

# Tender Points in Rheumatoid Arthritis — How Do They Help Us?



Decision making in rheumatoid arthritis (RA) is challenging. The disease is highly variable in its pattern of joint involvement, consequences of inflammation, course, and response to therapy. Pathologically, the primary disease process is synovial inflammation with resultant structural changes to joints, while clinically the patient is affected by pain and functional impairment. Since the introduction of gold compounds in 1932, the first RA disease-modifying drug<sup>1</sup>, a defined set of measures has been used to determine therapeutic efficacy: evaluation of joint swelling and tenderness, laboratory studies of inflammation, and radiography. Other assessment tools have been added, including instruments to measure functional impairment, genetic markers, and more advanced joint anatomic imaging studies. With the introduction of more effective RA therapies, the standard of care is now “treat to target,” with the target being remission of synovitis and improvement in its clinical manifestations<sup>2</sup>. While each disease assessment measure contributes to evaluating treatment response, all have limitations and must be used in concert for effective decision making.

In this issue of *The Journal*<sup>3</sup>, Ton and colleagues in the Utrecht Rheumatoid Arthritis Cohort study group assessed how the presence of tender points influenced the Disease Activity Score 28<sup>4</sup> (DAS28) in 196 patients with RA. They found that the tender point count significantly influenced the DAS28 score in the patient-reported components [tender joints and visual analog scale of global health (VAS-GH)] but not in the observer (swollen joint count) and laboratory-based [erythrocyte sedimentation rates (ESR)] components. Although the authors did not formally use the 1990 fibromyalgia (FM) classification criteria<sup>5</sup>, in individuals with  $\geq 11$  tender points at 18 survey sites, the DAS28 score was increased as compared to those with fewer tender points related to higher tender joint counts and VAS-GH scores. Similar results, but to a lesser extent, occurred in individuals in the 6–11 tender point group and the 1–5 tender point group. Finally, in individuals with DAS28 scores  $> 3.2$ , indicating active disease, 13% had no swollen joints. The authors concluded that tender points provided important

information to the DAS28 when making “treat to target” management decisions. In addition, evaluation of the individual components of the DAS28 composite score was helpful in disease activity assessment.

Pain is a particularly challenging musculoskeletal manifestation because there is no specific objective measurement; assessment relies solely on the patient’s description. The mechanism of RA pain is related to the effects of the synovitis on pain generators in joints, including the synovium, articular capsule, and subchondral bone, and the extension of the inflammatory process to the ligaments, tendons, and muscles around the joints. Secondary osteoarthritic changes can occur in RA, which can also cause pain. The correlation of pain and structural changes to radiographic and laboratory measures of inflammation are extremely variable. New understanding of pain processing has allowed further understanding of why these discrepancies may occur<sup>6</sup>. Although RA pain is initiated by nociceptive stimulation in joints, through inflammatory mediators including cytokines, there are other contributors, such as pain processing in the spinal cord and central brain and psychosocial factors<sup>7</sup>. Variations in spinal cord and brain processing have become increasingly well understood, including physiologic mechanisms and genetic factors such as polymorphisms of catechol-O-methyltransferase, GTP cyclohydrolase 1, and the voltage-gate sodium channel Nav 1.9<sup>8</sup>.

What do tender points tell us? Tender points are defined as localized specific areas in which pain is experienced on palpation<sup>9</sup>. The explanation of why various musculoskeletal tissues have different sensitivities to pain has not been fully elucidated<sup>10</sup>. Much of the focus of the specialty of rheumatology is on the immunologic inflammatory mechanisms involved in disease pathophysiology. Although pain is the cardinal manifestation of rheumatic disease, formal training and scientific investigation into pain mechanisms as a discipline has not typically been emphasized in the specialty. As rheumatologists, we must also be anatomists and pain physiologists in order to fully understand our patients’ pain. For example, of the 18 tender point survey sites in the 1990 FM

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See Look beyond the DAS28: tender points and DAS28 in RA, page 22

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classification criteria<sup>5</sup>, only 4 — the elbows and knees — are localized directly to joints, while 14 sites are found in muscle bodies, origins, or tendinous insertions. Like the manual examination of tender points for FM, the DAS28<sup>4</sup> provides a standardized protocol for the clinical evaluation of joint involvement in RA and is incorporated in many RA assessment tools. In the 28-joint count, pressure is applied to the joints, thus assessing pain generation directly from joint structures<sup>12</sup>. As demonstrated in the initial studies by Fuchs, *et al*<sup>13</sup> and van der Heijde, *et al*<sup>11</sup>, there may be discordance between the presence of observed joint swelling and the patient-reported joint tenderness. Further, of the 4 elements of the DAS28, the tender joint count, the swollen joint count, the VAS-GH, and the ESR, there is a differential weighting, with the tender joint count receiving twice the value of the swollen joint count. While the DAS28 is the standard-of-care measure for RA<sup>14</sup>, it has limitations, including the perception that it is difficult to perform, its sensitivity to determine change with lower or higher disease activity, it does not include function perimeters, and its validity in predicting remission.

Studies have shown that 12% to 17% of individuals with RA fulfill the 1990 FM classification criteria<sup>5</sup>, which can have an important influence on the manifestations of RA<sup>15</sup>. FM is thought to represent an alteration of pain processing with central amplification of pain<sup>16</sup>. The clinical criteria for FM include widespread pain lasting > 3 months; and ≥ 11 tender points in 18 survey sites may be present in other rheumatic diseases including systemic lupus erythematosus and Sjogren's syndrome. Studies evaluating RA and concomitant FM<sup>17,18,19,20,21</sup> demonstrate greater morning stiffness, impaired function, reduced quality of life, higher joint counts, and less erosive change on radiographs. These findings may contribute to higher DAS28 scores that are not directly related to inflammatory disease activity.

While synovitis is the anchoring point for assessment of RA, anchoring bias can arise because of the incomplete relationship among inflammation, structural change, and symptoms. The prediction models for managing RA have undergone a significant evolution, with decision making incorporating objective measures to determine levels of disease activity while allowing clinicians to use intuitive gestalt judgment. Yet the evaluation of joint swelling and tenderness, laboratory studies for inflammation and joint anatomic imaging alone have definite limitations in RA management, due to a lack of established criteria for their interpretation and to RA disease variability. It is clear that with the goal of achieving inflammatory and clinical remission in RA, proper pain assessment is also essential<sup>2</sup>. Care must be taken not to over- or under-adjust pharmacologic treatment related to pain that is not a reflection of inflammatory activity. Sir William Gowers stated in his 1904 article on lumbago<sup>22</sup>, which prompted interest in soft tissue rheumatism: We cannot wonder at our ignorance, still less complain of it,

for it is only quite recently that the minute structure of the sensory elements of muscle and tendon has been clearly perceived, and much of the normal structure still remains obscure.... We must therefore be content to wait, and content also meanwhile to rely on the apparent meaning of the symptoms of disease, as far as that meaning can be made out.

Gowers' statements remain true today. Tender points can provide important information for the evaluation and decision making in RA. Let's use them.

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