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How can we judge sympathetic denervation from the external manifestation in the human skin?

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Abstract

Sympathetic denervation is associated with many diseases. Most cutaneous external monitoring indicators are non-invasive and used widely in clinical medicine. The external monitoring indicators of sympathetic denervation are reviewed to facilitate the clinical diagnosis of sympathetic diseases and the results of sympathectomy. Useful indicators of sympathetic denervation include sweating, warm skin, increased blood flow, Electrodermal Activity (EDA), pain response, skin integrity, and skin wrinkling. Sympathetic denervation can be assessed simply and accurately using many external indicators to diagnose sympathetic-related diseases or evaluate the effectiveness, complications, and prognosis of sympathectomy.

Keywords: Skin physiological phenomena, Sympathectomy, Health status indicators, Skin diseases.

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Introduction

Sympathetic denervation is associated with many diseases. Sympathetic neuropathy is frequent in diabetic patients and reflects the severity of diabetes [1]. Patients with a spinal cord injury [1] or Parkinson's disease [2] may have symptoms of sympathetic denervation. Many localized lesions, such as diabetic foot [3], limb ischemia [4], Raynaud's disease [5], hyperhidrosis [6], and limb pain [7] are also closely related to the functions of the sympathetic nerve system. Surgical sympathectomy is an effective method for treating these localized lesions [8,9]. Skin sympathetic nerve activity is attenuated in aged human skin during hyperthermia [10]. External monitoring indicators of sympathetic denervation will facilitate the clinical diagnosis of sympathetic diseases and the results of sympathectomy.

The skin is the largest and most superficial organ of the body. The function of the skin also changes after sympathetic denervation. Most cutaneous external monitoring indicators are non-invasive and widely used in clinical medicine. This article reviews cutaneous external monitoring indicators of sympathetic denervation.

Sweating

Apocrine and eccrine sweat glands are innervated by the sympathetic nervous system. The sudomotor system is also controlled by sympathetic neurons. An iodine starch reaction is often used to observe the appearance of sweat spots and evaluate areas wetted by sweat. Some experts believe that the sweat spot test seems to be a more sensitive indicator than the commonly used cardiovascular tests in the observation of diabetic autonomic neuropathy [11].

After the removal or destruction of sympathetic trunks, sweating on the skin is reduced in more than 50% of patients (Table 1). However, 58.8% may develop Compensatory Sweating (CS) for a few months after a sympathectomy [6]. CS is the most common and serious complication of sympathectomy and often causes sweating on just one part of the body.

Skin Temperature

In humans, skin temperature is closely related to the production of sweat. A reduction in sweating decreases heat dissipation and consequently contributes to increased skin temperature. Intraoperative or postoperative monitoring of the change in skin temperature is used to guide surgeons performing sympathectomy, although skin temperature is also affected by surgical procedures (Table 2). The temperature of areas of skin dominated by sympathetic trunks will rise temporarily after sympathetic denervation, although the amplitude and duration of the temperature increase can differ. Successful sympathetic resection is indicated by an intraoperative increase in skin temperature exceeding 1°C. There are significant correlations between the range of postoperative CS and increases in temperature and blood flow [12].

However, the sensitivity of skin temperature monitoring is poor. Skin temperature is also affected by room temperature and the surgical procedure used. The removal of a unilateral sympathetic trunk increases ipsilateral skin temperature but does not increase or even decreases the contralateral skin temperature. Beginning approximately 1 w post-sympathectomy, skin temperature gradually returns to normal.

Skin Blood Flow

Sympathetic innervation is distributed heterogeneously in the blood vessels. After sympathetic denervation, the blood vessels will dilate in the skin dominated by sympathetic nerves. Increased blood supply is also one of the main causes of increases in skin temperature. Intraoperative monitoring of blood flow may be useful for assessing sympathectomy (Table 3). Laser Doppler flowmetry is an excellent non-invasive technique for measuring cutaneous microcirculation.

The degree of change in the blood flow exceeds that of the temperature. The time to the peak blood flow is more rapid than that to the peak temperature after sympathectomy [13]. Skin blood flow should be a faster, more reliable indication of sympathectomy than temperature. Patients with congenitally absent sweat glands have no active cutaneous vasodilation [14].

Electrodermal Activity

Electrodermal Activity (EDA) includes all electrical phenomena of the skin, and these are measured using skin potential, skin resistance, skin conductance, skin impedance, and skin admittance. A Galvanic skin reflex monitor can also be used to observe skin resistance, which is related to sweating and sympathetic nerves. Thoracic sympathetic blockade results in a significant increase in skin resistance [15]. The Sympathetic Skin Response (SSR) is the momentary change in the electrical potential of the skin, potentially generated by sweat in response to different stimuli.

SSR is used to assess sympathetic nerve function (Table 4). The amplitude of the SSR waveform tends to increase and several consecutive waves can be observed in patients with palmar hyperhidrosis [16]. The SSR waveforms abolished following a sympathectomy are restored gradually in palmar hyperhidrosis patients [17]. Intraoperative plantar skin temperature and perioperative SSR are correlated with these changes [18]. However, the SSR is not fully consistent with sudomotor dysfunction [19]. SSR outcomes are reliable but not stable indicators of spinal cord injury.

Others

Some other changes in the functions of skin are also associated with sympathetic nerves (Table 5). Sympathetic blockade can reduce sympathetic activity and pain, because sympathetic activity and catecholamines can activate primary afferent nociceptors. The integrity of the skin is also associated with sympathetic nerves. Patients with severe diabetes have dry, fissured skin [20]. Horner's syndrome comprises the triad of unilateral miosis, ptosis, and ipsilateral facial anhidrosis [21].

Skin wrinkling upon water immersion is a traditional method of observing peripheral sympathetic nerve activity. Skin wrinkling is stimulated by vasoconstriction through the loss of digit volume. After sympathetic blockade, skin wrinkling is reduced. The wrinkle test is more sensitive than the iodine starch test [22]. The improved wrinkle test replaces water with a eutectic mixture of local anesthetics and is a routine diagnostic test of sympathetic function [23].

Table 1. *Changes in skin sweating after sympathetic denervation.*

Disease	Intervention	Location	Skin sweating changes
Diabetic autonomic neuropathy	None	skin	Decreased [3]
Hyperhidrosis	Sympathectomy	Palms or soles	Decreased in 93% of patients [24]
Raynaud's phenomenon	Transthoracic sympathectomy	Limb	Decreased in 60% of patient [5]
Facial blushing	Transthoracic sympathectomy	Face	Decreased in 85% of patients [25]

Table 2. *Skin temperature changes after sympathetic denervation.*

Disease	Intervention	Location	Skin temperature changes
Herniorraphy	Anesthesia	Thigh	Rise of 1°C to 1.8°C within the first hour [26]
Hyperhidrosis	Unilateral transthoracic sympathectomy	Palms	62.3% synchronous bilateral elevation, 25.8% ipsilateral elevation, 11.8% no changes; [27] the ipsilateral hand

			gradually increased, the contralateral hand gradually decreased [28]
	Bilateral thoracic sympathectomy	Palms	Intraoperatively increased by 1.44-3°C; [6,29] bilateral elevation for 1 w [28]
Complex regional pain syndrome type I	Thermoregulation	Limbs	Temperature differences between both sides increased dynamically [30]
Critical limb ischemia	Lumbar sympathectomy	Limbs	A rise above 2°C [31]
Critical finger ischemia	Transvenous regional guanethidine	Finger	Markedly increased for 1 month [4]
Diabetes mellitus	None	Feet	Higher [20]

Table 3. *Skin blood flow changes after sympathetic denervation.*

Disease	**Intervention**	**Location**	**Skin blood flow changes**
Hyperhidrosis	Thoracic sympathectomy	Palms	Increased significantly intraoperatively [32]
Critical limb ischemia	Lumbar sympathectomy	Limbs	Lower leg blood flow doubled [33]
Critical finger ischemia	Transvenous regional guanethidine	Fingers	Marked hyperemia for 1 month [4]

Table 4. *Sympathetic skin response changes after sympathetic denervation.*

Disease	**Intervention**	**Location**	**The Sympathetic Skin Response (SSR)**
Hyperhidrosis	Thoracic sympathectomy	Palms	A marked decrease in palmar the SSR amplitude and its ratio [29]; abolition of the ipsilateral palmar SSR [16]
Diabetes mellitus	None	Feet	58.0% SSR (-) [20]
Spinal cord injury	None	Hands and feet	Slightly lower [34]

Table 5. *Other changes in the functions of skin after sympathetic denervation.*

Disease	**Intervention**	**Location**	**Other changes**
Diabetes mellitus	None	Feet	26.1% dry and fissured skin [20]
Peripheral vascular disease or sympathetic dystrophy	Lumbar sympathetic blockade or surgical sympathectomy	Soles	Relief of ischemic rest pain in 83.5% of patients at 1 week and 66.6% at 6 months [35]
Complex regional pain syndrome	Lumbar sympathetic block with Botox-b	Lower extremity	Pain intensity significantly reduced [36]

Conclusions

The external indicators of sympathetic denervation in the human skin include sweating, skin temperature, blood flow, EDA, pain response, integrity of the skin, and skin wrinkling. Sympathetic denervation results in reduced sweating, as assessed with an iodine starch reaction, in more than 50% of patients. Laser Doppler flowmetry can show increased skin blood flow after a sympathectomy. The temperature of skin dominated by sympathetic nerves will rise temporarily after sympathetic denervation, although the amplitude and duration of the temperature increase differ. Skin blood flow is a faster, more reliable indication of sympathectomy than temperature. EDA can be measured using skin potential, skin resistance, skin conductance, skin impedance, and skin admittance. The amplitudes of the sympathetic skin response waveforms decrease after sympathetic denervation. Sympathetic blockade can reduce pain and skin wrinkling. Sympathetic denervation can be assessed simply and accurately using many external indicators when we want to diagnose sympathetic-related diseases or evaluate the effectiveness, complications, and prognosis after sympathectomy. Multifunction devices that can monitor many indicators at one time should be developed for sympathetic monitoring.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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