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Review Article

Psoriasis and risk of chronic kidney disease: a meta-analysis

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Abstract: The association of psoriasis and renal disease remains controversial. We conducted this meta-analysis to determine the association between psoriasis and risk of chronic kidney disease (CKD) or end-stage renal disease (ESRD). PubMed and Embase were searched for observational studies published up to May 2017. Both retrospective and prospective studies that reported risk estimate of incident CKD or ESRD for patients with psoriasis versus participants without psoriasis. Four observational studies were included in the final analysis. Meta-analysis showed that psoriasis was associated with an increased risk of CKD (hazard ratio [HR]=1.14; 95% confidence interval [CI]=1.03-1.26) but not ESRD (HR=1.14; 95% CI=0.92-1.42). Subgroup analysis indicated that severe psoriasis significantly increased both CKD (HR=1.73; 95% CI=1.36-2.21) and ESRD (HR=3.25; 95% CI=2.04-5.18). However, mild psoriasis was not associated with an increased risk of CKD (HR=1.09; 95% CI=0.91-1.30) and ESRD (HR=0.94; 95% CI=0.73-1.20). This meta-analysis confirms that patients with severe psoriasis but not mild psoriasis have an increased risk of CKD or ESRD. Screening for renal disease in psoriatic patients may be warranted.

Keywords: Psoriasis, chronic kidney disease, end-stage renal disease, meta-analysis

Introduction

Psoriasis is a chronic inflammatory skin disorder characterized by relapsing thick scaling plaques [1]. The estimated prevalence of psoriasis ranged from 0.51% to 11.43% in the adult population [2]. Apart from negatively affect the quality of life, patients with psoriasis may increase the risk of comorbid diseases, such as diabetes mellitus, Crohn's disease, cancer, depression, non-alcoholic fatty liver disease, metabolic syndrome, and cardiovascular diseases [3]. Chronic kidney disease (CKD) and end-stage renal disease (ESRD) have become a global health burden [4]. Recent epidemiological studies have also linked psoriasis to renal disease [5]. The risk of renal disease was increased in psoriatic patients and particularly in those with severe psoriasis [6]. However, individual studies on the association of psoriasis with subsequent risk of CKD or ESRD have yielded inconsistent results.

To our knowledge, no previous meta-analysis has been performed to investigate the association of psoriasis with CKD or ESRD risk. This meta-analysis aimed to investigate whether psoriasis is independently associated with an increased risk of CKD or ESRD.

Materials and methods

Search strategy

We searched PubMed and Embase databases for eligible studies published from inception to May 2017. Search terms were "psoriasis" OR "psoriatic arthritis" AND "chronic kidney disease" OR "end-stage renal disease" OR "renal disease" OR "renal insufficiency". In addition, we scanned the reference lists of the included articles and relevant reviews to identify additional possible studies. This study was conducted in accordance with the recommendations of the Meta-Analysis of observational studies in epidemiology [7].

Study selection

Studies were considered eligible if they satisfied the following inclusion criteria: 1) studies of

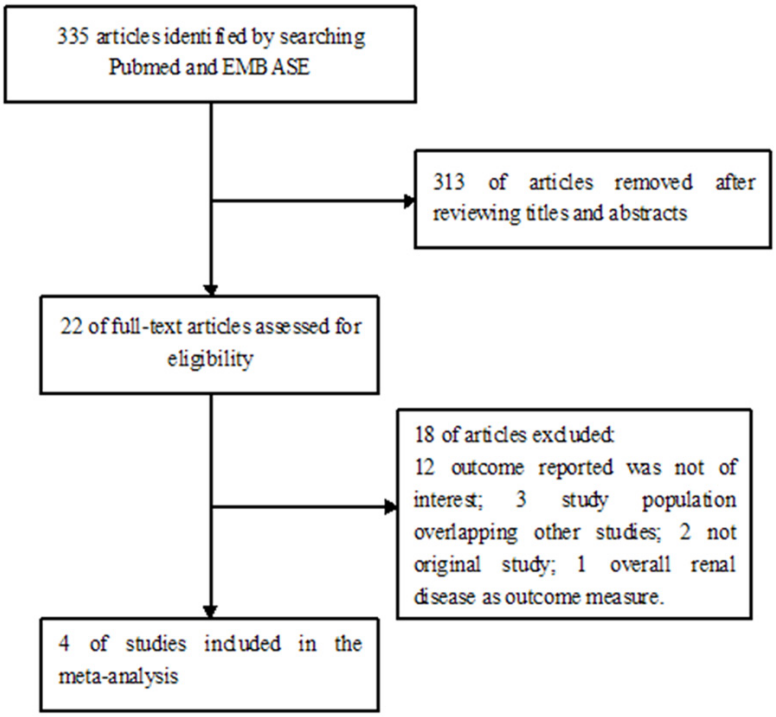

Figure 1. Flow chart showing the process for study selection.

observational design; 2) evaluation of the association between psoriasis and subsequent risk of CKD or ESRD; and 3) report of at least age adjusted risk ratio (RR) or hazard ratio (HR) with their corresponding 95% confidence interval (CI) of renal disease comparing with or without psoriasis. CKD was defined by a relevant diagnostic code and/or having an estimated glomerular filtration rate consistent with chronic renal disease. The definition of ESRD was by a relevant diagnostic code and/or undergoing dialysis. Severe psoriasis was defined as receiving systemic antipsoriatic treatment consistent with severe disease. Exclusion criteria were: 1) the study population overlapping other studies; 2) they did not provide the risk estimate of the association; and 3) conference abstracts, unpublished studies, or comments.

Data extraction and quality assessment

To ensure the accuracy, two authors independently retrieved data from included articles and performed quality assessment. Any discrepancy was resolved by discussion. The following data were abstracted: first author's last name, year published, study design, geographic origin of study, sample size, percentage of male, mean age or age range, severity of psoriasis, CKD/ESRD diagnosis, maximally adjusted HR with corresponding 95% CI, follow-up duration, and statistical adjustments for confounding factors. Methodological quality of included studies was evaluated using a 9-star Newcastle-Ottawa Scale (NOS) [8]. It is categorized into three items including selection of the study participants, comparability, and outcome measure. Studies with NOS score ≥7 were categorized as high quality.

Data analyses

Data analysis was performed using Stata software 12.0 (Statacorp, College Station, TX, USA). HR was used as a summary measure of the association of psoriasis with risk of CKD or ESRD. Heterogeneity in pooling risk estimates was tested using the I^2 statistic and Cochran's Q test. An I^2 statistic value <50% or Cochran's Q test of $p<0.05$ was considered statistically significant heterogeneity. In case of significant heterogeneity, we used a random effect model to pool risk summary. Otherwise, a fixed-effect model was applied. Potential publication bias was explored by Egger's test and Begg's test. Sensitivity analysis by removing individual study in turn was performed to test the stability of the pooling risk estimate.

Results

Search results and study characteristics

We identified 335 potentially relevant articles from the initial literature search. After reading the titles and abstracts, we retrieve 22 articles for detailed assessment. After reviewing the full-text articles, we further removed 22 studies with various reasons. Thus, only 4 studies [9-12] met our inclusion criteria and included in the final meta-analysis (**Figure 1**). The characteristics of the included studies are summarized in **Table 1**. This meta-analysis included 201,383 patients with psoriasis and 1, 833, 275 controls. The sample size of individual

Table 1. Basic characteristic of the included studies

Author/year	Region	Study design	Participants (% male)	Age (years)	Number/severity of psoriasis	Outcome ascertainment	No.CKD events HR (95% CI)	No.ESRD events HR (95% CI)	Follow-up (years)	Adjustments for confounding factors	Overall NOS
Wan et al. 2013 [9]	UK	Prospective cohort study	833,585 (45.9%)	18-90	Mild:136,529 Severe: 7,354	ICD code and/or eGFR	CKD:61,689 1.05 (1.02-1.07) Total 0.99 (0.97-1.02) Mild 1.93 (1.79-2.08) Severe	ESRD:NR 1.15 (0.84-1.58) Total 0.98 (0.69-1.38) Mild 4.15 (1.70-10.11) Severe	5.23	Age, sex, CVD, DM, hyperlipidemia, hypertension, and use of NSAIDs	8
Chi et al. 2015 [10]	Taiwan	Retrospective study	926,987 (49.49%)	33.9±19.8	Mild: 4,180; Severe:453	ICD-9 code	CKD:36,779 1.10 (0.95-1.29) Total 1.01 (0.85-1.19) Mild; 1.90 (1.33-2.70) Severe	ESRD:9,537 1.14 (0.85-1.53) Total 0.90 (0.64-1.29) Mild 2.97 (1.72-5.11) Severe	5.87	Age, gender, CVD, DM, hypertension, hyperlipidemia, gout, and use of NSAIDs ≥1 month	7
Chiu et al. 2015 [11]	Taiwan	Retrospective cohort study	17,376 (55.2%)	45.4±17.7	Mild: 3, 947; Severe: 397	ICD-9 code	CKD: 1,359 1.28 (1.14-1.44) Total 1.30 (1.14-1.46) Mild; 1.24 (0.85-1.81) Severe	—	5	Age, gender, DM, hypertension, hyperlipidemia, heart disease, NSAIDs use, and frequency of outpatient visits in 3 year	7
Parisi et al. 2015 [12]	USA	Retrospective cohort study	256,710 (43.6%)	Median age 47-48	Mild: 46,439 Severe: 2,084	ICD code	CKD:11,909 1.18 (1.07-1.31) Total	—	5.2	Age, gender, depression, calendar year, smoking, BMI, and socioeconomic status	7

Abbreviations: HR, hazard ratio; CI, confidence interval; DM, diabetes mellitus; BMI, body mass index; eGFR, estimated glomerular filtration rate; CVD, cardiovascular diseases; ESRD, end stage renal disease; NSAIDs, nonsteroidal anti-inflammatory drugs.

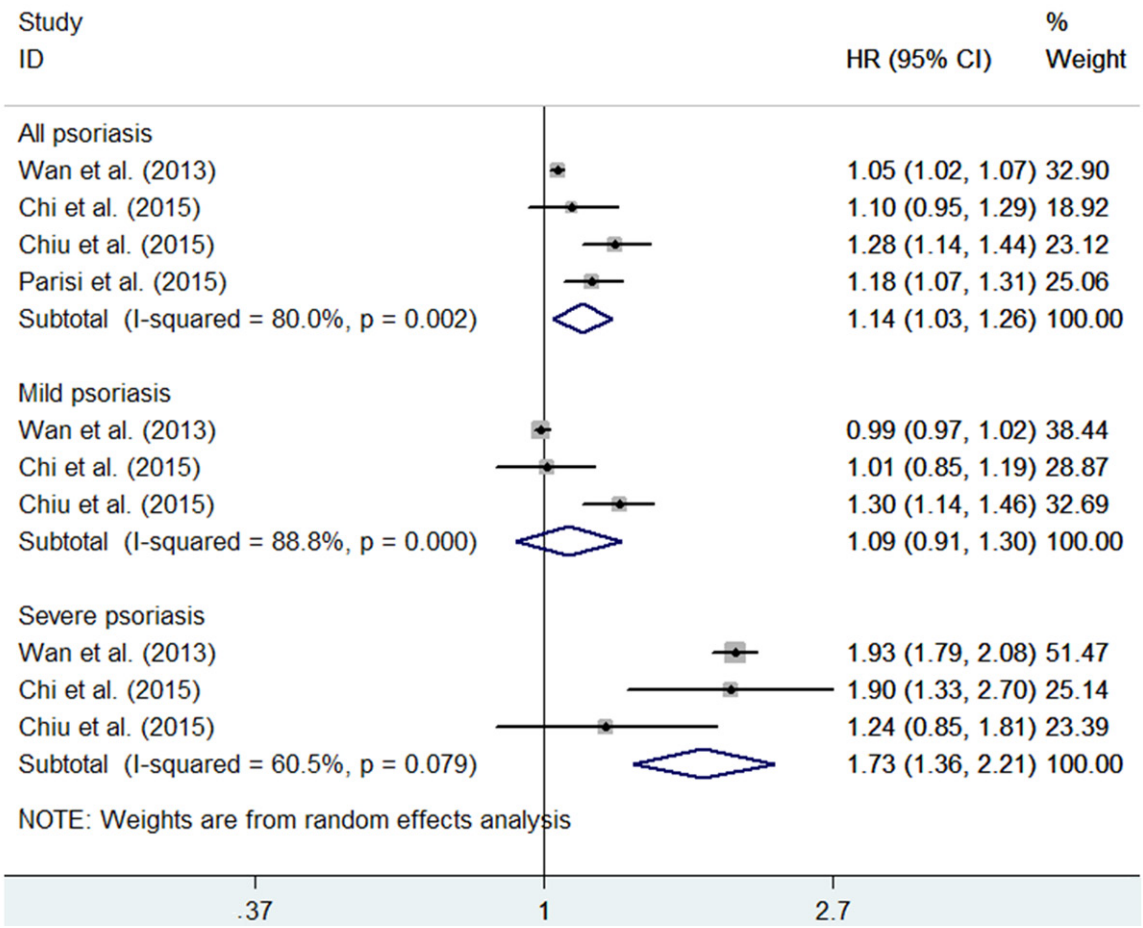

Figure 2. Forest plots showing the association of psoriasis with chronic kidney disease in a random effect model.

study ranged from 17,376 to 926,987. These studies were published from 2013 to 2015. Three studies [10-12] were retrospective design and one study [9] was prospective design. All included studies examined CKD risk and two studies [9, 10] examined ERSD risk. Two studies [10, 11] were performed in the Taiwan, one study each in the USA [12] and the UK [9]. According to the NOS, all studies showed a comparatively high quality (NOS ≥7).

Association of psoriasis with CKD risk

All the included studies provided risk estimates for the association of psoriasis with new-onset CKD. Overall, random effect model meta-analysis showed that psoriatic patients had a 14% (HR=1.14; 95% CI=1.03-1.26) higher risk of CKD compared to non-psoriatic patients (**Figure 2**). Substantial heterogeneity was found (I^2 =60.5%; p=0.079). The removal of any individual study did not alter the statistical significance and direction of overall pooled results. Subgroup analysis according to the severity of psoriasis indicated that this association was stronger among patients with severe psoriasis (HR=1.73; 95% CI=1.36-2.21) but not found among mild psoriasis patients (HR=1.09; 95% CI=0.91-1.30). Both of the Begg's test (p=0.734) and the Egger's test (p=0.151) did not show evidence of publication bias.

Association of psoriasis with ESRD risk

Two studies [10, 11] provided risk estimates for the association of psoriasis with ESRD. Overall, fixed-effect model meta-analysis showed that psoriasis was not associated with higher risk of ERSD (HR=1.14; 95% CI=0.92-1.42) compared to those without psoriasis (**Figure 3**). There was no evidence of significant heterogeneity (I^2 =0.0%; p=0.530) between two studies. Subgroup analysis by the severity of psoriasis indicated that severe psoriasis significantly in-

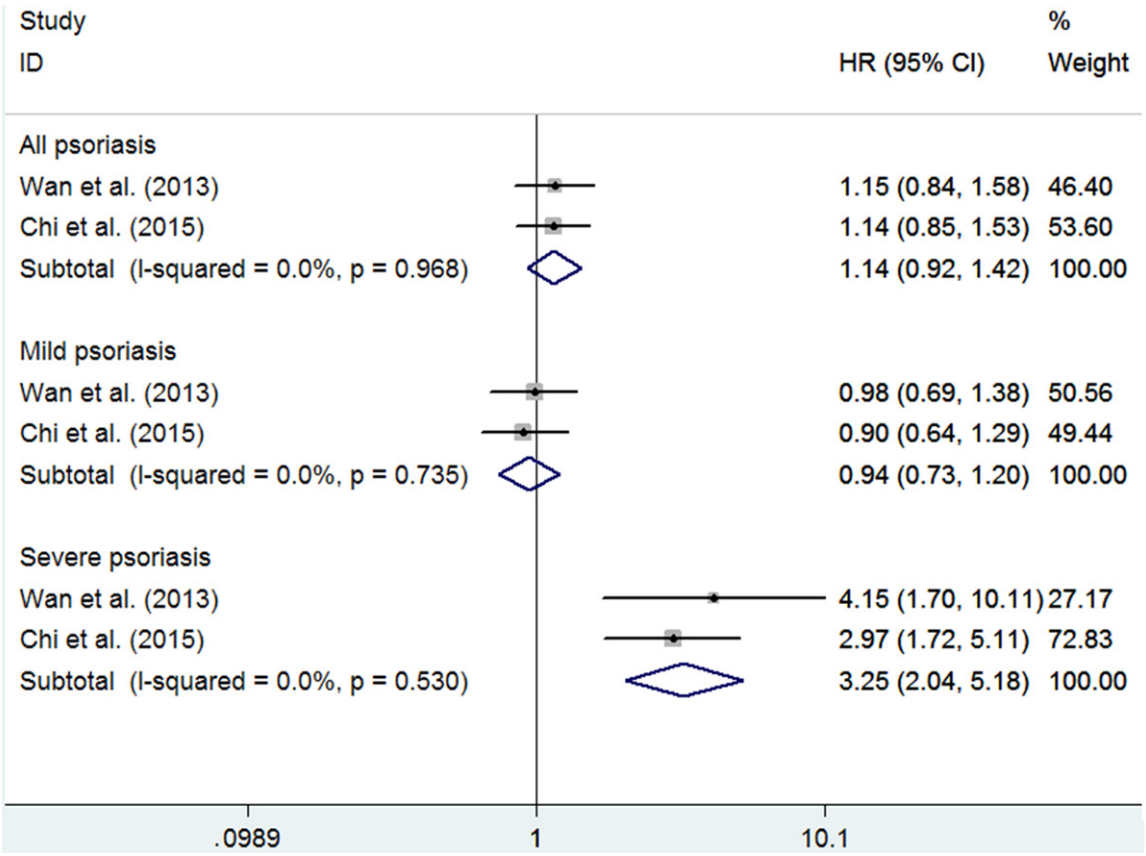

Figure 3. Forest plots showing the association of psoriasis with end-stage renal disease in a fixed-effect model.

creased risk of ESRD (HR=3.25; 95% CI=2.04-5.18) but not mild psoriasis (HR=0.94; 95% CI=0.73-1.20).

Discussion

This meta-analysis aimed to elucidate the association between psoriasis and risk of CKD or ESRD. Findings from the current meta-analysis suggested that patients with severe psoriasis had a higher risk of CKD and ESRD than non-psoriatic controls. After adjustment for potential confounders, severe psoriatic patients were associated with a 73% and 2.25-fold increase in the risk of CKD and ESRD, respectively. However, patients with mild psoriasis were not associated with increased risk of CKD and ESRD.

The severity of psoriasis ranges from a mild disease involving small body surface area to extensive skin involvement. A cross-sectional study of a Chinese population suggested that severe psoriatic patients had significantly higher prevalence of renal failure than the age and gender-matched controls, but the trend disappeared mild psoriatic patients [13]. Our meta-analysis demonstrated that severe psoriasis, but not mild psoriasis, was associated with increased risk of CKD and ESRD. Arterial hypertension, diabetes mellitus, hyperlipidemia, and use of nonsteroidal anti-inflammatory drugs (NSAIDs) in psoriasis may contribute to the impairment of renal function. However, the strength of the association was still robust in our analysis after pooling studies that adjusted these confounding factors. This finding demonstrated that severe psoriasis was associated with the development of CKD and ESRD independent of hypertension, diabetes mellitus, hyperlipidemia, and use of NSAIDs.

The underlying mechanisms of psoriasis in promoting renal diseases remain largely unknown. However, there are many possible explanations. First, systemic inflammatory burden of psoriasis can cause renal vascular injury through increased production of cytokines [14]. Second, autoimmune disorders associated with psoriasis can cause renal impairment [15,

16]. Third, antipsoriatic agents may modulate the association of psoriasis with renal disease. Increased risk of renal disease in patients with psoriasis may be at least partly attributed to use of nephrotoxic drugs [17, 18]. Therefore, monitoring of renal function is recommended when potentially nephrotoxic medications are prescribed, particularly in more severe psoriatic patients.

Several potential limitations should be acknowledged in this meta-analysis. First, most of the included studies (75%) were retrospective design and potential selection bias could not be totally excluded. Second, results from publication bias may be unreliable because of the small number of studies included. Third, identification of severe psoriasis based on systemic treatments or psoriatic arthritis may be yield ascertainment bias. However, use of treatments as a proxy measure of severity has been widely accepted in clinical practice [19, 20]. Fourth, individual studies did not consistently adjust confounding factors and lack of adjustment residual confounding factors might overestimate the risk summary. Finally, we could not determine the effects of nephrotoxic drugs on the progression of CKD or ESRD in the psoriatic patients.

This meta-analysis of observational studies suggests a statistically significant increased risk of CKD and ESED among patients with severe psoriasis. Patients with severe psoriasis should be screened for renal disease. However, more prospective studies are warranted to verify these associations or to explore their underlying mechanisms.

Disclosure of conflict of interest

None.

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