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ORIGINAL ARTICLE

Is psoriasis an independent risk factor of renal disease? A nationwide retrospective cohort study from 1996 to 2010

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ABSTRACT

Background: Psoriasis is a chronic inflammatory disease that affects the skin, joints, and cardiovascular system. Although a potential association of end-stage renal disease (ESRD) with psoriasis has been demonstrated in patients, the potential for the use of cyclosporin in these patients for the modulation of the course of ESRD remains doubted. Furthermore, the association between psoriasis and renal diseases in general remains unclear. This study aimed to investigate the risk of renal disease in psoriatic patients with or without the use of cyclosporin.

Methods: We performed a retrospective cohort study using the National Health Insurance Database of Taiwan from 1996 to 2010 to identify patients with psoriasis, renal disease, chronic renal failure, and ESRD, and the use of cyclosporin. Overall, 3502 psoriatic patients and 10,506 matched population comparisons were identified. The hazard ratios (HRs) for renal events during the follow-up period were computed.

Results: Patients with psoriasis had an increased risk of chronic renal failure [HR = 3.00; 95% confidence interval (CI), 2.30–3.93; $p < 0.0001$] and ESRD (HR = 2.03; 95% CI, 1.04–3.96; $p = 0.0393$). Cyclosporin increased the risk of renal disease in patients without psoriasis (HR = 6.34; 95% CI, 3.57–11.26; $p < 0.0001$), but not in patients with psoriasis (HR = 1.33; 95% CI = 0.66–2.69; $p = 0.4299$).

Conclusion: Psoriasis is an independent risk factor of chronic renal failure and ESRD. Cyclosporin, a commonly used antipsoriatic agent, does not significantly increase the risk of renal disease in patients with psoriasis. Further studies with larger sample size are indicated to validate this result.

Introduction

Psoriasis is a chronic inflammatory disease that affects not only the skin but also joints. Psoriasis is often associated with psychosocial burden that impairs patients' quality of life.[1,2] The etiology of psoriasis has not been fully elucidated, but a growing body of literature has indicated that psoriasis is highly related to dysregulated immune response.[3] In the past two decades, the development of biologics targeting specific immune molecules has led to dramatic advancements in therapeutics.[4,5] More specifically, the Th17 signaling pathway, which is polarized by interleukin (IL)-23, is critical in the development and maintenance of psoriasis.[6] Aberrant

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T cell polarization and abnormalities in the activation of chemokines and chemokine receptors might also play significant roles in the pathogenesis of psoriasis.[7,8] IL-23 recruits chemokine receptor 6 (CCR6)-expressing Th17, and CCR6 is essential for initiation of psoriatic lesions in the mouse model.[9]

Psoriasis has been associated with an increased risk of certain malignancies, cardiovascular diseases, and autoimmune diseases (e.g., ulcerative colitis). Moreover, population-based studies have suggested a relationship between psoriasis and metabolic syndrome.[10,11] A recent meta-analysis revealed that the pooled odds ratio for metabolic syndrome among patients with psoriasis was 2.26 [95% confidence interval (CI), 1.70–3.01] compared with the general population.[12] Epidemiologic studies also showed that psoriasis is associated with morbidity of circulatory diseases, including myocardial infarction, coronary artery disease, peripheral artery disease and stroke.[13] Taken together, psoriasis is a systemic disease involving more than merely the skin. As a disease with chronic inflammation status, psoriasis confers the risk of other diseases associated with chronic inflammation, including malignancies and atherosclerosis.

Risk factors for kidney failure include the use of nephrotoxic drugs [e.g., nonsteroidal anti-inflammatory drugs (NSAIDs)], concomitant hypertension, diabetes mellitus, lupus erythematosus, intrinsic renal parenchyma and vascular diseases. Among these risk factors, hypertension and diabetes mellitus have also been associated with psoriasis. The possible association of psoriasis with chronic renal disease corresponds with the finding that antipsoriatic biologic agents may induce autoimmune renal disorders.[14] In addition, the Th17 immune response, which is increased in psoriatic lesions, also plays an important role in renal inflammatory diseases, including lupus nephritis[15] and antiglomerular basement membrane glomerulonephritis.[16,17] An increasing body of data indicates that the chemokine receptor CCR6 recruits Th17 cells and participates in the pathogenesis of psoriasis[9] and glomerulonephritis.[18] For the reasons cited above, it is worthwhile to investigate the prevalence of renal disease in patients with psoriasis.

Cyclosporin is commonly used to treat moderate to severe psoriasis. However, renal function impairment is one of the adverse effects of cyclosporin. It is unclear whether cyclosporin use modifies the risk of renal disease in psoriasis patients. The aims of the present study were to investigate whether psoriasis is associated with renal disease, and whether the use of cyclosporin increases the risk of renal disease in psoriatic patients in a nationwide cohort in Taiwan.

Methods

Data source

In 1995, Taiwan launched the compulsory National Health Insurance (NHI) program, which covers 99% of the Taiwanese population.[19] The National Health Insurance Research Database (NHIRD) is a research database that includes data from the NHI program. The International Classification of Diseases, 9th revision, Clinical Modification (ICD-9-CM) was used to record diagnoses in the NHIRD. Based on registration files and claim data from hospitals, general practices, and community pharmacies, NHIRD is classified into specific data subsets for different research purposes. More than 1000 peer-reviewed publications used NHIRD as a data source (http://nhird.nhri.org.tw/talk_07.php). The NHIRD ensure enrollees' confidentiality through assigning an anonymous code to each enrollee. For the present study, we used the Longitudinal Health Insurance Database 2010 (LHID2010), which is a subset of data from NHIRD and contains longitudinal data of 1,000,000 enrollees randomly sampled from 2010. This study was approved by the Institutional Review Board (IRB) of the Kaohsiung Medical University Hospital, Kaohsiung, Taiwan.

Study cohort

We analyzed the 1-million-strong cohort of the LHID2010 database. We identified people older than 20 years who were still alive on December 31, 2010 (birth prior to January 1, 1990). The study cohort (psoriatic patients) was composed of enrollees diagnosed with psoriasis or psoriatic arthritis during the period from January 1, 1996 through December 31, 2010, whereas the population comparisons (nonpsoriatic patients) consist of enrollees who had not been diagnosed with psoriasis or psoriatic arthritis. The index date of psoriasis group was the date of first psoriasis diagnosis, whereas the index date of population comparisons was January 1, 1996. Follow-up ended at diagnosis with renal disease or on December 31, 2010.

The patient ascertainment was made based on the ICD-9-CM codes. In this database, patient diagnoses were coded according to the ICD-9-CM. Psoriatic patients were defined as enrollees with ICD-9-CM codes 696.0, 696.1, and 696.8. These codes have been used in psoriasis studies using NHIRD.[19–21] We excluded patients with these codes a maximum of three times during the study period. We also excluded patients who were diagnosed with renal disease before psoriasis was diagnosed. Finally, we identified 3502 psoriatic patients. For the population comparisons, we identified 10,506 individuals with a ratio of 1:3 by using propensity score to match age, age categories, and sex. The algorithm of patient selection is shown in Figure 1.

Construction of variables

The primary outcome of interest was renal disease, whereas the secondary outcomes were chronic renal failure and end-stage renal disease (ESRD). Renal disease was defined as ICD-9-CM codes 403.01, 403.11, 403.91, 404.02, 404.03, 404.12, 404.13, 404.92, 404.93, 582.x, 583.0–583.7, 585.x, 586.x, 588.0, V42.0, V45.1, and V56.x.[22] These ICD-9-CM codes include hypertensive kidney disease, chronic glomerulonephritis, nephritis and nephropathy, chronic kidney disease (CKD), and renal dialysis. Chronic renal failure was defined as ICD-9-CM code 585.x. For ESRD, the ICD-9-CM code 585.x was considered with concurrent use of hemodialysis or continuous ambulatory peritoneal dialysis defined by NHI administration codes D8 and D9, respectively.

Candidate predictors of renal disease and chronic renal failure included age and sex as well as comorbidities, including hypertension (ICD-9-CM code 401–405), diabetes mellitus (ICD-9-CM code 250.x), hyperlipidemia (ICD-9-CM code 272.x), and circulatory disease [ischemic heart disease (ICD-9-CM code 410-414) and cerebrovascular disease (ICD-9-CM code 430–438)]. The reliability of using these codes for comorbidities has been documented in previous studies.[19,23] Comorbidities were ascertained from ICD-9-CM codes with at least more than three diagnoses documented during the study period. We also considered use of cyclosporin during study period as a potential predictor.

Statistical analysis

We performed a propensity analysis using logistic regression to obtain a propensity score for each patient with the covariates, including age, age categories, and sex. It has been shown that a sample match on propensity score will be similar for all the covariates that went into computing the propensity score. Thus, matching on the propensity score can reduce the selection bias in

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