



## Review

## Subclinical cardiovascular disease in plaque psoriasis: Association or causal link?



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## ARTICLE INFO

## Article history:

Received 16 July 2013

Received in revised form

19 October 2013

Accepted 21 October 2013

Available online 1 November 2013

## Keywords:

Psoriasis

Atherosclerosis

Sub-endothelial dysfunction

Coronary artery calcium

Primary prevention

Carotid intima–media thickness

## ABSTRACT

**Background:** Psoriasis patients have a high prevalence of cardiovascular events and are thought to have a relative risk increase of 25% as compared to the general population. However, a causal relationship between psoriasis and cardiovascular disease has not been established. We sought to perform a systematic review of existing data regarding the presence of endothelial dysfunction and subclinical atherosclerosis in patients with plaque psoriasis.

**Methods:** A systematic literature search was performed, using Medline database and Ovid SP for relevant literature up to November 2012. Twelve studies met inclusion criteria from an initial search result of 529 articles.

**Results:** Among the twelve studies meeting inclusion criteria, two (17%) reported increased mean coronary artery calcification (CAC) in psoriatic patients. Six studies (50%) showed carotid intima–media thickness [CIMT] increase in psoriasis. Five studies (42%) examined flow mediated dilation [FMD], of which three showed decreased FMD in psoriasis patients. One study (8%) each demonstrated a decreased coronary flow reserve and increased arterial stiffness as assessed by pulse wave velocity.

**Conclusions:** Patients with psoriasis have an increased burden of subclinical atherosclerosis and endothelial dysfunction. Patients with greater severity and/or disease duration should be targeted for primary screening for cardiovascular disease risk reduction

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## 1. Background

Psoriasis is a chronic inflammatory skin disease that affects 2–3% of the US population and an estimated 125 million people worldwide [1]. Plaque psoriasis, which is characterized by recurring erythematous patches covered with silvery plaques, accounts for 80% of these patients. Psoriasis patients are known to have a high presence of traditional CVD risk factors [2–7]. The association of psoriasis with cardiovascular disease (CVD) has come under considerable scrutiny in recent years, with recent data suggesting that it is linked to increased cardiovascular outcomes independent of the clustering of traditional CVD risk factors [5,8]. A recent meta-analysis concluded that patients with psoriasis carry an about 25% increased relative risk of cardiovascular disease, independent of smoking, obesity and hyperlipidemia [9]. However, whether the relationship between clinical CVD and psoriasis extends to early atherosclerosis or preclinical disease is not well known. Such an association could provide potential insight regarding the role of psoriasis in the development of CVD and can potentially guide the discussion about whether detection and treatment of early subclinical CVD should be considered for this high risk group. The advent of non-invasive means to assess subclinical atherosclerosis has brought about a paradigm shift in CVD risk assessment. In spite of these advances, assessment of subclinical atherosclerosis and endothelial dysfunction in psoriatic patients using coronary artery calcium (CAC) screening, carotid intima–media thickness (CIMT) measurement and brachial artery flow mediated dilatation (FMD) has not been extensively studied. Therefore, in this systematic review, we sought to collect and summarize existing data regarding the presence of endothelial dysfunction and subclinical atherosclerosis as measured by non-invasive imaging techniques in patients with plaque psoriasis.

## 2. Methods

Systematic literature search was performed, using Medline database (National Library of Medicine, Bethesda, MD) and Ovid SP (Ovid, New York, NY). We used both MeSH terms and relevant free-text terms. The following search terms (synonyms and combinations) were used: 'psoriasis' AND 'coronary artery calci\*' OR 'coronary angiography' OR 'ankle brachial index' OR 'brachial artery' OR 'brachial artery reactivity' OR 'flow mediated dilation' OR 'intima media thickness' OR 'IMT' OR 'endothelial function' OR 'subclinical

atherosclerosis' OR 'arteriolosclerosis' (Fig. 1). The results obtained were then manually scanned for relevant articles by two independent reviewers. Discordances were discussed and a consensus was reached for each article in question. The search was conducted from 1996 to November 2012. References of obtained articles were manually scanned for other relevant studies.

Studies were included if they were in English, original research publications and contained data on subclinical atherosclerosis and psoriasis. The following data was extracted from the studies examined: number of patients and controls, age, inclusion/exclusion criteria, main findings (limited to techniques of interest) and statistical analyses. Review articles, case reports, studies on psoriatic arthritis alone and studies focusing on inflammatory markers alone were excluded from the analysis. Studies that analyzed heterogeneous groups of patients with both plaque psoriasis and psoriatic arthritis were also excluded. Using these methods, a total of 12 studies were included for review.

All studies included for review defined psoriasis as a chronic inflammatory skin disorder characterized by erythrosquamous plaques. All studies assessed psoriasis severity with the Psoriasis Area Severity Index (PASI), a subjective assessment of psoriasis severity subject to observer variation. However it remains the most validated approach to documenting psoriasis severity [10].

## 3. Results

### 3.1. Psoriasis and coronary artery calcification

Two studies analyzed CAC in patients with plaque psoriasis, with both demonstrating an increased mean CAC score in subjects vs controls [11,12] (see Table 1). Both were conducted in middle aged patient groups with plaque type psoriasis. One study recruited patients from outpatient discharge lists [12], while the second study recruited in patients whose diagnosis had been verified by a dermatologist [11]. Both studies did not exclude patients with cardiovascular risk factors. Control populations were selected from different sources in both studies.

Yiu et al. [12], which enrolled patients with >10% of body surface area involved, demonstrated that patients with psoriasis had a higher prevalence of coronary artery calcification ( $p < 0.01$ ), and a higher degree of coronary artery calcification estimated by the mean CAC score compared with controls, ( $p < 0.05$ ). C-Reactive protein levels were significantly higher in patients vs controls

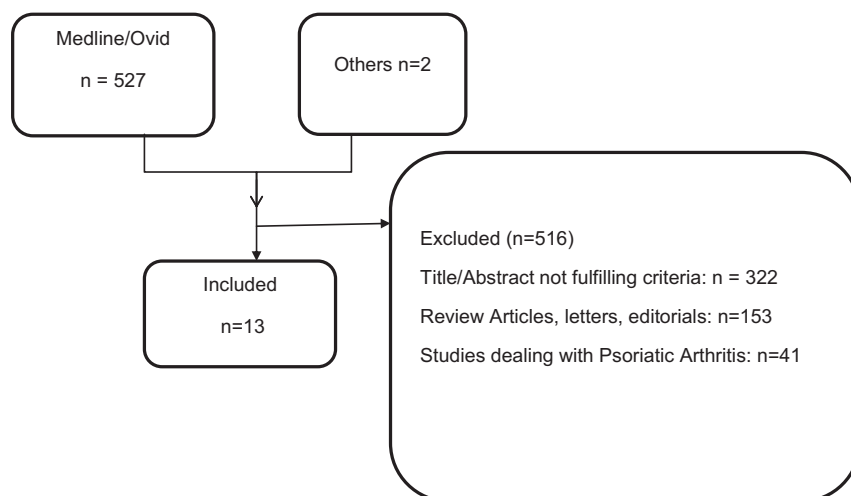


Fig. 1. Search strategy.

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