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Changes in the Skin Conductance Monitor as an End Point for Sympathetic Nerve Blocks

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Abstract

Objective. There is a lack of objective methods for determining the achievement of sympathetic block. This study validates the skin conductance monitor (SCM) as an end point indicator of successful sympathetic blockade as compared with traditional monitors.

Methods. This interventional study included 13 patients undergoing 25 lumbar sympathetic blocks to compare time to indication of successful blockade between the SCM indices and traditional measures, clinically visible hyperemia, clinically visible engorgement of veins, subjective skin temperature difference, unilateral thermometry monitoring, bilateral comparative thermometry monitoring, and change in waveform amplitude in pulse oximetry plethysmography, within a 30-minute observation period. Differences in the SCM indices were studied pre- and postblock to validate the SCM.

Results. SCM showed substantially greater odds of indicating achievement of sympathetic block in the next moment (i.e., hazard rate) compared with all traditional measures (clinically visible hyperemia, clinically visible engorgement of veins, subjective temperature difference, unilateral thermometry monitoring, bilateral comparative thermometry monitoring, and change in waveform amplitude in pulse oximetry plethysmography; $P \leq 0.011$). SCM indicated successful block for all (100%) procedures, while the traditional measures failed to indicate successful blocks in 16–84% of procedures. The SCM indices were significantly higher in preblock compared with postblock measurements ($P < 0.005$).

Conclusions. This preliminary study suggests that SCM is a more reliable and rapid response indicator of a successful sympathetic blockade when compared with traditional monitors.

Key Words. Sympathetic Nerve Block; Skin Conductance; Monitor; Complex Regional Pain Syndrome

Introduction

Lumbar sympathetic blocks are clinically used for both diagnosis and treatment of sympathetically mediated pain

in variety of neuropathic pain conditions including complex regional pain syndrome. Sympathetic nerve block has been found successful in about 40% of the patients with neuropathic pain to improve their pain conditions [1,2]. A sympathetic blockade refers to an injection of a local anesthetic around the sympathetic nerves to alter their functions [2]. The local anesthetic block, often repeated with intervals, may reduce the activity of spontaneous discharges in hyperactive neurons [2]. Reducing the sympathetic nerve activity in the painful region by blocking sympathetic nerve ganglia with a series of local anesthetic nerve blocks may therefore break the cycle of sympathetically mediated pain and provide pain relief [2]. Despite the frequent use of these blocks, there is still a lack of objective methods for determining the successful achievement of sympathetic block in the clinical setting.

In current clinical practice, the most commonly used monitoring methods to assess the success of a sympathetic block are observation of clinical signs of sympathetic blockade, skin temperature monitoring [3–6], pulse amplitude monitoring in pulse oximetry plethysmography [7], and any combination of these monitoring methods. The skin temperature and pulse amplitude in pulse oximetry plethysmography may increase after sympathetic block [3,8]. However, observation of clinical signs of sympathetic blockade, monitorization of skin temperature, and pulse amplitude often demonstrate an unpredictable or delayed response. Furthermore, confounding variables, such as ambient temperature, coexisting vascular disease, and use of other vasoactive medications, may contribute to inconsistencies in the temperature measurements, or pulse amplitude responses. Therefore, it is a clinical necessity to develop an objective monitoring method that is reliable, rapid response, and also not affected by the other confounders. One potential method is the examination of sympathetic nerve activity via a skin conductance monitor (SCM). Normal skin sympathetic nerve activity stimulates muscarinic receptors that subsequently stimulate the sweat glands to secrete and fill with sweat containing sodium and other electrolytes [9]. The electrolytes present in the sweat increase the electrical conductance while decreasing the electrical resistance at the skin level. The real-time changes in SCM indices can be monitored at the skin level by use of noninvasive electrodes attached to the skin (Figure 1) [9]. This is best monitored in the areas with relatively dense sweat glands, such as palm and plantar skin. A computer program analyzes the data and produces real-time graphic and numeric data demonstrating the skin conductance response (Figures 2 and 3) [9]. The initiation of successful sympathetic blockade can cause rapid cessation of the skin sympathetic nerve activity that leads to a decrease in skin conductance responses within seconds (Figure 3) [10]. Currently, there is no rapid response monitor with easy clinical applicability to assess the achievement of a successful sympathetic blockade. Such a monitor could increase procedural accuracy and efficiency, thereby improving patient care. This is especially important in evaluating the response to the sympathetic blocks as they are important for diagnostic purposes to differentiate neuropathic pain types as the sympathetically mediated/maintained pain (SMP), or sympathetically independent pain (SIP). The patients with neuropathic pain presenting with similar symptoms can be classified into two groups depending on their negative or positive response to selective sympathetic blockade. If the pain is relieved by the selective sympathetic block, it is considered SMP. Sympathetically mediated pain is defined as a symptom in a subset of patients with neuropathic pain. The significance of differentiating between SMP or SIP is that SMP has a greater chance of responding favorably to sympatholytic blockade. Therefore, a prospective therapy plan of performing repeated sympatholytic blocks may be considered as these blocks are more efficacious in SMP. On the contrary, as the chance of responding favorably to sympathetic blocks is less likely in SIP, alternative therapies must be considered in this group of patients. In order to plan the prospective treatment options, objective confirmation of sympathectomy created by the attempted sympathetic block is important to differentiate SMP vs SIP [11].

In this context, the utilization of a monitor with a rapid response and easy clinical applicability that can demonstrate effective sympathetic block would serve to function as an objective end point for the evaluation of sympathetic blockade both clinically and for future research. We hypothesize that the SCM is, on average, a more reliable rapid response indicator of a successful sympathetic blockade than traditional monitors such as clinical assessment, monitoring changes in the skin temperature, and pulse amplitude.

Methods

Subjects

After institutional review board (IRB) approval, a total of 25 recordings were included in the analysis from 13 patients recruited for this study after written informed consent was obtained. The patients were selected among patients who were scheduled for lumbar sympathetic block of the lower extremity. The inclusion criteria were that they were scheduled for lumbar sympathetic block at one of the lower extremities, and the other lower extremity was healthy. Inclusion ages were 18–99 years. The exclusion criteria were having pacemakers, cardiac defibrillators, and spinal cord stimulators; intravenous sedation for anxiety or analgesia or having dermatological conditions in the plantar aspect of the foot where SCM electrodes are attached; history of allergic reaction to adhesive tape; diagnosis of dysautonomia or sympathetic dysfunction (such as Raynaud disease or Buerger disease); disorders of sweating (such as acquired idiopathic generalized anhidrosis); and use of vasoactive drugs of which the mechanism of action is directly on the vascular tone. All the procedures were performed under fluoroscopy by the same practitioner using the same technique. The patients were positioned prone on the fluoroscopy table. After the monitors were placed, including the research monitors, the entry site was marked at the lumbar 3 vertebral body level in 30° oblique view ipsilateral to the affected extremity under

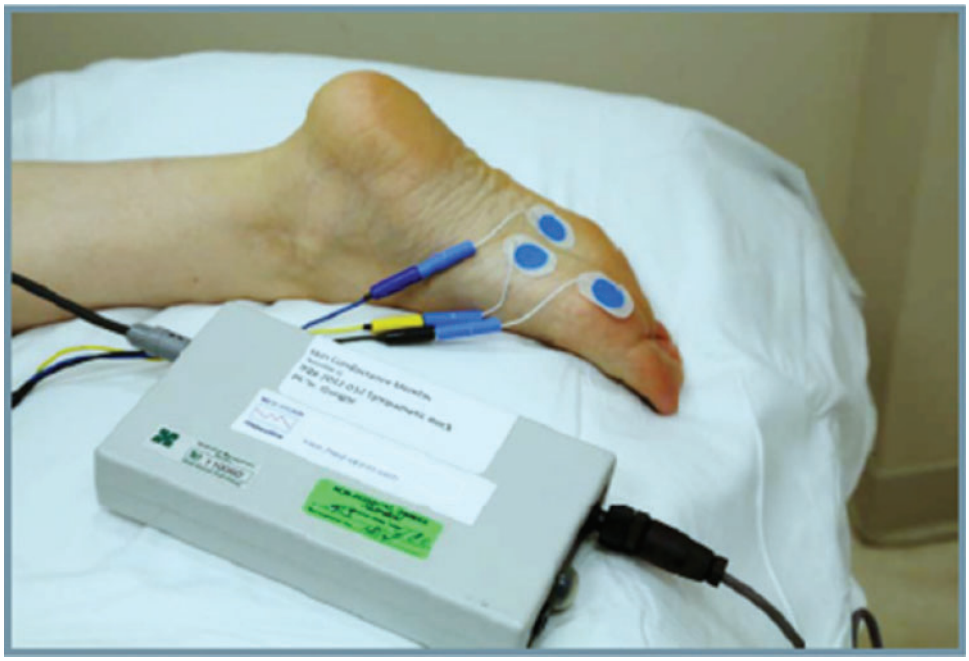

Figure 1 The self-adhesive electrodes, denoted C (current), R (reference), and M (measurement), are attached to plantar skin.

fluoroscopy. Two mL of lidocaine 1% was used for local anesthesia of the skin and subcutaneous tissues at the needle entry site. Then by using the 20-gauge 3.5-inch introducer needle and 25-gauge six-inch spinal needle, the needle was advanced to the anterolateral aspect of the lumbar 3 vertebral body on the affected side. After negative aspiration, 4 mL of Iohexol 180 mg/mL (Omnipaque 180) contrast was injected under live fluoroscopy, and the needle tip location with the spread of the contrast anterolateral to the lumbar 3 vertebral body was confirmed and intravascular uptake was ruled out. The contrast distribution was confirmed on anteroposterior, oblique, and lateral views. After negative aspiration, initially 3 mL of lidocaine 2% was given as a test dose, followed by 7 mL of bupivacaine 0.5% in all patients.

Clinicaltrial.gov number was NCT02390323.

Methods

Monitoring Temperature as a Measure for Sympathetic Block Assessment

Temperatures in the affected (T1) and unaffected (T2) limbs were continuously measured and recorded prior to the procedure, which constituted baseline, and at one-minute intervals thereafter until 10 minutes postprocedure. To determine the success of the sympathetic block, a thermometry score of 0–3 was assigned based on the recorded values (Table 1). Specifically, a bilateral (temperature difference between bilateral limbs) [4–6] or unilateral (temperature difference within measurements of the affected limb) [5] temperature score $>$ 3 (i.e., an increase in temperature $\geq 2\,^{\circ}C$) was used to indicate a successful sympathetic block. The temperature was assessed with dual channel monitor from Puritan-Bennett Corporation PB240 (Overland Park, KS, USA).

Monitoring Pulse Amplitude in Pulse Oximetry Plethysmography as a Measure for Sympathetic Block Assessment

Pulse amplitude [6,7] of the affected extremity was measured at baseline and then at one-minute intervals until 10 minutes after completion of procedure using plethysmography (Table 2). To determine the success of the sympathetic block, a plethysmography score of 0–4 was assigned based on the recorded values (Table 2). Specifically, a score that is ≥ 3 (i.e., a waveform amplitude reading of 20) was used to indicate a successful sympathetic block. The pulse pressure amplitude was assessed with plethysmography monitoring equipment from Puritan-Bennett Corporation PB240 (USA).

Skin Conductance Activity to Assess Sympathetic Block

The skin conductance measurement [12] was performed using three self-adhesive noninvasive electrodes attached to the participant's plantar skin surface of the affected lower extremity [13] (Figure 1). The skin conductance responses were assessed using the SCM equipment provided by Med-Storm Innovation, Oslo, Norway, software 1.0.6.33 [14]. The SCM is a device that primarily measures changes in skin conductance in real time [13] (Figures 2 and 3). A skin conductance

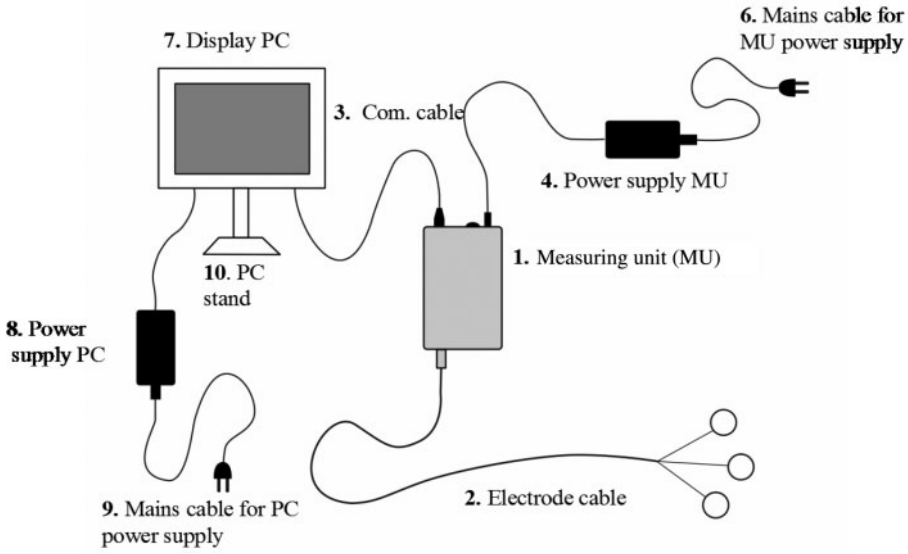

Figure 2 Overview of the skin conductance device.

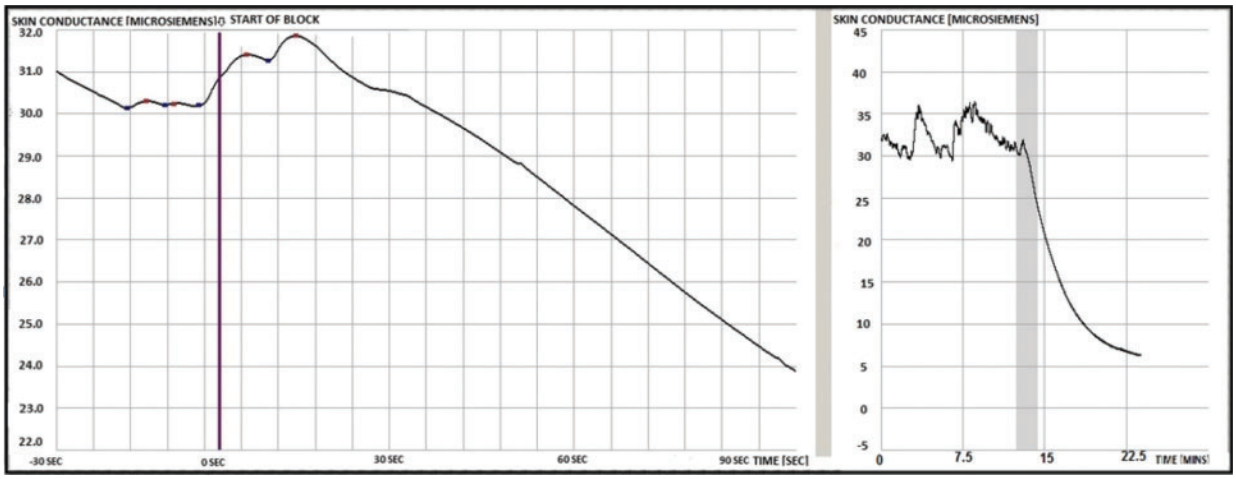

Figure 3 Left: Detail of recording from the skin conductance monitor (SCM) showing the time period from when the sympathetic nerve block injection was given, start of block (time period 0), until when the block worked. Right: Overview of the skin conductance recording before, at the start of block, and after the block worked. The detail is from the gray area in the overview.

response is defined as a minimum followed by a maximum in conductance values (mS). The measurement is performed using three self-adhesive electrodes, denoted C (current), R (reference), and M (measurement) attached to plantar skin (Figure 1). The measurement unit uses the C and R electrodes in a feedback configuration to apply an exact and constant alternating voltage between the R and M electrodes. The return current from the M electrode is recorded as its value provides direct information on the skin conductance. The recorded alternating current signal is subjected to advanced filtering, which removes noise and interference before the signal is sent on to the display computer (Figure 2). The three-electrode system used in our study allows us to only assess skin conductance activity underneath the M-electrode. The system can measure conductance values in the range of 1–200 mS, with a noise level (1 SD) below 0.002 mS. The threshold we used to define a skin conductance response was 0.005 microsiemens.

The measuring unit also has error detection that provides a warning for events caused by a loose electrode, external interference, or the use of electrocoagulation. The skin conductance responses per second are not influenced by environmental temperature [15]. This device has been issued a European Community

Table 1 Bilateral thermometry score (temperature difference between bilateral limbs), a score of 3 will be taken as an indicator of complete sympathetic block; unilateral temperature score (temperature difference within measurements of the affected limb), a score of 3 will be taken as an indicator of complete sympathetic block

0	No temperature difference or the affected limb is colder than the other extremity
1	Increase in temperature $\geq$ 1–1.4 °C
2	Increase in temperature $\geq$ 1.5–1.9 °C
3	Increase in temperature $\geq$ 2 °C

Table 2 Plethysmography scores will be assigned to each measurement as follows; an increase in the waveform reading score of 2 will be taken as an indicator of improvement in capillary circulation secondary to sympathetic block/vasodilatation; a reading of 3 and above will indicate a successful block

0	Waveform amplitude reading of 2/least capillary circulation
1	Waveform amplitude reading of 5
2	Waveform amplitude reading of 10
3	Waveform amplitude reading of 20
4	Waveform amplitude reading of 50/maximum capillary circulation

Declaration of Conformity but is not US Food and Drug Administration approved.

Skin Conductance Visual Observation Scale in Real Time

Easily recognizable changes on skin conductance graphs to determine the successful sympathetic block may have practical advantages (Figure 3). Definite and easily recognizable change in the SCM graph is usually a sudden decline in the graph (Figure 3), and in this study for research purposes this time point was defined as no observable skin conductance responses, that is to imply the skin conductance responses per second were 0.00 in a real-time 15-second time window. The SCM was applied to the affected lower extremity (Figure 1) immediately prior to the procedure to obtain baseline readings. Measurements were recorded at 0 minutes and every minute until 10 minutes after completion of procedure in real time to compare the data with the other sympathetic block assessment tools. The preset skin conductance analyzing window of 15 seconds was used on the SCM. A measurement of 0.00 responses per second was taken as an indicator of a successful block (Table 3). The visible/recognizable changes are determined when the skin responses per second reading were 0.00 in a 15-second analyzing window.

Validation of Reliability: Offline Skin Conductance Assessment

The skin conductance activity measurements for enrolled patients were saved as distinct registrations reflecting the precise time points when the test dose and the block were administered during the procedure. The purpose of in-depth analysis of 20 registrations after sampling the data was 1) to study the reliability of the method and 2) to see if we can further develop a more effective and accurate way of analyzing skin conductance responses rather than observing the registration curve (Figure 3) each minute in real time. During this analysis, we tested Med-Storm Innovation's software in various settings: Analyzing windows of 15 seconds, 30 seconds, and 60 seconds were defined and used from the start of block in order to gauge when the skin conductance responses disappeared, which was the definition of a successful block. We tracked this identical duration in time before the start of block to study what the lowest normal activity was in the affected extremity before the block for each individual. Moreover, the derivate of the skin conductance was obtained for these different time periods with the lowest number of skin conductance responses before and after the block for the different analyzing windows to study how the derivate of the skin conductance curve changed after the block.

Monitoring Clinical Assessment of Signs as a Measure of Sympathetic Block Assessment

Clinical assessment of signs included 1) clinically visible hyperemia, 2) clinically visible engorgement of veins, and 3) subjective warmth and temperature difference resultant of the comparison of the bilateral lower extremities as assessed by inspection and palpation. These clinical evaluations were performed every five minutes until 20 minutes postprocedure (Table 4). A score of 0–3 was assigned based on the clinical assessment values (Table 4). Specifically, a score $\geq$ 1 (i.e., mild difference) for each of the three parameters of clinical assessment was used as an indicator of successful sympathetic block.

These clinical evaluations were not studied each minute, but every five minutes until 20 minutes after the procedure for practical clinical feasibility reasons (Table 4).

The current limited evidence for using these traditional methods is presented (Table 5). The level of evidence was graded based on the reference by Xu et al. [16].

Table 3 Skin conductance graph visual observational scale is assessed to quickly evaluate and determine when the block starts work in real time; a reading of 2 will indicate a successful sympathetic block when there are 0.00 skin conductance responses in the 15-second analyzing window

0	No visible change in real-time graph
1	Questionable change in graph
2	Definite and easily recognizable change in graph defined as the skin conductance responses per second where 0.00 in a real-time 15-second time window

Table 4 Clinical assessment of signs is divided into 3 categories and was made with left and right comparison, with inspection and palpation; at least 1 (mild) change was considered a complete sympathetic block in all of the modalities

i. Clinically visible hyperemia, a score of 1 or above will be considered indication of complete sympathetic block
ii. Clinically visible engorgement of veins, a score of 1 or above will be considered indication of complete sympathetic block
iii. Subjective temperature difference, a score of 1 or above will be considered indication of complete sympathetic block

0	No differences
1	Mild
2	Moderate
3	Significant

Statistics

A clinically meaningful difference in time to indication of successful block between traditional and skin conductance measurement was taken to be five minutes (300 seconds). Assuming a standard deviation of 180 seconds, 10 sympathetic blocks and 10 stellate ganglion blocks would provide 80% power to detect a 300-second difference in time to indication of successful block between SCM and each of the six traditional measures at a Bonferroni-corrected alpha level of 0.004 (0.05 divided by 12 comparisons). The protocol was subsequently amended to include only lumbar sympathetic blocks to standardize the procedural technique, which allowed for over 99% power to detect the desired effect size at a Bonferroni-corrected alpha level of 0.008 (0.005 divided by six comparisons).

Continuous variables are presented as means with standard deviations or medians with first and third quartiles, depending upon the distribution of the data. Categorical variables are presented as counts and percentages. Kaplan-Meier curves were constructed to show the proportion of patients not yet displaying evidence of sympathetic blockade based on SCM and each of the traditional methods (Figure 4). A Cox proportional hazards model was used to compare each traditional method to SCM using a marginal approach with a working independence assumption to account for the correlation between measurements on the same patient.

The skin conductance responses were assessed on only the affected extremity. Therefore, the values before the block were compared with the values after the block offline in 20 registrations to explore the validity and the reliability of the method. In the same time period before and after the block, the minimum levels of skin conductance responses per second were studied. The length of the time period was defined by the time point at which the block started to work; that is, the SCM responses per second were 0.00, for analyzing windows of 15 seconds, 30 seconds, and 60 seconds. Regression based on the generalized estimating equations (GEE) approach was used to compare the difference in lowest peak value, and the difference in lowest average rise time before and after block dose administration. GEE was also used to evaluate the difference in time to start of decline in the SCM curve and difference in time to disappearance of peaks after test dose administration between 15-, 30-, and 60-second measurement windows. The GEE approach was used to account for lack of independence between measurements obtained from multiple blocks performed on the same patient. All statistical hypothesis tests were two-sided, with Bonferroni-adjusted P values of less than 0.05 defined as statistically significant. Statistical analyses were performed with SAS version 9.3 (SAS Institute, Cary, NC, USA).

Results

The 13 patients included had a mean ± SD age of 54 ± 13 years, body mass index (BMI) of 26 ± 3 kg/m^2, and 39% were female. There were 25 blocks in total, where seven patients received one block, three patients received two blocks, and three patients received four blocks. The SCM (Figure 2) and the temperature with pulse amplitude were displayed at two different monitors. All traditional methods of determining the achievement of sympathetic block had substantially smaller odds of indicating successful block compared with the observational skin conductance responses tested by the SCM in real time ($P \leq 0.011$) (Table 6 and Figure 4). Further, the observational SCM was the only method that indicated successful block for all patients within the

Table 5 Assessment of complete sympathetic block by using the skin conductance monitor, the plethysmography (wave form amplitude), bilateral thermometry, unilateral thermometry, subjective temperature difference, clinically visible engorgement of veins, clinically visible hyperemia, and the level of evidence graded based on the reference by Xu et al. [16] when using these methods

Monitor	Reference	Level of evidence	Comments
Skin conductance monitor	Kazansky et al. [8]	2C+	Twelve patients were studied, 11 obtained block according to the skin conductance monitor
Plethysmography (waveform amplitude)	Toshniwal et al. [6]	2C+	Thirty-three patients with complex regional pain syndrome 1 of upper extremity were assigned to either continuous stellate ganglion block or continuous infraclavicular brachial plexus block for 1 week; both groups showed clinically significant improvement after block according to the increase in the amplitude (waveform reading of 10) of the pulse wave assessed by the plethysmography within 30 minutes
	Beene and Eggers [7]	0	One patient was examined and showed increase in the amplitude of the pulse wave assessed by the plethysmography together with significant relief of pain after stellate ganglion block
Thermometry	Stevens et al. [5]	2C+	Fifty-nine stellate ganglion blocks were performed; successful sympathetic block was considered when: 1) change in ipsilateral and contralateral temperature of 1.5 °C; 2) Horner's syndrome present; and 3) sweat test changed from positive to negative; 36% of the blocks met all three criteria
	Park et al. [4]	2C+	Of 185 lumbar sympathetic blocks, successful block was considered to have occurred when changes in the ipsilateral temperature between preblock and postblock were ≥ 2 °C; the rate of 0.4 °C/min with a sensitivity of 89.5% and a specificity of 91.8% was achieved within approximately five minutes of the injection of local anesthetic
Clinically visible signs; engorgement of veins and clinically visible hyperemia	Toshniwal et al. [6]	2C+	Thirty-three patients with complex regional pain syndrome 1 of upper extremity were assigned to either continuous stellate ganglion block or continuous infraclavicular brachial plexus block for one week; both groups showed clinically significant improvement in edema score and range of motion all upper extremity joints when compared with the baseline and reported less neuropathic pain

observation period (Table 6 and Figure 4). Moreover, when the SCM readings were assessed offline on the affected extremity before and after the block using analyzing windows of 15 seconds, 30 seconds, and 60 seconds, the differences were statistically significant for all the windows studied ($N = 20$, $P < 0.005$) (Table 7). The mean of the lowest values before the block was similar for all analyzing windows, 15 seconds, 30 seconds, and 60 seconds with, respectively, 0.07 ± 0.08, 0.05 ± 0.06, and 0.07 ± 0.06 skin conductance responses per second (Table 7). Interestingly, when using the same window as the observational SCM score, 15 seconds, the skin conductance responses per second were 0.00 after 28.9 ± 21.4 seconds, which was a statistically significantly shorter time than using 30 seconds or 60 seconds, which were 74.1 ± 46.9 seconds and 150.6 ± 89.4 seconds, respectively, to reach 0.00 skin conductance responses ($P < 0.001$) (Table 8). Moreover, the derivate of the skin conductance curve changed statistical significance to negative only for the 30-second and 60-second analyzing windows from before to after the block.

Discussion

All the traditional methods of determining how fast the achievement of sympathetic block occurred had substantially smaller odds of indicating successful block in the next moment compared with the observational skin conductance testing by the SCM when validating these methods at one-minute intervals. Further, the observational SCM was the only method that indicated successful block for all patients (100%) within the observation period (i.e., skin conductance responses

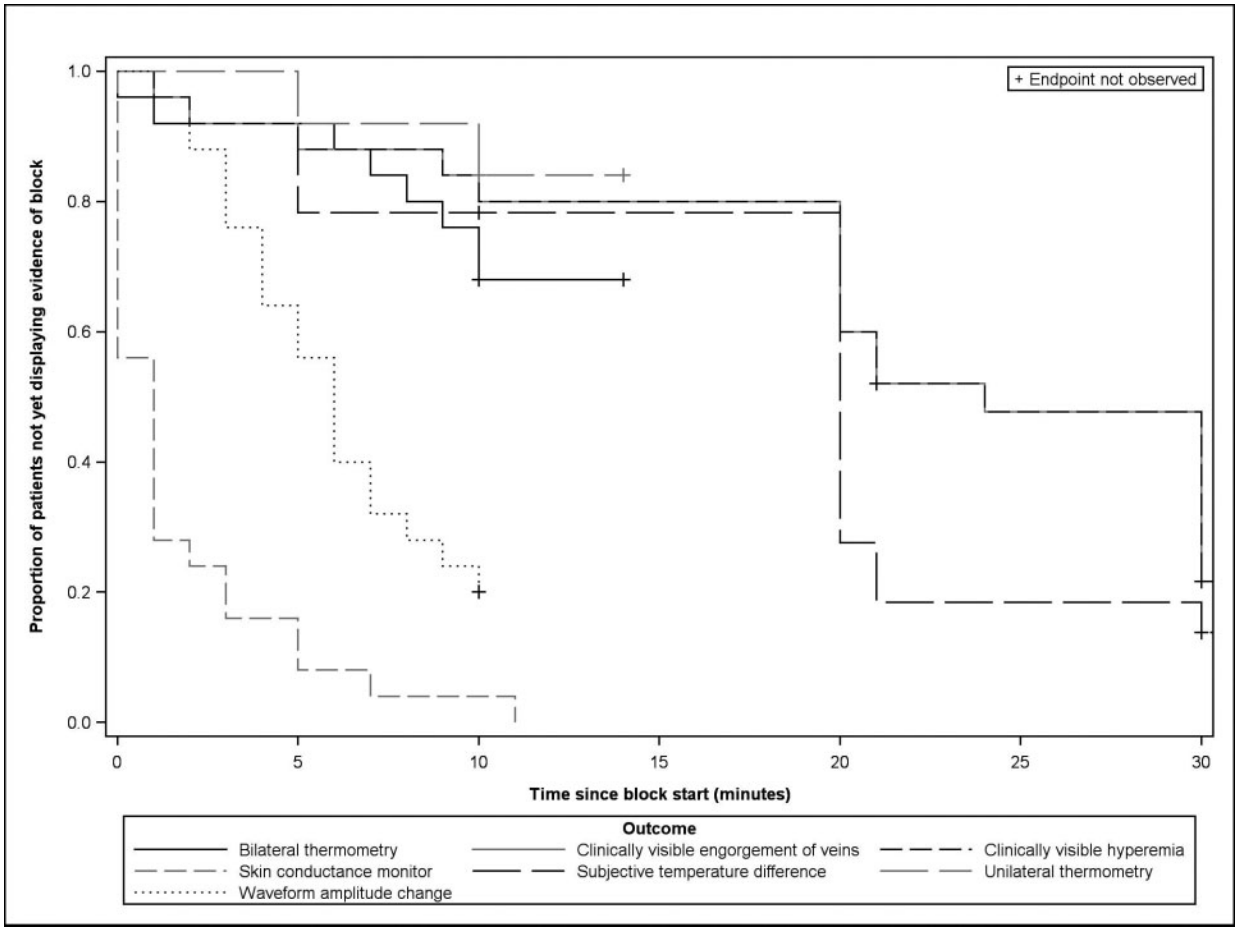

Figure 4 The observational real-time skin conductance monitor (SCM) compared with traditional assessment tools for sympathetic nerve blocks when assessed each minute or each five minutes. All traditional methods of determining the achievement of sympathetic block had substantially smaller odds of indicating successful block in the next moment compared with the observational skin conductance responses tested by the SCM in real time ($P < 0.001$). When analyzing the skin conductance responses in real time each minute, all patients had successful sympathetic block (defined as the skin conductance responses per second of 0.00 in a real-time 15-second window) within 10 minutes, which was statistically different than the traditional sympathetic block assessment tools ($P < 0.001$).

Table 6 The skin conductance monitor compared with the traditional assessment tools to show sympathetic block; number of end points not observed show the patients who did not receive the successful sympathetic block

	N	Count (%) no end point observed	HR (95% CI)	*P*
Skin conductance monitor	25	0	Reference	—
Waveform amplitude change from start of block	25	5 (20)	0.29 (0.14–0.63)	0.011
Bilateral thermometry	25	17 (68)	0.08 (0.04–0.17)	<0.001
Unilateral thermometry	25	21 (84)	0.04 (0.01–0.11)	<0.001
Subjective temperature difference	25	4 (16)	0.06 (0.02–0.17)	<0.001
Clinically visible engorgement of veins	25	6 (24)	0.04 (0.01–0.13)	<0.001
Clinically visible hyperemia	25	6 (24)	0.04 (0.01–0.13)	<0.001

CI = confidence interval; HR = hazard ratio.

Table 7 Differences in the lowest skin conductance responses (SCR) per second values, before and after the sympathetic block, with different analyzing time windows

Comparison	N	Time window, seconds	Mean ± SD	*P*
Difference in lowest SCR/sec value before and after block start	20	15	0.07 ± 0.08	0.013
Difference in lowest SCR/sec value before and after block start	20	30	0.05 ± 0.06	0.003
Difference in lowest SCR/sec value before and after block start	20	60	0.07 ± 0.06	0.001
Difference in lowest average rise time (microsiemens/sec) before and after block start	20	15	0 ± 0.03	0.999
Difference in lowest average rise time (microsiemens/sec) before and after block start	20	30	−0.01 ± 0.02	<0.001
Difference in lowest average rise time (microsiemens/sec) before and after block start	20	60	−0.01 ± 0.02	<0.001

SCR = skin conductance response.

Table 8 The time period from the sympathetic block start time until the skin conductance curve starts to decline; time period from the sympathetic block start time until the skin conductance responses per second is 0.00, defined as the complete sympathetic block

	15-second window		30-second window		60-second window		15- vs 30-second window	30- vs 60-second window	15- vs 60-second window
Measure	N	Mean ± SD	N	Mean ± SD	N	Mean ± SD		*P*	
Time between block start and start of decline, seconds	20	59.7 ± 69.5	20	56.1 ± 54.0	20	71.3 ± 35.1	0.999	0.999	0.560
Time between block start and disappearance of SCR/sec	20	28.9 ± 21.4	20	74.1 ± 46.9	19	150.6 ± 89.4	<0.001	<0.001	<0.001

SCR = skin conductance response.

disappeared after the block in all patients tested). The reliability was assessed by comparing the minimum skin conductance responses per second and the rise time of the curve before and after block start time point. Analysis of the offline registrations of SCM to validate the reliability of SCM demonstrated that SCR disappeared 28 ± 21 seconds after, when using the same analyzing window, 15 seconds, as used in the observational SCM test. Furthermore, when the lowest SCM values (skin conductance responses per second) were studied before the block, they were statistically different from the responses per second after the block. If the observational validation periods had been each 30 seconds and not each one minute, the sympathetic block probably would have been assessed earlier, also according to the observational SCM test.

Interestingly, when clinically observing the skin conductance curve graph, it was obvious that there was a sharp decline after the block (Figure 3). When studying the derivate of the curve for the different analyzing windows before and after the block, only the 30-second and 60-second analyzing windows showed statistically significant decreases. One may speculate that by reducing the Med-Storm software threshold value for defining the derivate of the curve to be negative, a statistically significant value for the 15-second analyzing window would also be obtained.

It has been questioned whether the patients in need of sympathetic block might have increased skin sympathetic nerve activity in the affected extremity. According to this study, the preblock skin sympathetic nerve activity that is mirrored by skin conductance responses per seconds was within normal range. The lowest levels were about 0.06 responses per second, which according to other studies show normal activity in relaxed patients [13].

The skin conductance response per second are assessed on the plantar aspect of the affected foot in

this study: The skin sympathetic nerve activity consists of four nerve types: vasoconstrictor, vasodilator, sudomotor, and pilomotor nerves [17]. The skin sympathetic sudomotor nerves have acetylcholine acting on muscarinic receptors, which are blocked by atropine. They increase in activity during hyperthermia and lead to release of sweat in the body [17], except palmary and plantar where the skin sympathetic sudomotor activity is released during emotional stress stimuli [15,18] and not influenced by environmental temperature [15,18]. Bini uses microneurography and monitors changes in skin resistance palmary, showing that temperature between 22°C and 40°C does not influence the sudomotor activity [15].

Multiple factors like sweating, status of the epithelium, and humidity of the skin will influence the mean skin conductance level, but not the "skin conductance responses per second" that was used in this study [15,17,18].

Common mode rejection and differential amplifiers were integrated in the skin conductance monitor used in this study. The threshold we use to define a skin conductance response is 0.005 microsiemens. After going through many hundreds of recordings manually, we have found that the threshold of 0.005 microsiemens is suitable to define a skin conductance response without any significant influence from noise. The way we performed these analyses is described for the prototype skin conductance monitor where we used a threshold value of 0.02 microsiemens [19].

The candidates for diagnostic/therapeutic sympathetic blocks are those patients with presentation of neuropathic pain mainly in the limbs, head, and neck. Lumbar sympathetic blocks are performed for lower extremity neuropathic pain conditions, and stellate ganglion blocks are performed for upper extremity, head, and neck neuropathic pain conditions. Some of the clinical conditions that may benefit from sympathetic blockade are either for pain relief in clinical conditions such as complex regional pain syndrome (CRPS), phantom limb pain, acute herpes zoster, and cancer patients with involvement of the sympathetic nervous system, or to improve blood flow in vasospastic disorders such as Raynaud disease, early frostbite, and obliterative arterial disease that is not suitable for vascular surgery [11].

It is recommended that the interdisciplinary approach is the most effective therapy in these patients, including pharmacologic, physical therapy with rehabilitation, psychological support, and interventional therapies [16,20]. Sympathetic blocks are also considered part of interventional therapy. The advantage of sympathetic blocks, despite the risks associated with them is that they help to differentiate SMP from SIP and may help reverse the disease process in a subset of patients with neuropathic pain [11]. There are also more invasive alternatives such as neuromodulation therapy with spinal cord stimulation [20].

This study examined lower extremity lumbar sympathetic blocks. Theoretically, this may also be valid for upper extremity sympathetic blocks, but this needs further exploration. In this study, the SCM is shown to be superior to other traditional ways of monitoring to determine whether a successful sympathetic block is achieved after administration of lumbar sympathetic blocks. As an objective end point, SCM has been shown to determine the achievement of successful sympathetic blocks significantly faster. In this study, all methods, except observation of clinical signs sympathectomy, were assessed in real time. Although the numeric values were measured and compared in this study for research purposes, by purely observing the trend of skin sympathetic activity in a real-time graph on SCM, the practitioner performing the block could easily determine whether a potentially successful sympathetic block is starting to work within seconds (Figure 3). One limitation was that the assessments were each minute and could beneficially be narrowed to 30 seconds to improve the reaction time for the SCM. Furthermore, the study included only lower extremity sympathetic blocks, and all procedures were performed by only one interventional pain management physician. The study design made it impossible to blind the participants. Another limitation of this study was that traditional measures such as clinically visible hyperemia, clinically visible engorgement of veins, subjective skin temperature difference, unilateral and bilateral comparative thermometry measurements, and change in waveform amplitude in pulse oximetry plethysmography were used to validate the skin conductance device. Although it would have been possible to assess microneurography in the blocked nerve and compare this method with the skin conductance device, the use microneurography was outside the scope of this study because of the invasiveness and complexity of this method.

Med-Storm Innovation's software was not developed to assess small decreases in the skin conductance curve when the derivate of the curve turns negative. All the patients studied showed a visual and recognizable decrease in the skin conductance curve when the block started to work (Figure 3). One improvement in Med-Storm Innovation's software could be to define the decrease in the curve as negative for smaller changes. Then, both the skin conductance responses and the derivate of the curve could be used to define the successful block. Currently, the SCM has the possibility to monitor only one extremity in real time. Hence, it would have been ideal to have dual-channel SCM equipment to monitor both extremities in real time for comparison purposes, between the affected extremity undergoing the block and the unaffected one as a reference standard.

To conclude, this preliminary study suggests SCM as a more reliable and rapid response indicator of a successful sympathetic blockade when compared with traditional monitors. As a noninvasive monitor with easy clinical applicability, it has a potential to improve procedural accuracy and efficiency during performance of lumbar sympathetic blocks.

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