High Prevalence of Subclinical Left Ventricular Dysfunction in Patients with Psoriatic Arthritis

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ABSTRACT. ***Objective.*** Endothelial dysfunction and early atherosclerosis have been found in patients with psoriatic arthritis (PsA) without cardiovascular disease (CVD) risk factors. Few studies have investigated whether there is any early impairment of myocardial function. The aims of our study were to determine the prevalence of subclinical left ventricular (LV) dysfunction in PsA patients and the disease-related risk factors.

Methods. Ninety-four PsA patients without clinical evidence of CVD and 63 healthy subjects were enrolled. All underwent conventional echocardiography and tissue Doppler imaging.

Results. Sixty-one (65%) patients with PsA had evidence of subclinical LV dysfunction as defined by mean myocardial peak systolic velocity (Sm) of basal 6 segments < 4.4 cm/s, lateral E' < 11.5 cm/s, and/or lateral E/E' > 10. Thirty-six (38%) patients had only diastolic dysfunction, 4 (4%) had only systolic dysfunction, and 21 (22%) had both systolic and diastolic dysfunction. PsA patients with subclinical LV dysfunction were older, had a higher age at diagnosis of PsA and of psoriasis, a longer disease duration, a higher prevalence of hypertension and hyperlipidemia, higher levels of serum creatinine, and more antihypertensive treatment than those with normal LV function. Multivariate regression showed that age at diagnosis of PsA > 40 years (OR 3.388, 95% CI 1.065–10.777, p = 0.039) and hypertension (OR 4.732, 95% CI 1.345–16.639, p = 0.015) were independent predictors of subclinical LV dysfunction.

Conclusion. PsA patients without established CVD disease and in the absence of traditional CV risk factors have a high prevalence of subclinical LV dysfunction. (First Release April 1 2011; J Rheumatol 2011;38:1363–70; doi:10.3899/jrheum.101136)

Key Indexing Terms:
ECHOCARDIOGRAPHY PSORIATIC ARTHRITIS MYOCARDIUM FUNCTION

Psoriatic arthritis (PsA) is an inflammatory arthritis associated with psoriasis. The prevalence of hyperlipidemia, hypertension, ischemic heart disease, congestive heart failure, peripheral vascular disease, cerebrovascular disease, and type II diabetes have been reported to be increased in patients with PsA[1]. A mortality study showed that cardiovascular diseases (CVD) are the leading causes of death in patients with PsA compared with controls, with a 1.3-fold risk of increased death rate due to CVD[2]. Gelfand, *et al*[3] prospectively compared the incidence of myocardial infarction among patients with and without a diagnosis of psoriasis, and suggested that psoriasis might be an independent risk factor for myocardial infarction. Despite these findings, however, psoriasis is still not considered a traditional risk factor for CV disease. Early diagnosis of atherosclerosis in a PsA population might allow more aggressive and targeted prophylaxis. Few studies have focused on the early detection of CV involvement in PsA and any association with traditional CV risk factors and specific disease-related risk factors. Tam, *et al*[4,5] found that, after adjustment for traditional CV risk factors, PsA remained associated with subclinical atherosclerosis, and that the increased prevalence of obesity, hypertension, dyslipidemia, and insulin resistance in PsA may be related to a shared inflammatory pathway. Gonzalez-Juanatey, *et al*[6,7] also demonstrated that PsA patients without traditional CV risk factors or clinically evident CVD exhibited endothelial dysfunction and had a high prevalence of macrovascular disease in the form of increased carotid artery intima-media thickness. Nonetheless, conventional echocardiography did not reveal any significant cardiac abnormalities in these patients.

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Compared to traditional echocardiography, tissue Doppler imaging (TDI) is a modified Doppler technique that allows direct measurement of myocardial contractile and relaxation velocities with high reproducibility and ease of performance[8,9]. Clinical studies have shown that TDI can detect subclinical myocardial disease otherwise not detectable by conventional 2-dimensional assessment of systolic function[10,11,12,13]. We hypothesized that in the milieu of chronic inflammation, patients with PsA might have a high propensity to experience subclinical cardiac dysfunction that has not been investigated. In this study, we employed conventional echocardiography and TDI to determine if subclinical left ventricular (LV) systolic and/or diastolic dysfunction is indeed present in patients with PsA, and whether this would be associated with PsA-related factors or as a result of other predisposing conditions.

MATERIALS AND METHODS

Study population. Ninety-four consecutive Chinese patients with PsA fulfilling the Classification of Psoriatic Arthritis criteria[14] were recruited from the rheumatology clinic of a university-affiliated teaching hospital. Exclusion criteria included pregnancy, hypothyroidism, clinically significant renal disease (serum creatinine level ≥ 270 μmol/l), those with history of angina, stable coronary artery disease, previous acute coronary syndromes, coronary revascularization, bundle-branch block, second-degree or higher atrioventricular block, atrial fibrillation, valvular stenosis or at least moderate valvular regurgitation, valvular replacement or repair, or mitral annular calcification. Patients were divided into 2 subgroups for comparison, PsA patients with and those without CVD risk factors, which included smoking status, hypertension (systolic BP ≥ 140 mm Hg or diastolic BP ≥ 90 mm Hg or the use of antihypertensive agents), diabetes mellitus (DM; defined as a history of DM, being on a DM-specific diet, taking oral hypoglycemic agent or insulin, or having fasting blood sugar ≥ 7.0 mmol/l), and hypercholesterolemia (total cholesterol ≥ 6.2 mmol/l or low-density lipoprotein cholesterol ≥ 4.13 mmol/l, or taking a lipid-lowering agent). Sixty-three healthy control subjects were enrolled, all with no history of overt CVD, and they were matched to patients without CVD risk factors for age, body mass index (BMI), and blood pressure.

The Ethics Committee of our institution approved the study, which was conducted in compliance with the Declaration of Helsinki (2000) of the World Medical Association and all patients provided written informed consent.

PsA clinical interview. Disease patterns. PsA patients who had ever had peripheral arthritis or had it at the time of assessment were included in the category of peripheral arthritis, and those with inflammatory arthritis of the back were included in the category of spondyloarthritis. Considering disease activity and severity: pain and physician and patient global assessments were evaluated using a 10-point visual analog scale (0, excellent well-being; 10, feeling extremely unwell). Examination recorded the number of tender and swollen joints using the 68 tender/66 swollen joint count, the presence of dactylitis, and the number of permanently deformed joints. Disease activity was assessed using the Disease Activity Score in 28 joints (DAS28)[15]. The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Bath Ankylosing Spondylitis Functional Index (BASFI) were used to assess disease activity and function in patients with predominant axial involvement[16,17]. Signs and symptoms of psoriasis (skin abnormality and nail lesions) were examined and the Psoriasis Area and Severity Index (PASI) was calculated to evaluate the severity of psoriasis[18]. Radiographs (spine, pelvis, feet, and hand) were reviewed for the presence of erosion at the time of the study.

Conventional echocardiography. Comprehensive standard 2-dimensional and Doppler echocardiography was performed in PsA patients and controls with Vivid 7 systems with a 3.5-MHz probe (GE Medical Systems, Milwaukee, WI, USA). Standard conventional echocardiographic assessments included measurement of LV dimensions, wall thickness, LV mass index, ejection fraction, and color Doppler imaging of all valves according to the recommendations of the American Society of Echocardiography[19]. LV hypertrophy was considered present if the mass index to body surface area exceeded 95 g/m^2 in women and 115 g/m^2 in men. Relative wall thickness (RWT) was calculated to categorize LV remodeling as normal geometry (normal LV mass with RWT ≤ 0.42), concentric remodeling (normal LV mass with increased RWT > 0.42), eccentric hypertrophy (increased LV mass with RWT ≤ 0.42), or concentric hypertrophy (increased LV mass with RWT > 0.42)[19]. The LV ejection fraction was evaluated by modified biplane Simpson's method. Stroke volume was calculated by difference between LV end-diastolic volume and end-systolic volume derived from Simpson's method, which was used to calculate the cardiac index.

Tissue Doppler imaging. We used apical views (apical 4-chamber, 2-chamber, and long-axis) for longitudinal motion with pulse repetition frequency adjusted to avoid aliasing, and with sector size and depth maximized to achieve highest possible frame rate (> 100 frames/s). Real-time pulse-wave tissue Doppler velocities were recorded from the septal and lateral sites of the mitral annulus in the apical 4-chamber view for measurements of peak systolic velocities (S') and early (E') diastolic peak velocities. Color TDI images in at least 3 consecutive beats were stored for offline analysis programs (EchoPac-PC 108.1.5; GE-Vingmed, Horten, Norway). The mean of peak systolic myocardial velocities (Sm) were measured from 6 basal LV segments to assess global systolic function. In our laboratory, the intraobserver and interobserver variability for tissue Doppler velocity data was 3% and 5%, respectively, as reported[12,20].

LV diastolic function. LV diastolic filling pattern was categorized according to pulse-wave Doppler examination of transmitral inflow before and during a Valsalva maneuver and of pulmonary venous inflow as well as TDI that assessed the lateral mitral annulus velocity. Normal LV relaxation pattern was defined with ratio of early to late diastolic mitral inflow velocities (E/A) between 0.75 and 1.5, normal early mitral inflow deceleration time > 140 ms and pulmonary venous flow pattern, and an early mitral inflow velocity/early lateral mitral annular motion (lateral E/E') ratio < 10 in the presence of normal LV ejection fraction and left atrial size. LV diastolic dysfunction was classified with increasing severity of abnormal relaxation, pseudonormal and restrictive filling pattern, as described and validated[21,22,23].

Assessment of subclinical LV dysfunction. Subclinical LV diastolic dysfunction was identified by lateral E' < 11.5 cm/s[24] and/or lateral E/E' > 10[22,23]; subclinical LV systolic dysfunction was defined by mean Sm from 6 basal LV segments < 4.4 cm/s[12]. Subclinical LV dysfunction included subclinical LV diastolic and/or systolic dysfunction.

Laboratory assessment in patients with PsA. Apolipoprotein A (apoA) and apoB were measured by automated analyzer (Cobas-Mira Plus, Hoffman-LaRoche Diagnostics, Mannheim, Germany) using a turbidimetric assay. Plasma insulin was measured using enzyme-linked immunosorbent assay (ELISA; Diagnostics Systems Laboratories, Webster, TX, USA). The homeostasis model assessment was used to determine insulin resistance: [fasting insulin (mU/l) × fasting glucose (mmol/l)]/22.5. Plasminogen activator inhibitor 1 (PAI-1) was measured by ELISA using commercial kits (Diagnostica Stago, Freres Chausson, France)[25]. Fibrinogen was measured using a modified clot-rate assay. High-sensitivity C-reactive protein (hsCRP) level was measured using an immunoturbidimetric assay performed with Olympus OSR6185 (Olympus Diagnostics, Lismeehan, Ireland). Erythrocyte sedimentation rate was measured by the Westergren method. Total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, and triglyceride were measured as described[5].

Statistical analysis. SPSS 17.0 for Windows (SPSS, Chicago, IL, USA) was used for the analyses. Results are expressed as the mean ± standard

deviation for normally distributed data and the median (interquartile range) for non-normally distributed data. Comparisons among groups were assessed using unpaired t test or ANOVA test for continuous variables and Pearson chi-square test for categorical variables. Mann-Whitney U test was used for continuous variables that were skewed. Pearson correlation and logistic regression (forward, conditional) analyses were performed to assess the relationship between echocardiographic and clinical variables. All tests were 2-tailed. P values < 0.05 were considered statistically significant.

RESULTS

Clinical characteristics in patients with PsA. In 94 patients with PsA, the mean age at diagnosis was 39.4 years and 58 (51.1%) patients had late-onset PsA (age > 40 yrs). Sixty-six (70.2%) patients had psoriasis with abnormal skin and nail lesion at the time of assessment. Forty-three (45.7%) patients had erosions on radiography. Seventy-eight (83.0%) patients had peripheral arthritis and 16 (17.0%) had spondyloarthritis. Based on the DAS28 score, 36 (38.3%) patients had inactive disease (DAS28 ≤ 3.2), 35 (37.2%) had moderate disease activity (3.2 < DAS28 ≤ 5.1), and 23 (24.5%) patients had very active disease (DAS28 > 5.1). Forty (42.6%) patients had hypertension, 18 (19.1%) had DM, and 12 (12.8%) had hyperlipidemia.

Comparisons of conventional echocardiography with TDI between controls and patients with PsA. PsA patients without CV risk factors had comparable epidemiologic data, ejection fraction, proportion of LV hypertrophy, and abnormal LV filling pattern compared to healthy controls (Table 1). Nonetheless, early LV remodeling was found in these patients, such as a thickened posterior wall, increased relative wall thickness, and higher prevalence of concentric remodeling, compared to controls ($p < 0.05$; Table 1). In addition, subclinical impairment of LV function was also detected, with 17 (47.2%) patients having evidence of subclinical LV dysfunction as defined by mean Sm < 4.4 cm/s, lateral E' < 11.5 cm/s, and/or lateral E/E' > 10. Among these patients, 7 (19.4%) had only diastolic dysfunction, 3 (8.3%) had only systolic dysfunction, while 7 (19.4%) had both systolic and diastolic dysfunction. In PsA patients with CV risk factors, LV subclinical dysfunction (75.9%) was more common than that in patients without ($p = 0.004$). In the whole PsA patient population, 61 (64.9%) had subclinical LV dysfunction. Among them, 36 (38.3%) patients had only diastolic dysfunction, 4 (4.3%) had only systolic dysfunction, and 21 (22.3%) had both systolic and diastolic dysfunction.

In patients with PsA, LV end-systolic dimension correlated significantly with hs-CRP ($r = 0.212$, $p = 0.046$), apoA-1 ($r = –0.314$, $p = 0.017$), and apoB/A-1 ($r = 0.357$, $p = 0.004$); the lateral E' ($r = –0.505$, $p < 0.001$) and lateral E/E' ($r = 0.230$, $p = 0.034$) correlated with the age at diagnosis of PsA; the mean Sm correlated with the age at diagnosis of PsA ($r = –0.355$, $p = 0.001$) and duration of PsA ($r = –0.211$, $p = 0.047$); and the category of LV dysfunction (1 = normal, 2 = only diastolic dysfunction, 3 = only systolic dysfunction, 4 = both systolic and diastolic dysfunction) correlated with the PsA duration ($r = 0.218$, $p = 0.039$).

Disease-related risk factors of LV dysfunction. Table 2 shows the comparison of clinical measures among patients with and those without subclinical LV dysfunction. Patients with subclinical LV dysfunction were older at the time of assessment and at diagnosis of PsA and psoriasis; and had a longer disease duration, a higher prevalence of hypertension and hyperlipidemia, higher levels of serum creatinine, and more antihypertensive treatment than those with normal LV function. There was no difference in other demographic measures, disease pattern, disease activity and/or severity, laboratory markers, and principal treatment between LV function subgroups. All the above risk factors were included in a univariate logistic regression and those with p values < 0.10 were included into the multivariate regression model. It was found that age at diagnosis of PsA (OR 1.071, $p = 0.021$) and hypertension (OR 4.444, $p = 0.022$) were independent risk factors for subclinical LV dysfunction. When age at PsA diagnosis > 40 years was included as a categorical variable, the ability to predict subclinical LV dysfunction remained present (OR 3.388, $p = 0.039$; Table 3).

DISCUSSION

In our study, comprehensive evaluation of LV systolic and diastolic function by conventional echocardiography and TDI revealed a high prevalence of subclinical LV dysfunction in patients with PsA, even in those without traditional cardiovascular risk factors. This finding confirms the hypothesis that subclinical LV systolic dysfunction can occur in PsA patients without traditional CV risk factors, probably associated with underlying inflammation.

LV remodeling in patients with PsA. Saricaoglu, *et al*[26] investigated 21 PsA patients with LV ejection fraction > 50% and reported increased LV end-diastolic and end-systolic diameters compared with controls. Our results are consistent with that study. Further, other indicators of LV remodeling, such as LV wall thickness, LV mass, and LV hypertrophy, were significantly abnormal in PsA patients without CV risk factors compared with the healthy control group matched for age, sex, BMI, and blood pressure. These findings suggest a direct PsA-related effect on LV structure, although the pathogenesis is not fully explained. We also found correlations between LV end-systolic dimension and hs-CRP, apoA-1, and apoB/A-1. Tsioufis, *et al*[27] investigated possible relations between LV concentric remodeling and plasma levels of hs-CRP; they found log of hs-CRP was significantly different between subjects with RWT > 0.44 and those with RWT < 0.44, after the adjustment for age, sex, BMI, and systolic/diastolic blood pressure ($p < 0.005$). Previous reports[28,29,30] showed that CRP decreases production of nitric oxide and upregulates angiotensin type-1 receptor expression, contributing to the pathogenesis of hypertension. Chronic systemic inflammation may induce

Table 1. Comparison of left ventricular (LV) function among healthy controls and patients with psoriatic arthritis (PsA) without or with cardiovascular (CV) risk factors.

Characteristics	Controls, n = 63	PsA patients without CV Risk Factors, n = 36	PsA Patients with CV Risk Factors, n = 58	ANOVA, p
Clinical measures				
Age, yrs	43.1 ± 13.6	44.4 ± 12.3	50.6 ± 11.5**†	0.004
Sex (M/F), n	25/38	17/19	34/24	0.113
Body mass index, kg/m^2	22.2 ± 3.1	24.4 ± 5.5	26.2 ± 3.9**†	< 0.001
Body surface area, m^2	1.62 ± 0.17	1.67 ± 0.24	1.77 ± 0.19**†	0.001
Systolic blood pressure, mm Hg	121 ± 11	119 ± 9	136 ± 18**††	< 0.001
Diastolic blood pressure, mm Hg	72 ± 8	75 ± 7	81 ± 10**††	< 0.001
Heart rate, beats per min	70 ± 12	72 ± 9	75 ± 13*	0.060
Conventional echocardiography with TDI				
Interventricular septum thickness, cm	0.82 ± 0.11	0.84 ± 0.15	0.93 ± 0.19**†	< 0.001
Posterior wall thickness, cm	0.72 ± 0.10	0.80 ± 0.13**	0.86 ± 0.14**†	< 0.001
LV end-diastolic diameter, cm	4.6 ± 0.4	4.6 ± 0.5	4.7 ± 0.4	0.151
LV end-systolic diameter, cm	2.8 ± 0.4	2.9 ± 0.4	2.9 ± 0.5	0.126
Relative wall thickness	0.32 ± 0.04	0.35 ± 0.07*	0.36 ± 0.06**	< 0.001
LV mass, g	117.4 ± 29.1	128.2 ± 33.0	148.3 ± 39.4**†	< 0.001
LV mass index, g/m^2	71.9 ± 14.1	76.5 ± 14.2	85.5 ± 21.2**†	< 0.001
LV hypertrophy, n (%)	0	2 (5.6)	8 (13.8)**	0.008
Normal geometry	63 (100)	29 (80.5)**	45 (77.6)**	0.004
Concentric remodeling	0	5 (13.9)	5 (8.6)	
Eccentric hypertrophy	0	1 (2.8)	5 (8.6)	
Concentric hypertrophy	0	1 (2.8)	3 (5.2)	
LV end-diastolic volume, ml	81.8 ± 15.8	71.7 ± 14.3*	81.6 ± 20.0†	0.011
LV end-systolic volume, ml	26.6 ± 6.8	25.1 ± 7.2	31.6 ± 8.8**††	< 0.001
LV stroke volume, ml	55.3 ± 11.8	46.6 ± 9.0**	50.0 ± 13.4*	0.002
LV ejection fraction, %	67.4 ± 5.9	65.6 ± 5.1	61.2 ± 5.5**††	< 0.001
Cardiac index, l/min·m^2	2.3 ± 0.5	2.0 ± 0.4**	2.1 ± 0.6	0.007
S' at mitral lateral annulus, cm/s	11.5 ± 2.4	9.0 ± 2.2**	9.1 ± 2.0**	< 0.001
Mean Sm of LV basal 6 segments, cm/s	6.2 ± 1.1	5.0 ± 1.1**	5.1 ± 1.1**	< 0.001
MV E, m/s	0.81 ± 0.13	0.76 ± 0.13	0.75 ± 0.16*	0.043
MV A, m/s	0.57 ± 0.12	0.62 ± 0.13	0.73 ± 0.21**††	< 0.001
MV deceleration time, ms	200 ± 48	210 ± 38	213 ± 48	0.244
E/A ratio	1.48 ± 0.39	1.26 ± 0.32*	1.11 ± 0.39**	< 0.001
Isovolumic relaxation time, ms	84 ± 13	81 ± 15	87 ± 18	0.231
E' at mitral lateral annulus, cm/s	14.3 ± 2.8	12.4 ± 2.7**	9.8 ± 3.2**††	< 0.001
E/E' (lateral annulus)	5.7 ± 1.3	6.4 ± 1.7	8.5 ± 3.2**††	< 0.001
LV filling pattern (using lateral E/E' > 10)				
Normal, n (%)	63 (100)	34 (94.4)	40 (69.0)**†	< 0.001
Abnormal relaxation pattern, n (%)	0	1 (2.8)	8 (13.8)	
Pseudonormal, n (%)	0	1 (2.8)	10 (17.2)	

S': peak systolic velocity of mitral annulus; MV E: early peak mitral inflow velocity; MV A: late peak mitral inflow velocity; E': early peak diastolic velocity of mitral annulus. * $p < 0.05$, ** $p < 0.005$ compared to controls; † $p < 0.05$, †† $p < 0.005$ compared to PsA patients without CV risk factors.

insulin resistance[31,32], which was associated with endothelial dysfunction, increased apoB and fibrinogen levels, and increased CRP and other inflammatory markers[33,34]. On the other hand, subclinical inflammation regulates cell growth, apoptosis, phenotype, and matrix turnover of cardiac tissue. All these factors can finally lead to adverse LV remodeling[27]. Pieretti, *et al*[35] reported that systemic lupus erythematosus, a chronic systemic disease, predicts increased LV mass. Similar associations between inflammation and CV end-organ damage may partly explain the link between LV remodeling and PsA.

Subclinical LV dysfunction and disease-related risk factors. Saricaoglu, *et al*[26] found that the presence of diastolic dysfunction was significantly associated with the presence of arthropathy and the duration of psoriasis. Gonzalez-Juanatey, *et al*[36,37,38,39,40] studied CVD in systemic diseases such as PsA, rheumatoid arthritis, and ankylosing spondylitis and suggested there were abnormalities of cardiac structure and function in those immune-mediated inflammatory diseases. Gladman, *et al*[41] demonstrated that high PASI score was a risk factor for CVD event. Compared to Gladman's study, our study detected early and subclinical

Table 2. Comparison of traditional cardiovascular risk factors and clinical characteristics between PsA patients with and those without subclinical LV dysfunction.

Characteristics	PsA Patients, n = 94	Subclinical LV Dysfunction		p
		No, n = 33	Yes, n = 61	
Age, yrs	48.2 ± 12.2	40.9 ± 10.7	52.1 ± 11.2	< 0.001
Hypertension, n (%)	40 (42.6)	6 (18.2)	34 (55.7)	< 0.001
Hyperlipidemia, n (%)	12 (12.8)	1 (3.0)	11 (18.0)	0.037
Age at psoriasis diagnosis, yrs	35.8 ± 14.3	30.4 ± 13.2	38.5 ± 14.2	0.012
Age at PsA diagnosis, yrs	39.4 ± 12.1	34.0 ± 11.0	42.6 ± 11.6	0.001
Age at PsA diagnosis > 40 yrs, n (%)	48 (51.1)	10 (30.3)	38 (63.3)	0.002
Psoriasis duration, yrs, median (IQR)	12.5 (5.0–16.7)	11.0 (4.1–15.7)	13.2 (6.5–17.1)	0.181
PsA duration, yrs, median (IQR)	7.9 (2.5–12.5)	5.3 (1.2–11.6)	9.4 (4.3–13.0)	0.046
PsA duration > 5 yrs, n (%)	45 (47.9)	11 (33.3)	34 (55.7)	0.038
Disease pattern				
Peripheral, n (%)	78 (83.0)	28 (84.8)	50 (82.0)	0.723
Spondylarthritis, n (%)	16 (17.0)	5 (15.2)	11 (18.0)	
DAS28, n (%)	3.7 ± 1.5	3.7 (1.4)	3.7 (1.5)	0.946
Inactive (DAS28 ≤ 3.2)	36 (38.3)	13 (39.4)	23 (37.7)	0.986
Moderate (3.2 < DAS28 ≤ 5.1)	35 (37.2)	12 (36.4)	23 (37.7)	
Very active (DAS28 > 5.1)	23 (24.5)	8 (24.2)	15 (24.6)	
Skin abnormal, n (%)				
Psoriasis vulgaris	44 (46.8)	19 (57.6)	25 (41.0)	0.124
Flexural psoriasis	44 (46.8)	15 (45.5)	29 (47.5)	0.847
Guttate	40 (42.6)	12 (34.6)	28 (45.9)	0.372
Erythrodema	47 (50.0)	13 (39.4)	34 (55.7)	0.130
Nail lesions, n (%)				
Pits	42 (44.7)	12 (36.4)	30 (49.2)	0.233
Onycholysis	35 (37.2)	12 (36.4)	23 (65.7)	0.898
Ridges	39 (41.5)	11 (33.3)	28 (45.9)	0.238
PASI, median (IQR)	2.4 (1.0–8.5)	2.1 (0.6–12.0)	2.6 (1.0–8.1)	0.955
HAQ, median (IQR)	0.4 (0.1–0.9)	0.4 (0–0.6)	0.4 (0.1–1.0)	0.498
Apo A-1, mg/dl	143.7 ± 33.5	135.6 ± 33.9	146.5 ± 33.3	0.284
Apo B, mg/dl	82.4 ± 17.3	81.0 ± 17.8	83.0 ± 17.3	0.704
hs-CRP, median (IQR), mg/l	4.7 (1.6–14.3)	5.6 (1.5–16.0)	4.3 (1.7–11.5)	0.598
Serum creatinine, μmol/l	74.8 ± 16.1	68.9 ± 16.8	77.0 ± 15.4	0.048
Current NSAID, n (%)	56 (59.6)	22 (66.7)	34 (55.7)	0.223
Current DMARD, n (%)	50 (53.2)	15 (44.5)	35 (57.4)	0.269
Corticosteroid ever, n (%)	8 (8.5)	4 (12.1)	4 (6.6)	0.238
Current antihypertensive therapy, n (%)	21 (22.3)	2 (6.1)	19 (31.1)	0.005
Calcium-channel blocker	10 (10.6)	0	10 (16.4)	0.014
ACEI/ARB	5 (5.3)	1 (3.0)	4 (6.6)	0.476
ß-blocker	11 (11.7)	1 (3.0)	10 (16.4)	0.054
Diuretics	2 (2.1)	0	2 (3.3)	0.293

IQR: interquartile range; DAS28: Disease Activity Score in 28 joints; PASI: Psoriasis Area and Severity Index; Apo A-1: apolipoprotein A 1; Apo B: apolipoprotein B; hs-CRP: high-sensitivity C-reactive protein; NSAID: nonsteroidal antiinflammatory drugs; DMARD: disease-modifying antirheumatic drugs; ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; HAQ: Health Assessment Questionnaire.

LV dysfunction in patients with relatively mild PsA, which may be due to inflammation-related myocardial fibrosis.

Although patients with overt CVD were excluded from the study, a number of the PsA patients had risk factors for CVD, particularly hypertension. A history of hypertension or use of antihypertensive medication was significantly more prevalent in those with subclinical LV dysfunction, which affected diastolic more than systolic function (Sm was not different). This is a potential confounding factor, but it is more likely that hypertension and PsA combine to adversely affect LV function, as illustrated in our results. However, LV diastolic and/or systolic impairment was associated with age at diagnosis of PsA, which was an independent risk factor for LV dysfunction, after adjustment for hypertension, hyperlipidemia, disease duration, and serum creatinine. Moreover, patients with late-onset PsA (age > 40 years) had a higher risk of having subclinical LV dysfunction. Although there is no well accepted definition of late-onset PsA, most cases of PsA are diagnosed in people aged 20–40 years, and late-onset cases tend to have more disease activity, poorer functional outcome, and immunological changes associated with aging[42,43,44]. In addition, Queiro, *et al*[45] compared young-onset and late-onset psoriatic spondylitis using the cutoff point of age > 40 years, and

Table 3. Predictors of subclinical cardiac dysfunction.

	Univariate			Multivariate		
	OR	95% CI	p	OR	95% CI	p
Age at PsA diagnosis	1.071	1.025–1.118	0.002	1.071	1.010–1.136	0.021
Age at PsA diagnosis > 40 yrs	3.977	1.600–9.863	0.003	3.388	1.065–10.777	0.039
Age at psoriasis diagnosis	1.044	1.008–1.081	0.015	—	—	—
PsA duration > 5 yrs	1.793	0.756–4.250	0.185	—	—	—
Hypertension	5.667	2.046–15.695	0.001	4.444	1.240–15.924	0.022
Hyperlipidemia	7.040	0.867–57.183	0.068	—	—	—
Serum creatinine	1.037	1.000–1.076	0.052	—	—	—
Calcium-channel blockers	1.045	0–∞	1.00			

Variables with $p < 0.10$ in univariate regression were included into multivariate regression.

found that patients with late-onset psoriatic spondylitis had a high frequency of polyarthritis. Thus, the definition of late-onset PsA (age > 40 years) used in our study appears to be acceptable.

Age, a traditional CV risk factor, was not included in the multivariate regression model possibly due to the following reasons. First, age is a confounding factor that can decrease the contribution of age at diagnosis of psoriasis/PsA and disease duration. Second, our results showed that the prevalence of LV dysfunction in patients without CV risk factors was higher than in age-matched healthy controls. Third, although the mean age at diagnosis of PsA in our study was younger than that in the study of Gonzalez-Juanatey, *et al*[7] (mean 39.4 ± SD 12.1 vs 42.4 ± SD 12.7 yrs, respectively), we still found a higher proportion of LV dysfunction. Finally, a recent mortality study[46] found that the relative risk of CV mortality was greatest in the younger patients with PsA; the adjusted relative risk of death resulting from CVD was 2.69 (95% CI 1.45–4.99) in 40-year-old patients, compared with 1.92 (95% CI 1.41–2.62) in 60-year-old patients.

All the above findings suggest that PsA itself contributes by a complicated pathway to cardiac involvement, and this contribution may be independent of age.

Limitations of our study include that the population was relatively small, and the study was cross-sectional and observational and no intervention was performed in those with LV remodeling and/or dysfunction. Although radial ventricular function was not assessed in this study, long-axis function measured by mitral annular motion has been proven to be a very sensitive indicator of subclinical LV dysfunction, more so than radial function[8,9]. TDI cannot effectively assess radial function because of the angle dependence of Doppler function. Radial and circumferential stress can be assessed by speckle tracking imaging, which would provide additional information. Finally, although psoriasis was not a risk factor of LV dysfunction in our patient cohort, some studies have shown an increased risk of coronary artery, cerebrovascular, and peripheral vascular diseases and mortality, and documented improvement of endothelial dysfunction under systemic therapy in patients with psoriasis[47,48,49,50]. Therefore, the potential influence of coexisting psoriasis on CVD in patients with PsA should not be neglected. We will enroll more patients with active and severe psoriasis to assess the relationship between severity of psoriasis and cardiac function in our future studies.

We have demonstrated a high prevalence of LV remodeling and subclinical LV dysfunction in patients with PsA, even in those without traditional CV risk factors. These changes in LV function may be associated with psoriasis, PsA, disease duration, and disease-related inflammatory markers. Future research should seek to clarify the mechanisms of cardiac dysfunction in patients with PsA and to identify interventional strategies that will slow the development of clinical CVD in this group.

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