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ORIGINAL ARTICLE

Association between cardio-cerebrovascular disease and systemic antipsoriatic therapy in psoriasis patients using population-based data: A nested case–control study

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Abstract

The effect of antipsoriatic therapy on cardio-cerebrovascular disease (CCVD) is not well described. Thus, we performed a population-based nested case–control study to investigate the effect of systemic antipsoriatic therapy on CCVD in psoriasis patients. Using nationwide cohort data from the Korean National Health Insurance Claims database, newly diagnosed psoriasis patients were identified. Among the enrolled participants, postenrollment development of CCVD events (ischemic heart disease, myocardial infarction, cerebral infarction, and cerebral hemorrhage) was investigated. To evaluate the effect of systemic antipsoriatic therapy on CCVD risk, we calculated the proportion of the treatment period with systemic antipsoriatic therapy during the study period (PTP [%]: the sum of all systemic antipsoriatic therapy durations divided by total observation period). Among 251 813 participants, 6262 experienced CCVD events during the study period (CCVD group). Controls included 245 551 patients without CCVD history during the study period (non-CCVD group). The non-CCVD group had greater PTP than the CCVD group (CCVD 2.12 ± 7.92, non-CCVD 2.64 ± 9.64; $P < 0.001$). In multiple logistic regression analysis, PTP was inversely associated with the CCVD risk after adjusting for age, sex, diabetes, hypertension, and dyslipidemia. A 10% increase in PTP reduced CCVD risk by 0.96 (95% confidence interval 0.93 to 0.99). Reduced CCVD risk was robust for both conventional antipsoriatic therapy and biologics. Our study found that systemic antipsoriatic therapy use was inversely associated with CCVD risk in psoriasis patients. These findings suggested that systemic antipsoriatic therapy could reduce CCVD development in patients with psoriasis.

Chong Won Choi and Sang Woong Youn contributed equally to this article as co-corresponding authors.

KEYWORDS
cardiovascular disease, cerebrovascular disease, comorbidity, psoriasis, systemic treatment

1 | INTRODUCTION

Psoriasis is a common chronic immune-mediated inflammatory disease.[1,2] In previous studies, psoriasis was associated with various comorbidities, such as inflammatory arthritis, Crohn's disease, and metabolic syndrome.[1–5] Furthermore, since proinflammatory cytokines and chemokines were reportedly elevated in the blood of psoriasis patients, recent studies suggested that psoriasis itself could induce a systemic inflammatory state in the affected patients,[1,2,6] therefore the "psoriatic march" concept, in which higher blood proinflammatory cytokines and adipokines in psoriasis patients induce insulin resistance and endothelial dysfunction, leading to major cardiovascular events, such as myocardial infarction and stroke, was proposed.[1,6]

Multiple epidemiological studies have revealed an association between psoriasis and major cardiovascular events. After the first report of a two-fold increase in the risk of arterial and venous diseases in psoriasis patients in 1973, several epidemiological studies and systematic reviews have reported an increased risk of cardiovascular and cerebrovascular diseases in psoriasis patients.[2,3,7–10] Despite the well-known association between psoriasis and elevated risk of cardio-cerebrovascular disease (CCVD) in psoriasis patients, the effect of systemic antipsoriatic therapy on CCVD risk remains unknown. In a few studies, reduced CCVD risk following systemic antipsoriatic therapy was observed, while other studies failed to document such effects.[6,11–14] However, previous studies had several limitations, such as the small number of enrolled psoriasis patients, analysis of the effect of single systemic antipsoriatic therapy, short-term observation period, and the lack of consideration of systemic antipsoriatic therapy duration.

This nationwide study investigated the effect of systemic antipsoriatic therapy on CCVD risk using data from the Korean Health Insurance Review and Assessment Service (HIRA). By summing up all systemic antipsoriatic treatment periods in each patient, we could assess the integrated effect of all systemic antipsoriatic treatment modalities used in Korea. We also investigated the effect of systemic antipsoriatic therapy duration on CCVD risk in psoriasis patients since the long-term cumulative effect of chronic inflammation induced by psoriasis might affect CCVD development.[15] Furthermore, we investigated and compared the effects of each systemic antipsoriatic treatment modality on CCVD risk. Using these integrated and comprehensive analyses, we can assess the effect of systemic antipsoriatic therapy on CCVD risk, which reflects the real-world psoriasis treatment pattern.

2 | METHODS

2.1 | Study design and data source

We performed a nested case–control study of a nationwide psoriasis population aged ≥20 years using data from HIRA from January 2010 to March 2021. The HIRA database contains information on the entire Korean population, which is related to all medical claims, and includes all diagnosis and treatment data. This study was exempt from the Institutional Review Board of Seoul National University Bundang Hospital (IRB number: X-2105686-901). The requirement for informed consent was waived because we only used de-identified data.

2.2 | Study cohort

We identified psoriasis patients aged ≥20 years with a diagnosis code for psoriasis (ICD-10 code L40) at least twice a year from January 2011 to March 2021.[16] The cohort entry date was set as the date of the first outpatient visit for psoriasis treatment. We excluded patients with a history of psoriasis or CCVD during the 1-year period before cohort entry (January–December 2010). Additionally, to ensure that only generally healthy patients were enrolled, we excluded those diagnosed with cancer, chronic obstructive pulmonary disease, chronic kidney disease, liver cirrhosis, or heart failure during the 1-year period before cohort entry, or those with a follow-up period <1 year. The remaining patients were followed up until the earliest CCVD outcome (defined in the outcome measurement), death, or end of the study period (March 31, 2021). The codes used to define the diseases are listed in Supporting Information Table S1.

2.3 | Definitions of cases and controls

We defined CCVD cases as patients with a diagnosis code of cardiovascular events, such as ischemic heart disease (I24) and myocardial infarction (I21), or cerebrovascular events, such as cerebral infarction (I63) and cerebral hemorrhage (I60, I61, and I62), during the study period.[17] Controls were defined as the remaining psoriasis patients, excluding CCVD cases in the study cohort.

2.4 | Exposure measurement

The exposure of interest was the proportion of systemic antipsoriatic treatment duration after psoriasis onset. For the analysis, the proportion of systemic antipsoriatic therapy treatment period (PTP, %) was defined by dividing the sum of all systemic antipsoriatic therapy durations by the total observation period. To calculate PTP, we examined all prescription records for systemic antipsoriatic therapy in both cases and controls. Systemic antipsoriatic therapy was classified into conventional agents (cyclosporine, methotrexate, or retinoids) and biologics (TNF-α inhibitor, anti-IL-12/23p40, IL-17A antagonist, or IL-23 antagonist), as described in Supporting

Information Table S1. The overall treatment period for conventional agents was calculated by adding the number of days prescribed for each drug, and the overall treatment period for biologics was determined by adding the administration days for each injection, assuming continuous treatment if prescribed within 12 weeks. The prevalence of psoriasis was calculated as the total number of days from psoriasis onset to the end of follow-up.

2.5 | Measurement of covariates

We identified demographic characteristics, including age and sex, and specific comorbidities, such as diabetes, hypertension, and hyperlipidemia, which were considered important CCVD determinants. Comorbidities at baseline were defined as the presence of at least one relevant diagnostic code between January 1 and December 31, 2010.

2.6 | Statistical analysis

We compared patient characteristics between cases and controls, using χ^2 tests for categorical variables and independent *t*-tests or Mann–Whitney U tests for continuous variables. Logistic regression was used to assess the association between CCVD risk and systemic antipsoriatic therapy usage in psoriasis patients. We calculated an unadjusted odds ratio (OR), followed by an adjusted odds ratio (aOR) and 95% confidence interval (CI), using multivariable logistic regression analysis with age, sex, diabetes, hypertension, and hyperlipidemia. We also used a nonlinear regression analysis with a generalized additive model to evaluate the relationship between the OR of CCVD risk and the PTP of systemic antipsoriatic therapy. In subgroup analyses, we evaluated the effect of each systemic antipsoriatic therapeutic modality on the association between CCVD risk and PTP in patients who received systemic therapy during the observation period. Data sets were constructed and analyzed using R statistical software (version 3.5.3; R Foundation for Statistical Computing). We defined results with a two-sided *P* value <0.05 as statistically significant.

3 | RESULTS

3.1 | PTP was low in patients with CCVD

Among 251 813 patients with newly diagnosed psoriasis who met the study cohort criteria for the nested case–control study (Figure 1), 6262 developed CCVD during the study period (CCVD group). The remaining patients without a CCVD history during the observation period were used as controls (non-CCVD group).

Table 1 and Supporting Information Table S2 summarized the baseline demographics and characteristics of the CCVD and non-CCVD groups. At baseline, CCVD patients were older and more likely to have diabetes, hypertension, and dyslipidemia than non-CCVD patients. Since the follow-up periods of the patients are different, we calculated the proportion of systemic antipsoriatic therapy treatment period (PTP [%]: the sum of all systemic antipsoriatic therapy durations divided by total observation period) and compared these values between the two groups. Interestingly, as indicated in Table 1, PTP showed a significant difference between the two groups. PTP

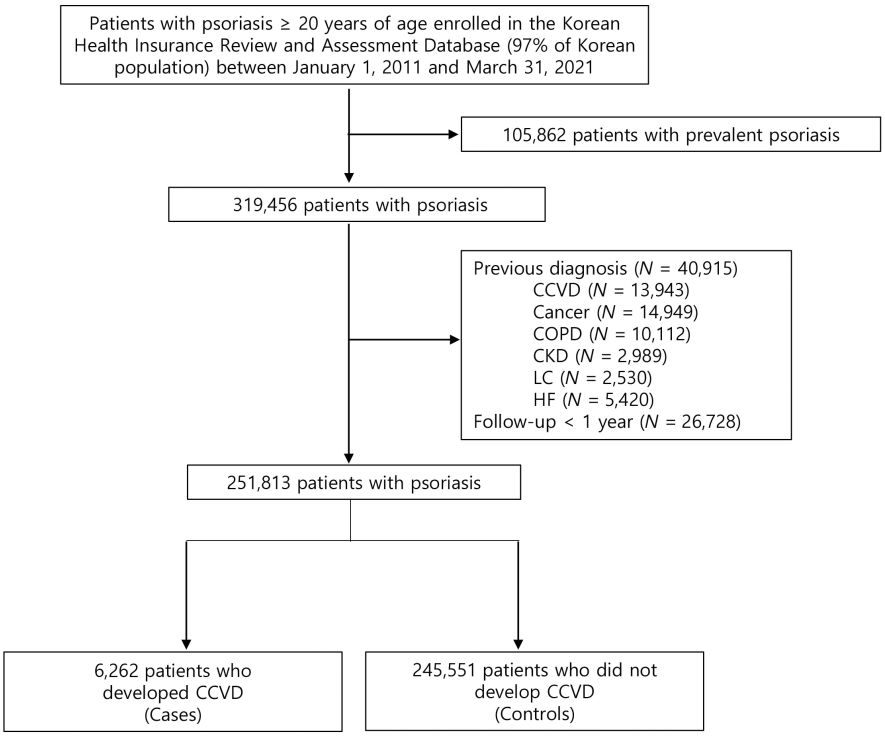

FIGURE 1 Study flow diagram outlining the selection of the study cohort. CCVD, cardio-cerebrovascular disease; CKD: chronic kidney disease; COPD, chronic obstructive pulmonary disease; HF, heart failure; LC, liver cirrhosis.

TABLE 1 Baseline demographics and characteristics of the study subjects ($N = 251\,813$).

Characteristics	CCVD group	Non-CCVD group	*P* value
Total number	6262	245 551	
Age, years	61.80 ± 12.79	45.45 ± 15.52	<0.001
20–29	53 (0.8)	44 577 (18.2)	<0.001
30–39	268 (4.3)	50 475 (20.6)	
40–49	779 (12.5)	51 544 (21.0)	
50–59	1499 (24.0)	51 549 (21.0)	
60–69	1694 (27.1)	29 233 (11.9)	
70–79	1545 (24.7)	14 565 (5.9)	
≥80	424 (1.7)	3608 (1.5)	
Sex			<0.001
Male	4190 (66.9)	136 390 (55.5)	
Female	2072 (33.1)	109 161 (44.5)	
Diabetes	1489 (23.8)	24 598 (10.0)	<0.001
Hypertension	2848 (45.5)	47 712 (19.4)	<0.001
Dyslipidemia	1901 (30.4)	52 520 (21.4)	<0.001
Median follow-up, years [IQR]	3.94 [2.32, 5.95]	5.81 [3.47, 8.05]	<0.001
Systemic anti-psoriatic therapy			
PTP of all systemic therapies, %	2.12 ± 7.92	2.64 ± 9.64	<0.001
PTP of conventional therapies, %	1.84 ± 6.74	2.11 ± 7.44	0.006
PTP of biologics, %	0.28 ± 3.62	0.54 ± 5.52	<0.001

Abbreviations: CCVD, cardio-cerebrovascular disease; IQR, interquartile range; PTP, proportion of treatment period with systemic antipsoriatic therapy during the study period.Data are presented as mean ± standard deviation or number (%).

for all systemic therapies and conventional and biologic antipsoriatic therapies of the CCVD group was lower than that of the non-CCVD group (CCVD vs. non-CCVD 2.12 ± 7.92 vs. 2.64 ± 9.64 for all systemic therapies, $P < 0.001$; 1.84 ± 6.74 vs. 2.11 ± 7.44 for conventional therapies, $P = 0.006$; 0.28 ± 3.62 vs. 0.54 ± 5.52 for biologics therapies, $P < 0.001$).

3.2 | PTP was negatively associated with CCVD risk in psoriasis patients

Since we found higher PTP in the non-CCVD group, suggesting that the non-CCVD group underwent more systemic antipsoriatic therapy than the CCVD group, we investigated the association between PTP and CCVD risk in psoriasis patients to determine the effect of systemic antipsoriatic therapy on CCVD risk (Table 2). In univariate logistic regression analysis, a greater PTP for all systemic therapies was associated with a reduced CCVD risk. A 10% increase in PTP decreased CCVD risk by 0.94 (95% CI 0.91–0.97). This negative association between PTP and CCVD risk was also significant after adjusting for age, sex, diabetes, hypertension, and dyslipidemia (adjusted OR 0.96, 95% CI 0.93–0.99).

Nonlinear regression analysis was used to further investigate the association between treatment duration for psoriasis and CCVD development. Nonlinear regression analysis demonstrated an inverse correlation between PTP and CCVD risk (Figure 2). Moreover, the inverse correlation was steady and consistent.

3.3 | Both conventional antipsoriatic therapy and biologics for psoriasis reduced CCVD risk in psoriasis patients

To evaluate the relationship between PTP and CCVD risk based on antipsoriatic therapy type, a subgroup analysis was performed in patients who had undergone systemic therapy for psoriasis during the observation period (Table 3). Evidently, the use of both conventional antipsoriatic therapy and biologics for psoriasis was negatively associated with CCVD risk. In logistic regression analysis, a greater PTP of conventional antipsoriatic therapy and biologics showed a reduced CCVD risk. A 10% increase in PTP decreased CCVD risk by 0.93 (95% CI 0.90–0.96) and 0.90 (95% CI 0.82–0.99) in conventional antipsoriatic therapies and biologics, respectively. Among the conventional antipsoriatic agents, the aOR of methotrexate was the lowest (aOR 0.79, 95% CI 0.62–0.99). Among biologics, interleukin-17A antagonist showed the lowest aOR, but without statistical significance (aOR 0.79, 95% CI 0.59–1.05).

3.4 | Sensitivity analysis

Our main finding of the negative association between PTP of all systemic antipsoriatic therapies and CCVD risk in psoriasis patients remained robust in the sensitivity analysis (Table 4). For the sensitivity analysis, we only investigated psoriasis patients who visited

TABLE 2 Impact of systemic antipsoriatic therapy duration on cardio-cerebrovascular risk in psoriasis patients ($N = 251\,813$).

	Crude OR (95% CI)	Adjusted OR (95% CI)[a]	*P* value (Wald's test)
PTP of all systemic therapies[b]	0.94 (0.91–0.97)	0.96 (0.93–0.99)	0.014
Age	1.07 (1.07–1.07)	1.07 (1.06–1.07)	<0.001
Sex	0.62 (0.59–0.65)	0.6 (0.57–0.63)	<0.001
Diabetes	2.8 (2.64–2.97)	1.24 (1.16–1.32)	<0.001
Hypertension	3.46 (3.29–3.64)	1.33 (1.26–1.42)	<0.001
Dyslipidemia	1.6 (1.52–1.69)	0.77 (0.73–0.82)	<0.001

Abbreviations: CI, confidence interval; OR, odds ratio; PTP, proportion of treatment period with systemic antipsoriatic therapy during the study period.

[a]Adjusted by age, sex, diabetes, hypertension, and dyslipidemia.

[b]OR for a 10% increase of PTP.

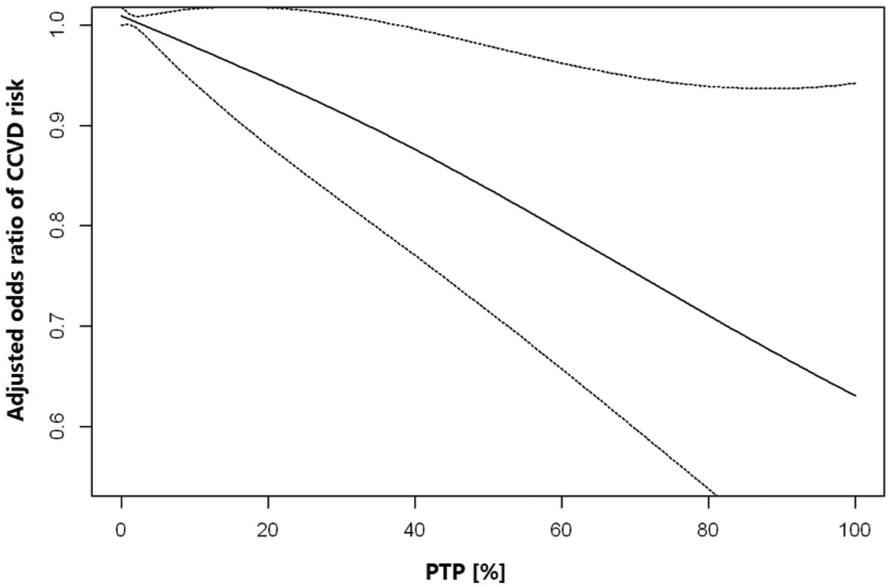

FIGURE 2 Association between PTP and adjusted odds ratio of CCVD risk with 95% confidence intervals. CCVD, cardio-cerebrovascular disease; PTP, proportion of treatment period with systemic antipsoriatic therapy during the study period.

medical institutes for two or more years among all patients. A total of 79 484 patients with psoriasis were enrolled, and 2076 patients with CCVD were identified. As shown in Table 4, a greater PTP of all systemic antipsoriatic therapies was related to a lower CCVD risk in the sensitivity analysis. A 10% increase in PTP reduced CCVD risk by 0.93 (95% CI 0.90–0.97). This negative association between PTP and CCVD risk was also significant after adjusting for age, sex, diabetes, hypertension, and dyslipidemia (aOR 0.96, 95% CI 0.92–1, $P = 0.029$).

4 | DISCUSSION

This nationwide nested case–control study with >250 000 participants revealed a negative association between systemic antipsoriatic therapy and CCVD risk in psoriasis patients. PTP during the observation period was significantly higher in psoriasis patients who did not have a CCVD event. Moreover, logistic regression analysis revealed that the PTP increase was inversely related to CCVD risk in psoriasis patients after adjusting for age, sex, diabetes, hypertension, and dyslipidemia, which was also evident in the nonlinear regression analysis. The results of our study provided evidence that systemic antipsoriatic therapy might reduce CCVD risk in psoriasis patients.

Several epidemiological studies reported increased incidence and prevalence of CCVD.[8,10,18] Moreover, psoriasis severity was associated with CCVD risk, with a higher CCVD risk in patients with severe disease.[9,10] Several mechanisms have been proposed to explain the increased incidence and prevalence of CCVDs in psoriasis patients. In this regard, inflammatory processes in psoriasis patients might not be limited to the skin but extend to systemic inflammatory conditions, and this chronic systemic inflammation can induce insulin resistance, endothelial dysfunction, and cardiovascular and cerebrovascular morbidities (termed the "psoriatic march").[1,8] Based on the presumed association between psoriasis and CCVD, several studies explored the effects of systemic antipsoriatic therapies on CCVD risk in psoriasis patients. Regarding conventional antipsoriatic agents, a few studies demonstrated the protective effect of methotrexate against CCVD development.[19,20] Moreover, some data indicated a cardioprotective effect of biologics in psoriasis patients.[13,21] Wu et al. found that anti-TNF-treated psoriasis patients

TABLE 3 Subgroup analysis of cardiocerebrovascular risk according to systemic antipsoriatic therapy types among psoriasis patients who had received systemic therapy.

PTP[a]	Crude OR (95% CI)	Adjusted OR (95% CI)[b]	*P* value (Wald's test)
All systemic therapies	0.94 (0.90–0.97)	0.93 (0.90–0.96)	<0.001
Conventional therapies	0.96 (0.91–1.00)	0.91 (0.87–0.95)	<0.001
Cyclosporine	1.00 (0.94–1.06)	0.94 (0.88–1.00)	0.049
Methotrexate	0.88 (0.71–1.08)	0.79 (0.62–0.99)	0.045
Oral retinoids	0.96 (0.89–1.02)	0.90 (0.84–0.97)	0.004
Biologics	0.93 (0.85–1.02)	0.90 (0.82–0.99)	0.031
TNF-α inhibitor	0.89 (0.75–1.05)	0.90 (0.75–1.07)	0.217
Anti-IL-12/23p40	0.98 (0.82–1.18)	0.95 (0.79–1.14)	0.553
Interleukin-17A antagonist	0.88 (0.68–1.14)	0.79 (0.59–1.05)	0.099
Interleukin-23 antagonist	0.95 (0.78–1.15)	0.88 (0.71–1.09)	0.241

Abbreviations: CI, confidence interval; OR, odds ratio; PTP, proportion of treatment period with systemic antipsoriatic therapy during the study period.

[a]OR for a 10% increase of PTP.

[b]Adjusted by age, sex, diabetes, hypertension, and dyslipidemia.

TABLE 4 Sensitivity analysis.

	Crude OR (95% CI)	Adjusted OR (95% CI)[a]	*P* value (Wald's test)
PTP of all systemic therapies[b]	0.93 (0.90–0.97)	0.96 (0.92–1)	0.029
Age	1.07 (1.07–1.07)	1.07 (1.06–1.07)	<0.001
Sex	0.62 (0.56–0.68)	0.58 (0.53–0.64)	<0.001
Diabetes	2.87 (2.59–3.19)	1.26 (1.12–1.41)	<0.001
Hypertension	3.43 (3.14–3.75)	1.33 (1.20–1.48)	<0.001
Dyslipidemia	1.68 (1.53–1.85)	0.81 (0.73–0.90)	<0.001

Abbreviations: CI, confidence interval; OR, odds ratio; PTP, proportion of treatment period with systemic antipsoriatic therapy during the study period.

[a]Adjusted by age, sex, diabetes, hypertension, and dyslipidemia.

[b]OR for a 10% increase of PTP.

had a decreased incidence of myocardial infarction as compared to those treated with only topical agents.[12] Despite the reported cardioprotective effects of a few treatment modalities for psoriasis in these studies, they had some limitations, including the enrollment of patients with rheumatoid arthritis as well as psoriasis patients,[19] the focus on the use of a single systemic antipsoriatic agent for a short treatment duration, or limited follow-up periods.[12,13,20,21] Considering real-world characteristics of psoriasis treatment, such as long-term treatment, rotational or sequential treatment using various treatment modalities, and intermittent treatment to avoid the side effects during long-term use of a single antipsoriatic treatment,[22–24] the cardioprotective effects of systemic antipsoriatic therapies in psoriasis patients can be properly investigated through an analysis that incorporates all systemic antipsoriatic therapies used in each patient. To examine the overall impact of systemic antipsoriatic therapy on CCVD development, we summed up the use of all systemic antipsoriatic treatments in each patient and analyzed the integrated effect of systemic antipsoriatic treatment on CCVD risk. Our results showed that PTP was significantly greater in psoriasis patients who did not experience a CCVD event. Moreover, multivariate logistic regression analysis adjusted for age, sex, and other comorbidities revealed a negative association between PTP and CCVD risk in psoriasis patients. Our results suggest a protective effect of systemic antipsoriatic treatment against CCVD development in psoriasis patients.

Regarding the adverse effects of long-term continuous use of conventional systemic antipsoriatic treatments, psoriatic patients cannot use systemic antipsoriatic therapy continuously, and physicians have devised treatment approaches, such as rotational or sequential treatment, to minimize the cumulative toxicity of the treatments.[22–24] Since conventional systemic antipsoriatic therapy is not continuous and the treatment duration of conventional systemic antipsoriatic therapy can vary among patients, it is important to consider the treatment duration when analyzing the effect of systemic antipsoriatic treatment on CCVD risk. By analyzing the association between PTP and CCVD risk, we showed that an increase in antipsoriatic treatment duration over the entire observation period was negatively associated with CCVD risk in psoriasis patients. Moreover, a nonlinear regression analysis demonstrated an inverse relationship between the PTP of all systemic antipsoriatic therapies

and CCVD risks in psoriasis patients. Our results of negative associations between PTP and CCVD risk implied that long-term control of psoriasis can decrease CCVD development in psoriasis patients. Moreover, our results also supported the beneficial effect of continuous treatment in reducing the CCVD risk. In this regard, long-term sustained control of psoriasis could reduce the cumulative effect of systemic inflammation observed in psoriasis patients.[15]

Previous studies compared the cardioprotective effects of various systemic antipsoriatic therapies to determine the appropriate treatment modality for psoriasis patients. Tsai et al. performed a head-to-head comparison between methotrexate and retinoid in CCVD risk and reported that methotrexate was associated with a reduced CCVD risk as compared to retinoid.[20] Additionally, recent studies showed a cardioprotective effect of biologics in psoriasis patients. Hong et al. reported a lower cardiovascular risk in patients who received biologics as compared to those who were treated with other antipsoriatic therapies.[13] Other studies also found a cardioprotective effect of anti-TNF therapy in psoriasis patients.[12,21] The results of our study were consistent with these previous findings as the reduction in risk by methotrexate was the greatest, followed by those of retinoid and cyclosporine in conventional systemic antipsoriatic treatment modalities. We also observed a decreased CCVD risk after treatment with biologics in psoriasis patients.

Our study had several advantages that deserve consideration. First, we investigated the integrated effects of various systemic antipsoriatic treatment modalities on CCVD development. Considering the characteristics of systemic antipsoriatic therapies, such as rotational and sequential approaches, the effect of systemic antipsoriatic therapies on CCVD development can be properly assessed by summing the effect of all types of systemic antipsoriatic therapies on each patient. Using the HIRA database, we calculated the use of systemic antipsoriatic therapies for each patient and investigated the integrated effect of systemic antipsoriatic therapies on CCVD development. Furthermore, as psoriasis is a chronic disease with no cure, systemic antipsoriatic therapy duration could affect CCVD risk. By adding all treatment durations of systemic antipsoriatic therapies for each patient, we investigated the effects of the cumulative duration of systemic antipsoriatic therapies on CCVD development and found that CCVD risk was lower in patients treated with systemic antipsoriatic treatment for longer periods. These results were clinically important for psoriasis management to prevent CCVD development and, to the best of our knowledge, no study has previously addressed this issue.

Interestingly, we found that the likelihood of developing CCVD in patients with psoriasis was less in women than in men, and in those with dyslipidemia compared to those without dyslipidemia. In Korea, since men are associated with more severe psoriasis than women,[25] it is assumed that the risk of psoriasis-related CCVD in men would be higher than that in women. As for dyslipidemia in psoriasis patients and the risk of CCVD, since dyslipidemia is a well-known risk factor for CCVD, it is unclear whether our results, which indicate a reduced risk of CCVD in psoriasis patients with dyslipidemia, are related to the characteristics of the Korean population or to the effect of lipid-lowering drugs used for dyslipidemia.

The following limitations of this study should be acknowledged. First, the identification of patients with psoriasis using International Classification of Diseases, tenth Revision (ICD-10) codes could be erroneous. To minimize misdiagnosis, we defined psoriasis patients as those with a diagnosis code for psoriasis at least twice a year. Additionally, we performed a sensitivity analysis by enrolling psoriasis patients who visited medical institutes for 2 or more years, and the association between PTP and CCVD risk in psoriasis patients remained robust. Second, since we obtained the data from the HIRA, we could not include determinants such as psoriasis severity and disease type (such as psoriatic arthritis, erythroderma, etc.) in the analysis despite previous studies revealing an increased risk of CCVD in severe patients and patients with psoriatic arthritis.[26] Moreover, we also could not include several important CCVD-related information, including family history, body mass index, smoking, alcohol consumption, and exercise habits, in the analysis. Third, certain clinical characteristics of the patient could influence the selection of treatment modalities for psoriasis. To overcome confounding factors, we obtained baseline comorbidities, such as diabetes, hypertension, and dyslipidemia, and included these comorbidities in the multivariable logistic regression analysis. Furthermore, we excluded patients diagnosed with cancer, chronic obstructive pulmonary disease, chronic kidney disease, liver cirrhosis, or heart failure to minimize the risk of these confounding variables. Lastly, because the use of biologics for psoriasis treatment has recently been approved and the requirement for insurance coverage for biologics is strict in Korea, this study could not include a sufficient number of cases to analyze the relationship between each biologic and CCVD risk.

In conclusion, we found that systemic antipsoriatic therapy was inversely associated with the risk of developing CCVDs in psoriasis patients. Furthermore, as antipsoriatic therapy duration increased, CCVD risk in psoriasis patients decreased. Our findings suggested that effective and long-term continuous control of psoriasis could lower CCVD risk in psoriasis patients.

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CONFLICT OF INTEREST STATEMENT

The authors have no conflict of interest to declare.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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