

# Advanced clinical and radiological features of ankylosing spondylitis: relation to gender, onset of first symptoms and disease duration

---

Grubišić, Frane; Jajić, Zrinka; Alegić-Karin, Anita; Borić, Igor; Jajić, Ivo

Source / Izvornik: *Collegium Antropologicum*, 2015, 39, 927 - 934

Journal article, Published version

Rad u časopisu, Objavljena verzija rada (izdavačev PDF)

Permanent link / Trajna poveznica: <https://urn.nsk.hr/urn:nbn:hr:105:674643>

Rights / Prava: [In copyright](#)/[Zaštićeno autorskim pravom.](#)

Download date / Datum preuzimanja: **2024-07-23**



Repository / Repozitorij:

[Dr Med - University of Zagreb School of Medicine Digital Repository](#)



# Advanced Clinical and Radiological Features of Ankylosing Spondylitis: Relation to Gender, Onset of First Symptoms and Disease Duration

Frane Grubišić<sup>1</sup>, Zrinka Jajić<sup>1</sup>, Anita Alegić-Karin<sup>2</sup>, Igor Borić<sup>3</sup>, Ivo Jajić<sup>1</sup>

<sup>1</sup>»Sestre Milosrdnice« University Hospital Center, Department of Rheumatology, Physical Medicine and Rehabilitation, Referral Center for the Spondyloarthropathies of the Ministry of Health and Social Welfare, Zagreb, Croatia

<sup>2</sup>University of Zagreb, University Hospital Dubrava, Department of Psychiatry, Regional Center for Psychotrauma, Referral of the Ministry of Health and Social Welfare of the Republic of Croatia, Zagreb, Croatia

<sup>3</sup>University of Zagreb, University Hospital Center »Sestre Milosrdnice«, Department for Diagnostic and Interventional Radiology, Zagreb, Croatia

## ABSTRACT

To determine the frequency of advanced clinical and radiological features of AS with reference to gender, onset of symptoms and disease duration. Fifty-seven patients diagnosed with AS were included in this study. Functional evaluation of the musculoskeletal system detected advanced clinical features: rubber-ball phenomenon, flattening of the chest anterior wall, diastasis of rectus abdominis muscle, steel back phenomenon, umbilical extrusion, skiing posture. Conventional radiographs of sacroiliac joints, pelvis and axial skeleton were obtained in order to analyze signs of sacroiliitis, syndesmophytes, vertebral squaring and ligamentous ossification. Statistical significance is found in the distribution of particular advanced clinical and radiological features of AS between men and women: rubber-ball phenomenon ( $p=0.002$ ), flat chest ( $p=0.002$ ), diastasis of rectus abdominis muscle ( $p=0.002$ ), skiing position ( $p=0.000$ ), syndesmophytes ( $p=0.009$ ) and ligamentous ossification ( $p=0.030$ ) in thoracic and lumbar spine. Onset of first disease symptoms ( $>20$  years of age) is significantly associated with radiological changes in thoracic spine (ligamentous ossification,  $p=0.015$ ) and cervical spine (vertebral squaring,  $p=0.032$ ). Longer disease duration ( $>10$  years) is significantly associated with the appearance of particular clinical features: rubber-ball phenomenon,  $p<0.01$ ; rectus abdominis diastasis,  $p=0.042$ ) and radiological changes of sacroiliac joints (grade IV sacroileitis,  $p=0.012$ ), thoracic and lumbar spine (syndesmophytes,  $p=0.015$ ; ligamentous ossification,  $p=0.027$ ). Our study shows that the occurrence of clinical and some radiological features of AS appears to be gender dependent. Furthermore, onset of first disease symptoms ( $>20$  years of age) and longer disease duration ( $>10$  years) are associated with the higher risk of developing particular clinical signs and radiological features in sacroiliac joints and axial skeleton.

**Key words:** ankylosing spondylitis; adult, aged; clinical features, radiography

## Introduction

Ankylosing spondylitis (AS) is a chronic progressive inflammatory rheumatic disease affecting primarily axial skeleton and sacroiliac joints. The prevalence of the AS is estimated between 0.2% and 1.2% with male:female ratio around 5:1 and the onset of first symptoms between 20 and 30 years<sup>1-3</sup>. Sacroiliitis is the hallmark of AS and is accompanied with the inflammation of entheses which can lead to the formation of syndesmophytes, followed by the appearance of ligamentous ossification and other tissue changes which contribute to the restriction of spinal mo-

bility and chest expansion<sup>4-6</sup>. Morphological changes of the axial skeleton and rib cage are responsible for the gradual flattening of the chest anterior wall, protraction of the humeroscapular girdle, changes from costal to abdominal breathing with abdomen becoming more protuberant. Subsequently, characteristic clinical features of AS may appear during the course of disease. Clinical features of advanced AS include: rubber-ball phenomenon, flattening of the chest anterior wall, diastasis of rectus abdominis muscle, steel back phenomenon, umbilical extrusion, skiing posture. Radiological features of advanced AS in spine include syndesmophytes, vertebral squaring, interverte-

**TABLE 1**  
CLINICAL AND DEMOGRAPHIC DATA

	Median (± SD)
Age of patients (years)	52.9±9.78
Onset of first symptoms (years)	29.3±8.8
Disease duration (years)	22.1±9.1
Delay in diagnosis (years)	10.7±9.7
Time interval between the onset of symptoms and appearance of advanced clinical features (years)	
Flattening of the chest anterior wall (years)	13±4
Rubber-ball phenomenon (years)	11.9±4.3
Umbilical extrusion (years)	19.2±6.1
Diastasis of rectus abdominis muscle (years)	13.2±4.3
Steel back phenomenon (years)	14.7±3.5
Skiing posture (years)	18.5±7.9
	N (%)
Gender	Male 36 (63.2)
	Female 21 (37.8)
B27	Positive 38 (71.2)
	Negative 8 (28.8)

bral joint ankylosis, ligamentous ossifications and atlantoaxial dislocation<sup>7</sup>.

The aim of this study is to determine the frequency of the particular clinical and radiological feature in patients with AS with reference to gender, onset of first symptoms and disease duration and to determine the time interval between the occurrence of the first symptoms of the disease and the occurrence of the particular advanced clinical and radiological features.

## Patients and Methods

### Study design and settings

This observational study was performed in the Department of Rheumatology, Physical Medicine and Rehabilitation, University Hospital Sestre Milosrdnice in Zagreb from September 2001 till September 2005. Study has been reviewed and approved by Ethic Committee of the School of Medicine, University of Zagreb and has been performed according to the ethical standards laid down in the Declaration of Helsinki<sup>8</sup>.

### Participants

Fifty-seven patients (thirty-six men and twenty-one women; age 25–73 years) diagnosed with ankylosing spondylitis, according to the modified New York 1984 criteria,

ten or more years ago in the Department of Rheumatology, Physical Medicine and Rehabilitation, University Hospital Sestre Milosrdnice in Zagreb were included<sup>9</sup>. The goals of this study were explained to each patient together with the information that no tissue or body liquid will be used. Each patient enrolled in the study signed the informed consent.

### Data collection

An expert experienced in clinical studies, prior to the physical examination, filled in a questionnaire. Structured questionnaire used in this study was divided into following sections: sociodemographic data, data on the history of disease, musculoskeletal examination, laboratory findings (including HLA antigens) and data on the pharmacological treatment and physical therapy. Additional patient's medical records were also used.

Data on the history of disease included: age of the onset of first symptoms, age when AS was diagnosed, time interval between onset of symptoms and established diagnosis. Although, there is no consensus on the definition of disease duration, we obtained this data retrospectively from the medical record as the time since diagnosis of AS by a healthcare provider.

Musculoskeletal examination included measures of spinal mobility and chest expansion index and detection of advanced clinical features: flattening of the chest anterior wall, rubber-ball phenomenon, umbilical extrusion, diastasis of rectus abdominis muscle, steel back phenomenon, skiing posture.

Flattening of the anterior chest wall, rubber ball phenomenon, umbilical extrusion, steel back phenomenon and skiing position are observed during physical examination while patient is in the standing position.

Diastasis of the rectus abdominis muscle is detected in patient's supine position while lifting up legs.

### Radiological analysis

Radiological findings analysed in this study included following features: signs of sacroiliitis, signs of syndesmophytes, vertebral squaring and ligamentous ossification in thoracic and lumbar spine and signs of intervertebral joint ankylosis, atlantoaxial dislocation, syndesmophytes and vertebral squaring in cervical spine.

Signs of sacroiliitis were assessed on standard anteroposterior radiography of sacroiliac joints with a 20° cranial tube angle and patient in supine position. Radiological signs of sacroiliitis were graded according to the New York scale<sup>10</sup>.

Cervical spine involvement was assessed on anteroposterior and full flexion lateral views. Thoracic and lumbar spine involvement was assessed on posteroanterior and lateral thoracic and lumbar standard radiography.

When analysing the distribution of advanced clinical and radiological features in relation to the age of onset of first symptoms, patients were divided in three categories: age of onset of first symptoms before 20 years, between 21 and 30 years and older than 31 years.

**TABLE 2**  
DISTRIBUTION OF ADVANCED CLINICAL FEATURES OF ANKYLOSING SPONDYLITIS ACCORDING TO THE GENDER

	Gender		Total	$\chi^2$	
	Male	Female		Chi square	p value
Advanced clinical manifestation	N (%)	N(%)	N	Chi square	p value
Rubber-ball phenomenon	32 (72.7)	12 (27.3)	44	9.164	0.002
Flattening of the chest anterior wall	20 (86.9)	3 (13.1)	23	9.960	0.002
Umbilical extrusion	3 (50)	3 (50)	6	0.448	0.503
Rectus abdominis muscle diastasis	23 (82.1)	5 (17.9)	28	9.219	0.002
Skiing posture	3 (75)	1 (25)	4	0.259	0.611
Steeled back phenomenon	26 (83.9)	5 (16.1)	31	13.532	<0.001

When analysing the distribution of advanced clinical and radiological features in relation to the disease duration, patients were divided in three categories: disease duration less than 10 years, between 11 and 20 years and more than 21 years.

### Statistical methods

Data were analysed using the methods of descriptive statistics and methods of parametric (ANOVA, t-test) and non-parametric statistics. Chi-square test was used in order to test significance of dichotomous variables (Fisher's exact test for 2x2 tables).

### Since expected frequency in some cells is less than 5, Yates' correction was used.

Kruskal-Wallis' test, which can be interpreted as hi square test as well, was used for the comparison of more independent samples. Both Kruskal-Wallis' and chi square test have same distribution. Results were considered to be significant with  $p < 0.05$ . Stat Soft Statistica 7.1 was used in the analysis.

### Results

Fifty-seven patients (thirty-six men and twenty-one women) were included in this study. Male:female ratio was 1.7:1. Mean age of patients was  $52.9 \pm 9.78$  years (men  $52.5 \pm 10.97$  years, women  $53.7 \pm 7.58$  years). Average age of the disease onset was  $29.3 \pm 8.8$  years (men  $28 \pm 8.1$  years, women  $31.6 \pm 9.7$  years). Average disease duration was  $22.1 \pm 9.1$  years (men  $24.5 \pm 12$  years, women  $23.6 \pm 11$  years). Average time of diagnosis delay was  $10.7 \pm 9.7$  years (men  $11.4 \pm 10.1$  years, women  $9.47 \pm 9.41$  years).

### Clinical and demographic data are shown in Table 1.

Average time between the onset of first symptoms of disease and appearance of particular clinical feature is as

follows: for rubber-ball phenomenon  $11.9 \pm 4.3$  years, for umbilical extrusion  $19.2 \pm 6.1$  years, for rectus abdominis muscle diastasis  $13.2 \pm 4.3$  years, for steel back phenomenon  $14.7 \pm 3.5$  years, for the flattening of the chest anterior wall  $13 \pm 4$  years, for the skiing posture of patient  $18.5 \pm 7.9$  years.

### Gender

Table 2 shows the distribution of advanced clinical manifestations of AS with reference to gender. Following clinical advanced features are more prominent in male patients: rubber-ball phenomenon in 72.7% patients, flattening of the chest anterior wall in 86.9% patients, rectus abdominis muscle diastasis in 50% patients, steeled back phenomenon in 83.9%. Significant difference is found in the distribution of particular advanced clinical features of AS between men and women: rubber ball phenomenon ( $p=0.002$ ), flattening of the chest anterior wall ( $p=0.002$ ), rectus abdominis muscle diastasis ( $p=0.002$ ), skiing posture ( $p<0.001$ ).

Table 3 shows the distribution of advanced radiological features of AS in sacroiliac joints and axial skeleton between male and female patients. No statistical significance is found in the distribution of advanced radiological features in sacroiliac joints between male and female patients. Statistical significance is found in the distribution of syndesmophytes and ligamentous ossification in thoracic and lumbar spine between male and female patients: syndesmophytes ( $p=0.009$ ), ligamentous ossification ( $p=0.030$ ).

### Age of the onset of disease

Table 4 shows distribution of advanced clinical manifestations of AS with reference to the age of onset of first symptoms. No statistical significance is found in the distribution of advanced clinical manifestations of AS between observed group of patients. Table 5 shows the distribution of advanced radiological manifestations of AS in sacroiliac joints and axial skeleton with reference to the age of onset of first symptoms. Radiological signs of bilat-

**TABLE 3**  
DISTRIBUTION OF ADVANCED RADIOLOGICAL FEATURES OF ANKYLOSING SPONDYLITIS ACCORDING TO THE GENDER

	Gender		Total	$\chi^2$	p value
	Male	Female			
Radiological features (sacroiliac joints)	N (%)	N (%)	N		
Grade II bilateral sacroiliitis	5 (55.5)	4 (44.5)	9	0.221	0.639
Grade III bilateral sacroiliitis	11 (50)	11 (50)	22	2.416	0.120
Grade IV bilateral sacroiliitis	19 (76)	6 (24)	25	3.512	0.061
Radiological features of thoracic and lumbar spine					
Syndesmophytes	30 (66.6)	15 (33.4)	45	0.982	0.009
Vertebral squaring	31 (64.6)	17 (35.4)	48	0.146	0.702
Ligamentous ossification	13 (86.6)	2 (13.4)	15	4.720	0.030
Radiological features of cervical spine					
I.v.joints ankylosis	10 (62.5)	6 (37.5)	16	0.013	0.911
Syndesmophytes	16 (69.6)	7 (30.4)	23	0.600	0.438
Vertebral squaring	20 (68.9)	9 (31.1)	29	0.753	0.386
Atlantoaxial joint dislocation	1 (50)	1 (50)	2	0.167	0.683

**TABLE 4**  
DISTRIBUTION OF ADVANCED CLINICAL FEATURES OF ANKYLOSING SPONDYLITIS ACCORDING TO THE AGE OF THE ONSET OF FIRST SYMPTOMS

Advanced clinical features	Age of the onset of first symptoms			$\chi^2$	p value
	<20 years	21-30 years	>31 years		
	N (%)	N (%)	N (%)		
Rubber-ball phenomenon	18 (40.4)	11 (25)	15 (34.6)	1.280	0.527
Flattening of the chest anterior wall	10 (43.4)	6 (26.1)	7 (30.5)	1.256	0.534
Umbilical extrusion	2 (33.3)	2 (33.3)	2 (33.3)	1.525	0.466
Rectus abdominis muscle diastasis	15 (53.5)	5 (17.8)	8 (28.7)	3.441	0.179
Skiing posture	2 (50)	2 (50)	0	4.780	0.092
Steeled back phenomenon	13 (42)	11 (35.4)	7 (22.6)	2.208	0.332

eral sacroiliitis are more prominent in patients with onset of first symptoms between 21 and 30 years. No statistical significance is found in their distribution between observed groups of patients. Radiological changes in axial skeleton are more prominent in patients with onset of first symptoms between 21 and 30 years. Statistical significance is found in the distribution of the ossification of yellow ligaments ( $p=0.015$ ) in thoracic and lumbar spine and vertebral squaring in cervical spine ( $p=0.032$ ) between observed groups of patients.

### *Disease duration*

Table 6 shows distribution of advanced clinical features of AS according to the disease duration. Several advanced

clinical features of AS are more prominent in patients in whom disease lasts longer than ten years: rubber-ball phenomenon, flattening of the chest anterior wall, rectus abdominis muscle diastasis and steeled back phenomenon. Statistical significance is found in the distribution of rubber-ball phenomenon ( $p<0.001$ ) and rectus abdominis muscle diastasis ( $p=0.042$ ) between observed groups of patients.

Table 7 shows distribution of advanced radiological features of AS according to the disease duration. Following advanced radiological features of AS in sacroiliac joints and thoracic and lumbar spine are more prominent in patients with disease lasting longer than 20 years: grade IV bilateral sacroiliitis, syndesmophytes, vertebral squaring and ligamentous ossification. In cervical spine,

**TABLE 5**  
DISTRIBUTION OF ADVANCED RADIOLOGICAL FEATURES OF ANKYLOSING SPONDYLITIS ACCORDING TO THE AGE OF THE ONSET OF FIRST SYMPTOMS

Advanced radiological features	Age of the onset of first symptoms			$\chi^2$	p value
	<20 years	21-30 years	>31 years		
	N (%)	N (%)	N (%)		
<b>Radiological features of sacroiliac joints</b>					
Grade II bilateral sacroiliitis	0	7 (77.7)	2 (22.3)	4.661	0.097
Grade III bilateral sacroiliitis	2 (9.1)	8 (36.3)	12 (54.6)	4.697	0.096
Grade IV bilateral sacroiliitis	7 (28)	11 (44)	7 (28)	5.143	0.076
<b>Radiological features of thoracic and lumbar spine</b>					
Syndesmophytes	9 (20)	21 (46.6)	15 (33.3)	2.644	0.267
Vertebral squaring	9 (20)	22 (47.3)	17 (37.7)	1.571	0.456
Ligamentous ossification	6 (40)	5 (33.4)	4 (26.6)	8.423	0.015
<b>Radiological features of cervical spine</b>					
I.v.joints ankylosis	4 (25)	7 (43.7)	5 (31.3)	1.250	0.535
Syndesmophytes	5 (21.8)	9 (39.1)	9 (39.1)	1.336	0.513
Vertebral squaring	7 (24.1)	9 (31.1)	13 (44.8)	6.896	0.032

**TABLE 6**  
DISTRIBUTION OF ADVANCED CLINICAL FEATURES OF ANKYLOSING SPONDYLITIS ACCORDING TO THE DISEASE DURATION

Advanced clinical features	Disease duration			$\chi^2$	p value
	<10 years	11-19 years	>20 years		
	N (%)	N (%)	N (%)		
Rubber-ball phenomenon	1 (2.3)	16 (36.4)	27 (61.3)	16.590	$\leq 0.001$
Flattening of the chest anterior wall	1 (4.3)	9 (39.1)	13 (56.5)	1.258	0.526
Umbilical extrusion	0	2 (33.3)	4 (66.4)	1.071	0.585
Rectus abdominis muscle diastasis	0	11 (39.3)	17 (60.7)	6.329	0.042
Skiing posture	0	1 (25)	3 (75)	1.121	0.571
Steeled back phenomenon	1 (3.2)	12 (38.7)	18 (58.1)	3.527	0.171

syndesmophytes, intervertebral joint ankylosis and vertebral squaring are more frequent in patients with disease duration over 20 years.

Statistical significance is found in the distribution of grade IV bilateral sacroiliitis ( $p=0.012$ ), syndesmophytes ( $p=0.015$ ) and ligamentous ossification ( $p=0.027$ ) in thoracic and lumbar spine between observed groups of patients.

## Discussion

Advanced clinical and radiological features of AS result from morphological changes of bone and soft tissues partially due to the delayed diagnosis and delayed pharmacological treatment. Clinical and radiological changes

evaluated in this research are indicative of advanced disease. These signs have not been thoroughly studied so far, which explains the lack of internationally acquired terminology. Furthermore, to our knowledge no study has been published on the issue of advanced clinical and radiological features of AS and their distribution with reference to gender and association with the age of onset of first symptoms and disease duration. Advanced clinical features do not represent the problem in terms of their detection, but in terms of getting the more precise answer about the time interval between the onset of first symptoms and their appearance. Average time interval of the appearance of advanced clinical features of AS is about 18 years in our study. Jajić published a paper about the umbilical extrusion in patients with AS which is considered to be the consequence of increased intraabdominal pressure due to

**TABLE 7**  
DISTRIBUTION OF ADVANCED RADIOLOGICAL FEATURES OF ANKYLOSING SPONDYLITIS ACCORDING TO THE DISEASE DURATION

Advanced radiological features	Disease duration			$\chi^2$	p value
	<10 years	11-19 years	>20 years		
	N (%)	N (%)	N (%)		
Radiological features of sacroiliac joints					
Grade II bilateral sacroiliitis	1 (11.1)	5 (56.5)	3 (33.3)	1.201	0.549
Grade III bilateral sacroiliitis	3 (13.6)	12 (54.5)	7 (31.9)	4.897	0.086
Grade IV bilateral sacroiliitis	1 (4)	6 (24)	18 (72)	8.805	0.012
Radiological features of thoracic and lumbar spine					
Syndesmophytes	3 (6.7)	15 (33.3)	27 (60)	8.368	0.015
Vertebral squaring	5 (10.4)	17 (35.4)	26 (54.2)	3.496	0.174
Ligamentous ossification	1 (6.7)	2 (13.3)	12 (80)	7.229	0.027
Radiological features of cervical spine					
I.v.joints ankylosis	1 (6.3)	5 (31.3)	10 (62.4)	1.629	0.443
Syndesmophytes	1 (4.3)	8 (34.8)	14 (60.9)	2.563	0.278
Vertebral squaring	1 (3.4)	11 (37.9)	17 (58.6)	3.505	0.173
Atlantoaxial joint dislocation	0	1 (50)	1 (50)	0.222	0.895

the changes of the breathing technique. Umbilical extrusion appeared three years after the morphological changes of the rib cage<sup>11</sup>. We showed that rubber-ball phenomenon developed firstly (11.9±4.3 years from the onset of first symptoms), followed by the appearance of rectus abdominis muscle diastasis (13.2±4.3 years from the onset of first symptoms) and umbilical extrusion (19.2±6.1 years from the onset of first symptoms).

Statistical significance is observed in the distribution of certain clinical and radiological features of AS between male and female patients. Therefore, distribution of advanced clinical and particular radiological features of AS in sacroiliac joint and axial skeleton is sex dependent what could be explained by the fact that AS is a disease more susceptible to male patients.

Several studies showed that male gender is considered as one of the constitutional factors related to worse prognosis of AS<sup>12</sup>. Jimenez et al. showed no significant clinical or radiological difference between male and female patients suffering from AS, although the course of AS was more serious in male patients in terms of more severe restriction of spinal mobility, more frequent findings of uveitis, bamboo spine and hip arthroplasty<sup>13</sup>. Radiological changes in patients with AS occur at typical levels during the course of disease and should be considered as the strong marker of both disease chronicity and progression. Also, these are irreversible and reflect the cumulative natural history of disease. Radiological assessment in patients with AS is very important not only for establishing the diagnosis, but also for the assessment of disease activity, differentiating other causes of low back pain (e.g. undifferentiated spondyloarthropathy, septic sacroiliitis,

osteoarthritis) and for the disease outcome. Sacroiliitis is the traditional hallmark of AS and is required by the modified New York criteria for the definite diagnosis<sup>9</sup>. Conventional radiographs of sacroiliac joints have certain limitations in patients with early disease because no specific changes in their morphology can be detected whereas computerized tomography or magnetic resonance imaging using STIR technique show early signs of inflammation and bone marrow oedema<sup>14,15</sup>. On the other hand, grade IV sacroiliitis which incorporates complete joint obliteration with/without residual sclerosis is typical advanced radiological feature of AS, although it can be detected in early and active AS in about 20% of patients. Our study shows that none of our patients had grade I sacroiliitis (suspicious, but not definite abnormality) which is consistent with data from literature that early inflammatory changes cannot be detected on conventional radiographs although clinical manifestation are typical for AS<sup>16,17</sup>.

In many of our patients, grade III and grade IV of sacroiliitis were detected on conventional radiographs, suggesting that their diagnosis is based on the modified New York criteria<sup>9</sup>.

Radiological changes of axial skeleton seen on the conventional radiographs of thoracic and lumbar spine include Roman's lesion, squaring of the vertebral body, formation of syndesmophytes and ligament ossification<sup>18</sup>. Later onset of first symptoms is associated with the higher risk of developing radiological changes in sacroiliac joints and in the axial skeleton. Particular clinical features of AS (rubber-ball phenomenon and rectus abdominis muscle diastasis) and radiological features (grade IV bilateral sacroiliitis, syndesmophytes and ligamentous os-

sification) are more frequent in patients with disease duration longer than 10 years which is consistent with data from Mau and Sai-Nahal research<sup>19,20</sup>.

Significant difference in the distribution of syndesmophytes and ligamentous ossification between male and female patients and in the distribution of ligamentous ossification between observed group in relation to the age of onset of first symptoms is found in our study. This finding could be explained by the more aggressive disease and higher incidence of AS in male patients.

Radiological changes of the advanced AS can be seen in cervical spine and may develop in later stages of disease, patients with longer disease duration, hip disease or more aggressive sacroiliitis<sup>21</sup>. Neck symptoms are rarely seen as the first signs of AS. Syndesmophytes and vertebral squaring are more prominent radiological findings in male patients and in patients with the onset of first symptoms above 21 years of age in our study and this findings correlate with the literature data<sup>16,22</sup>. Data on the distribution of radiological changes of cervical spine between male and female patients differ and do not confirm the domination of particular gender. El Maghraoui et al showed no significant difference in the distribution of clinical and radiological features of AS between men and women<sup>23</sup>.

Average time delay in diagnosing AS in our study is 10.7±9.7 years. Different publications show that average time delay in diagnosing AS varies from 5-10 years from onset of symptoms which may depend on the type of first symptoms and clinical training and experience of physician<sup>1,24-26</sup>. Study by Ozgocmen and colleagues show that delay in diagnosis is longer in patients with juvenile onset AS<sup>27</sup>. Furthermore, restricted spinal mobility as well as of the rib cage are not frequently seen in early stages of disease. Therefore, lack of radiological signs of sacroiliitis and lack of restricted spinal mobility in the early stages of disease might also contribute to the delay in diagnosing.

Early detection of AS, especially in preradiographic stage, is challenging for the several reasons. Low back pain is nowadays recognized as a very important public health problem and less than 5% of patients with low back pain develops AS<sup>28,29</sup>. Inflammatory back pain which is characteristic for the early stages of AS is present in more

than 70% of patients with AS, although can be observed in patients with so-called mechanical back pain as well. Established diagnostic criteria and classification criteria are based on the combination of clinical manifestations and changes observed on radiographs, these criteria lack sensitivity in the early stages of disease and there is no clinical sign or laboratory test specific for AS. Due to these reasons, AS is usually diagnosed with delay of several years.

1984 modified New York criteria cannot be applied to the preradiographic AS, specificity of ESSG criteria is not high enough, and new imaging techniques (computerized tomography and magnetic resonance imaging) are still not part of the existing criteria. The lower the specificity of the classification criteria, the higher proportion of misdiagnosed patients. This may be the problem with the application of ESSG criteria in patients with preradiographic AS. Amor criteria, on the other hand, are more superior compared to the ESSG criteria because they require at least three or four parameters for the precise classification of axial form of disease<sup>28-30</sup>. Magnetic resonance imaging for detection of early inflammatory changes in sacroiliac joints is an important diagnostic tool, especially in patients with inflammatory back pain, B27 positive patients and in those with family history of AS as suggested by several studies and are part of the recently developed ASAS (Assessment of SpondyloArthritis international Society) criteria<sup>31-35</sup>.

The limitations of our study may be small sample of observed patients, long time interval between the symptom onset and analysis of advanced features of disease and lack of control group. Furthermore, the analysis as not adjusted for the confounding effects, due to relatively small sample size and a number of described confounders. Results of our study emphasize the importance of patient's regular follow-up, of searching for clinical signs of AS and precise radiological assessment.

In conclusion, these features could be considered as the predictors of worse functional outcome and disease prognosis. Therefore, earlier diagnosis and adequate pharmacological treatment are necessary in order to decrease the inflammation, prevent structural changes of axial skeleton and prevent the functional impairment.

## REFERENCES

1. ELYAN M, KHAN MA, *J Rheumatol*, 33 Suppl 78 (2006) 12. — 2. MANSOUR M, CHEEMA GS, NAGUWA SM, GREENSPAN A, BORCHERS AT, KEEN CL, GERSHWIN ME, *Semin Arthritis Rheum*, 36 (2007) 210. — 3. JAJIĆ I, Ankilozantni spondilitis. In: JAJIĆ I, *Reumatologija (Medicinska knjiga, Zagreb, 1995)*. — 4. KHAN MA, *Ann Intern Med* 136 (2002) 896. — 5. JAJIĆ Z, GRAZIO S, NEMČIĆ T, JAJIĆ I, *Reumatizam* 45 (1997) 13. — 6. JAJIĆ I, *Orthop Med*, 21 (1999) 70. — 7. JAJIĆ I, JAJIĆ Z, *Rentgenska dijagnostika reumatskih bolesti (Medicinska naklada, Zagreb, 2001)*. — 8. World Health Organization. Declaration of Helsinki. *BMJ*, 313 (1996) 1448. — 9. VAN DER LINDEN S, VALKENBURG HA, CATS A, *Arthritis Rheum*, 27 (1984) 361. — 10. BENNET PH, BURCH TA, *Bull Rheum Dis*, 28 (1967) 453. — 11. JAJIĆ I, JAJIĆ Z, *Scand J Rheumatol*, 27(1998): 388. — 12. AMOR B, SANTOS RS, NAHAL R, LISTRAT V, DOUGADOS M, *J Rheumatol*, 21(1994) 1883. — 13. JIMENEZ-BALDERAS FJ, MINTZ G, *J Rheumatol*, 20 (1993) 2069. — 14. MAKSYMOWYCH WP, LANDEWE R, *Best Pract Res Clin Rheum*, 20 (2006) 507. — 15. HERMANN KG, LANDEWE RB, BRAUN J, VAN DER HEIJDE DM, *J Rheumatol*, 32 (2005) 2056. — 16. BAROZZI L, OLIVIERI I, DE MATTEIS M, PADULA A, PAVLICA P, *Eur J Radiol*, 27 Suppl (1998) S12. — 17. BRAUN J, GOLDBER W, BOLLOW M, SIEPER J, VAN DER HEIJDE D, *Clin Exp Rheumatol*, 20 Suppl.28 (2002) S178. — 18. BROPHY S, MACKAY K, AL-SAIDI A, TAYLOR G, CALIN A, *J Rheumatol*, 29 (2002) 1236. — 19. MAU W, ZEIDLER H, MAU R, *J Rheumatol* 15 (1988) 1109. — 20. SAI-NAHAL R, MICELI-RICHARD C, BERTHELOT JM, DUCHE A, DERNIS-LABOUS E, LE BIEVEC G, SARAUX A, PERDIGER A, GUISS S, CLAUDEPIERRE P, SIBILIA J, AMOR B, DOUGADOS M, BREBAN M, *Arthritis Rheum*, 43 (2000) 1356. — 21. LEE HS, KIM TH, YUN HR, PARK YW, JUNG



SS, BAE SC, JOO KB, KIM SY, Clin Rheum, 20 (2001) 262. — 22. DE VLAM K, MIELANTS H, VEYS EM, J Rheumatol, 26 (1999) 1738. — 23. EL MAGHRAOUI A, BENSABBAH R, BAHIRI R, BEZZA A, GUEDIRA N, HAJJAJ-HASSOUNI N, Clin Rheumatol, 22 (2003) 94. — 24. FELDTKELLER E, KHAN MA, VAN DER HEIJDE D, VAN DER LINDEN S, BRAUN J, Rheumatol Int, 23 (2003) 61. — 25. KHAN MA Ann Rheum Dis, 61 Suppl 3 (2002) iii3. — 26. KUMAR A, BANSAL A, BANSAL M, SRIVASTVA DN, PANDHI A, MENON A, MEHRA NK, MALAVIYA AN, Rheumatol Int, 20 (2001) 221. — 27. OZGOCMEN S, ARDICOGLU O, KAMANLI A, KAYA A, DURMUS B, YILDIRIM K, BAYSAL O, GUR A, KARATAY S, ALTAY Z, CEVIK R, ERDAL A, ERSOY Y, SARAC AJ, TEKEOGLU I, UGUR M, NAS K, SENEL K, ULUSOY H, J Rheumatol, 36 (2009) 2830. — 28. RUDWALEIT M, KHANMA, SIEPER J, Arthritis Rheum, 52 (2005) 1000. — 29. O'SHEA F, SALONEN D, INMAN R, J Rheumatol, 34 (2007) 5. — 30. DOUGADOS M, VAN DER LINDEN S, JUHLIN R, HUITFELDT B, AMOR B, CALIN A, CATS A, DIJKMANS B, OLIVIERI I, PASERO G, Arthritis

Rheum, 34 (1991) 1218. — 31. PUHAKKA KB, JURIK AG, SCHIOTTZ-CHRISTENSEN B, HANSEN GV, EGUND N, CHRISTIANSEN JV, STENGAARD-PEDERSEN K, Rheumatology (Oxford), 43 (2004) 234. — 32. BENNET AN, MCGONAGLE D, O'CONNOR P, HENSOR EM, SIVERA F, COATES LC, EMERY P, MARZO-ORTEGS H, Arthritis Rheum, 58 (2008) 3413. — 33. RUDWALEIT M, VAN DER HEIJDE D, VAN DER HEIJDE D, LANDEWER, LISTING J, AKKOC N, BRANDT J, BRAUN J, CHOU T, COLLANTES-ESTEVEZ E, DOUGADOS M, HUANG F, GU J, KHAN MA, KIRAZLI Y, MAKSYMOWYCH WP, MIELANTS H, SØRENSEN IJ, OZGOCMEN S, ROUSSOU E, VALLE-OÑATE R, WEBER U, WEI J, SIEPER J, Ann Rheum Dis, 68 (2009) 777. — 34. RUDWALEIT M, Curr Opin Rheumatol, 22 (2010) 375. — 35. RUDWALEIT M, VAN DER HEIJDE D, LANDEWÉ R, AKKOC N, BRANDT J, CHOU T, DOUGADOS M, HUANG F, GU J, KIRAZLI Y, VAN DEN BOSCH F, OLIVIERI I, ROUSSOU E, SCARPATO S, SØRENSEN IJ, VALLE-OÑATE R, WEBER U, WEI J, SIEPER J, Ann Rheum Dis, 70 (2011) 25.

#### F. Grubišić

University Hospital Center »Sestre Milosrdnice«, Referral Center for the spondyloarthropathies, Department of Rheumatology, Physical Medicine and Rehabilitation, Ministry of Health and Social Welfare of the Republic of Croatia, Vinogradska 29, 10 000 Zagreb, Croatia  
e-mail: franegrubisic@gmail.com

### UZNAPREDOVALA KLINIČKA I RADIOLOŠKA OBILJEŽJA ANKILOZANTNOG SPONDILITISA: POVEZANOST SA SPOLOM, DOBI POJAVE PRVIH SIMPTOMA I TRAJANJEM BOLESTI

#### SAŽETAK

Cilj je odrediti učestalost uznapredovalih kliničkih i radioloških manifestacija ankilozantnog spondilitisa obzirom na spol ispitanika, dužinu trajanja bolesti i dob pojave prvih kliničkih smetnji. U istraživanje je uključeno 57 bolesnika sa dijagnozom ankilozantnog spondilitisa. Uznapredovala klinička obilježja ankilozantnog spondilitisa otkrivena su kliničkim pregledom: fenomen gumene lopte, ravna prsa, dijastaza mišića rectus abdominisa, ekstruzija umbilikusa, fenomen očeličenih leđa, fenomen ravnih prsa, stav skijaša. Radiološke promjene u vidu sakroileitisa, sindezmofta, skveringa kralješka i osifikacije ligamenata analizirane su na standardnim rentgenogramima sakroilijakalnih zglobova, zdjelice i kralješnice. Statički značajna razlika nađena je u raspodjeli određenih uznapredovalih kliničkih i radioloških obilježja bolesti između muškaraca i žena: fenomen gumene lopte ( $p=0,002$ ), fenomen ravnih prsiju ( $p=0,002$ ), dijastaza mišića rektus abdominisa ( $p=0,002$ ), stav skijaša ( $p<0,001$ ), sindezmofti ( $p=0,009$ ) i osifikacija ligamenaza ( $p=0,003$ ) u području torakalne i slabinske kralješnice. Pojava prvih simptoma bolesti ( $>20$ . godine života) značajno je povezana sa radiološkim promjena na torakalnoj kralješnici (osifikacija ligamenata,  $p=0,015$ ) i vratnoj kralješnici (četvrtasti oblik kralješka,  $p=0,032$ ). Duži tijek bolesti ( $>10$  godina) značajno je povezan sa pojavom određenih kliničkih obilježja-fenomen gumene lopte ( $p<0,01$ ), dijastaza mišića rektus abdominisa ( $p=0,042$ ) i radioloških promjena na sakroilijakalnim zglobovima (IV. stadij sakroileitisa,  $p=0,012$ ), torakalnoj i slabinskoj kralješnici (sindezmofti,  $p=0,015$ , osifikacija ligamenata,  $p=0,027$ ). Istraživanje pokazuje da pojava uznapredovalih kliničkih i pojedinih radioloških obilježja bolesti ovisi o spolu. Nadalje, pojava prvih simptoma bolesti ( $>20$  godina života) i duži tijek bolesti ( $>10$  godina) povezani sa povećanim rizikom razvoja određenih kliničkih obilježja i radioloških obilježja na sakroilijakalnim zglobovima i aksijalnom skeletu.