Internal Medicine
The Japanese Society of Internal Medicine
doi: 10.2169/internalmedicine.3150-19
Intern Med 59: 45-53, 2020
http://internmed.jp

【 ORIGINAL ARTICLE 】

Effectiveness of Lifestyle Intervention Using the Internet of Things System for Individuals with Early Type 2 Diabetes Mellitus

Sawako Kato[1], Masahiko Ando[2], Hiroyuki Honda[3], Yasuko Yoshida[3], Takahiro Imaizumi[1], Naoki Yamamoto[4] and Shoichi Maruyama[1]

Abstract:
Objective Exercise therapy is used for glycemic control in type 2 diabetes mellitus (T2DM). We evaluated the effects of intensive health guidance using the Internet of things (IoT) among Japanese company workers with early T2DM.
Methods Fifty-three men (mean age: 54 years) with glycated hemoglobin (HbA1c) levels of >6.5% were enrolled in a 6-month exercise therapy program between August 2016 and January 2017. They used activity meters, scales, and sphygmomanometers connected to the Internet by Bluetooth. These devices automatically and continuously recorded daily information, and the participants simultaneously received health guidance from a public health nurse twice a month.
Results The number of daily steps significantly increased, whereas the amount of physical activity increased but was not significant. The mean decrease (±SD) in HbA1c levels after 3 and 6 months was estimated to be -0.40% (±0.45, p<0.0001) and -0.19% (±0.55, p=0.033), respectively, by a linear mixed model that included baseline HbA1c levels and age as covariates. The program failed to improve the body mass index and blood pressure of the participants. The percentage of active stage (action and maintenance stage) in stage of health behavior significantly increased from 48% to 68% (p=0.011).
Conclusion Intensive lifestyle intervention using a wearable monitoring system and remote health guidance improved diabetic control in middle-aged company workers.

Key words: exercise, healthy behavior, internet of things, lifestyle change, type 2 diabetes mellitus

(Intern Med 59: 45-53, 2020)
(DOI: 10.2169/internalmedicine.3150-19)

Introduction

Type 2 diabetes mellitus (T2DM) is one of the most prevalent metabolic disorders worldwide; the population of people living with diabetes had already increased to 415 million in 2015 and is estimated to reach 642 million by 2040 (1). According to the annual report from the Japanese Ministry of Health, Labour and Welfare in 2016, the number of diabetes patients is increasing rapidly, and although the number of deaths caused by diabetes mellitus was reported to be 13,327 (2), the much larger number of deaths caused by cardiovascular disease, stroke, and other afflictions caused by diabetes mellitus and poor diabetic control was not considered.

Although a healthy lifestyle has been reported to be effective for preventing incident T2DM (3-5), in most cases it is not easy for the individual to adopt and to continue to adhere to a healthy lifestyle (6, 7). According to the American Diabetes Association's (ADA) standards of medical care in diabetes-2016, as diabetic care must cover self-management, education, nutrition, counseling, physical activity, smoking

[1]Department of Nephrology, Nagoya University Graduate School of Medicine, Japan, [2]Center for Advanced Medicine and Clinical Research, Nagoya University Hospital, Japan, [3]Innovative Research Center for Preventative Medical Engineering, Nagoya University, Japan and [4]Safety and Health Promotion Division, Toyota Motor Corporation, Japan
Received for publication April 4, 2019; Accepted for publication July 15, 2019
Correspondence to Dr. Sawako Kato, kato07@med.nagoya-u.ac.jp

cessation, psychosocial care, and immunization, the health-care provider should take a holistic approach with the diabetic care program, accounting for all aspects of circumstances of the patients (8). Among them, exercise is a cornerstone for treating T2DM. The effect of exercise in patients already diagnosed with T2DM may still be unclear in terms of practicality and its contribution to reducing glycated hemoglobin (HbA1c) levels (9). In this study, we attempted to provide structured aerobic exercise. Aerobic exercise is adequate as a training modality for improving HbA1c levels (10). Aerobic exercise was reported to improve the function of pancreatic β-cells (11), induce the expression of M2 markers and peroxisome proliferative-activated receptor gamma in monocytes, resolve inflammation, and prevent insulin resistance (12). Intriguingly, it was recently reported that crosstalk between endurance exercise and the metabolic system in remote organs contributes to the upregulation of anti-inflammatory myokines and the release of exosomes containing antifibrotic particles and the circulatory dose increased according to the intensity of the endurance exercise (13). This means that exercise may play a role in preventing diabetic complications and improving energy expenditure.

Since 2014, we have been organizing a project aimed at promoting behavioral changes with the use of wearable monitoring devices connected to Internet of things (IoT) systems, in order to encourage participants to adopt healthy lifestyle habits. However, the scientific merits of our intervention remain unclear. Thus, the aim of this study was to evaluate whether participants using our IoT system made behavioral changes toward adopting healthy lifestyle habits and whether our system contributed to good diabetic control among Japanese company workers with early T2DM.

Materials and Methods

Study participants and design

The study participants were all male employees of Toyota Motor in Japan and participated in an annual health examination in March, April, and May of 2017. Individuals whose HbA1c levels were >6.5% and <7.9% were recruited. Subjects who were prohibited from exercising by their doctors were excluded. The study protocol was approved by the ethics committee of Nagoya University School of Medicine and was conducted in accordance with the guidelines of the Declaration of Helsinki. After being informed of the purpose of the study, all enrolled patients provided their written consent for participation in the study.

Lifestyle intervention

The participants were provided with Bluetooth-enabled activity meters (TOSHIBA Actiband WERAM1100, Tokyo, Japan), Bluetooth-enabled sphygmomanometers (A&D UA-851PBT-C, Tokyo, Japan), and Bluetooth-enabled body weight scales (A&D UC-411PBT-C). All devices promptly uploaded measurement data over a wireless network to a cloud server. We constructed a health care system, called the MY PAGE SYSTEM, to help with self-management, wherein the participants could view their unified individual data [exercise strength, exercise time, step count, body weight (BW), and blood pressure (BP)] on a website accessed by individual passwords. Moreover, the participants received health guidance from a public health nurse twice a month on the phone. During the phone call, which lasted approximately 20 minutes, the public health nurse, who was familiar with the specific health guidance determined by the Ministry of Health, Labour and Welfare of Japan, gave the guidance using a coaching, mindfulness, and motivation interview. She instructed the individuals on at least one goal that could be achieved before the next instruction for each diet and exercise item, according to the stage of health behavior (SHB) of the subject. She could simultaneously access and share the subjects' "MY PAGE." The MY PAGE SYSTEM is illustrated in Fig. 1.

Clinical data collection

We collected the following laboratory data: HbA1c, total cholesterol, triglyceride, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, serum creatinine, uric acid, blood sugar (fasting), and hemoglobin from the annual health checkups performed at the clinical chemistry facility at Good Life Design (Toyota, Japan). The HbA1c level was measured again at 3 and 6 months after the start of the program. We also measured height, BW, systolic BP (SBP), and diastolic BP (DBP) at baseline and after 6 months.

Assessment of physical activity and stage of health behavior

The number of daily steps was extracted from the uploaded data. Physical activity was assessed by the original physical activity score (PAS), which was calculated as follows: daily PAS=[(score of exercise strength)×(score of duration)×(score of frequency)]×(number of times/day). Each score was determined. Exercise strength scores of 1, 10, 100, and 1,000 corresponded to 3-3.9, 4-5.4, 5.5-6.9, and >7 metabolic equivalents (METs), respectively. Duration scores of 1, 10, and 100 corresponded to 10-29, 30-64, and >65 minutes, respectively. Frequency scores of 1, 10, and 20 corresponded to <2 times, 3-4 times, and >5 times per week, respectively.

We graded the stage of health behavior (SHB) using a self-administered questionnaire at baseline and after 6 months. The participants indicated their intentions regarding regular physical exercise, healthy dietary habits, and smoking cessation, by selecting one of the following options: 1) You have no intention of changing the behavior (pre-contemplation); 2) You acknowledge an intention to change the behavior (contemplation); 3) You actively plan to change the behavior (determination); 4) You have changed the behavior within the last 6 months (action); and 5) You have sustained the behavioral change for at least 6 months (main-

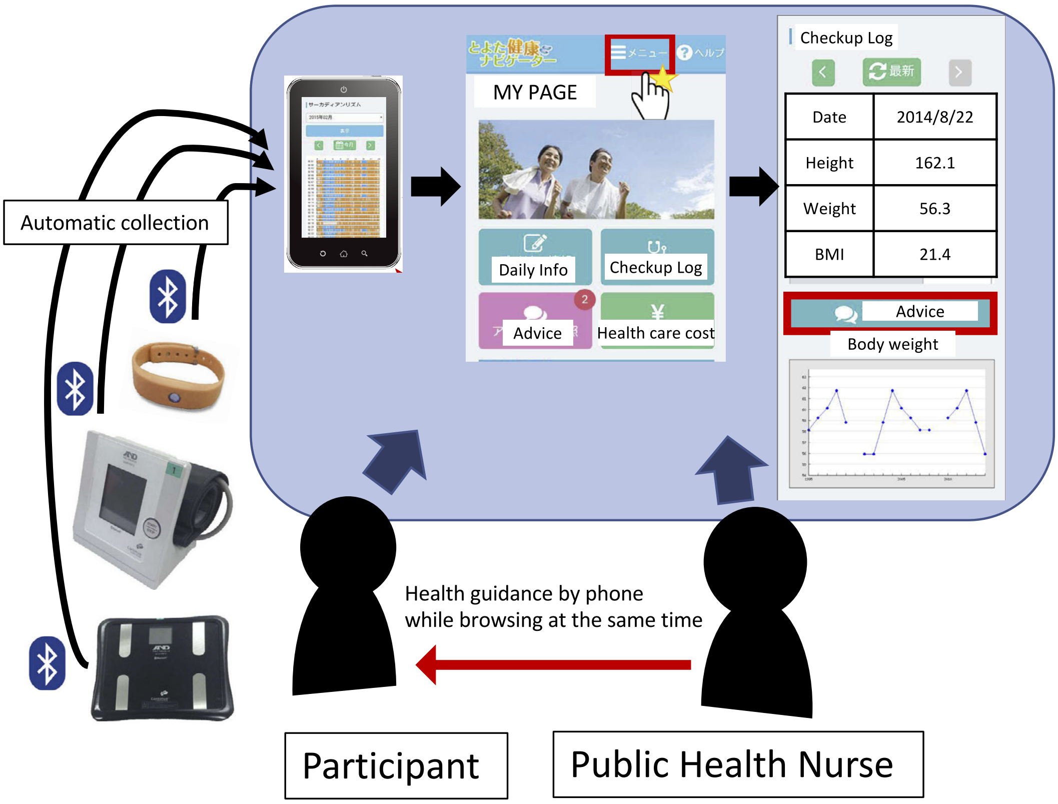

Figure 1. An overview of the “MY PAGE” system.

tenance).

Endpoints

The primary endpoint was the change in the HbA1c levels at 3 and 6 months after the start of the exercise program relative to the baseline values. Next, to remove seasonal fluctuations of HbA1c levels, we compared changes in the HbA1c levels, BMI, SBP, and DPB of the study subjects with those of concurrent nonrandomized control subjects. As controls, we selected workers from the same company with similar HbA1c levels at the same annual health check. The control subjects underwent routine health guidance. The secondary endpoints were the changes in daily steps and SHB at 6 months after the start of the exercise program relative to the baseline.

Statistical analysis

A linear mixed model that included age, time, and the HbA1c levels at baseline, was used to assess the change in HbA1c levels, which was the primary endpoint of the study. Next, to compare changes in HbA1c, BMI, SBP, and DPB between the intervention subjects and controls, an analysis of variance (ANOVA) was performed with age and HbA1c levels at baseline as covariates. For the assessment of the secondary endpoints, we used a paired *t*-test to evaluate the increase in daily steps and PAS and a Wilcoxon rank-sum test to evaluate the difference in SHB from baseline at the final time point. P values of <0.05 were considered to indicate statistical significance. All statistical analyses were performed using the SAS and JMP Pro software programs (versions 9.4 and 13, respectively; SAS Institute, Cary, USA).

Results

Study participants

In total, 650 subjects who took the abovementioned annual health examination above were screened, and 53 subjects fulfilled the inclusion criteria. Forty-nine participants completed the 6-month program. Four subjects dropped out of this study because of transfer (n=1) and withdrawal (n=3). This study had at least 85% statistical power to detect a significant between-group difference in the change in HbA1c from baseline, with a medium effect size of 0.5 standard deviations. The baseline characteristics of the subjects of this study are shown in Table. The subjects were all men and the mean age was 54.4±6.0 years. The mean BMI was 26.5±3.7 kg/m^2, and 36 of 53 participants (68%) were obese with a BMI of >25 kg/m^2. Among the subjects, 27 received oral medications for hypertension (51%) and 34 received antidiabetic drugs (64%), which had been prescribed by their general practitioner (insulin, n=1; oral antidiabetic drugs, n=33). Among the subjects, 42 (79%) had received guidance in relation to diet therapy for diabetes while 11 (21%) had not received treatment for diabetes.

Changes in activity scores and daily steps

The effects of this exercise intervention program on PAS

Table. Characteristics of Participants at Start of Lifestyle Intervention Program.

Characteristics			
	Mean age, years		54.4±6.0
	Men, n (%)		53 (100)
	Height (cm)		169.7±6.0
	Weight (kg)		76.5±12.4
	BMI (kg/m^2)		26.5±3.7
	Systolic blood pressure (mmHg)		126.5±10.9
	Diastolic blood pressure (mmHg)		76.9±8.3
Laboratory data	Total cholesterol (mg/dL)		196.3±27.7
	Triglyceride (mg/dL)		153.8±97.1
	LDL cholesterol (mg/dL)		120.2±23.0
	HDL cholesterol (mg/dL)		51.0±12.3
	HbA1c (%)		6.9±0.4
	Creatinine (mg/dL)		0.93±0.3
	Uric acid (mg/dL)		6.1±1.5
	Fasting blood sugar (mg/dL)		135.9±20.4
	Hemoglobin (g/dL)		15.2±1.1
Medications	Hypertension		
	Antihypertensive drug user, n (%)		27 (50.9)
	Diabetes		
	Antidiabetic drug user, n (%)	insulin	1 (1.9)
		oral	33 (62.2)
	Diet therapy, n (%)		42 (79.2)
	Untreated, n (%)		11 (20.8)
Stage of behavior changes	Smoking cessation, n (%)	Pre-contemplation	7 (14.0)
		Contemplation	3 (6.0)
		Determination	2 (4.0)
		Action	1 (2.0)
		Maintenance	37 (74.0)
	Diet therapy, n (%)	Pre-contemplation	0 (0)
		Contemplation	4 (7.5)
		Determination	27 (50.9)
		Action	1 (2.0)
		Maintenance	21 (39.6)
	Regular exercise, n (%)	Pre-contemplation	2 (4.0)
		Contemplation	6 (11.3)
		Determination	20 (37.7)
		Action	4 (7.5)
		Maintenance	21 (39.6)
	Duration of daily walking*, n (%)	Under 15 minutes	1 (2.0)
		15-30 minutes	15 (28.3)
		30-60 minutes	18 (34.0)
		Over 1 hour	19 (35.8)
	Daily steps*, n (%)	No estimation	14 (26.4)
		Under 5,000 steps	11 (20.8)
		5,000-10,000 steps	19 (35.8)
		Over 10,000 steps	9 (17.0)

*Self-assessment.

BMI: body mass index, HbA1c: glycated hemoglobin, HDL cholesterol: high density lipoprotein cholesterol, LDL cholesterol: low density lipoprotein cholesterol

and daily steps are shown in Fig. 2. The average number of daily steps (±standard deviation; SD) was 6,743 (±3,030) at the start (August), 8,188 (±3,008) after one month (September), 7,924 (±3,189) after 2 months (October), 8,432 (±3,478) after 3 months (November), 7,963 (±3,663) after 4 months (December), and 7,301 (±3,589) in the last month (January). This exercise intervention program significantly increased the daily steps from baseline by 1,443 (95% CI: 822-2,065, $p<0.0001$), 1,203 (95% CI: 631-1,775, $p<0.0001$), 1,561 (95% CI: 779-2,343, $p<0.0001$), and 960 (95% CI: 23-1,897, $p=0.045$) steps/day in September, October, November, and December, respectively. There was no

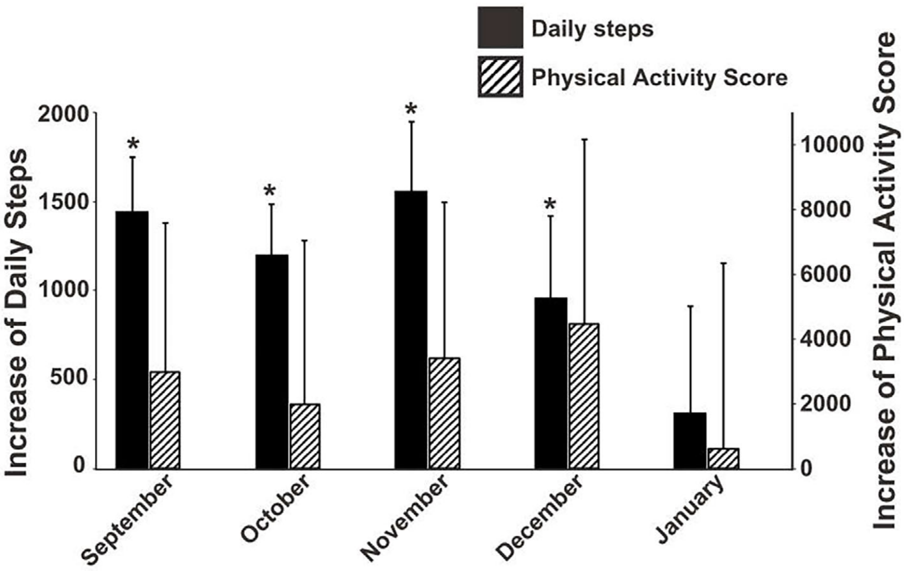

Figure 2. The monthly number of daily steps and physical activity scores. Daily steps were measured by activity meters worn on the wrist. Black bars show the average number of daily steps. Physical activity scores were calculated using our original formula from data uploaded by the same activity meter. Striped bars show the average weekly physical activity scores. *p<0.05 from baseline (August) to each time point, as determined by a paired t-test.

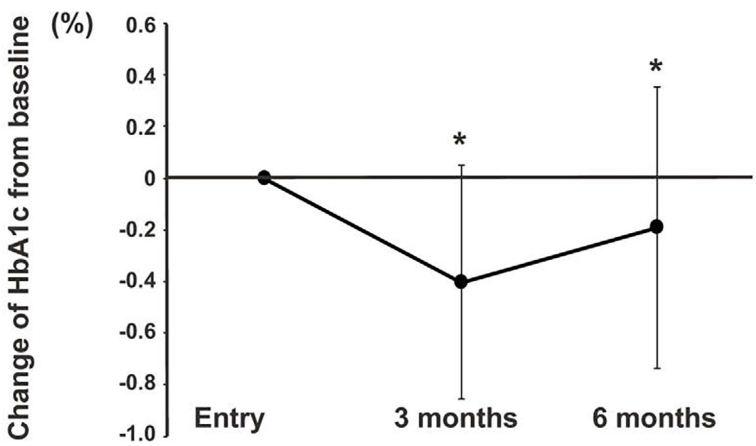

Figure 3. Changes in serum glycated hemoglobin (HbA1c) levels from baseline to 3 and 6 months. The HbA1c levels significantly deceased in the subjects enrolled in this exercise intervention program. This exercise program was effective for improving diabetic control. *p<0.05 from baseline to each time point, as calculated by a linear mixed model.

increase in daily steps in January.

The average PAS (±SD) in August, September, October, November, December and January was 8,844 (±34,247), 11,837 (±21,625), 10,842 (±18,217), 12,244 (±19,075), 13,327 (±24,341), and 9,456 (±21,310), respectively. The median (interquartile range) PAS values in August, September, October, November, December and January were 925 (331.3-3,218.8), 2,455 (593.8-8,625), 2,490 (975-7,610), 2,212.5 (650.0-19,906.3), 1,255 (19.2-9,000), and 738 (0-8,962.5), respectively. Thus, the majority of the study subjects showed low PASs. Although this exercise intervention program increased the PAS from baseline at all points, the differences were not statistically significant.

Effectiveness of the exercise program on reducing HbA1c levels

We checked the HbA1c levels to evaluate the effect of the exercise intervention program on diabetic control. A linear mixed model that included baseline HbA1c levels and age as covariates estimated that the decrease (±SD) in the HbA1c levels of the subjects was -0.40% (±0.45, p≤0.0001) after 3 months and -0.19% (±0.55, p=0.033) after 6 months (Fig. 3). The HbA1c levels at 3 and 6 months from baseline were not significantly different, and the decrease in the HbA1c level was attenuated at 6 months.

Next, we compared the changes in HbA1c levels of the

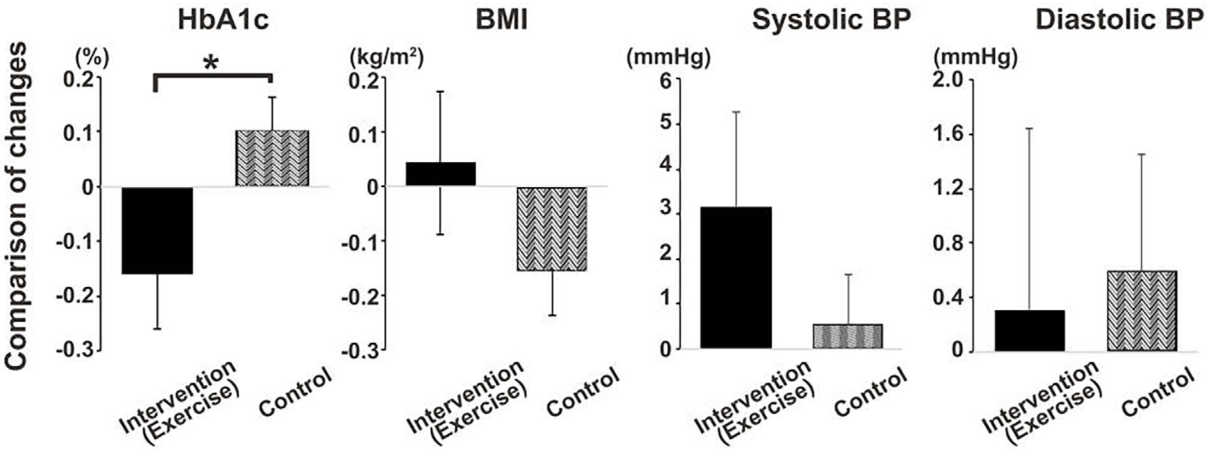

Figure 4. **Comparison of the changes in glycated hemoglobin (HbA1c) levels, body mass index and blood pressure between subjects in the exercise program and the nonrandomized controls. The controls were selected from the same pool of company workers who took the annual health check in the same season (month) and who were matched according to their HbA1c levels. This analysis was performed to verify that the decrease in the HbA1c levels of the active subjects was not an artefact of seasonal fluctuation. *p<0.05 between study subjects and controls, as determined by an ANOVA. ANOVA: analysis of variance**

study subjects to those of the controls. After 6 months, the exercise program group showed decreased HbA1c levels (delta; -0.16±0.10%), while the controls showed increased HbA1c levels (delta; 0.10±0.06%), with the difference in the delta HbA1c levels between the two groups being statistically significant (p=0.004) (Fig. 4). However, we failed to detect decreases in BMI, SBP, and DBP (delta; 0.04±0.13 kg/m^2, 3.17±2.11 mmHg and 0.31±1.33 mmHg, respectively). In contrast these values decreased in the controls (delta: -0.16±0.08 kg/m^2, 0.56±1.12 mmHg and 0.60±0.85 mmHg, respectively); however, the differences were not statistically significant (Fig. 4).

Improvement of SHB with respect to regular physical exercise, healthy dietary habits, and smoking cessation

The distribution of SHB is shown in Fig. 5. The number (percentage) of subjects with pre-contemplation, contemplation, determination, action, and maintenance of SHB at baseline is shown in Table. At six months, the proportion of patients who exhibited these behaviors in relation to regular physical exercise was as follows: pre-contemplation, 0%; contemplation, 8.3%; determination, 25.0%; action, 12.5%; and maintenance, 54.2% (p=0.005). At six months, the proportions of each SHB with respect to healthy diet were as follows: pre-contemplation, 2.1%; contemplation, 4.3%; determination, 25.5%; action, 14.9%; and maintenance, 53.2% (p=0.013). In contrast, at six months, the proportions of each SHB with respect to smoking cessation were as follows: pre-contemplation, 14.0%; contemplation, 6.0%; determination, 4.0%; action, 2.0%, and maintenance, 74.0%, with no statistically significant differences (p=0.40).

Discussion

This study demonstrated that the 6-month self-management support program using a wearable monitoring system connected to the IoT and with the provision of remote health guidance by a public nurse via phone was effective for improving glycemic control in Japanese company workers with early T2DM. The program participants took increased numbers of daily steps, although their PASs did not increase to a statistically significant extent. The participants gained confidence regarding the efficacy of healthy lifestyle with increasing SHB. HbA1c levels are generally affected by seasonal variations, being lower in summer and higher in winter. However, with standard care, the HbA1c levels of the program participants decreased from summer to winter in comparison to the control subjects, whose levels followed the common seasonal variation.

In this study, we instructed the participants on aerobic exercise, with programs that were individually tailored based on their level of obesity and the daily activities were uploaded with the aim of safely increasing the amount of high-impact exercise that each subject performed. Although there have been various reports on the assessment of optimal exercise intensity for patients with diabetes, in most of these studies, complex interventions in diet and exercise were attempted, and exercise was often unsystematic (14). According to the recommendations of the ADA, adults with diabetes should perform at least 150 min/week of moderate intensity aerobic physical activity, spread over at least 3 days/week with no more than 2 consecutive days without exercise (8). This ADA-recommended exercise intensity may be considered to be the equivalent of 1,000 points in our original PAS, although direct conversion is difficult. In this case,

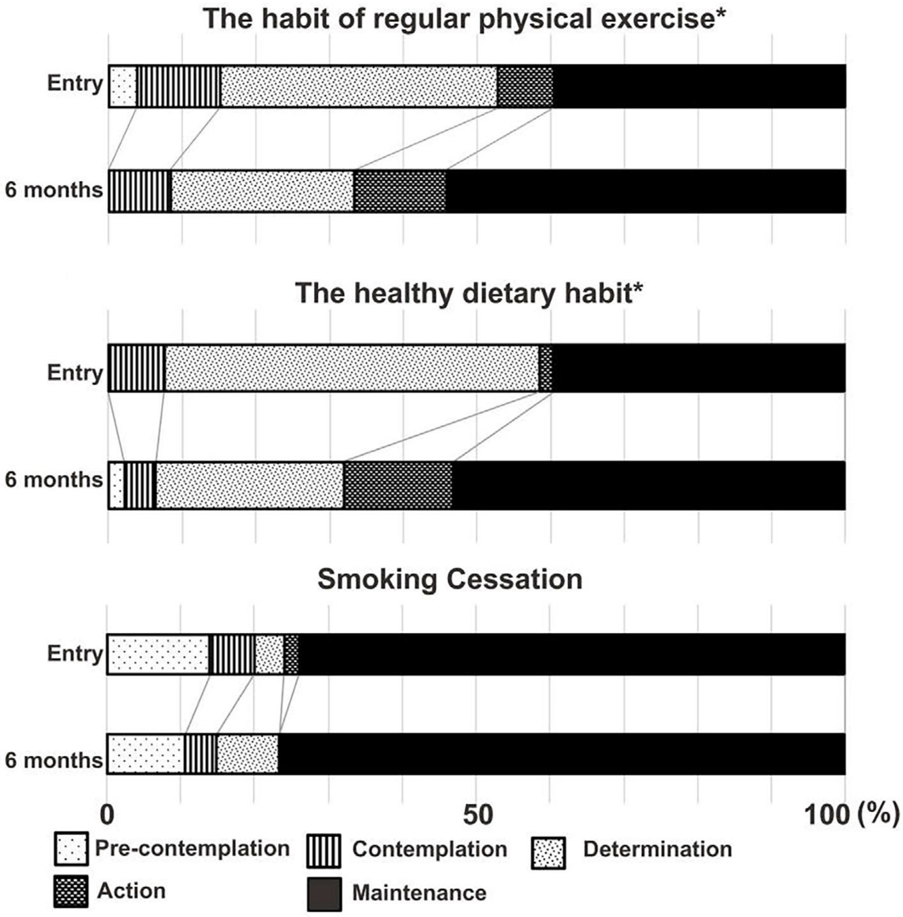

Figure 5. Changes in stage of health behavior with respect to regular physical exercise, healthy dietary habits, and smoking cessation. Stages of health behavior with respect to regular physical exercise and heathy dietary habits were significantly improved by the exercise intervention program. *p<0.05 between baseline and the end of this program, as determined by a Wilcoxon rank-sum test.

the PASs of the majority of our subjects were insufficient. In a meta-analysis, the performance of physical activity equivalent to the ADA recommendations reduced the risk of incident T2DM by 26%, and higher levels of physical activity further reduced the risk in comparison to inactive individuals (14). According to another meta-analysis that included 14 clinical trials involving patients already diagnosed with T2DM, exercising significantly reduced HbA1c levels by 0.66% in comparison to controls, although neither the exercise intensity (METs) nor the exercise volume (total MET hours) was associated with the degree of reduction in the HbA1c level (14). Interestingly, there were no significant differences in body weight loss between the exercise and control groups in this meta-analysis, and the authors hypothesized that the decrease in insulin resistance and increase in insulin disposal induced by exercise would be independent of body weight change (15). Moreover, sedentary behavior, which causes the exacerbation of postprandial glucose and insulin responses (16), may be a more noteworthy problem with respect to diabetes in company workers in modern society (17). In this study, we also demonstrated that even modest exercise interventions led to significant decreases in HbA1c levels, despite a lack of body weight loss, which points to the pleiotropic action of exercise, independent of energy expenditure. Liubaoerjijin et al. recently reported that higher-intensity exercise resulted in a greater reduction in HbA1c levels than lower-intensity exercise (18). Thus, if physical activity had been elevated to the recommended levels and the exercise program had been adhered to, better outcomes would have been expected.

One of the special characteristics of our program was the use of the wearable monitoring system connected to the IoT and the provision of remote health guidance by a public health nurse. Although each patient and medical staff member may recognize the importance of diet and exercise therapy for good control of T2DM, the majority of diet and physical activity interventions fail to foster consistently healthy lifestyles (9). Cradock et al. reviewed the main effective behavior modification techniques, namely "instruction on how to perform a behavior," "action planning," and "feedback and monitoring" (9). General physical activity advice alone was not associated with improved HbA1c levels, while structured exercise training regimens contributed to reducing HbA1c levels (19). In our study, "action planning" involved each subject starting to receive counselling from a public nurse about the start and goal of his/her exercise regime, according to his/her SHB, physical condition and clinical data. Self-management tools based on information and communication technology (ICT), such as personal computers and smartphones, might be available and useful (20). We provided a movie with commentary to instruct individuals on optimal exercise as "instruction on how to perform a behavior" via "MY PAGE." Regarding "feedback and monitoring," Jakicic et al. reported that-in comparison to standard care-the use of wearable technology monitoring energy expenditure and physical activity had no impact on weight loss in obese young adults (21). However, Ong et al. reported that a randomized control study of advanced chronic kidney disease using a smartphone and Bluetooth-enabled home BP monitoring gave the active group more confidence in self-management in comparison to the control group (22). In the study by Ong et al., both the subject and the public nurse could access daily uploaded data and discuss increasing or decreasing exercise intensity while the subjects had to manage this by themselves in the study by Jakcic et al. Our program had the benefit in that the medical staff supervised the subjects and provided encouraging advice. Since adherence to lifestyle changes is key to success in the treatment of T2DM (23), we believe that our programs would be useful for maintaining adherence, as well as economical, time-saving, practical, and effective.

The present study was associated with some limitations. First, the sample size was small and composed entirely of men; thus, the results could not be generalized. Moreover, because we provided only 6 months of observation, this timeframe may be insufficient to evaluate whether the participants had mastered the maintenance of a healthy lifestyle without reverting to old habits. Although there was no significant difference, the HbA1c values were aggravated after a significant decrease in the daily steps at the third month, and the meaningful increase in daily steps disappeared at the sixth month after the initiation of program. Continuity is important in lifestyle intervention; however, the long-term effects remained unclear. The observation period should have been at least one year to exclude influence of the seasonal variation. Furthermore, the study was single-armed and was not a randomized control study. Because the participants were all company workers at the same company, it was difficult for the health services of the company to assign any workers to the disadvantaged control group. Despite these limitations, we believe that this program demonstrated that the HbA1c levels of busy company workers were reduced by increasing physical activity, motivation and self-efficacy, and that these findings will be useful as an option of future diabetic therapy.

In conclusion, among middle-aged company workers, intensive lifestyle intervention using a wearable monitoring system connected to the IoT and the provision of remote health guidance resulted in improved diabetic control. Although further study is needed, encouraging physical activity with the use of monitoring devices and the provision of remote optimal advice may be a convincing, economical, and practical tool to help the self-management of patients with T2DM.

The authors state that they have no Conflict of Interest (COI).

Financial Support

This study was supported by the Ministry of Economy, Trade and Industry of Japan. Toyota Motor provided financial support for this study and for developing the health care system for promoting the health of their employees.

Acknowledgement

This study includes the following clinical research coordinators: Michiko Katagiri and Mieko Tori.

References

1. International Diabetes Federation. IDF Diabetes Altas. Brussels, 2015.
2. Japanese Ministry of Health LaW. Patient Survey. 2016.
3. Glechner A, Keuchel L, Affengruber L, et al. Effects of lifestyle changes on adults with prediabetes: a systematic review and meta-analysis. Prim Care Diabetes **12**: 393-408, 2018.
4. Hu FB, Manson JE, Stampfer MJ, et al. Diet, lifestyle, and the risk of type 2 diabetes mellitus in women. N Engl J Med **345**: 790-797, 2001.
5. Knowler WC, Barrett-Connor E, Fowler SE, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med **346**: 393-403, 2002.
6. Forhan M, Zagorski BM, Marzonlini S, Oh P, Alter DA. Predicting exercise adherence for patients with obesity and diabetes referred to a cardiac rehabilitation and secondary prevention program. Can J Diabetes **37**: 189-194, 2013.
7. Garcia-Perez LE, Alvarez M, Dilla T, Gil-Guillen V, Orozco-Beltran D. Adherence to therapies in patients with type 2 diabetes. Diabetes Ther **4**: 175-194, 2013.
8. Association AD. Foundations of care and comprehensive medical evaluation. Diabetes Care **39**: s23-s35, 2016.
9. Cradock KA, G OL, Finucane FM, Gainforth HL, Quinlan LR, Ginis KA. Behaviour change techniques targeting both diet and physical activity in type 2 diabetes: a systematic review and meta-analysis. Int J Behav Nutr Phys Act **14**: 18, 2017.
10. Schwingshackl L, Missbach B, Dias S, Konig J, Hoffmann G. Impact of different training modalities on glycaemic control and blood lipids in patients with type 2 diabetes: a systematic review and network meta-analysis. Diabetologia **57**: 1789-1797, 2014.
11. Lee SF, Pei D, Chi MJ, Jeng C. An investigation and comparison of the effectiveness of different exercise programmes in improving glucose metabolism and pancreatic beta cell function of type 2 diabetes patients. Int J Clin Pract **69**: 1159-1170, 2015.
12. Ruffino JS, Davies NA, Morris K, et al. Moderate-intensity exercise alters markers of alternative activation in circulating monocytes in females: a putative role for PPARgamma. Eur J Appl Physiol **116**: 1671-1682, 2016.
13. Safdar A, Saleem A, Tarnopolsky MA. The potential of endurance exercise-derived exosomes to treat metabolic diseases. Nat Rev Endocrinol **12**: 504-517, 2016.
14. Smith AD, Crippa A, Woodcock J, Brage S. Physical activity and incident type 2 diabetes mellitus: a systematic review and dose-response meta-analysis of prospective cohort studies. Diabetologia **59**: 2527-2545, 2016.
15. Boule NG, Haddad E, Kenny GP, Wells GA, Sigal RJ. Effects of exercise on glycemic control and body mass in type 2 diabetes mellitus: a meta-analysis of controlled clinical trials. JAMA **286**:

1218-1227, 2001.

16. Dunstan DW, Kingwell BA, Larsen R, et al. Breaking up prolonged sitting reduces postprandial glucose and insulin responses. Diabetes Care **35**: 976-983, 2012.
17. Wilmot EG, Edwardson CL, Achana FA, et al. Sedentary time in adults and the association with diabetes, cardiovascular disease and death: systematic review and meta-analysis. Diabetologia **55**: 2895-2905, 2012.
18. Liubaoerjijin Y, Terada T, Fletcher K, Boule NG. Effect of aerobic exercise intensity on glycemic control in type 2 diabetes: a meta-analysis of head-to-head randomized trials. Acta Diabetol **53**: 769-781, 2016.
19. Umpierre D, Ribeiro PA, Kramer CK, et al. Physical activity advice only or structured exercise training and association with HbA 1c levels in type 2 diabetes: a systematic review and meta-analysis. JAMA **305**: 1790-1799, 2011.
20. Shibuta T, Waki K, Tomizawa N, et al. Willingness of patients with diabetes to use an ICT-based self-management tool: a cross-sectional study. BMJ Open Diabetes Res Care **5**: e000322, 2017.
21. Jakicic JM, Davis KK, Rogers RJ, et al. Effect of wearable technology combined with a lifestyle intervention on long-term weight loss: the IDEA randomized clinical trial. JAMA **316**: 1161-1171, 2016.
22. Ong SW, Jassal SV, Miller JA, et al. Integrating a smartphone-based self-management system into usual care of advanced CKD. Clin J Am Soc Nephrol **11**: 1054-1062, 2016.
23. Tendas A, Sollazzo F, Niscola P, et al. Adherence to recommendation for chemotherapy-induced nausea and vomiting prophylaxis: the proposal of a score. Support Care Cancer **21**: 5-6, 2013.

Intern Med 59: 45-53, 2020