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Impaired heart rate recovery indices in psoriasis patients

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Background: Psoriasis is a systemic inflammatory disease associated with increased risk of cardiovascular diseases. The heart rate recovery index (HRRI) is an indicator of autonomic nervous system function and is an independent prognostic risk factor for cardiovascular diseases. The aim of this study was to evaluate the heart rate recovery indices in patients with psoriasis.

Material/methods: Thirty-three psoriasis patients (22 male; mean age 41±11 years) and 26 healthy individuals (15 male; mean age 39±11 years) as a control group were included in the study. Baseline electrocardiography, transthoracic echocardiographic examinations, and exercise stress tests were performed in psoriasis and control groups. The heart rate recovery of the psoriasis group at 1, 2, 3, 4, and 5 minutes after maximal exercise were calculated and compared to those of the control group.

Results: Baseline demographic and clinical characteristics of psoriasis and control groups including age, sex, body mass index, systolic blood pressure, and echocardiographic parameters were similar. Total cholesterol, low-density lipoprotein cholesterol, and triglyceride levels were significantly higher and high-density lipoprotein cholesterol levels were significantly lower in the psoriasis group ($p<0.05$). Heart rate recovery at 1, 2, 3, 4, and 5 minutes after maximal exercise were found to be significantly lower in the psoriasis group ($p<0.05$). Additionally, baseline heart rates before exercise were significantly higher in the psoriasis group ($p<0.05$).

Conclusions: We found that impaired HRRI in psoriasis patients, which indicates the underlying autonomic nervous system dysfunction, is a pathophysiologic mechanism for increased cardiovascular disease risk.

MeSH Keywords: Cardiovascular Risk • Psoriasis • Heart Rate

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Background

Psoriasis is a chronic inflammatory skin disease with an unknown etiology. It was initially thought of as being primarily a skin disease, but with understanding of the immunopathogenesis and genetics of the disease it has been accepted as a systemic inflammatory condition [1,2]. Chronic inflammation in psoriasis is supposed to predispose patients to other diseases in which inflammation plays a role, such as cardiovascular and metabolic disorders [3]. Psoriasis has been shown to be associated with metabolic syndrome, diabetes, obesity, hypertension, and dyslipidemia [4–8]. The association of psoriasis with comorbidities increasing the risk of cardiovascular diseases was highlighted in many studies and psoriasis was also found to be independently related with myocardial infarction [3,4,9,10]. Psoriasis patients seem to be at higher risk of cardiovascular diseases compared to individuals without psoriasis.

Heart rate recovery (HRR) is the rapidly decline in heart rate after exercise and is considered to be a function of parasympathetic reactivation and sympathetic withdrawal [11,12]. This rapid decrease is thought to be an important mechanism to prevent excessive cardiac action [13]. The prognostic value of the rate of decrease in heart rate was studied in heart failure patients and found to provide valuable prognostic information [14]. As well as in cardiac patients, HRR was found to be impaired when compared to healthy subjects in different inflammatory diseases in the literature such as Behçet's disease, familial Mediterranean fever, and systemic lupus erythematosus [15–17]. Moreover, a delayed decrease in heart rate after exercise was reported to be a robust and independent predictor of the risk of death [11]. In this study, we aimed to evaluate the HRR indices of patients with psoriasis, which is a chronic inflammatory disease and has been shown to be associated with several risk factors for cardiovascular disease.

Material and Methods

Thirty-three psoriasis patients (22 male; mean age 41±11 years) and 26 healthy individuals (15 male; mean age 39±11 years) were included in this study. The diagnosis of psoriasis was based on clinical or histopathological examination. Current disease severity was quantified by the Psoriasis Area and Severity Index (PASI), which determines the affected body surface area, together with erythema, thickness and scaling. In the PASI system, the head, trunk, upper extremities, and lower extremities are assessed separately. The PASI score ranges from 0 to 72 (from no psoriasis to maximal disease); higher PASI scores indicate more severe psoriasis [18].

Patients aged younger than 18 and older than 65 years, and those with history of any cardiovascular disease, and comorbidities such as hypertension, chronic renal failure, anemia (Hgb <10 g/dl), autonomic nervous system disorder, rheumatoid diseases, diabetes mellitus, hyperthyroidism, or hypothyroidism were excluded from the study.

Baseline electrocardiograms (ECG) were evaluated for all patients with psoriasis and healthy controls. All participants underwent echocardiographic examinations by a Vivid Seven Echocardiography device (GE Vingmed Ultrasound A/S, Norway) equipped with a 2.5 MHz probe. The exercise stress tests in accordance with modified Bruce protocol were performed to calculate the HRR index in both groups. Both psoriasis patients and healthy controls aimed to reach at least 85% of age-adjusted maximum heart rate. The ECG was continuously recorded during the exercise stress test. The heart rates were recorded at rest, during the 5 minutes after exercise. HRRs were calculated by subtracting the heart rates at 1 (HRR1), 2 (HRR2), 3 (HRR3), 4 (HRR4), and 5 (HRR5) minutes from the heart rate at peak exercise.

The study has been approved by and carried out according to the instructions of the institutional Ethics Committee. Informed consents were obtained from all patients and healthy individuals included in this study.

Statistical analysis

Continuous variables are presented as mean ± standard deviation; categorical variables are given as percentages. The variables were investigated by Kolmogorov-Smirnov test to determine if they were normally distributed. Student's t test was used to compare continuous variables between 2 groups. Nonparametric values were compared with Mann-Whitney U test. Chi-square test was used to compare the categorical data. $P<0.05$ was considered as significant.

Results

The baseline clinical characteristics of psoriasis and control groups are presented in Table 1. There was no significant difference between the 2 groups regarding age, sex, body mass index, systolic blood pressure, and resting pulse. Total cholesterol, LDL-cholesterol, triglyceride levels were significantly higher and HDL-cholesterol levels were significantly lower in the psoriasis group. Additionally, diastolic blood pressure levels were significantly lower in the psoriasis group. The echocardiographic parameters, including left ventricle ejection fraction, were similar in both groups. The mean duration of disease was 8±6 years and mean PASI score of patients was 9.5±5 in the psoriasis group.

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Table 1. Baseline demographic and clinical characteristics of psoriasis and control groups.

	Psoriasis group n=33	Control group n=26	p Value
Male gender	22	15	NS*
Age (years)	41±11	39±11	NS*
BMI (kg/m^2)	28.2±4.6	26.8±3.0	NS*
Total cholesterol (mg/dl)	206.8±38.5	169.7±34.5	.001
HDL-C (mg/dl)	42.1±10.2	54.0±14.7	.001
LDL-C (mg/dl)	121.1±26.1	95.1±33.9	.004
Triglycerides (mg/dl)	219.7±170.5	102.1±67.2	.004
Hb (g/dl)	14.5±1.8	13.9±1.7	NS*
Systolic BP (mmHg)	131±16	124±16	NS*
Diastolic BP (mmHg)	73±10	79±8	.016
Resting Pulse (beat/minute)	78±9	76±12	NS*
LVEDD (mm)	45±4	45±3	NS*
LVESD (mm)	29±4	29±5	NS*
LVEF (%)	63±3	63±3	NS*

* Not significant.

Table 2. Exercise stress test parameters of the psoriasis and control groups.

	Psoriasis group n=33	Control group n=26	p Value
Duration (seconds)	603±98	657±135	NS*
Baseline heart rate (bpm)	94±14	81±12	.001
Maximum HR (bpm)	168±12	171±15	NS*
Percentage of age-adjusted HR (%)	94±5	95±6	NS*
HRR1	23±7	31±9	.000
HRR2	48±11	57±11	.004
HRR3	55±12	65±11	.001
HRR4	59±13	70±11	.001
HRR5	64±14	77±12	.000

* Not significant.

All psoriasis patients and healthy controls completed the exercise stress tests without difficulty. Both groups reached at least 85% of predicted maximum heart rates. The exercise duration, maximum heart rates, and percentage of maximum heart rate reached on peak exercise were similar in both groups. However, mean baseline heart rate was significantly higher in the psoriasis group. All of the calculated heart rate recovery indices were significantly lower in the psoriasis group (Table 2).

Discussion

In this study we demonstrated that HRR at 1, 2, 3, 4 and 5 minutes after maximal exercise testing were significantly impaired in psoriasis patients when compared to the healthy control group. Our findings support the presence of impaired autonomic nervous system functions as a potential explanation for increased cardiovascular disease risk in psoriasis patients.

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The risk of cardiovascular diseases in psoriasis has been shown in several studies [2–4]. In a cohort study that included a total of 34 371 patients with mild psoriasis and 2621 with severe psoriasis; psoriasis was reported to be associated with increased risk of adverse cardiovascular events. The event rates and rate ratios of all-cause mortality, cardiovascular death, myocardial infarction (MI), coronary revascularization, stroke, and a composite of MI, stroke, and cardiovascular death were found to be increased in psoriasis patients. Risk increased with disease severity and decreased with age at onset [19]. Psoriasis was identified as an independent risk factor for coronary artery calcification. There was a significantly higher prevalence and severity of coronary artery calcification in patients with psoriasis compared with control subjects [20]. In systematic review and meta-analysis of observational studies, an increased risk of cardiovascular events in psoriasis was reported [4,21], but the exact mechanisms that contribute to increased risk of cardiovascular events in psoriasis patients have not been clarified yet. Psoriasis and cardiovascular diseases have common risk factors, such as smoking and alcohol consumption. A higher prevalence of conventional cardiovascular risk factors such as obesity, dyslipidemia, and systemic medications used for treatment are other possible factors that could have roles in the risk of heart disease in psoriasis patients [2]. Additionally, inflammatory activity, presence of circulating proinflammatory factors, and endothelial activation may increase the risk, as in other systemic inflammatory conditions [1,2].

Heart rate recovery after exercise is the result of sympathetic withdrawal and parasympathetic reactivation [12]. Vagal reactivation plays an important role during this period, and heart rate decreases after termination of exercise. This mechanism is important for decreasing cardiac overload, and an impaired heart-rate recovery was suggested to increase the risk of cardiovascular death [11,13]. HRR has been studied in several inflammatory diseases. HRR index was reported to be impaired in ankylosing spondylitis patients, although there was no apparent active articular or cardiac involvement [22]. Sarcoidosis is an inflammatory granulomatous disease associated with cardiac disorders such as ventricular arrhythmias and sudden cardiac death. HRR index was also found to be impaired in patients with sarcoidosis and was suggested to be the possible cause of cardiac disorders in these patients [23]. There were significant differences in 1st minute and 2nd minute indices between patients with familial Mediterranean fever and a control group, and HRR index was reported to be impaired in patients with FMF [16]. Furthermore, to identify the high risk patients with Behçet's disease regarding cardiovascular dysfunction, use of HRR was suggested [15]. Psoriasis, a systemic inflammatory disease, has also been evaluated for HRR index, but the findings are controversial. Bulur et al. failed to demonstrate a significant difference in patients with mild to moderate psoriasis regarding HRR indices [24], but Sarli et al. reported lower HRR indices in psoriasis patients and demonstrated that first-minute HRR index was significantly correlated with duration of psoriasis and psoriasis area and severity index score [25]. Our findings support the results of Sarli et al. We also found decreased HRR indices in psoriasis patients compared to the healthy control group. One potential explanation for the different results might be the severity of psoriasis disease, which is reflected by PASI scores. The mean PASI scores of the patients in the study by Bulur et al. was 6.3 [24], but mean PASI scores were higher in our study and in a study by Sarli et al. [25]. An additional finding of our study was the significantly higher baseline heart rates of the psoriasis patients compared to healthy individuals. This finding may also reflect the presence of impaired parasympathetic nervous system functions in psoriasis patients.

Conclusions

We found that HRR indices were decreased in psoriasis patients. These findings may indicate the presence of autonomic nervous system dysfunction, which could be one of the factors that increase cardiovascular risk in psoriasis patients. HRR may be used as a simple and non-invasive test to identify high-risk psoriasis patients.

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