Equilibrium Res Vol. 79(1) 57～65, 2020

原　著

Influence of vascular risk factors on postural stability in a community-dwelling population: Results from the Iwaki Health Promotion Project

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Abstract

Background: Dizziness and balance dysfunction are common complaints associated with falls. The mechanisms of postural instability are complex and multifactorial and have not yet been fully elucidated.

Objective: The purpose of this study was to examine the relationships between postural stability and vascular risk factors.

Methods: The subjects of this study were 1037 volunteers (401 men, 636 women) who had participated in the Iwaki Health Promotion Project. We evaluated the postural stability of the subjects by static posturography and assessed the effects of vascular risk factors on the sway length.

Results: In both men and women, the age and blood hemoglobin A 1 c level were found to be significantly related to the sway length. In postmenopausal women, the brachial-ankle pulse wave velocity (baPWV) was also significantly associated with the sway length.

Conclusion: The results of this study suggested that arteriosclerosis and diabetes affected postural stability. In addition, rapid deterioration of arteriosclerosis due to menopause could also be associated with deterioration of postural stability.

Key words: static posturography, postural stability, arteriosclerosis, diabetes, menopause

Introduction

Dizziness and balance dysfunction occur in various diseases and are one of the common chief complaints. The prevalence of dizziness ranges from approximately 20% to 30%[1)]. Postural stability deteriorates with age, and postural balance disorders in older people lead to falls[2)]. Patients with vestibular dysfunction who are clinically symptomatic exhibit a 12-fold increase in the odds of falling[3)]. Moreover, falls are the leading cause of hospital admission and

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Table 1 Characteristics of subjects in men and women

Characteristics	men (N = 401)	women (N = 636)	p value
age (years)	49.1 ± 15.3	52.2 ± 15.2	0.002
BMI (kg/m^2)	23.7 ± 3.1	22.2 ± 3.6	0.000
baPWV (cm/s)	1480.0 ± 367.0	1415.0 ± 370.7	0.006
SBP (mmHg)	128.1 ± 15.3	125.5 ± 20.7	0.032
HbA 1 c (%)	5.8 ± 0.6	5.8 ± 0.6	0.168
TG (mg/dl)	121.9 ± 89.7	80.6 ± 45.5	0.000
HDL-C (mg/dl)	58.6 ± 16.3	69.3 ± 16.1	0.000
alcohol (g/day)	23.8 ± 28.0	4.5 ± 10.1	0.000
pack years	12.9 ± 16.7	2.7 ± 6.9	0.000
sway length with EO (cm)	99.6 ± 31.4	87.5 ± 28.5	0.000
sway length with EC (cm)	144.9 ± 60.0	116.3 ± 46.1	0.000

Values represent mean ± standard deviation.
BMI = body mass index; baPWV = brachial-ankle pulse wave velocity; SBP = systolic blood pressure; TG = triglycerides; HDL-C = high-density lipoprotein cholesterol; pack years = number of cigarettes packs per day × years of smoking; EO = eyes open; EC = eyes closed.

accidental death[1)] and can lead to decline in activities of daily living (ADL) and quality of life (QOL) in older people. With increased longevity in older people, their QOL and general health have become important and controversial issues[4)]; therefore, postural stability is important in maintenance of the ADL in older people.

Postural stability is maintained by the integration of vestibular, visual and somatosensory inputs to the central nervous system, followed by outputs to the musculoskeletal system[1)5)6)]. The underlying mechanisms of postural instability are complex and multifactorial and have thus far not been fully elucidated[1)7)]. There have been some reports that increased vascular risk factors are associated with dizziness[7)~10)] and falls[11)12)].

We believed that it is important to identify risk factors for postural stability could aid in preventing its progression, thereby preserving ADL and QOL. Therefore, we evaluated postural stability by conducting static posturography and performed an epidemiological investigation of the effects of vascular risk factors on postural stability. Most previous papers have targeted patients with specific symptoms of dizziness or a history of falls. In comparison, we targeted a community-dwelling population.

Material and methods

1. Study subjects

The Iwaki Health Promotion Project is a large-scale epidemiological survey in the Iwaki district of Hirosaki city. We invited all residents over 20 years of age living in this district to this project. There were approximately 9,500 residents over 20 years of age, of which 1,113 and 1,148 participated in this project in 2015 and 2016, respectively. For residents who provided data in both 2015 and 2016, we used data from 2016. This study included 1,449 subjects (559 men, 890 women) for the entire study period; 84 subjects were excluded due to missing data. Additionally, 328 subjects were excluded because they met one or more of the following exclusion criteria: (1) presence of vestibular disease (e.g. Meniere's disease, vestibular neuritis or benign paroxysmal positional vertigo), (2) presence of intracranial disease (e.g. cerebral infarction, cerebral hemorrhage or brain tumors), (3) presence of cardiovascular disease (e.g. myocardial infarction, angina or heart failure), (4) presence of neurologic disease (e.g. myasthenia gravis or spinocerebellar degeneration), (5) presence of malignant tumor, (6) history of surgery

Table 2 Multiple linear regression analysis of sway length with vascular risk factors in men and women

	men (N=401)				women (N = 636)			
	sway length with EO $r^2 = 0.241$		sway length with EC $r^2 = 0.149$		sway length with EO $r^2 = 0.219$		sway length with EC $r^2 = 0.164$	
	β	p value	β	p value	β	p value	β	p value
age	0.378	0.000	0.226	0.002	0.273	0.000	0.238	0.000
BMI	0.031	0.519	− 0.001	0.989	− 0.003	0.945	− 0.032	0.468
baPWV	0.036	0.648	0.053	0.523	0.230	0.001	0.217	0.002
SBP	0.065	0.298	0.055	0.400	− 0.089	0.125	− 0.096	0.107
HbA 1 c	0.107	0.043	0.123	0.028	0.096	0.014	0.074	0.064
TG	− 0.105	0.052	− 0.076	0.185	0.023	0.563	0.035	0.395
HDL-C	− 0.062	0.224	− 0.010	0.852	− 0.079	0.050	− 0.059	0.153
alcohol	0.053	0.282	0.098	0.058	0.055	0.146	0.072	0.065
pack years	− 0.039	0.403	0.023	0.644	0.008	0.820	0.013	0.737

BMI = body mass index; baPWV = brachial-ankle pulse wave velocity; SBP = systolic blood pressure; TG = triglycerides; HDL-C = high-density lipoprotein cholesterol; pack years = number of cigarettes packs per day × years of smoking; EO = eyes open; EC = eyes closed.

of the spine or legs, (7) use of anxiolytic drugs or sleeping pills. Finally, a total of 1,037 subjects (401 men, 636 women) were included in the analysis.

Data collection for the present study and the overall Iwaki Health Promotion Project were approved by the Ethics Committee of Hirosaki University School of Medicine (Authorisation number: 2015–075, 2016–085), and written consent to participate in the project was obtained from all subjects.

2. Data collection

(1) Lifestyles and physical measurements

We obtained lifestyle information by a self-administered questionnaire and face-to-face interviews regarding age, sex, medical history, drug information, smoking habits and drinking habits. For smoking habits, we calculated pack years (number of cigarettes packs per day × years of smoking); for drinking habits, we calculated the daily alcohol intake (g/day). Menopause was determined by interviews in which subjects confirmed that they had no menstrual periods in the past year. Height and weight were measured and body mass index (BMI, kg/m^2) was calculated.

(2) Blood test

Venous blood samples were obtained in the early morning on an empty stomach. Hemoglobin A 1 c (HbA 1 c), triglycerides (TG) and high-density lipoprotein cholesterol (HDL-C) levels were examined. HbA 1 c (%) was expressed as a National Glycohemoglobin Standardization Program equivalent value (%) and used as an index of diabetes. TG and HDL-C were used as lipid parameters for metabolic syndrome criteria.

(3) Blood pressure and brachial-ankle pulse wave velocity (baPWV)

We measured blood pressure and baPWV using a volume-plethysmographic apparatus (Form PWV/ABI, Colin Co., Komaki, Japan). Subjects rested in a supine position on the bed in a partitioned space; cuffs for blood pressure measurement were attached to both upper arms and distal parts of both tibias and electrocardiogram clips were attached to both wrists. The left and right PWV between the brachial and ankle arteries were measured and the mean values of both sides were used in the analysis. Systolic blood pressure (SBP) was measured at the time of PWV measurement.

(4) Static posturography

We evaluated postural stability by using a Gravicorder GP 31 platform (Anima Co., Tokyo, Japan).

Table 3 Characteristics of subjects in premenopausal and postmenopausal women

Characteristics	premenopausal women (N = 287)	postmenopausal women (N = 349)	p value
age (years)	38.4 ± 8.3	63.5 ± 9.0	0.000
BMI (kg/m^2)	21.7 ± 3.9	22.6 ± 3.2	0.001
baPWV (cm/s)	1153.8 ± 192.5	1629.7 ± 343.2	0.000
SBP (mmHg)	114.3 ± 16.1	134.7 ± 19.6	0.000
HbA 1 c (%)	5.6 ± 0.5	6.0 ± 0.6	0.000
TG (mg/dl)	69.7 ± 37.7	89.4 ± 49.4	0.000
HDL-C (mg/dl)	70.0 ± 15.6	68.8 ± 16.5	0.346
alcohol (g/day)	6.2 ± 12.0	3.1 ± 7.9	0.000
pack years	2.9 ± 5.8	2.5 ± 7.8	0.380
sway length with EO (cm)	76.9 ± 18.7	96.3 ± 32.0	0.000
sway length with EC (cm)	101.5 ± 32.0	128.4 ± 52.1	0.000

Values represent mean ± standard deviation.
BMI = body mass index; baPWV = brachial-ankle pulse wave velocity; SBP = systolic blood pressure; TG = triglycerides; HDL-C = high-density lipoprotein cholesterol; pack years = number of cigarettes packs per day × years of smoking; EO = eyes open; EC = eyes closed.

The sampling frequency was 20 Hz. During the examination, subjects maintained static upright posture on the foot plate with their feet together and their arms at the sides of the body. We instructed subjects not to speak or move during the examination. We conducted the examination twice, first with the subjects' eyes open and then with their eyes closed, for 1 minute each. When we examined the subjects with their eyes open, we instructed them to gaze at a target placed 150 cm ahead of their eyes. We used sway length (the total length determined from the center of pressure movement for 60 seconds, cm) and enveloped area (the envelopment area tracing by the movement of center of pressure, cm^2) for analysis of the magnitude of postural sway. In addition, we also analyzed Romberg's ratio (the ratio of a measured value with eyes closed to that with eyes open) of sway length and enveloped area.

3. Statistical analysis

Subjects were divided into two groups for statistical analysis, based on their sex. The characteristics of subjects were compared between men and women by unpaired t-tests. Data were expressed as mean ± standard deviation. Multiple linear regression analysis was used to examine the effects of vascular risk factors on the sway length with eyes open (EO) and with eyes closed (EC); β refers to the slope of the linear regression. Furthermore, to demonstrate changes in sway length due to menopause, women were divided into two groups, premenopausal and postmenopausal, and multiple linear regression analysis was performed in a similar manner. SPSS Statistics, version 25.0 (IBM Corp., Armonk, NY, USA) was used for data analysis. P values less than 0.05 were considered statistically significant.

Results

1. Subjects' characteristics

Characteristics of men and women in this study are shown in Table 1. The mean ages were 49.1 years for men and 52.2 for women; men were significantly younger than women. Compared to women in the study, men had significantly higher values of BMI, baPWV, SBP, TG, daily alcohol intake, pack years and sway length; in addition, men had significantly lower values of HDL-C. Only HbA 1 c values did not significantly differ between sexes.

2. Risk factors for postural stability

Table 2 shows the results of multiple linear regression analysis of risk factors for postural stabil-

Table 4 Multiple linear regression analysis of sway length with vascular risk factors in premenopausal and postmenopausal women

	premenopausal women (N = 287)				postmenopausal women (N = 349)			
	sway length with EO (cm) $r^2 = 0.108$		sway length with EC (cm) $r^2 = 0.090$		sway length with EO (cm) $r^2 = 0.142$		sway length with EO (cm) $r^2 = 0.116$	
	β	p value	β	p value	β	p value	β	p value
age	0.121	0.075	0.062	0.368	0.220	0.001	0.212	0.001
BMI	0.003	0.972	−0.021	0.785	0.010	0.863	−0.030	0.601
baPWV	0.139	0.177	0.155	0.137	0.171	0.023	0.150	0.049
SBP	−0.144	0.178	−0.122	0.261	−0.051	0.451	−0.070	0.302
HbA 1 c	0.016	0.807	−0.068	0.295	0.123	0.019	0.125	0.019
TG	0.100	0.145	0.101	0.146	0.023	0.678	0.038	0.506
HDL-C	−0.127	0.049	−0.123	0.060	−0.040	0.505	−0.009	0.884
alcohol	0.061	0.325	0.068	0.275	0.066	0.211	0.093	0.085
pack years	0.155	0.014	0.172	0.007	−0.015	0.774	−0.016	0.765

BMI = body mass index; baPWV = brachial-ankle pulse wave velocity; SBP = systolic blood pressure; TG = triglycerides; HDL-C = high-density lipoprotein cholesterol; pack years = number of cigarettes packs per day × years of smoking; EO = eyes open; EC = eyes closed.

ity. In men, sway length (both EO and EC) increased with age and HbA 1 c. In women, sway length during the EO trial increased with increasing age, baPWV and HbA 1 c; sway length during the EC trial increased with increasing age and baPWV. We also analyzed the enveloped area and Romberg's ratio in the same way as the sway length. However, we thought that the results were not effective because their coefficient of determination was extremely low (data not shown).

3. Menopause-related characteristics

Characteristics of premenopausal and postmenopausal women in this study are shown in Table 3. There were no significant differences in HDL-C and pack years. Compared to premenopausal women, postmenopausal women were significantly older and had significantly higher values of BMI, baPWV, SBP, HbA 1 c, TG and sway length; postmenopausal women also had significantly lower values of daily alcohol intake.

4. Risk factors for postural stability (menopausal effect)

Table 4 shows the results of multiple linear regression analysis of risk factors for postural stability in premenopausal and postmenopausal women. In premenopausal women, sway length during the EO trial increased with increasing HDL-C and pack years; sway length during the EC trial increased with increasing pack years. In postmenopausal women, sway length (both EO and EC) increased with increasing age, baPWV and HbA 1 c. We also analyzed the enveloped area and Romberg's ratio in the same way as the sway length. However, we thought that the results were not effective because their coefficient of determination was extremely low (data not shown).

Discussion

Postural stability is maintained by the integration of vestibular, visual and somatosensory inputs to the central nervous system, followed by outputs to the musculoskeletal system[1)5)6)]. The functions of these components deteriorate with age[6)]. There have been many reports that vestibular function declines with age[13)14)]; age-related changes in postural stability have also been reported, using static posturography assessment[5)15)]. In the present study, age was significantly related to the sway length in static posturography, both in men and women. Thus, this study suggested that postural stability deteriorated with age, as in previous reports.

In the present study, increasing HbA 1 c was related to sway length in both men and women; this suggests that diabetes might affect postural stability. Diabetes is presumed to affect postural stability because it causes peripheral neuropathy[15)~17)], retinopathy[16)] and vestibular dysfunction[3)18)]. Especially, there have been many reports that diabetic peripheral neuropathy is a major cause of alterations in postural stability. Somatosensory information, together with visual and vestibular information, plays an important role in postural control. Postural instability in patients with diabetic peripheral neuropathy is often attributed to the absence of accurate peripheral sensory information from the feet. In posturography assessment, patients who had symptoms of bilateral numbness and/or paresthesia in the feet had higher postural sway length and enveloped area levels, compared to patients without symptoms[16)]. Although we did not investigate the presence of peripheral neuropathy and retinopathy, we suspect that diabetes might affect postural stability in both men and women.

Furthermore, women exhibited a significant positive association between sway length and baPWV in both EO and EC, regardless of adjustment for the influence of ageing. This finding suggests that the progression of arteriosclerosis causes deterioration of postural stability. An association has been reported between falls and arteriosclerosis; for example, fallers had significantly higher PWV[12)]. It has been suggested that peripheral vestibular diseases are associated with arteriosclerosis; the frequency of abnormal intima-media-thickness was significantly higher in subjects in the benign paroxysmal positional vertigo group[7)] and the metabolic syndrome score and baPWV of subjects in the vestibular neuritis group were significantly higher than control subjects[8)]. In the central nervous system, an abnormal middle cerebral artery in intracranial magnetic resonance angiography has been reported to be closely related to dizziness[9)]. Risk factors for arteriosclerosis include diabetes, dyslipidemia and smoking, which are expected to cause impaired blood flow not only in the central nervous system but also in peripheral blood vessels, such as the vestibule. In fact, there have been many reports that arteriosclerosis and circulatory disorders related to balance disorders; however, to the best of our knowledge, there have been few studies in which the relationship between arteriosclerosis and postural stability was evaluated in subjects who were not patients with specific symptoms of dizziness or a history of falls. In the present study, we demonstrated an association between arteriosclerosis and postural stability in an examination of community-dwelling subjects. However, it is not clear whether stenosis of blood vessels or blood flow disorder actually exists in the central nervous system and peripheral vestibule, because we did not measure the diameter and blood flow of the vertebral and carotid arteries. In addition, there are other factors that affect arteriosclerosis; for example, it is relatively cold in the Iwaki district, and the cold temperature may increase the prevalence of arteriosclerosis. But we do not consider that the prevalence of arteriosclerosis has a significant impact, because we indicated that sway length increased with increasing baPWV value not but prevalence of arteriosclerosis.

Regarding sex differences, it has been reported that falls are more common in women[2)]. Koo M et al. reported a significant association between vertigo and peripheral artery occlusive disease in female patients but not in male patients[10)]. However, the underlying causes of sex differences in the relationship between balance disorders and arteriosclerosis have not been clarified. Therefore, we presumed that the involvement of female hormones may contribute to these sex differences and examined the effect of menopause on postural stability. Before menopause, there were significant positive associations between sway length and pack years and HDL-C. Presumably, risk factors of arteriosclerosis, such as smoking and dyslipidemia, are related to postural stability; baPWV has not been reflected in postural stability at this stage in premenopausal women. While, after menopause, estrogens with vasodilator and anti-atherosclerotic effects are rapidly depleted and arteriosclerosis rapidly progresses. In addition, changes in lipid metabolism and insulin resistance due to menopause can cause increased onset and deterioration of diabetes[19]. These prior findings suggested that arteriosclerosis and diabetes are rapidly worsened after menopause and might accelerate postural instability. Naessen T et al. reported that, in postmenopausal women, the sway velocity significantly decreased in the balance test and dizziness also improved after hormonal therapy[20]. Taken together, our findings and those of prior studies suggest that rapid deterioration of arteriosclerosis might be a source of postural instability due to a reduction in female hormones. In the present study, men had worse lifestyle habits (drinking and smoking) than women and had higher baPWV, blood pressure and lipid levels. However, the relationship between arteriosclerosis and postural stability was observed only in women, which is potentially because women exhibit vulnerability to impaired blood flow with regard to postural stability.

Ageing and menopause cannot be prevented. In the present study, diabetes and arteriosclerosis were found to be related to postural stability; therefore, care for these diseases should be regarded as important for prevention of future balance disorders and falls. Specifically, improving lifestyle habits such as exercise might reduce future balance impairment. It has been reported that 6 months of participation in a twice-per-week exercise program, with an emphasis on swimming, improved baPWV and balance[4]; moreover, older patients with diabetes who exercised by walking and balance exercises for 12 weeks exhibited a reduction in the postural sway index[17]. It is well-known that arteriosclerosis is a risk factor for cerebrovascular and cardiovascular diseases; the results of the present study suggest that arteriosclerosis may also affect postural stability. Therefore, because of the super-aged nature of society in Japan, it is important to improve lifestyles in order to prevent balance disorders and associated falls.

The strengths of this study were its large sample size, detailed medical examination and comprehensive data sampling. Furthermore, it targeted the general population rather than patients with dizziness symptoms and a history of falls, and analyzed not categorical outcome measures but continuous outcome measures. In addition, this research assessed sex differences, include the influence of menopause, on postural stability.

Nevertheless, there were limitations in this study. First, we assessed the effects of female hormones but did not directly measure hormone levels. Second, although posturography is a test that objectively evaluates postural stability, it is difficult to identify specific lesions involved in balance dysfunction and additional tests may be necessary for such detailed diagnosis. Because this study was performed on the basis of routine health checkups, we used posturography, which is an easy-to-use and non-invasive test for the evaluation of postural stability[5]. To determine the specific sites at which impairments are located that directly affect deteriorated balance function, more comprehensive investigations are needed. Third, we used baPWV in this study. However, baPWV is an index of arterial stiffness and it is not clear if there are stenosis of blood vessels or blood flow disorder. In order to clarify them, it is necessary to use other useful tests such as carotid ultrasound, but it was difficult in such a large-scale health checkups. Finally, about enveloped area, we could not get high coefficient of determination. We consider that the low sampling frequency in the static posturography is one of the reasons of this results. It has been suggested that lower sampling frequency may result in smaller enveloped area[21]. Therefore, there is a possibility that the individual difference became smaller in enveloped area compared with the sway length, resulting in the extremely low coefficient of determination. In addition, it has been reported that the results of sway length and enveloped area are dissociated, and these values may represent different aspects of the balance function[22]. However, future researches are required since the difference between the sway length and enveloped area is unclear.

In this study, we evaluated postural stability in a large cohort study of community-dwelling population. We found that age and HbA1c level affected postural stability in both men and women. Moreover, baPWV affected the sway length in static posturography in women. In addition, our findings suggested that the rapid deterioration of arteriosclerosis due to menopause might contribute to deteriorated postural stability.

Acknowledgements

This work was supported by JST COI Grant Number JPMJCE1302. The authors would like to thank all of their coworkers on this study for their skillful contributions to the collection and management of the data.

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Disclosure of interest: No potential conflict of interest was reported by the authors.

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