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Psoriasis risk in patients with type 2 diabetes in German primary care practices

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ABSTRACT

Aim: To analyze psoriasis risk in type 2 diabetes mellitus (T2DM) patients treated in German primary care practices.

Methods: The study included 87,964 T2DM patients aged 40 years or over who received their initial diabetes diagnosis between 2004 and 2013. Patients were excluded if they had been diagnosed with psoriasis prior to diabetes diagnosis or if the observation period prior to the index date was less than 365 days. After applying these exclusion criteria, 72,148 T2DM patients were included. A total of 72,148 non-diabetic controls were matched (1:1) to T2DM cases based on age, gender, type of health insurance (private or statutory), number of medical visits, and index date. The primary outcome was the diagnosis of psoriasis. Skin infections, dermatitis/eczema, hyperlipidemia, and medications associated with psoriasis (beta blockers, angiotensin-converting enzyme (ACE) inhibitors, lithium, antimalarials, nonsteroidal anti-inflammatory drugs, and benzodiazepines) were included as potential confounders.

Results: The mean age was 68.7 years (SD = 12.7 years) and 48.6% of subjects were men. Hyperlipidemia, dermatitis/eczema, and skin infections were more frequent in T2DM patients than in controls. Beta blockers, ACE inhibitors, and nonsteroidal anti-inflammatory drugs were also more commonly used in people with T2DM than in controls. A total of 3.4% of T2DM patients and 2.8% of matched controls developed psoriasis within ten years of follow-up (p-value <0.001). T2DM patients were at a higher risk of developing psoriasis than controls (HR = 1.18, 95% CI: 1.08–1.29).

Conclusion: T2DM was positively associated with psoriasis in patients treated in German primary care practices.

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1. Introduction

Approximately 422 million people worldwide are affected by diabetes [1]. This chronic condition is predicted to become the seventh global leading cause of death by 2030. In Germany, around one in every 13 persons has diabetes [2]. In the past decades, overweight, obesity, and an unhealthy diet have become more frequent in European countries, resulting in an increase of the prevalence of diabetes and indirectly in an increase of the related health burden. As a matter of fact, diabetes can favor the development of other diseases, complicate the treatment/management of co-occurring disorders, and impair patients' quality of life [3–5].

The association between diabetes and psoriasis has been known for several years [6–9]. In 2007, Shapiro and colleagues found that the age-adjusted proportion of diabetes was significantly higher in psoriasis patients compared to controls in 46,095 psoriasis patients and 1,579,037 controls [6]. Cohen et al. subsequently corroborated these results and showed that psoriasis increased the risk of developing diabetes (OR = 1.38, p-value <0.05) [7]. More recently, a meta-analysis including 27 observational studies found that both mild and severe psoriasis increased the odds of being diagnosed with diabetes (ORs equal to 1.53 and 1.97, respectively) [9]. The hypothesis to explain such findings maintains that psoriasis notably involves a persistent secretion of tumor necrosis factor-alpha (TNF-α), leading to chronic inflammation precipitating diabetes [7].

Although the causal relation between psoriasis and diabetes is clearly described in the literature, little is known about the potential impact of diabetes on psoriasis. Thus, the goal of the present study was to analyze psoriasis risk in type 2 diabetes mellitus (T2DM) patients treated in primary care practices in Germany.

2. Methods

2.1. Database

The Disease Analyzer database (IMS HEALTH) compiles drug prescriptions, diagnoses, basic medical and demographic data obtained directly and in anonymous format from computer systems used in the practices of general practitioners [10]. Diagnoses (ICD-10), prescriptions (Anatomical Therapeutic Chemical (ATC) classification system), and the quality of reported data are monitored by IMS based on a number of criteria (e.g., completeness of documentation, linkage between diagnoses and prescriptions).

In Germany, the sampling methods used for the selection of physicians' practices were appropriate to obtain a representative database of primary care practices [10]. Prescription statistics for several drugs were very similar to data available from pharmaceutical prescription reports [10]. The age groups for given diagnoses in the Disease Analyzer database corresponded well with those in relevant disease registries [10]. Finally, this database has been already used in several studies focusing on T2DM [11–13].

2.2. Study population

The current study sample included 87,964 T2DM patients aged 40 years or over from 1250 practices who received their initial diabetes diagnosis during the index period (January 2004–December 2013). Follow-up lasted until December 2015. Patients were excluded if they had been diagnosed with psoriasis (ICD-10: L40, L41) prior to diabetes diagnosis (index date). In order to guarantee the accuracy of the diagnoses, patients with a previous observation period of less than 365 days were excluded. After applying these exclusion criteria, 72,148 T2DM patients were included in the study. There were 5,888,987 primary care patients without any diabetes diagnosis or antidiabetic prescriptions during the index period. After applying similar exclusion criteria, 4,506,658 non-diabetic patients were eligible to be included in the present investigation. Finally, 72,148 non-diabetic controls were matched (1:1) to T2DM cases based on age (in years), gender, type of health insurance (private or statutory), number of primary care physician visits, and index date. In the control group, a random date (visit) was selected and designated the index date, again ensuring that the observation period prior to the index date covered at least 365 days. When more than one matching partner was available in the control group for a diabetes patient in the case group, one of these controls was randomly selected.

2.3. Study outcome

The primary outcome was the diagnosis of psoriasis (ICD-10: L40, 41) recorded in the database between the index date and the end of follow-up. Skin infections (ICD 10: L00-08), dermatitis and eczema (L20-30), hyperlipidemia (E78, which indirectly reflects obesity), and medications associated with psoriasis [14] (beta blockers (ATC: C07), angiotensin-converting enzyme (ACE) inhibitors (C09A, C09B), lithium (N06A3), antimalarials (P01B), nonsteroidal anti-inflammatory drugs (M01A), and benzodiazepines (N05C0)) were included as potential confounders. These diagnoses and prescriptions were to be documented within 12 months prior to the index date. Interferons, terbinafine, and lithium also associated with psoriasis were found to be taken by less than 1% of patients and not included in the analyses.

2.4. Statistical methods

Descriptive analyses were obtained for all demographic and clinical variables using paired t-tests, Wilcoxon-tests for paired samples, or McNemar's tests. Psoriasis-free survival analyses were carried out using product-limit methods. Log-rank tests were performed to compare T2DM patients and nondiabetic controls. Cox proportional hazards models (dependent variable: incident psoriasis) were used to adjust for confounders. Cox regressions were performed for patients as a whole and then separately for patients in the age groups $\leq$70 and >70 years, men, women, and patients with and without dermatitis/eczema. p-values <0.05 were considered as statistically significant. The analyses were carried out using SAS version 9.3.

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