

## The association of neuropathic pain and disease activity, functional level, and quality of life in patients with ankylosing spondylitis: a cross-sectional study

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**Background/aim:** Increased neuropathic pain (NP) symptoms are seen in rheumatologic diseases such as fibromyalgia, osteoarthritis, and rheumatoid arthritis, but no studies have demonstrated a relationship between ankylosing spondylitis (AS) and NP except for a brain imaging study. The aim of this study was to estimate the presence of NP in patients with AS and to investigate how NP was related to disease activity, functional status, and quality of life.

**Materials and methods:** A total of 100 AS patients (71 males and 29 females; median age: 37 years, range: 18–71 years) were included in the study. Pain (visual analog scale (VAS) and the painDETECT questionnaire), disease activity (Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Maastricht Ankylosing Spondylitis Enthesitis Score (MASES), Patient Global Assessment of Disease Activity (PGA), and Ankylosing Spondylitis Disease Activity Score (ASDAS)), functional level (Bath Ankylosing Spondylitis Functional Index (BASFI)), and health-related quality of life (36-Item Short Form Survey (SF-36)) were evaluated. Patients were divided into two groups. Group 1 included patients with possible or likely NP symptoms (painDETECT score of  $\geq 13$ ) and Group 2 included patients without NP symptoms (painDETECT score of  $< 13$ ).

**Results:** Low back pain-VAS, peripheral joint-VAS, BASDAI, PGA, ASDAS, and BASFI scores were significantly higher in Group 1 compared to those of Group 2 ( $P < 0.05$ ). The SF-36 physical component (PC) score was significantly lower in Group 1 compared to that of Group 2 ( $P < 0.05$ ). There were no significant differences between the groups regarding SF-36 mental component (MC) scores, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) values and MASES scores. Total painDETECT scores correlated positively with low back pain-VAS, peripheral joint-VAS, morning stiffness-VAS, BASDAI, ASDAS-CRP, ASDAS-ESR, PGA, BASFI, and MASES scores and ESR values, and inversely with SF-36 PC scores.

**Conclusion:** Our results suggest that AS patients should be evaluated in terms of NP in order not to underestimate NP. If clinicians find evidence of likely NP, they should treat the patient with drugs that target NP.

**Key words:** Neuropathic pain, ankylosing spondylitis

### 1. Introduction

Ankylosing spondylitis (AS) is a rheumatic disease characterized by chronic inflammatory back pain due to sacroiliac joint and spine involvement. Peripheral joints and extraarticular findings should also be seen (1). It is now known that mixed pain patterns may develop in chronic diseases by the addition of a neuropathic pain (NP) component to existing pain mechanisms (2,3).

NP is caused by a lesion or disease affecting the somatosensory nervous system (4). It is maladaptive and continues even when the stimulus disappears (5). Burning, stinging pain is typically described. Abnormal sensations such as allodynia or hyperalgesia may be observed. The presence of symptoms of NP has been shown in rheumatic

diseases such as fibromyalgia (6,7), osteoarthritis (8,9), and rheumatoid arthritis (10,11).

There is only one recent study that indicated the presence of NP in AS (12). In that study, correlations of painDETECT scores and abnormal brain gray matter findings were shown. However, so far the relationship between NP and disease activity, functional status, quality of life, and demographic characteristics have not been investigated in AS.

AS differs from other rheumatic diseases such as rheumatoid arthritis as acute-phase reactants such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) values are not highly correlated with disease activity (13). Disease activity is evaluated with subjective

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methods in AS. The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) is the most widely used scale to determine disease activity in AS (14). The BASDAI has an important role in deciding treatment and follow-up. However, it is a subjective assessment consisting of questions about neck, hip, and back pain; peripheral joint pain; stiffness; fatigue; and tenderness on pressure and palpation (14). This index may be affected by accompanying NP symptoms. The NP symptoms cannot be treated with traditional antiinflammatory or disease-modifying drugs or biological agents. High disease activity and low functional level despite treatment in patients with AS may be due to the NP component.

The painDETECT questionnaire is the most widely used and accepted quantitative tool in the diagnosis of NP (15). It has been used in the diagnosis of NP in many musculoskeletal disorders such as fibromyalgia, low back pain, osteoarthritis, and rheumatoid arthritis (10,11,16–18). To date, use of the painDETECT questionnaire has not been reported widely in assessments of people with AS.

We aimed to investigate the presence of NP in patients with AS using the painDETECT questionnaire and to investigate the relationship between NP and disease activity, functional status, and quality of life.

## 2. Materials and methods

We conducted a study of 100 participants (71 males and 29 females) with AS diagnosed based on the modified New York criteria (19) from the Rheumatologic Diseases Outpatient Clinic of the Physical Medicine and Rehabilitation Department. Demographic data including age, sex, education level, current tobacco or alcohol use, current treatment, use of nonsteroid antiinflammatory drugs (NSAIDs) or disease-modifying antirheumatic drugs (DMARDs), and biological therapies were also recorded. Ethical approval for this study was provided by the local ethics committee. All patients provided written informed consent.

Participants were interviewed during routine clinic appointments and identified from clinic records. They were eligible to participate in the study if their treatment had been stable for the previous 3 months. Patients who had neuropsychiatric conditions (e.g., radiculopathy, polyneuropathy, neuropathy, depression, fibromyalgia) and/or musculoskeletal disorders (e.g., surgery, fracture) and/or endocrine diseases (e.g., diabetes mellitus) and/or malignancy were excluded based on their history and clinical examination.

## 2.1. Measures

### 2.1.1. Pain assessment tools

#### 2.1.1.1. Visual analog scale (VAS) (0–10)

The VAS was used to record each patient's current level of low back pain and peripheral joint pain, with 0 indicating no pain and 10 indicating the worst pain that the patient had ever experienced. Using a ruler marked in centimeters, the examiner obtained the exact values along a 10-cm VAS line.

#### 2.1.1.2. Morning stiffness

The patient's current duration of morning stiffness was recorded, with 0 indicating no stiffness and 10 indicating stiffness lasting  $\geq 2$  h.

#### 2.1.1.3. painDETECT questionnaire

NP symptoms were assessed using the Turkish version of the painDETECT questionnaire (20). It consists of seven items evaluating pain qualities, one evaluating the course of pain, and one evaluating pain radiation. Additionally, the questionnaire contains three numerical rating scales (NRSs) of 0–10 for current, worst, and average pain severity. An overall score is generated that summarizes everything but the pain intensity NRS, which ranges between –1 and 38. An overall score of  $>18$  indicates likely NP, 13–18 possible NP, and  $<13$  unlikely NP. The Turkish validation of the painDETECT questionnaire was reported by Alkan et al. (20).

### 2.1.2. Assessment of disease activity

#### 2.1.2.1. Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)

The BASDAI has six NRSs of 0–10 to measure the severity of fatigue, spinal and peripheral joint pain, localized tenderness, and morning stiffness in patients with AS. The final BASDAI score has a range of 0–10, with lower numbers representing less severe disease activity (14). A score of 4 has been determined as the BASDAI cut-off value for assessment of disease activity; that is, BASDAI values of greater than 4 indicate the presence of active disease. The Turkish validation of the BASDAI was reported by Akkoc et al. (21).

#### 2.1.2.2. Maastricht Ankylosing Spondylitis Enthesitis Score (MASES)

The number of tender entheses is rated by the MASES. To assess the MASES, the investigator applies pressure over 13 different entheses. The patients' response to firm palpation over these entheses is noted (0 = absence of tenderness; 1 = presence of tenderness). The entheses sites assessed were the bilateral first costochondral joints, seventh costochondral joints, posterior superior iliac spines, anterior superior iliac spines, iliac crests, proximal insertion of the Achilles tendons, and fifth lumbar spinal process. The total score ranges from 0 to 13 (22).

### 2.1.2.3. Patient Global Assessment of Disease Activity (PGA)

The PGA is scored from 0 (very well) to 10 (very bad) based on a VAS. All aspects of disease including activity, function, and structural damage are evaluated from the patient's point of view. The Assessment of Spondyloarthritis International Society (ASAS) recommends the use of the PGA as an important component of clinical assessment (22).

### 2.1.2.4. Ankylosing Spondylitis Disease Activity Score (ASDAS)

The ASDAS is a composite score of patient-reported measures and acute-phase reactants that was developed in order to capture both the subjective and objective aspects of AS disease activity (23,24). There are four versions of the ASDAS. We used the ASDAS-ESR and ASDAS-CRP. The ASDAS has been validated and found to be discriminatory in assessing disease activity (25).

### 2.1.3. Assessment of functional level

#### 2.1.3.1. Bath Ankylosing Spondylitis Functional Index (BASFI)

The BASFI is used for the assessment of physical functioning in patients with AS. It includes tasks for which the patients rate their own ability by marking a vertical line on a 100-mm horizontal line. The ten tasks comprising the BASFI are as follows: 1) putting on socks, 2) bending forward to pick up a pen, 3) reaching a high shelf, 4) getting up from an armless chair, 5) getting up from the floor from lying supine, 6) standing unsupported, 7) climbing steps without a handrail, 8) looking over one's shoulders, 9) performing physically demanding activities, and 10) doing a full day's activities. The total BASFI score is calculated by adding all ten scores and dividing by 10. The Turkish validation of the BASDAI was reported by Kartepe et al. (26).

### 2.1.4. Assessment of health-related quality of life

Health status was measured using the 36-Item Short Form (SF-36) Health Survey, version 2 (SF-36v2), which assesses eight different aspects of health (27). Item scores can be aggregated into physical component (PC) summary and mental component (MC) summary scores. The Turkish validation of the SF-36 was shown by Koçyiğit et al. (28).

### 2.2. Statistical analyses

All data were analyzed using the Number Cruncher Statistical System (2007). Normality of distribution of variables was analyzed by the Shapiro–Wilk test. Patients were divided into two groups as Group 1, including patients with possible or likely NP symptoms (painDETECT score of  $\geq 13$ ), and Group 2, including patients without NP symptoms (painDETECT score of  $< 13$ ). Since variables were distributed nonnormally, differences between the groups were examined using Mann–Whitney U tests for continuous variables and chi-square tests (with the Yates

continuity correction as appropriate) for categorical variables. Continuous variables were presented as descriptive statistics (median, minimum–maximum) and categorical variables were recorded as numbers (n) and percentages (%). Statistical significance was considered at  $P < 0.05$ .

In order to evaluate the correlations between painDETECT scores and the other parameters, Spearman correlations were used.

Post hoc power levels of differences that were statistically meaningful were calculated and these observed differences had a very high rate of fixation capabilities (99.4%–100%). The G\*Power program was used (Tables 1 and 2).

## 3. Results

### 3.1. Patient characteristics

One hundred patients (median age: 37 years, range: 18–71 years; females/males (n): 29/71) fulfilled the criteria and completed the study. Median disease duration of patients was 5 years (1–32 years). Percentage of smoking history and alcohol use was 55% and 16%, respectively. Of the 100 patients, 47% were being treated with sulfasalazine and/or NSAIDs and 53% were being treated with a biologic agent alone or combined with sulfasalazine at the time of the study.

### 3.2. Pain evaluation

The median low back pain-VAS score was 5 (0–10) and the median peripheral joint pain-VAS score was 4 (0–10). The median stiffness VAS score was 2 (0–10). Of the 100 patients, 75% had unlikely NP components, 11% had possible NP components, and 14% had likely NP components according to painDETECT scores.

### 3.3. Disease activity

Most patients had well-controlled disease activity according to their BASDAI scores. Fifty-four of the 100 patients (54%) were in remission (BASDAI score of  $< 4$ ). The PGA disease activity median score was 5 (0–10). The MASES median score was 1 (0–13). The ASDAS-CRP and ASDAS-ESR median scores were 2.1 and 2.6, respectively. Twenty-one patients (21%) and 4 patients (4%) were in remission according to the ASDAS-CRP and ASDAS-ESR, respectively.

### 3.4. Functional level and quality of life

The median BASFI score was 2.7 (0–9). The median PC and MC score of the SF-36 was 36.9 (19.8–61.0) and 44.2 (21.5–57.8), respectively.

### 3.5. Comparison of groups according to painDETECT scores

Patients were divided into two groups: Group 1, patients with possible or likely NP symptoms (painDETECT score of  $\geq 13$ ), and Group 2, patients without NP symptoms (painDETECT score of  $< 13$ ). There was no significant

**Table 1.** Comparison of pain level, disease activity, functional level, and quality of life between groups.

|                                                                   | Group 1 (n = 22)           | Group 2 (n = 78)           | P       | Power  |
|-------------------------------------------------------------------|----------------------------|----------------------------|---------|--------|
| Low back pain-VAS score, median (min-max) / mean $\pm$ SD         | 7.0 (0-10) / 6.6 $\pm$ 2.4 | 4.0 (0-10) / 3.6 $\pm$ 2.7 | <0.0001 | 98.6%  |
| Peripheral joint pain-VAS score, median (min-max) / mean $\pm$ SD | 6.0 (0-10) / 6.1 $\pm$ 2.4 | 2.0 (0-8) / 2.8 $\pm$ 2.5  | <0.0001 | 100%   |
| Stiffness-VAS score, median (min-max) / mean $\pm$ SD             | 5.0 (0-10) / 5.3 $\pm$ 2.9 | 2.0 (0-10) / 2.5 $\pm$ 2.6 | 0.003   | 99.99% |
| BASDAI score                                                      | 5.0 (2.2-9)                | 3.2 (0-10)                 | <0.0001 | 99.99% |
| PGA score                                                         | 6.0 (0-10)                 | 4.0 (0-10)                 | 0.004   | 98.5%  |
| MASES score                                                       | 2.5 (0-11)                 | 1.0 (0-13)                 | 0.055   | 99.99% |
| ASDAS-CRP score                                                   | 2.9 (0.6-4.6)              | 2.0 (0.6-3.9)              | <0.0001 | 99.99% |
| ASDAS-ESR score                                                   | 3.2 (1-4.6)                | 2.4 (0.6-4.5)              | <0.0001 | 99.99% |
| BASFI score                                                       | 5.4 (0-9)                  | 2.05 (0-9.1)               | 0.001   | 99.99% |
| SF-36 PC score                                                    | 31.9 (19.8-48.7)           | 41.3 (23.6-61.0)           | <0.0001 | 99.99% |
| SF-36 MC score                                                    | 40.7 (21.5-58.4)           | 44.5 (20.9-57.8)           | 0.482   |        |
| Erythrocyte sedimentation rate, mm/h                              | 12.0 (4-82)                | 9.0 (1-76)                 | 0.381   |        |
| C-reactive protein, mg/dL                                         | 0.4 (0.1-4.4)              | 0.32 (0.02-1.6)            | 0.312   |        |

Variables are presented as median (min-max) and were analyzed by Mann-Whitney U test.

VAS: Visual analog scale; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; PGA: Patient Global Assessment of Disease Activity; BASFI: Bath Ankylosing Spondylitis Functional Index; ASDAS: Ankylosing Spondylitis Disease Activity Score; SF-36 PC: SF-36 Short Form Physical Component; SF-36 MC: SF-36 Short Form Mental Component.

**Table 2.** Correlation of painDETECT scores with outcome parameters.

|                                  | painDETECT |         | Power |
|----------------------------------|------------|---------|-------|
|                                  | r          | P       |       |
| Low back pain-VAS (0-10)         | 0.477      | <0.0001 | 100%  |
| Morning stiffness-VAS (0-10)     | 0.413      | <0.0001 | 99.4% |
| Patient global assessment (0-10) | 0.403      | <0.0001 | 99.3% |
| Peripheral joint-VAS (0-10)      | 0.406      | <0.0001 | 99.4% |
| BASDAI                           | 0.589      | <0.0001 | 100%  |
| BASFI                            | 0.509      | <0.0001 | 100%  |
| MASES (0-13)                     | 0.248      | 0.013   |       |
| SF-36 MC                         | 0.264      | 0.015   | 77%   |
| ESR                              | 0.228      | 0.022   | 52.8% |
| ASDAS-CRP                        | 0.503      | <0.0001 | 100%  |
| ASDAS-ESR                        | 0.523      | <0.0001 | 100%  |

difference between groups regarding demographic characteristics (Table 3). Low back pain-VAS scores, peripheral joint-VAS scores, BASDAI scores, PGA scores,

ASDAS-CRP and ASDAS-ESR scores, and BASFI scores were significantly higher in Group 1 compared to those of Group 2. SF-36 PC scores were significantly lower in

**Table 3.** Comparison of demographic properties between groups.

|                                                           | Group 1 (n = 22)                 |          | Group 2 (n = 78)                 | P     |
|-----------------------------------------------------------|----------------------------------|----------|----------------------------------|-------|
| Age, median (min–max) / mean $\pm$ SD, years              | 39.5 (27–66) / 41.7 $\pm$ 8.9    |          | 36.0 (18–71) / 38.4 $\pm$ 9.4    | 0.080 |
| Sex, n (%)                                                | 7 females (31%), 15 males (49%)  |          | 22 females (29%), 56 males (71%) | 0.466 |
| Disease duration, median (min–max) / mean $\pm$ SD, years | 4.0 (1–30) / 9.5 $\pm$ 9.7       |          | 6.0 (1–32) / 8.9 $\pm$ 7.8       | 0.776 |
| Education status                                          |                                  | n (%)    | n (%)                            | 0.759 |
|                                                           | Primary school                   | 10 (10%) | 26 (26%)                         |       |
|                                                           | Junior high school               | 3 (3%)   | 8 (8%)                           |       |
|                                                           | High school                      | 4 (4%)   | 21 (21%)                         |       |
|                                                           | University                       | 5 (5%)   | 22 (22%)                         |       |
| Current treatments                                        |                                  | n (%)    | n (%)                            | 0.389 |
|                                                           | NSAIDs                           | 5 (5%)   | 20 (20%)                         |       |
|                                                           | NSAIDs and sulfasalazine         | 5 (5%)   | 18 (18%)                         |       |
|                                                           | Sulfasalazine                    | 1 (1%)   | 0 (0%)                           |       |
|                                                           | Biologic agent                   | 8 (8%)   | 33 (33%)                         |       |
|                                                           | Biologic agent and sulfasalazine | 3 (3%)   | 7 (7%)                           |       |
| Smoking                                                   | 15 (68.2%)                       |          | 40 (51.3%)                       | 0.404 |
| Alcohol use                                               | 4 (18.1%)                        |          | 14 (17.9%)                       | 0.599 |

Continuous variables are presented as median (min–max) and categorical data are presented as n (%). Categorical data were analyzed using the chi-square test ( $\chi^2$ ) and continuous variables were analyzed by the Mann–Whitney U test.

Group 1 compared to Group 2. There was no significant difference between groups regarding SF-36 MC scores, ESR values, CRP levels, and MASES scores (Table 1).

### 3.6. Correlation of painDETECT scores and other parameters

Total painDETECT scores correlated moderately with BASDAI scores ( $r < 0.589$ ,  $P < 0.0001$ ), low back pain-VAS scores ( $r = 0.477$ ,  $P < 0.0001$ ), peripheral joint-VAS scores ( $r = 0.406$ ,  $P < 0.0001$ ), morning stiffness-VAS scores ( $r = 0.413$ ,  $P < 0.0001$ ), PGA scores ( $r = 0.403$ ,  $P < 0.0001$ ), ASDAS-CRP scores ( $r = 0.503$ ,  $P < 0.0001$ ), ASDAS-ESR scores ( $r = 0.523$ ,  $P < 0.0001$ ), and BASFI scores ( $r = 0.509$ ,  $P < 0.0001$ ). A weak correlation between painDETECT scores and MASES scores ( $r = 0.248$ ,  $P = 0.013$ ) and ESR values ( $r = 0.228$ ,  $P = 0.022$ ), along with a weak inverse correlation with SF-36 PC scores ( $r = -0.264$ ,  $P = 0.015$ ), were also observed (Table 2).

### 4. Discussion

In this study, we found that 25% of patients with AS probably have NP as determined by the painDETECT questionnaire. Patients with NP symptoms have higher VAS scores for low back pain, peripheral joint pain,

morning stiffness, and PGA, along with higher BASDAI scores and lower BASFI and SF-36 scores, as compared to patients without NP symptoms.

There may be a neuropathic component that affects pain perception in AS. It was proposed by Pollard et al. that arthritic joints expand their total receptive field to the surrounding noninflamed tissue, called peripheral sensitization (29). Another peripheral mechanism in the development of neuropathic pain in AS patients could be the focal demyelination of nonnociceptive, large myelinated fibers in those patients (30).

Inflammatory radiculopathy without any mechanic compression advanced by local inflammation of the axial spine in AS may be another peripheral mechanism (31). Dysregulation of central pain processing mechanisms and central sensitization is the underlying pathology of NP. Wu et al. (12) showed that higher painDETECT scores in AS patients were found to be correlated with thinning of the primary somatosensory cortex and thickening of the primary motor cortex. The study of Wu et al. is valuable since it showed objective findings of central sensitization, which supports the reliability of painDETECT in assessing neuropathic pain.

Wu et al. also demonstrated that back pain includes a NP component in more than half of patients with AS (12). In our study, we found this rate to be 25%. We investigated 100 AS patients and the associations between painDETECT scores and clinical parameters. However, Wu et al. included only 17 patients in their study. The reason for this higher ratio may be the smaller sample size. However, the aim of Wu et al. was to investigate the correlation between painDETECT scores and the sensory thresholds measured by a standardized set of von Frey filaments and a computer-controlled Peltier device (TSA-II NeuroSensory Analyzer, Medoc) and the functional MRI findings, and their sample size was adequate for such a study.

Despite almost 60% of patients being in remission according to BASDAI scores, 65% still reported clinically significant low back pain and 53% peripheral pain. According to the painDETECT questionnaire, 14% of all patients had likely NP, while 11% had possible NP features.

These patients were shown to have more severe pain, lower functional level and quality of life, and higher disease activity. Clinically significant pain was defined as an average pain score of  $\geq 4$ . This threshold was based on several previous studies that identified pain intensity levels of  $\geq 4$  out of 10 as moderate to severe or unacceptable (32,33).

In our study, patients receiving treatment for at least for 3 months were included in order to exclude untreated patients. This suggests that other pain mechanisms together with inflammation may play a role since pain control remains inadequate although patients are in remission (34).

There are some recent studies that evaluated NP in rheumatic diseases. Koop et al. (11) found similar results in patients with rheumatoid arthritis. They found 17% likely and 24% probable NP in their survey. Similar to our results, they found high VAS scores ( $>4$ ), although the majority of the patients were in remission according to the DAS-28. In another study by Meirinhos et al. (35), 19% of rheumatoid arthritis patients having likely NP prevalence was reported. Contrary to these results, Ahmed et al. (10) showed that a large proportion of subjects with rheumatoid arthritis demonstrated likely or probable NP features based on painDETECT scores. However, the proportion of AS patients with likely NP was lower than that reported by Wu et al. (12). NP symptoms have been reported much more in patients with osteoarthritis (8,9,36) and fibromyalgia (6,7). Further studies should be designed to evaluate NP frequency in AS patients with larger sample sizes.

No previous studies examined correlations of NP symptoms with disease activity, functional level, and quality of life in patients with AS. In the current study,

NP symptoms were not related to any of the demographic features. However, painDETECT scores were correlated with BASDAI scores, PGA scores, BASFI scores, and the PC of SF-36 scores. A similar relationship was shown in rheumatoid arthritis patients by Koop et al. (11). Ahmad et al. (10) found that people with rheumatoid arthritis prescribed a combination of biologics and DMARDs had an overall high mean VAS score compared with other groups, despite DAS-28 scores suggesting good control of disease activity. In our study, we did not evaluate the subgroups according to current medications. However, scores for the VAS, BASDAI, BASFI, PC of SF-36, and other parameters did not differ between patients with NP and patients without NP. On the other hand, we showed that although 60% of patients were in remission according to the BASDAI, 65% of the patients had high VAS scores. The results of our study and those of Ahmad et al. suggest that disease activity measures may be affected by NP rather than by inflammation alone (10).

The BASDAI is the most widely used activity indicator in both routine clinical practice and drug trials in which the efficacy of novel drugs are tested (14,37). However, the BASDAI is a self-reported questionnaire and does not include any objective parameters. It may be influenced by other diseases. Potential factors that may influence these scores should also be taken into account, such as NP, other coexisting musculoskeletal disorders such as fibromyalgia, and depression (38). Otherwise, overtreatment or inadequate treatment could be an outcome in some AS patients since treatment strategies are planned according to BASDAI scores. We also utilized the ASDAS since it is a more objective disease activity assessment tool because it includes CRP and/or ESR values in addition to patient-reported assessments. Some researchers have concluded that the ASDAS-CRP and ASDAS-ESR discriminate high and low disease activity better than the BASDAI or acute-phase reactants (39,40). However, we found similar results from the ASDAS and BASDAI. The reason for this result may be the normal ranges of ESR and CRP values of the patients who received at least 3 months of therapy before the study. We thus concluded that the reason for this difference was not inflammation.

Medications are expensive and can have serious side effects. Although drugs targeting inflammation are known to have no effect on NP mechanisms, one study by Wu et al. (41) showed that after tumor necrosis factor inhibitor (TNFi) treatment, AS patients had partially reversed hyposensitivity in thermal and mechanical detection, compared with healthy subjects, of the foot. They showed that TNFi attenuates the NP component of AS in addition to reversing sensory loss and improving lateral spinal mobility. However, in our study, there were no differences in terms of medications between AS patients with NP and

patients without NP. Despite the findings of Wu et al., we recommend that treatment decisions and alterations be made after the treatment of accompanying NP.

Our study has several strengths. First, it showed the correlation between the painDETECT questionnaire and clinical data, BASDAI and BASFI scores, and quality of life. This gives insight into the origin of pain in AS patients, and also the effect of NP on the daily life (42). Another strength of our study was excluding patients with comorbidities, including obesity, fibromyalgia, diabetes mellitus, smoking, and secondary osteoarthritis, which might exacerbate pain in AS (43). Recent studies have shown that the majority of AS patients have accompanying fibromyalgia (44–46), often considered the prototypical central pain syndrome (47). Based on this knowledge, we evaluated our patients with the 2010 American College of Rheumatology fibromyalgia criteria and excluded the patients with fibromyalgia.

Depression and anxiety also contribute to BASDAI scores. Although we excluded patients who had known depression or mood disorders and were receiving antidepressants, we did not evaluate the patients with a

screening tool for depression or anxiety. This may be a potential limitation of our study. There are some other limitations of this study. The number of patients was relatively small, with 100 participants recruited. NP in patients with AS should be further studied with larger sample sizes. The patients included in this study were recruited from normal daily clinical practice and were receiving at least 3 months of therapy, and therefore closely resembled current ‘well-controlled’ AS patients. The findings, however, may not be applicable to all AS populations. Additionally, the cross-sectional nature of this study does not allow any determination of the direction of associations between NP symptoms and clinical variables.

In conclusion, mixed pain patterns may be seen in some patients with AS. This condition is related to high disease activity and poor functional level and quality of life. Clinicians could evaluate people with AS using painDETECT in order not to underestimate NP. If clinicians find evidence of likely NP, they should treat the patient with drugs targeting NP. Disease activity should be reevaluated after NP treatment in order to avoid overtreatment of patients with AS.

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