Association of Peripheral Autonomic Neuropathy and Sympathetic Skin Response in the Patients with Diabetic Polyneuropathy: A Pilot Study in Thailand

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Objective: *Investigate the association of peripheral autonomic neuropathy (PAN) symptoms and sympathetic skin response (SSR) in the patients with diabetic polyneuropathy (DPN) as a pilot study in Thai patients.*
Material and Method: *Sixty-eight DPN patients' limbs, conducted retrospectively between June 2012 and January 2014, were included and divided into two groups, 48 abnormal SSR limbs and 20 control limbs, respectively. All clinical data, demographic characteristics, PAN symptoms, and other associated factors were compared and analyzed.*
Results: *A comparison between abnormal and normal SSR groups in DPN limbs showed no significant differences of age, gender, body mass index (BMI), comorbidity of hypertension and dyslipidemia, duration of PAN symptoms, associated neurological signs of impaired light touch sensation, and muscle weakness or atrophy (p-value >0.05). The PAN symptoms, either anhidrosis or hypohidrosis, and hyporemia showed significantly correlated to abnormal SSRs (p-value = 0.003 and 0.028, respectively). Among symptoms of somatic small fiber neuropathy (SFN), burning paresthesia, and reduced thermal sensation revealed significantly correlated to abnormal SSRs (p-value = 0.032 and 0.021, respectively). Moreover, the study showed that history of fall in six months, history of foot ulcer in three months, impaired pinprick sensation, impaired proprioceptive sensation, decreased deep tendon reflex, burning paresthesia, reduced thermal sensation, either anhidrosis or hypohidrosis, and hyporemia had significantly associated with the occurrence of abnormal SSRs (p-value <0.05).*
Conclusion: *There was the association between PAN symptoms and abnormal SSRs in DPN patients' limbs. These data support the recent findings of several studies that abnormal SSR has the association with history of foot ulceration in diabetic patients. It warrants further investigation into the clinical utility of the SSR in diabetic patients.*

Keywords: *Sympathetic skin response, Autonomic neuropathy, Peripheral neuropathy, Small fiber neuropathy, Diabetic mellitus*

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Peripheral sensorimotor neuropathy and autonomic neuropathy are the most common neuropathies in patients with diabetic mellitus (DM), with a prevalence of 30 to 70%[1-3]. The diabetic autonomic neuropathy (DAN), either clinical or subclinical, is more difficult to diagnose or probably undiagnosed[4]. Several studies demonstrated that diabetic peripheral neuropathy (DPN) does not necessarily coexist with DAN in diabetic patients[1,5-7]. For autonomic innervation of the peripheral nervous system (PNS), it is known that autonomic nerves consist of small myelinated and unmyelinated fibers[3,4]. They are present in skin (somatic fibers and sudomotor fibers), peripheral nerves, and organs, which involve the autonomic nervous system (ANS)[8]. Damage of theses fibers is characterized by small fiber neuropathy (SFN)[8-10].

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Peripheral autonomic neuropathy (PAN) results in the atrophy of sweat glands and decreased sudomotor response that may affect the skin's suppleness and flexibility that prevent skin cracks and ulceration and may also reduce sweating, leading to abnormal skin conditions, such as dryness, fissures, and blisters[11-13]. The prevalence of PAN, as determined by the presence of two or more clinical signs, has recently been estimated to affect about 40% of diabetic patients aged 40 to 70 years[14,15]. PAN is usually evaluated through sweat function, using the sympathetic skin response (SSR), or by quantitative sudomotor axon reflex test (QSART)[11,15,16]. Clinically high-special skill and instruments, such as the QSART, skin vasomotor reflex (SVR) test, or microneurographic study, are performed in relatively few research or medical centers[1,16-18], and this subject is still controversial. These methods require specialized training and are time-consuming procedures, not widely available. Therefore, the diagnosis or assessment of PAN is difficult and needs more specific autonomic

markers for analysis[18-20]. Moreover, this analysis lacks a reliable quantitative method for clinical practice. An important limitation is the insufficiency of the other standard diagnostic methods or techniques accepted to investigate definitely autonomic SFN[16,18,21-25].

SSR is a simple, non-invasive test of skin sympathetic activity, which can be readily performed in most electrodiagnostic (EDX) laboratories to explore the effector organ response involving SFN. It is a reflex change in the sweat related electrical potential of an area of skin as elicited by various unexpected adrenergic stimuli, such as an electrical shock to a somatic nerve[8,11,16,17]. However, it does not reflect a selective post-ganglionic dysfunction[18,26,27]. Nevertheless, SSR is a widely available and inexpensive method for assessing small fiber sudomotor function in PAN[8,9,15]. Therefore, this method is suitable to investigate PAN. Because there is no published study in Thai patients, the present study aimed to investigate the association of PAN symptoms and SSR tests in the Thai patients with DPN.

Material and Method

Participants

Twenty consecutive diabetic participants with 80 limbs were recruited to the study. They were obtained from the EDX laboratory of the Faculty of Medicine at Naresuan University. The present study was conducted retrospectively between June 2012 and January 2014.

Study protocol

According to the study protocol, all recruited participants' limbs were included and divided in two groups. Group I was the abnormal SSR group. The patients' limbs (n = 48 from 12 diabetic patients) diagnosed DPN with abnormal SSR findings using clinical assessment and EDX method. The inclusion criteria were 1) patients' limbs diagnosed as DPN were enrolled by history of known diabetes, 2) there was EDX evidence of mixed sensorimotor polyneuropathy, 3) presented at least one of clinically PAN or somatic SFN symptoms, 4) the SSR findings were obtained from all DPN limbs, and 5) examined by the same physiatrist. A history of limb surgery or trauma, peripheral nerve injury or neuropathy, plexopathy/plexitis, and cervical or lumbosacral radiculopathy were excluded. According to variability of polyneuropathy, diabetic patients with EDX findings exhibiting a chronic inflammatory demyelinating polyneuropathy (CIDP) or other advanced DPN were excluded because these abnormalities may confound the association between the PAN symptoms and SSR findings.

The second group was the control group. They were the patients' limbs (n = 20 from 5 diabetic patients) diagnosed as having normal SSR findings by the EDX evidence.

Evaluation of PAN, SSR, and DPN

The clinical diagnosis of PAN was based on one or more of the follows, 1) skin sodomotor symptoms, including anhidrosis or hypohidrosis, and hyperhidrosis, 2) skin vasomotor symptoms, including hyporemia and hyperemia. In addition, the diagnosis of somatic SFN was based on one or more of the following: burning paresthesia, allodynia, and reduced thermal sensation[9,10,21].

The SSR parameters were established by the presence or absence of a SSR waveform. The absence of a SSR waveform was determined to be abnormal[8,18]. The SSR tests were performed using a Micromed electromyography machine in a supine position and relax in a warm and quiet room. The skin temperature of the hands and feet was maintained at or above 32°C. The room temperature was kept at 20 to 25°C. Active surface electrodes were placed in the center of palm and sole, and reference electrodes were placed on the dorsum of hand and foot. The stimulus consisted of a brief square wave electrical pulse, duration of 0.2 ms, intensity 15 to 30 mA, filter settings of 0.6 to 60 Hz, time interval of 1 second/division, sensitivity of 0.1 to 1.0 mV/cm, and the total analysis time was set at 10 seconds. The nerve stimulations of bilateral median nerves at wrist and tibial nerves in the ankles were applied to all four limbs consecutively. The SSR stimulus was performed four repetitions per test[8,15,18,22]. The SSR characteristics were measured and recorded.

The DPN was diagnosed by EDX evidences of mixed sensorimotor polyneuropathy in known diabetic patients[14,28,29].

Fig. 1 showed a flow chart of all recruited participants' limbs. The study was approved by the Ethics Committee of the Naresuan University Institutional Review Board (IRB No. 229/57).

Statistical analysis

Statistical analysis was performed using SPSS for Windows version 17.0. The data and each EDX parameter were analyzed using descriptive statistics, including mean and standard deviation (SD). Numbers and percentage were also presented for clinical and demographic characteristics. Comparison

of demographic data and all EDX parameters between groups of patients' limbs were evaluated by Mann-Whitney U, Fisher's exact, or Chi-square test. Spearman correlation coefficient and binary logistic regression were applied to determine independent correlation and association between the PAN and SSR in DPN limbs. Crude odds ratio (crude OR) with a 95% confidence interval (95% CI) was used to measure strength of the association. A *p*-value <0.05 was considered statistically significant.

Results

Five DPN patients with normal SSR (n = 20 limbs) with a mean age of 56.8±6.7 years served as controls, and 12 DPN patients with abnormal SSR (n = 48 limbs) with a mean age of 58.1±7.3 years, respectively. Three DPN patients were excluded from the study, consisted of two patients that had EDX evidence of bilateral carpal tunnel syndrome (CTS) and one patient that had CIDP. Compared with the controls, there was no significant difference of age, gender, body mass index (BMI), comorbidity of hypertension and dyslipidemia, duration of PAN symptoms, associated neurological signs of impaired light touch sensation, and muscle weakness or atrophy. History of fall in six months[30], history of foot ulcer in three months[31], impaired pinprick sensation, impaired proprioceptive sensation, decreased deep tendon reflex showed markedly significant differences (*p*-value = 0.005, 0.001, <0.001, 0.003, and <0.001, respectively). The comparison of these demographic and clinical characteristics between the abnormal and normal SSRs is summarized in Table 1.

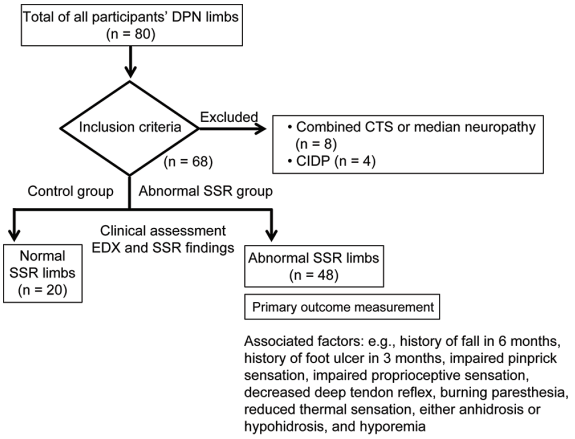

Fig. 1 Flow chart of all recruited participants' limbs.

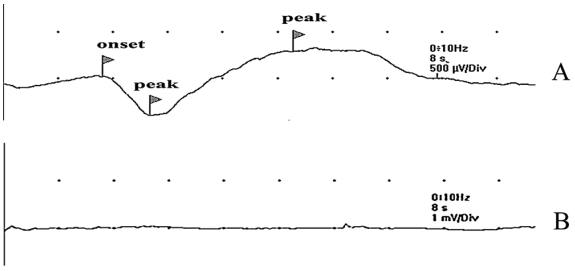

Fig. 2 Examples of the SSR waveforms were demonstrated (A) Presence of SSR waveform or normal SSR, and (B) Absence of SSR waveform or abnormal SSR.

The correlation between PAN symptoms and SSR findings in Table 2, either anhidrosis or hypohidrosis, and hyporemia had significantly correlated to abnormal SSRs (*p*-value = 0.003 and 0.028, respectively). However, there was no significant correlation between hyperhidrosis and abnormal SSR (*p*-value = 0.901). Moreover, there was no DPN limbs presented hyperemia in both abnormal and normal SSR groups.

Among the symptoms of somatic SFN, Table 3 showed that burning paresthesia and reduced thermal sensation had significantly correlated to abnormal SSRs (*p*-value = 0.032 and 0.021, respectively), but the presence of allodynia showed no significant correlation (*p*-value = 0.270).

The binary logistic regression analysis of the neurological signs and symptoms related to abnormal SSRs, these results showed that history of fall in six months, history of foot ulcer in three months, impaired pinprick sensation, impaired proprioceptive sensation, decreased deep tendon reflex, burning paresthesia, reduced thermal sensation, either anhidrosis or hypohidrosis, and hyporemia had significantly associated with the occurrence of the abnormal SSR findings (*p*-value <0.05) as summarized in Table 4.

Discussion

PAN is one of the most common neuropathies in diabetic patients. It is a frequently coexisting neuropathic disorder with DPN. However, there is controversy about the gold standard diagnostic methods in clinical practice[16,18,21-25]. Routine EDX studies conventionally test function of the large myelinated fibers and are mostly normal in the patients with somatic or autonomic SFN[8,22]. Several previous studies demonstrated that sensitivity as well as specificity of SSR is considered to be low[3,8,21,22,24,25]. However, some authors have argued that the SSR is most usefully to investigate sweat gland dysfunction or foot ulceration in diabetic patients[11,12,14-16]. For the present study, the results showed that the absence of

Table 1. Comparison of demographic and clinical characteristics between abnormal and normal sympathetic skin response in diabetic patients (n = 17)

	SSR		*p*-value
	Abnormal (n = 12)	Normal (n = 5)	
Limbs (n)	48	20	
Age (years), mean ± SD	58.1±7.3	56.8±6.7	0.830
Female, n (%)	6 (50.0)	4 (80.0)	0.338
BMI (kg/m^2), mean ± SD	27.4±3.4	25.6±3.1	0.286
Comorbidity, n (%)			
Known hypertension	8 (66.7)	2 (40.0)	0.593
Known dyslipidemia	7 (58.3)	4 (80.0)	0.600
Duration of PAN symptoms (months), median (range)	8 (4 to >60)	8 (4 to 12)	0.283
History of fall in 6 months†, n (%)	10 (83.3)	3 (60.0)	0.005
History of foot ulcer in 3 months‡, n (%)	7 (58.3)	1 (20.0)	0.001
Associated neurological signs (limbs), n (%)			
Impaired pinprick sensation (yes)	48 (100.0)	11 (55.0)	<0.001
Impaired light touch sensation (yes)	35 (72.9)	10 (50.0)	0.093
Impaired proprioceptive sensation (yes)	20 (41.7)	1 (5.0)	0.003
Decreased deep tendon reflex (yes)	48 (100.0)	14 (70.0)	<0.001
Muscle weakness or atrophy (yes)	20 (41.7)	6 (30.0)	0.422

SSR = sympathetic skin response; BMI = body mass index; PAN = peripheral autonomic neuropathy
† History of fall in 6 months was defined as at least one self-reported fall in the last six months of duration
‡ History of foot ulcer in 3 months was defined as at least one history of foot ulceration occurred in the last three months of duration

Table 2. Correlation between symptoms of peripheral autonomic neuropathy and abnormal sympathetic skin response in diabetic limbs (n = 68)

PAN symptoms	r_s	95% CI		*p*-value
		Lower	Upper	
Anhidrosis or hypohidrosis	0.361	0.127	0.629	0.003
Hyperhidrosis	0.015	-0.228	0.258	0.901
Hyporemia	0.267	0.026	0.521	0.028

PAN = peripheral autonomic neuropathy; r_s = Spearman correlation coefficient; 95% CI = 95% confidence interval

Table 3. Correlation between symptoms of somatic small fiber neuropathy and abnormal sympathetic skin response in diabetic limbs (n = 68)

Somatic SFN symptoms	r_s	95% CI		*p*-value
		Lower	Upper	
Burning paresthesia	0.261	0.020	0.514	0.032
Allodynia	0.136	-0.107	0.381	0.270
Reduced thermal sensation	0.279	0.039	0.534	0.021

SFN = small fiber neuropathy; r_s = Spearman correlation coefficient; 95% CI = 95% confidence interval

SSR was significant associated with the presence of history of foot ulceration (crude OR 2.364; 95% CI 0.797-3.932; *p*-value = 0.003). This finding supports the recent findings of other studies that abnormal SSR or sudomotor dysfunction may result in dryness of foot skin and has been significantly associated with foot ulceration[15,16]. However, some previous studies have not used the findings to explain the association between sudomotor dysfunction and foot ulcers in diabetes[32-37].

For the control group in the present study, the results demonstrated that all of DPN limbs were impaired pinprick and light touch sensations, but the results showed only about 50% of theses sensory impairments (55% of impaired pinprick sensation and 50% of light touch sensation) were presented abnormal SSRs. Because of the most common utilities of the SSR tests, they were recommended to detect the SFN more than large fiber neuropathy or mixed (small and large) fiber neuropathy[11,12,15,17,18,20]. According to the recent studies, they did not have enough data to demonstrate or identify the subtypes of peripheral neuropathy (e.g., pure SFN, pure large myelinated fiber neuropathy, or mixed (small and large) fiber neuropathy) involved with the risk factor of foot ulceration in diabetes[11-15,20]. Although sudomotor dysfunction is common in many subtypes of neuropathy (pure somatic or autonomic SFN and mixed fiber

Table 4. Binary logistic regression of associated factors related to abnormal sympathetic skin response in diabetic limbs (n = 68)

	Crude OR	95% CI		*p*-value
		Lower	Upper	
History of fall in 6 months	1.618	0.499	2.738	0.005
History of foot ulcer in 3 months	2.364	0.797	3.932	0.003
Impaired pinprick sensation	3.850	1.684	6.016	<0.001
Impaired proprioceptive sensation	2.608	0.517	4.699	0.015
Decreased deep tendon reflex	3.649	1.482	5.817	0.001
Burning paresthesia	1.327	0.071	2.582	0.038
Reduced thermal sensation	1.362	0.161	2.563	0.026
Anhidrosis or hypohidrosis	1.902	0.549	3.254	0.006
Hyporemia	1.266	0.105	2.426	0.033

Crude OR = crude odds ratio; 95% CI = 95% confidence interval

neuropathy), SSR is not the only the method to detect the sudomotor dysfunction or abnormality in peripheral SFN. Other techniques, such as the QSART, the thermoregulatory sweat test (TST), and the quantitative direct and indirect reflex test (QDIRT)[3,8,11,12,16-21] are more accurate diagnostic techniques for assessment of sudomotor function or SFN. Compared with the definitive diagnostic method, such as a skin biopsy, some previous studies of these techniques had demonstrated that QSART was capable of detecting peripheral SFN with both high sensitivity and specificity[16-18,21-25]. However, they had not yet been assessed in epidemiological or in randomized controlled trials (RCTs). These results should be considered a reference method for the detection of sudomotor dysfunction or SFN in further clinical and research studies[16-18,21-25,32,38-41]. In the present study, there were excluded, two patients had EDX findings of bilateral CTS and one patient had CIDP, respectively. This result supported the finding that diabetic patients can also develop CIDP. CIDP should be considered, especially in the patients with advanced DPN[42].

Either impaired pinprick or proprioceptive sensation, and decreased deep tendon reflex occurred significant differences between the abnormal and normal SSR groups (*p*-value <0.001, 0.003, and <0.001, respectively). These findings support the results of other previous studies, implying that these neurological signs are mostly associated with sudomotor dysfunction or abnormal SSRs because the abnormality of large myelinated fibers frequently coexists with small myelinated or unmyelinated fibers in patients with mixed fiber neuropathy[8,11-16,22-25,32,38-41].

Among the PAN symptoms, either anhidrosis or hypohidrosis, and hyporemia had significantly correlated to abnormal SSRs (*p*-value = 0.003 and 0.028, respectively). However, there was no significant correlation between the occurrence of hyperhidrosis and abnormal SSR (*p*-value = 0.901). This finding is controversial, it is suggested that the PAN symptoms of hyperhidrosis is the least likely to be associated with the abnormal SSR or sudomotor dysfunction. However, these results supported the several studies revealed that the hyperhidrosis is not characterized clinical diagnostic criteria for SFN[18,21-25].

According to the results of somatic SFN symptoms, burning paresthesia and reduced thermal sensation had significantly correlated to abnormal SSRs (*p*-value = 0.032 and 0.021, respectively), but the presence of allodynia showed no significant correlation to abnormal SSRs. These data imply that most of the somatic SFN symptoms are associated with the sudomotor abnormalities. In the present study, allodynia significantly showed no correlation to the abnormal SSR (*p*-value = 0.270). However, the previous studies also demonstrated that SSR had low sensitivity as well as specificity in the diagnosis of SFN[11,16,21-25]. They suggested that high accuracy diagnostic tools, such as QSART, TST, and QDIRT should be considered to diagnose SFN more than the SSR test.

The binary logistic regression analysis of the neurological signs and symptoms related to abnormal SSRs, these results showed that history of fall in six months, history of foot ulcer in three months, impaired pinprick sensation, impaired proprioceptive sensation, decreased deep tendon reflex, burning paresthesia,

reduced thermal sensation, either anhidrosis or hypohidrosis, and hyporemia had significantly associated with the occurrence of the abnormal SSR findings (p-value <0.05). Furthermore, this analysis showed both PAN and somatic SFN symptoms had significantly associated with abnormal SSRs (p-value <0.05). It suggests that SSR should be recommended to detect autonomic or somatic SFN.

As a limitation of the present study, there was no comparative study of the high accuracy diagnostic tools, as the gold standard methods to diagnose PAN and somatic SFN symptoms. Although the skin biopsy to determine SFN, used with the pan-neuronal marker against the protein gene product (PGP) 9.5 is considered the gold standard test as the reliable method of intraepidermal nerve fibers (IENF) density analysis, it is the extreme gold standard technique to obtain the definitive diagnosis of both PAN and SFN because it is a very invasive technique and so more useful in the animal models than human studies or clinical practice[2,11,16,18,21,25-28,38-41]. Another limitation is the small numbers for statistical analysis in each subgroup of the DPN patients. However, there were not enough data to support the role of SSR to diagnose PAN or SFN in DPN. Finally, the utility role of SSR in clinical practice is still controversial.

Conclusion

These results demonstrated that there was the association between PAN symptoms and abnormal SSRs in DPN patients' limbs. These data support the recent findings of several studies that SSR has the association with history of foot ulceration in diabetic patients. It warrants further investigation into the clinical utility of the SSR in diabetic patients.

What is already known on this topic?

The diagnosis or assessment of PAN is more difficult to ascertain. SSR is a simple, non-invasive test of skin sympathetic activity to explore the effector organ response involving SFN, but it does not reflect a selective post-ganglionic dysfunction[18,26,27]. Several studies demonstrated that sensitivity as well as specificity of SSR is considered to be low[3,8,21,22,24,25]. However, some authors have argued that the SSR is most usefully to investigate sweat gland dysfunction or foot ulceration in diabetic patients[11,12,14-16]. Some previous studies have not used the findings to explain the association between sudomotor dysfunction and foot ulcers in diabetes[32-37]. To confirm and clarify the utility role of SSR in diagnosis of the PAN and somatic SFN are essential.

What this study adds?

Findings of the present study were in agreement with the several previous studies that SSR is most usefully to investigate sweat gland dysfunction or foot ulceration in diabetic patients[11,12,14-16]. For the present study, the results showed that the abnormal SSR was significantly associated with the history of foot ulceration (crude OR 2.364; 95% CI 0.797-3.932; p-value = 0.003). This finding again supports the recent findings of several studies that abnormal SSR or sudomotor dysfunction has significantly associated with foot ulceration[15,16]. Furthermore, the present study showed both PAN and somatic SFN symptoms had significantly associated with the abnormal SSRs (p-value <0.05). It suggested that SSR should be recommended to detect autonomic or somatic SFN in the clinical practice.

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Potential conflicts of interest

None.

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ความสัมพันธ์ของ peripheral autonomic neuropathy และผลการตรวจ sympathetic skin response ในผู้ป่วยเบาหวานที่มีภาวะเส้นประสาทเสื่อมหลายเส้น: การศึกษานำร่องในประเทศไทย

ชินภัทร์ จิระวรพงศ์

วัตถุประสงค์: เพื่อสืบค้นความสัมพันธ์ของอาการของ PAN และผลการตรวจ SSR ในผู้ป่วยเบาหวานที่มีภาวะเส้นประสาทเสื่อมหลายเส้น เป็นการศึกษานำร่องในผู้ป่วยไทย

วัสดุและวิธีการ: วิเคราะห์ผลการตรวจรยางค์แขนขามีภาวะเส้นประสาทเสื่อมหลายเส้นจากผู้ป่วยเบาหวาน จำนวนทั้งสิ้น 68 ข้าง แบ่งเป็น รยางค์ที่มีความผิดปกติของ SSR จำนวน 48 ข้าง และรยางค์ที่มี SSR ปกติ จำนวน 20 ข้าง เก็บข้อมูลย้อนหลังระหว่างเดือนมิถุนายน พ.ศ. 2555 ถึง มกราคม พ.ศ. 2557 โดยนำข้อมูลพื้นฐานทางคลินิก ลักษณะทางประชากร อาการของ PAN และปัจจัยต่าง ๆ มาเปรียบเทียบ และวิเคราะห์ผล

ผลการศึกษา: ผลการเปรียบเทียบระหว่างกลุ่มที่มีและไม่มีความผิดปกติของ SSR พบว่า ไม่มีความแตกต่างของอายุ, เพศ, ดัชนีมวลกาย, โรคประจำตัว ได้แก่ ความดันโลหิตสูง และภาวะไขมันในเลือดสูง, ช่วงเวลาที่มีอาการของ PAN, อาการแสดงร่วมทางระบบประสาท ได้แก่ impaired light touch sensation และ muscle weakness หรือ atrophy (p-value >0.05) สำหรับอาการของ PAN พบว่า ทั้งอาการ anhidrosis หรือ hypohidrosis, และ hyporemia สัมพันธ์กับ SSR ที่ผิดปกติอย่างมีนัยสำคัญทางสถิติ (p-value มีค่าเท่ากับ 0.003 และ 0.028 ตามลำดับ) ส่วนอาการของ somatic SFN พบว่า อาการ burning paresthesia และ reduced thermal sensation สัมพันธ์กับ SSR ที่ผิดปกติอย่างมีนัยสำคัญทางสถิติ (p-value มีค่าเท่ากับ 0.032 และ 0.021 ตามลำดับ) นอกจากนี้ ยังพบว่าปัจจัยต่าง ๆ ได้แก่ ประวัติการหกล้มภายใน 6 เดือน, ประวัติการเกิดแผลเท้าเบาหวานภายใน 3 เดือน, impaired pinprick sensation, impaired proprioceptive sensation, decreased deep tendon reflex, burning paresthesia, reduced thermal sensation, ทั้ง anhidrosis หรือ hypohidrosis, และ hyporemia มีความสัมพันธ์กับการตรวจพบความผิดปกติของ SSR อย่างมีนัยสำคัญทางสถิติ (p-value <0.05)

สรุป: มีความสัมพันธ์ระหว่างอาการของ PAN และผลการตรวจ SSR ในรยางค์ของผู้ป่วยเบาหวานที่มีภาวะเส้นประสาทเสื่อมหลายเส้น ผลการศึกษานี้ยังสนับสนุนผลการศึกษาอีกหลายการศึกษาในปัจจุบันที่ว่า ผลการตรวจ SSR มีความสัมพันธ์กับประวัติการเกิดแผลเท้าเบาหวาน และให้ความเชื่อมั่นในการสืบค้นเกี่ยวกับการใช้ประโยชน์ทางคลินิกของการตรวจ SSR ในผู้ป่วยเบาหวานต่อไปภายหน้า