FINGER SYSTOLIC BLOOD PRESSURES AFTER COLD PROVOCATION IN HEALTHY MALES AND FEMALES: EFFECT OF ROOM TEMPERATURE

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Abstract

Vibration-induced white finger (VWF) is the vascular component of the hand-arm vibration syndrome (HAVS). International Standard 14835-2:2005 defines how the measurement of finger systolic blood pressure, FSBP, after finger cooling can be used to assist the diagnosis of VWF, but it requires that room temperature is maintained at 21±1°C. This study investigates the effects of room temperature on finger systolic blood pressures after cold provocation. Twelve healthy males and twelve healthy females participated in two sessions with the room temperature at either 20 or 28°C. The FSBP after warming or cooling the fingers to 30, 15, and 10°C was measured in both sessions. There were significant reductions in FSBP at both 15 and 10°C compared with 30°C, and lower FSBPs with the room temperature at 20°C than at 28°C. The percentage reductions in FSBPs at 15 and 10°C from those at 30°C, corrected for any changes in blood pressure in the thumb, (i.e., %FSBP) did not differ between the two room temperatures. Females had lower FSBPs than males at 30, 15, and 10°C, but %FSBPs were similar in males and females. The study suggests that the calculation of percentage changes in finger systolic blood pressure reduces the effects of room temperature and gender, and that the test may be used in conditions where the ±1°C tolerance on room temperature cannot be achieved.

1. Introduction

Workers who are regularly exposed to hand-transmitted vibration from powered hand tools are at risk of developing disorders in the fingers, hands or arms, collectively known as the hand-arm vibration syndrome (Griffin, 1997; Griffin and Bovenzi, 2002). One consequence of exposure to hand transmitted vibration can be impaired circulation in the fingers, with 'attacks' of finger blanching commonly provoked by exposure to cold. The blanching may occur on the distal, middle, or proximal phalanges of the fingers and is called 'vibration-induced white finger', VWF, sometimes considered a form of secondary Raynaud's disease (Griffin, 1990).

The diagnosis of vibration-induced white finger is currently heavily reliant on the reporting of relevant symptoms, such as cold-induced finger blanching, and an appropriate history of exposure to hand-transmitted vibration. Cold provocation of the fingers and hands is commonly used in clinical and epidemiological studies to confirm the existence of an abnormal response to cold in the digital vessels of workers reporting relevant symptoms. Two vascular tests involving exposure to cold have been standardised: the measurement of finger rewarming times after cold provocation (in ISO 14835-1:2005) and the measurement of finger systolic blood pressures during cold provocation (in ISO 14835-2:2005).

The measurement of finger systolic blood pressures (FSBPs) after cold provocation has long been considered a promising laboratory test for quantifying the degree of cold-induced digital vasospasm in vibration-exposed workers (Olsen *et al.*, 1995; Gemne, 1997; Bovenzi, 2002). The results of the test are usually expressed in terms of percentage FSBP (%FSBP), which is the systolic blood pressure in a test finger cooled to 15, 10 or 6 °C expressed as a percentage of the systolic blood pressure at 30°C, corrected for the change of pressure in an ipsilateral non-cooled reference finger during the cold test (Olsen *et al.*, 1982; Ekenvall and Lindblad, 1986; Bovenzi, 1988, 1993). During cold provocation of the fingers, the blood vessels constrict and finger systolic blood pressure falls (Nielsen and Lassen, 1977; Nielsen *et al.*, 1980). The cold-induced reductions in finger systolic blood pressures seem to be related to reports of finger blanching with high repeatability, sensitivity, and specificity (e.g., Olsen *et al.*, 1982; Hack *et al.*, 1986; Kurozawa *et al.*, 1991; Carnicelli *et al.*, 1992; Nasu and Kurozawa, 1995; Gemna, 1997; Olsen, 2000).

Published studies of FSBP after cold provocation have been conducted with different room temperatures (in the range 16 to 26°C) in healthy control groups, in workers without symptoms but exposed to vibration, and in VWF patients (Ekenvall and Lindblad, 1986; Kurozawa *et al.*, 1991; Bovenzi, 1993). In ISO 14835-2 (2005), the room temperature during the FSBP test is set at 21±1°C for the duration of the test and air circulation is controlled to avoid the skin cooling. Although environmental temperature influences peripheral circulation (Mirbod *et al.*, 1998; Harada *et al.*, 1998; Ye and Griffin, 2011a), there is no known study designed to understand the relationship between room temperature and finger systolic blood pressure after local cooling.

This study investigated: (i) how room temperature influences changes in finger systolic blood pressure after cold provocation in the digits of healthy males and females, and (ii) gender differences in finger systolic blood pressures after cold provocation. The study was undertaken at two room temperatures: 20 and 28°C. The tests were performed in the same conditions by an experimenter experienced in applying the tests according to the HSE recommended procedure (Lindsell and Griffin, 1998). It was hypothesised that there would be higher finger systolic blood pressures after digital cooling at 15 and 10°C when the FSBP test was conducted in the higher room temperature. It was also hypothesised that there would be a higher FSBP before and after the cold provocation in males than in females.

2. Methods

2.1 <u>Apparatus</u>

Finger systolic blood pressures (HVLab multi-channel plethysmograph, University of Southampton).

An *HVLab* plethysmograph was used to measure finger systolic blood pressures following cold provocation of the digits. Water-perfusable cuffs were placed around the middle phalanx of each finger, with a separate air cuff around the thumb as a reference. Strain gauges were placed at the base of the finger nails of the cuffed fingers. Subjects lay supine and motionless on a couch with both hands resting in a comfortable position at the level of the heart so as to minimise effects of hydrostatic variations. The tips of the fingers were squeezed to reduce blood volume and then the cuffs were inflated to 220 mm Hg (a suprasystolic pressure to prevent arterial inflow) by perfusing the cuffs with

thermostatically controlled water. After 5 min of ischaemia, the cuff pressure was reduced at a rate of 2 mm Hg/s. Finger systolic blood pressures were measured on the right hand after cooling by water circulating at 30, 15, and 10°C. The finger systolic blood pressure was calculated as the cuff inflation pressure at which arterial inflow returned to the finger at 30°C, 15°C and 10°C. The percentage changes in finger systolic blood pressure (%FSBP) from 30 to 15°C, and from 30 to 10°C, were calculated according to the following equation:

$$\%FSBP_{t°C} = \frac{FSBP_{test,t°C}}{FSBP_{test,30°C} - (FSBP_{ref,30°C} - FSBP_{ref,t°C})} \times 100\%$$

$FSBP_{t°C}$ is the finger systolic pressure of the test finger after thermal provocation at 10°C or 15°C;

$FSBP_{test,30°C}$ is the finger systolic blood pressure measured on the test digit after thermal provocation at 30°C;

$FSBP_{ref,30°C}$ is the finger systolic blood pressure measured on the reference finger after thermal provocation of the test finger at 30°C;

$FSBP_{ref,t°C}$ is the finger systolic blood pressure measured on the reference finger after thermal provocation of the test finger at 10°C or 15°C.

Finger skin temperature (FST) was measured using k-type thermocouples attached by micro pore tape to the distal phalanges of the right and left middle fingers. The room temperature was measured by a mercury-in-glass thermometer to an accuracy of ± 0.5°C. The thermometer was located close to the heads of the subjects.

2.2 Subjects

Twenty four healthy volunteers, twelve males and twelve females, participated in the study. All subjects were University students (aged 19 to 31 years) with no history of significant (regular or prolonged) exposure to hand-transmitted vibration in occupational or leisure activities. They completed a health questionnaire, read a list of medical contraindications, and gave their written informed consent to the study. None of the subjects reported cardiovascular or neurological disorders, connective-tissue diseases, injuries to the upper extremities, or a family history of Raynaud's phenomenon. All were right-handed and non-smokers.

The subjects were requested to avoid consuming caffeine for 4 hours and alcohol for 12 hours prior to the testing. The study was approved by the Ethics Committee of the Faculty of Engineering and the Environment (application number: 12795).

2.3 Procedure

Initially, subjects stayed in one of two room temperatures (20 or 28°C) for at least 30 minutes or until they had a constant finger skin temperature (<1°C variation over 10 minutes) before the tests started. Each subject participated in two sessions conducted on two separate days. In each session, the finger systolic blood pressures at three water temperatures (30, 15 and then 10°C) on the right hand were measured with the room temperature at either 20 or 28°C. The order of presentation of room

temperatures was randomized. The finger skin temperatures at the right and left middle fingers and the room temperature were measured before and after the finger systolic blood pressure measurements at the three water temperatures (30, 15 and 10°C).

2.4 Statistical methods

Data analysis was performed using the software package SPSS (version 22.0). The data were summarised with the median as a measure of central tendency and the inter-quartile range (IQR) as a measure of dispersion. Non-parametric tests were employed to analyse the data, which were not normally distribution. The Wilcoxon test was used to investigate differences between the measures of FSBP and %FSBP: (i) at two room temperatures (i.e. 20 and 28°C), and (ii) at two water temperatures (i.e., 15 and 10°C). The Friedman test was used to investigate differences between measurement locations for both FSBP and %FSBP. The Mann-Whitney U test was used to investigate differences between males and females. The Spearman rank correlation coefficient was used to investigate associations between finger skin temperatures, finger systolic blood pressures, and individual body and finger sizes.

The criterion for statistical significance was $p<0.05$. The reported p-values have been adjusted for multiple comparisons.

3. Results

The medians and IQRs of the age, body size, and vibration perception thresholds of the male and female subjects are shown in Table 1. There were significant differences between male and female subjects in their stature ($p=0.008$, Mann-Whitney), weight ($p<0.001$, Mann-Whitney), finger volume ($p<0.01$, Mann-Whitney), and body mass index (BMI) ($p<0.001$, Mann-Whitney). The male and female subgroups did not differ in age ($p=0.36$, Mann-Whitney).

Table 1 Median and inter-quartile range (IQR) of the age, body size, finger size and baseline finger skin temperature with room temperatures of 20 and 28°C for male and female subjects.

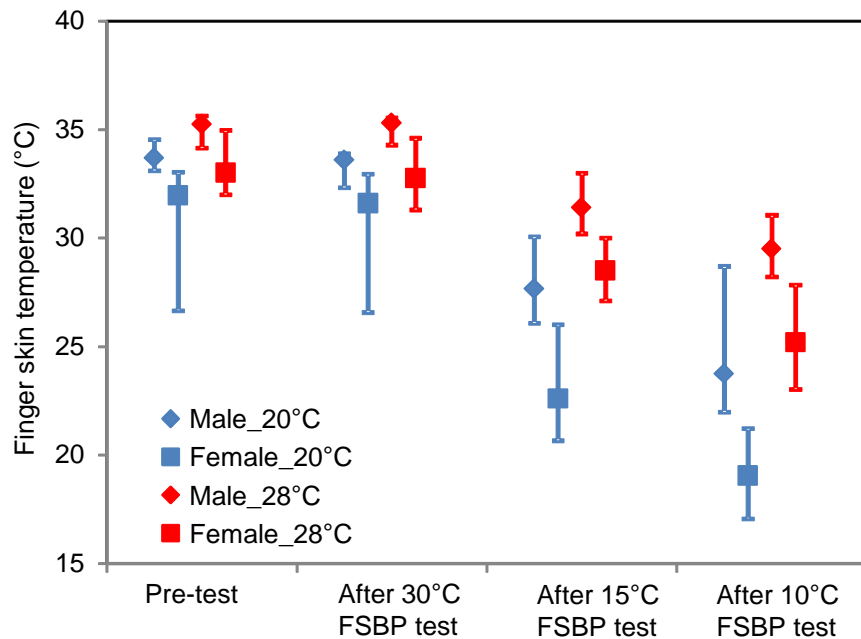|		Females	Males
Age (year)		24 (21-27)	23.5 (20-26)
Height (m)		1.61 (1.56-1.66)	1.76 (1.72-1.80)
Weight (kg)		53 (47-61)	75 (60-87)
Finger volume (cm³)	Right middle	12.5 (11.2-13.6)	15.4 (12.9-17.4)
	Left middle	12.3 (11.0-13.8)	15.0 (13.3-17.1)
Body mass index (BMI)		20.5 (2.1)	23.1 (3.3)
Baseline finger skin temperature (°C)	Room temperature 20°C	31.9 (26.6-33.0)	33.7 (33.1-34.5)
	Room temperature 28°C	33.0 (32.0-34.9)	35.3 (34.1-35.6)

Figure 1 Median and inter-quartile range (IQR) of finger skin temperature (FST) on the right middle finger before and after FSBP tests at 30, 15, and 10°C water temperature with room temperatures of 20 and 28°C. Data from 12 males and 12 females.

3.1 Room temperature

In the two sessions, the temperature in the laboratory was either in the range 19.5°C to 21.0°C or in the range 27.5°C to 28.5°C. The room temperature did not change significantly during either session (at 20°C, p=0.346; at 28°C, p=0.512; Friedman).

3.2 Finger skin temperature

Throughout the sessions, the median finger skin temperature was lower with the room at 20°C than at 28°C, for both male and female subjects (Figure 1).

Before the tests, the baseline finger skin temperature varied between subjects as shown in Table 1. The finger skin temperatures on the right and left middle fingers did not differ before and after the FSBP test at 30°C with either of the two room temperatures (20 and 28°C) in either male or female subjects (p=0.166-0.604; Wilcoxon).

There was a significant reduction in finger skin temperature on the right middle finger after the FSBP tests conducted at 15 and 10°C compared with before and after the FSBP test at 30°C at both room temperatures for males and females (20°C, p=0.003-0.008; 28°C, p<0.001; Wilcoxon). On the left middle finger, significant reductions in finger skin temperature after the FSBP tests at 15 and 10°C were also obtained at both room temperatures for males and females (p=0.019-0.027; Wilcoxon), except for FST with the room temperature of 28°C for male subjects (p=0.056; Wilcoxon). There was a greater reduction in FST on the right middle finger compared with the unexposed left middle finger (p<0.001; Wilcoxon).

At both room temperatures and during and in all four measurements, the median finger skin temperatures on the right middle finger were lower in females than males (pre-test, after FSBP test at 30, 15, 10°C) ($p<0.001$; Mann-Whitney). The FSTs within the male and female subgroups were not correlated with stature, weight, BMI, or age ($p=0.17$-0.78; Spearman). At both room temperatures there was a positive correlation between the FST and finger volume in both males ($p=0.001$-0.023; Spearman) and females ($p=0.007$-0.036; Spearman).

3.3 Finger systolic blood pressures

The median and inter-quartile ranges of finger systolic blood pressures measured at 30, 15 and 10°C, and the %FSBP calculated for 15 and 10°C with room temperatures of 20 and 28°C for males and females are shown in Table 2.

Table 2 Median and inter-quartile range (IQR) of finger systolic blood pressures (FSBP) at 30, 15 and 10°C, and the %FSBP calculated at 15 and 10°C with room temperatures of 20 and 28°C. Data from 12 males and 12 females.

	Females		Males	
Room temperature	20°C	28°C	20°C	28°C
$FSBP_{30°C}$ (mm Hg)	119 (116-122)	120 (114-125)	126 (115-130)	125 (120-129)
$FSBP_{15°C}$ (mm Hg)	110* (105-114)	113 (109-117)	118* (109-124)	121 (116-124)
$FSBP_{10°C}$ (mm Hg)	105** (102-111)	110 (105-115)	114** (108-116)	118 (115-121)
$\%FSBP_{15°C}$ (%)	95 (92-97)	95 (93-99)	97 (95-100)	98 (96-101)
$\%FSBP_{10°C}$ (%)	92 (89-95)	94 (88-96)	94 (90-97)	95 (94-96)

* $p<0.05$, ** $p<0.001$: statistical significance of reductions in FSBP at 15 and 10°C with room temperatures of 20°C (Wilcoxon test).

At neither room temperature did the finger systolic blood pressure measured in air on the reference right thumb differ when the temperature of the other fingers was varied to 30, 15 or 10°C, in either males or females ($p=0.56$-0.61, Friedman).

At neither room temperature did the finger systolic blood pressure obtained at 30, 15 or 10°C differ across the index, middle, ring and little fingers in either males or females ($p=0.29$-0.56; Friedman), except on the little finger where there was a lower FSBP at 10°C with the room temperature of 20°C in females ($p=0.013$-0.047; Wilcoxon).

The finger systolic blood pressures at 30°C did not differ between the 20 and 28°C room temperatures in either males or females ($p=0.19$-0.33; Friedman). However, the FSBPs at 15°C were lower with the room temperature at 20°C than at 28°C ($p=0.017$-0.024; Wilcoxon) and the FSBPs at 10°C were also lower with the room temperature at 20°C than at 28°C ($p=0.001$-0.008; Wilcoxon), in both males and females.

Notwithstanding the reductions in FSBPs, the %FSBPs calculated at 15 and 10°C did not differ between room temperatures of 20 and 28°C in either males or females ($p=0.081$-0.28; Wilcoxon).
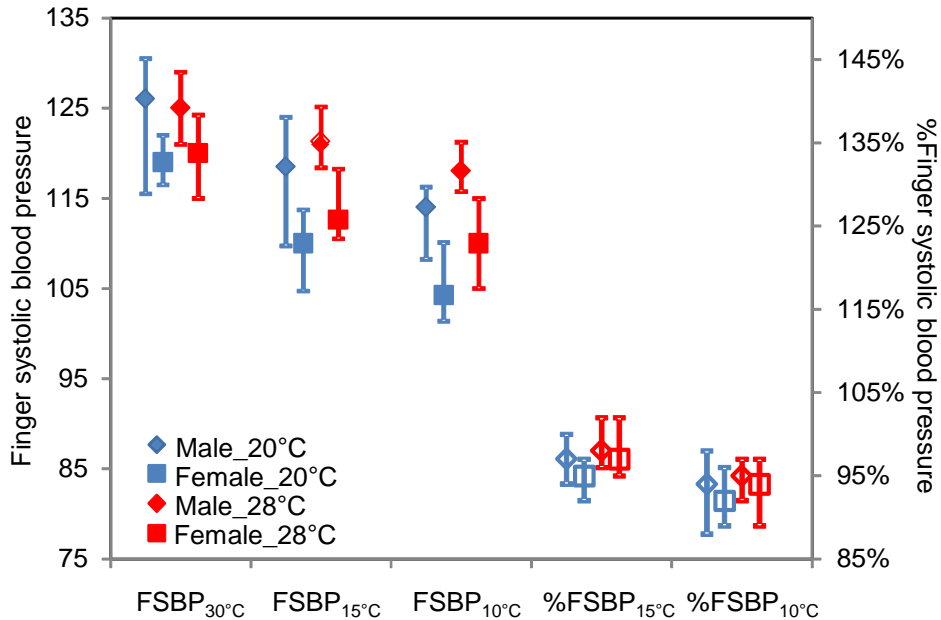
Figure 2 Median and inter-quartile range (IQR) of finger systolic blood pressure (FSBP) with 30, 15, and 10°C water temperatures and %FSBP calculated with 15 and 10°C water temperatures and room temperatures of 20 and 28°C. Data from 12 males and 12 females.

The %FSBPs obtained with 10°C water were generally lower than those obtained with 15°C water at both room temperatures for males and females (p=0.001-0.038; Wilcoxon), except with a room temperature of 20°C in females (p=0.064; Wilcoxon).

The finger systolic blood pressures at 30, 15 and 10°C were lower in females than in males with both room temperatures (p<0.001; Mann-Whitney U). However, the %FSBPs calculated at 15 and 10°C did not differ between males and females (p=0.38-0.71; Mann-Whitney U).

The FSBPs within the male and female subgroups were not correlated with stature, weight, BMI, age or finger volume (p=0.33-0.52; Spearman). The FSBPs at 30, 15 and 10°C were not correlated with finger skin temperature after the corresponding FSBP tests within either males or females (p=0.284-0.803; Spearman). Similarly, there was no correlation between the %FSBPs calculated at either 15 or 10°C and the FSTs within the males and females (p=0.407-0.936; Spearman).

4. Discussion

Finger skin temperature

Finger skin temperatures were reduced after FSBP tests with water circulating at 15 and 10°C. The reduction in FST was found both on fingers of the right hand exposed to cold and also on fingers of the unexposed hand. The reduced finger skin temperature contralateral to vibration stimulation has been reported in studies using thermography (Nasu, 1977) and k-type thermocouples (Ye and Griffin, 2011a). Vasoconstriction in both hands after exposing one hand to either cold or vibration might be explained by reflex control of digital circulation mediated through central sympathetic activity (Fox and Edholm, 1963; Roddie, 1983).

The findings show that finger skin temperature is dependent on room temperature, consistent with expectations and previous studies (e.g., Muhbub *et al.*, 2006, 2008; Ye and Griffin, 2011a). The pre-test finger skin temperature was greater with the higher room temperature. The human body controls the body core temperature partly by regulating skin temperature, which is partly dependent on the environmental temperature. When the external environment is cold, dermal blood vessels constrict causing the warm blood to bypass the skin and allow the skin temperature to drop towards the temperature of the environment.

Finger systolic blood pressures

Over the 24 subjects, the median %FSBP was 96.3% at 15°C and 93.8% at 10°C, with a lowest individual %FSBP of 79% at 15°C and 74% at 10°C. This is slightly higher than in 22 male subjects aged 20 to 29 years where the median value was 94.8% at 15°C and 90.3% at 10°C, with a lowest individual %FSBP of 75% at 15°C and 67% at 10°C (Bovenzi, 1988). The greater reduction in FSBP with finger cooling from 30 to 15 or 10°C in the previous study may due to different tobacco consumption within subjects, as smokers experienced a more intense digital vasoconstriction than non-smokers (Bovenzi, 1988).

When FSBPs were measured after digital cooling to 15 and 10°C, higher FSBPs were found with a room temperature of 28°C than 20°C. However, there was a similar percentage change in FSBPs at 15 and 10°C relative to FSBPs at 30°C when corrected for any changes in FSBP in the thumb. The results confirm that room temperature influenced FSBP after cold provocation, but that by calculating the %FSBP the effect of room temperature is minimised. There is a similar trend with changes in finger blood flow before and during exposure to vibration at the same two room temperatures (i.e., 20 and 28°C): reduced finger blood flow and smaller reductions in finger blood flow during exposure to vibration with a room temperature of 20°C, but the percentage change in finger blood flow provoked by vibration is similar with both room temperatures (Ye and Griffin, 2011a). Although the stimulus for vasoconstriction was vibration not cold, the effect of room temperature on finger skin temperature, finger blood flow, and finger blood pressure seems broadly consistent irrespective of whether the local stimulus is applied to the fingers or to the hand.

Gender effect

The study found lower baseline finger skin temperatures in females than males, consistent with previous studies suggesting increased sympathetic tone in females (Cooke *et al.*, 1990; Kellogg *et al.*, 2001; Ye and Griffin, 2011b).

The males had higher finger blood pressures before and after the application of local cooling. Although the measurement location, measurement method, and environmental conditions differed, the current findings are consistent with previous studies (Khoury *et al.*, 1992; Wiinber *et al.*, 1995). In 352 normotensive (for age) Danish males and females aged 20 to 79 years, Wiinber *et al.* (1995) found blood pressure increased with age in both males and females, but that males had higher 24-hour mean blood pressure, by approximately 6 to 10 mm Hg, than females, until the age of 70 to 79 years, when blood pressure was similar in males and females. A higher blood pressure among males has

also been reported by Khoury *et al.* (1992) during ambulatory blood pressure monitoring on 131 males and females (aged 50 to 60 years).

Although the mechanisms responsible for gender differences in blood pressure control are not clear, there is evidence that androgens, such as testosterone, play a role in gender-associated differences in blood pressure regulation. Studies using ambulatory blood pressure monitoring in children have found that blood pressure increases with increasing age in both boys and girls. However, after the onset of puberty, boys have higher blood pressure than age-matched girls (Bachmann *et al.*, 1987; Harshfield *et al.*, 1994).

Body size may also contribute to differences in blood pressure between males and females. High body weight is linked with higher systolic and diastolic blood pressure (Seidman *et al.* 1991; Rosner *et al.* 2000). There was lower body weight and reduced body mass index in the females of the current study but no significant correlations between body weight or body mass index and finger systolic blood pressure. This might be explained by the small variations of body weight and body mass index mass in the subject group.

Diagnostic criteria

The diagnostic indicators of abnormal finger systolic blood pressure used in ISO 14835-2:2005 are the percentage changes in FSBP after cold provocation at 15 and 10°C. A %FSBP lower than 80% is currently used to indicate 'possible dysfunction' and a %FSBP lower than 60% is considered to indicate 'definite dysfunction' (Lindsell and Griffin, 1998).

In this study, the calculated individual %FSBPs at 15 and 10°C were all greater than 80%, except for one female subject with %FSBPs of 79% and 74% at 15 and 10°C, respectively. In other groups of 'normal' subjects, the lowest reported individual %FSBPs at 15 and 10°C are 68% and 66% (Nielsen *et al.*, 1980), 84% and 77% (Thulesius *et al.*, 1981), 65% and 60% (Ekenvall and Lindblad, 1986) and 74% and 63% (Bovenzi, 1988). Some of these are lower than in this study, possibly due to a wider age group, greater tobacco and alcohol consumption, and greater body weight.

Using a %FSBP of 60% as a threshold for distinguishing patients with VWF from healthy individuals, none of the current healthy subjects showed an abnormal cold reaction. The specificity of the test to disclose vibration-induced digital arterial hyper-responsiveness to cold was therefore high, consistent with previous studies (e.g., Ekenvall and Lindblad, 1986; Kurozawa *et al.*, 1991, 1992; Bovenzi, 1988, 1993, 2002; Bovenzi *et al.*, 2008).

Although the absolute FSBPs at 15 and 10°C were lower with the room temperature of 20°C (in females), the %FSBP calculated at 15 and 10°C did not differ significantly between two room temperatures, or between males and females. This suggests that using the calculated %FSBP as a diagnostic indicator, the variations in FSBP introduced by room temperature and gender can be minimised. This is consistent with a previous study that found the calculated %FSBP (corrected for changes in a reference finger) has a higher diagnostic accuracy than other finger systolic blood pressure indices (Bovenzi, 2002).The findings also imply that if %FSBP is used as the diagnostic criterion, room temperature is not a major factor influencing the accuracy of the test when in other

respects it is performed according to ISO 14835-2:2005. The tight control of room temperature (±1°C) stated in ISO 14835:2 seems unnecessary, allowing the test to be performed in environments where control of room temperature is difficult or impossible.

5. Conclusions

The reduction in finger systolic blood pressure due to local cooling of the fingers at 15 and 10°C is dependent on the room temperature (either 20 or 28°C). The absolute reduction in FSBP is greater with a lower room temperature, but the percentage change in blood pressure (i.e., %FSBP) is similar. Females have lower finger systolic blood pressures both before and after the application of local cooling of the fingers. The use of %FSBP as a diagnostic indicator, as in ISO 14835-2:2005, minimises the influence of room temperature and the difference between males and females. However, the study shows that close control of room temperature required by ISO 14835-2:2005 is not necessary when measuring finger systolic blood pressures after finger cooling. None of subjects in this study showed an abnormal reaction to cold according to the current diagnostic criteria, consistent with the high specificity claimed for %FSBP.

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