Correlation between clinical neuropathy scores and nerve conduction studies in patients with diabetic peripheral neuropathy

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Background
Diabetic peripheral neuropathy (DPN) represents one of the most common complications of diabetes mellitus.
Objective
The aim of this study was to assess the correlation between clinical neuropathy scores and nerve conduction studies (NCS).
Patients and methods
This study included 30 (12 men and 18 women) Egyptian patients with type 2 diabetes mellitus complaining of symptoms suggestive of DPN. All patients underwent a clinical evaluation using three clinical scores: the Neuropathy Disability Score (NDS), the Neuropathy Impairment Score in the Lower Limbs (NIS-LLs), and the Diabetic Neuropathy Examination (DNE) score. Neurophysiological studies using NCS as well as measurement of glycated hemoglobin (HbA_1C) were carried out.
Results
HbA_1C was significantly correlated with NDS, NIS-LL, and DNE. The NDS was statistically correlated to median nerve sensory amplitude, sensory conduction velocity; ulnar nerve sensory amplitude, sensory conduction, motor amplitude, motor conduction velocity; and peroneal nerve sensory amplitude, sensory conduction velocity, motor amplitude, and motor conduction velocity. NIS-LL was significantly correlated with median nerve sensory amplitude, sensory conduction velocity; motor amplitude, motor conduction velocity; ulnar nerve sensory amplitude, sensory conduction velocity, motor conduction velocity; and peroneal nerve sensory amplitude, sensory conduction velocity, motor amplitude, and motor conduction velocity. DNE was significantly correlated with median nerve sensory amplitude, sensory conduction velocity, motor amplitude, motor conduction velocity; ulnar nerve sensory amplitude, sensory conduction velocity, motor amplitude, motor conduction velocity; and peroneal nerve sensory amplitude, sensory conduction velocity, motor amplitude, and motor conduction velocity.
Conclusion
Clinical neuropathy scores represent a simple tool for evaluation and follow-up of patients with DPN in comparison with NCS, and we recommend the use of these scores in clinical practice on a routine basis.

Keywords:
clinical scores, diabetic neuropathy, Diabetic Neuropathy Examination, nerve conduction studies, Neuropathy Disability Score, Neuropathy Impairment Score in the Lower Limbs

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Introduction

Diabetic peripheral neuropathy (DPN) represents one of the most common complications of diabetes mellitus (DM) encountered by a neurologist in clinical practice [1]. Diabetic neuropathy may or may not be symptomatic.

Electrodiagnostic tests represent a standard part of the workup for diagnosis of DPN and provides a high level of specificity [2]. Nerve conduction studies (NCS) represent a noninvasive technique that is reliable, objective, and sensitive for detection of neuropathy. Yet its availability may be limited and it may be difficult to be used in routine follow-up [3].

Clinical scores have been developed and validated as measures of severity of neuropathy. Many scores have been used in clinical practice, such as the neuropathy symptom score (NSS) [4], and the Neuropathy Disability Score (NDS) [5,6] among others.

The aim of this study was to evaluate the correlation between clinical neuropathy scores and NCS in a sample of Egyptian patients with DPN.

Patients and methods

This study included 30 (12 men and 18 women; mean age 50.90±9.18 years) Egyptian patients with type 2 DM who had symptoms suggestive of peripheral neuropathy. The patients were selected from consecutive outpatients at outpatient clinics of Cairo University Hospitals, Egypt, during the period April 2015 to November 2015. The institutional review board approved the study and all patients signed an informed consent form before enrollment in the study.

Patients with evidence of nerve entrapment or neuropathy due to causes other than DM (e.g. drug induced, hereditary neuropathies) were excluded.

Methods

(1) Clinical scoring systems:

Scoring of peripheral neuropathy was done for all patients using the following:

(a) NDS [5,6]: The NDS is the most widely used and accepted scoring system for diabetic neuropathy. It includes examination of vibration (using a 128-Hz tuning fork), sensation (pain and temperature), and ankle reflex. The score of vibration and sensation is '0' if present and normal, and '1' if absent, reduced, or uncertain. The ankle reflex scores '0' if present and normal, and '2' if absent, with a maximum total score of '10'. The grades of severity of neuropathy are classified as follows: mild (scores: 3–5), moderate (scores: 6–8), and severe (scores: 9–10).

(b) Neuropathy Impairment Score in the Lower Limbs (NIS-LLs) [4]: This score evaluates quantitatively the changes in motor, sensory, and reflex activity in the lower limbs. It examines motor power, sensations, and deep reflexes. The graded scale ranges from 0 (normal) to 88 (loss of all motor, sensory, and reflex activities in the lower limbs).

(c) Diabetic Neuropathy Examination (DNE) score [7]: Only the limbs of the right side are examined in this score, with a maximum score of 16 points. A score greater than three is considered abnormal.

(2) Neurophysiologic studies:

All participants underwent neurophysiologic evaluation by an expert examiner in the Clinical Neurophysiology Unit, Department of Neurology, Cairo University. NCS were performed using Dantec NCV/EMG machine (Keypoint, Pleasanton, California, USA). Patients' limbs were placed in relaxed position as any movement of the limb could hamper the results; room temperature was maintained between 21 and 23°C. Reduction of electrode impedance was achieved by applying an electrode gel under the electrode and by affixing the electrode with adhesive tape to the skin. Median nerve motor and sensory fibers on both sides were studied. The median nerve compound muscle action potential was recorded using surface electrodes placed over the main bulk of the abductor pollicis brevis. The median sensory responses were measured by the antidromic technique using finger ring electrodes on the index finger while stimulating the wrist. Motor stimulation was applied at the palm, the wrist, and at the mid-forearm. Velocity was calculated at the palm–wrist segment (distal segment) and at the wrist/mid-forearm segment (proximal segment). The ulnar nerve was stimulated at the wrist and mid-forearm and the compound muscle action potential was recorded using surface electrodes applied over the abductor digiti minimi muscle while the sensory responses were measured using ring electrodes applied over the ring finger to record antidromic responses. The peroneal nerve motor responses were measured by stimulation at the ankle and neck of the fibula and recording by surface electrodes applied over the extensor digitorum brevis muscle. The peroneal sensory responses were measured using surface electrodes applied at the ankle over the intermediate superficial sensory branch while stimulation was applied over the anterolateral aspect of the leg.

(3) Measurement of glycated hemoglobin (HbA_1C).

Statistical analysis

Analysis was performed using the statistical package for the social sciences (SPSS), version 23 (IBM Inc., Chicago, Illinois, USA). Numerical data were expressed as mean±SD and comparisons were made using Student's *t*-test. Pearson's correlation coefficient (*r*) was used to test the correlation between variables. The χ^2-test was used to test distribution and associations among nominal (non-numerical data) variables. *P*-values less than 0.05 were considered statistically significant.

Results

The mean duration of DM was 11.8±7.63 years and the mean duration of symptoms was 3.67±2.63. The mean HbA_1C was 9.49±1.94.

HbA_1C was significantly correlated to NDS (r=0.470, P=0.008), NIS-LL (r=0.527, P=0.003), and DNE (r=0.547, P=0.002). In addition, the duration of DM was significantly correlated to NDS (r=0.434, P=0.017), NIS-LL (r=0.466, P=0.009), and DNE (r=0.500, P=0.005). The duration of symptoms of neuropathy was significantly correlated to NDS (r=0.447, P=0.013), NIS-LL (r=0.509, P=0.004), and DNE (r=0.578, P=0.001) (Table 1).

NDS was significantly correlated to median nerve sensory amplitude (r=−0.611, $P\leq$0.001), sensory conduction velocity (r=−0.496, P=0.005); ulnar nerve sensory amplitude (r=−0.776, $P\leq$0.001), sensory conduction velocity (r=−0.547, P=0.002), motor amplitude (r=−0.617, $P\leq$0.001), motor conduction velocity (r=−0.711, $P\leq$0.001); and peroneal nerve sensory amplitude (r=−0.533, P=0.002), sensory conduction velocity (r=−0.480, P=0.007), motor amplitude (r=−0.642, $P\leq$0.001), and motor conduction velocity (r=−0.680, $P\leq$0.001) (Table 2).

NIS-LL was significantly correlated to median nerve sensory amplitude (r=−0.462, P=0.01), sensory conduction velocity (r=−0.541, P=0.002); motor amplitude (r=−0.612, $P\leq$0.001), motor conduction velocity (r=−0.395, P=0.031); ulnar nerve sensory amplitude (r=−0.591, P=0.001), sensory conduction velocity (r=−0.372, P=0.043), motor conduction velocity (r=−0.494, P=0.006); and peroneal nerve sensory amplitude (r=−0.486, P=0.006), sensory conduction velocity (r=−0.472, P=0.008), motor amplitude (r=−0.435, P=0.016), and motor conduction velocity (r=−0.698, $P\leq$0.001) (Table 2).

DNEs was significantly correlated to median nerve sensory amplitude (r=−0.704, $P\leq$0.001), sensory conduction velocity (r=−0.659, $P\leq$0.001); motor amplitude (r=−0.463, P=0.01), motor conduction velocity (r=−0.454, P=0.012); ulnar nerve sensory amplitude (r=−0.798, $P\leq$0.001), sensory conduction velocity (r=−0.490, $P\leq$0.001), motor amplitude (r=−0.659, $P\leq$0.001), motor conduction velocity (r=−0.762, $P\leq$0.001); peroneal nerve sensory amplitude (r=−0.502, P=0.005), sensory conduction velocity (r=−0.468, P=0.009), motor amplitude (r=−0.692, $P\leq$0.001), and motor conduction velocity (r=−0.726, $P\leq$0.001) (Table 2).

The three clinical scores were correlated to each other. There was statistically significant correlation between

Table 1 Correlation between clinical scores and clinical and laboratory variables in patients with DPN

Variables	NDS		NIS-LL		DNEs	
	r	*P*-value	*r*	*P*-value	*r*	*P*-value
Duration of DM	0.470	0.009*	0.412	0.009*	0.565	0.001*
Duration of Symptoms	0.524	0.003*	0.509	0.004*	0.669	<0.001*
HbA_1C	0.494	0.005*	0.583	0.007*	0.578	0.01*

DM, diabetes mellitus; DNEs, Diabetic Neuropathy Examination; DPN, diabetic peripheral neuropathy; HbA_1C, glycated hemoglobin; NDS, Neuropathy Disability Score; NIS-LL, Neuropathy Impairment Score in the Lower Limb. *P<0.01, significant.

Table 2 Correlation between clinical scores and different parameters in patients with DPN

Variables	NDS		NIS-LL		DNEs	
	R	*P*-value	*R*	*P*-value	*R*	*P*-value
Median nerve sensory amplitude	−0.611	<0.001**	−0.462	0.01**	−0.704	<0.001**
Median nerve sensory conduction velocity	−0.496	0.005**	−0.541	0.002**	−0.659	<0.001**
Median nerve motor amplitude	−0.282	0.131	−0.612	<0.001**	−0.463	0.01**
Median nerve motor conduction velocity	0.323	0.082	−0.395	0.031*	−0.454	0.012*
Ulnar nerve sensory amplitude	−0.776	<0.001**	−0.591	0.001**	−0.789	<0.001**
Ulnar nerve sensory conduction velocity	−0.547	0.002**	−0.372	0.043*	−0.490	<0.001**
Ulnar nerve motor amplitude	−0.617	<0.001**	−0.494	0.006**	−0.659	0.005**
Ulnar nerve motor conduction velocity	−0.711	<0.001**	−0.328	0.077	−0.762	<0.001**
Peroneal nerve sensory amplitude	−0.533	0.002**	−0.486	0.006**	−0.502	0.005**
Peroneal nerve sensory conduction velocity	−0.480	0.007**	−0.472	0.008**	−0.468	0.009**
Peroneal nerve motor amplitude	−0.642	<0.001**	−0.435	0.016*	−0.692	<0.001**
Peroneal nerve motor conduction velocity	−0.680	<0.001**	−0.689	<0.001**	−0.726	<0.001**
Duration of DM	0.470	0.009**	0.412	0.009**	0.565	0.001**
Duration of Symptoms	0.524	0.003**	0.509	0.004**	0.669	<0.001**
HbA_1C	0.494	0.005**	0.583	0.007**	0.578	0.01**

DM, diabetes mellitus; DNEs, Diabetic Neuropathy Examination; DPN, diabetic peripheral neuropathy; HbA_1C, glycated hemoglobin; NDS, Neuropathy Disability Score; NIS-LL, Neuropathy Impairment Score in the Lower Limb. *P<0.05, significant. **P<0.01, significant.

NDS, NIS-LL (r=0.570, P=0.001), and DNE (r=0.869, P<0.001) and between NIS-LL and DNE (r=0.730, P<0.001)

There was significant difference in median nerve sensory amplitude (P=0.018), sensory conduction velocity (P=0.029); motor conduction velocity (P=0.047); ulnar nerve sensory amplitude (P≤0.001), motor conduction velocity (P=0.032); peroneal nerve sensory amplitude (P=0.003), sensory conduction velocity (P<0.001), and motor amplitude (P=0.017), with worse results in patients with moderate-to-severe neuropathy according to NDS categories compared with those with mild neuropathy.

NDS was able to detect neuropathy in all patients (100%) with abnormal NCS (n=24) and also in six patients with normal NCS, with significant difference in NDS score between the two groups (P=0.007). Similarly, NIS-LL was able to detect neuropathy in all patients (100%) with abnormal NCS (n=24) and also in six patients with normal NCS, with significant difference in NIS-LL score between the two groups (P=0.002). NE was able to detect neuropathy in all patients (100%) with abnormal NCS (n=24) and also in two out of six (33.3%) patients with normal NCS, with significant difference in DNE between the two groups (P=0.004).

Discussion

The standardization of the diagnosis of diabetic neuropathy has been an issue of discussion and no single 'gold' standard tool has been adopted by clinicians. Despite that, the San Antonio consensus, in a trial to be as objective as possible, recommended the use of at least one of five diagnostic tests: symptom scoring, physical examination scoring, quantitative sensory testing, cardiovascular autonomic function testing, and electrodiagnostic studies [8].

Although neurophysiologic studies represent an objective and sensitive tool in the diagnosis of DPN [9], it remains limited by the availability of equipment, expert physicians, and trained technicians, in addition to cost, inconvenience to patients, and pain. These limitations are more evident when used as a follow-up tool or screening tool in an outpatient setting [7]. There is thus a need to develop simpler tools that can fit into this gap, hence the development of neuropathy scores [10].

In this study we studied three clinical examination neuropathy scores used in clinical practice [4–7] to evaluate DPN in comparison with neurophysiologic, clinical, and lab variables. We found a significant correlation between the three scores and most clinical and neurophysiologic results.

NDS was statistically correlated to HbA_1C, duration of diabetes and symptoms of neuropathy, median nerve sensory amplitude, sensory conduction velocity; ulnar nerve sensory amplitude, sensory conduction, motor amplitude, motor conduction velocity; peroneal nerve sensory amplitude, sensory conduction velocity, motor amplitude, and motor conduction velocity. In addition, NDS was significantly higher in patients on insulin therapy compared with that in patients on Oral antidiabetics (OADs).

NDS is a widely used clinical score with a high predictive value and reproducibility [11]. It has been shown to be significantly associated with neuropathological changes in peripheral nerves [12] and significantly correlated to NCS [13]. It has also been proven to be the most reliable neurological test for detecting and grading DPN [14]. However, some NDS items have been found to be not essentially abnormal in DPN and therefore the neuropathy impairment score, revised on the basis of the NDS, has been proposed [15].

The performance of the NIS-LL in the detection of DPN is almost similar to that of the NDS, but the main drawback is too much emphasis on motor nerve function and no recognized diagnostic threshold for neuropathy [16].

In the present study, NIS-LL was significantly correlated to HbA_1C; median nerve sensory amplitude, sensory conduction velocity, motor amplitude, motor conduction velocity; ulnar nerve sensory amplitude, sensory conduction velocity, motor conduction velocity; and peroneal nerve sensory amplitude, sensory conduction velocity, motor amplitude, and motor conduction velocity.

DNE is modified from the NDS and is fast, easy to perform, hierarchical, and sensitive for neuropathy [7]. It has been shown to relate significantly to abnormalities in NCS [17].

DNE was significantly correlated to median nerve sensory amplitude sensory conduction velocity, motor amplitude, motor conduction velocity; ulnar nerve sensory amplitude, sensory conduction velocity, motor amplitude, motor conduction velocity; peroneal nerve sensory amplitude, sensory conduction velocity, motor amplitude, and motor conduction velocity.

The clinical scores showed the ability to detect neuropathy in patients with normal NCS. However, although this may be explained by the possible presence of small fiber neuropathy that is not readily detected by conventional NCS, the small number of patients remains a limitation.

Generally, most clinical neuropathy scores are noninvasive, inexpensive, sensitive–specific, and highly predictive of clinical endpoints. Furthermore, combining multiple scores has been shown to be better than using a single test [14]. Yet, these scales lack a mechanism for measuring anatomic spread of sensory loss, an important clinical aspect of early neuropathy progression [16].

Conclusion

We find that the three clinical neuropathy scores are simple and easy-to-use tools for screening and evaluation of DPN, being feasible in an outpatient setting, and can be readily performed by a trained neurologist. These scores complement clinical symptoms and signs and NCS and we recommend their use on a routine basis.

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Conflicts of interest

There are no conflicts of interest.

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