

Effects of weight- and age-related syndesmophytes on patients with ankylosing spondylitis.

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Abstract

Objective: To determine contributors of syndesmophytes and evaluate their effects on various aspects of quality of life among patients with ankylosing spondylitis (AS).

Methods: we conducted a cross-sectional study and 85 AS patients received the X-ray examination and completed the questionnaire including demographic variables, clinical variables, psychological variables and quality of life.

Results: There were 44(51.8%) with syndesmophytes among AS patients. Age, gender, body mass index (BMI), waist hip ratio (WHR), education level, disease duration and the level of ESR were different between AS patients with or without syndesmophytes. AS patients with syndesmophytes have more problems in functional status, spinal mobility, night or global pain, disability and health related quality of life.

Conclusions: Syndesmophytes had negative effects on AS patients in the field of functional status, spinal mobility, pain, disability and quality of life. In addition, aging, gender, WHR was the key predictor of syndesmophytes formation.

Introduction

Ankylosing spondylitis(AS) is a chronic inflammatory rheumatic disease with unclear etiology characterized by inflammation of the sacroiliac joint and spinal column with poor health related quality of life (HRQoL)(1). Other and our study have shown that HRQoL of AS patients was impaired and relevant with socioeconomic status (SES), psychological factors and body image disturbance(2–4). One of distinguishing characteristics of AS is that new bone formation in the form of syndesmophytes and its occurring at the cortical bone compartment of the axial skeleton impair the spinal mobility and function (5). 16% patients had syndesmophytes at baseline and 13.4% patients developed new syndesmophytes in their lumbar spines after 2 years in female AS patients in South Korea(6). One study in Netherlands showed that only 33% AS patients had no syndesmophytes(7). New syndesmophytes developed in 33% patients within 2 years and in 48% patients within 4 years(8). Actually, the cause of syndesmophytes formation is still ambiguous. Longer disease duration and elevated C-reactive protein (CRP) levels at baseline were associated with the occurrence of new syndesmophytes(6, 9). Meanwhile, inflammatory factors were related to syndesmophytes formation and systemic inflammation, indicating that continuous, systemic, and low-dose inflammation played crucial roles in the process of syndesmophytes formation (10, 11). As we all know, aging, obesity, anxiety, depression and other SES or psychological factors are correlated with inflammation and have negative effect on functional status and HRQoL(12, 13). Nevertheless, it is still unclear about the relationships among SES, psychological status, inflammation and syndesmophytes in AS patients. Thus, we conducted this study to evaluate the prevalence and predictors of syndesmophytes and identify the effects of syndesmophytes on HRQoL in Chinese patients with AS.

Patients And Methods

A cross-sectional study was conducted among both inpatients and outpatients from Affiliated Hospital of Nantong University from February 2017 to September 2017. A total of 85 AS patients who were fulfilled the modified New York criteria for AS were constantly enrolled and complete the questionnaire under the researchers' supervision in a clinical setting. At the same time, these patients were required to receive free X-ray examination of cervical and lumbar with the informed consent of themselves.

Measures

Patients with AS who joined in this study should complete self-report questionnaires as the followings:

Demographic variables contained the following: age, gender, body mass index (BMI), waist hip ratio (WHR), marital status, education level, employment, yearly per capita income, medical insurance, place of residence, hospitalization, tobacco use, alcohol use, family history, disease duration, etc.

The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) was applied for measuring disease activity of AS patients according to its score definition(14). Impaired functioning was assessed by Bath Ankylosing Spondylitis Functional Index (BASFI)(15). Researchers measured the distance from the tragus to the wall, lumbar flexion, cervical rotation, lumbar side flexion, and maximal intermalleolar distance for AS patients to assess spine and hip mobility according to the Bath Ankylosing Spondylitis Metrology Index (BASMI)(15, 16). Night pain and general pain was assessed by visual-analogue-scale (VASs). The Health Assessment Questionnaire (HAQ) was applied for quantifying the difficulty in functional areas about daily activities such as dressing and grooming, arising, eating, walking, hygiene, reaching, gripping, etc. with higher scores indicating more disability(17). The revised Self-Rating Anxiety Scale (SAS) can indicating the level of anxiety symptoms with scores ≤ 50 (18). The revised Self-Rating Depression Scale (SDS) can show the depressive symptoms with score ≤ 53 (19). Participants completed the paper questionnaire under the researchers' supervision in a clinical setting. Raw data were obtained and added to database by two blinded researchers who rechecked totals prior to entering the data.

Short-Form 36 (SF-36) questionnaire was used to assess general health status including physical functioning (PF), Role-Physical (RP), Bodily Pain (BP), General Health (GH), Vitality (VT), social functioning (SF), Role-Emotional (RE), Mental Health (MH) with two distinct high-order summary scores: the physical component summary (PCS) and the mental component summary (MCS)(20). The level of Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were measured in AS patients.

Radiographic evaluation

Conventional radiographs including X-rays are still regarded as the gold standard in assessing the chronic structural changes of the spine in AS patients(21–23). The modified Stokes AS Spine Score (mSASSS) is the sum of the lumbar and cervical spine score which is a well validated scoring system (range 0–72)(24). A corresponding scoring system was used as follows: 0 = no abnormality; 1 = erosion, sclerosis or squaring; 2 = syndesmophyte; and 3 = total bony bridging at each site. Worsening of

mSASSS score ≥ 2 was defined as the growth of syndesmophytes which might lead to chronic structural changes of the spine, diminished physical function and restricted spinal motion(25–27). The diagnosis of syndesmophyte relying on X-ray was evaluated by two radiologists independently and blindly and the final mSASSS score was the average value of the them. If the radiologists hold scores with huge disparities, another radiologist will be invited to evaluate duplicate.

Analytic Strategy

Descriptive statistics are provided using the median (IQR), mean (\pm standard deviation) or quantity (percentage) based on the parameter distribution of the measured variables. The conformity to the normal distribution was assessed by using the Shapiro-Wilk test. The chi-square test is used to estimate the difference in the proportions. Differences in numerical variables between independent groups were studied by using the independent sample t test while satisfying the parametric test hypothesis and using the Mann-Whitney U test without satisfying the hypothesis. Multivariate analysis was used to explore how several variables affect the results of syndesmophytes. All variables obtained by univariate test were logistic regression models with $P < 0.05$ as independent variables. Demographic, clinical, and psychological characteristics were defined as independent risk factors, included in the model if $P < 0.05$, or removed according to forward (LR) selection techniques if $P > 0.10$. Data was analyzed using SPSS (version 21.0). Statistical significance was defined as $P < 0.05$.

Results

Sample characteristics

Demographic, clinical characteristics of the study population and the difference between them are described in Table 1. There are 65(76.5%) males with median (IQR) age of 32(14.5) years, A total of 66 (77.6%) married patients and 63 (74.1%) were employed. The duration of these patients was 5 (8), and 35.3% of the patients had an education level of no more than 9 years. More than one-third of patients have an annual per capita income of less than RMB15,000. 11(12.9%) patients were found with AS familiarity, and 22(25.9%) patients had a hospitalization before. 27.1% AS patients with smoking and 20% with alcohol consumption. The score of BASDAI is 2.7(2.79) and night pain was 3(5) with global pain is 4(4). Based on blood test result, the median (IQR) of ESR was 21(34.5) mm/h and the level of CRP was 14.95(22.88) mg/L. There were 44(51.8%) patients have syndesmophytes. Age, gender, BMI, WHR, education level, disease duration, BASFI, BASMI, pain and the level of ESR were different between AS patients with or without syndesmophytes. In addition, these two groups have no differences in annual per capita income, smoking, drinking, BASDAI, CRP, etc. ($P > 0.05$).

Syndesmophytes was associated with age, gender, obesity, education level, disease duration, BASMI, BASFI, pain and inflammation.

Correlation between socioeconomic status, disease activity, ESR, CRP and syndesmophytes is presented in Table 2. Age, gender, BMI, WHR, education level, disease duration, BASMI, BASFI, pain and the level of

ESR were related to syndesmophytes.

Syndesmophytes had negative effects on quality of life in AS patients.

Comparison of quality of life between groups of syndesmophytes formation or not is given in Table 3. Physical related quality of life (PCS, PF, RP, BP) were found to be different between AS patients with or without syndesmophytes. In addition, there were no difference ($P > 0.05$) in mental related quality of life (MCS, GH, VT, SF, RE, MH) between the two groups.

Older and fatter male AS patients are more likely to form syndesmophytes.

the results of logistic regression analysis was showed in Table 4. We conducted the predictors ($P \leq 0.05$ in table 1), such as age, gender, BMI, WHR, education level, disease duration, pain and ESR into the model of logistic regression analysis and found that gender (odds ratio = 0.007; $P = 0.004$), age (odds ratio = 1.148; $P = 0.001$), WHR (odds ratio = 2.251; $P = 0.023$) were the predictors of the syndesmophytes formation. Considering that the score of BASMI and BASFI were the reflect of the outcome of syndesmophytes, we ignored it in logistic regression analysis.

Discussion

AS patients have high incidence of syndesmophytes. In Netherlands, of the 81(61%) patients, 17 (45%) were female and 64 (65%) were male, with a common syndesmophytes(28). In South Korea, Kang KY, et al reported that 16% female AS patients had syndesmophytes at baseline and 13.4% of patients developed new syndesmophytes in the lumbar spine after 2 years. In the present study, we revealed that 51.8% of AS patients suffered from syndesmophytes in China.

Although the cause of syndesmophyte formation has not been resolved, continuous inflammation plays an important role in it(10, 27, 29–33). Aging, obesity, depression, anxiety and other SES or psychological factors as an inflammatory state may had a greatly influences on the occurrence of syndesmophytes(34, 35). Many other researchers have found that the effect of age on the number of syndesmophytes depends on the duration of the disease(35, 36)^[39]. During long-term treatment with TNF- α inhibitors, more radiographic damage were associated with baseline syndesmophytes, male gender and older age(37). There is associated relationship between not only aging and the inflammatory activity but also obesity and reactive bone formation of the knee joint compartments(38, 39). WHR is an important measure of central obesity, because the key to obesity is the accumulation of body fat, not just weight. Recently, a study conducted on European population demonstrated a close relevance of obesity with higher disease activity and lower functional performance in AS patients(40, 41). However, there were still none study reporting the relationship between inflammation, SES factors and syndesmophytes in Chinese AS patients. In this study, we reported that older age, higher WHR and longer disease duration were correlated with occurrence of syndesmophytes in AS patients. Besides, older age and higher WHR might be an independent predictor of syndesmophytes according to the results of logistic analysis.

Poor QoL is significantly associated with high disease activity, poor functional status, and decreased spinal activity in AS(42). The results in this study were in line with previous studies, showing that syndesmophytes have negative influence on physical related QoL. Additionally, the rate of anxiety and depression in AS patients was higher than controls and it had a negative effect on HRQoL(2, 43–45). However, no significant correlation was found between the syndesmophytes and psychological status, such as anxiety and depression in this study.

In summary, the syndesmophytes had negative effects on quality of life in AS patients. By the logistic analysis, we found that age, WHR and male was the predictors of syndesmophytes in AS. These findings also suggested the role of inflammation in radiographic progress. According to the results of logistic analysis, clinicians need to pay more attention to the older and fatter male in AS patients due to their susceptibility of syndesmophytes.

List Of Abbreviations

ankylosing spondylitis (AS), body mass index (BMI), waist hip ratio (WHR), health related quality of life (HRQoL), socioeconomic status (SES), Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), body mass index (BMI), waist hip ratio (WHR), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI), Bath Ankylosing Spondylitis Metrology Index (BASMI), visual-analogue-scale (VAS), Health Assessment Questionnaire (HAQ), Self-Rating Anxiety Scale (SAS), Self-Rating Depression Scale (SDS), Short-Form 36 questionnaire (SF–36), physical functioning (PF), Role-Physical (RP), Bodily Pain (BP), General Health (GH), Vitality (VT), social functioning (SF), Role-Emotional (RE), Mental Health (MH), physical component summary (PCS), mental component summary (MCS), modified Stokes AS Spine Score (mSASSS).

Declarations

Ethics approval and consent to participate

This survey was approved by the Ethics Committee of Affiliated Hospital of Nantong University and the ethics approval number for this study is 2017-K003. Informed consent was obtained from all individual participants included in the study.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

All authors contributed to the study conception and design, especially [Ting Fu, Zhifeng Gu]. Data collection were performed by [Chen Dong], [Jing Wang] and [Rui Zhao]. Data analysis was performed by [Juan Ji] and [Yuanyuan Chen]. The first draft of the manuscript was written by [Chen Dong] and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Acknowledgements

Not applicable

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Tables

Table 1. Differences between socioeconomic status, disease activity, psychological status between groups with syndesmophytes or not.

Variables	All patients (N=85)	With syndesmophytes (n=44)	Without syndesmophytes (n=41)	P
Age, year	32(14.5)	40(18.75)	29(9)	<0.001**
Sex, man	65(76.5)	38(86.4)	27(65.9)	0.026*
BMI	23.44(5.26)	24.08(4.91)	22.47(3.91)	0.038*
WHR	0.88(0.11)	0.9(0.12)	0.86(0.12)	0.009**
Place of residence				0.406
Urban	50(58.8)	24(54.5)	26(63.4)	
Rural	35(41.2)	20(45.5)	15(36.6)	
Marital status				0.14
Married	66(77.6)	37(84.1)	29(70.7)	
Other marital status	19(22.4)	7(15.9)	12(29.3)	
Education level				0.013*
≤9 years	30(35.3)	21(47.7)	9(22)	
≥9 years	55(64.7)	23(52.3)	32(78)	
Employed, yes	63(74.1)	32(72.7)	31(75.6)	0.762
Yearly per capita income, yuan				0.901
≤15000	30(35.3)	16(36.4)	14(34.1)	
15000-33000	28(32.9)	15(34.1)	13(31.7)	
≥33000	27(31.8)	13(29.5)	14(34.1)	
Medical insurance, yes	58(68.2)	32(72.7)	26(63.4)	0.357
Tobacco use, yes	23(27.1)	12(27.3)	11(26.8)	0.963
Alcohol use, yes	17(20)	8(18.2)	9(22)	0.664
Hospitalization, yes	22(25.9)	10(22.7)	12(29.3)	0.491
Family history, yes	11(12.9)	6(13.6)	5(12.2)	0.843
Disease duration, year	5(8)	5.5(8.5)	4(6.5)	0.043*
BASFI	0.9(2.4)	1.6(3.05)	0.3(1.1)	<0.001**
BASMI	1.5(3)	3(3)	1(2)	<0.001**
BASDAI	2.7(2.79)	2.9(3.08)	2.63(1.98)	0.232
Patient night pain, VAS (mm)	3(5)	3(6.5)	2(3.5)	0.036*
Patient global pain, VAS (mm)	4(4)	5(5)	3(4)	0.005**
HAQ	0.13(0.38)	0.19(0.63)	0(0.31)	0.056
Anxiety, yes	20(23.5)	12(27.3)	8(19.5)	0.399
Depression, yes	24(28.2)	15(34.1)	9(22)	0.214
ESR, mm/h	21(34.5)	28(33.75)	10(36)	0.006**
CRP, mg/L	14.95(22.88)	16.9(20.23)	11.8(23.8)	0.112
Syndesmophyte, yes	44(51.8)	--	--	--

Notes: Data presented as n (%), mean ± standard deviation, median (IQR). Data are means ± SD for continuous variables, or percentages for categorical variables. P values were obtained with the chi-square test for categorical variables and the two-tailed t test for continuous variables. * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$.

Abbreviations: AS=ankylosing spondylitis; BMI=Body Mass Index; WHR=waist-to-hip ratio; BASFI=Bath Ankylosing spondylitis Functional index; BASMI=Bath Ankylosing spondylitis Metrology index; BASDAI=Bath Ankylosing spondylitis Disease Activity index; VAS=visual analog scale; HAQ=health Assessment Questionnaire; ESR=erythrocyte sedimentation rate; CRP=c-reactive protein.

Table 2. Correlation between socioeconomic status, disease related status, psychological status and syndesmophytes.

Variables	syndesmophyte	
	R	P-value
age	0.456 ^{***}	<0.001^{**}
Sex, man	-0.242 [*]	0.026[*]
BMI	0.227 [*]	0.037[*]
WHR	0.287 ^{**}	0.008^{**}
Place of residence	0.09	0.412
Marital status	-0.16	0.143
Education level	-0.27 [*]	0.013[*]
Employed, yes	-0.033	0.765
Yearly per capita income, yuan	-0.041	0.708
Medical insurance, yes	0.1	0.363
Tobacco use, yes	0.005	0.964
Alcohol use, yes	-0.047	0.669
Hospitalization, yes	-0.075	0.497
Family history, yes	0.021	0.845
Disease duration, year	0.221 [*]	0.042[*]
BASDAI	0.131	0.234
BASFI	0.418 ^{***}	<0.001^{**}
BASMI	0.479 ^{***}	<0.001^{**}
Patient night pain, VAS (mm)	0.228 [*]	0.035[*]
Patient global pain, VAS (mm)	0.305 ^{**}	0.005^{**}
HAQ	0.209	0.055
Anxiety, yes	0.091	0.405
Depression, yes	0.135	0.219
ESR	0.319 ^{**}	0.006[*]
CRP	0.194	0.113

Notes: Spearman's correlation was used for categorical variables. Pearson's correlation was used for continuous variables. * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$.

Abbreviations: BMI=Body Mass Index; WHR=waist-to-hip ratio; BASDAI, Bath Ankylosing spondylitis Disease Activity index; BASFI, Bath Ankylosing spondylitis Functional index; BASMI, Bath Ankylosing spondylitis Metrology index; VAS, visual analog scale; HAQ, health Assessment Questionnaire; ESR, erythrocyte sedimentation rate; CRP, c-reactive protein.

Table 3. Differences in quality of life between AS patients with syndesmophytes or not.

	All patients N=85	With syndesmophytes, n=44	Without Syndesmophytes, n=41	P
SF-36				
PCS	56.29±22.88	50.13±21.21	63.1±23.01	0.011*
MCS	66.78±21.96	65.8±20.45	67.87±23.76	0.681
PF	80(63.75, 95)	75(45, 87.5)	85(75, 95)	0.01*
RP	50(0, 100)	25(0, 75)	75(12.5, 100)	0.026*
BP	55.05±22.47	48.49±21.1	62.32±21.96	0.006**
GH	48.42±20.88	46.93±19.2	50.08±22.76	0.509
VT	61.41±16.75	61.34±15.97	61.49±17.79	0.97
SF	75(50, 100)	75(50, 87.5)	87.5(62.5, 100)	0.168
RE	100(0, 100)	66.67(0, 100)	100(0,100)	0.723
MH	71.64±16.95	72.29±16.45	70.92±17.68	0.723

Notes: Data are means ± SD or median (IQR) for continuous variables. P values were obtained with the two-tailed t test for continuous variables. * $P < 0.05$; ** $P < 0.01$.

Abbreviations: SF-36=Short Form 36 Health Survey. PCS=physical components summary. MCS=mental components summary. PF=physical functioning. RP= role limitations due to physical problems. BP=body pain. GH=general health perception. VT= energy/vitality. SF=social functioning. RE=role limitations due to emotional problems. MH=mental health.

Table 4. Results of multivariate analysis using forward stepwise logistic regression model in AS patients with syndesmophytes.

syndesmophyte	B	SE	Wald	OR	95%CI	P-value
Gender, man	-2.659	0.928	8.22	0.07	0.011, 0.431	0.004**
Age, years	0.138	0.04	11.633	1.148	1.06, 1.242	0.001**
WHR (0.1)	0.812	0.357	5.157	2.251	1.118, 4.536	0.023*
constant	-8.54	3.35	6.499	0.000		0.011*

$R^2=0.49$. Notes: * $P < 0.05$; ** $P < 0.01$.

Abbreviations: WHR=waist-to-hip ratio.