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SHORT REPORT

Assessment of vibratory sensation with a tuning fork at different sites in Japanese patients with diabetes mellitus

Mitsuyoshi Takahara[1]*, Yuko Fujiwara[2], Fumie Sakamoto[1], Naoto Katakami[1], Taka-aki Matsuoka[1], Hideaki Kaneto[1], Iichiro Shimomura[1]

[1]Department of Metabolic Medicine, Graduate School of Medicine, Osaka University, and [2]Division of Nursing, Diabetic & Foot Care Center, Osaka University Hospital, Osaka, Japan

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***Correspondence**
Mitsuyoshi Takahara
Tel.: 81-6-6879-3743
Fax: 81-6-6879-3739
E-mail address: takahara@endmet.med.osaka-u.ac.jp

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ABSTRACT

The current study compared the vibratory sensations at different sites, using a retrospective database of 547 Japanese diabetic patients. The vibratory sensation was assessed with a 128-Hz tuning fork at the medial malleolus, the great toe and the fifth toe. The vibratory sensations at different sites were significantly associated with one another (all $P < 0.01$). The vibratory sensation at one site corresponding to 10 s at another site was calculated to be 9–11 s. Although the vibratory sensations at the three sites had different associations with the pressure sensation and the ankle reflex, they showed similar *C*-statistics for the impaired pressure sensation and the disappeared ankle reflex. In conclusion, the vibratory sensations at different sites were strongly associated with one another. They would be clinically acceptable alternatives to one another in the assessment of diabetic peripheral neuropathy.

INTRODUCTION

Peripheral neuropathy is a major complication of diabetes mellitus[1–3]. It is not only associated with unpleasant symptoms, which impairs quality of life, but is also associated with diabetic foot, resulting in tissue loss and amputation[4–7]. Its periodic assessment is clinically important in the management of diabetes mellitus.

In clinical practice, diabetic peripheral neuropathy is evaluated by the combination of several examinations, including the assessment of vibratory sensation[4–8]. In Japan, vibratory sensation in diabetic patients is often assessed with a 128-Hz tuning fork at the medial malleolus[8,9], whereas it is often assessed at the great toe overseas[4–7]. However, to date, few data are available about the association between the test at the medial malleolus and at the great toe in Japanese diabetic patients, which has made it difficult to compare the reports from Japan and those from overseas about vibratory sensation.

In addition, some diabetic patients will suffer from foot lesions at the very site where it is generally recommended to carry out the neurological assessment. It would be of clinical use if the assessment at some alternative sites was clinically validated.

The aim of the current study was to compare the vibratory sensations assessed by a 128-Hz tuning fork at different sites in Japanese diabetic patients.

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MATERIALS AND METHODS

Study Population and Definitions

We used a retrospective clinical database of 547 Japanese patients with diabetes mellitus who had their peripheral neurological findings assessed between 2004 and 2012. The study was in accordance with Ethical Guidelines for Epidemiological Research in Japan, and was approved by the human ethics committee of Osaka University. The vibratory sensation, the Achilles tendon reflex and the pressure sensation were assessed by one certified diabetes educator. The vibratory sensation was evaluated by a 128-Hz tuning fork at the medial malleolus, the great toe and the fifth toe, as follows[8,10,11]. The examiner stroked the end of a 128-Hz tuning fork hard enough that the sides touched, and immediately placed the vibrating tuning fork firmly on the bony prominence of the site of interest. At the same time, the examiner began counting the seconds. The patient was instructed to tell the examiner when the patient felt

the vibration stop. The examiner recorded the time (seconds) for which the patient could perceive the vibration. The examination was repeated three times per site, and the vibratory sensation at a site was evaluated by the mean value of the three records at the site. Note that before the examinations, the examiner applied the vibrating tuning fork on the patient's wrist, to make sure that the patient could recognize the vibration.

The pressure sensation was assessed by the Semmes Weinstein 4.31 monofilament at the planter aspects of the great toe, the first metatarsal and the fifth metatarsal. The impaired pressure sensation was determined when the patient could not perceive the applied pressure at one or more of the three sites.

The database was consecutively constructed, excluding the cases with data missing, as well as duplicative cases. We also excluded from the current analysis the patients with considerable bilateral difference in vibratory sensations (≥5 s), because the bilateral difference indicated the possibility that some neurological disorders other than diabetic peripheral neuropathy would exist. We used the neurological findings in the right lower extremity as their representative values in every patient.

Statistical Analysis

The differences in continuous variables and dichotomous variables between the patients with and without diabetic peripheral neuropathy were assessed by the unpaired *t*-test and the Fisher's exact test, respectively. Note that the presence of diabetic peripheral neuropathy was judged according to the criteria proposed by Diagnostic Neuropathy Study Group in Japan[8]. The association of the vibratory sensation at one site with that at another site was assessed by calculating the Pearson's correlation coefficient, the intraclass correlation coefficient, the corresponding value based on the univariate linear regression analysis and the *C*-statistic.

We also investigated whether the vibratory sensations at different sites had any different impacts on other neurological findings. We carried out the trivariate logistic regression analysis whose dependent variable was either impaired pressure sensation or disappeared ankle reflex, and whose explanatory variables were the vibratory sensations at the three sites. Furthermore, we assessed the *C*-statistic of the vibratory sensation at each site for other neurological findings.

Data are given as means and standard deviation for continuous variables or as percentages for dichotomous variables. Hemoglobin A1c levels were converted to a National Glycohemoglobin Standardization Program equivalent value with the conversion equation reported by the Japan Diabetes Society[12]. A P-value <0.05 was considered to be significant and 95% confidence intervals (CI) were given when required. All statistical analyses were carried out using IBM SPSS Statistics Version 19 (SPSS Inc., Chicago, IL, USA).

Table 1 | Characteristics of patients with and without peripheral neuropathy

	Patients without neuropathy (n = 251)	Patients with neuropathy (n = 296)	P-value
Males	156 (62%)	172 (58%)	$P = 0.38$
Age (years)	62 ± 13	66 ± 10	$P < 0.01$
Body mass index (kg/m^2)	23.9 ± 4.0	23.8 ± 4.1	$P = 0.66$
Type 1 diabetes mellitus	33 (13%)	20 (7%)	$P = 0.01$
Diabetic duration	14 ± 10	19 ± 12	$P < 0.01$
Hemoglobin A1c (%)	7.3 ± 1.0	7.5 ± 1.4	$P = 0.08$
Insulin use	99 (39%)	155 (52%)	$P < 0.01$
Vibratory sensation (s)			
Medial malleolus	12 ± 3	8 ± 3	$P < 0.01$
Great toe	11 ± 3	7 ± 4	$P < 0.01$
Fifth toe	11 ± 3	7 ± 4	$P < 0.01$
Disappeared ankle reflex	10 (4%)	118 (40%)	$P < 0.01$
Impaired pressure sensation	9 (4%)	89 (30%)	$P < 0.01$
Diabetic retinopathy	61 (24%)	141 (48%)	$P < 0.01$
Diabetic nephropathy	60 (24%)	126 (43%)	$P < 0.01$
Hypertension	127 (51%)	180 (61%)	$P = 0.02$
Dyslipidemia	122 (49%)	135 (46%)	$P = 0.49$
Cardiovascular disease	46 (18%)	97 (33%)	$P < 0.01$

Data are mean ± standard deviation or n (%).

Table 2 | Associations among the vibratory sensations assessed at three different sites

	Medial malleolus	Great toe	Fifth toe
Correlation coefficient r			
Medial malleolus	–	0.78 (0.75, 0.81)	0.75 (0.71, 0.78)
Great toe	0.78 (0.75, 0.81)	–	0.81 (0.78, 0.84)
Fifth toe	0.75 (0.71, 0.78)	0.81 (0.78, 0.84)	–
Intraclass correlation coefficient			
Medial malleolus	–	0.78 (0.75, 0.81)	0.73 (0.69, 0.77)
Great toe	0.78 (0.75, 0.81)	–	0.81 (0.78, 0.84)
Fifth toe	0.73 (0.69, 0.77)	0.81 (0.78, 0.84)	–
Corresponding value to			
10 s at medial malleolus	–	9.3 (9.1, 9.5)	9.1 (8.8, 9.3)
10 s at great toe	10.5 (10.3, 10.7)	–	9.7 (9.5, 9.9)
10 s at fifth toe	10.6 (10.4, 10.8)	10.0 (9.8 10.2)	–
C-statistic for predicting			
<10 s at medial malleolus	–	0.88 (0.85, 0.91)	0.86 (0.83, 0.89)
<10 s at great toe	0.90 (0.87, 0.92)	–	0.89 (0.86, 0.92)
<10 s at fifth toe	0.86 (0.83, 0.89)	0.89 (0.86, 0.92)	–
Impaired pressure sensation	0.80 (0.75, 0.85)	0.84 (0.80, 0.88)	0.82 (0.77, 0.87)
Disappeared ankle reflex	0.75 (0.70, 0.79)	0.74 (0.69, 0.79)	0.73 (0.68, 0.78)

Data are shown with 95% confidence intervals. Corresponding values were obtained from univariate linear regression models.

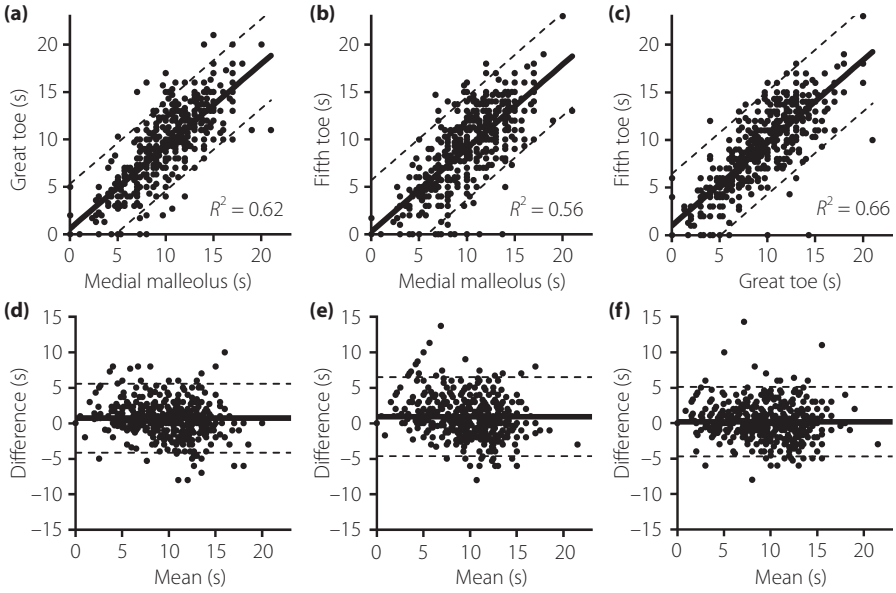

Figure 1 | (a–c) Scatter plots and (d–f) Bland–Altman plots among the vibratory sensations assessed at three different sites. (a–c) Scatter plots between the vibratory sensations (a) at the medial malleolus and the great toe, (b) between those at the medial malleolus and the fifth toe and (c) between those at the great toe and the fifth toe are shown. Bold solid line and thin dotted lines represent the regression line and 95% prediction intervals, respectively. (d–f) Bland–Altman plots of (d) the medial malleolus vs the great toe, (e) the medial malleolus vs the fifth toe and (f) the great toe vs the fifth toe are shown. Bold solid line represents the mean difference, whereas thin dotted lines represent mean ± 2 standard deviations of the difference.

RESULTS

The patients were aged 64 ± 12 years and 328 (60%) were male. Diabetic duration was 17 ± 11 years and hemoglobin A1c levels were 7.4 ± 1.2%. Table 1 shows the characteristics of those with and without diabetic peripheral neuropathy.

Table 2 and Figure 1 show the association among the vibratory sensations at different sites. They were significantly correlated with one another (all $P < 0.01$). The vibratory sensation at one site corresponding to 10 s at another site was calculated to be from 9 to 11 s. The *C*-statistics for the vibratory sensation <10 s at another site ranged from 0.86 to 0.90.

Table 3 shows the association of the vibratory sensations with other neurological findings. In logistic regression models, the vibratory sensations at the great toe and the fifth toe were independently associated with impaired pressure sensation (both $P < 0.01$), but not with disappeared ankle reflex (both $P > 0.05$). In contrast, that at the medial malleolus was associated with disappeared ankle reflex ($P = 0.01$). Nevertheless, as shown in Table 2, the vibratory sensations at different sites demonstrated similar *C*-statistics for predicting the impaired pressure sensation and the disappeared ankle reflex.

Table 3 | Logistic regression models for different neurological findings

	Trivariate model for predicting impaired pressure sensation	Trivariate model for predicting disappeared ankle reflex
Vibratory sensation at the medial malleolus	0.86 (0.51, 1.46)	0.57 (0.37, 0.88)*
Vibratory sensation at the great toe	0.32 (0.15, 0.66)*	0.67 (0.38, 1.19)
Vibratory sensation at the fifth toe	0.36 (0.17, 0.73)*	0.65 (0.36, 1.15)

Data are adjusted odds ratios (95% confidence interval) per interquartile range increment. *$P < 0.05$.

DISCUSSION

The current study investigated the vibratory sensations at the medial malleolus, the great toe and the fifth toe in Japanese diabetic patients, suggesting that they are strongly associated with one another, as shown in Table 2. In contrast, they had some different associations with other neurological findings (Table 3). One possible explanation of these findings could be the closeness in distance of the sites where neurological findings were assessed. Indeed, the vibratory sensations at the toes had significantly independent associations with the pressure sensation, assessed at the toe and metatarsal. In contrast, the vibratory sensation at the medial malleolus was associated with the ankle reflex. Nevertheless, interestingly, the predictive performances of respective vibratory sensations for neurological findings were almost the same (Table 2). These findings indicate that, despite their independent associations with other neuro-

logical findings, the vibratory sensations at different sites would clinically complement one another, as to assessing peripheral neuropathy.

The current study had some limitations. First, this was a single-center study. However, the current single-center design enabled the neurological evaluation of the entire study population by one examiner, which could minimize measurement error. Second, we constructed the database in a retrospective manner, which might cause some selection biases. Future studies will be required to validate the current findings.

In conclusion, the vibratory sensations at the medial malleolus, the great toe and the fifth toe were strongly associated with one another in Japanese diabetic patients. They would be clinically acceptable alternatives to one another in the assessment of diabetic peripheral neuropathy.

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