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# Effect of weight loss on circulating fatty acid profiles in overweight subjects with high visceral fat area: a 12-week randomized controlled trial

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## Abstract

**Background:** Significant associations between visceral fat and alterations in plasma fatty acids have been identified in overweight individuals. However, there are scant data regarding the relationships of the visceral fat area (VFA) with the plasma fatty acid profiles and desaturase activities following weight loss. We investigated the effect of weight loss with mild calorie restriction on the circulating fatty acid profiles and desaturase activities in nondiabetic overweight subjects with high VFA.

**Methods:** Eighty overweight subjects with high VFA (L4 VFA  $\geq 100$  cm<sup>2</sup>) were randomized into the 12-week mild-calorie-restriction (300 kcal/day) or control groups.

**Results:** Comparison of the percent of body weight changes between groups revealed that the weight-loss group had greater reductions in body weight. The VFA decreased by 17.7 cm<sup>2</sup> from baseline in the weight-loss group ( $P < 0.001$ ). At follow-up, the weight-loss group showed greater reductions in serum triglycerides, insulin, and HOMA-IR than the control group. Significantly greater reductions in total saturated fatty acids, palmitic acid, stearic acid, total monounsaturated fatty acids, palmitoleic acid, oleic acid, eicosadienoic acid, and dihomo- $\gamma$ -linolenic acid levels were detected in the weight-loss group compared with the control group after adjusting for baseline values. Following weight loss, C16  $\Delta 9$ -desaturase activity was significantly decreased and  $\Delta 5$ -desaturase activity was significantly increased, and the changes were greater in the weight-loss group than in the control group.

**Conclusions:** The results suggest that mild weight loss improves abdominal obesity, overall fatty acid profiles, and desaturase activities; therefore, mild calorie restriction has potential health benefits related to obesity-related diseases in overweight subjects with high VFA.

**Trial registration:** NCT02992639. Retrospectively registered 11 December 2016.

**Keywords:** Fatty acid, Fatty acid desaturase, Visceral fat, Weight loss, Obesity-related disease

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## Background

A visceral fat area (VFA) cutoff of 100 cm<sup>2</sup> was established to predict the risk of obesity-related health risks, including insulin resistance (IR), metabolic syndrome, and diabetes, in Asian populations [1]. Compared with abdominal subcutaneous fat, visceral fat is more metabolically active in the fasting state [2, 3]. Compared with other weight-loss methods, calorie restriction tends to reduce more visceral than subcutaneous adipose tissue [4]. It is known that plasma fatty acid composition mirrors not only dietary fatty acid composition but also endogenous fatty acid synthesis, in which desaturases play important roles [5]. In endogenous fatty acid synthesis, C16  $\Delta$ 9-desaturase (C16:1/C16:0) activity is known to be high in conditions of diabetes and abdominal obesity. Additionally, an inverse relation between  $\Delta$ 5-desaturase activity (C20:4, n-6/C20:3, n-6) and diabetes risk and a direct relation between  $\Delta$ 6-desaturase activity (C18:3, n-6/C18:2, n-6) and IR have been reported. Pan et al. [6] reported that obesity is related to increased  $\Delta$ 9-desaturase activity and reduced  $\Delta$ 5-desaturase activity. Several previous studies observed that low  $\Delta$ 5-desaturase activity is linked to increased risk of type 2 diabetes and insulin resistance among Japanese adults [7, 8]. Zhao et al. [9] also noted that  $\Delta$ 5-desaturase activity is inversely associated with metabolic abnormalities among obese Chinese subjects. In a Swedish study,  $\Delta$ 5-desaturase activity was found to be inversely associated with obesity and insulin resistance, whereas  $\Delta$ 6-desaturase activity demonstrated positive associations [10].

Significant associations between visceral fat amount and alterations in serum fatty acids have been identified in overweight individuals [11]. However, there are scant data regarding the relations between changes in VFA and changes in circulating fatty acid profiles and desaturase activities following weight loss. Research is required to determine the amount of visceral fat reduction with calorie restriction that is necessary to induce favorable metabolic changes in the overall fatty acid profile. Therefore, in this study, we investigated the effects of weight loss with mild calorie restriction (a 300 kcal/day intake reduction) on circulating fatty acid profiles and desaturase activities in nondiabetic overweight subjects with high VFA [VFA at the 4th lumbar vertebrae (L4 VFA)  $\geq$  100 cm<sup>2</sup>].

## Methods

### Study subjects

Study subjects were recruited through advertisements posted in Seoul. Based on the data screened by the Clinical Nutrition Lab, Yonsei University, overweight subjects [25.0 kg/m<sup>2</sup>  $\leq$  body mass index (BMI) < 30 kg/m<sup>2</sup>] were referred to the Department of Internal Medicine, Yonsei University Severance Hospital. After their health and basic blood tests, including serum glucose, were rechecked,

individuals who met the study criteria were recommended for study participation. The inclusion criteria were as follows: age between 20 and 60 years; absence of pregnancy or breastfeeding; stable body weight (body weight change < 1 kg in the 3 months before screening); BMI between 25 and 30 kg/m<sup>2</sup>; high L4 VFA (L4 VFA  $\geq$  100 cm<sup>2</sup>); absence of hypertension, type 2 diabetes, cardiovascular disease, and thyroid disease; and no use of medication affecting body weight, energy expenditure, or glucose control for 6 months prior to screening. Subjects were excluded if they had a history of Cushing syndrome, malignancy, or liver disease, including chronic viral hepatitis, autoimmune hepatitis, primary biliary cirrhosis, and drug-induced liver disease. Male and female subjects whose alcohol consumption was > 40 and > 20 g/day, respectively, and subjects with a history of intentional weight reduction in the 6 months before the current study were excluded. Finally, those who consented to participate in the program were included in this study. The purpose of the study was carefully explained to all participants, and written consent was obtained prior to their participation. The protocol was approved by the Institutional Review Board of Yonsei University and Yonsei University Severance Hospital in accordance with the Helsinki Declaration.

### Study design and intervention

The basic framework of the present study was based on a previous study [12]. A 12-week, placebo-controlled, randomized study was conducted with 80 high VFA, nondiabetic overweight subjects (L4 VFA  $\geq$  100 cm<sup>2</sup>). Subjects were divided into two groups: a weight-loss group with 12 weeks of mild calorie restriction (a 300 kcal/day intake reduction) or a control group with no treatment (NCT02992639; <http://www.clinicaltrials.gov/>). Randomization was achieved by computer-generated block randomization (placebo:test = 1:1).

### Protocol for weight loss

The subjects in the weight-loss group followed a 12-week weight-loss program comprising a 300 kcal/day reduction of their usual caloric intake. Basically, the subjects were instructed to remove 1/3 of a bowl of rice (approximately 100 kcal; a bowl of rice is approximately 300 kcal per meal, according to the food composition table from the Rural Development Administration of Korea [13]) from one meal a day for easier application of the 300 kcal/day deficit. Moreover, based on each subject's reported food intake, an individualized and nutritionally balanced diet plan was produced by a trained nutritionist to achieve the goal of losing a minimum of 3% of initial body weight. The instructions included food choices, cooking methods, reductions in snack consumption frequency, low-calorie substitutions for high-calorie foods, low-fat foods, and limitations on simple sugar consumption. The subjects in the

control group were instructed to maintain their usual dietary and physical activity habits during the study period.

#### Daily energy intake and physical activity measurements

At baseline, the subjects' usual dietary intakes were assessed via 24-h recall and semiquantitative food frequency questionnaires completed with the nutritionist's assistance. In addition, a standardized 3-day dietary record was obtained from each participant at week 6 and 12. These records were completed at home following detailed instructions from the nutritionist. A computerized version of the Korean Nutrition File (Can-Pro 3.0; The Korean Nutrition Society, Seoul, Korea) was used to determine the macronutrient contents of foods and total daily energy intakes. On the same days as the dietary records, 3-day physical activity records were completed at home. The total energy expenditure (TEE) (kcal/day) was calculated from activity patterns, including the basal metabolic rate (BMR), physical activity for 24 h, and the specific dynamic action of food. Each subject's BMR was calculated using the Harris-Benedict equation.

#### Anthropometric parameters and body composition measurements

Detailed information was previously published [14]. Briefly, all data were acquired at baseline and week 12. Body weight (Inbody370; Biospace, Cheonan, Korea), height, waist circumference, and blood pressure (BP) were measured. BMI was calculated in units of kilogram per square meter ( $\text{kg}/\text{m}^2$ ). The abdominal fat distribution was measured at L4 by computed tomography (CT). The scanning parameters were a slice thickness of 1 mm at 200 mA and 120 kVp, with a 48-cm field of view. Abdominal adipose tissue was determined using the attenuation range from  $-150$  to  $-50$  Hounsfield units in the CT images. The body composition of the study participants was measured via dual-energy X-ray absorptiometry (DEXA) to determine the fat percentage, fat mass, and lean body mass.

#### Blood collection and biochemical assessments

Details were provided previously [14]. Blood samples were collected after an overnight fast of at least 12 h. Venous blood specimens were collected in EDTA-treated tubes and serum tubes. The blood samples were centrifuged to obtain plasma and serum samples, which were then stored at  $-70$  °C. The levels of serum-fasting glucose, insulin, triglycerides (TGs), total cholesterol, and high-density lipoprotein (HDL) cholesterol were measured [15]. The IR and low-density lipoprotein (LDL) cholesterol levels were calculated using the equations of homeostatic model assessment (HOMA) and the Friedewald formula, respectively:  $\text{HOMA-IR} = [\text{fasting insulin } (\mu\text{IU}/\text{mL}) \times \text{fasting glucose } (\text{mg}/\text{dL})]/405$ ;

Friedewald formula:  $\text{LDL cholesterol} = \text{total cholesterol} - [\text{HDL cholesterol} + (\text{TG}/5)]$ .

#### Metabolite extraction and gas chromatography–mass spectrometry (GC-MS) analysis

The details of the GC-MS procedure have been previously published [16]. Briefly, plasma samples (100  $\mu\text{L}$ ) were placed into PTEE screw-capped Pyrex tubes. An internal standard compound containing heptadecanoic acid (500  $\mu\text{L}$ , 25 ppm in n-hexane) and methanol (2 mL) were added to the samples. After vortexing, acetyl chloride (100  $\mu\text{L}$ ) was added slowly, and the tubes were then heated at 95 °C for 1 h. After cooling on ice, 6% potassium carbonate (5 mL) was added to the tubes. The tubes were centrifuged (4 °C, 3000 rpm, 5 min), and the clear n-hexane top layer (100  $\mu\text{L}$ ), including the fatty acid methyl esters (FAME), was then transferred into a vial prior to GC-MS analysis.

GC-MS analyses were performed on an Agilent Technologies 7890 N gas chromatograph coupled with an Agilent Technologies 5977A quadrupole mass selective spectrometer with a triple-axis detector (Agilent, Palo Alto, CA, USA) in the electron ionization (70 eV) and full scan monitoring ( $m/z$  50–800) modes. The injection volume of the samples was 1  $\mu\text{L}$  in the splitless mode. The fatty acid methyl esters of all samples were separated on a VF-WAX column (Agilent Technologies, Middelburg, Netherlands) with helium as a carrier gas. The temperature program was as follows: (1) initial temperature of 50 °C for 2.3 min, (2) increase to 175 °C at 50 °C/min, and (3) increase to 230 °C at 2 °C/min. The metabolites in the samples were identified by comparing their relative retention times and mass spectra with those of authentic reference standards. The relative levels of metabolites were calculated by comparing their peak areas to those of the internal standard compound.

#### Statistical analysis

The statistical analyses were conducted with SPSS version 23.0 software (IBM/SPSS, Chicago, IL, USA). Skewed variables were logarithmically transformed. An independent *t*-test compared continuous variables between the control and weight-loss groups. A paired *t*-test was used to compare continuous variables at baseline and follow-up within each group. For the comparison of categorical variables, a chi-squared test was conducted. A general linear model test was performed to adjust the baseline values of the changed values. A Pearson's correlation coefficient was used to examine the relations among variables. A heat map was created using Multiple Experiment Viewer (MeV) version 4.9.0 (<http://www.tm4.org/>) to visualize and evaluate the relations among variables in the study population. The results are

expressed as the mean  $\pm$  standard error (SE). A two-tailed  $P < 0.05$  was considered statistically significant.

## Results

The dropout rate was less than 10% in the control ( $n = 2$ ) and weight-loss ( $n = 3$ ) groups. Participants were excluded for personal reasons ( $n = 4$ ) and lack of a blood sample for GC-MS analysis ( $n = 1$ ).

### Effects of mild calorie restriction on clinical and biochemical characteristics at baseline and follow-up

The age, sex distribution, smoking, and drinking did not significantly differ between the two groups (Table 1). At baseline, no significant differences were observed in all clinical and biochemical parameters between the control and weight-loss groups; after the 12-week intervention, the BMI, serum insulin levels, HOMA-IR score, and serum TG levels were significantly decreased in the weight-loss group compared with the control group (Table 1). In the control group, the subjects showed slight but significant weight gain (weight and BMI; all  $P < 0.001$ ) during the intervention, whereas the subjects in the weight-loss group showed significant reductions in not only the weight and BMI (both  $P < 0.001$ ) but also the waist circumference ( $P < 0.001$ ), systolic BP ( $P = 0.049$ ), insulin levels ( $P = 0.001$ ), and HOMA-IR score ( $P = 0.003$ ) following the intervention (Table 1). In addition, these reductions in weight, BMI, and waist circumference in the weight-loss group were greater than those in the control group after adjusting for the baseline values (all  $P < 0.001$ ) (Table 1). The serum insulin levels, HOMA-IR score, and serum TG levels also showed significantly greater decreases in the weight-loss group than in the control group after adjusting for the baseline values ( $P = 0.020$ ,  $P = 0.034$ , and  $P = 0.022$ , respectively) (Table 1). The estimated TEE ( $2144.6 \pm 45.3$  kcal/d vs.  $2201.3 \pm 59.3$  kcal/d;  $P = 0.519$ ), total calorie intake (TCI) ( $2105.8 \pm 40.0$  kcal/d vs.  $2200.5 \pm 50.3$  kcal/d;  $P = 0.159$ ), and percentage of macronutrient intakes (%CHO:%PRO:%FAT = 61:15:22 in both groups) did not significantly differ between the two groups at baseline (data not shown). The subjects' overall compliance with the weight-loss plan was good. The estimated TCI of the weight-loss group at 12-week follow-up was, on average, 1949.4 kcal (%CHO:%PRO:%FAT = 59:19:22); and the types of dietary fats [saturated fatty acids (SFAs), monounsaturated fatty acids (MUFAs), and polyunsaturated fatty acids (PUFAs)] ingested by the study participants did not demonstrate any changes during the intervention (data not shown).

### Effects of a 12-week mild calorie restriction on percent of body weight change, abdominal fat areas (CT), and body composition (DEXA)

Table 2 presents the effects of a 12-week mild calorie-restricted diet on the percent of body weight change,

abdominal fat area measured by CT, and body composition measured by DEXA. Comparison of the percent of body weight changes (differences from baseline) revealed that the weight-loss group had greater reductions in the percent of body weight change than the control group ( $0.63 \pm 0.15$  vs.  $-3.44 \pm 0.34$ ;  $P < 0.001$ ). Regarding the results of CT, no significant differences were observed in the L4 abdominal fat area (whole fat area and VFA), L4 subcutaneous fat area, or visceral-to-subcutaneous area ratio (VSR) at baseline between the control and weight-loss groups. At follow-up, the L4 VFA in the weight-loss group was lower than in the control group ( $P < 0.001$ ). The VFA decreased by  $17.7 \text{ cm}^2$  (15%) from baseline in the weight-loss group ( $P < 0.001$ ), and the VSR decreased by 0.09 from baseline in the weight-loss group ( $P < 0.001$ ). Significantly greater reductions in the L4 VFA and VSR were observed in the weight-loss group compared with the control group (all  $P < 0.001$ ). No statistically significant shifts in the VFA, subcutaneous fat area, or VSR were identified in the control group (Table 2). With regard to the DEXA results, there were no significant differences in the fat percentage, fat mass, or lean body mass between the two groups at both baseline and follow-up (Table 2). After the intervention, significant decreases in the fat percentage and fat mass were observed in both the control and weight-loss groups; however, greater reductions in the fat percentage and fat mass were observed in the weight-loss group than in the control group after adjustment for the baseline values ( $P = 0.006$  and  $P < 0.001$ , respectively). The control group showed a significant increase in the lean body mass, whereas the weight-loss group showed a significant decrease in the lean body mass at the 12-week follow-up; these changes were significantly different between the two groups ( $P < 0.001$ ) (Table 2).

### Effects of mild calorie restriction on circulating fatty acid profiles and desaturase activities at baseline and follow-up

Table 3 presents the effects of a 12-week mild calorie-restricted diet on plasma fatty acid profiles. At baseline, no significant difference was observed in the SFAs, MUFAs, n-6 PUFAs, and n-3 PUFAs between the control and weight-loss groups. The total SFAs, including palmitic acid (C16:0) and stearic acid (C18:0), decreased from baseline in the weight-loss group; in addition, these reductions were significantly greater than those in the control group after adjusting for the baseline values ( $P = 0.027$ ,  $P = 0.033$ , and  $P = 0.021$ , respectively). At follow-up, the weight-loss group showed significantly lower levels of total SFAs ( $P = 0.029$ ), lauric acid (C12:0) ( $P = 0.032$ ), and palmitic acid (C16:0) ( $P = 0.028$ ) than the control group. Similarly, the total MUFAs, including palmitoleic acid (C16:1, n-7) and oleic acid (C18:1, n-9), decreased from baseline in the weight-loss group, and

**Table 1** Clinical and biochemical characteristics of the weight-maintenance (control) and weight-loss groups at baseline and 12-week follow-up

	Weight-maintenance group (n = 38)		Weight-loss group (n = 37)		p <sup>a</sup>	p <sup>b</sup>	p <sup>c</sup>	p <sup>d</sup>
	Baseline	Follow-up	Baseline	Follow-up				
	Age (year)	46.0 ± 1.35		44.1 ± 1.92				
Male/female n, (%)	11 (28.9)/27 (71.1)		15 (40.5)/22 (59.5)		0.292			
Cigarette smoker n, (%)	4 (10.5)		5 (13.5)		0.691			
Drinker of alcohol n, (%)	21 (55.3)		22 (59.5)		0.713			
Weight (kg)	71.6 ± 1.51	72.1 ± 1.49 <sup>***</sup>	73.8 ± 1.54	71.4 ± 1.52 <sup>***</sup>	0.321	0.743	< 0.001	< 0.001
Change	0.44 ± 0.10		-2.42 ± 0.24		0.994	0.002	< 0.001	< 0.001
BMI (kg/m <sup>2</sup> )	27.3 ± 0.25	27.4 ± 0.24 <sup>***</sup>	27.3 ± 0.23	26.4 ± 0.24 <sup>***</sup>	0.994	0.002	< 0.001	< 0.001
Change	0.17 ± 0.04		-0.90 ± 0.08		0.648	0.103	< 0.001	< 0.001
Waist (cm)	93.6 ± 0.82	93.4 ± 0.83	93.0 ± 0.86	91.5 ± 0.80 <sup>***</sup>	0.648	0.103	< 0.001	< 0.001
Change	-0.13 ± 0.21		-1.48 ± 0.31		0.214	0.431	0.001	< 0.001
Systolic BP (mmHg)	122.4 ± 1.99	123.0 ± 2.49	126.1 ± 2.20	122.9 ± 2.09 <sup>*</sup>	0.214	0.431	0.001	< 0.001
Change	-2.09 ± 1.87		-3.23 ± 1.59		0.871	0.930	0.645	0.919
Diastolic BP (mmHg)	77.6 ± 1.67	76.9 ± 1.60	78.0 ± 1.52	76.7 ± 1.47	0.871	0.930	0.758	0.794
Change	-0.70 ± 1.26		-1.26 ± 1.30		0.940	0.638	0.651	0.303
Glucose (mg/dL) <sup>‡</sup>	89.5 ± 1.46	90.8 ± 1.45	89.5 ± 1.65	89.9 ± 1.45	0.940	0.638	0.651	0.303
Change	1.32 ± 1.40		0.41 ± 1.44		0.240	< 0.001	0.031	0.020
Insulin (μU/dL) <sup>‡</sup>	15.5 ± 1.19	17.5 ± 2.25	13.5 ± 0.92	11.0 ± 0.75 <sup>***</sup>	0.240	< 0.001	0.031	0.020
Change	1.99 ± 1.91		2.99 ± 0.20	2.42 ± 0.17 <sup>**</sup>	0.256	< 0.001	0.046	0.034
HOMA-IR <sup>‡</sup>	3.43 ± 0.26	4.00 ± 0.59	2.99 ± 0.20	2.42 ± 0.17 <sup>**</sup>	0.256	< 0.001	0.046	0.034
Change	0.57 ± 0.52		-0.57 ± 0.19		0.271	0.010	0.565	0.022
Triglycerides (mg/dL) <sup>‡</sup>	166.4 ± 18.4	159.6 ± 12.9	135.9 ± 9.38	115.3 ± 7.56	0.271	0.010	0.565	0.022
Change	-6.74 ± 14.1		-16.3 ± 8.36		0.577	0.738	0.690	0.857
Total-cholesterol (mg/dL) <sup>‡</sup>	220.30 ± 7.10	220.0 ± 6.93	213.8 ± 5.46	216.0 ± 6.18	0.577	0.738	0.690	0.857
Change	-0.37 ± 4.22		2.22 ± 4.90		0.568	0.409	0.427	0.352
HDL-cholesterol (mg/dL) <sup>‡</sup>	51.0 ± 1.97	51.6 ± 1.86	52.0 ± 1.60	54.0 ± 1.92	0.568	0.409	0.427	0.352
Change	0.53 ± 1.34		2.00 ± 1.27		0.911	0.855	0.901	0.933
LDL-cholesterol (mg/dL) <sup>‡</sup>	136.0 ± 6.00	136.5 ± 6.31	134.6 ± 4.78	135.9 ± 4.90	0.911	0.855	0.901	0.933
Change	0.45 ± 3.51		1.10 ± 3.86					

Mean ± SE. <sup>‡</sup>tested following logarithmic transformation. p<sup>a</sup>-values derived from an independent t-test between the groups at baseline. p<sup>b</sup>-values derived from an independent t-test between the groups at follow-up. p<sup>c</sup>-values derived from an independent t-test between the groups at changed values. p<sup>d</sup>-values are p<sup>c</sup>-values adjusted with the baseline values. \*P < 0.05, \*\*P < 0.01, and \*\*\*P < 0.001 derived from a paired t-test

**Table 2** CT and DEXA evaluation of the weight-maintenance (control) and weight-loss groups at baseline and 12-week follow-up

	Weight-maintenance group (n = 38)		Weight-loss group (n = 37)		P <sup>a</sup>	P <sup>b</sup>	P <sup>c</sup>	P <sup>d</sup>
	Baseline	Follow-up	Baseline	Follow-up				
Percent weight change	0.63 ± 0.15		-3.44 ± 0.34		< 0.001			
CT evaluation (L4)								
Whole fat area (cm <sup>2</sup> )	327.0 ± 6.32	333.3 ± 6.23	319.8 ± 6.65	298.5 ± 7.23***	0.435	< 0.001		
Change	6.34 ± 4.72		-21.3 ± 4.70				< 0.001	< 0.001
Visceral fat area (cm <sup>2</sup> )	118.2 ± 2.34	121.9 ± 3.26	118.3 ± 3.14	100.6 ± 3.67***	0.989	< 0.001		< 0.001
Change	3.65 ± 2.31		-17.7 ± 3.30				< 0.001	< 0.001
Subcutaneous fat area (cm <sup>2</sup> )	208.7 ± 6.98	211.4 ± 6.24	201.5 ± 7.06	197.8 ± 6.90	0.468	0.148		
Change	2.69 ± 4.17		-3.66 ± 2.54				0.200	0.099
Visceral/subcutaneous fat ratio (%)	0.60 ± 0.03	0.60 ± 0.03	0.62 ± 0.03	0.53 ± 0.03***	0.556	0.101		< 0.001
Change	0.00 ± 0.02		-0.09 ± 0.02				< 0.001	< 0.001
DEXA evaluation								
Fat percentage (%)	31.5 ± 0.94	31.0 ± 0.94**	29.8 ± 1.03	28.5 ± 0.98***	0.209	0.067		0.014
Change	-0.50 ± 0.18		-1.26 ± 0.24					0.006
Fat mass (g)	22,826.7 ± 616.6	22,536.71 ± 606.1*	22,038.8 ± 685.1	20,768.91 ± 651.1***	0.395	0.050		< 0.001
Change	-290.0 ± 128.4		-1269.9 ± 221.4				< 0.001	< 0.001
Lean body mass (g)	48,289.8 ± 1471.4	48,934.6 ± 1497.4***	50,875.5 ± 1598.1	49,726.2 ± 1567.7***	0.237	0.716		< 0.001
Change	644.8 ± 168.6		-1149.3 ± 164.3				< 0.001	< 0.001

Mean ± SE. \*tested following logarithmic transformation. P<sup>a</sup>-values derived from an independent t-test between the groups at baseline. P<sup>b</sup>-values derived from an independent t-test between the groups at follow-up. P<sup>c</sup>-values derived from an independent t-test between the groups at changed values. P<sup>d</sup>-values are P<sup>c</sup>-values adjusted with the baseline values. \*P < 0.05, \*\*P < 0.01, and \*\*\*P < 0.001 derived from a paired t-test

**Table 3** GC-MS analysis of fatty acids in the weight-maintenance (control) and weight-loss groups at baseline and 12-week follow-up

Fatty acids (Relative peak area)	Weight-maintenance group (n = 38)		Weight-loss group (n = 37)		p <sup>a</sup>	p <sup>b</sup>	p <sup>c</sup>	p <sup>d</sup>
	Baseline	Follow-up	Baseline	Follow-up				
	Saturated fatty acids	7.292 ± 0.211	7.287 ± 0.215	7.166 ± 0.177				
Change	-0.005 ± 0.216		-0.601 ± 0.228				0.062	
Lauric acid (C12:0)	0.033 ± 0.003	0.040 ± 0.005	0.027 ± 0.002	0.027 ± 0.003	0.063	0.032		
Change	0.007 ± 0.005		0.000 ± 0.003				0.313	
Myristic acid (C14:0)	0.307 ± 0.022	0.319 ± 0.029	0.260 ± 0.017	0.241 ± 0.031	0.105	0.068		
Change	0.013 ± 0.028		-0.019 ± 0.029				0.210	
Pentadecylic acid (C15:0)	0.045 ± 0.002	0.046 ± 0.003	0.041 ± 0.002	0.046 ± 0.006	0.182	0.978		
Change	0.001 ± 0.002		0.005 ± 0.006				0.505	
Palmitic acid (C16:0)	4.762 ± 0.148	4.729 ± 0.135	4.646 ± 0.118	4.333 ± 0.113*	0.545	0.028		
Change	-0.033 ± 0.152		-0.313 ± 0.120				0.155	
Stearic acid (C18:0)	2.011 ± 0.055	2.014 ± 0.059	2.054 ± 0.048	1.778 ± 0.108**	0.557	0.058		
Change	0.004 ± 0.056		-0.276 ± 0.100				0.016	
Arachidic acid (C20:0)	0.040 ± 0.002	0.041 ± 0.002	0.041 ± 0.001	0.041 ± 0.002	0.623	0.859		
Change	0.001 ± 0.002		0.000 ± 0.003				0.808	
Behenic acid (C22:0)	0.096 ± 0.005	0.098 ± 0.004	0.098 ± 0.004	0.099 ± 0.004	0.663	0.880		
Change	0.003 ± 0.004		0.001 ± 0.005				0.759	
Monounsaturated fatty acids	1.472 ± 0.052	1.457 ± 0.054	1.442 ± 0.046	1.235 ± 0.078**	0.663	0.021		
Change	-0.015 ± 0.050		-0.207 ± 0.068				0.017	
Palmitoleic acid (C16:1, n-7)	0.196 ± 0.011	0.197 ± 0.012	0.192 ± 0.011	0.156 ± 0.012**	0.777	0.018		
Change	0.001 ± 0.011		-0.035 ± 0.009				0.013	
cis-10-Heptadecenoic acid (C17:1, n-7)	0.015 ± 0.001	0.014 ± 0.001	0.014 ± 0.001	0.014 ± 0.003	0.264	0.998		
Change	0.000 ± 0.001		0.001 ± 0.003				0.675	
Oleic acid (C18:1, n-9)	1.193 ± 0.041	1.176 ± 0.042	1.171 ± 0.036	0.997 ± 0.066**	0.693	0.024		
Change	-0.016 ± 0.039		-0.174 ± 0.057				0.025	
Eicosenoic acid (C20:1, n-9)	0.011 ± 0.001	0.012 ± 0.001	0.010 ± 0.001	0.011 ± 0.002	0.158	0.638		
Change	0.001 ± 0.001		0.001 ± 0.001				0.889	
Erucic acid (C22:1, n-9)	0.008 ± 0.001	0.007 ± 0.001	0.007 ± 0.001	0.008 ± 0.001	0.576	0.476		
Change	-0.001 ± 0.001		0.001 ± 0.001				0.278	
Nervonic acid (C24:1, n-9)	0.049 ± 0.002	0.050 ± 0.003	0.048 ± 0.002	0.049 ± 0.002	0.669	0.731		
Change	0.001 ± 0.002		0.000 ± 0.003				0.979	

**Table 3** GC-MS analysis of fatty acids in the weight-maintenance (control) and weight-loss groups at baseline and 12-week follow-up (Continued)

Fatty acids (Relative peak area)	Weight-maintenance group (n = 38)		Weight-loss group (n = 37)		p <sup>d</sup>	
	Baseline	Follow-up	Baseline	Follow-up		
Polyunsaturated fatty acids (n-6)	2.965 ± 0.065	2.971 ± 0.069	2.844 ± 0.070	2.800 ± 0.067	0.208	0.080
Change	0.006 ± 0.055		-0.044 ± 0.071			0.577
Linoleic acid (C18:2, n-6)	2.203 ± 0.052	2.194 ± 0.054	2.097 ± 0.051	2.089 ± 0.050	0.149	0.156
Change	-0.009 ± 0.049		-0.008 ± 0.052			0.992
γ-linolenic acid (C18:3, n-6)	0.038 ± 0.003	0.041 ± 0.005	0.030 ± 0.002	0.028 ± 0.002	0.065	0.033
Change	0.003 ± 0.004		-0.002 ± 0.002			0.222
Eicosadienoic acid (C20:2, n-6)	0.022 ± 0.001	0.023 ± 0.001	0.021 ± 0.001	0.016 ± 0.001***	0.519	< 0.001
Change	0.001 ± 0.001		-0.005 ± 0.001			< 0.001
Dihomo-γ-linolenic acid (C20:3, n-6)	0.122 ± 0.005	0.125 ± 0.006	0.111 ± 0.005	0.096 ± 0.006*	0.168	0.001
Change	0.004 ± 0.005		-0.015 ± 0.007			0.028
Arachidonic acid (C20:4, n-6)	0.547 ± 0.018	0.553 ± 0.020	0.550 ± 0.020	0.537 ± 0.021	0.927	0.584
Change	0.006 ± 0.013		-0.013 ± 0.019			0.421
Docosatetraenoic acid (C22:4, n-6)	0.033 ± 0.002	0.034 ± 0.002	0.034 ± 0.002	0.033 ± 0.002	0.826	0.670
Change	0.001 ± 0.002		-0.001 ± 0.002			0.490
Polyunsaturated fatty acids (n-3)	0.477 ± 0.025	0.496 ± 0.040	0.477 ± 0.028	0.469 ± 0.034	0.999	0.619
Change	0.018 ± 0.035		-0.008 ± 0.025			0.542
α-linolenic acid (C18:3, n-3)	0.115 ± 0.010	0.121 ± 0.009	0.099 ± 0.007	0.093 ± 0.010	0.182	0.037
Change	0.005 ± 0.008		-0.007 ± 0.008			0.296
Eicosapentaenoic acid (C20:5, n-3)	0.112 ± 0.008	0.115 ± 0.016	0.110 ± 0.010	0.116 ± 0.013	0.867	0.978
Change	0.003 ± 0.015		0.006 ± 0.012			0.894
Docosapentaenoic acid (C22:5, n-3)	0.048 ± 0.003	0.050 ± 0.004	0.046 ± 0.002	0.044 ± 0.003	0.696	0.193
Change	0.002 ± 0.004		-0.003 ± 0.002			0.257
Docosahexaenoic acid (C22:6, n-3)	0.203 ± 0.016	0.210 ± 0.024	0.223 ± 0.019	0.217 ± 0.018	0.425	0.808
Change	0.007 ± 0.015		-0.005 ± 0.012			0.513
Ratio n-6/n-3	6.786 ± 0.352	7.243 ± 0.493	6.600 ± 0.346	7.519 ± 0.673	0.707	0.742
Change	0.457 ± 0.421		0.919 ± 0.544			0.502



**Table 3** GC-MS analysis of fatty acids in the weight-maintenance (control) and weight-loss groups at baseline and 12-week follow-up (Continued)

Fatty acids (Relative peak area)	Weight-maintenance group (n = 38)		Weight-loss group (n = 37)		P <sup>d</sup>	P <sup>c</sup>	P <sup>b</sup>	P <sup>a</sup>
	Baseline	Follow-up	Baseline	Follow-up				
	C16 Δ9-desaturase <sup>a</sup>	0.041 ± 0.001	0.041 ± 0.002	0.041 ± 0.002				
Change	0.000 ± 0.001		-0.005 ± 0.002			0.016	0.014	
C18 Δ9-desaturase <sup>b</sup>	0.593 ± 0.012	0.583 ± 0.011	0.569 ± 0.009	0.561 ± 0.010	0.111	0.144	0.111	
Change	-0.010 ± 0.013		-0.008 ± 0.012			0.903	0.331	
Δ6-desaturase <sup>c</sup>	0.017 ± 0.002	0.019 ± 0.002	0.014 ± 0.001	0.014 ± 0.001	0.122	0.049	0.122	
Change	0.001 ± 0.002		-0.001 ± 0.001			0.264	0.211	
Δ5-desaturase <sup>d</sup>	4.725 ± 0.201	4.689 ± 0.214	5.141 ± 0.190	6.157 ± 0.336**	0.137	< 0.001	0.137	
Change	-0.035 ± 0.154		1.017 ± 0.351			0.008	0.001	
Elongase <sup>e</sup>	0.426 ± 0.008	0.428 ± 0.007	0.444 ± 0.006	0.406 ± 0.014*	0.092	0.161	0.092	
Change	0.001 ± 0.010		-0.038 ± 0.014			0.024	0.101	

Mean ± SE. <sup>a</sup>tested following logarithmic transformation. <sup>b</sup>P-values derived from an independent t-test between the groups at baseline. <sup>c</sup>P-values derived from an independent t-test between the groups at follow up. <sup>d</sup>P-values derived from an independent t-test between the groups at changed values. <sup>e</sup>P-values are P-values adjusted with the baseline values. \*P < 0.05, \*\*P < 0.01, and \*\*\*P < 0.001 derived from a paired t-test. <sup>a</sup>C16 Δ9-desaturase = palmitoleic acid/palmitic acid. <sup>b</sup>C18 Δ9-desaturase = oleic acid/stearic acid. <sup>c</sup>Δ9-desaturase = γ-linolenic acid/linoleic acid. <sup>d</sup>Δ5-desaturase = arachidonic acid/dihomo-γ-linolenic acid. <sup>e</sup>Elongase activity = stearic acid/palmitic acid

these decreases were significantly greater than those in the control group after adjustment for the baseline values ( $P = 0.017$ ,  $P = 0.006$ , and  $P = 0.018$ , respectively). At follow-up, the weight-loss group showed significantly lower levels of total MUFAs ( $P = 0.021$ ), palmitoleic acid (C16:1, n-7) ( $P = 0.018$ ), and oleic acid (C18:1, n-9) ( $P = 0.024$ ) than did control group. Although the total n-6 and n-3 PUFA levels did not significantly change, eicosadienoic acid (C20:2, n-6) and dihomo- $\gamma$ -linolenic acid (C20:3, n-6) decreased from baseline in the weight-loss group. Both showed greater reductions in the weight-loss group than in the control group after adjusting for the baseline values ( $P < 0.001$  and  $P = 0.003$ , respectively). At follow-up, the weight-loss group showed significantly lower levels of eicosadienoic acid (C20:2, n-6) ( $P < 0.001$ ) and dihomo- $\gamma$ -linolenic acid (C20:3, n-6) ( $P = 0.001$ ) than the control group (Table 3).

C16  $\Delta 9$ -desaturase activity significantly decreased from baseline in the weight-loss group, and this reduction was greater in the weight-loss group than in the control group after adjusting for the baseline values ( $P = 0.014$ ). The activity of  $\Delta 5$ -desaturase significantly increased from baseline in the weight-loss group, and this increase was greater in the weight-loss group than in the control group after adjusting for the baseline values ( $P = 0.001$ ). In addition, at follow-up,  $\Delta 5$ -desaturase activity was significantly higher in the weight-loss group than in the control group ( $P < 0.001$ ). Elongase activity significantly decreased after the intervention (Table 3).

#### Relations between changes in L4 VFA and changes in clinical/biochemical characteristics and fatty acid levels

Overall, 22 variables showed significant changes in the weight-loss group compared with the control group after adjusting for the baseline values [Table 1: weight, BMI, waist circumference, insulin, HOMA-IR, and TGs; Table 2: whole fat area, VFA, VSR, fat percentage, fat mass, and lean body mass; Table 3: SFAs, palmitic acid (C16:0), stearic acid (C18:0), MUFAs, palmitoleic acid (C16:1, n-7), oleic acid (C18:1, n-9), eicosadienoic acid (C20:2, n-6), dihomo- $\gamma$ -linolenic acid (C20:3, n-6), C16  $\Delta 9$ -desaturase, and  $\Delta 5$ -desaturase]. A correlation analysis between changes in L4 VFA and changes in these variables was performed. Of the total study subjects ( $n = 75$ ), the changes in L4 VFA demonstrated significant positive correlations with changes in weight ( $r = 0.596$ ,  $P < 0.001$ ), BMI ( $r = 0.596$ ,  $P < 0.001$ ), waist circumference ( $r = 0.317$ ,  $P = 0.006$ ), insulin ( $r = 0.259$ ,  $P = 0.025$ ), fat percentage ( $r = 0.241$ ,  $P = 0.037$ ), fat mass ( $r = 0.381$ ,  $P = 0.001$ ), lean body mass ( $r = 0.464$ ,  $P < 0.001$ ), and dihomo- $\gamma$ -linolenic acid (C20:3, n-6) ( $r = 0.235$ ,  $P = 0.042$ ) and a significant negative correlation with changes in  $\Delta 5$ -desaturase activities ( $r = -0.277$ ,  $P = 0.016$ ) (Fig. 1).

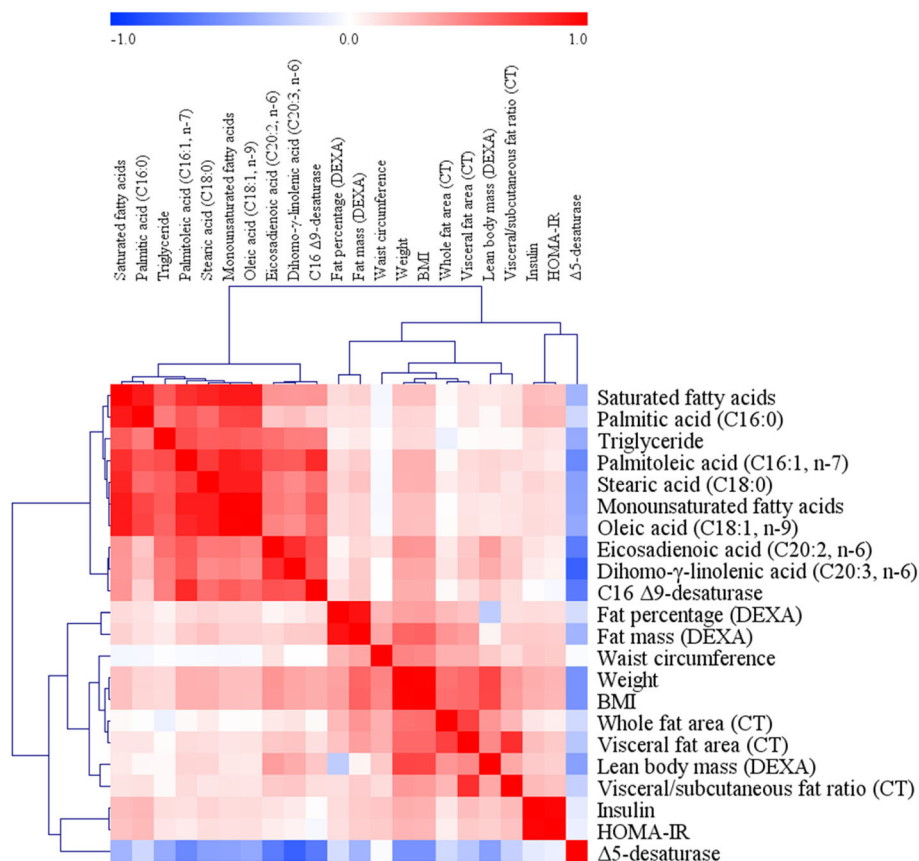
#### Discussion

VFA is associated with plasma fatty acid profiles and lifestyle patterns [17]. We investigated the effects of weight loss by mild calorie restriction (a 300 kcal/day intake reduction) on circulating fatty acid profiles and desaturase activities in nondiabetic and overweight subjects with high VFA (L4 VFA  $\geq 100$  cm<sup>2</sup>). The 12-week intervention led to a 3.4% body weight loss and a 15% VFA loss in the participants in the weight-loss group. In addition, the study showed enhancement of plasma fatty acid profiles (SFAs and MUFAs), greater decreases in C16  $\Delta 9$ -desaturase activity, and greater increases in  $\Delta 5$ -desaturase activity in the weight-loss group compared with the control group.

An inverse relation between  $\Delta 5$ -desaturase activity and diabetes risk [18] and direct relations among C16  $\Delta 9$ -desaturase activity, insulin resistance, and abdominal obesity [5] have been reported. In the present study, a VFA loss was significantly related to  $\Delta 5$ -desaturase activity but not to C16  $\Delta 9$ -desaturase activity. Although some evidence supports the inverse relation between  $\Delta 5$ -desaturase activity and diabetes risk [18–22], the  $\Delta 5$ -desaturase activity of this study did not correlate to insulin and HOMA-IR, which are risk factors of type 2 diabetes. However, the weight-loss group showed greater reductions in the serum insulin levels and HOMA-IR scores than the control group; furthermore, changes in insulin and HOMA-IR were positively correlated with changes in weight and BMI, which showed a significant negative correlation with changes in  $\Delta 5$ -desaturase activity. Because weight and BMI are also closely related to the risk of type 2 diabetes [23, 24], our results might indicate an indirect inverse association between  $\Delta 5$ -desaturase activity and the risk of type 2 diabetes (Fig. 2). Consequently, mild calorie-restriction-induced weight loss in individuals with high VFA might lead to the potential benefit of a reduced risk of type 2 diabetes by improving fatty acid desaturase activity.

Estimated  $\Delta 5$ -desaturase activity was expressed as the ratio of arachidonic acid (20:4, n-6) to dihomo- $\gamma$ -linolenic acid (20:3, n-6). The increase in  $\Delta 5$ -desaturase activity observed in the weight-loss group might result from the greater decrease of dihomo- $\gamma$ -linolenic acid (20:3, n-6) than that observed in the control group because there were no significant changes in arachidonic acid (20:4, n-6) in the control and weight-loss groups. Indeed, changes in VFA were positively correlated with changes in dihomo- $\gamma$ -linolenic acid (20:3, n-6) (Fig. 1). Therefore, the study indicated that the inverse relation between VFA and  $\Delta 5$ -desaturase activity might be mediated by an alteration of dihomo- $\gamma$ -linolenic acid (20:3, n-6), which is also significantly associated with VFA.

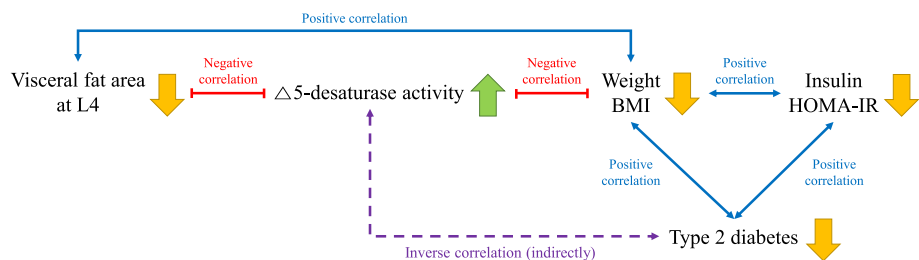
Although the total n-6 PUFAs did not significantly change during the intervention, the subjects in the weight-loss group showed decreases in not only dihomo-



**Fig. 1** Correlation matrix among major clinical parameters, fatty acids, and fatty acid desaturases (changed values). Correlations were obtained by identifying a Pearson's correlation coefficient. Red indicates a positive correlation, and blue indicates a negative correlation

$\gamma$ -linolenic acid (C20:3, n-6) but also eicosadienoic acid (C20:2, n-6); and these reductions were greater than the reductions detected in the control group (Table 3). Consistent with our results, other studies have found that obese individuals showed higher levels of dihomo- $\gamma$ -linolenic acid (C20:3, n-6) in plasma phospholipids, TGs, and sterol esters than the controls [25, 26]. A recent study emphasized the proadipogenic properties of n-6

PUFAs [27]; indeed, several studies have found that n-6 PUFAs promote adipogenesis and increase the expression of lipogenic genes [27, 28]. Muhlhausler BS et al. [27] concluded that n-6 PUFAs promote the expansion of fat depots by up-regulating both hyperplasia and hypertrophy; in other words, an accumulation of n-6 PUFAs might exacerbate an obese status by enhanced adipogenesis, which could lead to several obesity-related



**Fig. 2** Summary of an indirect association between  $\Delta$ 5-desaturase activity and the risk of type 2 diabetes in the present study. Although no significant and direct correlation between  $\Delta$ 5-desaturase activity and the risk of type 2 diabetes was observed in this study, connections among  $\Delta$ 5-desaturase activity, weight, BMI, serum insulin level, and HOMA-IR score indicate an indirect inverse correlation between  $\Delta$ 5-desaturase activity and the risk of type 2 diabetes. Because the visceral fat area (VFA) has a significant negative correlation with  $\Delta$ 5-desaturase activity and  $\Delta$ 5-desaturase activity is inversely related to the risk of type 2 diabetes, VFA and the risk of type 2 diabetes might be positively correlated. Thus, mild calorie-restriction-induced weight loss that affects VFA at L4 decrease might lead to health benefits

health risks, including IR, metabolic syndrome, and diabetes [1]. Therefore, lowering the n-6 PUFA levels by calorie-restriction-induced weight loss is necessary, and the reduction of VFA to lower n-6 PUFAs is important.

In this study, the weight-loss group showed significant decreases in total SFAs, including palmitic acid (C16:0) and stearic acid (C18:0), which have previously been observed to be related to the incidence of type 2 diabetes [29, 30]. Total MUFAs, including palmitoleic acid (C16:1, n-7) and oleic acid (C18:1, n-9), were also significantly decreased in the weight-loss group of this study. The palmitoleic acid (C16:1, n-7) plasma concentrations mostly showed *de novo* hepatic fatty acid synthesis from palmitic acid (C16:0) by C16  $\Delta$ 9-desaturase [31, 32]; in the present study, both palmitic acid (C16:0) and C16  $\Delta$ 9-desaturase activity were significantly decreased during the 12-week intervention in the weight-loss group, which indicates that these alterations might affect plasma concentrations of palmitoleic acid (C16:1, n-7). Mice supplemented with palmitoleic acid exhibit higher fat deposition, hepatic steatosis, and increased hepatic expression of sterol regulatory element-binding protein 1c and fatty acid synthase, demonstrating the pro-lipogenic effect of this MUFA [33]. Moreover, studies conducted on humans have observed a detrimental influence of this MUFA on health [34, 35]. A previous study found that high levels of palmitoleic acid (C16:1, n-7) are associated with an increased risk of cardiovascular disease [34] and are positively associated with metabolic syndrome [35], including hypertriglyceridemia [34] and abdominal obesity [36]. In the present study, the weight-loss group, which presented significantly decreased levels of palmitoleic acid (C16:1, n-7), showed greater reductions in serum TGs and waist circumference than the control group. Therefore, reduced levels of SFAs and MUFAs via calorie-restriction-induced weight and VFA loss might yield future health benefits.

One of the major points of the present study is the correlation of weight loss with a significant reduction of VFA. As discussed thus far, many changes observed in the weight-loss group of this study might be explained by the VFA change. However, there is controversy regarding whether visceral fat is more harmful to circulating fatty acids than subcutaneous fat. Jensen MD [37] reported that visceral fat is not a source of excess systemic free fatty acid availability; conversely, Björntorp P [38] concluded that visceral fat tissue could be a significant source of free fatty acids that might exert complex metabolic effects. Indeed, several studies have suggested that large visceral fat depots flooded the liver and the systemic circulation in the form of free fatty acids [39, 40]. In addition, Klein S [41] observed that excess visceral fat is more harmful than excess subcutaneous fat because the lipolysis of TGs in visceral adipose tissue releases free fatty acids into the portal vein,

which directly delivers them to the liver. Nielsen et al. [42] demonstrated that the contribution of free fatty acids derived from visceral fat to the portal and systemic circulation increases with increases in the visceral fat mass. Because evidence that supports our results exists, we believe that visceral fat is an important factor affecting the circulating fatty acid profiles.

A limitation of this study is its small sample size. Additionally, our results might not be generalizable because the study subjects were limited to nondiabetic overweight Korean subjects. Finally, we did not exclude subjects who took a medication that affects lipid metabolism. Only two subjects in the control group took a lipid-lowering medication; the clinical/biochemical parameters and fatty acid profiles did not show any significant differences between the control groups according to medication [ $n=38$  (original control group) vs.  $n=36$  (control group w/o medication)] (data not shown). In addition, the baseline value-adjusted statistical significance of the changed values between the control group without medication and the weight-loss group was identical to the present results (data not shown). Therefore, in this study, medication was not considered a confounding factor in interpreting the research results. Despite these limitations, this study demonstrates that a weight-loss intervention based on a hypocaloric diet in overweight subjects with high visceral fat levels improved not only the anthropometric and biochemical parameters but also the fatty acids plasma levels.

## Conclusions

An analysis of plasma fatty acid profiles identified significant decreases in palmitic acid (C16:0), stearic acid (C18:0), palmitoleic acid (C16:1), oleic acid (C18:1), eicosadienoic acid (C20:2, n-6), and dihomo- $\gamma$ -linolenic acid (C20:3, n-6) as well as a decrease in C16  $\Delta$ 9-desaturase activity and an increase in  $\Delta$ 5-desaturase activity. These results suggest that maintenance of high VFA levels without treatment does not produce changes in the plasma fatty acid profiles, whereas even mild weight loss with reduced VFA improves the overall plasma fatty acid profile and desaturase activities. Through enhancement of the plasma fatty acid profiles, individuals may receive potential health benefits of reduced future risks of type 2 diabetes and cardiovascular disease. Moreover, eating behavior modification (mild calorie restriction) might be an effective therapy for the treatment of diseases such as type 2 diabetes and cardiovascular disease.

## Abbreviations

BMI: Body mass index; BMR: Basal metabolic rate; BP: Blood pressure; CT: Computed tomography; DEXA: Dual-energy X-ray absorptiometry; HDL: High-density lipoprotein; HOMA-IR: Homeostasis model assessment insulin resistance; IR: Insulin resistance; L4: 4th lumbar; LDL: Low-density lipoprotein; MUFA: Monounsaturated fatty acid; PUFA: Polyunsaturated fatty acid; SE: Standard error; SFA: Saturated fatty acid; TCI: Total calorie intake;

TEE: Total energy expenditure; TG: Triglyceride; VFA: Visceral fat adiposity; VSR: Visceral-to-subcutaneous area ratio

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Not applicable

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#### Availability of data and materials

The data that support the findings of this study are available on request from the corresponding author [JHL].

#### Authors' contributions

YJL contributed to the acquisition, analysis, and interpretation of the data and helped draft the manuscript. HJY, MK, and MK contributed to the analysis and interpretation of the data and helped draft the manuscript. AL contributed to the acquisition and analysis of the data. SHJ contributed to the conception and design of the study. DYS contributed to the acquisition of the data. JHL contributed to the conception and design of the study and to the analysis and interpretation of the data and helped draft the manuscript. All authors critically revised, read, and approved the final manuscript and agreed to be fully accountable for ensuring the integrity and accuracy of the work.

#### Ethics approval and consent to participate

The purpose of the study was carefully explained to all participants, and written consent was obtained prior to their participation. The protocol was approved by the Institutional Review Board of Yonsei University and Yonsei University Severance Hospital in accordance with the Helsinki Declaration.

#### Consent for publication

Not applicable

#### Competing interests

The authors declare that they have no competing interests.

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#### References

- Katsuki A, Sumida Y, Urakawa H, et al. Increased visceral fat and serum levels of triglyceride are associated with insulin resistance in Japanese metabolically obese, normal weight subjects with normal glucose tolerance. *Diabetes Care*. 2003;26:2341–4.
- Hannukainen JC, Kalliokoski KK, Borra RJ, et al. Higher free fatty acid uptake in visceral than in abdominal subcutaneous fat tissue in men. *Obesity*. 2010;18:261–5.
- Bucci M, Borra R, Nägren K, et al. Human obesity is characterized by defective fat storage and enhanced muscle fatty acid oxidation, and trimetazidine gradually counteracts these abnormalities. *Am J Physiol Endocrinol Metab*. 2011;301:E105–12.
- Chaston TB, Dixon JB. Factors associated with percent change in visceral versus subcutaneous abdominal fat during weight loss: findings from a systematic review. *Int J Obes*. 2008;32:619–28.
- Warensjö E, Ohrvall M, Vessby B. Fatty acid composition and estimated desaturase activities are associated with obesity and lifestyle variables in men and women. *Nutr Metab Cardiovasc Dis*. 2006;16:128–36.
- Pan DA, Hulbert AJ, Storlien LH. Dietary fats, membrane phospholipids and obesity. *J Nutr*. 1994;124:1555–65.
- Akter S, Kurotani K, Sato M, et al. High serum phospholipid dihomogamma-linoleic acid concentration and low  $\Delta 5$ -desaturase activity are associated with increased risk of type 2 diabetes among Japanese adults in the Hitachi health study. *J Nutr*. 2017;147:1558–66.
- Pouidel-Tandukar K, Sato M, Ejima Y, et al. Relationship of serum fatty acid composition and desaturase activity to C-reactive protein in Japanese men and women. *Atherosclerosis*. 2012;220:520–4.
- Zhao L, Ni Y, Ma X, et al. A panel of free fatty acid ratios to predict the development of metabolic abnormalities in healthy obese individuals. *Sci Rep*. 2016;6:28418.
- Warensjö E, Rosell M, Hellenius ML, et al. Associations between estimated fatty acid desaturase activities in serum lipids and adipose tissue in humans: links to obesity and insulin resistance. *Lipids Health Dis*. 2009;8:37.
- Kishino T, Watanabe K, Urata T, et al. Visceral fat thickness in overweight men correlates with alterations in serum fatty acid composition. *Clin Chim Acta*. 2008;398:57–62.
- Shin MJ, Hyun YJ, Kim OY, et al. Weight loss effect on inflammation and LDL oxidation in metabolically healthy but obese (MHO) individuals: low inflammation and LDL oxidation in MHO women. *Int J Obes*. 2006;30:1529–34.
- Department of Agrofood Resources. 8th revision standard food composition table. Suwon: Rural Development Administration; 2011.
- Jung S, Lee YJ, Kim M, et al. Supplementation with two probiotic strains, *Lactobacillus curvatus* HY7601 and *Lactobacillus plantarum* KY1032, reduced body adiposity and Lp-PLA<sub>2</sub> activity in overweight subjects. *J Funct Foods*. 2015;19:744–52.
- Kim M, Kim M, Lee YJ, et al. Supplementation with nutrients modulating insulin-like growth factor-1 negatively correlated with changes in the levels of pro-inflammatory cytokines in community-dwelling elderly people at risk of undernutrition. *J Hum Nutr Diet*. 2017;30:27–35.
- Kim M, Kim M, Lee YJ, et al. Effects of  $\alpha$ -linolenic acid supplementation in perilla oil on collagen-epinephrine closure time, activated partial thromboplastin time and Lp-PLA<sub>2</sub> activity in non-diabetic and hypercholesterolaemic subjects. *J Funct Foods*. 2016;23:95–104.
- Oshima Y, Rin S, Kita H, et al. The frequency of fish-eating could negatively associate with visceral adiposity in those who eat moderately. *J Nutr Sci Vitaminol (Tokyo)*. 2015;61:426–31.
- Kröger J, Schulze MB. Recent insights into the relation of  $\Delta 5$  desaturase and  $\Delta 6$  desaturase activity to the development of type 2 diabetes. *Curr Opin Lipidol*. 2012;23:4–10.
- Kröger J, Zietemann V, Enzenbach C, et al. Erythrocyte membrane phospholipid fatty acids, desaturase activity, and dietary fatty acids in relation to risk of type 2 diabetes in the European prospective investigation into cancer and nutrition (EPIC)-Potsdam study. *Am J Clin Nutr*. 2011;93:127–42.
- Krachler B, Norberg M, Eriksson JW, et al. Fatty acid profile of the erythrocyte membrane preceding development of type 2 diabetes mellitus. *Nutr Metab Cardiovasc Dis*. 2008;18:503–10.
- Patel PS, Sharp SJ, Jansen E, et al. Fatty acids measured in plasma and erythrocyte-membrane phospholipids and derived by food-frequency questionnaire and the risk of new-onset type 2 diabetes: a pilot study in the European prospective investigation into cancer and nutrition (EPIC)-Norfolk cohort. *Am J Clin Nutr*. 2010;92:1214–22.
- Chow LS, Li S, Eberly LE, et al. Estimated plasma stearoyl co-a desaturase-1 activity and risk of incident diabetes: the atherosclerosis risk in communities (ARIC) study. *Metabolism*. 2013;62:100–8.
- Lee S, Kuk JL, Davidson LE, et al. Exercise without weight loss is an effective strategy for obesity reduction in obese individuals with and without type 2 diabetes. *J Appl Physiol* (1985). 2005;99:1220–5.
- Kopp HP, Krzyzanowska K, Möhlig M, et al. Effects of marked weight loss on plasma levels of adiponectin, markers of chronic subclinical inflammation and insulin resistance in morbidly obese women. *Int J Obes*. 2005;29:766–71.

25. Decsi T, Molnár D, Koletzko B. Long-chain polyunsaturated fatty acids in plasma lipids of obese children. *Lipids*. 1996;31:305–11.
26. Decsi T, Csábi G, Török K, et al. Polyunsaturated fatty acids in plasma lipids of obese children with and without metabolic cardiovascular syndrome. *Lipids*. 2000;35:1179–84.
27. Muhlhauser BS, Ailhaud GP. Omega-6 polyunsaturated fatty acids and the early origins of obesity. *Curr Opin Endocrinol Diabetes Obes*. 2013;20:56–61.
28. Lorente-Cebrián S, Costa AG, Navas-Carretero S, et al. Role of omega-3 fatty acids in obesity, metabolic syndrome, and cardiovascular diseases: a review of the evidence. *J Physiol Biochem*. 2013;69:633–51.
29. Iggman D, Arnlöv J, Vessby B, et al. Adipose tissue fatty acids and insulin sensitivity in elderly men. *Diabetologia*. 2010;53:850–7.
30. Kurotani K, Sato M, Ejima Y, et al. High levels of stearic acid, palmitoleic acid, and dihomo- $\gamma$ -linolenic acid and low levels of linoleic acid in serum cholesterol ester are associated with high insulin resistance. *Nutr Res*. 2012; 32:669–675.e3.
31. Ntambi JM, Miyazaki M. Regulation of stearoyl-CoA desaturases and role in metabolism. *Prog Lipid Res*. 2004;43:91–104.
32. Zong G, Ye X, Sun L, et al. Associations of erythrocyte palmitoleic acid with adipokines, inflammatory markers, and the metabolic syndrome in middle-aged and older Chinese. *Am J Clin Nutr*. 2012;96:970–6.
33. Guo X, Li H, Xu H, et al. Palmitoleate induces hepatic steatosis but suppresses liver inflammatory response in mice. *PLoS One*. 2012;7:e39286.
34. Paillard F, Catheline D, Duff FL, et al. Plasma palmitoleic acid, a product of stearoyl-coA desaturase activity, is an independent marker of triglyceridemia and abdominal adiposity. *Nutr Metab Cardiovasc Dis*. 2008;18:436–40.
35. Warensjö E, Risérus U, Vessby B. Fatty acid composition of serum lipids predicts the development of the metabolic syndrome in men. *Diabetologia*. 2005;48:1999–2005.
36. Gong J, Campos H, McGarvey S, et al. Adipose tissue palmitoleic acid and obesity in humans: does it behave as a lipokine? *Am J Clin Nutr*. 2011;93:186–91.
37. Jensen MD. Is visceral fat involved in the pathogenesis of the metabolic syndrome? *Human Model Obesity*. 2006;14:20S–4S.
38. Björntorp P. Metabolic difference between visceral fat and subcutaneous abdominal fat. *Diabetes Metab*. 2000;26:10–2.
39. Björntorp P. "Portal" adipose tissue as a generator of risk factors for cardiovascular disease and diabetes. *Arterioscler Thromb Vasc Biol*. 1990; 10:493–6.
40. Kissebah AH, Peiris AN. Biology of regional body fat distribution: relationship to non-insulin-dependent diabetes mellitus. *Diabetes Metab Rev*. 1989;5:83–109.
41. Klein S. The case of visceral fat: argument for the defense. *J Clin Invest*. 2004;113:1530–2.
42. Nielsen S, Guo Z, Johnson CM, et al. Splanchnic lipolysis in human obesity. *J Clin Invest*. 2004;113:1582–8.

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