

Review

Unfavorable cardiovascular risk profiles in untreated and treated psoriasis patients

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Abstract

Psoriasis is a chronic inflammatory skin disease that is associated with an increased cardiovascular risk profile. The systemic inflammation present in psoriasis, various systemic treatments for psoriasis and an increased prevalence of unhealthy life style factors may all contribute to this unfavorable risk profile. The purpose of this article is to provide an overview of what is known about these risk factors in psoriasis, the way they influence the cardiovascular risk of psoriasis patients, and what can be done to reduce this risk.

Genetic studies demonstrate that psoriasis and cardiovascular disease share common pathogenic features in which, for example inflammatory cytokines like TNF- α and IL-1 play an important role. The chronic inflammation in psoriasis has an unfavorable effect on the cardiovascular risk profile. Multiple cardiovascular risk factors seem to be influenced; the blood pressure, oxidative stress, dyslipidemia, endothelial cell dysfunction, homocysteine levels and blood platelet adhesion. Moreover, classic cardiovascular risk factors like smoking and obesity that have an increased prevalence among patients with psoriasis, indirectly also worsen the cardiovascular risk profile by stimulating the psoriasis activity. Systemic treatments in psoriasis reduce the cardiovascular risk by diminishing the inflammation, but it should be taken into account that most therapies also have adverse cardiovascular effects like dyslipidemia, hyperhomocysteinemia and hypertension. As a consequence preventive measures may be indicated at least during long-term treatments. Prospective research is warranted to accurately estimate the increased cardiovascular risk in psoriasis, to determine the underlying processes and to consider preventive measures according to the absolute risk of cardiovascular disease. The present overview provides data to advice health care providers to pay more attention to the cardiovascular risk profile in psoriasis patients.

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1. Introduction

Psoriasis is a chronic inflammatory skin disorder affecting approximately 2% of the general population. It is characterized by epidermal hyperproliferation, abnormal differentiation of epidermal keratinocytes and a lymphocyte infiltration consisting mostly of T-lymphocytes. In the pathogenesis of psoriasis many different inflammatory cells are involved with major roles for the T-lymphocyte and the cytokine network and chemokines [1]. At the site of inflammation activated T-lymphocytes predominantly release type 1 cytokines like interferon- γ (IFN- γ), tumor necrosis factor- α (TNF- α) and interleukin-2 (IL-2). IFN- γ may contribute to hyperproliferation of keratinocytes in the skin by inhibiting their apoptosis [2]. IL-2 stimulates the T-lymphocyte proliferation and TNF- α activates and increases keratinocyte proliferation. Other effects of TNF- α are stimulation of production of cytokines from T-lymphocytes and macrophages, chemokine release from macrophages, and the expression of adhesion molecules on vascular endothelial cells. In case of such an extended inflammation, it is conceivable also to assume systemic consequences. Most health care providers, including dermatologists, do not associate psoriasis with an unfavorable cardiovascular risk profile, but more and more evidence is emerging that this might be the case. The higher prevalence of classic cardiovascular risk factors, like smoking, hypertension and obesity contribute to atherogenesis in psoriasis patients, but psoriasis itself and its systemic treatment may also stimulate premature atherogenesis, increasing the cardiovascular risk. In rheumatoid arthritis (RA), which is also a chronic inflammatory disease with a comparable pathogenesis, it has already been demonstrated that these patients have an increased prevalence of atherosclerosis compared to the general population [3]. The atherosclerosis in RA is not only associated with classic cardiovascular risk factors, but with the inflammatory process as well [4]. Additional support for this notion has come from research with laboratory mice. A mouse was created with a deficiency in the interleukin (IL)-1 receptor antagonist gene that normally functions as a naturally occurring inhibitor of IL-1 [5]. These mice developed three apparently spontaneous inflammatory diseases arthritis, psoriasis-like dermatitis and arteritis [6]. This suggests that the inflammatory process in psoriasis may also affect

the arterial wall, promoting the atherosclerotic process. In the present review, we describe all available evidence for the association between psoriasis and cardiovascular disease to assess the indication for risk evaluation and preventive measures in these patients.

2. Methods

A literature search was performed using the PubMed database. We identified 926 articles that were published in the English language from January 1970 to January 2006. The following MeSH terms were used: psoriasis, cardiovascular diseases, inflammation, atherogenesis, hydroxymethylglutaryl-coa reductase inhibitors, obesity, smoking, hypertension, homocysteine, insulin resistance, blood platelets, oxidative stress and endothelial cells. The following text words were also searched for: cardiovascular risk, PSORS1, dyslipidemia and therapy. The identified studies were reviewed on the presence of information on the cardiovascular risk profile of psoriasis patients, resulting in a final selection of 78 studies.

3. Psoriasis and cardiovascular disease risk

Mallbris et al. performed a historical cohort study to assess the risk for cardiovascular mortality among psoriasis patients [7]. Remarkably, patients who were treated at least once as inpatient had a 50% increased overall risk for cardiovascular death compared to the general population. The excess risk was clearly associated with the severity of psoriasis expressed as the number of hospital admissions. Especially patients admitted at young age had an unexpectedly high excess cardiovascular mortality, whereas no increased cardiovascular mortality among outpatients with psoriasis was observed. These data suggest on the one side, that psoriasis patients with more severe disease have a substantially increased risk for cardiovascular death. On the other side, it can be argued that the available in-hospital treatment modalities contribute to this risk as well. A large 10-year prospective cohort study of psoriasis outpatients showed no increase of cardiovascular mortality compared to the general population

[8]. This follow up study was performed among patients on photochemotherapy, who had an average severity of psoriasis of more than 30% affected body surface area (BSA) at entry. Unfortunately, no analysis was performed according to the affected BSA. McDonald assessed the cardiovascular morbidity by combining psoriasis data from three studies and concluded that the occurrence rate of occlusive vascular events was significantly greater in psoriatic than in the non-psoriatic dermatologic patient [9]. In this study, the percentage of body surface area affected by psoriasis appeared to influence the incidence of cardiovascular diseases particularly in the older patient. Henseler and Christophers conducted a hospital-based cross-sectional study and found an overall increase in heart failure among psoriasis inpatients [10]. Taken together, these data support the notion that an association exists between psoriasis and an unfavorable cardiovascular risk profile, especially in patients with severe psoriasis. However, differences with regard to the type of study, the selection procedures and whether or not age and the severity of psoriasis were taken into account resulted in an intricate set of combined results. For example, Wong and co-workers found that patients with psoriatic arthritis had an increased death rate of 1.3 due to cardiovascular diseases, but Shbeeb et al. did not observe a difference in lifetime survival between patients with psoriatic arthritis and the general population [11,12]. These conflicting results may be based on the differences in disease severity. The work by Gladman et al. confirmed a selection of patients with the highest disease severity to referral centers: markers of previously active and severe disease as manifested by the prior use of medication, a high erythrocyte sedimentation rate at presentation and evidence of radiological joint damage are associated with increased mortality in psoriatic arthritis patients [13]. Moreover, a shift from hospital based to effective outpatient care has arisen, and the present day treatment whereby the inflammatory process is modulated, may reduce the risk of subsequent cardiovascular mortality associated with psoriasis.

4. Psoriasis genetics and cardiovascular disease risk

Twin studies support a genetic basis of psoriasis [14,15]. Although the way gene variants influence the disease is complex, a clear association was found with the PSORS1 gene locus on chromosome 6, accounting for approximately 35–50% of the genetic contribution to psoriasis [16,17]. Carriers of this HLA-Cw*0602 allele exhibit an earlier disease onset, more extensive skin lesions and a more severe disease [18]. Psoriasis patients who are predisposed to have such an extended inflammation may also be at higher risk for cardiovascular complications. Since cytokines are thought to play a pivotal role in psoriasis, the genes that encode them are also potential candidate genetic markers for disease susceptibility and severity, as well as cardiovascular disease risk. For example, IL-1 receptor antagonist-deficient

mice that develop both psoriasis and arteritis, fit well with the reported dysregulation of the IL-1 family of cytokines in psoriasis [6,19]. Furthermore, TNF- α is overexpressed in lesional skin, in the circulation of patients with psoriasis, as well as in failing myocardium [20,21]. Studies on transgenic mice that overexpress TNF- α specifically in the heart, showed that they develop myocardial inflammation and subsequent heart failure [22]. Another interesting association has been demonstrated between the apolipoprotein (apo) E4 allele and chronic plaque psoriasis and guttate psoriasis, suggesting a possible pathogenic role of ApoE in psoriasis [23]. Apo E is also involved as a ligand in the clearance of triglyceride-rich lipoproteins from the circulation. Individuals with the ApoE4 isoform tend to have increased total cholesterol, low-density lipoprotein (LDL) cholesterol and apolipoprotein B, and a high prevalence of heart disease [24]. The underlying mechanism is not fully understood and possibly involves downregulation of LDL receptors.

5. Psoriasis treatment and cardiovascular disease risk

Depending on the severity of the psoriasis various treatments are available. Anti-psoriatic therapies are mainly targeted at reducing the inflammatory process in the skin. Topical treatments, corticosteroids, Vitamin D analogues, dithranol and tar are preferred in mild forms of psoriasis (<10% of the body area affected). The next option will be phototherapy, which can be divided into UVB-light therapy and photochemotherapy (PUVA). In more severe forms of psoriasis (>10% of the body area affected) systemic therapy is used. We will shortly discuss the available systemic therapies and their adverse systemic effects with special focus on cardiovascular effects.

Methotrexate (MTX) is a frequently prescribed agent. MTX blocks DNA synthesis in rapidly proliferating epidermal cells, T- and B-lymphocytes and disrupts cytokine secretion [25]. Hepatotoxicity is a well-known adverse effect of MTX. After a cumulative dose of 1.5 g a liver biopsy is recommended to examine if there are hepatotoxic effects. MTX also reduces plasma and red blood cell folate levels via reduced activity of dihydrofolate reductase, which subsequently increases homocysteine levels [26]. Therefore folic acid is usually added to methotrexate to reduce its toxicity and its effect on homocysteine levels [27].

The immunosuppressive drug cyclosporin inhibits T-cell activation and the transcription of IL-2 and other cytokines important in the pathogenesis of psoriasis [28]. Cyclosporin is associated with renal toxicity that is related to the dose and the duration of treatment [29]. Other side effects of cyclosporin are metabolic abnormalities like hypertriglyceridemia and hypercholesterolemia.

Acitretin is an oral retinoid that by binding to retinoic acid receptors alters the transcription of genes coding for proteins involved in the pathogenesis of psoriasis, especially

in keratinocytes. The most common side effects are dose-dependent and are mucocutaneous adverse effects such as cheilitis and hair loss, requiring dose reduction in some patients. Hepatotoxicity and hypercholesterolemia, triglyceridemia and low high-density lipoprotein (HDL) cholesterol are also side effects of acitretin [30].

Oral fumaric acid ester therapy is another systemic treatment for psoriasis in Western Europe. Fumaric acid esters promote the secretion of type 2 cytokines (IL-4, IL-5 and IL-10) that may inhibit type 1 cytokines. The cytokine switch appears to be beneficial in psoriasis [31]. Gastrointestinal complaints and flushing are often reported and frequently a relative lymphocytopenia occurs [32]. No significant changes in cholesterol levels have been noticed with the use of fumaric acid esters [33].

Biological response modifiers are protein molecules constructed to specifically target a particular molecule on cells or a cytokine involved in the pathogenesis of psoriasis. At this moment they can be classified into T-cell modifying agents and TNF- α inhibitors. Primary concerns with the use of biologicals are increased risk of infection and relative uncertainty about the long-term adverse effects and safety. The effect of TNF- α inhibitors on serum HDL levels has been investigated in patients with rheumatoid arthritis. On the first day it decreases HDL, but most likely it favorably increases HDL during prolonged treatment [34,35]. Irace et al. also observed a transitory improvement in endothelial function after anti-TNF- α treatment [35].

In summary, the iatrogenic effects of systemic psoriasis therapies might also enhance the cardiovascular risk profile: the increased homocysteine level after MTX use, the dyslipidemic changes related to the use of cyclosporin and acitretin, but also a potential beneficial increase of HDL occurs when using TNF- α inhibitors.

6. Classic cardiovascular risk factors in psoriasis

6.1. Lipid profile

In moderate to severe psoriasis, a significantly deteriorated lipid profile was observed compared to healthy controls with higher values of cholesterol, triglycerides, LDL and low HDL [36]. In less severe cases, only values of HDL were significantly lower compared to controls [37]. Moreover, the lipid profile may be affected during systemic treatment with anti-psoriatic medication like acitretin or cyclosporin, potentially increasing the overall risk for cardiovascular diseases.

6.2. Hypertension

In a hospital-based study, Lindegard and co-workers observed that psoriasis was significantly associated with hypertension and also Henseler and Christophers found it twice as frequent in psoriasis as in control subjects [10,38]. Inerot et al. reported no increased frequency of hyperten-

sion in a population of patients with psoriasis sampled from a patient organization [39]. A probable explanation for this difference is that in the latter study patients had a mild form of psoriasis, which was also suggested by the authors, while Henseler and Christophers described that the majority of their psoriasis patients were hospitalized at first diagnosis. Another explanation might be the relatively low mean age of approximately 40 in the study of Inerot et al.

Factors contributing to the association between psoriasis and hypertension may be the production of endothelin-1, the inflammatory process itself and the adverse effects of cyclosporin treatment. Endothelin-1 is a peptide produced by keratinocytes as an autocrine growth factor for these cells. Bonifati et al. reported that endothelin-1 was increased in both the sera and lesional skin of patients with psoriasis compared to normal subjects and the values also correlated with the psoriasis severity [40]. Endothelin-1 has very potent systemic vasoconstricting properties and may therefore have systemic effects and contribute to elevated blood pressure in psoriasis patients. If the inflammatory process in psoriasis influences the blood pressure has not been investigated yet, although other work does provide circumstantial evidence. Like oxidative stress, also present in mild psoriasis, has been implicated to play a role in hypertension by the nitric oxide (NO) destructive effects of reactive oxygen species (ROS), which impair the endothelium dependent vasodilatation [41]. The third contributing factor is the frequent prescription of cyclosporin that is known for its hypertensive side effect, especially in long-term maintenance therapy [42].

6.3. Obesity

In a case-control study, Naldi et al. showed that psoriasis of recent onset was positively correlated with body mass index (BMI), with an odds ratio of 1.6 for over weighted and 1.9 for obese patients [43]. Moreover, a Croatian study suggested that a low energy diet might be beneficial in psoriasis vulgaris treatment as a significant reduction in psoriatic skin lesions was observed after a low-energy diet [44]. Obesity is associated with a state of chronic low-grade inflammation observed by increased circulatory levels of TNF- α , C-reactive protein and IL-6 positively related to the BMI [45,46]. Macrophages that infiltrate the adipose tissue in obesity are likely to be responsible for the production of these pro-inflammatory cytokines [47]. This pro-inflammatory state in obesity may explain the association between psoriasis and obesity. When patients with psoriasis are more likely to be obese that implies they will also have the comorbid conditions of those with obesity. The risks of diabetes, hypertension and dyslipidemia start to rise from a BMI of about 21.0 kg/m² thereby deteriorating the cardiovascular risk profile [48,49].

In both obesity as well as diabetes mellitus, TNF- α is an important mediator of insulin resistance through its ability to decrease the tyrosine kinase activity of the insulin receptor [50]. Several chronic inflammatory diseases like rheumatoid arthritis have also been associated with the presence

of insulin resistance [51]. Reynoso-von Drateln et al. investigated whether this is the case in patients with psoriasis, however no differences were found in insulin secretion or sensitivity compared with control patients [37]. Nonetheless, a significant correlation was observed between the duration of psoriasis and insulin sensitivity. Henseler and Christophers, and Binazzi et al. both found an association between psoriasis and diabetes mellitus, which was probably the result of an increased prevalence of obesity in the psoriasis patients [10,52].

6.4. Smoking

A number of studies have examined the association between psoriasis and smoking. The most striking link has been established between smoking and pustular psoriasis [43]. Naldi et al. showed in the same paper that the risk for plaque psoriasis was also higher in current smokers and ex-smokers than in patients who had never smoked. A cross-sectional study by Herron et al., demonstrated that in their psoriasis population the prevalence of smoking was higher than in the general Utah population and higher than in the non-psoriatic patients [53]. Using questionnaires, they found that 78% smoked before the onset of psoriasis. Smoking may not only be a trigger, but it might be associated with clinical severity as well. A high intensity of smoking (>20 cigarettes daily) relative to a lower level of consumption (≤ 10 cigarettes daily) was associated with a more than two-fold increased risk of clinically more severe psoriasis [54].

Recently, it has been shown that cigarette smoking induces an overproduction of IL-1 β , increases the production of TNF- α and enhances the transforming of growth factor- β from mononuclear blood cells [55]. These cytokines are also raised in psoriasis and may partly explain the association with smoking [56,57]. Nicotine also stimulates dendritic cell (DC) expression of costimulatory molecules, MHC class II and adhesion molecules [58]. This DC activation augments their capacity to stimulate the proliferation of T-lymphocytes, which also play an important role in the pathogenesis of psoriasis. Moreover, nicotine induces a significant increase in the secretion of the pro-inflammatory type I cytokine interleukin-12 by human DC, further contributing to the inflammatory process.

7. Other cardiovascular risk factors in psoriasis

7.1. Oxidative stress

Patients with psoriasis exhibit several markers of oxidative stress and show impaired antioxidant status. The oxidative stress develops when the antioxidant capacity is overwhelmed leading to oxidative damage of lipids and proteins. Oxidative stress and increased free radical generation, reactive oxygen species and superoxide anion liberation occur in inflamed skin in psoriasis [59]. Malondialdehyde (MDA),

a marker of lipid peroxidation, is increased in plasma and red blood cells of patients with psoriasis. Antioxidants like β -carotene and α -tocopherol show decreased plasma levels [60]. Both function as scavengers of free radicals like lipid peroxy radicals. The activity of glutathione peroxidase, an antioxidant enzyme is also reduced in psoriasis. This imbalance between oxidants and antioxidants is also observed in mild forms of psoriasis [61]. High levels of oxidants may favor the progression of the atherosclerotic process by promoting LDL oxidation. Oxidized LDL (Ox-LDL) is not only important for the formation of the fatty streak but it also damages the endothelium allowing continued transport of inflammatory cells and mediators into the vessel wall and all these processes generate ROS [60]. It is also clear that ROS are involved in signaling vascular smooth muscle cell migration and proliferation during the formation of atherosclerotic lesions.

7.2. Homocysteine

Hyperhomocysteinemia may constitute an independent risk factor for cardiovascular disease [62]. Homocysteine promotes many processes involved in atherosclerosis and also affects the coagulation system. Vanizor Kural et al. examined serum total homocysteine levels and its relationship with atherothrombotic markers in 30 patients with psoriasis and 30 sex and aged matched healthy volunteers [63]. The mean levels of serum total homocysteine, fibrinogen, fibronectin, soluble intercellular adhesion molecules-1, plasminogen activator inhibitor-1 (PAI-1), total cholesterol, triglycerides and autoantibodies against oxidized LDL (AuAb-oxLDL) were increased whereas tissue plasminogen activator, Vitamin B₁₂ and folate levels were decreased compared with healthy controls. Total homocysteine levels were negatively correlated with Vitamin B₁₂ and positively correlated with plasminogen activator inhibitor-1 and AuAb-oxLDL. Hyperhomocysteinemia may be a risk indicator, but high levels of homocysteine change the homeostatic balance towards a prothrombotic state by increased PAI synthesis as well as by an increased fibrinogen level and stimulate atherosclerosis by the increased level of AuAb-oxLDL resulting in LDL oxidation.

7.3. Endothelial cell dysfunction

Blann suggested that one of the mechanisms of endothelial cell damage is caused by a chronic inflammatory state [64]. Chronic stimulation of the endothelial cell by cytokines may result in dysfunctional changes. Other factors like smoking, hyperinsulinemia, hypertension and hypercholesterolemia, which are often associated with psoriasis, are also deleterious to the endothelium and may accelerate endothelial cell dysfunctioning. Vascular endothelial cell dysfunction is seen as one of the early markers of atherosclerosis and is recognized as a predictor of cardiovascular events [65]. Damage to endothelium can be determined by assessing the levels

of soluble endothelial cell markers, such as soluble intercellular adhesion molecule-1 (sICAM-1) and von Willebrand factor in the plasma or non-invasively by postocclusion flow-mediated vasodilatation of the brachial artery using high sensitivity brachial ultrasonography [66–68]. We propose that psoriasis might be associated with endothelial dysfunction, both because of the abundance of pro-inflammatory cytokines as well as the metabolic abnormalities found in psoriasis.

7.4. Blood platelets

Patients with psoriasis were reported to have normal platelet counts and fibrinolytic activity. Circulating platelet aggregates were not raised significantly, but a higher spontaneous platelet hyperaggregability was noticed using a platelet aggregation test [69]. This hyperaggregation of platelets is probably due to enhanced cyclooxygenase activity in these platelets [70]. It is, however, not clear whether or not this contributes to a higher risk of occlusive vascular disease. Blood platelets might contribute to the cardiovascular risk in psoriasis by another mechanism. Inflammatory signals induce the expression of proteins on the endothelial cell surface that promote the adhesion and extravasation of activated immune cells from the circulation into the underlying tissue. P-selectin and E-selectin are among the molecules expressed on the endothelial cells. Platelets also adhere to the activated human endothelial cell monolayer by attaching to the selectins [71]. Thereafter, platelets firmly adhere to the vascular endothelium via β_3 integrins, release other pro-inflammatory substances and induce a proatherogenic phenotype of ECs. Subsequently, they recruit circulating leukocytes, bind them and activate them, thereby initiating leukocyte transmigration and foam cell formation. Thus, platelets provide the inflammatory cellular basis for plaque formation and may contribute to the early processes of atherosclerosis in psoriasis [71].

8. Possible role of statins in psoriasis

HMG-CoA reductase inhibitors (statins) have pleiotropic effects and may be beneficial to patients with psoriasis: in addition to cholesterol lowering, statins have other anti-atherosclerotic, cardiovascular risk reducing effects [72]. Statins directly upregulate endothelial nitric oxide synthase *in vitro*, which reduces the monocyte adhesion to the endothelial surface and the oxidation of LDL. Moreover, statins also have immunomodulatory activities that may improve the psoriasis skin [73]. By binding to HMG-CoA reductase statins inhibit the cholesterol biosynthesis and reduce isoprenoid levels in the mevalonate pathway. Especially mevalonate is an important substrate in cholesterol biosynthesis that activates inflammation via intracellular signal transduction systems [74]. In this way statins may cause a shift from pro-inflammatory to anti-inflammatory conditions in psoriasis patients that might be beneficial to the skin disorder as well as the cardiovascu-

lar risk profile [75,76]. These observations suggest a potential role for statins in psoriasis patients.

9. Discussion

It is clear that psoriasis is associated with a higher risk of cardiovascular disease. The excess risk is influenced by the psoriasis severity, indicating an inflammation dependent effect. This association is corroborated by genetic studies confirming overlapping pathogenic features, like overexpression of pro-inflammatory cytokines in both psoriasis and cardiovascular disease. It would be interesting to be able to confirm the association of PSORS1 with cardiovascular disease in future research.

If systemic inflammation promotes atherosclerosis, then it follows that the use of anti-inflammatory agents in psoriasis may decrease the cardiovascular disease burden in this population. Unfortunately most of these drugs also have adverse effects on the cardiovascular risk profile, resulting in a more ambivalent effect. Methotrexate treatment in RA has proven to offer substantial protection against cardiovascular disease, far outweighing the potential effect of hyperhomocysteinemia [77]. The resultant of other therapies has not been investigated yet, but we assume that side effects like hypertension or dyslipidemia will dramatically reduce the advantageous anti-inflammatory effects.

As discussed in detail, the systemic inflammation in psoriasis acts on many different cardiovascular risk factors; hypertension, oxidative stress, dyslipidemia, endothelial cell dysfunction, homocysteine levels and blood platelet adhesion. Although for some cardiovascular risk factors the association with psoriasis is more robust than others, there is unquestionably a considerable impact of this systemic inflammation on the cardiovascular risk profile. The presence of unhealthy life style factors like smoking and obesity are associated with psoriasis onset and severity by creating a pro-inflammatory environment. These classic cardiovascular risk factors affect the process of atherosclerosis directly, but in the same way also indirectly by stimulating the psoriasis activity.

10. Conclusion

Psoriasis is associated with an unfavorable cardiovascular risk profile: many clinical studies confirm this association. The cardiovascular risk factors are accumulating in psoriasis patients. Three elements contribute to the cardiovascular risk profile in psoriasis patients (Fig. 1). The most important one is the systemic inflammation in psoriasis; this deteriorates the complete cardiovascular risk profile. Secondly, systemic therapies of which its effect depends on the sum of anti-inflammatory effects and atherogenic side effects. Finally, life style factors like smoking and obesity, that add to the cardiovascular risk profile directly as a classic cardiovascular risk factor, and also indirectly by increasing the psoriasis

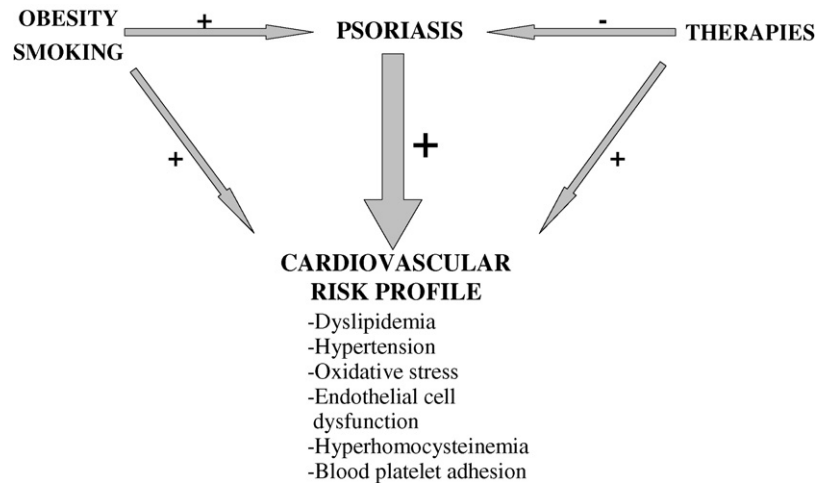


Fig. 1. Psoriasis represents a state of systemic inflammation with subsequent unfavourable effects on the cardiovascular risk profile. The increased prevalence of unhealthy life style factors like smoking and obesity influence the cardiovascular risk profile directly and also indirectly by stimulating the psoriasis severity. Anti-psoriatic therapies have a more bivalent effect, they reduce the chronic inflammation, but cardiovascular side-effects may reduce this beneficial effect.

activity. The assemblage of risk factors seems to increase the risk of cardiovascular disease, which is supported by a number of epidemiological studies. The future impact of an unfavorable cardiovascular risk profile in psoriasis can be of great importance, not only for the care of patients with psoriasis, but also in the research field of psoriasis. Based on the carefully collected evidence, we propose to estimate the absolute risk of cardiovascular disease in psoriasis patients, to take this into account when choosing a psoriasis treatment and to treat them when necessary according to the international consensus statement on prevention of cardiovascular disease in which statins may play a key role [78]. Further study may identify targets that enable simultaneous intervention for psoriasis and cardiovascular risk.

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