those without, there did not appear to be a gender effect; however, there was no specific analysis comparing men and women.

Duruoz et al[14] investigated gender effect in PsA in a cohort of 1038 patients included in a multicenter Turkish study, of whom 65% were women. They found that although men were more likely to have spondylitis, women had higher disease activity scores (measured by the Disease Activity Score in 28 joints and Clinical Disease Activity Index for Psoriatic Arthritis scores, which include patient-reported outcomes [PROs]). Women also had higher levels of pain and fatigue and worse QOL. Further, they were less likely to achieve a state of minimal disease activity (MDA).

Mease et al[15] investigated differences between men and women within the axial spondyloarthritis cohort of the Corrona registry. They found that women had higher disease activity measured by the Bath Ankylosing Disease Activity Index, as well as higher tender joint counts. Higher scores of PROs were also reported by women.

In this issue of *The Journal of Rheumatology*, Gossec et al[16] report on sex effect in a multicenter multinational cross-sectional study of 2270 patients with PsA, of whom 46% were women. Information was collected from physicians who performed clinical assessments, including skin and joint examinations, and from patients who completed patient-reported questionnaires. The only demographic difference between men and women was that

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more men were in full employment. The authors noted a higher mean swollen joint count in men, although more men had one or fewer swollen joints. The main differences were in PROs where women reported worse QOL (EuroQol 5-dimension questionnaire), higher levels of disability (Health Assessment Questionnaire [HAQ]–Disability Index), and higher 12-item Psoriatic Arthritis Impact of Disease scores, with both pain and fatigue being higher. Overall activity impairment measured by the Work Productivity and Activity Impairment questionnaire was also higher in women. In regression models that controlled for a number of variables, only HAQ scores and less activity impairment were retained. This information is important as it demonstrates that there are differences in the impact of disease between men and women. However, a major limitation was the lack of assessment of FM. As was shown in a previous study, the presence of FM affects the clinical assessment of patients with PsA.[13]

The observation that there are differences in reporting of pain and other PROs in patients with PsA is important, as it may have an effect on the results of clinical trials. Iannone et al[17] investigated the effect of FM, which includes many of the features previously reported to be worse in women, on response to therapy in patients with PsA. Of the 238 patients included in the study, 59 had concomitant FM. There were more women in the FM group, which had polyarticular disease and higher BMI than the group without FM. Importantly, drug survival was significantly lower among patients with FM, as were the rates of remission, low disease activity, or MDA.

There has been increasing interest in analyzing results of clinical trials by sex. In the SEAM-PsA (Study of Etanercept and Methotrexate in Subjects with Psoriatic Arthritis) trial comparing etanercept (ETN) monotherapy to methotrexate (MTX) monotherapy and combination ETN and MTX, men responded better only in the combination therapy group.[18] Other studies are currently underway.

In a disease that affects men and women equally, recognizing sex effect is important. Whether this effect is mediated through the presence of FM is not clear. Further studies are clearly needed to understand the mechanism of this sex effect.

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