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ORIGINAL ARTICLE

Usefulness of the Psoriatic Arthritis Screening and Evaluation Questionnaire to Monitor Disease Activity in Management of Patients with Psoriasis: Findings from the EPI-PSODE Study

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Background: Psoriasis and psoriatic arthritis (PsA) are included in the group of immune-mediated inflammatory diseases (IMIDs) caused by systemic inflammation; however, indicators for monitoring inflammatory activity in patients with psoriasis, such as the Psoriasis Area and Severity Index (PASI), are limited. **Objective:** To determine whether the Psoriatic Arthritis Screening and Evaluation (PASE) questionnaire can be used to monitor disease activity in patients with psoriasis. **Methods:** This was a multicenter, non-interventional, cross-sectional study. Demographic factors and PASI and PASE scores were collected to investigate associations between each. **Results:** PASE data were available for 1,255 patients, of whom 498 (39.7%) had a score of ≥ 37. Compared with the group with PASE score < 37, the group with score ≥ 37 had a higher proportion of women (34.9% vs. 48.8%, $p < 0.0001$), older mean age at diagnosis (36.4 vs. 41.7 years, $p < 0.0001$), more severe disease activity using PASI and body surface area measures ($p = 0.0021$ and $p = 0.0008$, respectively), and higher mean body mass index (23.7 vs. 24.1, $p = 0.0411$). In a multiple linear regression model, PASE score was positively associated with cutaneous disease activity ($p < 0.0001$). **Conclusion:** After risk-adjustment, PASE was positively associated with PASI, which suggests that PASE can be sensitive to disease activity. Since psoriasis is regarded as one of the IMIDs, PASE may be utilized as a tool not only to screen PsA but also to monitor disease activity. **(Ann Dermatol 31(1) 29~36, 2019)**

-Keywords-
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INTRODUCTION

Psoriasis is a chronic inflammatory skin disease with prevalence of 1%～3% worldwide. Skin lesions are characterized by multiple, well-demarcated, raised, red plaques with a white scaly surface[1]. It is considered to be a systemic disease because it is frequently accompanied by comorbidities that include psoriatic arthritis (PsA), diabetes, dyslipidemia, and cardiovascular disease[2,3]. PsA is an inflammatory arthritis associated with psoriasis and its prevalence varies between 0.02% and 0.42% in the general population[4,5] and between 6% and 48% in psoriasis patients[6]. The skin manifestations of psoriasis precede symptoms of arthritis by 10 years on average and, in 15% of the total cases, PsA and psoriasis either occur simultaneously or PsA precedes the skin disease[7].

Early diagnosis of and prompt intervention for PsA are crucial because delaying treatment may result in devastating, irreversible joint damage. Moreover, PsA is known to be an important determinant of vascular comorbidities in psoriatic patients[8]. Dermatologists, therefore, have an important role in examining other body systems as well as the skin lesions associated with psoriasis that might be involved in this immune-mediated inflammatory disease (IMID).

However, there is no specific indicator for monitoring systemic inflammation in patients with psoriasis, such as the C-reactive protein levels used in clinical practice to monitor disease activity in rheumatic and inflammatory bowel disease. On the other hand, some screening tools have been developed for the identification of PsA in patients with psoriasis; these include the Psoriatic Arthritis Screening and Evaluation (PASE)[9], the Psoriatic and Arthritic Questionnaire[10], the Psoriasis Epidemiology Screening Tool[11], the Toronto Psoriatic Arthritis Screen[12], and the Early Arthritis for Psoriatic Patients[13]. Of these, PASE has the most questions, with possible scores of 0 to 75, with a broader range to screen arthritis-related symptoms and functions. In this analysis, we sought to determine whether the symptoms of inflammatory arthritis, and their effect on patient functioning, are positively associated with cutaneous disease activity in order to enable better management of patients with psoriasis, in a holistic approach to IMID.

MATERIALS AND METHODS

Study design

The EPI-PSODE[14] study was a multicenter, noninterventional, cross-sectional study. The 25 participating centers were primarily university hospitals, located across Korea (with the exception of the Jeju island region). This study was reviewed and approved by the Institutional Review Board of each center (Corresponding author's institution [Asan Medical Center]: IRB no. 2013-0161). To extract a representative sample reflecting the distribution of psoriasis in Korea, the numbers and locations of the study centers were selected on the basis of population distribution and health insurance reimbursement data of patients with psoriasis. Patients were examined and enrolled consecutively in order of visiting the center. After obtaining informed consent, all study procedures were performed on 1 day. The study patients were adults aged 20 years or older diagnosed with psoriasis. Data were collected by interviewing and assessing the patients on demographic factors (age, gender, height, weight, waist circumference, disease duration, age at diagnosis, family history in first-degree relative, drinking/smoking history, and medication history). Physical examinations for disease-severity measures (Psoriasis Area and Severity Index [PASI] and body surface area [BSA]) and blood pressure were performed. Quality of life was evaluated by the Dermatologic Life Quality Index (DLQI) and Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36)[15]. In order to evaluate patient satisfaction with various therapies, questions from the existing Medication Satisfaction Questionnaire (MSQ) were included[16]. Lastly, the PASE tool was used to assess arthritis-related symptoms and functions.

Statistical analysis

Descriptive statistics for continuous variables are presented as means with standard deviation (SD), and dichotomous variables are presented as frequencies with percentages in parentheses. Respective proportions are presented using 37 points[17,18], 44 points[19], and 47 points[9] as cut-off values in PASE, and variables collected were compared to assess the statistical significance of any differences among the groups using a cutoff threshold of 37 points of PASE (PASE <37 and PASE ≥ 37) based on a validation study for Korean patients (sensitivity of 77.8%, specificity of 82.3%, positive predictive value of 37.8% and negative predictive value of 96.4%)[17]. We used, where appropriate, the Mann-Whitney U-test and t-test for continuous variables and Pearson's chi-square test and Fisher's exact test for dichotomous variables, without missing data imputation. In addition, multiple linear regression analysis was used to assess association between disease activity (using PASI) and inflammatory arthritis-related symptoms and functions (using PASE) after excluding the effect of each confounder such as gender, age, and body mass index (BMI) which are considerably related to occurrence of arthritis. All stat-

istical tests were performed using 2-sided tests and *p*-values <0.05 were considered statistically significant. Analyses were performed using the statistical software package SAS 9.4 (Statistical Analysis System; SAS-Institute, Cary, NC, USA).

RESULTS

Of 1,260 patients who completed the study, PASE data were available for 1,255 patients. The proportions of patients scoring ≥ 47, ≥ 44, and ≥ 37 points were 18.6% (n= 233), 24.0% (n=301), and 39.7% (n=498), respectively (Fig. 1).

At the 37-point cut-off, there were 757 patients in the group with PASE <37 and 498 in the group with PASE ≥ 37. The group with PASE ≥ 37 had a higher proportion of women than the group with PASE <37 (48.8% vs. 34.9%, $p<0.0001$); older mean age (50.5 years vs. 44.7 years, $p<0.0001$); and older mean age at diagnosis (41.7 years vs. 36.4 years, $p<0.0001$). The higher-score PASE group (PASE ≥ 37) had more severe disease activity using PASI and BSA (difference of PASI=1.5; $p=0.0021$ and difference of BSA=3.1; $p=0.0008$, respectively) than the lower-score PASE group (PASE <37). Nail involvement and family history of psoriasis were more frequent in the PASE ≥ 37 group but this did not reach statistical significance. The group with PASE ≥ 37 had higher mean BMI (24.1 vs. 23.7, $p=0.0411$) and greater waist circumference (85.87 cm vs. 83.22 cm, $p=0.0002$) but there was no significant relationship with blood pressure between the 2 groups. A significantly lower percentage of patients in the group with PASE ≥ 37 had a smoking and drinking history than the group with PASE <37, but this appears to be affected by the difference in the gender ratio (no statistical significance based on Cochran-Mantel-Haenszel [CMH] test between the 2 groups stratified by gender; smoking (pCMH=0.9297) and drinking (pCMH=0.1261) (data not shown). Regarding medication history, only use of systemic treatment was significantly greater in the group with PASE ≥ 37 than the group with PASE <37 (66.3% vs. 58.0%, $p=0.0032$). DLQI and both physical and mental component SF-36 scores were significantly higher in the group with PASE ≥ 37 compared to the group with PASE <37, and satisfaction with treatment was lower in the group with PASE ≥ 37 ($p=0.0015$) (Table 1).

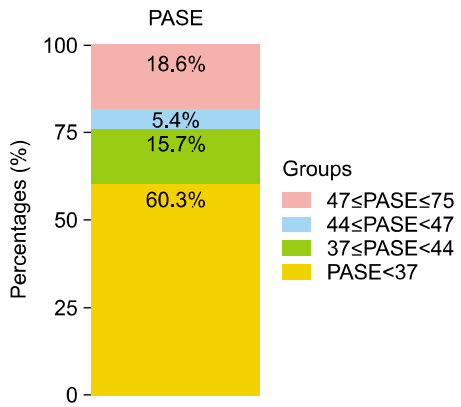

Fig. 1. Proportion of patients by PASE cut-off values. PASE: Psoriatic Arthritis Screening and Evaluation.

A multiple linear regression model was used to explore the potential for an association between disease severity represented by PASI and PASE scores by designating factors with representativeness among significant independent variables in the univariate analysis. It appeared that female gender, age, and BMI affected arthritis symptoms and function. PASE and PASI were associated with each other, even after adjustment for the these factors ($p<0.0001$) (Table 2).

The comparison of scores between the group with PASE ≥ 37 and the group with PASE <37 for each question of the PASE questionnaire is shown in Fig. 2 and Table 3 for the symptom subscale and Fig. 3 and Table 4 for the function subscale. For the symptom subscale, the highest score difference between the 2 groups was for question 2, "My joints hurt". The highest score in both groups was for question 1, "I feel tired for most of the day", and the lowest score in both groups was for question 5, "My joints feel hot". This last question had the lowest score difference between the groups. For the function subscale, the score difference between the 2 groups was highest for question 8, "I feel that my joint problems have affected my ability to work", then question 12, "I am unable to be as active as I used to be" and question 13, "I feel stiff for more than 2 hours after waking up in the morning". Lastly, the question with the lowest score in both groups and the lowest score difference between the 2 groups was question 10, "I have trouble wearing rings on my fingers or my watch".

DISCUSSION

The prevalence of PsA in Korea according to previous studies was approximately 9.0%~14.1%[20-22]. When PASE scores of ≥ 47, ≥ 44, and ≥ 37 were applied as cut-off values, the proportions of screened patients in each group were 18.6%, 24.0%, and 39.7%, respectively. Of these, approximately 40% of patients with a cut-off score of ≥ 37 validated in the Korean population may require additional assessments to confirm a diagnosis of PsA. In our study, the prevalence of PsA in patients with psoriasis was nu-

Table 1. Comparison of related factors between 2 groups divided by PASE 37

Category	n'	PASE <37 (n=757)	PASE ≥37 (n=498)	*p*-value
Demographics				
Gender	1,255			
Male	748	493 (65.1)	255 (51.2)	<0.0001
Female	507	264 (34.9)	243 (48.8)	
Age (yr)	1,255	44.7±13.92	50.5±14.66	<0.0001
Age at diagnosis (yr)	1,252	36.4±15.72	41.7±17.11	<0.0001
Disease duration (mo)	1,252	106.6±121.13	113.7±123.58	0.3574
PASI	1,255	6.87±6.409	8.38±7.905	0.0021
BSA	1,253	11.9±13.21	15.0±16.36	0.0008
Nail involvement	1,255	90 (11.9)	65 (13.1)	0.5401
Family history	1,255	91 (12.0)	68 (13.7)	0.3947
BMI (kg/m^2)	1,254	23.70±3.308	24.12±3.746	0.0411
Waist circumference (cm)	1,108	83.22±10.218	85.87±12.304	0.0002
SBP≥140 mmHg or DBP≥90 mmHg	1,160	134 (19.3)	97 (20.9)	0.4900
Smoking history	1,255	391 (51.7)	216 (43.4)	0.0041
Drinking history	1,255	512 (67.6)	291 (58.4)	0.0009
Medication history				
Topical	1,255	712 (94.1)	463 (93.0)	0.4420
Phototherapy	1,255	394 (61.7)	245 (49.2)	0.3230
Systemics	1,255	439 (58.0)	330 (66.3)	0.0032
Biologics	1,255	38 (5.0)	34 (6.8)	0.1779
Patient-reported outcome				
PASE total score	1,255	24.8±6.81	47.2±7.95	<0.0001
PASE symptom score	1,255	12.2±3.64	22.0±4.08	<0.0001
PASE function score	1,255	12.6±4.17	25.2±5.01	<0.0001
DLQI	1,251	10.3±6.80	14.6±7.12	<0.0001
SF-36 (physical)	1,253	52.1±6.07	43.8±7.86	<0.0001
SF-36 (mental)	1,253	46.0±10.29	37.4±10.61	<0.0001
Satisfaction in MSQ	1,250	461 (61.2)	271 (54.5)	0.0015

Values are presented as number (%) or mean±standard deviation. Percentages were based on the total number of subjects with each available result in each group. n': Total number of subjects with each available result, PASE: Psoriatic Arthritis Screening and Evaluation, PASI: Psoriasis Area and Severity Index, BSA: body surface area, BMI: body mass index, SBP: systolic blood pressure, DBP: diastolic blood pressure, DLQI: Dermatology Life Quality Index, SF-36: Medical Outcomes Study 36-Item Short-Form Health Survey, MSQ: Medication Satisfaction Questionnaire.

Table 2. Association between PASE and PASI in a multiple linear regression model

Variable	PASE	
	β	*p*-value
PASI	0.235	<0.0001
Female gender	3.920	<0.0001
Age	0.161	<0.0001
BMI	0.136	0.2014

PASE: Psoriatic Arthritis Screening and Evaluation, PASI: Psoriasis Area and Severity Index, β: regression coefficient, BMI: body mass index.

merically estimated to be 15.0% by applying positive predictive value of 37.8% to the patients screened with a cut-off of 37 points[17]. In addition, a recent study performed in Japan showed that the prevalence of PsA in patients with psoriasis reached around 20% in some areas[23]. Continued studies are required to further characterize the prevalence of PsA in Korea.

The maximum score for the PASE is 75; for a continuous variable with such a wide range, the ability to detect changes becomes relatively greater and sensitivity is higher than a continuous variable with a narrow range. In general, most patients who develop PsA progress from psoriasis alone to psoriasis with PsA and these patients have more severe psoriasis[24]; this finding aligns with our analysis in which the group with PASE ≥37 showed higher PASI scores and BSA affected than the group with PASE <37. Moreover, disease severity in psoriasis is associated with elevated proinflammatory cytokines[25] and this level of inflammation is related to the development of hyper-

tension[26]. A systematic review found that there is a greater prevalence of hypertension in patients with psoriasis, and patients with severe psoriasis are more likely to have hypertension than those with mild psoriasis[27], consistent with hypertension considered as a type of inflammatory disease[28].

The disease severity of psoriasis has been shown to be related to the activity of inflammation. In our analysis, PASE scores were positively associated with PASI scores after

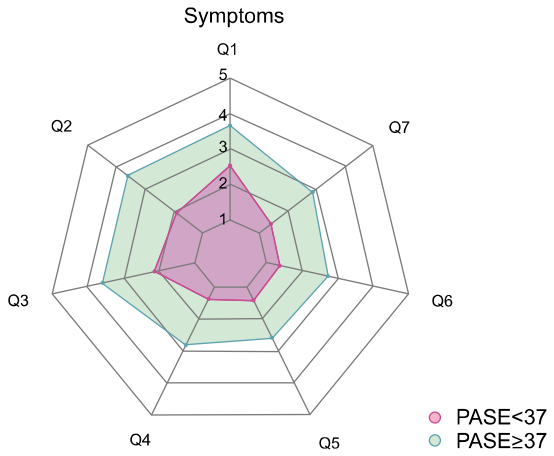

Fig. 2. Comparisons in symptom subscale of PASE. PASE: Psoriatic Arthritis Screening and Evaluation.

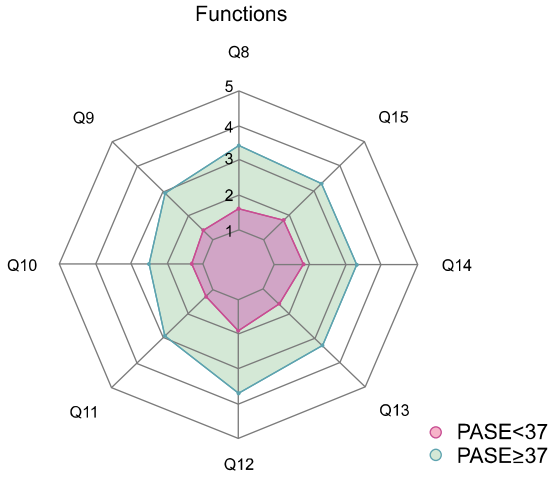

Fig. 3. Comparisons in function subscale of PASE. PASE: Psoriatic Arthritis Screening and Evaluation.

Table 3. Comparisons in symptom subscale of PASE

PASE Questionnaire	PASE <37 (n=757)	PASE ≥37 (n=498)	Difference
1. I feel tired for most of the day	2.5±1.10	3.7±0.87	−1.2±1.01
2. My joints hurt	1.9±0.99	3.6±0.92	−1.7±0.96
3. My back hurts	2.1±1.11	3.6±0.92	−1.5±1.04
4. My joints become swollen	1.4±0.63	2.8±1.07	−1.4±0.83
5. My joints feel "hot"	1.4±0.61	2.6±1.04	−1.2±0.81
6. Occasionally, an entire finger or toe becomes swollen, making it look like a "sausage"	1.4±0.68	2.7±1.12	−1.3±0.88
7. I have noticed that the pain in my joints moves from one joint to another, e.g. my wrist will hurt for a few days then my knee will hurt and so on	1.4±0.66	2.9±1.09	−1.4±0.85

Values are presented as mean±standard deviation. Difference=PASE≥37−PASE <37. PASE: Psoriatic Arthritis Screening and Evaluation.

Table 4. Comparisons in function subscale of PASE

PASE Questionnaire	PASE <37 (n=757)	PASE ≥37 (n=498)	Difference
8. I feel that my joint problems have affected my ability to work	1.6±0.82	3.4±1.01	−1.9±0.90
9. My joint problems have affected my ability to care for myself, e.g. getting dressed or brushing my teeth	1.4±0.70	2.9±1.08	−1.5±0.87
10. I have had trouble wearing rings on my fingers or my watch	1.3±0.63	2.5±1.11	−1.2±0.86
11. I have had trouble getting into or out of a car	1.3±0.59	2.9±1.11	−1.5±0.84
12. I am unable to be as active as I used to be	1.9±1.02	3.7±0.97	−1.8±1.00
13. I feel stiff for more than 2 hours after waking up in the morning	1.6±0.80	3.3±1.00	−1.7±0.88
14. The morning is the worst time of day for me	1.8±0.95	3.3±1.01	−1.5±0.97
15. It takes me a few minutes to get moving to the best of my ability, any time of the day	1.8±0.92	3.3±0.94	−1.5±0.93

Values are presented as mean±standard deviation. Difference=PASE≥37−PASE <37. PASE: Psoriatic Arthritis Screening and Evaluation.

adjusting for confounding factors such as female gender, age, and BMI which affect arthritis symptoms and our result also showed positive linearity through each regression coefficient (β) in Table 2. In addition, Husni et al.[29] confirmed that the PASE tool is sensitive to changes in response of patients treated with biological therapy, which might be applied similarly to change in disease activity or systemic inflammation. Therefore, the use of PASE could monitor changes in inflammatory activity, in other words disease activity, in patients with psoriasis. PASE is not only used for PsA screening but also for management of psoriasis as an IMID. Patients with PsA showed more severe psoriasis than patients without PsA in some studies[24,30,31]. In line with these results, our analysis showed that the group with PASE $\geq$37 had significantly higher PASI and BSA affected than the group with PASE $<$37; greater and more active systemic inflammation may affect many body systems so this increased disease activity may promote the development of PsA. The most common identified risk factor for development of PsA was the presence of nail disease in many studies[30,32,33]. In our study, nail involvement was higher in the group with PASE $\geq$37 than the group with PASE $<$37, but this was not statistically significant. Obesity has also been shown to increase the risk of occurrence of PsA in some studies[34,35]; this suggests that weight loss may alleviate disease severity and reduce the risk of developing PsA. Consistent with this, the BMI of the group with PASE $\geq$37 was significantly higher in our study than that of the group with PASE $<$37. However, further studies are needed to determine the relationship between obesity and development of PsA in Korean patients with psoriasis because the difference in BMI between groups was small (0.42 kg/m^2) and weight gain may increase the risk of osteoarthritis, which is not related to systemic inflammation[36].

The association between smoking/drinking and PsA is controversial because there have been opposing results from a variety of studies[37]. In our analysis, the percentage of patients with a history of smoking was higher in the group with PASE $<$37 using a univariate model, though there was no statistically significant difference between the 2 groups when stratified by gender. In other words, no association between smoking and PASE score was identified in our analysis. Drinking was also not associated with PsA when stratified by gender. Tey et al.[38] reported that sex, age of onset of psoriasis, and a family history of psoriasis were not associated with PsA, but our study showed that age at diagnosis was significantly higher in the group with PASE $\geq$37 than the group with PASE $<$37.

A potential limitation of the PASE questionnaire is its length, and it may be difficult for patients to complete all 15 questions in the real-world setting of dermatology clinic practice. However, it may be sufficient to use only the questions that showed the greatest difference between the two groups. Question 2, "My joints hurt" in the symptom subscale and question 8, "I feel that my joint problems have affected my ability to work" showed the greatest difference between the 2 groups in our analysis. According to the Turkish PASE tool validation study[39], questions 2, 8, and 12 indicated the highest sensitivity (77%) for the answers "agree" or "strongly agree". This result is closely aligned with our analysis. If the scores for these questions are increased, physicians may consider completing the entire PASE questionnaire with the patient or performing regular follow-up, at least once every 6 or 12 months so that changes in inflammatory activity, which might not be apparent by examination of the skin, may be checked by evaluation of joint symptoms. Lastly, further studies are needed to support results from the present study. For example, a study on specific population excluding confounders could be conducted or a study to follow up changes in intra-subject setting.

In conclusion, PASE scores is independently associated with PASI scores after risk adjustment and can be sensitive to disease activity. From the perspective that psoriasis is treated as one of the IMIDs, PASE may be utilized as a tool to monitor changes in inflammatory activity and their effect on the course of the disease.

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CONFLICTS OF INTEREST

Dae Young Yu and Youngdoe Kim are employees of Janssen Korea. Other authors have no conflict of interest to declare.

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