Psoriasis and risk of diabetes-associated microvascular and macrovascular complications

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Background: Psoriasis's effect on diabetes onset is well documented, but its effect on course of diabetes is poorly understood.

Objective: We sought to compare risks of developing microvascular and macrovascular complications between diabetic patients with and without psoriasis.

Methods: Adults with 2 or more diabetes diagnoses selected from MarketScan databases (Truven Health Analytics Inc, Ann Arbor, MI) (2000-2006) were classified into 2 cohorts: 2 or more psoriasis diagnoses and without psoriasis diagnosis. Patients with psoriasis were matched using propensity score, and exactly matched using age, sex, and diabetes characteristics with patients without psoriasis. Outcomes were compared between cohorts using Cox regression models.

Results: In all, 6164 diabetic patients with psoriasis (27% moderate to severe) were matched to 6164 diabetic patients without psoriasis. Patients with psoriasis were significantly more likely to develop microvascular events than patients without psoriasis overall (hazard ratio [HR] 1.14, $P < .001$) and by psoriasis severity (mild: HR 1.13, $P = .004$; moderate to severe: HR 1.16, $P = .038$). Risk of macrovascular events was higher for patients without psoriasis overall (HR 1.13, $P = .001$) and those with mild psoriasis (HR 1.15, $P = .003$), but not for moderate to severe cases (HR 1.10, $P = .210$).

Limitations: Psoriasis to diabetes association may be underestimated.

Conclusion: Among diabetic patients, psoriasis is generally associated with higher rates of microvascular and macrovascular complications. Greater psoriasis severity did not increase risk of diabetic complications. (J Am Acad Dermatol 2015;72:968-77.)

Key words: complications; diabetes; inflammation; macrovascular; microvascular; observational study; psoriasis.

Recent studies have begun to explicate the role inflammation plays in the pathogenesis of chronic diseases such as psoriasis[1] and diabetes.[2] For psoriasis, advancements in understanding immune pathogenesis have led to the development of biologics that inhibit pathologic pathways in the innate[3-5] and adaptive[6] immune systems. Shared immunologic mechanisms may underlie

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epidemiologic observations that patients with psoriasis are at risk for developing other immune-mediated diseases (eg, diabetes).[7] Comparatively, individuals with psoriasis are more likely to have diabetes[8-10] and to develop new-onset diabetes.[11,12] One class of biologics, the tumor necrosis factor (TNF) inhibitors, not only improves psoriasis but decreases the risk of new-onset diabetes among treated patients.[13,14] Possible explanations for the reduced risk of new-onset diabetes in patients with psoriasis treated with TNF inhibitors include either a direct effect of TNF inhibitors on diabetes onset and/or a psoriasis-mediated indirect effect.

CAPSULE SUMMARY

- Patients with psoriasis and those with diabetes have both been shown to have an increased risk of developing vascular complications.
- In this study, we provide epidemiologic evidence for an increased risk of microvascular and macrovascular complications among patients having both diabetes and psoriasis compared with patients having diabetes only, without psoriasis.
- More aggressive screening for diabetic complications may be needed in diabetic patients with psoriasis.

In the pathogenesis of type 2 diabetes, inflammation is thought to arise from metabolic stress through several mechanisms.[15-18] These metabolic stresses activate proinflammatory TNF and interleukin (IL)-1 pathways, including the nuclear factor-$_k$B pathway. However, although IL-1[19] and nuclear factor-$_k$B[20] inhibitors have been shown to improve B-cell function and glucose control in preliminary human studies, TNF inhibitors seem to exert these effects only among patients with specific inflammatory disorders such as psoriasis or rheumatoid arthritis,[21,22] but not in patients from the general population.[23] Furthermore, inflammation from metabolic stress also plays a role in the pathogenesis of microvascular complications of diabetes, such as retinopathy,[24] neuropathy,[25] and nephropathy,[26] and the pathogenesis of macrovascular complications.[27] It is not well understood what impact psoriatic inflammation has in the development of these complications, but a recent study showing that patients with psoriasis have more difficulty managing hypertension than patients without psoriasis supports the hypothesis that psoriasis may have an inflammation-mediated effect on the progression of metabolic and cardiovascular diseases.[28]

To investigate the hypothesis that psoriatic inflammation plays a role in the pathogenesis of diabetic microvascular and macrovascular complications, we compared the risk of developing these complications in diabetic patients with and without psoriasis using a large administrative database with coverage in all US census regions.

METHODS

Data source

The study sample was derived from Truven Health MarketScan Research Databases[29] that include data for approximately 25 million individuals annually, covered by more than 130 health plans and self-insured employers (January 1, 2000, to December 31, 2006). The data comprise service-level claims for inpatient services, outpatient services, outpatient prescriptions, enrollment history, and demographic information for US patients with primary or Medicare supplemental coverage through privately insured health plans.

Sample selection

Enrollees were included if the diabetes sample if they had 2 or more diagnoses for diabetes (*International Classification of Diseases, Ninth Revision, Clinical Modification*: 250.xx) over the 7-year observation period. Within the diabetes sample, we retained 2 patient cohorts: (1) the psoriasis cohort, which included patients with 2 or more diagnoses for psoriasis (*International Classification of Diseases, Ninth Revision, Clinical Modification* 696.1x) during the observation period, and (2) the cohort without psoriasis, which included patients without any psoriasis diagnosis during the observation period. To be included in the final sample, patients in the psoriasis cohort also had to be age 18 years or older and have 1 or more eligible index dates, ie, a diabetes claim date that: (1) was preceded by a diagnosis of psoriasis, and (2) was preceded by 6 months or longer and followed by 12 months or longer of continuous eligibility in their health plan. Among eligible patients with psoriasis, we selected randomly a unique index date to ensure representation of patients with various disease durations and severity.

Matching

Patients in the psoriasis cohort were matched with patients in the cohort without psoriasis based on propensity score, and age, gender, diabetes duration, prior use of diabetes medication, and prior microvascular and macrovascular events. Propensity scores were estimated using a multivariable logistic