EDITORIAL

Embracing fibromyalgia amongst spondyloarthritis – what's hidden behind extreme patient reported outcomes

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Fibromyalgia (FM) is an intricate disease in which the pain profile, being nociplastic in nature, carries most frequently hyperbolic descriptions by patients. This widespread pain syndrome is commonly surrounded by other characteristic traits as sleep disturbances, fatigue, headaches, depression and/or anxiety states, memory and concentration disruptions, and so on[1]. Estimates on the global FM prevalence circle 2-7%[2], and diagnosing it requires a clinically qualified physician. While some cases present themselves as undoubtedly FM, others might (at least initially) truly defy alternative differential hypothesis such as inflammatory myopathies, hyperparathyroidism or osteomalacia. Thus, some diagnostic/classification criteria have been proposed like the 1990 American College of Rheumatology (ACR) ones[3] or the Fibromyalgia Rapid Screening Tool (FiRST), the latter with sensitivity and specificity reports of 90.5% and 85.7%, respectively, for the detection of FM[4]. Further convoluting this interaction, FM may very well coexist with inflammatory rheumatic diseases as rheumatoid arthritis or spondyloarthritis (SpA), where a higher FM prevalence has been reported comparing to that of the general population[5].

SpA are a group of joint inflammatory diseases that might encompass axial and peripheral joint involvement, along with features of enthesitis, dactylitis, psoriasis, inflammatory bowel disease and uveitis[6], to name the most common ones. Especially on the axial disease, inflammatory back pain poses as the hallmark symptom, mainly due to sacroiliac joint or spine inflammation, but other conditions may superimpose such as vertebral fractures (in a higher osteoporosis risk disease) and degenerative musculoskeletal entities (either primary or secondary to the structural changes of a refractory/untreated SpA). Likewise, FM might emerge, and it has been projected to have a prevalence ranging from 11-25%[7,8] in these patients. In fact, FM tender points might overlap with enthesitis sites in around 10% of patients[9], and musculoskeletal morning stiffness might coexist as well, contributing to a disguised SpA diagnosis. Hence, it has been created a consensus-based definition of ultrasound-detected enthesitis in SpA and psoriatic arthritis, discerning it from non-inflammatory enthesitis[10]. Moreover, FM in SpA patients appears to associate with high baseline scores for Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Widespread Pain Index (WPI)[11]. One might conclude that high levels of disease activity may expedite FM's display, since a greater index of nociceptive pain (as in active SpA), mostly if unattended to, links in the long run to central sensitization, a peculiar element to FM. Nevertheless, clinicians must not belittle the uncertainty surrounding patient reported outcomes (PRO) when measuring disease activity. PRO imply a patient-centered report of a specific aspect of his health/disease status, and thus rely on the patient's level of education about his own condition, and whether channeling a specific event to it is a correct link. This is one of the reasons why patient's education on the rheumatic disease is of surmount value. Patients with both SpA and FM knowingly report higher BASDAI scores[5]. This instrument covers fatigue, morning stiffness, axial and entheseal pain, while the Bath Ankylosing Spondylitis Functional Index (BASFI) comprises everyday physical functioning. Both these scores, BASDAI and BASFI, have been significantly associated with WPI and Symptom Severity Scale (SSS) scores, but care should be taken since there is a fair overlap between questions under the BASDAI, SSS and WPI scores[8], while BASFI also relates to functions impacted by fatigue. Ergo, a definition of "extreme PRO" has been proposed[12], settled on a score ≥ 8 (on a 0-10 scale) on three out of the first five BASDAI questions: fatigue, spinal pain, peripheral arthritis, enthesitis and intensity of morning stiffness. The DESIR cohort[12] data amounted an "extreme PRO" prevalence of 13.4% among SpA patients, while others have stretched this number to 23.4%[13], and these patients were more likely to be female, with a lower educational level and a higher intake of antidepressants, a portrait that mimics some idiosyncrasies of most FM patients. These "extreme PRO"-stating subjects also receive TNFα-inhibitors more frequently, with lower response rates[12], undergo more biologic disease-modifying anti-rheumatic drugs (bDMARDs) switches

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and have lower retention rates for the first bDMARD[14]. So, recognizing concomitant FM is imperative to avoid overemphasizing the disease activity, which leads to unmatching therapeutic escalation. In this regard, "extreme PRO" has been validated, against FM's 1990 ACR classification criteria and the FiRST, as a highly specific surrogate marker of FM, in SpA patients[13]. When comparing a population of SpA patients going for a first-time use of TNFα-inhibitor at baseline and 12 weeks after, "extreme PRO" performed with a higher sensitivity and lower specificity at baseline (capturing some false FM diagnosis), progressing to a lower sensitivity but a higher specificity at the 12-week mark[13]. Initial high levels of pain and fatigue might indeed associate with SpA's high disease activity but, following treatment, those symptoms are more likely to be FM-related. On account of the established repercussion of this comorbidity on perceiving the treatment effect of anti-rheumatic drugs in SpA[15], appraising "extreme PRO" as plausible exclusion criteria in organized trials might be a prudent approach.

Physicians must not overlook that "extreme PRO" might be FM's manifestation of its native catastrophization, and thusly one has to integrate it in the overall clinical picture, counterbalancing it with the available biological and imaging markers, to most accurately assess SpA's circumstances. Due to its prevalence in SpA, FM must be screened, with a more vigorous intention if: we are inclined to initiate a bDMARD, we are evaluating a treatment's efficacy, the patient has a present or past history of peripheral joint symptoms or enthesitis, and in the presence of "extreme PRO". When firmly adamant of a coeval FM diagnosis, one should act upon it as well, exploring the benefits of long-term exercise (and other non-pharmacological options), supported by few symptomatic medications. Mitigating FM's distress will arguably decrease the "extreme PRO" construct and enhance the patient's quality of life.

Respecting the many virtues of Metrology applied to Medicine, and chiefly, to Rheumatology, one also has to esteem the physician (and his medical sense), who detains the required awareness to articulate that which is not integrable: the quantity with the quality, the symptoms with the scores, the biological markers with the array of its possible causative agents. A conscientious practice should be wary of the "extreme PRO".

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