REVIEW ARTICLE

Cardiovascular risk factors in patients with plaque psoriasis: a systematic review of epidemiological studies


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Abstract

Introduction Many epidemiological studies have associated psoriasis with an increased risk of coronary artery disease, resulting from a higher prevalence of cardiovascular risk factors in psoriasis patients compared with unmatched controls. However, the results of epidemiological studies vary depending upon the populations studied. The aim of this systemic review was to evaluate the risk of diabetes, hypertension, dyslipidaemia and obesity in adults with plaque psoriasis. In addition, we assessed the relationship between the risk of cardiovascular risk factors and psoriasis severity.


Results The initial literature search identified 353 articles. The final selection included 18 cross-sectional case-control studies. An increased risk of metabolic syndrome was observed in psoriatic patients (OR = 1.3–5.92), and a trend for a higher risk of obesity (OR = 1.18–5.49), especially in patients with severe psoriasis. For hypertension, hypertriglyceridaemia, and diabetes, the association was not significant in all studies.

Discussion There was important heterogeneity in study design preventing from pooling results. Most often lifestyle factors such as smoking, alcohol consumption, physical activities were not taken into account.

Conclusion There is an increased risk of obesity and metabolic syndrome in psoriasis. For hypertension, diabetes and dyslipidaemia no consistency was found across studies. Prospective epidemiological studies with thorough recording of cardiovascular risk factors are required in psoriasis patients.

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Keywords cardiovascular diseases, comorbidity, diabetes, dyslipidemia, hypertension, metabolic syndrome, obesity, psoriasis, review literature

Sources

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Conflicts of interest

C. Paul has received research grants and has been a paid consultant of Abbott France; S. Aractingi has given conferences in symposia sponsored by Wyeth and has been a consultant for Abbott and Schering-Plough; the remaining authors declare no conflicts of interests.
Introduction
Psoriasis is a common disease, affecting 2–3% of the population worldwide. Psoriasis is a multigenic inflammatory disease and more than 20 predisposition genes have been identified. The role of environmental factors such as infection, drugs, stressful events and smoking has been suggested. The association of psoriasis with cardiovascular disease dates back from 1961. Recent epidemiological studies in registry databases have confirmed a consistent association between adult psoriasis and an increased risk of coronary heart disease and stroke. In this study, we systematically evaluated the relationship between psoriasis and cardiovascular risk factors (diabetes, hypertension, dyslipidaemia, obesity and metabolic syndrome) from published epidemiological studies.

Material and methods
We performed a systematic review of all epidemiological studies (prospective and retrospective) investigating the risk of cardiovascular comorbidities in psoriasis patients and published between January 1980 and June 2009. The Cochrane, Pubmed and Embase databases were systematically searched. The research used different combinations of the Medical Subject Headings (MeSH): 'Psoriasis [title] AND (diabetes OR hypertension OR high blood pressure OR dyslipidaemia OR metabolic syndrome OR obesity)'. We limited the literature search to articles on human subjects, articles written in English or in French, and articles including original data.

For all the articles, the following data were retrieved: type of database, author, year, inclusion period, number of psoriatic patients, number and origin of control subjects (i.e. general population or dermatology patients), existence of matching, criteria used for the definition of the comorbidity (e.g. patients’ history, measurement), odds ratio and 95% confidence interval.

To determine the effect of disease severity, we attempt when possible to separate data for patients with ‘moderate to severe psoriasis’ versus patients with ‘mild psoriasis’. Patients with moderate to severe psoriasis were defined as patients treated with systemic therapy (cyclosporine, methotrexate or biological therapy).

Two reviewers (SP, CP) independently performed parts of the systematic electronic search and the data extraction. When not provided in the paper, odds ratio (OR) and the corresponding 95% confidence intervals (CI) were calculated from the available data of the selected articles. When statistical significance was reassessed, uncorrected P-values are given. All computations were performed using Stata V.10 (StataCorp College Station, TX, USA).

Results
We identified a total of 353 eligible articles by searching Medline, Cochrane and Embase databases, five by hand-searching reference lists. The majority of articles (N = 264) were excluded by reading the abstract because they did not directly deal with the subject, 13 were not written in English or in French, 12 were reviews, 38 were out of scope and in five articles there was no control group. Eight studies for which there was not enough information to recompute OR were excluded. A total of 18 articles were finally selected (Fig. 1).

The control population used in the studies originated from the general population from registry databases in 12 articles, outpatients attending dermatology departments in five studies performed in dermatology departments and female nurses in one study. Analytical approaches were heterogeneous between studies. Adjustment for age, sex, smoking or area of living was not systematically performed.

Diabetes
Fourteen cross sectional studies were found, three were performed in the USA, and the others in Europe (Table 1 and Fig. 2). Eleven studies were based on automated databases (General Practice Research Database = GPRD in the UK, Clalit Health Service and Maccabi Healthcare Services in Israel, National Health Wellness Survey, IMS Health, Marketscan and Nurses’ Health Study = NHS in US) and four were performed in dermatology departments.

The definition of diabetes varied from one study to another: code in databases, the use of diabetic medications, diabetes mellitus type II in medical history or fasting blood glucose higher than 6.1 mmol/L.

A significant association between diabetes and psoriasis was found in 11 studies with OR varying from 1.20, CI = [1.14–1.25] to 2.80, CI = [2.68–2.99]. In three studies, no significant association was found. In a recent study by Qureshi et al., the multivariable analysis (adjusting for weight, smoking, physical activity and alcohol) showed an increased risk of diabetes in...
psoriasis patients with an OR of \(= 1.63\), CI \([1.25–2.12]\). In studies investigating the effect of psoriasis severity on the risk of diabetes \((n = 4)\), the risk of diabetes appeared to be higher in patients with 'moderate to severe psoriasis' (OR ranged from 1.62, CI \([1.30–2.01]\) to 1.91, CI \([0.91–4.04]\)) when compared with patients with 'mild psoriasis'.

**Dyslipidaemia**

Twelve studies were selected.\(^3,5,6,8,10,12–14,16–18,20\) (Table 2 and Fig. 3) Definition of dyslipidaemia was very heterogeneous between studies: code in databases, use of dyslipidaemia medications, hypertriglyceridaemia or hypercholesterolaemia in medical history or results of serum tests (hypertriglyceridaemia > 1.7 mmol/L, HDL-cholesterol < 0.9–1.0 mmol/L in men or 1.0–1.3 mmol/L in women).

When considering all criteria, there was a trend for a higher risk of dyslipidaemia, which was significant in seven of 12 studies,\(^3,5,6,8,13,16,17\) with OR ranging from 1.0 CI \([1.0–1.3]\) to 2.09 CI \([1.23–3.54]\) for psoriatic patients compared with the control population.

For hypertriglyceridaemia, the OR varied from 1.0, CI \([1.0–1.3]\) to 2.0, CI \([1.4–2.8]\) and was significant in three studies.\(^12,14,16\) For HDL-cholesterol, there was no increased risk. For total cholesterol, only one study showed a significant increased risk (OR = 1.35, CI \([1.11–1.63]\)).\(^6\) No apparent effect of psoriasis severity on the risk of dyslipidaemia was observed.

**Hypertension**

Twelve studies evaluated the risk of hypertension in psoriatic patients.\(^3,5–8,10–14,16,17\) (Table 3 and Fig. 4).
The definition of hypertension in the studies was heterogeneous: specific code in the database, the use of anti-hypertensive medications, hypertension in medical history or results of systolic blood pressure > 135 mmHg or 140 mmHg for the systolic, and diastolic blood pressure > 85 mmHg or 90 mmHg.

The increased risk of hypertension was significant in 10 of 12 studies, with an OR ranging between 1.09, CI = [1.05–1.14] and 3.27, CI = [2.41–4.43].3,5–8,10,12,13,16,17 It is unclear whether the level of risk was influenced by psoriasis severity. The multivariable analysis of Qureshi et al.7 showed a persisting modest increased risk of hypertension in psoriatic patients with an OR = 1.17 CI = [1.06–1.30].

Obesity
The definition of obesity used in studies was a body mass index (weight/height²) higher than 30 kg/m² as defined by the World Health Organization.19 Eight articles analysed the risk of obesity10–14,17,20,21 (Table 4 and Fig. 5). They showed a significant increased risk with an OR ranging from 1.18, CI = [1.14–1.23] to 5.49, CI = [3.09–9.74] in all studies but one.14 The level of risk appeared to be influenced by the severity of psoriasis. OR of the ‘moderate and severe psoriasis’ population varied from 1.79, CI = [1.55–2.05] to 5.49, CI = [3.09–9.74] vs. 1.27, CI = [1.24–1.31] to 1.7, CI = [1.1–2.6] for ‘mild’ psoriasis.

Metabolic syndrome
Three studies evaluated the metabolic syndrome in psoriasis patients, with different criteria for each14,16,22 (Table 5 and Fig. 6).
The study of Gisondi et al.\(^{14}\) used the criteria of the National Cholesterol Education Program’s Adult Panel: central obesity (waist circumference > 102 cm \(\varnothing\), > 88 cm \(\varnothing\)), hypertriglyceridaemia > 1.7 mmol/L, HDL-cholesterol < 1.0 mmol/L \(\varnothing\) or < 1.3 mmol/L \(\ominus\), blood pressure > 135/85 mmHg and fasting plasma glucose > 6.1 mmol/L.

The study of Sommer et al.\(^{16}\) used the World Health Organization criteria: the presence of diabetes mellitus type II plus at least 2 of the following: antihypertensive medication and/or high blood pressure (> 140 mmHg systolic or > 90 mmHg diastolic); plasma triglycerides > 1.7 mmol/L; HDL-cholesterol < 0.9 mmol/L \(\varnothing\), < 1.0 mmol/L \(\ominus\); BMI > 30 kg/m\(^2\) and/or waist : hip ratio > 0.9 \(\varnothing\), > 0.85 \(\ominus\); urinary albumin excretion rate ≥ 20 µg/min or albumin:creatinine ratio ≥ 30 mg/g.

The study of Cohen et al.\(^{22}\) used as criteria the presence of obesity plus any of two of the following criteria: raised triglycerides, reduced HDL-cholesterol, hypertension or diabetes. Each item was extracted from an automated database.

In all articles, there was a significant increased risk of metabolic syndrome in psoriasis patients, with OR from 1.3, CI = [1.1–1.4] to 5.92, CI = [2.78–12.8]. Gisondi et al.\(^{14}\) who studied the metabolic syndrome on patients with ‘mild’ psoriasis, still found an increased risk with an OR = 1.66, CI = [1.20–2.40] in this population.\(^{14}\)

**Discussion**

There is a significant increased risk of obesity and metabolic syndrome in patients with psoriasis. For other risk factors, hypertension, diabetes mellitus type 2 and dyslipidemia, the results were less consistent across studies, some studies showing a strong association between psoriasis and these risk factors, others failed to show such an association. Despite different criteria used to define metabolic syndrome across studies a significant association between metabolic syndrome and psoriasis was consistently found.
The magnitude of the association between psoriasis and cardiovascular comorbidities appeared to be influenced by the study size and by the nature of the control population. Small studies including controls originating from dermatology outpatients tended to show the stronger association (i.e. Table 5).

We found a substantial heterogeneity in design between epidemiological studies as regards: retrospective or prospective nature of the recruitment and the outcome assessment, definition of risk factors, type of database used, type of control population, matching and adjustment strategies. Nijsten et al. have reported on the ‘Strengthening the Reporting of OBservational Studies in Epidemiology’ (STROBE) which provide important information on the quality of observational studies. Most studies evaluated in the present analysis failed to provide a rationale for sample size selection.

A potential limitation of cross sectional studies concerned the selection of the control subjects: studies performed in dermatology departments used outpatients as controls; however, outpatients without psoriasis attending a dermatology department may not adequately represent the general population. The main advantage of the prospective studies conducted in dermatology department is the more thorough collections of data regarding cardiovascular risk-factors and psoriasis phenotype. Life style factors such as alcohol, smoking, sedentarity and the use of

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![Figure 5](image-url)

**Figure 5** Cross sectional studies about risk of obesity in psoriatic patients (OR with 95% confidence interval) Control: Dermatological patients (red), General population from databases (green). Matching: Yes (x), No (>). Type of psoriasis: Severe (V), Mild and moderate (<).

### Table 4 Cross sectional studies about risk of obesity in psoriasis

<table>
<thead>
<tr>
<th>References</th>
<th>Country</th>
<th>Psoriasis Nb</th>
<th>Control Nb</th>
<th>Type</th>
<th>Match</th>
<th>OR obesity</th>
<th>Definition</th>
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<tr>
<td>Driessen 2008</td>
<td>the Netherlands</td>
<td>107</td>
<td>396</td>
<td>D</td>
<td>N</td>
<td>5.49 [3.09–9.74]</td>
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<tr>
<td>Naldi 2008</td>
<td>Italia</td>
<td>560</td>
<td>690</td>
<td>D</td>
<td>Y</td>
<td>1.7 [1.1–2.6]</td>
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<tr>
<td>Cohen 2008</td>
<td>Israel</td>
<td>16851</td>
<td>48677</td>
<td>G</td>
<td>N</td>
<td>1.7 [1.5–1.9]</td>
<td>Code</td>
</tr>
<tr>
<td>Gisondi 2007</td>
<td>Italia</td>
<td>338</td>
<td>334</td>
<td>G</td>
<td>N</td>
<td>1.19 [0.91–1.55]</td>
<td>BMI≥30</td>
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<tr>
<td>Neumann 2006</td>
<td>UK</td>
<td>131560</td>
<td>479317</td>
<td>G</td>
<td>Y</td>
<td>1.29 [1.26–1.32]</td>
<td>BMI≥30</td>
</tr>
<tr>
<td>Naldi 2005</td>
<td>Italia</td>
<td>560</td>
<td>690</td>
<td>D</td>
<td>N</td>
<td>1.9 [1.2–2.8]</td>
<td>BMI≥30</td>
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<tr>
<td>Herron 2005</td>
<td>USA</td>
<td>557</td>
<td>4080</td>
<td>G</td>
<td>N</td>
<td>2.39 [1.98–2.90]</td>
<td>BMI≥30</td>
</tr>
</tbody>
</table>

Control population: G, General population; D, Dermatologic outpatients; Matching: Y, yes – N, no.

### Table 5 Cross sectional studies about risk of metabolic syndrome in psoriasis

<table>
<thead>
<tr>
<th>References</th>
<th>Pays</th>
<th>Psoriasis</th>
<th>Control Nb</th>
<th>Type</th>
<th>Match</th>
<th>OR metabolic syndrome</th>
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<td>48681</td>
<td>G</td>
<td>N</td>
<td>1.3 [1.1–1.4]</td>
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<tr>
<td>Gisondi 2007</td>
<td>Italia</td>
<td>338</td>
<td>334</td>
<td>D</td>
<td>N</td>
<td>1.66 [1.20–2.40]</td>
</tr>
<tr>
<td>Sommer 2006</td>
<td>Germany</td>
<td>625</td>
<td>1044</td>
<td>D</td>
<td>N</td>
<td>5.92 [2.78–12.8]</td>
</tr>
</tbody>
</table>

Control population: G, General population; D, Dermatologic outpatients; Matching: Y, yes – N, no.
Cardiovascular risk factors in patients with plaque psoriasis

systemic therapy for psoriasis (i.e. cyclosporine, retinoids) are major confounding bias as these factors can influence cardiovascular risk and also may have a negative effect on some risk factors (e.g. alcohol consumption and hypertension). Lifestyle factors were most often not accounted for in the analysis. Such heterogeneity between the studies prevents from pooling the results and the lack of adjustment for possible confounding factors in some studies raises uncertainty regarding the strength of the association.

The pathophysiology of the relation between psoriasis and cardiovascular risk is still debated. Some authors suggest that the high incidence of metabolic syndrome in psoriasis may be at least in part explained by the chronic systemic inflammation present in psoriasis. Obese psoriasis patients have low level of adiponectine (compared with normal weight psoriasis) and an increased level of IL-6 and glutation redox status (oxidative stress). Genetic studies performed in the UK on 1256 psoriatic patients (vs. 2938 controls) showed a significant association between psoriasis and CDKAL1 gene, implicated in diabetes mellitus. A case-control study made on 70 psoriatic patients (red). General population from databases (green). Matching: Yes (x), No (○). Type of psoriasis: Severe (△), Mild and moderate (○). Figure 6 Cross sectional studies about risk of metabolic syndrome in psoriasis (OR with 95% confidence interval) Control: Dermatological patients (red). General population from databases (green). Matching: Yes (x), No (○). Type of psoriasis: Severe (△), Mild and moderate (○).

The evidence that psoriasis patients have an increased risk of cardiovascular risk factors should be confirmed by prospective epidemiological studies including thorough recording of cardiovascular risk factors, life style elements, psoriasis severity and parameters for systemic inflammation. In the mean time, it appears advisable to:

1. Document personal and familial history of cardiovascular risk in psoriasis patients and systematically evaluate weight, body mass index and blood pressure.
2. Propose blood testing for fasting glucose and lipid profile in relation with the primary care physicians.
3. As part of psoriasis management, the dermatologist may want to provide recommendations concerning diet and physical activity to reduce cardiovascular risk factors.

References


