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Metabolic syndrome is associated with an increased risk of psoriasis: A nationwide population-based study

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ABSTRACT

Background: Psoriasis is a chronic inflammatory skin disease characterized by an abnormal T-cell-mediated immune response, and is associated with metabolic syndrome (MetS) and components thereof. However, few prospective studies have investigated the associations between MetS and its components, on the one hand, and the risk of psoriasis, on the other. Therefore, we investigated the association between the presence of MetS and its components and the prospective risk of psoriasis development.
Methods: In total, 9,718,591 adults (2,595,878 in the MetS group and 7,122,713 in the comparison group) were evaluated using data from the Korean National Health Insurance Service (2009 to 2017).
Results: MetS was positively associated with an increased risk of psoriasis over an 8-year follow-up period after adjusting for age, sex, smoking status, alcohol consumption, physical activity, household income, and body mass index (hazard ratio 1.05, 95% confidence interval 1.04–1.06). The risk of psoriasis tended to increase as the number of MetS components increased, and this trend was significant in obese subjects (P for trend <0.001).
Conclusion: Psoriasis was significantly and positively associated with MetS and several components thereof; MetS severity and obesity affected these associations over 8 years of follow-up, suggesting that MetS is a risk factor for the development of psoriasis.

1. Introduction

Metabolic syndrome (MetS), a cluster of metabolic risk factors including hyperglycemia, atherogenic dyslipidemia, elevated blood pressure, and abdominal obesity [1], is associated with an increased risk of cardiovascular disease and all-cause mortality [2]. The prevalence of MetS is increasing rapidly worldwide [3]; thus, MetS has become a major medical issue. MetS not only reflects a complex interaction of maladaptive characteristics associated with impairment of insulin-mediated effects on target organs [4]; increased oxidative stress or chronic inflammation also affect MetS development and aggravation [5,6].

Psoriasis is a chronic inflammatory skin disease characterized by dysregulation of the T-cell-mediated immune response [7] that has been associated with metabolic syndrome (MetS) and its components [8–10]. However, prospective studies investigating the associations between MetS and components thereof that may predispose to psoriasis, and the risk of psoriasis, are scarce, especially for Asian populations [11]. Therefore, we aimed to investigate the prospective risk of psoriasis development among the patient with MetS using the database established by the Korean National Health Insurance Service (KNHIS).

2. Materials and methods

2.1. Data source

We extracted data from the KNHIS national health claims database [12]. The KNHIS provides comprehensive medical care to 97% of the Korean population and maintains a database of inpatient and outpatient medical service records, diagnostic and procedural codes, prescribed medications, and demographic data. A Medical Aid program covers the low-income population (the remaining 3% of Koreans). Since 2006, Medical Aid data have been included in the KNHIS database, so the database now covers all Koreans. No record is duplicated or omitted because all Koreans receive a unique identification number at birth. The KNHIS uses the standard codes of the International Statistical Classification of Diseases and Related Health Conditions, 10th revision (ICD-10).

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The KNHIS also provides general health checkups and a cancer-screening program. All Koreans can receive free health checkups at any age. The data that we accessed were anonymized (thus devoid of personal information), and our work was approved by the Institutional Review Board of the KNHIS (approval no. NHIS-2019-1-075). The Ethics Committee of Seoul St. Mary's Hospital, the Catholic University of Korea, also approved the study design and waived the need for informed subject consent (approval no. KC18ZESI0643).

2.2. Study design and population

This was a prospective study, and we retrieved patient's data from the KNHIS 2009–2017. Of the 10,490,491 civilians aged ≥20 years who received general health checkups in 2009, those for whom data were missing (n = 510,925), and those diagnosed with psoriasis prior to enrollment (n = 260,975) were excluded. Thus, 9,718,591 subjects were finally included (Fig. 1). All included subjects were tracked over the 8 years from 2009 to 2017 to identify those who developed psoriasis (ICD-10: L40).

The MetS and the comparison groups consisted of 2,595,878 and 7,122,713 subjects, respectively, in 2009. MetS was defined using the revised criteria of the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) [13]; thus, by the presence of three or more of the following: waist circumference ≥ 90 cm for males and ≥ 85 cm for females [14]; triglyceride level ≥ 150 mg/dL or on medication to reduce triglyceride levels; high-density lipoprotein (HDL) cholesterol level < 40 mg/dL for males or < 50 mg/dL for females, or on medication to reduce HDL-cholesterol levels; systolic blood pressure ≥ 130 mmHg or diastolic blood pressure ≥ 85 mmHg or on antihypertensive medication; and fasting glucose levels ≥100 mg/dL or on medication to reduce glucose levels. MetS severity was defined as the number of components increased in MetS.

2.3. Clinical, laboratory, and anthropometric measurements

Information on age, sex, household income, smoking status, alcohol consumption, and physical activity was obtained from data recorded at regular, medical KNHIS checkups. Household income was estimated as total income divided by the square root of the number of household members, and was dichotomized at the lower 20% border (≤20% vs. >20%). Cigarette smoking was divided into three categories based on current use: non-smoker, ex-smoker, and current smoker. Alcohol consumption was classified as abstinence (no alcoholic drinks within the past year), moderate (<30 g pure alcohol per day), and heavy (≥30 g pure alcohol per day). Physical activity was classified as moderate-to-intense or not, and moderate-to-intense activity was defined as moderate or vigorous exercise on at least 1 day a week. Comorbidities (hypertension, dyslipidemia, and diabetes mellitus [DM]) were identified based on clinic and pharmacy ICD-10 codes and medicine lists. Venous blood samples for assay of fasting glucose, lipid, and creatinine levels were obtained after an overnight fast. Body mass index (BMI) was the weight (kg) divided by the square of the height (m), and was classified as underweight, normal weight, overweight, obese, or severely obese (<18.5, 18.5 to 22.9, 23 to 24.9, 25 to 29.9, and ≥30 kg/m^2 respectively) [15].

2.4. Statistical analysis

We used the independent *t*-test to compare continuous variables and the chi-squared test to compare dichotomous variables. Skewed variables were log-transformed. Data are expressed as means ± standard deviations, or as numbers with percentages, or as geometric means with 95% confidence intervals (CIs) if the distributions were skewed. Univariate and multivariate Cox's proportional hazard regression analyses were performed to identify any association between MetS status and psoriasis development. The multivariate analysis was adjusted for age, sex, smoking status, alcohol consumption, physical activity, household income, and BMI. Psoriasis-free status during follow-up was analyzed using the Kaplan-Meier method; we used the log-rank test to analyze differences in psoriasis incidence between the two groups. Incidence of psoriasis by the number of MetS components and obesity was analyzed using the Cox's proportional hazard regression analyses after adjusting for age, sex, smoking status, alcohol consumption, physical activity, and household income. All analyses were performed with the aid of SAS software ver. 9.4 (SAS Institute, Cary, NC, USA). A *P*-value <0.05 was regarded as statistically significant.

3. Results

3.1. Characteristics of the study population

A total of 9,718,591 adults were included in this study (2,595,878 [26.7%] for the adults with MetS). During the 8-year follow-up, 207,059 psoriasis cases developed (63,660 [2.45%] for the MetS group and 143,399 [2.01%] for the comparison group). Table 1 lists the characteristics of the MetS and comparison groups. The incidence of psoriasis in the MetS group was higher than in the other group (2.45% vs. 2.01%, $P < 0.001$). The MetS group tended to be older; had higher proportions of females and heavy drinkers; lower proportions of current smokers and those engaging in moderate-to-intense physical activity; and higher proportions of those with hypertension, dyslipidemia, and DM.

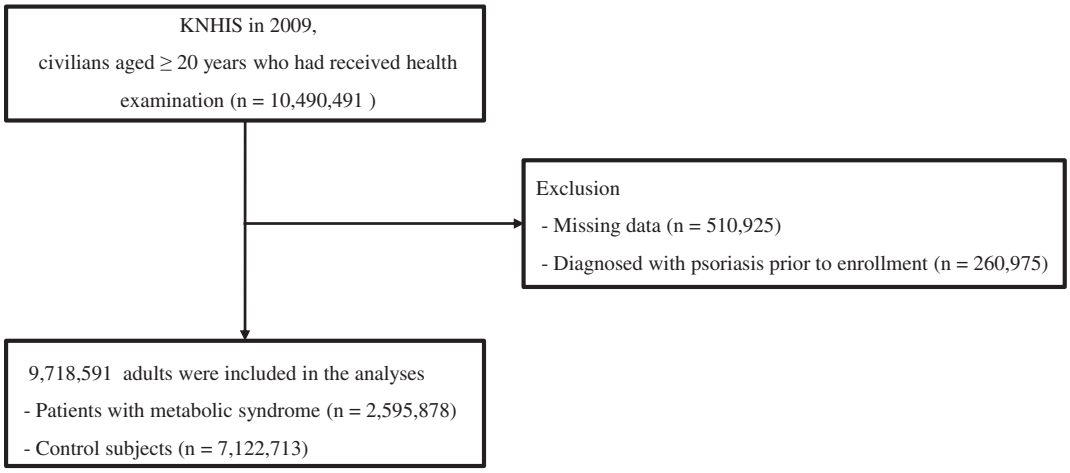

Fig. 1. Study population: data from the Korean National Health Insurance Service.

Table 1
Characteristics of the study population.

	Metabolic syndrome (n = 2,595,878)	Comparison (n = 7,122,713)	*P*
New-onset psoriasis	63,660 (2.45)	143,399 (2.01)	<0.001
Age (years)	54.7 ± 13.0	44.3 ± 13.4	<0.001
Male	1,404,676 (54.1)	3,908,853 (54.9)	<0.001
Current smoker (%)	632,861 (24.4)	1,905,369 (26.8)	<0.001
Heavy drinker (%)	209,839 (8.1)	455,311 (6.4)	<0.001
Exercise (yes) (%)	1,262,259 (48.6)	3,735,067 (52.4)	<0.001
Low income (%)	665,005 (25.6)	1,898,752 (26.7)	<0.001
Comorbidities			
Diabetes	618,529 (23.8)	221,387 (3.1)	<0.001
Dyslipidemia	1,119,023 (43.1)	648,533 (9.1)	<0.001
Hypertension	1,492,702 (57.5)	996,144 (14.0)	<0.001
Body mass index (kg/m^2)	25.8 ± 3.1	22.9 ± 2.9	< 0.001
Waist circumference (cm)	86.8 ± 7.9	77.8 ± 8.2	<0.001
Systolic pressure (mmHg)	131.3 ± 14.7	119.2 ± 13.7	<0.001
Diastolic pressure (mmHg)	81.1 ± 9.9	74.6 ± 9.4	<0.001
Total cholesterol (mg/dL)	204.5 ± 41.1	191.6 ± 34.2	<0.001
HDL-cholesterol (mg/dL)	49.4 ± 19.5	57.6 ± 18.2	<0.001
LDL-cholesterol (mg/dL)	116.5 ± 38.9	112.0 ± 31.5	<0.001
Triglycerides (mg/dL)[a]	172.2 (172.1–172.3)	97.6 (97.5–97.6)	<0.001
Metabolic syndrome components			
Elevated waist circumference	1,265,340 (48.7)	636,327 (8.9)	<0.001
Elevated blood pressure	2,136,680 (82.3)	2,098,848 (29.5)	<0.001
Elevated fasting glucose level	1,683,799 (64.9)	1,356,015 (19.0)	<0.001
Reduced HDL-cholesterol level	1,716,366 (66.1)	952,374 (13.4)	<0.001
Elevated triglyceride level	2,107,168 (81.5)	1,275,989 (17.9)	<0.001

Values are expressed as means ± standard deviations or as numbers with percentages (%) and were compared using the independent t-test (continuous variables) or chi-squared test (dichotomous variables). Values are expressed as geometric means with 95% confidence intervals if the distributions were skewed[a]. Low income was defined as a household income ≤20% of the median. HDL, high-density lipoprotein; LDL, low-density lipoprotein.

3.2. Metabolic syndrome and its components as predictors of psoriasis

As shown in Table 2, the MetS group was at a greater risk of psoriasis than the comparison group (unadjusted hazard ratio [HR] 1.23, 95% confidence interval [CI] 1.22–1.24); the association remained significant after adjusting for age, sex, smoking status, alcohol consumption, exercise status, income, and BMI (multivariate-adjusted HR [aHR] 1.05, 95% CI 1.04–1.06). Compared to the comparison group, the MetS group exhibited an increasing trend toward psoriasis development as the number of components increased (aHR 1.02, 95% CI 1.01–1.04 for the number of MetS components of 3, aHR 1.06, 95% CI 1.04–1.08 for the number of 4, and aHR 1.09, 95% CI 1.06–1.12 for the number of 5, respectively). Those with elevated waist circumference or triglyceride levels, or reduced HDL-cholesterol levels, were more likely to develop psoriasis than those of normal waist circumference or with normal metabolite levels after adjusting for the aforementioned covariates (aHR 1.11, 95% CI 1.09–1.12; aHR 1.04, 95% CI 1.03–1.05, and aHR 1.07, 95% CI 1.06–1.08, respectively). The HR for psoriasis trended upward as overweight or obese status became more marked (aHR 1.02, 95% CI 1.01–1.03 for overweight, aHR 1.06, 95% CI 1.04–1.07 for obesity, and aHR 1.12, 95% CI 1.09–1.15 for severe obesity, respectively).

3.3. Cumulative effects of metabolic syndrome on psoriasis incidence

Fig. 2 presents the results of Kaplan-Meier curves assessing the psoriasis-free rate by the presence of MetS and components thereof. A total of 69,804,956 person-years were examined (18,503,023 person-years for the MetS group and 51,301,933 person-years for the comparison group). The cumulative incidence of psoriasis was higher in the MetS group ($P < 0.0001$; log-rank test, Fig.2, A). Compared to subjects without any MetS components, those with one or more MetS components had a greater probability of psoriasis development in a dose-dependent manner ($P < 0.0001$; log-rank test, Fig.2, B).

3.4. Incidence of psoriasis by the number of metabolic syndrome components and obesity

The psoriasis risk increased significantly as the number of MetS components increased in obese subjects (*P* for trend <0.0001) after

Table 2
Associations between metabolic syndrome, components thereof, and the incidence of psoriasis.

	Cases	Person-years	Incidence rate[a]	HR (95% CI)			
				Unadjusted	Model 1	Model 2	Model 3
Metabolic syndrome	63,660	18,503,023	3.44	1.23 (1.21–1.23)	1.07 (1.06–1.08)	1.07 (1.06–1.08)	1.05 (1.04–1.06)
Number of MetS components							
0	46,601	18,137,201	2.57	1	1	1	1
1	51,905	18,484,625	2.81	1.09 (1.08–1.11)	0.99 (0.97–1.01)	0.99 (0.98–1.00)	0.98 (0.97–1.00)
2	44,893	14,680,105	3.05	1.19 (1.17–1.21)	1.01 (1.00–1.03)	1.01 (0.99–1.02)	0.99 (0.98–1.01)
3	33,403	10,110,838	3.30	1.29 (1.27–1.30)	1.05 (1.04–1.07)	1.05 (1.03–1.06)	1.02 (1.01–1.04)
4	21,317	6,009,344	3.54	1.38 (1.36–1.40)	1.09 (1.07–1.11)	1.09 (1.07–1.10)	1.06 (1.04–1.08)
5	8940	2,382,839	3.75	1.46 (1.43–1.49)	1.13 (1.10–1.16)	1.12 (1.10–1.15)	1.09 (1.06–1.12)
Metabolic syndrome components							
Elevated waist circumference	47,286	13,590,867	3.48	1.22 (1.21–1.24)	1.11 (1.10–1.12)	1.11 (1.10–1.12)	1.11 (1.09–1.12)
Elevated blood pressure	97,263	30,182,944	3.22	1.16 (1.15–1.17)	0.99 (0.98–1.00)	0.99 (0.98–1.00)	0.97 (0.96–0.98)
Elevated fasting glucose level	69,609	21,629,536	3.21	1.13 (1.12–1.14)	1.00 (0.99–1.01)	1.00 (0.99–1.01)	0.99 (0.98–1.00)
Reduced HDL-cholesterol level	62,720	19,124,666	3.28	1.15 (1.14–1.16)	1.08 (1.07–1.09)	1.08 (1.07–1.08)	1.07 (1.06–1.08)
Elevated triglyceride level	79,856	24,295,646	3.29	1.18 (1.17–1.19)	1.06 (1.05–1.07)	1.05 (1.04–1.06)	1.04 (1.03–1.05)
BMI (kg/m^2)							
< 18.5	6609	2,614,928	2.53	0.91 (0.88–0.93)	0.99 (0.97–1.03)	0.99 (0.97–1.02)	–
18.5–22.9	76,683	27,497,678	2.79	1	1	1	–
23–24.9	52,492	17,310,693	3.03	1.09 (1.07–1.10)	1.01 (1.00–1.03)	1.02 (1.01–1.03)	–
25–29.9	63,570	19,973,051	3.18	1.14 (1.13–1.15)	1.05 (1.04–1.06)	1.06 (1.04–1.07)	–
≥30	7705	2,408,604	3.20	1.15 (1.12–1.17)	1.12 (1.09–1.15)	1.12 (1.09–1.15)	–

Values are expressed as HRs (with 95% CIs) derived via Cox's proportional hazard regression analysis. Model 1: adjusted for age and sex; Model 2: adjusted for age, sex, smoking status, alcohol consumption, physical activity, and household income; Model 3: adjusted for all items in model 2 plus BMI… [a]per 1000 person-years. BMI, body mass index; CI, confidence interval; HR, hazard ratio; MetS, metabolic syndrome.

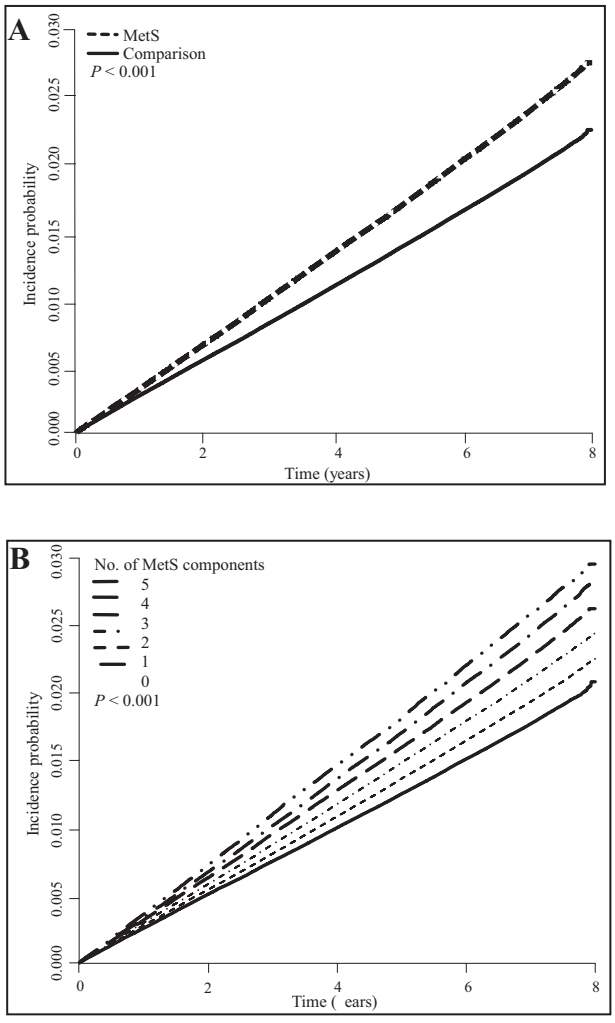

Fig. 2. Cumulative incidence of psoriasis by metabolic syndrome presence/absence (A) and the number of metabolic syndrome components (B) over 8 years of follow-up. *P* values were determined using the log-rank test. MetS: metabolic syndrome.

adjusting for age, sex, smoking status, alcohol consumption, exercise status, and income (Fig. 3).

4. Discussion

This large-scale nationwide study of a general population included 2,595,878 subjects with MetS and 7,122,713 matched controls. MetS was positively associated with an increased risk of psoriasis over the 8-year follow-up period, after adjusting for age, sex, smoking status, alcohol consumption, physical activity, household income, and BMI. The risk of psoriasis trended upward as the number of MetS components increased; this trend was more marked in obese subjects. Some MetS components (elevated waist circumference and an elevated triglyceride level, and a reduced HDL-cholesterol level) were associated with the psoriasis risk, but neither elevated blood pressure nor fasting glucose level was associated.

Studies have widely reported that psoriasis is associated with MetS [16], but most research has been cross-sectional in nature, not longitudinal [17–19]. A prospective cohort study from Norway reported a positive association between MetS and psoriasis development [11], but no study has yet examined an Asian population. We found that the incidence of psoriasis increased significantly in MetS subjects; a dose-response relationship was evident, consistent with what was found in a previous prospective study [11]. Several explanations may be advanced. First, in MetS subjects, elevated levels of inflammatory cytokines [including tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), and plasminogen activator inhibitor-1 (PAI-1)] released by visceral fat, and decreases in the levels of adiponectin (reducing insulin-sensitivity and anti-inflammatory action) and C-reactive protein [20,21], may stimulate T-cell proliferation and activation, triggering the development of inflammatory and immune-mediated psoriatic skin lesions [22]. Second, oxidative stress, which plays a critical role in MetS development/aggravation, may contribute to the development of psoriasis [23] via endothelin overexpression in vascular endothelial cells and keratinocytes, and endothelial dysfunction characterized by reduced production of nitric oxide by endothelial cells [24]. Third, insulin resistance, which plays a key role in MetS pathogenesis [25], affects psoriasis development and severity by increasing keratinocyte proliferation and inflammation, and by upregulating various vascular adhesion molecules [26]. Therefore, MetS management considering the severity of the condition might reduce the incidence of psoriasis.

We found that high triglyceride and low HDL-cholesterol levels and abdominal obesity were associated with an increased incidence of psoriasis, as did the previous prospective study [11]. The pathophysiology of MetS is largely attributable to an excessive flux of circulating fatty acids released by visceral fat, and the development of insulin resistance [1]. The circulating fatty acids increase triglyceride production and the secretion of very low density lipoproteins; the associated lipid/lipoprotein abnormalities include reductions in HDL-cholesterol levels [1]. An overabundance of circulating fatty acids is closely linked to abdominal obesity, and high triglyceride but low HDL-cholesterol levels. These MetS components significantly influenced psoriasis development.

Notably, we found a negative association between elevated blood pressure and psoriasis development. However, a study of 77,728 American females found that long-term hypertensive status (≥6 years) was associated with a risk of psoriasis [27], and hypertension was significantly associated with an increased risk of psoriasis in a population-based cohort study of Koreans [28]. In terms of blood pressure level, the use of a systolic blood pressure ≥ 130 mmHg or a diastolic blood pressure ≥ 85 mmHg to define MetS may be associated with less psoriasis than use of a systolic blood pressure ≥ 140 mmHg or a diastolic blood pressure ≥ 90 mmHg; the use of antihypertensive medication must also be considered. We found that a fasting glucose level ≥ 100 mg/dL was not associated with psoriasis development, but DM significantly predicted psoriasis in another prospective study [29]. Therefore, further studies considering the stepped effects of elevated fasting glucose and blood pressure levels are needed to confirm associations with psoriasis development.

Obesity is a risk factor for psoriasis development and aggravates existing psoriasis [30,31]. We found that obese individuals were not

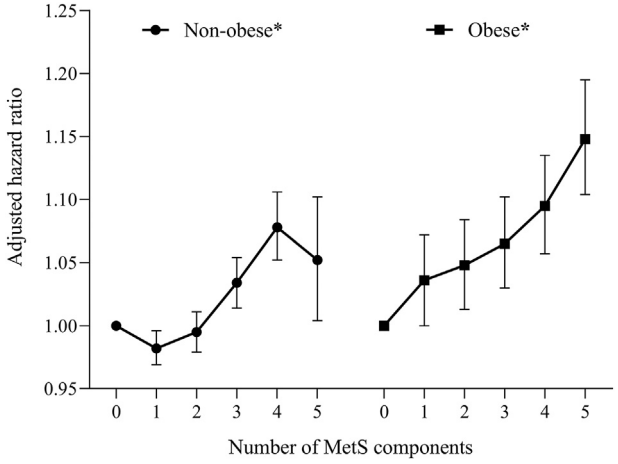

Fig. 3. The association between the number of metabolic syndrome components and the incidence of psoriasis by obesity status. Obesity was defined as body mass index ≥ 25 kg/m^2. **P* value <0.0001. MetS: metabolic syndrome.

only likely to develop psoriasis, but also that the risk increased as the number of MetS components increased, consistent with previous studies. Obese patients require careful management of both obesity per se [32] and MetS components, and should be screened for psoriasis even before MetS diagnosis.

In this study, aHR of psoriasis incidence for MetS was 1.05 (95% CI 1.04–1.06), and is relatively lower than that in the previous prospective study conducted in a Norwegian population (aHR 1.66, 95% CI 1.30–2.14) [11]. The differences may be due to the prevalence gap of psoriasis between races. The prevalence of psoriasis is lower in East Asians than in Caucasians. The prevalence of psoriasis is estimated to be 0.47% in China [33], 0.34% in Japan [34], 0.24% in Taiwan [35], and 0.54% in Korea [36], but is estimated to affect about 2–4% of the population in the US and Europe [7,37]. In spite of the relatively low prevalence of psoriasis, psoriasis has major effects on life since it is not only results in functional and social morbidities with socioeconomic cost [38], but also associated with an increased risk of various accompanying disease [39,40]; thus, psoriasis has become a medical concern, and finding the related factors as predictors of psoriasis is important.

The strengths of this study include the fact that we used nationwide data on the entire Korean population, performed the 8-year longitudinal follow-up, and enrolled 2,595,878 patients with MetS and 7,122,713 controls. This is the first large prospective study investigating the association between MetS and its components, and the psoriasis risk, in a representative nationwide Asian population. The database also contained sociodemographic information (smoking status, alcohol consumption, physical activity, household income, and BMI), so we could adjust for confounding factors. However, our work had certain limitations. First, MetS, psoriasis, hypertension, DM, and dyslipidemia were identified by ICD-10 codes in the claims database. Therefore, coding/mismatching/misclassification errors are possible. However, approximately 70% of diagnostic codes on KNHIS claim records were identical to those of medical records [12]. Second, we lacked data on the severity, involved area, types, or onset of psoriasis, and psoriasis assessment tools such as Psoriasis Area and Severity Index score, or Physician Global Assessment. Third, information was not available on family history and medication use, which are potential confounders of the association. Fourth, we included only Koreans; it is unclear whether our findings can be generalized to other ethnicities.

5. Conclusions

We found significant positive associations between psoriasis development and MetS and components thereof (waist circumference, and triglyceride and HDL-cholesterol levels). MetS severity and obesity affected these associations over 8 years of follow-up; MetS is a risk factor for psoriasis development.

Declaration of Competing Interest

None.

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None.

Author Contributions

Conceptualization: Ha-Na Kim, Yong-Gyu Park, Ji Hyun Lee.
Data curation: Kyungdo Han.
Formal analysis: Kyungdo Han, Yong-Gyu Park.
Supervision: Yong-Gyu Park, Ji Hyun Lee.
Writing - original draft: Ha-Na Kim.
Writing - review & editing: Ha-Na Kim, Yong-Gyu Park, Ji Hyun Lee.

References

[1] Eckel RH, Alberti KG, Grundy SM, Zimmet PZ. The metabolic syndrome. Lancet 2010;375:181–3.
[2] Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of obesity. Circulation 2009;120:1640–5.
[3] Grundy SM. Metabolic syndrome pandemic. Arterioscler Thromb Vasc Biol 2008;28:629–36.
[4] Gill H, Mugo M, Whaley-Connell A, Stump C, Sowers JR. The key role of insulin resistance in the cardiometabolic syndrome. Am J Med Sci 2005;330 290–4.
[5] Roberts CK, Sindhu KK. Oxidative stress and metabolic syndrome. Life Sci 2009;84 705–12.
[6] Sutherland JP, McKinley B, Eckel RH. The metabolic syndrome and inflammation. Metab Syndr Relat Disord 2004;2:82–104.
[7] Nestle FO, Kaplan DH, Barker J. Psoriasis. N Engl J Med 2009;361:496–509.
[8] Fernandez-Armenteros JM, Gomez-Arbones X, Buti-Soler M, Betriu-Bars A, Sanmartin-Novell V, Ortega-Bravo M, et al. Psoriasis, metabolic syndrome and cardiovascular risk factors. A population-based study. J Eur Acad Dermatol Venereol 2019;33 128–35.
[9] Gisondi P, Fostini AC, Fossa I, Girolomoni G, Targher G. Psoriasis and the metabolic syndrome. Clin Dermatol 2018;36 21–8.
[10] Rodriguez-Zuniga MJM, Garcia-Perdomo HA. Systematic review and meta-analysis of the association between psoriasis and metabolic syndrome. J Am Acad Dermatol 2017;77 657–66.[e8].
[11] Snekvik I, Nilsen TIL, Romundstad PR, Saunes M. Metabolic syndrome and risk of incident psoriasis: prospective data from the HUNT study, Norway. Br J Dermatol 2019;180:94–9.
[12] Song SO, Jung CH, Song YD, Park CY, Kwon HS, Cha BS, et al. Background and data configuration process of a nationwide population-based study using the Korean national health insurance system. Diabetes Metab J 2014;38:395–403.
[13] Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA, et al. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute scientific statement. Circulation 2005;112:2735–52.
[14] Lee SY, Park HS, Kim DJ, Han JH, Kim SM, Cho GJ, et al. Appropriate waist circumference cutoff points for central obesity in Korean adults. Diabetes Res Clin Pract 2007;75:72–80.
[15] Wen CP, David Cheng TY, Tsai SP, Chan HT, Hsu HL, Hsu CC, et al. Are Asians at greater mortality risks for being overweight than Caucasians? Redefining obesity for Asians. Public Health Nutr 2009;12:497–506.
[16] Singh S, Young P, Armstrong AW. An update on psoriasis and metabolic syndrome: a meta-analysis of observational studies. PLoS One 2017;12:e0181039.
[17] Langan SM, Seminara NM, Shin DB, Troxel AB, Kimmel SE, Mehta NN, et al. Prevalence of metabolic syndrome in patients with psoriasis: a population-based study in the United Kingdom. J Invest Dermatol 2012;132:556–62.
[18] Miller IM, Ellervik C, Zarchi K, Ibler KS, Vinding GR, Knudsen KM, et al. The association of metabolic syndrome and psoriasis: a population- and hospital-based cross-sectional study. J Eur Acad Dermatol Venereol 2015;29:490–7.
[19] Parodi A, Aste N, Calvieri C, Cantoresi F, Carlesimo M, Fabbri P, et al. Metabolic syndrome prevalence in psoriasis: a cross-sectional study in the Italian population. Am J Clin Dermatol 2014;15:371–7.
[20] Trayhurn P, Wood IS. Adipokines: inflammation and the pleiotropic role of white adipose tissue. Br J Nutr 2004;92 347–55.
[21] Shibata S, Tada Y, Hau CS, Mitsui A, Kamata M, Asano Y, et al. Adiponectin regulates psoriasiform skin inflammation by suppressing IL-17 production from gammadelta-T cells. Nat Commun 2015;6:7687.
[22] Wolk K, Sabat R. Adipokines in psoriasis: an important link between skin inflammation and metabolic alterations. Rev Endocr Metab Disord 2016;17 305–17.
[23] Schluter K, Diehl S, Lang V, Kaufmann R, Boehncke WH, Burger C. Insulin resistance may contribute to upregulation of adhesion molecules on endothelial cells in psoriatic plaques. Acta Derm Venereol 2016;96:162–8.
[24] Lynch M, Ahern T, Sweeney CM, Malara A, Tobin AM, O'Shea D, et al. Adipokines, psoriasis, systemic inflammation, and endothelial dysfunction. Int J Dermatol 2017;56 1103–18.
[25] Kahn SE, Hull RL, Utzschneider KM. Mechanisms linking obesity to insulin resistance and type 2 diabetes. Nature 2006;444 840–6.
[26] Polic MV, Miskulin M, Smolic M, Kralik K, Miskulin I, Berkovic MC, et al. Psoriasis severity-a risk factor of insulin resistance independent of metabolic syndrome. Int J Environ Res Public Health 2018;15.
[27] Wu S, Han J, Li WQ, Qureshi AA. Hypertension, antihypertensive medication use, and risk of psoriasis. JAMA Dermatol 2014;150 957–63.
[28] Kim HN, Han K, Song SW, Lee JH. Hypertension and risk of psoriasis incidence: an 11-year nationwide population-based cohort study. PLoS One 2018;13:e0202854.
[29] Kim ES, Han K, Kim MK, Park YM, Baek KH, Moon SD, et al. Impact of metabolic status on the incidence of psoriasis: a Korean nationwide cohort study. Sci Rep 2017;7:1989.
[30] Gisondi P, Girolomoni G. The multifaceted association between psoriasis and obesity. Br J Dermatol 2019;180:24.

[31] Budu-Aggrey A, Brumpton B, Tyrrell J, Watkins S, Modalsli EH, Celis-Morales C, et al. Evidence of a causal relationship between body mass index and psoriasis: a Mendelian randomization study. PLoS Med 2019;16:e1002739.
[32] Mahil SK, McSweeney SM, Kloczko E, McGowan B, Barker JN, Smith CH. Does weight loss reduce the severity and incidence of psoriasis or psoriatic arthritis? A critically-appraised topic. Br J Dermatol 2019. https://doi.org/10.1111/bjd.17741 [Epub ahead of print].
[33] Ding X, Wang T, Shen Y, Wang X, Zhou C, Tian S, et al. Prevalence of psoriasis in China: a population-based study in six cities. Eur J Dermatol 2012;22 663–7.
[34] Kubota K, Kamijima Y, Sato T, Ooba N, Koide D, Iizuka H, et al. Epidemiology of psoriasis and palmoplantar pustulosis: a nationwide study using the Japanese national claims database. BMJ Open 2015;5:e006450.
[35] Chang YT, Chen TJ, Liu PC, Chen YC, Chen YJ, Huang YL, et al. Epidemiological study of psoriasis in the national health insurance database in Taiwan. Acta Derm Venereol 2009;89 262–6.
[36] Han JH, Lee JH, Han KD, Seo HM, Bang CH, Park YM, et al. Epidemiology and medication trends in patients with psoriasis: a nationwide population-based cohort study from Korea. Acta Derm Venereol 2018;98:396–400.
[37] Kurd SK, Gelfand JM. The prevalence of previously diagnosed and undiagnosed psoriasis in US adults: results from NHANES 2003-2004. J Am Acad Dermatol 2009;60 218–24.
[38] Michalek IM, Loring B, John SM. A systematic review of worldwide epidemiology of psoriasis. J Eur Acad Dermatol Venereol 2017;31 205–12.
[39] Yeung H, Takeshita J, Mehta NN, Kimmel SE, Ogdie A, Margolis DJ, et al. Psoriasis severity and the prevalence of major medical comorbidity: a population-based study. JAMA Dermatol 2013;149 1173–9.
[40] Takeshita J, Grewal S, Langan SM, Mehta NN, Ogdie A, Van Voorhees AS, et al. Psoriasis and comorbid diseases: epidemiology. J Am Acad Dermatol 2017;76 377–90.