Determination of Hiesho among Young Japanese Females using Thermographic Technique

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Abstract Hiesho is the condition of having a cold sensation in one's hands or feet. This is a well-known health problem for young Asian females. However, the definition of Hiesho is still controversial. In this study, we aimed to develop a quantitative and non-invasive approach to determine Hiesho. Sixty-three young females participated in this research. Temperature difference (ΔT) between the forehead and foot sole was utilized to define Hiesho or non-Hiesho condition, and the result was crosschecked with that of a self-reported questionnaire. Central systolic blood pressure and augmentation index were measured to evaluate subjects' physiological indicators. The results of the questionnaire showed that 49% of young females (31 of 63 people) reported Hiesho. There was a significant difference in ΔT between non-Hiesho and Hiesho (1.85°C and 5.55°C, respectively, $p < 0.01$). After cross-checking with the self-reported questionnaire, ΔT of 3.64°C demonstrated acceptable reliability and accuracy for defining Hiesho. Central systolic blood pressure and augmentation index were not different between Hiesho and non-Hiesho. In conclusion, young females with Hiesho had drastically different temperatures at the forehead and foot sole. The temperature difference between the forehead and foot could be used as a quantitative and objective parameter for defining Hiesho.

Keywords: Hiesho, thermographic technique, non-invasive method.

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1. Introduction

Hiesho, also known as a cold sensation, is frequently observed in Asian females [1–3]. The characteristic symptom of Hiesho is a cold feeling, particularly in the hands and feet, at an environmental temperature at which a healthy person does not feel cold [4]. Hiesho is not only related to several health problems in daily life but is also associated with a higher frequency of chronic disease [4, 5]. In Western medicine, Hiesho is not perceived as a

remarkable symptom [6]. However, in Japan, approximately 30% of the patients used Kampo medicines because of Hiesho [7].

Currently, the diagnosis of Hiesho is still controversial. The most popular method for defining Hiesho is through a questionnaire-based survey called “Terasawa Hiesho Questionnaire” [8–10]. As this questionnaire is in Japanese, applying this method in other countries is difficult. Nakamura [8] reported that there was a significantly higher skin temperature difference in pregnant women with Hiesho. However, young Hiesho patients are still unaware of different skin temperatures.

Cutaneous blood flow is controlled by two types of sympathetic nerve systems: cutaneous vasoconstrictor (CVC) and cutaneous vasodilator (CVD). Increased CVC activity results in constriction of cutaneous blood vessels, while increased activity of CVD results in dilation of skin vessels. CVC does not affect cutaneous blood flow at the forehead, whereas peripheral blood flow is affected by CVC activity [11].

We hypothesized that a difference in forehead and foot plantar temperatures exist in young females with Hiesho. To test this hypothesis, we subjectively defined Hiesho using a questionnaire, performed thermal check using thermographic technique, and investigated the usefulness of the proposed method in determining Hiesho. The result of this study is expected to provide a quantitative and non-invasive approach to determine Hiesho.

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2. Subjects and Methods

2.1 Human Subjects

Sixty-three female students (age: 21.5 ± 1.7 years, height: 157.92 ± 6.07 cm, weight: 51.45 ± 6.16 kg, body mass index: 20.60 ± 2.03 kg/m²) with regular menstrual cycles participated in our experiment. No subject reported a history of health problems including endocrinopathy, cardiovascular disease, gynecological conditions, and connective tissue disease. Subjects were required to abstain from alcohol and caffeine for at least one day and from any food at least 2 h before the experiment.

Before the experiment, all subjects were informed of the purpose and methods of this study and provided written informed consent. Subjects were free to withdraw from the study at any time. This study was approved by the Ethics Committee of Osaka University Hospital (No. 19162, August 2019).

2.2 Experimental Environment and Methods

The experiment was conducted from 31st July to 21st October 2019, from 10 a.m. to 4 p.m. Considering that body temperature fluctuates depending on the phase of the menstrual cycle, the experiment was conducted only during the follicular phase. The local temperature during our experiment was: maximum $30.1 \pm 12.3^\circ\text{C}$, minimum $22.8 \pm 4.7^\circ\text{C}$, and average $26.9 \pm 4.4^\circ\text{C}$ [12]. The indoor temperature was $24.6 \pm 0.6^\circ\text{C}$, and humidity was $54.5 \pm 12.3\%$.

Before the experiment, we asked the subject to rest for 20 min to adapt to the experimental environment. Then, each subject responded to a Hiesho questionnaire. A thermal check that captures temperatures from the forehead and the foot (at dominant foot) was utilized to define Hiesho. Finally, we measured blood pressure, pulse wave and augmentation index to investigate the subject's physiological indicators.

2.3 Defining Hiesho

In this research, "Terasawa Hiesho Questionnaire" was used to define Hiesho. This questionnaire contains twenty questions, comprising three main questions, five related questions, and twelve minor questions [8, 10]. A subject who answers positively to (1) two or more main questions, or (2) one main and two or more related questions, or (3) four or more related questions, is defined to be Hiesho; otherwise, a subject is considered to be non-Hiesho.

Figure 1 shows the proposed method for defining Hiesho using a quantitative approach. In this study, an infrared thermometer (©Fluke Thermometer Ti450) was utilized to measure skin temperature. This thermal equipment is loaded with MultiSharp FocusTM, which pro-

Fig. 1 Image of thermal check.

vides sharp focusing of one image data so that we can acquire high-quality temperature data from the thermal graph. The resolution of this thermometer is 320×240 pixels, and the noise equivalent temperature difference is 0.03°C [13]. The thermometer used in this study has been proved to be a highly reliable equipment for collecting temperature data [14].

We asked the subject to sit still on a chair, with their legs stretched on the chair, and ensure that their feet were perpendicular to the ground. Then, we captured a thermal graph image of their entire body. Forehead was defined as the area above the subject's eyebrows and below the hairline. Temperature difference (ΔT) was calculated as follows:

$$\Delta T = T_{\text{forehead}} - T_{\text{plantar}} \quad (1)$$

where T_{forehead} represents the average forehead temperature and T_{plantar} represents the average planar temperature at the dominant foot.

To define the optimal ΔT , the thermal check result was verified and evaluated in terms of sensitivity and specificity of the questionnaire results, as well as by the area under the receiver operating characteristics (ROC) curve (AUC) analysis of the validation data.

2.4 Physiological Indicators

A non-invasive automated blood pressure monitor with augmentation index function (Omron HEM-9000AI; Omron Healthcare, Kyoto, Japan) was used to measure central systolic blood pressure (cSBP), pulse wave and augmentation index (AI) [15]. A scene of measurement is shown in **Fig. 2**. Systolic blood pressure, diastolic blood pressure, cSBP, pulse pressure, pulse rate, and AI were measured in each subject.

2.5 Data Analysis

Average forehead and plantar temperatures were utilized for calculating the temperature difference. The results of the Hiesho questionnaire and ΔT for each subject were used to calculate the optimal cut-off value. ROC analyses were conducted using the statistical software MedCalc® (version 19.2.5). Disease prevalence was calculated as the percentage of Hiesho based on the ques-

Fig. 2 Measurement of cSBP and AI.

tionnaire results. Student's *t*-test was used to test the significance of difference between two groups, with the significance level set at 5%. The *t*-test was performed using JASP (version 0.13.1.0, The Netherlands).

3. Results

According to the "Terasawa Hiesho Questionnaire", 49.2% of the subjects (31 in 63 people) were defined to have Hiesho. **Figure 3(a)** shows examples of thermal images of a non-Hiesho and a Hiesho subject. Dark blue indicates low temperature, while dark red represents high temperature. Compared with healthy subjects (non-Hiesho group at the left), the colors of the feet and the forehead in the Hiesho group (right image) were totally different, indicating that the temperature at the foot sole was much lower than that at the forehead.

Figure 3(b) shows the results of the ROC curve to define ΔT and Hiesho. Optimal ΔT was 3.64°C , with sensitivity 77.4% and specificity 71.9%. The ΔT of 3.64°C showed acceptable accuracy for defining Hiesho (AUC = 0.753, standard error: 0.061, 95% confidence interval: 0.634 to 0.857, $p < 0.001$).

The subjects' basic information and their thermal check results are summarized in **Table 1**. There were no significant differences in height, weight, and BMI between the two groups ($p > 0.05$). There was a difference in age between Hiesho and non-Hiesho groups (22.0 ± 1.5 versus 21.1 ± 1.8 years, $p < 0.05$), Cohen's *d* suggested that this was a medium effect size.

Table 2 shows the results of thermal check. For the Hiesho group, the average forehead temperature was 35.08°C , which was higher than that in the non-Hiesho group ($p < 0.01$). On the contrary, non-Hiesho young females had a higher plantar temperature than those with Hiesho (32.60 versus 29.51°C). The ΔT between the forehead and plantar showed significant difference between the two groups (1.85°C in the non-Hiesho group

Fig. 3 Example of thermal check and result of the ROC curve. (a) Samples of thermal check in two groups. The left thermal image is the non-Hiesho subject, and the right thermal image is a Hiesho subject. The color bar indicates the temperature range in the images. (b) Receiver operating characteristics curve to predict optimal ΔT for defining Hiesho.

Table 1 Age and physical characteristics.

	non-Hiesho (<i>N</i> = 32)	Hiesho (<i>N</i> = 31)	<i>p</i> value	Cohen's <i>d</i>
Age (years)	21.1 (1.8)	22.0 (1.5)	< 0.05	0.524
Height (cm)	158.70 (6.28)	157.11 (5.84)	0.30	-0.263
Weight (kg)	52.39 (7.04)	50.47 (5.03)	0.22	-0.312
BMI (kg/m^2)	20.75 (2.01)	20.48 (2.08)	0.60	-0.133

Value: mean (standard deviation)

BMI: body mass index

versus 5.55°C in the Hiesho group, $p < 0.01$). Cohen's *d* indicated that these were large effects.

Table 3 shows the results of physiological indicators. There were no significant differences between non-

Table 2 Results of thermal check.

	non-Hiesho (<i>N</i> = 32)	Hiesho (<i>N</i> = 31)	<i>p</i> value	Cohen's <i>d</i>
FT (°C)	34.43 (0.69)	35.08 (0.57)	< 0.01	1.020
PT (°C)	32.60 (1.20)	29.51 (1.36)	< 0.01	−2.403
ΔT (°C)	1.85 (1.23)	5.55 (1.40)	< 0.01	2.854

Value: mean (standard deviation)

FT: forehead temperature

PT: plantar temperature

ΔT: Temperature difference

Table 3 Results of physiological indicators.

	non-Hiesho (<i>N</i> = 32)	Hiesho (<i>N</i> = 31)	<i>p</i> value	Cohen's <i>d</i>
SBP (mmHg)	101.3 (9.3)	101.4 (6.9)	0.52	0.163
DBP (mmHg)	68.5 (7.2)	69.0 (6.0)	0.96	0.012
cSBP (mmHg)	98.9 (8.4)	100.1 (7.0)	0.76	0.078
PP (mmHg)	32.8 (5.5)	32.4 (6.3)	0.78	−0.070
PR (BPM)	70.4 (9.7)	72.3 (8.9)	0.41	0.211
AI (%)	52.5 (10.7)	56.1 (10.9)	0.20	0.331

Value: mean (standard deviation)

SBP: systolic blood pressure

DBP: diastolic blood pressure

cSBP: central systolic blood pressure

PP: pulse pressure

PR: pulse rate

AI: augmentation index

Hiesho and Hiesho groups. However, there was a trend that Hiesho group had higher cSBP than non-Hiesho group (100.1 ± 7.0 versus 98.9 ± 8.4 mmHg). Hiesho group also showed a tendency of higher pulse rate (72.3 ± 8.9 BPM) compared to non-Hiesho group (70.4 ± 9.7 BPM). Higher AI in Hiesho group ($56.1 \pm 10.9\%$) indicated a trend of stiffer peripheral blood vessel than in non-Hiesho group ($52.5 \pm 10.7\%$).

4. Discussion

In this study, we defined Hiesho among young females based on a questionnaire. As a result, 31 in 63 people (49%) were defined to have Hiesho. Previous studies also reported that approximately half of young women in

Japan suffered from Hiesho [16–18], similar to our finding. However, it has to be emphasized that body temperature in Hiesho patients varies in different seasons [19], and performing experiments in the same season is recommended. The age of Hiesho group was higher than that of non-Hiesho group (22 versus 21.1 years), even though the difference was less than one year. Most of the subjects aged 22 years were in their fourth year of university, and were facing job hunting and undergoing hospital training. Compared to more junior students, they may have had more mental stress, irregular diet, and lack of sleep, which were related to Hiesho [20].

The average skin temperature at the forehead in the Hiesho group (35.08°C) was significantly higher than that in the non-Hiesho group (34.43°C). A similar result was also found in a previous study [8], in which Nakamura observed that Hiesho patients had a higher core temperature at the forehead, resulting in higher skin temperature. During our experiment, the indoor temperature was set at approximately 25°C . Under similar conditions, the forehead skin temperature of females ranged from 34 to 35°C [21]. However, owing to lower metabolism, heat production in the Hiesho group was lower than that in the non-Hiesho group [22]. The heat loss must be decreased to maintain a balance between heat production and heat loss to keep a constant core temperature. Accordingly, cutaneous vasoconstrictor reduced blood flow at the extremities, resulting in a low skin temperature but higher core temperature [23]. We considered that this was the reason why Hiesho patients felt cold in an environment where healthy subjects did not.

Nakamura [20] summarized two main factors that resulted in Hiesho. The first is internal factors such as sympathetic nerve, blood flow, female hormones, vasomotor nerve, and *ying-yang* balance. The second is external factors including mental stress, smoking, overworking, and sleep deprivation. The exact mechanism of Hiesho is still unclear, but some studies have indicated that Hiesho might be a heritable phenotype [1] and associated with hypersensitive to the surrounding environment [24, 25]. Although Hiesho is not perceived as a remarkable symptom, a new concept that deals with cold feeling at extremities, called Flammer syndrome (FS), has been observed recently in Western medicine [6]. According to Flammer et al. [26], FS describes the phenotype of people with a predisposition for an altered reaction of the blood vessels to stimuli such as coldness, emotional stress, and hypoxia. Symptoms of patients with FS seem to be consistent with those of females with Hiesho in Japan. Similar to a statistical report [27], FS occurs more often in females than males in Europe [28, 29]. We acknowledged the significance of investigating the reasons for Hiesho both from the viewpoints of West-

ern and Eastern medicine, but it was beyond the scope of this paper. More studies on the relation between Hiesho and Flammer syndrome are expected.

In this research, we proposed a quantitative method for defining Hiesho by the skin temperature difference between the forehead and the foot sole. After cross-checking with the result of a subjective questionnaire, our proposed method had a sensitivity of 77.4% and a specificity of 71.9%. Meanwhile, measuring different temperatures using an infrared thermometer provided a non-invasive method to discriminate Hiesho rapidly and with acceptable accuracy. Recently, several researchers have sought to solve this health problem. A previous study proposed to measure the blood flow from the radial artery at the wrist of Hiesho patients by studying Doppler ultrasound peripheral vascular flow [30]. In this six-month follow-up study, the authors observed that blood flow could be an effective approach for monitoring personal health of Hiesho patients. However, the difference in blood flow between Hiesho patients and healthy subjects was not known because they did not perform control experiment and there were only four subjects in their study.

In this study, we measured blood pressure, pulse wave, and augmentation index to evaluate physiological indicators. Although there were no differences in systolic and diastolic blood pressures between non-Hiesho and Hiesho groups, central blood pressure showed a higher trend in subjects who had Hiesho. Previous studies also reported no difference in blood pressure between subjects with Hiesho and healthy subjects [10, 31]. It was interesting to notice that pulse rates in both non-Hiesho and Hiesho groups in this study (72.3 BPM in Hiesho and 70.4 BPM in non-Hiesho) were higher than those in previous report (60 BPM in Hiesho and approximately 65 BPM in non-Hiesho group) [10]. Meanwhile, it seemed that young females with Hiesho had higher heart rates. Ogata *et al.* [10] summarized that higher heart rate in Hiesho group was due to higher sympathetic nerve activity, which can be analyzed through heart rate variability (HRV). However, we did not perform HRV analysis in this study.

It has been shown that augmentation index is closely related to arterial stiffness, and a positive relationship between age and AI has also been reported [32]. We also observed a trend that AI was higher in Hiesho than in non-Hiesho group, and age was different between the two groups. Kohara *et al.* [33] reported that AI was approximately 65% in women aged from the 20 s, which was higher than those of both Hiesho and healthy groups in our study (52.5% and 56.1% respectively). We speculated that because all subjects recruited in our study were in their early 20s, peripheral blood vessel was softer compared to the average.

There were several limitations in this study. According to an epidemiological survey [34], the percentage of women who self-reported Hiesho increased from 30% (under 40 years) to 50% (50 years or older). Hiesho seems to be an age-related health problem. However, only young females in their early twenties were recruited for this research. As physical and psychological conditions change continuously with age for females, examining more subjects across different age groups would be necessary in future study. Meanwhile, as it has been reported that 67% of pregnant women have Hiesho [8] and that Hiesho might be a heritable phenotype [1], a follow-up study on this topic could provide more information on Hiesho and its pathogeny.

In this study, all subjects were Japanese. Hiesho is also known in other countries [1–3]. Due to the differences in habits and living conditions, the reason of Hiesho may be different. Thus it is difficult to generalize the findings of this research. Meanwhile, 153 men out of 10,000 from the general population in Japan were reported to have Hiesho [27]. As such, Hiesho affects both genders. We did not recruit male subjects in this study.

5. Conclusion

In this paper, we proposed an objective and quantitative approach to define Hiesho. Thermal check results indicate that young females with Hiesho have considerable temperature difference between the forehead and the foot sole. A difference in temperature of 3.64°C between the forehead and the foot sole can be utilized as the threshold for distinguishing Hiesho.

Competing Interests

The authors declare no competing financial interests.

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