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Simplified diagnostic criteria for diabetic distal polyneuropathy

Preliminary data of a multicentre study in the Campania region

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Abstract. The diagnostic procedures recommended for diabetic neuropathy are rather complex and there is the risk that they may be applied only in highly specialized research centres and not in other more basic health service centres that recruit large numbers of diabetic patients. This consideration highlights the need for rapid and precise diagnostic procedures for the screening and follow-up of diabetic patients. In this paper we describe a simplified diagnostic protocol for distal polyneuropathy (DP), which is the most common form of peripheral neuropathy associated with diabetes. We performed an electroneurographic examination (ENG) based on a five-nerve evaluation in 204 diabetic subjects, and took it as the standard. Its reproducibility preliminarily assessed with a test–retest evaluation was 100%. DP was found in 47 of the 204 diabetic patients on the basis of an alteration in at least two nerves. Other clinical parameters, including a questionnaire on symptoms, a clinical neurological examination (NE), and the vibration perception threshold (VPT) were evaluated. The variability coefficient was not significant for all clinical parameters in a selected group of diabetic patients (questionnaire = 21,2%, NE = 5%, VPT = 16.5%). The sensitivities and specificities of the questionnaire, NE, and VPT in comparison with ENG were 87% and 60% for the questionnaire, 94% and 92% for NE, and 64% and 97% for VPT, respectively. Thus, the use of ENG permitted the recognition of DP in 14% of patients who were still asymptomatic. Finally, a four-nerve ENG was compared with the five-nerve procedure, and the concordance between the two tests was 100%.

Key words: Distal polyneuropathy – Electroneurography – Diagnostic criteria – Vibration sensitivity

Introduction

Various criteria have been proposed for the diagnosis of diabetic neuropathy based either on clinical parameters only [1–3] or on clinical and sometimes complex instrumental tests [4–6]. Therefore, prevalence data are rather variable between studies. The San Antonio Consensus Conference [7] as well as the Rochester Study [5] have indicated that both the clinical data and the results of complex instrumental procedures must be considered in diagnosis. These criteria permit an accurate diagnosis to be obtained both in the more frequent distal polyneuropathy (DP) [1] and in the less frequent mononeuritis and predominantly autonomic neuropathies [5, 8]. However, the previously proposed criteria are rather complex and require the use of complicated and time-consuming methodologies for each patient. Therefore, their extensive and systematic use in large series of diabetic patients is extremely difficult and their enforcement is perhaps limited to highly specialized research institutions. A fast and reliable screening method to be used for the maximum possible number of patients is one of the primary goals of diabetologists. A task force of the Italian Society of Diabetology (SID) on diabetic neuropathy recently proposed a fast screening method based on symptoms, clinical signs and the assessment of vibratory sensitivity and autonomic signs [9]. This method is fairly simple but requires electroneurographic confirmation. On these grounds, we set up a study to evaluate the diagnostic accuracy of the easily collectable data on signs, symptoms and evaluation of the vibratory sensitivity versus the more sensitive and specific electroneurography (ENG) [5, 8, 10–12] as the standard. This approach was directed toward the more frequent distal diabetic neuropathy, deliberately excluding the less frequent mononeuropathies and autonomic neuropathies.

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Table 1. Clinical data of the 204 subjects studied

Sex (M/F)	89/115
Age (years)	
Mean ± SD	58 ± 9
Range	23–76
Diabetes type[a] (*n*)	
I	6
II	198
Diabetes duration (years)	
Mean ± SD	9 ± 7
Range	5–28
Height (cm)	
Mean ± SD	160.4 ± 9.5
Range	138–190
Body mass index	
Mean ± SD	27.3 ± 4.2
Range	23.1–32.9
Fasting glycaemia (mg/dl)	
Mean ± SD	154.5 ± 14.3
Range	51–318
HbA_{1c}[b] (%)	
Mean ± SD	8.1 ± 1.8
Range	4.4–15.5

[a] Defined according to WHO criteria [16]
[b] Normal range 3.7–6.7 (BioRad method)

Table 2. Questionnaire on symptoms of neuropathy[a]

1. Have you ever felt tingling, numbness, heaviness in your hands or legs?	0	1	2
2. Have you ever felt burning, stabbing pain, pains or cramps in your legs or arms?	0	1	2
3. Have you ever felt as if you were walking on foam or cotton wool or have you been unable to feel the uneveness (roughness) of the ground while walking?	0	1	2
4. Are you unable to feel the pain of burning or a cut?	0	1	2
5. Have you ever felt weakness in your legs while climbing or descending stairs?	0	1	2
6. Have you ever felt faint or dizzy upon rising from bed?	0	1	2
7. Do you have difficulty in starting to urinate or loss of control of bladder function?	0	1	2
8. Do you have diarrhoea, particularly in the night?	0	1	2
9. Have you ever sweated abundantly from your face only?	0	1	2
10. (Males only) Do you have difficulty in maintaining an erection?	0	1	2

[a] Modified from SID study group [9]
0 = No, 1 = sometimes, 2 = often

Materials and methods

Selection of patients

Enrolled in the study were 204 diabetic outpatients presenting to the clinic during a 6-month period in 1993. The main clinical data of the patients are shown in Table 1. The cohort under study (204 subjects) was selected to be fully representative of the total population of subjects ($n = 1000$). The 204 patients were consecutively enrolled according to the exclusion criteria. Serum HbA_{1c} (BioRad method) and fasting glycaemia (Boehringer, Mannheim, glucose-oxidase method) were determined in each patient before the neurological examination (NE). The clinical data were collected on the day of the NE. Patients with a glycaemia >199 mg/dl before the NE were not considered. Informed consent was obtained from all patients prior to their enrollment. The study was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and was approved by the local Ethics Committee.

Exclusion criteria

Individuals with the following characteristics were excluded from the study: (1) radicular pathology of a osteoarticular, toxic–metabolic, congenital, alcoholic, lead poisoning or paraneoplastic aetiology; (2) ulcerations and scars on the limbs; (3) chronic liver diseases, renal and emathological diseases, connective tissue disorders, malignancies; (4) mononeurites and symptomatic entrapment neuropathies syndrome [13]; (5) previous or current treatment with aldosoreductase inhibitors, gangliosides, diuretics, beta-blockers or other drugs which are known to interfere with the state of alertness, nerve conduction efficiency or the hydroelectrolyte balance, topical creams (therapeutic and/or cosmetic), acupuncture or reflexotherapy, (6) alcohol or drug abuse; (7) symptoms or sequelae of vascular cerebropathy; (8) Winsor's index values below 90% (9) creatinaemia values above 1.5 mg/dl; (10) any type of chronic endocrinological disorder; (11) use of a pacemaker; and (12) phlogosis and/or leg oedema due to local or systemic pathologies.

Protocol of the study

All investigators participated in a 2-month pretrial observation period including repeated (five to seven) measurements performed under the guidance of skilful investigators and followed by group discussion with the aim of reducing inter- and intraobserver variability.

All patients underwent a series of tests performed and evaluated on the basis of the procedures proposed by the neuropathy study group of the SID [6–9]. These included (1) a questionnaire on symptoms of diabetic neuropathy (Table 2); (2) a muscle strength test; (3) a foot examination; (4) NE including ankle and achilles jerk reflexes, trophism and muscle strength of the lower limbs; (5) the vibration perception threshold (VPT); and (6) the nerve conduction velocity (ENG) in the lower limbs.

The test were carried out in a peaceful and comfortable environment with a stable temperature of 25 °C. Before the VPT and nerve conduction studies the patients' legs were maintained at a constant temperature of 32 °C during recordings by means of surface thermistors and longitudinal infrared lamp.

Questionnaire

The questionnaire included ten questions (Table 2), of which questions 1–5 were aimed at evaluating the function of the peripheral nervous system (1 and 2, positive symptoms; 3 and 4, sensitivity abnormalities; 5, motor abnormality). Although the questionnaire also included questions aimed at detecting autonomic symptoms (6–10), which were outside the scope of the present study, it was used without modification because it was well known to Italian diabetologits and simpler than other symptoms questionnaires reported in the literature [4, 6, 10–12, 14]. Questions were asked in the simplest possible manner, independent of the patient's education. In considering answers, doctors could exclude possible causes other than diabetic neuropathy. For each question a score from 0 to 2 was attributed (0, absent; 1, sometimes; 2, often). The final score was the sum of the scores of all the questions. A final

score >4 (including a score or 2 for one of the questions 3, 4, 9 and 10) was needed for the result of the test to be considered abnormal [6].

Neurological examination

Deviations of several clinical parameters from normality were graded:

1. Muscle stretch reflexes in lower limbs (knee and ankle). Evaluation: 0, normal; 1, decreased; 2, absent.

2. Muscle trophism of lower limbs (dorsiflector muscles of the foot and of the big toe). Evaluation: 0, normal; 1, reduced; 2, severely impaired.

3. Muscle strength in lower limbs by bilateral dorsiflection of the foot against resistance. Evaluation: 0, normal; 1, reduced; 2, absent.

4. Capacity of the patient to walk on heels. Evaluation: 0, normal; 1, reduced; 2, absent.

5. Inspection of foot. Evaluation: 0, normal; 1, dry corny skin or bone deformity; 2, ulcerations.

In judging the impairment, the neurologist took into consideration the patient's age, weight, sex and his or her general condition. A bilateral score of more than 3 was considered as abnormal.

Sensory examination of vibration perception threshold

The VPT was assessed using a digital Biothesiometer, model VPT 3, as previously described [15, 24]. In particular, before beginning, the test was explained to the patient and a trial vibratory stimulus was administered. Five different levels of vibratory threshold were determined at two different sites on the dominant side. The impulse intensity was increased to about 1 V/s beginning from 0 until the vibration was felt by the patient. Particular attention was paid to standardizing the pressure of the probe on the skin. The two sites studied were: (1) the dorsal surface of the phalanx of the big toe near the nail bed, and (2) the external malleolus. The first test was applied with the patient in the supine position with the legs bent such that the entire plantar surface was in contact with the bed, and the second test was applied with the patient lying on his or her side so that the whole medial part of the foot was in contact with the bed. The VPT value has been determined as the mean value of five determinations, but in this study the two extreme values were not taken into account for the determination of the mean value. In the analysis of the data collected common errors relating to false alarms and to the perception–response latency were taken into consideration [17, 18].

Reference values for age and sex were based on 178 healthy subjects without neuropathy or disorders known to predispose to neuropathy. Values greater than the 95th percentile were considered abnormal. The VPT was considered to be altered when an abnormal result was obtained from both sites studied. When only one site gave an abnormal result the diagnosis of neuropathy was based on all the other parameters studied. However, in none of the 47 patients diagnosed as having DP did this extra evaluation have to be carried out.

Nerve conduction (ENG) study

Peripheral nerve conduction was measured with a Medelec Sapphire 1500 System in the median, sural and peroneal nerves using both stimulating and recording surface electrodes. Motor conduction (MC) was measured in the ulnar and peroneal nerves, and sensory conduction (SC) in the median, ulnar and sural nerves. To record MC, the ulnar nerve was stimulated at the wrist and elbow (5 cm above the epitrochlear–olecranic douche), and the peroneal nerve was stimulated at the ankle and at the capitulum fibulae. Evoked muscle action potentials were recorded from the abductor of the fifth finger and from the extensor digitorum brevis (EDB) muscles, respectively.

To study SC, the median nerve was stimulated at digit III and evoked responses were orthodromically recorded at the wrist (standard distance, 15 cm). The ulnar nerve was stimulated at digit V and evoked responses were orthodromically recorded at the wrist (standard distance, 14 cm). The sural nerve was stimulated at the sura and the evoked potentials were the result of a 64-sweep electronic averaging. The latency of the muscle potentials was measured at the potential onset, the latency of the sensory potentials was measured at the first positive peak, and the amplitude was measured peak-to-peak. Reference values for age and sex were based on a population of healthy subjects without neuropathy or disorders known to predispose to neuropathy, divided into four age groups (25 for each of the following groups: 10–29, 30–49, 50–60, 61–70 and >70 years). Values greater than the 95th percentile were considered abnormal.

Criteria for nerve abnormality

A nerve was judged to be abnormal when an alteration of even a single parameter was found.

Criteria for a diagnosis of distal neuropathy

The requirements for arriving at a diagnosis of diabetic DP [5] were: (1) neuropathic symptoms and findings judged to be due to diabetes mellitus; (2) symptoms and/or signs of neuropathy predominantly in the distal segments of the lower limbs; and (3) findings almost symmetrical (differences between sides <25%).

Neuropathy was diagnosed by ENG in the presence of alterations in two or more nerves, one at least of which was in the lower limbs. When one of the two abnormal nerves was the median nerve the concomitant normality of Phalen's test [19, 20] was required to achieve a diagnosis of DP to ensure the exclusion of asymptomatic carpal tunnel syndrome. However, because of the low specificity of Phalen's test, when the result was normal, the symmetrical nerve in the opposite limb was also studied. Abnormalities of two nerves both in upper limbs were not observed.

Reproducibility of clinical and instrumental assessments

The reproducibility (test–retest variability) of the questionnaire, NE and VPT was assessed in 26 diabetic patients (15 with DP and 9 without DP) and in 15 comparable healthy controls. All the subjects underwent a second examination performed by an independent skilled observer under standard conditions. A 3–5 day period elapsed between the tests. A second ENG was repeated by the same neurologist in all the 15 controls and the 26 diabetic patients under standard conditions and after a similar time interval, as discussed above. Further evaluation of interobserver variability could not be performed because the subjects refused to undergo a third instrumental examination.

Statistical analysis

The variability coefficient was derived from the mean of the individual variability coefficients for each test (questionnaire, NE, VPT) repeated several times. A P-value less than 0.05 was considered statistically significant. Student's t-test for paired data was used to discriminate between normal and abnormal values.

The age-related normal values and ranges expressed as percentiles (5th and 95th) were calculated by the method of regression with replication. Data were normalized by logarithmic conversion after performing a Lovene test. The sensitivity and specificity of the questionnaire, NE and VPT compared with ENG was evaluated according to the method of Galen and Gambino [19]. The concordance coefficient was evaluated according to the method of Fleiss [20].

Results

Selection bias

Considering diabetics of all ages, the studied cohort (204 patients) did not differ from the non-participants (796 patients) in the community with respect to sex, therapy (insulin, oral hypoglycaemic agents, or no treatment), or duration and type of diabetes (as assessed from the medical record). Co-morbidity was less common. Among the 30 medical disorders evaluated, stroke (2% and 7%, $P<0{,}001$), congestive heart failure (2% and 9%, $P<0.001$), ischaemic leg ulcer (3% and 7%, $P=0.003$), cataract (8% and 15%, $P=0.002$), and macular degeneration (2% and 4%, $P=0.03$) were significantly less frequent in the cohort than in the non-participants.

Among the patients, there were no co-morbidity differences between the enrolled and non-enrolled cohort, and none of the various medical conditions was significantly less prevalent in the enrolled patients than in the non-enrolled patients.

Diagnosis of peripheral neuropathy based on ENG

The test–retest variability of the ENG was $\leq 2\%$ for each single parameter studied and the concordance between the final diagnoses was 100% both in healthy controls and diabetic patients. Based on ENG, 47 diabetic subjects affected by DP (30 male and 17 female; 23.5%) and 157 non-affected subjects (72 male and 85 female) were identified. The frequency of alterations of the tested nerves in the 47 patients with DP was: ulnar (motor conduction), 29/47 (61.6%); peroneal, 39/47 (82.9%); median, 24/47 (51.06%); sural 37/47 (78.8%); ulnar (sensory conduction), 12/47 (25.5%). In Tables 3–6 the mean $\pm$SD and ranges are shown of the nerve parameters of the 47 diabetic patients with DP compared with the 157 without DP. It should be noted that in the 47 neuropathic patients the mean of each nerve parameter is strictly related to the reported frequency of alteration. In 5/47 patients, only two nerves were altered (case nos. 13, 80, 165, 191 and 200), of which one was the median nerve. In all these five patients the Phalen's test [19, 20] result was normal. In order to verify the accuracy of the diagnosis of DP the corresponding symmetrical nerve was also evaluated by ENG. In all five patients the result was also abnormal, confirming the diagnosis of DP.

Clinical evaluations

Tables 7 and 8 show the variability (test–retest) of the questionnaire, NE and VPT in healthy controls and patients, respectively. In the controls the variance of the single observations was not statistically significant for the questionnaire, NE or VPT. In the diabetic patients the mean variability coefficient of the three tests was higher than in the controls, but in no case did the difference attain statistical significance. Table 9 shows the values of the diagnostic sensitivity and specificity of the questionnaire, NE and VPT compared with ENG. It is clear that (1) VPT had a high specificity and a low sensitivity, (2) the questionnaire had a relatively good sensitivity and a very low specificity, and (3) NE was the most sensitive and has a very good specificity. In particular, among patients with an altered ENG, 14.3% were asymptomatic (questionnaire negative), 36.3% had a normal VPT, and only 6.4% had a normal NE. Conversely, among patients with a normal ENG, 21% revealed abnormalities by questionnaire and 7.6% by NE, and only 2.5% showed an altered VPT.

Table 3. Sural nerve sensory conduction values

	Conduction velocity sura–lateral malleolus (m/s)	Potential amplitude lateral malleolus (μV)
Patients without DP	52.1±5.7 45–61	14.5±4.7 8–27
Patients with DP	40.7±6.2 30–54	5.6±3.7 1.5–15
No. of absent responses	–	3
Mean difference (%)	−21.8	–

Values are mean±SD (range)

Table 4. Median nerve sensory conduction values

	Conduction velocity digit III–wrist (m/s)	Potential amplitude at wrist (μV)
Patients without DP	49.0±5.4 43–62	13.0±7.1 3.4–24
Patients with DP	41.4±8.6 21–64	6.5±4.2 1.5–16.6
No. of absent responses	–	0
Mean difference (%)	−15.5	–

Values are mean±SD (range)

Table 5. Peroneal nerve motor conduction values

	Distal latency (ms)	Maximal velocity capitulum fibulae–ankle (m/s)	Potential from capitulum fibulae (mV)	Amplitude from ankle (mV)
Patients without DP	4.0±0.9 2.5–5.6	49.2±2.3 45.5–53.2	3.8±2.4 1.2–8.7	4.8±2.9 3.6–11
Patients with DP	5.2±1.0 3.8–7.4	36.3±4.2 32–43	6.2±3.4 0.2–11	5.7±2.6 1.5–12
No. of absent responses	–	–	0	0
Mean difference (%)	+23	−26.2	–	–

Values are mean±SD (range)

Table 6. Ulnar nerve conduction values

	Motor conduction				Sensory conduction	
	Distal latency (ms)	Maximal velocity (m/s)	Potential at wrist (mV)	Amplitude at elbow (mV)	Conduction velocity digit V–wrist (m/s)	Potential amplitude at wrist (μV)
Patients without DP	3.0±0.5 2.2–3.4	55.1±3.2 50–62	10.0±2.1 8–12	9.4±1.6 7–11	50.2±3.5 45–60	6.2±2.1 4.5–10
Patients with DP	3.6±0.6 2.8–0.6	42.2±4.2 40–61	7.4±1.7 5.4–10.6	6.2±1.3 4.6–8.5	40.2±5.2 32–58	5.5±2.7 2.6–9.2
No. of absent responses	–	–	0	3	–	–
Mean difference (%)	+20	−23.4	–	–	−19.9	–

Values are mean±SD (range)

Table 7. Variability coefficient (%) of the questionnaire, NE and VPT results in healthy controls

	Mean	SD	Range
Questionnaire	13.5	5.7	8–20
Neurological examination	3.9	4.5	0–6
VPT			
Big toe	12.5	4.6	0–18
Malleolus	14.2	9.2	0–28

Table 8. Variability coefficient (%) of the questionnaire, NE and VPT results in diabetic patients

	Mean	SD	Range
Questionnaire	21.6	9.8	8–32
Neurological examination	5.0	3.5	0–6.5
VPT			
Big toe	16.5	5.8	4–21
Malleolus	18.6	9.5	4.4–28

Table 9. Diagnostic sensitivity and specificity of symptoms using the questionnaire, clinical neurological examination and vibratory threshold (VPT) compared with the diagnosis of peripheral neuropathy by ENG

	Sensitivity (%)	Specificity (%)
Questionnaire	87.0	60.0
Neurological examination	94.0	92.0
VPT	64.0	97.0

Discussion

We describe a simiplified protocol for the diagnosis of diabetic DP. A five-nerve ENG study was used as the standard because it was considered the most reproducible, accurate and sensitive diagnostic tool for the diagnosis of diabetic neuropathy [5, 8, 10, 12], and it was recommended as such at the San Antonio Consensus Conference on Diabetic Neuropathy [7]. We evaluated the diagnostic accuracy of a four-nerve ENG study in comparison with a five-nerve study in a selected group of diabetic patients. We also determined the sensitivity and specificity of a set of clinical tests proposed by a study group of the SID, which were simpler than those previously proposed [4, 7]. We focused on DP, the most common form of diabetic neuropathy (>80% of the total) [1, 5, 8], to the exclusion of less frequent forms such as mononeuritis and autonomic neuropathy. Therefore, we did not perform the autonomic tests included in the SID protocol, although we used the full SID questionnaire, retaining the questions on autonomic symptoms [6–10] because of the widespread use of this questionnaire among Italian diabetologists.

In a pretrial study undertaken to standardize the investigational methodologies and to reduce the investigational biases, the test–retest diagnostic concordance of the ENG test was 100%. The positivity criterion for this diagnostic procedure, i.e. the alteration of at least two nerves, one in the lower limbs, was satisfied in 89.3% of the symptomatic patients in our series. However, the diagnosis was still uncertain in 5 out of 47 cases (10.7%) in which only two nerves, one the median nerve were abnormal. In fact, an asymptomatic median nerve, entrapment syndrome had to be excluded. Even Phalen's test [19, 20] was not sufficient to exclude the carpal syndrome [5]. In these cases the diagnosis was reached by studying an additional nerve other than median nerve. ENG was of particular value in establishing the diagnosis of DP in the absence of clinical symptoms. Indeed,. 14.3% of the patients with altered ENG were asymptomatic. The least frequently affected nerve was the sensory ulnar nerve. It was abnormal only in 12 out of 47 neuropathic patients, always in association with two other abnormal nerves. In contrast, alterations in the sensory ulnar nerve were observed in none of the non-neuropathic patients. Thus, the study of the sensory nerve was in no case critically important for the diagnosis of diabetic neuropathy, and a 100% concordance existed between the diagnoses of diabetic neuropathy reached by the five-nerve study and by the four-nerve study (Table 10). Besides confirming that the ENG study is the most accurate method for diagnosis of DP [5, 8, 10–12], our results show that a simplified four-nerve ENG study is as accurate as a five-nerve study.

Table 10. Concordance in the diagnosis of DP achieved including (5 nerves) or not (4 nerves) the assessment of the sensory fibres of the ulnar nerve in the 204 patients in the study

		Neuropathy (4 nerves)	
		Yes	No
Neuropathy (5 nerves)	Yes	47	0
	No	0	157

Clinical tests have also been recommended in conjunction with ENG for the diagnosis of DP [7]. However, those so far proposed [4, 7] are rather complex [5] and difficult to adopt in clinical practice other than in highly specialized settings [7]. Other simpler clinical tests, such as those proposed by the SID study group [6, 9] had not previously been evaluated as to their accuracy and inter- and intraobservational variability. In our series we found that (1) the symptom questionnaire, as far as questions 1 to 5 are concerned, had a sensitivity of 87%, but a specificity of only 60%, compared with ENG, (2) the VPT had a fairly high specificity (97%), but a relatively low sensitivity (64%); and (3) NE had both a high sensitivity (94%) and moderately high specificity (92%). All tests were characterized by a low variability. The NE was the most consistent method. The VPT had a variability coefficient similar to that reported by others [15]. The questionnaire had the highest variability, possibly because of the impact of educational, social and relational factors. Question numbers 1, 2, and 6 had the highest variability coefficients.

The results of the clinical tests were of particular value in those symptomatic cases (10.7%) in which one of the two nerves found to be abnormal by ENG examination was the median nerve making the study of an additional nerve necessary to arrive at a diagnosis. In all of these cases (as well as in all symptomatic patients with two abnormal nerves other than the median nerve) either the VPT or NE showed abnormalities. It thus appears that in symptomatic cases the positivity of simple clinical tests such as VPT or NE could be sufficient to confirm the diagnosis of DP, thus eliminating the need for the ENG examination of an additional nerve. On the other hand, in none of the asymptomatic cases diagnosed by means of ENG (14.3%) was the median nerve abnormal, which makes it less probable, in our opinion, that the median nerve may be abnormal and that the ENG study of an additional nerve may be required in an asymptomatic neuropathic patient. These observations support our proposal of a simplified four-nerve ENG study for the diagnosis of diabetic DP in both clinically symptomatic and asymptomatic patients.

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