Diabetic Neuropathy Examination

A hierarchical scoring system to diagnose distal polyneuropathy in diabetes

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OBJECTIVE — Existing physical examination scoring systems for distal diabetic polyneuropathy (PNP) do not fulfill all of the following criteria: validity, manageability, predictive value, and hierarchy. The aim of this study was to adapt the Neuropathy Disability Score (NDS) to diagnose PNP in diabetes so that it fulfills these criteria.

RESEARCH DESIGN AND METHODS — A total of 73 patients with diabetes were examined with the NDS. Monofilaments and biothesiometry were used as clinical standards for PNP to modify the NDS.

RESULTS — A total of 43 men and 30 women were studied; mean duration of diabetes was 15 years (1–43), and mean age was 57 years (19–90). A total of 24 patients had type 1 diabetes, and 49 patients had type 2 diabetes. Clinically relevant items were selected from the original 35 NDS items (specific item scored positive in >3 patients). The resulting 8-item Diabetic Neuropathy Examination (DNE) score could accurately predict the results of the clinical standards and is strongly hierarchical (H value 0.53). The sensitivity and specificity of the DNE at a cutoff level of 3 to 4 were 0.96 and 0.51 for abnormal monofilament scores, respectively. For abnormal vibration perception threshold scores, these values were 0.97 and 0.59, respectively. Reproducibility as assessed by inter- and intrarater agreement was good.

CONCLUSIONS — The DNE is a sensitive and well-validated hierarchical scoring system that is fast and easy to perform in clinical practice.

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E arly detection of symmetrical distal sensorimotor polyneuropathy (PNP) is important in patients with diabetes because preventive interventions can be applied to decrease morbidity (1). Unfortunately, no "gold standard" exists for diagnosing PNP, but a consensus panel has recommended that at least 1 measurement should be performed in 5 different diagnostic categories. One of these categories is a standardized physical examination (2,3). In our opinion, diagnostic tests should fulfill the following criteria: validation (presence of an independent reference standard, adequate spectrum and number of patients, standardization, soundly based item selection), predictive value, manageability (reproducibility, performance in clinical

practice), and hierarchy. Frequently used and accepted examination scores for diabetic neuropathy are the Neuropathy Disability Score (NDS) (4), the Neuropathy Impairment Score in the Lower Limbs (NIS-LL) (5,6), various modified NDS scores (7,8), the Neuropathy Deficit Score (9), the Michigan Neuropathy Screening Instrument (MNSI) (10), and the Clinical Examination Score of Valk (CE-V) (11).

The NDS was designed for neuropathy in general (4). Although the score is well founded and complete, it is difficult to perform in clinical practice on patients with diabetic foot problems. Precise descriptions of how the tests should be performed and how items should be scored are lacking. The NIS-LL is a modification of the NDS specific for distal PNP, although motor activity grading is the focus and involves 64 of a maximum of 88 points (5,6). The NIS-LL has not been validated. Various other modified NDS scoring systems have been used, such as those of Veves et al. (7) and Young et al. (8); however, these instruments also have not been validated, and no information is available on their predictive value regarding the results of clinical standards. The Neuropathy Deficit Score is a neurological examination score aimed at anatomical levels in the legs and arms (9). It has not been validated, and no information is available about how to interpret modifications, which is also the case for the other modified NDS scoring systems (7,8). Feldman et al. (10) developed a combination of 2 scoring systems: the MNSI (symptom and examination score) and the Michigan Diabetic Neuropathy Score (neurological examination and nerve conduction studies). These scores do not have a separate examination score as advised by consensus reports (2,3). The CE-V can be used to examine sensory functions, tendon reflexes, and muscle strength in the lower extremities (11). The scoring systems of Feldman et al. (10) and Valk et al. (11) have been validated and are easy to perform in clinical practice. None of the aforementioned scores is known to be hierarchical.

The aim of this study was to adapt the NDS into a valid, easily managed, graded, and accurate scoring system for diagnosing

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Table 1—*Patient characteristics*

n	73
Mean age (years)	56.9 ± 16.1 (19–90)
Mean duration of diabetes (years)	14.9 ± 9.9 (1–43)
Sex (M/F)	43/30
Type of diabetes (type 1/type 2)	24/49
Mean HbA$_{1c}$ (%)	8.7 ± 1.4 (6.6–13.5)

Data are *n* or means ± SD (ranges).

PNP, the Diabetic Neuropathy Examination (DNE) score.

RESEARCH DESIGN AND METHODS

Patients
Our study group consisted of 73 patients with diabetes. Exclusion criteria were factors that may interfere with the neurological condition of the subjects other than PNP. A total of 50 patients were randomly selected from the diabetes outpatient clinic of University Hospital (Groningen, the Netherlands). A total of 23 patients with obvious diabetic foot complications or clinical neuropathy were selected from the Department of Diabetes at the Rehabilitation Centre Beatrixoord. The characteristics of these 73 patients are shown in Table 1.

Methods
The same researcher (J.-W.G.M.) examined all 73 patients. First, the NDS and NIS-LL were performed followed by quantitative sensory tests that acted as a clinical standard.

NDS and NIS-LL
The NDS is the most widely used and widely accepted scoring system for diabetic neuropathy; it has also been recommended in consensus reports (2–4). The instrument examines cranial nerves, muscle weakness, reflexes, and sensation (4). The scale consists of 35 items for testing the left and right sides of the body; scores range from 0 to 4. A sum score is obtained with a maximum of 280 points.

The NIS-LL is a modified version of the NDS to quantify diabetic PNP. The lower-limb items of the NDS are used complemented with 2 muscle power items (toe extension and toe flexion). The NIS-LL has 14 items: 8 items evaluate muscle power (0–4 points), 2 items evaluate reflexes (0–2 points), and 4 items evaluate sensory modalities (0–2 points). All items are tested on both sides. The maximum score is 88 points.

The NDS, as the most complete and accepted score, was used for item selection to develop the DNE.

Clinical standards
Semmes-Weinstein monofilaments and biothesiometry were chosen as clinical standards to study the construct validity of the scoring system for PNP. Semmes-Weinstein monofilaments were tested on the plantar surface of the hallux and centrally at the heel (when necessary after removal of excessive calluses). This method was standardized according to generally accepted guidelines (12–15). The "yes/no" method was used, which means that the patient says "yes" each time he or she senses the application of a monofilament. Six trials were administered; when the patient was unable to respond correctly in more than 1 trial, a heavier monofilament was used. The 1-, 10-, and 75-g monofilaments were used. We present the results in 4 categories: category 1, 1-g monofilament felt; category 2, 10-g monofilament felt and 1-g monofilament not felt; category 3, 75-g monofilament felt and 10-g monofilament not felt; and category 4, 75-g monofilament not felt.

Vibration perception thresholds (VPTs) were determined using a hand-held biothesiometer (Biomedical Instruments, Newbury, OH). VPT was tested at the dorsum of the hallux on the interphalangeal joint. It was performed in a standardized way (15,16). The voltage of vibration was increased until the patient could perceive a vibration. This was done 3 times. The mean of these 3 trials was used to determine the VPT.

Reproducibility
To test reproducibility, inter- and intrarater agreement were assessed in a separate study of 10 patients. The 6 women and 4 men with a mean ± SD age of 50.0 ± 15.9 years had a wide range of neuropathy severity. The mean duration of diabetes was 11.5 ± 10.5 years; 3 participants had type 1 diabetes, and 7 participants had type 2 diabetes. Two experienced physicians, an endocrinologist (E.E.B.) and a physiatrist (J.-W.G.M.), both experienced in diagnosing diabetic neuropathies, rated these patients twice within 1 week.

Statistical analyses
The internal consistency of the DNE was assessed by calculating Cronbach's α and reliability coefficient ρ (17), which are comparable with α. In addition to internal consistency, scalability coefficient *H* was computed with the probabilistic scaling program of Mokken Scaling Polychotomous (MSP) items to assess the hierarchical structure of the items (17). High values of coefficient *H* increase the likelihood that patients with the same scale score have difficulties or problems with the same items.

The statistical package SPSS-PC (Chicago) was used to compute the descriptive statistics, factor analysis, reliability coefficient Cronbach's α, Pearson's correlation coefficient *r*, and Student's *t* test.

Inter- and intrarater agreement were assessed on a scale level by computing Pearson's correlation coefficients and *t* test values for differences in means.

RESULTS — Items were excluded from the original NDS if they conformed to the following definition of clinical irrelevance: specific item scored positive in >3 patients. After examining the patients, 9 of the original 35 items remained. No relevant differences were found between the measurements made on the left and right sides, so only the right-side items were used in the analyses.

Factor analysis was performed on the 9 items to investigate coherence. The coherence of the 8 items was good; only item 22 (muscle strength in triceps surae) had poor coherence compared with the other items.

Calculation of hierarchy was performed using the MSP items. This resulted in a hierarchical scale of 8 items. Item 22 disturbed the hierarchy severely. Logistical regression analysis was performed to study whether item 22, in addition to the 8-item hierarchical scale, could predict the results of the clinical standards VPT and monofilaments. Item 22 did not make any significant contribution, so it was excluded.

Modification of the NDS resulted in an 8-item scale, the DNE. The DNE is shown in the Appendix. The reliability of the scale was assessed by measuring the internal consistency. According to both Cronbach's

α (0.78) and reliability coefficient ρ (0.81), the scale appears to be reliable. The *H* value for hierarchy was 0.53, which indicates the presence of a strong hierarchical scale (17).

Table 2 shows characteristics of the DNE, NDS, and NIS-LL. As expected, the correlation between the DNE and the NDS (Pearson's *r* = 0.96, *P* < 0.001) and NIS-LL (Pearson's *r* = 0.92, *P* < 0.001) were both high. The reliability of the scoring systems was good.

The DNE is fast and easy to perform in clinical practice; application takes ~5 min.

Relationship of the NDS, NIS-LL, and DNE with the clinical standards

Pearson's correlation coefficient *r* for monofilaments with the NDS, NIS-LL, and DNE was similar with values of 0.76 (*P* < 0.001), 0.74 (*P* < 0.001), and 0.75 (*P* < 0.001), respectively. Pearson's correlation coefficient *r* for VPT with the NDS, NIS-LL, and DNE was similar with values of 0.73 (*P* < 0.001), 0.71 (*P* < 0.001), and 0.75 (*P* < 0.001), respectively. The NDS, NIS-LL, and DNE predicted the results of the clinical standards very accurately (*P* < 0.001).

At a cutoff point of 3 to 4, the sensitivity and specificity of the DNE were 0.96 and 0.51, respectively, for an abnormal result using monofilaments. For an abnormal result using the VPT, these values were 0.97 and 0.59, respectively.

Reproducibility

Reproducibility of the DNE was assessed by comparing the scores of 2 raters obtained on 2 occasions (interval of 1 week). The interrater correlation was 0.97 at t_1 and 0.92 at t_2. Differences in mean scores were <10% and were not significant (*P* = 0.08 and *P* = 0.55, respectively). The intrarater correlation was 0.89 for 1 rater and 0.99 for the other. The mean scores of the 2 raters did not differ significantly at t_1 and t_2 (*P* = 0.17 and *P* = 0.60, respectively).

CONCLUSIONS — The NDS is a widely accepted and validated physical examination scoring system used to diagnose neuropathy. Its predictive value and reproducibility are high. It is well correlated with neurophysiological and sural nerve morphometric abnormalities in patients with diabetes (4,18–21). Because the aim of the NDS is to evaluate neuropathy in general, it is not completely suitable for use at an outpatient diabetic foot clinic. Consequently, several other scoring systems have been developed, but they do not sufficiently fulfill all of the criteria necessary for adequate diagnostic tests. One of these tests is the NIS-LL (a score for distal diabetic PNP), which has 14 items. The score has not been validated and focuses more on motor problems than on sensory problems (5,6).

In this study, the NDS was modified once again with the aim of achieving a new physical examination scoring system for diagnosing distal symmetrical PNP in diabetes. The new instrument is the DNE, which is a scoring system with 8 items. It was validated in diabetic patients with a wide spectrum of complications. The DNE is hierarchical, sensitive, fast, and easy to perform in clinical practice (application took ~5 min). Hierarchy implies that patients with the same scale score have difficulties or problems with the same items, which makes this scoring system able to differentiate between severity levels of PNP and to compare groups or individuals over time. The NDS, NIS-LL, and the other instruments for evaluating PNP have not been documented to represent a hierarchical scale.

Our modifications were validated with monofilament measurements and VPTs. These are both semiquantitative reliable measurements with proven predictive value for the development of clinical problems such as foot ulcers and amputations. They are noninvasive, patient friendly, independent, and complementary (12–16). Monofilaments and VPTs only assess large fiber function; no small fiber tests have been used in this study. Testing the DNE on a random sample from the outpatient clinic in addition to a set of patients with definite neuropathy means that the results are generalizable to the complete range of patients with diabetes.

Many clinicians prefer using electrodiagnostic techniques to diagnose diabetic PNP. Although neurophysiological examination is sensitive, specific, and reproducible regarding the presence and severity of peripheral nerve involvement in patients with diabetes (18), it is not suitable for making a quick preliminary diagnosis at a diabetes outpatient clinic. No data are available on the predictive value of these techniques in relation to the development of clinical problems such as diabetic foot disease.

Because the aim of this study was to develop a screening instrument as a tool in the detection and prevention of patients at risk for diabetic foot complications, the observed sensitivity and specificity of the DNE are satisfactory. Because sensitivity is of greater importance than specificity for screening instruments, the chosen cutoff value results in the desired high sensitivity with an acceptable specificity. A low specificity might burden prevention education programs. The combined use of different diagnostic tools, as advised in consensus reports, will enhance specificity.

The selection of the muscle strength of the quadriceps femoris item in the DNE is surprising and suggests the presence of mononeuropathy. Nevertheless, all patients with quadriceps dysfunction also showed other abnormalities regarding sensations in the feet that were not related to the same peripheral nerves, which makes mononeuropathy less probable. The ankle dorsiflexion item was excluded because of poor coherence and disturbance of hierarchy. It did not contribute to the 8 definite items. Perhaps this discrepancy in muscle strength and its assessment is because of other factors such as limited joint mobility.

The results of validation and the predictive value of the NDS, NIS-LL, and DNE were very satisfactory. The strengths of the DNE are its manageability in clinical practice and its hierarchy. The DNE is the most efficient according to the criteria shown in Table 2.

Table 2—*Characteristics of the NDS, NIS-LL, and DNE in our study population* (n = 73)

	NDS	NIS-LL	DNE
Mean score	19.7 ± 14.5	9.7 ± 7.9	5.0 ± 3.6
Reliability (α)	0.88	0.87	0.78
Items	70	28	8
Maximum score	280	88	16
Maximum scored	56	32	13
Items not scored	44	1	0
<3 scores	8	3	0

Data are *n* or means ± SD, unless otherwise indicated.

In conclusion, the DNE as modified from the NDS is fast, easy to perform, hierarchical, and sensitive for PNP, and patient scores are more differentiated.

APPENDIX: DIABETIC NEUROPATHY EXAMINATION

Diabetic Neuropathy Examination
Muscle strength
1. Quadriceps femoris: extension of the knee
2. Tibialis anterior: dorsiflexion of the foot

Reflex
3. Triceps surae

Sensation: index finger
4. Sensitivity to pinpricks

Sensation: big toe
5. Sensitivity to pinpricks
6. Sensitivity to touch
7. Vibration perception
8. Sensitivity to joint position

Only the right leg and foot are tested.
Scoring from 0 to 2:
0 = Normal
1 = Mild/moderate deficit
- Muscle strength: Medical Research Council scale 3–4
- Reflex: decreased but present
- Sensation: decreased but present

2 = Severely disturbed/absent
- Muscle strength: Medical Research Council scale 0–2
- Reflex: absent
- Sensation: absent

Maximum score: 16 points

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