Sonographic Evaluation of the Peripheral Nerve in Diabetic Patients

The Relationship Between Nerve Conduction Studies, Echo Intensity, and Cross-sectional Area

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Objective. Early detection of nerve dysfunction is important to provide appropriate care for patients with diabetic polyneuropathy. The aim of this study was to assess the echo intensity of the peripheral nerve and to evaluate the relationship between nerve conduction study results and sonographic findings in patients with type 2 diabetes mellitus. ***Methods.*** Thirty patients with type 2 diabetes (mean ± SD, 59.8 ± 10.2 years) and 32 healthy volunteers (mean, 53.7 ± 13.9 years) were enrolled in this study. The cross-sectional area (CSA) and echo intensity of the peripheral nerve were evaluated at the carpal tunnel and proximal to the wrist (wrist) of the median nerve and in the tibial nerve at the ankle. ***Results.*** There was a significant increase in the CSA and hypoechoic area of the nerve in diabetic patients compared with controls (wrist, 7.1 ± 2.0 mm^2, 62.3% ± 3.0%; ankle, 8.9 ± 2.8 mm^2, 57.6% ± 3.9%; and wrist, 9.8 ± 3.7 mm^2, 72.3% ± 6.6%; ankle, 15.0 ± 6.1 mm^2, 61.4% ± 5.3% in controls and diabetic patients, respectively; $P < .05$). Cross-sectional areas were negatively correlated with reduced motor nerve conduction velocity and delayed latency. ***Conclusions.*** These results suggest that sonographic examinations are useful for the diagnosis of diabetic neuropathy. ***Key words:*** cross-sectional area; diabetic neuropathy; echo intensity; median nerve; sonography; tibial nerve.

Abbreviations
BMI, body mass index; BSA, body surface area; CMAP, compound muscle action potential; CSA, cross-sectional area; CTS, carpal tunnel syndrome; DPN, diabetic polyneuropathy; MCV, motor nerve conduction velocity; MMCV, median motor nerve conduction velocity; NCS, nerve conduction study; ROC, receiver operating characteristic; TMCV, tibial motor nerve conduction velocity; TTS, tarsal tunnel syndrome

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The World Health Organization estimates that more than 180 million people worldwide have diabetes mellitus. This figure is estimated to more than double by 2030.[1] In Japan, the number of diabetic patients has increased and reached 8 million, and it is assumed that 35% to 45% of diabetic patients have symmetric diabetic polyneuropathy (DPN). Advanced DPN causes serious complications, such as diabetic foot ulcers, gangrene, and Charcot joint, all of which worsen the quality of life of diabetic patients.[2] Therefore, early detection of nerve dysfunction is important to provide appropriate care for patients with DPN.[3]

The diagnosis of diabetic neuropathy is based primarily on characteristic symptoms and is confirmed with a nerve conduction study (NCS). Although imaging analyses for neuropathy have not been used for diagnosis, high-resolution diagnostic ultrasound equipment has improved greatly, making revelation of minute peripheral nerves by sonographic evaluation possible.[4] Recent

studies using sonography for entrapment neuropathy such as carpal tunnel syndrome (CTS)[4–9] have been presented. However, there are few reports of DPN diagnosis using sonography. We showed previously that the cross-sectional area (CSA) of the median nerve in the carpal tunnel of patients with DPN is greater than that of controls and correlates with NCS.[10] The aim of this study was to assess the echo intensity of the peripheral nerve and to evaluate the relationship between NCS results and sonographic findings in diabetic patients.

Materials and Methods

Participants

Thirty patients with type 2 diabetes were enrolled in this study at the Gifu University Hospital from October 2007 to January 2009 (17 men and 13 women; age range, 36–83 years; mean ± SD, 59.8 ± 10.2 years). Our control group consisted of 32 healthy volunteers without diabetes mellitus or CTS (25 men and 7 women; age range, 24–72 years; mean, 53.7 ± 13.9 years). Patients' wrists with symptoms of CTS were not included in the study; those that were included had negative Phalen test results. Every participant was able to walk unaided, and none had received hemodialysis.

We studied a total of 95 peripheral nerves (including 62 median nerves and 33 tibial nerves) of 62 participants who received both sonography and NCS. This study was approved by the Institutional Review Board of Gifu University Hospital, and informed consent was obtained from all participants.

Sonographic Examinations

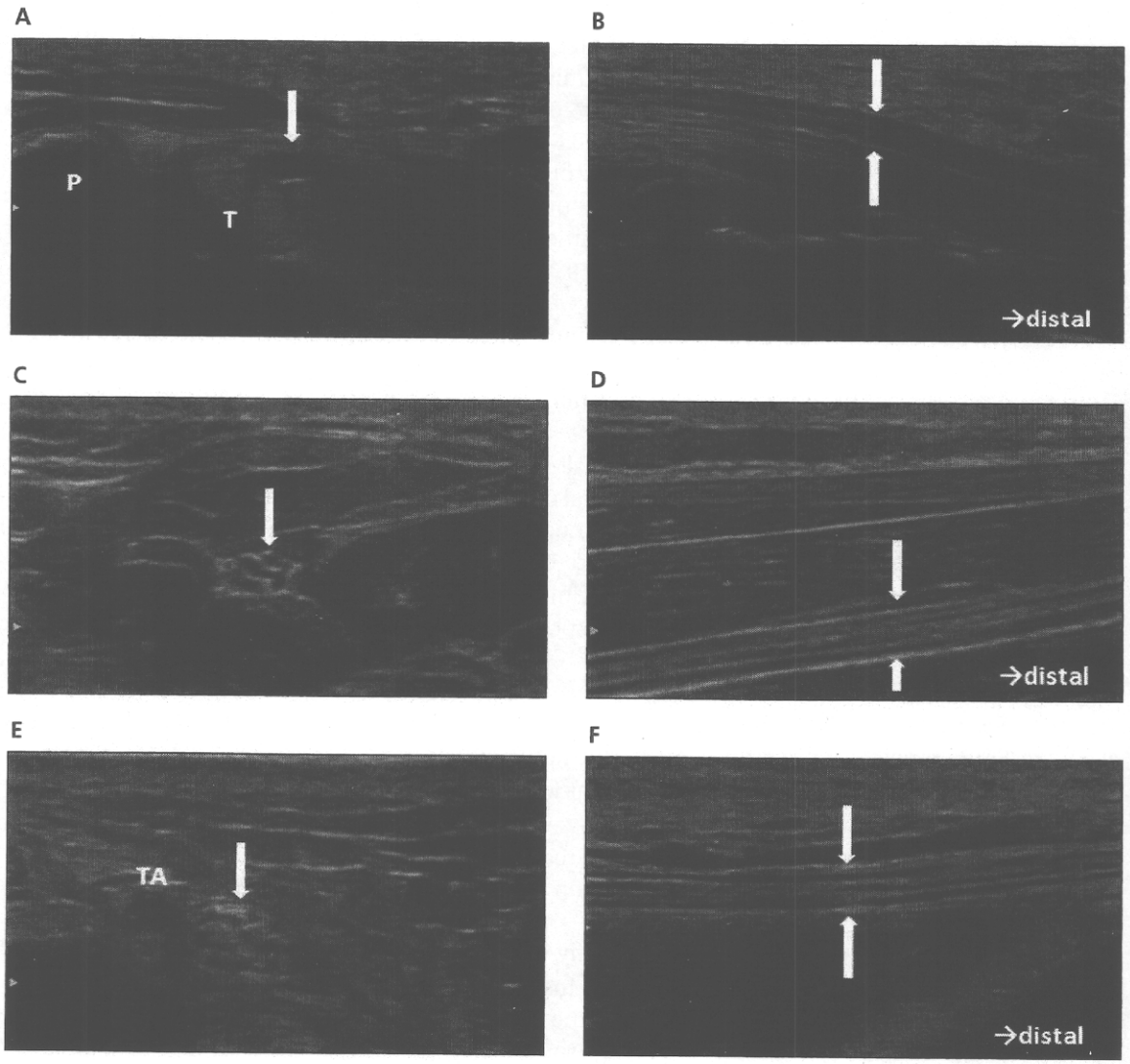
Sonographic examinations were performed by 1 of 2 experienced sonographers (with at least 10 years of ultrasound experience) using a 6.0- to 14.0-MHz linear array probe (portable real-time apparatus: EUB-7500; Hitachi Corporation, Tokyo, Japan; or ProSound Alpha 10; Aloka Co, Ltd, Tokyo, Japan). Sonograms were quantitatively analyzed using ImageJ software (National Institutes of Health, Bethesda, MD), and only the image obtained by a specific zoom setting was used. Computer analyses were performed by 2 other sonographers who did not have any knowledge of the electrodiagnostic results (observer A had 15 years of experience, and observer B had 6 years of experience). All participants were in the supine position on a table with fingers semiextended during examination of the median nerve and in the prone position during examination of the tibial nerve. The major axis, minor axis, and CSA of the median nerve were measured at the carpal tunnel and at 5 cm proximal to the wrist (wrist). The major axis, minor axis, and CSA of the tibial nerve were measured at the posterior medial malleolus (ankle). The CSA was calculated by the indirect method using the formula major axis × minor axis × π × 1/4 (square millimeters). There are 2 sonographic measurement methods of the nerve CSA: the indirect method (ellipsoid formula) and the direct method (tracing). Recently, Alemán et al[11] reported that median nerve CSA measurements are reproducible by either the direct or indirect method when a standardized sonographic examination protocol is applied. In addition, Sernik et al[12] also reported a high correlation (r = 0.99) between the areas calculated by the indirect and direct methods; consequently, we used the easier indirect method in our study. The volar wrist crease and pisiform bone or medial malleolus were used as initial external reference points and landmarks during scanning. Transverse and longitudinal sonograms of the nerve at each position were recorded (Figure 1). The peripheral nerve's speckled pattern on sonography enabled us to assess its size and echo intensity.

Of the 62 participants, 26 (42%; 13 diabetic patients and 13 controls) were recorded as specific zoom images on the Hitachi EUB-7500 ultrasound equipment. The stored images were further analyzed by 2 sonographers on a personal computer using ImageJ. Each observer received training specific to this study before initiation of the data collection. The images were saved as JPEG files and transferred to a personal computer for analysis. The monochrome sonogram was quantized to 8 bits (ie, 256 gray levels). Histogram analysis on sonography has been expected to offer an objective index for estimating echo intensity such as in diagnosis of fatty liver. The region of interest was set to cover the entire nerve, excluding its hyperechoic rim. The bright-

ness of the pixels ranged from 0 (black) to 255 (white). We used the percentage of the hypoechoic area as the index after the effects of the gain shift on the echo intensity in the median nerve were confirmed (Figure 2).

The normal appearance of the peripheral nerve should be readily recognized. The nerve consists of multiple hypoechoic bands corresponding to neuronal fascicles, which are separated by hyperechoic lines that correspond to the epineurium. Thus, the mean echogenicity was used as a threshold level for the analysis of the percentage of the hypoechoic area because the echogenicity of the peripheral nerve was obtained as a graded echo density from black to white. The percentage of the hypoechoic area was studied using computer analysis. Using ImageJ, the amount of the hypoechoic area falling below the threshold echo intensity level was calculated (Figure 3). Each measurement was taken 5 times, and the mean value was used in the analysis.

Figure 1. Transverse and longitudinal sonograms of the median and tibial nerves at each level. **A**, **C**, and **E**, Transverse sonograms showing the median nerve in the carpal tunnel (**A**) and 5 cm proximal to the wrist (**C**) and the tibial nerve in the posterior medial malleolus (**E**). The nerve (arrows) shows speckled pattern. **B**, **D**, and **F**, Longitudinal sonograms showing the median nerve in the carpal tunnel (**B**) and 5 cm proximal to the wrist (**D**) and the tibial nerve in the posterior medial malleolus (**F**). P indicates pisiform bone; T, tendon; and TA, tibial artery.



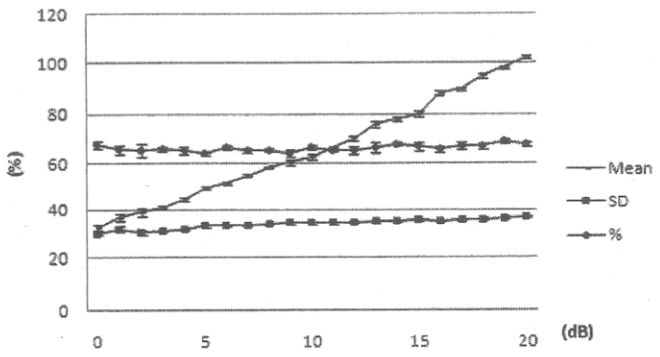


Figure 2. Effects of gain shift on the echo intensity in the median nerve. The line connecting rectangles shows a change of the mean; the line connecting squares shows a change of the SD; and the line connecting circles shows a change of the percentage according to the gain shift.

Intraobserver reproducibility was expressed as the difference between 2 repeated measurement results from the same observer. Interobserver reproducibility was expressed as the difference between 2 measurements obtained by 2 observers. Intraobserver reproducibility and interobserver reproducibility were estimated according to intraclass and interclass correlation coefficients.

Electrophysiologic Examinations

Routine NCS was performed using conventional procedures and standard electromyography (Neuropack MEB-2200; Nihon Kohden Corporation, Tokyo, Japan). All examinations were performed in a room with an ambient temperature of 25°C. The skin surface temperature in all cases was 31°C to 33°C. Motor nerve conduction velocity (MCV) was calculated from the distance of 2 stimulating points and the difference in each response time, and the compound muscle action potential (CMAP) was recorded from the abductor pollicis brevis muscle of the median nerve and the extensor digitorum brevis of the tibial nerve.

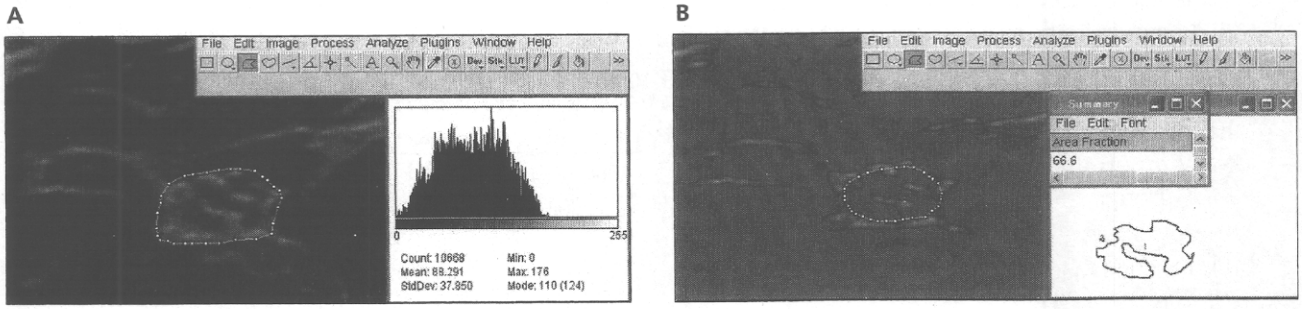
The rough reference ranges for the MCVs from the Gifu Laboratory are 50 m/s for the median motor nerve conduction velocity (MMCV) and 40 m/s for the tibial motor nerve conduction velocity (TMCV); therefore, we divided the patients into 4 groups (median nerve >50 and <50 m/s [high- and low-MMCV groups] and tibial nerve >40 and <40 m/s [high- and low-TMCV groups]) and compared them with the controls.

Statistical Analysis

The Mann-Whitney *U* test was used to compare the data between 2 groups. Pearson correlation coefficients were used to investigate the correlation of the CSA and percentage of the hypoechoic area with clinical parameters. Results are given as mean ± SD, and statistical significance was assessed as $P < .05$.

A receiver operating characteristic (ROC) curve was fitted to sonographic measurements using clinical DPN criteria as the reference standards to determine the optimum cutoff point and to evaluate the diagnostic accuracy of sonographic measurements. Receiver operating characteristic curves are plots of the true-positive rate (sensitivity) against the false-positive rate (1.0 – specificity) for the different possible cutoff points of a diagnostic test. The cutoff value at the Younden index point indicates the optimum threshold. To see the change of diagnostic accuracy according

Figure 3. Method of quantitative analysis for echo intensity using ImageJ software. **A**, The region of interest was set to cover the entire nerve, including the hyperechoic rim surrounding the nerve. The mean pixel brightness value was used for further analysis as a threshold. **B**, The percentage was calculated using the Analyze Particles function on the hypoechoic area in the nerve after threshold input.



to reference standards, another ROC curve was fitted using MCV results, and the sensitivity and specificity of sonography and NCS were calculated and compared between 2 examinations.

Results

Detailed demographic data for the diabetic patients and controls are shown in Table 1. There were no significant differences in age, height, weight, or body mass index (BMI) between controls and diabetic patients. Intraobserver reproducibility was high for both observers (observer A, intraclass correlation coefficient = 0.998; observer B, intraclass correlation coefficient = 0.987); interobserver reproducibility was also high (interclass correlation coefficient = 0.995). Results of the sonographic examinations and NCS of the diabetic patients and controls are shown in Table 2. Cross-sectional areas in the high-MMCV group were 8.8 ± 2.1 mm^2 in the carpal tunnel and 6.7 ± 1.4 mm^2 in the wrist. Cross-sectional areas in the low-MMCV group were 14.0 ± 6.1 mm^2 in the carpal tunnel and 9.8 ± 3.7 mm^2 in the wrist. Cross-sectional areas in the controls were 8.3 ± 1.8 mm^2 in the carpal tunnel and 7.1 ± 2.0 mm^2 in the wrist. There was a significant increase in the median nerve CSA in the low-MMCV group compared with that in the controls (carpal tunnel, $P < .001$; wrist, $P < .05$) and the high-MMCV group (carpal tunnel, $P < .001$; wrist, $P < .01$). Cross-sectional areas in the ankle were 15.0 ± 6.1 mm^2 in the low-TMCV group, 8.8 ± 2.9 mm^2 in the high-TMCV group; and 8.9 ± 2.8 mm^2 in the controls. There was a significant increase in the tibial nerve CSA in the low-TMCV group compared with that in the controls ($P < .01$) and the high-TMCV group ($P < .05$).

The percentage of the hypoechoic area was significantly increased in the low-MMCV group compared with that in the controls ($P < .01$) and the high-MMCV group ($P < .05$). Sonograms and histograms of the diabetic patients and controls are shown in Figure 4.

The MCV and CMAP of both the median and tibial nerves in the low-MCV group showed a significant decrease compared with those in the controls and the high-MCV group. On the other hand, latency was significantly slower in the low-MCV group than in the controls and the high-MCV group.

Table 3 shows the correlation results between several sonographic findings and characteristics in the median nerve. The CSA in the carpal tunnel showed a significant correlation with age ($r = 0.306$; $P < .05$), MCV ($r = -0.655$; $P < .001$), latency ($r = 0.552$; $P < .001$), and CMAP ($r = -0.311$; $P < .05$). In the wrist, the CSA was also significantly correlated with age ($r = 0.266$; $P < .05$), body surface area (BSA; $r = 0.271$; $P < .05$), MCV ($r = -0.502$; $P < .001$), latency ($r = 0.296$; $P < .05$), and CMAP ($r = -0.285$; $P < .05$). The percentage of the hypoechoic area showed a significant correlation with MCV ($r = -0.624$; $P < .001$) and latency ($r = 0.595$; $P < .01$).

Table 4 shows the correlation results between several sonographic findings and characteristics in the tibial nerve. The CSA in the ankle showed a significant correlation with age ($r = 0.493$; $P < .01$), weight ($r = 0.359$; $P < .05$), BMI ($r = 0.454$; $P < .05$), MCV ($r = -0.532$; $P < .01$), latency ($r = 0.525$; $P < .01$), and CMAP ($r = -0.414$; $P < .05$). The percentage of the hypoechoic area showed a significant correlation with weight ($r = 0.432$; $P < .05$), BMI ($r = 0.432$; $P < .05$), BSA ($r = 0.435$; $P < .05$), MCV ($r = -0.565$; $P < .01$), and latency ($r = 0.466$; $P < .05$).

The latency period of the median nerve was divided into 3 groups: latency of less than 3.5 milliseconds, latency of 3.5 to 4.0 milliseconds, and latency of greater than 4.0 milliseconds. The MCV of the median nerve was also divided into 3 groups: MCV of less than 50 m/s, MCV of 50 to 55 m/s, and MCV of greater than 55 m/s.

Table 1. Characteristics of All Participants

Parameter	Controls	Diabetic Patients
n	32	30
Male/female	25/7	17/13
Age, y	53.7 ± 13.9	59.8 ± 10.2
Height, cm	164.9 ± 6.9	161.2 ± 7.7
Weight, kg	62.6 ± 9.5	62.6 ± 10.2
BMI, %	22.6 ± 2.8	24.1 ± 2.9
Duration, y	NA	15.4 ± 10.7
HbA1c, %	NA	8.9 ± 1.9
CVRR, %	NA	1.96 ± 1.19
Presence of sensory symptoms, n (%)	NA	47 (14/30)
Bilaterally decreased or absent Achilles tendon, n (%)	NA	66.7 (20/30)
Decreased vibratory sensation, n (%)	NA	66.7 (20/30)

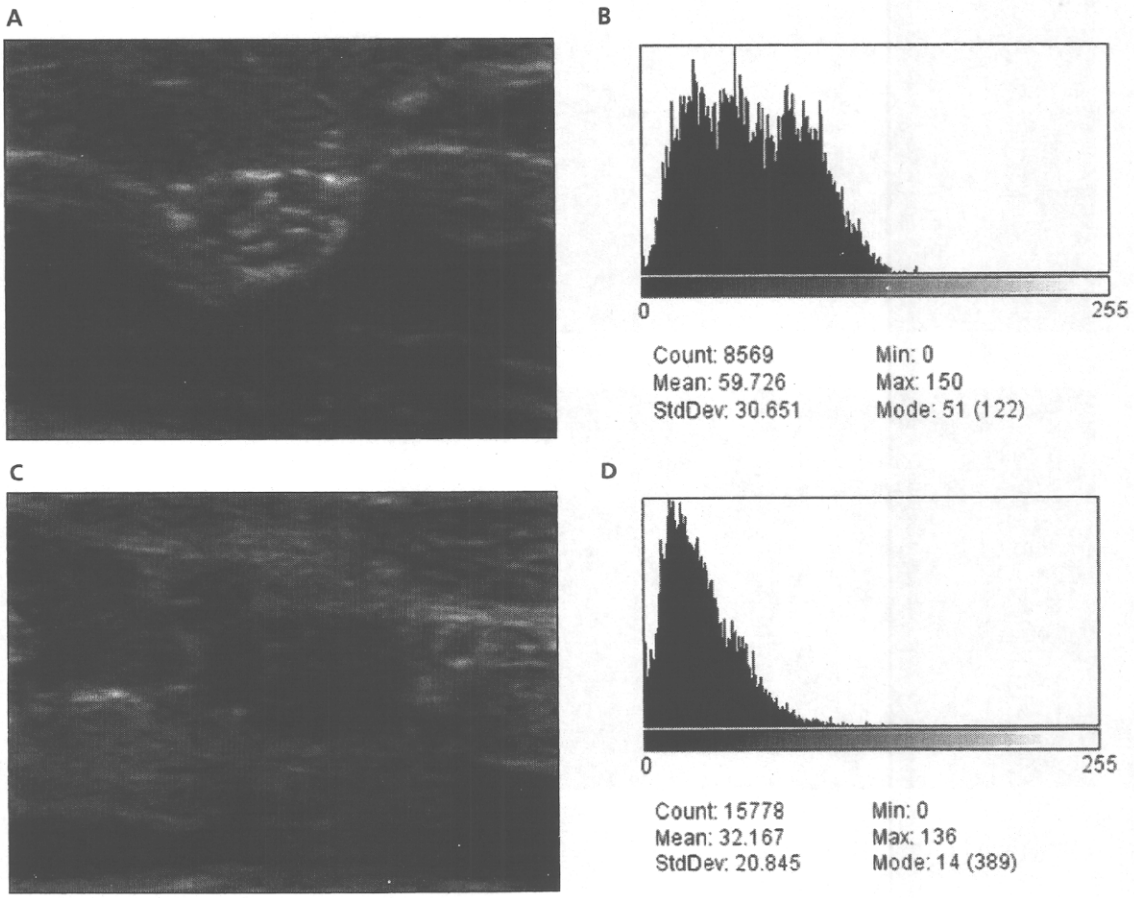
CVRR indicates coefficient of variation of R-R intervals; HbA1c, hemoglobin A1c; and NA, not applicable.

Table 2. Sonographic and Electrophysiologic Measurements of Patients With Diabetes Mellitus and Controls

Parameter	Median Nerve			Tibial Nerve		
		Diabetic Patients			Diabetic Patients	
	Controls (n = 32)	High MMCV (n = 16)	Low MMCV (n = 14)	Controls (n = 14)	High TMCV (n = 5)	Low TMCV (n = 14)
Sonographic measurements (CSA)						
Level of carpal tunnel, mm^2	8.3 ± 1.8	8.8 ± 2.1	14.0 ± 6.1[a,b]			
Level of 5 cm proximal to the wrist, mm^2	7.1 ± 2.0	6.7 ± 1.4	9.8 ± 3.7[c,d]			
Level of posterior medial malleolus, mm^2				8.9 ± 2.8	8.8 ± 2.9	15.0 ± 6.1[e,f]
Sonographic measurements (echo intensity)						
SD	31.3 ± 3.2	31.3 ± 4.5	26.0 ± 5.1[c,g]	28.3 ± 3.4	27.3 ± 1.2	26.5 ± 3.5
Hypoechoic area, %	62.3 ± 3.0	61.8 ± 5.0	72.3 ± 6.6[e,g]	57.6 ± 3.9	60.3 ± 2.7	61.4 ± 5.3
Electrophysiologic measurements						
MCV, m/s	54.9 ± 4.3	53.1 ± 2.8	45.3 ± 3.5[a,b]	50.1 ± 3.3	42.1 ± 1.9[e]	35.8 ± 2.4[a,h]
Latency, ms	3.7 ± 0.6	3.8 ± 0.5	4.7 ± 1.3[e,g]	4.1 ± 0.5	4.5 ± 0.8	5.6 ± 1.0[a,f]
CMAP, mV	13.7 ± 4.9	6.4 ± 3.2[a]	5.8 ± 3.2[a]	18.7 ± 6.8	10.3 ± 4.1[c]	5.9 ± 5.1[a]

Mann-Whitney *U* test: [a]$P < .001$ versus controls; [b]$P < .001$ versus high MMCV; [c]$P < .05$ versus controls; [d]$P < .01$ versus high MMCV; [e]$P < .01$ versus controls; [f]$P < .05$ versus high TMCV; [g]$P < .05$ versus high MMCV; [h]$P < .01$ versus high TMCV.

Figure 4. Transverse sonograms and histograms of the nerve at each level. **A**, Sonogram of the median nerve in a control participant's wrist. **B**, Histogram of the median nerve in a control participant's wrist. **C**, Sonogram of the median nerve in a diabetic patient's wrist. **D**, Histogram of the median nerve in a diabetic patient's wrist (continued).



Categorizing of participants into tertiles of latency yielded 3 separate groups. Compared with the first tertile, CSAs of the median nerve increased significantly with each tertile. Moreover, after combining tertiles of latency and the MCV, even more comprehensive CSA stratification was possible, with all CSAs ranging from 7.1 mm^2 in participants in the lowest tertile of both parameters to 14.6 mm^2 in participants in the highest tertile (Figure 5). The latency period of the tibial nerve was divided into 3 groups: latency of less than 4.5 milliseconds, latency of 4.5 to 5.0 milliseconds, and latency of greater than 5.0 milliseconds. The MCV of the tibial nerve was also divided into 3 groups: MCV of less than 40 m/s, MCV of 40 to 50 m/s, and MCV of greater than 50 m/s. The CSA of the tibial nerve stratification was 16.3 mm^2 in participants in the highest tertile for both parameters (Figure 6).

In the ROC analysis (Figure 7), the following cutoff values corresponded to the highest diagnostic accuracy: 11 mm^2 for the sonographic CSA of the carpal tunnel, 8 mm^2 for the sonographic CSA of the wrist, and 10 mm^2 for the sonographic CSA of the ankle; 62% for the hypoechoic area of the wrist and 66% for the hypoechoic area of the ankle; 52 m/s for the NCS MCV of the median nerve and 42 m/s for the NCS MCV of the tibial nerve; and 4.0 milliseconds for latency in the median nerve and 4.4 milliseconds for latency in the tibial nerve. According to the cutoff values derived from ROC analysis, the most effective sonographic parameter was the CSA of the carpal tunnel (68.2% sensitivity and 85% specificity), whereas the most effective NCS parameter was the tibial nerve MCV (87.5% sensitivity and 93.5% specificity). The sensitivity was lower with sonog-

Figure 4. (continued) **E**, Sonogram of the tibial nerve in a control participant's ankle. **F**, Histogram of the tibial nerve in a control participant's ankle. **G**, Sonogram of the tibial nerve in a diabetic patient's ankle. **H**, Histogram of the tibial nerve in a diabetic patient's ankle.

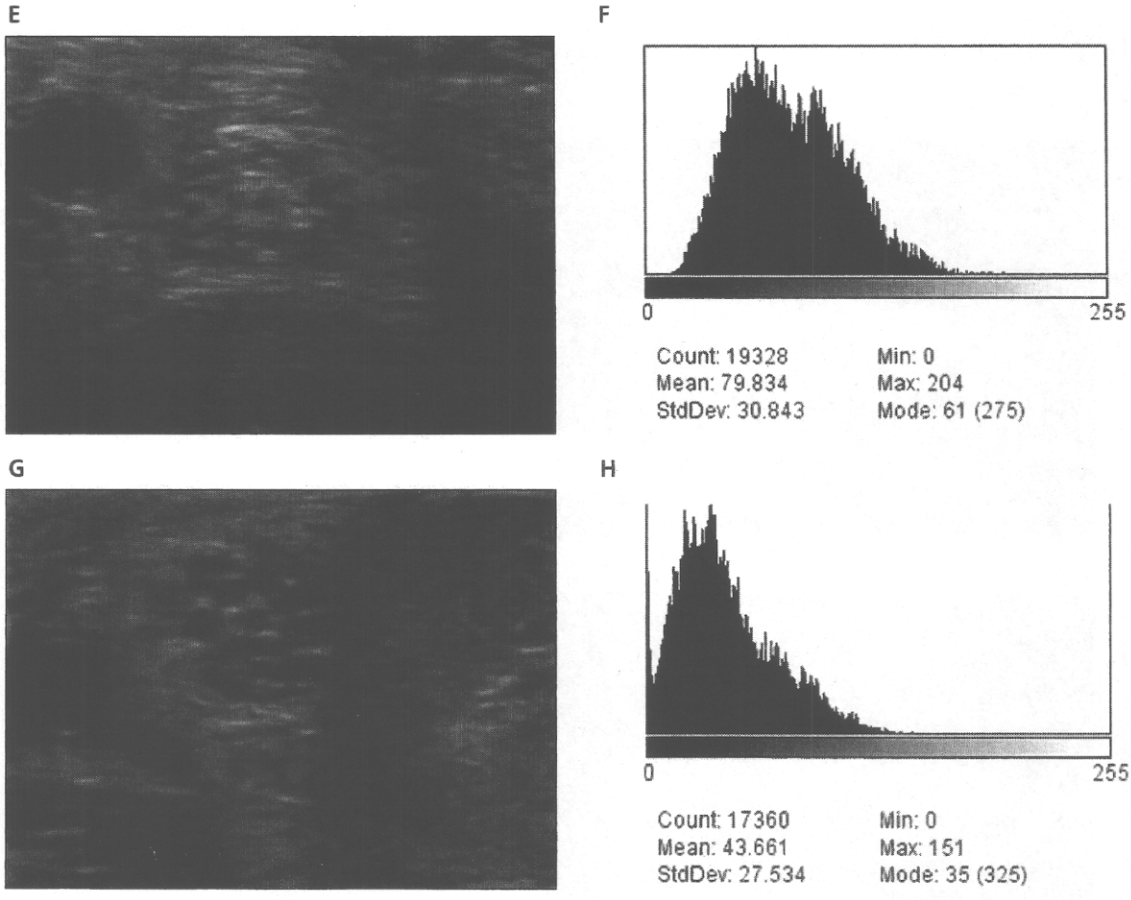


Table 3. Correlation Between Several Sonographic Findings and Characteristics in the Median Nerve

	Correlation Coefficient		
	CSA		Percentage of
Parameter	Carpal Tunnel	Wrist	Hypoechoic Area
Age	0.306[a]	0.266[a]	0.358
Height	−0.041	0.187	−0.020
Weight	0.131	0.217	0.232
BMI	0.186	0.189	0.328
BSA	0.123	0.271[a]	0.182
CVRR	−0.050	0.125	0.101
HbA1c	−0.251	−0.098	0.301
Duration	0.298	0.173	−0.219
MCV	−0.655[b]	−0.502[b]	−0.624[b]
Latency	0.552[b]	0.296[a]	0.595[c]
CMAP	−0.311[a]	−0.285[a]	−0.336

The CSA and percentage of the hypoechoic area were compared with the participant's age, physical parameters, coefficient of variation of R-R intervals (CVRR), hemoglobin A1c (HbA1c) level, duration, and nerve conduction study by Pearson correlation coefficients.
[a]$P < .05$; [b]$P < .001$; [c]$P < .01$.

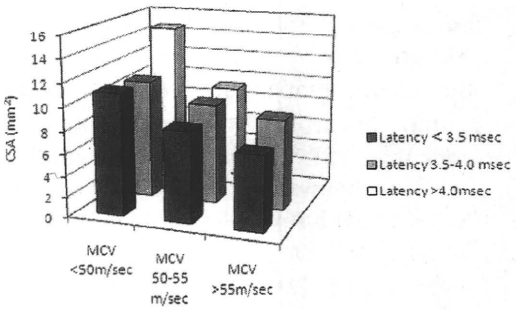


Figure 5. Cross-sectional area stratification in the median nerve by combining tertiles of latency and MCV. The CSA increased from 7.1 mm² in participants in the first tertiles of both nerve conduction study parameters to 14.6 mm² in participants in the third tertile of latency and MCV. The latency was divided into 3 groups: latency of less than 3.5 milliseconds, latency of 3.5 to 4.0 milliseconds, and latency of greater than 4.0 milliseconds. The MCV was also divided into 3 groups: MCV of less than 50 m/s, MCV of 50 to 55 m/s, and MCV of greater than 55 m/s.

raphy than NCS, but the specificity was similar between sonography and NCS (Table 5).

Discussion

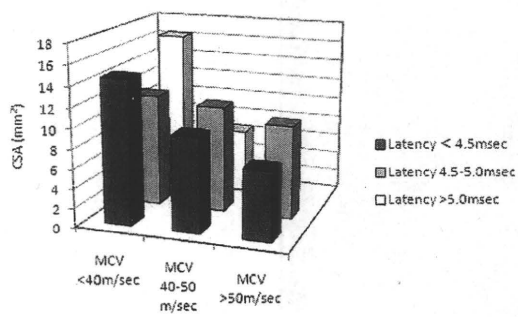
Diabetes mellitus is becoming a major cause of premature disability in Japan, and peripheral neuropathy is a common complication of diabetes.[13] The diagnosis of diabetic neuropathy is based on its characteristic symptoms and can be confirmed with NCS.[13–16] However, NCS is time-consuming, slightly invasive, and generally not well tolerated for repeated evaluations.[17] In contrast, sonographic examinations can be performed to assess peripheral nerves with less discomfort and have already been used for the evaluation of disorders of the peripheral nervous system.[4–10]

Table 4. Correlation Between Several Sonographic Findings and Characteristics in the Tibial Nerve

	Correlation Coefficient	
Parameter	CSA	Percentage of Hypoechoic Area
Age	0.493[a]	0.062
Height	−0.079	0.182
Weight	0.359[b]	0.432[b]
BMI	0.454[b]	0.432[b]
BSA	0.229	0.435[b]
CVRR	0.115	−0.038
HbA1c	0.241	0.156
Duration	0.018	−0.109
MCV	−0.532[a]	−0.565[a]
Latency	0.525[a]	0.466[b]
CMAP	−0.414[b]	−0.321

The CSA and percentage of the hypoechoic area were compared with the participant's age, physical parameters, coefficient of variation of R-R intervals (CVRR), hemoglobin A1c (HbA1c) level, duration, and nerve conduction study by Pearson correlation coefficients.
[a]$P < .01$; [b]$P < .05$.

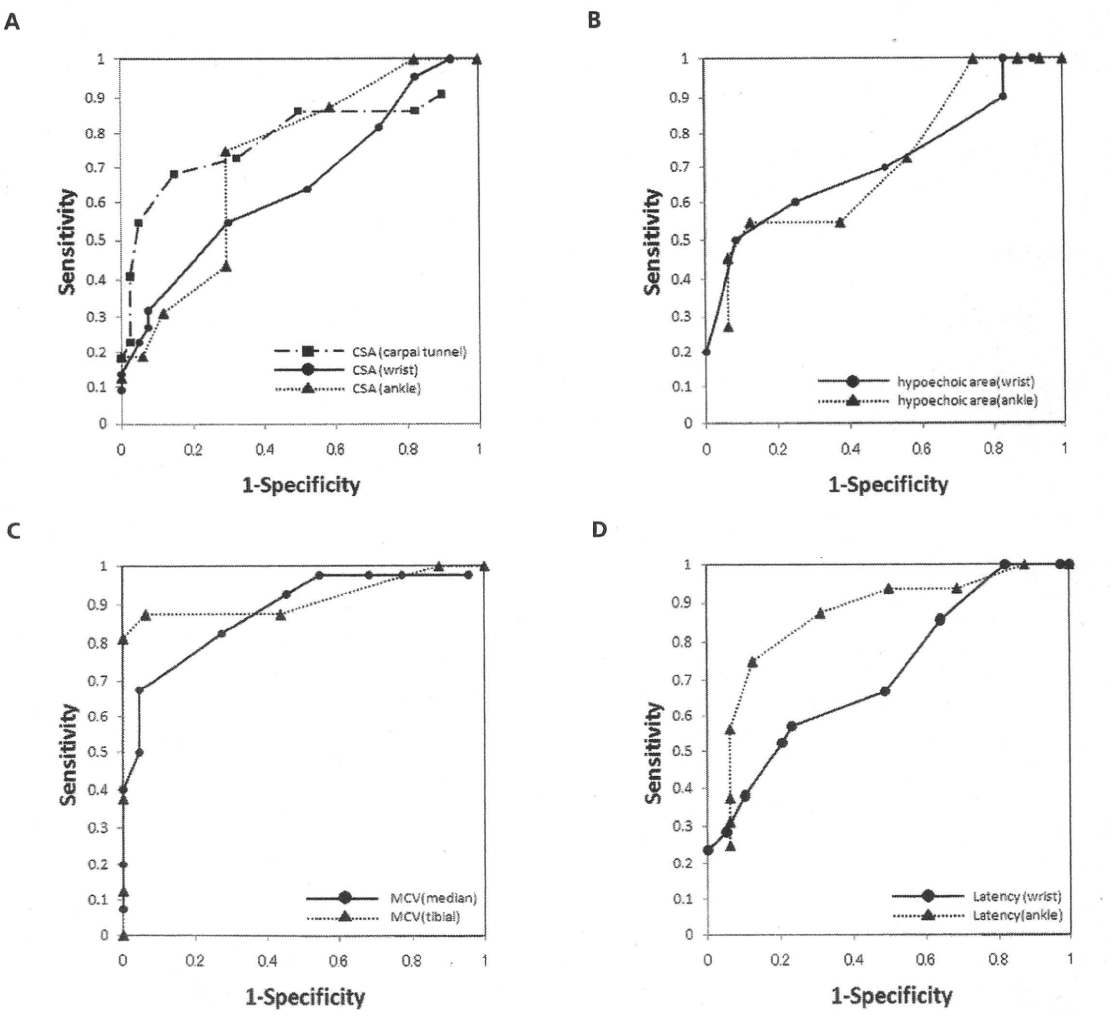
Figure 6. Cross-sectional area stratification in the tibial nerve by combining tertiles of latency and MCV. The CSA was 16.3 mm² in participants in the highest tertile of both latency and MCV. The latency was divided into 3 groups: latency of less than 4.5 milliseconds, latency of 4.5 to 5.0 milliseconds, and latency of greater than 5.0 milliseconds. The MCV was also divided into 3 groups: MCV of less than 40 m/s, MCV of 40 to 50 m/s, and MCV of greater than 50 m/s.



Conventional motor and sensory NCS has been widely used to diagnose DPN.[18–24] Symptoms of DPN appear bilaterally from the toes or the soles of the feet. Thus, NCS in the lower limbs should be more suitable to assess DPN severity. However, NCS in the lower limbs is time-consuming, and the action potential in the lower limbs sometimes cannot be evoked in cases of patients with advanced DPN. Some previous studies have reported that nerve conduction velocity slowing in the upper limbs is similar to that in the lower limbs of diabetic patients.[25,26] Skin temperature and humidity, however, easily affect the sensory nerve conduction velocity at the time of measurement. Mizumoto et al[27] reported that they chose instead to look at distal motor latency and the MCV because the sensory nerve conduction velocity was not measurable in many patients and appeared to be an unsuitable parameter. For the reasons above, we performed only the motor nerve conduction study.

Sonographic criteria for the diagnosis of neuropathy have been proposed by several studies. Cartwright et al[28] evaluated the CSA reference value studied for nerve sonography. In their study, the mean area of the tibial nerve at the

Figure 7. Receiver operating characteristic curves fitted for difference modality. **A**, When the ROC curve was fitted using sonographic CSA results, the CSA of the carpal tunnel was most effective. **B**, When the ROC curve was fitted using the sonographic hypoechoic area, the area of the tibial nerve was most effective. **C**, When the ROC curve was fitted using NCS MCV results, the MCV of the tibial nerve was most effective. **D**, When the ROC curve was fitted using NCS latency results, the latency of the tibial nerve was most effective.



ankle was 13.7 mm^2, which was greater than the value of 8.9 mm^2 that we obtained. They also reported that age and height showed weak correlations with the nerve CSA, whereas weight and BMI showed stronger correlations with the nerve CSA. Their study participants' mean BMI and weight were 26.5 and 74.5 kg, respectively, which were markedly greater than those of our participants, explaining the discrepancy with our findings. Mean normal median nerve CSA values cited in the literature vary between 6.1 and 10.4 mm^2; the difference between these normal values constitutes 51% of the normal median nerve CSA (8.4 mm^2), which is similar to our result of 8.3 mm^2.[29] The aim of our study was to evaluate whether the sonographic findings in the median and tibial nerves corresponded to the results of motor NCS in diabetic patients. We found that the CSA of both median and tibial nerves in diabetic patients were significantly larger than those in controls. Carpal tunnel syndrome and tarsal tunnel syndrome (TTS) are the most common entrapment neuropathies. A cross-sectional study of diabetic neuropathy reported by Dyck et al[16] found that polyneuropathy was the most common form of diabetic neuropathy, followed by CTS. It is well known that diabetic neuropathies are frequently asymptomatic. Kim et al[15] reported that 6.8% of diabetic patients had asymptomatic electrophysiologic CTS. The most common etiologies of TTS are mass lesions in the tunnel such as lipomas, ganglions, osteochondromas, varicosities, and synovitis because of rheumatoid arthritis or chronic uremia; however, to our knowledge, TTS is a rare complication of diabetes mellitus. Using sonography in the median nerve, Sernik et al[12] showed decreased echogenicity of the median nerve in symptomatic CTS wrists. Although sonography provides excellent detail of peripheral nerve parenchymal changes, there is currently a lack of quantitative examinations of peripheral nerve echogenicity. We therefore attempted to create a standardized quantitative analysis of sonographic images to allow a more objective assessment of nerve echogenicity in diabetic patients. This study was not designed to compare sonographic findings with histological changes; rather, the intent of this initial study was to develop a method of computer quantitation of echogenicity changes and to assess for a correlation with NCS. In our data, it appears that the percentage of the hypoechoic area of the peripheral nerve was significantly greater in lower-MCV patients with diabetes mellitus compared with controls and higher-MCV patients with diabetes mellitus. It is likely that these findings reflect pathologic changes, although the pathogenesis of nerve enlargement and an increasing percentage of the hypoechoic area in peripheral nerves are uncertain because affected median or tibial nerves have rarely been biopsied in patients with diabetes mellitus.

Table 5. Comparison of Sensitivity and Specificity Between Sonography and NCS

Parameter	Sensitivity, %	Specificity, %
Sonography		
CSA (median nerve, carpal tunnel)	68.2	85.0
CSA (median nerve, wrist)	54.5	70.0
CSA (tibial nerve, ankle)	75.0	70.6
Hypoechoic area (median nerve, wrist)	50.0	91.7
Hypoechoic area (tibial nerve, ankle)	54.5	87.5
NCS		
MCV (median nerve)	67.5	95.5
MCV (tibial nerve)	87.5	93.8
Latency (median nerve)	57.1	76.9
Latency (tibial nerve)	87.5	68.8

Diabetic neuropathy is characterized by axonal loss combined with demyelination, which is reflected in typical neuropathophysiologic findings, including reduced CMAP amplitudes combined with slowed nerve conduction. With regard to the relationship between sonography and NCS in this study, we found an increased CSA of the peripheral nerve in diabetic patients, especially those with a low MCV, compared with healthy controls. Moreover, the percentage of the hypoechoic area in the median nerve increased significantly compared with the controls and diabetic patients with a high MCV. According to ROC curve analysis, to investigate whether using sonography and NCS could judge the diagnostic accuracy for DPN, we compared the sensitivity and specificity of different modalities. Both the sensitivity and specificity were higher for NCS than sonography. These results are consistent with current widely accepted status of NCS as being more sensitive than sonography in the evaluation of polyneuropathy and CTS. However, although sonographic measurement had insuffi-

cient sensitivity, its specificity was similar to that of NCS. In addition, sonography was able to directly show morphologic change in the peripheral nerve. Compared with NCS, sonography caused less discomfort to patients and took less time. For these reasons, we have insisted on the possibility of using sonography to diagnose DPN.

Severinsen and Andersen[30] reported that the nerve conduction velocity may be reduced not only because of loss of the fastest conducting axons but also because of demyelination and acute metabolic dysregulation, which may cause lower nerve conduction velocity. Suzuki et al[31] reported that sorbitol itself and secondary sodium accumulation caused by an increase in sorbitol may be major contributors to the increase in intracellular hydration using a ^{1}H-nuclear magnetic resonance study. It has further been hypothesized that the peripheral nerve is swollen in individuals with diabetes mellitus because of increased water content related to increased aldose reductase conversion of glucose to sorbitol.[32] We hypothesize that an increased hypoechoic area of the peripheral nerve in diabetic patients may occur because of increased water content, which is also a cause of an enlarged peripheral nerve. Furthermore, our data showed that CSAs were negatively correlated with both a reduced MCV and delayed latency. Our findings may reveal that asymptomatic CTS or TTS exists in diabetic patients, and both entrapment and other factors such as metabolic or vascular causes affect DPN.

Finally, our study was an sonographic examination only; therefore, it remains unknown exactly what causes increased the hypoechoic area or CSA. In addition, there were some limitations of our study that warrant discussion because advanced sonographic techniques such as color and power Doppler imaging were not used. However, sonography is a noninvasive method that can be used to evaluate detailed nerve structures. Further studies are needed to confirm these findings in larger groups of diabetic patients and in other types of neuropathy.

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Synergistic effect of α-glucosidase inhibitors and dipeptidyl peptidase 4 inhibitor treatment

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ABSTRACT

Monotherapy of α-glucosidase inhibitor (α-GI) or dipeptidyl peptidase 4 (DPP4) inhibitor does not sufficiently minimize glucose fluctuations in the diabetic state. In the present study, we evaluated the combined effects of various of α-GI inhibitors (acarbose, voglibose or miglitol) and sitagliptin, a DPP4 inhibitor, on blood glucose fluctuation, insulin and active glucagon-like peptide-1 (GLP-1) levels after nutriment loading in mice. Miglitol and sitagliptin elicited a 47% reduction ($P < 0.05$) of the area under the curve of blood glucose levels for up to 2 h after maltose-loading, a 60% reduction ($P < 0.05$) in the range of blood glucose fluctuation, and a 32% decrease in plasma insulin compared with the control group. All three of the combinations elicited a 2.5–4.9-fold synergistic increase in active GLP-1 ($P < 0.05$ *vs* control). Thus, combined treatment with the α-GI miglitol, which more strongly inhibits the early phase of postprandial hyperglycemia, and DPP4 inhibitor yields both complementary and synergistic effects, and might represent a superior anti-hyperglycemic therapy. (J Diabetes Invest, doi: 10.1111/j.2040-1124.2010.00081.x, 2010)

KEY WORDS: Postprandial hyperglycemia, Insulin, Glucagon-like peptide-1

INTRODUCTION

Although active intervention for postprandial hyperglycemia by acarbose, an α-glucosidase inhibitor (α-GI), prevents development of cardiovascular events[1], it is also important to flatten the postprandial glucose fluctuation to prevent macroangiopathy. α-GI not only inhibits the rapid elevation of postprandial blood glucose level without excessive insulin secretion, but also enhances active glucagon-like peptide-1 (GLP-1) secretion[2]. In contrast, the dipeptidyl peptidase 4 (DPP4) inhibitor, sitagliptin, increases insulin secretion and reduces late-phase elevation of postprandial blood glucose level. We hypothesized that a combination of α-GI and sitagliptin might yield a greater minimizing effect on blood glucose fluctuation while conserving insulin secretion and enhancing active GLP-1 secretion to prevent atherosclerosis[3–5]. Recently, the combined effects of voglibose, an α-GI, and a DPP4 inhibitor on plasma insulin and active GLP-1 levels were reported in mice[6,7]. However, comparison of the combined effect of various α-GIs and sitagliptin on blood glucose fluctuation has not been reported.

In the present study, we showed that combination therapy of α-GIs and sitagliptin can yield complementary and synergistic beneficial effects in mice.

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MATERIALS AND METHODS

Because α-GIs are inhibitors of α-glucosidase, which converts disaccharide to glucose, 7–9-week-old male C57BL/6J mice (Charles River Japan, Tokyo, Japan) were subjected to an overnight fast and orally loaded with 2.5 g/kg of maltose. Blood was collected from the end of the tail just before loading until 2 h after loading, and blood glucose level was measured using the glucose dehydrogenase method. The area under the curve of blood glucose levels for up to 2 h after maltose-loading ($\Delta AUC_{0-2\ h}$) was calculated using the trapezoid method. The range of blood glucose fluctuation was determined as the difference between the maximal and minimal blood glucose levels for up to 2 h.

To evaluate initial insulin-secreting capacity, plasma insulin concentration in blood collected from the end of the tail at 0.25 h after loading was measured using an ELISA kit (Morinaga Institute of Biological Science, Yokohama, Japan).

Ten-week-old male C57BL/6J mice freely fed a high-fat diet (D12492 Rodent Diet; Research Diets, New Brunswick, NJ, USA) for 6 weeks were orally loaded with 10 mL/kg of enteral nutrition (Ensure H; Abbot Japan, Tokyo, Japan) to stimulate GLP-1 secretion. To analyze the delayed effect of GLP-1 secretion by α-GI, blood was collected after 0.5 h from the abdominal vein using a syringe containing diprotin A and EDTA at a final concentration of 3 mmol/L and 0.15%, respectively. The concentration of plasma active GLP-1 was measured using an ELISA kit (Millipore Corporation, Billerica, MA, USA).

α-Glucosidase inhibitors (acarbose 10 mg/kg, voglibose 0.1 mg/kg or miglitol 3 mg/kg) was given orally at the time of maltose or enteral nutrition-loading, and sitagliptin (0.3 mg/kg)

was given 0.5 h before oral loading. Test doses of α-GIs were determined from the ED_{50} doses of the inhibition effect on sucrose or maltose-loading in normal rats, respectively.

The experiment was carried out according to the guidelines of Gifu University. Results are expressed as mean ± SD. Significance of difference among groups was analyzed using Dunnett's or Tukey's multiple comparison test based on ANOVA. *P*-values of <0.05 were considered to show statistical significance.

RESULTS

In the maltose-loading test, treatment with each of the three α-GIs alone significantly suppressed the blood glucose peak level at 0.5 h. Administration of miglitol alone significantly suppressed the blood glucose elevation as early as 0.25 and 0.5 h, and delayed the blood glucose peak until 1 h after loading. With administration of sitagliptin alone, the blood glucose level peaked at 0.25 h and was significantly lower at 0.5 and 1 h. Consequently, a complementary suppression of blood glucose elevation was observed at 0.25, 0.5 and 1 h in the combined miglitol and sitagliptin group (Figure 1c). As a result, the $\Delta AUC_{0-2\,h}$ of the blood glucose concentration of the group receiving miglitol alone was almost equal to that with acarbose or voglibose alone. The rate of decrease of the $\Delta AUC_{0-2\,h}$ of the blood glucose concentration in the miglitol and sitagliptin combination group was 47% ($P < 0.05$) compared with the control group, which was larger than that observed in the combined groups with acarbose or voglibose at the tested doses (Table 1). Similarly, combined treatment of miglitol and sitagliptin showed a 60% reduction ($P < 0.05$) of the range of blood glucose fluctuation compared with the control group, and also a significant decrease compared with miglitol or sitagliptin alone (Table 1).

Enhancement of plasma insulin occurred with sitagliptin at 0.25 h after loading (1.6–2.0-fold). In contrast, miglitol alone or combined treatment with miglitol and sitagliptin decreased the plasma insulin concentration by 39 or 32% compared with the control group, respectively (Table 1).

When enteral nutrition was orally loaded in mice fed a high-fat diet, the plasma active GLP-1 concentration was increased by 1.5–1.9-fold after administration of sitagliptin compared with the control group. In contrast, a synergistic increase in the GLP-1 concentration was observed after treatment with a combination of α-GI and sitagliptin (2.5–4.9-fold, $P < 0.05$ *vs* control; Table 1).

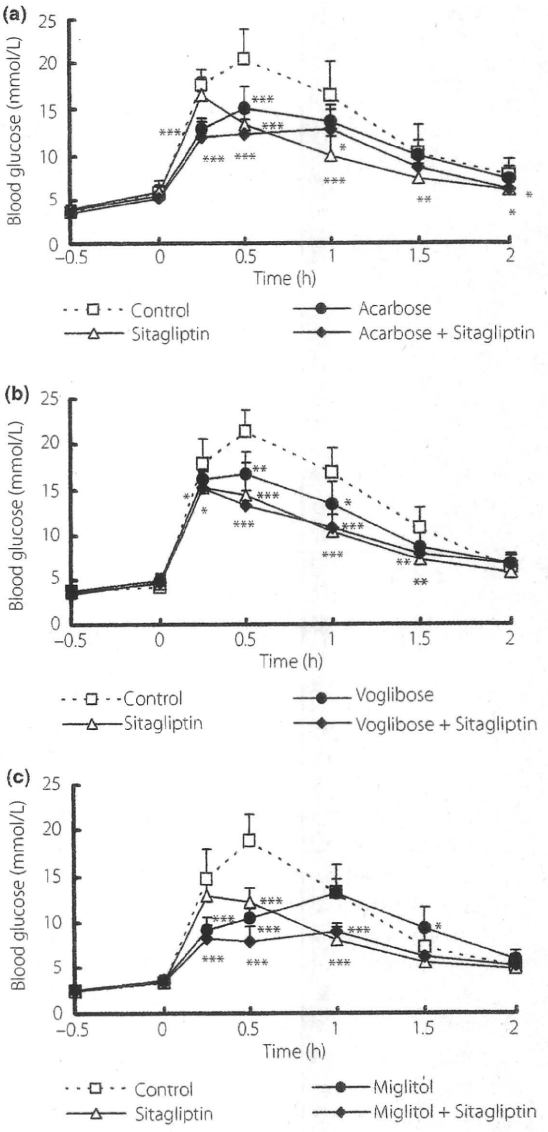

Figure 1 | Blood glucose profiles after oral administration of α-glucosidase inhibitor (α-GI) and sitagliptin (0.3 mg/kg) in maltose-loaded normal mice. (a) Acarbose, 10 mg/kg; (b) voglibose, 0.1 mg/kg; (c) miglitol, 3 mg/kg. Each value represents mean ± SD of 8–10 mice. $^*P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$ *vs* the control group using to Dunnett's multiple comparison test.

DISCUSSION

Recently, suppression of postprandial hyperglycemia has come to be considered important for prevention of atherosclerosis[3]. Repeated episodes of blood glucose fluctuation accelerate the adhesion of monocytes to vascular endothelial cells and enhance the development/progression of atherosclerosis[8]. In the present study, the combined administration of α-GI and sitagliptin complementarily lowered the blood glucose level. Furthermore, the combination of miglitol with sitagliptin significantly minimized blood glucose fluctuations. Thus, such combined treatment should reduce the risk of atherosclerosis.

The suppression of postprandial hyperglycemia by α-GI alone and combination treatment with sitagliptin enables insulin secretion to be conserved, and therefore can be expected to mitigate dysfunction of pancreatic β-cells[9]. In contrast, sitagliptin decreases the blood glucose level by enhancing insulin secretion. Thus, long-term administration of this agent might create a

Table 1 | Incremental blood glucose, range of glucose fluctuation and plasma insulin in maltose-loaded mice and plasma active glucagon-like peptide-1 in enteral nutrition-loaded mice

Test compound	Blood glucose concentration $\Delta AUC_{0-2\ h}$		Range of glucose fluctuation	Plasma insulin at 15 min after maltose loading	Plasma active GLP-1 at 30 min after EN loading
	(h*mmol/L)	Inhibition rate (%)	mmol/L	pmol/L	pmol/L
Control	20.9 ± 4.6^{a}	–	15.3 ± 2.6^{a}	111.9 ± 44.8^{ab}	2.18 ± 0.90^{a}
Acarbose, 10 mg/kg	15.6 ± 2.6^{b}	25.4	10.0 ± 2.5^{b}	89.5 ± 25.8^{a}	2.37 ± 0.76^{a}
Sitagliptin, 0.3 mg/kg	12.3 ± 3.3^{b}	41.1	10.9 ± 1.7^{b}	173.9 ± 53.4^{b}	3.33 ± 1.44^{a}
Combination	13.8 ± 2.3^{b}	34.0	8.5 ± 2.3^{b}	118.8 ± 68.9^{ab}	10.76 ± 6.34^{b}
Control	20.9 ± 3.2^{a}	–	17.2 ± 2.4^{a}	113.7 ± 48.2^{a}	2.23 ± 1.86^{a}
Voglibose, 0.1 mg/kg	16.1 ± 3.2^{b}	23.0	12.3 ± 1.7^{b}	111.9 ± 17.2^{a}	2.78 ± 1.23^{a}
Sitagliptin, 0.3 mg/kg	12.7 ± 2.9^{b}	39.2	11.6 ± 2.4^{b}	229.0 ± 93.0^{b}	3.54 ± 2.33^{ac}
Combination	13.6 ± 1.3^{b}	34.9	10.7 ± 1.8^{b}	142.9 ± 43.1^{a}	5.52 ± 2.34^{bc}
Control	17.9 ± 3.6^{a}	–	15.5 ± 2.6^{a}	158.9 ± 44.8^{a}	2.37 ± 1.33^{a}
Miglitol, 3 mg/kg	14.4 ± 1.7^{b}	19.6	9.7 ± 1.3^{b}	96.4 ± 18.9^{a}	3.29 ± 1.13^{a}
Sitagliptin, 0.3 mg/kg	11.5 ± 1.6^{bc}	35.8	10.0 ± 1.8^{b}	252.5 ± 86.1^{b}	4.62 ± 3.06^{a}
Combination	9.4 ± 1.3^{c}	47.5	6.2 ± 1.3^{c}	107.3 ± 20.7^{a}	11.22 ± 9.72^{b}

Maltose-loading tests used for normal mice. Enteral nutirition (EN)-loading tests used for mice fed high-fat diet for 6 weeks. Each value represents the mean ± SD of 8–10 mice. Means with different letters (a, b, and c) are significantly different at $P < 0.05$ by Tukey's multiple comparison test. $AUC_{0-2\ h}$, the area under the curve of blood glucose levels for up to 2 h after maltose-loading; GLP-1, glucagon-like peptide-1.

burden on pancreatic β-cells. In addition, a correlation between hyperinsulinemia and the level of high-sensitivity C-reactive protein (CRP), a marker of inflammation, has been reported[10]. Because the CRP elevation is related to coronary heart disease, stroke and mortality[5], insulin secretion should be reduced as much as possible. In the present study, when α-GI and sitagliptin were used in combination, insulin secretion was suppressed to a level almost the same as that with α-GI alone. Furthermore, after chronic combined treatment of miglitol and sitagliptin for 8 weeks in high-fat diet fed mice, the elevation of fasting plasma insulin level was significantly suppressed compared with that of control mice (normal diet group: 137.8 ± 84.4 pmol/L; high-fat control group: 253.1 ± 72.3 pmol/L, $P < 0.05$ *vs* normal diet group; miglitol alone group: 189.4 ± 110.2 pmol/L; sitagliptin alone group: 359.9 ± 187.7 pmol/L; combination group: 161.9 ± 84.4 pmol/L, $P < 0.05$ *vs* high fat control; Y.H. and J.T., unpublished data). Thus, combined treatment might reduce risk of the development/progression of atherosclerosis as well as dysfunction of pancreatic β-cells.

In patients with type 2 diabetes, miglitol has been reported to increase plasma active GLP-1 levels[2,11]. GLP-1 has several physiological activities, including a trophic effect on the pancreatic islets and suppression of gastric emptying and appetite[12], in addition to enhancement of insulin secretion and inhibition of glucagon secretion. When combined with sitagliptin, each α-GI tested increased the active GLP-1 concentration synergistically. The GLP-1 secretion induced by α-GI might result from delayed absorption of carbohydrate into the lower parts of the digestive tract[13], although the details of this mechanism remain unclear.

In conclusion, combined treatment with α-GI miglitol, which more strongly inhibits the early phase of postprandial hyperglycemia, and sitagliptin can yield complementary and synergistic effects and therefore might represent a better antihyperglycemic therapy.

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M-3-2 大学生の健康に対する取り組みと生活環境に関する検討

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健康、生活習慣、学校保健

【はじめに】

大学生世代は健康を大きく崩すことの少なく、学業やスポーツなどへの活動性が高い時期であるが、どの程度健康を意識して、生活に反映させているかに関する調査報告は少ない。このため、今回我々は健康維持への取り組みと仕事や睡眠等の生活環境を調べるために質問調査を実施した。

【方法】

平成 21 年度定期健康診断を受診した岐阜大学生 6288 名を対象に健康に関する取り組みの有無やアルバイトや睡眠、疲労感等の生活状況についてアンケート調査を行った。本検討では、調査に同意し回答の得られた 4657 名（男性 2827 名、女性 1830 名、回収率 74.1%）の結果を解析した。質問は、Q1「健康のために、時間やお金をかけていますか？」、Q2「Q1 で『はい』の人へ、何に取り組んでいますか？」、Q3「疲労をどの程度感じますか？」、Q4「毎日の睡眠時間はどれくらいですか？」、Q5「生活の中で仕事をしていますか？」の項目とした。

【結果】

Q１「健康のために時間やお金をかけていますか？」の問いに「はい」と回答した学生は799名（17.2%）であり、女性で有意に多かった。Q2で設問の健康への取り組みの内訳は調査項目では多いものより、「サプリメント（402名）」「健康食品（154名）」「マッサージ(79名)」の順であった。その他の取り組みについての質問では、筋トレや部活、水泳など運動の取り組みが合計で170名程と最も多かった。Q3の疲労に関する質問では「ひどく疲れている」が109名、「疲れている」が788名、「時々疲れを感じる」が2854名、「疲れていない」が872名であった。Q4の睡眠時間に関する質問では「5－7時間」が3459名と最も多かった。

Q5の生活の中での仕事の有無に関する質問では、仕事をしている学生が2830名（60.8%）であった。仕事の有無により睡眠時間に有意な影響が認められた。また、睡眠時間について、「5時間以下」を１、「5-7時間」を２、「7-9時間」を３、「9-11時間」を４、「11時間以上」を５とし、疲労感について、「疲れていない」を１、「時々疲れる」を２、「疲れている」を３、「非常に疲れている」を４とし、spearmanの順位相関を検討すると、同順位補正後の相関係数－0.158、$p<0.0001$の結果であった。

【考察】

調査学生の約 1／6 が健康のために時間やお金をかけているが、多くはサプリメントや健康食品等の摂取等比較的時間やお金がかからず手軽に取り組めるものであった。また、本検討では、学生の生活環境、睡眠時間について調査したが、仕事のある人の場合で睡眠時間が短い傾向が認められた。学生の健康支援のために、食品や栄養に関する正しい情報提供や無理の無い運動やストレッチ方法の紹介、日常スケジュール管理に関する指導等の活動の推進が今後ますます求められていると考えられた。

【結語】

良い生活習慣や健康法を学生が身につけることは将来的な健康増進、疾病予防のため効果が期待されるため、健康教育の中で質の良い情報を提供し、指導を行っていく取り組みが大切であると思われた。

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優秀演題選定結果

優秀演題選定委員長(藤女子大学)**藤井　義博**

一般演題143題の中から、選定委員の先生方により優秀演題の選定をいただき、下記の演題が選ばれました。閉会式において、選定委員長の藤井より賞状と記念品の贈呈が行われました。選ばれた演題は、CAMPUS HEALTH 47 (1) に論文として掲載されます。

氏　名	大　学　名	演　題　名	演題番号
八田文裕子	立命館大学 保健センター	学生定期健康診断に胸部X線検査は必要か?	(B-2-2)
早渕　純子	徳島大学 保健管理センター	徳島大学における特定保健指導の導入	(C-3-2)
田山　　淳	長崎大学保健・ 医療推進センター	女子大学生を対象とした運動習慣形成プログラムの実践と課題	(F-2-1)
田中　生雅	岐阜大学 保健管理センター	大学生の健康に対する取り組みと生活環境に関する検討	(M-3-2)
中川　　克	立命館大学 保健センター	新型インフルエンザ(A/H1N1)の経験	(J-2-1)
楠田　康子	神戸大学 保健管理センター	麻疹排除への取り組み～「麻疹(風疹)登録制度」と、入学時に予防接種証明書、抗体検査結果証明書を求めることの意義～	(L-2-2)
長沼　洋一	獨協大学 保健センター	保健センターの健康管理サービスに対する学生の認知と利用及びニーズに関する調査(10) 大学生のGHQ30得点の推移とストレス緩衝要因の関連	(O-2-1)
國中　咲枝	日本福祉大学学生 相談保健センター	心理社会的介入プログラムの展開(2) －ケースマネジメントの充実とICF導入の試み－	(Q-2-2)

H-1-3 岐阜県内の大学・短大等学生の喫煙実態調査—岐阜県大学保健管理研究会の調査結果より—

岐阜大学保健管理センター

○山本眞由美、田中生雅、佐渡忠洋、臼井るり子、高井郁恵、端元加奈子、長瀬江利、加納晃子、浅田修市、清水克時

敷地内禁煙、喫煙率、禁煙指導

【はじめに】

大学生の生涯にわたる健康度向上のためには、禁煙・防煙教育により、将来のタバコ関連疾患の予防をはかることが重要である。本学でも、禁煙啓発活動、禁煙宣言、敷地内禁煙の実施などの各種とりくみを行なってきた。これらの努力が、学生の喫煙率低下に寄与しただろうと推察しているものの、大学生の喫煙実態を調査した報告は少ない。特に、大学生に対する禁煙啓発活動と喫煙率の関係の検討はほとんどなく、科学的根拠の確立に至っていない。今回、岐阜県保健管理研究会の協力で、岐阜県下の大学・短大・高専等の学生を対象に喫煙実態調査を実施した。その中から、大学全体の取り組みとして敷地内禁煙措置がなされているか否かと、学生の喫煙率の結果をまとめたので報告する。

【方法】

大学便覧、短大便覧等から、岐阜県下の大学・高専・短大・専門学校を抽出し、学生の保健管理担当者あてに協力を要請した。同意の得られた 25 校で、全学生を対象に自己記入式質問用紙（図１）の配布と回収を依頼した。回収された 22180 名（男性 14340 名、女性 7708 名、性別不明 132 名）の回答結果について検討した。喫煙率の比較はカイ２乗を用いた。

【結果】

協力参加 25 校のうち、学内の取り決めとして、敷地内禁煙としているのは 3 校（以下、禁煙校）、他の 22 校は校内分煙（以下、分煙校）であった。

全体の喫煙率は 14.7%（男性 19.7%、女性 5.4%）、禁煙校では 12.3%（男性 18.0%、女性 3.9%）、分煙校では 16.3%（男性 20.6%、女性 6.8%）であった。禁煙校と分煙校を比較した表を表１にまとめた。性別、学部、学年、年齢別の喫煙率を禁煙校と分煙校で比較すると、学部別では工学系、学年では 1・2 年生、年齢別では 19 歳以下で有意差をもって、禁煙校の方が喫煙率が低かった。

学年別の喫煙率は、禁煙校、分煙校ともに増加しており、大学入学後に喫煙を開始する危険度の高さが推察できた。

禁煙校でも１年生 6.4%から２年生 10.9%に増加していたが、分煙校ではさらに、11.5%から 17.4%に増加していた。

１年生、２年生ともに、それぞれの学年の喫煙率は、禁煙校の方が有意に分煙校より低かったが、１年生から２年生の１年間での喫煙率増加は、禁煙校、分煙校ともに著しく、禁煙校の増加分 4.5（6.4→10.9）%、分煙校の 5.9（11.5→17.4）%の間に有意差はなかった。入学後が喫煙開始の一番誘惑の多い時期と考えられ、敷地内禁煙措置のみでは不十分であることも示唆された。

【考察】

工学系の学部、１年生、２年生、19 歳以下では、禁煙校のほうが学生の喫煙率が低いことより、敷地内禁煙措置は学生の禁煙・防煙教育に有用であることが示唆された。敷地内禁煙措置という「環境改善」により、「喫煙しない」という「生活習慣」を身につけさせてしまう。これは、喫煙開始年齢層の大学生をターゲットにした「ポプレーションアプローチ」の実践であり、喫煙を開始してから禁煙指導をするよりも、敷地内禁煙措置をとるほうが、人的・時間的・予算的にはるかに効率的であると推察された。

今回の調査に参加した分煙校の１年生は、4361 名で現在の喫煙者は 501 名(11.5%)であるが、このままの大学環境であれば、4 年生には、今回の調査の 4 年生喫煙率 20.1%レベルまで増加することも十分予想される。すると、4361 名×0.201=877 名と 376 名もの学生が大学在学中に喫煙を開始することになってしまう。仮に、喫煙開始後に、保健師が 1 時間程度 4 回の禁煙指導を実施するとすれば、1(回)×4(時間)×376 名=1504 時間もの業務が発生することとなり、6 時間/日の時間を費やしても 250 日という業務量である。これを実施することは不可能に近い。あまり科学的ではないが、仮に、4 年生の喫煙率が分煙校の 17.9%のレベルでおさえられたなら、4361 名×0.179=781 名と、96 名を喫煙開始から回避できる可能性も期待できる。個別の保健指導は、重要な業務であるが、「敷地内を禁煙にする」という環境改善戦略を大学が打ち出すだけで保健指導業務の削減につながり、効率的になると言えよう。ところで、

禁煙校の１年生で有意に喫煙率が少ないことは、「敷地内禁煙」であることが大学選択理由のひとつになっている可能性もある。禁煙対策は学生募集に関わる問題といっても過言ではないだろう。中学高校での喫煙開始を阻止するためにも大学が敷地内禁煙を実施することは有用と考えられる。今回の調査で喫煙率が増加するのは、1年から2年と2年から3年の間であった。入学後ならびに成人直後が喫煙開始の一番誘惑の多い時期と考えられる。喫煙開始をより阻止するには、敷地内禁煙措置のみでは不十分で、健康診断管理・保健指導業務においては優先度の高い内容として注意する必要があると示唆された。禁煙校でも喫煙開始者はおり、特に低学年での開始者が多いことから、在学中の禁煙指導の充実も敷地内禁煙措置と同時に重要であると考えられた。Willcox らは、大学内の環境改善や、大学内厚生施設の有効利用によって、喫煙者を増やさないようにする事が、比較的容易である事を報告しており[1)]、今回の我々の調査結果をサポートするものである。

【結語】

敷地内禁煙措置は学生の禁煙・防煙教育に有用であることが示唆された。敷地内禁煙措置は、「ポプレーションアプローチ」の実践であり、喫煙を開始してから禁煙指導をするよりも、敷地内禁煙措置をとるほうが、効率的と推察できる。ただ、敷地内禁煙措置だけでは、喫煙開始者を完全に阻止することはできず、健康診断管理・保健指導業務ならびに在学中の禁煙指導の充実が不可欠である。

【引用文献】

1) Willcox ML. Tabacco control programmes for universities: a feasibility study, J Public Health Med 1997; 19: 37-44.

【調査協力】

加藤澄代(朝日大学)、三尾美紀(岐阜経済大学)、恩田晶代(岐阜高専)、松本ヨシ子、高橋ひろみ、平下千穂(岐阜聖徳学園大学)、篠田あさ江(岐阜市立女子短大)、塩内美春、森倭子、山田信子(中部学院大学)、上村明美(東海学院大学)、山田登(中日本航空専門学校)、矢島すみ江（名古屋工業大学）、織笠スズエ(名城大学)(大学 50 音順)

また、データ解析について、川邉敬子氏、川島恵子氏（岐阜大学保健管理センター）の協力を得た。

"A Survey of the Percentage of Smoking Students in Gifu Prefecture- Effect of Total Smoking Ban on the Smoking Attitude"
Health Administration Center, Gifu University; Yamamoto M. et al.
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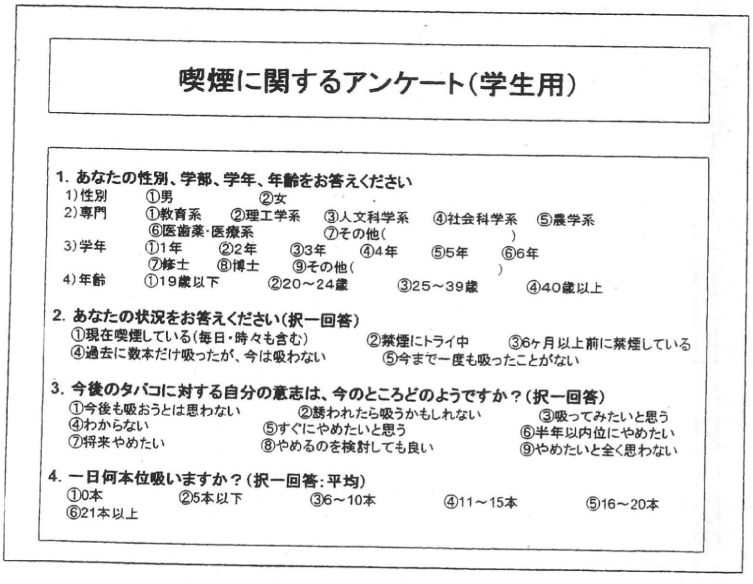
図１



喫煙に関するアンケート(学生用)

1. あなたの性別、学部、学年、年齢をお答えください
1)性別 ①男 ②女
2)専門 ①教育系 ②理工学系 ③人文科学系 ④社会科学系 ⑤農学系 ⑥医歯薬・医療系 ⑦その他(　　)
3)学年 ①1年 ②2年 ③3年 ④4年 ⑤5年 ⑥6年 ⑦修士 ⑧博士 ⑨その他(　　)
4)年齢 ①19歳以下 ②20～24歳 ③25～39歳 ④40歳以上

2. あなたの状況をお答えください(択一回答)
①現在喫煙している(毎日・時々も含む) ②禁煙にトライ中 ③6ヶ月以上前に禁煙している
④過去に数本だけ吸ったが、今は吸わない ⑤今までに一度も吸ったことがない

3. 今後のタバコに対する自分の意志は、今のところどのようですか？(択一回答)
①今後も吸おうとは思わない ②誘われたら吸うかもしれない ③吸ってみたいと思う
④わからない ⑤すぐにやめたいと思う ⑥半年以内位にやめたい
⑦将来やめたい ⑧やめるのを検討しても良い ⑨やめたいと全く思わない

4. 一日何本位吸いますか？(択一回答:平均)
①0本 ②5本以下 ③6～10本 ④11～15本 ⑤16～20本 ⑥21本以上