An Initial Evaluation of a Proof-of-Concept 128-Hz Electronic Tuning Fork in the Detection of Peripheral Neuropathy

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Background: Diabetic peripheral neuropathy (DPN) is an essential precursor leading to diabetic limb loss. Neurologic screening tests, including the 128-Hz tuning fork (TF), have long been used to identify and track the progression of DPN, thereby guiding the implementation of preventive strategies. Although a sensitive indicator of neuropathy, shortcomings of TF testing include the lack of standardization and quantification of clinical findings. In an attempt to overcome these limitations, a novel 128-Hz electronic TF (ETF) prototype has been developed that is capable of performing accurate timed vibration tests (TVTs). This study was designed to assess the ability of the ETF to detect sensory impairment compared with three established neurologic screening methods: the Semmes-Weinstein monofilament test, the biothesiometer, and the sharp/dull discrimination test.

Methods: Fifty-five test patients were recruited from the primary author's practice and enrolled according to an approved protocol. The 10-g Semmes-Weinstein monofilament test and the sharp/dull discrimination test were administered in standard fashion to the plantar aspects of digits 1 and 5 bilaterally. The ETF and the biothesiometer (25-V setting) were applied to the dorsal aspects of the distal phalanx of the hallux and fifth metatarsal head bilaterally.

Results: The sensitivity and specificity of neuropathy detection for the ETF were 0.953 and 0.761, respectively, using conventional tests as reference standards.

Conclusions: Performance of TVTs with the ETF detected sensory impairment compared with three conventional neurologic screening methods. Given these findings, the ETF could facilitate the use of standardized TVTs as an indicator of DPN progression. (J Am Podiatr Med Assoc 104(2): 134-140, 2014)

Diabetic peripheral neuropathy (DPN) has been identified as a key pathophysiologic precursor leading to diabetic foot ulcers, infections, and subsequent lower-extremity amputations.[1] It is known to affect most diabetic patients, and its progression is thought to be directly proportional to the duration and severity of the disease.[2,3]

The importance of prompt diagnosis of DPN and implementation of preventive strategies designed to reduce complications leading to limb loss has been recognized as an essential element in the care of patients with diabetes.[1,4] Despite recent studies documenting a marked reduction in the diabetic

amputation rate in the United States, lower-extremity amputations still occur eight times more often in diabetic than nondiabetic patients.[5] Moreover, diabetic lower-extremity amputations continue to have a staggering human and financial impact globally.[6-8]

In light of the insidious role that DPN plays in the diabetic foot, simple neurologic screening methods have been developed to identify patients with the condition. Two techniques predominate among these tests: the 5.07/10-g Semmes-Weinstein monofilament test (SWMT) for assessing loss of protective sensation and the 128-Hz tuning fork (TF) for assessing vibratory sensation.[9-11] Both of these methods are classified as semiquantitative and psychophysical in nature, owing to their reliance on patient feedback.[12] Further contributing to their inaccuracy are variations in user technique, testing

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site selection, and material fatigue.[13-18] Given each test's unique characteristics, some controversy has arisen as to which is superior. In particular, several authors have begun advocating for use of the TF over the SWMT, noting reports of ambiguous clinical efficacy.[19,20]

Although acknowledged for its sensitivity, concerns have been raised regarding TF testing as well. The lack of standardization and uncertainty regarding how to interpret clinical findings are cited as shortcomings.[21,22] In an attempt to overcome these limitations, a novel 128-Hz electronic TF (ETF) prototype has been developed. This device electronically reproduces the same vibration output and decay rate as the traditional TF. An integrated timer facilitates performance of accurate and reproducible timed vibration tests (TVTs); TVTs have been shown to be a valid method for detecting neuropathy.[23,24]

This study was designed to assess the ability of the ETF to detect sensation loss compared with three established neurologic screening methods: the SWMT, the biothesiometer, and the sharp/dull discrimination test.

Research Design and Methods

Patients

Fifty-five patients were enrolled for participation in the study at Health Access Network (Lincoln, Maine). The inclusion criterion was age older than 18 years. The exclusion criteria included foot amputation, open foot ulcers, and foot infection. The study protocol was approved by the institutional review board administered by Portable Ethics Inc (Windham, Maine). All of the participants provided written informed consent in accordance with good clinical practice guidelines.

Methods

Each test patient underwent neurologic testing with a 5.07/10-g SWMT (Touch-Test; North Coast Medical, Morgan Hill, California), a biothesiometer (Bio-Medical Instrument Co, Newbury, Ohio), a sharp/dull discrimination test, and an ETF (O'Brien Medical LLC, Orono, Maine). Each test was administered in a treatment room with an ambient temperature of 70°F to 72°F. Patients had their socks removed for 5 to 10 min before testing. For the purposes of this study, each foot was treated as a single statistical element. This was deemed appropriate because some patients may have had

normal test results on one foot and abnormal results on the other. Test sites and their nerve distributions are shown in Figures 1 and 2.

Testing Protocols

The four testing protocols—SWMT, biothesiometer, sharp/dull discrimination test, and EFT—are described in the following paragraphs.

SWMT. The accuracy of monofilaments was assessed daily before testing with a digital scale. Monofilaments registering beyond ±5% of the desired 10 g of pressure were not used. A standard technique[4] was used when applying the monofilaments to the plantar aspects of the first and fifth digits. Test patients, with eyes closed, indicated perception of the monofilament touch verbally by saying "yes." Lack of an expected response at any location constituted an abnormal reading.

Biothesiometer. The biothesiometer was set at the 25-V level and was applied to the dorsal aspect of the distal phalanx of the hallux and to the dorsal aspect of the fifth metatarsal head. Test patients indicated whether they perceived vibrations verbally with a "yes" or "no." Lack of patient perception at any location was recorded as an abnormal reading.
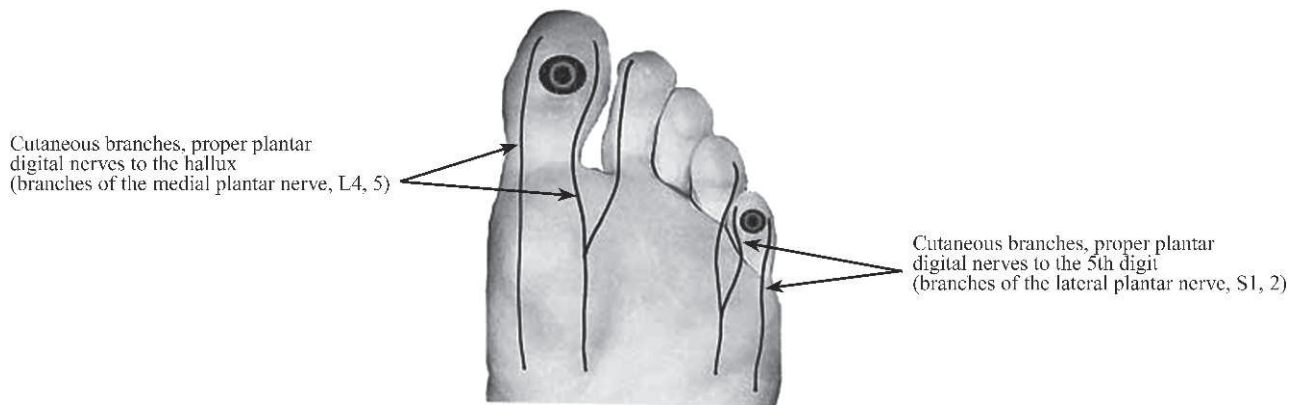
Sharp/Dull Discrimination Test. A sharply cut monofilament imparting 60 g, ±5%, was applied for sharp touch. A monofilament terminating in a blunt polyisoprene tip imparting 225 g, ±5%, was applied for dull touch. A standard technique was used when applying the monofilaments to the plantar aspects of the first and fifth digits. Test patients, with eyes closed, indicated whether they perceived the touch of the instrument as either "sharp" or "dull." An incorrect response at any location constituted an abnormal reading.

ETF. The contact point of the ETF was applied to the dorsal aspect of the distal phalanx of the hallux (Fig. 3) and to the dorsal aspect of the fifth metatarsal head (Fig. 4). The device was activated, simultaneously starting the vibrations and the integrated timer. Test patients indicated whether they perceived vibrations verbally with a "yes" or "no." Those indicating "no" were recorded as 0 sec of elapsed time. Those indicating "yes" were asked to state when the vibrations subsided beyond their perception by saying "now." At this point, the device was stopped and the elapsed time was recorded.

The cumulative diagnostic results of all of the conventional methods were compared with the ETF data to derive sensitivity and specificity. For the
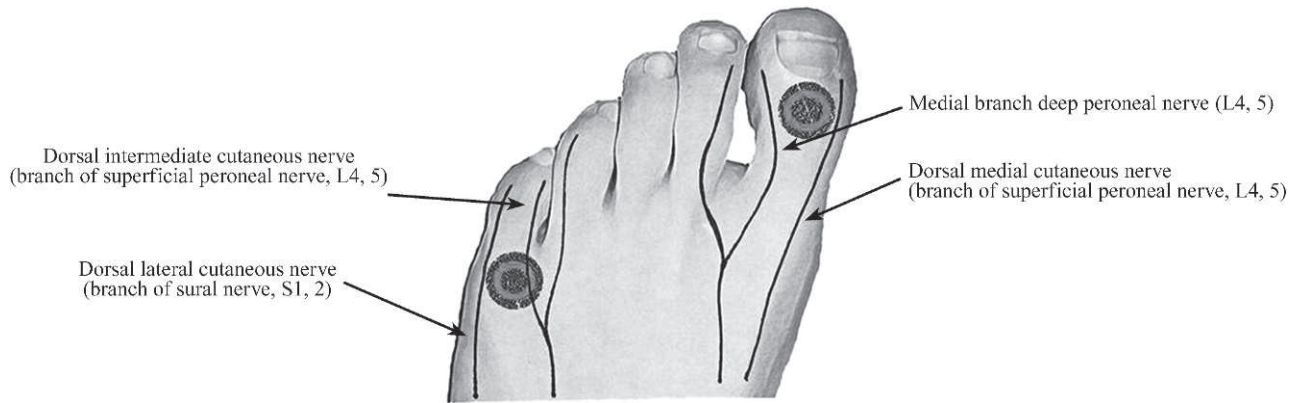
Figure 1. Electronic tuning fork and biothesiometer test sites and their associated sensory nerve distributions are shown in the dorsal view.

Figure 2. Semmes-Weinstein monofilament test and sharp/dull discrimination test sites and their associated sensory nerve distributions are shown in the plantar view.

purposes of this study, a false-positive occurred when the ETF TVT values were abnormal and the results of all three of the conventional methods were negative. A false-negative occurred when the ETF TVT values were normal and any of the results of the conventional methods were positive. All of the data were recorded on data collection sheets and were later entered into a password-protected database. A χ^2 analysis was used to determine whether an association ($P < .05$) existed between patients diagnosed as having diabetes and patients diagnosed as having neuropathy. A Tukey mean separation test was used to evaluate differences ($P < .05$) in age among patients with different neuropathic diagnoses. No transformation of patient data was necessary to meet the assumptions of normality. Normality was assessed by examining skewness, kurtosis, and the Shapiro-Wilk W statistic. To detect differences in ETF readings between

nonneuropathic and neuropathic patients (based on conventional methods), a Student's t test was used.

Results

Fifty-five patients consented to participating in the

Figure 3. Electronic tuning fork applied to the hallux.

Figure 4. Electronic tuning fork applied to the fifth metatarsal head.

study. Of these patients, 69.1% had been diagnosed as having diabetes (Table 1). Patient age ranged from 20 to 88 years, but more than half were 60 years or older.

Based on the cumulative diagnoses of three conventional examination methods (the SWMT, the biothesiometer, and the sharp/dull discrimination test) and patient medical record review (ie, established pedal peripheral neuropathy documented by the patient's physician), there was a 58.2% prevalence of neuropathy in 110 patient feet examined (Table 2). Most patients with neuropathy exhibited loss of sensation in both feet (73%) compared with those with sensation loss in one foot (27%).

No association between patient diagnosis of diabetes and neuropathy was evident in this

Table 1. Demographic Variables for the 55 Study Participants

Variable	Descriptive Statistic Result
Male sex (No. [%])	22 (40.0)
Age (years)	
Mean ± SD	59.9 ± 15.3
Median	61.0
Range	20–88
Diabetic (No. [%])	38 (69.1)

Table 2. Examination Results Based on the Three Conventional Methods

Neuropathy Diagnosis	No. of Patients (%)	Age (Mean ± SD [Years])
Negative	18 (32.7)	50.9 ± 15.4
One foot	10 (18.2)	58.2 ± 16.4
Both feet	27 (49.1)	66.4 ± 11.6

population ($\chi^2_1 = 2.295$, $P = .130$). Pairwise comparisons showed that the group without neuropathy was younger than the group with neuropathy in both feet ($P = .001$); no other age differences were detected among these groups (Table 2).

After examining the hallux and fifth metatarsal head of 109 patient feet (218 test sites), the maximum ETF reading corresponding to an abnormal biothesiometer result was 8.9 sec (Table 3). Therefore, based on this result, an abnormal parameter of less than 9 sec was established for the ETF. Overall, the ETF mean TVT value seen in the nonneuropathic patient group (per biothesiometer results) was 11.1 sec. This value was substantially higher than the mean of the neuropathic group, which was 1.1 sec ($P < .001$). Based on an abnormal reading of less than 9 sec, the ETF detected 71 additional test sites having sensation loss that the biothesiometer did not. Using the cumulative diagnostic results of all of the conventional methods, the sensitivity and specificity of the ETF were 0.953 and 0.761, respectively. Only three of the 110 patient feet examined were false-negatives by the ETF. However, these same feet were also classified as negative by the biothesiometer and the SWMT; only the sharp/dull discrimina-

Table 3. ETF Timed Vibration Test Readings Compared With Biothesiometer Results

Variable	Biothesiometer Results	
	Abnormal	Normal
No. of test sites	47	171
ETF readings (sec)		
Mean	1.1[a]	11.1
SD	2.4	6.8
Range	0–8.9	0–29.3

Abbreviation: ETF, electronic tuning fork.
[a]A statistically significant difference from patients not diagnosed as having neuropathy by the biothesiometer ($P < .001$).

tion test identified these feet as positive for neuropathy. Conversely, the ETF identified 11 of 110 patient feet (10%) as positive for neuropathy that conventional methods did not.

Overall, patients without neuropathy felt the diminishing vibration from the ETF substantially longer than patients with neuropathy ($P < .001$). Similarly, diabetic patients without neuropathy felt the diminishing vibrations longer than diabetic patients with neuropathy ($P < .001$) (Fig. 5).

A comparison of SWMT results and ETF readings is presented in Table 4. All of the patients exhibiting abnormal SWMT results had an ETF reading of 5.8 sec or less. However, some test patients having normal SWMT results still exhibited ETF readings of 5.8 sec or less.

Discussion

In this study, a proof-of-concept ETF based on the 128-Hz TF was tested and compared with established neurologic screening tests. The TVTs performed by the ETF were shown to be sensitive (0.953) and specific (0.761) at detecting neuropathy unilaterally in ten patients and bilaterally in 27 patients. These results were comparable with those of TVTs performed by Perkins et al.[24]

In particular, the study by Perkins et al included 478 individuals who underwent screening with four simple neurologic screening tests (the SWMT, superficial pain sensation, and the 128-Hz TF vibration test by the on-off method and by the timed method). The results of these screening tests were compared against the criterion standard of nerve conduction velocity studies. Vibration testing by the timed method in this study resembled, to some extent, the TVTs performed in the present study, with some important differences. The technique used involved three steps: 1) vibration perception duration (VPD) at the dorsal aspect of the distal phalanx of the hallux was measured bilaterally and the values were added, 2) the VPD of the examiner's thumb was measured bilaterally and the values were added, and 3) nonneuropathic and neuropathic patients were defined through comparison of the VPDs at the patient's hallux and the examiner's thumb. If the examiner detected vibration for less than 20 sec in total duration above the total for the patient's total hallux score (10 sec per hallux), the patient was considered to have normal sensation. A score greater than 40 sec (20 sec per hallux) indicated neuropathy. The sensitivity and specificity of this technique at detecting neuropathy
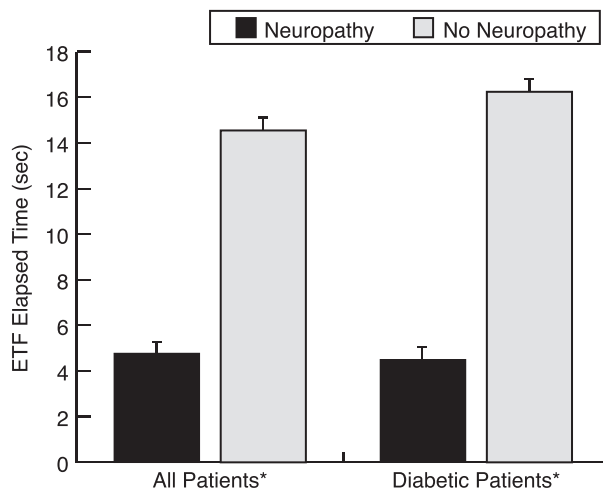
Figure 5. Differences in the length of time patients with neuropathy can detect electronic tuning fork (ETF) vibration versus patients without neuropathy. Sample size represents the cumulative number of examination sites for patients with or without neuropathy. Error bars represent the SEM. *A difference between patients with and without neuropathy ($P < .001$).

against the criterion standard were 80% and 98%, respectively.

Perkins et al[24] noted that their technique was time intensive and potentially difficult to interpret, a conclusion we agree with compared with the relative simplicity of the present test protocol. One of the key differences between the method of Perkins et al and ours was the reliance on the examiner's hand sensation as the standard for identification of neuropathy. This dependence on examiner feedback added another level of subjectivity and variation to the test protocol that was not present in our study. Another contrast was the use of nerve conduction velocities as their criterion

Table 4. ETF Timed Vibration Test Readings Compared with SWMT Results

	SWMT Results	
Variable	Abnormal	Normal
No. (%)	29 (13.4)	187 (86.6)
ETF readings (sec)		
Mean	1.3	10.1
SD	2.1	7.2
Range	0–5.8	0–29.3

Abbreviations: ETF, electronic tuning fork; SWMT, Semmes-Weinstein monofilament test.

standard. The present study used a combination of simple neurologic screening tests as standards, chief among them the biothesiometer. We concluded that biothesiometer testing was the closest reference standard. This comparison between biothesiometer and ETF results provided the neuropathy cutoff value of less than 9 sec.

A recent study by Oyer et al[20] is perhaps the best direct comparison to ours. They describe a novel "clanging tuning fork" test to screen for DPN. This test involves hitting a 128-Hz TF with sufficient force to hear an audible clang before applying it to the patient's hallux. The VPD was then measured and recorded. Oyer et al compared the results from their version of the TVT with the SWMT results. It was concluded that values of less than 5 sec were indicative of severe neuropathy. A retrospective medical record review of 81 diabetic patients was also performed. It was found that patients with values of 4 sec or less were at a 15-fold higher risk of diabetic foot ulcers. This was despite often normal SWMT findings. For this reason, the authors strongly advocated replacing the SWMT with the TF TVT for the detection of DPN.

In another related study, Botez et al[23] evaluated the reliability of TF TVTs as part of the bedside neurologic examination. This investigation, performed on 25 healthy volunteers, found that interrater and intrarater reliability of the TVT was high at various anatomical sites, including the hallux. The authors concluded that the TVT is a reliable bedside examination when performed using a standardized protocol.

Taken together, Perkins, Oyer, and Botez and their colleagues confirm the sensitivity, specificity, and reliability of TF TVTs. As far as the clinical ramifications of TVT values regarding the diabetic foot are concerned, Oyer et al[20] alone provide guidance. As noted previously herein, they suggested a cutoff time of less than 5 sec for identification of diabetic patients with severe DPN, further advising prevention of diabetic foot complications through the use of protective footwear.

In contrast, the present study simply identified sensory impairment as less than 9 sec with the ETF. Although we did not endeavor to do so, it is possible to define a cutoff value for loss of protective sensation based on these data. We suggest that loss of protective sensation exists at 5.8 sec or less with ETF testing. This cutoff time corresponds to the highest ETF reading seen in any test patient with an abnormal SWMT result. This cutoff value of 5.8 sec or less is comparable with the cutoff value of less than 5 sec for severe neuropathy suggested by Oyer et al. It should be understood that this proposed cutoff value is hypothetical and requires further research to validate any predictive value regarding diabetic foot complications.

One of the discrepancies in this study was the number of false-positives, which necessarily lowered specificity values. This may have been the result of using less sensitive conventional screening methods as standards. Even the biothesiometer, known as the gold standard of vibration testing, did not identify some patients with neuropathic findings. This could have been due to the choice of using the accepted 25-V neuropathy cutoff value instead of age-adjusted vibration perception threshold standards.[25] A large coefficient of variation, especially in patients older than 70 years, has also been identified as a potential source of inaccuracy in biothesiometry.[26,27]

Another source of false-positives was the identification of patients with isolated entrapment neuropathies. Several of these patients had abnormal ETF readings in one specific anatomical location and clinical examination findings consistent with entrapment neuropathy despite normal findings with the other methods. Although not an anticipated finding, this quantitative confirmation of entrapment neuropathy may prove to be a clinically useful feature of the ETF.

Another limitation of this study was the individual patient population derived from a single physician practice. Although statistically significant findings were clearly evident, a larger, multisite study performed by multiple clinical researchers would serve to confirm the results.

The fact that a unique prototype was used in this study may be a limiting factor. Although the ETF was designed to replicate the output of a traditional TF, there could be subtle differences between the two. It is not clear whether these differences are clinically significant because the present findings are comparable with those of Perkins et al[24] and Oyer et al.[20] In addition, the reproducible vibrations created by the device likely mitigated against significant variation between tests, although this was not specifically assessed.

Regardless of these limitations, the results of this study suggest that neuropathy in diabetic patients can be identified as measured by the ETF prototype. Further refinement of this prototype could lead to the development of an instrument capable of providing quantitative tracking of neurologic status in this patient population.

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