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ORIGINAL PAPER

Increased prevalence of the metabolic syndrome in patients with moderate to severe psoriasis

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Abstract The role of chronic inflammation causing metabolic and vascular disorders is increasingly recognized. It is hypothesized that proinflammatory cytokines contribute to atherogenesis, peripheral insulin resistance, and the development of hypertension and type II diabetes. Psoriasis as a chronic inflammatory skin disorder is characterized by a variety of immunologic and inflammatory changes and may similarly predispose for those disorders. The objective of this study was to elucidate the association of psoriasis with chronic vascular and metabolic disorders. We investigated a total of 581 adult patients hospitalised for plaque type psoriasis as compared to 1,044 hospital-based controls. A distinct pattern of chronic disorders was found to be significantly associated with psoriasis, including diabetes mellitus type II [odds ratio (OR)=2.48], arterial hypertension (OR = 3.27), hyperlipedemia (OR = 2.09), and coronary heart disease (OR = 1.95). The combined presence of these conditions together with obesity, known as the metabolic syndrome, was clearly more prevalent in psoriasis patients (OR = 5.29). In addition, psoriasis patients were significantly more likely to be smokers (OR = 2.96) and to have a regular or heavy consumption of alcohol (OR = 3.33 and 3.61, respectively). In conclusion, psoriasis patients appear to be at higher risk for diabetes mellitus and cardiovascular disease. This could likely be due to the effects of chronic inflammatory changes, in particular the secretion of proinflammatory cytokines. The risk of late term cardiovascular complications might support the use of systemic treatment in psoriasis.

Keywords Inflammation · Clinical epidemiology · Insulin resistance syndrome · Comorbidity

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Introduction

Chronic plaque type psoriasis has been linked to the occurrence of cardiovascular disease and diabetes in several studies [9, 16, 18]. A recent study found an excess cardiovascular mortality in patients hospitalised for psoriasis [13]. Psoriasis is regarded as a chronic inflammatory disorder confined to the skin as the solely manifestation. The only exception is the association of psoriasis with an inflammatory arthropathy, termed psoriatic arthritis (PsA). The nature of this disorder of the joints was clearly defined by Moll and Wright in 1973 as an arthritis that is negative for rheumatoid factor and associated with psoriasis [17, 27]. In recent epidemiological surveys, PsA proved to be much more common than previously estimated [20, 28], and in a Scandinavian study on more than 5,000 patients, nearly 30% were found to suffer from concomitant arthritis [29].

The association between chronic inflammation, as seen in rheumatoid arthritis (RA), and the development of cardiovascular disease has repeatedly been reported. The mode of action underlying this

phenomenon has been uncertain so far. More recently, however, the induction of insulin resistance caused by proinflammatory cytokines has been suggested to play a key role [4]. PsA bears striking similarities to RA and psoriasis is known to exhibit systemic inflammatory changes [27]. It seems therefore reasonable that chronic inflammation may be involved in the association of psoriasis with chronic metabolic and cardiovascular disorders.

In a previous study, we have shown that psoriasis was associated with diabetes mellitus, obesity, and chronic heart disease [9]. We have now further analysed data from hospitalised psoriasis patients treated during 1995–2002. This study provides additional information on phenotypical patterns as a basic feature of the clinical heterogeneity of psoriasis and elucidates a possible role of plaque type psoriasis as a risk factor for cardiovascular disease.

Materials and methods

Data of 625 patients (323 males and 302 females) hospitalised for psoriasis in the Department of Dermatology during the years 1996–2002 were retrieved from the patient's charts. Relevant items included demographical data, age of onset of disease, type and extent of psoriatic skin lesions, and the presence of PsA. Severity of disease was scored following a suggestion of Gudjonsson et al. [8] taking into account not only body surface involvement, but also presence of PsA and course and intensity of treatment. Among these patients, 581 adults had chronic plaque type psoriasis with or without other accompanying clinical features and were hospitalised because of severity or treatment resistance of the disease (Table 1).

Table 1 Clinical characteristics of study patients

		Male	Female
Number	*n*	308	273
Age of onset	Median (years)	32	30
	Range	3–95	2–86
Duration of disease	Median (years)	13	16
	Range	0–75	0–78
Type of psoriasis[a] [*n* (%)]	Type I	187 (60.7)	163 (59.7)
	Type II	111 (36.0)	103 (37.8)
	Uncertain	10 (3.2)	7 (2.6)
Psoriatic arthritis	No	250 (81.2)	205 (75.1)
	Yes	49 (15.9)	49 (17.9)
	Uncertain	9 (2.9)	19 (7.0)

Clinical characteristics of 581 adult (age 18 and over) patients with plaque type psoriasis

[a] Type pf psoriasis : type I: <40 years; type II: >40 years. There were no significant differences between male and female patients

As controls, the charts of 1,044 patients treated surgically for localized stage I melanoma during the same period of time were evaluated similarly.

The charts of all patients were screened for the presence of symptomatic or medically treated concomitant forms of chronic internal diseases. These included arterial hypertension, coronary artery disease, diabetes mellitus, hyperlipedemia, and renal disease, as defined below.

The body mass index (BMI) was calculated as BMI = weight (kg)/height $(cm)^2$, and obesity was defined as BMI > 30 kg/m^2. Metabolic syndrome (MBS) was defined according to WHO criteria [1]. Briefly, these consist of a diagnosis of insulin resistance, in our study defined by the presence of diabetes mellitus type II plus at least two of the following:

- antihypertensive medication and/or high blood pressure (>140 mmHg systolic or >90 mmHg diastolic);
- plasma triglycerides >150 mg/dl (>1.7 mmol/l);
- HDL cholesterol < 35 mg/dl (<0.9 mmol/l) in men or <39 mg/dl (<1.0 mmol/l) in women;
- BMI > 30 kg/m^2 and/or waist:hip ratio >0.9 in men, >0.85 in women;
- urinary albumin excretion rate ≥ 20 μg/min or albumin:creatinine ratio ≥ 30 mg/g.

Furthermore, the amount of alcohol intake and smoking habits, consistently recorded in the patient's charts, were evaluated. Alcohol consumption was classified based upon the average frequency of consumption of any kind of alcoholic beverages as:

- "none/low": less than one alcoholic beverage per week;
- "moderate": one up to three alcoholic beverages per week;
- "regular": four alcoholic beverages per week up to one per day;
- "heavy": more than one alcoholic beverage per day.

Statistical analysis

Analyses were made using the SPSS (V.9.0, SPSS, Munich, Germany) and the SAS (v.8.0, SAS, Freiburg, Germany) software packages. Descriptive statistics were done according to standard methods. Rates and ratios were compared between patients and controls using chi-square statistics.

Data were stratified for age and sex and analysed using the Cochran–Mantel–Haenszel Statistics and Mantel–Haenszel common odds ratios (ORs) were calculated together with their 95% confidence intervals (CI). Homogeneity of the ORs was tested by the Breslow–Day test.

Table 2 Associated diseases in psoriasis

Condition		Prevalence in		
		Psoriasis *n* (%)	Control patients *n* (%)	OR[a] (95% CI)
Number (*n*)		581	1,044	
M/F		308/273	478/566	†
Median age (years) (range)		54.4 (18–95)	58.5 (20–100)	†
Metabolic syndrome		25 (4.3)	11 (1.1)	5.92 (2.78–12.8)***
Diabetes mellitus type II		68 (11.7)	61 (5.8)	2.48 (1.70–3.61)***
Arterial hypertension		127 (21.9)	106 (10.2)	3.27 (2.41–4.43)***
Hyperlipoproteinemia		30 (5.2)	29 (2.8)	2.09 (1.23–3.54)**
Coronary heart disease		32 (5.5)	38 (3.6)	1.77 (1.07–2.93)*
Alcohol consumption				
None versus	Moderate	246 (42.3)	257 (24.6)	2.78 (2.14–3.62)***
	Regularly	75 (12.9)	58 (5.5)	3.33 (2.20–5.05)***
	Heavy[b]	24 (4.1)	18 (1.7)	3.61 (1.85–7.07)***
Cigarette smoking		264 (45.4)	219 (21.0)	2.96 (2.27–3.84)***

The prevalence of diseases in plaque type psoriasis patients ($n = 581$) was compared to hospital-based controls ($n = 1,044$)

[a] Common odds ratios adjusted for age and sex are presented with their 95% CI

[b] Due to low numbers only adjusted for sex

*$P < 0.05$

**$P < 0.01$

***$P < 0.0001$ by Mantel–Haenszel test

† Not statistically significant

In order to determine interacting effects from age, sex, the type of psoriasis, presence of PsA, duration of the disease, and from smoking or alcohol intake, logistic regression analysis was performed with these variables on each concomitant condition that was significantly associated by univariate measures.

Results

In this study, hyperlipidemia, arterial hypertension, coronary artery disease, as well as diabetes mellitus type II occurred significantly more frequent in patients with psoriasis as compared to the hospital-based controls (Table 2).

Determination of the BMI also revealed significant differences between psoriasis patients and control patients (Fig. 2). Both male and female patients demonstrated increased BMI values at 40–69 years of age in males and age 18–79 years in females. Females showed much higher rates of obesity than male psoriatic patients.

The simultaneous occurrence of these conditions, designated as "Metabolic Syndrome" [7], was at least twice as common in patients with psoriasis as compared to controls. The increased OR for MBS in psoriasis was found to start at mid age (40–49 years) and to persist throughout further life.

Among the individual abnormalities of the MBS, arterial hypertension was present in psoriasis patients of all age groups. The highest ORs are seen at the age of 40–49 years, whereas in the youngest as well as in the oldest group statistical significance is not reached (Fig. 1).

Similar to hypertension, increased ORs are seen for coronary heart disease (CHD) in sex- and age-adjusted comparisons. The calculated overall OR is 1.77 (95% CI 1.07–2.93; $P < 0.05$) adjusted for sex and age.

Diabetes mellitus revealed as occurring more often in psoriasis patients as compared to controls. Significant differences were seen in non-insulin-dependent diabetes mellitus (type II). This disorder was noted with an overall adjusted OR of 2.48 (95% CI 1.70–3.61; $P < 0.0001$). This was not restricted to old age, but already seen in the younger age groups (40–49 years; adjusted OR 17.2, 95% CI; Fig. 1).

Considering the data for body weight, hyperlipidemia, diabetes mellitus, and CHD, it appears that deviations from normal are most prevalent as the fourth and fifth decade of life and while in the older age groups these alterations become less marked. No apparent differences were noted between male and female patients with psoriasis.

An increased rate of alcohol consumption was noted both genders as psoriasis patients appeared to frequently consume alcohol at occasional and regular

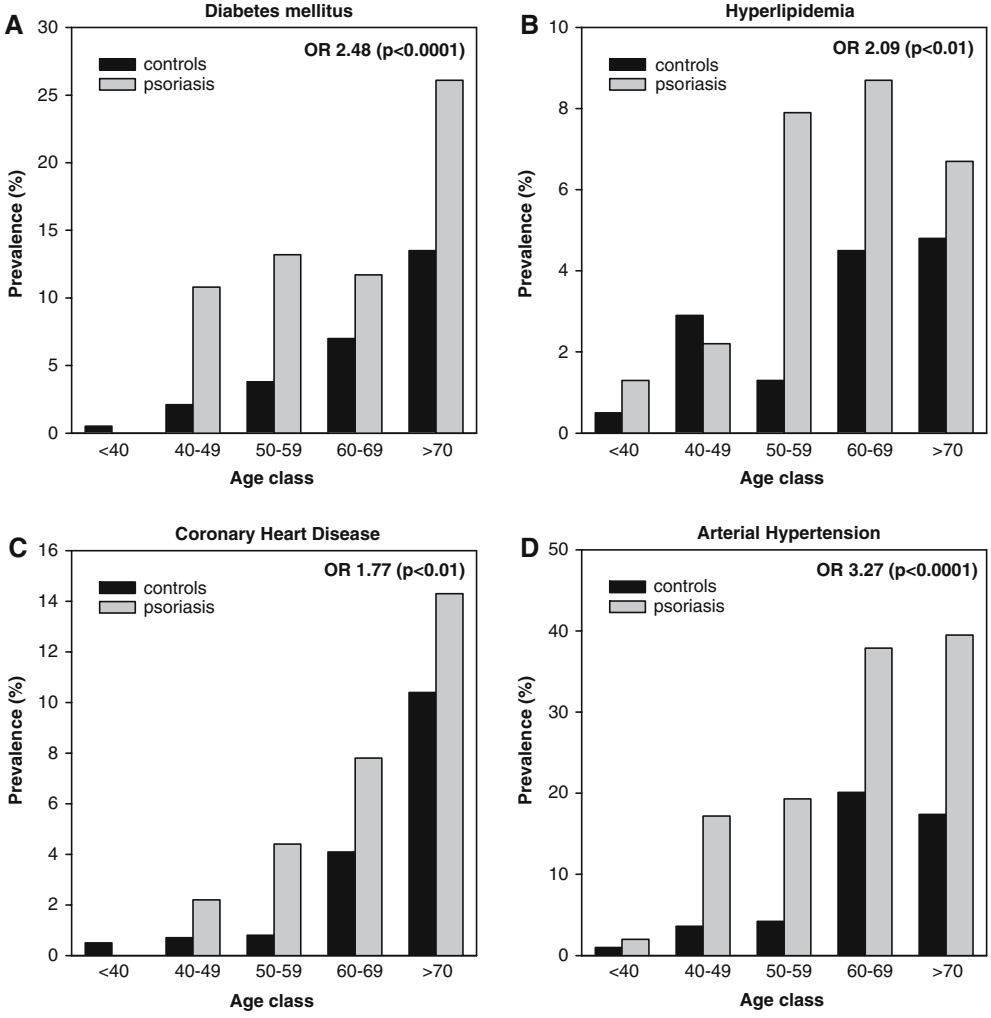

Fig. 1 Prevalence of diabetes mellitus type II (**a**), hyperlipidemia (**b**), coronary artery disease (**c**), and arterial hypertension (**d**) in psoriasis patients as compared to normal controls. *OR* common odds ratio adjusted for sex, age class, smoking, and alcohol consumption

intervals. As compared to controls of the same gender, the respective OR was similar for females as for males (data not shown). Likewise, smoking was significantly more often noted in psoriasis patients compared with control cohorts and was more prevalent in male (60.7%) versus female patients (45.6%). The OR was not significantly different between males (OR 3.07) and females (OR 2.66). In order to control for the potentially confounding effects of cigarette smoking and alcohol ingestion, a logistic regression analysis including disease status (psoriasis yes/no), gender, age, smoking, and alcohol consumption as covariates was performed, which confirmed the independent association of psoriasis with diabetes mellitus type II (OR 2.61; $P < 0.0001$), CHD (OR 1.72; $P < 0.05$), HT (OR 2.54; $P < 0.0001$), HLP (OR 3.76; $P < 0.0001$), and obesity (OR 2.30; $P < 0.0001$).

Testing effects from a variety of factors on the presence of concomitant diseases revealed that age and sex were significant determinants of most conditions. The presence of PsA was a significant indicator for arterial hypertension. Diabetes, hypertension, and CHD were also more likely in patients who had a severe disease or elevated C-reactive protein as an indicator of active inflammation. The type of psoriasis, HLA-C genotype, and duration of disease were not unequivocally associated with the risk for concomitant disorders (Table 3).

Discussion

Psoriasis is a paradigm of a chronic and relapsing inflammatory skin disease which so far was supposed to be restricted to the skin with the exception of PsA. PsA represents a seronegative arthropathy showing overlapping features with RA [27]. Several clinical signs including the absence of rheumatoid factor, lack of evidence for B-cell activation as well as different HLA

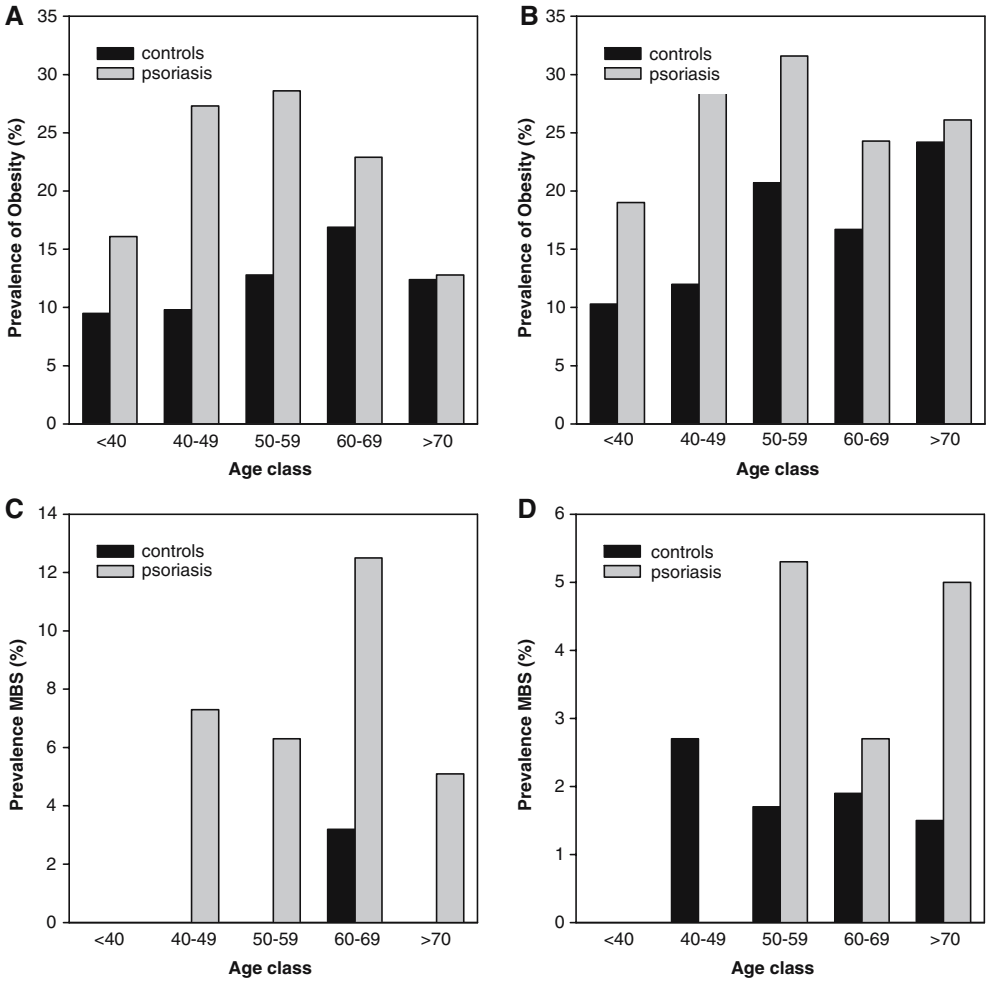

Fig. 2 Prevalence of obesity as measured by body mass index (BMI) > 30 (A—males; B—females) and the metabolic syndrome (MBS; C—males, D—females). Overall, the rate of obesity was significantly higher in both men ($P = 0.001$) and women ($P < 0.001$). For MBS, there were significant risk estimates for men (OR 10.6; 95% CI 3.2–34.7) and for women (OR 3.4; 95% CI 1.2–9.5)

associations [6] are reasons for considering it a distinct entity separate from RA [27]. Recent reports on patients with RA bearing an enhanced risk for insulin resistance and cardiovascular disease [24] led us to investigate these association in patients with psoriasis and PsA.

In this report, we describe the development of non-cutaneous disorders diagnosed in psoriasis patients hospitalised for treatment. The results show that these patients are prone to develop a distinct cluster of concomitant diseases, including diabetes mellitus, arterial hypertension, dyslipidemia, obesity, and cardiac disease. The combination of such abnormalities is known as MBS or—more recently—the insulin resistance syndrome (IRS) [2] which was highly more prevalent in patients with psoriasis than in controls. This association was not restricted to patients with accompanying PsA, although there was a tendency for arterial hypertension to occur more often in patients with PsA.

Patients analysed in the present study were submitted to inpatient care because of the extent of disease or treatment resistance. The majority (nearly two thirds) demonstrated early onset (type I) and suffered from long lasting moderate to severe form of the disease.

An increased frequency of cardiovascular disease was noted independently from gender and age. Importantly, although smoking and alcohol consumption were more frequent in psoriasis patients, multivariate analysis revealed that the increased prevalence of metabolic and vascular disorders appeared not to be due to the confounding effect of these factors. Still, like in any hospital-based study, our investigations might have been be prone to some degree of statistical bias, but most relevant parameters like BMI, blood pressure, or

Table 3 Subgroup analysis comparing odds ratios for different factors in psoriasis patients

	DM II	HT	CHD	HLP
Psoriasis type				
Type I	2.24 (1.3–3.8)	3.78 (2.5–5.8)	0.86 (0.4–2.2)	2.10 (1.0–4.3)
Type II	2.63 (1.7–4.1)	2.94 (2.1–4.2)	2.38 (1.4–4.1)	2.18 (1.2–4.0)
HLA status				
Cw6 positive	1.95 (1.0–3.8)	2.90 (1.8–4.7)	1.21 (0.5–3.3)	1.85 (0.8–4.4)
Cw6 negative	2.80 (1.7–4.7)	3.19 (2.1–5.0)	1.36 (0.6–3.0)	1.82 (0.8–4.0)
PsA				
Yes	2.48 (1.1–5.4)	6.03 (3.3–11.0)	1.51 (0.4–5.2)	3.54 (1.5–8.7)
No	2.50 (1.7–3.7)	2.96 (2.1–4.1)	1.88 (1.1–3.2)	1.78 (1.0–3.2)
CRP				
Elevated	2.90 (1.7–4.8)	3.64 (2.3–5.7)	2.11 (1.1–4.2)	2.01 (0.9–4.3)
Normal	2.21 (1.4–3.4)	3.09 (2.2–4.4)	1.58 (0.9–2.9)	2.10 (1.2–3.8)
Severity				
Severe	3.67 (2.0–6.9)	3.83 (2.2–6.6)	2.61 (1.1–6.0)	2.64 (1.1–6.3)
Moderate	2.24 (1.5–3.4)	3.19 (2.3–4.4)	1.61 (0.9–2.8)	1.96 (1.1–3.4)
Duration of Dx				
15+ years	2.37 (1.5–3.8)	3.12 (2.1–4.6)	1.37 (0.7–2.7)	2.01 (1.1–3.8)
<15 years	2.64 (1.7–4.2)	3.44 (2.4–5.1)	2.45 (1.2–4.2)	2.35 (1.2–4.6)

Presence or absence of concomitant disease in psoriasis patients ($n = 581$) as associated with various clinical factors. Odds ratios were calculated using Mantel–Haenszel's common odds ratios for data stratified for sex, age class, smoking, and alcohol consumption. The 95% confidence intervals are given in parentheses

PsA psoriatic arthritis, *CRP* C-reactive protein, *DM II* diabetes mellitus type II, *HT* arterial hypertension, *HLP* hyperlipidemia, *CHD* coronary heart disease

medication for chronic conditions are usually very reliable, even in short-stay patients, and only diagnoses being present at admission haven been evaluated. However, some degree of admission bias might still be present, and the results should be verified in different patient populations.

Several risk factors related to life-style, e.g. smoking, alcohol consumption, obesity, and diabetes, have previously already been observed in psoriasis patients [9, 19, 21]. A direct proof of a causative role of these factors in eliciting or worsening psoriasis is lacking. On the other hand, previous reports [9, 13, 19] indicate that the risk for CHD as well as the symptoms of MBS in psoriasis patients increases with the duration of disease as well as with the extent of body involvement (severity). Our investigations revealed a consistent trend for an enhanced OR when comparing patients with severe disease to those with moderate extent. It can be speculated that this effect might even be pronounced when including patients with mild forms of psoriasis. Similar correlations are seen in patients with RA with a fourfold increased risk of cardiovascular events and twice as many patients suffering from CHD as compared to control population [4]. The risk for development of these complications is positively correlated with the disease severity (number of joints involved and length of disease).

In a recent study involving 5,000 Swedish psoriasis patients, excess risk for cardiovascular death compared to the general population was observed in those patients who were hospitalised due to severe psoriasis [13].

Similarly, in a cross-sectional study of hospitalised patients, McDonald observed a significant proportion of patients with psoriasis showing cardiovascular disease as compared to other dermatological inpatients [15]. Also, in a longitudinal population-based study, Lindegard found hypertension to be significantly associated with psoriasis. Diabetes, obesity, and myocardial infarction were significantly enhanced in the female subgroup [12].

Data raised in our study as well as those obtained in the aforementioned reports deal with patients undergoing hospital treatment for severe psoriasis. Of interest, the study of Mallbris et al. [13] demonstrated that outpatients who are likely to be affected by mild psoriasis failed to show cardiovascular complications. Likewise, Stern and Lange failed to show a increase in cardiovascular mortality among their cohort of 1,380 patients, most of them being outpatients [25]. From these observations, it appears that the occurrence of cardiovascular complications like CHD is restricted to severe forms of psoriasis.

During recent years, the various metabolic factors leading to CHD such as hypertension, low HDL cholesterol, obesity, and altered glucose tolerance have been defined as the consequence of hyperinsulinemia [10], although recent results suggest that lipid

alterations may also be genetically determined in psoriasis patients [14].

Prospective studies and an overwhelming fundus of epidemiological data point towards the primary role of insulin resistance in this cluster of diseases. More recently, chronic inflammation has been suggested as part of the IRS [5]. Data from studies in RA have confirmed a correlation between lasting arthritis and the development of IRS eventually terminating in CHD. Among the cytokines involved, TNFα and IL-6 are shown to play a central role [5, 23]. Therapeutical intervention by use of anti-inflammatory drugs including methotrexate (MTX) and TNFα antagonists seems to diminish the risk [3, 11]. In a recent report involving patients with RA and patients with psoriasis, the effect of MTX was most pronounced in the patients with psoriasis reducing the risk for vascular disease by 45% [22]. These observations suggest that chronic subclinical inflammation eventually leads into CHD after years of developing overt morbidity due to the IRS.

Regarding the impressive association of psoriasis with diabetes in the present study, it seems interesting that a significant association has been found between polymorphisms in the gene encoding the receptor for advanced glycation end products and plaque psoriasis [26]. The associated risk was related to the presence of common cardiovascular disorders and this might be yet another mechanism posing psoriasis patients at risk for chronic vascular disease.

In the present report on comorbidity in psoriasis patients, the similarities to the outcome of other chronic non-cutaneous inflammatory disorders are striking. It is shown for the first time that in psoriasis, patients are at risk of developing a cluster of disorders known as IRS. These observations categorize lasting psoriasis as an eventually life-threatening disorder showing great similarities to outcomes of chronic RA. This emphasizes the need for treatment of patients with moderate to severe psoriasis and, in addition, makes it mandatory to more closely pay attention to concomitant diseases particularly of the IRS.

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References

1. Alberti KG, Zimmet PZ (1998) Definition, diagnosis and classification of diabetes mellitus and its complications. Part: 1 diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. Diabet Med 15(7):539–553
2. Bloomgarden ZT (2004) Definitions of the insulin resistance syndrome: the 1st World Congress on the insulin resistance syndrome. Diabetes Care 27(3):824–830
3. Choi HK, Hernan MA, Seeger JD, Robins JM, Wolfe F (2002) Methotrexate and mortality in patients with rheumatoid arthritis: a prospective study. Lancet 359(9313):1173–1177
4. Dessein PH, Joffe BI, Stanwix AE (2003) Inflammation, insulin resistance, and aberrant lipid metabolism as cardiovascular risk factors in rheumatoid arthritis. J Rheumatol 30(7):1403–1405
5. Fernandez-Real JM, Ricart W (2003) Insulin resistance and chronic cardiovascular inflammatory syndrome. Endocr Rev 24(3):278–301
6. Gladman DD, Farewell VT, Rahman P, Schentag CT, Pellett F, Ng CM, Wade JA (2001) HLA-DRB1*04 alleles in psoriatic arthritis: comparison with rheumatoid arthritis and healthy controls. Hum Immunol 62(11):1239–1244
7. Grundy SM, Brewer HB Jr, Cleeman JI, Smith SC Jr, Lenfant C (2004) Definition of metabolic syndrome: report of the National Heart, Lung, and Blood Institute/American Heart Association conference on scientific issues related to definition. Circulation 109(3):433–438
8. Gudjonsson JE, Karason A, Antonsdottir AA, Runarsdottir EH, Gulcher JR, Stefansson K, Valdimarsson H (2002) HLA-Cw6-positive and HLA-Cw6-negative patients with psoriasis vulgaris have distinct clinical features. J Invest Dermatol 118(2):362–365
9. Henseler T, Christophers E (1995) Disease concomitance in psoriasis. J Am Acad Dermatol 32:982–986
10. Kendall DM, Sobel BE, Coulston AM, Peters Harmel AL, McLean BK, Peragallo-Dittko V, Buse JB, Fonseca VA, Hill JO, Nesto RW, Sunyer FX (2003) The insulin resistance syndrome and coronary artery disease. Coron Artery Dis 14(4):335–348
11. Kiortsis DN, Mavridis AK, Vasakos S, Nikas SN, Drosos AA (2005) Effects of infliximab treatment on insulin resistance in patients with rheumatoid arthritis and ankylosing spondylitis. Ann Rheum Dis 64(5):765–766
12. Lindegard B (1986) Diseases associated with psoriasis in a general population of 159,200 middle-aged, urban, native Swedes. Dermatologica 172:298–304
13. Mallbris L, Akre O, Granath F, Yin L, Lindelof B, Ekbom A, Stahle-Backdahl M (2004) Increased risk for cardiovascular mortality in psoriasis inpatients but not in outpatients. Eur J Epidemiol 19(3):225–230
14. Mallbris L, Granath F, Hamsten A, Stahle M (2006) Psoriasis is associated with lipid abnormalities at the onset of skin disease. J Am Acad Dermatol 54(4):614–621
15. McDonald CJ (1989) Cardiovascular disease in psoriasis. J Invest Dermatol 92:646–647
16. McDonald CJ, Calabresi P (1978) Psoriasis and occlusive vascular disease. Br J Dermatol 99(5):469–475
17. Moll JM, Wright V (1973) Psoriatic arthritis. Semin Arthritis Rheum 3(1):55–78
18. Montagnani A, Tosti A, Patrizi A, Salardi S, Cacciari E (1985) Diabetes mellitus and skin diseases in childhood. Dermatologica 170:65–68
19. Naldi L, Parazzini F, Brevi A, Peserico A, Veller Fornasa C, Grosso G, Rossi E, Marinaro P, Polenghi MM, Finzi A et al (1992) Family history, smoking habits, alcohol consumption and risk of psoriasis. Br J Dermatol 127:212–217
20. Offidani A, Cellini A, Valeri G, Giovagnoni A (1998) Subclinical joint involvement in psoriasis: magnetic resonance imaging and x-ray findings. Acta Derm Venereol 78:463–465
21. Poikolainen K, Reunala T, Karvonen J, Lauharanta J, Karkkainen P (1990) Alcohol intake: a risk factor for psoriasis in young and middle aged men? BMJ 300:780–783

22. Prodanowich S, Ma F, Taylor JR, Pezon C, Fasihi T, Kirsner RS (2005) Methotrexate reduces incidence of vascular diseases in veterans with psoriasis or rheumatoid arthritis. J Am Acad Dermatol 52(2):262–267
23. Rotter V, Nagaev I, Smith U (2003) Interleukin-6 (IL-6) induces insulin resistance in 3T3-L1 adipocytes and is, like IL-8 and tumor necrosis factor-alpha, overexpressed in human fat cells from insulin-resistant subjects. J Biol Chem 278(46):45777–45784
24. Sattar N, McCarey DW, Capell H, McInnes IB (2003) Explaining how "high-grade" systemic inflammation accelerates vascular risk in rheumatoid arthritis. Circulation 108(24):2957–2963
25. Stern RS, Lange R (1988) Cardiovascular disease, cancer, and cause of death in patients with psoriasis: 10 years prospective experience in a cohort of 1,380 patients. J Invest Dermatol 91:197–201
26. Vasku V, Kankova K, Vasku A, Muzik J, Izakovicova Holla L, Semradova V, Vacha J (2002) Gene polymorphisms (G82S, 1704G/T, 2184A/G and 2245G/A) of the receptor of advanced glycation end products (RAGE) in plaque psoriasis. Arch Dermatol Res 294(3):127–130
27. Winchester R (1993) Psoriatic arthritis. In: Fitzpatrick TB, Eisen AZ, Wolff K, Freedberg IM, Austen KF (eds) Dermatology in general medicine, 4th edn. McGraw-Hill Book Company, New York, pp 515–527
28. Zachariae H (2003) Prevalence of joint disease in patients with psoriasis: implications for therapy. Am J Clin Dermatol 4(7):441–447
29. Zachariae H, Zachariae R, Blomqvist K, Davidsson S, Molin L, Mork C, Sigurgeirsson B (2002) Quality of life and prevalence of arthritis reported by 5,795 members of the Nordic Psoriasis Associations. Data from the Nordic Quality of Life Study. Acta Derm Venereol 82(2):108–113