Original Article

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Relationship between arteriosclerotic indicators and range of motion of foot joints in diabetic patients

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Abstract

Foot ulcers cause gait disturbances, decreased quality of life, and high rates of mortality in diabetic patients. High plantar pressure and failure of peripheral circulation dynamics have been mentioned as risk factors for diabetic foot ulcers. It has been reported that plantar pressure is affected by the limited joint mobility (LJM) of foot joints. Therefore, preventing LJM of foot joints is important for prevention of diabetic foot ulcers. Failure of peripheral circulation dynamics can be evaluated by measuring brachial-ankle pulse wave velocity (baPWV) . The LJM of foot joints and arteriosclerosis are involved in the etiology of diabetic foot ulcers, but there have been no studies regarding the relationship between these two factors. We investigated the relationship between the range of motion (ROM) of foot joints and baPWV in diabetic patients.

The study population consisted of 48 diabetic patients admitted to hospital for glycemic control and diabetes education. The LJM parameters measured were passive ROM of plantar flexion and dorsiflexion of the ankle joint, flexion and extension of the first metatarsophalangeal joint, and pronation and supination of the subtalar joint. baPWV was measured using an automated device. Pearson's and partial correlation coefficients of patients' baPWV and ROM values were calculated. The control conditions were age, gender, diabetes condition (diabetes duration, HbA1c levels, and diabetic polyneuropathy) , and arteriosclerosis status (systolic and diastolic blood pressure) .

The mean age of the subjects was 57.4±11.8 years. ROM values for ankle, first metatarsophalangeal, and subtalar joints were 56.9°±8.8°, 89.7°±11.8°, and 27.0°±7.1°, respectively. Partial correlation analysis revealed a negative correlation between baPWV and ankle ROM ($r=-0.35$, $p=0.03$) after controlling for age, sex, systolic and diastolic blood pressure, diabetes duration, HbA1c level, and diabetic polyneuropathy. No significant associations of these outcomes were found in other joints.

In diabetic patients, baPWV and ankle ROM were significantly negatively correlated when controlling for factors such as age, systolic and diastolic blood pressure, diabetes duration, HbA1c level, and diabetic polyneuropathy. However, additional studies are needed to draw clinical conclusions.

KEY WORDS

Diabetes mellitus, Range of motion, Brachial-ankle pulse wave velocity, Ankle joint, Atherosclerosis

Introduction

Since diabetic foot ulcers cause gait disturbances, decrease the quality of life, and lead to high mortality in diabetic patients, the prevention of diabetic ulcers is very important[1-3]. To date, in addition to poor peripheral circulation dynamics and decreased defense sensation,

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high plantar pressure has also been mentioned as a risk factor for diabetic foot ulcers[4]. Plantar pressure is considered to be affected by limited joint mobility (LJM) of the foot joints. It has been revealed that a decrease in the dorsiflexion range of motion (ROM) of the ankle joint and extension ROM of the first metatarsophalangeal joint causes an increase in plantar pressure of the forefoot during walking[5),6)]. This LJM occurs frequently not only in patients who have experienced foot injuries, such as ankle sprains, but also in those with diabetes[5),7)]. For diabetic patients who are prone to foot ulcers triggered by poor peripheral circulation dynamics and reduced defense sensation, LJM in the foot additively increases the risk of foot ulceration through an increase in plantar pressure[8-12)]. Thus, preventing LJM of foot joints is important in the prevention of diabetic foot ulcers. The causes of LJM in diabetic patients include the influence of advanced glycated end-products (AGEs) and a sedentary lifestyle[7)]. In particular, AGEs promote the formation of collagen crosslinks and decrease soft tissue flexibility[13)].

On the other hand, the failure of peripheral circulation dynamics is also an important risk factor for diabetic foot ulcers, and accurate assessment of arteriosclerosis is necessary for their prevention. Among several arteriosclerotic indices, brachial-ankle pulse wave velocity (baPWV) reflects the hardness of the peripheral and central arterial walls[14)]. The hardness of the arterial wall is affected by deposition of the extracellular matrix including collagen and elastin, calcification of vascular smooth muscle, and deterioration of endothelial cell function[15)]. An increase in collagen crosslinking and destruction of elastin are associated with arteriosclerosis in the extracellular matrix deposition[16)]. Carotid-femoral pulse wave velocity showed a positive correlation with relative contents of collagen, and a negative correlation with relative contents of elastin[17)]. Age-related changes of the arterial wall is accelerated by glycation stress[18)].

As described above, LJM of foot joints and arteriosclerosis are individually involved in the formation of diabetic foot ulcers; however, no studies on the relationship between the two have been found. Collagen crosslinking is a histologic common factor causing LJM or arteriosclerosis. In the current study, we hypothesized that there is a relationship between LJM of foot joints and arteriosclerosis in diabetic patients. To test this hypothesis, we investigated the relationship between the baPWV and ROM of foot joints in diabetic patients.

Method

Subjects consisted of 48 diabetic patients admitted to Japanese Red Cross Kanazawa Hospital for glycemic control and diabetes education between March 2016 and June 2017. All patients were able to walk without an assistive device. No patients had a history of diabetic foot ulcers and arteriosclerosis obliterans. Moreover, ankle brachial index were 1.13 ± 0.07. Therefore, we considered that patients have no gait disturbances caused by poor peripheral hemodynamics. Exclusion criteria for the present study were severe orthopedic and central or peripheral nervous system disease affecting gait pattern. Patient characteristics are shown in Table 1. Information on diabetes status (i.e., duration of diabetes, status of diabetic polyneuropathy, and HbA1c levels at admission) and lipid status (i.e., HDL-cholesterol, LDL-cholesterol, and triacylglycerol) were collected. Diabetic polyneuropathy was defined as an abnormality in nerve condition velocity or attenuation of protective sensation determined by Semmes-Weinstein 4.56 monofilament test. Examinations were performed according to the Declaration of Helsinki. All patients provided informed consent for participation in the present study.

The LJM measurement was made using the right foot. Measured parameters were passive ROM of plantar flexion and dorsiflexion of the ankle joint, flexion and extension of the first metatarsophalangeal joint, and pronation and supination of the subtalar joint. All ROMs were measured using established methods[19),20)]. Measurements of the ankle and first metatarsophalangeal joints were performed with patients in the supine position, with a roll placed under the knee to position the knee in slight flexion. The subtalar joint was maintained in an anatomical position. The stationary arm was the longitudinal axis of the fibula, and the movable arm was the sole of the heel. The ankle and toes were maintained in the neutral position. The axis was placed over the dorsum of the first metatarsophalangeal joint of the toe being measured. The stationary arm was the longitudinal axis of the metatarsal, and the movable arm was the longitudinal axis of the proximal phalanx. Measurements of the subtalar joint were performed with patients in the prone position, with the foot protruding from the bed. The ankle and first metatarsophalangeal joints were maintained in an anatomical position. The stationary arm was the center line on the back of the lower leg, and the movable arm was the longitudinal axis of the calcaneus. All measurements were performed by a physiotherapist, who was not a primary investigator on this research project, using a double-armed digital goniometer (GM-180, nihon-ikakikaiseisakusyo, Japan) calibrated in 1-degree increments. The maximum ROM of each joint was measured three times and the average value was calculated.

baPWV was measured using an automatic device (form PWV/AVI, Omron Colin, Japan) . After 1 min of rest, the spine, brachial, and ankle arterial pressure waveforms were recorded by wrapping the cuff connected to the plethysmograph and the oscillometric sensor around the upper arm and ankle. baPWV was calculated by dividing the difference in distance between the two sensors by the transit time. In the present study, the baPWV value on the right side was analyzed as the measurement value. Systolic and diastolic blood pressure and ankle-brachial index were recorded at the same time.

Correlation analysis was carried out between each ROM and age, gender, diabetes condition (diabetes duration, HbA1c levels, and diabetic polyneuropathy) , and arteriosclerosis status (systolic and diastolic blood pressure) . The correlation ratio was calculated for variables on the nominal scale. Pearson's correlation coefficient was calculated f for variables normally distributed, and Spearman's correlation coefficient was calculated for variables non-normally distributed. Pearson's and partial correlation coefficients of baPWV and ROM values were calculated per patient. The control conditions were age, gender, diabetes condition, and arteriosclerosis status. The significance level was set at $p < 0.05$. Statistical analyses were performed using SPSS for Windows (SPSS, Inc., Chicago, IL, USA) .

Table 1. Patient characteristics (n=48)

Age (years)	57.4±11.8
Gender (male/female)	34/14
Body weight (kg)	70.3±15.0
Body mass index (kg/m^2)	25.5±4.5
Diabetes duration (months)	8.1±8.3
HbA1c level (%)	9.7±1.6
Diabetic polyneuropathy	11/37
Systolic blood pressure (mmHg)	131.8±20.7
Diastolic blood pressure (mmHg)	81.3±14.1
Pulse rate (beat/minutes)	77.3±13.5
Triacylglycerol (mg/dl)	207.4±185.2
HDL-cholesterol (mg/dl)	50.0±11.3
LDL- cholesterol (mg/dl)	116.3±43.0
baPWV (cm/sec)	1620.9±310.8
Ankle joint ROM (°)	56.9±8.8
First metatarsophalangeal joint ROM (°)	89.7±11.8
Subtalar joint ROM (°)	27.0±7.1

ROM: range of motion

Results

Patient characteristics, diabetes status, lipid status, baPWV, and ROM of foot joints are shown in Table 1. Mean subject age was 57.4 ± 11.8 years. ROM values for the ankle, first metatarsophalangeal, and subtalar joints were 56.9 ± 8.8°, 89.7 ± 11.8°, and 27.0 ± 7.1°, respectively. The correlation coefficients between each ROM and age, gender, diabetes condition, and arteriosclerosis status are shown in Table 2. Partial correlation analysis revealed a negative correlation between baPWV and ankle ROM ($r = -0.35$, $p = 0.03$) after controlling for age, sex, systolic blood pressure, diastolic blood pressure, diabetes duration, HbA1c levels, and diabetic polyneuropathy (Table 3) . No significant relationship in these outcomes was found in other joints.

Discussion

The primary finding of this study was that baPWV and ankle ROM were significantly associated after adjusting for arteriosclerosis risk factors such as age, systolic blood pressure, diastolic blood pressure, and indices of short- and long-term glycosylation stress (diabetes duration, HbA1c levels, and diabetic polyneuropathy) . In the present study, the mean ankle ROM of subjects was 56.9 ± 8.8°, which was

Table 2. Correlation coefficients between each ROM and age, gender, diabetes condition, and arteriosclerosis status

	Ankle joint	First metatarsophalangeal joint	Subtalar joint
Age (years)	0.06	-0.07	0.12
Gender (male/female)	0.12	0.33	0.35
Diabetes duration (months)	-0.17	0.03	-0.09
HbA1c level (%)	0.02	0.10	0.12
Diabetic polyneuropathy	0.04	0.28	0.06
Systolic blood pressure (mmHg)	0.11	0.02	0.20
Diastolic blood pressure (mmHg)	0.07	0.29*	-0.04

*p<0.05

Table 3. Single and partial correlation coefficient of brachial-ankle pulse wave velocity and each range of motion of foot joints

		Single correlation coefficient	Partial correlation coefficient
Ankle joint	r	-0.16	-0.35*
First metatarsophalangeal joint	r	0.03	0.013
Subtalar joint	r	0.04	-0.077

The partial correlation coefficient was controlled by sex, age, systolic blood pressure, diastolic blood pressure, HbA1c levels, diabetes duration, and diabetic polyneuropathy.
*p<0.05

lower than the mean ankle joint angle (72.6° for males, 88.1° for females) found in a previous study in healthy Japanese subjects[21]. A number of previous studies have addressed LJM of the ankle joint in diabetic patients, and the results of the current study support the findings of these studies[5),10),11]. Several factors have been shown as causes of ROM limitations in diabetic patients. A lengthened duration of diabetes, an accumulation of AGEs in collagen tissues, and decreased physical activity levels have previously been mentioned as contributing factors[7]. Collagen denaturation is greatly affected in tissues with low turnover, such as joint capsule, and in tendon tissue in particular[22]. Histologically, abnormal crosslinking between collagen fibers reduces the viscoelasticity of the tissue[23]. Thus, LJM of the ankle joint in diabetic patients has a great influence on the degeneration of collagen tissue exposed to glycation stress.

Incidentally, in recent years, correlations between trunk flexibility and baPWV have been observed in healthy subjects[24]. According to previous research, scores on the sit and reach test as an indicator of trunk flexibility were negatively correlated with baPWV in middle-aged and elderly subjects. This was believed to be caused by the degeneration of collagen tissue in the arterial wall and the hypertonic tone of the vascular smooth muscle. In fact, the deterioration of baPWV represents the stiffness of the peripheral artery and the central artery from the brachial to the ankle joint. Furthermore, histologically, the influence of the extracellular matrix deposition of the arterial wall, such as collagen and elastin, has been pointed out in previous research[15),16)]. Based on these factors, we controlled for systolic and diastolic blood pressure in our analysis, as these are factors affecting aspects of arteriosclerosis such as hypertonic vascular smooth muscle and collagen degeneration.

Results of this study suggest that the ankle ROM decreased when baPWV was high. From a clinical standpoint, in order to prevent diabetic foot ulcers, it is necessary to carefully observe, over time, the state of the ankle ROM and plantar skin of diabetic patients whose baPWV is becoming high. Histologically, correlations between baPWV and ROM were found even when controlling for factors influencing atherosclerosis and LJM of the foot joint. Thus, it is possible that the degeneration of collagen tissues is a commonality between the two variables. The cross-sectional design was a limitation of this study, and as such, we could not draw conclusions regarding the mechanism of association between the deterioration of baPWV and ROM of foot joints. Since the baPWV and ROM values collected herein are the results of a noninvasive examination, in the future it will be necessary to conduct histological and longitudinal studies examining the relevance of the periarticular soft tissue and the collagenous tissue of the arterial wall.

Conclusion

In a sample of diabetic patients in Japan, baPWV and ankle ROM were significantly negatively correlated after controlling for factors such as age, systolic blood and diastolic blood pressure, diabetes duration, HbA1c levels, and diabetic polyneuropathy. However, additional studies are needed to draw clinical conclusions regarding the influence of baPWV and ROM on diabetic foot ulcers.

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糖尿病患者における足部関節可動域と動脈硬化指標の関係

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要　　旨

糖尿病性足部潰瘍は歩行障害、QOL の低下、死亡率の上昇を引き起こす。糖尿病性足部潰瘍の危険因子として高すぎる足底圧と末梢循環動態の障害が報告されている。足底圧は、足部関節の可動域制限の影響を受けることが示されている。従って、足部関節の関節可動域制限を予防することは、糖尿病性足部潰瘍の予防において重要である。末梢循環動態は、上腕 - 足首脈波速度（baPWV）で評価できる。足部関節の可動域制限および動脈硬化は糖尿病性足部潰瘍に個々に関与しているが、両者の関係は不明である。そこで本研究の目的は、糖尿病患者の足部関節の関節可動域と baPWV の関係を調べることとした。

対象は、血糖コントロールと糖尿病教育のために入院した 48 人の糖尿病患者とした。測定された関節可動域は、足関節の背屈および底屈、第 1 中足趾節間関節の屈曲および伸展、および距骨下関節の回内および回外方向の他動関節可動域とした。baPWV は専用の自動計測装置で測定した。対象の baPWV および各関節の関節可動域のピアソンおよび偏相関係数を計算した。偏相関係数の統制条件は、年齢、性別、糖尿病の状態（糖尿病罹病期間、HbA1c 値および糖尿病性多発性神経障害）および動脈硬化に関連する値（収縮期血圧および拡張期血圧）とした。

対象の平均年齢は 57.4 ± 11.8 歳であった。足関節、第 1 中足趾節間関節、距骨下関節の関節可動域は、それぞれ 56.9 ± 8.8°、89.7 ± 11.8°、27.0 ± 7.1° であった。偏相関分析は、年齢、性別、収縮期血圧および拡張期血圧、糖尿病期間、HbA1c 値および糖尿病性多発性神経障害の有無で制御した後、baPWV と足関節の関節可動域との間に負の相関を示した（$r = -0.35$、$p = 0.03$）。他の関節では有意な関連は認められなかった。

糖尿病患者では、年齢、収縮期および拡張期血圧、糖尿病期間、HbA1c 値および糖尿病性多発性神経障害の因子で統制しても、baPWV および足関節の関節可動域は有意に負の相関関係を認めた。しかしながら、臨床的結論を引き出すためにはさらなる研究が必要である。