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Evaluating the Usefulness of the Diabetic Peripheral Neuropathy Screening Process

Huijuan Yuan[1], Jing Zhang[1], Rui Tian[1], Limin Wang[1], Chunling Zhang[2], Zhigang Zhao[1]* and Linong Ji[3]*

[1]*Department of Internal Medicine, Henan Provincial People's Hospital, Zhengzhou, China*
[2]*Henan University of Economics and Law, Zhengzhou, China*
[3]*Department of Internal Medicine, Peking University People's Hospital, Beijing, China*

Summary

Aims: To evaluate the clinical utility of the diabetic peripheral neuropathy (DPN) screening process in the diagnosis of DPN among diabetic patients.

Methods: A total of 816 diabetic patients performed nerve conduction velocity (NCV), Somatosensory evoked potential (SEP), Toronto clinical scoring system (TCSS), and DPN screening process at baseline. The NCV and SEP were used as the 'gold standard' against which the sensitivity, specificity, positive predictive value, negative predictive value and Youden's index of the TCSS and the DPN screening process determined by the Chinese Diabetes Society of the Chinese Medical Association in 2010.

Results: According to the DPN screening process, 602 patients (73.77%) were positive while 458 patients (56.13%) were positive according to the TCSS score. The sensitivity, specificity, positive predictive value, negative predictive value, and Youden's index of DPN screening process were 89.49%, 66.56%, 81.99%, 78.82%, and 0.5605, respectively. Patients with DPN exhibited numbness (46.02%), pain (15.71%), paresthesia (16.59%), pinprick sensation (12.17%), and others (10.62%). The sensitivity and specificity of the various DPN checks were as follows: pressure sensation (19.44% and 95.62%), vibration perception (77.78% and 60.87%), temperature sensation (35.19% and 89.13%), and pinprick (31.48% and 84.78%). The sensitivity, specificity, positive predictive value, negative predictive value, and Youden's index of a TCSS score ≥ 6 were 78.21%, 84.11%, 89.33%, 69.40%, and 0.6232, respectively. DPN screening process took an average of 5.89 minutes, while TCSS spent an average of 10.32 minutes.

Conclusion: DPN screening process is economical, simple, fast, accurate, and could be used for early clinical screening of DPN in patients with diabetes.

Keywords: Diabetic peripheral neuropathy; TCSS; DPN screening process

Introduction

Diabetic polyneuropathy is the main pattern of Diabetic peripheral neuropathy (DPN) [1]. Furthermore, Diabetic distal symmetrical polyneuropathy (DSPN), which is characterized by chronic, symmetrical, length-dependent sensory and motor polyneuropathy that spreads from the lower limbs to upper limbs, is the most common type of DPN. Therefore, a method could be designed to screen out different levels of diabetic polyneuropathy by using clinical symptoms and signs, as well as an electrophysiological examination of the nervous system. Late stage DPN may lead to serious consequences, such as foot ulceration, gangrene, amputation, and neuropathic pain. The prevalence of type 2 diabetes in China is estimated to be 9.7% [2]. An accurate and early diagnosis can lead to a timely treatment, and prevent a potential risk of disease progression. Nearly half of diabetes patients do not exhibit any signs and symptoms of peripheral neuropathy. Electrophysiological examination of the nervous system is the only way to identify subclinical DPN. In the present study, we evaluated the usefulness of the DPN screening process, which proposed by the Chinese Diabetes Society of the Chinese Medical Association, by comparing this process with an electrophysiological examination of the nervous system and the Toronto clinical scoring system (TCSS) in patients with diabetes mellitus.

Subjects and Methods

Subjects

The study was conducted at Henan Provincial People's Hospital from October 2010 to June 2011. All included patients had DM, as defined according to the 1999 World Health Organization (WHO) criteria. The subjects were consisted of 468 males (57.35%) and 348 females (42.65%), with average age of 56.2 ± 9.72 years. The mean duration of disease was 7.05 ± 6.36 years and the mean HbA1c level was 8.82 ± 2.23%. Patients with lumbar intervertebral discprotrusion, cerebral hemorrhage, peripheral vascular disease or neuropathy caused by other relevant factors, including family history, alcoholism, trophism, and uremia, were excluded.

Methods

Somatosensory evoked potential and nerve conduction velocity examination: Somatosensory evoked potentials (SEP) and nerve conduction velocity (NCV) were measured using an electromyograph (MEB-5504K, Photoelectric Company, Japan). The surface electrode

***Corresponding authors:** Zhigang Zhao, 7 Weiwu Lu, Department of Internal Medicine, Henan Provincial People's Hospital, Zhengzhou, Henan 450003, P.R. China, Tel: +86 13803859882; Fax: +86 0371-65897717; E-mail: lmls3712@163.com

Linong Ji, 11 Xizhimen Nandajie, Xicheng District, Department of Endocrinology, Peking University People's Hospital, Beijing, 100044, P.R. China, Tel: +86 10-88325373; Fax: +86 10-68318386; E-mail: jilinong@gmail.com

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was used during stimulation and record. The results were compared to a table of normal data from our hospital electromyography lab. Patients were diagnosed with DPN when either the SEP or NCV results were abnormal.

DPN clinical screening:

- **DPN screening:** Firstly, each patient was asked whether they had symptoms of neuropathy (pain, numbness, acantesthesia or other sensory abnormalities). Subsequently, ankle reflex, pressure sensation, vibration sensation, pinprick sensation and temperature sensation were tested which being commonly used in daily treatment work.
- **Diagnostic criteria of DPN screening process:** Primarily, neuropathy symptoms, such as pain, numbness, acantesthesia, and weakness were assessed while cervical or lumbar degenerative diseases, nerve root compression, paraneoplastic syndrome, cerebrovascular disease, spinal cord disease or other causes of peripheral neuropathy were excluded. Then, neuropathy signs, including ankle reflex, pressure sensation, vibration sensation, pinprick sensation and temperature sensation, were estimated. DPN screening process was considered as suspected diagnoses which had mere nerve symptoms or any one symptom among ankle reflex, pressure sensation, vibration sensation, pinprick sensation and temperature sensation. Whereas Clinical diagnoses was assigned with both symptoms and signs of DPN. Both suspected diagnoses and clinical diagnoses were used to analyze the sensitivity, specificity, positive predictive value, negative predictive value and Youden's index.
- DPN screening process established by Chinese Diabetes Society of the Chinese Medical Association in 2010 (Figure 1).
- **Toronto clinical scoring system:** The Toronto Clinical Scoring System (TCSS) included a symptom score, reflection score, and sensory score, all of which totaled a possible 19 points. A score of greater than six was considered positive.

Symptom scores including lower extremity pain, numbness, tingling, weakness, walking imbalance and upper extremity symptoms, normal was drafted as 0 point, exception as 1 point, a total of 6 points.

Reflex scores, including the bilateral patellar reflex and ankle reflex, were normal 0 point, weakened 1 point and disappeared 2 points, a total of 8 points.

Sensory score, including a light touch in the right great toe joint position sense, vibration sense, pinprick, temperature sensation, were normal 0 point, exception 1 point, a total of 5 points.

TCSS and DPN screening

TCSS and DPN screening process were conducted by the same physician and examination time was recorded when each case were inspected.

Statistical analysis

The data were analyzed using SPSS software package, version 17.0 (SPSS Inc., Chicago, IL, USA). The sensitivity, specificity, positive

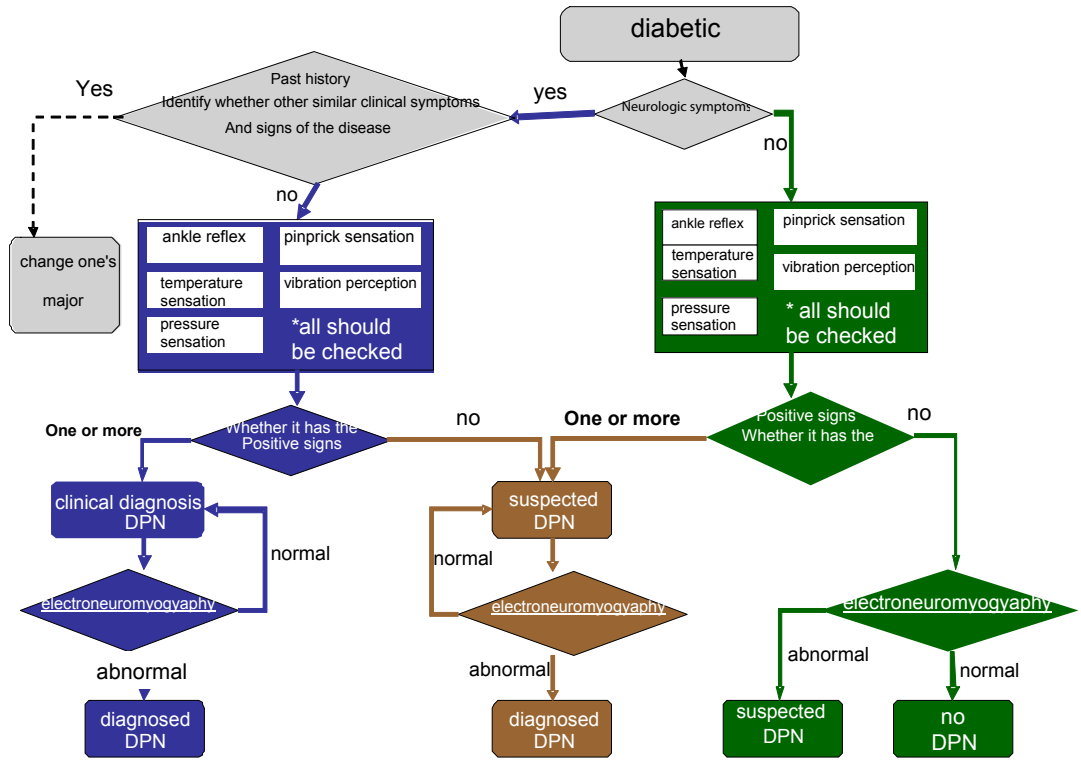

Figure 1: DPN screening process (Chinese Diabetes Society of the Chinese Medical Association, 2010).

predictive value, negative predictive value and Youden's index of the two screening methods were carried out comprehensive analysis under comparison. We calculated the abnormal rates of all test results between patients with neural symptoms and patients who had no neurologic symptoms. The comparison of diagnostic methods was assessed with chi-square tests of paired, fourfold table data. P value < 0.05 was taken for statistically significant.

Results

Basic analysis of the general information

According to the completed assessments, among 816 cases had nerve symptoms which were 561 cases (68.75 %), none of nerve symptoms were 255 cases (31.25 %). The abnormal rate of Symptoms of DPN included numbness (46.02%), pain (15.71%), paresthesia (16.59%), pinprick sensation (12.17%), and weakness (10.62%).

During the electrophysiological examination 514 patients were positive (62.99%). 602 patients in the DPN group were positive (73.77%), and 458 patients in the TCSS group were positive (56.13%). In other words, the positive rate of DPN screening was higher than with TCSS.

Sensitivity, specificity, positive predictive value, negative predictive value and Youden's index of the two screening methods

We divided the 816 diabetics into positive group and negative group by taking the results of the NCV and SEP as the 'gold standard'. The sensitivity, specificity, positive predictive value, negative predictive value and Youden's index of both the DPN screening process and TCSS were summarized in Table 1.

The result of temperature sensation, pinprick, pressure and vibration perception could be seen in table 2.

The comparison of the time of the two kinds of screening

We recorded how much time was required to screen for DPN using the clinical screening process and TCSS among DM patients. DPN screening process took an average of 5.89 minutes, while the TCSS expended an average of 10.32 minutes.

Discussion

Many methods can be used to diagnose DPN, including the Michigan Neuropathy Screening Instrument (MNSI), Michigan Diabetic Neuropathy Score (MDNS), TCSS and so forth. In addition to these systems, nerve and skin biopsies can be used for evaluation of peripheral neuropathy. However, these morphological examinations are currently used predominantly in research rather than in medical institution. Depending on the screening method employed, the prevalence of DPN can range from 2.4 to 75.1% [3,4]. A nerve electrophysiological examination is more objective and realistic compared to other methods, and is considered to represent the "gold standard" [5]. Despite its high sensitivity, specificity and repeatability, nerve electrophysiological examination is expensive and time-consuming, and has not been widely adopted in the hospital setting. The incidence of DPN rises along with the progression of diabetes, and could be as high as 60%-90% [1]. Since DPN can often be dormant and inconsistent with clinical symptoms, numerous patients stay in delitescence without symptoms. Since peripheral neuropathy is a pivotal element in the causal pathway to foot ulceration and amputation, selecting a quick, inexpensive, and accurate method to evaluate the high-risk patient is essential for clinical decision making [6].

The DPN screening process was formulated by the Chinese Diabetes Society of the Chinese Medical Association in 2010, and aimed at searching for an economical, simple, fast and accurate method. Is it a practical and useful method of DPN screening process in daily clinical work? Our study found that the sensitivity, specificity, positive predictive value, negative predictive value, and Youden's index of the DPN screening process were 89.49%, 66.56%, 81.99%, 78.82%, and 0.5605, respectively. Thus, this screening process had a moderate consistency with electrophysiological examination.

TCSS was an apparently useful method to screen DPN, however the processes and contents were too complicated which were arduous to conduct in clinical work, meanwhile might cost too much time for clinical doctors. We used the two methods of DPN screening process and TCSS with 816 T2DM cases in studies, the results were compared with NCV and SEP which were used as the 'gold standard'. We found that the advantage of DPN screening process was more sensitive and less time-consuming, which could lead to the accurate completion of the screening program in a relative short time, the specificity was less lower, but through adjusting Youden's index, its clinical value was close to TCSS. The results showed that, on average, the DPN screening process took approximately half the time required for completion of the TCSS. The diversity in time made the screening of peripheral neuropathy in diabetic patients more practical for clinicians.

In addition, selection of ankle reflex, pressure sensation, vibration sensation, pinprick sensation and temperature sensation of the inspection and electrical physiological detection control study to evaluate the practicality of the DPN screening process is possible in theory. Although DPN is one of the diabetic foot risk factors, there may be no obvious clinical symptoms during the early part of the disease process. Indeed, if a physician merely based diagnosis on the presence of patient symptoms, a proper diagnosis and early intervention of DPN will likely be delayed. From a pathophysiological perspective,

Item	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	Youden's index
DPN screening process	89.49	66.56	81.99	78.82	0.5605
TCSS ≥ 6	78.21	84.11	89.33	69.40	0.6232

Table 1: Comparison of the DPN screening process and TCSS.

	Temperature sensation	Pinprick perception	Pressure sensation	Vibration perception
Sensitivity (%)	35.19	31.48	19.44	77.78
Specificity (%)	89.13	84.78	95.62	60.87

Table 2: Sensitivity and specificity of all DPN checks.

the effect of diabetes on the nervous system starts at the myelinated and unmyelinated nerve fibers, causing pain and diminishing temperature sensation and finally bringing about myelinated nerve fiber damage, which led to cause vibration hypoesthesia. While conventional electrophysiological examination, such as NCV, can detect large myelinated fibers and pain nerve fibers, it could not detect autonomic neuropathy fibrosis. However, small fiber involvement often occurs during the early phase of DM that may be identified using sensory quantitative testing. With the progression of symptoms, large fibers become involved, and these changes may be detected by electrophysiological testing. Our study also used TCSS for assessing peripheral neuropathy. TCSS includes a nerve symptom score, reflex score, and a sensory function check. As established by Perkins, et al. in 2001 [7], the TCSS is a valid instrument for detecting the presence and severity of DPN as measured by sural nerve morphology and electrophysiology. In our study, the sensitivity, specificity, positive predictive value, negative predictive value and Youden's index of a TCSS score ≥ 6 were 78.21%, 84.11%, 89.33%, 69.40%, and 0.6232, respectively.

In our study, using nerve electrophysiology as 'gold standard', we confirmed that the DPN screening process and TCSS both had a comparably high sensitivity, specificity and similar Youden's index, and had considerable clinical value. The advantages of TCSS included its clear rating classification system, which could be used for the diagnosis of DPN, as well as for judging the severity of DPN. The study suggested that the peripheral neuropathy patients with diabetes be in 47.12% of the mild disease, moderate 33.85%, severe degree occupy 9.07%, very severe be up to 9.96%. Clinical observations indicated that as the TCSS score increased, its consistency with NCV also gradually increased. Domestic and foreign researches had confirmed the correlation between TCSS neuropathy grading and NCV, suggesting the utility of TCSS in the evaluation of DPN severity [8]. Our study was conducted to explore the value of the DPN screening process, and whether it had a better clinical value compared with TCSS. The results indicated that the DPN screening process was more economical, accurate, and easier method. Thus, when a diagnosis of DPN needs to be determined, particularly in large-scale epidemiological investigations involving general hospital outpatients, this simple DPN screening process could be utilized.

Conclusion

In conclusion, the limitations of the various DPN check methods cause difficulties in epidemiological investigations and limit their widespread use in the out-patient setting. The American Diabetes Association (ADA) recommends that patients with diabetes should annually use at least one of the screening methods to screen for DPN [9]. The results of this study indicate that both the DPN screening process and TCSS score have good consistency with a NCV check and can be used for DPN screening in the clinical setting and in epidemiological surveys.

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