

Comparison of different screening tests for diagnosis of diabetic peripheral neuropathy in Primary Health Care setting

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Abstract:

Background: DPN is an important complication and contributes to the morbidity of diabetes mellitus. Evidence indicates early detection of DPN results in fewer foot ulcers and amputations.

Objective: The purpose of this study was to compare different screening tests in the detection of DPN in primary care setting.

Methodology: It is a cross-sectional study in a random sample (N = 242) of type 2 diabetes mellitus participants at primary care setting. Different screening tests for detecting DPN such as Michigan Neuropathy Screening Instrument (MNSI), Semmes-Weinstein *Monofilament* (SWM), vibration sensation and ankle reflex were performed for each patient and compare between them.

Results: 45% of the participant had DPN based on MNSI, The detection rate using the 128-Hz tuning fork and 10-g SWM was nearly same (32.6 & 31.4%) respectively and significantly higher than ankle reflexes (23.1%). Although, the prevalence of DPN determined by the combined two tests (38.79%) was higher than that through the single test.

Conclusion: this study showed different results of DPN screening tests, even in the same group of patients. However there was a significant correlation between them. 128-Hz tuning fork and 10-g SWM monofilament would appear to be an appropriate, cheap and easy to use tool for identifying patients at risk of having neuropathy in primary care setting.

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Introduction

Diabetic Peripheral Neuropathy (DPN) is one of the most common complications of diabetes and stands as a major pathophysiological risk factor for foot ulcers and amputation. It is defined by international consensus guidelines as "the presence of symptoms and/or signs of peripheral nerve dysfunction in people with diabetes after exclusion of other causes". It's accounts for 50–75% of non-traumatic amputations in diabetic patients.^(1,2,3) Foot disorders remain a major source of morbidity and a leading cause of hospitalization among people with diabetes mellitus.^(4, 5)

As the incidence of type 2 diabetes mellitus (T2DM) increases⁽⁶⁾ every year, it has been recommended that prevention of DPN and/or early diagnosis should become high priority matters at the primary care level, where the majority of health care visits for diabetic patients take place.⁽⁷⁾ Early intervention strategies can prevent foot ulcers and amputation while preserving the quality of life^(8–10) and ameliorating the social and economic costs of diabetic foot disease.^(11–13)

While the gold standard for diagnosis of DPN continues to be a nerve conduction study, that is time consuming, requires a separate patient visit, and is costly which cannot be recommended for screening. A simple method that has ease of use for the regular evaluation and diagnosis of DPN in the primary care setting is needed.⁽¹⁴⁾

A number of methods can be used as a screening for detecting diabetic peripheral neuropathy. It's ranging from quantitative methods, such as nerve conduction studies and vibration sense testing, to validated questionnaires such as MNSI or clinical examinations such as pressure sensation by using 10 g Semmes-Weinstein *Monofilament* (SWM), vibration sensation by tuning fork and ankle reflex.^(15, 16)

Therefore, the objective of this study was to compare between this screening tests in the detection of DPN in primary health care (PHC) setting.

Methodology

Study design

This was a multicenter cross-sectional study carried out in Primary Health Care clinics in National Guard in Riyadh. Subject inclusion

criteria were as follows: (1) Patients aged 35 to 70 years; (2) male or female; (3) diagnosis of Type 2 diabetes mellitus according to World Health Organization 1999 criteria; (4) willingness to sign informed consent form. Exclusion criteria were (1) type 1 diabetes mellitus; (2) history of nerve root compression, cerebral vascular disease, hypothyroidism, pernicious anemia, alcoholism and using of drugs that's may cause neuropathy.

In each research center, doctors advised patients who were in accordance with inclusion criteria to become familiar with the study information and obtain informed consent then referred to the investigator to conduct the screening. The investigators at each center who performed the screening were trained in the standard operating methods (10-g SWM and 128-Hz tuning fork and Ankle reflex) before the survey and were given CDs containing a video tutorial. The study was approved by King Abdullah International Medical Research Center, Riyadh.

Randomization method and sample size:

The sample size was estimated based on 18-23% proportion of DPN among type 2 diabetics detected by monofilament or validated score^(17, 18) using 0.05 precision with 95% C.I and power of 0.80. Subjects were selected from Family Medicine follow up clinics, patients who is carrying odds number in patient list was enrolled in the study.

Data collection Instrument:

A data collecting sheet was filled by the investigators to record demographic data and relevant medical history of diabetes, then were screened for diabetic peripheral neuropathy. Body mass index (BMI) was calculated from weight in kilogram divided by height in meter square. Categorized as Normal (< 25 kg/m²), overweight (25-30 kg/m²) and obese (>30 kg/m²).

DPN screening:

The skillful, trained investigators from each center performed the screening for DPN in a quite environment using Michigan Neuropathy Screening Instrument (MNSI). It consists of a two-step program:

The first part: assessed a Neuropathic symptoms by a history questionnaire

consists of 15 "yes or no" questions on foot sensation including pain, numbness and temperature sensitivity. The detailed scores are shown in Table 1.

The second part: is a brief physical examination involving an inspection of the feet and evaluation of ankle reflexes, vibration sensation and fine touch. The detailed scores are shown in Table 2.

Neuropathy is defined operationally as seven or more positive responses on the MNSI questionnaire or a score >2.0 on the MNSI examination, thresholds defined by prior validation studies.^(19, 20)

The screening method for fine touch sensation, vibration perception and ankle reflex using 10-g SWM, 128-Hz tuning fork and reflex hammer was followed the practical guideline from Michigan Diabetes Research and Training Center.⁽²¹⁾

All above-mentioned tests were performed by the same investigator to control for inter-rate reliability.

Statistical analyses

Data entry and analysis was carried out using Statistical Package of Social Sciences (SPSS, windows version 18.0). It was done by statistician to ensure blind assessment of the result. Overall percentage of presence or absence of DPN and descriptive analysis was carried out on the main study variables. Mean values of age, duration of diabetes, BMI, HgA1C and total MNSI scores were compared between groups: "DPN" and "No DPN" using t-test. In addition, ankle reflex, vibration sensation (128-Hz tuning fork) and monofilament (10-g SWM) individual scores (within MNSI) were compared between the two groups and also correlated with the total MNSI scores of the patient. P value was set at a significance of < 0.05 . Pearson's R and Spearman rho were used as correlation coefficients in comparing the screening tests.

Results

A total of 242 patients were studied and their characteristics were presented in Table 3. The majority (60.7%) of the patient was female, the median age was 56 years and the mean duration of diabetes was 9 years. The mean BMI was 25 Kg/m². Over 47.5% had normal BMI, while 36.3% were overweight and only 16.1% were obese. There was significant difference in prevalence of DPN with age and HbA1c level.

The screening results revealed that overall prevalence of diabetic peripheral neuropathy as assessed by MNSI was 45%. 81.7% of them were symptomatic and 18.3% were having asymptomatic DPN. Among those with DPN (45%), only 7.4% have met the MNSI questionnaire criteria for diagnosed neuropathy (7 or more in MNSI questionnaires part).

The detection rate using the 128-Hz tuning fork and 10-g SWM was nearly same (32.6 & 31.4%) respectively and significantly higher than ankle reflexes (23.1%). Although, the prevalence of DPN determined by the combined two test (128-Hz tuning fork & 10-g SWM) was higher than that through the single test, but lesser than that determined by total MNSI score (38.79 & 45%) respectively (Figure 1).

Table 4 gives the sensitivity, specificity and predictive value of each diagnostic modality compared with Michigan Neuropathy Screening Instrument (MNSI), which is taken as the gold standard (as 100%). As shown, 128-Hz tuning fork test and 10-g SWM monofilament were the most sensitive (72.5%, 69.7) and accurate (81.4%, 79.7) of all the diagnostic tests and the combination of both test will increased the sensitivity and accuracy to (89.5%, 86.5).

In Table 5, the correlation between the different screening tests and MNSI are shown to be significant.

Table (1). Michigan Neuropathy Screening Instrument (Questionnaire part):

1- Are you legs and/or feet numb?	1 Yes	0 No
2- Do you ever have any burning pain in your legs and/or feet?	1 Yes	0 No
3- Are your feet too sensitive to touch?	1 Yes	0 No
4- Do you get muscle cramps in your legs and/or feet?	0 Yes	0 No
5- Do you ever have any prickling feelings in your legs or feet?	1 Yes	0 No
6- Does it hurt when the bed covers touch your skin?	1 Yes	0 No
7- When you get into the tub or shower, are you able to tell the hot water from the cold water?	0 Yes	1 No
8- Have you ever had an open sore on your foot?	1 Yes	0 No
9- Has your doctor ever told you that you have diabetic neuropathy?	1 Yes	0 No
10- Do you feel weak all over most of the time?	0 Yes	0 No
11- Are your symptoms worse at night?	1 Yes	0 No
12- Do your legs hurt when you walk?	1 Yes	0 No
13- Are you able to sense your feet when you walk?	0 Yes	1 No
14- Is the skin on your feet so dry that it cracks open?	1 Yes	0 No
15- Have you ever had an amputation?	1 Yes	0 No
	Total: points	/13

Table (2). Michigan Neuropathy Screening Instrument (Examination part):

	Right	Left
Appearance of feet: (Deformity, dry skin, callus, infection, fissure)	Normal = 0 Abnormal = 1	Normal = 0 Abnormal = 1
Ulceration	Absent = 0 Present = 1	Absent = 0 Present = 1
Ankle Reflexes	Present = 0 Present/reinforced = 0.5 Absent = 1	Present = 0 Present/reinforced = 0.5 Absent = 1
Vibration perception at great toe	Present = 0 Decreased = 0.5 Absent = 1	Present = 0 Decreased = 0.5 Absent = 1
Monofilament	Present = 0 Reduced = 0.5 Absent = 1	Present = 0 Reduced = 0.5 Absent = 1

Table (3). Characteristics of study population:

Demographic	Total N (%)	DPN N (%)	NO DPN N (%)	P value
N (%)	242 (100%)	109 (45%)	133 (55%)	
Age	56.4±7.9	57.5±8.3	55.2±7.4	0.002
Gender:	1:1.5			
Male	95 (39.3%)	43 (45.3%)	52 (54.7%)	NS*
Female	147 (60.7%)	66 (44.9%)	81 (55.1%)	
Body mass Index:	25.65±4.69			
Normal	115 (47.5%)	52 (45.2%)	63 (54.8%)	NS
Overweight	88 (36.4%)	38 (43.2%)	50 (56.8%)	
Obese	39 (16.1%)	19 (48.7%)	20 (51.3%)	
Duration of Diabetes:	8.99±6.18			
<5 year	63 (26%)	25 (39.7%)	38 (60.3%)	NS
5-10 year	103 (42.6%)	47 (45.6%)	56 (54.4%)	
>10 year	76 (31.4%)	37 (48.7%)	39 (51.3%)	
Family History of Diabetes:				
Yes	162 (67%)	77 (47.5%)	85 (52.5%)	NS
NO	80 (33%)	32 (40%)	48 (60%)	
Glycosylated haemoglobin (%)				
Controlled (<7.5)	64 (26.5%)	21 (32.8%)	43 (67.2%)	0.002
High (7.5-9.0)	81 (33.5%)	31 (38.3%)	50 (61.7%)	
Very high (>9)	97 (40%)	57 (58.8%)	40 (41.2%)	

* NS: Not significant.

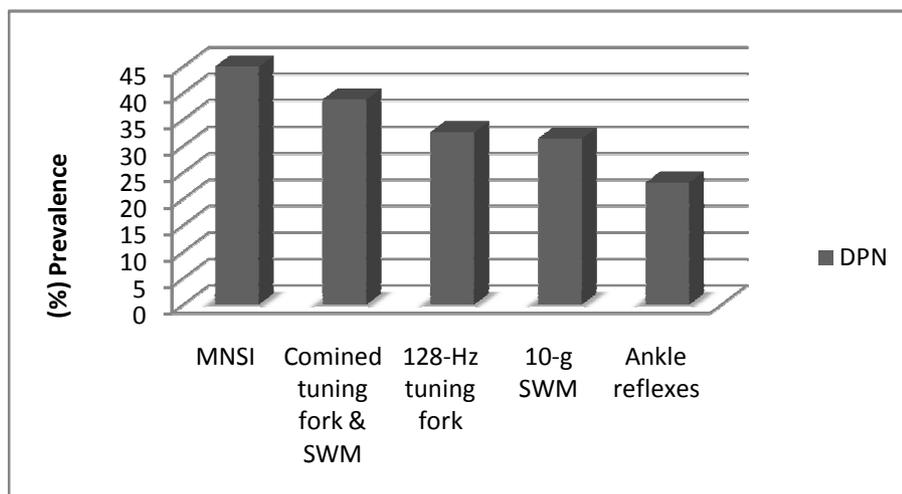
Table (4). Diagnostic accuracy of different tests compared to Michigan Neuropathy Screening Instrument (MNSI):

Test	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Ankle reflexes	51.4	97.7	94.9	71	76.8
10-g SWM	69.7	87.9	82.6	78	79.7
128-Hz tuning fork	72.5	88.7	84	79.7	81.4
Combined tuning fork & SWM	89.5	84.9	92.8	89.5	86.5

Table (5). The correlation between the different screening tests and Michigan Neuropathy Screening Instrument (MNSI):

		MNSI	MNSI questionnaires part	Ankle Reflex	128-Hz tuning fork	10-g SWM
MNSI	CC	1.000	.250	.569	.625	.591
	Sig.	.	.000	.000	.000	.000
	N	242	242	242	242	242
MNSI questionnaires part	CC	.250	1.000	.169	.226	.297
	Sig.	.000	.	.008	.000	.000
	N	242	242	242	242	242
Ankle Reflex	CC	.569	.169	1.000	.377	.309
	Sig.	.000	.008	.	.000	.000
	N	242	242	242	242	242
128-Hz tuning fork	CC	.625	.226	.377	1.000	.441
	Sig.	.000	.000	.000	.	.000
	N	242	242	242	242	242
10-g SWM	CC	.591	.297	.309	.441	1.000
	Sig.	.000	.000	.000	.000	.
	N	242	242	242	242	242

Fig. (1). The prevalence of DPN using different diagnostic test.



Discussion

The current randomized, multicenter cross-sectional study showed that the prevalence of diabetic peripheral neuropathy among Type II diabetes at PHC setting in Riyadh is 45%, on screening patients with MNSI method.

In this study, we used different screening tests for detecting diabetic neuropathy and compared the results in order to finding a simple, reliable and accurate DPN selection method designed for ease of implementation in primary care settings, and for use by multiple levels of care providers. Also, to see whether there was a significant correlation between them.

As shown in (Table 4), 128-Hz tuning fork test and 10-g SWM monofilament were the most sensitive (72.5%, 69.7) and accurate (81.4%, 79.7) of all the diagnostic tests which is almost similar to Jayaprakash P. study.⁽²²⁾ Though the ankle reflex was most specific (97.7%), it had poor sensitivity and accuracy.⁽²²⁾

The combination of two test (128-Hz tuning fork test and 10-g SWM monofilament), will increase the sensitivity and accuracy to (89.5%, 86.5), which is not seen in the previous study.⁽²³⁾

These differences exist could be because each method has a unique way of detecting neuropathy; in the symptom score the result depends on what patients say and in the sign score, the examiner plays the major role. Another reason, some methods such as deep tendon reflexes, is operator-dependent and may include inter-personal bias.

Although the prevalence of neuropathy in each method was different from the others, there was a significant correlation between them ($P < 0.01$).

Reports on diabetic peripheral neuropathy screening using a combination of several simple methods have shown the diagnostic value of these sensation tests, but most were single-center studies with somewhat controversial results. Perkins, et. al. showed that the point estimate of the positive likelihood ratios for vibration testing by the on-off method was the highest (26.6%), followed by the timed method vibration (18.5%), SWM (10.2%) and superficial pain sensation test (9.2%) and that the combination of two simple tests did not add value to each individual screening test.⁽²³⁾ However, as concluded by previous study,⁽¹⁸⁾

our study determined that the combination of two tests (128-Hz tuning fork & 10-g SWM) could indeed increase the detection rate of diabetic peripheral neuropathy relative to 10-g SWM or 128-Hz tuning fork alone in the total population (Figure 1).

The two simple methods require a total of less than two minutes of inspection time per individual. As a result, the combined 10-g SWM and 128-Hz tuning is a practical, highly efficient method suitable for screening diabetic peripheral neuropathy in T2DM patients in the PHC clinics.⁽¹⁴⁾

Our results concurs with the literature, indicating that questionnaire part of the Michigan Neuropathy screening instrument alone has relatively poor diagnostic accuracy in predicting the presence of diabetic neuropathy in comparison with the part based on clinical examination, since only 7.4% from those with DPN have met the MNSI questionnaire criteria for diagnosed neuropathy.⁽²⁰⁾ And perhaps should not be used as a stand-alone test without a neurological examination.⁽¹⁹⁾

In conclusion, this study showed that the results of different DPN screening tests, even in the same group of patients, are different. However there was a significant correlation between them. In summary, for the purposes of screening in general practice, 128-Hz tuning fork and 10-g SWM monofilament would appear to be an appropriate, cheap and easy to use tool for identifying patients at risk of having neuropathy and consequently at risk of developing foot ulcers. The combination of both tests will increase the sensitivity and accuracy.

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