

The Influence of Vertebral Fracture on the Functional Disability of Patients with Rheumatoid Arthritis

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The aim of the present study was to identify the influence of vertebral fracture (VF) on the functional disability in patients with rheumatoid arthritis (RA). This study consecutively enrolled 100 female patients aged 50 yr or older with RA. All participants underwent lateral imaging of the thoracolumbar spine by simple radiography to identify any VFs. They also completed questionnaires via interview regarding demographics, medical history, and disease outcomes including functional disability. We used univariate analysis to evaluate associations between functional disability and VF, and made multivariate logistic regression models to test independent effect of the presence of VF, the number of VFs, and the severity of VF on functional disability. Among the 100 RA patients, 47 had at least one VF, but 34 of them were asymptomatic that they had experienced a fracture. The multiple VFs ≥ 3 (OR, 8.95; 95% CI, 1.77-44.15, $P = 0.01$) and moderate or severe VF (OR, 3.38; 95% CI, 1.26-9.04, $P = 0.02$) were related to disability in univariate analysis. The multiple VFs ≥ 3 (OR, 6.13; 95% CI, 1.02-36.94, $P = 0.048$) was associated with functional disability of RA patients after adjusting various confounders and it was mainly in walking and arising. The VF might be an important factor which affects functional disability in RA patients.

Keywords: Arthritis, Rheumatoid; Spinal Fractures; Health Assessment Questionnaire

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic, painful, and disabling disease associated with reduced health-related quality of life (HRQOL) compared to the general population (1, 2). Disease-related factors, such as disease activity, disease duration, and pain, are likely to affect the physical disability and quality of life of patients with RA (3). In addition, higher levels of comorbidity can make the physical disability of RA patients even worse (4). Osteoporosis leading to bone fracture is one of the main comorbidities of RA, and approximately one-third of women with RA report a fracture within 5 yr of follow-up (5). Recent study showed the prevalence of vertebral fracture (VF) in RA patients of age more than 40 yr including both women and men was 13% and it was increased to 65% in patients of age more than 50 (6). Several studies have shown that VF can affect the development of subsequent vertebral and non-vertebral fractures (7-12), and patients with VF have higher mortality than patients without VF (13). However, few studies have examined the influence of VF on the outcome of patients with RA. The purpose of this study was to determine how the presence and severity of VF affects functional disability in RA patients.

MATERIALS AND METHODS

Study participants

All female RA patients aged 50 yr or older who visited one university hospital for periodic examination between April and August 2011 were asked to participate in this study. Of these 169 patients, 100 were consecutively enrolled after excluding 69 patients who either did not wish to participate or recently had a routine examination for osteoporosis.

Data collection

Participants completed questionnaires via interview regarding demographic characteristics (age, gender, height, and weight) and lifestyle characteristics (alcohol use, smoking use, exercise habits). Functional disability as a primary outcome was evaluated with the Health Assessment Questionnaire Disability Index (HAQ-DI) (14), and disease activity was measured in terms of the number of tender and swollen joints, patients' global health visual analog scale (VAS), and the disease activity score (DAS) using 28 joints. Clinical information related to RA, such as disease duration, the positivity of rheumatoid factor (RF) and anti-cyclic-citrullinated protein antibody (ACPA), and the use of glu-

corticosteroid and disease modifying anti-rheumatic drugs (DMARD) were collected through medical record review.

Assessment of vertebral fracture

Each participant underwent thoracolumbar radiography, and the results were evaluated by two radiologists. Genant visual semiquantitative criteria were used to describe each patient's VF status as follows: i) presence or absence of fracture, ii) fracture number (no VFs, a single VF, multiple VFs), iii) severity of VF (normal vertebra, mild fracture, moderate or severe fracture). In questionable cases, two radiologists discussed the case until a consensus was formed.

Statistical analysis

As appropriate, the chi-square or Fisher's exact test was used to compare categorical data between independent groups. The Student's t-test or Mann-Whitney U-test was used to compare continuous data distribution between two independent samples. We used univariate and multivariable logistic regression analysis to evaluate the impact of VF on disability (HAQ-DI ≥ 1). We performed three separate logistic regression models to evaluate the impact of the presence of VF, the number of VFs and the severity of VF on disability. The chi-square test for nominal variables and independent t-tests for continuous variables were used to identify demographic and clinical characteristics of patients who were unaware their VF.

All data were analyzed with SPSS 21.0 (SPSS, Chicago, IL, USA), and *P* values < 0.05 were considered statistically significant.

Ethics statement

This study was approved by our institutional review board of the Hanyang University Hospital (HYUH IRB 2010-R-53). All participants provided informed consent under a protocol approved by the Institutional Review Board.

RESULTS

Prevalence of VF in patients with RA and their clinical features

Forty-seven patients had at least one VF, and the other 53 patients had no VFs. Among patients with VF, only 11 patients (23.3%) were aware of their fractures, while 36 patients (76.6%) had occult fractures of the vertebrae that had not been diagnosed previously. Thirteen among 36 patients were unaware of their VF despite their VF was moderate or severe, and 14 patients with multiple VF more than two were also unaware of their VF.

When patients were divided into two groups according to the presence or absence of VF, the mean age was higher among the patients with VF (65.5 \pm 8.0 yr) than the patients without VF (57.4 \pm 6.2 yr; *P* < 0.001), but disease duration, body mass index (BMI), the positivity of RF and ACPA did not show statistically

significance between two groups. Disease activity was higher in patients with VF than patients without VF, but this result was not quite statistically significant (3.5 \pm 0.9 vs 3.1 \pm 1.1, *P* = 0.06). With regards to medication use, two groups did not differ in the use of DMARDs, including methotrexate (*P* = 0.60). Although patients with VF tended to use glucocorticoids more frequently and at a higher dosage than patients without VF, this difference was not statistically significant (*P* = 0.37). With regards to osteoporosis or fracture, the mean BMD score for the total L-spine did not differ between groups; the frequency of osteopenia and osteoporosis also did not differ between groups. In terms of functional disability, the HAQ-DI scores tended to be higher in the patients with VF (0.94 \pm 0.60) than the patients without VF (0.73 \pm 0.54), but this difference was not quite statistically significant (*P* = 0.07) (Table 1).

Comparison of responses to individual questions in the HAQ-DI between patients without and with VF

Patients with VF had greater difficulty in arising and walking than patients without VF. Greater difficulty in the response to questions of "Are you able to stand up from an armless straight chair?" showed in the patients with VF than patients without VF (57.4% vs 35.9%, *P* = 0.02). Patients with VF showed more difficulty than them without VF in the questions of "Are you able to walk outdoors on flat ground?" and "Are you able to climb up five steps?" (59.6% vs 39.6%; *P* = 0.04, 83.0% vs 66.0%, *P* = 0.02, respectively.) One question of hygiene category: "Are you able to get on and off the toilet?" also showed different results (57.4% in patients with VF vs 30.2% in patients without VF, *P* = 0.01.) There were no different difficulties in dressing, eating, hygiene, reach, grip, or usual activities. Table 2 presented results for all 20 items in the HAQ-DI.

Impact of VF on functional disability

The unadjusted analysis revealed a significant association between disability (HAQ-DI ≥ 1) and old age (OR, 1.06; 95% CI, 1.004-1.11, *P* = 0.03), disease activity (OR, 1.82; 95% CI, 1.19-2.79, *P* = 0.01), multiple VFs more than three (OR, 8.95; 95% CI, 1.77-45.15, *P* = 0.01), and moderate or severe VF (OR, 3.38; 95% CI 1.26-9.04, *P* = 0.01). The presence of VF was not significantly associated with disability after multivariable regression analysis adjusting for age, disease duration, BMI, glucocorticoid use, and previous history of VF, while disease activity was independently associated with disability (OR, 1.91; 95% CI, 1.17-3.12, *P* = 0.01) (model 1). When separate multivariable regression model was used to evaluate the impact of number of VF on disability, multiple VFs more than three (OR, 6.31; 95% CI, 1.02-36.94, *P* = 0.048) was independently associated with disability along with disease activity (OR, 2.01; 95% CI, 1.21-3.33, *P* = 0.01) (model 2). To determine the effect of severity of VF on disability, we performed multivariable analysis of model 3. The signifi-

Table 1. Demographic and clinical characteristics of participants

Characteristics	Patients without VF (n = 53)	Patients with VF (n = 47)	P value	
Demographic and clinical factors				
Age (yr)*	57.4 ± 6.2	65.5 ± 8.0	< 0.01	
Disease duration (yr)*	5.7 ± 5.6	7.4 ± 6.3	0.11	
BMI (kg/m ²)*	23.0 ± 3.5	22.7 ± 2.	0.64	
Alcohol (No., %)	8	3	NC	
Current smoking (No., %)	0 (0)	1 (2.1)	NC	
Regular exercise (No., %)	23 (43.4)	23 (48.9)	0.58	
RF positivity (No., %)	52 (98.1)	45 (95.7)	0.49	
ACPA positivity (No., %)	42/49 (85.7)	36/39 (92.3)	0.50	
Swollen joint (No.)*	1.0 ± 1.3	1.5 ± 1.8	0.19	
Tender joint (No.)*	0.9 ± 1.4	1.1 ± 1.7	0.41	
ESR (mm/hr) *	28.6 ± 24.5	35.5 ± 20.4	0.04	
DAS28*	3.1 ± 1.1	3.5 ± 0.9	0.06	
Current medication				
Glucocorticoid use (No., %)	28 (52.8)	29 (61.7)	0.37	
Glucocorticoid dose (users, mg/day)*	2.7 ± 1.0	2.8 ± 1.5	0.50	
Methotrexate (No., %)	48 (90.6)	41 (87.2)	0.60	
Methotrexate dose (mg/week) [†]	9.7 ± 4.0	9.8 ± 1.0	0.75	
Osteoporosis medication (No., %) [‡]	28 (52.8)	27 (57.4)	0.64	
Osteoporosis and related features				
No previous history of non VF (No., %)	8 (15.1)	11 (23.4)	0.29	
BMD (T score of L-spine)*	-1.55 ± 1.11	-1.69 ± 1.28	0.55	
Normal (T score ≥ -1.0)	18 (34.0)	15 (31.9)	0.94	
Osteopenia (-2.5 < T score < -1.0) (No., %)	22 (41.5)	19 (40.4)		
Osteoporosis (T score ≤ -2.5) (No., %)	13 (24.5)	13 (27.7)		
Number of VFs (No., %)				
0	53 (100)	0	NC	
1	0 (0)	23		
≥ 2	0 (0)	24		
Severity of VF (No., %)				
Normal	53 (100)	0	NC	
Mild	0 (0)	21		
Moderate or severe	0 (0)	26		
Functional disability	HAQ-DI*	0.73 ± 0.54	0.94 ± 0.60	0.07

*Data are expressed as mean ± SD; [†]Methotrexate were treated orally; [‡]Osteoporosis medication included bisphosphonate, calcium/vitamin D. RA, rheumatoid arthritis; VF, vertebral fracture; BMI, body mass index; RF, rheumatoid factor; anti-CCP, anti-cyclic citrullinated protein antibody; DAS 28, disease activity score 28; ESR, erythrocyte sedimentation rate; BMD, bone mineral density; NC, not calculated.

Table 2. Comparison of responses to individual questions in the HAQ-DI between patients without and with VF

Questions: 'Are you able to ...'	Patients without VF (n = 53) Disability (+) (No., %)	Patients with VF (n = 47) Disability (+) (No., %)	P value
Dressing			
Dress yourself, including tying shoelaces and doing buttons?	11 (20.8)	8 (17.0)	0.64
Shampoo your hair?	8 (15.1)	7 (14.9)	0.98
Arising			
Stand up from an armless straight chair?	19 (35.8)	27 (57.4)	0.03
Get in and out of bed?	31 (58.5)	28 (59.6)	0.91
Eating			
Cut your meat?	8 (15.1)	8 (17.0)	0.79
Lift a full cup or glass to your mouth?	7 (13.2)	6 (12.8)	0.95
Open a new milk carton?	21 (39.6)	23 (48.9)	0.35
Walking			
Walk outdoors on flat ground?	21 (39.6)	28 (59.6)	0.04
Climb up five steps?	35 (66.0)	39 (83.0)	0.05
Hygiene			
Wash and dry your entire body?	5 (9.4)	4 (8.5)	1.00
Take a tub bath?	6 (11.3)	5 (10.6)	0.91
Get on and off the toilet?	16 (30.2)	27(57.4)	0.01
Reach			
Reach and get down a 5-pound object from just above your head?	26 (49.1)	23 (48.9)	0.99
Bend down to pick up clothing from the floor?	25 (47.2)	26 (55.3)	0.42
Grip			
Open car doors?	11 (20.8)	8 (17.0)	0.64
Open jars which have been previously opened?	27 (50.9)	25 (53.2)	0.82
Turn taps on and off?	13 (24.5)	11 (23.4)	0.90
Usual activities			
Run errands and shop?	33 (62.3)	30 (63.8)	0.87
Get in and out of a car?	17 (32.1)	21 (44.7)	0.20
Do chores such as vacuuming or yard work?	43(81.1)	35 (74.5)	0.42

cance of severity of VF (OR, 2.38; 95% CI, 0.71-8.04, *P* = 0.16) was disappeared and disease activity (OR, 1.99; 95% CI, 1.20-

3.29, *P* = 0.01) showed consistent association with functional disability (Table 3).

Table 3. Factors influencing functional disability in patients with RA (n=100)

Variables	Unadjusted analysis		Adjusted analysis Model* 1 ($r^2 = 0.198$) [†]		Adjusted analysis* Model 2 ($r^2 = 0.262$) [†]		Adjusted analysis* Model 3 ($r^2 = 0.222$) [†]	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Age	1.06 (1.004-1.11)	0.03	1.05 (0.99-1.11)	0.12	1.05 (0.98-1.12)	0.17	1.04 (0.98-1.11)	0.18
Disease duration (yr)	1.03 (0.96-1.10)	0.41	1.01 (0.93-1.09)	0.90	1.00 (0.92-1.08)	0.98	1.00 (0.92-1.08)	0.96
BMI	1.04 (0.92-1.17)	0.57	1.06 (0.93-1.22)	0.39	1.05 (0.91-1.22)	0.51	1.06 (0.92-1.21)	0.44
Glucocorticoid use	1.25 (0.56-2.77)	0.58	0.91 (0.36-2.35)	0.85	0.81 (0.30-2.19)	0.68	0.75 (0.28-2.03)	0.58
Glucocorticoid dose (mg/day)	0.74 (0.47-1.14)	0.17						
DAS28	1.82 (1.19-2.79)	0.01	1.91 (1.17-3.12)	0.01	2.01 (1.21-3.33)	0.01	1.99 (1.20-3.29)	0.01
Previous history of non VF	0.66 (0.24-1.85)	0.43	0.41 (0.13~1.31)	0.13	0.41 (0.12-1.40)	0.15	0.39 (0.12-1.27)	0.12
Presence of VF	2.22 (0.99-4.95)	0.05	1.44 (0.54-3.85)	0.46	-	-	-	-
Number of VFs								
0	1				1			
1	1.64 (0.61-4.42)	0.33	-		1.18 (0.37-3.76)	0.79	-	
2	1.28 (0.36-4.59)	0.71			0.71 (0.15-3.28)	0.66		
≥ 3	8.95 (1.77-45.15)	0.01			6.13 (1.02-36.94)	0.048		
Severity of VF								
None	1						1	
Mild	1.34 (0.48-3.76)	0.58	-		-		0.92 (0.29-2.98)	0.89
Moderate or severe	3.38 (1.26-9.04)	0.02					2.38 (0.71-8.04)	0.16

*Analysis Model was performed after adjusting for age, disease duration, BMI, current glucocorticoid use, DAS28, previous history of non VF; [†]Nargelkerke R square. RA, rheumatoid arthritis; VF, vertebral fracture; BMI, body mass index; DAS 28, disease activity score 28.

DISCUSSION

The prevalence of VF was high (47%); and among patients with VF, more than two thirds of patients (76.6%) were unaware that they had a VF. Previous reports showed the prevalence of VF of 13% in RA patients of age more than 40 including both women and men (6), and that for women RA patients was higher as 21.7%-36% (15, 16). The prevalence of our study was slightly higher, but our study population was older than previous study. The prevalence of asymptomatic VF was comparable to that reported in a previous study of post-menopausal women receiving glucocorticoid therapy (17). Some patients were unaware of their VF despite their VF was multiple or severe. This unawareness of their VF might be related with using of glucocorticoid or NSAIDs. These results suggest that to judge the VF based on RA patients' subjective assessment of pain might miss the presence of VF. Additionally, the number of VFs did not always correspond with the severity of VF (Spearman's correlation 0.32, $P = 0.029$), it is important to consider both variables when evaluating VF status in patients with RA. Therefore, it would be helpful to detect VF rigorously in postmenopausal RA patients in order to reduce their functional disability.

Recent study suggested that incident VF were associated with reduced functional status in postmenopausal patients with RA (18). Furuya et al. showed that the increased HAQ score was associated with VF as relative risk of 2.42 (19). Our results suggest that the multiple VFs may independently affect the functional disability of patients with RA. Interestingly, we found that patients who were aware of their VF showed worse functional disability comparing to patients who were unaware of their VF. The factors related with osteoporosis or VF were worse in patients

who were aware of their VF, although their disease activity was lower. Moreover, patients with VF had greater difficulty walking and arising than patients without VF, although they were not more likely to have difficulty in dressing, eating, hygiene, reach, grip, or usual activities, as suggested by our analysis using 20 questions in the HAQ-DI. These results imply that VF can influence the disability of patients with RA regardless of their disease activity.

Our study showed that the multiple VF and severity of VF was associated with higher functional disability in the unadjusted analysis, although a statistically significant difference was not found for the presence of VF (OR, 2.22; 95% CI, 0.99-4.95). The multiple VF showed consistent association with functional disability after adjusting confounding factors. The age and disease duration was not associated with functional disability, while disease activity showed consistent association. These results indicate that the presence of VF might affect functional disability more importantly in postmenopausal RA patients in addition to age, disease duration and disease activity which were known predictors of functional disability in RA patients (3).

Our study has important strengths. The information about clinical characteristics focused on RA patients who were unaware of their VF would help us to approach old patients with bad functional disability despite low disease activity.

There are several limitations to our study. First, relatively small number of patients did not allow us to determine the impact of VF on different subgroups of patients. Second, we could not evaluate the impact of incident VF on functional disability, because our study was cross-sectional design. We expect that a further follow-up study would allow us to identify the incident case of VF and to evaluate its impact on functional disability.

In conclusion, we identified that about half of RA patients had VF and a large number of patients among them were unaware of their VF. The VF might important factor which affects functional disability in postmenopausal RA patients in addition to age, disease duration and disease activity.

DISCLOSURE

All authors have no conflicts of interest to disclose.

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