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Original

Peripheral Cold Sensation in Patients with Chronic Heart Failure

Ryo Kayashima[1,2], Shichiro Abe[1)], Kaori Kono[2)], Yu Ogata[3)], Tomoko Fukuoka[3)], Akira Taneichi[4)], Kentaro Kaneko[5)], Machiko Yamamoto[3)], Toshiaki Nakajima[1)], Shigeru Toyoda[1)]

1) Department of Cardiovascular Medicine, Dokkyo Medical University School of Medicine, Tochigi, Japan
2) Department of Fundamental Nursing, Dokkyo Medical University School of Nursing, Tochigi, Japan
3) Ibaraki Christian University School of Nursing
4) Department of Nursing, Aomori University of Health and Welfare
5) Miyagi University School of Nursing

Summary

In patients with chronic heart failure (CHF), blood is redistributed to the major organs and blood perfusion of peripheral tissues decreases. Consequently, the skin temperature decreases, and patients experience a peripheral cold sensation (PCS). Blood reallocation involves autonomic nervous system control. In other words, a decrease in skin temperature and variation in autonomic nervous activity may be predictors of CHF severity. Forty-five patients with CHF were identified by New York Heart Association (NYHA) functional classification and divided into NYHA class I and NYHA class II-III groups. The temperature of the eardrum, toe, and skin were measured and the autonomic nervous activity was estimated by heart rate variability. We compared the results between the NYHA groups. The temperature of the left dorsum pedis and right pollex pedis were significantly lower in the NYHA class II-III group than in the NYHA I group. The difference in temperature between the eardrum and the left dorsum pedis and that between eardrum and right pollex pedis was significantly greater in the NYHA class II-III group than in the NYHA I group. However, there was no significant intergroup difference in autonomic nervous activity was noted. Body surface versus deep body temperature in patients with CHF were significantly lower in those with NYHA class II-III versus NYHA class I disease. Thus, PCS might be associated with CHF severity.

Key Words: autonomic nerve activity, chronic heart failure, cold sensation, heart rate variability

Introduction

In chronic heart failure (CHF), decreased cardiac output is redistributed to prioritize blood flow to the main organs such as the kidneys and brain. As a result, the skin's blood perfusion decreases. This redistribution is regulated by the autonomic nervous system. In addition, as CHF worsens, sympathetic nerve activity increases and vasoconstriction persists[1)]; a peripheral cold sensation (PCS) is among its major clinical symptoms. Blood flow in the extremities of patients with CHF is lower than that in healthy subjects[2)]. A decreased peripheral blood flow is closely related to susceptibility to fatigue and impaired exercise tolerance in patients with CHF[3)] and affects their psycho-

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Reprint requests to: Shichiro Abe
abenana@dokkyomed.ac.jp
Department of Cardiovascular Medicine, Dokkyo Medical University School of Medicine, 880 Kitakobayashi, Mibu, Tochigi 321-0293, Japan

logical quality of life[4]. Furthermore, patients with CHF have lower parasympathetic nerve activity at rest than healthy subjects and are vulnerable to stress and fatigue[5]. Therefore, PCS could be a potential predictor of worsening CHF. In patients with CHF, the skin surface temperature decreases versus the deep body temperature according to disease severity, but no studies have elucidated its implications in the pathophysiology of CHF. Thus, this study aimed to clarify PCS and autonomic nervous activity in relation to CHF severity.

Materials and Methods

The subjects were 45 patients with CHF with a mean 66.6 years of age who attended the cardiac rehabilitation center of Dokkyo Medical University Hospital and met the following inclusion criteria: 1) age 50-80 years old at the time providing consent; and 2) New York Heart Association (NYHA) cardiac function classification I-III. We excluded patients who: 1) were undergoing dialysis; 2) had active malignant tumors; 3) were classified as NYHA class IV; 4) had peripheral arterial disease; 5) were participating in other intervention trials; and 6) were deemed inappropriate participants by physicians.

The study was conducted between January and November 2019. Physiological parameters were performed in a room with controlled temperature and relative humidity of 23.6 ± 0.9℃ and 38.6 ± 18.2%, respectively. After setting the adaptation period to the environment for 20 min, the experiment was performed for 15 min. During this process, the patient was covered from the neck to the toes with a towel to keep them in the supine position with bare feet and avoid the influence of outside air. The measurement was performed before cardiac rehabilitation considering the influence of cardiac rehabilitation on peripheral skin temperature and skin blood flow.

The blood pressure was measured of the right arm using an electronic sphygmomanometer (ES-H55; Terumo Co., Ltd., Tokyo, Japan) at the beginning of the adaptation and at the end of measurement. The eardrum temperature was taken to represent the deep body temperature, while the peripheral skin temperature was taken at four points of the foot (i.e., both dorsum pedis and both pollex pedis). The eardrum temperature was measured in the right outer ear using an earplug-type temperature probe (ITPO10-27; Nikkiso-Therm Co., Ltd., Tokyo, Japan) and a temperature thermistor (Precision 8-channel data logger N540 series; Nikkiso-Therm Co., Ltd.). Foot temperature was measured using a temperature thermistor (Precision 8-channel data logger N540 series; Nikkiso-Therm Co., Ltd.).

After each participant rested in the supine position for 20 min, heart rate (HR) was measured using wireless radiofrequency and electrocardiography sensors (GMS Co., Ltd., Tokyo, Japan) applied to the chest. Electrocardiographic complexes were recorded for 15 min. HR variability (HRV) was calculated using the maximum entropy method with MemCalc/Bonaly Light real-time analysis software (GMS Co., Ltd.) based on R-R intervals. In the frequency analysis, the low-frequency (LF) domain (0.04-0.15 Hz) and high-frequency (HF) domain (0.15-0.40 Hz) were categorized. The HF domain is generally considered a true indicator of vagal nerve activity, while the LF/HF ratio is generally considered an indicator of sympathetic nervous activity.

Statistical analysis

The participants were divided into NYHA class I and NYHA class II-III groups and compared for each index. The chi-square test was used to examine categorical variables. The Mann-Whitney U-test was used as the test method. Statistical processing was performed using SPSS software (SPSS Statistics version 25; IBM, Armonk, NY, USA), and a p value of less than 0.05 was considered significant.

Results

Clinical background

Of the 45 patients, 21 (mean age, 65.9 ± 8.6 years) were in the NYHA class I group, while 24 (mean age, 67.3 ± 9.2 years) were in the NYHA class II-III group. The incidence of diabetes and hypertension was significantly higher in the NYHA class I group than in the NYHA class II-III group. No other significant intergroup differences were found (Table 1).

Comparison of measurement data

There was no difference in eardrum temperature between the NYHA class I and NYHA class II-III

Table 1 Patient characteristics of the NYHA class I versus NYHA class II-III groups

		NYHA class I (n = 21)	NYHA class II-III (n = 24)	P value
Female sex	n (%)	10 (47.6)	12 (50.0)	0.118
Age	years	65.9 ± 8.6	67.3 ± 9.2	0.531
Height	cm	158.8 ± 9.2	158.7 ± 7.3	0.991
Body weight	kg	61.2 ± 14.0	60.4 ± 15.2	0.724
BMI	kg/m²	24.4 ± 4.9	23.9 ± 5.1	0.625
History of smoking	n (%)	3 (14.3)	1 (4.2)	0.326
Heart rate	bpm	62.4 ± 9.9	64.2 ± 11.5	0.611
SBP	mmHg	119.1 ± 15.3	107.9 ± 16.2	0.470
DBP	mmHg	66.7 ± 11.4	66.7 ± 11.4	0.437
Comorbidity				
Diabetes	n (%)	15 (71.4)	10 (41.7)	0.045*
Hypertension	n (%)	14 (66.7)	7 (29.2)	0.012*
Dyslipidemia	n (%)	9 (42.9)	7 (29.2)	0.338
Hyperuricemia	n (%)	5 (23.8)	2 (8.3)	0.225
Renal dysfunction	n (%)	5 (23.8)	9 (37.5)	0.322
Sleep apnea syndrome	n (%)	2 (9.5)	4 (16.7)	0.670
Thyroid dysfunction	n (%)	2 (9.5)	0 (0)	0.212
Causative disease				
Myocardial infarction	n (%)	7 (33.3)	5 (20.8)	0.501
Angina pectoris	n (%)	1 (4.8)	1 (4.2)	0.923
Dilated cardiomyopathy	n (%)	4 (19.0)	7 (29.2)	0.503
Myocarditis	n (%)	0 (0)	2 (8.3)	0.176
Cardiac sarcoidosis	n (%)	0 (0)	2 (8.3)	0.176
Hashimoto's thyroiditis	n (%)	1 (4.8)	0 (0)	0.280
Hypertension	n (%)	4 (19.0)	0 (0)	0.025*
Aortic valve stenosis	n (%)	0 (0)	2 (8.3)	0.176
Aortic Regurgitation	n (%)	1 (4.8)	1 (4.2)	0.923
Mitral regurgitation	n (%)	3 (14.3)	1 (4.2)	0.234
Tachycardia-induced cardiomyopathy	n (%)	0 (0)	2 (8.3)	0.176
Systemic lupus erythematosus	n (%)	0 (0)	1 (4.2)	0.344
Treatment				
ACE/ARB	n (%)	16 (76.2)	18 (75.0)	1.000
Statin	n (%)	12 (57.1)	9 (37.5)	0.188
β-blocker	n (%)	17 (81.0)	21 (87.5)	0.689
Cardiac rehabilitation	n (%)	13 (61.9)	17 (70.8)	0.546

NYHA, New York Heart Association; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; ACE, angiotensin converting enzyme inhibitor; ARB, angiotensin II receptor blocker; bpm, beats per minute; Values are expressed as mean ± SD; $^*p < 0.05$.

groups. Each skin temperature trend was lower in the NYHA class II-III group than in the NYHA class I group. The temperatures of the left and right dorsum pedis were significantly lower in the NYHA class II-III group than in the NYHA class I group. The temperature difference between the eardrum and peripheral skin tended to be greater in the NYHA class II-III group than in the NYHA class I group. The difference in temperature between the eardrum and the left dorsum pedis/right pollex pedis was significantly greater in the NYHA class II-III group (Table 2).

Comparison of HRV

Of the 45 subjects, 25 were able to undergo HRV measurements (12 in the NYHA I group, 13 in the NYHA class II-III group). No significant intergroup differences were observed in HF (Fig. 1) and LF/HF (Fig. 2).

Table 2 Mean body temperatures of the NYHA class I versus NYHA class II-III groups

Body location	NYHA class I (n = 21) Body temperature (℃)	NYHA class II-III (n = 24) Body temperature (℃)	P value
Eardrum	36.1 ± 0.4	36.0 ± 0.5	0.339
Rt. dorsum pedis	31.9 ± 2.3	30.5 ± 2.2	0.065
Lt. dorsum pedis	32.0 ± 2.2	30.5 ± 2.1	0.020*
Rt. pollex pedis	30.3 ± 3.9	27.8 ± 3.8	0.036*
Lt. pollex pedis	30.3 ± 3.5	28.0 ± 4.1	0.056
Eardrum-Rt. dorsum pedis	4.2 ± 2.5	5.5 ± 2.2	0.072
Eardrum-Lt. dorsum pedis	4.1 ± 2.3	5.5 ± 2.0	0.020*
Eardrum-Rt. Pollex pedis	5.8 ± 3.9	8.2 ± 3.7	0.038*
Eardrum-Lt. pollex pedis	5.8 ± 3.5	8.0 ± 4.0	0.056

Lt, left; Rt, right. Values are expressed as mean ± SD; *p < 0.05.

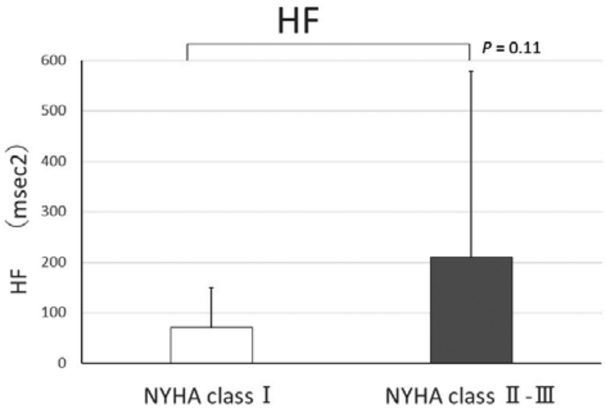

Figure 1 Comparison of HF between the NYHA class I and NYHA class II-III groups
HF, high frequency; NYHA, New York Heart Association. Values are expressed as mean ± SD.

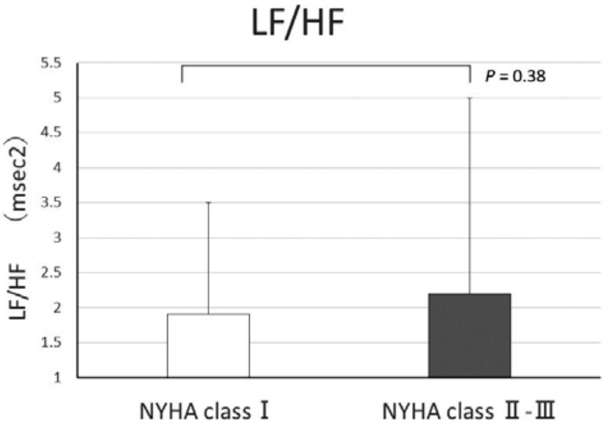

Figure 2 Comparison of LF/HF between the NYHA class I and NYHA class II-III groups
LF/HF, low frequency/high frequency; NYHA, New York Heart Association. Values are expressed as mean ± SD.

Discussion

When cardiac output decreases due to CHF, blood is redistributed to the major organs and blood perfusion of the peripheral tissues and skin decreases. Consequently, the skin temperature decreases in patients with CHF and they feel PCS. Blood reallocation involves autonomic nervous system control. In other words, a decrease in skin temperature and variation in autonomic nervous activity may be predictors of CHF severity. Our results suggested significant intergroup differences in the deep body and body surface temperatures. On the other hand, there was no difference in autonomic nervous activity by CHF severity. The attenuation of all frequency components was reported as a characteristic finding of HRV in patients with CHF[6]. Sympathetic nerve activity decreases and parasympathetic nerve activity increases due to the oral administration of β-blockers and exercise load[7]. In this study, no intergroup differences were found in the ratio of beta-blocker use and cardiac rehabilitation. Moreover, the incidence of diabetes was significantly higher in the NYHA class I group than in the NYHA class II-III group. Denervation due to diabetes may affect autonomic nervous activity. Therefore, there might be a loss of difference in the power of the HRV spectrum.

CHF can be considered a syndrome accompanied by autonomic neuropathy; therefore, the imbalance between sympathetic and parasympathetic nerve activity can be corrected. This supports the usefulness of the β-blockade in patients with CHF. Sympathetic nerve activity regulates peripheral arterial constriction. Thus, αβ-blocker, such as carvedilol, may be more suitable for patients with PSC than a β1 selective agonist. PCS is an indefinite symptom that depends on subjective sensation. In this study, we found that skin temperature was related to CHF severity, but we did not investigate the association between body surface temperature and the presence of PSC. Thus, an actual survey of symptomatic PCS should be conducted to improve the quality of life of patients with CHF. Thus, we may have to perform further large-scale studies in the future.

Study limitations

Since the size of the current cohort was too small, we divided the patients into NYHA class I and NYHA class II-III groups. Hence, a larger cohort of each NYHA class should be investigated in the future.

Conclusion

Peripheral skin temperature was significantly lower than deep body temperature in patients with NYHA class II-III versus NYHA class I CHF.

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