Test Battery for Assessing Vascular Disturbances of Fingers

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Abstract

The diagnosis of vibration-induced white finger (VWF) is difficult, often relying on medical interview and history. The condition is characterized by an exaggerated vasoconstriction of digital arteries in response to cold. The complete closure of digital arteries is episodic and results in a characteristic blanching that is rarely observed by a clinician. Objective measurements of the response of the digital circulation to cold can assist in evaluating a patient for VWF. Finger systolic blood pressure (FSBP) following local cooling is a measure of cold-induced vasoconstriction in digital arteries and is an assessment of vasomotor tone. Low FSBPs following cooling are indicative of dysfunction. Finger skin temperature (FST) following hand cooling is a measure of cutaneous blood flow. The mechanism underlying the recovery of cutaneous blood flow following cooling is as yet not fully understood, but a delayed recovery is believed to arise from persistent vascular disturbances of the fingers or from a delayed release of vasospasm, or both. There are various methods of conducting both of these tests, resulting in conflicting opinions concerning the utility of the measurements, a scarcity of comparable data from epidemiological investigations, and limited normative data to aid clinicians in decision-making. This review of evidence on which the tests are based is aimed at providing clinicians and researchers with an understanding of the factors that must be considered when conducting the tests, interpreting the results, and comparing results between different studies.

Key words: cold provocation tests, vibration-induced white finger, finger systolic blood pressure, finger skin temperature, rewarming test

Introduction

Exposure to hand-transmitted vibration can cause a variety of disorders collectively known as the hand-arm vibration syndrome. The vascular component of this syndrome is vibration-induced white finger (VWF), which manifests as episodic blanching of the fingers in response to cold. The blanching is due to a cessation of blood flow in the affected finger resulting from exaggerated cold-induced vasoconstriction (1). This vasospasm is most likely mediated partly locally by changes in the fingers and partly centrally in response to the central sympathetic nervous system (2, 4). Due to the episodic nature of the condition, a clinician rarely observes the blanching, thus VWF has often been diagnosed based only on medical history and vibration exposure history (5, 6). Indeed, such a medical

interview is commonly considered the gold standard for the diagnosis of VWF (7).

Reliance on medical interview either for the diagnosis of VWF or for screening workers exposed to hand-transmitted vibration may have limitations; there is evidence suggesting that vascular dysfunction can be present but not yet manifest in the complete closure of digital arteries that is required to cause blanching (6, 8). Furthermore, workers may under-report or downplay their symptoms, and claimants in medicolegal cases may overestimate their symptoms (8, 9). Measuring the response of peripheral circulation to local cold provocation can be used to quantify the extent of cold-induced vasoconstriction. Such measurements may be used to support a diagnosis of VWF, for epidemiological investigations, and for health surveillance in the workplace. The measurements of responses of finger skin temperature (FST) and the response of finger systolic blood pressure (FSBP) to cold provocation are the two most widely used methods.

The measurement of FSBP following local cooling provides a measure of vasomotor tone; a higher vasomotor tone results in an increased cold-induced vasoconstriction (10), which is measured as a drop in blood pressure after local

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cooling (6, 11, 12). The measurement of FST following cold provocation is based on the principle that skin temperature tends to correlate with cutaneous blood flow (13, 14). The measurement primarily provides information on the recovery from cold-induced vasoconstriction; a slow recovery suggests prolonged vasoconstriction, which is a sign of vibration-induced white finger (13). The measurement of FST following cold provocation is fundamentally different from that of FSBP in that it measures the release from vasospasm, and not the extent of vasospasm (15). The two measures may not correlate within the same subjects (16), and there is evidence suggesting that in workers with VWF, a poor cutaneous skin flow can occur even when there is no measurable abnormality of the vasoconstriction in response to cold provocation (17).

Various methods of conducting both of these cold provocation tests have been reported, resulting in conflicting opinions concerning the utility of the measurements, a scarcity of comparable data from epidemiological investigations, and limited normative data to aid clinicians in their diagnosis of VWF. This review of evidence on which the tests are based is aimed at providing clinicians and researchers with an understanding of the factors that must be considered when conducting the tests, interpreting the results, and comparing results between different studies. Consideration is given to conditions under which the test are conducted, and to combining these two tests into a battery for measuring both the extent of vasospasm and release from vasospasm when evaluating an individual for VWF.

Finger systolic blood pressure

A method for FSBP measurement with local cooling was first proposed by Nielsen and Lassen in 1977 (10). Briefly, the medial phalanx of one finger was cooled for 5 to 7 minutes using a thin-walled, plastic cuff perfused with water controlled at different temperatures. During this time, the finger was held in an ischemic state using a pressure cuff placed proximal to the cooling cuff. After the cooling period, the pressure cuff was slowly deflated until blood flow was detected distal to the cooling cuff. Blood flow was detected using a mercury-in-elastic strain gauge wrapped around the distal phalanx; blood entering the distal phalanx through the digital arteries causes a volume increase that is measured by the expansion of the strain gauge. To maximize this volume change, the finger was emptied of venous blood by a light external compression prior to pressure application and the distal phalanx was warmed during cooling to maintain the vasomotor tone in this part of the finger. In addition to blood pressure measured on the test finger, a reference measurement was carried out simultaneously on a reference finger without cooling; the reference measurement allows changes in systemic systolic pressure (SSP) to be considered when explaining how FSBP changes in response to thermal provocation. Blood pressure was assessed at between 30°C and 10°C with a 5°C stepwise reduction in temperature between measurements such that the vasomotor tone could be obtained at different temperatures and compared between temperatures. The procedure was later adapted to combine water perfusion and pressure into the same cuff (18). The

method has been widely adopted for the measurement of FSBP in response to local cold provocation and forms the basis of the current international standard (19).

Equipment for conducting measurements of FSBP in response to cold provocation

The device used in measuring FSBP in response to local cold provocation is generally referred to as a plethysmograph. Under the strict definition, a plethysmograph is an instrument for measuring variations in the volume of an organ or limb resulting from changes in the amount of blood present or passing through it. The term has been adopted to include the device used to provide pressure and temperature-controlled water, and to acquire data, regardless of whether volume change is used as the primary method of detecting blood flow. Pressure and cooling cuffs, and transducers for measuring blood flow are connected to the plethysmograph.

In the measurement method described above, mercury-in-elastic strain gauges are used to detect a volume increase when blood enters the finger. Several other types of transducer have been used successfully for the detection of blood flow in distal phalanges. Photoelectric cells can detect changes in skin color that are indicative of changes in digital circulation. Doppler methods can detect a shift in the frequency of reflected electromagnetic or sound waves that occurs when there is blood flow in the finger. The use of different transducers can result in different FSBPs. Laser-Doppler flowmetry, for example, may be more sensitive to detecting blood flow than strain gauge methods in patients exhibiting strong vasospasm (20), although experience suggests that Doppler shift methods are more variable than strain gauge and photocell techniques.

In addition to selecting a transducer for measuring blood flow, attention must be paid to the selection of pressure cuffs. Cuffs of 24 mm width placed on the medial phalanges of the index, middle and ring fingers result in systolic blood pressure similar to that in the arms, while on the little finger, a 24 mm cuff placed on the proximal phalanx, or a 20 mm cuff placed on the medial phalanx, results in FSBP similar to arm systolic blood pressure (21). Cuffs wider than the length of the phalanx may not conform to finger shape during inflation and may result in additional variability.

The material from which a pressure cuff is made can influence the test outcome; a stiff material prevents the cuff maintaining contiguity with the surface of the finger, whereas softer cuffs adapt to finger shape. Too elastic a material can result in a loss of cuff shape under pressure, and hence a loss of control over cuff size. The adaptation of thin-walled plastic cuffs to finger shape has been shown to be better than that of rubber cuffs (21). As well as the stretch and flexibility of the cuff, thermal conductivity must be considered; the rate of attainment of thermal equilibrium of the finger is dependent on the rate of energy flow through the cuff material.

Cold provocation

The temperature, duration and area of cold provocation influence the degree of cold-induced vasoconstriction apparent in blood vessels (15). As the temperature of cold provocation decreases, the vasoconstriction of digital arteries increases.

The sensitivity of FSBP to VWF improves with decreasing temperature of cold provocation (22, 23). There is a critical temperature below which the complete closure of digital arteries is achieved; this temperature is indicative of the severity of primary Raynaud's phenomenon, the idiopathic form of the condition (10). Too low a temperature of cold provocation, however, can result in the occurrence of the hunting phenomenon, a cyclical cold-induced vasodilation (23).

A single measurement of FSBP following cooling is not objectively meaningful without a comparison with a measurement of the vasomotor tone at some baseline; therefore, a basal measurement is usually made at a temperature inhibiting vasoconstriction. A procedure for the measurement of FSBP at more than two or three temperatures is prohibitively lengthy for use in routine diagnosis and screening programs; in most studies, two or three temperatures of cold provocation are used. Generally, 30°C or 35°C is used to obtain a measure of basal vasomotor tone, and then 15°C or 10°C is used to measure cold-induced vasoconstriction.

The duration of cold provocation affects the temperature achieved by the arterial wall and hence the degree of vasoconstriction of digital arteries. After five minutes of cooling with ischemia, the temperature of the superficial subcutaneous tissue, in which digital arteries lie, is within 1°C of cuff temperature (10). It has been argued that an increased duration of local cooling, combined with whole-body cooling, may be required to detect mild VWF (24). Most likely, the addition of whole-body cooling and not increasing the duration of local cooling improves the sensitivity of this measure to mild VWF; in mild cases of primary Raynaud's phenomenon the addition of whole-body cooling increases the hyper-response of finger circulation (25). Whole-body cooling increases sympathetic discharge to the fingers, and it may be helpful in cases when an investigator is attempting to induce the complete closure of digital arteries (18, 26).

Duration of recovery between provocations

The measurements of FSBP at different temperatures are usually carried out in quick succession. Little consideration has been given to any lasting influence of thermal provocation on either central sympathetic activity or the local response to thermal provocation. Central sympathetic activity increases when the hands are exposed to cold, and this central sympathetic activity is enhanced in workers with VWF (27, 28). Central sympathetic activity then decreases during recovery following cold provocation (29, 30). This change might influence subsequent measurements. With a five to fifteen minute recovery period between tests, subjects exhibit lower blood pressures at the second test than at the first (31, 32). Moreover, lasting vasospasm in response to cold provocation has been observed (33). Patients exhibiting blanching of the fingers during a measurement may require some recovery time for additional tests to cause vasospasm (25).

Test measurement

Both the finger assessed, and the positions of the pressure cuff, cooling cuff, and the transducer on a finger may cause variability in FSBP. Differences between fingers in patients

with VWF are likely influenced by the distribution of blanching on the fingers; the measurements of FSBP following cold provocation are more sensitive to VWF when blanching is observed in the tested finger as opposed to on a finger of the test hand that does not blanch (24, 34). If VWF is primarily a local dysfunction, then the measurement may not only be finger-specific but also phalanx-specific.

Recent advances in the measurement of FSBPs have included simultaneous measurements on multiple test fingers; the increased area of the cold stimulus applied to the fingers has not been shown to increase the vasoconstriction of digital arteries, or to increase vasomotor tone in the reference finger (35). However, increased repeatability is observed with simultaneous cold provocation of multiple fingers. The greater consistency of response with an exaggerated stimulus is possibly due to a dominance of the effect of thermal provocation over the effects of other factors influencing sympathetic activity such as noise, environmental conditions and mental stress (36).

Reference measurement

A reference measurement is usually carried out simultaneously with test measurements and is used to adjust the change in FSBP due to cold provocation for any changes in systemic systolic pressure. The need for a reference measurement has been questioned (37), although including a reference measurement maximizes the discriminative power of the test (38). There is an incomplete consensus on the most appropriate location for the reference measurement. Differences between FSBPs of different digits, between FSBPs measured along the lengths of the digits and between measurements of systolic pressure on the arm and the fingers have been shown (20, 21, 25). The effects of hydrostatic pressure in the body may suggest that systolic pressure at an elevation different from that of the test measurement may not be reflective of systemic systolic pressure at the test location. The repeatability of measurements at different locations has also been shown to vary, perhaps due to measurement accuracy (39). The use of a finger with vascular dysfunction as a reference might result in low reference measurements (37). In healthy subjects, any effects of cold provocation of one finger on pressure measured on the arm or other fingers have been shown to be small and not repeatable (40). Because the thumb may be symptomatic, the use of the arm has been encouraged by some (8). For the purpose of diagnosing VWF, maximal sensitivity and specificity are achieved when a finger or the thumb of the test hand is used as the reference when compared with the use of the arm (38).

Pressure indices

An FSBP measurement usually consists of four separate components: 1) a measurement of basal vasomotor tone at the test site ($FSBP_{TEST,r^{\circ}C}$), 2) a measurement of vasomotor tone in response to cold provocation at the test site ($FSBP_{TEST,i^{\circ}C}$), 3) a measurement of systemic systolic pressure during the basal vasomotor tone measurement ($FSBP_{REF,r^{\circ}C}$), and 4) a measurement of systemic systolic pressure during the cold provocation measurement ($FSBP_{REF,i^{\circ}C}$). Various methods have been suggested for computing a pressure index that combines the information from the four components (12, 23, 37). The

pressure index most frequently used is the %FSBP (Equation 1) (25). This index has been shown to be repeatable and to discriminate between groups with and without VWF most consistently (12, 38).

$$\%FSBP_{T^{\circ}C} = \frac{FSBP_{TEST,T^{\circ}C}}{FSBP_{TEST,T^{\circ}C} - (FSBP_{REF,T^{\circ}C} - FSBP_{REF,1^{\circ}C})} \cdot 100\% \quad (1)$$

Normative data

While there is a wide range of %FSBPs reported in the literature for groups of patients with VWF, there appears to be some consistency with regard to healthy workers and lower normal limits. A review of data from eight studies suggests mean lower normal limits of 67°C for %FSBP_{15°C} and 64.5% for %FSBP_{10°C} (41). A lower normal limit of 60% for %FSBP_{10°C} results in sensitivities ranging between 74% and 87% and specificities between 94% and 100% (38). A normal limit of 60% may be useful as an indicator of potent vasospasm resulting from an exaggerated cold response (6). This limit can be used for both %FSBP_{15°C} and %FSBP_{10°C} although measurements at 15°C are likely to be less sensitive to VWF.

The complete closure of digital arteries has been argued to be the only means of confirming VWF (6). However, achieving the complete closure of digital arteries is not always possible, particularly in mild VWF; whole-body cooling is advised if this strict criterion is used (18, 24, 26).

Finger skin temperature

A general method for measuring the response of FST to cold provocation involves the immersion of a hand in cold water for some period, removing the hand, and then monitoring skin temperature at selected locations until the hand has warmed. A delayed warming is believed to result from either persistent vascular disturbances of the fingers (42), a delayed release from vasospasm (15, 36), or some combination of these.

Equipment for measuring finger skin temperature response to cold provocation

There are two main components required for measuring the FST response to cold provocation, a cold water bath and transducers for measuring the temperature of the skin. Additional equipment is required for controlling water temperature and acquiring data. Using environmental chambers and cold air have been suggested as possible methods of applying cold provocation (43, 44), but little research has been conducted with these alternatives and their utility is not well understood.

Several different transducers are available for monitoring FST, each has advantages and disadvantages. Thermocouples and thermistors (point transducers) are often used as these are relatively inexpensive, simple to use, and allow continuous data acquisition both during and following cold provocation. Thermal imaging devices have been successfully employed, but these are difficult to adapt to measurements during cooling. They can, however, provide much more extensive information about the temporal and spatial changes in FST (45). The use of point transducers are appropriate for the diagnosis of VWF if

several precautions are taken: transducers should have a low heat capacity and be of small contact area to avoid influencing temperature changes at the measurement site; transducers should be placed so as to maintain good contact with the skin; transducers should not be in contact with surfaces other than the skin at the measurement site; and transducers should be allowed to equilibrate until the recorded temperature stabilizes (46).

Site of measurement

The site at which the FST is measured is reflective of blood flow at that site. Point transducers are limited to assessing blood flow in the region immediately surrounding the transducer, while thermal imaging devices can evaluate blood flow over the entire hand. When using a thermal imaging device, the dorsal and volar surfaces of the fingers tend to indicate similar FSTs in healthy people (45). When using point transducers, the measurement site may significantly affect sensitivity to VWF; the measurements are most likely fingerspecific (47).

Conditions of cold provocation

As with the measurement of FSBP, the temperature, duration and site of cold provocation affect the extent of cold-induced vasoconstriction (13). The time taken for FST to increase following cooling depends, in part, on the extent of cold-induced vasoconstriction in the digits (13). The conditions of cold provocation should be chosen so as to achieve maximal vasoconstriction with minimal subject discomfort (46).

Exposure durations reported in the literature vary between 1 minute and 30 minutes, water temperatures between 0°C and 20°C, and hand conditions between wet or dry and ischemic or nonischemic (48). Different areas of application of cold provocation have been reported. For example, a single finger (13), a part of the hand (1), and the entire arm to the level of the shoulder (49). While both hands can be immersed in cold water, this causes loss of data from a reference site: this can provide useful information about central sympathetic discharge to the fingers during cooling (30). A majority of studies have involved the immersion of one hand in cold water up to the wrist (48). Some have suggested that the hand should grip an iron bar during cooling to maximize the cold-induced vasoconstriction (1, 50, 51), but this practice is uncommon.

Temperatures of cooling below about 10°C can cause a cold-induced vasodilation (46), the hunting phenomenon (52), and pain (53, 54). Warmer temperatures are preferable to cooler temperatures because they are tolerated better by subjects. However, too high a temperature will be insufficient to cause vasoconstriction in patients with VWF. The maximum vasoconstriction of digital arteries has been found to occur between 10°C and 20°C (13, 55). It has been argued that there is currently insufficient evidence that supports the diagnostic value of cooling at a temperature of 15°C (48). In comparison studies, a temperature of 10°C inhibits postischemic reactive hyperemia more effectively than 15°C in patients with VWF (56, 57). Recent analyses of a large claims database have questioned the diagnostic utility of a 15°C cold provocation test (58, 60), although these reports have met with some criticism regarding the conduct of the test (61, 62) and interpretation of results (63). With appropriate conduct of the test and inter-

pretation of the results, a 15°C cold provocation may have a sensitivity to VWF similar to a 10°C cold provocation, causes less discomfort and is easier to achieve (47). It seems that temperatures between 10°C and 15°C are most useful in avoiding cold-induced vasodilation, pain, and the hunting phenomenon while achieving maximal cold-induced vasoconstriction. Regardless of temperature, a minimum FST is achieved after about 5 minutes of cooling (15, 53, 64). Durations of cold provocation greater than this have not been shown to improve the diagnostic sensitivity and specificity of this test (65).

Hand conditions during immersion

The removal of the hand from a cold water bath while wet allows continued cooling by evaporation, which is either avoided by keeping the hands dry during immersion by wearing waterproof gloves (59, 66), or minimized by immediately drying the hand with a towel (67). Whether or not the hand is covered during cold provocation is not believed to affect the degree of cold provocation, provided the hand is not insulated against the cold and the covering does not influence the circulation (61). Covering and drying the hands with a towel might increase variability of the test and no evidence has yet been provided to recommend one method over another.

The use of a tourniquet to induce an ischemic state in the hand during cooling allows a more rapid decrease in both FST and internal hand temperature (1) and has been recommended by some (13, 46, 51, 67). In addition, the removal of a tourniquet during cooling allows the evaluation of an inhibited reactive hyperemia (68). The reproducibility and diagnostic value of the hyperemic temperature achieved on removal of a tourniquet at the wrist is similar to those of recovery temperatures after cold provocation (56, 57). The addition of ischemia may not be necessary.

Hand conditions during recovery

While much attention has been given to the nature of cold provocation, little has been reported on hand conditions during the recovery from cold provocation. There is no evidence based on which one can recommend the most appropriate hand conditions during the recovery phase of this test. One suggestion is to rest the hands on a nylon net to achieve maximum exposure to air with minimum insulation effects (69). Another recommendation is that the hand should be dry, any covering used during immersion should be removed, and the compression of blood vessels should be avoided (65).

Interpretation of finger skin temperature response to cold provocation

The response of FST to cold provocation is a complex and poorly understood phenomenon. A multitude of different parameters have been used to quantify the decrease in FST during cooling and the subsequent increase in FST following cooling. Rewarming time, rewarming rate, recovery temperature, immersion temperature and the hyperemic temperature have been considered. Rewarming time, defined as the time taken for the finger skin to increase in temperature by a specified amount following cooling, is among the more repeatable parameters in healthy subjects (64, 70), but has limited diagnos-

tic utility (47, 59). No single parameter can fully quantify the response to cold provocation; there are at least four distinct patterns of response to cold provocation (68). The entire response profile should be considered when interpreting the results of this test (71). One method suggested for quantifying the entire response profile involves combining 11 parameters that describe the equilibration, immersion and recovery periods (72), whereas another involves the use of the area above the response profile; larger areas indicate a prolonged vasoconstriction and a delayed recovery of cutaneous blood flow relative to cutaneous blood flow prior to cold provocation (47).

In addition to measuring the FST response to cold provocation at a single test site, comparison between sites may be useful in interpreting results. The presence of asymmetry between the hands, and differences between the fingers, have been used to provide a differential diagnosis of vibration-induced white finger; a symmetrical distribution of diminished blood flow following cold provocation is likely to be indicative of primary Raynaud's phenomenon (72). Also, in patients with VWF the fingers have been observed to rewarm from the tip to the base whereas in normal subjects, the fingers rewarm from the base to the tip, suggesting that the temperature gradient along a finger can be used in diagnosis (66, 73). The measurement of FST on a contralateral hand can also provide an indication of sympathetic discharge that may differ between healthy subjects and patients with VWF (30).

Because the vasodilation process following cold provocation is not as yet completely understood, the interpretation of test results and the provision of normative data remain difficult. Receiver operating characteristics for various indices and methods of interpretation can be used to assist clinicians in deciding the utility of additional information provided by the test. For example, the slope of the receiver operating characteristic curve is equal to the positive likelihood ratio (74), and some indices of recovery can give a high positive likelihood ratio even when the test has little negative predictive power (47, 63).

Test environment

Various factors that are not intrinsic to cold provocation tests must be considered during their conduct, and when performing the tests within the same test session. These include environmental factors, factors influencing the peripheral circulation outside of cold provocation, and carry over effects between repeated applications of cold provocation.

Environment

Environmental temperature is an important factor in the thermoregulation of the human body. Thermoregulation has a significant effect on blood flow in the peripheral circulatory system. In cold environments, the blood supply is directed away from the extremities to the body core. In warm environments, as core body temperature increases, blood flow to the extremities increases. In moderate temperature environments, the change in blood flow is generally mediated by the vasoconstriction or vasodilation of arteries through increases or decreases in sympathetic tone. Because cutaneous blood flow is highly

dependent on local environmental conditions, strict control of such conditions is required (13).

Cold environments may be sufficient to cause vasoconstriction in digital arteries in patients with VWF extraneous to cold provocation tests (37), and they can result in the occurrence of the hunting phenomenon (33). Such effects may be detrimental to the diagnosis of VWF. Through an increased sympathetic discharge to the fingers, however, cold environments can enhance vasoconstriction in response to cold provocation, which may be useful in detecting mild VWF when measuring FSBPs (15, 75). A cold environment can also result in a decreased FST and a slower recovery from cold provocation (76). Warm environments have the effect of inhibiting sympathetic discharge to the fingers and minimizing cold-induced vasoconstriction in VWF (68). The %FSBP_{10°C} may increase by as much as 2 mmHg per 1°C between 20°C and 28°C (41).

Whole-body cooling or warming has the same effect as changing environmental temperature; whole-body cooling exaggerates the response to local cold provocation whereas whole-body warming inhibits it (24, 51, 68). A complication of whole-body cooling is the transient increase in sympathetic discharge to the fingers that results from the sudden application of cold packs (25).

In addition to the environment in which the tests are conducted, exposure to uncomfortable environments prior to cold provocation can result in lasting changes in central sympathetic activity (53, 77). Furthermore, if the prior environment is sufficiently cold to provoke the complete closure of digital arteries, it may be difficult to induce further exaggerated vasoconstriction (25).

Seasonal variations in vascular measurements

The results of vascular tests depend, in part, on the season during which the test is performed, with higher FSTs reported in the summer months than in winter months (76). Several authors recommend that measurements should be performed during the winter months (55, 72, 78).

Noise

A reduced peripheral circulation has been observed during exposure to an auditory stimulus (79). It has been suggested that noise can trigger an attack of blanching (80) and hence might influence the measurements of vascular function.

Vibration

There are significant changes in peripheral blood flow following acute exposures to hand-transmitted vibration. Immediately after exposure to vibration, vasodilation occurs in digital blood vessels, followed by a vasoconstriction (81, 84). The vasoconstriction can last at least 45 minutes but the maximum duration is currently unknown. How these acute effects of vibration exposure influence the response of digital arteries and FST to cold provocation are not currently known.

Disease and injury

No lists of diseases or injuries that might influence test results are exhaustive. The principal condition that confounds

the diagnosis of VWF is primary Raynaud's phenomenon. This is because of the 1–3% prevalence of this idiopathic condition among the normal population (85). Although it is sometimes argued that cold provocation tests cannot discriminate between primary Raynaud's phenomenon and VWF (86), the pattern of vascular dysfunction may be useful; a symmetrical distribution of dysfunction is likely to be indicative of primary Raynaud's phenomenon, whereas in VWF asymmetrical injury is observed (72).

Age

It is unlikely that age contributes significantly to variability in the cold response of FSBP (12, 15, 41, 75, 87). The effect of age on FST is more significant. Older subjects tend to achieve lower FST during immersion (88), and lower FST during recovery (41, 89, 90).

Sex

It is as yet unknown if there is a systematic difference between males and females in the vascular response to cold provocation. In women, there are cyclic variations in circulation and variations in the cardiovascular response to a cold stress test that are related to ovulation (91, 92). Males and females have been shown to have similar FSBPs (18).

Drug intake

There are many substances that can significantly affect peripheral circulation, and some that can cause episodic blanching (11). Nicotine, caffeine and alcoholic drinks are the common substances with vasoactive effects that can be controlled when evaluating a patient for VWF.

Nicotine interferes with endothelial function and hence vasospasm in response to cold (31). An exaggerated response to cold has been observed amongst smokers compared with non-smokers (11, 12). Nicotine has an acute effect of increasing cold-induced vasoconstriction (31). Although several studies have found no effects of smoking status on either the FST response to cold provocation (93) or on FSBP (15, 75, 87), the acute effects should be considered when interpreting test results. In contrast to nicotine, alcohol has a direct effect on the response of digital arteries to cold provocation by abolishing or relieving vasospasm (10, 37). Caffeine results in small increases in heart rate and blood pressure, and a decreased peripheral blood flow. These acute effects of caffeine disappear within about 2 hours (94, 95). It is unknown whether the cold response of the hands changes with caffeine consumption.

Time of day

The time of day has a direct effect on FST (91), and cutaneous vasoconstriction in response to whole-body cooling (96). It is unknown whether daily variations have a significant effect on the FST response to cold provocation or FSBP.

Food intake

Food intake does not significantly alter the vasoconstrictive response to cold (76).

Pain

Pain is often experienced during the tests of vascular function involving cold provocation (11, 12). Pain and discomfort, although subjective feelings, can result in physiological changes in the peripheral vasculature through a stress response (52).

Considerations for combining both tests into a single test battery

It often occurs that both FSBP and FST following cold provocation are measured in the same session (15, 37, 49). The exposure of the hand to cold provocation increases central sympathetic activity (28, 30). This change in central sympathetic activity can influence the results of a subsequent test, either by exaggerating vasoconstriction in healthy subjects (31, 33) or, in patients with VWF in whom an episode of blanching has occurred immediately prior to testing, the inhibition of vasospasm (25). The repeatability of measurements is dependent on the order in which they are conducted; in patients with VWF, the application of cold provocation during a prior test increases the variability in response during the second test, consistent with prior cooling affecting vasomotor tone and central sympathetic activity (32). When performing both tests in the same session, it is suggested that FST measurements be performed before the FSBP measurements. The recovery period in the FST measurements allows for the effects of cold provocation to dissipate in healthy subjects, whereas any lasting increases in sympathetic activity or in vasomotor tone might maximize vasoconstriction during the measurement of FSBP among patients with VWF. If the complete closure of digital arteries is observed during any of the measurements, subsequent measurements are not required because such an observation can be considered evidence for a vascular disturbance (6). Repeated tests are also likely to result in false negative findings (25).

Summary

For measuring cold-induced vasoconstriction, FSBP following cold provocation can be used. The medial phalanx of a finger should be cooled using a cuff perfused with water at a controlled temperature. The cuff should be pressurized, or a pressure cuff should be placed proximal to the cooling cuff, to induce ischemia. After cooling, the pressure should be deflated until blood flow is detected distal to the cuff using a strain gauge or a photocell, or using the Doppler principle. The cuff pressure at which blood flow is detected is equal to FSBP. A simultaneous measurement should be made without local cooling at a reference site not affected with VWF, the thumb is the most likely to satisfy this criteria. The test should be conducted at 30°C to inhibit vasoconstriction, and at 15°C or 10°C to provoke vasoconstriction. %FSBP, corrected for

changes in systemic systolic pressure, should be calculated. Measurements at different temperatures should be performed in rapid succession. Test fingers should be selected as those most affected by VWF. The addition of whole-body cooling increases the cold-induced vasoconstriction, which can help in detecting vascular disturbances in mild VWF, or if the complete closure of digital arteries is required. An abnormally potent vasospasm should be considered to have occurred if FSBP with cooling is lower than 60% of FSBP at 30°C. The complete closure of digital arteries, resulting in an FSBP of zero, may be considered definitive evidence of a vascular disturbances.

The measurement of the response of FST to cold provocation involves the immersion of a hand in cold water, removing the hand, and then monitoring FST until the hand has warmed. FST can be measured using point transducers (e.g., thermocouples), or using thermal imaging devices. The site at which FST is measured is reflective of blood flow at that site; the measurements are specific to vascular disturbances at the site of measurement. The temperature of cold provocation should be between 10°C and 15°C with low temperatures being more sensitive to VWF and warm temperatures being more easily tolerated by subjects. The minimum FST is achieved after 5 minutes of cooling; longer durations are not beneficial. The use of a tourniquet does not improve the diagnostic value of this test and is not necessary. The entire rewarming curve must be considered when evaluating the FST response to cold provocation; the response is a complex phenomenon that cannot be fully characterized by a single measure. Generally, low FSTs for more than 5 minutes after cooling has finished should indicate an increased likelihood of vascular dysfunction.

When performing both tests in the same session, carry over effects should be minimized. FST measurements should be performed before FSBP measurements. If the complete closure of digital arteries is observed during any measurements, subsequent measurements are not required.

The temperature of the examination room should be controlled so as not to cause vasoconstriction or vasodilation. Exposure to uncomfortable environments, particularly cold environments, should be avoided prior to testing. Noise exposure should be minimized. A decreased blood flow following exposure to hand-transmitted vibration should be allowed to recover prior to testing. Pain and discomfort during testing should be minimized. Disease or injury that might influence peripheral circulation should be considered when interpreting results. Age does not influence FSBPs but lower FSTs following cold provocation may be observed in older subjects than in younger subjects. There do not appear to be any systematic gender differences in test results, but in women, the stage of the menstrual cycle may alter the cold response of peripheral circulation. The intake of drugs with vasoactive effects should be avoided if possible, particularly nicotine, caffeine and alcoholic drinks.

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