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Role of psoriasis as independent predictor of cardiovascular disease: A meta-regression analysis

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ABSTRACT

Background: Despite the proved association between psoriasis and cardiovascular risk exposure, there are no data about the role of psoriasis as an independent predictor of such risk. The aim of this study was to investigate whether any association between psoriasis and excess cardiovascular risk exposure is independent from confounding factors.
Methods: Meta-analysis and meta-regression analysis were performed using data extracted from observational studies (identified by MEDLINE, EMBASE and CINAHL) investigating the relationship between psoriasis and cardiovascular disease with at least 6 points on the New Castle-Ottawa quality scale. Two reviewers with methodological expertise conducted data extraction independently.
Results: Thirteen studies including patients with psoriasis showed an increased risk of cardiovascular disease (RR = 1.24 [1.18–1.31]; P = 0.0001). These patients still presented a significantly larger cardiovascular risk in the presence of smoking (RR = 1.14 [CI = 1.13–1.15] P<0.0001), obesity (RR = 1.11 [CI = 1.07–1.14] P = 0.0003) and hyperlipidemia (RR = 1.05 [CI = 1.03–1.07] P = 0.0006), but not in the presence of hypertension (RR = 1.03 [CI = 0.98–1.09] P = 0.4647) and diabetes (RR = 0.95 [CI = 0.90–1.01] P = 0.6502).
Conclusions: Patients with psoriasis carry an about 25% increased relative risk of cardiovascular disease. This risk appears to be independent of smoking, obesity and hyperlipidemia.

1. Introduction

Psoriasis is a chronic inflammatory dermatological disease affecting people of all ages although disease onset in early adulthood has been described in patients developing this disease secondary to a genetic transmission. Psoriasis is relatively rare in Blacks and Asians [1,2], while its prevalence is 1.5% in the United Kingdom and between 2 and 3% in the Caucasian population [2,3]. The pathophysiology of psoriasis is supposed to be mainly determined by an inappropriate activation of the cellular immune system [4]. Various environmental factors including stress, withdrawal of systemic corticosteroid and other environmental factors have been suggested as aggravating psoriasis. In addition to cutaneous manifestations, psoriasis is frequently accompanied by impairment in quality of life, depression and arthritis [5–7].

In the last decade, the interest of investigators in evaluating the relationship between psoriasis and cardiovascular diseases has increased considerably. Several studies have suggested that patients with psoriasis are exposed to an increased cardiovascular risk [8–28]. Other conditions such as hyperlipidemia, hypertension, vascular endothelial cell dysfunction, oxidative stress, hyper-homocysteinemia, diabetes, smoking habits, high alcohol consumption, obesity, metabolic syndrome and intra-abdominal adipose visceral tissue syndrome have also been reported in association with psoriasis [29]. The causes underlying the relationship of psoriasis with the above mentioned diseases are unknown, although some authors have suggested the possible role of a common chronic inflammatory pathway. Other authors have postulated that some genes encoding cytokine markers of cardiovascular risk are also involved in clinical expression of psoriasis [8].

To date, it is not clear whether psoriasis is independently associated with the risk of developing cardiovascular diseases and what is the excessive exposure to cardiovascular diseases, if at all, in patients with psoriasis. Also unclear is the role that correction of cardiovascular risk factors has on the expression of psoriasis as well as the role of therapy for psoriasis in the exposure to subsequent cardiovascular events. The present study provides a meta-analysis of all recent high-quality observational studies about the association between psoriasis and presence of cardiovascular disease. Using meta-regression analysis, we investigated

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whether any association between psoriasis and excess cardiovascular risk exposure was independent of confounding factors (smoking, obesity, dyslipidemia, hypertension and diabetes) commonly observed in this population.

2. Methods

2.1. Data source

Studies were identified by searching electronic databases and scanning reference lists of articles. This search was applied to MEDLINE, EMBASE and CINAHL using psoriasis, cardiovascular disease, myocardial infarction and hypertension as keywords. Additionally, hand searches of the reference lists of included studies, reviews, meta-analyses and guidelines on psoriasis and cardiovascular disease were performed. To investigate to what extent metabolic syndrome influence cardiovascular risk a second search having psoriasis, cardiovascular risk, diabetes, hypertension, obesity, hyperlipidemia and metabolic syndrome as keywords was performed.

2.2. Study selection

The literature search was independently conducted and in duplicate by 2 investigators (MG and SC). The same authors independently selected potentially eligible studies for inclusion. Disagreements between reviewers were resolved by consensus; if no agreement could be reached, it was planned that a third senior author (GP) would decide.

2.3. Data extraction and quality assessment

Studies screened according to the selection criteria quoted above were included if they: 1) provided comparative data investigating the relationship between psoriasis and cardiovascular diseases; 2) reported one or more of the following outcomes: cardiovascular disease, infarction, and cardiovascular mortality; and 3) presented with 6 or more points according to the New Castle-Ottawa (NOS) quality scale. All selected studies were cross-sectional, prospective, observational, case–control or cohort studies. The flow chart of paper selection is reported in Fig. 1.

Methodological quality was independently assessed by two investigators (MG and CR). NOS was used for prospective (cohort and case–control) and retrospective studies (case–control). This scale is provided with three grouping items: selection, exposure/outcome and comparability. A study can be awarded a maximum of one star for each numbered item in 'patient selection' (four items) and 'exposure' (three items) categories and a maximum of two stars in the 'comparability of study groups' (two items), thus enabling a total maximum score of nine stars. In our meta-analysis, the NOS score varied between a minimum of six to a maximum of nine stars.

3. Statistical methods

We developed a data extraction sheet, pilot-tested it on three randomly-selected included studies, and refined it accordingly. The following data were extracted from selected studies and entered in a data extraction form by one investigator (MG): author, study design, study year, participants, outcomes and country. A second investigator (CR) checked the extracted data to ensure accurate reporting. Disagreements were resolved by discussion between the two investigators; if no agreement could be reached, it was planned that a third investigator would decide (RC).

We first aggregated myocardial infarction, cardiovascular disease and cardiovascular death data by performing an overall cardiovascular risk evaluation (Fig. 2, panel A). Effects of psoriasis on overall cardiovascular outcome were also investigated based on disease severity. To this aim, the severity of psoriasis was considered as mild or severe according to definitions encountered in the selected studies. If the heterogeneity evaluated by the I [2] was greater than 50%, the random effects model described by DerSimonian and Laird [30] was selected over the fixed effects model. Small study and publication bias effects were assessed by funnel plot visual inspection. Both Harbord and Egger [31] tests were applied, if more than 5 studies were included. Finally, robustness of results was evaluated by sensitivity analysis. Sensitivity analysis was performed on all meta-analyses excluding one study at a time and evaluating robustness of the risk estimate.

P-values lower than 0.05 were considered statistically significant and all statistical tests were 2-sided. Meta-analysis panels and funnel plots were obtained by RevMan5 [32], and Harbord and Egger tests were performed by the SAS [33] software package vers. 9.1.3.

The extent to which each confounding factors could explain the increased cardiovascular risk in psoriatic patients was then explored using random effect meta-regression analysis. For this analysis, several meta-regression models were generated to assess the role of selected confounders (i.e., smoking, obesity, diabetes, hyperlipidemia and hypertension) one by one. According to this model, the logarithm of overall cardiovascular relative risk was the response variable, the ratio between psoriatic patients and healthy controls (both having the investigated confounding factor) was the explanatory co-variate, and the overall number of subjects was the weight variable. To compensate for inhomogeneous distribution of confounding factors between psoriatic patients and healthy controls, the cardiovascular relative risk was calculated by projecting on the corresponding ordinate the abscissa value of 1 as obtained after reaching the solution of the meta-regression equation for each confounding factor (Fig. 3). To investigate for the effect of two or more confounders a Bayesian analysis was applied. In

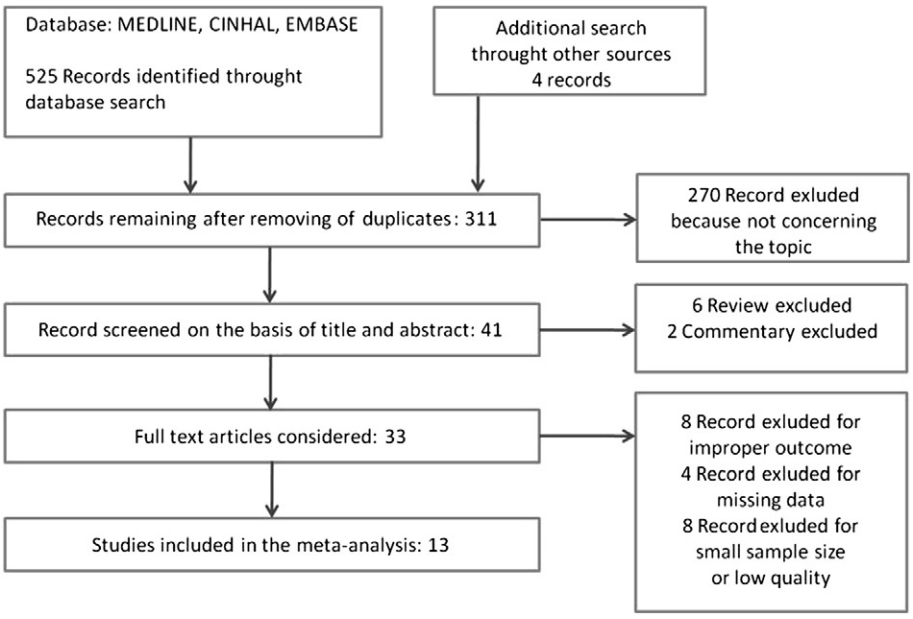

Fig. 1. Flow chart of paper selection.