

Cold-Provocation Testing for the Vascular Component of Hand-Arm Vibration Syndrome in Health Surveillance

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Abstract: The aim was to investigate whether the use of infra-red thermography (I-R) and measurement of temperature gradients along the finger could improve the diagnostic accuracy of cold-provocation testing (15°C for 5 min) in vascular hand-arm vibration syndrome (HAVS). Twenty-one controls and 33 individuals with stages 2/3V HAVS were studied. The standard measurement of time to rewarm by 4°C (T4°C) and temperature gradients between the finger tip, base and middle (measured using I-R) were calculated. Receiver Operating Characteristics (ROC) analysis to distinguish between the two groups revealed that for T4°C the area under the ROC curve was not statistically significantly different from 0.5 (0.64 95% confidence interval 0.49–0.76). The difference between the tip and middle portion of the finger during the sixth minute of recovery was the most promising gradient with an area of 0.76 (95% confidence interval 0.62–0.87), and sensitivity and specificity of 57.6% and 85.7% respectively. However, this was not significantly different from that for the time to rewarm by 4°C. In conclusion, the cold-provocation test used in this study does not appear to discriminate between individuals with stage 2/3V HAVS and controls and this is not improved by the measurement of temperature gradients along the fingers using I-R.

Keywords: Hand-arm vibration, HAVS, Cold-provocation, Diagnosis, Vibration white finger

Introduction

Hand-arm vibration syndrome (HAVS) is a complex condition with vascular, sensorineural, and musculoskeletal components affecting workers who handle vibratory tools extensively. The sensorineural component is characterised by tingling and numbness in the affected fingers, and reduced sensitivity to temperature and vibration. The vascular component manifests itself as periodic blanching of the affected fingers provoked by cold, loss of sensitivity and painful throbbing (vibration white finger (VWF)).

Tests designed to assess the vascular component of HAVS and aid in grading disease severity have focused on measuring the responsiveness of the digital blood vessels to a cold

stimulus. The most commonly applied test involves immersion of the hands in cold water for a period of time to elicit cold-induced vasoconstriction. The recovery of finger skin temperature following the cold-stimulus is used as a measure of responsiveness of the digital blood vessels to the cold stimulus. While there has been many variants of this test^{1,2}, the procedure that has been recently used most widely in the UK involves immersion of the hands in 15°C water for 5 min and recording of finger skin tip temperature during recovery using thermocouples^{3–5}. However, the diagnostic usefulness of this technique has been questioned^{4,6,7}.

Infra-red thermography is an alternative technique that has been used to measure skin temperature in response to cold-provocation⁸. The advantage of using such a technique is that an image of the entire hand can be assessed, which may potentially yield more information concerning the

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pattern of rewarming of the whole hand, rather than simply monitoring the temperature of the finger tip. It may be that additional information concerning the temperature gradients along the finger, which can be obtained using infra-red thermography, is more useful diagnostically. It has been reported that using infra-red thermography with a water temperature of 5°C for 1 minute gives a good sensitivity, specificity, positive predictive value and negative predictive value for the diagnosis of digital vasospasm⁸.

The aim of this study was to establish whether the measurement of temperature gradients along the finger using infra-red thermography aids the diagnostic ability in HAVS of a cold-provocation test based on a 15°C challenge for 5 min.

Materials and Methods

Subjects

Individuals who attended the HAVS referral centre at the Health and Safety Laboratory (HSL) between April 2002 and March 2003, had a standard cold-provocation test performed as part of their assessment, and had been assigned a Stockholm Workshop staging of 2/3V, were invited to take part in this study.

Male members of HSL staff who had not been occupationally exposed to vibration, and after being interviewed by a medical practitioner to exclude primary Raynaud's phenomenon formed the control group. All testing took place in a temperature controlled laboratory between the hours of 10am and 4pm.

Ethics committee approval for this study was obtained from the HSE Research Ethics Committee and informed consent obtained from each subject.

Procedure

Standard cold-provocation test using thermocouples

When individuals first arrived in the laboratory they were asked to sit quietly for at least 15 min to adjust to the laboratory temperature. Thermocouples (Institute of Sound and Vibration Research, Southampton) were then attached to the fleshy part of the tips of the four fingers of both hands using transpore tape. A thin plastic glove was then placed on each hand and taped loosely at the wrist to exclude air entrapment. Whilst seated subjects positioned their hands and forearms at approximately heart level with the palms facing upwards for 2 min. At the end of this settling period the subject was instructed to stand up and immerse both hands up to the wrist crease in water thermostatically controlled at 15°C for 5 min. Immediately following the

hand-immersion period the subject removed their hands from the water, the gloves were removed, the subject sat down, and the hands and forearms were supported at heart level to rewarm for 10 min. Skin temperatures of the eight fingers during the settling, hand-immersion and rewarming periods were recorded on an IBM compatible computer.

Infra-red thermography

Infra-red thermograms of the right hand were taken using an Infra-red camera (Land Cyclops T135) during the baseline period before the plastic gloves were placed on the hand and then every minute during the rewarming period of the standard cold-provocation test.

Data analysis

For the standard cold-provocation test with thermocouples the time taken for skin temperature to increase by 4°C following hand-immersion (T4°C) was calculated for each finger. On those occasions where a finger failed to rewarm by 4°C during the rewarming period the time used for analytical purposes was 600 s, the total duration of the rewarming period.

For the Infra-red thermograms the following parameters were calculated for each finger from the baseline image and for each minute of recovery:

- Absolute finger tip temperature
- Absolute temperature of the middle of the finger
- Absolute temperature of the base of the finger
- Gradient (difference) between finger tip and base temperature (tip-base)
- Gradient (difference) between finger tip and middle temperature (tip-middle)
- Gradient (difference) between the middle of the finger and the base (middle-base)

Statistical analysis

Data for the standard cold-provocation test and infra-red thermography were plotted to investigate whether they were normally distributed. Where data appeared to differ significantly from a normal distribution, non-parametric statistical tests were used.

Differences between the two groups; cases (stage 2/3V) and controls for the cold-provocation test were assessed using the Mann-Whitney U-test (SPSS version 11). Differences between groups over time for infra-red thermography were investigated using two-way analysis of variance.

The diagnostic accuracy of either of these tests was investigated using Receiver Operating Characteristics (ROC) analysis to establish the optimum outcome metric for

distinguishing between groups that minimised the false positive and negative results (MedCalc, version 7.3, Belgium). The area under the ROC curve was also derived and tested to determine if this were significantly greater than 0.5 as this would suggest that the diagnostic test has power to distinguish between the two groups. Sensitivity and specificity were also defined from the ROC analysis. A disease prevalence of 40%, similar to that seen in the HAVS referral centre, was applied to the sensitivity and specificity data to derive the positive and negative predictive values for the tests (PPV and NPV respectively).

Results

Twenty-one normal healthy male controls and 33 vascular HAVS cases, stage 2/3V on the right hand were studied. The mean (SD) age at time of testing in the two groups was 37.6 (8.4) and 48.2 (7.5) years respectively ($p < 0.001$). The mean (SD) room temperature at time of testing was 23.1°C (1.4) respectively.

In 85% of the HAVS cases individuals were also classified with the same staging on their left hands. In the remaining cases the staging was different on the two hands, with the right hand being more severely staged in most cases. The median reported Griffin score⁹⁾ was the same for each finger on the right hand (median 3, range 0–6), and therefore subsequent comparisons have been performed on one finger, the middle finger, of the right.

Differences between groups in rewarming of skin temperature following cold-provocation

The median value for the time to rewarm by 4°C was highest in the stage 2/3V group when compared to the laboratory control group (488 and 249 s respectively), but these differences were not statistically significant ($p > 0.05$).

The mean (SD) temperature of the finger tip and base in the laboratory controls in the settling period was 32.2°C (4.0) and 33.1°C (2.4) respectively, and 31.0°C (4.1) and 31.9°C (3.1) in the HAVS cases. There were no significant differences ($p > 0.05$) between groups.

Changes in finger tip, middle and base temperatures following cold-provocation over time were investigated (Fig. 1). Over time the mean temperature had a tendency to be lower in the HAVS cases compared to controls. These differences appeared to get larger as time went on, particularly for the finger tip. There was a statistically significant difference between the groups over time but there were no significant differences at individual time points ($p > 0.05$).

Changes in differential temperatures between finger tip,

middle and base were also investigated (Fig. 2). The mean difference in temperature between the finger tip and base was negative to start with in both groups, suggesting that the base of the finger rewarmed more quickly than the finger tip. After around 7 min of recovery the mean gradient reversed in the controls to become positive, showing that the finger tip was now warmer than the base. However, the mean gradient remained negative for the HAVS cases for the duration of the recovery period. These differences were variable but were found to be significantly different between groups overall ($p < 0.001$), but again there were no significant differences at individual time points. This gradient reversed in 61.9% of controls and 33% of stage 2/3V at mean times of 5.3 and 6.8 min respectively.

After around 2 min of recovery the finger tip became warmer than the middle of the finger resulting in a positive gradient, the finger base was warmer than the middle of the finger throughout recovery. There were no significant differences between groups at any individual time point.

Diagnostic accuracy of rewarming of skin temperature following cold-provocation

The sensitivity, specificity, PPV and NPV for T4°C based on thermocouple fingertip measurements to distinguish between HAVS cases and controls were 69.7%, 66.7%, 58.3% and 76.8% respectively. The area under the ROC curve was 0.64 (95% CI 0.49 to 0.76) and was not significantly different from a value of 0.5 ($p > 0.05$), which indicates that the variable cannot distinguish between groups.

The diagnostic accuracy of the infra-red measurements for the same challenge was also investigated for each of the outcome parameters at each time point. The sensitivity, specificity, PPV, NPV and area under the ROC curve for the settling period and three time points during recovery are presented in Tables 1 and 2. For the majority of parameters at the three time points during recovery the area under the ROC curve was not found to be significantly different from 0.5, suggesting that these parameters are not able to distinguish between individuals with stage 2/3V and laboratory controls. On three occasions the area under the ROC curve was significantly different from 0.5 (Table 2) suggesting that these parameters may be useful diagnostically. There were no significant differences between the areas under the ROC curve for these three parameters. The parameter with the greatest area under the curve was the difference in temperature between the finger tip and the middle part of the finger at the sixth minute of recovery with an area under the curve of 0.76, sensitivity of 57.6%, specificity of 85.7%, PPV of 72.9% and NPV of 75.2%. This area was not

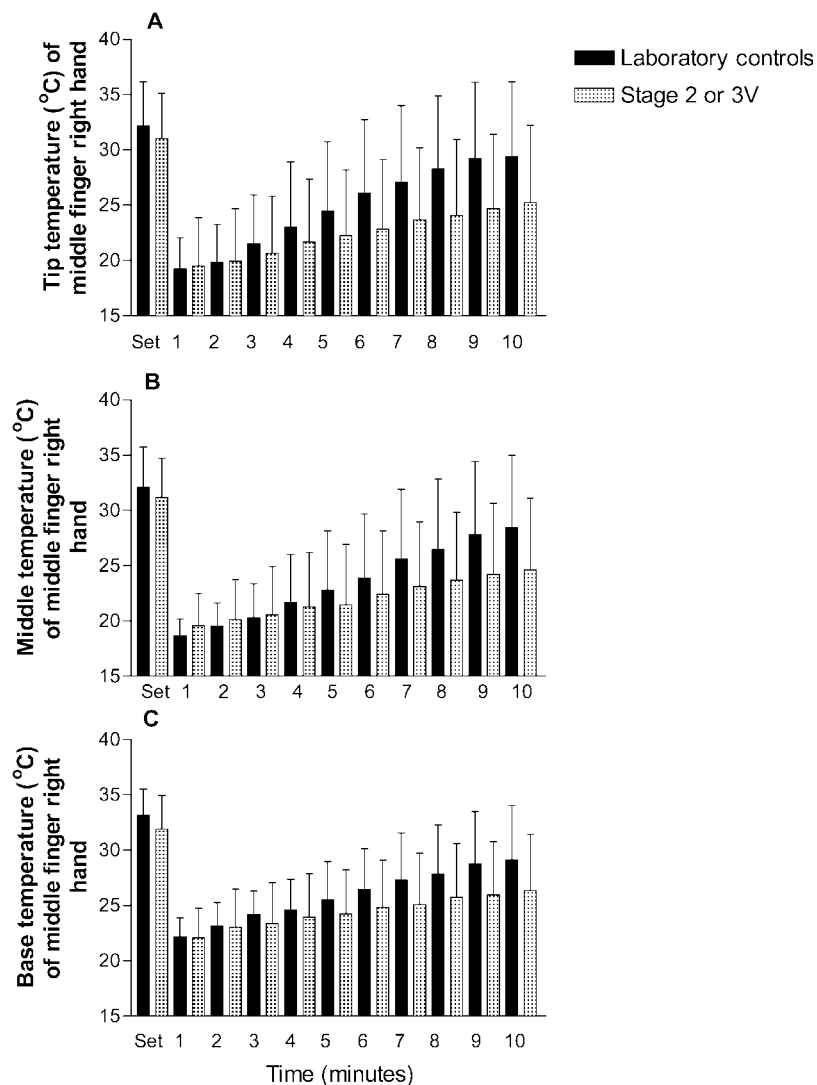


Fig. 1. Changes in finger tip, middle and base temperature of the middle finger on the right hand following cold-provocation.

Each bar represents the mean + 1 standard deviation. A presents data for the tip of the middle finger, B presents data for the middle part of the middle finger, and C presents data for the basal part of the middle finger. 'Set' represents the settling period.

significantly different to that found for T4°C ($p=0.143$) (Fig. 3).

Discussion

This study has aimed to compare two methods for measuring recovery of skin temperature following a standardised cold-provocation in hand-arm vibration syndrome to investigate which may be the most useful diagnostically.

Using a cold-provocation test (15°C for 5 min) that has been most notably used in the DTI scheme for coalminers'

compensation⁵), the median time to rewarm by 4°C increased in individuals with HAVS stage 2/3V but was not found to be statistically significantly different from controls. This specific combination of outcome metric and cold-provocation has been suggested to be of limited diagnostic value based on the data from the miners' compensation scheme^{4,7}). Here we confirm this measurement did not seem to discriminate between stage 2/3V HAVS cases drawn from a health surveillance population and controls.

However, finger rewarming after cold provocation in various forms has had substantial history of use in epidemiological HAVS investigations and diagnosis.

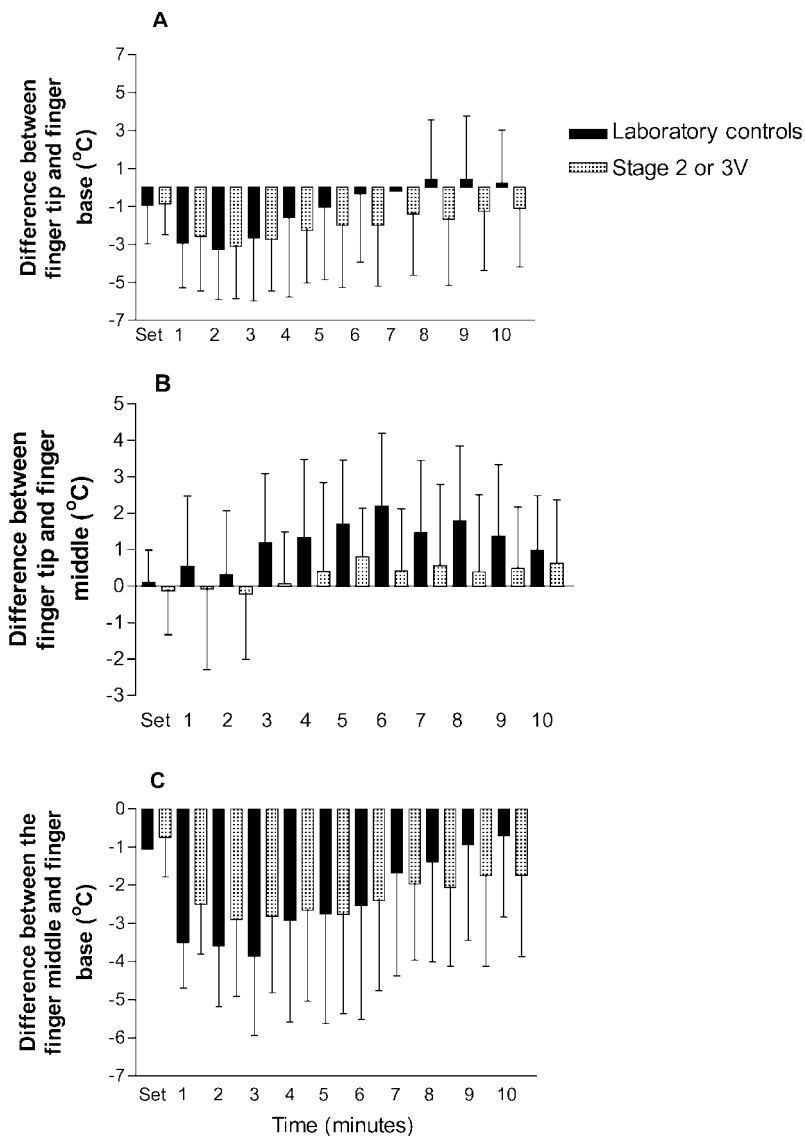


Fig. 2. Differences between the tip, middle and base of the middle finger during recovery in the three groups.

Each bar represents the mean +1 standard deviation. 'Set' represents the settling period.

Table 1. Sensitivity, specificity, positive predictive value and negative predictive value for outcome parameters comparing HAVS cases and laboratory controls at different times during recovery

	0				2				6				10			
	Sens	Spec	PPV	NPV	Sens	Spec	PPV	NPV	Sens	Spec	PPV	NPV	Sens	Spec	PPV	NPV
Tip temperature	66.7	66.7	57.2	75	18.2	100	100	64.7	72.7	57.1	53	75.8	78.8	61.9	58	81.4
Middle temperature	69.7	61.9	54.9	75.4	15.2	100	100	63.9	72.7	52.4	50.5	74.2	81.8	52.4	53.4	81.2
Base temperature	63.6	61.9	52.7	71.8	30.3	85.7	58.6	64.8	75.8	52.4	51.5	76.5	60.6	71.4	58.6	73.1
Tip-base	97	19	44.4	90.5	87.9	23.8	43.5	74.7	78.8	47.6	50.1	77.1	72.7	52.4	50.5	74.2
Tip-middle	30.3	85.7	58.6	64.8	27.3	95.2	79.1	66.3	57.6	85.7	72.9	75.2	27.3	90.5	65.7	65.1
Middle-base	100	19	45.2	100	30.3	90.5	68	66.1	84.8	33.3	45.9	76.7	72.7	66.7	59.3	78.6

Sens relates to sensitivity, Spec relates to specificity, PPV relates to positive predictive value and NPV relates to negative predictive value.

Table 2. Area below ROC curve (95% confidence interval) for each parameter at different time points comparing stage 2/3V and laboratory controls middle finger right hand

Parameter	Time (min)			
	0	2	6	10
Tip temperature	0.62 (0.47, 0.75)	0.55 (0.41, 0.68)	0.65 (0.50, 0.77)	0.63 (0.49, 0.76)
Middle temperature	0.62 (0.48, 0.75)	0.49 (0.35, 0.63)	0.57 (0.42, 0.70)	0.59 (0.44, 0.72)
Base temperature	0.63 (0.49, 0.76)	0.51 (0.37, 0.65)	0.62 (0.48, 0.75)	0.65* (0.51, 0.78)
Tip-base	0.5 (0.36, 0.64)	0.50 (0.36, 0.64)	0.62 (0.47, 0.74)	0.64 (0.49, 0.79)
Tip-middle	0.54 (0.40, 0.67)	0.57 (0.43, 0.71)	0.76* (0.62, 0.87)	0.53 (0.39, 0.67)
Middle-base	0.54 (0.40, 0.68)	0.56 (0.42, 0.70)	0.53 (0.39, 0.66)	0.66* (0.52, 0.78)

*Area under ROC curve significantly different from 0.5, $p < 0.05$.

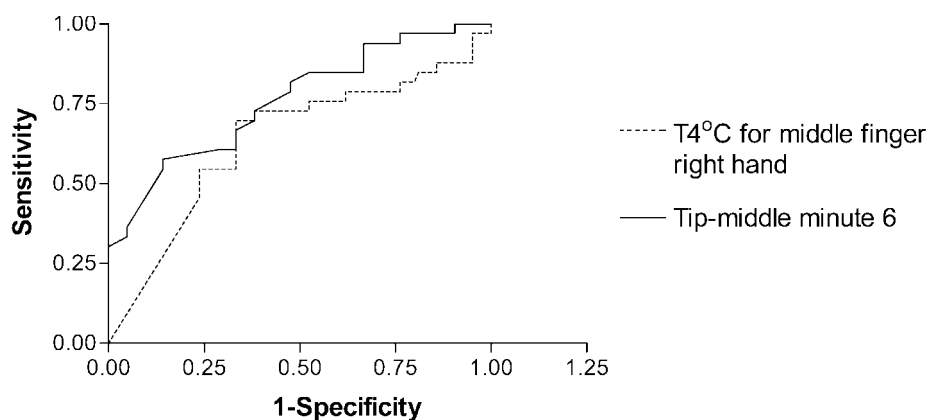


Fig. 3. Comparison of ROC curves for T4°C and difference between finger tip and middle temperature for 6th min of recovery.

Therefore questions arise whether it is the nature of the cold challenge or the method of defining the test outcome metric may be influencing the poor diagnostic value we have reported. Infra-red thermography has advantages over thermocouples in allowing thermal images of the whole hand to be collected and differential temperature gradients along the finger to be analysed. Coughlin *et al.*⁸⁾ have reported using thermography to distinguish between normal healthy volunteers and patients diagnosed as Stockholm Workshop scale 3 using a cold-provocation test of 5°C for 1 min. They found that during the pre-cooling period and at each time point during rewarming that the finger tip, base and gradient between tip and base were significantly different between HAVS patients and controls. They reported sensitivities and

specificities often substantially greater than 80% for the detection of HAVS, although from the data presented in publications, it is difficult to substantiate such high diagnostic parameters from the single outcome metrics presented in the authors' paper. We have failed in this study to replicate Coughlin's diagnostic power. When the infra-red measurement technique was applied to our population with our cold-provocation test (15°C for 5 min) there was a tendency for the mean temperatures to be lower in the HAVS stage 2/3V group compared to control groups. However, there were no significant differences between groups in any of the outcome parameters at any time point pre or post immersion. ROC analysis suggested that the most significant outcome metric for comparisons between controls groups

and abnormal was the difference between finger tip and middle at the sixth minute of rewarming. However, these results were derived from multiple comparisons and the chance that this is a spurious result cannot be ruled out. The sensitivity, specificity, PPV and NPV for this parameter were calculated as 57.6%, 85.7%, 72.9% and 75.2%, which in themselves do not indicate a diagnostically powerful test. The results suggested that infra-red thermography and measurement of more complex temperature gradients along the finger does not necessarily improve the diagnostic power over the use of single point thermocouple. The present study is larger than Coughlin's study and therefore it seems unlikely that the number of subjects could account for the differences between the two studies. It remains unclear whether the nature of the cold provocation, Coughlin's being shorter and more severe a challenge, could have contributed to these differences in diagnostic power.

We have considered possible biases in our study that may have led to poorer diagnostic outcomes for the cold-provocation test. Mis-classification of cases appears unlikely; individuals were assigned to this group after a prior full HAVS assessment⁵⁾ as part of health surveillance rather than within a medicolegal context. Prior to testing these individuals underwent a repeat of the symptom questionnaire of this assessment to confirm their staging. It is understood that laboratory controls may not reflect workers undertaking manual activity, but this may be expected to exaggerate any group differences if it has any influence at all. However, these volunteers were assessed by a physician for likely confounding influences and were unlikely (because of their positive attitude to research) to with-hold or misrepresent any relevant medical or familial conditions. Overall we do not believe that miss-classification of subjects is an issue within the study.

Using the test conditions applied in this study there is little evidence that this cold-provocation test (15°C for 5 min) using thermocouples or infra-red thermography is a useful diagnostic test for vascular HAVS. A single infra-red thermography metric out of many comparisons was more diagnostically useful while using the same cold provocation

but only when based on a ratio of temperature measurements at a highly specific time point. This needs to be confirmed. The data does not exclude the diagnostic use of thermography (or thermocouples) to measure rewarming in some form, but the nature of the cold challenge or the simplistic use of a single outcome metric is not appropriate.

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