Should Psoriasis Patients be Screened for Heart Disease?

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Abstract

Psoriasis is a systemic, immune-mediated disorder that manifests as chronic skin and joint inflammation. While the prevalence of psoriasis worldwide is 2%, its prevalence in developed countries is on average about 4.6%. Psoriasis is associated with cardiovascular disease (CVD). For this literature review, Pubmed and Medline were used to source articles using the keywords 'psoriasis' and 'cardiovascular disease'. The inclusion criteria were studies with sample sizes of 100 or more published in English from 2000 onwards. Out of 1,657 papers retrieved, 37 were deemed relevant. Of these, 36 papers contained evidence in support of screening for CVD while one paper had evidence against screening for CVD. Substantial evidence suggested a higher CVD prevalence in psoriasis patients compared to populations without psoriasis. Furthermore, the risk of developing CVD correlated highly with increased psoriasis severity and duration in addition to other CVD risk factors. The pathophysiological link between psoriasis and CVD is a common immunological pro-inflammatory state. In conclusion, psoriasis is an independent risk factor for CVD, particularly in younger patients with severe psoriasis, and is associated with increased mortality. Further research is required to better understand the relationship between psoriasis, traditional risk factors and development of CVD.

Introduction

Psoriasis is a systemic, immune-mediated disorder that manifests as a chronic skin and joint inflammation[1]. While the prevalence of psoriasis worldwide is 2%, its prevalence in developed countries is on average about 4.6%[2]. The gold standard for measuring psoriasis is the Psoriasis Area and Severity Index (PASI)[3]. Nearly two thirds of people with psoriasis have a mild form of the disease, classified as less than 3% of the skin surface affected[4].

The pathogenesis of psoriasis shows an association with certain types of human leukocyte antigen (HLA), suggesting a genetic component[5]. Furthermore, the genesis of new lesions at sites of trauma suggests a role for exogenous stimuli. Sensitized CD4+ T-helper (Th)-1 and Th-17 cells, and activated cytotoxic T lymphocytes that accumulate in the epidermis may drive keratinocyte proliferation by elaborating cytokines[5]. In particular, Th-1, Th-17 and Th-22 cell populations are expanded and stimulated to release inflammatory cytokines, including tumor necrosis factor-α (TNF-α), interleukin (IL)-17 and IL-22[6, 7, 8]. The inflammation that drives psoriatic pathology is systemic and there is evidence to suggest that it contributes to immunological and metabolic changes that enhance and perpetuate psoriasis, as well as to the development of co-morbidities[9].

CLINICAL POINTS

Psoriasis is a systemic, immune-mediated disorder

Psoriasis is an independent risk factor for CVD, particularly in younger patients with severe disease

Psoriasis is associated with increased mortality

The NICE guidelines recommend that patients with severe psoriasis be offered screening for any potential CVD risk

The literature shows that moderate to severe psoriasis is associated with diseases such as ischaemic heart disease, stroke, hypertension, dyslipidaemia and diabetes[4].

This paper will review the evidence for CVD screening in patients with psoriasis of all severities, evaluate the strength of the association and deliberate

table 1 Vascular disease and mortality - psoriasis and traditional cardiovascular risk factors[13]

Risk factor	Peripheral vascular disease	Ischaemic heart disease	Cerebrovascular Disease	Any Vascular Disease	Mortality
Hypertension	3.52 (2.44-5.07)	2.92 (2.48-3.44)	3.32 (2.59-4.25)	3.21 (2.76-3.73)	1.13 (0.95-1.34)
Diabetes	2.40 (1.84-3.13)	2.30 (1.96-2.70)	2.08 (1.70-2.54)	2.38 (2.04-2.79)	1.27 (1.05-1.52)
Dyslipidaemia	1.81 (1.39-2.36)	2.39 (2.05-2.80)	1.56 (1.27-1.90)	2.16 (1.86-2.52)	0.35 (0.28-0.43)
Tobacco use	1.78 (1.20-2.63)	1.83 (1.42-2.37)	1.78 (1.32-2.40)	2.14 (1.67-2.74)	0.80 (0.59-1.09)
Psoriasis	1.98 (1.38-2.82)	1.78 (1.51-2.11)	1.70 (1.33-2.17)	1.91 (1.64-2.24)	1.86 (1.56-2.21)

Patient group	Mortality (% total patients)
Patients with psoriasis (n=3236)	19.6
Controls (n=2500)	9.9

when CVD screening may become necessary for psoriasis patients. It also discusses whether earlier and more stringent control of the disease-driving inflammatory processes could potentially prevent the development and worsening of CVD. This has important implications in terms of risk stratifying patients with psoriasis for CVD risk and eventually improving overall patient outcomes.

Currently various CVD risk scores are being used. Equations derived from the American Framingham cohort study are the most widely used in the United Kingdom (UK)[10]. A 2007 study by Hippisley-Cox et al. derived a new CVD risk score (QRISK) for the UK and its performance validated against the Framingham algorithm and ASSIGN (used in Scotland). The Framingham algorithm over-predicted CVD risk at 10 years by 35%, ASSIGN by 36%, and QRISK by 0.4%. The study concluded that QRISK, which includes additional variables of positive family history and antihypertensive treatment, provides a more appropriate risk estimate for UK patients on the basis of age, sex, and social deprivation[11].

Methods

For this literature review, Pubmed and Medline were used to source articles using the keywords 'psoriasis' and 'cardiovascular disease'. The inclusion criteria were studies with sample sizes of 100 or more, published in English from 2000 onwards. Out of 1,657 papers retrieved, 37 were deemed relevant. Of these, 36 papers contained evidence in support of screening for CVD while one paper had evidence against it.

Results

36 papers with evidence supporting screening psoriasis patients for CVD were relevant. Of these,

- 26 papers concluded that psoriasis causes a higher incidence of CVD
- 4 papers suggested that pharmacological treatment of psoriasis increases the risk of CVD
- 3 papers assessed the risk of patients with

psoriasis and psoriatic arthritis developing CAD, peripheral vascular disease and cerebrovascular accidents

- 3 papers showed a causal link between psoriasis and metabolic disease, predisposing to CVD

A systematic literature review (1980 – 2011) by Horreau C et al[12]. assessed cardiovascular morbidity and mortality in psoriasis and psoriatic arthritis patients. This research identified 33 observational studies, which compared psoriasis and psoriatic arthritis patients with a control group. A common link, immunological and inflammatory pathways, was observed between psoriasis and psoriatic arthritis patients who developed stroke, coronary artery disease (CAD), or peripheral vascular disease (PVD). Psychological stress, sedentary lifestyle and poor compliance to CVD risk factor management contributed to the link. Psoriasis and psoriatic arthritis were shown to be significant risk factors for a cardiovascular event, although, there was no correlation with CVD mortality. The limitations of this study include: heterogeneity in study design, outcome definition and assessment methods.

A 2009 observational study by Prodanovich et al[13]. compared 3,236 psoriasis patients with 2,500 control subjects. It was concluded that psoriasis is an independent risk factor for CVD mortality, usually linked to atherosclerosis development. Psoriasis increases the occurrence of diabetes mellitus, hypertension and dyslipidemia, resulting in atherosclerosis. A 2009 literature review by Kimball et al[14]. of articles sourced from Medline (1995 – 2007) reached similar conclusions. Both studies showed evidence of pro-inflammation in psoriasis and CVD. This is consistent with the literature regarding the role of inflammation in vaso-occlusive cardiac disease.

table 2 Cardiovascular risk factors associated with psoriasis

Risk Factor	Mild Psoriasis	Controls (mild)	Odds ratio (95% CI) (mild)*	Severe Psoriasis	Controls (severe)	Odds ratio (95% CI) (severe)*
Diabetes	4.4%	3.3%	1.27 (1.23-1.31)	7.1%	3.3%	1.86 (1.58-2.19)
Hyperlipidaemia	4.7%	3.3%	1.28 (1.24-1.33)	6.0%	3.6%	1.31 (1.11-1.56)
Hypertension	14.7%	11.8%	1.16 (1.14-1.18)	20.0%	13.2%	1.25 (1.13-1.39)
Smoking	28.0%	21.1%	1.40 (1.38-1.43)	30.1%	22.5%	1.31 (1.20-1.44)
BMI = 25 – 30	35.0%	32.9%	1.12 (1.10-1.14)	37.7%	33.4%	1.28 (1.15-1.43)
BMI > 30	15.8%	13.1%	1.29 (1.26-1.32)	20.7%	13.0%	1.84 (1.60-2.11)

*Abbreviations: BMI - body mass index. *after adjustment for age, sex, and person-years, CI - confidence interval*

A 2011 study by Johnsson et al[15]. concluded that a raised BMI and psoriasis could increase risk of diabetes mellitus. Psoriatic patients were shown to have elevated visceral fat, which promotes liver insulin resistance and non-alcoholic fatty liver disease.

A 2013 systematic review and meta-analysis by Samarasekera et al[16]. examined studies regarding the incidence of CVD in psoriasis patients from 1984 to 2013. The systematic review included 14 cohort studies with sample sizes ranging from 130 to 462 subjects (n = 976). Results were classified into two subgroups based on the severity of disease, with those requiring systemic treatment or hospital admission being classified as severe psoriasis. Patients with severe psoriasis were reported to have increased

incidence of CVD mortality in all cohorts, with the absolute increase being 1 in 283 patients per year. However, the evidence for CVD mortality associated with mild psoriasis was inconsistent and hence weak. Inadequate awareness of concomitant CVD risk factors existing in psoriatic patients is a limitation that affects the study outcome preventing a causal relationship from being drawn between psoriasis and CVD. The review concluded that patients with severe psoriasis should be screened for CVD.

Another study by Farajzadeh et al[17]. in 2012 investigated the prevalence of CVD risk factors in psoriasis patients. In the study, 73 psoriatic patients aged 20 to 50 years were age and sex matched to 73 control subjects. The patients included had mild psoriasis according to the PASI scoring system. Individuals with thyroid disease, familial hyperlipidemia, nephrotic syndrome, cholestasis, people on drugs affecting lipid metabolism, and pregnant women were excluded. Relevant risk factors were assessed. Of these, hypertension, diabetes mellitus, hypercholesterolemia, hypertriglyceridemia, impaired fasting glucose and elevated BMI were shown to be more prevalent in the psoriasis patients than in the control group. There was no significant difference in the prevalence of cigarette smoking between both groups. It should be noted that this study is limited by its small sample size and inclusion of patients with mild psoriasis, therefore, the results may not be representative of all psoriasis severity groups.

In 2013, a population-based study by Dowlatshahi et al[18]. included 262 psoriasis patients and 8,009 reference subjects, all above 55 years. They were followed-up for a mean period of 11 years. The results indicated no significant difference in atherosclerosis and cardiovascular events incidence between patients with mild psoriasis and reference subjects. The study was limited by including only subjects above 55 years old; hence it is not representative of all psoriasis patients. The small psoriasis patient sample size may have resulted in the absence of a statistically significant difference observed between the groups. In addition, the prevalence of CVD in patients with severe psoriasis was not addressed in this study.

A 2013 meta-analysis by Gaeta et al[19]. showed a relative risk of 1.24 for CVD in psoriasis patients. Psoriasis patients showed a 25% increased relative risk of CVD. Thirteen studies were included, with sample sizes ranging from 598 to 4,042,257 and subjects aged between 45 and 57.1 years. Duplicate studies, literature reviews, commentaries, poor quality studies and small sample size studies were excluded. The limitation of this study was its heterogeneity in the assessment of psoriasis between studies, thereby inhibiting an association between the effects of psoriasis severity on cardiovascular risk being formed.

NICE guidelines

Current NICE Guidelines recommend: "Offer adults with severe psoriasis of any type a cardiovascular risk assessment at presentation using a validated risk estimation tool. Offer further assessment of cardiovascular risk every 5 years, or more frequently if indicated following assessment."[20]

However, no data was available regarding the adherence to these guidelines.

Discussion

The literature reviewed suggests a significant relationship exists between psoriasis and CVD compared to populations without psoriasis. Specifically, the risk of developing CVD correlated highly with increased psoriasis severity and duration in addition to other CVD risk factors such as smoking, obesity and sedentary lifestyle. The pathophysiological link between psoriasis and heart disease is a common immunological pro-inflammatory state, which occurs with the release of inflammatory cytokines, such as IL1, commonly present in kerati-

nocytes[21]. These act as mediators in initiating and maintaining psoriatic plaques in skin. Co-existence of dyslipidaemia and pro-inflammatory cytokines thus accelerate atherosclerotic lesion and plaque formation, leading to hypertension and CVD due to vaso-occlusive effects. There is also an association between these events and an increase in the inflammatory cytokine IL8. In addition, elevated visceral fat in psoriatic patients can lead to hepatic insulin resistance predisposing to diabetes, which is a significant risk factor of CVD.

Conclusion

There is strong evidence to suggest that psoriasis is an independent risk factor for CVD, particularly in younger patients with severe psoriasis[13], and is associated with increased mortality[14]. However, further research is required to better understand the relationship between psoriasis, traditional risk factors and development of CVD. While no major studies have yet shown whether screening for CVD in psoriasis patients in other countries have been beneficial, we recommend early screening for CVD and risk factors in this patient group be implemented in Irish health systems to improve patient outcomes[17]. In addition, because the study concerning screening of patients with mild psoriasis was not strong, and in view of the underlying common pro-inflammatory state behind CVD and psoriasis, further research is necessary regarding whether screening for CVD is potentially beneficial for all psoriasis patients. This would be beneficial to determine if more stringent control of the disease driven inflammation could potentially prevent the development and worsening of CVD.

Acknowledgements

We would like to thank Dr. Shivashini Jeyarajan of Adelaide and Meath Hospital Dublin incorporating the National Children's Hospital (AMNCH) for her guidance in writing this literature review.

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