# Initial Diagnosis of Lumbar Disc Herniation Is Associated with a Delay in Diagnosis of Ankylosing Spondylitis

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ABSTRACT. Objective. There is often a considerable delay in diagnosis of ankylosing spondylitis (AS). In this multicenter study, we analyzed the delay and possible associated factors, including an initial diagnosis of lumbar disc herniation (LDH), which we frequently encounter in daily clinical practice.
Methods. The study included 393 consecutive patients [258 men (65.6%), mean age 39.3 ± 10.8 yrs] with AS according to the modified New York criteria. Face-to-face interviews were done using a structured questionnaire, addressing all the potentially relevant factors.

**Results.** The mean diagnostic delay was  $8.1 \pm 8.6$  years in the whole study population. The shortest delay was observed when rheumatologists were the first physicians consulted  $(2.9 \pm 5.3 \text{ yrs})$ . An initial diagnosis of LDH was reported by 33% of the patients. The diagnostic delays in patients with an initial diagnosis of LDH and those without were  $9.1 \pm 8.5$  years and  $6.2 \pm 7.4$  years, respectively (p = 0.002). In a regression model, predictive factors for delay in diagnosis were age at onset of spondyloarthritic symptoms, back pain, education level, prior diagnosis of LDH, and surgical history for LDH.

*Conclusion.* These results indicate the need to increase awareness of the concept of axial spondyloarthritis among specialists who might be the first physicians consulted by patients with AS for their back pain. There is also a need to develop strategies for early referral of such patients to rheumatologists. (J Rheumatol First Release Aug 1 2012; doi:10.3899/jrheum.120106)

Key Indexing Terms: ANKYLOSING SPONDYLITIS LUMBAR DISC HERNIATION

INTERVERTEBRAL DISC DISPLACEMENT LOW BACK PAIN DELAYED DIAGNOSIS

Ankylosing spondylitis (AS) is a chronic inflammatory disease that affects mainly sacroiliac joints and spine with an estimated prevalence around  $0.5\%^1$ . This prevalence figure is comparable to that of rheumatoid arthritis in the general population<sup>2,3</sup>; however, there is a considerable delay in diagnosing AS in Turkey, similar to other countries<sup>4,5,6,7</sup>. Although the age at onset of the symptoms is typically 20 to 30 years, time elapsed from onset of the symptoms to diag-

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nosis ranges from 5 to 10 years. Factors associated with the diagnostic delay may include (1) difficulty in diagnosis of inflammatory back pain (IBP), which is the leading symptom in most patients; (2) the absence of pathognomonic clinical and laboratory tests; (3) the lack of diagnostic criteria; and (4) the available classification criteria for AS depend on the presence of unequivocal radiographic sacroiliitis, which usually takes several years to develop<sup>8,9</sup>. In recent years the correct and early diagnosis of AS has become more important because of the availability of effective new treatments, such as anti-tumor necrosis factor (TNF) agents<sup>9,10</sup>.

In our clinical practice, like other authors<sup>4,6</sup>, we commonly see patients with AS who had been previously diagnosed as having lumbar disc herniation (LDH). We have speculated that inappropriate overuse of lumbar spinal magnetic resonance imaging (MRI) in patients with AS may result in an overdiagnosis of LDH because of its incidental finding on MRI, and consequently lead to possibly unnecessary surgical interventions. Therefore we evaluated the diagnostic delay in AS and the possible contributing factors, including a prior diagnosis of LDH.

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Gerdan, et al: AS diagnosis delay

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## MATERIALS AND METHODS

A total of 393 consecutive patients [258 men (65.6%), mean age 39.3  $\pm$  10.8 yrs] with AS according to the modified New York criteria<sup>11</sup> from 5 rheumatology clinics in 4 different cities were included in the study. A face-to-face interview was done using a structured questionnaire that addressed the factors that might lead to delayed diagnosis, including education level, age at onset of spondyloarthritic symptoms and back pain in particular, the presence of characteristics of IBP and other features of spondyloarthritis (SpA), the specialty of the first physician consulted and the one who first made the correct diagnosis, the type of imaging done first, the first clinical and radiographic diagnoses including LDH, surgical history for LDH, family history for SpA, HLA-B27 status, erythrocyte sedimentation rate, and C-reactive protein levels. Total duration of delay in diagnosis was defined as the time interval from the first visit to the physician for back pain to the diagnosis of AS. The time elapsed from the onset of any SpA-related symptom until the correct diagnosis was also recorded.

The study was approved by the local ethics committee (approval number: 89-IOC/2010) and informed consent was obtained from each patient. *Statistics*. Unless otherwise stated, values are presented as mean  $\pm$  SD or percentage, as appropriate. Kruskal-Wallis and Mann-Whitney U tests were used for group comparisons. Possible factors related to delay in diagnosis were evaluated by Spearman's correlation for continuous variables. The point-biserial correlation coefficient was used to test the association of a quantitative variable and a dichotomous or nominal variable. A linear regression method was used to determine predictive factors for delay in diagnosis of AS. All statistical tests were 2-tailed and a p value < 0.05 was considered to be statistically significant. The statistical analysis was carried out using SPSS version 13.0 (SPSS, Chicago, IL, USA).

#### RESULTS

Some of the demographic and clinical characteristics of the study group are summarized in Table 1. The mean diagnostic delay was  $8.1 \pm 8.6$  years in all patients with AS. Mean time from symptom onset to the correct diagnosis was  $9.7 \pm$ 

*Table 1*. Demographic and clinical characteristics of patients with ankylosing spondylitis (AS). Data are mean (SD) unless otherwise indicated.

Characteristic	
Age, yrs	39.3 (± 10.8)
Men, %	65.6
Education level, yrs	9.3 (± 4.3)
Smoking, %	61
Initial symptom, n (%)	
Back pain	241 (61.3)
Arthritis, dactylitis, or enthesitis	128 (32.6)
Other	24 (6.1)
Age at onset of symptoms, yrs	24.1 (± 8.7)
Age at onset of back pain, yrs	25.7 (± 8.4)
Age at onset of arthritis, dactylitis, or enthesitis, yrs	20.7 (± 8.8)
Age at diagnosis of AS, yrs	33.9 (± 10.8)
Inflammatory back pain at any time, n (%)	369 (93.9)
Hip prosthesis, n (5)	13 (3.3)
Uveitis, n (%)	54 (13.7)
Inflammatory bowel disease, n (%)	11 (2.8)
Psoriasis, n (%)	6 (1.5)
HLA-B27 positivity, n (%)	95/156 (61)
BASDAI score	3.7 (± 2.4)
BASFI score	3.3 (± 2.6)

BASDAI: Bath Ankylosing Spondylitis Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index.

9.3 years. Only 4% (n = 16) of patients presented to rheumatologists for the first visit for back pain, whereas 30% (n = 118) consulted a physiatrist, 25% (n = 99) an orthopedist, and 16% (n = 63) a neurosurgeon. The correct diagnosis was made by rheumatologists in 261 patients (66.4%). In the study sample, the mean delay in diagnosis was  $8.12 \pm 8.57$ years and differed significantly among the specialties consulted for the first visit. Diagnostic delay was  $2.9 \pm 5.3$  years for rheumatologists when they were the first-contacted physicians,  $6.3 \pm 7.6$  years for physiatrists,  $9.6 \pm 9.1$  years for orthopedists, and  $8.8 \pm 6.6$  years for neurosurgeons. There were significant differences among specialties consulted at first visit and time elapsed from the initial visit to the diagnosis (Table 2).

Of the 393 patients, 269 could recall the features of their back pain at onset; of them, 247 (92%) fulfilled the Calin criteria for IBP<sup>2</sup>. Initial diagnosis was recalled by 302 of the 393 patients and LDH was reported by 130 of them (33%). Only 54 patients (13.7%) stated that SpA or AS were diagnosed as the cause of their back pain at their initial presentation. Nonspecific back pain was diagnosed in another 98 patients (24.9%). In the rest of the patients (n = 111), initial clinical diagnoses were either not reported or were nonspecific.

The delay in diagnosis was significantly longer in patients with a prior diagnosis of LDH in comparison with others (9.1 ± 8.5 vs 6.2 ± 7.4 years; p = 0.002). Spinal computerized tomography (CT) or MRI examinations had been performed in 85% of the patients who were given an initial diagnosis of LDH. Initial diagnosis of LDH was negatively associated with early diagnosis, defined as within 5 years after first visit (OR 0.59, 95% CI 0.36–0.95). A history of LDH surgery was reported by 26 patients (6.6%) and the diagnostic delay was significantly longer in those patients compared to those without a history of such surgery (13.3 ± 11.3 vs 7.8 ± 8.2 yrs; p = 0.023).

Factors correlated with the diagnostic delay were ages at onset of any spondyloarthritic symptom, age at onset of back pain, prior diagnosis of LDH, surgical history for LDH, first specialty consulted for back pain, and education level. In a regression model, these factors were found to be associated with delay in diagnosing AS: age at onset of spondyloarthritic symptom, age at onset of back pain, prior diagnosis of LDH, surgical history for LDH, and education level (Table 3).

## DISCUSSION

Our study, like others<sup>4,5,6,7</sup>, illustrates that patients with AS are diagnosed unacceptably late and that an initial diagnosis of LDH and previous history of surgery for LDH is associated with a later diagnosis. In confirmation of the findings of some previous studies, age at onset of back pain, age at onset of spondyloarthritic symptom, education level, and medical specialty consulted for back pain were also found to

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Table 2. Diagnostic delay among various specialists consulted, with first visit and comparisons of groups.

First Specialist Consulted	Mean Diagnostic Delay, yrs ± SD	Comparison Between Groups	р
Rheumatologists, n = 16	$2.9 \pm 5.3$	Rheumatologists vs physiatrists	0.002
		Rheumatologists vs orthopedists	0.001
		Rheumatologists vs neurosurgeons	0.002
Physiatrists, $n = 118$	$6.3 \pm 7.6$	Physiatrists vs orthopedists	0.012
		Physiatrists vs neurosurgeons	0.021
Orthopedists, $n = 99$	$9.6 \pm 9.1$	Orthopedists vs neurosurgeons	NS
Neurosurgeons, $n = 63$	$8.8 \pm 6.6$	1 0	
All specialties, $n = 349$	$8.1 \pm 8.6$	Rheumatologists vs other specialties	< 0.001

NS: nonsignificant.

*Table 3*. Factors related to the delay in diagnosis of patients with ankylosing spondylitis (results of the correlation and regression analysis).

	Correlation Analysis		Regression Analysis	
	r or R <sup>2</sup>	р	В	р
Age at onset of spondylitic symptons, yrs*	-0.216	< 0.001	-0.178	0.003
Age at onset of back pain, yrs*	-0.140	0.006	0.080	0.002
Education level, yrs*	-0.189	< 0.001	-0.252	0.018
Specialty of the first physician consulted**	-0.012	0.024	-0.400	0.343
Prior diagnosis of lumbar disc herniation**	0.032	0.001	2.278	0.018
Surgical history for lumbar disc hernation**	0.025	0.015	6.014	< 0.001

\* Spearman's correlation coefficient (r). \*\* Point-biserial correlation coefficient (R<sup>2</sup>).

be correlated with diagnostic delay. However, in contrast to some previous studies, no correlation was found between HLA-B27 status and diagnostic delay<sup>5,13</sup>.

The mean time between onset of symptoms and clinical diagnosis of AS has been reported to range from 5.0 to 8.6 years in previous studies from Turkey. The corresponding timespan (from onset of symptom to correct diagnosis) in our study was 9.8 years. The difference between the studies may be due to differences in the study populations. Two study cohorts, including ours, with the longest delay in diagnosis had lower male/female ratios (1.8/1) compared to those with shorter delay times (from 3/1 to 13/1). Delay in diagnosis of AS may be longer for women than for men, possibly because of the frequent predominant peripheral joint and/or cervical spine involvement and less severe radiographic damage in women<sup>14</sup>.

About two-thirds of adults suffer low back pain at some time<sup>15</sup>; however, in only around 10% of these patients, pain does not resolve within 12 weeks, and in up to 90% of the patients with chronic back pain, the anatomic cause cannot be determined<sup>16</sup>. Among all adult patients with low back pain, prevalence of herniated disc is estimated at 4%. In our study cohort, the prevalence of a previous diagnosis of LDH was 33%, which is within the range of the 22%–40% frequency of herniated disc reported as an incidental finding on

MRI of asymptomatic adults<sup>17,18,19</sup>. Diagnostic imaging for evaluation of patients with low back pain is recommended in special situations such as the presence of trauma, persistent neurologic deficit, severe pain, or a symptom suggestive of a systemic disease (infections, cancer). However, advanced imaging modalities are used indiscriminately in daily clinical practice, as illustrated by the frequent use (85%) of spinal MRI or CT examinations in our study cohort. This frequency contributed to an overdiagnosis of LDH, due to incidental findings on MRI. We speculate that the explanatory diagnosis given to those patients for their back pain led to a delay in consulting with rheumatologists and to a greater delay in diagnosis. This view is supported by a lower chance of early diagnosis of AS (within  $\leq$  5 years of symptom onset) among patients with an initial diagnosis of LDH.

The performance of physicians with different specialties may vary. One study reported that the correct diagnosis of AS was most frequently made by rheumatologists<sup>11</sup>. Another study found that diagnosis is made significantly earlier by physiatrists and rheumatologists compared to general practitioners, internists, orthopedists, and neurosurgeons<sup>13</sup>. In our study, the correct diagnosis was made by rheumatologists in two-thirds of the patients. For the purpose of our study we defined the diagnostic delay as the time

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from first physician visit for back pain to correct diagnosis, because we were particularly interested in factors that may be related to the clinical practice. When rheumatologists were the first contacted specialists, the mean diagnostic delay was significantly shorter than that for the other specialties. Physiatrists also performed better than orthopedists and neurosurgeons in diagnosing AS earlier. However, our results may be biased in favor of rheumatologists making an earlier diagnosis because the study included only patients followed at rheumatology clinics. Moreover, in regression analysis, the specialty of the first physician consulted was not found to be a significant predictor of diagnostic delay (Table 3).

The main limitation of our study is the use of patientcollected data without any validation by means of medical records. Therefore it was not possible to verify the patientreported initial diagnosis. Retrospective questioning of patients who may have introduced recall bias is another limitation of our study. However, to minimize the recall bias we collected the data using a standardized form for the definition and articulation of the questions and answers.

In the past, early diagnosis of patients with AS might not have been too much of a concern for physicians because of the unavailability of adequate treatment options. However, the introduction of TNF antagonists, which are very effective in treating signs and symptoms of AS, has changed this situation. Lack of any pathognomonic symptoms or a predictive laboratory test, and longtime requirement for development of radiological signs of sacroiliitis (according to the modified New York criteria), should be considered among the major causes of delay in diagnosis. However, the new axial SpA (axSpA) classification criteria, which do not require the presence of radiographic sacroiliitis<sup>20</sup>, and the early referral strategies may help physicians make an earlier diagnosis<sup>21</sup>.

Our study indicates that an initial diagnosis of LDH may lead to late presentation of patients with AS to rheumatologists, and consequently to a delay in diagnosis. The relatively common history of LDH surgery among patients with AS, which is associated with a significantly longer diagnostic delay, is also of concern. These findings underscore the necessity for increasing the awareness of the new axSpA classification criteria among physicians who might be consulted for back pain, and the importance of developing strategies to identify patients for early referral to rheumatologists.

# REFERENCES

- Onen F, Akar S, Birlik M, Sari I, Khan MA, Gurler O, et al. Prevalence of ankylosing spondylitis and related spondyloarthritides in an urban area of Izmir, Turkey. J Rheumatol 2008;35:305-9.
- Akar S, Birlik M, Gurler O, Sari I, Onen F, Manisali M, et al. The prevalence of rheumatoid arthritis in an urban population of Izmir-Turkey. Clin Exp Rheumatol 2004;22:416-20.
- 3. Akkoc N. Are spondyloarthropathies as common as rheumatoid

arthritis worldwide? A review. Curr Rheumatol Rep 2008;10:371-8.

- Aggarwal R, Malaviya AN. Diagnosis delay in patients with ankylosing spondylitis: Factors and outcomes — an Indian perspective. Clin Rheumatol 2009;28:327-31.
- Feldtkeller E, Khan MA, van der Heijde D, van der Linden S, Braun J. Age at disease onset and diagnosis delay in HLA-B27 negative vs. positive patients with ankylosing spondylitis. Rheumatol Int 2003;23:61-6.
- Ibn Yacoub Y, Amine B, Laatiris A, Bensabbah R, Hajjaj-Hassouni N. Relationship between diagnosis delay and disease features in Moroccan patients with ankylosing spondylitis. Rheumatol Int 2012;32:357-60.
- Ozgocmen S, Ardicoglu O, Kamanli A, Kaya A, Durmus B, Yildirim K, et al. Pattern of disease onset, diagnostic delay, and clinical features in juvenile onset and adult onset ankylosing spondylitis. J Rheumatol 2009;36:2830-3.
- Mau W, Zeidler H, Mau R, Majewski A, Freyschmidt J, Stangel W, et al. Clinical features and prognosis of patients with possible ankylosing spondylitis. Results of a 10-year followup. J Rheumatol 1988;15:1109-14.
- Rudwaleit M, van der Heijde D, Khan MA, Braun J, Sieper J. How to diagnose axial spondyloarthritis early. Ann Rheum Dis 2004;63:535-43.
- Braun J, Sieper J, Breban M, Collantes-Estevez E, Davis J, Inman R, et al. Anti-tumour necrosis factor alpha therapy for ankylosing spondylitis: International experience. Ann Rheum Dis 2002;61 Suppl 3:iii51-60.
- van der Linden S, Valkenburg HA, Cats A. Evaluation of diagnostic criteria for ankylosing spondylitis. A proposal for modification of the New York criteria. Arthritis Rheum 1984;27:361-8.
- Calin A, Porta J, Fries JD, Schurman DJ. Clinical history as a screening test for ankylosing spondylitis. JAMA 1977;237:2613-4.
- Dincer U, Cakar E, Kiralp MZ, Dursun H. Diagnosis delay in patients with ankylosing spondylitis: Possible reasons and proposals for new diagnostic criteria. Clin Rheumatol 2008; 27:457-62.
- Feldtkeller E, Bruckel J, Khan MA. Scientific contributions of ankylosing spondylitis patient advocacy groups. Curr Opin Rheumatol 2000;12:239-47.
- Deyo RA, Weinstein JN. Low back pain. N Engl J Med 2001;344:363-70.
- Rathmell JP. A 50-year-old man with chronic low back pain. JAMA 2008;299:2066-77.
- Boden SD, Davis DO, Dina TS, Patronas NJ, Wiesel SW. Abnormal magnetic-resonance scans of the lumbar spine in asymptomatic subjects. A prospective investigation. J Bone Joint Surg Am 1990;72:403-8.
- Jensen MC, Brant-Zawadzki MN, Obuchowski N, Modic MT, Malkasian D, Ross JS. Magnetic resonance imaging of the lumbar spine in people without back pain. N Engl J Med 1994;331:69-73.
- Weishaupt D, Zanetti M, Hodler J, Boos N. MR imaging of the lumbar spine: Prevalence of intervertebral disk extrusion and sequestration, nerve root compression, end plate abnormalities, and osteoarthritis of the facet joints in asymptomatic volunteers. Radiology 1998;209:661-6.
- 20. Rudwaleit M, van der Heijde D, Landewe R, Listing J, Akkoc N, Brandt J, et al. The development of Assessment of SpondyloArthritis international Society classification criteria for axial spondyloarthritis (Part II): Validation and final selection. Ann Rheum Dis 2009;68:777-83.
- Poddubnyy D, Vahldiek J, Spiller I, Buss B, Listing J, Rudwaleit M, et al. Evaluation of 2 screening strategies for early identification of patients with axial spondyloarthritis in primary care. J Rheumatol 2011;38:2452-60.

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