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Cardiovascular risk profile of patients with psoriatic arthritis compared to controls—the role of inflammation

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Objective. To examine the distribution of traditional and novel risk factors of cardiovascular disease (CVD) in patients with PsA compared with healthy controls.
Methods. We compared risk factors for CVD between 102 consecutive PsA patients and 82 controls, adjusting for BMI. We also assessed the role of inflammation on the CVD risk factor by using a BMI and high-sensitivity CRP (hsCRP)-adjusted model.
Results. The BMI of PsA patients were significantly higher than healthy controls. After adjusting for the BMI, PsA patients still have a higher prevalence of diabetes mellitus (DM) [odds ratio (OR) 9.27, 95% CI 2.09, 41.09) and hypertension (OR 3.37, 95% CI 1.68, 6.72), but a lower prevalence of low high density lipoprotein (HDL) cholesterol (OR 0.16, 95% CI 0.07, 0.41). PsA patients have significantly increased systolic and diastolic blood pressures, insulin resistance and inflammatory markers (hsCRP and white cell count) compared to controls. PsA patients have higher HDL cholesterol and apolipoprotein (Apo) A1 levels; and lower total cholesterol (TC) and low density lipoprotein cholesterol levels; and a lower TC/HDL ratio. However, the Apo B level ($P < 0.05$), and the Apo B/Apo A1 ratio ($P = 0.07$) were higher in PsA patients. Further adjustment for hsCRP level rendered the differences in the prevalence of hypertension and DM; the TC, and sugar levels; and white cell count non-significant between the two groups; while the differences in other parameters remained significant.
Conclusion. These data support the hypothesis that PsA may be associated with obesity, hypertension, dyslipidaemia and insulin resistance because of the shared inflammatory pathway.

Key words: PsA, Obesity, Hypertension, Dyslipidaemia, Insulin resistance, Inflammatory markers.

PsA is a chronic inflammatory arthropathy that occurs in association with psoriasis. Patients with PsA may experience substantial morbidity and unfavourable outcomes at referral centres [1, 2], although investigators from other centres report that in unselected patients [3], this condition is not associated with a significant increase in mortality. In a mortality study in PsA patients from Toronto, the first leading causes of death were diseases of the circulatory (36.2%) system [1]. An increase in death rate of 1.3 due to cardiovascular diseases (CVD) was noted compared with general population [1]. Han *et al.* [4] reported that the prevalence ratio of overt CVD were higher in patients with PsA than controls in the USA. Two recent studies also demonstrated that PsA patients had a higher prevalence of subclinical atherosclerosis by exhibiting greater intimal medial thickness (IMT) than healthy controls [5, 6]. Gonzalez-Juanatey *et al.* [7] also found that endothelial dysfunction was evident in PsA patients without overt CVD, although the same group failed to demonstrate subclinical echocardiographic abnormalities [8].

In RA studies, traditional CVD risk factors, RA disease characteristics, inflammatory indicators and medications used to treat RA (e.g. NSAID and cox-II inhibitor) may all play a role in promoting CVD. In patients with PsA, markers of disease activity as reflected by prior use of medication, a high ESR at presentation and evidence of radiological damage are associated with an increased cardiovascular mortality [2]. Unlike in other rheumatic diseases, studies assessing CVD risk factors in PsA are scanty [9]. Three previous studies demonstrated that PsA patients with active synovitis had lower total cholesterol (TC), low density lipoprotein (LDL) cholesterol and high density lipoprotein (HDL) cholesterol [10–12]. Nonetheless, Jones *et al.* [12] demonstrated that the most dense subfraction of LDL, LDL (3), was significantly increased in PsA patients. Whether incidence of other CVD risk factors among persons with PsA differ from those in the general population had not been thoroughly studied [9]. In the study by Kimhi *et al.* [5], the prevalence of traditional CVD risk factors including smoking, altered lipid profile, hypertension and diabetes mellitus (DM) were similar between the 30 PsA patients and the age-matched controls, although the BMI was significantly increased in the patient group. On the contrary, Han *et al.* [4], using a large administrative database, reported a higher prevalence ratio of type II DM, hyperlipidaemia and hypertension in PsA patients compared with controls. We therefore undertake this large-scale study to answer the central question of whether individuals with PsA have an increased prevalence of CVD risk factors.

The aim of this study was to elucidate whether patients with PsA have an increased prevalence of CVD risk factors compared with healthy controls.

Patients and methods

Patients

One hundred and two consecutive PsA patients from two regional hospitals (the Prince of Wales Hospital and the Alice Ho Miu Ling Nethersole Hospital) were recruited to participate in this cross-sectional study including clinical assessment and fasting blood samples. All patients fulfilled the Moll and Wright criteria [13]. Hong Kong has a dual system with public and private provision for both ambulatory and hospital inpatient care. Public care is available to all residents and is heavily subsidized, and therefore over 95% of patients with chronic illnesses were under public care. These two public hospitals are the only referral centres for a well-defined population of almost a million people, out of a total population of around seven million in Hong Kong. All patients are Southern Chinese. History of DM, hypertension

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and hypercholesterolaemia, overt CVD including myocardial infarction, angina, stroke and transient ischaemic attack and drug history were retrieved from case notes. The Hong Kong Hospital Authority has been utilizing compulsory ICD coding since 1995 for all patients under the public system. Data can be accessed throughout the city. Therefore, if patients had prior history of CVD managed outside these two hospitals, this part of the history could easily be retrieved. Body height, weight, waist and hip circumference, cigarette smoking and blood pressure (BP) were elicited during the clinical assessment. Eighty-two healthy ethnicity-, age- and sex-matched controls were recruited in the same community for comparison of the traditional and metabolic risk factors. Healthy controls were recruited from a broad spectrum of hospital staff, without prior history of overt CVD. The catchment area of the Prince of Wales Hospital and the Alice Ho Miu Ling Nethersole Hospital has only been developed since the 1960s. The majority of its inhabitants, including staff at the hospital, are a typical socio-economic representation of first- or second-generation migrants from Southern China now living in a westernized environment. The protocol was approved by the Ethics Committee of The Chinese University of Hong Kong and the Hong Kong Hospital Authority. Written informed consent was obtained according to the Declaration of Helsinki from all subjects before participating in the study.

Evaluation of disease activity and severity

Pain and patients' global self-estimation of well-being were evaluated using a 10-point visual analogue scale, where 0 indicates excellent well-being and 10 indicates feeling extremely unwell. Physical examination included recording the number of tender and swollen joints using the 68 tender/66 swollen joint count, the presence of dactylitis, as well as the number of permanently deformed joints. Laboratory markers of disease activity included high-sensitivity CRP (hsCRP) and complete blood count.

Disease activity for the whole group was assessed based on the 28 joint disease activity score (DAS 28) [14]. The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Bath Ankylosing Spondylitis Functional Index (BASFI) were used to measure disease activity and functional ability in patients with predominant axial involvement [15, 16]. The Psoriasis Area and Severity Index (PASI) was used to assess the extent of skin involvement [17].

Clinical risk factors and biomarkers of CVD

The clinical variables included smoking status, BMI, DM (a history of DM on diet, oral hypoglycaemic agent or insulin, or fasting sugar $\geq$7.0 mmol/l), hypertension (systolic BP $\geq$140 mmHg or a diastolic BP $\geq$90 mmHg or the use of anti-hypertensive agents) and hypercholesterolaemia (TC $\geq$6.2 mmol/l, or LDL cholesterol $\geq$4.13 mmol/l or on lipid lowering agent). For Asians, overweight is a BMI between 25 and 29.9 kg/m^2 and obesity is a BMI $\geq$30 kg/m^2 [18]. Waist hip ratio (WHR) was calculated as the ratio of waist-to-hip circumferences. Abdominal obesity was defined as: (i) a waist circumference of $\geq$80 cm for women, and $\geq$90 cm for men, as recently proposed by the International Association for the Study of Obesity (IASO) [19]; (ii) a WHR of 0.9 or greater, as proposed by the World Health Organization (WHO) [20].

The National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) guidelines classify individuals as having the metabolic syndrome (MetS) if they possess three or more of the following components [21]: (i) fasting plasma glucose $\geq$ 6.1 mmol/l or receiving glucose-lowering drugs; (ii) hypertension (systolic and/or diastolic BP $\geq$130/85 mmHg or receiving BP lowering drugs); (iii) fasting plasma triglycerides (TG) $\geq$1.7 mmol/l; (iv) fasting HDL cholesterol $<$1.04 or 1.29 mmol in males and females, respectively and (v) central obesity (waist circumference $\geq$80 or $\geq$90 cm in females and males, respectively) [18].

Fasting blood samples were collected for TC and TG measured by an autoanalyser enzymatic method; HDL cholesterol was determined enzymatically with polythelene glycol-modified enzymes. LDL cholesterol was calculated by the Friedewald formula. If the triglyceride levels are above 4.0 mmol/l, then the LDL levels were measured directly by ultracentrifugal single spin analysis. Apolipoprotein (Apo) A1 and Apo B were measured by automated analyzer (Cobas-Mira Plus, Hoffman-LaRoche Diagnostics, Germany), using a turbidimetric assay. Plasma insulin was measured using ELISA (Diagnostics Systems Laboratories, Inc Corporate Webster, TX, USA) [22]. As a measure of insulin resistance the Homeostasis Model Assessment (HOMA-IR) Index was used: fasting plasma glucose (mmol/l) $\times$ fasting serum insulin (mU/l) divided by 22.5 [23]. HsCRP was measured by an ELISA assay (Diagnostic Systems Laboratories, Inc.) with a detection limit: of 1.6 ng/ml. ESR was measured by the Westergren method having a normal range of $<$15 mm/1st h.

Statistical analysis

First, we examined the frequency of clinical CVD risk factors between the PsA patients and controls. The frequencies were compared using chi-squared tests for categorical variables. Next, we ascertained whether there are differences in the traditional and novel CVD risk factors between the PsA patients and controls. Student's *t*-tests or Mann–Whitney U-tests were used for continuous variables where appropriate. Because of potential confounding effect, BMI-adjusted models were used to assess differences between the patients with PsA and the non-PsA controls using logistic regression and multivariate general linear models where appropriate. Association between the traditional and metabolic risk factors and the hsCRP level were assessed using Spearman's correlations. Finally, we also assessed the role of inflammation on the CVD risk factor by using a BMI and hsCRP-adjusted model. Continuous variables that were not normally distributed were log-transformed. *P*-value $<$0.05 was considered statistically significant. All tests were two-tailed. The Statistics Package for Social Sciences (SPSS for Windows, version 13.0, 2006, SPSS Inc, Chicago, IL, USA) was used for the analyses.

Results

Clinical features of PsA patients

The clinical characteristics are summarized in Table 1. Sixty-two percent of the patients had psoriasis preceding PsA, and most had a polyarticular pattern of arthritis. Seventy-four (72.5%) patients had psoriasis at the time of assessment. No patients had clinically overt CVD.

Medications used by the patients

At the time of the study, sixty patients (58.8%) were on NSAIDs. Forty-seven (46.1%) patients were currently on DMARD. MTX was by far the most frequently used medication (used by 31/102, 30.4% of the patients). One (1.0%) patient was on corticosteroids, one (1.0%) on anti-TNF-α and 14 (13.7%) on salazopyrine. Eleven (10.8%) patients were on oral hypoglycaemic agents, 27 (26.5%) were on anti-hypertensives and three (2.9%) on statins.

Demographic and traditional CVD risk factors in patients and controls

Table 2 summarized the demographic data and the prevalence of traditional CVD risk factors, and Table 3 summarized the BP and metabolic risk factors of the entire study cohort. The age, gender distribution, smoking habit (Table 2) and serum creatinine level

TABLE 1. Clinical characteristics of the PsA patients

	PsA patients ($n=102$)
PsA disease duration (yrs)	9.0 (3.5–13.9)
Age at diagnosis of PsA	40 ± 12
Age at diagnosis of psoriasis	37 ± 14
Disease patterns	
Distal joint disease, *n* (%)	8 (8)
Oligoarthritis involving ≤ 4 joints, *n* (%)	28 (28)
Polyarthritis affecting ≥ 5 joints, *n* (%)	34 (33)
Arthritis mutilans, *n* (%)	1 (1)
SpA, *n* (%)	31 (30)
Disease activity	
DAS 28	3.4 ± 1.3
No of tender joints	2.0 (0–7.0)
No of swollen joints	0 (0–3)
PASI ($n=74$)	2.8 (1.0–7.3)
Physician's global assessment (VAS 0–10)	1.0 (0.0–3.0)
Pain (VAS 0–10)	4.8 ± 2.7
Patient's global assessment (VAS 0–10)	4.6 ± 2.4
BASDAI ($n=31$)	4.6 ± 2.1
BASFI ($n=31$)	2.4 (0.3–4.7)
No. of damaged joints	1 (0–5)
Health assessment questionnaire	0.5 (0.1–1.1)

Data are expressed as mean ± S.D. or median (interquartile range).

(Table 3) for the two groups was similar. The PsA group had a significantly higher mean BMI and WHR, and the prevalence of overweight, obesity and abdominal obesity (according to the WHO criteria) was also significantly increased.

The role of BMI

After adjusting for the BMI, traditional risk factors, such as DM [odds ratio (OR) 9.27, 95% CI 2.09, 41.09] and hypertension (OR 3.37, 95% CI 1.68, 6.72) were found in a significantly higher proportion of patients with PsA (Table 2). Despite 27 (26.5%) PsA patients were on anti-hypertensives, both the systolic and diastolic BP were significantly elevated compared with controls (Table 3).

PsA patients had a significantly lower prevalence of low HDL cholesterol (OR 0.16, 95% CI 0.07, 0.41) (Table 2), while the prevalence of hypercholesterolaemia and hypertriglyceridaemia (TG >1.7 mmol/l) was similar in both the groups. The TC and LDL cholesterol levels were significantly lower, while the HDL cholesterol, Apo A1 and Apo B levels were significantly increased in PsA patients compared to controls (Table 3). The TG levels were similar between the two groups. Overall, the Apo B/Apo A1

TABLE 2. Demographic data and the prevalence of traditional CVD risk factors in PsA patients and controls

	PsA ($n=102$)	Controls (n = 82)	Unadjusted *P*-value	OR (95% CI)	
				BMI-adjusted model	BMI and hs CRP adjusted model
Age (yrs)	48.7 ± 12.2	48.1 ± 7.7	0.67		
Sex (M:F)	48:54	34:48	0.45		
Current smokers, *n* (%)	9 (8.8)	8 (9.8)	0.83		
BMI (kg/m^2)	25.4 ± 4.3	23.7 ± 2.9	0.002		
Overweight, *n* (%)	60 (58.8)	42 (51.2)	0.002		
Obese, *n* (%)	14 (13.7)	2 (2.4)			
Waist circumference (cm)	83.9 ± 12.4	81.1 ± 9.4	0.09		
WHR	0.89 ± 0.08	0.85 ± 0.08	0.04		
Abdominal obesity, *n* (%)					
IASO	41 (40.1)	38 (46.3)	0.40		
WHO	41 (40)	21 (25.6)	0.04		
Hypertension, *n* (%)	50 (49)	16 (19.5)	<0.001	3.37 (1.68, 6.72)	NS
Anti-hypertensives, *n* (%)	27 (26.5)	–			
Low HDL cholesterol, *n* (%)	9 (8.8)	25 (30.5)	<0.001	0.16 (0.07, 0.41)	0.16 (0.07, 0.41)
Hypertriglyceridemia, *n* (%)	28 (27.4)	17 (20.7)	0.29	NS	NS
Hypercholesterolemia, *n* (%)	12 (11.8)	18 (22.0)	0.063	NS	NS
Statins, *n* (%)	3 (2.9)	–			
DM, *n* (%)	19 (18.6)	2 (2.4)	0.001	9.27 (2.09, 41.09)	NS
Oral hypoglycaemic agents, *n* (%)	11 (10.8)	–			
Metabolic syndrome, *n* (%)					
NCEP ATP III, *n* (%)	24 (23.5)	13 (15.9)	0.19	NS	NS

Data are presented as mean ± S.D. NS:non-significant.

TABLE 3. Blood pressure and metabolic risk factors in PsA patients and controls

	PsA patients (n=102)	Controls (n=82)	Unadjusted *P*-value	B (95% CI for B)	
				BMI-adjusted model	BMI and hsCRP adjusted model
Systolic BP (mmHg)	136 ± 23	119 ± 19	<0.001	15.84 (9.45, 22.24)	15.84 (9.45, 22.24)
Diastolic BP (mmHg)	82 ± 13	74 ± 12	<0.001	6.92 (3.33, 10.51)	6.92 (3.33, 10.51)
TC (mmol/l)	5.09 ± 0.94	5.47 ± 0.94	0.007	−0.38 (−0.66, 0.11)	NS
LDL cholesterol (mmol/l)	2.86 ± 0.75	3.33 ± 0.73	<0.001	−0.47 (−0.69, −0.25)	−0.47 (−0.69, −0.25)
HDL cholesterol (mmol/l)	1.60 ± 0.46	1.51 ± 0.42	0.16	0.16 (0.04, 0.29)	0.21 (0.08, 0.35)
TG (mmol/l)	1.43 ± 0.84	1.37 ± 1.12	0.68	NS	NS
Apo-A1 (mg/dl)	137.8 (120.7–166.9)	107.4 (66.8–126.7)	<0.001	0.19 (0.14, 0.25)	0.19 (0.14, 0.25)
Apo-B (mg/dl)	81.5 ± 17.5	60.9 ± 18.9	<0.001	0.14 (0.10, 0.17)	0.14 (0.10, 0.17)
TC/HDL	3.37 ± 0.91	3.84 ± 1.06	0.01	−0.62 (−0.90, −0.34)	−0.62 (−0.90, −0.34)
Apo-B/Apo-A1	0.59 (0.47–0.71)	0.54 (0.40–0.89)	0.004	NS	0.28 (0.10, −0.47)
Glucose (mmol/l)	5.1 (4.7–6.1)	5.1 (4.8–5.4)	0.04	0.07 (0.03, 0.11)	NS
Insulin (pmol/l)	57.4 ± 31.1	33.3 ± 23.4	<0.001	18.45 (11.22, 25.68)	18.45 (11.22, 25.68)
HOMA-IR	12.1 (8.1–18.6)	6.5 (3.8–10.0)	<0.001	0.25 (0.16, 0.34)	0.25 (0.16, 0.34)
Urate (mmol/l)	0.33 ± 0.10	0.30 ± 0.08	0.015	NS	NS
Platelet count × 10^9/l	300 ± 77	246 ± 56	<0.001	53.74 (33.49, 73.99)	34.13 (13.36, 54.90)
High-sensitivity CRP (mg/l)	4.80 (1.55–15.00)	0.42 (0.22–0.71)	<0.001	1.03 (0.89, 1.18)	–
White cell count × 10^9/l	6.8 (5.5–8.5)	5.9 (5.3–7.2)	0.002	0.68 (0.10, 1.25)	NS
Serum creatinine (μmol/l)	74.4 ± 15.0	73.6 ± 14.3	0.72	NS	NS

Data are presented as mean ± S.D. or median (interquartile range).

TABLE 4. Spearman's correlation between hsCRP level and the traditional and metabolic risk factors for the whole group ($n=184$)

	rho	*P*-value
Age	−0.005	0.96
BMI (kg/m^2)	0.21	0.04
Waist circumference (cm)	0.36	<0.001
WHR	0.44	<0.001
Systolic BP (mmHg)	0.33	0.001
Diastolic BP (mmHg)	0.27	0.005
TC (mmol/l)	−0.23	0.22
LDL cholesterol (mmol/l)	−0.01	0.90
HDL cholesterol (mmol/l)	−0.45	<0.001
TG (mmol/l)	0.03	0.74
Apo-A1(mg/dl)	−0.45	<0.001
Apo-B (mg/dl)	0.06	0.56
TC/HDL	0.31	0.002
Apo-B/Apo-A1	0.39	<0.001
Glucose (mmol/l)	0.32	0.001
Insulin (pmol/l)	0.16	0.13
HOMA-IR	0.22	0.04
Urate (mmol/l)	0.12	0.23
Platelet count $\times 10^9$/l	0.35	<0.001
White cell count $\times 10^9$/l	0.38	<0.001
Serum creatinine (μmol/l)	0.06	0.39

ratio was slightly increased ($P=0.07$), although the TC/HDL ratio was significantly lower in PsA patients compared with the controls, after adjusting for the BMI.

Insulin resistance as reflected by the HOMA-IR was significantly increased in the PsA patients compared with the controls (Table 3). Nonetheless, the urate level as well as the prevalence of metabolic syndrome was similar between the two groups (Tables 2 and 3).

As expected, the hsCRP level, platelet and white cell counts were significantly increased in the PsA group reflecting underlying inflammation.

The role of inflammation

Table 4 summarized the correlation of the risk factors with hsCRP levels for the whole group ($n=184$). Inflammation, as reflected by the hsCRP level, was associated with an increase in traditional risk factors including a higher BMI, waist circumference, WHR, systolic and diastolic BP, sugar and insulin resistance (HOMA-IR) and dyslipidaemia (lower HDL cholesterol and Apo A1 levels; higher TC/HDL and Apo B/Apo A1 ratios). It is also associated with an increased thrombotic tendency as demonstrated by the increased platelet count. As expected, the white cell count was also associated with hsCRP as an inflammatory marker. No association was found between hsCRP and patient's age, TC, LDL cholesterol, TG, Apo B, insulin, urate and serum creatinine levels. The results were similar when only PsA patients were included in the analysis, except that the hsCRP level correlated inversely with TC ($\rho=-0.23$, $P=0.02$).

Further adjustment for hsCRP level rendered the differences in the prevalence of hypertension and DM, the TC and sugar levels and white cell count non-significant between the two groups. However, PsA patients still had a significantly lower prevalence of low HDL cholesterol. The differences between the two groups including the systolic and diastolic BP; the LDL and HDL cholesterol levels; Apo A1 and Apo B levels; the TC/HDL and the Apo B/Apo A1 ratio; insulin resistance (HOMA-IR) and platelet count remained statically significant. The results in Table 3 remained unchanged when current use of NSAID and DMARDs were included into the model (data not shown).

Discussion

In the present study, patients with PsA had increased BMI and other traditional and novel risk factors compared with controls. Only one previous study reported a higher BMI in PsA patients [5]. However, the prevalence of other CVD risk factors were similar to controls ($n=30$) after adjusting for the age in the subgroup analysis of 30 PsA patients [5]. In contrast, increased prevalence of DM and hypertension was found in our group of PsA compared with age- and sex-matched controls, even after adjusting for the BMI. The study by Han *et al.* [4] also reported similar finding using an administrative database, although no information regarding the BMI and inflammatory markers was available. In patients with psoriasis, an increased prevalence of obesity, DM and hypertension was also reported [24]. These findings may suggest that obesity, insulin resistance, psoriasis and PsA may share a common predisposition in terms of low grade inflammation. There is now a wealth of evidence indicating close ties between metabolic and immune systems [25]. For instance, IL-6 is a key pro-inflammatory cytokine that can stimulate the hypothalamic–pituitary axis, which is associated with central obesity, hypertension and insulin resistance [26]. IL-6 also induces CRP production. Even in patients with mild or inactive disease such as in our group of PsA patients, low grade inflammation as reflected by the hsCRP level was associated with obesity, insulin resistance, hypertension and dyslipidaemia. Further adjustment for hsCRP level rendered the differences in the prevalence of hypertension and DM; the TC and sugar levels and white cell count non-significant between the two groups; while the differences in other parameters remained significant suggesting that other inflammatory pathway (e.g. TNF-α) may also play a role. TNF-α may lead to insulin resistance by several mechanisms [27, 28]. Our group previously had demonstrated that TNF blocker therapy improved insulin resistance in RA patients [29]. Sattar *et al.* [30] also reported that TNF blockade lead to an increase in the sex hormone-binding globulin concentration, a surrogate marker for insulin sensitivity. Therefore, it is possible that the association of the obesity, insulin resistance and PsA is explained by inflammatory pathways shared by these seemingly disparate diseases. Another explanation for the predisposition of PsA patients to develop obesity and insulin resistance may be that certain behaviours or the psychological impact of PsA or psoriasis itself (e.g. poor eating habits, alcohol consumption, stress, decreased exercise due to psoriasis symptoms, joint pain or stigmatization).

In agreement with the three previous studies, we also demonstrated that PsA patients had lower TC and LDL cholesterol [10–12]. In contrast, we noticed an elevated level of HDL cholesterol. In addition, we also studied novel CVD risk factors including Apo A1 and Apo B. Apo A1 has been advocated as a strong predictor of cardiovascular events, with potential advantages over HDL cholesterol since Apo A1 transports and acts as the major anti-atherogenic protein in the HDL particles [31]. Moreover, with inflammation, HDL particles become depleted of Apo A1 and enriched with serum amyloid A [32]. Apo B transports all potentially atherogenic very low-density lipoprotein (VLDL), intermediate-density lipoprotein (IDL) and LDL particles. The cholesterol balance determined as the Apo B/Apo A1 ratio has been shown to be a better marker than lipids, lipoproteins and lipid ratios [31], although the true value of the Apo B/Apo A1 ratio is still under debate in the literature. In our study, we noticed the levels of both Apo A1 and Apo B were significantly increased. However, the Apo B/Apo A1 ratio was significantly increased compared with controls after adjusting for the BMI and hsCRP, suggesting an overall unfavourable lipid profile despite the apparently lower TC and LDL cholesterol and higher HDL cholesterol. The mechanisms for such changes in lipid levels in patients with inflammatory conditions are not clear form the literatures. Moreover, serum lipid levels are affected by several factors, including diet and the use of DMARDs or biologics. Our group has demonstrated that TC, HDL cholesterol, LDL cholesterol, TG and Apo B levels all increased significantly in RA patients after given TNF blocker [29]. Likewise, Apo B and TG levels were increased in PsA patients after given TNF blocker [30]. These findings may suggest normalization

with suppression of inflammation. Dietary intervention prevented the increase in total and LDL cholesterol upon acute phase response suppression [33]. Further work in this area should address these confounding factors.

Epidemiological observation suggests that in RA, mechanisms other than the classic atherosclerotic risk factors may play a pivotal role in the increase prevalence of CVD complications [34]. In this regard, recent reports have emphasized the importance of chronic inflammation in the pathogenesis of accelerated atherosclerosis observed in PsA patients [5–8]. The present study is novel for several reasons. It is potentially the first to comprehensively examine a range of traditional (including insulin resistance) and novel (Apo A1 and Apo B) risk factors for CVD in patients with PsA compared with age- and sex-matched healthy controls. Furthermore, we attempted to dissect the relevance of systemic inflammation to the risk factor pattern in PsA by examining the influence of hsCRP concentrations after adjusting for the BMI.

There are potential limitations of our methods. First, since it is a cross-sectional comparative study, the results do not prove a causal relationship between PsA and the CVD risk factors, and the study did not relate the clinical CVD risk factors or biomarkers to end points such as myocardial infarction. A prospective study with a long-term follow-up period is needed to clearly address the relative risk in these populations for the incidence of CVD and the relationship between inflammation and the CVD risk factors. Second, only patients who were ethnic Chinese attending referral centers were studied. We cannot exclude the possibility that patients with milder diseases may be under the care of primary care physicians or dermatologists, and this may limit the generalizability of our findings. However, the age at onset, sex distribution and presentation (predominantly polyarthritis) are similar to PsA patients in other observational cohorts [35]. Moreover, most of the patients in our group were having mild disease with low PASI, tender, swollen and damage joint counts, as well as HAQ score. Thirdly, other risk factors including menopausal status, drinking habit, family history of coronary artery disease, homocysteine, lipoprotein (a) levels or other inflammatory markers, e.g. TNF-α or IL-6 levels were not available in our study. Lastly, PsA patients who die soon after diagnosis would be excluded from the current study.

The analyses of associations between novel and traditional risk factors, PsA involved multiple tests of significance and multiple comparisons are associated with an increased chance of type I error. However, the utility of formal adjustments for multiple comparisons in an epidemiological context has been questioned [36–38]. We therefore chose not to perform any formal α-adjustments in the present study, but we acknowledge the need to consider with caution the statistical significance of such associations.

In conclusion, there was an increased prevalence of traditional and novel CVD risk factors in patients with PsA. The results should be confirmed in a larger number of 'unselected' patients. Not-withstanding the limitations, this data support the hypothesis that PsA may be associated with obesity, hypertension, insulin resistance and dyslipidaemia because of the shared inflammatory pathway. Our data suggest a need for better monitoring of traditional and novel atherosclerotic risk factor in PsA patients to reduce cardiovascular mortality and morbidity.

Rheumatology key messages

- After adjusting for the BMI, PsA patients still have a higher prevalence of CVD risk factors.
- Further adjustment for hsCRP level rendered the differences in the prevalence of most risk factors non-significant.
- PsA may be associated with CVD risk factors because of the shared inflammatory pathway.

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