

Tobacco Smoking Was Positively Associated with Disease Relapse at week 24 and 48 Among Patients with Psoriasis Vulgaris in Shanghai: A Prospective Study

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Purpose: Tobacco smoking is an unhealthy behavior associated with the onset, severity, and treatment response of psoriasis. However, evidence regarding the impact of tobacco smoking on the relapse of psoriasis remains limited. This study aims to examine the relapse condition in psoriasis patients and explore the association between tobacco smoking and psoriasis relapse.

Patients and Methods: We conducted an observational study with 551 psoriasis patients recruited from 2022 to 2024 in Shanghai Skin Disease Hospital. A structured questionnaire and physical examination were used to collect data at baseline, week 12, week 24 and week 48. PASI50 and PASI75 were used to evaluate the improvement of psoriasis patients after treatment at week 12, and disease relapse was defined as the loss of 50% PASI improvement during clinical remission after the achievement of PASI50 or PASI75 at week 12.

Results: 75.7% of the 551 psoriasis patients were males, with an average age of 45.8 years, and 282 (51.2%) were tobacco smokers. 41.2% and 61.6% of psoriasis patients with PASI50 achievement at week 12 encounter disease relapsed at week 24 and 48, respectively, while for patients with PASI75 achievement at week 12, the relapse rate was 27.6% and 51.7% at week 24 and 48, respectively. Logistic regression indicated that patients with tobacco smoking had a higher relapse rate, especially among those with PASI75 achievement at week 12. The odds ratio was 2.10 (95% CI: 1.17–3.78) and 1.84 (95% CI: 1.07–3.14) at week 24 and week 48 respectively, even after adjusting for potential confounding factors. Moreover, patients with longer smoking duration and more daily cigarette consumption had higher relapse rate.

Conclusion: Tobacco smoking was positively correlated with the relapse, especially among those with longer smoking duration and more daily cigarette consumption. Therefore, patients with psoriasis should quit smoking to reduce the risk of relapse.

Keywords: psoriasis, tobacco smoking, relapse, psoriasis area severity index, PASI

Introduction

Psoriasis is an inflammatory skin disease characterized by a chronic relapsing-remitting course, and currently there is no complete cure.^{1,2} It is estimated that psoriasis affects 1–5% of the global population.³ In China, the number of psoriasis patients is substantial, and the prevalence rate shows an overall increasing trend.⁴ As a systemic disease, psoriasis not only manifests with cutaneous symptoms but also increases the risk of other inflammatory diseases and systemic comorbidities, particularly in patients with severe conditions.⁵ Psoriasis can also affect psychological health and social participation, with patients often facing anxiety and depression, work restrictions, and social stigmatization, which impose a great burden on patients.⁶

Although significant advancements have been achieved in the efficacy of psoriasis treatment through the application of biologics and systemic therapies in recent years, the relapse of psoriasis remains a major challenge in clinical practice. In clinical evaluation of psoriasis, the psoriasis area and severity index (PASI) is a commonly used quantitative evaluation tool. National Psoriasis Foundation Medical Advisory Board defines psoriasis relapse as a 50% loss of PASI improvement from baseline in patients who achieve a clinically meaningful response.⁷ Previous studies have shown that more than half of the patients relapse within 6 months after discontinuing treatment.⁸ The recurrent episodes and long-term treatment of psoriasis increase the economic burden among psoriasis patients and undermine their confidence in treatment as well.^{6,9}

The exact mechanisms underlying the relapse of psoriasis remain unclear. Current perspectives suggest that existing treatments for psoriasis can only suppress the activity of pathogenic immune cells rather than eliminate them. After the discontinuation of treatment, these cells may be reactivated and trigger the recurrence of lesions.⁷ The notion of local “immune memory” is supported by evidence.¹⁰ Tissue resident memory T cells (TRM) in the skin tissue are likely to be an important factor contributing to the relapse of psoriasis. Upon antigen activation, TRM cells can re-initiate the inflammatory cascade, leading to the relapse of the disease.¹¹

Growing evidence indicates that environmental factors (such as diet and obesity, tobacco smoking and alcohol drinking, psychological factors) play an important role in psoriasis development.¹² Tobacco smoking, as a modifiable lifestyle factor, has received widespread attention for its impact on psoriasis. Previous studies have indicated that tobacco smoking increases the risk of developing psoriasis, exacerbates disease severity in patients, and is detrimental to achieving better treatment efficacy.^{4,13,14} However, evidence regarding the association between tobacco smoking and psoriasis relapse is still limited. In this study, we aimed to investigate the relapse rate among psoriasis patients and explore the impact of tobacco smoking on disease relapse, so as to provide more precise lifestyle intervention recommendations for patients with psoriasis.

Materials and Methods

Study Design

This observational study was based on a cohort of psoriasis patients established at Shanghai Skin Disease Hospital from 2022 to 2024. In this study, we applied the sample size calculation formula $n = [\mu_{\alpha}^2 \times p(1-p)] / \delta^2$ for observational study and set $p=30\%$ (Zheng et al¹⁵ reported that the prevalence of tobacco smoking was 31% in Shanghai), $\alpha=0.05$, $\delta=15\%$ of p , and a non-response rate of 10%, the sample size calculation result indicated that at least 445 psoriasis patients should be recruited. In this study, 551 patients with psoriasis were finally recruited and analyzed. The institutional ethical review board of the Shanghai Skin Disease Hospital reviewed and approved this study (2022–25). We have registered this study in the Chinese clinical trial registry (ChiCTR2200066894), and implemented it in line with the Declaration of Helsinki.

Psoriasis Patient Diagnosis and Enrollment

In this study, the diagnosis of psoriasis was confirmed according to the Chinese Clinical Dermatology, which is in line with the global guidelines for psoriasis diagnosis and treatment.¹⁶ In this study, the inclusion criteria were patients with psoriasis vulgaris aged ≥ 18 years for both sexes, and without migration plan within a year. The exclusion criteria were patients who were unable to provide informed consent, or with neurological or psychiatric disorders.

Data Collection

In this study, patients with psoriasis underwent physical examination, the psoriasis area and severity index (PASI), physician global assessment (PGA), and body surface area (BSA) evaluations were administered and information was collected through questionnaire interviews by dermatologists during patients' hospital visits. The questionnaire includes: (1) demographic features: age, gender, education, etc; (2) lifestyle habits: tobacco smoking, alcohol drinking, etc; (3) treatment plan: topical only, non-biological systemic, and biological systemic; and (4) family history of psoriasis, medical history of non-communicable disease (NCD), disease duration and psoriasis severity (BSA, PASI, PGA). The evaluation of diseases severity and treatment effects was conducted at baseline, week 12, week 24 and week 48, respectively.

Definition and Classification

In this study, PASI was used to assess the severity of psoriasis lesions. PASI improvement refers to the improvement in a patient's PASI score compared to baseline and was calculated by the formula $[(\text{PASI at baseline} - \text{PASI at week } t) / \text{PASI at baseline}] \times 100\%$, which was used to evaluate the efficacy of psoriasis treatment. PASI50 and PASI75 were defined as patients achieving $\geq 50\%$ and $\geq 75\%$ PASI score improvement, respectively. The relapse of psoriasis was defined as the loss of 50% PASI improvement from baseline among patients who achieved a clinically meaningful response (PASI50 or PASI75) and discontinued their treatment at week 12.

A smoker was defined as a person who smoked at least 100 cigarettes in his or her lifetime. The collected smoking-related data included the age of tobacco smoking initiation, daily cigarette consumption, and the total duration of tobacco smoking in years. Years of smoking was defined as the years of time interval between the age at smoking initiation and the age at investigation or tobacco smoking cessation, and then was classified into ≤ 10 , 11–20, 21–30, 31–40, and > 40 years. Daily cigarette consumption was categorized as < 20 and ≥ 20 cigarettes. An alcohol drinker was defined as a person who drank alcohol at least twice a week for at least six months.

In this study, the age of psoriasis patients was categorized as < 35 , 35–45, 46–60 and ≥ 60 years. Education was classified as primary school and lower, junior high, senior high, and college and above. Individual monthly income was categorized as < 3000 , 3001–5000, 5001–10000 and > 10000 (Chinese Yuan, RMB). Marital status was categorized as unmarried, married and divorced/widows/others. Body mass index (BMI) was calculated weight/height^2 (kg/m^2), and was classified into < 23.9 (low or normal weight), 24.0–28.0 (overweight) and > 28.0 (obesity). NCD comorbidity was defined as patients with ≥ 1 type of common comorbidity abnormality, such as diabetes, stroke, hypertension, etc. Disease duration of psoriasis was calculated as the time interval (years) between the initial psoriasis diagnosis and the investigation, and was then classified as < 5 , 5–10 and > 10 years.

Statistical Analysis

Statistical analysis was performed by using SAS 9.4 software in this study. Mean and standard deviation (SD) or median and interquartile range (IQR) were used to describe quantitative variables as appropriate, and Student's *t*-test or Mann–Whitney *U*-test was applied to examine the difference between groups. Frequency counts and proportions (%) were used to describe qualitative variables, and the chi-square test was used for comparison between groups. Logistic regression was performed to calculate the odds ratio (OR) and 95% confidence interval (CI) to explore factors associated with the diseases relapse at week 24 and 48 among patients with psoriasis, with a particular focus on the association between tobacco smoking and psoriasis relapse. Subgroup analysis was performed to show the association between tobacco smoking and disease relapse among psoriasis patients in different treatment plan groups. In this study, all performed statistical tests were two-tailed and a *p*-value of less than 0.05 was considered as statistically significant.

Results

Baseline Characteristics of Patients with Psoriasis

The average age of 551 psoriasis patients was 45.8 years, with approximately 70% of patients aged 35 and above, of which 417 (75.7%) were male. 40.3% of patients had college and above education, and 58.8% reported a monthly income $> 5,000$ RMB, and 68.8% of them were married. Nearly 58.4% of patients were classified as overweight or obese based on BMI criteria. In this study, 51.2% of patients reported tobacco smoking, 10.3% reported alcohol drinking, and 42.6% had NCD comorbidities. The median disease duration was 12 years (IQR: 6–21), and the median values of the PASI, BSA, and PGA scores were 11.4 (IQR: 8.0–16.8), 14.2 (IQR: 9.0–25.3) and 2.7 (IQR: 2.0–3.0), respectively. The proportion of psoriasis patients in the acitretin, methotrexate, narrow band ultraviolet B (NB-UVB), and biologics groups were 8.3%, 31.6%, 25.2%, and 34.8%, respectively.

Data in Table 1 indicated that at week 12, 373 patients (67.7%) achieved PASI50, and 300 patients (54.4%) achieved PASI75. Psoriasis patients without PASI50 achievement had higher prevalence of tobacco smoking than those with PASI50 achievement, the finding was similar for PASI75 achievement among patients at week 12. The median disease duration was

Table 1 The Baseline Characteristics of Patients with Psoriasis in Shanghai ^a

Characteristics	Total (n=551)	PASI50 Achieved at wk12		PASI75 Achieved at wk12	
		Yes (n=373)	No (n=178)	Yes (n=300)	No (n=251)
Age (years), mean (SD)	45.8 (18.2)	45.3 (18.5)	46.7 (17.5)	44.9 (18.9)	46.8 (17.2)
Age group, (n, %)					
<35 years	169 (30.7)	121 (71.6)	48 (28.4)	104 (61.5)	65 (38.5)
35-45 years	97 (17.6)	64 (66.0)	33 (34.0)	49 (50.5)	48 (49.5)
46-60 years	132 (24.0)	85 (64.4)	47 (35.6)	62 (46.9)	70 (53.1)
>60 years	153 (27.8)	103 (67.3)	50 (32.7)	85 (55.6)	68 (44.4)
Gender, n (%)					
Male	417 (75.7)	283 (67.9)	134 (32.1)	216 (51.8)	201 (48.2)
Female	134 (24.3)	90 (67.2)	44 (32.8)	84 (62.7)	50 (37.3)
Education, (n, %)					
Primary and lower	108 (19.6)	71 (65.7)	37 (34.3)	66 (61.1)	42 (38.9)
Junior high	107 (19.4)	72 (67.3)	35 (32.7)	52 (48.6)	55 (51.4)
Senior high	114 (20.7)	68 (59.7)	46 (40.4)	56 (49.1)	58 (50.9)
College and above	222 (40.3)	162 (73.0)	60 (27.0)	126 (56.8)	96 (43.2)
Monthly income, (RMB)					
<3000	90 (16.3)	66 (73.3)	24 (26.7)	58 (64.4)	32 (35.6)
3000-5000	137 (24.9)	87 (63.5)	50 (36.5)	71 (51.8)	66 (48.2)
5001-10000	290 (52.6)	200 (69.0)	90 (31.0)	156 (53.8)	134 (46.2)
>10000	34 (6.2)	20 (58.8)	14 (41.2)	15 (44.1)	19 (55.9)
Marital status, (n, %)					
Married	379 (68.8)	254 (67.0)	125 (33.0)	198 (52.2)	181 (47.8)
Unmarried	80 (14.5)	54 (67.5)	26 (32.5)	44 (55.0)	36 (45.0)
Divorced/widow/others	92 (16.7)	65 (70.7)	27 (29.3)	58 (63.0)	34 (37.0)
BMI (kg/m ²), mean (SD) ^b	25.0 (3.9)	25.0 (3.9)	25.1 (3.9)	25.1 (4.0)	24.9 (3.8)
BMI (kg/m ²), n (%)					
<23.9 (low or normal weight)	229 (41.6)	160 (69.9)	69 (30.1)	125 (54.6)	104 (45.4)
24.0-28.0 (overweight)	210 (38.1)	137 (65.2)	73 (34.8)	112 (53.3)	98 (46.7)
>28.0 (obesity)	112 (20.3)	76 (67.9)	36 (32.1)	63 (56.3)	49 (43.8)
Tobacco smoking, n (%) [†]	282 (51.2)	171 (45.8)	111 (62.4)	128 (42.7)	154 (61.4)
Alcohol drinking, n(%)	57 (10.3)	36 (9.7)	21 (11.8)	32 (10.7)	25 (10.0)
NCD comorbidity, n (%)	235 (42.6)	159 (42.6)	76 (42.7)	130 (43.3)	105 (41.8)
Family history, n (%)	109 (19.8)	75 (20.1)	34 (19.1)	61 (20.3)	48 (19.2)
DD (year), median (IQR) [‡]	12 (6-21)	12 (6-21)	13 (5-23)	13 (7-22)	12 (4-20)
PASI at wk0, median (IQR) ^c	11.4 (8.0-16.8)	11.2 (8.0-16.9)	11.7 (7.8-16.2)	12.0 (9.0-18.1)	10.5 (7.4-14.8)
BSA at wk0 (%), median (IQR) ^d	14.2 (9.0-25.3)	14 (8.5-25.0)	15 (10-26)	16 (10-29)	13 (8-22)
PGA at wk0, median (IQR) ^e	2.7 (2.0-3.0)	2.7 (2.0-3.0)	2.7 (2.0-3.0)	2.7 (2.0-3.0)	2.3 (2.0-3.0)
Treatment plan, n (%) ^{††}					
Acitretin	46 (8.3)	12 (26.1)	34 (73.9)	8 (17.4)	38 (82.6)
Methotrexate	174 (31.6)	100 (57.5)	74 (42.5)	74 (42.5)	100 (57.5)
NB-UVB	139 (25.2)	94 (67.6)	45 (32.4)	64 (46.0)	75 (53.9)
Biologics (ustekinumab, etc)	192 (34.8)	167 (86.9)	25 (13.1)	154 (80.2)	38 (19.8)

Notes: ^a Data represented as mean (SD), median (IQR) or frequency (%) as appropriate. ^b BMI was calculated as weight in kilograms divided by height in meters squared. ^c PASI indicate the severity of psoriasis, with a higher value represents a more severe condition (0[better]-72[worse]). ^d BSA indicate the affected body surface, with a higher value represents a more severe condition (0%[better]-100%[worse]). ^e PGA indicate the physician's overall evaluation of psoriasis with a higher score represents a more severe condition (0[better]-5[worse]). [†] the difference of PASI₅₀ achievement at wk 12 between groups was statistically significant (P<0.05). [‡] the difference of PASI₇₅ achievement at wk 12 between groups was statistically significant (P<0.05).

Abbreviations: SD, standard deviation; RMB, Chinese Yuan; BMI, body mass index; NCD, non-communicable diseases; DD, diseases duration; IQR, Interquartile range; PASI, psoriasis area and severity index; BSA, body surface area; PGA, Physician's Global Assessment; NB-UVB, narrow band ultraviolet; wk, week.

slightly longer in patients who achieved PASI75. Furthermore, patients with biologic treatment had higher response rates in achieving both PASI50 and PASI75 compared to other treatments. The differences were all statistically significant ($p<0.05$).

Relapse Condition at week 24 and 48 Among Patients

Data in Table 2 showed the relapse condition at week 24 and week 48 among patients with psoriasis after the achievement of PASI50 and PASI75 at week 12. For patients who achieved PASI50 at week 12, the relapse rate was 41.2% at week 24 and 61.6% at week 48, and patients with relapse had higher score in PASI, BSA, PGA, lower PASI75 achievement and PGA (1/0) rate at week 24 and week 48 as well than those without relapse ($p<0.05$). Among patients who achieved PASI75 at week 12, the relapse rates were 27.6% and 51.7% at week 24 and 48, respectively. Patients with relapse also had higher PASI, BSA, and PGA scores, but lower PASI75 achievement and PGA (1/0) rate both at week 24 and week 48 than those without relapse ($p<0.05$).

Association Between Tobacco Smoking and Disease Relapse at week 24 and 48

Univariate logistic regression analysis indicated that psoriasis patients with tobacco smoking had higher relapse rate than those without tobacco smoking, the OR was 1.06 (95% CI: 0.69–1.62) and 1.38 (95% CI: 0.88–2.15) at week 24 and week 48 for patients achieved PASI50 at week 12, and the OR was 2.20 (95% CI: 1.31–3.71) and 1.83 (95% CI: 1.12–2.97) at week 24 and week 48 respectively for patients achieved PASI75 at week 12 (Table 3). Findings in Table 3 also indicated that patients with overweight or obesity, NCD comorbidities, longer disease duration also had higher relapse rate. Moreover, patients with NB-UVB or biologic treatment had higher relapse rate than those with acitretin/methotrexate.

In this study, multivariate logistic regression analysis with the adjustment of potential confounding factors (alcohol consumption, BMI, NCD comorbidity, family history, disease duration, and treatment plan) indicated that psoriasis patients with tobacco smoking had a higher relapse rate at week 24 and 28 both for patients who achieved PASI50 or PASI75 at week 12. The OR was 1.12 (95% CI: 0.70–1.80) at week 24 and 1.40 (95% CI: 0.86–2.28) at week 48 for patients achieved PASI50, and the OR was 2.10 (95% CI: 1.17–3.78) at week 24 and 1.84 (95% CI: 1.07–3.14) at week 48 for patients achieved PASI75, respectively (Figure 1).

Table 2 The Relapse Condition at week 24 and 48 After the Achievement of PASI50 and PASI75 at week 12 Among Patients with Psoriasis in Shanghai ^a

Indexes	Patients with PASI50 at wk12		Patients with PASI75 at wk12	
	Relapse	Not-Relapse	Relapse	Not-Relapse
Week 24				
Patients, n (%)	147 (41.2)	210 (58.8)	80 (27.6)	210 (72.4)
PASI, median (IQR)†‡	1.2 (0.0–3.4)	1.2 (0.3–2.1)	2.7 (1.5–5.3)	0 (0–1.2)
BSA, median (IQR)†‡	0.6 (0–3.5)	0.2 (0–2.0)	2.0 (0.5–6.8)	0 (0–1.0)
PGA, median (IQR)†‡	1.0 (0–2.0)	1.0 (0–2.0)	2.0 (1.0–2.0)	0 (0–1.0)
PASI75 achievement, n (%)††‡	99 (67.4)	180 (85.7)	38 (47.5)	205 (97.6)
PGA (1/0) rate, n (%)†‡	97 (65.9)	154 (73.3)	37 (46.3)	178 (84.8)
Week 48				
Patients, n (%)	205 (61.6)	128 (38.4)	139 (51.7)	130 (48.3)
PASI, median (IQR)††‡	2.1 (0.4–4.4)	0.8 (0–1.9)	2.7 (1.5–4.8)	0 (0–0.8)
BSA, median (IQR)††‡	0.8 (0.1–4.0)	0.5 (0–2.0)	1.5 (0.5–4.0)	0 (0–0.5)
PGA, median (IQR)††‡	2.0 (1.0–2.0)	1.0 (0–1.0)	2.0 (1.0–3.0)	0 (0–1.0)
PASI75 achievement, n (%)††‡	121 (59.0)	114 (89.1)	73 (52.5)	128 (98.5)
PGA (1/0) rate, n (%)††‡	101 (49.5)	103 (80.5)	55 (39.9)	117 (90.0)

Notes: ^a Data represented as median (IQR) or frequency (%) as appropriate. †: the difference between patients with relapse and without relapse based on the PASI50 achievement at wk 12 was statistically significant ($P<0.05$). ‡: the difference between patients with relapse and without relapse based on the PASI75 achievement at wk 12 was statistically significant ($P<0.05$).

Abbreviations: IQR, Interquartile range; PASI, psoriasis area and severity index; BSA, body surface area; PGA, Physician's Global Assessment.

Table 3 Factors Associated with the Relapse at week 24 and 48 After the Achievement of PASI50 and PASI75 at week 12 Among Patients with Psoriasis in Shanghai

Characteristics	Relapse at wk24 based on PASI50 at wk12		Relapse at wk48 Based on PASI50 at wk12		Relapse at wk24 based on PASI75 at wk12		Relapse at wk48 Based on PASI75 at wk12	
	n (%)	OR 95% CI	n (%)	OR 95% CI	n (%)	OR 95% CI	n (%)	OR 95% CI
Age group								
<35 years	49 (42.6)	1.00	69 (62.7)	1.00	23 (22.8)	1.00	49 (50.5)	1.00
35-45 years	28 (45.2)	1.11 (0.60–2.07)	30 (57.7)	0.81 (0.41–1.59)	16 (33.3)	1.70 (0.79–3.62)	21 (52.5)	1.08 (0.52–2.26)
46-60 years	29 (36.7)	0.78 (0.43–1.41)	45 (60.0)	0.89 (0.49–1.63)	17 (29.8)	1.41 (0.69–3.00)	27 (50.0)	0.98 (0.50–1.91)
>60 years	41 (40.6)	0.92 (0.54–1.58)	61 (63.5)	1.04 (0.59–1.83)	24 (28.6)	1.36 (0.70–2.63)	42 (53.9)	1.14 (0.63–2.08)
Gender								
Male	114 (42.1)	1.00	154 (61.1)	1.00	63 (30.3)	1.00	97 (50.5)	1.00
Female	33 (38.4)	0.86 (0.52–1.41)	51 (62.9)	1.08(0.65–1.82)	17 (20.7)	0.60 (0.33–1.11)	42 (54.6)	1.18 (0.69–2.00)
Education								
Primary and lower	28 (39.4)	1.00	46 (64.8)	1.00	15 (22.7)	1.00	34 (51.5)	1.00
Junior high	27 (39.1)	0.98 (0.50–1.95)	38 (62.3)	0.90 (0.44–1.83)	14 (28.0)	1.32 (0.57–3.08)	24 (55.8)	1.19 (0.55–2.57)
Senior high	25 (38.5)	0.96 (0.48–1.91)	38 (62.3)	0.90 (0.44–1.83)	15 (27.8)	1.31 (0.57–2.99)	26 (52.0)	1.02 (0.50–2.13)
College and above	67 (44.1)	1.21 (0.68–2.15)	83 (59.3)	0.79 (0.44–1.43)	36 (30.0)	1.46 (0.73–2.92)	55 (50.0)	0.94 (0.51–1.73)
Monthly income, (RMB)								
<3000	28 (42.4)	1.00	45 (69.2)	1.00	14 (24.1)	1.00	32 (56.1)	1.00
3000-5000	26 (30.6)	0.60 (0.31–1.17)	41 (51.9)	0.48 (0.24–0.95)	13 (18.6)	0.72 (0.31–1.68)	25 (39.1)	0.50 (0.24–1.03)
5001-10,000	84 (45.2)	1.12 (0.63–1.97)	107 (62.9)	0.76 (0.41–1.39)	47 (31.9)	1.48 (0.74–2.96)	72 (54.1)	0.92 (0.49–1.72)
>10000	9 (45.0)	1.11 (0.41–3.04)	12 (63.2)	0.76 (0.26–2.22)	6 (40.0)	2.10 (0.63–6.92)	10 (66.7)	1.56 (0.47–5.16)
BMI (kg/m ²)								
<23.9 (low or normal)	61 (40.1)	1.00	82 (57.3)	1.00	29 (24.4)	1.00	51 (46.4)	1.00
24.0–28.0 (overweight)	63 (47.0)	1.32 (0.83–2.12)	86 (68.9)	1.64 (1.00–2.72)	36 (32.7)	1.51 (0.85–2.69)	60 (59.4)	1.69 (0.98–2.92)
>28.0 (obesity)	23 (32.4)	0.72 (0.40–1.29)	37 (56.9)	0.98 (0.54–1.78)	15 (24.6)	1.01 (0.49–2.07)	28 (48.3)	1.08 (0.57–2.04)
Tobacco smoking								
Yes	70 (41.9)	1.06 (0.69–1.62)	106 (65.4)	1.38 (0.88–2.15)	46 (36.5)	2.20 (1.31–3.71)	73 (59.8)	1.83 (1.12–2.97)
No	77 (40.5)	1.00	99 (57.9)	1.00	34 (20.7)	1.00	66 (44.9)	1.00
Alcohol drinking								
Yes	18 (50.0)	1.49 (0.75–2.97)	25 (71.4)	1.64 (0.76–3.54)	12 (37.5)	1.68 (0.78–3.61)	17 (56.7)	1.25 (0.58–2.70)
No	129 (40.2)	1.00	180 (60.4)	1.00	68 (26.4)	1.00	122 (51.1)	1.00
NCD comorbidity								
Yes	68 (43.6)	1.19 (0.78–1.83)	103 (67.8)	1.63 (1.04–2.55)	44 (34.4)	1.83 (1.09–3.08)	70 (56.5)	1.43 (0.88–2.31)
No	79 (39.3)	1.00	102 (56.4)	1.00	36 (22.2)	1.00	69 (47.6)	1.00
Family history								
Yes	31 (43.1)	1.10 (0.65–1.86)	45 (67.2)	1.36 (0.77–2.39)	14 (23.7)	0.78 (0.40–1.51)	25 (46.3)	0.76 (0.42–1.39)
No	116 (40.7)	1.00	160 (60.2)	1.00	66 (28.6)	1.00	114 (53.1)	1.00
Disease duration (year)								
<5	27 (32.1)	1.00	43 (54.4)	1.00	16 (27.1)	1.00	29 (52.7)	1.00
5-10	24 (35.3)	1.15 (0.59–2.26)	41 (65.1)	1.56 (0.79–3.08)	15 (26.3)	0.96 (0.42–2.19)	31 (58.5)	1.26 (0.59–2.70)
>10	96 (46.8)	1.86 (1.09–3.17)	121 (63.5)	1.45 (0.85–2.46)	49 (28.2)	1.06 (0.54–2.04)	79 (49.1)	0.86 (0.47–1.59)
Treatment plan								
Acitretin/Methotrexate	27 (25.0)	1.00	51 (49.5)	1.00	17 (21.0)	1.00	36 (47.4)	1.00
NB-UVB	43 (46.2)	1.42 (1.42–4.69)	65 (70.6)	2.45 (1.36–4.44)	32 (50.0)	3.78 (1.82–7.78)	48 (75.0)	3.33 (1.62–6.87)
Biologics	77 (49.4)	1.71 (1.71–5.00)	89 (64.5)	1.85 (1.10–3.12)	31 (21.4)	1.02 (0.53–1.99)	55 (42.6)	0.83 (0.46–1.46)

Notes: bold text indicates statistical significance (P<0.05).

Abbreviations: RMB, Chinese Yuan; BMI, body mass index; NCD, non-communicable diseases; NB-UVB, narrow band ultraviolet; wk, week; OR, odds ratio; CI, confidence interval.

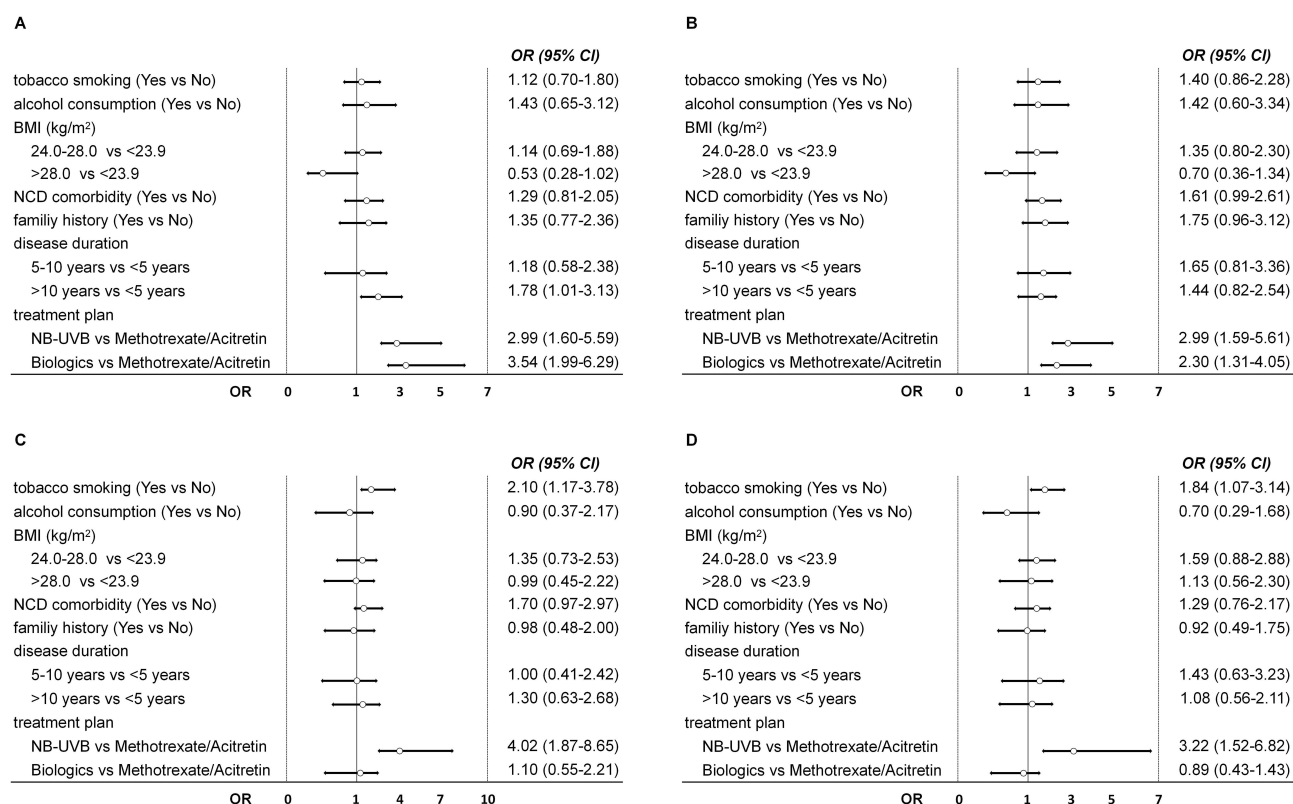


Figure 1 Factors associated with the relapse at week 24 and 48 based on multivariate logistic regression after the achievement of PASI50 or PASI75 at week 12 among psoriasis patients in Shanghai. **(A)** Relapse at wk24 based on PASI50 at wk12 (n=357). **(B)** Relapse at wk48 based on PASI50 at wk12 (n=333). **(C)** Relapse at wk24 based on PASI75 at wk12 (n=290). **(D)** Relapse at wk48 based on PASI75 at wk12 (n=269).

Abbreviations: OR, odds ratio; CI, confidence interval; BMI, body mass index; NCD, non-communicable diseases; NB-UVB, narrow band ultraviolet.

Association Between Tobacco Smoking Feature and Diseases Relapse

We also explored the association between tobacco smoking features and diseases relapse condition at week 24 and 48 among 171 psoriasis patients who smoked and achieved PASI50 at week 12, and 128 patients who smoked and achieved PASI75 at week 12. Data in Table 4 showed that psoriasis patients with relapse had longer years of tobacco smoking (the median value was 30 vs 23 at week 24, and 30 vs 22 at week 48 with PASI50 achievement at week 12; 32 vs 20 at week 24 and 29 vs 25 at week 48 with PASI75 achievement at week 12). Moreover, psoriasis patients with more years of tobacco smoking were inclined to have higher relapse rate at week 24 as well as at week 48, regardless of the PASI 50 or PASI75 achievement at week 12. This study also indicated that psoriasis patients with at least 20 daily cigarette consumption had higher relapse rate at week 24 and at week 48 than those with less than 20 daily cigarette consumption, regardless of the PASI 50 or PASI75 achievement at week 12, but without statistical significance.

Subgroup and Sensitivity Analysis

Subgroup analysis was performed to demonstrate the association between tobacco smoking and diseases relapse among psoriasis patients achieved PASI50 or PASI75 at week 12 with different treatment plans. Table 5 indicated that patients with tobacco smoking had higher relapse rates at both week 24 and week 48 compared to those without tobacco smoking, regardless of the PASI50 or PASI75 achievement at week 12 in the acitretin/ methotrexate, NB-UVB and biologics groups. For patients received NB-UVB treatment and achieved PASI50 at week 12, patients with tobacco smoking had a relapse rate of 47.9% at week 24 and 76.6% at week 48, respectively, whereas the relapse rate was 44.4% at week 24 and 64.4% at week 48 among patients without tobacco smoking, the difference was statistically significant ($p < 0.05$). For patients received NB-UVB treatment and achieved PASI75 at week 12, patients with tobacco smoking had a relapse rate

Table 4 The Association Between Smoking Initiation Age, years of Smoking, Cigarette Consumption Amount and Relapse Incidence at wk 24 and wk48 After the Achievement of PASI50 or PASI75 at wk 12 Among Psoriasis Patients with Tobacco Smoking Habits

Tobacco smoking condition	All smokers (n=282)	Relapse based on PASI50 at wk12 (n=171) ^a				Relapse Based on PASI75 at wk12 (n=128) ^b			
		Relapse at wk24		Relapse at wk48		Relapse at wk24		Relapse at wk48	
		Yes (n=70)	No (n=97)	Yes (n=106)	No (n=56)	Yes (n=46)	No (n=80)	Yes (n=73)	No (n=49)
Smoke initiation age, mean (SD)	24.3 (5.9)	23.9 (5.2)	24.9 (6.5)	24.8 (6.3)	24.2 (5.3)	23.6 (5.3)	24.8 (5.9)	24.2 (6.1)	25.1 (5.1)
Smoke initiation age, median (IQR)	24 (20–27)	24.5 (20–27)	23 (20–28)	25 (20–28)	23.5 (20–26)	24 (20–25)	25 (21–29)	25 (20–27)	25 (22–30)
Years of smoking, mean (SD)†‡	25.4 (15.9)	27.6 (16.9)	22.9 (16.0)	25.8 (17.8)	22.9 (14.4)	29.4 (15.8)	21.9 (17.5)	24.8 (18.3)	23.8 (15.9)
Years of smoking, median (IQR)†‡	28.5 (12–39)	30 (13–40)	23 (10–36)	30 (10–40)	22 (13–35)	32 (15–40)	20 (0.5–37)	29 (7–40)	25 (10–37)
Years of smoking, n (%)†‡									
≤10 years	68 (24.1)	16 (36.4)	28 (63.6)	31 (70.5)	13 (29.5)	8 (22.2)	28 (77.8)	23 (63.9)	13 (36.1)
11–20 years	49 (17.4)	8 (29.6)	19 (70.4)	11 (44.0)	14 (56.0)	7 (36.8)	12 (63.2)	9 (50.0)	9 (50.0)
21–30 years	51 (18.1)	13 (41.9)	18 (58.1)	17 (58.6)	12 (41.4)	7 (35.0)	13 (65.0)	10 (52.6)	9 (47.4)
31–40 years	67 (23.8)	17 (46.0)	20 (54.0)	23 (63.9)	13 (36.1)	14 (48.3)	15 (51.7)	17 (60.7)	11 (39.3)
>40 years	47 (16.7)	16 (57.1)	12 (42.9)	24 (85.7)	4 (14.3)	10 (45.5)	12 (54.5)	14 (66.7)	7 (33.3)
Cigarettes/day, mean (SD)	16.2 (7.6)	16.8 (6.4)	16.5 (8.6)	17.2 (7.5)	15.5 (8.3)	17.2 (6.9)	17.5 (8.6)	17.8 (7.8)	16.6 (8.5)
Cigarettes/day, median (IQR)	20 (10–20)	20 (10–20)	20 (10–20)	20 (10–20)	16.5 (10–20)	20 (10–20)	20 (10–20)	20 (10–20)	20 (10–20)
Daily cigarette consumption, n (%)									
<20	129 (45.7)	28 (36.6)	45 (61.4)	42 (59.1)	29 (40.9)	18 (36.0)	32 (64.0)	27 (55.1)	22 (44.9)
≥20	153 (54.3)	42 (44.7)	52 (55.3)	64 (70.3)	27 (29.7)	28 (36.8)	48 (63.2)	46 (63.1)	27 (36.9)

Notes: ^a the number of missing data was 4 at wk 24 and 9 at wk48. ^b the number of missing data was 2 at wk 24 and 6 at wk48. †: the difference between patients with and without relapse at wk 24 base on PASI50 achievement at wk12 was statistically significant. ‡: the difference between patients with and without relapse at wk 48 base on PASI50 achievement at wk12 was statistically significant. §: the difference between patients with and without relapse at wk 24 base on PASI75 achievement at wk12 was statistically significant.

Abbreviations: SD, standard deviation; IQR, Interquartile range; PASI, psoriasis area and severity index; wk, week.

Table 5 The Association Between Tobacco Smoking and Treatment Relapse at week 24 and 48 After the Achievement of PASI50 or PASI75 at week 12 Among Psoriasis Patients with Different Treatment Plan in Shanghai

Treatment plan	Patients n (%)	Patients with PASI50 at wk12		Patients with PASI75 at wk12	
		Relapse Rate at wk24	Relapse Rate at wk48	Relapse Rate at wk24	Relapse Rate at wk48
Acitretin/Methotrexate					
With tobacco smoking	134 (60.9)	15 (25.4)	32 (55.2)	10 (26.3)	20 (54.1)
Without tobacco smoking	86 (39.1)	12 (24.5)	19 (42.2)	7 (16.3)	16 (41.0)
NB-UVB†‡					
With tobacco smoking	70 (50.4)	23 (47.9)	36 (76.6)	20 (64.5)	28 (90.3)
Without tobacco smoking	69 (49.6)	20 (44.4)	29 (64.4)	12 (36.4)	20 (60.6)
Biologics					
With tobacco smoking	78 (40.6)	32 (53.3)	38 (66.7)	16 (28.1)	25 (46.3)
Without tobacco smoking	114 (59.4)	45 (46.9)	51 (62.9)	15 (17.1)	30 (40.0)

Notes: †: the relapse rate between patients with and without tobacco smoking at wk 24 base on PASI75 achievement at wk12 was statistically significant.

‡: the relapse rate between patients with and without tobacco smoking at wk 48 base on PASI75 achievement at wk12 was statistically significant.

Abbreviations: PASI, psoriasis area and severity index; NB-UVB, narrow band ultraviolet; wk, week.

of 64.5% at week 24 and 90.3% at week 48, respectively, whereas the relapse rate was 36.4% at week 24 and 60.6% at week 48 among patients without tobacco smoking, the difference was statistically significant ($p < 0.05$).

Discussion

Previous studies have shown that tobacco smoking is an independent risk factor for psoriasis.¹⁷ It is positively correlated with disease severity and negatively associated with treatment efficacy.^{4,14,18} However, evidence on the association between tobacco smoking and psoriasis relapse was still limited. In this study, we recruited 551 patients with psoriasis to explore the influence of tobacco smoking on disease relapse, findings indicated that tobacco smoking is positively associated with diseases relapse at week 24 and 48 in psoriasis patients, and psoriasis patients with longer smoking duration and more daily cigarette consumption had higher relapse rate.

Over the past decades, significant progress has been achieved in exploring the pathogenesis of psoriasis, which has also been successfully translated into effective therapies. However, psoriasis patients usually experience relapses after discontinuing treatment or even during the treatment course.⁷ The definition of “relapse” varies across different studies, with the common criteria of a 50% loss of maximum PASI improvement or a loss of $\text{PGA} \leq 2$.¹⁹ In this study, we defined relapse as the loss of 50% PASI improvement in patients who achieved PASI50 or PASI75 at week 12. We noticed that patients who achieved PASI50 at week 12, the relapse rates at week 24 and week 48 were 41.2% and 61.6%, respectively. Meanwhile, for patients with PASI75 achievement at week 12, the relapse rates were 27.6% and 51.7% at week 24 and week 48, respectively. These findings suggested that patients who achieved a higher therapeutic response (PASI75) had a relatively lower relapse rates during the same observation time points, which was in line with previous studies.²⁰ This study also showed that a higher improvement in PASI and a shorter time to achieve the improvement during treatment were important predictors for longer relapse-free duration. An 8-year multi-center retrospective study conducted by Chiu et al²⁰ indicated that the cumulative probabilities of relapse-free at 6 months and 12 months after the withdrawal from ustekinumab treatment were 49.3% and 12.6%, respectively. Blauvelt et al²¹ reported 75.1% patients treated with secukinumab experienced relapse during a 1-year follow-up period. The differences in treatment plans and criteria for relapse assessment maybe the primary reasons for the observed discrepancies in relapse rates compared with those in previous studies.

In this study, we found that tobacco smoking was positively associated with relapse rate at week 24 and week 48, especially among patients who achieved PASI75 at week 12. Patients with tobacco smoking had a 2.10 and 1.84 times higher risk of relapse at week 24 and week 48 than those without tobacco smoking, which was consistent with the findings in previous studies. Warren et al²² revealed that psoriasis patients who smoke had a twofold greater odds of relapse than non-smokers ($\text{OR} = 2.04$, 95% CI: 1.02–4.07). A meta-analysis also indicated that tobacco smoking is one risk factor for relapse in psoriasis patients after discontinuation of biologics ($\text{RR} = 1.09$, 95% CI: 1.02–1.17).⁸ Furthermore, we also noticed that psoriasis patients

with more years of tobacco smoking had a higher relapse rate, suggesting that long-term tobacco smoking may be an important risk factor for relapse in psoriasis patients. The impact of smoking on relapse is likely associated with multiple mechanisms. Smoking can induce oxidative stress and generate free radicals, which interfere with signaling pathways related to psoriasis, including nuclear factor kappa B (NF- κ B), mitogen activated protein kinase (MAPK) and janus kinase signal transducers and activators of transcription (JAK-STAT).²³ Moreover, nicotine and other harmful substances in cigarette smoke can induce the activation of immune cells, promote inflammatory events, and thereby worsen or initiate psoriasis.^{23,24} Neutrophils are one of the most abundant innate immune cells, and tobacco smokers often exhibit enhanced neutrophil chemotaxis.²³ The infiltration of neutrophils into the lesion areas promotes the formation of Munro's microabscesses, which is one of the major histopathological hallmarks of psoriasis.^{25,26} From a clinical perspective, these findings suggest that psoriasis patients should be advised to quit smoking during treatment to reduce the risk of relapse.

In this study, we also noticed that patients with higher BMI, NCD comorbidities, and longer disease duration may be risk factors for psoriasis relapse. Previous studies indicate that an increase in BMI is significantly correlated with the increased risk of relapse.²² The underlying mechanisms may be related to pro-inflammatory cytokines and adipocytokines secreted by adipose tissue, which may exacerbate the pathological processes of psoriasis.^{27,28} In addition, meta-analyses have shown that obesity is associated with lower treatment efficacy of anti-tumor necrosis factor agents, and weight loss may prevent from de novo psoriasis.²⁸ For disease duration, a longer course of psoriasis often implies increased opportunities for reactive oxygen species activation and inflammation which is closely related to the relapse of psoriasis, and previous studies confirm that patients with a shorter disease duration tend to respond better to treatment and maintain a longer relapse-free period.^{29–31} Regarding NCD comorbidities, since psoriasis is a systemic inflammatory disease, it is often accompanied by multiple comorbidities, with metabolic diseases being the most common.³² Previous research indicates that patients with psoriasis and metabolic syndrome do not exhibit significant improvement in systemic inflammatory biomarkers, even after achieving complete or nearly complete skin lesion clearance. These residual inflammatory factors appear to promote psoriasis relapse, thereby shortening the period of clinical remission.³³

In this study, we found that psoriasis patients treated with NB-UVB and biologics were more prone to relapse compared with those treated with acitretin and methotrexate. This may be attributed to the fact that biologics can reduce or clear skin lesions in the short term, leading to relatively better PASI improvement at week 12, but for patients achieved the same PASI improvement with acitretin and methotrexate treatment, the proportion was lower and most of them had relatively mild skin lesion, which might also contribute to the lower relapse rate. In this study, the subgroup analysis indicated that regardless of patients achieved PASI50 or PASI75 at week 12, patients with tobacco smoking had higher relapse rates in any treatment plan, and this was more pronounced among patients with NB-UVB treatment. Previous studies indicate that tobacco smoking may have adverse effects on the therapeutic efficacy of NB-UVB through the pathway mediated by tumor necrosis factor alpha converting enzyme,³⁴ which might contribute to a higher risk of diseases relapse.

The major strength of this study is the real-world clinical circumstances, which provides evidence that is more reflective of actual clinical practice, and the 48 weeks of follow-up time also provides a relatively long-term clinical data for diseases relapse evaluation. Moreover, the clinical data of psoriasis patients were directly extracted from the health information system (HIS), which ensuring the high data quality, is another strength of current study.

There are several limitations should be considered in this study. First, patients were enrolled in one hospital, so the generalization and representation of the results was limited. Second, the information regarding patients' tobacco smoking was collected through questionnaire interview, which might lead to recall bias. Third, the evaluation of treatment efficacy and relapse in patients was mainly based on the changes in PASI scores, which may not be sufficient for patients with psoriasis in special areas. All of these aforementioned limitations would restrict the interpretations of clinical findings in some degree, and some improvement should be considered in future study.

Conclusion

Psoriasis patients had high relapse rate at week 24 at week 48, even with the PASI50 or PASI75 achievement at week 12, and tobacco smoking was positively correlated with the relapse, especially among those with longer smoking duration and more daily consumption. Therefore, we recommend that patients with psoriasis should quit smoking and combine this with a healthy lifestyle and standardized treatment to prevent the risk of relapse.

Abbreviations

BMI, Body Mass Index; BSA, Body Surface Area; CI, Confidence Interval; RMB, Chinese Yuan; IQR, Interquartile Range; NB-UVB, Narrow Band Ultraviolet; NCD, Non-communicable Disease; OR, Odds Ratio; PASI, Psoriasis Area and Severity Index; PGA, Physician Global Assessment; SD, Standard Deviation; TRM, Tissue Resident Memory T Cells.

Data Sharing Statement

The data for this study are available upon request from the corresponding author. The request should state the title and aim of the research for which the data are requested.

Ethics Approval and Informed Consent

This study was approved by the Institutional Review Boards of Shanghai Skin Disease Hospital, Shanghai, China (2022-25). Informed consent was obtained before starting the study, and the study was strictly performed in accordance with the Declaration of Helsinki.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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