

Productivity Loss of Rheumatoid Arthritis Patients according to the Their Stages of the Disease Activity Score

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Objective. Productivity loss was compared by 3-stage of disease activity and associations between higher disease activity and high productivity loss were identified. **Methods.** Data were extracted from Rheumatoid Arthritis (RA) Patient-reported Outcomes Research, which enrolled 2,000 RA patients (> 20-year) on disease-modifying-antirheumatic-drugs (DMARDs) (\geq 6-month) from December 2012 to June 2013. This included 1,457 RA patients with the disease activity score (DAS-28-ESR) in their medical charts. Productivity loss in time and indirect cost was estimated using The World Health Organization Health and Work Performance Questionnaire (HPQ). Baseline characteristics and productivity loss outcomes were compared according to DAS-28-ESR groups. **Results.** 84.4% were females, 54.2% had low DAS-28-ESR ($<$ 3.2), and 38.2% and 7.6% had moderate (3.2 ~ 5.1) and high DAS-28-ESR ($>$ 5.1). Patients with moderate to high DAS-28-ESR had higher lost productivity time (LPT) and monthly costs of LPT than those with low DAS-28-ESR (time in hours: 110.0 ± 58.4 vs. 132.4 ± 57.2 vs. 71.5 ± 52.0 , $p < 0.0001$; monthly costs of LPT in 1,000 Korean won: $1,097 \pm 607$ vs. $1,302 \pm 554$ vs. 741 ± 531 , $p < 0.0001$). Multiple regression analyses revealed significant associations with high LPT in high (adjusted odds ratio [OR] = 3.87, 95% confidence interval [CI]: 2.18 ~ 6.87) and moderate DAS-28-ESR (adjusted OR = 1.88, 95% CI: 1.41 ~ 2.52) compared to low DAS-28-ESR. In addition, positive associations with high monthly costs of LPT were observed in high (adjusted OR = 3.45, 95% CI: 1.98 ~ 5.99) and moderate DAS-28-ESR (adjusted OR = 1.93, 95% CI: 1.43 ~ 2.54) compared to low DAS-28-ESR. **Conclusion.** Timely therapeutic strategies should be taken into consideration given that the RA patients with moderate to high DAS-28-ESR showed strong associations with high productivity loss for effective management of RA. (**J Rheum Dis 2018;25:122-130**)

Key Words. Rheumatoid arthritis, Productivity loss, Disease activity score, Patient reported outcome measures

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INTRODUCTION

Rheumatoid arthritis (RA) is a chronic inflammatory disease associated with progressive joint destruction within the first two years of disease onset [1]. Thus, prompt disease control is critical to prevent the further progression of disease severity and reduce the burden of illness [2]. Disease activity score-28-erythrocyte sedimentation rate (DAS-28-ESR) is widely used to measure disease activity in RA patients [3]. DAS-28-ESR is used as a tool to guide treatment decision recommended by American College of Rheumatology (ACR), since it has been proved to be the most accurate tool when discriminating low from high disease activity [4-6]. Therefore, systemic monitoring of DAS-28-ESR could bring an influential impact on improving health outcomes of patients [7]. One interventional study with RA patients showed clinical improvements in the group treated with DAS-28-ESR-driven therapy compared to a group treated with usual care in mean health assessment questionnaire (HAQ) and DAS-28-ESR scale after two years of observation [7].

Numerous studies have covered that RA patients suffer from a considerable socio-economic burden as well as worse health-related quality of life (HRQoL) and functional disability than general population [8-11]. Recent findings have identified that one of the strongest determinants of lower patient reported outcomes (PROs) in Korean RA patients was higher disease activity [12]. In order to minimize the socio-economic burden of disease, it is important to determine the association between DAS-28-ESR and productivity loss.

Reducing productivity loss along with functional disability is also considered important in an effort to improve PROs in RA patients [13]. In fact, RA patients' total costs of illness were dominated by the indirect cost coming from productivity loss [14-16]. Since impaired physical function, which is mostly dependent on the level of disease severity, is the main cause of decreased work capacity in RA patients, we expect to observe relatively higher productivity loss in moderate to high DAS-28-ESR groups compared to low DAS-28-ESR group [17-19]. Although a number of literatures have reviewed productivity loss in RA, there is a lack of studies specifically observing productivity loss by disease activity of RA patients [19-21]. Therefore, this analysis was triggered to compare productivity loss by 3-stage of disease activity (low, moderate, high) and identify associations between

higher disease activity and high productivity loss using the data from the Rheumatoid Arthritis Patient-reported Outcomes Research [22].

MATERIALS AND METHODS

Patients (study population)

The Rheumatoid Arthritis Patient-reported Outcomes Research population included 2,000 RA patients recruited from rheumatology department of 22 tertiary hospitals during December 2012 and June 2013 in Korea [22]. For this specific analysis, we included patients recorded DAS-28-ESR in their medical chart, and the most recent records from baseline were extracted for the analysis. 543 patients whose records of DAS-28-ESR were not retrievable from the medical chart were excluded. Eligibility criteria at baseline were patients older than 20 years who and were diagnosed with RA, and have been treated with disease-modifying antirheumatic drugs (DMARDs) for at least past 6 months. Anyone in severe acute or chronic clinical/mental condition other than RA, that may affect quality of life of a patient, was excluded from the study by physician's discretion during the recruitment period. This study was approved by Institutional Review Board (IRB) of all participating hospitals (IRB no. 2012-09-027). All procedures in this study have therefore been performed in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. All participants provided their informed consent prior to their enrollment in the study [22].

Data collection

Data on socio-demographic and clinical characteristics including gender, age, date of RA diagnosis, the most recent Disease Activity Score (DAS-28-C-reactive protein [CRP]/ESR), rheumatoid factor serology, anti-cyclic citrullinated peptide (anti-CCP) antibody, treatment patterns, and Charlson comorbidity index (CCI) were obtained from the medical record [22]. The DAS-28-ESR is an index consisting of a 28 tender joint count (range: 0~28), a 28 swollen joint count (range: 0~28), ESR and an optional general health assessment on a visual analogue scale (range: 0~100) [23]. Its continuous scale ranges from 0 to 9.4 and the stage of disease activity categorizes into low (DAS-28-ESR: <3.2), moderate (DAS-28-ESR: 3.2~5.1), and high (DAS-28-ESR: >5.1) [23]. Also, func-

tional disability was measured using the Korean Health Assessment Questionnaire (KHAQ) through patients self-report. All data on the outcome variables were obtained from the self-reported questionnaires. Productivity loss was also estimated using Health and Work performance Questionnaire (HPQ) in terms of time and indirect cost on monthly basis [24]. Calculation of lost productivity time (LPT) and the monthly cost of LPT due to

absenteeism and presenteeism were performed as follows [24-29]. Monthly cost of LPT was calculated using the hourly wage (Korean won [KRW]/hour) based on average wage of Korean workers by their age, gender, and occupation [25].

$$\text{LPT} = [\text{absenteeism} + \text{presenteeism}]$$

- Absenteeism = {[entire work days missed due to RA over past four weeks] × 8 (hours)/day} + {[partial days

Table 1. Patient characteristics by disease activity score (DAS-28-ESR)

Variable	Total (n=1,457)	DAS-28-ESR < 3.2 (n=790, 54.2%)	DAS-28-ESR 3.2~5.1 (n=557, 38.2%)	DAS-28-ESR > 5.1 (n=110, 7.6%)	p-value*
Gender					0.0003
Male	227 (15.6)	151 (19.1)	62 (11.1)	14 (12.7)	
Female	1,230 (84.4)	639 (80.9)	495 (88.9)	96 (87.3)	
Age (yr)					0.0092
N	1,457	790	557	110	
Mean ± SD	55.7 ± 11.9	54.8 ± 11.7 [†]	56.7 ± 11.9 [†]	56.7 ± 12.5	
Median	55.0	55.0	57.0	57.0	
Min, max	20, 87	20, 87	25, 86	20, 80	
Duration of disease (yr)					0.0003
N	1,358	746	516	96	
Mean ± SD	8.4 ± 7.1	7.8 ± 6.8 [†]	9.2 ± 7.5 [†]	9.9 ± 7.5 [†]	
Median	6.4	5.5	7.5	8.3	
Min, max	0, 44	0.0, 44.4	0.3, 44.5	0.0, 30.7	
RF positivity					0.0479
Positive	1,124 (77.1)	591 (74.8)	440 (79.0)	93 (84.6)	
Negative	307 (21.1)	187 (23.7)	104 (18.7)	16 (14.6)	
Unknown	26 (1.8)	12 (1.5)	13 (2.3)	1 (0.9)	
Anti-CCP positivity					0.0636
Positive	1,016 (69.7)	545 (69.0)	393 (70.6)	78 (70.9)	
Negative	209 (14.3)	129 (16.3)	71 (12.7)	9 (8.2)	
Unknown	232 (15.9)	116 (14.7)	93 (16.7)	23 (20.9)	
CCI					0.3671
1~2	1,311 (90.0)	720 (91.1)	493 (88.5)	98 (89.1)	
3~4	126 (8.6)	62 (7.9)	55 (9.9)	9 (8.2)	
≥5	20 (1.4)	8 (1.0)	9 (1.6)	3 (2.7)	
Current steroid use					< 0.0001
Yes	1,042 (71.5)	516 (65.3)	434 (77.9)	92 (83.6)	
No	415 (28.5)	274 (34.7)	123 (22.1)	18 (16.4)	
Current NSAID use					0.0211
Yes	1,099 (75.4)	578 (73.2)	428 (76.8)	93 (84.6)	
No	358 (24.6)	212 (26.8)	129 (23.2)	17 (15.5)	
KHAQ score					< 0.0001
Mean ± SD	0.7 ± 0.7	0.4 ± 0.5 [†]	0.9 ± 0.7 [†]	1.3 ± 0.8 [†]	
Median	0.5	0.3	0.9	1.1	
Min, max	0, 3	0, 3	0, 3	0, 3	

Values are presented number (%) otherwise indicated. DAS-28-ESR: disease activity score-28-erythrocyte sedimentation rate, SD: standard deviation, RF: rheumatoid factor, CCP: cyclic citrullinated peptide, CCI: Charlson comorbidity index, Connective tissue disease was considered for all rheumatoid arthritis patients, NSAID: nonsteroidal anti-inflammatory drug, HAQ: health assessment questionnaire. *p-value by chi-square test or analysis of variance. [†]A post hoc analysis showed the significant difference between groups at p-value < 0.05.

missed due to RA over past four weeks]×4(hours)/day}
 - Presenteeism=[actual days worked if not sick due to RA over past four weeks]×{[10-overall job performance]/10}

Monthly cost of LPT=LPT×hourly wage (KRW/hour)

Statistical analysis

Analysis of variance (ANOVA) or chi-square test was performed to observe the distribution and mean variance of each characteristic among different stages of DAS-28-ESR groups. Mean absenteeism and presenteeism and their sub-item means were estimated with their standard deviation within each DAS-28-ESR groups. LPT in hours and monthly cost of LPT in 1,000 KRW were calculated by low, moderate and high DAS-28-ESR groups and were compared using ANOVA. To evaluate the association between high lost productivity time (≥100 hours) and disease activity stage, we used multiple logistic regression analysis. Likewise, association between high monthly cost of LPT (≥1,000,000 KRW) and disease activity stage was measured using multiple logistic regression analysis. In the multiple logistic regression analyses, variables that were found to be significant from simple logistic analyses and also determined clinically meaningful were included. All analyses were performed using SAS version 9.3 (SAS Institute, Cary, NC, USA).

RESULTS

Characteristics of the RA patients by DAS-28-ESR groups

Table 1 describes the characteristics of RA patients with DAS-28-ESR measurements (n=1,457) by low (DAS-28-ESR: <3.2), moderate (DAS-28-ESR: 3.2~5.1), high (DAS-28-ESR: >5.1) DAS-28-ESR groups including socio-demographic factors and clinical factors overall. Among those 1,457 patients with DAS-28-ESR recorded, each group had 80.9%, 88.9%, 87.3% females in low, moderate, high DAS-28-ESR groups, respectively (p=0.0003). Mean age was 54.8±11.7, 56.7±11.9, 56.7±12.5 in low, moderate, high DAS-28-ESR groups, respectively (p=0.0092). Mean duration of illness was approximately 8 years for patients having low DAS-28-ESR, while it was approximately 9 and 10 years for patients having moderate to high DAS-28-ESR, respectively (p=0.0003). Patients with positive rheumatoid factor (RF) were 74.8%, 79.0%, 84.6% (p=0.0479) and with positive anti-CCP antibody were 69.0%, 70.6%, 70.9% in each group. Steroid and nonsteroidal anti-inflammatory drugs (NSAIDs) use were 65.3%, 77.9%, 83.6% and 73.2%, 76.8%, 84.6% in each group, respectively. For functional disability, KHAQ scores differed by levels of DAS-28-ESR, and patients with high DAS-28-ESR showed highest scores indicating the most impairment comparing to patients with low and moderate DAS-28-ESR groups.

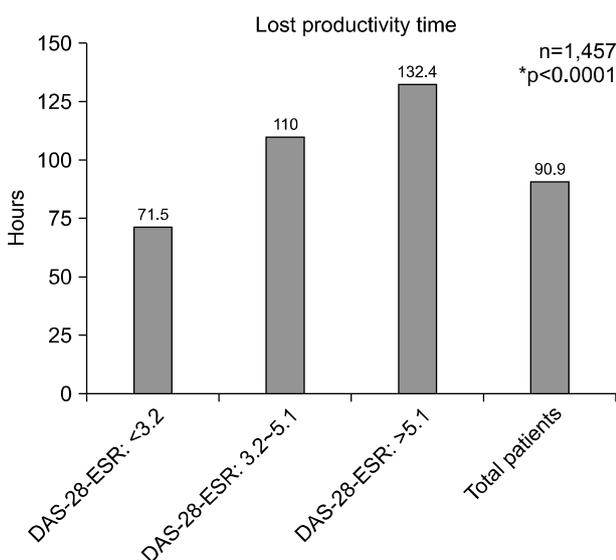


Figure 1. Lost productivity time in hours by DAS-28-ESR in the past one month. DAS-28-ESR: disease activity score-28-erythrocyte sedimentation rate. *p-value by analysis of variance.

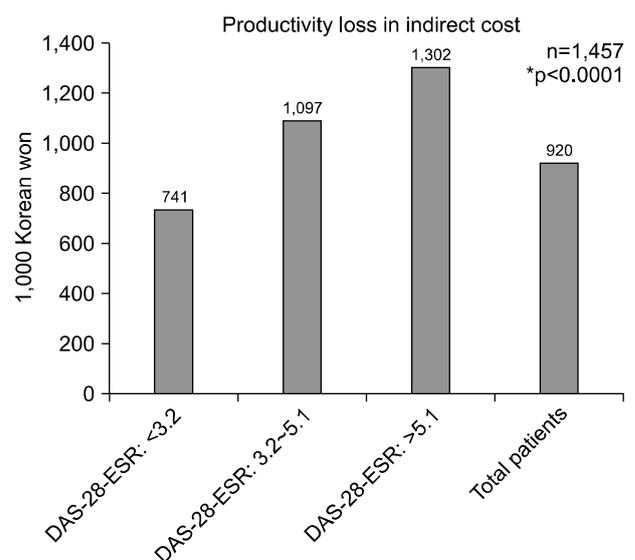


Figure 2. Productivity loss in indirect cost by DAS-28-ESR per month. DAS-28-ESR: disease activity score-28-erythrocyte sedimentation rate. *p-value by analysis of variance.

Table 2. Productivity loss in rheumatoid arthritis over past four weeks

Variable	Total (n = 1,457)	DAS-28-ESR < 3.2 (n = 790, 54.2%)	DAS-28-ESR 3.2 ~ 5.1 (n = 557, 38.2%)	DAS-28-ESR > 5.1 (n = 110, 7.6%)	p-value*
Absenteeism					
Actual days worked if not sick due to RA (d)					0.4202
Mean ± SD	26.0 ± 3.8	25.9 ± 3.7	26.1 ± 3.8	25.7 ± 4.7	
Median	28.0	28.0	28.0	28.0	
Min, max	5, 28	8, 28	5, 28	8, 28	
Entire work days missed due to RA (d)					< 0.0001
Mean ± SD	1.7 ± 5.0	0.7 ± 3.2 [†]	2.5 ± 5.9 [†]	4.3 ± 7.7 [†]	
Median	0.0	0.0	0.0	0.0	
Min, max	0, 28	0, 28	0, 28	0, 28	
Partial days missed due to RA (d)					< 0.0001
Mean ± SD	3.0 ± 6.5	1.7 ± 4.8 [†]	4.3 ± 7.4 [†]	6.4 ± 8.7 [†]	
Median	0.0	0.0	0.0	1.8	
Min, max	0, 28	0, 28	0, 28	0, 28	
Lost productivity time in hours					< 0.0001
Mean ± SD	90.9 ± 59.0	71.5 ± 52.0 [†]	110.0 ± 58.4 [†]	132.4 ± 57.2 [†]	
Median	85.6	67.0	112.0	128.0	
Min, max	0, 224	0, 224	0, 224	0, 224	
Presenteeism					
Performance of most workers in a similar job [†]					0.0629
Mean ± SD	7.8 ± 1.9	7.9 ± 1.8	7.7 ± 1.9	7.5 ± 2.0	
Median	8.0	8.0	8.0	8.0	
Min, max	0, 10	0, 10	0, 10	0, 10	
Overall performance [†]					< 0.0001
Mean ± SD	6.1 ± 2.4	6.9 ± 2.1 [†]	5.4 ± 2.3 [†]	4.4 ± 2.4 [†]	
Median	5.0	7.0	5.0	5.0	
Min, max	0, 10	0, 10	0, 10	0, 10	
Overall performance compared to others [§]					< 0.0001
Mean ± SD	4.7 ± 1.6	4.3 ± 1.5 [†]	5.1 ± 1.5 [†]	5.6 ± 1.5 [†]	
Median	4.0	4.0	5.0	6.0	
Min, max	1, 7	1, 7	1, 7	2, 7	
Monthly cost of lost productivity time (1,000 Korean won)					< 0.0001
Mean ± SD	920 ± 597	741 ± 531 [†]	1,097 ± 607 [†]	1,302 ± 554 [†]	
Median	858	673	994	1,369	
Min, max	0, 3,626	0, 3,626	0, 3,506	0, 2,671	

DAS-28-ESR: disease activity score-28-erythrocyte sedimentation rate, RA: rheumatoid arthritis, SD: standard deviation. *p-value by analysis of variance. [†]A post hoc analysis showed the significant difference between groups at $p < 0.05$. [†]Rating on a scale from 0 to 10 (worst to top performance). [§]Rating on a scale from 1 to 7 (a lot better to a lot worse).

Of all 1,457 patients, mean LPT was 90.9 hours during the past one month, and monthly cost of LPT was 920,000 KRW (Table 2, Figures 1 and 2). When moderate to high DAS-28-ESR groups were compared to low DAS-28-ESR group, longer missed work days were observed in moderate to high DAS-28-ESR groups ($p < 0.0001$). Overall work performance also got worse as DAS-28-ESR stage of RA patients became more severe ($p < 0.0001$) (Table 2). Compared to patients with low DAS-28-ESR, those with moderate to high DAS-28-ESR had increasingly higher LPT and monthly costs of LPT (time in hours: 110.0 ± 58.4 ,

132.4 ± 57.2 vs. 71.5 ± 52.0 , $p < 0.0001$; monthly costs of LPT in 1,000 KRW: $1,097 \pm 607$, $1,302 \pm 554$ vs. 741 ± 531 , $p < 0.0001$) (Table 2). In multiple regression analyses, significant positive associations with high LPT (≥ 100 hours) were shown in high (adjusted odds ratio [OR]=3.87, 95% confidence interval [CI]: 2.18 ~ 6.87) and moderate DAS-28-ESR (adjusted OR=1.88, 95% CI: 1.41 ~ 2.52) compared to low DAS-28-ESR. Female compared to male (adjusted OR=1.85, 95% CI: 1.21 ~ 2.83), age per 1 year (adjusted OR=1.03, 95% CI: 1.02 ~ 1.04), and KHAQ ≥ 1.0 compared to KHAQ < 1.0 (adjusted OR=5.51, 95%

Table 3. Univariate and multivariate analysis of factors associated with high lost productivity time (≥ 100 hours)

Variable	Unadjusted OR (n = 1,457)	95% CI	Adjusted OR (n = 1,159)	95% CI
DAS-28-ESR				
3.2 ~ 5.1 (ref. < 3.2)	2.75	2.19 ~ 3.45	1.88	1.41 ~ 2.52
> 5.1 (ref. < 3.2)	6.05	3.90 ~ 9.38	3.87	2.18 ~ 6.87
Gender				
Female (ref. male)	2.11	1.54 ~ 2.89	1.85	1.21 ~ 2.83
Age (yr)	1.04	1.03 ~ 1.05	1.03	1.02 ~ 1.04
Duration of disease (yr)	1.03	1.02 ~ 1.05	0.99	0.97 ~ 1.01
RF positivity				
Positive (ref. negative)	1.04	0.81 ~ 1.35	0.76	0.54 ~ 1.08
Anti-CCP positivity				
Positive (ref. negative)	0.99	0.73 ~ 1.34	1.13	0.76 ~ 1.68
CCI (1 point)	1.25	1.11 ~ 1.41	1.13	0.97 ~ 1.33
Current steroid use				
Yes (ref. no)	1.63	1.29 ~ 2.07	1.31	0.96 ~ 1.79
Current NSAID use				
Yes (ref. no)	1.10	0.86 ~ 1.40	0.94	0.68 ~ 1.29
HAQ score ≥ 1.0 (ref. < 1.0)	7.65	5.94 ~ 9.86	5.51	3.99 ~ 7.59

OR: odds ratio, CI: confidence interval, DAS-28-ESR: disease activity score-28-erythrocyte sedimentation rate, RF: rheumatoid factor, CCP: cyclic citrullinated peptide, CCI: Charlson comorbidity index, Connective tissue disease was considered for all rheumatoid arthritis patients, NSAID: nonsteroidal anti-inflammatory drug, HAQ: health assessment questionnaire.

Table 4. Univariate and multivariate analysis of factors associated with high monthly cost of lost productivity time ($\geq 1,000,000$ Korean won)

Variable	Unadjusted OR (n = 1,457)	95% CI	Adjusted OR (n = 1,159)	95% CI
DAS-28-ESR				
3.2 ~ 5.1 (ref. < 3.2)	2.48	1.98 ~ 3.11	1.93	1.43 ~ 2.54
> 5.1 (ref. < 3.2)	5.42	3.52 ~ 8.32	3.45	1.98 ~ 5.99
Gender				
Female (ref. male)	0.97	0.73 ~ 1.30	0.52	0.36 ~ 0.76
Age (yr)	1.01	1.01 ~ 1.02	0.99	0.98 ~ 1.01
Duration of disease (yr)	1.02	1.00 ~ 1.03	0.99	0.97 ~ 1.01
RF positivity				
Positive (ref. negative)	0.88	0.68 ~ 1.13	0.66	0.47 ~ 0.92
Anti-CCP positivity				
Positive (ref. negative)	0.85	0.63 ~ 1.16	1.02	0.70 ~ 1.50
CCI (1 point)	1.16	1.03 ~ 1.30	1.10	0.94 ~ 1.28
Current steroid use				
Yes (ref. no)	1.63	1.28 ~ 2.08	1.18	0.87 ~ 1.61
Current NSAID use				
Yes (ref. no)	1.16	0.90 ~ 1.48	0.92	0.67 ~ 1.25
HAQ score ≥ 1.0 (ref. < 1.0)	5.65	4.43 ~ 7.21	6.07	4.39 ~ 8.40

OR: odds ratio, CI: confidence interval, DAS-28-ESR: disease activity score-28-erythrocyte sedimentation rate, RF: rheumatoid factor, CCP: cyclic citrullinated peptide, CCI: Charlson comorbidity index, Connective tissue disease was considered for all rheumatoid arthritis patients, NSAID: nonsteroidal anti-inflammatory drug, HAQ: health assessment questionnaire.

CI: 3.99~7.59) were also positively associated with high LPT (Table 3).

Also, significant positive associations with high monthly cost of LPT ($\geq 1,000,000$ KRW) were shown in high DAS-28-ESR (adjusted OR=3.45, 95% CI: 1.98~5.99) and moderate DAS-28-ESR groups (adjusted OR=1.93, 95% CI: 1.43~2.54) compared to low DAS-28-ESR group. Also, female compared to male (adjusted OR=0.52, 95% CI: 0.36~0.76), RF positivity compared to RF negativity (adjusted OR=0.66, 95% CI: 0.47~0.92), and KHAQ ≥ 1.0 compared to KHAQ < 1.0 (adjusted OR=6.07, 95% CI: 4.39~8.40) showed positive association with high monthly costs of LPT (Table 4).

DISCUSSION

This is a unique large-scale multicenter, cross-sectional, observational research representing a large number of RA patients in Korea. Previously, characteristics of entire patients in this research has been determined as average age of fifties, mostly females, having over eight years of disease duration, and more than half had low stage of disease activities [22]. In this particular analysis, we investigated Korean RA patient characteristics and their productivity loss outcomes by different stage of DAS-28-ESR groups among those with DAS-28-ESR measurement. With an ultimate goal of improving patient's HRQoL and functional disability for treatment of RA, treatment guidelines recommend an adequate treatment of patients by different stage of DAS-28-ESR considering factors associated with those poor outcome measures [4]. Since DAS-28-ESR is one of the most influential factors associated with HRQoL and functional disability, we now compared productivity loss, which is directly and indirectly related to quality of life of RA patients, by DAS-28-ESR stage.

Although a majority of studies on productivity loss in RA observed its association with functional disability as a primary predictor [30-32], this analysis was focused on the relationship of productivity loss with disease activity which can be an objective approach to the evaluation of disease prognosis. Through this study, we were specifically able to determine the strength of association between two measures of productivity loss and DAS-28-ESR stages for the past 1-month adjusting for all other determinants. The results of productivity loss measures were consistent both in LPT and monthly costs of LPT, and the associations were shown to be stronger as DAS-28-ESR stage increases although some adjusted fac-

tors were found to be marginally significant when monthly costs of LPT were measured as productivity loss outcome. The interpretation of these results may be limited to transient associations between higher DAS28 and impaired LPT in time and indirect cost since the data used in this analysis was achieved from relatively short observation. However, a prospective study targeting patients with axial Spondyloarthritis found that the prominent impacts of decreasing disease activity on remarkable improvement in work productivity for the 1-year study duration [33]. Similarly, previous studies including rheumatoid arthritis showed that higher disease activity was a predictive factor that yields compromised productivity in both time and indirect cost [34-36].

There have been many approaches to study disease-induced costs as health outcomes, and costs have been calculated in various ways including the expected cost estimation using economic models and standard cost estimation performed by a panel of clinicians [14,37]. In spite of the fact these approaches would bring more accurate and reliable results than that from the study proposed herein, this analysis should come to attention the way in which it adds values since it utilizes the clinical observational data from the real world practice and patient surveys on the LPT measuring both the socio-economic burden and the health-related disease burden at the same time.

Nevertheless, this study has several limitations. Firstly, we cannot infer temporality in this cross-sectional study although we determined the strength of association between productivity loss outcomes and DAS-28-ESR. Second, there may be possible respondent bias when patients administered questionnaire used for the measurement of the productivity loss. Even though this study is valuable for presenting the data of a representable population of Korean RA patients, the results could not be generalized to other populations with different social and economic characteristics. Third, this study may selectively include healthy patients with minimal impairment in their clinical conditions who were sufficiently able to complete patients' self-administered questionnaires. Lastly, the fact that no specific socio-economic data such as education and actual income status did not include in the analysis should be taken into consideration while interpreting study results.

In conclusion, patients with moderate to high DAS-28-ESR had more productivity loss in time and monthly cost of lost productivity time than patients with low DAS-28-ESR, and stronger association was found to be present

between higher disease activity and high LPT as well as high monthly cost of LPT. Although all patients were being treated with either biologic DMARDs or conventional DMARDs, burden of patients still remained high among RA patients and these results could be easily discriminated when outcomes were observed by different stages of DAS-28-ESR as in this study. Based on the results obtained from this analysis of Korean RA patients, treatment should be considered in a timely manner after the onset of disease to control the disease activity which may lead to higher socio-economic burden and physical impairment based on higher productivity loss in time and indirect cost. Therefore, focused treatments on patients with moderate to high DAS-28-ESR could not only enhance suppression of further progression, but also be positively associated with low burden of illness.

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CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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