Factors Contributing to Postural Sway in Patients with Diabetes in an In-Hospital Education Program

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Key Words
Postural sway · Posturography · Diabetes mellitus · Diabetic nephropathy · Diabetic retinopathy · Diabetic neuropathy · Nerve conduction study · Hearing loss

Abstract

Objective: We investigated the effect of polyneuropathy, nephropathy, and retinopathy on postural sway in patients with poorly controlled diabetes mellitus (DM) who were hospitalized for DM education. We also investigated the relationship between postural sway and hearing disturbances. Methods: We included 50 subjects who were hospitalized for the purpose of DM education. Mean age was 57.2 years, mean HbA\textsubscript{1c} was 9.4\%, and mean DM duration was 11.1 years. Renal function, retina condition, and nerve conduction were evaluated in relation to DM complications (nephropathy, retinopathy, and neuropathy). Static posturography was performed to assess DM-related postural sway. Nerve conduction studies were used to obtain information on the condition of peripheral nerves. Pure-tone audiometry was measured. Stepwise multiple linear regression was used to assess DM-related factors that affected postural sway. Results: Deterioration of median nerve compound muscle action potential (CMAP) amplitude, tibial nerve CMAP conduction velocity, and peroneal nerve CMAP latency were associated with deterioration of postural sway. Deterioration of hearing in the worse ear was also associated with postural sway. Conclusion: In patients with poorly controlled DM, postural sway was particularly associated with deterioration of motor nerve conduction study.
parameters represented by median nerve CMAP amplitude, tibial nerve CMAP conduction velocity, and peroneal nerve CMAP latency. A link between diabetic polyneuropathy, diabetes-related postural sway, and diabetes-related hearing loss was recognized.

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**Introduction**

Complex interactions between visual, vestibular, and somatosensory information and the cerebellar system help people maintain an upright posture [Dichgans et al., 1976; Nashner et al., 1989]. Diabetes mellitus (DM) is a metabolic disease that produces vascular and neurologic complications [Shamoon et al., 1993]. The degree of instability has been reported to be greater in subjects with diabetes than in subjects without diabetes [Giacomini et al., 1996; Simoneau et al., 1994; Uccioli et al., 1995, 1997]. Several studies have used posturography to assess posture stability and reported an association between neuropathy and instability in patients with DM [Aranda et al., 2009; Emam et al., 2009; Fioretti et al., 2010; Uccioli et al., 1997; Yamamoto et al., 2001]. Postural instability was found to be significantly associated with sensory neuropathy, but not with diabetes per se [Emam et al., 2009; Yamamoto et al., 2001]. In these studies, the level of DM control was generally not bad and DM-related factors, including diabetic nephropathy and retinopathy, were not sufficiently investigated.

Posture stability is closely associated with the vestibular system, which is adjacent to the auditory system. Some authors have reported that hearing difficulties were risk factors for postural instability and fall-related injuries [Sprince et al., 2003; Valente Coimbra et al., 2010; Viljanen et al., 2009]. Several studies have reported that people with DM have greater hearing loss compared with people without DM [Austin et al., 2009; Bainbridge et al., 2008; Kakkarlapudi et al., 2003; Uchida et al., 2010]. However, the relationship between postural sway and hearing in patients with DM has not been assessed.

We attempted to investigate the effect of polyneuropathy, nephropathy, and retinopathy on postural sway in patients with poorly controlled DM who were hospitalized for the purpose of DM education. We also investigated the relationship between postural sway and hearing disturbances.

**Materials and Methods**

**Subjects**

Subjects were adults with poorly controlled DM who were hospitalized in the Department of Endocrinology and Diabetes of the Nagoya University Hospital for the purpose of DM education between October 2009 and April 2013. Demographic characteristics, personal history, family history, lifestyle habits, and medical history were obtained from detailed questionnaires. Patients with cerebral apoplexy and spinal cord diseases were excluded. The study protocol was reviewed by the Ethics Committee of the Nagoya University Hospital (authorization number: 810), and written informed consent was obtained from all participants.

**Variables Assessed**

Age, sex (1 male; 0 female), body mass index, DM duration, and medical history of insulin treatment were obtained from medical records and a self-reported questionnaire. Biochemical parameters, including HbA1c level, serum creatinine concentration, creatinine clearance, microalbuminuria and proteinuria, were measured. Fasting blood sugar concentration was
measured in venous blood collected early in the morning after a fast of ≥12 h and was usually measured the day after hospitalization.

After otological inspection, pure-tone audiometry was performed by laboratory technicians using an AA-79 diagnostic audiometer (Rion, Tokyo, Japan) in a soundproof compartment. Air-conduction audiometric measurement thresholds at octave intervals from 125 to 8,000 Hz and at the interoctave frequencies of 3,000 and 6,000 Hz were obtained using 5-dB steps. Four pure-tone averages (500, 1,000, 2,000, and 4,000 Hz thresholds) were calculated and used to determine the better ear and worse ear in order not to overlook subjects with at least one affected ear.

Nerve conduction studies were performed using a Nicolet Viking Electrodiagnostic System (Nicolet Instrument Corp., Madison, Wisc., USA), and the values were used as independent variables. The nerves on one side of the body were usually studied. Motor nerve studies included the median, ulnar, peroneal, and tibial nerves. The following parameters were measured: compound muscle action potential (CMAP) amplitude, conduction velocity (CV) and latency, and F-wave minimal latency (median and tibial nerves only). Sensory nerve studies were performed in the median, ulnar, and sural nerves. The following parameters were measured: sensory nerve action potential (SNAP) amplitude, CV to positive peak (first negative-going deflection), and negative latency. The stimulus duration was 0.2 ms for median and ulnar studies, and 0.3 ms for peroneal, tibial, and sural nerve studies. For all studies, the strength was always tested for a maximum response.

Polyneuropathy was defined as present if there were two or more nerves with abnormalities in the nerve conduction studies. Nephropathy was defined as present if there was microalbuminuria or proteinuria, and/or the patient was undergoing regular dialysis. An ophthalmological evaluation was performed to determine whether there was evidence of diabetic retinopathy and was graded as follows: 0 = no evidence of diabetic retinopathy; 1 = simple diabetic retinopathy; 2 = preproliferative diabetic retinopathy, and 3 = proliferative diabetic retinopathy.

Static posturography was performed using a UM-BAR (Unimec Corporation, Tokyo, Japan). Subjects were asked to maintain an upright posture for 60 s with their eyes open and then closed. A statokinesigram showing the entire range of postural sway from the central position in a chart was obtained. Total wavelength and envelope area surrounded by the circumference of the wave pattern in postural sway were calculated. These parameters obtained with the patients’ eyes both open and closed were used in this study. The Romberg quotient was calculated by dividing the outcome value of the test administered when the subject’s eyes were closed by that of the test administered when the subject’s eyes were open.

Statistical Analysis

Stepwise multiple linear regression was used to assess DM-related factors that affected the postural sway. Age, sex, body mass index, DM duration, medical history of insulin treatment, HbA1c level, fasting blood sugar, serum creatinine concentrations, creatinine clearance, presence of DM complications (nephropathy, retinopathy, and polyneuropathy), grade of diabetic retinopathy (grades 0–3), pure-tone audiometry threshold average in the better and worse ear, and nerve conduction study parameters (CMAP amplitude, CV and latency in the median, ulnar, peroneal and tibial nerves, F-wave minimal latency in the median and tibial nerves, and SNAP amplitude, CV and negative latency in the median, ulnar and sural nerves) were included as the investigation factors. Medical history of insulin treatment and DM complications (nephropathy, retinopathy, and polyneuropathy) were treated as binary variables (presence = 1, absence = 0). Similarly, total length (open and closed eyes), envelope area (open and closed eyes), and Romberg quotient (total length and envelope area) were included as independent variables.
The significance of the multiple linear regressions was evaluated using the F test. A variable was added to the model if its associated p value for the F test was <0.05 and removed if its p value was >0.1. The relationships between clinical characteristics, pure-tone audiometry thresholds and nerve conduction study, and posturography parameters were analyzed using Pearson’s correlation and Spearman rank correlation. Posturography parameters with or without nephropathy, retinopathy or polyneuropathy were compared using the t test. Statistical analyses were conducted using SPSS version 21 (IBM Corporation, Armonk, N.Y., USA). A p value <0.05 was considered significant.

**Results**

Subjects included 50 adults (33 men, 17 women; mean age, 57.2 years; range, 21–82 years). Demographic and clinical data of the subjects are shown in table 1. Almost all patients (47; 94.0%) had type 2 DM and 19 (38.0%) used insulin. HbA1c level, which reflects the control of DM, was poor. Twenty-three patients (46.0%) exhibited polyneuropathy.

Posturography parameters with or without diabetic nephropathy, retinopathy, and polyneuropathy are presented in table 2. Most posturography parameters deteriorated more in patients with nephropathy, retinopathy, and polyneuropathy than in patients without these complications, except for the Romberg quotient.

Thresholds of pure-tone audiometry are shown in table 3. A gently down-sloping configuration characterized most pure-tone audiograms. The hearing difference between the better ear and worse ear was significant for most pure-tone audiometry thresholds (500–4,000 Hz and average), as shown by the t test.

Some clinical characteristics showed significant relationships with posturography parameters in both Pearson’s correlation and Spearman rank correlation [age and Romberg quotient (total length), serum creatinine and total length (open eyes), creatinine clearance and total length (open and closed eyes), and grade of diabetic retinopathy and total length (open eyes)].

In terms of pure-tone audiometry thresholds, only total length (closed eyes) and Romberg quotient (total length) showed significant relationships with hearing in both Pearson’s correlation and Spearman rank correlation [total length (closed eyes), at 6,000–8,000 Hz in the worse ear; Romberg quotient (total length), at 3,000–4,000 Hz and average in the better ear.

| **Table 1.** Demographic characteristics and clinical data (n = 50) |
|---------------------------------------------------------------|
| **Age, years** | 57.2 (14.5) |
| **Sex (male/female)** | 33/17 |
| **Body mass index** | 24.9 (4.6) |
| **Type of DM (type 1/type 2)** | 3/47 |
| **Diabetes duration, years** | 11.1 (8.9) |
| **Medical history of insulin treatment, %** | 38.0 |
| **HbA1c, %** | 9.4 (2.0) |
| **Fasting blood sugar, mg/dl** | 157.9 (40.6) |
| **Serum creatinine, mg/dl** | 0.8 (0.6) |
| **Creatinine clearance, ml/min** | 100.3 (44.6) |
| **Diabetic nephropathy, %** | 32.0 |
| **Diabetic retinopathy, %** | 38.0 |
| **Grade of diabetic retinopathy (0/1/2/3)** | 31/10/4/5 |
| **Diabetic polyneuropathy, %** | 46.0 |

Figures in parentheses are standard deviation.
and 5,000–8,000 Hz and average in the worse ear. In these relationships, deterioration of pure-tone audiometry thresholds was related to deterioration of postural sway.

The correlation between nerve conduction study and posturography parameters is shown in table 4. A large number of relationships were observed in total length (open and closed eyes) and several relationships were detected in the envelope area (open and closed eyes) in both Pearson’s correlation and Spearman rank correlation. No relationship was found between nerve conduction studies and the Romberg quotient except between the median nerve CMAP CV and the Romberg quotient (envelope area).

Table 5 shows the results of multiple linear regression analysis to investigate DM-related factors that affected postural sway. Some nerve conduction study parameters, mainly motor nerve parameters, were independent predictors of all posturography parameters. Median nerve CMAP amplitude and CV, tibial nerve CMAP CV, peroneal nerve CMAP latency, sural

Table 2. Posturography parameters

|                        | Total length | Envelope area | Romberg quotient |
|------------------------|--------------|---------------|------------------|
|                        | open eyes    | closed eyes   | open eyes        | closed eyes     | total length | envelope area |
| Total                  | 1,119.3 (309.7) | 1,616.6 (579.1) | 386.3 (179.4)    | 521.3 (267.5)  | 1.45 (0.30)  | 1.44 (0.61)   |
| Diabetic nephropathy   |              |               |                  |                  |              |               |
| Without                | 1,028.3 (231.9)* | 1,460.1 (504.5)* | 360.8 (169.1)    | 480.0 (268.9)  | 1.42 (0.31)  | 1.39 (0.53)   |
| With                   | 1,312.6 (369.2) | 1,949.3 (601.6) | 440.5 (193.8)    | 609.1 (250.1)  | 1.50 (0.29)  | 1.54 (0.76)   |
| Diabetic retinopathy   |              |               |                  |                  |              |               |
| Without                | 1,044.2 (292.0)* | 1,544.5 (612.0) | 370.3 (172.9)    | 537.6 (310.5)  | 1.47 (0.31)  | 1.51 (0.63)   |
| With                   | 1,241.8 (305.5)* | 1,734.3 (514.9) | 412.3 (191.3)    | 494.7 (181.1)  | 1.40 (0.30)  | 1.33 (0.57)   |
| Diabetic polyneuropathy|              |               |                  |                  |              |               |
| Without                | 1,002.1 (243.7)* | 1,410.7 (532.8)* | 330.5 (153.6)*  | 481.8 (283.5)  | 1.41 (0.29)  | 1.50 (0.56)   |
| With                   | 1,256.8 (326.7) | 1,858.3 (546.2) | 451.7 (188.3)    | 567.7 (245.3)  | 1.49 (0.31)  | 1.36 (0.66)   |

Figures in parentheses are standard deviation. Asterisks show the significance of the comparison between each posturography parameter value with or without diabetic nephropathy, retinopathy and neuropathy.

Table 3. Thresholds of pure-tone audiometry

| Frequency, Hz | Better ear | Worse ear |
|--------------|------------|-----------|
| 125          | 21.1 (8.2) | 21.6 (10.4) |
| 250          | 20.4 (8.9) | 20.6 (10.2) |
| 500*         | 17.6 (8.9) | 19.3 (9.4) |
| 1,000***     | 16.5 (12.6)| 19.5 (13.1)|
| 2,000***     | 19.3 (16.4)| 23.0 (15.6)|
| 3,000**      | 20.4 (18.4)| 23.6 (18.4)|
| 4,000***     | 26.6 (22.3)| 31.7 (22.0)|
| 6,000        | 27.0 (22.3)| 27.7 (24.2)|
| 8,000        | 37.1 (24.9)| 38.3 (24.2)|
| Average***   | 22.9 (13.3)| 25.0 (13.4)|

Figures in parentheses are standard deviation. Asterisks show the significance of the comparison between audiological values of the better and worse ear. * p < 0.05; ** p < 0.01; *** p < 0.001.
nerve SNAP latency, and ulnar nerve SNAP CV were significantly related to postural sway. Deterioration of pure-tone audiometry threshold average in the worse ear was significantly related to deterioration of postural sway. Fasting blood sugar levels also showed a significant relationship to postural sway. In these detected factors, nerve conduction study parameters were particularly related to postural sway.

**Discussion**

In the present study, we collected data on DM-related complications, performed nerve conduction studies and hearing and posturography assessments to understand more clearly the association between DM and postural sway in patients with poorly controlled DM.
The postural control is a complex system that controls the orientation and balance of the body when it is in an upright posture [Horak, 2006; Macpherson et al., 1997]. Imbalance is commonly found in patients with polyneuropathy due to impaired proprioception and motor function [Shepard et al., 1990; Voorhees, 1990]. The afferent sensory input from the proprioceptors as well as the efferent motor nerves must be intact to maintain balance [Nashner, 1976]. Our multiple linear regression results showed that nerve conduction study parameters were major independent predictors of posturography parameters. In sensory nerve conduction studies, two parameters (sural nerve SNAP latency and ulnar nerve SNAP CV) were associated with postural sway. In motor nerve conduction studies, four parameters (median nerve CMAP amplitude and CV, tibial nerve CMAP CV, and peroneal nerve CMAP latency) were associated with postural sway. Yamamoto et al. [2001] also reported that mainly motor nerve conduction study parameters showed significant correlations with posturography parameters.

Tibial and peroneal muscles are crucial muscles directly related to standing. In multiple linear regression analysis, median nerve CMAP amplitude and CV showed an association with postural sway. It is thought that DM mainly damages peripheral nerves, especially the inferior limb sensory nerves. When peripheral neuropathy occurs in the upper limbs, the diabetic neuropathy is already well advanced in the legs and feet [Lewko et al., 2013]. This finding means that the function of the median motor nerve could reflect the advancement of diabetic neuropathy, and this characteristic of the median nerve might have a relationship with postural sway. We
have also examined patients with poorly controlled DM and reported that hearing disturbance was associated with renal dysfunction and diabetic neuropathy, represented by decreases in median nerve CMAP amplitude [Sugimoto et al., 2013]. A link between diabetic polyneuropathy, diabetes-related postural sway, and diabetes-related hearing loss was recognized.

Our multiple linear regression analysis showed that deterioration of pure-tone audiometry threshold average in the worse ear had a direct relationship to deterioration of total length (closed eyes) and the Romberg quotient (total length). Hearing and vestibular organs are anatomically close, share fluid-filled bony compartments and blood circulation, are both served by the eighth cranial nerve, and have similar mechanosensory receptor hair cells, which detect sound, head movements, and orientation in space. The structure and function of the inner ear suggest that these organs may share etiological factors and that deterioration of hearing might reflect deterioration of vestibular organs.

Decreases in fasting blood glucose levels were related to deterioration of the Romberg quotient (envelope area). One third of our patients, who were hospitalized for the purpose of DM education, started insulin treatment for the first time because of poorly controlled DM. Those who started insulin treatment had relatively shorter diabetes duration but higher fasting blood glucose levels than the others. Generally, fasting blood glucose levels reflect control of DM over a short time, and the special circumstances of hospitalization for the purpose of DM education might lead to an association between fasting blood glucose levels and the Romberg quotient (envelope area).

Except for nerve conduction study parameters, only a few factors showed a significant relationship to postural sway in multiple linear regression analysis. It is possible that nerve conduction study parameters that are related to diabetic polyneuropathy may have affected postural sway more in these patients and may have hidden the effect of other DM-related factors in this study. Our multiple linear regression analysis showed that deterioration of most detected nerve conduction study parameters was associated with deterioration of postural sway. However, deterioration of median nerve CMAP CV showed a relationship to improvement of the Romberg quotient (envelope area). Further work is needed to explore these relationships.

Some limitations of the present study should be mentioned. Our study focused on patients with poorly controlled DM and did not include a control group. However, we examined in detail DM-related factors that affect postural sway and found relationships between some DM-related factors and postural sway. These results may provide clues for a better understanding of DM-associated postural sway.

Conclusions

In patients with poorly controlled DM, postural sway was associated with deterioration of motor nerve conduction study parameters represented by median nerve CMAP amplitude, tibial nerve CMAP CV, and peroneal nerve CMAP latency. Deterioration of hearing in the worse ear was also associated with postural sway. A link between diabetic polyneuropathy, diabetes-related postural sway, and diabetes-related hearing loss was recognized.

Acknowledgments

This study was supported by research grants (21390460, 20591979) from the Ministry of Education, Culture, Sports, Science, and Technology and a research grant for Longevity Sciences (25-2) from the Ministry of Health, Labour and Welfare of Japan.
Disclosure Statement

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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