Incidence rates of comorbidities among patients with psoriasis in the United States

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Abstract

Psoriasis is associated with a substantial burden of comorbidities; however, incidence rates (IRs) of these comorbidities following psoriasis diagnosis are not well characterized. Using administrative claims data from the Truven Health Analytics MarketScan Commercial and Medicare Supplemental Databases between January 1, 2002 and September 30, 2015, we compared the incidence of newly diagnosed comorbidities among patients with psoriasis versus demographically matched (birth year, gender, and geographic region) control patients without psoriasis in the United States. Comorbidities of interest were identified using ICD-9-CM codes. A total of 114,824 matched pairs of patients with psoriasis and control patients were included. IRs of all selected comorbidities were significantly higher among patients with psoriasis compared with controls ($P<0.05$). The most common newly diagnosed comorbidities in both groups were hyperlipidemia (psoriasis versus control, IR per 1,000 patient-years, 127.5 versus 102.8) and hypertension (94.3 versus 80.6). The greatest differences in IRs between patients with psoriasis and controls were observed for rheumatoid arthritis (9.7 versus 3.1; IR ratio [IRR], 3.15) and psoriatic arthritis (24.0 versus 0.2; IRR, 151.57). In this real-world study, patients with psoriasis were more likely to develop new selected comorbidities after diagnosis compared with demographically matched patients without psoriasis.

Keywords: administrative claims data, comorbidity, incidence rate, psoriasis, psoriatic arthritis, rheumatoid arthritis

Introduction

Psoriasis is a chronic, immune-mediated disease that affects approximately 7.4 million adults (2%-4%) in the United States, with men and women affected at approximately equal rates [1, 2]. Patients with psoriasis can experience significant physical, psychosocial, and economic health burdens that negatively impact their health-related quality of life [3-6].

Psoriasis is a disease associated with adverse conditions in multiple body systems beyond the skin [5, 7]. The abnormal immune response that promotes the clinical manifestations of psoriasis includes increased activity of T cells, B cells, antigen-presenting cells, and T helper 17 cell–related cytokines [1]. This aberrant immune function causes systemic inflammation that may lead to other comorbidities, resulting in an increased prevalence of comorbidities in patients with psoriasis compared with the general population [8]; alternatively, patients with comorbidities driven by similar mechanisms of inflammation, such as obesity, may predispose patients to psoriasis [9]. Whether due to genetics, inflammation, or the effect of the disease on patient lifestyle, patients with psoriasis have an increased risk of comorbidities compared with the general population [3, 5, 7]. An estimated 6% to 42% of patients with psoriasis develop psoriatic arthritis, which can lead to joint damage and disability [1, 10, 11]. Psoriasis has also been shown to be associated with a higher prevalence of cardiovascular disease, malignancy, metabolic syndrome, and other autoimmune diseases [3, 7, 12-18]. Additionally,

patients with psoriasis may develop mental health conditions, such as depression and anxiety [19].

Owing to the common inflammatory mechanisms shared by psoriasis and many associated comorbidities, therapies that target the underlying inflammation may treat both psoriasis and comorbidities [9, 20]. When treatments are chosen for patients with psoriasis, specific comorbidities should be considered because these conditions may affect disease activity, response to treatment, and costs to patients [9]. Some treatment options may affect the likelihood of developing comorbidities or the options for management of comorbidities [20]. For example, patients with psoriasis treated with methotrexate have a lower risk of vascular disease compared with those receiving other therapies [21]; however, methotrexate is contraindicated in patients with hepatic impairment [22, 23]. Obesity can reduce the response to treatment with biologics, particularly those administered at fixed doses rather than based on body weight [20, 24].

While psoriasis is associated with higher prevalence rates of comorbidities [3, 5], there are limited data on the incidence rates (IRs) of comorbidities in U.S. patients with psoriasis. A prospective analysis of the Nurses' Health Study II, which included a cohort of 116,671 U.S. female nurses, demonstrated that women with psoriasis had significantly higher risks of developing diabetes and hypertension over 14 years of follow-up than those without psoriasis [25]. Among the 1,813 women with psoriasis enrolled in the study, 3.3% developed incident diabetes and 21.3% developed incident hypertension compared with 2.0% and 20.1%, respectively, of those without psoriasis. Similarly, in a pooled analysis of 184,395 U.S. women and men enrolled in the Nurses' Health Study (1996-2008), the Nurses' Health Study II (1991-2007), and the Health Professionals' Follow-Up Study (1986-2006), patients with psoriasis aged<60 years had a 26% increased risk of developing incident type 2 diabetes compared with those without psoriasis (relative risk, 1.26 [95% CI, 1.08-1.46]), [26].

The objective of this retrospective observational study was to examine the incidence of newly diagnosed comorbidities among patients with psoriasis compared with matched control patients without psoriasis in the United States using healthcare claims data.

Methods

Data Source

This retrospective, observational cohort study used US administrative claims data from January 1, 2000, to September 30, 2015, obtained from the Truven Health Analytics MarketScan Commercial and Medicare Supplemental Databases. These databases contain inpatient, outpatient, and outpatient prescription drug experiences of patients covered under a variety of health plans. The MarketScan Commercial Claims and Encounters Database includes data from employees and their dependents with employer-sponsored private health insurance. The Medicare Supplemental Database includes data from retirees with employer-sponsored Medicare supplemental insurance and comprises the Medicare-covered portion of payment, the employer-paid portion, and patient out-of-pocket patient expenses. The databases include all pharmacy fills with positive health plan payment or patient copayment; written prescriptions that are not filled are not included in the claims database. Demographic and diagnosis data, prescribing physician specialty, insurance plan type, copayment, charges, and reimbursed amount are recorded at the time the prescription is filled.

Study Design and Patient Selection

Patients with ≥ one International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) code for psoriasis (696.1) were identified from the Truven Health Analytics MarketScan Commercial and Medicare Supplemental Databases. Claims for laboratory, pathology, or radiology services were not used to identify individuals with psoriasis because their use could incorrectly identify individuals as having psoriasis based on the reason for testing (e.g., screening) rather than the test results; therefore, claims for laboratory, pathology, or radiology services associated with psoriasis diagnosis were ignored during patient selection, and these diagnoses were termed non–rule-out psoriasis. Patients eligible for inclusion had ≥1 inpatient or ≥2 non–rule-out diagnoses for psoriasis ≥30 days apart

but within 365 days from January 1, 2002, to September 30, 2015. The first occurrence of non–rule-out psoriasis diagnosis (ICD-9-CM code 696.1) was defined as the index diagnosis, and the date of the index diagnosis was defined as the index date. Patients included in the analyses were enrolled in the Commercial or Medicare Supplemental Database with medical and pharmacy benefits for ≥24 months before the index date (pre-index period) and were ≥20 years of age at the index date (to ensure that all patients were ≥18 years old during 24-month pre-index period).

Patients with psoriasis were matched 1:1 to control patients on birth year, gender, and geographic location. Control patients were assigned the same index date as the matched patient with psoriasis. Eligible control patients were those without a diagnosis of psoriasis during the study period (January 1, 2002, to September 30, 2015) who were aged ≥20 years at the index date and enrolled in the Commercial or Medicare Supplemental Database for ≥24 months before the index date. Both patients with psoriasis and matched controls were followed until loss of follow-up, end of enrollment, or end of study.

Study Variables and Outcomes

Patient characteristics were recorded at the index date and included age, gender, geographic region of residence, insurance type, calendar year of index date, and Deyo-Charlson Comorbidity Index score. Comorbidities of interest were selected based on expert opinion and previous psoriasis studies, and were identified using ICD-9-CM codes (**Table 1**), [3, 5-7, 13, 27-29]. Selected comorbidities of interest included hypertension, hyperlipidemia, diabetes mellitus, obesity, depression, anxiety, coronary heart disease, cerebrovascular disease (stroke), peripheral vascular disease, multiple sclerosis, Crohn disease or ulcerative colitis, rheumatoid arthritis, psoriatic arthritis, other autoimmune disorders, lymphoma, skin cancer, and other malignancies. The prevalence of comorbidities of interest during the 24-month

Table 1: *ICD-9-CM codes for identification of comorbidities of interest.*

Comorbidity	ICD-9-CM Codes
Hypertension	401-404
Hyperlipidemia	272.0-272.4
Diabetes mellitus	250
Obesity	278.0
Depression	296.2, 296.3, 298.0, 300.4, 309.1, 311
Anxiety	300.0
Coronary heart disease	410-414
Cerebrovascular disease	430-438
Peripheral vascular disease	440, 441, 443, 447.1, 557.1, 557.9, V43.3
Multiple sclerosis	340
Crohn disease or ulcerative colitis	555-556
Rheumatoid arthritis	714.0
Psoriatic arthritis	696.0
Other autoimmune disorders	255.4 (Addison disease), 446.5 (giant cell arteritis), 515, 516.31 (pulmonary fibrosis), 579.0 (celiac disease), 582 (chronic glomerulonephritis), 704.01 (alopecia areata), 708 (chronic urticaria), 709.01 (vitiligo), 710.0 (systemic lupus erythematosus), 710.1 (systemic sclerosis), 710.2 (Sjögren syndrome)
Lymphoma	200.0-200.7, 202.1, 202.2, 202.7 (non-Hodgkin lymphoma), 201.0-201.9 (Hodgkin lymphoma)
Skin cancer	172 (melanoma skin cancer), 173 (non-melanoma skin cancer)
Other malignancies	146, 155, 156, 157, 162, 174, 184.4, 187, 189 (cancers of the pharynx, liver, bladder, pancreas, lung, breast, vulva, penis, and kidney)

ICD-9-CM, International Classification of Diseases, Ninth Revision, Clinical Modification.

pre-index period was determined for both groups, and patients with an existing comorbidity of interest were excluded from further analysis for development of that comorbidity. The first event of the newly diagnosed comorbidity of interest with ICD-9-CM code (**Table 1**) was used to define the incidence of that comorbidity.

Statistical Analyses

Patient characteristics and the prevalence of comorbidities during the 24-month pre-index period were examined using descriptive statistics. Continuous variables were summarized using means with SDs; categorical variables were summarized using frequency counts and percentages. IRs were calculated as the number of patients newly diagnosed with the comorbidity of interest after psoriasis diagnosis divided by the total observation time (in years) and reported as incidence per 1,000 patient-years. The observation time was the time from the index date to the first diagnosis of the comorbidity of interest or the end of follow-up for patients not diagnosed with the comorbidity of interest. Time to first diagnosis was evaluated separately for each comorbidity of interest, so that diagnosis with one comorbidity of interest did not exclude patients from the analyses for other comorbidities of interest. The IRs of comorbidities of interest newly diagnosed during the follow-up period were determined for both groups and compared descriptively between patients with psoriasis and control patients with IR ratios (IRRs). IRRs were calculated as IR among patients with psoriasis divided by IR among matched controls. The 95% CIs for IRs per 1,000 patient-years and IRRs were calculated based on Poisson distribution for each comorbidity. Cox proportional hazards models were used to assess the difference in the risk of having a comorbidity between patients with psoriasis and control patients; hazard ratios (HRs) were adjusted for baseline Deyo-Charlson Comorbidity Index score, index year, and insurance plan type. Patients with a

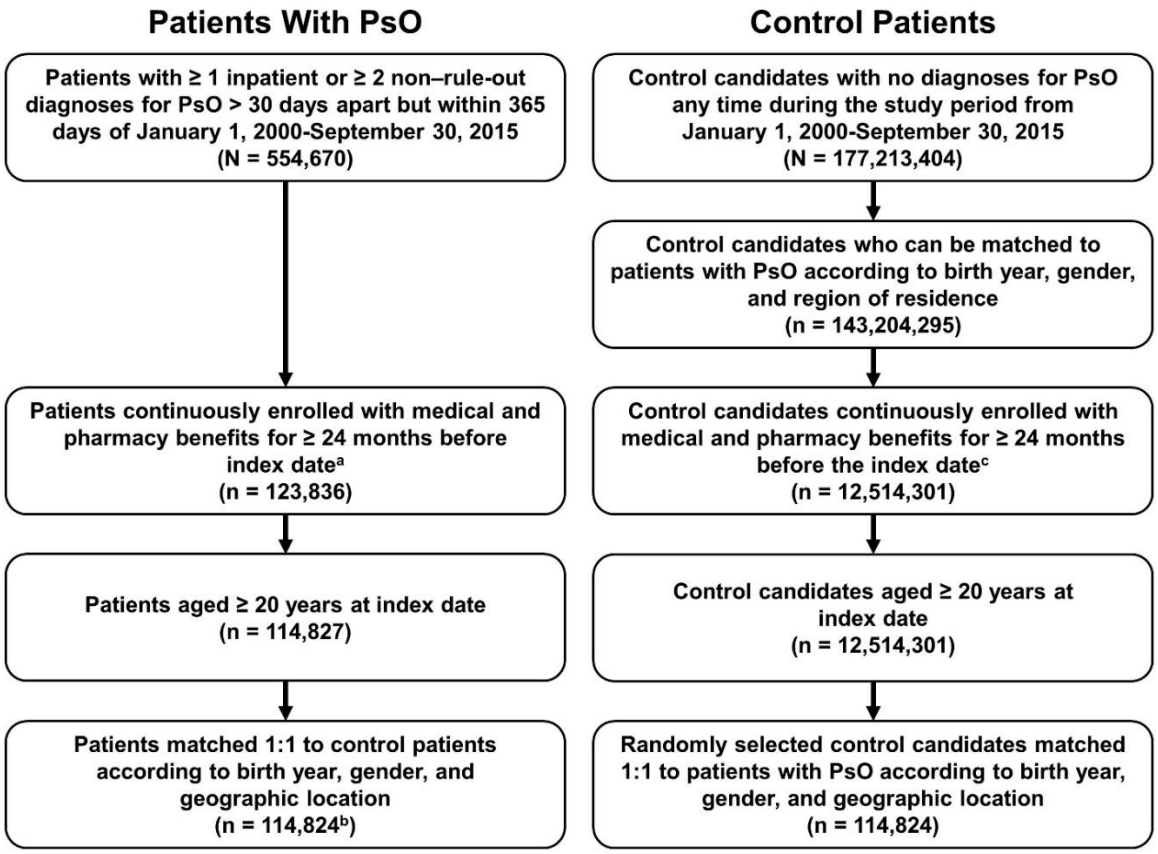

Figure 1. *Selection of study cohorts. [a]The index date was the date of the first psoriasis diagnosis. [b]Three patients with psoriasis could not be matched to control patients. [c]Control patients were assigned the same index date as the matched patients with psoriasis. PsO, psoriasis.*

comorbidity of interest in the 24-month pre-index period were excluded from analyses of IRs, IRRs, and HRs for that comorbidity of interest; ie, only individuals at risk for each comorbidity were included in the analyses. Unadjusted time to first event analyses were performed using Kaplan-Meier estimates.

Results

Patient Characteristics at Index Date

Table 2. *Patient characteristics at the index date.*

Patient Characteristics	Patients With PsO (N = 114,824)	Control Patients (N = 114,824)
Age, years, mean (SD)	53 (15)	53 (15)
Age group, n (%)		
20-34	13,242 (11.5)	13,242 (11.5)
35-44	17,536 (15.3)	17,536 (15.3)
45-54	27,563 (24.0)	27,563 (24.0)
55-64	33,210 (28.9)	33,210 (28.9)
≥ 65	23,273 (20.3)	23,273 (20.3)
Gender, n (%)		
Male	53,001 (46.2)	53,001 (46.2)
Female	61,823 (53.8)	61,823 (53.8)
Region, n (%)		
Northeast	19,049 (16.6)	19,049 (16.6)
North Central	32,078 (27.9)	32,078 (27.9)
South	41,949 (36.5)	41,949 (36.5)
West	20,918 (18.2)	20,918 (18.2)
Unknown	830 (0.7)	830 (0.7)
Plan type, n (%)[a]		
Fee for service	89,335 (77.8)	92,278 (80.4)
HMO and POS capitation	21,716 (18.9)	20,522 (17.9)
Unknown	3,773 (3.3)	2,024 (1.8)
Year of index date, n (%)		
2002	5,131 (4.5)	5,131 (4.5)
2003	4,177 (3.6)	4,177 (3.6)
2004	4,903 (4.3)	4,903 (4.3)
2005	5,916 (5.2)	5,916 (5.2)
2006	7,131 (6.2)	7,131 (6.2)
2007	7,615 (6.6)	7,615 (6.6)
2008	8,344 (7.3)	8,344 (7.3)
2009	9,647 (8.4)	9,647 (8.4)
2010	11,941 (10.4)	11,941 (10.4)
2011	12,094 (10.5)	12,094 (10.5)
2012	12,082 (10.5)	12,082 (10.5)
2013	10,537 (9.2)	10,537 (9.2)
2014	10,379 (9.0)	10,379 (9.0)
2015	4,927 (4.3)	4,927 (4.3)
Deyo-Charlson Comorbidity Index score, mean (SD)[a]	0.9 (1.6)	0.8 (1.5)
Duration of follow-up, days, mean (SD)[a]	1,276 (1,049)	1,164 (1,039)

[a]*P*<0.001.
HMO, health maintenance organization; POS, point of service; PsO, psoriasis.

A total of 114,824 eligible patients with psoriasis were identified. Of the 12,514,301 patients without psoriasis eligible for the control cohort, 114,824 were randomly selected and matched 1:1 with patients with psoriasis by birth year, gender, and geographic location. Thus, 114,824 patients with psoriasis and 114,824 matched control patients without psoriasis were included in the analyses (**Figure 1**).

Demographics were comparable between patients with psoriasis and control patients (**Table 2**). The mean age was 53 years, 53.8% of patients were female, and more than one-third of patients (36.5%) were from the Southern region of the United States. The majority of patients in both groups had fee-for-service insurance plans (patients with psoriasis, 77.8%; control patients, 80.4%). The mean duration of follow-up was 1,276 days in the psoriasis group and 1,164 days in the control group.

Patients with psoriasis had a higher mean Deyo-Charlson Comorbidity Index score at the index date compared with control patients (mean [SD], 0.9 [1.6] versus 0.8 [1.5]; $P<0.001$), (**Table 2**). The most common comorbidities among both patient groups during the 24-month pre-index period were hypertension, hyperlipidemia, and diabetes (patients with psoriasis, 39.7%, 38.7%, and 15.5%, respectively; control patients, 33.7%, 32.7%, and 12.8%, respectively; **Table 2**). The proportion of patients with a comorbidity of interest during the 24-month pre-index period was higher ($P<0.001$) among patients with psoriasis than control patients for all comorbidities except other malignancies (**Table 3**). Of note, 5.2% of patients with psoriasis had psoriatic arthritis compared with 0.1% of control patients.

Incidence of Comorbidities During Follow-Up Period

Incidence rates of newly diagnosed comorbidities including cardiovascular and metabolic diseases, autoimmune conditions, depression, anxiety, skin cancer, and lymphoma were significantly ($P<0.05$) higher among patients with psoriasis compared with

Table 3. *Prevalence of comorbidities of interest during the 24-month pre-index period*

Comorbidity, n (%)	Patients with PsO (N = 114,824)	Control Patients (N = 114,824)
Metabolic		
Hypertension[a]	45,637 (39.7)	38,752 (33.7)
Hyperlipidemia[a]	44,489 (38.7)	37,526 (32.7)
Diabetes mellitus[a]	17,796 (15.5)	14,738 (12.8)
Obesity[a]	7,598 (6.6)	5,069 (4.4)
Mental Health		
Depression[a]	11,718 (10.2)	8,788 (7.7)
Anxiety[a]	8,507 (7.4)	6,602 (5.7)
Cardiovascular		
Coronary heart disease[a]	12,288 (10.7)	9,986 (8.7)
Cerebrovascular disease[a]	6,908 (6.0)	5,677 (4.9)
Peripheral vascular disease[a]	5,981 (5.2)	4,483 (3.9)
Autoimmune		
Multiple sclerosis[b]	479 (0.4)	388 (0.3)
Crohn's disease or ulcerative colitis[a]	1,897 (1.7)	898 (0.8)
Rheumatoid arthritis[a]	3,930 (3.4)	1,294 (1.1)
Psoriatic arthritis[a]	5,932 (5.2)	66 (0.1)
Other autoimmune disorder[a]	5,671 (5.1)	3,959 (3.4)
Cancer		
Lymphoma[a]	461 (0.4)	204 (0.2)
Skin cancer[a]	5,859 (5.1)	3,959 (3.4)
Other malignancy	2,773 (2.4)	2,616 (2.3)

[a]$P<0.001$; [b]$P<0.05$; PsO, psoriasis.

controls in both unadjusted and adjusted models. The most common newly diagnosed comorbidities during the follow-up period in both groups were hyperlipidemia and hypertension (patients with psoriasis: IR per 1,000 patient-years=127.5 and 94.3, respectively; control patients: IR per 1,000 patient-years=102.8 and 80.6, respectively), (**Table 4**). The greatest differences in IRs between patients with psoriasis and control patients were observed for rheumatoid arthritis and psoriatic arthritis. Patients with psoriasis had an IR of rheumatoid arthritis approximately 3× higher than control patients (IR per 1,000 patient-years=9.7 versus 3.1; IRR=3.15). The IR of psoriatic arthritis among patients with psoriasis was approximately 150× higher than that of control patients (IR per 1,000 patient-years=24.0 versus 0.2; IRR=151.57).

Adjustment for baseline Deyo-Charlson Comorbidity Index score, index year, and insurance plan type resulted in similar outcomes. Patients with psoriasis were significantly ($P<0.05$) more likely to develop all comorbidities of interest, with the exception of other malignancies, during the follow-up period compared with control patients (**Figure 2**). The HRs (95% CI) for developing rheumatoid arthritis or psoriatic arthritis were 3.13 (2.93 to 3.35) and 151.86 (117.33 to 196.55), respectively, in patients with psoriasis versus control patients (**Figure 2**). Unadjusted time to first event analyses for patients with psoriasis and matched controls were also performed and were consistent with our other findings (data not shown).

Discussion

With data from a large U.S. administrative claims database, this retrospective observational study

Table 4. Incidence of newly diagnosed comorbidities of interest during the follow-up period.

Comorbidity, n (%)	Patients With PsO[a]	Matched Control Patients[a]	IRR (95% CI)[b]
Metabolic			
Hypertension	94.3 (93.0-95.7)	80.6 (79.4-81.9)	1.17 (1.15-1.19)[c]
Hyperlipidemia	127.5 (125.9-129.1)	102.8 (101.4-104.2)	1.24 (1.22-1.26)[c]
Diabetes mellitus	30.9 (30.3-31.5)	23.7 (23.2-24.3)	1.30 (1.26-1.34)[c]
Obesity	33.1 (32.5-33.7)	24.1 (23.6-24.7)	1.37 (1.33-1.41)[c]
Mental Health			
Depression	33.3 (32.7-33.9)	24.9 (24.3-25.4)	1.34 (1.30-1.38)[c]
Anxiety	32.3 (31.7-32.9)	25.1 (24.6-25.7)	1.28 (1.25-1.32)[c]
Cardiovascular			
Coronary heart disease	28.4 (27.8-29.0)	23.3 (22.8-23.8)	1.22 (1.18-1.25)[c]
Cerebrovascular disease	27.3 (26.7-27.8)	23.6 (23.1-24.1)	1.16 (1.12-1.19)[c]
Peripheral vascular disease	25.6 (25.1-26.1)	20.2 (19.8-20.7)	1.27 (1.23-1.30)[c]
Autoimmune			
Multiple sclerosis	0.7 (0.6-0.8)	0.5 (0.5-0.6)	1.34 (1.12-1.61)[c]
Crohn's disease or ulcerative colitis	3.2 (3.0-3.3)	1.9 (1.8-2.1)	1.64 (1.49-1.80)[c]
Rheumatoid arthritis	9.7 (9.4-10.0)	3.1 (2.9-3.3)	3.15 (2.95-3.37)[c]
Psoriatic arthritis	24.0 (23.5-24.5)	0.2 (0.1-0.2)	151.57 (117.09-196.21)[c]
Other autoimmune disorder	19.7 (19.2-20.1)	11.8 (11.5-12.2)	1.66 (1.60-1.72)[c]
Cancer			
Lymphoma	1.4 (1.3-1.5)	0.7 (0.6-0.8)	1.97 (1.70-2.28)[c]
Skin cancer	20.1 (19.6-20.5)	15.2 (14.8-15.6)	1.32 (1.28-1.37)[c]
Other malignancy	7.4 (7.1-7.6)	6.9 (6.6-7.2)	1.07 (1.01-1.12)[c]

[a]Patients with the comorbidity of interest during the 24-month pre-index period were excluded from the analysis. [b]Patients with PsO vs matched control patients.[c]$P<0.05$.
IR, incidence rate; IRR, incidence rate ratio; PsO, psoriasis.

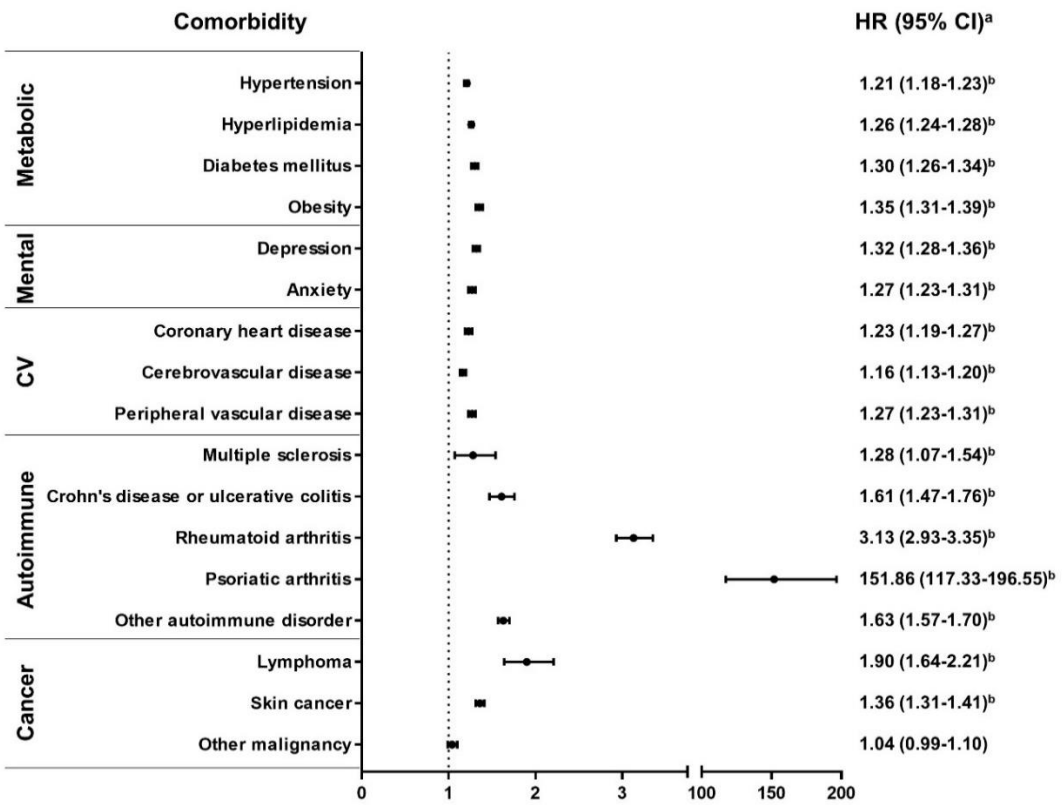

Figure 2. *Hazard ratios for developing comorbidities of interest during follow-up in patients with psoriasis versus controls. * P<0.05. [a]Adjusted for baseline Deyo-Charlson Comorbidity Index score, index year, and insurance plan type. Patients with the comorbidity of interest in the 24-month pre-index period were excluded from the analysis. CV, cardiovascular; HR, hazard ratio; PsO, psoriasis.*

demonstrated that patients with psoriasis were more likely to have a medical claim with an incident diagnosis of selected comorbidities compared with matched control patients without psoriasis. Patients with psoriasis had higher IRs of hypertension, hyperlipidemia, diabetes mellitus, obesity, depression, anxiety, coronary heart disease, cerebrovascular disease, peripheral vascular disease, multiple sclerosis, Crohn disease or ulcerative colitis, rheumatoid arthritis, psoriatic arthritis, other autoimmune disorders, lymphoma, skin cancer, and other malignancies during follow-up compared with control patients. The greatest differences in IRs between patients with psoriasis and controls were observed for psoriatic arthritis (24.0 versus 0.2; IRR, 151.57) and rheumatoid arthritis (9.7 versus 3.1; IRR, 3.15).

Psoriatic arthritis is a common immune-mediated comorbidity associated with psoriasis. Psoriatic arthritis is an inflammatory arthritis that results in joint destruction and deformity, reduced functional status and quality of life, and increased risk of death [11]. An estimated 6% to 42% of patients with psoriasis also have psoriatic arthritis, with most patients developing arthritis approximately 8 to 10 years after the onset of psoriasis [1, 10, 11, 30]. In our study, psoriatic arthritis was identified during the pre-index period in approximately 5% of patients eventually diagnosed with psoriasis compared with 0.1% of control patients. After the index date (i.e., after psoriasis diagnosis), the IR of newly diagnosed psoriatic arthritis among patients with psoriasis in our study population was 24.0/1,000 patient-years, approximately 150× greater than that among matched control patients. However, this IR may be low due to underreporting of psoriatic arthritis in claims data and a mean duration of follow-up in this study of 4 years after diagnosis of psoriasis. Prior studies suggest that 10% to 40% of patients with psoriasis have undiagnosed psoriatic arthritis [31-33]. A delay in psoriatic arthritis diagnosis of 6 months can lead to peripheral joint damage and functional disability [34]. Early diagnosis and treatment are therefore critical to improve patient outcomes. Screening for psoriatic arthritis sooner

after the diagnosis of psoriasis may lead to earlier identification of psoriatic arthritis, thereby allowing earlier treatment and prevention of joint damage and disability.

The IRs of cardiovascular and metabolic comorbidities in our study are consistent with results of previous population-based studies comparing the risk of these comorbidities in patients with psoriasis with that of patients without psoriasis. Large cohort studies in the United Kingdom and the United States found that patients with psoriasis had higher prevalence rates of diabetes, obesity, and coronary heart disease compared with their respective control populations [17, 35]. Similarly, patients eventually diagnosed with psoriasis in our study had higher prevalence rates of diabetes, obesity, and coronary heart disease, as well as other coronary and metabolic comorbidities, in the 24-month pre-index period compared with control patients. Multiple studies using data from the U.K. General Practice Research Database have shown higher incidence rates of diabetes and risk factors for cardiovascular disease, including hypertension, hyperlipidemia, obesity, and peripheral vascular disease, among patients with psoriasis compared with control patients [36, 37]. Additionally, analyses of the U.S.-based Nurses' Health Study, Nurses' Health Study II, and Health Professionals' Follow-Up Study found that patients with psoriasis have greater IRs of diabetes and hypertension than those without psoriasis [25, 26]. Consistent with these observations, patients diagnosed with psoriasis in our study were more likely to develop diabetes (HR=1.30), hypertension (HR=1.21), hyperlipidemia (HR=1.26), obesity (HR=1.35), and peripheral vascular disease (HR=1.27) after diagnosis of psoriasis compared with matched control patients with the same index date.

Prior administrative database studies found that hyperlipidemia and hypertension were the most prevalent comorbidities among a general population of patients with psoriasis (27% and 25%, respectively), [5] and among patients with moderate to severe psoriasis (33% for both), [3]. In our study, hyperlipidemia and hypertension were the most common newly diagnosed comorbidities during follow-up in patients with psoriasis, and patients with psoriasis were more likely to develop hyperlipidemia and hypertension after psoriasis diagnosis compared with matched control patients with the same index date (HR=1.26 and 1.21, respectively; $P<0.05$).

In addition to psoriatic arthritis and cardiovascular and metabolic comorbidities, patients with psoriasis have an increased risk of other comorbidities compared with those without psoriasis. Large cohort studies previously conducted in the United States and Europe showed that patients with psoriasis had higher prevalence rates of skin cancer, lymphoma, depression, and autoimmune comorbidities compared with patients without psoriasis [3, 14, 18, 19]. Consistent with these studies, patients eventually diagnosed with psoriasis in our study had higher prevalence rates of skin cancer, lymphoma, depression, and autoimmune comorbidities, including rheumatoid arthritis and Crohn disease, prior to index compared with control patients. Population-based cohort studies using data from the U.K. General Practice Research Database showed that patients with psoriasis in the United Kingdom were more likely to develop incident depression (HR=1.39), anxiety (HR=1.31), and lymphoma (HR=1.35) than matched patients without psoriasis [38, 39]. Similarly, patients with psoriasis in our study were more likely to develop depression (HR=1.32), anxiety (HR=1.27), and lymphoma (HR=1.90) during follow-up than matched controls. In a nationwide cohort study in Denmark, patients with mild or severe psoriasis had higher incidence rates of multiple sclerosis than those without psoriasis (mild: IRR=1.84; severe: IRR=2.61), [40]. Patients with psoriasis in our study also had a higher IR of multiple sclerosis than those without psoriasis (IRR=1.34).

Limitations

This study is subject to the general limitations of retrospective studies based on healthcare claims data, such as possible coding errors or omissions of claims. For example, comorbidities were identified using administrative ICD-9-CM codes, which may have resulted in inaccurate capture of medical conditions due to undercoding, upcoding, or miscoding, leading to classification bias in comorbidities identified in the pre-index period or in

follow-up IRs. Thus, follow-up IRs of comorbidities of interest in the study population may be underestimated. Additionally, the IRs of some comorbidities may not be stable over time; for such comorbidities, the IRs may be biased due to the slightly longer follow-up time in the psoriasis cohort compared with the control cohort (42 versus 38 months, respectively). Furthermore, limiting the pre-index period to 24 months did not allow capture of full medical history; patients may have had the comorbidity of interest before the start of the pre-index period, leading to bias in the IRs during follow-up. The study population only included patients with commercial and Medicare supplemental insurance; thus, results may not be generalizable to all patients with psoriasis, particularly those with Medicaid, other types of insurance, or no insurance. Also, the databases did not capture potential confounding factors such as race/ethnicity or body mass index. Patients with psoriasis may have had more frequent healthcare utilization (e.g., office, emergency room, or hospitalization visits) during the pre-index or follow-up periods compared with the control patients, which could have contributed to the higher prevalence of comorbidities during the pre-index period or higher IRs of comorbidities during follow-up. Lastly, causality of comorbidities was not examined in this study; the IRs of new-onset comorbidities does not imply whether psoriasis has a causal relationship to the comorbidities of interest.

Conclusion

Using data from a U.S. administrative healthcare claims database, this study suggested that patients with psoriasis were more likely to develop metabolic, cardiovascular, autoimmune, depression/anxiety, and cancer-related comorbidities compared with demographically matched control patients. In addition, patients with psoriasis were more likely to develop new comorbidities after diagnosis compared with patients without psoriasis. Patients with psoriasis were 150× more likely to be newly diagnosed with psoriatic arthritis and 3× more likely to be newly diagnosed with rheumatoid arthritis compared with control patients. Further studies are needed to assess the impact of patient demographic and clinical characteristics and the effects of psoriasis treatment on the incidence of comorbidities after onset or diagnosis of psoriasis. The results of this study provide insight into the IRs of comorbidities in patients with psoriasis compared with those without psoriasis in U.S. clinical practice.

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