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ORIGINAL

Ipragliflozin effectively reduced visceral fat in Japanese patients with type 2 diabetes under adequate diet therapy

Chiho Yamamoto[1)], Hideaki Miyoshi[1)], Kota Ono[2)], Hajime Sugawara[1)], Reina Kameda[1)], Mei Ichiyama[1)], Kohei Yamamoto[1)], Hiroshi Nomoto[1)], Akinobu Nakamura[1)] and Tatsuya Atsumi[1)]

[1)] *Division of Rheumatology, Endocrinology and Nephrology, Hokkaido University Graduate School of Medicine, Sapporo 060-8638, Japan*
[2)] *Clinical Research and Medical Innovation Center, Hokkaido University Hospital, Sapporo 060-8648, Japan*

Abstract. To investigate if ipragliflozin, a novel sodium-glucose co-transporter 2 inhibitor, alters body composition and to identify variables associated with reductions in visceral adipose tissue in Japanese patients with type 2 diabetes mellitus. This prospective observational study enrolled Japanese participants with type 2 diabetes mellitus. Subjects were administered ipragliflozin (50 mg/day) once daily for 16 weeks. Body composition, visceral adipose tissue volume and plasma variables were measured at 0, 8, and 16-weeks. The subjects' lifestyle habits including diet and exercise were evaluated at baseline and 16 weeks. The primary endpoint was defined as the decrease of visceral adipose tissue mass. Twenty-four of 26 enrolled participants completed the study. The visceral adipose tissue decreased significantly (110 ± 33 to 101 ± 36 cm^2, $p = 0.005$) as well as other parameters for metabolic insufficiency including hemoglobin A1c. Seventy-one % of the total body weight reduction (-2.49 kg) was estimated by a decrease in fat mass (-1.77 kg), and the remaining reduction (22%) by water volume (-0.55 kg). A minor but significant reduction in the skeletal muscle index was also observed. Correlation analyses were performed to identify variables associated with changes in visceral adipose tissue and the only significant variable identified was diet therapy (Spearman's $r = -0.416$, $p = 0.043$). Ipragliflozin significantly decreased visceral adipose tissue, and improved parametres for metabolic dysfunction. Adequate diet therapy would be necessary to induce and enhance the therapeutic merit.

Key words: Diet therapy, Ipragliflozin, Visceral adipose tissue

THE BODY MASS INDEX (BMI) of Japanese patients with type 2 diabetes mellitus (T2DM) has been progressively increasing, with recent reports indicating that the current average BMI is now 25.0 kg/m^2 [1]. Although the average BMI of Asian patients with T2DM is apparently low, these patients characteristically tend to possess a large amount of visceral adipose tissue (VAT) [2], presumably leading to the increase of metabolic complications associated with their T2DM.

Sodium-glucose co-transporter 2 (SGLT2) inhibitors improve glycaemia and reduce body weight in patients with T2DM by enhancing urinary glucose excretion [3-5]. These characteristics are suitable for treatment strategy for obese patients. While the SGLT2-associated weight loss is mainly caused by a reduction of fat mass, reduced lean muscle mass due to an increase in compensatory gluconeogenesis has been assumed in response to increased glucose excretion. Accordingly, sarcopenia related with SGLT2 inhibitor administration has been one of the major concerns in daily clinical practice [6-8], as well as compensatory hyperphagia associated with increased glucose excretion [9-11].

Given the significantly lower average BMI of Asian patients with T2DM as compared to that found in Western populations, it is important to evaluate potential changes in body composition (VAT and lean mass) associated with SGLT2 inhibitor therapy in Asian people.

SGLT2 inhibitors are a class of oral anti-hyperglycemic drugs that were recently approved for use in Japan in 2014. To date, most of clinical information related to this therapeutic class have been available from evi-

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Correspondence to: Hideaki Miyoshi, M.D., Ph.D., Division of Rheumatology, Endocrinology and Nephrology, Hokkaido University Graduate School of Medicine, North 15, West 7, Kita-ku, Sapporo, 060-8638, Japan. E-mail: hmiyoshi@med.hokudai.ac.jp
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dence established by studies on the effects of dapagliflozin, canagliflozin, or empagliflozin in Western populations. Ipragliflozin (ASP1941; Astellas Pharma Inc. Tokyo, Japan and Kotobuki Pharmaceutical Co., Ltd, Nagano, Japan) is a novel and selective SGLT2 inhibitor, being one of the first C-aryl glycoside compounds. Ipragliflozin was designed to have better bioavailability compared to original O-glycoside molecules susceptible to glucosidase degradation [12].

The aim of the current study was to investigate changes in body composition resulting from administration of ipragliflozin in Japanese patients with T2DM, and to identify potential relationships with their lifestyle.

Materials and Methods

Participants

This study included patients with T2DM who were undergoing outpatient treatment at Hokkaido University Hospital from June 2014 to February 2015. Participants were given a detailed description of the study and were informed of possible risks and benefits of participation prior to providing their written informed consent and study enrollment. The inclusion criteria were as follows; all patients should be deemed suitable by a physician to receive ipragliflozin (between 20 and 75 years old, hemoglobin A1c (HbA1c) level above 7.0%, BMI above 22 kg/m^2 and estimated glomerular filtration rate (eGFR) above 45 mL/min). In addition, patients must have had stable blood pressure/lipid control and predicted to require no additional drugs during the study period. We excluded subjects with unstable diabetic retinopathy, serious hepatic dysfunction, renal failure, heart complications, those who were pregnant, lactating, or had a history of hypersensitivity to the ingredients of ipragliflozin. The study was approved by the Institutional Review Board of Hokkaido Hospital, and was carried out based on the Declaration of Helsinki.

Methods

This was a prospective observational study. After obtaining the subjects' informed consent, once daily ipragliflozin (50 mg/day) was given for 16 weeks according to the study protocol (Fig. 1). During the 16-week study period, changes of base-line medication use were not allowed with the exception of reducing sulfonylurea and insulin doses to prevent hypoglycemia. The subjects' lifestyle including diet and exercise were assessed at base-line and 16th week using a questionnaire with the modified check lists [13, 14] (Supplementary Table 1).

The primary endpoint of this study was defined as VAT change and body composition measured by two different bioelectrical impedance methods, a Dual Scan® (HDS 2000®, employing dual bioelectrical impedance analysis; Omron Healthcare Company, Limited) and an InBody 720® (InBody Company, Limited, employing the Direct Segmental Multi-frequency Bioelectrical Impedance Analysis Method). VAT and subcutaneous adipose tissue (SAT) were indicated by the area under the umbilical section. The body composition including fat mass, soft lean mass, body water was expressed by the systemic volume weight. The skeletal muscle index (SMI) was calculated from the limb muscle volume divided by height squared [15].

The secondary endpoints included changes of body weight, abdominal circumference, fasting plasma glu-

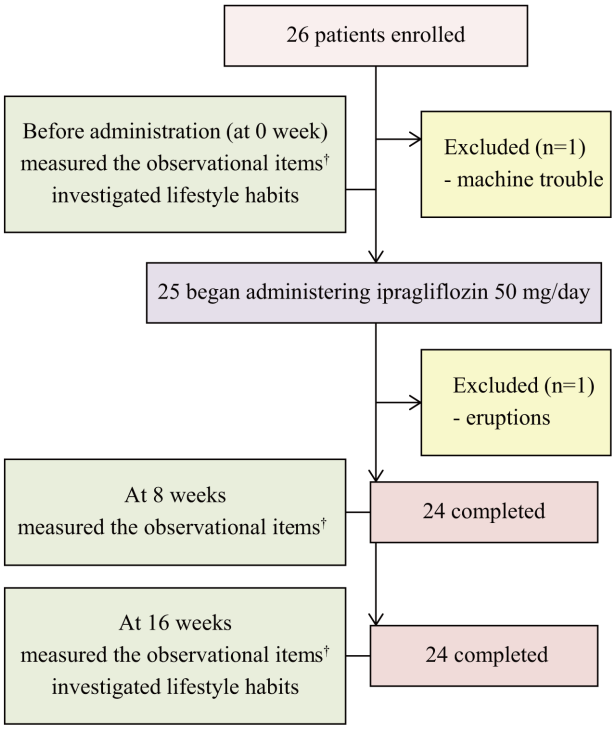

Fig. 1 Flow diagram
† Observational items; visceral adipose tissue and subcutaneous adipose tissue measured using a Dual Scan®: body mass measurements (body fat mass, body water, and lean mass), measured using an InBody 720®: fasting plasma glucose: hemoglobin A1c: weight: abdominal circumference: and changes in blood sample items such as metabolism and inflammatory markers.

cose, HbA1c, liver and renal function, ketone bodies, adipokines (adiponectin and leptin), the score for lifestyle assessment, and subanalysis of body composition. Data were collected following an overnight fast at baseline and 8th and 16th week of observation.

Statistical Analysis

Results were expressed as means ± SD or medians (25^{th}–75^{th} percentiles). Mean changes between baseline and post-treatment of parameters were analyzed descriptively as the secondary analyses. We employed repeated measure ANOVA with Dunnett's adjustment or Wilcoxon signed test between baseline and post-treatment of parameters. The relationship between change in VAT and other variables was assessed using Pearson's correlation coefficients or Spearman's rank correlation coefficients. A p-value < 0.05 was considered statistically significant. Data were analyzed using JMP Pro 12 (SAS Institute Japan, Tokyo, Japan).

Results

Participants' characteristics

A total of 26 patients with T2DM was enrolled in this study. Two individuals did not complete the protocol; one was failed to be evaluated at the base-line due to a mechanical trouble, and the other discontinued ipragliflozin due to eruptions. Twenty-four participants completed the full protocol (8 men and 16 women; Fig. 1) and were included in the statistical analyses. Among these 24 patients, the adverse side effects of ipragliflozin treatment, including genital or urinary tract infections, did not occur during the study period. Patient characteristics were as follows: age, 52.7 ± 11.9 years; morbidity period, 9.9 ± 4.9 years; HbA1c, 7.7 ± 0.7%; BMI, 28.9 ± 5.4 kg/m^2; and eGFR, 84.3 ± 23.8 mL/min. Prior to ipragliflozin administration, subjects were receiving sulfonylurea (n = 14), biguanide (n = 20), dipeptidyl peptidase-4 inhibitor (n = 17), α-glucosidase inhibitor (n = 5), thiazolidinedione (n = 5), glucagon-like peptide-1 receptor agonists (n = 3), and insulin (n = 2). According to the Japan diabetes society with information regarding the source of the recommendation, the sulfonylurea treatment was reduced for three patients and stopped for five who were taking a low dose of sulfonylurea at the time that the SGLT2 inhibitor treatment began. Similarly, insulin was reduced for one patient when SGLT2 inhibitor treatment was started and four patients during the study required further reductions of their insulin dose to prevent hypoglycemia.

Body weight was decreased significantly at the 16th week (75.6 ± 17.2 to 73.1 ± 17.3 kg, $p < 0.001$). Abdominal circumference was also decreased significantly. VAT, the primary endpoint, was significantly reduced at both week 8 and week 16 (from 110 ± 33 to 102 ± 36 and 101 ± 34 cm^2, respectively, $p = 0.005$) (Fig. 2). Although SAT was more variable individually than VAT, it was also significantly decreased at week 16 (262 ± 93 to 247 ± 94 cm^2, $p = 0.037$) (Table 1).

Total fat mass was significantly decreased by week 8 (27.9 ± 11.9 to 26.9 ± 11.8 kg, $p < 0.001$), and remained decreased at the final measurement (week 16) (26.2 ± 11.6 kg) (Table 1). Seventy-one percent of the final body weight reduction (-2.49 kg) was estimated by the decrease in fat mass (-1.77 kg) (Fig. 3). Body water was also decreased significantly at week 8 (35.1 ± 7.3 to 34.6 ± 7.2 kg, $p < 0.001$), without further change at week 16 (34.5 ± 7.4 kg) (Table 1). Lean mass was significantly reduced by week 8 (44.9 ± 9.4 to 44.3 ± 9.3 kg, $p < 0.001$) and remained similar at week 16 (44.3 ± 9.5 kg). A similar pattern of change was observed for the skeletal muscle index [15, 16] with a significant reduction at week 8 (7.5 ± 1.1 to 7.3 ± 1.2 kg/m^2, $p < 0.001$) but no further change at week 16 (7.3 ± 1.2 kg/m^2 at week 16) (Table 1). The majority of body

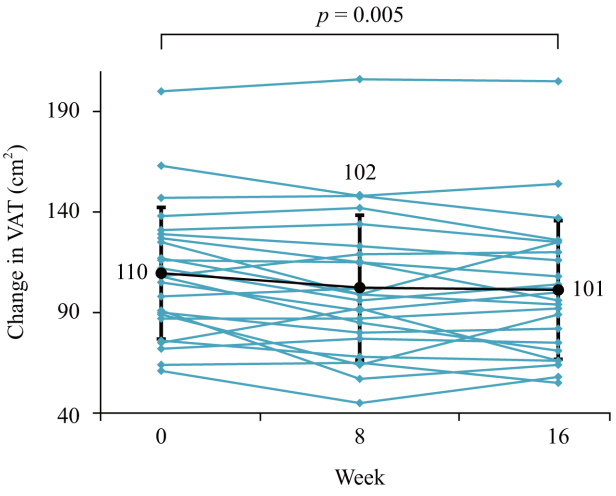

Fig. 2 Change in the VAT
VAT was indicated by the area under the umbilical section using a Dual Scan®. The data showed mean value of the VAT at 0, 8, and 16-weeks. VAT, visceral adipose tissue. p value: ANOVA Dunnet, 0 week *vs*. 16 weeks.

Table 1 The changes in various items of 24 participants from the administration of ipragliflozin

	Week 0	Week 8	*p* value W0 *vs*. 8	Week 16	*p* value W0 *vs*. 16
BW (kg)	75.6 ± 17.2 ††	73.8 ± 17.3 ††	<0.001	73.1 ± 17.3 ††	<0.001
AC (cm)	99 ± 11 ††	97 ± 11 ††	0.020	96 ± 10 ††	0.002
Body composition					
Body fat mass (kg)	27.9 ± 11.9 ††	26.9 ± 11.8 ††	0.001	26.2 ± 11.6 ††	<0.001
VAT (cm^2)	110 ± 33 ††	102 ± 36 ††	0.016	101 ± 34 ††	0.005
SAT (cm^2)	262 ± 93 ††	257 ± 94 ††	0.601	247 ± 94 ††	0.037
Body water (kg)	35.1 ± 7.3 ††	34.6 ± 7.2 ††	0.001	34.5 ± 7.4 ††	<0.001
Protein (kg)	9.3 ± 2.0 ††	9.2 ± 2.0 ††	<0.001	9.2 ± 2.0 ††	0.001
Soft lean mass (kg)	44.9 ± 9.4 ††	44.3 ± 9.3 ††	0.001	44.3 ± 9.5 ††	<0.001
SMI (kg/m^2)	7.5 ± 1.1 ††	7.3 ± 1.2 ††	<0.001	7.3 ± 1.2 ††	<0.001
Mineral (kg)	3.2 ± 0.6 ††	3.2 ± 0.6 ††	0.090	3.2 ± 0.6 ††	0.041
FPG (mg/dL)	162 ± 34 ††	142 ± 31 ††	0.003	141 ± 33 ††	0.002
HbA1c (%)	7.7 ± 0.7 ††	7.2 ± 0.5 ††	<0.001	7.3 ± 0.5 ††	0.002
UA (mg/dL)	5.6 ± 1.2 ††	4.8 ± 1.4 ††	<0.001	4.9 ± 1.2 ††	<0.001
AST (U/L)	34 ± 17 ††	31 ± 18 ††	0.466	31 ± 16 ††	0.498
ALT (U/L)	44 ± 27 ††	40 ± 30 ††	0.232	36 ± 24 ††	0.020
HOMA-IR	3.6 ± 1.5 ††	2.6 ± 1.3 ††	0.001	2.4 ± 1.0 ††	<0.001
Ht (%)	41 ± 6 ††	42 ± 7 ††	0.472	44 ± 4 ††	0.006
eGFR (mL/min)	87 ± 26 ††	82 ± 25 ††	0.078	84 ± 24 ††	0.462
Total ketone body (μmol/L)	102 ± 71 ††	199 ± 186 ††	0.172	247 ± 323 ††	0.030
Acetoacetic acid (μmol/L)	24 ± 14 ††	47 ± 47 ††	0.085	47 ± 53 ††	0.075
β-hydroxybutyric acid (μmol/L)	77 ± 59 ††	153 ± 140 ††	0.209	198 ± 272 ††	0.028
FFA (μEq/L)	539 ± 185 ††	595 ± 176 ††	0.351	606 ± 213 ††	0.236
Pyruvic acid (mg/dL)	0.6 ± 0.4 ††	0.4 ± 0.3 ††	0.733	0.7 ± 1.4 ††	0.970
Lactic acid (mg/dL)	11.0 ± 4.0 ††	10.8 ± 5.4 ††	0.982	10.7 ± 5.0 ††	0.962
Leptin (ng/mL)	18 ± 16 ††	18 ± 15 ††	0.373	15 ± 11 ††	0.320
Adiponectin (μg/mL)	3.3 ± 1.1 ††	3.2 ± 2.1 ††	0.541	3.4 ± 2.5 ††	0.809
Lifestyle score					
Total score	22 (16-24) ‖	-	-	24 (19-25) ‖	0.332 ‡
Diet score	17 (13-19) ‖	-	-	18 (15-19) ‖	0.459 ‡
Exercise score	4 (3-8) ‖	-	-	6 (4-8) ‖	0.398 ‡

Data are †† mean ± standard deviation or ‖medians (25^{th}–75^{th} percentiles) where indicated. BW, body weight; AC, abdominal circumference; VAT, visceral adipose tissue; SAT, subcutaneous adipose tissue; SMI, skeletal muscle index; FPG, fasting plasma glucose; HbA1c, hemoglobin A1c; UA, uric acid; AST, aspartate amino transferase; ALT, alanine amino transferase; HOMA-IR, homeostasis model assessment of insulin resistance; Ht, Hematocrit; eGFR, estimated glomerular filtration rate; FFA, free fatty acid. *p* value: ANOVA with Dunnett's adjustment. ‡ Wilcoxon rank sum test.

weight reduction was due to loss of fat mass (71%, -1.77 ± 1.84 kg), with the remainder (22%) coming from water volume (-0.55 ± 0.80 kg). A minor but significant reduction in protein and mineral content was also observed (-0.14 ± 0.21 kg and -0.03 ± 0.08 kg, respectively) (Fig. 3).

The subjects' lifestyle was evaluated using a questionnaire before and after the study. The mean total lifestyle scores did not differ significantly between baseline and the end of the study. When the individual category scores were analyzed to assess diet and exercise separately, there were still no significant differences.

For better understanding the mechanism behind the VAT changes observed with ipragliflozin, we exam-

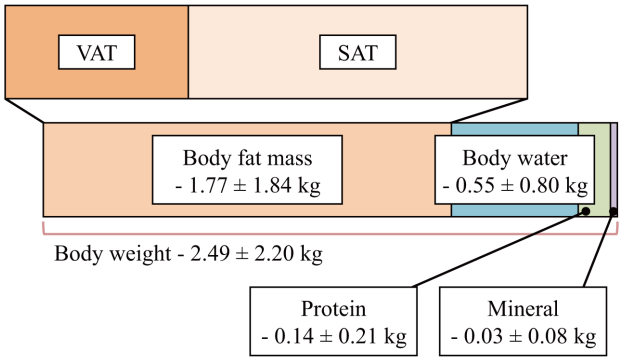

Fig. 3 The composition of body weight reduction following administration of ipragliflozin for 16 weeks. These were measured by two different bioelectrical impedance methods, Dual Scan® and InBody 720®. The body composition including fat mass, soft lean mass, body water was expressed by the systemic volume weight. VAT and SAT were indicated by the ratio from the results of area under the umbilical section. VAT, visceral adipose tissue; SAT, subcutaneous adipose tissues. The data showed mean ± standard deviation.

Table 2 The relationship between changes in VAT (%) and various items

	r	*p*
0W		
Age (years)	-0.136 §	0.527 §
Duration of disease (years)	-8.327 §	0.397 §
HbA1c (%)	-0.244 §	0.242 §
BMI (kg/m^2)	0.208 §	0.329 §
AC (cm)	0.146 §	0.495 §
eGFR (mL/min)	-0.029 §	0.894 §
HOMA-IR	0.367 §	0.078 §
VAT (cm^2)	0.065 §	0.763 §
Diet score	-0.097 ¶	0.829 ¶
Exercise score	0.053 ¶	0.888 ¶
16W		
HbA1c (%)	-0.157 §	0.464 §
BMI (kg/m^2)	0.314 §	0.135 §
AC (cm)	0.276 §	0.191 §
HOMA-IR	0.403 §	0.051 §
Diet score	-0.416 ¶	0.043 ¶
Exercise score	0.004 ¶	0.735 ¶

HbA1c, hemoglobin A1c; BMI, body mass index; AC, abdominal circumference; eGFR, estimated glomerular filtration rate; HOMA-IR, homeostasis model assessment of insulin resistance; VAT, visceral adipose tissue. § Pearson's correlation coefficient. ¶ Spearman's rank correlation coefficient.

ined the correlation between changes in VAT (%) and a number of other measured parameters. The week 16 diet therapy scores were the only variable identified to have a significant correlation with change in VAT (Spearman's r = -0.416, p = 0.043) (Table 2, Fig. 4). There was no correlation between the change in HbA1c and in visceral fat. The correlation coefficients for the other variables were listed in Table 2. Although the levels of fasting plasma glucose and HbA1c decreased significantly over the study period, these changes were not associated with the changes in diet score during the study or the diet score at 16 weeks.

Alanine aminotransferase levels and uric acid values also decreased significantly. There was a significant improvement in the homeostasis model assessment of insulin resistance (HOMA-IR) in the 22 subjects without using insulin. Although hematocrit levels arose significantly, eGFR remained unchanged. Total ketone body and β-hydroxybutyric acid levels increased significantly, but acetoacetic acid levels showed no clear changes (Table 1).

Discussion

In this study, we showed three novel findings. First, we demonstrated that an SGLT2 inhibitor reduces VAT in relatively lean Asian people with T2DM. Second, this reduction was predominantly due to a loss of fat mass, accompanied by a minor but significant decrease

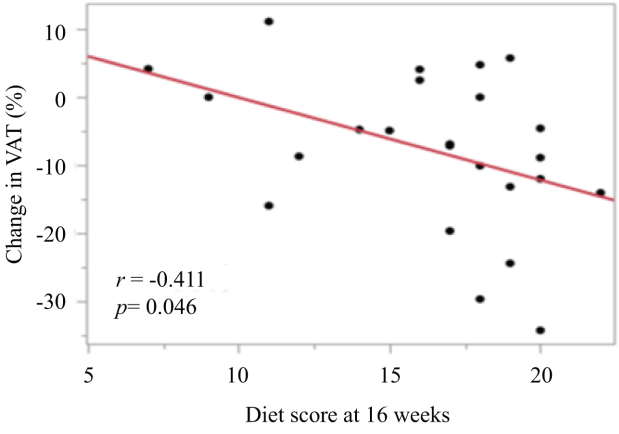

Fig. 4 Significant correlation between diet therapy and VAT. The week 16 diet therapy scores were the only variable identified to have a significant correlation with change in VAT among a number of other measured parameters. VAT, visceral adipose tissue.

in lean mass. Third, we showed that adequate diet therapy was the most important factor correlated with the SGLT2 inhibitor-associated reduction in VAT.

Although the body weight reduction associated with the administration of SGLT2 inhibitors has been widely recognised in clinical practice, it has been obscure how body composition is affected with this weight loss. Recently two studies published, showing body composition changes associated with dapagliflozin or canagliflozin use in Caucasians with an average of BMI greater than 30 kg/m^2 (32.1 kg/m^2 and 31.2 kg/m^2) [6, 7]. The results from these studies were very similar that approximately two-thirds of the reduction in body weight was from fat mass while the remaining third was due to loss of lean mass [6, 7]. However, those data did not provide any information on body composition changes in more lean Asian population on the SGLT2 inhibitor. In this population, there has been a major concern regarding lean mass decrease leading to sarcopenia. In the current study, the average BMI of participants was 28.9 kg/m^2, largely lower than that in the Caucasian studies. After 16 weeks of ipragliflozin treatment, 71% of the body weight loss (2.49 kg) was due to a reduction in fat mass, which is comparable to the previous studies described above (75% and 61%, respectively). This is the first study to investigate the effects of ipragliflozin on VAT area in an Asian population. Our data demonstrate that the observed decrease in fat mass was associated with an 8.2% reduction in VAT area, which is also comparable the results reported in Caucasian populations (-13.7% by 10 mg dapagliflozin for 24 weeks [7], and -8.1% by 300 mg canagliflozin for 52 weeks) [6].

A reduction in VAT increases insulin sensitivity and improves metabolic dysfunction. A 3% reduction in body weight has been shown to be the minimum requirement to improve metabolic disorders in obese and overweight people in Japan [17]. In this study, administration of ipragliflozin for 16 weeks resulted in a 3.3% reduction in body weight and an 8.2% decrease in VAT. However, improvements in a number of metabolic endpoints were already apparent after 8 weeks of treatment when body weight and VAT were reduced by 2.4 and 7.3%, respectively (Table 1).

In this study, we observed a significant decrease in lean mass. However, the lean mass calculation performed by InBody 720® combines body water, protein, and mineral content with bone components excluded [18, 19], probably implying that loss of body water would be reflected as a decrease in lean mass even if the protein or mineral fractions are not dramatically altered. This is a limitation associated with dual-energy x-ray absorptiometry (DXA) or impedance methods for assessing body composition. Future evaluations of the effects of SGLT2 inhibitors on body composition should not only assess muscle volume but also muscle quality, using methods such as an evaluation of grip strength or gait tests [20]. The initial reductions in lean mass and skeletal muscle index observed at week 8 did not advance by week 16. Change in body water followed a similar pattern suggesting the muscle related changes observed in this study were greatly affected by changes in body water content.

A couple of recent studies using rodents revealed that compensatory hyperphagia occurs following administration of SGLT2 inhibitors [9, 10]. In humans SGLT2 inhibitors cause substantially less weight loss than expected from the energy excreted *via* glycosuria in human. Very recently, Ferrannini *et al*. [11] reported in a human study that increased glycosuria would elicit an adaptive increase in energy intake and therefore combining SGLT2 inhibition with caloric restriction would be expected to be associated with major weight loss. In this study we showed for the first time a correlation between diet therapy and VAT reduction with an SGLT2 inhibitor therapy (Table 2, Fig. 4). We suggest that adequate diet therapy is the most important and the most useful to elicit the benefit of SGLT2 inhibitors in order to reduce VAT. We observed a reduction in VAT in patients who adhered to an appropriate diet before and throughout the study, and in those whose diet score improved during the study even if their score was bad at the start (data not shown). These results suggest that the compensatory hyperphagia caused by SGLT2 inhibitors may reduce the beneficial effects of SGLT2 inhibitors on VAT; to achieve a reduction in VAT it may be necessary to overcome the compensatory hyperphagia associated with SGLT2 use. Ferrannini *et al.* [11] suggested that increased calorie intake was inversely related to baseline BMI and positively to baseline eGFR. However, there was no correlation between those factors and the VAT change observed in the current study.

The lack of a comparator is a major limitation in this observational study. As previously discussed, the use of impedance methods does not provide a means to measure actual protein volume or assess the quality of muscle. Small sample size and the short dura-

tion are other potential limitations of the current study. However, power calculations determined that the number of patients included in this study was sufficient for an exploratory observational study in clinical practice. Additional studies using a larger sample size and more sophisticated methods for assessing muscle volume and quality will be required to confirm and extend our current findings.

In conclusion, ipragliflozin significantly decreased VAT, and improved metabolic diseases in Japanese with type 2 diabetes. Adequate diet therapy would be necessary to induce and enhance its therapeutic merit.

Acknowledgements

C.Y. contributed to the data analysis and wrote the manuscript. H.M. designed and performed the research, and wrote the manuscript. K.O. contributed to the statistical analysis. H.M., H.S., R.K., M.I., K.Y., H.N., A.N. and T.A. contributed to discussion, reviewed and edited the manuscript.

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Disclosure Statement

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H.M. has received honoraria for lectures from Astellas Pharma Inc., AstraZeneca, Dainippon Pharma Co, Eli Lilly, Kissei, Mitsubishi Tanabe Pharma Co., MSD, Novartis Pharma, Novo Nordisk Pharma and Sanofi; and received research funding from Astellas Pharma Inc., AstraZeneca, Daiichi Sankyo, Eli Lilly, Mitsubishi Tanabe Pharma Co., MSD, Novo Nordisk Pharma, Sanofi, Takeda Pharmaceutical Co., Ltd. and Taisho Toyama Pahrmaceutical Co., Ltd.

A.N. has received honoraria for lectures from Sanofi.

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C.Y., K.O., H.S., R.K., M.I., K.Y. and H.N. declare no conflict of interest.

Supplementary Table 1 Questionnaire about the lifestyle

Question		
Answer	:	Point
Diet		
1. Do you skip your ordinary meal (for example, skip breakfast, etc.)?		
Never	:	3 points
1-3 times in a week	:	2 points
4-6 times in a week	:	1 point
Almost every day	:	0 point
2. Do you eat your dinner later than 9 PM?		
Never	:	3 points
1-3 times in a week	:	2 points
4-6 times in a week	:	1 point
Almost every day	:	0 point
3. Are you taking care of the amount and content of your meal (for example, cutting down total energy, sugar, or oil. eating a lot of vegetables, etc.)?		
Almost kept it	:	6 points
Occasionally not keep it	:	4 points
Often not keep it	:	2 points
Not careful	:	0 point
4. Do you have a snack between meals?		
Never	:	3 points
1-3 times in a week	:	2 points
4-6 times in a week	:	1 point
Almost every day	:	0 point
5. Do you eat out in the evening?		
Never	:	3 points
1-3 times in a week	:	2 points
4-6 times in a week	:	1 point
Almost every day	:	0 point
6. Do you drink alcohol?		
Never	:	3 points
1-3 times in a week	:	2 points
4-6 times in a week	:	1 point
Almost every day	:	0 point
7. How much is the speed of the meal?		
Slowly	:	2 points
Average	:	1 point
Speedy	:	0 point
8. Do you eat until full?		
Never	:	3 points
Sometimes	:	2 points
Frequently	:	1 point
Always	:	0 point
Exercise		
9. How often do you exercise a week?		
Every day	:	6 points
4 to 6 days	:	4 points
1 to 3 day(s)	:	2 points
Never	:	0 point
10. How long do you exercise a day?		
More than 1 hour	:	6 points
Within 1 hour more than 30 minutes	:	4 points
Within 30 minutes	:	2 points
Never (who answered ‘never’ in question 8)	:	0 point

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