ORIGINAL ARTICLE

Effects of sedentary behavior and daily walking steps on body mass index and body composition: Prospective observational study using outpatient clinical data of Japanese patients with type 2 diabetes

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ABSTRACT

Aims/Introduction: This study examined the effect of daily walking steps on glycated hemoglobin, body mass index (BMI) and body composition while taking into consideration sedentary time (ST) in Japanese type 2 diabetes patients over a period of 12 months.

Materials and Methods: Self-administered ST values and information regarding daily walking steps were obtained and analyzed for 236 patients with type 2 diabetes who regularly visited the outpatient clinic. The patients – divided into three categories of daily walking steps: non-step counter user, <7,500 daily walking steps and ≥7,500 daily walking steps (HS) – were prospectively observed considering ST through the monitoring of glycated hemoglobin, BMI waist circumference (WC) and visceral fat accumulation (VFA) for 12 months.

Results: After 12 months, the participants categorized as the HS group had significantly reduced BMI and VFA independent of ST, as well as significantly reduced WC with high ST. WC and VFA disparities widened significantly at 12 months between the participants categorized as being in the non-step counter user group and the HS group with long ST. However, no difference in glycated hemoglobin levels and BMI were found among the three categories independent of ST. Compared with non-step counter users, the odds ratios with logistic regression models of improvement in BMI and VFA in the <7,500 daily walking steps and HS groups, and WC in the HS group after 12 months were significantly higher only among those with long ST.

Conclusions: These results suggest that consideration of sedentary behavior in combination with daily walking steps might be essential for type 2 diabetes management.

INTRODUCTION

Type 2 diabetes mellitus is a pandemic that threatens worldwide health and economic growth due to the disease's micro- and macrovascular complications in patients[1-3]. The goal for diabetes management is to extend healthy life of patients by avoiding diabetic complications and thereby improving the quality of life equivalent to that of their counterparts without diabetes. To achieve this objective, it is important to manage blood glucose levels and control bodyweight.

Regular exercise is considered to have potential for enhancement of health benefits not only for diabetes patients, but also for healthy individuals, because it increases energy

consumption. Most adults with diabetes are instructed to engage in a total of at least 150 min of moderate-to-vigorous physical activity each week, at a frequency of at least 3 days/week, with no more than two consecutive days without activity[4]. Aerobic exercise, such as walking, increases daily energy expenditure and assists with bodyweight management through the use of the body's large muscle groups. Pedometers, or step counters, have gained popularity recently and, along with smartphone step-counting apps, are widely used by both patients with type 2 diabetes and healthy adults. One reason for the increase in popularity is that software technology used to calculate walking steps taken has become accurate and affordable. Based on the use of step counters, adults with type 2 diabetes are recommended to take no fewer than 5,000 steps/day and to strive to exceed 7,500 steps/day[4-6].

Furthermore, patients with type 2 diabetes are encouraged to decrease the amount of time spent in daily sedentary behavior, because extended sedentary time (ST) is associated with poorer glycemic control[7]. Regularly breaking up prolonged sitting with light-intensity physical activity led to significantly lower post-prandial insulin and glucose levels among individuals without known type 2 diabetes[8]. In addition, a prospective study of a USA national cohort suggested that reducing total ST and breaking up prolonged, uninterrupted sedentary bouts was associated with a reduction in all-cause mortality risk, particularly among study participants who were less active[9]. Another study provided evidence that higher levels of total physical activity, regardless of intensity level, and lesser amounts of ST were associated with lower risk for premature mortality in middle-aged and older people[10].

Such recommendations speak to the importance of both exercising regularly and reducing ST for people diagnosed with type 2 diabetes mellitus. Such results raise a clinical question regarding whether the impact of such exercise as walking would be affected by the degree of sedentary behavior, as well as whether the benefit from walking could change depending on lifestyle, including the level of sedentary behavior, for treatment of type 2 diabetes. In this prospective, observational study, to assess the impact of exercise calculated by the number of daily walking steps on glycated hemoglobin (HbA1c), body mass index (BMI), waist circumference (WC) and visceral fat accumulation (VFA), while also taking into consideration sedentary behavior, outpatients with type 2 diabetes were followed for 12 months by monitoring changes in stratified ST and daily walking steps. The study's aim was to clarify the association between daily walking steps and ST to formulate effective advice about exercise with personalized benefits for patient-centered glycemic management.

MATERIALS AND METHODS

Study population and patient preparation
A total of 274 patients with type 2 diabetes who regularly visited the diabetes outpatient clinic at Kawasaki Medical School Hospital, Okayama, Japan, from July 2018 to October 2020 and who underwent measurements for WC and VFA were eligible to participate in the present study. ST was estimated in all patients using the Japanese version of the International Physical Activity Questionnaire short form[11,12] at the beginning of the study. Among that total, patients with active retinopathy, end-stage renal disease, steroid use, difficulties in carrying out physical activity due to orthopedic and other impairments, and those deemed to be inappropriate for this questionnaire by the attending physician were excluded from the study in advance. During the 12-month period, one, 33 and four patients were excluded, because they refused to visit the clinic, were referred to another medical facility or underwent hospitalization for another disease, respectively. With this in mind, the full, final analysis study sample consisted of 236 patients.

The participants were prospectively observed for 12 months, with monitoring of HbA1c and BMI taking place. In addition, WC and VFA were measured at the beginning of the study, after 6 months, and after 12 months. Diabetes treatment with respect to diet, exercise, and medication was encouraged and prescribed by the attending physician based on a patient-centered approach that took into consideration the best available evidence regarding benefit, harm, patient values, preferences, various situations and target HbA1c level in a regular outpatient setting. Among the participants, 112 with pedometers attached to a belt or built in to their mobile phones were monitored for the number of walking steps at every outpatient visit, with the walking steps calculated using mean daily values based on the data collected at 12 months. WC was measured at the umbilical level in the late expiration phase with participants standing; VFA around the waist was estimated by bioelectrical impedance analysis (Panasonic EW-FA90, Shiga, Japan), as reported previously[13]. In brief, voltage at the umbilicus position correlated significantly with VFA and was affected by subcutaneous fat only negligibly, which suggested that VFA could be calculated based on voltage. The correlation of bioelectrical impedance analysis with the computed tomography measurement results was 0.88[13]. BMI was calculated by dividing weight in kilograms by height in meters squared. 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 were expressed as numerals and percentages. Continuous variables were expressed as the mean and standard deviation, or the median and interquartile ranges. The χ^2-test was used for testing associations between categorical variables. Residual analyses were used to identify the specific cells making the greatest contribution to the χ^2-test results. As the data regarding HbA1c, BMI, WC and VFA were not normally distributed, analysis took place after logarithmic transformation. To find the impact of the mean daily walking steps according to ST, three categories were established for daily

walking steps: non-step counter user (NU), <7,500 steps (LS) and ≥7,500 (HS). In addition, the three categories were further divided into long or short ST by the median among the study participants (300 min/day), resulting in the creation of six categories: (i) long ST and NU; (ii) long ST and LS; (iii) long ST and HS; (iv) short ST and NU; (v) short ST and LS; and (vi) short ST and HS.

First, HbA1c, BMI, WC and VFA taken at the 6- and 12-month visits were compared with measurements taken at the beginning of the study, using the Wilcoxon signed-rank test for the six categories. In addition, these four variables at the beginning of the study, at 6 months and at 12 months were compared using analysis of covariance (ANCOVA) for comparisons among the three categories by long or short ST among (i), (ii) and (iii), as well as among (iv), (v) and (vi). After multivariate tests, to determine if there were significant differences, Tukey's tests were carried out for post-hoc analysis. All results were expressed after adjustment was made for the following confounders: age, sex, and the use of sulfonylureas, sodium–glucose cotransporter 2 inhibitors, glucagon-like peptide-1 receptor agonists or insulin at 12 months, with these four medications included because they are known to affect not only patient bodyweight, but also HbA1c levels.

Next, to clarify the significance of daily walking steps as a predictor of improved HbA1c, BMI, WC and VFA, the odds ratios of LS and HS for improvements in comparison with the NU group were estimated with logistic regression models, after adjustment for the six aforementioned factors. "Improvement" was defined as decreases observed in each of the four indicators after 12 months. That is, when the value subtracted from the indicator after 12 months at the beginning

was positive, the indicator was considered to be "improved." 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, BMI, WC and VFA for all participants at the beginning of the study were 65.0 ± 11.6 years, 7.1 ± 1.0%, 25.8 ± 5.1 kg/m^2, 93.4 ± 12.4 cm and 121.2 ± 54.2 cm^2, respectively. The mean ST was 361 ± 241 min/day. The distribution of ST among all participants is shown in Figure 1. The mean number of walking steps among 112 pedometer users was 6,666 ± 2,981/day. Oral medications, insulin injection therapy for diabetes and medications for hypertension were few in number among the HS group compared with the NU group, but not significant at the study's start. Table 1 shows the clinical characteristics of patients categorized by the three categories of NU, LS and HS, among short ST and long ST. At the beginning of the study, no differences were observed regarding sex, age, systolic and diastolic blood pressure, or estimated glomerular filtration rate.

Changes in HbA1c, BMI, WC and VFA in each group divided based on daily walking steps (NU, LS and HS) and ST (short ST and long ST)
The mean BMI, WC and VFA at the beginning of the study among patients in each category of short STs were lower than those among patients in corresponding categories of long STs, although the difference was not statistically significant. In
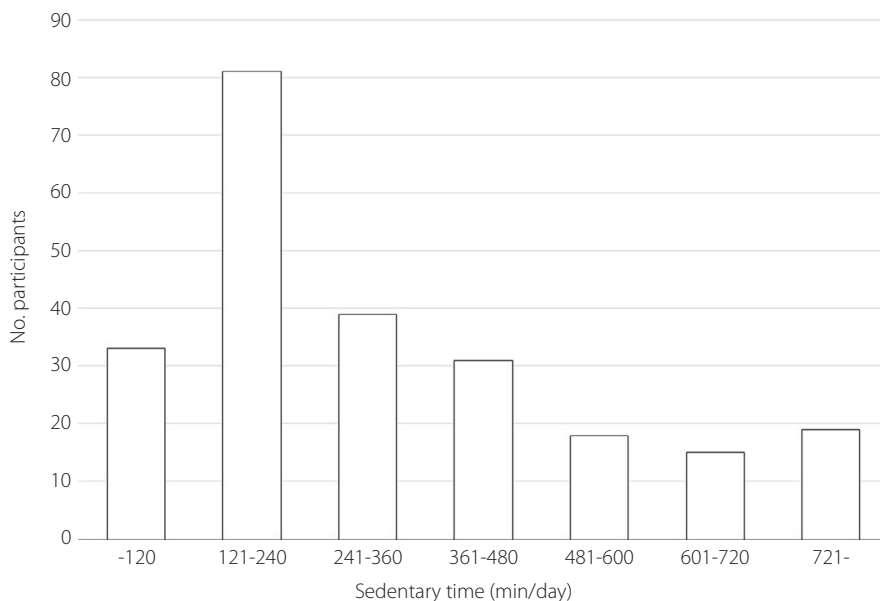
Figure 1 | Distribution of sedentary time among all participants.

Table 1 | Changes in clinical characteristics for each group based on walking steps and sedentary status among patients with type 2 diabetes

	Short sedentary time			Long sedentary time		
	NU	LS	HS	NU	LS	HS
M/F (n)	25/35	18/16	15/9	43/21	25/8	16/5
Age (years)	68.0 ± 11.1	68.1 ± 9.7	64.2 ± 9.6	62.3 ± 13.8	62.7 ± 9.5	64.0 ± 11.1
SBP (mmHg)	133 ± 15	132 ± 13	132 ± 14	131 ± 16	131 ± 14	129 ± 15
DBP (mmHg)	76 ± 11	74 ± 10	78 ± 13	77 ± 12	79 ± 13	76 ± 12
eGFR (ml/min/1.73 m^2)	75.3 ± 19.2	74.8 ± 18.0	75.4 ± 17.7	74.9 ± 22.9	76.9 ± 16.5	78.7 ± 20.1
Sedentary time (min/day)	180 ± 61	179 ± 49	173 ± 60	584 ± 211	544 ± 239	426 ± 131
Walking steps (/day)	No data	4715 ± 1624	9520 ± 1281	No data	4494 ± 1416	9976 ± 2089
HbA1c (%)						
At beginning	7.27 ± 1.12	7.09 ± 0.91	7.00 ± 0.80	7.13 ± 1.14	7.12 ± 0.87	6.88 ± 0.67
After 6 months	7.31 ± 1.02	6.95 ± 0.67	6.85 ± 0.63	7.51 ± 1.40***	7.20 ± 0.82	7.07 ± 0.48
After 12 months	7.45 ± 1.12	7.06 ± 0.64	6.82 ± 0.62	7.48 ± 1.38***	7.22 ± 1.14	6.95 ± 0.59
BMI (kg/m^2)						
At beginning	25.5 ± 4.5	24.0 ± 4.3	23.7 ± 4.7	27.2 ± 5.6	27.7 ± 5.5	24.5 ± 4.1
After 6 months	25.2 ± 4.3	23.6 ± 4.0	23.4 ± 4.4	27.3 ± 5.6	27.5 ± 5.3	24.7 ± 4.0
After 12 months	25.3 ± 4.4	23.8 ± 4.5	23.3 ± 4.6**	27.5 ± 5.9	27.2 ± 5.3‡	23.9 ± 4.1***
WC (cm)						
At beginning	92.4 ± 11.3	88.8 ± 11.4	87.6 ± 10.5	97.6 ± 13.8	98.1 ± 11.0	90.3 ± 10.4
After 6 months	92.5 ± 11.5	87.9 ± 11.1	86.5 ± 10.1	97.8 ± 13.5	98.1 ± 10.5	89.8 ± 10.5
After 12 months	92.2 ± 11.1	88.7 ± 11.0	86.8 ± 9.9	98.8 ± 14.0**	96.8 ± 10.4	89.0 ± 9.9*·**
VFA (cm^2)						
At beginning	114.5 ± 49.0	102.8 ± 49.8	95.0 ± 51.6	140.1 ± 58.5	143.2 ± 46.4	108.1 ± 49.5
After 6 months	109.3 ± 47.2	98.6 ± 50.3	85.9 ± 49.8**	138.2 ± 56.0	141.8 ± 45.9	108.5 ± 48.5
After 12 months	108.6 ± 51.0	97.6 ± 51.5	83.8 ± 49.6***	145.2 ± 57.9	135.0 ± 48.1†	95.9 ± 45.8*·***
Medication for HT (n)	28	15	7	29	17	6
Medication for DL (n)	36	17	10	35	17	9
Treatment for diabetes using insulin/SGLT2i/GLP-1RA/TZD (n)						
At beginning	10/23/7/3	4/14/2/0	0/8/1/0	7/25/6/0	5/17/8/0	0/2/0/0
After 12 months	9/23/11/1	5/13/2/0	1/11/0/0	7/33/6/0	6/17/8/0	0/5/0/0
Treatment for diabetes using SU/glinide/BG/α-GI/DPP-4I (n)						
At beginning	7/7/33/3/27	3/3/12/1/14	4/0/8/0/7	7/2/34/2/21	6/0/14/1/10	3/2/6/0/7
After 12 months	4/7/30/2/25	3/3/13/2/17	3/0/9/0/7	7/3/32/1/23	8/0/16/1/10	2/1/6/0/5

Data are shown as the mean ± standard deviation. *$P < 0.05$ compared with non-step counter users (NU after) adjustment for confounders; **$P < 0.05$ compared with data at beginning of the study; and ***$P < 0.01$ compared with the data at the beginning. α-GI: alpha-glucosidase inhibitors; BG, biguanide; BMI, body mass index; DBP, diastolic blood pressure; DL, dyslipidemia; DPP-4I, dipeptidyl peptidase-4 inhibitors; eGFR, estimated glomerular filtration rate; GLP-1RA, glucagon-like peptide-1 receptor agonist; HbA1c, glycated hemoglobin; HS, ≥7,500 daily walking steps; HT, hypertension; LS, <7,500 daily walking steps; NU, non-step counter user; SBP, systolic blood pressure; SGLT2i, sodium–glucose co-transporter 2 inhibitors; SU, sulfonylureas; TZD, thiazolidinedione; VFA, visceral fat accumulation; WC, waist circumference.

addition, the mean BMI, WC and VFA at the beginning of the study were the lowest levels among participants in the HS group, followed in order by the LS group and then the NU group among participants with both short and long ST, although the differences were not statistically significant. After adjustment was carried out for the six confounders described earlier, no difference in HbA1c levels and BMI were found among the three categories based on ANCOVA analysis at 12 months. In contrast, WC and VFA after 12 months were found to be significantly lower in the HS group than the NU group with long ST ($P < 0.05$, each), but not in the participants with short ST.

By Wilcoxon's signed-rank tests, HbA1c was significantly worsened among the NU group with long ST at 6 and

12 months compared with the HbA1c at the start of the study ($P < 0.0001$ and $P = 0.0005$, respectively). BMI was significantly improved among the HS group at 12 months for both the short and long ST groups ($P = 0.030$ and 0.005, respectively), and among the LS group at 12 months with the long ST groups ($P = 0.003$) compared with BMI at the start of the study. WC was significantly worsened and improved among the NU and HS group with long ST at 12 months compared with WC at the beginning of the study ($P = 0.014$ and 0.039, respectively). VFA was significantly improved among the HS group with short ST at 6 and 12 months ($P = 0.043$ and 0.009, respectively), and the LS and HS group with long ST at 12 months ($P = 0.038$ and 0.003, respectively) compared with VFA at the start of the study. These results imply that the

effect of habitual walking on improved bodyweight and body composition in each category might be significant, especially among patients with long ST rather than short ST (Table 1).

Impact of walking steps in consideration of ST on HbA1c, BMI, WC and VFA

After adjustment was carried out for six confounders and ST as a continuous variable, the odds ratios of walking steps as numerical values were not statistically significant for HbA1c, BMI, WC or VFA. After adjustment was carried out for the six confounders, and ST as a continuous variable, the LS and HS groups compared with the NU group had high odds ratios of 1.93 (95% confidence interval [CI] 1.04–3.57, $P = 0.037$) and 1.87 (95% CI 0.90–3.86, $P = 0.092$), 2.08 (95% CI 1.11–3.89, $P = 0.023$) and 2.85 (95% CI 1.33–6.09, $P = 0.007$), 1.19 (95% CI 0.64–2.21, $P = 0.590$) and 2.39 (95% CI 1.13–5.07, $P = 0.023$), and 1.48 (95% CI 0.79–2.74, $P = 0.218$) and 2.45 (95% CI 1.12–5.34, $P = 0.025$), for HbA1c, BMI, WC and VFA improvements, respectively. After adjustment was carried out for six confounders, the LS and HS groups compared with the NU group with short ST had high odds ratios of 1.88 (95% CI 0.77–4.58, $P = 0.16$) and 3.61 (95% CI 1.23–10.56, $P = 0.019$) regarding HbA1c improvement ($P = 0.016$ for trend). The LS and HS groups compared with the NU group with long ST had odds ratios of 2.45 (95% CI 0.98–6.14, $P = 0.06$) and 1.41 (95% CI 0.49–4.05, $P = 0.52$) regarding HbA1c improvement. On the contrary, the LS and HS groups compared with the NU group with long ST had significantly high odds ratios of 4.73 (95% CI 1.75–12.82, $P = 0.002$), and 4.54 (95% CI 1.48–13.92, $P = 0.008$) regarding BMI improvement, respectively

($P = 0.001$ for trend). The LS and HS groups compared with the NU group with long ST had high odds ratios of 2.35 (95% CI 0.94–5.85, $P = 0.07$) and 5.27 (95% CI 1.69–16.47, $P = 0.004$) for WC improvement ($P = 0.002$ for trend), and 2.86 (95% CI 1.12–7.28, $P = 0.028$) and 6.96 (95% CI 1.98–24.45, $P = 0.003$) for VFA improvement ($P = 0.0007$ for trend; Figure 2). The results imply that the effect of walking on improved bodyweight and body composition in each category tended to be significant, especially among patients with long ST.

DISCUSSION

The present prospective observational study clarified that the number of daily walking steps affected both bodyweight and body composition among patients with type 2 diabetes in a group of participants with long ST. The results suggest that sedentary status should be taken into consideration for the successful practice of physical activity, such as daily walking, to prevent Japanese patients with type 2 diabetes from becoming overweight or obese and thereby exacerbate their diabetes condition.

Previously, the significance of maintaining short ST in addition to, or in place of, increased physical activity for preventing bodyweight gain in Japanese patients with type 2 diabetes was clarified in a cross-sectional study[14]. This prospective observational study found that the effects of physical activity expressed by the number of walking steps on bodyweight, and composition control might be affected by the ST of each individual among Japanese patients with type 2 diabetes. Walking is a simple exercise that can be used to increase daily energy
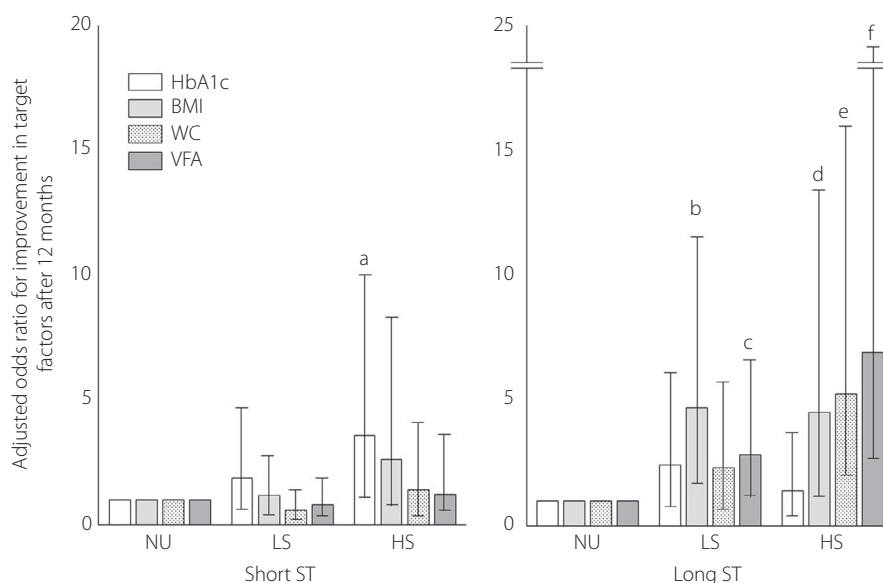
Figure 2 | Adjusted odds ratio for improvement of glycated hemoglobin (HbA1c), body mass index (BMI), waist circumference (WC) and visceral fat accumulation (VFA) among patients categorized into the three groups – non-step counter user (NU), <7,500 steps (LS) and ≥7,500 (HS) – stratified by short and long sedentary time (ST). $^{a}P = 0.019$, $^{b}P = 0.002$, $^{c}P = 0.028$, $^{d}P = 0.008$, $^{e}P = 0.004$ and $^{f}P = 0.003$ compared with NU.

expenditure and assist with bodyweight management. Based on a representative sample of adults in the USA using an accelerometer, a greater number of daily steps was reported to be significantly associated with lower all-cause mortality[15]. However, there was no significant association observed between step intensity and mortality after adjustment was made for total steps per day[15]. The present study found that participants taking <7,500 steps, as well as ≥7,500, had improved BMI and VFA, among participants with high levels of ST. Such improvements observed in these groups might indicate that the participants were able to achieve reduced bodyweight and maintain lean body mass, which could also help to prevent sarcopenia. The results suggest that patients with long ST should be encouraged to exercise, even if only a small number of walking steps, with the aim of interrupting prolonged ST. Indeed, a population-based study in the USA showed that both the total volume of ST and its accrual in prolonged and uninterrupted bouts were associated with all-cause mortality[16], which could be reduced by interrupting such sedentary bouts among less active individuals[9].

The present study surprisingly did not find an increased benefit from walking on BMI, WC and VFA among the participants with low levels of ST, except for participants in the HS group. However, that result does not imply that walking was wasteful for patients with short ST. As a premise, HS groups had significantly improved BMI, WC and VFA after adjustment was made for minutes of ST in this study. It might indicate that participants with low levels of ST were potentially more active compared with long ST participants, and as a result, they might have been able to better manage bodyweight and body composition, given the original baseline data. Accordingly, energy expenditures from walking would be additional and therefore not as significant for participants with short ST, but potentially contribute to the maintenance of bodyweight and body composition.

According to a self-recorded questionnaire carried out in Japan[17], 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. A cross-sectional study carried out in 13 countries found that the type 2 diabetes patient-reported success rate for exercise was just 37%[18]. Taking such circumstances into consideration, the results of the present study might permit a simple, but intriguing, approach in which patients with long ST would be encouraged to simply interrupt prolonged sitting to promote glucose metabolism[8], and patients with short ST would be encouraged mainly to continue managing their daily lifestyle. An impressive report explaining the contrast in non-exercise activity thermogenesis observed between lean and obese individuals suggested that weight gain could be prevented by merely decreasing sedentary activities or by increasing behaviors such as standing, walking and fidgeting[19]. Indeed, Hamasaki et al.[20] showed that non-exercise activity thermogenesis is associated with improvement of insulin sensitivity in patients with Japanese type 2 diabetes. Accordingly, maintaining low levels of ST is an important and critical strategy for the management of patients with type 2 diabetes.

Caloric expenditure from walking seemed to have a small effect on HbA1c in the present study. However, this could have been the result of the use of diabetes medications prescribed by the attending physician to target HbA1c level. In other words, the physician might try to maintain glycemic control by prescribing medication even in cases in which physical activity and ST were not ideal, with such medication affecting patient bodyweight. Interestingly, HbA1c levels were comparable among the participants in the LS and HS groups, although the levels had significantly worsened among only the NU group with long ST during the observation period as expected. To clarify the association between glycemic control and ST or daily walking, further study is necessary.

The present study had several limitations. First, it was of a prospective, single-centered, observational design, neither randomized nor interventional, with a limited participant population. The generalizability of the results of the present study would therefore be limited. Assessment of the precise effect of walking and ST was therefore difficult to achieve in the study. Second, the four diabetes medications – sulfonylureas, sodium–glucose cotransporter 2 inhibitors, glucagon-like peptide-1 receptor agonists and insulin – were considered to be confounders, because they have the potential to modify patient bodyweight. The prescribed amount of diabetes medications was likely increased in patients with higher HbA1c levels. 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 physical activity of several patients categorized as being in the NU group was simply not monitored, even though they exercised regularly. Such a lack of monitoring could have affected the results. Fifth, ST was asked on the basis of the International Physical Activity Questionnaire short form, without use of any monitoring devices. This might be one reason why ST per se did not appear to be associated with HbA1c, BMI or body composition. Daily walking steps were assessed with various wearable devices having varying degrees of reliability and validity for walking. Such difficulties in collecting data could have created biases. Finally, VFA was methodologically assessed only by bioelectrical impedance analysis, not computed tomography. Further prospective study is required to clarify the precise effect of ST on physical activity and management of type 2 diabetes.

In conclusion, to manage quantity and quality of bodyweight in individuals with type 2 diabetes, assessment of physical activity should be taken into consideration together with patients' ST. The present study's results suggest that instruction regarding physical activity for treatment of type 2 diabetes should be adapted on the basis of individual characteristics and health status, with consideration also paid to ST.

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