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Impact of physical activity and sedentary time on glycated hemoglobin levels and body composition: Cross-sectional study using outpatient clinical data of Japanese patients with type 2 diabetes

Shuhei Nakanishi[1,*], Hidenori Hirukawa[1], Masashi Shimoda[1], Fuminori Tatsumi[1], Kenji Kohara[1], Atsushi Obata[1], Seizo Okauchi[1], Yukino Katakura[1], Junpei Sanada[1], Yoshiro Fushimi[1], Momoyo Nishioka[1], Yuki Kan[1], Akiko Tomita-Mizoguchi[1], Hayato Isobe[1], Hideyuki Iwamoto[1], Kaio Takahashi[1], Tomoatsu Mune[1], Kohei Kaku[2], Hideaki Kaneto[1]

[1]Division of Diabetes, Metabolism and Endocrinology, Kawasaki Medical School, Okayama, Japan, and [2]Department of Internal Medicine, Kawasaki Hospital, Kawasaki Medical School, Okayama, Japan

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***Correspondence**
Shuhei Nakanishi
Tel.: +81-86-462-1111
Fax: +81-86-464-1046
E-mail address:
n-shuhei@umin.net

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ABSTRACT

Aims/Introduction: This study examined the association among sedentary time (ST), physical activity (PA), glycated hemoglobin and body composition in Japanese type 2 diabetes patients.

Materials and Methods: Patients with type 2 diabetes who visited the outpatient clinic at Kawasaki Medical School Hospital, Okayama, Japan, comprised the study's participants. Self-administered International Physical Activity Questionnaire short forms were obtained and analyzed for 1,053 patients, including 158 patients for whom waist circumference and visceral fat accumulation were measured. From the questionnaire, three categorical data (low, moderate, high) and continuous data (METs/h/week) regarding PA and ST (min/day), respectively, were obtained.

Results: The patients categorized as having low PA had significantly higher body mass index than those categorized as having high levels, after adjustment was made for confounders. Continuous data of PA were negatively associated with waist circumference and visceral fat accumulation. ST was positively associated with body mass index. After dividing the participants into four groups according to medians of ST and PA, the following categories were established: long ST and low PA, long ST but high PA, short ST but low PA and short ST and high PA. In terms of body mass index, short ST and high PA measured significantly lower than long ST and low PA. For waist circumference and visceral fat accumulation, short ST but low PA and short ST and high PA measured significantly lower than long ST and low PA and long ST but high.

Conclusions: These results imply that the combination of avoiding sedentary behavior and increasing PA might be important in the prevention bodyweight gain and in the avoidance of central obesity, respectively, in Japanese type 2 diabetes patients.

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INTRODUCTION

The goal for patients with diabetes is to secure years of healthy life by controlling the disorder and thereby maintaining a quality of life equivalent to that of their healthy counterparts. To achieve this objective, it is important to manage blood glucose levels and prevent obesity. Accordingly, the adoption and maintenance of physical activity (PA) are critical for these patients.

Patients with type 2 diabetes are encouraged to decrease the amount of time spent in daily sedentary behavior[1], because extended sedentary time is associated with poorer glycemic control[2]. Most adults with diabetes are called on to engage in a total of at least 150 min of moderate-to-vigorous intensity PA every week, at a frequency of at least 3 days/week, with no more than two consecutive days without activity[1]. For younger and more physically fit individuals with type 2 diabetes, however, a shorter duration (minimum 75 min/week) of vigorous intensity PA or interval training might be sufficient[1].

Such recommendations speak to the importance of both the quantity and quality of exercise. Exercise quantity, such as moderate-to-high volumes of aerobic activity, is associated with substantially lower cardiovascular and overall mortality risk[3]. Exercise quality, such as high-intensity interval training, promotes glycemic control in adults with type 2 diabetes[4]. In addition, these two kinds of exercises can reduce visceral adipose tissue, which is thought to play a central role in metabolic syndrome through the release of large numbers of cytokines and bioactive mediators[5], although abdominal fat reduction accompanying weight loss can vary by obesity phenotype (i.e., intra-abdominal vs abdominal subcutaneous fat storage)[6].

Commonly, however, it is difficult to promote behavioral changes in patients in terms of increased frequency of PA and exercise in accordance with recommendations, because patients have different lifestyles and medical needs as outpatients. Self-reported success in the use of exercise among patients with type 2 diabetes was just 35%, according to a 2005 paper[7]. It is first and foremost challenging to accurately assess individual PA and sedentary time in the daily life of each patient. As a result, it is still nearly impossible to assess sedentary time and quality and quantity of PA for Japanese patients with type 2 diabetes, as well as to show the relationship between these factors and the management of glycemic control or bodyweight on a clinical basis. As such, clinicians have a difficult time promoting physical exercise to patients with type 2 diabetes without being able to provide clear evidence of the benefit of such activity. Indeed, the rate of utilization of exercise therapy, based on guidance provided chiefly by physicians, was only approximately 50% in diabetes patients, with 30% of such patients never receiving instruction regarding exercise and just 9.9% of patients ever receiving instruction about nutrition, according to a self-recorded questionnaire carried out in Japan[8].

In the present cross-sectional study, data of the self-administered International Physical Activity Questionnaire (IPAQ) short form from outpatient patients with type 2 diabetes were obtained and used to assess the impact of sedentary behavior and PA on glycated hemoglobin (HbA1c), body mass index (BMI), waist circumference (WC) and visceral fat accumulation (VFA). The study's aim was to clarify the underlying clinical question of how best to effectively advise individual patients about exercise and its benefits.

METHODS

Study population and patient preparation

Patients eligible for this study were those diagnosed with type 2 diabetes who regularly visited the diabetes outpatient clinic at Kawasaki Medical School Hospital, Okayama, Japan, over the course of >1 year. The amount of PA carried out by each patient was calculated using the Japanese version of the IPAQ short form[9,10]. Among the total of 2,145 patients, 314 patients aged <20 years or >80 years were excluded. Also excluded were 778 patients with active retinopathy, end-stage renal disease, steroid use, difficulties in carrying out PA due to orthopedic and other impairments, those deemed to be inappropriate for this questionnaire by the physician in charge, and those with incomplete answers to the questionnaire that prevented the calculation of PA. The final study sample thus consisted of 1,053 patients.

From the IPAQ responses, the following measures were used for assessment of PA in the study participants: (i) category of PA (high, moderate, low); (ii) total PA (METs/h/week); and (iii) sedentary time (min/day). BMI was calculated by dividing weight in kilograms by height in meters squared. Among the total participants, the WC of 158 patients was randomly measured at the umbilical level in the late expiration phase while the participants were standing, and VFA around the WC was estimated by bioelectrical impedance analysis (Panasonic EW-FA90, Shiga, Japan), as reported previously[11], with the personal IPAQ results being concealed from the recorders of these data. Briefly, voltage at the umbilicus position correlated significantly with VFA and was affected by subcutaneous fat only negligibly, which suggested that the VFA could be calculated based on voltage. The correlation of bioelectrical impedance analysis with the computed tomography measurement results was 0.88[11].

The effect of these three datasets regarding PA was investigated in the clinical setting on HbA1c levels, BMI, WC and VFA. The hospital's ethics committee approved the study protocol, and information pertaining to the study was provided to the public through the Internet, instead of informed consent being obtained from each individual patient (No. 3125).

Statistical analysis

Categorical variables are expressed as numerals and percentages. Continuous variables are expressed as the mean and standard deviation, or median and interquartile ranges. The χ^2-test was used for testing relationships between categorical variables. Residual analyses were used to identify the specific cells making the greatest contribution to the χ^2-test results. Continuous variables were compared using analysis of covariance (ANCOVA) for comparisons with categorical variables. After multivariate tests, to determine if there were significant differences, Tukey's tests were carried out for *post-hoc* analysis. Multiple regression analyses were carried out to compare continuous variables. HbA1c, BMI, WC and VFA were used as dependent variables, and PA and sedentary time were each used as an independent variable. In addition, all results were expressed after adjustment was made for seven confounders: age, sex, experience of dietary therapy led by a nutritionist, as well as use of sodium–glucose cotransporter 2 inhibitor, glucagon-like peptide 1 receptor agonist, thiazolidinedione or insulin, with these four medications included because they are known to affect not only patient bodyweight, but also HbA1c levels. As data of HbA1c, BMI, WC, VFA, PA and sedentary time were not normally distributed, they were analyzed after logarithmic transformation. In addition, to compare the impact of sedentary time and PA on HbA1c, BMI, WC, and VFA, the data were divided into four groups: long sedentary time and low PA (LL), long sedentary time but high PA (LH), short sedentary time but low PA (SL), and short sedentary time and high PA (SH). *P*-values of <0.05 were considered to show statistical significance. Statistical analyses were carried out using JMP software (version 13.2 for Windows; SAS Institute, Cary, NC, USA).

RESULTS

Clinical characteristics of study participants

The mean age, HbA1c and BMI for all participants were 62.7 ± 11.3 years, 7.0 ± 1.1% and 26.0 ± 4.9 kg/m^2, respectively. Table 1 shows the clinical characteristics of patients categorized by three categories of low, moderate and high. Male patient numbers were statistically high in the high-activity category ($P = 0.0125$), but no differences in treatment for diabetes among the three categories were observed. The clinical characteristics of the patients having WC and VFA data are also presented, along with numbers of patients.

Relationship between three categories (low, moderate, high) of PA and HbA1c, BMI, WC or VFA

After adjustment was carried out for the seven confounders described above, no difference in HbA1c levels was found among these three categories based on ANCOVA analysis. In contrast, BMI was found to be significantly higher among participants categorized as high PA than those categorized as low PA ($P = 0.003$). In addition, sedentary time was found to be significantly lower among participants categorized as high PA than in those categorized as middle and low PA ($P < 0.0001$ each). Among subgroups whose WC and VFA were measured, no difference was observed for WC and VFA among the three categories. Accordingly, the results suggest that patients with high PA also had significantly short sedentary times, and consequently benefitted in terms of quantity of bodyweight, as indicated by BMI. However, quality of bodyweight and HbA1c, as shown by WC and VFA, might not have been directly related to intensity of PA (Table 1).

Impact of PA (METs/h/week) on HbA1c, BMI, WC and VFA

After adjustment was carried out for the seven confounders described above, HbA1c and BMI were found not to be related to PA based on multiple regression analysis, whereas WC and VFA were significantly inversely related ($P = 0.008$ and 0.007, respectively). These data suggest a benefit derived from PA for quality of bodyweight shown by WC and VFA, but not quantity of bodyweight shown by BMI (Table 2).

Table 1 | Clinical characteristics in each group based on the intensity of physical activity among patients with type 2 diabetes

	High activity	Moderate activity	Low activity	Total
Sex, male/female (*n*)	204/113	183/145	225/183	612/441
Age (years)	63.6 ± 11.6	63.7 ± 10.9	61.2 ± 11.4	62.7 ± 11.3
Duration of type 2 diabetes (years)	15.1 ± 9.9	14.1 ± 8.0	12.6 ± 8.1	13.9 ± 8.8
BMI (kg/m^2)	25.2 ± 4.7*	25.7 ± 4.5	26.7 ± 5.2	26.0 ± 4.9
HbA1c (%)	7.00 ± 1.06	6.89 ± 0.94	7.04 ± 1.20	6.98 ± 1.08
SBP (mmHg)	129 ± 16	132 ± 15	129 ± 15	130 ± 15
DBP (mmHg)	76 ± 12	77 ± 11	77 ± 12	76 ± 11
Physical activity (METs/h/week)	5,598 (4,158–8,262)**,***	1,445 (990–2,117)**	198 (0–529)	1,386 (347–3,672)
Sedentary times (min/day)	180 (120–300)**,***	240 (180–480)	300 (180–600)	240 (180–480)
Waist circumference, cm (*n*)	92.1 ± 11.2 (48)	91.5 ± 10.5 (47)	97.9 ± 14.6 (63)	94.2 ± 12.8 (158)
Visceral fat accumulation, cm^2 (*n*)	113.5 ± 51.5 (48)	113.8 ± 45.4 (47)	138.5 ± 62.1 (63)	123.6 ± 55.4 (158)
Treatment for diabetes (*n*)				
Insulin/SU/glinides/TZD	66/50/26/62	45/37/32/52	68/59/34/63	179/146/92/177
BG/α-GI/DPP-4I	158/34/165	150/36/175	202/34/206	510/104/546
SGLT2I/GLP-1RA	65/21	77/17	90/36	232/74

Data are shown as mean ± standard deviation or median (interquartile range). *$P = 0.0028$, **$P < 0.0001$ compared to category of low activity and ***$P < 0.0001$ compared to category of moderate activity after adjustment for confounders, respectively. α-GI, alpha-glucosidase inhibitors; BG, biguanide; BMI, body mass index; DBP, diastolic blood pressure; DPP-4I, dipeptidyl peptidase-4 inhibitors; GLP-1RA, glucagon-like peptide 1 receptor agonist; HbA1c, glycated hemoglobin; SBP, systolic blood pressure; SGLT2I, sodium–glucose cotransporter 2 inhibitors; SU, sulfonylureas; TZD, thiazolidinedione.

Table 2 | Impact of physical activity and sedentary time on glycated hemoglobin, body mass index, waist circumference and visceral fat accumulation

	HbA1c	BMI	Waist circumference	Visceral fat accumulation
Physical activity (METs/h/week)				
β	0.008	–0.045	–0.209	–0.211
P	0.788	0.135	0.008	0.007
Sedentary time (min/day)				
β	–0.010	0.110	0.120	0.126
P	0.719	<0.0001	0.106	0.086

Glycated hemoglobin (HbA1c), body mass index (BMI), waist circumference and visceral fat accumulation were used as dependent variables, and physical activity and sedentary time were each used as an independent variable. Data were expressed after adjustment of confounders. β, standardized regression coefficient.

Impact of sedentary time (min/day) on HbA1c, BMI, WC or VFA

After adjustment was carried out for the seven confounders described above, BMI was positively related to sedentary time based on multiple regression analysis ($P < 0.0001$), but HbA1c was not ($P = 0.72$). In contrast, among the subgroups with WC and VFA data, these measures were found to not be related ($P = 0.11$, and 0.09, respectively). These data suggest long sedentary time might harm quantity rather than quality of bodyweight (Table 2).

Comparison of effects of sedentary time and PA on HbA1c, BMI, WC or VFA

As described above, the data were divided into four groups according to the cut-off lines, as medians were 240 min for sedentary time and 1,386 METs/h/week for total PA. Patient numbers for the four different groups (LL, LH, SL and SH) described above were 290, 288, 236 and 239, respectively. After dividing the study participants into the quartiles after adjustment for the seven confounders, no difference was found in HbA1c among the four categories, based on ANCOVA. In addition, no differences were found in SBP or in DBP, although serum high-density lipoprotein cholesterol ($P = 0.012$) and triglycerides ($P = 0.013$) were higher and lower, respectively, among patients categorized as SH than among those categorized as LL (data not shown). In contrast, BMI was significantly lower among patients categorized as SH than among those categorized as LL or LH in *post-hoc* testing ($P = 0.0007$ and 0.002, respectively). In addition, WC was significantly lower among patients categorized as SH, SL or LH than among those categorized as LL ($P = 0.002$, 0.019 and 0.006, respectively), and VFA was significantly lower among patients categorized as SH, SL and LH than among those categorized as LL ($P = 0.001$, 0.023 and 0.004, respectively), as shown in Figure 1. Considering these results, a combination of enhanced PA and shortened sedentary time could be useful for improvement in both quality and quantity of bodyweight.

DISCUSSION

This cross-sectional study clarified the significance of sedentary time and intensity levels of PA for preventing bodyweight gain in Japanese patients with type 2 diabetes. In addition, total PA was found to be significantly related to WC and VFA. A combination of reduced sedentary time and increased PA might positively affect BMI, WC and VFA. These results suggest the importance of both reducing sedentary time and elevating intensity of PA for the prevention of becoming overweight and obese in Japanese patients with type 2 diabetes.

Glycemic control is a fundamental tool in effective diabetes management. To prevent diabetic microangiopathy, for example, it is recommended that a patient have an HbA1c level of <7.0% as a reasonable goal for non-pregnant adults[12,13]. To maintain good glycemic control, prevention of bodyweight gain with a focus on quantity of bodyweight is a clinically crucial factor for patients with type 2 diabetes[14]. Furthermore, in general, central fat distribution, or the quality of bodyweight, is associated with increased insulin resistance, risk of developing type 2 diabetes and cardiovascular disease[15]. Accordingly, in individuals with type 2 diabetes, the adoption and maintenance of PA are critical foci for blood glucose control, and both quality and quantity of bodyweight management. The present study suggests that a focus should be maintained on reducing sedentary time, as well as on increasing total PA in terms of the quality and quantity of bodyweight for the management of type 2 diabetes mellitus.

The intensity of PA was positively related to BMI in the present study. Furthermore, patients categorized as low PA tended to have high WC and VFA levels, although not statistically significant, compared with patients with moderate or high PA (Table 1). It is difficult to assess whether these relationships were directly or indirectly related clinically, because patients categorized as high PA had significantly short sedentary time. Accordingly, this difference was derived from not only the intensity of PA, but also from a short duration of sedentary time. In addition, medication used to treat type 2 diabetes differed among the three categories, even after statistical adjustment. However, one report showed that individuals with low PA tended to consume more calories compared with high-activity groups[16]. Accordingly, high PA levels could, at least in part, directly affect bodyweight not only through calorie expenditure, but also through relative caloric restriction.

The World Health Organization reported that the leading global risks for mortality worldwide were hypertension (responsible for 13% of deaths globally), tobacco use (9%), high blood glucose (6%), physical inactivity (6%) and being overweight or obese (5%) in 2009[17]. In addition, a report explaining the significant difference in non-exercise activity thermogenesis observed between obese and lean individuals implies that obesity might be prevented by simply limiting sedentary activities

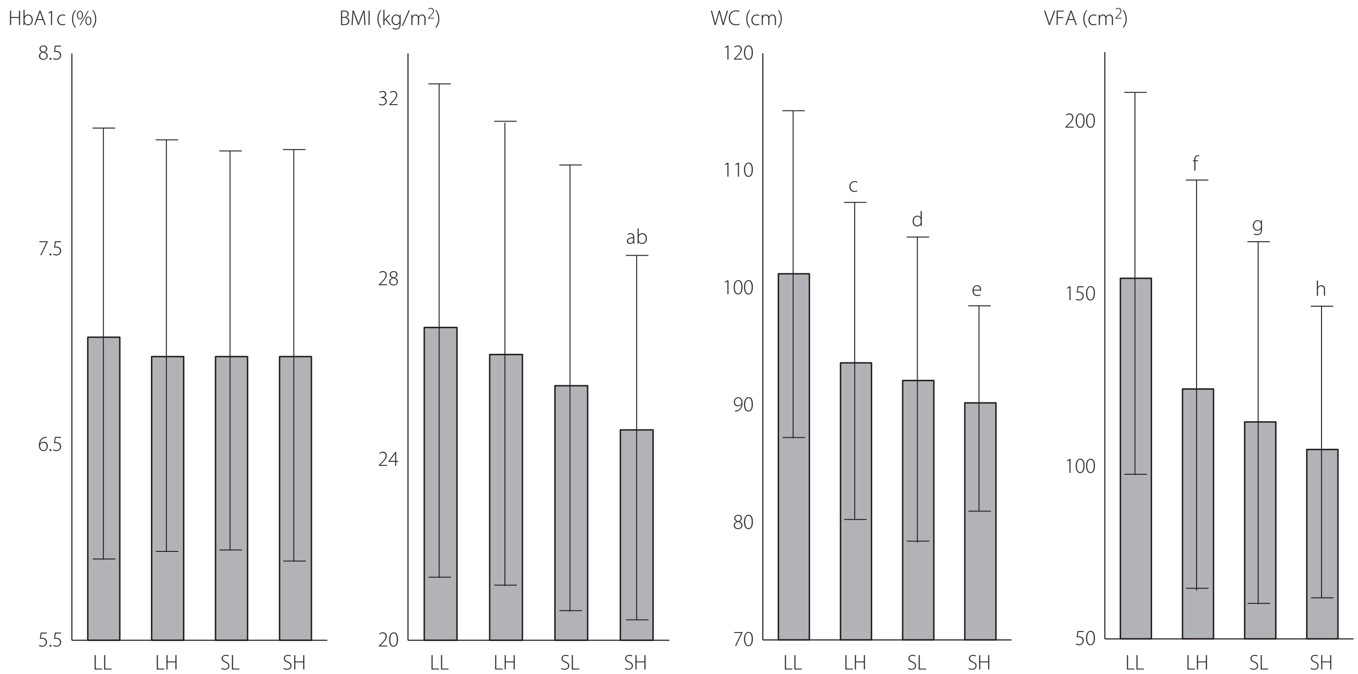

Figure 1 | Glycated hemoglobin (HbA1c), body mass index (BMI), waist circumference (WC) and visceral fat accumulation (VFA) among patients categorized into the four groups: long sedentary time and low physical activity (PA) (LL), long sedentary time but high PA (LH), short sedentary time but low PA (SL), and short sedentary time and high PA (SH). The cut-off lines were medians. Regarding HbA1c and BMI, the numbers of participants in the LL, LH, SL and SH groups were 290, 288, 236 and 239, respectively. Regarding WC and VFA, the numbers were 38, 41, 38 and 41, respectively. $^{a}P = 0.0007$ compared with group LL, and $^{b}P = 0.002$ compared with group LH. $^{c}P = 0.006$, $^{d}P = 0.019$, $^{e}P = 0.002$, $^{f}P = 0.004$, $^{g}P = 0.023$ and $^{h}P = 0.001$ compared with group LL.

or by increasing behaviors, such as standing, walking and fidgeting[18]. Indeed, Hamasaki *et al.*[19] showed that non-exercise activity thermogenesis is associated with amelioration of insulin sensitivity in Japanese patients with type 2 diabetes, and the reduction of WC and elevation of high-density lipoprotein cholesterol in Japanese women with type 2 diabetes. Accordingly, reducing sedentary time in any way possible is an important and critical strategy for the management of patients with type 2 diabetes. The present study supports these findings. In addition, central fat distribution is now recognized as an important predictor and modifier of adverse health consequences, such as hypertension, insulin resistance, type 2 diabetes mellitus, dyslipidemia and coronary heart disease, through various mechanisms[20,21], although central fat distribution indicated by WC and VFA was not related to sedentary time in the present study. In contrast, PA was statistically related to both WC and VFA, but not to BMI. These results support the interpretation that increased PA leads to increased lean body mass as a compensation for decreased BMI. In contrast, in the present study, sedentary time did not affect body composition, but did affect bodyweight directly. Indeed, the combination of reduced sedentary time and increased PA might be favorable for preventing increased BMI, WC or VFA, as described in Figure 1, although the study could not clarify which of long sedentary time and low PA was statistically worse for bodyweight gain and central obesity. One speculation is that both of the factors might, at least in part, affect bodyweight independently. Accordingly, first of all, patients with type 2 diabetes who are sedentary in varying degrees could be advised to break the habit of “staying still,” and patients who exercise regularly could be told to focus on intensity, although further study is required to resolve this ambiguity.

Intensity and caloric expenditure of PA and sedentary time were not related to HbA1c. However, these relationships were not surprising. Because the design of the present study was cross-sectional, the relationship was the result of diabetes medication prescribed by the physician in charge based on a patient-centered approach considering the best available evidence in terms of benefit, harm, patient values, preferences, various situations and target HbA1c level. In other words, the physician might try to keep glycemic control appropriate by prescribing medication even if PA and sedentary time were not ideal, and such medication might have affected patient bodyweight. To clarify the relationship between glycemic control and sedentary time or PA, further study is necessary.

The present study had several limitations. First, it was of a cross-sectional design with a limited participant population. As described above, it was difficult to distinguish causes and results in the study. Second, the four diabetes medications – sodium–glucose cotransporter 2 inhibitor, glucagon-like peptide 1 receptor agonist, thiazolidinedione and insulin – were considered confounders, because they have potential for modifying patient bodyweight. The prescribed amount of diabetes medication likely increased in patients with poor HbA1c level. It was therefore difficult to assess the effect that medication might have had on the study design. Third, also not considered were habits and comorbidity factors, such as smoking, cognitive function, frailty and daily activities. Fourth, the results of the present study might not be applicable to different ethnicities. The definition of obesity differs in Japan Society for the Study of Obesity[22] and World Health Organization[23], because the proportion of Asian people with a higher risk of type 2 diabetes and cardiovascular disease was substantially large, even though their BMIs were lower than the existing World Health Organization cut-off point for the overweight classification of ≥25 kg/m^2. Finally, PA was only calculated on the basis of the IPAQ short form, without use of any monitoring devices. Furthermore, it was difficult to clearly distinguish between aerobic and resistance exercise. In addition, VFA was methodologically assessed only by bioelectrical impedance analysis, not by computed tomography. Further prospective study is required to clarify the precise relationships between sedentary time or PA, and management of type 2 diabetes, although the method using IPAQ appeared to be practical for obtaining these data from >1,000 patients thus far.

In conclusion, to manage the quantity and quality of bodyweight in patients with type 2 diabetes, a primary goal should be the promotion of increased PA and reduced sedentary time. It is likely that the combination of seeking out PA and avoiding sedentary behavior is important for the management of bodyweight in Japanese patients with type 2 diabetes.

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