

# Determinants of diagnostic delay in spondyloarthritis: How do demographic attributes, sub-phenotypes, and extra-musculoskeletal manifestations affect the delay?

Spondiloartritte tanı gecikmesinin belirleyicileri: Demografik özellikler, alt fenotipler ve kas-iskelet dışı tutulumlar gecikmeyi nasıl etkiler?

Emel Oğuz Kökoğlu<sup>1</sup>, Hüseyin Kaplan<sup>2</sup>, Melih Kızıltepe<sup>1</sup>, Tuğba Kahraman Denizhan<sup>3</sup>, Celil Barlas Cengiz<sup>4</sup>,  
Abdurahman Soner Şenel<sup>4</sup>

<sup>1</sup>Kayseri City Education and Research Hospital, Clinic of Internal Medicine, Division of Rheumatology, Kayseri, Türkiye

<sup>2</sup>Aksaray Training and Research Hospital, Clinic of Rheumatology, Aksaray, Türkiye

<sup>3</sup>Malatya Training and Research Hospital, Clinic of Rheumatology, Malatya, Türkiye

<sup>4</sup>Erciyes University Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, Kayseri, Türkiye

## Abstract

**Objective:** To investigate the determinants of diagnostic delay in patients with spondyloarthritis (SpA), focusing on the complex interplay of demographic attributes, clinical sub-phenotypes, and extra-musculoskeletal manifestations (EMMs).

**Methods:** This retrospective cohort study included 371 patients diagnosed with SpA according to Assessment of SpondyloArthritis International Society criteria, comprising 289 axial SpA (70.6% radiographic, 29.4% non-radiographic), 82 peripheral SpA, 12 psoriatic arthritis, and 24 enteropathic arthritis phenotypes. Demographic data, presence of EMMs (uveitis, psoriasis, inflammatory bowel disease), and disease-related parameters were recorded. Diagnostic delay was defined as the time between symptom onset and formal diagnosis, with a prolonged interval categorized as >3 years based on the cohort's median delay. Multivariable logistic regression analyses were performed to identify independent predictors.

**Results:** The median diagnostic delay was 3.0 years. In the multivariable model, a younger age at symptom onset emerged as a robust independent predictor of prolonged diagnostic delay ( $p<0.001$ ). Furthermore, female sex was significantly and independently associated with an increased risk of prolonged delay (adjusted odds ratio: 1.723, 95% confidence interval: 1.075-2.761,  $p=0.024$ ). Conversely, the consolidated peripheral SpA sub-phenotype was significantly associated with a reduced diagnostic interval ( $p<0.05$ ). Notably, the individual presence of specific EMMs (uveitis, psoriasis, inflammatory bowel disease) or body mass index did not independently accelerate or significantly influence the diagnostic timeline.

## Özet

**Amaç:** Spondiloartrit (SpA) hastalarında tanı gecikmesinin belirleyicilerini; demografik özellikler, klinik alt fenotipler ve kas-iskelet dışı tutulumların (EMM'lerin) arasındaki karmaşık etkileşime odaklanarak incelemektir.

**Yöntem:** Bu retrospektif kohort çalışmasına, *Assessment of SpondyloArthritis International Society* kriterlerine göre SpA tanısı almış, 289 aksiyel SpA (%70,6 radyografik, %29,4 non-radyografik), 82 periferik SpA, 12 psöriyatik artrit ve 24 enteropatik artrit fenotipinden oluşan toplam 371 hasta dahil edilmiştir. Demografik veriler, EMM varlığı (uveit, psöriyazis, enflamatuvar barsak hastalığı) ve hastalık aktivite parametreleri kaydedilmiştir. Tanı gecikmesi, semptomların başlaması ile resmi tanı konulması arasındaki süre olarak tanımlanmış; uzamış tanı süresi, kohortun medyan gecikme süresi temel alınarak >3 yıl olarak kategorize edilmiştir. Bağımsız öngördürücüler belirlemek amacıyla regresyon analizleri uygulanmıştır.

**Bulgular:** Medyan tanılama gecikme süresi 3,0 yıl olarak saptanmıştır. Çok değişkenli (multivaryant) modelde, semptom başlangıcında genç yaşta olmanın, uzamış tanı gecikmesinin güçlü bir bağımsız öngördürücüsü olduğu belirlenmiştir ( $p<0.001$ ). Ayrıca, kadın cinsiyeti uzamış gecikme riski ile anlamlı ve bağımsız bir şekilde ilişkili bulunmuştur (düzeltilmiş olasılık oranı: 1,723, %95 güven aralığı: 1,075-2,761,  $p=0,024$ ). Aksine, konsolide periferik SpA alt fenotipinin tanı süresini anlamlı derecede kısalttığı görülmüştür ( $p<0,05$ ). Dikkat çekici bir şekilde, spesifik EMM'lerin (uveit, psöriyazis, enflamatuvar barsak hastalığı) bireysel varlığının veya vücut kitle indeksinin tanı sürecini bağımsız olarak hızlandırdığı veya tanı takvimi üzerinde anlamlı bir etki göstermediği belirlenmiştir.

**Correspondence / İletişim:** Emel Oğuz Kökoğlu MD,

Kayseri City Education and Research Hospital, Clinic of Internal Medicine, Division of Rheumatology, Kayseri, Türkiye

**E-mail:** dr\_eoguz@hotmail.com **ORCID ID:** orcid.org/0000-0002-5475-2182

**Received / Geliş Tarihi:** 13.04.2026 **Accepted / Kabul Tarihi:** 30.09.2026 **Epub:** 01.10.2026

**Cite this article as / Atf:** Oğuz Kökoğlu E, Kaplan H, Kızıltepe M, Kahraman Denizhan T, Cengiz CB, Şenel AS. Determinants of diagnostic delay in spondyloarthritis: how do demographic attributes, sub-phenotypes, and extra-musculoskeletal manifestations affect the delay? J Turk Soc Rheumatol. [Epub Ahead of Print]

## Abstract

**Conclusion:** Our findings demonstrate that early-onset disease and female sex are primary clinical barriers to timely diagnosis in SpA, whereas the consolidated peripheral sub-phenotype significantly accelerates clinical recognition. Paradoxically, the presence of specific EMMs does not provide a distinct diagnostic advantage in accelerating this process, underscoring the urgent need for multi-faceted screening strategies and heightened clinical suspicion in primary care.

**Keywords:** Spondyloarthritis, diagnostic delay, extra-musculoskeletal manifestations, age at symptom onset, clinical sub-phenotypes

## Introduction

Spondyloarthritis (SpA) represents a diverse group of chronic inflammatory rheumatic diseases characterized by axial skeleton involvement, which can lead to severe pain, structural damage, and significant disability.<sup>[1]</sup> SpA is predominantly characterized by inflammation within the sacroiliac joints; however, its clinical manifestations frequently encompass the vertebral column, peripheral joints, and various entheses, such as capsules and ligaments.<sup>[2]</sup> Beyond the musculoskeletal system, SpA is renowned for its heterogeneous extra-musculoskeletal manifestations (EMMs), which vary significantly in both frequency and severity.<sup>[3]</sup> Acute anterior uveitis, psoriasis, and inflammatory bowel disease (IBD) represent the most frequent extra-musculoskeletal features, whereas less common systemic complications involving the cardiovascular, respiratory, integumentary, and renal systems are also recognized in the clinical literature.<sup>[3]</sup> These manifestations not only increase the disease burden but also necessitate a multidisciplinary diagnostic approach.

Despite advancements in imaging modalities and the widespread use of the Assessment of SpondyloArthritis International Society (ASAS) classification criteria<sup>[4]</sup>, diagnostic delay remains a formidable challenge in SpA management.<sup>[5]</sup> Literature indicates that the delay between symptom onset and formal diagnosis typically ranges from 8 to 10 years—a duration considerably longer than that seen in many other rheumatic conditions.<sup>[5]</sup> This prolonged delay is closely associated with poorer clinical outcomes, including irreversible functional impairment, structural progression, and diminished quality of life.<sup>[5]</sup>

Recent studies have identified several factors influencing this diagnostic gap, such as specific demographic attributes including sex (with longer delays often noted in females), age at symptom onset, as well as clinical sub-phenotypes like the presence or absence of peripheral arthritis.<sup>[6-8]</sup> However, while the impact of musculoskeletal symptoms is well-studied, the literature specifically examining how the presence of EMMs influences the diagnostic journey remains relatively sparse and conflicting. Some reports suggest that EMMs may facilitate earlier diagnosis by prompting specialist referrals, while others indicate they may obscure the primary rheumatological diagnosis.<sup>[5,9]</sup> Therefore,

## Özet

**Sonuç:** Bulgularımız, erken yaşta başlayan hastalığın ve kadın cinsiyetinin SpA'da zamanında tanı konulmasının önündeki temel klinik engeller olduğunu; konsolide periferik alt fenotipin ise klinik tanınmayı anlamlı derecede hızlandığını göstermektedir. Paradoksik olarak, spesifik EMM'lerin varlığı bu süreci hızlandırmada belirgin bir tanısal avantaj sağlamamakta; bu durum, birinci basamak sağlık hizmetlerinde çok yönlü tarama stratejilerine ve klinik şüphenin artırılmasına duyulan acil ihtiyacı vurgulamaktadır.

**Anahtar Kelimeler:** Spondiloartrit, tanısal gecikme, ekstra-muskuloskeletal manifestasyonlar, semptom başlangıç yaşı, klinik alt fenotipler

this study aims to investigate the complex interplay of these demographic attributes, sub-phenotypes, and EMMs, and to delineate their direct impact on diagnostic delay within a large SpA cohort.

## Materials and Methods

### Study Design and Patient Selection

A retrospective cohort was established by identifying patients who satisfied the standardized ASAS classification criteria framework for SpA in general<sup>[4,10]</sup> and were followed up at the Erciyes University Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, between December 2011 and December 2024. Depending on their predominant clinical presentation at baseline, patients were classified under the respective axial or peripheral SpA criteria algorithms. The overall study cohort comprised a comprehensive, real-world spectrum of axial and peripheral SpA, including patients with psoriatic arthritis (PsA) and IBD-associated SpA phenotypes. Patients with PsA were identified according to the Classification Criteria for Psoriatic Arthritis (CASPAR).<sup>[11]</sup> IBD-associated SpA (enteropathic arthritis) was defined by the presence of confirmed IBD (Crohn's disease or ulcerative colitis) together with associated SpA. All patients were subsequently classified according to their predominant musculoskeletal phenotype using the ASAS classification criteria for axial SpA or peripheral SpA. Thus, PsA and IBD-associated SpA represented clinical phenotypes within the study cohort, whereas axial versus peripheral SpA classification was used as the SpA subtype variable in the analyses.

The study cohort consisted of 371 patients whose data were extracted from medical records. This study was approved by the Erciyes University Health Sciences Research Ethics Committee (approval no: 2025/149, date: 19.03.2025). The Ethics Committee waived the need for informed consent because our study was retrospective in nature.

### Data Collection and Clinical Parameters

For each participant, an extensive range of information encompassing clinical history, demographic characteristics,

and socioeconomic status was collected using a structured data collection form.

**Demographics and Socioeconomic Status:** Recorded parameters included age, sex, and body mass index (BMI, kg/m<sup>2</sup>). Socioeconomic factors were categorized by educational level (primary school, high school, or university), marital status (married, single, divorced, or widowed), and residential area (rural or urban).

### Disease Chronology

- Age at symptom onset: Defined as the age at which the patient first experienced inflammatory back pain or other SpA-related symptoms.
- Age at diagnosis: Defined as the age at which the formal SpA diagnosis was established by a rheumatologist.
- Diagnostic delay: Calculated as the time interval (years) between the age at symptom onset and the age at diagnosis.
- Disease duration: Calculated as the time elapsed (years) from the date of formal diagnosis to the time of study enrollment (or the last follow-up visit).

**Clinical Phenotype and Manifestations:** EMMs, specifically uveitis, psoriasis, and IBD, were recorded as present or absent, strictly defining their presence as manifestation onset before or synchronous with the formal diagnosis of SpA. Any extra-musculoskeletal feature emerging subsequent to the SpA diagnosis was excluded from the baseline analysis to accurately evaluate their potential chronological impact on the diagnostic timeline.

**Comorbidities:** Concomitant chronic conditions, such as hypertension, diabetes mellitus, cardiovascular diseases, and other associated rheumatic conditions, were documented for each patient.

Therapeutic management variables, including the use of non-steroidal anti-inflammatory drugs (NSAIDs), conventional synthetic disease-modifying antirheumatic drugs (DMARDs), and biological DMARDs (bDMARDs), were recorded based on the patients' current treatment regimens documented at their last follow-up visit.

### Laboratory and Disease Activity Assessments

Laboratory evaluations were performed both at the time of diagnosis and at the most recent follow-up visit. The following parameters were analyzed:

- Laboratory markers: Laboratory assessments encompassed a full hemogram, a comprehensive biochemical profile, and the measurement of systemic inflammatory markers, specifically C-reactive protein (CRP) and the erythrocyte sedimentation rate (ESR).
- Genetic marker: HLA-B27 status was documented for all available cases.

Patient inflammatory status was multifaceted; therefore, we utilized the BASDAI and both variants of the Ankylosing Spondylitis Disease Activity Score (ASDAS) (incorporating ESR and CRP, respectively) to quantify the degree of disease burden across the cohort.

### Statistical Analysis

Statistical analysis was performed using SPSS for Windows (version 23.0; IBM Corp., Armonk, NY, USA). The normality of data distribution was evaluated using the Shapiro-Wilk test. Continuous variables are reported as mean  $\pm$  standard deviation or median and interquartile range (IQR, 25<sup>th</sup>-75<sup>th</sup> percentiles), while categorical variables are presented as frequencies and percentages. To compare continuous variables between patients with a diagnostic delay of  $\leq 3$  years and  $> 3$  years, the independent samples t-test was used for normally distributed data, whereas the Mann-Whitney U test was applied for non-normally distributed variables. The distribution of categorical frequencies across groups was analyzed using chi-square statistics to identify potential disparities. Factors associated with diagnostic delay were identified using logistic regression analyses. Results were expressed as odds ratios (ORs) and 95% confidence intervals (CIs). A p-value of less than 0.05 was considered statistically significant.

### Results

A total of 371 patients were included in the study. The mean age of the participants was  $46.5 \pm 11.4$  years, with a predominance of female patients (62.3%). Regarding the clinical and phenotypic composition of the overall SpA cohort (n=371), axial SpA (axSpA) was the predominant phenotype, observed in 289 patients (77.9%), while peripheral SpA criteria were satisfied by 82 patients (22.1%). Within the axial SpA subgroup, 204 patients (70.6%) were classified as radiographic axSpA (r-axSpA) and 85 patients (29.4%) as non-r-axSpA.

In terms of specific underlying disease manifestations, PsA was present in 12 patients (3.2%), and enteropathic arthritis (IBD-associated SpA) was documented in 24 patients (6.5%).

Regarding therapeutic management at the last follow-up visit, 43.9% (n=163) of the patients were receiving NSAIDs, while 20.8% (n=77) were on sulfasalazine treatment. Notably, a majority of the cohort, 65.5% (n=243), was being treated with bDMARDs.

Table 1 details the core characteristics of the participants, providing a comprehensive breakdown of the study group's clinical and demographic background.

Regarding EMMs, uveitis was the most common involvement observed in 36 patients (9.7%), followed by IBD in 24 patients (6.5%) and psoriasis in 13 patients (3.5%) (Table 1).

| Table 1. Demographic and clinical characteristics of the patients |                |
|-------------------------------------------------------------------|----------------|
|                                                                   | Total patients |
| <b>Characteristic</b>                                             |                |
| Age (years) <sup>#</sup> ,                                        | 46.5±11.4      |
| Female sex, n (%)                                                 | 231 (62.3%)    |
| BMI <sup>#</sup> , kg/m <sup>2</sup>                              | 28.7±5.2       |
| Smoking history <sup>#</sup> , n (%)                              | 131 (35.3%)    |
| <b>Education<sup>#</sup>, n (%)</b>                               |                |
| Illiterate                                                        | 5 (1.3%)       |
| Primary school                                                    | 172 (46.3%)    |
| High school                                                       | 102 (27.5%)    |
| College/university                                                | 92 (24.8%)     |
| <b>Residential area<sup>#</sup>, n (%)</b>                        |                |
| Urban                                                             | 330 (88.9%)    |
| Rural                                                             | 41 (11.1%)     |
| <b>Marital status<sup>#</sup>, n (%)</b>                          |                |
| Single                                                            | 35 (9.4%)      |
| Married                                                           | 320 (86.6%)    |
| Divorced                                                          | 15 (4%)        |
| Presence of comorbidity <sup>#</sup> , n (%)                      | 209 (56.3%)    |
| <b>Additional diseases<sup>#</sup>, n (%)</b>                     |                |
| Hypertension                                                      | 79 (21.3%)     |
| Fibromyalgia                                                      | 45 (12.1%)     |
| Diabetes mellitus                                                 | 54 (14.6%)     |
| Polyneuropathy                                                    | 34 (9.2%)      |
| Asthma                                                            | 42 (11.3%)     |
| Hyperlipidemia                                                    | 31 (8.4%)      |
| Hypothyroidism                                                    | 28 (7.5%)      |
| CAD                                                               | 19 (5.1%)      |
| Other comorbidities*                                              | 17 (4.5%)      |
| <b>SpA subtype<sup>†</sup>, n (%)</b>                             |                |
| AxSpA                                                             | 289 (77.9%)    |
| pSpA                                                              | 82 (22.1%)     |
| <b>Rheumatological findings<sup>#</sup>, n (%)</b>                |                |
| Dactylitis                                                        | 40 (10.8%)     |
| Arthritis <sup>†</sup>                                            | 115 (31%)      |
| Enthesitis <sup>#</sup>                                           | 34 (9.2%)      |
| <b>Extra-musculoskeletal manifestations, n (%)</b>                |                |
| Uveitis                                                           | 36 (9.7%)      |
| Psoriasis                                                         | 13 (3.5%)      |
| IBD                                                               | 24 (6.5%)      |
| Age at symptom onset (years) <sup>†</sup>                         | 31.9±11.6      |
| Age at diagnosis (years) <sup>†</sup>                             | 37.1±11.3      |
| Diagnostic delay (years) <sup>†</sup>                             | 3 [0-7.5]      |
| Disease duration (years) <sup>#</sup>                             | 8 [4-12]       |

| Table 1. Continued                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------|
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | Total patients |
| <b>HLA-B27 positivity<sup>#</sup>, n (%)</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                |
| Negative                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 204 (55%)      |
| Positive                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 160 (43.1%)    |
| Unknown                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 7 (1.9%)       |
| ESR <sup>†</sup> , mm /h                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 21.9±18.9      |
| CRP <sup>†</sup> , mg/L                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 12.7±18        |
| ESR <sup>#</sup> , mm /h                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 16.2±13.2      |
| CRP <sup>#</sup> , mg/L                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 5.3±7.1        |
| VAS GLOBAL <sup>#</sup> (0-10)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 5 [3-7]        |
| BASDAI <sup>#</sup>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 4 [2.2-5.8]    |
| ASDAS-ESR <sup>#</sup>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 2.5 [1.9-3.1]  |
| ASDAS-CRP <sup>#</sup>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 2.4 [1.55-3]   |
| <sup>†</sup> : Assessment at the time of diagnosis (including extra-musculoskeletal manifestations present prior to or at formal diagnosis), <sup>#</sup> : Final visit assessment, *: Other comorbidities include COPD (n=6, 1.6%), CKD (n=6, 1.6%), and malignancy (n=5, 1.3%)<br>Continuous variables are presented as mean ± standard deviation or median [IQR]<br>ASDAS: Ankylosing Spondylitis Disease Activity Score, axSpA: axial spondyloarthritis, BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, BMI: Body mass index, CAD: Coronary artery disease, CKD: Chronic kidney disease, COPD: Chronic obstructive pulmonary disease, CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate, IBD: Inflammatory bowel disease, IQR: Interquartile range, pSpA: Peripheral spondyloarthritis, VAS: Visual analogue scale |                |

When patients were categorized based on the median diagnostic delay ( $\leq 3$  years vs.  $> 3$  years), several significant differences were identified. Patients with a longer diagnostic delay ( $> 3$  years) were significantly older ( $48.5 \pm 10.2$  vs.  $45 \pm 12$  years;  $p=0.004$ ) and had a higher BMI ( $p=0.010$ ) compared to those with a shorter delay. A critical finding was the age at symptom onset: patients in the shorter delay group ( $\leq 3$  years) experienced their first symptoms at a later age (median: 35 years) compared to the long-delay group (median: 28 years;  $p<0.001$ ). Furthermore, the presence of comorbidities was significantly more frequent in patients with a delay  $> 3$  years ( $p=0.034$ ), specifically hypertension ( $p=0.032$ ). Regarding disease activity at the last visit, patients with a longer diagnostic delay exhibited significantly higher ASDAS-CRP scores ( $p=0.023$ ). The demographic and clinical features of the patients, stratified by diagnostic delay ( $\leq 3$  years vs.  $> 3$  years), are summarized in Table 2.

When evaluating EMMs based on the diagnostic interval, no statistically significant differences were observed between patients with a diagnostic delay of  $\leq 3$  years and those with a delay of  $> 3$  years (Table 2).

Logistic regression analyses were conducted based on baseline clinical data collected at the time of diagnosis. In the univariate analyses, the following factors were identified as associated predictors of prolonged diagnostic delay: age at symptom onset (OR: 0.959, 95% CI: 0.941-0.978,  $p<0.001$ ), age at diagnosis (OR: 1.039, 95% CI: 1.019-1.059,  $p<0.001$ ), and SpA subtype (OR: 0.514, 95% CI: 0.305-0.869,  $p=0.013$ ). Then, candidate predictors were

| Table 2. Comparison of demographic and clinical characteristics between patients with diagnostic delay ≤3 years and >3 years |                        |                        |                  |
|------------------------------------------------------------------------------------------------------------------------------|------------------------|------------------------|------------------|
| Characteristic                                                                                                               | Delay ≤3 years (n=213) | Delay >3 years (n=158) | p-value          |
| Age (years) <sup>#</sup> ,                                                                                                   | 45±12                  | 48.5±10.2              | <b>0.004</b>     |
| Female sex, n (%)                                                                                                            | 125 (58.7%)            | 106 (67.1%)            | 0.099            |
| BMI <sup>#</sup> , kg/m <sup>2</sup>                                                                                         | 27.7 [24.4-31.2]       | 28.8 [26.3-32.1]       | <b>0.010</b>     |
| Smoking history <sup>#</sup> , n (%)                                                                                         | 82 (38.5%)             | 49 (31.0%)             | 0.178            |
| <b>Education<sup>#</sup>, n %</b>                                                                                            |                        |                        |                  |
| Illiterate                                                                                                                   | 1 (0.5%)               | 4 (2.5%)               | 0.054            |
| Primary school                                                                                                               | 88 (41.3%)             | 84 (53.2%)             |                  |
| High school                                                                                                                  | 62 (29.1%)             | 40 (25.3%)             |                  |
| College/university                                                                                                           | 62 (29.1%)             | 30 (19.0%)             |                  |
| <b>Residential area<sup>#</sup>, n (%)</b>                                                                                   |                        |                        |                  |
| Urban                                                                                                                        | 189 (88.7%)            | 141 (89.2%)            | 0.508            |
| Rural                                                                                                                        | 24 (11.3%)             | 17 (10.8%)             |                  |
| <b>Marital status<sup>#</sup>, n (%)</b>                                                                                     |                        |                        |                  |
| Single                                                                                                                       | 26 (12.2%)             | 9 (5.7%)               | 0.076            |
| Married                                                                                                                      | 177 (83.1%)            | 143 (90.5%)            |                  |
| Divorced                                                                                                                     | 9 (4.2%)               | 6 (3.8%)               |                  |
| <b>Presence of comorbidity<sup>#</sup>, n (%)</b>                                                                            | 110 (51.6%)            | 99 (62.7%)             | <b>0.034</b>     |
| <b>Number of comorbidities</b>                                                                                               | 1 [0-1]                | 1 [0-2]                | <b>0.024</b>     |
| <b>Additional diseases<sup>#</sup>, n (%)</b>                                                                                |                        |                        |                  |
| Hypertension                                                                                                                 | 37 (17.4%)             | 42 (26.6%)             | <b>0.032</b>     |
| Fibromyalgia                                                                                                                 | 24 (11.3%)             | 21 (13.3%)             | 0.555            |
| Diabetes Mellitus                                                                                                            | 28 (13.1%)             | 26 (16.5%)             | 0.371            |
| Polyneuropathy                                                                                                               | 15 (7.0%)              | 19 (12.0%)             | 0.100            |
| Asthma                                                                                                                       | 23 (10.8%)             | 19 (12.0%)             | 0.712            |
| Hyperlipidemia                                                                                                               | 16 (7.5%)              | 15 (9.5%)              | 0.495            |
| Hypothyroidism                                                                                                               | 15 (7.0%)              | 13 (8.2%)              | 0.669            |
| CAD                                                                                                                          | 11 (5.2%)              | 8 (5.1%)               | 0.965            |
| <b>SpA subtype<sup>†</sup>, n (%)</b>                                                                                        |                        |                        |                  |
| AxSpA                                                                                                                        | 156 (73.2%)            | 133 (84.2%)            | <b>0.012</b>     |
| pSpA                                                                                                                         | 57 (26.8%)             | 25 (15.8%)             |                  |
| <b>Rheumatological findings<sup>#</sup>, n (%)</b>                                                                           |                        |                        |                  |
| Dactylitis                                                                                                                   | 28 (13.1%)             | 12 (7.6%)              | 0.088            |
| Arthritis <sup>‡</sup>                                                                                                       | 70 (32.9%)             | 45 (28.5%)             | 0.367            |
| Enthesitis <sup>#</sup>                                                                                                      | 20 (9.4%)              | 14 (8.9%)              | 0.861            |
| <b>Extra-musculoskeletal manifestations, n (%)</b>                                                                           |                        |                        |                  |
| Uveitis                                                                                                                      | 21 (9.9%)              | 15 (9.5%)              | 0.906            |
| Psoriasis                                                                                                                    | 8 (3.8%)               | 5 (3.2%)               | 0.487            |
| IBD                                                                                                                          | 17 (8.0%)              | 7 (4.4%)               | 0.169            |
| <b>Age at symptom onset (years)<sup>†</sup></b>                                                                              | 35 [25-42]             | 28 [20-35]             | <b>&lt;0.001</b> |
| <b>Age at diagnosis (years)<sup>†</sup></b>                                                                                  | 35 [26-43]             | 40 [33-47]             | <b>&lt;0.001</b> |
| <b>Disease duration (years)<sup>#</sup></b>                                                                                  | 9 [5-13]               | 8 [4-12]               | 0.082            |

| Table 2. Continued                           |                        |                        |              |
|----------------------------------------------|------------------------|------------------------|--------------|
| Characteristic                               | Delay ≤3 years (n=213) | Delay >3 years (n=158) | p-value      |
| <b>HLA-B27 positivity<sup>#</sup>, n (%)</b> |                        |                        |              |
| Negative                                     | 120 (56.3%)            | 84 (53.2%)             | 0.574        |
| Positive                                     | 88 (41.3%)             | 72 (45.6%)             |              |
| Unknown                                      | 5 (2.4%)               | 2 (1.3%)               |              |
| <b>ESR<sup>‡</sup>, mm/h</b>                 | 14 [7-29]              | 18 [9-32]              | 0.155        |
| <b>CRP<sup>‡</sup>, mg/L</b>                 | 5.8 [3.2-12.4]         | 8.1 [3.4-14.7]         | 0.130        |
| <b>ESR<sup>#</sup>, mm/h</b>                 | 12 [6-21]              | 15 [6-23]              | 0.457        |
| <b>CRP<sup>#</sup>, mg/L</b>                 | 3 [1.3-6.1]            | 3.7 [1.5-7.2]          | 0.395        |
| <b>VAS GLOBAL<sup>#</sup> (0-10)</b>         | 5 [3-7]                | 5 [3-7]                | 0.471        |
| <b>BASDAI<sup>#</sup></b>                    | 4 [2.2-5.5]            | 4.1 [2.3-6]            | 0.174        |
| <b>ASDAS-ESR<sup>#</sup></b>                 | 2.5 [1.7-3.1]          | 2.6 [2-3.2]            | 0.053        |
| <b>ASDAS-CRP<sup>#</sup></b>                 | 2.3 [1.5-2.9]          | 2.6 [1.8-3.1]          | <b>0.023</b> |

<sup>†</sup>: Assessment at the time of diagnosis (including extra-musculoskeletal manifestations present prior to or at formal diagnosis). <sup>#</sup>: Final visit assessment  
Continuous variables are presented as mean ± standard deviation or median [IQR].  
Bold emphasis in p-values indicate statistical significance  
ASDAS: Ankylosing Spondylitis Disease Activity Score, axSpA: Axial spondyloarthritis, BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, BMI: Body mass index, CAD: Coronary artery disease, CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate, IBD: Inflammatory bowel disease, IQR: Interquartile range, pSpA: Peripheral spondyloarthritis, VAS: Visual analogue scale

entered into the multivariate model. Due to the inherent strong correlation between age at symptom onset and age at diagnosis, only age at symptom onset was prioritized for inclusion in the multivariate model to avoid potential multicollinearity and to better reflect the clinical impact of early-onset disease. Extra-articular manifestations (IBD, psoriasis, and uveitis), as well as disease subtypes, HLA-B27 status, and sex, which have previously been reported to influence diagnostic delay in SpA cohorts, were also included in the multivariate model. Arthritis, enthesitis, and dactylitis were excluded from the multivariate model, as they constitute the hallmark manifestations of peripheral SpA—a disease subtype already incorporated into the model—and did not demonstrate significant associations in the univariable analyses. After adjusting for the effects of SpA-related extra-articular manifestations and HLA-B27 status in the enter model, age at symptom onset (OR: 0.953, 95% CI: 0.933-0.973,  $p<0.001$ ), female sex (OR: 1.723, 95% CI: 1.075-2.761,  $p=0.024$ ), and SpA subtype (OR: 0.457, 95% CI: 0.264-0.794,  $p=0.005$ ) were identified as significant predictors of prolonged diagnostic delay (>3 years). The comprehensive results of both univariate and multivariate logistic regression analyses, including ORs and 95% CIs for all evaluated clinical and demographic factors, are detailed in Table 3.

## Discussion

This study provides a comprehensive evaluation of the clinical and demographic determinants influencing the diagnostic journey of patients with SpA in a large cohort. Our findings highlight a persistent and substantial diagnostic gap,

with a median delay of 3 years, reinforcing the global challenge of timely SpA recognition. The most compelling observation of our adjusted analysis is that age at symptom onset serves as a potent independent predictor of this delay; specifically, younger patients face a significantly more protracted path to formal diagnosis, potentially due to the misattribution of early inflammatory symptoms to mechanical causes. Interestingly, despite their high clinical specificity and potential role as “red flags,” EMMs such as uveitis, psoriasis, and IBD did not significantly accelerate the diagnostic process in our cohort. Furthermore, multivariate model demonstrated that female sex significantly and independently increases the risk of prolonged diagnostic delay. This strong association aligns perfectly with the global literature, where atypical clinical presentations and the historically male-dominant perception of SpA often delay the recognition of the disease in female patients. Conversely, the peripheral SpA sub-phenotype was found to significantly reduce the diagnostic delay interval, likely due to the more overt and visible nature of peripheral joint and enthesal involvements which prompt faster specialized referral. This underscores the complex nature of SpA and suggests that early-onset disease is the primary clinical barrier to timely diagnosis in our setting, overriding the influence of other demographic factors.

In a large-scale European study involving 432 patients, Masson Behar et al.<sup>[12]</sup> reported a mean diagnostic delay of 4.9 (6.3) years, median 2.0 (IQR: 1-7; range: 0-43) years. Our cohort

demonstrated a comparable mean delay of 5.3 years and a median delay of 3 years (IQR: 0-7.5). Our findings regarding diagnostic delay are consistent with the broader global landscape. According to a recent systematic review by Hay et al.<sup>[9]</sup>, the median diagnostic delay worldwide typically ranges between 2 and 6 years. While some countries like Denmark report delays as short as 0.67 years, others, such as South Korea, experience delays reaching up to 8 years.<sup>[9]</sup> It is crucial to note that reporting “median” values provides a more accurate clinical picture than “mean” values; the aforementioned review highlights that mean data can be skewed by outliers, potentially overestimating the delay by approximately 2.7 years. By focusing on the median, our study provides a more representative clinical picture of the patient experience. Furthermore, our results are in agreement with previous Turkish studies summarized in the systematic review by Hay et al.<sup>[9]</sup>, which reported median diagnostic delays ranging from 2 to 5 years, including 2 years in Bodur et al., 3 years in Ozgocmen et al., 4 years in Zengin et al., and 5 years in Gerdan et al. This consistency suggests that our cohort reflects a typical diagnostic trajectory within the Turkish healthcare system, sitting squarely within both national and international range.

In our multivariate model, age at symptom onset emerged as the most robust independent predictor of diagnostic delay, suggesting that the impact of early-onset disease on the diagnostic timeline is independent of sex, BMI, or current age.

| Table 3. Identification of factors associated with prolonged diagnostic delay (>3 years) using data at the time of diagnosis                                                                                                                                                                                                                                                                 |                  |        |       |                  |                    |        |       |                  |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------|--------|-------|------------------|--------------------|--------|-------|------------------|
|                                                                                                                                                                                                                                                                                                                                                                                              | Univariate model |        |       |                  | Multivariate model |        |       |                  |
|                                                                                                                                                                                                                                                                                                                                                                                              | OR               | 95% CI |       | p-value          | OR                 | 95% CI |       | p-value          |
| <b>Demographics</b>                                                                                                                                                                                                                                                                                                                                                                          |                  |        |       |                  |                    |        |       |                  |
| Age at symptom onset (years) <sup>†</sup>                                                                                                                                                                                                                                                                                                                                                    | 0.959            | 0.941  | 0.978 | <b>&lt;0.001</b> | 0.953              | 0.933  | 0.973 | <b>&lt;0.001</b> |
| Age at diagnosis (years) <sup>†</sup>                                                                                                                                                                                                                                                                                                                                                        | 1.039            | 1.019  | 1.059 | <b>&lt;0.001</b> |                    |        |       |                  |
| Female sex (Ref. male)                                                                                                                                                                                                                                                                                                                                                                       | 1.435            | 0.934  | 2.205 | 0.099            | 1.723              | 1.075  | 2.761 | <b>0.024</b>     |
| SpA subtype (Ref. AxSpA)                                                                                                                                                                                                                                                                                                                                                                     |                  |        |       |                  |                    |        |       |                  |
| pSpA                                                                                                                                                                                                                                                                                                                                                                                         | 0.514            | 0.305  | 0.869 | <b>0.013</b>     | 0.457              | 0.264  | 0.794 | <b>0.005</b>     |
| <b>Extra-musculoskeletal clinical manifestations<sup>†</sup> (Ref. no)</b>                                                                                                                                                                                                                                                                                                                   |                  |        |       |                  |                    |        |       |                  |
| IBD                                                                                                                                                                                                                                                                                                                                                                                          | 0.534            | 0.216  | 1.322 | 0.175            | 0.847              | 0.320  | 2.243 | 0.738            |
| Psoriasis                                                                                                                                                                                                                                                                                                                                                                                    | 0.837            | 0.269  | 2.610 | 0.760            | 1.159              | 0.356  | 3.773 | 0.807            |
| Uveitis                                                                                                                                                                                                                                                                                                                                                                                      | 0.959            | 0.478  | 1.926 | 0.906            | 0.984              | 0.467  | 2.073 | 0.966            |
| <b>Clinical parameters</b>                                                                                                                                                                                                                                                                                                                                                                   |                  |        |       |                  |                    |        |       |                  |
| Arthritis                                                                                                                                                                                                                                                                                                                                                                                    | 0.814            | 0.520  | 1.204 | 0.367            |                    |        |       |                  |
| Enthesitis                                                                                                                                                                                                                                                                                                                                                                                   | 0.938            | 0.458  | 1.920 | 0.861            |                    |        |       |                  |
| Dactylitis                                                                                                                                                                                                                                                                                                                                                                                   | 0.543            | 0.267  | 1.105 | 0.092            |                    |        |       |                  |
| HLA-B27 positivity <sup>#</sup> (Ref. negative)                                                                                                                                                                                                                                                                                                                                              | 1.169            | 0.769  | 1.775 | 0.465            | 0.974              | 0.616  | 1.542 | 0.911            |
| <b>Disease activity parameters</b>                                                                                                                                                                                                                                                                                                                                                           |                  |        |       |                  |                    |        |       |                  |
| ESR <sup>†</sup>                                                                                                                                                                                                                                                                                                                                                                             | 1.005            | 0.993  | 1.017 | 0.417            |                    |        |       |                  |
| CRP <sup>†</sup>                                                                                                                                                                                                                                                                                                                                                                             | 1.000            | 0.988  | 1.012 | 0.997            |                    |        |       |                  |
| <sup>†</sup> : Assessment at the time of diagnosis (including extra-musculoskeletal manifestations present prior to or at formal diagnosis), <sup>#</sup> : Bold emphasis in p-values indicate statistical significance<br>axSpA: Axial spondyloarthritis, CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate, IBD: Inflammatory bowel disease, pSpA: Peripheral spondyloarthritis |                  |        |       |                  |                    |        |       |                  |

This observation is strongly supported by the recent global meta-analysis by Zhao et al.<sup>[5]</sup>, which demonstrated that patients with juvenile-onset SpA experience substantially longer trajectories to diagnosis compared to those with adult-onset disease. Consistent with our findings, a large-scale German study by Redeker et al.<sup>[13]</sup> involving 1,677 patients, reported mean delay of 5.7 years is remarkably similar to our finding of 5.3 years and a younger age at symptom onset was a significant predictor of prolonged diagnostic delay. Also Aggarwal and Malaviya<sup>[14]</sup> highlighted that juvenile age at symptom onset emerged as a critical factor significantly associated with late diagnosis. In a multicenter study from Turkey, Gerdan et al.<sup>[15]</sup> evaluated 393 patients with AS and reported a mean diagnostic delay of 8.1 years. Notably, they found that one-third of these patients were initially misdiagnosed with lumbar disc herniation, which significantly extended the delay to 9.1 years compared to 6.2 years in those without such a misdiagnosis. Furthermore, the study identified younger age at symptom onset as a significant predictor of prolonged diagnostic delay, highlighting that patients who develop symptoms earlier in life often face a more protracted path to a formal diagnosis. This suggests that clinical mimicry, initial management by non-rheumatologists, and the misinterpretation of early-onset inflammatory symptoms remain major barriers to timely diagnosis in the local healthcare setting.

The impact of EMMs on the diagnostic trajectory SpA remains a subject of significant debate, with our findings contributing to the existing lack of consensus in global literature. In our study, the presence of uveitis, IBD, and psoriasis was not significantly associated with diagnostic delay. This outcome reflects the clinical complexity highlighted by Hay et al.<sup>[9]</sup> in their recent systematic review. In their analysis of 47 different factors across multiple studies, the authors found conflicting evidence regarding the role of uveitis in reducing diagnostic delay. Specifically, among the five studies evaluated for this factor, only one reported a decrease in delay, while another suggested an increase, and three found no significant impact. Consequently, Hay et al.<sup>[9]</sup> concluded that no definitive association could be established between uveitis and the timing of diagnosis. Furthermore, other common EMMs, such as IBD and psoriasis, lacked sufficient longitudinal data to be consistently correlated with diagnostic outcomes. This lack of consensus in global literature underscores the complexity of the diagnostic journey and suggests that the influence of EMMs may be highly dependent on regional healthcare structures and the referral patterns of non-rheumatology. Our results contrast with some regional reports where EMMs served as diagnostic “red flags.” For instance, Hajjalilo et al.<sup>[16]</sup> identified acute anterior uveitis as a potent accelerator, reducing delay to 2.4 years, while Aggarwal and Malaviya<sup>[14]</sup> observed that the absence of EMMs significantly correlated with a longer diagnostic trajectory

(8.7 years vs. 5.9 years). These researchers attributed such accelerations to efficient referral chains from ophthalmologists to rheumatologists. Interestingly, Sykes et al.<sup>[6]</sup>, who analyzed a large UK cohort of 1,193 patients with SpA, reported that while peripheral arthritis and IBD were predictors of a shorter delay (median 4.0 years), the presence of uveitis was paradoxically associated with a longer median delay of 10.0 years. Therefore, the presence of EMMs does not uniformly guarantee early recognition. In some clinical scenarios, these manifestations may lead to localized management of the specific symptom rather than prompting a timely rheumatological referral for the underlying systemic condition. Ultimately, the discrepancy between our findings and existing literature underscores that the influence of EMMs is likely highly dependent on regional healthcare structures and the clinical suspicion levels of non-rheumatology specialists.

In our logistic regression model, while structural phenotypic and demographic attributes such as female sex and the consolidated peripheral SpA sub-phenotype emerged as significant independent determinants of the diagnostic timeline, a select array of baseline parameters including individual peripheral manifestations (such as isolated arthritis, dactylitis, and enthesitis), education level, HLA-B27 positivity, and acute phase reactants—did not independently influence the diagnostic interval. Regarding patient sex, our findings contrast with the systematic review by Hay et al.<sup>[9]</sup>, which observed no definitive link between sex and diagnostic delay in the vast majority of evaluated studies. But rather align with growing global evidence indicating that the atypical or more peripheral presentation of SpA in female patients, coupled with a historically lower clinical suspicion for axial disease in women, frequently misleads primary care clinicians and delays rheumatological referral.<sup>[17,18]</sup>

Similarly, the impact of HLA-B27 and inflammatory markers remains a subject of intense debate; while Hajjalilo et al.<sup>[16]</sup> identified HLA-B27 positivity and elevated ESR/CRP as “diagnostic catalysts” capable of nearly halving the delay, our data support the counter-evidence where these biological markers show no significant predictive power. Crucially, while individual peripheral features such as isolated arthritis, dactylitis, or enthesitis did not reach statistical significance when analyzed independently in our cohort—reflecting the global ambiguity often reported in the literature—the consolidated peripheral SpA sub-phenotype emerged as a powerful determinant of reduced diagnostic latency. This phenomenon can be attributed to the clinical synergy and cumulative diagnostic weight of these manifestations in real-world practice. While some European cohorts<sup>[6]</sup> suggest that peripheral “red flags” facilitate earlier recognition, our data indicate that a single, isolated peripheral feature may occasionally be misdiagnosed or managed supportively in primary care, or even paradoxically

prolong the journey due to its frequent misinterpretation as a mechanical issue.<sup>[16]</sup> Conversely, the coexistence of multiple peripheral involvements or their combination presents a highly overt, classical clinical picture that naturally amplifies diagnostic suspicion and accelerates prompt rheumatological referral. Furthermore, from a statistical perspective, aggregating these interconnected signs into a unified phenotypic category enhances the biostatistical power of the model, allowing the overarching impact of peripheral disease to be robustly captured. Ultimately, these discrepancies highlight a clear divergence: while “classic” symptoms are traditionally expected to accelerate diagnosis, their influence is often overshadowed by systemic factors. As emphasized by Zhao et al.<sup>[5]</sup>, socio-economic determinants such as education levels may represent more consistent barriers in certain populations, suggesting that the diagnostic path in SpA is shaped by a complex interplay of regional clinical practices and patient-related dynamics rather than uniform clinical or laboratory phenotypes alone.

To the best of our knowledge, this is one of the most comprehensive studies in our region evaluating the clinical and demographic determinants of diagnostic delay in SpA. The present study has several notable strengths that reinforce the validity of our findings. It is based on a substantial and well-characterized cohort of 371 patients followed over a 13-year period at a tertiary referral center, providing robust real-world data on the diagnostic journey. Furthermore, our analysis utilized an extensive set of variables, including detailed EMMs and various comorbidities, allowing for a nuanced understanding of potential diagnostic barriers. Methodologically, by reporting both mean and median values for diagnostic delay, we ensured a more accurate representation of the patient experience that is less sensitive to outliers, aligning with current global recommendations.

### Study Limitations

Despite its clinical relevance, certain limitations associated with this study deserve scrutiny to ensure a balanced evaluation of the reported outcomes. First, its retrospective design relies on medical records, which may be inherently prone to variations in reporting. Second, although our total cohort size is substantial, the low prevalence and small absolute numbers of certain EMMs—specifically psoriasis and IBD—may have resulted in insufficient statistical power. Consequently, the possibility of a type II error cannot be entirely excluded, and subtle but clinically meaningful differences regarding the impact of these specific phenotypes on diagnostic delay might have been obscured. Additionally, diagnostic delay was dichotomized into  $\leq 3$  and  $> 3$  years based on the cohort’s median value to facilitate clinical stratification and ensure balanced group sizes for comparison. We acknowledge that converting a continuous variable into

a binary outcome can lead to a loss of statistical information and reduce statistical power near the threshold. Third, being a single-center study conducted at a tertiary referral hospital, our findings may reflect specific regional referral patterns and may not be fully generalizable to the broader population or primary care settings. Fourth, the determination of “age at symptom onset” is based on patient recall, introducing a potential for recall bias in calculating the exact duration of diagnostic delay. Lastly, while our cohort is substantial, the lack of HLA-B27 data in a small minority of patients may have limited our ability to fully characterize its impact on the diagnostic interval.

### Conclusion

In conclusion, our study demonstrates that despite the availability of advanced classification criteria and biological therapies, a significant diagnostic delay persists in the management of SpA. Our findings reveal that younger age at symptom onset and female sex are the most critical independent predictors of a protracted diagnostic journey, while the consolidated peripheral SpA sub-phenotype significantly accelerates the time to definitive diagnosis. Paradoxically, highly specific EMMs such as uveitis, psoriasis, and IBD do not appear to consistently accelerate the path to diagnosis in our cohort, indicating that their impact on the diagnostic timeline is complex and requires conservative interpretation. These results underscore an urgent need for increased clinical suspicion among non-rheumatology specialists and the development of more efficient referral pathways, particularly for younger patients presenting with early inflammatory symptoms. Improving the recognition of the interplay between these diverse clinical phenotypes and demographic attributes is essential to reduce diagnostic delay, prevent irreversible structural damage, and ultimately enhance the long-term quality of life for patients with SpA.

### Ethics

**Ethics Committee Approval:** This study was approved by the Erciyes University Health Sciences Research Ethics Committee (approval no: 2025/149, date: 19.03.2025).

**Informed Consent:** The ethics committee waived the need for informed consent because our study was retrospective in nature.

### Footnotes

#### Author Contributions

Surgical and Medical Practices: E.O.K., Concept: E.O.K., H.K., Design: E.O.K., H.K., Data Collection or Processing: E.O.K., M.K., T.K.D., C.B.C., Analysis or Interpretation: E.O.K., H.K., A.S.Ş., Literature Search: E.O.K., M.K., T.K.D., C.B.C., Writing: E.O.K., H.K., A.S.Ş.

**Conflict of Interest:** No conflict of interest was declared by the authors.

**Financial Support:** The authors declared that they received no financial support.

## References

1. Juanola X, Ramos MJM, Belzunegui JM, Fernández-Carballido C, Gratacós J. Treatment failure in axial spondyloarthritis: insights for a standardized definition. *Adv Ther.* 2022;39:1490-501.
2. Simone D, Al Mossawi MH, Bowness P. Progress in our understanding of the pathogenesis of ankylosing spondylitis. *Rheumatology (Oxford).* 2018;57(suppl\_6):vi4-9.
3. El Maghraoui A. Extra-articular manifestations of ankylosing spondylitis: prevalence, characteristics and therapeutic implications. *Eur J Intern Med.* 2011;22:554-60.
4. Rudwaleit M, van der Heijde D, Landewé R, et al. The Assessment of SpondyloArthritis International Society classification criteria for peripheral spondyloarthritis and for spondyloarthritis in general. *Ann Rheum Dis.* 2011;70:25-31.
5. Zhao SS, Pittam B, Harrison NL, Ahmed AE, Goodson NJ, Hughes DM. Diagnostic delay in axial spondyloarthritis: a systematic review and meta-analysis. *Rheumatology (Oxford).* 2021;60:1620-8.
6. Sykes MP, Doll H, Sengupta R, Gaffney K. Delay to diagnosis in axial spondyloarthritis: are we improving in the UK? *Rheumatology (Oxford).* 2015;54:2283-4.
7. Seo MR, Baek HL, Yoon HH, et al. Delayed diagnosis is linked to worse outcomes and unfavourable treatment responses in patients with axial spondyloarthritis. *Clin Rheumatol.* 2015;34:1397-405.
8. Redeker I, Callhoff J, Hoffmann F, et al. The prevalence and impact of comorbidities on patients with axial spondyloarthritis: results from a nationwide population-based study. *Arthritis Res Ther.* 2020;22:210.
9. Hay CA, Packham J, Ryan S, Mallen CD, Chatzixenitidis A, Prior JA. Diagnostic delay in axial spondyloarthritis: a systematic review. *Clin Rheumatol.* 2022;41:1939-50.
10. Rudwaleit M, Landewé R, van der Heijde D, et al. The development of Assessment of SpondyloArthritis international Society classification criteria for axial spondyloarthritis (part I): classification of paper patients by expert opinion including uncertainty appraisal. *Ann Rheum Dis.* 2009;68:770-6. Erratum in: *Ann Rheum Dis.* 2011;70:1519.
11. Taylor W, Gladman D, Helliwell P, Marchesoni A, Mease P, Mielants H; CASPAR Study Group. Classification criteria for psoriatic arthritis: development of new criteria from a large international study. *Arthritis Rheum.* 2006;54:2665-73.
12. Masson Behar V, Dougados M, Etcheto A, et al. Diagnostic delay in axial spondyloarthritis: a cross-sectional study of 432 patients. *Joint Bone Spine.* 2017;84:467-71.
13. Redeker I, Callhoff J, Hoffmann F, et al. Determinants of diagnostic delay in axial spondyloarthritis: an analysis based on linked claims and patient-reported survey data. *Rheumatology (Oxford).* 2019;58:1634-8.
14. Aggarwal R, Malaviya AN. Diagnosis delay in patients with ankylosing spondylitis: factors and outcomes--an Indian perspective. *Clin Rheumatol.* 2009;28:327-31.
15. Gerdan V, Akar S, Solmaz D, et al. Initial diagnosis of lumbar disc herniation is associated with a delay in diagnosis of ankylosing spondylitis. *J Rheumatol.* 2012;39:1996-9.
16. Hajjalilo M, Ghorbanihaghjo A, Khabbazi A, Kolahi S, Rashtchizadeh N. Ankylosing spondylitis in Iran; late diagnosis and its causes. *Iran Red Crescent Med J.* 2014;16:e11798.
17. Neuenschwander R, Hebeisen M, Micheroli R, et al. Differences between men and women with nonradiographic axial spondyloarthritis: clinical characteristics and treatment effectiveness in a real-life prospective cohort. *Arthritis Res Ther.* 2020;22:233.
18. Rusman T, van Bentum RE, van der Horst-Bruinsma IE. Sex and gender differences in axial spondyloarthritis: myths and truths. *Rheumatology (Oxford).* 2020;59(Suppl 4):iv38-46.