

A Comparison of the DN4 and LANSS Questionnaires in the Assessment of Neuropathic Pain: Validity and Reliability of the Turkish Version of DN4

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Abstract: A screening tool that quickly and correctly differentiates neuropathic pain from non-neuropathic pain is essential. Although there are many screening tools in the assessment of neuropathic pain, many physicians still have the problem of not being able to identify their neuropathic pain patients easily. In this study, we assessed the test-retest reliability, internal consistency, and validity of the Turkish version of DN4 questionnaire. Within the same group of patients, we also compared the DN4 with the LANSS questionnaire. A total of 180 patients (n = 121 with neuropathic pain and n = 59 with non-neuropathic pain characteristics) were enrolled. In our study population, peripheral origin of neuropathic pain, mainly radiculopathies and polyneuropathies, dominated. The reliability and validity of Turkish version of DN4 were found to be high. The sensitivities of the DN4 and the LANSS were 95% and 70.2%, respectively. The specificity of both tests was 96.6%. The strengths and weaknesses of these questionnaires are discussed.

Perspective: The Turkish version of DN4 questionnaire is reliable and valid. It is also an easier, quicker, and more sensitive screening tool (1-minute test) compared with the Turkish version of LANSS questionnaire. These features of the DN4 may help clinicians to identify their neuropathic pain patients accurately in daily clinical practice and research studies.

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Key words: Neuropathic pain, non-neuropathic pain, visual analog scale, pain assessment, screening tool.

A group of experts from the neurology and pain community has redefined neuropathic pain as: "Pain arising as a direct consequence of a lesion or disease affecting the somatosensory system."²⁶ However, the diagnosis of neuropathic pain is still challenging. A working grading system includes a history of pain suggesting a neuroanatomically relevant lesion or disease, examination of negative or positive sensory signs confined to the innervation territory of the nervous system with any diagnostic test confirming a lesion or disease to explain the neuropathic pain.²⁶ Symptomatology of neuropathic pain includes spontaneous or trigger-induced chronic pain, characteristically burning, stabbing, electric-like shocks, sharp, shooting, lancinating or

sometimes as dull, aching, pressure, squeezing, deep, cold pain, and neuropathic itch.^{5,16,17} The estimated prevalence of neuropathic pain characteristics in the general population may be as high as 7%.⁷ However, many physicians still have the problem of not being able to identify neuropathic pain patients.¹⁵ Without an appropriate suspicion of neuropathic pain, many patients are under the burden of productivity loss and/or loss of desire to live and are to be faced with inappropriate or under-treatment. Besides, there is an unnecessary occupation of higher-level health care systems with the same pain complaints, which all result in a huge economic loss for the country.

The first suspicion of neuropathic pain can be identified by screening tools. In literature, screening tools to identify neuropathic pain have been developed since 2001.⁴ There are many reported screening tools (LANSS, DN4, NPQ, PainDETECT, ID-pain, StEP questionnaire and etc) to identify neuropathic pain.^{1,3,6,13,21,22} Recently, an expanded and revised form of Short-form McGill Pain Questionnaire (SF-MPQ-2) has been validated in neuropathic pain patients as well.¹¹ The SF-MPQ-2

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questionnaire has the advantage of evaluating the pain intensity as well as measuring sensory, affective, and evaluative qualities of pain. The response to treatment may also be assessed.¹¹ Based on pain symptoms and clinical examinations, all screening tools have strengths and weaknesses.^{4,10} The strength of the ID-pain scale is to assesses pain limited to joints (used to identify non-neuropathic pain); pain-DETECT assesses radiation of pain and pain evoked by mild pressure, heat, or cold; NPQ assesses pain evoked by changes in weather; LANSS assesses autonomic changes; and DN4 assesses both itching and raised soft touch threshold.⁴ A recently reported screening tool to differentiate radicular back pain from axial low back pain is named StEP (Standardized Evaluation of Pain).²² All screening tools have self-assessment questions. However, sensory examination is present in LANSS, DN4, and StEP questionnaires, which give them an objective significance and crucial findings for the diagnosis of neuropathic pain, among all the others.

The DN4 questionnaire (Douleur Neuropathique 4 questions) was originally developed and validated by a French group of experts.⁶ Linguistic validation of the DN4 for use in international studies has been reported as well.²⁷ In this study, we aimed to assess the validity and reliability of the Turkish version of the DN4 questionnaire and whether it is an easy and accurate screening tool to identify neuropathic pain patients. This may enable us to identify very quickly and standardize the neuropathic pain patients in daily clinical practice and in research studies. Within the same group of patients, we also wanted to compare the strengths or weaknesses of the DN4 questionnaire with the LANSS questionnaire.

Materials and Methods

The DN4 questionnaire consists of 10 items.⁶ The first 7 items are related to pain characteristics and sensations and the remaining 3 items are related to the examination (see Appendix A). For each item, a score of "1" is given if the answer is "yes" and a score of "0" is given if it is "no." The patient is defined to have neuropathic pain if the sum of all 10 items is calculated to be 4 or more.⁶

Adaptation Procedure Into Turkish of the DN4 Questionnaire

After approval of the study by the local ethics committees (applied by one of the authors [I.U.C.] to both Ufuk University Faculty of Medicine Local Ethics Committee and Medicana International Ankara Hospital Local Ethics Committee), the DN4 was adapted to Turkish population using recommended guidelines for cross-cultural adaptation.² Initially the English questionnaire was translated into Turkish by 4 native Turkish-speaking physicians, an expert engineer in methodology, and an English linguist (forward translation). The Turkish questionnaire was back-translated into English by a native English speaker who spoke Turkish fluently and did not see the original questionnaire. Later, the Turkish translations of most accurate, understandable, and compatible to Turkish

DN4 and LANSS Scales in the Assessment of Neuropathic Pain culture were decided by the authors. The questionnaire was tested to a pilot group of 30 patients with pain complaints who were asked to report any difficulty in both meaning and conceptual framework of the questionnaire. Finally, the last revision was made to assess the clarity or appropriateness of wording of the translated questionnaire (see Appendix B). The investigators involved in this study were a neurologist and pain specialist (I.U.C.) and physiatrists (S.S.A. and D.E.). The study was conducted in Ufuk University Faculty of Medicine, Departments of Neurology and Physical Medicine and Rehabilitation. One of the authors (I.U.C.) also recruited patients from Medicana International Ankara Hospital Pain Center.

Patients

Patients aged over 18, having a chief pain complaint in 1 anatomical location, either diagnosed to have neuropathic pain (NP) or non-neuropathic pain (NPP) were included. Patients who had an adequate level of understanding of the questionnaire were enrolled and written informed consents were obtained. The Turkish version of the DN4 questionnaire was administered to the same patient twice, 2 days apart, by the same investigator. Differential diagnosis of patients with neuropathic pain was based on medical history, clinical examinations, and appropriate diagnostic techniques including neuroimaging and electrophysiological studies when indicated. The patients diagnosed to have definite or probable neuropathic pain were included for data analysis.²⁶ Patients with possible neuropathic pain were not included in the study. The musculoskeletal and neurological examinations of the patients with cervical and lumbar pain were performed appropriately. Only the patients whose main clinical findings were consistent with radiculopathy (characterized by radicular pain toward the affected limb and clinical signs of nerve root involvement, including sensory or motor deficits in the limb and a diminution or loss of tendon reflexes) were enrolled in neuropathic pain group. The non-neuropathic pain group included osteoarthritis, mechanical low back pain (defined as axial pain accompanied by limitation of the range of motion in the neck or low back area without any sign of radiculopathy), myofascial pain syndrome, carpal tunnel syndrome (defined as mild paresthesia and indistinct discomfort present only at night), and somatoform disorders. A detailed form that included the demographic characteristics of the patient and clinical characteristics of their pain assessed by 10-cm visual analog scale (VAS) and the duration and ease of use of DN4 and LANSS questionnaires was filled by the physician. The physician recorded the time consumed in filling both questionnaires by a stop watch.

Statistics

For the statistical analysis, SPSS for Windows Release 16.0 (SPSS Inc, Chicago, IL) was used. All data for normality was tested by using the Kolmogorov-Smirnov test. To compare the differences between the groups, the Mann-Whitney *U* test was used.

Reliability

Reliability of the Turkish version of the DN4 was tested by internal consistency and test-retest reliability. Test-retest reliability gives an opinion that there has been no change in condition between 2 successive administrations. It was evaluated by using intraclass correlation coefficient (ICC) with 95% confidence interval, ranged between 0 and 1, and the results over 0.70 were accepted adequate for reliability.^{12,18,19} Internal consistency determines the homogeneity of the subscale and it can also be described as intercorrelation of the items in an instrument and was expressed by Cronbach's α coefficient.⁹ Cronbach's α coefficient ranges from 0 to 1, and higher values indicate higher internal consistency reliability.^{9,12}

Validity

Validity was assessed by construct validity, ROC (receiver operating characteristic), AUC (area under the curve), along with sensitivity and specificity.²⁵ Construct validity was determined by testing for expected associations between the adapted instrument and other valid measures. Spearman correlation coefficient² was used for statistical analysis. Construct validity was evaluated with correlation between Turkish LANSS questionnaire.²⁸ ROC curve analysis was used to determine the cut-off value of the questionnaire score for neuropathic pain diagnosis. The AUC was calculated by the trapezoid method.

Results

Patient Characteristics

A total of 180 patients ($n = 121$ with neuropathic pain characteristics and $n = 59$ with non-neuropathic pain) were enrolled to the study. Among the neuropathic pain patients ($n = 121$), the definite and probable neuropathic pain groups consisted of 71.1% ($n = 86$) and 28.9% ($n = 35$), respectively. Demographic and clinical features of the participants are shown in Table 1. There was no difference in sex, body mass index, educational level, occupation, and presence of the use of any medication to relieve pain between the groups. However, neuropathic pain patients were slightly older, and VAS scores were higher than the non-neuropathic pain patients ($P < .05$). The etiology of pain in the study patients is summarized in Table 2. Patients with neuropathic pain components consisted of both peripheral and central origin. Non-neuropathic pain patients consisted of those with osteoarthritis (knee and hip), mechanical low back pain, myofascial pain syndrome, carpal tunnel syndrome (without neuropathic pain components), and somatoform disorders.

Features of NP and NNP According to DN4 Questionnaire

We compared the frequency of positive score for each item of the DN4 questionnaire between neuropathic and non-neuropathic patients (Table 3). Each item was re-

Table 1. Demographic Data of the Neuropathic and Non-Neuropathic Pain Patients

	NP (n = 121)	NNP (n = 59)	P VALUE
Age (y)	53.3 ± 14.1	48.7 ± 13.1	.035
Sex (female/male)	78/43	34/25	.376
BMI (kg/m ²)	26.3 ± 15.1	23.4 ± 15.5	.603
Education level n, (%)			.126
Low (≤8 y)	66 (54.6%)	25 (42.4%)	
High (>8 y)	55 (45.4%)	34 (67.6%)	
Occupation n, (%)			.436
Employed	69 (57.0%)	30 (50.9%)	
Unemployed	52 (43.0%)	29 (49.1%)	
Drug therapy n, (%)			.259
Medication (for pain relief)	86 (71.1%)	37 (62.7)	
No medication (for pain relief)	35 (28.9%)	22 (37.3%)	
Patients' global VAS assessment	5.3 ± 1.6	4.7 ± 1.5	.002
Physicians' global VAS assessment	5.9 ± 1.7	5.0 ± 1.9	.023

BMI, body mass index; NP, pain associated with neuropathic pain component; NNP, pain associated with non-neuropathic pain component; VAS, visual analog scale (0 to 10).

ported to be statistically significant in neuropathic pain patients compared to non-neuropathic pain patients (all $P < .05$). The prominent sensory descriptive of DN4 questionnaire in neuropathic pain patients were tingling, burning, pins and needles, electric shocks, painful cold, and numbness. The least symptom reported was itching (30.6%). On examination hypoesthesia to touch, hypoesthesia to prick, and brush allodynia was present in more than 50% of neuropathic pain patients and less than 5% in non-neuropathic pain patients ($P < .05$).

Table 2. Etiology of Pain in the Study Patients

	n (%)
Neuropathic pain (n = 121)	
Radiculopathy (cervical or lumbar)	63 (52.1%)
Non-diabetic polyneuropathy	13 (10.7%)
Diabetic polyneuropathy	12 (9.9%)
Carpal tunnel syndrome	8 (6.6%)
Postherpetic neuralgia	5 (4.1%)
Post-surgical pain	5 (4.1%)
Trigeminal neuralgia	4 (3.3%)
Medulla spinalis benign lesion	2 (1.7%)
Spinal stenosis	2 (1.7%)
Post-stroke pain	1 (0.8%)
Nerve trauma	1 (0.8%)
Thoracic outlet syndrome	1 (0.8%)
Neuralgia paresthetica	1 (0.8%)
Occipital neuralgia	1 (0.8%)
Phantom pain	1 (0.8%)
Non-neuropathic pain (n = 59)	
Osteoarthritis	27 (45.8%)
Mechanical low back pain	22 (37.3%)
Myofascial pain syndrome	6 (10.2%)
Carpal tunnel syndrome	2 (3.3%)
Somatoform disorder	1 (1.7%)

Table 3. Frequency of the DN4 Questionnaire 10 Items Between Groups

	NP n (%)	NNP n (%)	P VALUE
Burning	103 (85.1%)	20 (33.9%)	.000
Painful cold	67 (55.4%)	9 (15.3%)	.000
Electric shocks	94 (77.7%)	7 (11.9%)	.000
Tingling	107 (88.4%)	8 (13.6%)	.000
Pins and needles	102 (84.3%)	5 (8.5%)	.000
Numbness	73 (60.3%)	4 (6.8%)	.000
Itching	37 (30.6%)	7 (11.9%)	.006
Hypoesthesia to touch	89 (73.6%)	2 (3.4%)	.000
Hypoesthesia to prick	64 (52.9%)	3 (5.1%)	.000
Brushing	68 (56.2%)	1 (1.7%)	.000

Reliability

The DN4 questionnaire was reliable for both neuropathic and non-neuropathic pain patients, with Cronbach's α coefficients of 0.97 and 0.98, respectively (Table 4). Each 10 items of DN4 questionnaire had a Cronbach's α coefficient greater than the recommended value (0.70) in neuropathic and non-neuropathic pain groups (Cronbach's α coefficient values ranged from 0.93 to 1.00 in the neuropathic group and 0.79 to 1.00 in the non-neuropathic group). The total score of the DN4 questionnaire test and retest reliability was also good, with a high intraclass correlation coefficient between the 2 time periods in both neuropathic and non-neuropathic pain groups (ICC, 0.95 and 0.96, respectively) (Table 4).

Validity

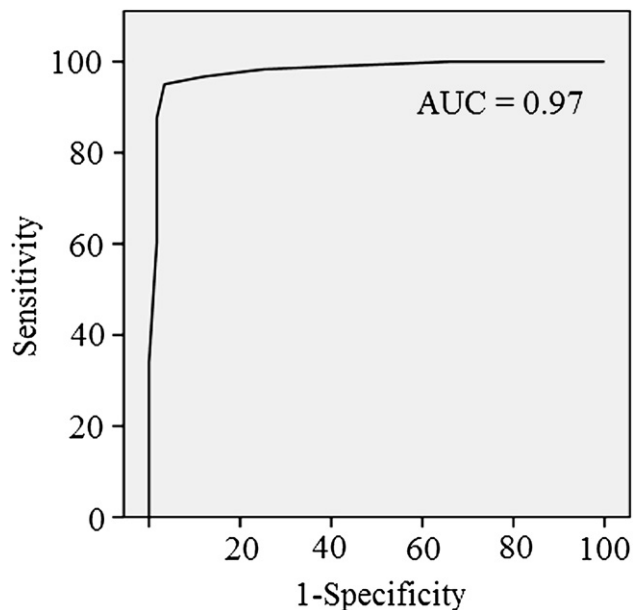
To differentiate NP from NNP, the indicators of validity tested by construct validity, sensitivity, and specificity of the DN4 questionnaire were found to be good. Total scores of DN4 questionnaire in neuropathic and non-neuropathic patients were high, which correlated with the total scores in LANSS questionnaire (construct validity $r = 0.60$, $P = 0.000$ in neuropathic patients and $r = 0.61$, $p = 0.000$ in non-neuropathic pain patients). The DN4 questionnaire validity was also tested by ROC curve and AUC analysis. A total score ≥ 4 points in the DN4 questionnaire was very effective to discriminate between neuropathic and non-neuropathic patients (Fig 1).

Comparison of DN4 and LANSS Questionnaires

In the neuropathic pain group, for the DN4 and the LANSS, the sum of median scores were 6.6 and 16,

Table 4. Internal Consistency and Test-Retest Reliability of the Turkish Version of the Total Score of DN4 Questionnaire in Patients With Neuropathic Pain and Non-Neuropathic Pain

	INTERNAL CONSISTENCY (CRONBACH'S α)	TEST	RE-TEST	ICC (95% CI)
NP	0.97	6.64 \pm 1.87	6.65 \pm 1.78	0.95 (0.94-0.97)
NNP	0.98	1.11 \pm 1.26	1.03 \pm 1.29	0.96 (0.94-0.97)

**Figure 1.** ROC curve and AUC of the DN4 questionnaire (total score ≥ 4) in patients with NP.

respectively, whereas in the non-neuropathic group these scores were 1 for both. The sensitivity and specificity of the DN4 questionnaire (with a cut-off value ≥ 4 of the total score) in the diagnosis of neuropathic pain within neuropathic pain patients were found to be 95% and 96.6%, respectively. The sensitivity of the LANSS questionnaire (with a cut-off value ≥ 12 of the total score) within neuropathic pain patients was 70.2%, whereas the specificity of the scale was 96.6% (Table 5). These results indicate a strong relationship between clinical diagnosis (gold standard) and DN4 questionnaire scores with accepted cut-off values (≥ 4). The physicians completed the DN4 questionnaire in 1 minute \pm 15 seconds and the LANSS questionnaire in 3 minutes \pm 30 seconds. Compared with the LANSS questionnaire, the DN4 questionnaire was noted to be easy to apply by the physicians and to get a quick reply from the patients. These results suggest that the DN4 questionnaire can be administered in a very short time without any burden on patients or physicians.

Discussion

The diagnosis of neuropathic pain is still very challenging. Clinicians who are not pain specialists have a request for a short, simple, but accurate tool to identify the neuropathic pain patients in their daily practice. Besides, there is a need of a standardized identification of neuropathic pain patients in research studies. In this study we validated the Turkish version of the DN4 questionnaire to be used in neuropathic pain patients. Our results confirmed test-retest reliability and internal consistency. We also reviewed all the current screening tools and compared the strengths and weaknesses of the DN4 with the LANSS questionnaire.

Table 5. Accuracy of the Two Screening Tools in Identifying Patients With Neuropathic Pain

	<i>SENSITIVITY</i>	<i>SPECIFICITY</i>	<i>PPV</i>	<i>NPV</i>
DN4	95 (89.6-97.7)	96.6 (88.5-99.1)	98.3 (94.8-99.5)	90.5 (85.0-94.2)
LANSS	70.2 (61.6-77.7)	96.6 (88.5-99.1)	97.7 (93.9-99.2)	61.3 (53.7-68.4)

Abbreviations: PPV, positive predictive value; NPV, negative predictive value.

NOTE. All numbers are presented as percentages within a 95% confidence interval.

Our study population consisted of 180 pain patients. Similar to the original report, the etiology of our neuropathic pain patients was more common with peripheral rather than central origin.⁶ In our study, neuropathic pain associated with radiculopathies and polyneuropathies dominated. A ratio of 10:1 among peripheral versus central neuropathic pain and a dominance of diabetic polyneuropathy and radiculopathy was reported in a European neurologist survey as well.²⁴ Thus, with our study population, we were able to determine the neuropathic pain components in more complex pain conditions of mixed origin. Radiculopathies associated with the neuropathic pain component has been also shown by recent studies.^{13,14,22} In clinical trials with neuropathic pain, a patient's VAS score of ≥ 3 is usually needed as an inclusion criteria,²³ and our study patients had VAS score >5 . The adaptation procedure was followed according to the established protocols.²⁷ Patients of neuropathic pain or non-neuropathic pain group did not differ according to sex, occupation, or educational level. This enabled us to interpret that there was no difference in level of understanding of the questionnaires in both groups. Reliability of the DN4 questionnaire, tested with internal consistency and test-retest, was very good, and our results were also comparable with the Spanish version of the DN4 study.²⁰ The validity of Turkish version of the DN4 questionnaire led us to notice its high diagnostic properties. We applied both DN4 and LANSS questionnaires to each patient, which enabled us to test and compare neuropathic pain terms at the same time in the same patient. The presence of each 10 items (7 descriptive and 3 examination parts) of the DN4 questionnaire was statistically significant in the neuropathic pain group. The most important features of neuropathic pain were tingling, burning, and pins and needles and electric shocks, the same as in the original study.⁶ Itch as a neuropathic pain symptom was assessed in the DN4⁶ and in the SF-MPQ-2 questionnaires.¹¹ We found that 30.6% reported itching in the neuropathic pain group, similar to the original report.⁶ We conclude that as neuropathic itch may be a very bothersome problem for the patients seeking treatment, this symptom must be correctly diagnosed and treated appropriately as previously reported.⁵

The sensitivity of the DN4 questionnaire (total score ≥ 4) was higher than in the LANSS questionnaire (total score of ≥ 12). In a validation study of the Turkish version of the LANSS questionnaire, the sensitivity and specificity (from 44 neuropathic pain patients and 49 nociceptive pain patients) were found to be 89.9% and 94.2%, respectively.²⁸ We may assume that this discrepancy might

be due to the lesser number of patients and different clinical characteristics of their study population. In their neuropathic pain group, the median LANSS score was reported to be 18,²⁸ whereas our neuropathic pain patients had a LANSS median score of 16. In contrast to the DN4 questionnaire, which gives 1 score to each item, the LANSS questionnaire gives different scores according to each positive question.³ For example, in the LANSS, the second question, related to the change in color of the skin (autonomic dysfunction), gives 5 points when it is present. This feature is most commonly observed in CRPS patients. In our study, 81.8% of the neuropathic pain patients responded "no," so the total score automatically dropped down to 19. The 4th question related with electric shocks and the 5th question related with the feeling of hot or burning are weighted very low (scores of 2 and 1, respectively) in the LANSS questionnaire.³ However, burning pain and electric shocks are very dominant sensory descriptors both in our study population and in previously reported neuropathic pain patients.^{6,8} In the LANSS questionnaire, the presence of mechanical allodynia is scored in both the 3rd and 6th items. If a patient does not have mechanical allodynia, then the total score drops automatically down to 16. We think these may all account for the low sensitivity of the LANSS questionnaire in detection of neuropathic pain patients, compared with the DN4 questionnaire in our study. We think, as both questionnaires have the same specificity, due to the higher sensitivity of DN4 questionnaire, it will be less likely to miss the identification of neuropathic pain patients. Many clinicians, either non-pain specialist or primary care physicians, are dealing with chronic pain patients. However, they usually complain of not having adequate skill or enough time to evaluate these patients. In this study, we documented that the DN4 was an easy and very short (1 minute test) compared with the LANSS. The DN4 questionnaire was found to be very definite (easy to be applied by the physician) and the LANSS to be very descriptive (for the patient).

We conclude that the Turkish version of DN4 questionnaire is a reliable, valid, short, and quick screening tool in identification of neuropathic pain patients to be used in daily clinical practice and multicenter clinical research studies.

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Appendix A: Questionnaire DN4

Please complete this questionnaire by ticking 1 answer for each item in the 4 questions below:

Interview of the Patient

Question 1. Does the pain have one or more of the following characteristics?

	YES	NO
1. Burning		
2. Painful cold		
3. Electric shocks		

Question 2. Is the pain associated with one or more of the following symptoms in the same area?

	YES	NO
4. Tingling		
5. Pins and Needles		
6. Numbness		
7. Itching		

Examination of the Patient

Question 3. Is the pain located in an area where the physical examination may reveal one or more of the following characteristics?

	YES	NO
8. Touch hypoesthesia		
9. Pricking hypoesthesia		

Question 4. In the painful area, can the pain be caused or increased by:

	YES	NO
10. Brushing		

Patient score: /10.

Appendix B: DN4 Anketi

Lütfen bu anketi aşağıdaki 4 sorunun her bir maddesi için bir cevap işaretleyerek doldurunuz:

Hasta ile Görüşme

Soru 1. Ağrı, aşağıdaki bir veya daha fazla özelliğe sahip mi?

	EVET	HAYIR
1. Yanma		
2. Ağrılı soğuk hissi		
3. Elektrik çarpması		

Soru 2. Ağrı, aynı bölgede aşağıdaki yakınmalardan bir veya daha fazlası ile ilişkili mi ?

	EVET	HAYIR
4. Karıncalanma		
5. İğnelenme		
6. Hissizlik		
7. Kaşınma		

Hastanın muayenesi

Soru 3. Ağrı ; fizik muayenenin yapıldığı bir alana lokalize ve aşağıdaki özelliklerden bir veya daha fazlasını açığa çıkarıyor mu?

	EVET	HAYIR
8. Dokunma hipoestezisi		
9. İğne hipoestezisi		

Soru 4. Ağrılı bölgede, ağrıya neden olabiliyor ya da arttırabiliyor mu:

	EVET	HAYIR
10. Fırçalama		

Hastanın puanı: /10.