

# Cardiovascular Disease and Risk Factors in Patients with Psoriasis and Psoriatic Arthritis

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**ABSTRACT.** *Objective.* Patients with psoriasis and psoriatic arthritis (PsA) have an increased incidence of cardiovascular disease (CVD) and cardiovascular risk factors such as smoking, hypertension, and metabolic syndrome compared to the normal population. Patients with psoriasis and PsA may also have increased risk from nonconventional risk factors such as raised levels of homocysteine and excessive alcohol consumption. We conducted a comprehensive review of the literature on CVD and all cardiovascular risk factors in patients with psoriasis and PsA.

*Methods.* Data sources: All studies identified from a Medline ([www.ncbi.nlm.nih.gov](http://www.ncbi.nlm.nih.gov)) search pertaining to CVD, individual risk factors in psoriasis, and PsA were included. Study selection: Studies included a healthy reference population, were published between 1975 and 2009, and were written in English.

*Results.* Our search yielded 14 studies that documented rates of CVD in patients with psoriasis and PsA compared to controls. Substantial evidence points to elevated risk of CVD in patients with psoriasis and PsA.

*Conclusion.* It remains difficult to conclude if risk factors are caused by psoriasis or share a common pathogenesis. Physicians treating patients with psoriasis and PsA must be aware of all potential cardiovascular risk factors in their patients. (J Rheumatol First Release May 15 2010; doi:10.3899/jrheum.090822)

*Key Indexing Terms:*

PSORIASIS

CARDIOVASCULAR DISEASE

PSORIATIC ARTHRITIS

CARDIOVASCULAR RISK FACTORS

Psoriasis is now recognized as one of the commonest immune-mediated inflammatory disorders<sup>1</sup>. Its incidence has been assessed at 1%–3% of the population<sup>2,3</sup>. Ten percent of patients with psoriasis develop psoriatic arthritis (PsA), a seronegative spondyloarthropathy<sup>4</sup>. It is now apparent that patients with psoriasis and PsA suffer other morbidities in addition to their skin and joint disease. In particular, both populations have an increased risk of cardiovascular disease (CVD).

The objective of our review was to provide a current overview of the literature supporting the increased risk of CVD and all relevant risk factors. It is important that dermatologists and rheumatologists assess patients for CVD. Knowledge of a patient's risk profile may enable early intervention and modification of risk factors.

## MATERIALS AND METHODS

We conducted a literature search using the scientific literature database Medline up to June 30, 2009. We used different combinations of the following search terms: "psoriasis," "psoriatic arthritis," "cardiovascular disease," "smoking," "hypertension," "cholesterol," "diabetes," "homocysteine," "alcohol," "thrombosis," and "inflammation" with limits set to include humans. Our initial search yielded more than 2000 abstracts, which were reviewed to include only studies with a reference population, published between 1975 and 2009, and written in English. This yielded 47 studies, of which the full articles were then reviewed by the first and last authors.

## RESULTS

*Increased risk of CVD in patients with psoriasis and PsA.* Our search yielded 14 studies that documented rates of CVD in patients with psoriasis and PsA compared to controls. The increased incidence of cardiovascular events in patients with psoriasis was recognized by McDonald and Calabresi in

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1978<sup>5</sup>. They reported patients with psoriasis had a 2.2 times higher incidence of arterial and venous vascular disease compared to controls in a clinic-based case-control study<sup>5</sup>.

Since then most studies have been large retrospective or prospective database studies (Table 1)<sup>5-14</sup>. The largest prospective study was that published by Gelfand, *et al* in 2006 using the UK General Practice Database<sup>6</sup>. Psoriasis appeared to confer an independent risk of myocardial infarction. The investigators controlled for diabetes, hyperlipidemia, hypertension, body mass index (BMI), age, sex, and smoking. Patients with psoriasis still had excess cardiovascular mortality compared to controls. This risk was greater for younger patients with severe psoriasis<sup>6</sup>. A second group utilizing the same data found an increased incidence of risk factors for CVD, as well as increased rates of myocardial infarction, angina, stroke, and peripheral vascular disease<sup>7</sup>. A more recent study using this database restricted diagnosis to patients with early psoriasis and did not find an increased risk of myocardial infarction<sup>8</sup>. Patients less than 60 years of age with more severe disease, however, had an increased risk [1.66, confidence interval (CI) 1.03–2.66]<sup>8</sup>.

Retrospective studies from Sweden, Germany, and Finland previously documented increased rates of risk factors such as hypertension, diabetes, and obesity in patients with psoriasis<sup>9-14</sup>. Poikolainen, *et al*<sup>11</sup> and Mallbris, *et al*<sup>12</sup> reported increased cardiovascular mortality in patients who were hospitalized. Patients managed as outpatients, however, did not have excess risk, suggesting that more severe disease was associated with a higher risk of CVD. This association is replicated in studies by Brauchli, *et al*<sup>8</sup> and Kimball, *et al*<sup>14</sup>, where more severe disease was associated with increased rates of CVD.

In a mortality study the leading cause of death in 428 Canadian patients with PsA was circulatory diseases (36.2%)<sup>15,16</sup> (Table 2)<sup>15-19</sup>. An increase in the death rate of 1.3 (CI 7.72–1.53) (standard mortality rate, SMR) due to CVD was found compared to the general population<sup>15</sup>. In a subsequent study of 648 patients, patients with PsA had a significantly higher prevalence of myocardial infarction and hypertension<sup>17</sup>. Data generated from an administrative database identifying 3066 patients with PsA confirmed these findings<sup>18,19</sup>.

*Increased risk of subclinical CVD in psoriasis and PsA.* Evidence also exists that demonstrates subclinical CVD in psoriasis and PsA. In 39 patients with moderate to severe psoriasis, arterial stiffness as measured by carotid and radial arterial wave velocity was significantly higher in patients than controls<sup>20</sup>. In another study of 43 patients, flow-mediated dilatation of the brachial artery and intimal medial thickness of the carotid were significantly lower and higher, respectively, in psoriasis patients without CVD risk factors, versus controls<sup>21</sup>. In 25 patients, 9 of whom had PsA, carotid wave pulse velocity, a measure of arterial stiffness, was significantly higher in patients with both psoriasis and PsA<sup>22</sup>. Patients with psoriasis were found to have increased coronary artery calcification in a recent direct imaging study compared to controls<sup>23</sup>.

Two case-control studies also demonstrated that patients with PsA had a higher prevalence of subclinical atherosclerosis as measured by arterial intima-media wall thickness<sup>24,25</sup>. Gonzalez-Juanatey, *et al* also found evidence of endothelial dysfunction in PsA patients without overt CVD<sup>24</sup>. A larger study of 82 patients with PsA in patients without clinical CVD found that 35% of patients had

Table 1. Studies identifying cardiovascular disease and risk factors in patients with psoriasis.

Study	Design	Findings
McDonald <sup>5</sup>	Clinic-based control study of 323 patients and 325 controls	Higher rates (2.2) of occlusive vascular disease in patients with psoriasis compared to controls
Gelfand <sup>6</sup>	Retrospective, population-based cohort study based on the UK General Practice Research Database (130,976 patients)	Increased rates of diabetes, obesity, hypertension, hyperlipidemia, and smoking in patients with psoriasis
Kaye <sup>7</sup>	Retrospective Cohort Study based on the UK General Practice Research Database (44,164 patients)	Increased rates of myocardial infarction, angina, and peripheral vascular disease, also increased diabetes, smoking, hypertension, and hyperlipidemia
Brauchli <sup>8</sup>	Cohort study of 36,702 patients from UK General Practice database	Found no increased risk for myocardial infarction overall but, in patients < 60 yrs with severe disease, risk was increased
Lindgard <sup>9</sup>	Retrospective review of database (2941 patients)	Increased rates of hypertension and diabetes and myocardial infarction in women with psoriasis
Henseler <sup>10</sup>	Retrospective cohort identified from dermatology database (42,461 patients)	Increased rates of cardiovascular disease, diabetes, obesity and hypertension
Poikolainen <sup>11</sup>	Retrospective review of patients identified from in-patient registry (5687 patients)	Increased rates of cardiovascular disease in men and women (M 1.49, F 1.7)
Mallbris <sup>12</sup>	Retrospective cohort study from Inpatient Registry and Psoriasis Association (8991 patients and 19,757 outpatients)	Increased risk of death from cardiovascular disease of 1.86 for inpatients and 0.94 for outpatients
Shapiro <sup>13</sup>	Retrospective cross-sectional study based on an Israeli database (46,095 patients)	Increased rates of atherosclerosis and diabetes in psoriasis
Kimball <sup>14</sup>	Retrospective case control study of 2 US healthcare databases (46,170 patients)	Increased cardiovascular disease and diabetes

Table 2. Studies identifying cardiovascular disease and risk factors in patients with psoriatic arthritis.

Study	Design	Findings
Wong <sup>15</sup>	Prospective study of 428 patients registered on PsA database	Myocardial infarction was leading cause of death and PsA patients had higher cardiovascular mortality (1.33) compared to controls.
Gladman <sup>16</sup>	Prospective study of 428 outpatients	Increased mortality in patients overall and increased rates of circulatory disease
Gladman <sup>17</sup>	Prospective follow up of 648 patients from PsA database	Increased risk of myocardial infarction and hypertension
Han <sup>18</sup>	Retrospective database study of 3066 patients	Increased risk of cardiovascular disease
Kimhi <sup>19</sup>	Prospective cohort study of 42 patients	Increased rates of hypertension and hyperlipidemia as well as evidence of increased arterial intimal thickness

increased intimal medial thickness despite having low cardiovascular risk<sup>26</sup>.

*Conventional risk factors in psoriasis.* Cardiovascular risk factors found with increased frequency in patients with psoriasis include the conventional risk factors obesity, diabetes mellitus, hypertension, dyslipidemia, and smoking. Oxidative stress, endothelial cell dysfunction, abnormal platelet adhesion, and hyperhomocysteinemia, which may also increase cardiovascular risk, may all be regarded as risk factors specific to psoriasis and PsA and arise with greater prevalence in psoriasis.

*Smoking in psoriasis.* The increased rates of smoking in psoriasis are well documented<sup>27-32</sup>. Poikolainen, *et al* found excess mortality related to smoking in both male and female patients [SMR for men: 1.44 (CI 1.33–1.56), SMR for women: 1.61 (CI 1.45–1.77)]<sup>30</sup>. Other retrospective database studies also document increased rates of smoking in patients with psoriasis compared to controls<sup>10-14</sup>.

Smoking also appears to adversely affect the natural history of psoriasis<sup>33</sup>. In a hospital-based cross-sectional study of Italian patients admitted to hospital for treatment of psoriasis, smoking more than 20 cigarettes a day confers a 2-fold higher risk of clinically more severe psoriasis<sup>33</sup>. Behnam, *et al* in their review found both sexes who were smokers had reduced improvement rates<sup>31</sup>.

*Hypertension in psoriasis.* Preece first described an association between psoriasis and raised blood pressure in 1977<sup>34</sup>. An increased prevalence of hypertension in patients with psoriasis compared to controls has also been documented in those studies of cardiovascular risk factors using databases<sup>6,7,9,10,14</sup>.

In a hospital-based case-control study, Ena, *et al* reported a significantly higher prevalence of essential hypertension in 100 patients with psoriasis compared to controls<sup>35</sup>. Enhanced activity of the renin-angiotensin system was found in patients with psoriasis. Endothelin-1, a potent vasoconstrictor released from vascular endothelium, is increased in the serum of patients with psoriasis and may contribute to the increased incidence of hypertension in patients with psoriasis<sup>36</sup>.

*Dyslipidemia in psoriasis.* There are more than 9 published

case-control studies measuring serum lipids in psoriasis, as summarized in Table 3<sup>37-44</sup>. The largest study has been by Mallbris, *et al* — lipids at the onset of psoriasis in 200 patients demonstrated significantly higher very low-density lipoprotein (VLDL) and high-density lipoprotein (HDL) fractions<sup>45</sup>. This study controlled for sex, blood pressure, BMI, physical activity, smoking, alcohol consumption, and C-reactive protein (CRP). Two early studies by Ferretti, *et al* of 30 children with psoriasis found that they had increased total plasma cholesterol, increased HDL cholesterol, and a decrease in ratio of HDL to LDL cholesterol<sup>46,47</sup>. This suggests that psoriasis per se may be associated with dyslipidemia. Although there are inconsistencies between studies, it appears safe to conclude that patients with psoriasis have raised levels of triglycerides, raised VLDL and LDL cholesterol, and raised lipoprotein A1 and apolipoprotein A1.

Hyperlipidemia was also found to be more common in patients with psoriasis than controls from studies utilizing databases<sup>6,7</sup>. In Gelfand's study, patients with psoriasis had a hazard ratio of 3.08–3.18 (CI 2.93–3.23 and 3.02–3.36) of having hyperlipidemia compared to controls<sup>6</sup>.

Dyslipidemia observed in psoriasis is compounded by increased oxidative stress and decreased antioxidant capacity<sup>42,48,49</sup>. Autoantibodies recognizing oxidized LDL have been found in psoriasis, their level correlating with disease activity as measured by the Psoriasis Area and Severity Index<sup>48</sup>.

*Diabetes mellitus in psoriasis.* An association between psoriasis and hyperglycemia was documented as early as 1967 by Lynch<sup>50</sup>. Numerous studies have since confirmed the association of psoriasis, hyperglycemia, and relative insulin resistance<sup>7,9,10,13,51-60</sup>. Genetic analysis of 2 non-major histocompatibility complexes in patients with psoriasis found the strongest phenotypic marker for a loci mapping to chromosome 6p22 (rs6908425;  $p = 0.00015$ )<sup>61</sup>. This marker maps to *CDKALI*, a gene associated with type II diabetes, suggesting a possible role for pleiotropic susceptibility loci for both conditions<sup>61</sup>.

Patients with psoriasis also demonstrate hyperinsulinemia and insulin resistance, with an apparent correlation between disease severity and insulin secretion<sup>62,63</sup>. It is possible that increased levels of insulin result in excessive

Table 3. Summary of studies of dyslipidemia in patients with psoriasis.

Study	Design	Patients/Controls, no.	Results
Vahlquist <sup>37</sup>	Case-control	20 male/36	Raised VLDL cholesterol; raised total, VLDL, and LDL triglycerides
Seckin <sup>38</sup>	Case-control	32 male/13	No difference in cholesterol, triglycerides, or lipoproteins
Seishima <sup>39</sup>	Case-control	38/40	Raised triglycerides; raised apolipoprotein B, CII, and CIII
Uyanik <sup>40</sup>	Case-control	72/30	Raised triglycerides; raised lipoprotein A1
Vanizor Kural <sup>41</sup>	Case-control	35/35	Raised total and LDL cholesterol; lower HDL cholesterol; raised triglycerides
Piskin <sup>41</sup>	Case-control	100/100	Raised total, VLDL, LDL cholesterol; lower HDL cholesterol; raised triglycerides
Rocha-Pereira <sup>42</sup>	Case-control	88/40	Raised total, VLDL, LDL and HDL cholesterol; raised triglycerides; raised lipoprotein A1
Akhyani <sup>43</sup>	Case-control	50/50	Raised total, VLDL, and LDL cholesterol; raised triglycerides
Mallbris <sup>45</sup>	Case-control	200/285	Raised total, VLDL, HDL cholesterol; raised apolipoprotein A1

levels of insulin-like growth factors (IGF), which appear to have a role in epidermal hyperproliferation in psoriasis<sup>64-66</sup>. Induction of interleukin 6 and vascular endothelial growth factor has been postulated as underpinning IGF's role in the development of psoriatic plaques<sup>67,68</sup>.

*Obesity and metabolic syndrome in psoriasis.* In a case-control study we found patients with psoriasis had higher BMI compared to controls ( $p < 0.004$ )<sup>69</sup>. In 2 case-control studies obesity was associated with increased frequency of psoriasis (OR 1.9), and psoriasis was associated with increased prevalence of obesity compared to the control population, respectively (8.4% vs 3.6;  $p < 0.001$ )<sup>52,53</sup>.

The prospective Nurses' Health Study of 78,626 nurses found that increased adiposity and weight gain were strong risk factors for development of psoriasis<sup>70</sup>. When age, smoking status, and alcohol intake were all controlled for, a significant association was found, clearly indicating a graded association between BMI and risk of incident psoriasis<sup>71</sup>. Obesity is one of the major components of the metabolic syndrome. Metabolic syndrome may be considered to consist of central obesity, hypertension, dyslipidemia, and insulin resistance.

Sommer, *et al* found increased prevalence of metabolic syndrome in psoriasis patients admitted to hospital compared to other hospital-based controls (odds ratio 5.29, CI 2.78–12.8)<sup>51</sup>. Another hospital-based case-control study found that metabolic syndrome was significantly more common in psoriatic patients than in controls (30.1% vs 20.6%; odds ratio 1.65, CI 1.16–2.35,  $p = 0.005$ )<sup>52</sup>. In their cross-sectional study of patients with psoriasis identified from an Israeli database, Cohen, *et al* demonstrated that psoriasis was associated with metabolic syndrome (OR 1.3, CI 1.1–1.4)<sup>53</sup>.

*Conventional risk factors in PsA.* There has been less research on CVD and risk factors in PsA. It is apparent, however, that patients with PsA have an increased prevalence of cardiovascular risk factors<sup>18,19,72,73</sup>. In 2004, Peters, *et al* reviewed the literature regarding cardiovascular risk factors in the spondyloarthropathies, including PsA<sup>72</sup>. There had been no studies of the prevalence of smoking or

hypertension in PsA. Patients did, however, have an atherogenic lipid profile, with a suggestion that as disease activity receded, lipid profile improved<sup>72</sup>.

In a cross-sectional comparative study of PsA patients identified from a US database, Han, *et al* found patients with PsA had a higher prevalence ratio for type II diabetes, hyperlipidemia, and hypertension compared to controls (1.5, 1.3, and 1.2, respectively)<sup>18</sup>. Kimhi, *et al* compared 47 patients with PsA to 100 healthy controls and found significantly higher levels of hypertension and hyperlipidemia compared to controls<sup>19</sup>.

One hundred two patients with PsA were screened for cardiovascular risk factors and compared to 82 control patients<sup>73</sup>. Patients had a higher prevalence of diabetes mellitus (OR 9.27, 95% CI 2.09, 41.09) and hypertension (OR 3.37, 95% CI 1.68, 6.72), and an increased prevalence of lower HDL cholesterol (OR 0.16, 95% CI 0.07, 0.41) following adjustment for BMI<sup>73</sup>. This atherogenic lipid profile was confirmed by Jones, *et al* in 50 patients with PsA<sup>74</sup>. Tam, *et al* found a slightly different pattern of dyslipidemia in their case-control study of 102 patients: patients with PsA had higher HDL cholesterol and apolipoprotein A1 levels, lower total cholesterol and LDL cholesterol levels, and a lower total cholesterol to HDL cholesterol ratio<sup>73</sup>. Two older studies had demonstrated that PsA patients with active synovitis had lower total cholesterol, LDL cholesterol, and HDL cholesterol<sup>75,76</sup>.

Raised BMI in patients with PsA has been documented in the 2 case-control studies by Kimhi, *et al* and Tam, *et al*<sup>19,26</sup>. The full spectrum of metabolic syndrome has not been formally studied in patients with PsA. Individual components of the metabolic syndrome such as obesity<sup>18,26</sup>, hypertension<sup>18,19,72</sup>, insulin resistance<sup>18,72</sup>, and dyslipidemia<sup>18,19,72,73</sup> have been reported.

*Nonconventional risk factors in psoriasis and PsA. Inflammation.* Chronic inflammation has been shown to play a role in the development of atherosclerosis<sup>77,78</sup>. A picture of atherosclerosis as an inflammatory, autoimmune-like disease is emerging<sup>79</sup>. Both the innate immune system and T helper-1 lymphocytes appear to be involved in atherogen-



esis<sup>80,81</sup>. This is similar to the pattern of immune-mediated inflammation in psoriasis and PsA<sup>82-84</sup>. It is possible that psoriasis and PsA produce chronic, systemic inflammation, with higher levels of inflammatory cells and cytokines invoking endothelial inflammation and plaque formation<sup>85,86</sup>.

The increased prevalence of obesity seen in patients with psoriasis and PsA may also increase the burden of inflammation<sup>87</sup>. White adipose tissue accumulates in deposits close to blood vessels, where (as noted above) it secretes cytokines, chemokines, and hormone-like proteins<sup>88</sup>.

CRP has emerged as one of the predictors of CVD<sup>89-91</sup>. As its levels correlate well with joint inflammation, CRP is measured routinely in PsA<sup>92-95</sup>. A recent large cohort study from Italy, however, suggests that CRP is possibly more valuable in patients with more severe joint disease<sup>96</sup>. In a study of cardiovascular risk factors, Tam, *et al* reported that low-grade inflammation as measured by high sensitivity CRP (hs-CRP) was associated with obesity, hypertension, insulin resistance, and dyslipidemia<sup>73</sup>.

Fibrinogen is the other major acute-phase protein known to be associated with vascular events<sup>97,98</sup>. Fibrinogen levels are known to be increased in psoriasis and PsA<sup>14,49,72,98-101</sup>. Both these elevated markers indicate chronic inflammation in psoriasis and PsA and a possible role in elevating a patient's cardiovascular risk.

*Endothelial cell dysfunction.* Atherosclerotic plaques may be considered the result of chronic inflammation of vessel endothelium, leading to endothelial dysfunction and plaque formation in the milieu of raised plasma lipids.

Oxidative stress and the generation of free radicals is believed to play a critical role in causing damage to the endothelial cells<sup>101</sup>. Increased levels of oxidized low-density lipoproteins in psoriatic plaques of 84 patients have been reported compared to healthy controls<sup>99,100</sup>. This finding was confirmed in a study that also reported decreased antioxidant capacity and a lipid and lipoprotein profile susceptible to oxidation<sup>102</sup>. Rocha-Pereira, *et al* reported that patients with psoriasis may be at increased risk of oxidative and proteolytic stress from neutrophils<sup>42</sup>.

Endothelial activation in patients with psoriasis is known to be important in the formation of plaques. Treatment of patients with anti-tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) led to the downregulation of the vascular growth factors angiopoietin 1 and 2 and their receptor Tie-2, underpinning the role of angiogenesis in plaque formation<sup>103</sup>. There does not appear to be a reliable marker of either endothelial dysfunction or endothelial activation, however.

*Atherothrombotic markers: fibronectin and platelets.* Atherothrombosis is the result of atherosclerotic progression that can result in vessel occlusion<sup>104</sup>. Atherosclerotic plaques rupture, and plaque contents interact with blood components, triggering the coagulation cascade involving platelets, thrombin, fibrin, and inflammatory cells<sup>105</sup>.

Increased coagulation factors, decreased fibrinolysis, and increased or more reactive platelets all promote thrombus formation<sup>105</sup>.

Low levels of fibronectin have been suggested as a marker of atherothrombosis. Studies of fibronectin in psoriasis have been conflicting; Vanizor and colleagues found that levels of fibronectin were raised in patients with psoriasis<sup>99</sup>. Fibronectin levels were lower in patients with psoriasis in a second study; however, this was true of patients with active disease and not those in remission<sup>106</sup>. Fibronectin levels have been shown to be raised in patients with PsA compared to healthy controls<sup>107</sup>.

Increased platelet aggregation in patients with psoriasis compared to controls has been documented<sup>108</sup>. Thrombocytosis has also been documented in PsA: platelets may be acting as an acute-phase reactant in this instance<sup>109</sup>.

*Homocysteine.* Raised levels of homocysteine have been shown to be an independent risk factor for the development of CVD<sup>110</sup>. Homocysteine is believed to cause endothelial dysfunction by causing accumulation of asymmetrical dimethyl arginine, a natural inhibitor of nitric oxide synthase. It thus reduces the production of the vasodilator nitric oxide, which also protects the vessel wall against the pathogenesis of atherosclerosis and thrombosis.

In our case-control study, patients with psoriasis had a relative risk 7.1 times greater than controls of having significantly raised levels of homocysteine<sup>69</sup>. A recent controlled study has shown that patients with psoriasis have raised levels of homocysteine and lower levels of plasma folate compared to normal controls<sup>111</sup>; this is supported by 2 other uncontrolled studies, one of them in patients taking methotrexate<sup>100,112</sup>. It is proposed that keratinocyte turnover is accelerated in patients with psoriasis, and folate, which is used to methylate DNA in actively dividing cells, may be consumed, leading to higher levels of homocysteine<sup>113-115</sup>. High levels of homocysteine have been documented in a small number of patients with PsA<sup>116</sup>.

*Increased alcohol consumption.* Although moderate alcohol consumption has been shown in several epidemiological studies to be cardioprotective, excessive alcohol consumption increases cardiovascular risk and mortality<sup>117</sup>. Poikolainen, *et al* found alcohol in a retrospective study to be the leading cause of excess mortality in patients hospitalized for treatment of psoriasis<sup>11</sup>. Excessive alcohol consumption is widely documented in patients with psoriasis<sup>118,119</sup>. We have shown a higher prevalence and incidence of psoriasis in a population of patients with alcoholic liver disease<sup>120,121</sup>. There is also a suggestion that alcohol consumption may adversely affect treatment outcomes in patients who continue to consume excess alcohol<sup>122</sup>.

There have been few studies of alcohol consumption in patients with PsA apart from those being treated with methotrexate.

*Conclusion.* The evidence that patients with psoriasis and

PsA have an elevated risk of developing CVD is substantial. This may be due to the increased prevalence of conventional risk factors but also other risk factors that are disease-specific. From published studies it would appear that risk is greatest in those with more severe disease and longer disease. This implies that aggressive treatment of both diseases should lower cardiovascular risk. Data from the British Biologics Registry do support the reduction in myocardial infarction in patients with rheumatoid arthritis treated with TNF inhibitors<sup>123</sup>. It may be too early, however, for registries to fully conclude the benefits of TNF inhibitors. Two studies have looked at the effects of TNF inhibitors on cardiovascular risk factors in PsA<sup>124,125</sup>. In a double-blind study the TNF inhibitor oncept significantly lowered lipoprotein(a) and homocysteine but also increased triglyceride levels<sup>124</sup>. In a review of published studies, Channal, *et al* found that etanercept and infliximab appeared to have no effect on dyslipidemia, and treatment with each resulted in significant weight gain in both psoriasis and PsA<sup>125</sup>. Hence the benefit of lowering inflammation would appear to be counteracted by unique effects of individual drugs. Methotrexate decreased cardiovascular mortality in a large cohort of patients with psoriasis<sup>125</sup>. This may be due to the concomitant use of folic acid and to beneficial effects on homocysteine. A placebo-controlled clinical trial on methotrexate use in patients with stable CVD may further elucidate the role of methotrexate<sup>126</sup>. To date there is insufficient evidence to conclude that aggressive disease control improves cardiovascular risk. Biologics registries may be helpful in providing an answer to this question.

The European League Against Rheumatism has issued guidelines based on a systematic literature search of cardiovascular risk management in PsA<sup>127</sup>. It recommends annual screening of PsA patients for cardiovascular risk and management according to the SCORE or Framingham model, or national guidelines. They note commonly used thresholds are a systolic blood pressure of 140 mm Hg and LDL cholesterol of 2.5 mmol/l. The initiation of antihypertensives and statins should be similar to the general population. They also recommend being mindful of the associated increased cardiovascular risk associated with nonsteroidal antiinflammatory drugs, cyclooxygenase-2 inhibitors, and corticosteroids. Smoking cessation is to be recommended.

In a consensus document published in the *American Journal of Cardiology* the following was recommended for patients with psoriasis<sup>128</sup>: Patients with psoriasis and  $\geq 1$  abnormal serum lipid level, and/or elevated plasma hs-CRP, should adopt a multifaceted lifestyle approach to reduce risk. This involves weight loss, increased physical activity, and alcohol reduction. If this is unsuccessful in achieving target LDL cholesterol levels then a statin should be introduced. Cigarette smoking cessation should be promoted. Patients with hypertension should first undertake lifestyle changes, including reduction of weight and dietary sodium

and, if unsuccessful, antihypertensive medication should be commenced. Beta-blockers, angiotensin-converting enzyme inhibitors, and angiotensin II blockers can worsen psoriasis. The National Psoriasis Foundation recommends implementing the American Heart Association guidelines<sup>129</sup>, which recommend smoking cessation by age 40 years, alcohol reduction, and exercising for 30 minutes 3 times a week in patients without risk factors. More intensive intervention is warranted for people with risk factors, as outlined on the website of the American Heart Association: [www.american-heart.org](http://www.american-heart.org).

There is a paucity of information on the effects of lipid-lowering agents and antihypertensives on cardiovascular risk and no data on the optimal use of aspirin. Large prospective cohort studies are required to produce adequate evidence-based guidelines. Further, a comprehensive study of nonconventional risk factors in patients with psoriasis and PsA has not been done. It is important that such studies be conducted to define patients who are at risk and identify potential biomedical markers of cardiovascular risk.

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