

Association between Retinal Vein Occlusion and Psoriasis in Korea: A Nationwide Population-based Prospective Cohort Study

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Psoriasis is a chronic inflammatory skin disease imparting increased risk of cardiovascular diseases. Until now, few studies have reported an increased incidence of ophthalmological retinal vasculopathy in individuals with psoriasis. This study aimed to investigate the association between psoriasis and retinal vein occlusion in the Korean population. Data collected by the National Health Insurance Service between 2009 and 2015 in Korea were analysed. Participants who underwent national health examinations from 2009 to 2012 were enrolled in this study and were divided into either the psoriasis group ($n=3,088$) or the control group ($n=465,205$). All occurrences of retinal vein occlusion were observed, and the incidence rate of retinal vein occlusion was compared between the psoriasis and control groups. A Cox proportional hazards regression analysis was used to assess the association between psoriasis and newly developed retinal vein occlusion. During a mean 4.37-year follow-up period, 2,034 patients developed retinal vein occlusion. According to multivariable Cox proportional hazard models, individuals with psoriasis had a significantly higher risk of retinal vein occlusion compared with controls (hazard ratio 1.72, 95% confidence interval 1.18–2.51) after adjustments for covariates. This study found that psoriasis was positively associated with retinal vein occlusion.

Key words: epidemiology; incidence; psoriasis; retinal vein occlusion; risk.

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Psoriasis is considered a systemic disease and is associated with various comorbidities, such as cardiovascular disease, stroke, hypertension, dyslipidaemia, diabetes, and obesity (1–3). Therefore, cardiovascular complications are a problem in individuals with psoriasis. However, relatively few studies have focused on microvascular complications compared with macrovascular complications.

Retinal vein occlusion is a heterogeneous group of disorders that impairs venous return from the retinal

SIGNIFICANCE

Psoriasis is a chronic inflammatory skin disease with various multi-systemic complications. This study investigated the association between psoriasis and retinal vein occlusion. Data collected by the National Health Insurance Service between 2009 and 2015 in Korea were analysed, dividing participants into either the psoriasis group or the control group. All occurrences of retinal vein occlusion were observed and the incidence rates between the 2 groups were compared. Statistical analysis showed that individuals with psoriasis had 1.72 times higher risk of retinal vein occlusion compared with controls.

circulation (4). Retinal vein occlusion causes visual impairment, with macular oedema and neovascularization of the retina and optic disc, which lead to vitreous haemorrhage, retinal detachment, and neovascular glaucoma (4). The worldwide prevalence of branch retinal vein occlusion is estimated at 0.4%, while that of central retinal vein occlusion is approximately 0.08% with an equal distribution between males and females and increased risk with older age (5). The mean incidence rate of retinal vein occlusion in Korea has been reported as 48.09 per 100,000 person-year, with a peak in the late 70s, and females showed a 1.24-times higher incidence rate compared with males (6). To date, the comorbidities of retinal vein occlusion have not been evaluated in any previous Korean study.

Retinal vein occlusion is known to develop at an elderly age and is associated with typical atherosclerosis risk factors (7). It is also caused by inflammation, vasospasm, or compression (8). Therefore, the chronic autoimmune inflammatory diseases are characterized in retinal vein occlusion. In branch retinal vein occlusion, major risk factors are arterial hypertension, arteriosclerosis, and diabetes mellitus (4). In addition, thrombophilia and homocystinuria are known to increase the risk of retinal vein occlusion (9). Considering that psoriasis is a chronic inflammatory disease and associated with metabolic syndrome, there is also the possibility of an association between psoriasis and retinal vein occlusion (10). Recently, a Taiwan study reported increased risk of retinal vascular (both arterial and venous) occlusion in individuals with psoriasis (11). Visual impairment or even blindness due to retinal vein occlusion is a very important complication, and more research on this as-

sociation is needed to predict and educate patients about retinal vein occlusion in individuals with psoriasis.

The aim of this study was to investigate the association between psoriasis and retinal vein occlusion using Korean Health Insurance Review and Assessment Service data obtained from 2002 to 2015. Since Koreans are obliged to join the National Health Insurance Program, and information from their visits to health institutions and insurance claims is stored in this system, this database is suitable for obtaining a national level of epidemiological information on psoriasis and retinal vein occlusion.

MATERIALS AND METHODS

Data source and study population

This was a nationwide population-based retrospective cohort study using the Korean National Health Insurance Service (KNHIS) Claims Database (in which diagnoses are recorded using the International Classification of Diseases, Tenth Revision (ICD-10) code), which contains all claims data for the KNHIS programme, the Korean Medical Aid programme, and long-term care insurance from 1 January 2002 until 31 December 2015. The KNHIS is a universal healthcare system that provides almost 99% coverage for the entire Korean population. The computerized KNHIS database contains almost all patient medical data (12). The current study used a random sample of 1 million people (representing 2% of the total population) among the KNHIS database to gather data for analysis. KNHIS staff confirmed that multi-level sampling is a representative group of the Korean population from 2002 to 2015 (13). Each patient's information was anonymized to protect individual privacy. The study was approved by the Institutional Review Board and the ethics committee of Uijeongbu St. Mary's Hospital at The Catholic University of Korea (UC22ZISI0032). The Institutional Review Board at the Korea Centers for Disease Control and Prevention approved the protocol according to the principles of the Declaration of Helsinki. Anonymized and de-identified information was used for analysis, and informed consent was not required due to the retrospective nature of this study.

Study population and design

The study is designed as a nationwide population-based prospective cohort study. All participants who underwent health screening from January 2009 to December 2012 ($n=484,410$) were included. Participants younger than 20 years ($n=1,555$) were excluded. The year the participant underwent the health examination was considered the index year of the participant. To evaluate the association between retinal vein occlusion and psoriasis, patients who had been diagnosed with retinal vein occlusion prior to the index year were excluded ($n=2,187$). Individuals who died within 1 year of the health examination were also excluded ($n=1,913$). After excluding participants with missing values of any of the covariables ($n=10,462$), our analysis was conducted on a total of 468,293 participants. Death of the participants was censored. The development of retinal vein occlusion was observed from the index year until 31 December 2015 (Fig. S1).

Definition of the psoriasis group

Of the 468,293 participants who underwent a national health examination from 2009 to 2012, individuals with psoriasis were defined as those who visited an outpatient clinic and received

treatment under the diagnosis of psoriasis (ICD-10 code L40.0, L40.1, L40.2, L40.3, L40.4, L40.5, L40.8, and L40.9). In total, 3,088 participants were placed in the psoriasis group, and the other 465,205 individuals were classified in the control group.

Primary outcome of incidence of retinal vein occlusion

The incidence of retinal vein occlusion was observed from the index year to December 2015 in all participants ($n=468,293$). Newly developed retinal vein occlusion was defined when a patient visited an ophthalmology clinic and was treated for a diagnosis of retinal vein occlusion (ICD-10 code H34.8) without a prior history of retinal vein occlusion before the index year. The primary endpoint was newly diagnosed retinal vein occlusion that occurred between the baseline visit and the follow-up visit until 31 December 2015.

Measurements from the health examination

Enrolees in the National Health Insurance Corporation are recommended to undergo a standardized medical examination every 2 years. These medical examinations include measurements of height, weight, waist circumference, and blood pressure and laboratory tests such as fasting glucose, total cholesterol, high-density lipoprotein cholesterol, and urinalysis. Health-related behaviours (such as smoking, drinking, and physical activity) were collected using standardized self-reporting questionnaires. Age and sex data were obtained for all participants. Anthropometric measurements were performed while the patients wore light clothing. Body mass index (BMI) was calculated as the participant's weight (in kg) divided by the square of the participant's height (in m). Blood pressure was measured while the individual was seated after resting for at least 5 min. Smoking status was categorized as never smoker, ex-smoker, or current smoker. Alcohol drinking status was defined as non-drinker, mild drinker, or heavy drinker based on a question regarding frequency of alcohol consumption per week. The participants' income levels were dichotomized at the lowest 20%. Blood samples were drawn after an overnight fast and were assessed for serum levels of glucose and total cholesterol. The hospitals in which the health examinations were performed were certified by the KNHIS and are subject to regular quality control.

Baseline comorbidities and subgroup classifications

Baseline comorbidities were obtained from the health examination database and were assessed during the screening period from 2009 to 2012. Baseline characteristics of the comorbidities were extracted from the medical claims according to ICD-10 codes, prescription codes, and procedure codes. The study also included diabetes mellitus, hypertension, and dyslipidaemia diagnoses. A diagnosis of type 2 diabetes was confirmed by the ICD-10 codes E11–E14 and prescription of antidiabetic drugs (sulphonylureas, metformin, meglitinides, thiazolidinediones, dipeptidyl peptidase-4 inhibitors, α -glucosidase inhibitors, or insulin) or fasting blood sugar ≥ 126 mg/dl. Presence of hypertension was defined as at least 1 claim per year for prescription of an antihypertensive agent under ICD-10 codes I10–I13 and I15 or systolic/diastolic BP $\geq 140/90$ mmHg. The presence of dyslipidaemia was defined as at least 1 claim per year for prescription of an antihyperlipidaemic agent under ICD-10 code E78 or total cholesterol level ≥ 240 mg/dl.

Statistical analysis

When presenting the baseline characteristics, the continuous variable was marked as mean with SD and was compared between groups using Student's *t*-test. The categorical variables

were presented as numbers and percentages and were analysed using a χ^2 test. The incidence rate of retinal vein occlusion was calculated by dividing the number of incident cases by the total follow-up period and was expressed as per 1,000 person-years. A Cox proportional hazards regression analysis was used to assess the association between psoriasis and newly developed retinal vein occlusion. The hazard ratio (HR) and 95% confidence interval (CI) values for retinal vein occlusion in individuals with psoriasis were calculated with a reference of non-psoriasis individuals. In Model 1, only 2 variables (psoriasis and retinal vein occlusion) were used for univariate analysis. In Model 2, age and sex were considered confounding variables. In addition, in Model 3, age, sex, BMI, smoking status, alcohol consumption, physical activity, income level, diabetes mellitus, hypertension, and dyslipidaemia were adjusted as confounding variables. Subgroup analysis was conducted on the underlying characteristics, and Cox proportional hazard regression analysis was conducted to analyse the occurrence rates of both psoriasis and retinal vein occlusion between the subgroups with adjustment for age, sex, BMI, smoking status, alcohol consumption, physical activity, income level, diabetes mellitus, hypertension, and dyslipidaemia.

The cumulative incidence of retinal vein occlusion in the presence of psoriasis was presented using a Kaplan–Meier curve. The proportional hazards assumption was tested through using Schoenfeld residuals. A log-rank test was also performed to analyse the differences between individuals with psoriasis and controls. Statistical significance was defined as a 2-sided p -value < 0.05 . Tukey's method was used for multiple mean comparisons of groups. All statistical analyses were performed using SAS software (ver. 9.4; SAS Institute, Cary, NC, USA) and R programming, version 3.1.0 (The R Foundation for Statistical Computing, Vienna, Austria; <http://www.R-project.org>).

RESULTS

Baseline characteristics of the study population

The participants ($n=468,293$) were divided into a psoriasis group ($n=3,088$) and a control group ($n=465,205$). The baseline characteristics of the participants are shown in **Table I**. Patients with psoriasis were older (mean age 50.5 ± 14.5 years) with a higher proportion of males (57.3%) than in the non-psoriasis group. Patients with psoriasis were more likely to be current smokers (28.9%) and heavy drinkers (8.1%) than those without psoriasis. Individuals with psoriasis had greater proportions of comorbid diabetes mellitus (11.8%), hypertension (34.6%), and dyslipidaemia (24.0%) than those without psoriasis (all, $p < 0.001$).

Incidence rates and risks of retinal vein occlusion among the psoriasis group

During a mean follow-up of 4.37 ± 1.1 years, 2,034 patients developed retinal vein occlusion. Twenty-seven cases of retinal vein occlusion occurred in individuals with psoriasis. In addition, 2,007 participants in the control group developed retinal vein occlusion. The incidence rate of retinal vein occlusion per 1,000 person-years was 2.00 (95% CI 1.37, 2.92) in the psoriasis group and was higher than that of the control group, 0.99 (0.95, 1.03). In Model 1, the crude HR for retinal vein

Table I. Baseline characteristics of the study population

	Controls $n = 465,205$	Psoriasis $n = 3,088$	p -value
Age, years, mean \pm SD	47.73 \pm 14.32	50.52 \pm 14.46	< 0.001
Follow-up years, mean [IQR]	4.58 [3.67–5.25]	4.58 [3.75–5.25]	0.68
Age group, n (%)			< 0.001
< 40 years	133,576 (28.71)	717 (23.22)	
40–64 years	267,146 (57.43)	1,800 (58.29)	
≥ 65 years	64,483 (13.86)	571 (18.49)	
Sex, n (%)			< 0.001
Male	233,579 (50.21)	1,768 (57.25)	
Female	231,626 (49.79)	1,320 (42.75)	
Income low (20%), n (%)	73,217 (15.74)	497 (16.09)	0.59
Smoking, n (%)			< 0.001
Never smokers	288,817 (62.08)	1,629 (52.75)	
Ex-smokers	63,127 (13.57)	566 (18.33)	
Current smokers	113,261 (24.35)	893 (28.92)	
Drinking, n (%)			0.09
Non-drinkers	248,953 (53.51)	1,702 (55.12)	
Mild drinkers	180,156 (38.73)	1,136 (36.79)	
Heavy drinkers	36,096 (7.76)	250 (8.1)	
Regular exercise, n (%)	82,265 (17.68)	588 (19.04)	< 0.05
BMI, kg/cm ² , mean \pm SD	23.7 \pm 3.3	23.93 \pm 3.3	< 0.001
BMI level, kg/cm ² , n (%)			< 0.01
< 18.5	18,929 (4.07)	101 (3.27)	
18.5–23	184,275 (39.61)	1,156 (37.44)	
23 < 25	113,086 (24.31)	760 (24.61)	
< 30	131,473 (28.26)	945 (30.6)	
≥ 30	17,442 (3.75)	126 (4.08)	
Diabetes mellitus, n (%)	42,827 (9.21)	365 (11.82)	< 0.001
Hypertension, n (%)	127,875 (27.49)	1,068 (34.59)	< 0.001
Dyslipidaemia, n (%)	88,803 (19.09)	742 (24.03)	< 0.001
SBP, mean \pm SD	122.23 \pm 15.27	123.72 \pm 15.53	< 0.001
DBP, mean \pm SD	76.07 \pm 10.18	76.8 \pm 10.26	< 0.001
Glucose, mean \pm SD	97.59 \pm 24.17	99.3 \pm 26.15	< 0.001
Total cholesterol, mean \pm SD	194.84 \pm 40.62	197.04 \pm 45.31	< 0.01

SD: standard deviation; IQR: interquartile range; BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure.

occlusion was 2.03 (95% CI 1.39–2.97) in the psoriasis group compared with the controls. After adjustments for age and sex in Model 2 and for age, sex, BMI, income level, smoking status, drinking status, regular exercise frequency, diabetes mellitus, hypertension, and dyslipidaemia in Model 3, the HR for retinal vein occlusion in the psoriasis group was significantly increased compared with that of the controls (HR 1.77, 95% CI 1.21–2.59 in Model 2 and HR 1.72, 95% CI 1.18–2.51 in Model 3, all $p < 0.01$, **Table II**) As shown in **Fig. 1**, the psoriasis group showed an increased incidence probability of retinal vein occlusion after 2 years compared with the controls (**Fig. 1**).

Subgroup analysis of risk of retinal vein occlusion in individuals with psoriasis

To verify the increased risk of retinal vein occlusion in individuals with psoriasis, subgroup analysis was performed according to age, sex, BMI, smoking status, drinking status, regular exercise frequency, and the presence of comorbid disease including diabetes mellitus, hypertension, and dyslipidaemia (**Table III**). Regardless of the covariates, the increased risk of retinal vein occlusion was consistent in individuals with psoriasis. The increased risk of retinal vein occlusion was significantly higher in

Table II. Incidence and overall risk of retinal vein occlusion according to the presence of psoriasis

Groups	Number	Retinal vein occlusion	Duration (person-years)	Incidence rate per 1,000 person-years	Model 1 HR (95% CI)	Model 2 HR (95% CI)	Model 3 HR (95% CI)
Psoriasis							
No	465,205	2,007	2,032,203.25	0.99	1	1	1
Yes	3,088	27	13,487.83	2.00	2.03 (1.39, 2.97)	1.77 (1.21, 2.59)	1.72 (1.18, 2.51)
<i>p</i> -value					<0.001	<0.01	<0.01

Model 1: Crude. Model 2: Age, sex. Model 3: Age, sex, BMI, income level, smoking status, drinking status, regular exercise frequency, diabetes mellitus, hypertension, and dyslipidaemia. HR: hazard ratio; CI: confidence interval; BMI: body mass index.

individuals with psoriasis who were <65 years old (HR 2.14, 95% CI 1.38–3.34), male (HR 1.88, 95% CI 1.16–3.03), currently smoking (HR 2.25, 95% CI 1.11–4.54), non-heavy drinking (HR 1.78, 95% CI 1.21–2.62), and regular exercisers (HR 2.37, 95% CI 1.17–4.77) compared with the risk of retinal vein occlusion in control. Increased hazard ratio for retinal vein occlusion in individuals with psoriasis was significantly high when the individuals had no comorbidities, including diabetes mellitus (HR 1.85, 95% CI 1.21–2.81), hypertension (HR 2.93, 95% CI: 1.86–4.62), and dyslipidaemia (HR 1.85, 95% CI 1.17–2.9) compared to controls. The *p*-value for interaction showed significance in subgroup analysis on hypertension (Table III).

DISCUSSION

This population-based study showed increased risk of retinal vein occlusion in individuals with psoriasis. The findings suggest that psoriasis is an independent risk factor for retinal vein occlusion.

Psoriasis is a chronic inflammatory cutaneous disease. The prevalence of psoriasis varies from 0.14% in East Asia to 1.99% in Australasia.(14) A previous Korean

study reported the prevalence of psoriasis in Korea according to the Korean national insurance database was 0.44–0.45% of the general population (15). Psoriasis is associated with increased cardiovascular risk, including myocardial infarction, heart failure, and cardiovascular mortality (16–19). The association between psoriasis and ocular disease has not been well elucidated. Recently, a Taiwan study reported increased risk of retinal vascular (both arterial and venous) occlusion in individuals with psoriasis (11). Although the clinical finding, cause, and prognosis are different between retinal artery occlusion and retinal vein occlusion, the incidence rate of retinal vein occlusion was not specified in the previous Taiwan study (11). The retinal vasculopathy in individuals with psoriasis has not been evaluated in Korea. A previous Korean study reported the development of psoriasis in diabetic patients with diabetic retinopathy (20). That study also included the psoriasis incidence in diabetic patients, although the risk of ophthalmic vascular complications in individuals with psoriasis was not evaluated in the previous Korean study. In this study, the subgroup analysis showed that the psoriasis patients without hypertension, diabetes mellitus, or dyslipidaemia had high risk of retinal vein occlusion compared with individuals without psoriasis. The results might suggest that psoriasis itself is a risk factor for retinal vein occlusion regardless of metabolic syndrome, the powerful risk factor for retinal vein occlusion.

The mechanisms that underlie these associations are not well understood. However, inflammatory status and increased vascular complications in individuals with psoriasis are thought to play roles in retinal vein occlusion.

This association is based on the hypothesis that the 2 conditions share pathological mechanisms as follows. First, psoriasis and retinal vein occlusion share common risk factors, such as hypertension, diabetes mellitus, and hyperlipidaemia. Metabolic syndrome is considered a risk factor for both psoriasis and retinal vein occlusion (4, 21). Secondly, homocysteinaemia is commonly observed in both psoriasis and retinal vein occlusion patients, and the increased level of homocysteine in both populations might play a critical role in the development of both psoriasis and retinal vein occlusion. In individuals with psoriasis, the homocysteine level is significantly higher than that seen in healthy controls (22–24). Homocysteinaemia is also a risk factor for retinal vein occlusion (25, 26). Homocysteine promotes inflammation by activating

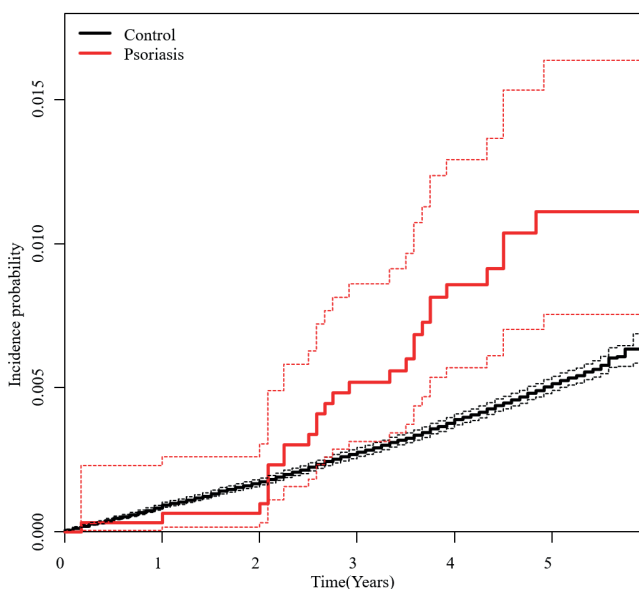


Fig. 1. Cumulative incidence of retinal vein occlusion according to the presence of psoriasis. Red line represents the incidence probability of psoriasis patients and red dotted line represents 95% confidence interval. Black colour is for controls.

Table III. Subgroup analysis of incidence and risk of retinal vein occlusion according to psoriasis

	Group	Number	Retinal vein occlusion	Duration	Incidence rate per 1,000-person years	HR (95% CI)*	p-value for interaction
Age, years	Control	400,722	1,263	1,750,898.58	0.72	1	0.1033
	Psoriasis	2,517	20	11,054.92	1.81	2.14 (1.38, 3.34)	
≥65	Control	64,483	744	281,304.67	2.64	1	1.08 (0.51, 2.27)
	Psoriasis	571	7	2,432.92	2.88	1.08 (0.51, 2.27)	
Sex	Control	233,579	929	1,030,392.25	0.90	1	0.5917
	Psoriasis	1,768	17	7,771.67	2.19	1.88 (1.16, 3.03)	
Female	Control	231,626	1,078	1,001,811	1.08	1	1.49 (0.80, 2.78)
	Psoriasis	1,320	10	5,716.17	1.75	1.49 (0.80, 2.78)	
BMI (kg/cm ²)	Control	148,915	771	652,858.25	1.18	1	0.9669
	Psoriasis	1,071	11	4,699.42	2.34	1.79 (0.99, 3.24)	
25–	Control	316,290	1,236	1,379,345	0.90	1	1.68 (1.03, 2.76)
	Psoriasis	2,017	16	8,788.42	1.82	1.68 (1.03, 2.76)	
Present smoking	Control	351,944	1,678	1,539,015.33	1.09	1	0.3084
	Psoriasis	2,195	19	9,603.67	1.98	1.54 (0.98, 2.42)	
Yes	Control	113,261	329	493,187.92	0.67	1	2.25 (1.11, 4.54)
	Psoriasis	893	8	3,884.17	2.06	2.25 (1.11, 4.54)	
Heavy drinker	Control	429,109	1,867	1,874,819.33	1.00	1	0.5034
	Psoriasis	2,838	26	12,395.25	2.10	1.78 (1.21, 2.62)	
Yes	Control	36,096	140	157,383.92	0.89	1	0.89 (0.12, 6.36)
	Psoriasis	250	1	1,092.58	0.92	0.89 (0.12, 6.36)	
Regular exercise	Control	382,940	1,604	1,667,345.42	0.96	1	0.272
	Psoriasis	2,500	19	10,872	1.75	1.53 (0.97, 2.41)	
Yes	Control	82,265	403	364,857.83	1.10	1	2.37 (1.17, 4.77)
	Psoriasis	588	8	2,615.83	3.06	2.37 (1.17, 4.77)	
Diabetes mellitus	Control	422,378	1,570	1,848,456.5	0.85	1	0.4492
	Psoriasis	2,723	22	11,950.17	1.84	1.85 (1.21, 2.81)	
Yes	Control	42,827	437	183,746.75	2.38	1	1.29 (0.54, 3.12)
	Psoriasis	365	5	1,537.67	3.25	1.29 (0.54, 3.12)	
Hypertension	Control	337,330	934	1,473,863.25	0.63	1	0.0031
	Psoriasis	2,020	19	8,880.83	2.14	2.93 (1.86, 4.62)	
Yes	Control	127,875	1,073	558,340	1.92	1	0.86 (0.43, 1.73)
	Psoriasis	1,068	8	4,607	1.74	0.86 (0.43, 1.73)	
Dyslipidaemia	Control	376,402	1,388	1,645,744.33	0.84	1	0.5591
	Psoriasis	2,346	19	10,330.83	1.84	1.85 (1.17, 2.9)	
Yes	Control	88,803	619	386,458.92	1.60	1	1.48 (0.73, 2.97)
	Psoriasis	742	8	3,157	2.53	1.48 (0.73, 2.97)	

*Age, sex, BMI, income level, smoking status, drinking status, regular exercise frequency, diabetes mellitus, hypertension, and dyslipidaemia were adjusted in analysis. HR: hazard ratio; 95% CI: 95% confidence interval; BMI: body mass index.

Th1 and Th17 cells and neutrophils while suppressing regulatory T cells. Moreover, it enhances the production of pro-inflammatory cytokines by inducing nuclear factor kappa B activation, which is critical in the immunopathogenesis of psoriasis and retinal vein occlusion. Thirdly, interleukin-17 is a potential mechanistic link between psoriasis and retinal vein occlusion. Interleukin 17 is produced by Th17 cells and is a pivotal cytokine in the pathogenesis of psoriasis. High serum level of interleukin 17 can disrupt endothelial function and vascular health and result in vascular dysfunction. The pathological role of interleukin 17 is also indicated in retinal vein occlusion (27). Fourthly, tumour necrosis factor alpha, another key cytokine in psoriasis, might be associated with a common pathogenesis of psoriasis and retinal vein occlusion. A previous study reported that anti-tumour necrosis factor alpha treatment improved the symptoms of retinal vein occlusion in patients with rheumatoid arthritis (28). As

such, the 2 conditions share a common cytokine that is probably involved in their pathogenesis. Although the complications of retinal vein are severe including vitreous haemorrhage, retinal detachment, neovascular glaucoma, and even visual loss, the vascular alterations can progress without any clinical evidence of ocular inflammation sign (29). Therefore, the recommendation of regular eye examination is considered to be important for individuals with psoriasis.

Study limitations

This study has some limitations. First, psoriasis, retinal vein occlusion, and other comorbidities were defined by claims data from the KNHIS database, which might not have been accurate. Secondly, the severity of the diseases and the types of medications prescribed were not considered in the analysis, so we could have missed some

important factors. Thirdly, the data about the articular involvement in individuals with psoriasis and the diagnosis of psoriatic arthritis were analysed in this study. The association between psoriatic arthritis and retinal vein occlusion should be evaluated in further study. Fourthly, lifestyle factors were based on self-report, a problematic aspect given the potential for social desirability bias.

Conclusion

Despite the limitations of this nationwide cohort study, the study found that psoriasis was an independent risk factor for retinal vein occlusion, after adjustment for covariates including diabetes mellitus, hypertension, and dyslipidaemia. Therefore, physicians should recommend regular eye examinations throughout the retina in order to monitor the development of retinal problems in individuals with psoriasis. Further studies are needed to identify the pathological mechanism of increased retinal vasculopathy in individuals with psoriasis with more large-scale study and to identify factors that can predict increased risk of microvascular complications in individuals with psoriasis.

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