Ann Med Res 2021;28(4):759-66

Annals of Medical Research

DOI: 10.5455/annalsmedres.2020.11.1097

Original Article

Validation and Cross-cultural Adaptation and Reliability of the Turkish Version of the Michigan Neuropathy Screening Instrument in the Eastern Anatolia Region of Turkey

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Abstract

Aim: Distal symmetric polyneuropathy is a common complication causing foot ulcers and amputations in diabetic patients. The Michigan Neuropathy Screening Instrument (MNSI) is one of the screening methods of diabetic neuropathy, which also provides a comprehensive foot evaluation. The aim of this study was to evaluate the validation, cross-cultural adaptation, and reliability of Turkish Version of the MNSI in the Eastern Anatolia region of Turkey.

Materials and Methods: One hundred twenty-six patients with diabetes mellitus were randomly assigned to the study. The questionnaire section of the MNSI was completed by the patients, and the physical examination section was evaluated by health professionals. Nerve conduction studies were performed to 123 patients as the gold standard for diabetic neuropathy. All nerve conduction studies and patients were evaluated by a neurologist.

Results: The inter-rater agreement of questionnaire section [ICC: 0.957 (95% CI: 0.940-0.969), p<0.001] and physical examination section [ICC: 0.917 (95% CI: 0.884-0.941), p<0.001] were excellent. The intra-rater agreement of the questionnaire section [ICC: 0.880 (95% CI: 0.833-0.914), p<0.001] and physical examination section [ICC: 0.920 (95% CI: 0.889-0.943), p<0.001] showed a high stability. The area under curve (AUC) for the questionnaire section and physical examination section of the MNSI were 0.588 (p=0.205) and 0.880 (p<0.001), respectively. The optimum cut-off value of the physical examination section determined using both Youden's index and Index of Union as >3, with the sensitivity of 76.2%, specificity of 91.2%, positive predictive value of 64%, negative predictive value of 94.9%.

Conclusion: The physical examination section of Turkish version of the MNSI is valid and reliable.

Keywords: Diabetic neuropathy; distal symmetric polyneuropathy; michigan neuropathy screening instrument; nerve conduction study

INTRODUCTION

Diabetes mellitus (DM) is a serious, long-term disease that affects patients' quality of life, their families, and societies (1). The number of patients with DM worldwide in 2019 was estimated as 463 million by the International Diabetes Federation (1). A cross-sectional survey, 'The Turkish Epidemiology Survey of Diabetes, Hypertension, Obesity and Endocrine Disease (TURDEP II)' which was conducted in 2010, demonstrated that the prevalence of DM was 16.5% in adult Turkish population (2). Distal symmetric polyneuropathy (DSP) is one of the most common complications causing morbidity and mortality in patients with DM (3). Foot ulcers and amputation are common as consequences of DSP and/or peripheral arterial disease (4). The prevalence of DSP was reported as 11-50% in Type 1 (T1DM), 8-51% in patients with Type 2 DM (T2DM) (3). In addition the American Diabetes Association (ADA) reported that up to 50% of diabetic peripheral neuropathy might be asymptomatic (4). Early diagnosis and treatment is very important for preventing both long- and short-term morbidity because patients with DM are at risk for foot injuries. The ADA recommended that all patients should be assessed for diabetic neuropathy starting at the diagnosis of T2DM and five years after the diagnosis of T1DM (4).

Received: 03.11.2020 **Accepted:** 31.12.2020 **Available online:** 22.04.2021
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Several methods are used for determining DSP such as the monofilament test, the physical evaluation scoring system, vibration test and nerve conduction studies (NCS), and skin biopsy (5,6). NCS are objective, sensitive, reliable, and the gold standard method for DSP (7,8). However, NCS are time-consuming and expensive methods. The ideal screening method should be practical, inexpensive, and non-invasive (7). The Michigan Neuropathy Screening Instrument (MNSI) was created by Feldman et al. in 1994 (9). The MNSI provides standardization for clinical assessment and referring patients to relevant departments for the treatment of DSP and follow-up (7). The MNSI has also been used in large cohort studies (10).

Our aim was to perform the cross-cultural adaptation, validation and reliability study of Turkish version of the MNSI in the Eastern Anatolia region of Turkey.

MATERIALS and METHODS

Study Population

A total of 144 patients with T1DM (five-year after diagnosis) and T2DM (starting at the diagnosis) who presented to outpatient internal medicine clinic, aged at least 18 years and literate, were randomly assigned into the cross-sectional study between May 2019 and Dec 2019. The (7xnumber of items and ≥100) method was used for determining sample size, which was described by Terwee et al (11). Before performing the MNSI evaluation, a pilot study was performed with 15 patients with diabetes and 15 health professionals. Patients with renal failure (estimated glomerular filtration rate (eGFR) <60 mL/min/1.73m^2), visual problems, liver disease, infections causing neuropathy (eg. HIV), alcohol abuse, B12 deficiency, drug abuse, peripheral vasculitis or autoimmune disease, cerebrovascular disease, cancer, history of receiving radiotherapy or chemotherapy, mental or physical conditions affecting cognitive functions and clinical radiculopathy were excluded. Ethics approval for the study was granted by Erzincan Binali Yildirim University Clinical Research Ethics Committee (date: 05.03.2019, no: 01/06). Written informed consent was obtained from all patients. The patients were informed about leaving the study on request in any time of the study process.

Socio-demographic characteristics of patients, age, education duration (year), occupation, type of DM, duration of DM (year), and body mass index (BMI) (kg/m^2) were recorded. Laboratory tests including glycated hemoglobin (HbA1c) (%) level, fasting plasma glucose level, liver and renal function tests were performed.

Michigan Neuropathy Screening Instrument (MNSI)

The MNSI is a two-step method that includes a questionnaire section completed by patients, and a physical assessment section evaluated by physician (9). The questionnaire section includes 15 questions about the sensation of the feet and legs of the patient. Thirteen questions of questionnaire are related to DSP, the 10th question is related to general weakness, and the 4th question is related to peripheral vascular disease. 'Yes' answers receive one point for questions 1-3, 5-6, 8-9, 11-12,14-15. 'No' answers receive one point for questions 7 and 13 (7,9,12). Patients receive scores between 0 and 13 in the questionnaire section (12).

The second section of the MNSI includes clinical evaluations performed by health professionals. It is composed of four clinical assessments including inspection of both feet (dry skin, calluses, fissures, deformities and infection), presence of ulceration, and vibration sensation of great toe and ankle reflexes. Each foot with any abnormality or ulcer in inspection receives a score of 1. Foot deformities included hammer toes, overlapping toes, halux valgus, joint subluxation, prominent metatarsal heads, and medial convexity (Charcot foot). If the ankle reflex is normal, the score is 0. If the reflex is present with the Jendrassic maneuver, the score is 0.5. If the reflex is absent with Jendrassic maneuver, the score is 1. A 128-Hz tuning fork is used for vibration evaluation. Vibration is scored as present (scored as 0) if the examiner senses the vibration on their finger for shorter than 10 seconds after the patient expresses the end of vibration feeling in the great toe. Vibration is scored as decreased if sensed for ≥ 10 seconds (scored as 0.5). If vibration sensation is absent, it is scored as 1 (9,12). The score of physical assessment is between 0 and 8.

Cross-cultural adaptation of Turkish Version of Michigan Neuropathy Screening Instrument

The cross-cultural adaptation of the Turkish version of MNSI was conducted through steps including preparation, translation from English to Turkish, reconciliation, back translation into English, harmonization, cognitive debriefing, finalization and proofreading (13). As part of the preparation, permission to use the MNSI was obtained from Feldman who was one of the creators of the MNSI via e-mail. The original version of the MNSI was translated from English to Turkish by a medical expert interested in pain medicine and a non-medical professional translator, independently, both of whom were fluent in the English language. The translation of the MNSI into Turkish version was compared by researchers. The fifth question was translated from English to Turkish by two different bilingual persons independently because the researchers could not come to an agreement in the word 'prickling'. 'prinkling' was translated as 'karıncalanma/iğnelenme/batma' in the fifth question because it expresses multiple meanings in Turkish. After reconciliation, the Turkish version of the MNSI was back translated into English by two professional translators who were blinded to original version of the instrument. The original version of the MNSI and re-translation of the instrument were almost the same. The words 'bath and shower' were used in the seventh question because 'bathtub' is not as common as 'bath and shower' in Turkish culture. The words 'your doctor' were changed as 'any doctor' in the ninth question because patients can present to different doctors in the Turkish healthcare system. 'Amputation' is not commonly

used in Turkish. Therefore, the meaning of amputation was explained in brackets in the fifteenth question. In addition, 'toe of foot/foot/leg' words were added into the fifteenth question to prevent any misunderstanding of amputation location in the harmonization section.

The final version of Turkish translation of the MNSI was back translated into English by two different persons who were fluent in English and did not know the original version of instrument. The researchers evaluated and compared the final version of the MNSI and no changes were needed. After harmonization, the appropriateness of the instrument for Turkish language was evaluated by a person who was professional in Turkish education. Removal of the word 'shower' was recommended in the seventh question because the word 'bath' includes 'shower' in Turkish. It was remarked that using 'your feet' instead of 'your foot' was more suitable for consistency with question in Turkish. Recommendations were accepted by common accord by the researchers. Fifteen patients and 15 physicians were included in a pilot study and 86% of the patients did not understand the term 'diabetic neuropathy'. Therefore, its meaning was explained in brackets in the ninth question. After revision the rate of understanding of the ninth question was 100%.

One hundred and forty-four patients fulfilled the including criteria. The questionnaire section of the Turkish version of the MNSI was completed by patients twice on the same day. In addition, the physical examination part of the instrument was evaluated by an internal medicine expert, and a physical medicine and rehabilitation (PMR) specialist independently on the same day. Eighteen patients left the study on their request. One hundred twenty-six patients completed the questionnaires and they were re-evaluated by the same physicians after 15 days. Nerve conduction studies (NCS) were performed as the gold standard test to evaluate for DSP in 123 patients because two patients did not accept NCS and NCS could not be performed in one of patient because of ulcers in the feet and cellulitis in the legs.

Definition of Distal Symmetric Polyneuropathy

Nerve conduction studies were performed using Medelec Synergy electromyography device (Medelec Synergy, Oxford, UK) and all patients were evaluated by a neurologist who was blinded to the MNSI scores. NCS includes decreased nerve conduction velocity, prolonged distal motor latency, reduced compound muscle action potential (CMAP), and reduced sensory nerve action potential (DSAP) in DSP (14). DSP was diagnosed as nerve conduct abnormalities in one or more attribute(s) among the sural, peroneal or median nerves affecting at least two extremities (9,12).

Monofilament Test

The 10-g Semmes-Weinstein monofilament test is recommended for DSP screening by the ADA (4). Therefore, 10-g monofilament test was performed in all patients for comparing sensitivity and specificity with MNSI. There is no a standard protocol for the monofilament test because of variability of pressure points reported as three points, four points, eight points, and ten points, besides different cut-off points (5). For the 10 g-monofilament test to the dorsal surface of the great toe, the plantar surface of the first, third, and fifth toes, the first, third, and fifth metatarsal heads, the medial and lateral mid-foot, and the heels on both feet were used in our study. The 10 g-monofilament test was classified as 'normal' when the patients sensed 8-10 points of 10 points, 'decreased' when the patients sensed 1-7 points, and 'absent' if patients sensed none of points.

Statistical Analysis

All statistical analyses were performed using IBM SPSS 22 (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp) and R version 3.5.1. The data are presented as mean ± standard deviation (SD) or median and interquartile range (IQR) for continuous variables or scores, and number and percentage [n, (%)] for categorical variables. The normality of distribution for continuous variables was confirmed with the Shapiro-Wilk test. For comparison of independent continuous variables between two groups, the Student's t-test or Mann–Whitney U test was used depending on whether the statistical hypotheses were fulfilled or not. The reliability and stability of the scale were evaluated using intraclass correlation coefficients (ICC), and intra-rater and inter-rater agreements were reported. ICC categories less than 0.40 were accepted as poor, between 0.40 and 0.59 as fair, between 0.60 and 0.74 as good, and between 0.75 and 1.00 as excellent (15). For both questionnaire and examination sections of the Turkish version of the MNSI, internal validity and factor structures were confirmed using confirmatory factor analysis (CFA). The fit indexes obtained from CFA, model Chi-square, relative Chi-square ($\chi 2/df$), root mean square error of approximation (RMSEA), comparative fit index (CFI), standardized root mean square residual (SRMR) were reported. The model fit acceptable ranges for indexes were $\chi 2/df$:2/1, RMSEA<0.07, CFI>0.95, SRMR<0.08 (16). For CFA, the lavaan R package was used and path diagram was created using the semPlot R package (17). For the validity of the Turkish version of the MNSI, NCS was used as the gold standard test for diagnosing DSP and diagnostic measures were obtained for the scale. Receiver operating characteristic (ROC) curve analysis was used for total scores and Chi-square test was used for each item for both questionnaire and physical examination sections. Diagnostic accuracy measures, sensitivity, specificity, positive predictive values (PPV), and negative predictive values (NPV) were calculated. In ROC curve analysis, the area under the curve (AUC) was reported with 95% confidence intervals (CI). Youden's index and Index of union (IU) were used to definite an optimal cut-off point after ROC curve analysis. For Youden's index the

point that which had the highest index value was chosen as the optimal cut-off point (18) and for IU, the point that had the lowest index value was chosen as optimal cut-off point (19). For all tests a p-values less than 0.05 were considered statistically significant.

RESULTS

A total of 126 patients completed the study. 79 patients (62.7%) were female and 47 patients (37.3%) were male. The mean age of the patients was 57.2 ± 9.5 years. The median duration of DM was 7 (IQR, 2.75-13.25) years. Three (2.4%) patients had T1DM. The median HbA1C level was 7.1 (IQR, 6.5-8.7). The median BMI was 29.4 (IQR, 27.3-33.2) kg/m².

One hundred twenty-three patients underwent NCS because two patients did not agree to participate in the NCS and NCS could not be performed on one patient due to foot ulcers and cellulitis in the legs. According to NCS, 17.1% of patients were diagnosed as having distal symmetrical polyneuropathy, and 25.2% of patients had carpal tunnel syndrome, 57.7% of patients had normal NCS findings. The DSP distribution by sex was 27.3% in male and 11.4% in female patients (p=0.025). DSP was not related to age (p=0.232), education level (p=0.537), occupation (p=0.092), HbA1C level (p=0.254), and BMI (p=0.186). Only long-duration DM was related to DSP (p=0.006). The demographic characteristics of male and female patients and their relationship with DSP are presented in Table 1.

Table 1. Demographic Characteristics of Patients and Their Relationship between DSP

	Female (n=79)			Male (n=44)		
	Patients without DSP (n=70)	Patients with DSP (n=9)	p	Patients without DSP (n=32)	Patients with DSP (n=12)	p
Age (year) mean±SD	57.1±7.9	58.2±7.9	0.693	55.2±13.1	60.8±7.6	0.175
Education (year) median (IQR)	5.0 (5.0-5.0)	5.0 (5.0-5.0)	0.155	8.0 (5.0-11.0)	5.0 (5.0-8.0)	0.414
Height (cm) median (IQR)	160.0 (157.0-163.0)	157.5 (155.0-163.5)	0.855	170.0 (168.0-175.0)	172.0 (168.0-180.0)	0.483
Weight (kg) median (IQR)	75.0 (70.0-85.0)	88.0 (74-93.5)	0.179	83.5 (75.5-91.0)	90.0 (75.5-98.5)	0.290
BMI (kg/m²) median (IQR)	29.6 (27.6-33.3)	34.7 (29.4-36.7)	0.108	28.6 (26.0-31.0)	29.6 (27.3-32.4)	0.328
Duration of DM (year) median (IQR)	6.5 (2.0-15.0)	15.0 (10.0-20.0)	**0.014**	5.0 (1.0-10.0)	10.0 (5.0-14.5)	**0.040**
Fasting plasma glucose level (mg/dL) median (IQR)	120.5 (102.5-155.2)	129.0 (109.0-177.5)	0.379	117.5 (107.7-156.0)	116.0 (99.0-326.0)	0.941
HbA1c level (%) median (IQR)	7.1 (6.5-8.3)	7.5 (6.7-8.5)	0.584	6.8 (6.4-8.7)	8.4 (6.2-9.0)	0.413
ALT level (IU/L) median(IQR)	19.0 (15.7-24.0)	15.0 (11.0-25.0)	0.171	26.0 (16.7-30.0)	19.0 (12.0-38.0)	0.606
Creatinine level (mg/dL) median (IQR)	0.8 (0.7-0.82)	0.7 (0.7-0.85)	0.445	0.9 (0.87-1.07)	0.8 (0.7-1.06)	0.129

DM: Diabetes Mellitus; DSP: Distal Symmetric Polyneuropathy; SD: Standard Deviation; IQR, Interquartile Range; BMI: Body Mass Index; HbA1C: Glycated Hemoglobin; ALT: Alanine Aminotransferase

Table 2. Stability of the Turkish version of the Michigan Neuropathy Screening Instrument

N= 126	Initial score median (IQR)	Re-test score median (IQR)	ICC
Intra-rater agreement of Section A	4.5 (IQR, 2-6)	4 (IQR, 2-6)	0.880 (95% CI: 0.833-0.914)
Intra-rater agreement of Section B	2.25 (IQR, 1-3)	2.5 (IQR,1.5-3.0)	0.920 (95% CI: 0.889-0.943)
	Score of Rater 1	Score of Rater 2	
Inter-rater agreement of Section A	4.5 (IQR, 2-6)	5 (IQR, 2-6)	0.957 (95% CI: 0.940-0.969)
Inter-rater agreement of Section B	2.25 (IQR, 1-3)	2 (IQR, 1.5-3.0)	0.917 (95 CI%: 0.884-0.941)

ICC: Intraclass Correlation Coefficient; CI: Confidence Interval; Section A, the questionnaire section of the Michigan Neuropathy Screening Instrument; Section B, the physical evaluation section of the Michigan Neuropathy Screening Instrument

The inter-rater agreement of the questionnaire section [ICC: 0.957 (95% CI: 0.940-0.969), p<0.001] and physical examination section [ICC: 0.917 (95% CI: 0.884-0.941), p<0.001] of the MNSI were excellent. In addition, the intra-rater agreement of the questionnaire section [ICC: 0.880 (95% CI: 0.833-0.914), p<0.001] and physical examination section [ICC: 0.920 (95% CI: 0.889-0.943), p<0.001] of MNSI showed a high stability (Table 2).

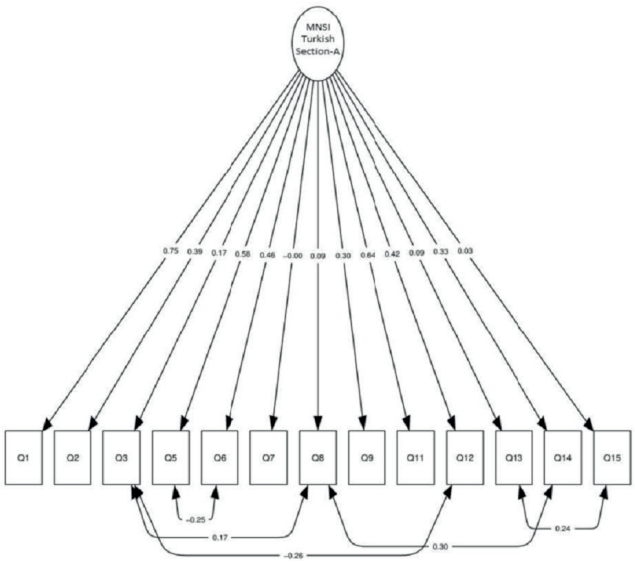

Figure 1. Path diagram of the questionnaire section of the Turkish version of the MNSI

CFA was performed in order to establish construct validity. Unidimensional models including all items for both questionnaire and examination sections show good fit. The indices of goodness of fit for questionnaire section were χ2: 50.56, χ2/df: 0.842, RMSEA: 0.001 (90% CI: 0.0-0.036), CFI: 1.0, SRMR: 0.059. For the examination section indices were χ2:0.471, χ2/df: 0.235, RMSEA: 0.001 (95% CI: 0.0-0.113), CFI:1.0, SRMR: 0.019. One-dimensional structure of the questionnaire section was shown in Figure 1.

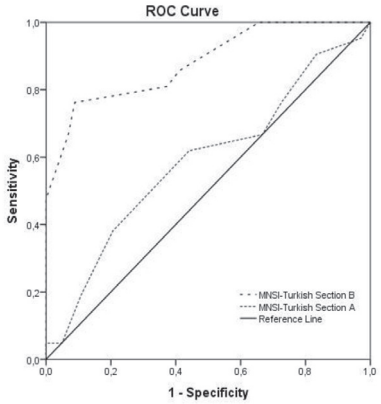

Figure 2. The diagnostic performance of the Turkish version of the MNSI for both sections: Section A (Questionnaire section) and Section B (Physical examination section)

The Area under Curve (AUC) was estimated using ROC analysis between the NCS and both sections of the MNSI to validate the instrument (Figure 2). The AUC for questionnaire section was 0.588 (95% CI: 0.446-0.730) (p=0.205). In question 13 and 15, the expected counts of cells were less than 5; therefore, the diagnostic accuracy measures could not be reliable. The AUC for the physical examination section was 0.880 (95% CI: 0.792-0.968) (p<0.001). The optimum cut-off value determined using Youden's index of >3, had a sensitivity of 76.2%, specificity of 91.2%, PPV of 64%, and NPV of 94.9%. Regarding a cut-off >2 for the physical examination section, the sensitivity was 85.7%, specificity was 58.8%, the PPV was 30.0%, and the NPV was 95.2%. In the physical examination section, 44.4% of patients had abnormal appearance (dryness/callus/infection/deformity) in their feet. Only one patient with DSP had ulceration. The ankle reflex was normal in 65.9% of patients, was present with Jendrassic maneuver in 17.0% of patients and was absent in 17.1% of patients. Vibration sensation was normal in 25.2% of patients, reduced in 51.2% of patients and absent in 23.6% of patients.

Table 3. Diagnostic accuracy measures of the questionnaire Section of the MNSI

Question number	Sensitivity	Specificity	PPV	NPV	χ2	p*
Question 1	57.1%	48.0%	18.5%	84.5%	0.188	0.665
Question 2	85.7%	26.7%	19.6%	90.0%	1.453	0.228
Question 3	38.1%	61.8%	17.0%	82.9%	0.001	0.990
Question 4	76.2%	25.5%	17.4%	83.9%	0.026	0.872
Question 5	52.4%	37.3%	14.7%	79.2%	0.786	0.375
Question 6	23.8%	91.2%	35.7%	85.3%	3.877	0.063
Question 7	9.5%	99.0%	66.7%	84.2%	3.170	0.075
Question 8	14.3%	92.2%	27.3%	83.9%	0.888	0.346
Question 9	14.3%	92.2%	27.3%	83.9%	0.888	0.346
Question 10	71.4%	32.4%	17.9%	84.6%	0.115	0.735
Question 11	47.6%	50.0%	16.4%	82.3%	0.039	0.842
Question 12	61.9%	32.4%	15.9%	80.5%	0.258	0.611
Question 13	0.0%	99.0%	0.0%	82.8%	0.208	0.649
Question 14	52.4%	69.6%	26.2%	87.7%	3.148	0.076
Question 15	4.8%	100.0%	100.0%	83.6%	1.873	0.171

* the p-value of Chi-Square test

There was a negative correlation between age and vibration sensation (r=-0.345, p<0.001). The diagnostic accuracy measures of the questionnaire and physical examination sections of the MNSI were presented in Table 3 and Table 4.

There was a weak positive correlation between the questionnaire score and the physical examination score (r=0.303, p=0.001). The questionnaire score was positively correlated with BMI (r=0.275, p=0.002) and duration of DM (p=0.245, p=0.006). There was no correlation between the questionnaire score and age (r=0.160, p=0.074), education level (r=-0.039, p=0.667), and HbA1C level (r=0.084, p=0.365). In addition, the questionnaire score was not related to sex (p=0.285). The physical examination score was positively correlated with age (r=0.300, p=0.001), HbA1C level (p=0.252, p=0006), BMI (r=0.283, p=0.001) and duration of DM (r=0.270, p=0.002). There was no correlation between the physical examination score and education level (r=-0.070, p=0.442).

The 10-g monofilament test's sensitivity was 47.6%, specificity was 87.3%, PPV was 43.5, NPV was 89.0 (p<0.001).

Table 4. Diagnostic accuracy measures of the physical examination section of the MNSI

Number of questions	Sensitivity	Specificity	PPV	NPV	χ2	p*
1. Foot appearance, normal/abnormal	66.7%	60.8%	25.9%	89.9%	5.328	**0.021**
2. Ulceration, Present/absent	4.8%	100 %	100%	83.6%	4.897	**0.027**
3. Achilles reflex present/ absent	71.4%	88.2%	55.6%	93.8%	36.184	**<0.001**
4. Vibration present/ absent	71.4%	79.4%	41.7%	93.1%	21.743	**<0.001**

DISCUSSION

A total of 126 patients with DM completed the study, 123 patients accepted NCS tests for DSP. The prevalence of DSP was 17.1%. DSP was related to longer duration of DM and male gender in this study. Consistent with our results, the prevalence of DSP was reported as 11-50% in T1DM, 8-51% in patients with T2DM in a review article (3). In addition, the main risk factors for diabetic neuropathy were reported as longer duration of DM and HbA1C level in previous studies (3,8).

The inter-rater and intra-rater reliability of the Turkish version of the MNSI were excellent. Although the questionnaire section (AUC=0.588) did not have diagnostic accuracy in our study population, the physical examination section (AUC=0.880) of the MNSI was diagnostic for DSP with diagnostic accuracy of 76.2% sensitivity, 91.2% specificity with an optimal cut-off of >3. Herman et al. reported that the physical examination section of the MNSI, with a cut-off of ≥2.5, had a 61% sensitivity and 79% specificity (AUC=0.73) (12). Feldman et al. reported that the sensitivity was 80% and specificity was 95% with a cut-off of >2 in the physical examination section (9). However, when we considered the cut-off value as >2, the sensitivity increased to 85.7%, but the specificity reduced to 58.8%. Therefore, the optimal cut-off value was above 3 for our study population. Barbosa et al. reported that the sensitivity of physical examination section was 86% and the specificity was 61%, when regarding the cut-off value as ≥2 (AUC=0.79) (7). Fateh et al. reported that the physical examination section had a sensitivity of 75.2% and specificity of 33.3% with the cut-off of ≥2 (8). There are two publications about the Turkish validation and reliability of the MNSI performed in the Aegean region in Western Turkey in 2020. A Reyhanioglu et al. reported that the sensitivity was 87.5%, and the specificity was 93.6% with the cut-off of 2.75 (AUC=0.939) (20). The other study with smaller sample size determined that when the cut-off value was considered as ≥2, the sensitivity was 100% and the specificity was 97.6% (AUC=1.00) (21). The higher cut-off value may be related to the high rate of foot abnormalities in patients with DM. De Macedo et al. reported that the prevalence of skin disorders varied between 51.1% and 97.7% in patients with T1DM and T2DM (23). Pavicic et al. reported that xerosis was very common in patients with DM with rate between 75% and 82.1% (24). 44.4% of patients had abnormal appearance in their feet in our study. The reasons of skin disorders were explained by high glucose level causes inhibition of keratinocyte proliferation, migration, and protein biosynthesis, in addition to induction of endothelial cell apoptosis (23). 51.2% of our patients had reduced vibration sensation in our study. Absence of vibration had diagnostic accuracy with 71.4% sensitivity and 79.4% specificity. In contrast, reduced vibration sensation was not diagnostic. In addition, age was negatively correlated with vibration sensation. There are a few studies about the normative values of vibration perception threshold (VPT) (25,26). Prabhakar et al. determined the normative data of age-wise timed vibration sense and they showed that the optimal cut-off value of timed vibration sense (AUC=0.73) was <8 s with a sensitivity of 85% and specificity of 42.8%. In addition there are various techniques for determining vibration abnormality (25–27). Further studies determining age and gender-wise timed vibration sense, which provide to identify the best technique for Turkish population, may be useful for early detection of DSP and specifying the optimal cut-off value of the physical evaluation section of the MNSI. Pourhamidi et al. compared the diagnostic usefulness of tuning fork, monofilament, biothesiometer,

and skin biopsy of distal symmetric neuropathy in patients with varying glucose metabolism (6). The tuning fork test identified small nerve neuropathy in 12 of 27 patients with a sensitivity of 44%. The researchers emphasized that assessing vibration sensation with a 128-Hz tuning fork might be useful in detecting early neuropathy (6). Some patients in our study may have had small fiber neuropathy because of the shorter duration of DM. However, we could not prove this idea because we did not performe skin biopsies. The physical examination score was positively correlated with age, HbA1C level, BMI, and DM duration.

The questionnaire section (AUC=0.588) did not have diagnostic accuracy in our study population. Herman et al. performed a study including 1184 patients with T1DM. They reported that the sensitivity of the questionnaire section was 13% and the specificity was 99% with a cut-off of ≥7 sensitivity. When the cut-off ≥4 was used, the sensitivity was 40%, specificity was 92% (12). The sensitivity of questionnaire section was lower than the physical examination section in this study. A Reyhanioglu et al. reported that the sensitivity of questionnaire section was 75.5% and specificity was 68.1% with a cut-off of 3.5 (20). The sensitivity and specificity of questionnaire section were lower than the physical examination section in this study. The questionnaire section not being diagnostic for DSP, may be related to the education level of our study population or regional differences. The median education duration was five years in our study. Another possibility is that NCS might have been normal due to the shorter duration of DM. Perkins et al. reported that NCS might be within the normal range in patients with mild and early neuropathy (28). They added that NCS might be normal even in the presence of symptoms or clinical findings in patients with mild neuropathy. NCS only determine large fiber activity (28). Some of patients may have small nerve fiber neuropathy, as mentioned before. Fillingim reported that many factors affected the prevalence of chronic pain such as sex, age, and ethnic groups (29). Higher questionnaire scores in patients without polyneuropathy might be associated with cultural differences of Turkish people or Turkish people living in the Eastern Anatolia region of Turkey. Some of patients may have lower pain thresholds. Multicenter studies including different countries and different cities of Turkey are needed to assess pain thresholds of patients with DM. Considering some of the studies that concluded that fibromyalgia may have a neuropathic pain component, this may be caused by accompanying fibromyalgia syndrome in some patients, but we did not evaluate fibromyalgia in this study (30). Further studies identifying fibromyalgia pathogenesis are needed.

There are many different protocols and diagnostic thresholds for the monofilament test. Wang et al. reported that the 10 g-monofilament test had limited sensitivity as a screening tool for DM (5). The sensitivity and specificity of the monofilament test in our study were 47.6% and 87.3%, respectively. Both the sensitivity and specificity of the physical evaluation section of the MNSI were higher than the monofilament test. Supporting to our data, Gin et al. reported that the monofilament test was determinant for DSP, but had less sensitivity for screening patients (27). In the light of this information, the physical evaluation section of the MNSI was more accurate than the monofilament test as a screening tool for DSP providing a comprehensive foot evaluation, patient education, and preventing morbidities.

The strengths of the study were including considerably accepted sample size, excluding the conditions causing DSP, performing NCS as a gold standard diagnostic test for DSP, determining diagnostic accuracy of all items of both sections of the MNSI, comparing the sensitivity and specificity of the MNSI and monofilament test as a screening tool for DSP, determining risk factors for DSP in patients with DM. The limitations of the study were the short duration of DM, low educational level of the patients, the patients were not evaluated for fibromyalgia syndrome, and no skin biopsies were performed for small nerve neuropathy.

CONCLUSION

The physical examination section of the Turkish version of the MNSI is valid and reliable for screening DSP with a cut-off of > 3 in the Eastern Anatolia region of Turkey.

Competing interests: The authors declare that they have no competing interest.

Financial Disclosure: There are no financial supports.

Ethical approval: Ethics approval for the study was granted by Erzincan Binali Yildirim University Clinical Research Ethics Committee (date: 05.03.2019, no: 01/06).

REFERENCES

1. Saeedi P, Petersohn I, Salpea P, et al. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. Diabetes Res Clin Pract 2019;157:107843.
2. Satman I, Omer B, Tutuncu Y, Kalaca S, Gedik S, Dinccag N, et al. Twelve-year trends in the prevalence and risk factors of diabetes and prediabetes in Turkish adults. Eur J Epidemiol 2013;28:169-80.
3. Feldman EL, Callaghan BC, Pop-Busui R, et al. Diabetic neuropathy. Nat Rev Dis Prim 2019;5:41.
4. American Diabetes Association. 10. Microvascular Complications and Foot Care: Standards of Medical Care in Diabetes-2018. Diabetes Care. 2018;41:105-18.
5. Wang F, Zhang J, Yu J, et al. Diagnostic Accuracy of Monofilament Tests for Detecting Diabetic Peripheral Neuropathy: A Systematic Review and Meta-Analysis. J Diabetes Res. 2017;2017:8787261.
6. Pourhamidi K, Dahlin LB, Englund E, Rolandsson O. Evaluation of clinical tools and their diagnostic use in distal symmetric polyneuropathy. Prim Care Diabetes 2014;8:77-84.

7. Barbosa M, Saavedra A, Severo M, et al. Validation and Reliability of the Portuguese Version of the Michigan Neuropathy Screening Instrument. Pain Pract 2017;17:514-21.
8. Fateh HR, Madani SP, Heshmat R, et al. Correlation of Michigan neuropathy screening instrument, United Kingdom screening test and electrodiagnosis for early detection of diabetic peripheral neuropathy. J Diabetes Metab Disord 2015;15:8.
9. Feldman EL, Stevens MJ, Thomas PK, et al. A practical two-step quantitative clinical and electrophysiological assessment for the diagnosis and staging of diabetic neuropathy. Diabetes Care 1994;17:1281-9.
10. Pop-Busui R, Lu J, Lopes N, et al. BARI 2D Investigators. Prevalence of diabetic peripheral neuropathy and relation to glycemic control therapies at baseline in the BARI 2D cohort. J Peripher Nerv Syst 2009;14:1-13.
11. Terwee CB, Bot SDM, de Boer MR, et al. Quality criteria were proposed for measurement properties of health status questionnaires. J Clin Epidemiol 2007;60:34-42.
12. Herman WH, Pop-Busui R, Braffett BH, et al. Use of the Michigan Neuropathy Screening Instrument as a measure of distal symmetrical peripheral neuropathy in Type 1 diabetes: results from the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications. Diabet Med 2012;29:937-44.
13. Wild D, Grove A, Martin M, et al. Principles of Good Practice for the Translation and Cultural Adaptation Process for Patient-Reported Outcomes (PRO) Measures: report of the ISPOR Task Force for Translation and Cultural Adaptation. Value Health 2005;8:94–104.
14. Bae JS, Kim BJ. Subclinical diabetic neuropathy with normal conventional electrophysiological study. J Neurol 2007;254:53-9.
15. Cicchetti DV. Guidelines, criteria, and rules of thumb for evaluating normed and standardized assessment instruments in psychology. Psychol Assess 1994;6:284-90.
16. Hooper D, Coughlan J, Mullen M. Structural Equation Modelling: Guidelines for Determining Model Fit. Electron J Bus Res Methods 2008;6:53-60.
17. Epskamp, S.,&Stuber S. semPlot: Path diagrams and visual analysis of various SEM packages' output. R Packag version 2014;1.
18. Youden WJ. Index for rating diagnostic tests. Cancer. 1950;3:32-5.
19. Unal I. Defining an Optimal Cut-Point Value in ROC Analysis: An Alternative Approach. Comput Math Methods Med 2017;2017:1-14.
20. Aktar Reyhanioglu D, Adiyaman SC, Bektas M, et al. Turkish validity and reliability of the Michigan Neuropathy Screening Instrument. Turkish J Med Sci 2020.
21. Kaymaz S, Alkan H, Karasu U, et al. Turkish version of the Michigan Neuropathy Screening Instrument in the assessment of diabetic peripheral neuropathy: a validity and reliability study. Diabetol Int 2020;11:283-92.
22. Barbosa M, Saavedra A, Severo M, et al. Validation and Reliability of the Portuguese Version of the Michigan Neuropathy Screening Instrument. Pain Pract. 2017;17:514-21.
23. de Macedo GMC, Nunes S, Barreto T. Skin disorders in diabetes mellitus: an epidemiology and physiopathology review. Diabetol Metab Syndr 2016;8:63.
24. Pavicic T, Korting HC. Xerosis and callus formation as a key to the diabetic foot syndrome: Dermatologic view of the problem and its management. JDDG 2006;4:935-41.
25. Kästenbauer T, Sauseng S, Brath H, et al. The value of the Rydel-Seiffer tuning fork as a predictor of diabetic polyneuropathy compared with a neurothesiometer. Diabet Med 2004;21:563-7.
26. Prabhakar AT, Suresh T, Kurian DS, et al. Timed Vibration Sense and Joint Position Sense Testing in the Diagnosis of Distal Sensory Polyneuropathy. J Neurosci Rural Pract 2019;10:273-7.
27. Gin H, Rigalleau V, Baillet L, et al. Comparison between monofilament, tuning fork and vibration perception tests for screening patients at risk of foot complication. Diabetes Metab 2002;28:457-61.
28. Perkins B, Bril V. Electrophysiologic testing in diabetic neuropathy. Handb Clin Neurol 2014;126:235-48.
29. Fillingim RB. Individual Differences in Pain: Understanding the Mosaic that Makes Pain Personalitle. Pain 2017;158:11-8.
30. Cheng CW, Wong CS, Hui GK, et al. Fibromyalgia : is it a neuropathic pain ? Pain Manag 2018;8:377-83.