ORIGINAL RESEARCH

Effects of a moderate low-carbohydrate diet on preferential abdominal fat loss and cardiovascular risk factors in patients with type 2 diabetes

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Background: Reports have shown that visceral adipose tissue (VAT) is more closely linked to cardiovascular risk factors (CRFs) than subcutaneous adipose tissue (SAT). We aimed to elucidate preferential abdominal fat loss and the correlations between abdominal fat reductions and changes in CRFs achieved with a moderate low-carbohydrate diet (LCD) in patients with type 2 diabetes (T2DM).

Patients and methods: Fifty-two outpatients (28 men and 24 women, mean age $\pm$ SD: 60.0 ± 10.5 years) with hemoglobin A_{1c} (HbA_{1c}) levels $\geq 6.5\%$ were on an LCD for 6 months. Over a 6-month period, we measured their abdominal fat distribution (using CT) and assessed CRFs, including body mass index (BMI), HbA_{1c}, fasting blood glucose (FBG), serum insulin, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglyceride levels.

Results: The patients showed good compliance with the LCD (1812 ± 375 kcal/day, % carbohydrate:fat:protein = 35:40:19 for men; 1706 ± 323 kcal/day, % carbohydrate:fat:protein = 41:36:21 for women). Significant decreases ($P = 0.05$) in BMI and HbA_{1c} levels were observed, along with an increase in HDL-C ($P = 0.021$) in men and a decrease in LDL-C ($P = 0.001$) in women. VAT (-21.6 cm², $P < 0.001$ in men; -19.6 cm², $P < 0.001$ in women) and SAT (-13.5 cm², $P = 0.004$ in men; -19.1 cm², $P = 0.003$ in women) significantly decreased. The loss of VAT (%ΔVAT) was greater than that of SAT (%ΔSAT) in women ($P = 0.022$). A similar but not significant predominance of VAT loss was detected in men ($P = 0.111$). In women, the %ΔSAT significantly correlated with changes in FBG (ΔFBG) ($r = 0.417$) and HDL-C (ΔHDL) ($r = -0.720$), as was %ΔVAT with changes in triglyceride (ΔTG) ($r = 0.591$).

Conclusion: Six months of a moderate LCD resulted in preferential VAT loss only in women, with significant correlations between %ΔSAT and both ΔHDL and ΔFBG, as well as between %ΔVAT and ΔTG. Our results suggest that an LCD has the potential to reduce abdominal fat in patients with T2DM and deterioration of serum lipid profiles.

Keywords: low-carbohydrate diet, visceral adipose tissue, subcutaneous adipose tissue, cardiovascular risk factors

Introduction

Low-carbohydrate diets (LCDs) have attracted interest for weight loss, glycemic control, and the management of cardiovascular risk factors in overweight patients with type 2 diabetes (T2DM).[1,2] Among their reported advantages over high-carbohydrate diets (HCDs) are improvements in both serum high-density lipoprotein cholesterol (HDL-cholesterol) levels and triglyceride levels in obese patients.[3–5]

The proportion of energy obtained from carbohydrates in East Asian populations is generally higher (about 60%) and the fat percentage generally lower (about 25%)

compared with Western populations.[6–9] Therefore, compared with HCDs, moderate (non-ketogenic) LCDs, but not strict (ketogenic) LCDs, may be sufficiently effective for glycemic control in East Asian patients with T2DM. Moreover, a moderate LCD is more acceptable to patients with T2DM because they are not required to strictly limit carbohydrates.[10,11] Indeed, we demonstrated the efficacy of a moderate LCD (30%–45% carbohydrate diet) in glycemic control, weight loss, and improvement of serum lipid profiles in T2DM patients with a low attrition rate.[11,12] Even in the Western population, strict and moderate LCDs are reported to be equally effective in controlling body weight and serum lipid profiles.[13]

It has been proposed that abdominal fat accumulation raises cardiovascular risk. As compared with subcutaneous adipose tissue (SAT), visceral adipose tissue (VAT) in particular is more closely linked to glucose intolerance, hypertension, dyslipidemia, and insulin resistance.[14–16] Therefore, VAT is widely assumed to be a major predictor of metabolic syndrome and insulin resistance. Indeed, experimental studies have demonstrated that VAT and SAT play different physiological and biochemical roles.[16] Men have significantly more VAT than women, which may explain why women have fewer cardiovascular events than men.[17] Thus, if moderate LCDs result in a greater decrease in VAT than SAT, such LCDs may be useful for controlling not only blood glucose levels, but also abdominal fat.

Many intervention studies involving HCDs and either exercise or drugs have been conducted to assess changes in abdominal fat distribution in obese subjects. However, although HCDs can result in absolute VAT and SAT loss, these diets do not result in preferential abdominal fat loss.[18] To date, only a few studies have examined the effects of LCDs on preferential abdominal fat loss and the associations between the loss of adipose tissue and improvement in cardiovascular risk factors in nonobese and obese patients with and without T2DM.[19]

Therefore, in the present study, we investigated which abdominal fat tissues (VAT or SAT) would be preferentially reduced by a 6-month moderate LCD. The subjects were non-obese patients with T2DM who were typical of those commonly treated in Japan.[20,21] We also sought to determine whether decreases in VAT or SAT were associated with changes in cardiovascular risk factors (body mass index [BMI], blood pressure [BP], hemoglobin A_{1c} [HbA_{1c}] levels, fasting blood glucose [FBG], serum insulin [IRI] and serum lipid profiles).

Patients and methods

We invited all new outpatients with T2DM and HbA_{1c} levels of 6.5% or above to participate in a 6-month intervention study from April 2007 to November 2008 at the Haimoto Clinic. Patients with serum creatinine levels > 1.5 mg/dL, severe complications from diabetes (proliferative retinopathy, symptomatic neuropathy, or a diabetic foot), ketoacidosis, soft drink ketosis, cancer, severe heart failure, and liver cirrhosis were excluded. Five patients on hormone and/or insulin treatment were also excluded due to the considerable effects of these drugs on body weight (BW) and serum insulin levels. The remaining 63 patients participated in the study.

We measured the participants' BW, BP, and HbA_{1c} levels every month. Levels of FBG and serum insulin, triglyceride (TG), low-density lipoprotein cholesterol (LDL-C) and HDL-C were analyzed in the fasting state at baseline and after 6 months. Changes in VAT, SAT, total adipose tissue (TAT) and waist circumference (WC) were also assessed at baseline and after 6 months by computed tomography (CT).

All participants gave informed consent, and the study protocol was approved by the Ethics Committee of the Nagoya Tokushukai General Hospital.

Laboratory methods

Plasma glucose concentrations were determined by enzymatic methods (Shino-Test Co. Kanagawa, Japan). Serum insulin levels were measured using the standard double antibody radioimmunoassay method (Fujirebio Inc. Tokyo, Japan). Enzymatic methods were used to measure TG levels (Daiichi Pure Chemicals Co., Tokyo, Japan). Direct methods were used to assay serum LDL-C and HDL-C levels (Daiichi Pure Chemicals Co., Tokyo, Japan). HbA_{1c} levels were measured using high-performance liquid chromatography (Arkley Co., Kyoto, Japan).

Assessment of body composition

BW was determined using an electronic scale while patients were wearing only underwear. BMI was calculated by dividing weight in kilograms by the square of height in meters. To eliminate the effect of sex and age, we used the standard deviation score of BMI as well as crude BMI values. The score was computed using the following formula: (BMI – mean)/SD. We used the average and standard deviation of BMI by sex and 10-year age group in the National Health and Nutrition Survey, Japan, 2009[22] because of the small number of participants in some age groups in the present study.

The surface areas of VAT and SAT were measured by CT (Hitachi Medical Corporation X-ray CT system Pronto Si), and

patients were scanned at the navel. These areas and WC were measured using image analysis software (Hitachi Medical Corporation Fat Pointer, version 1.10) as described previously.[23]

The carbohydrate-reduced diet

The main principle of the LCD used in this study was to eliminate carbohydrate-rich foods depending on each patient's HbA_{1c} levels, as described previously.[11,12] In brief, patients with HbA_{1c} levels $< 9.0\%$ were asked to eliminate carohydrate-rich foods from their dinner, whereas patients with an HbA_{1c} level $\geq 9.0\%$ were asked to eliminate carbohydrates twice a day (from breakfast and dinner). It was easy for patients to stay on the LCD because no strict protein:fat:carbohydrate (PFC) ratio was prescribed, and they were permitted to eat as much protein and fat as they wanted, including saturated fat. There were no other restrictions.

A dietician (TS) gave instructions to all participants 3 times during the first month and once a month thereafter. The participants were instructed to maintain their baseline physical activity level throughout the study period. Their dietary intake was assessed after 5 months from 3-day food records and an interview with a dietitian and the data were analyzed using the HealthyMaker432 (mushroomsoft, Okayama, Japan). The participants had not previously been instructed to follow a LCD before this intervention. They were asked about changes in their physical activity levels on a questionnaire that they filled out at the end of the study.

Statistical analysis

Data are presented as mean ± SD. Either the paired t-test or its nonparametric counterpart (Wilcoxon signed rank test) was used to assess changes in all the parameters during the 6-month period. The unpaired t-test was applied to assess the differences in VAT and SAT at baseline and in the percentage of dietary macronutrient intake between men and women.

We compared the ratio of VAT area to SAT area (V/S ratio) at baseline and after the 6-month period. The changes in some variables during the 6-month study period (ie, 6-month value minus baseline value) are presented as Δvariable (eg, ΔBMI, ΔSBP, ΔDBP, ΔFBG, ΔIRI, ΔHbA_{1c}, ΔTG, ΔLDL-C, and ΔHDL-C). We used %ΔVAT, %ΔSAT and ΔV/S as indicators of differential changes in VAT or SAT, although various parameters have been used in previous intervention studies (eg, ΔVAT, ΔSAT, ΔVAT/ΔSAT, %ΔVAT, %ΔSAT, %ΔVAT/%ΔSAT, V/S, and ΔV/S).[18,19,24–29] The parameters %ΔVAT and %ΔSAT were computed using the following formula: 100 – (100 × [FAT area at 6 months/FAT area at baseline]).

The correlations between abdominal fat distribution and either cardiovascular risk factors or body composition at baseline and the correlations between changes in these variables over the 6-month period were assessed with Spearman correlation coefficients. Multiple regression analyses adjusted for age were performed on the significant and strong correlations between changes in abdominal fat and cardiovascular risk factors. All statistical analyses were performed using the SPSS statistical package (version 11.0; SPSS, Inc., Chicago, IL). P values less than 0.05 were considered to be statistically significant.

Results

Baseline characteristics of patients

Of the 63 patients enrolled in the study, 2 patients voluntarily dropped out, 2 refused the CT assessment at 6 months, 3 began to require insulin treatment, and 4 were hospitalized because of diseases other than T2DM. After excluding these patients, 52 were left for the analyses (28 men, mean age ± SD: 57.3 ± 10.6 years, range: 35–73 years and 24 women, mean age ± SD: 63.6 ± 9.5 years, range: 34–82 years). All but one of the female participants were postmenopausal.

The patients' characteristics at baseline are shown in Table 1. The mean BMI was 25.4 ± 4.5 kg/m² for men and 23.9 ± 3.4 kg/m² for women, and only 5 patients exceeded 30.0 kg/m². The mean standard deviation score of BMI was 0.49 ± 1.34 for men and 0.30 ± 0.93 for women.

HbA_{1c} levels were 8.4% ± 1.5% in men and 8.6% ± 2.0% in women. VAT was much larger in men than in women (men: 150.9 ± 57.5 cm², women: 99.6 ± 51.7 cm²), whereas SAT was larger in women (men: 123.4 ± 70.7 cm², women: 187.3 ± 70.0 cm²). No changes in physical activity levels during the study period were reported in the questionnaire.

As for the correlations of VAT or SAT distribution and WC with cardiovascular risk factors in men, we found a strong positive correlation between VAT and BMI (Spearman correlation coefficient $[r] = 0.669$, $P < 0.001$). There were also strong, positive correlations between SAT, TAT, or WC and either BMI ($r = 0.590$, 0.819 or 0.806, respectively and $P \leq 0.001$ for all) or serum insulin levels ($r = 0.655$, 0.565, 0.673 and $P < 0.001$, $P = 0.002$, $P < 0.001$, respectively). Moderate inverse correlations between either SAT or WC and serum HDL-C levels ($r = -0.473$, -0.472 and $P = 0.020$ or $P = 0.020$, respectively) were also observed. In women, we found strong positive correlations between VAT, SAT, TAT, or WC and either BMI ($r = 0.652$, 0.730, 0.796, or 0.865 and $P \leq 0.001$ for all) or serum insulin levels ($r = 0.658$, 0.663, 0.762, or 0.759 and $P < 0.001$ for all). A significant

Table 1 Changes in abdominal fat distribution and cardiovascular risk factors during the 6-month moderate low-carbohydrate diet

	Men (n = 28)			Women (n = 24)		
	Baseline	After 6 months	P	Baseline	After 6 months	P
Body weight (kg)	70.7 ± 13.6	68.7 ± 12.7	0.004*	55.8 ± 7.2	54.1 ± 7.4	0.002
Body mass index (kg/m²)	25.4 ± 4.5	24.6 ± 4.1	0.003*	23.9 ± 3.4	23.2 ± 3.4	0.002
Standard deviation score of body mass index	0.49 ± 1.34	0.26 ± 1.24	0.004*	0.30 ± 0.93	0.08 ± 0.93	0.002
Systolic blood pressure (mmHg)	132 ± 23	133 ± 16	0.864	143 ± 22	134 ± 19	0.142
Diastolic blood pressure (mmHg)	81 ± 15	78 ± 9	0.813	80 ± 13	78 ± 9.6	0.460
Hemoglobin A_{1c} (%)	8.4 ± 1.5	6.5 ± 0.6	0.000	8.6 ± 2.0	7.0 ± 1.0	0.000*
Fasting blood glucose (mg/dL)	157 ± 47	136 ± 29	0.024	164 ± 50	144 ± 33	0.059
Fasting serum insulin (μIU/mL)	9.11 ± 9.11	8.18 ± 5.15	0.467*	6.63 ± 3.61	6.87 ± 3.81	0.634*
Serum triglyceride (mg/dL)	126 ± 120	110 ± 77	0.361*	112 ± 63	105 ± 59	0.468*
Serum LDL cholesterol (mg/dL)	134 ± 39	125 ± 29	0.076*	157 ± 35	133 ± 28	0.001*
Serum HDL cholesterol (mg/dL)	47 ± 13	52 ± 14	0.021*	59 ± 14	60 ± 16	0.319
VAT (cm²)	150.9 ± 57.5	129.4 ± 57.8	0.000	99.6 ± 51.7	80.0 ± 40.7	0.000*
ΔVAT (cm²)		−21.6 ± 26.2			−19.6 ± 19.5	
%ΔVAT		−14.2 ± 21.6			−18.9 ± 19.0	
SAT (cm²)	123.4 ± 70.7	109.9 ± 63.8	0.004	187.3 ± 70.0	168.1 ± 67.3	0.003*
ΔSAT (cm²)		−13.5 ± 22.8			−19.1 ± 29.9	
%ΔSAT		−9.0 ± 23.1			−8.8 ± 17.9	
TAT (cm²)	274.4 ± 106.4	239.3 ± 103.6	0.000	286.9 ± 103.5	248.1 ± 94.6	0.000
ΔTAT (cm²)		−35.1 ± 42.1			−38.8 ± 36.0	
%ΔTAT		−12.8 ± 19.3			−13.4 ± 15.2	
V/S ratio	1.40 ± 0.67	1.30 ± 0.58	0.069*	0.57 ± 0.30	0.49 ± 0.21	0.013*
Waist circumference (cm)	88.9 ± 10.1	86.3 ± 10.2	0.000	87.0 ± 8.8	84.6 ± 9.0	0.002

Notes: Values are means ± SD. Patients receiving lipid-lowering drugs (4 men and 5 women) were excluded from the analysis of lipid profiles, as were patients receiving antihypertensive drugs (11 men and 10 women) from the analysis of blood pressure; *Nonparametric counterpart (Wilcoxon signed rank test).
Abbreviations: VAT, visceral adipose tissue; SAT, subcutaneous adipose tissue; TAT, total adipose tissue; V/S ratio, ratio of visceral adipose tissue area to subcutaneous adipose tissue area.

inverse correlation between VAT and serum HDL-C levels ($r = 0.567$ and $P = 0.011$) was also observed. Applying the standard deviation score of BMI did not materially change the correlations of VAT, SAT, TAT, or WC with BMI in both sexes ($P \leq 0.001$ for all).

Assessment of dietary intake

Total energy intake, assessed by 3-day food records, was 1812 ± 375 kcal/day for men and 1706 ± 323 kcal/day for women. The average daily percentages of intake for carbohydrates, fat, and protein (% energy) were 34.5% ± 8.0%, 39.6% ± 9.0%, and 19.1% ± 3.4% for men and 40.6% ± 8.1%, 36.4% ± 7.4%, and 20.5% ± 2.4% for women, respectively (Table 2). The carbohydrate intake (% energy) was significantly higher in women than in men ($P = 0.010$).

Changes in anthropometric variables, cardiovascular risk factors, and antidiabetic drug use over 6 months

In men, the mean BMI (−0.7 ± 1.2 kg/m²), the standard deviation score of BMI (−0.23 ± 0.37), HbA$_{1c}$ (−1.8% ± 1.4%) and FBG (−20 ± 42 mg/dL) were significantly decreased, and serum

HDL-C (4.5 ± 8.8 mg/dL) levels were significantly increased after 6 months. However, no significant changes were observed in the serum LDL-C and TG levels (Table 1). In women, however, the mean BMI (−0.8 ± 1.0 kg/m²), the standard deviation score of BMI (−0.22 ± 0.30), HbA$_{1c}$ (−1.7% ± 1.6%) and LDL-C levels (−24 ± 27 mg/dL) were significantly decreased, whereas the mean serum TG and HDL-C levels were not significantly altered after 6 months (Table 1).

Sixteen of the patients had already been prescribed antidiabetic drugs by other physicians before initiation of the study. The number of patients (n) who took sulfonylureas decreased and some of the remaining patients' doses were lowered over the 6 months (glibenclamide: n; from 5 to 1, mean dose; from 5 to 2.5 mg/day; glimepiride: n; from 6 to 7, mean dose; from 2.8 to 1.5 mg/day; gliclazide: n; from 1 to 1, mean dose; from 80 to 20 mg/day). As for other antidiabetic drugs, the number of patients (n) who received nateglinide, mitiglinide, voglibose, and pioglitazone also decreased (nateglinide: n; from 1 to 0, mitiglinide: n; from 1 to 0, pioglitazone: n; from 4 to 1, voglibose: n; from 8 to 3). The number of patients who took metformin slightly increased (from 5 to 7), although mean dose decreased from 600 to 500 mg/day.

Table 2 Daily dietary intake at 5 months after baseline

	Men (n = 28)	Women (n = 24)
Total energy intake (kcal)	1812 ± 375	1706 ± 323
Carbohydrate (g)	153.8 ± 37.7	171.8 ± 40.5
Soluble fiber (g)	2.7 ± 1.0	3.1 ± 1.0
Insoluble fiber (g)	10.1 ± 3.7	10.6 ± 4.0
Carbohydrate (% energy)	34.5 ± 8.0	40.6 ± 8.1
Fat (g)	79.4 ± 24.3	69.6 ± 21.7
Saturated fat (g)	21.7 ± 7.2	17.4 ± 6.8
Monounsaturated fat (g)	32.7 ± 11.1	27.7 ± 10.0
Polyunsaturated fat (g)	15.5 ± 5.6	15.8 ± 5.7
Fat (% energy)	39.6 ± 9.0	36.4 ± 7.4
Protein (g)	85.4 ± 19.7	86.8 ± 15.4
Protein (% energy)	19.1 ± 3.4	20.5 ± 2.4
Foods rich in carbohydrate		
Rice (g)	166 ± 85	160 ± 57
Noodles (g)	41 ± 46	57 ± 61
Bread (g)	24 ± 35	19 ± 29
Potatoes (g)	18 ± 34	22 ± 46
Fruit (g)	34 ± 73	64 ± 78
Confectioneries (g)	17 ± 24	19 ± 16
Sugar (g)	7 ± 7	8 ± 7

Note: values are means ± SD.

Changes in abdominal fat distribution

The parameters ΔVAT, ΔSAT, and WC were significantly decreased in both men and women during the 6-month period ($P < 0.05$ for all, Table 1).

In men, despite an absolute decrease in VAT (-21.6 ± 26.2 cm²), %ΔVAT ($-14.2\% \pm 21.6\%$) was not significantly different from %ΔSAT ($-9.0\% \pm 23.1\%$) ($P = 0.111$). However, a significant decrease in V/S ($P = 0.069$) was not observed (Table 1). In women, along with an absolute decrease in VAT (-19.6 ± 19.5 cm²), %ΔVAT ($-18.9\% \pm 19.0\%$) was significantly higher than %ΔSAT ($-8.8\% \pm 17.9\%$) ($P = 0.022$), and V/S was also significantly decreased ($P = 0.013$).

Associations between changes in abdominal fat distribution and cardiovascular risk factors

In men, no significant correlations were observed between changes in abdominal adipose tissue distribution (ΔVAT, ΔSAT, ΔTAT, %ΔVAT, %ΔSAT, and %ΔTAT) and changes in cardiovascular risk factors (Table 3). Meanwhile, ΔTAT, %ΔSAT, and %ΔTAT were strongly correlated with ΔFBG in women ($r = 0.533$ for ΔTAT, $r = 0.417$ for %ΔSAT, and $r = 0.461$ for %ΔTAT, Table 3). Similarly, ΔSAT, ΔTAT, %ΔSAT, and %ΔTAT were all strongly and inversely correlated with ΔHDL-C in women ($r = -0.699$ for ΔSAT,

$r = -0.567$ for ΔTAT, $r = -0.720$ for %ΔSAT, and $r = -0.554$ for %ΔTAT, Table 3). In addition, a significant inverse correlation between ΔWC and ΔHDL-C was detected ($r = -0.622$), as was a similar correlation between either ΔSAT or ΔWC and ΔSBP ($r = -0.543$ for ΔSAT and $r = -0.550$ for ΔWC, Table 3). In contrast, only %ΔVAT significantly correlated with ΔTG ($r = 0.591$, Table 3).

In multiple regression analyses that were adjusted for age, the following associations remained significant in women: between %ΔVAT and ΔTG ($P = 0.005$), between ΔSAT and ΔHDL-C ($P < 0.001$), between %ΔSAT and ΔHDL-C ($P < 0.001$), and between ΔWC and ΔHDL-C ($P < 0.001$). When five patients who had received pioglitazone, which influences abdominal fat distribution and serum lipid profiles, were excluded, the strong correlations observed in women were not materially altered (data not shown).

Discussion

This study is the first to show that, in outpatients with T2DM, a significant decrease in both VAT and SAT in men and women with good glycemic and BMI control, as well as a tapering off of sulfonylurea use and an improvement in serum lipid profiles, can be achieved with a moderate LCD (about a 38% carbohydrate diet). Significant preferential VAT loss was achieved in women. VAT loss was greater than SAT loss in men as well, but the difference did not reach statistical significance. At the same time, significant correlations of %ΔSAT with ΔFBG and ΔHDL-C and significant correlations of %ΔVAT with ΔTG were observed only in women.

Limitations

First, the use of antidiabetic drugs (especially pioglitazone) that influence SAT and HDL-C may have affected the results.[30,31] However, in the analysis that excluded the 4 patients who took pioglitazone, a strong correlation remained between the change in abdominal fat distribution and ΔHDL-C in women. Second, all the participants in this study were non-obese, with an average BMI ($\pm$SD) of 24.7 ± 4.0. Caucasians tend to be more obese and insulin resistant than East Asian populations.[32,33] Therefore, studies of non-obese patients with T2DM may be more relevant to East Asian populations. Cross-sectional studies of apparently lean Japanese individuals demonstrated that a significant accumulation of VAT was associated with increased risk factors for cardiovascular disease and diabetes. These results were similar to what has been observed in obese patients with T2DM.[23,34,35] Third, MRI abdomen is more accurate in

Table 3 Spearman correlation coefficients between the change in abdominal fat distribution or WC and cardiovascular risk factors during the 6-month moderate low-carbohydrate diet

	r							
	ΔVAT (cm²)	ΔSAT (cm²)	ΔTAT (cm²)	%ΔVAT	%ΔSAT	%ΔTAT	ΔV/S ratio	ΔWC (cm)
Men (n = 28)								
ΔBody mass index (kg/m²)	0.533**	0.747**	0.735**	0.656**	0.707**	0.742**	−0.173	0.678**
ΔStandard deviation score of body mass index	0.544**	0.729**	0.731**	0.662**	0.697**	0.743**	−0.150	0.667**
ΔSystolic blood pressure (mmHg)	0.076	0.123	0.174	0.022	0.211	0.081	−0.350	0.159
ΔDiastolic blood pressure (mmHg)	0.001	0.114	0.117	0.021	0.204	0.077	−0.347	0.150
ΔFasting blood glucose (mg/dL)	−0.083	−0.125	−0.138	−0.094	−0.088	−0.096	0.021	0.140
ΔFasting serum insulin (μIU/mL)	−0.236	0.070	−0.137	−0.075	0.123	−0.042	−0.292	0.119
ΔHemoglobin A_{1c} (%)	0.210	−0.041	0.115	0.050	−0.080	0.028	−0.006	0.055
ΔTriglyceride (mg/dL)	−0.110	−0.173	−0.173	−0.004	−0.128	−0.089	0.228	0.176
ΔLDL–cholesterol (mg/dL)	0.058	0.174	0.078	−0.026	0.142	−0.009	−0.357	0.026
ΔHDL–cholesterol (mg/dL)	−0.166	0.075	−0.119	−0.243	0.085	−0.213	−0.268	−0.005
Women (n = 24)								
ΔBody mass index (kg/m²)	0.365	0.390	0.462*	0.596**	0.448*	0.609**	−0.047	0.538**
ΔStandard deviation score of body mass index	0.377	0.394	0.468*	0.606**	0.451*	0.615**	−0.049	0.542**
ΔSystolic blood pressure (mmHg)	−0.037	−0.543*	−0.292	−0.081	−0.455	−0.275	0.240	−0.550*
ΔDiastolic blood pressure (mmHg)	−0.524	−0.249	−0.444	−0.442	−0.242	−0.469	−0.213	−0.441
ΔFasting blood glucose (mg/dL)	0.282	0.381	0.533**	0.283	0.417*	0.461*	−0.110	0.444*
ΔFasting serum insulin (μIU/mL)	0.293	−0.059	0.189	0.218	−0.105	0.104	0.291	0.335
ΔHemoglobin A_{1c} (%)	0.002	−0.025	0.006	0.101	0.007	0.062	0.068	0.099
ΔTriglyceride (mg/dL)	0.335	−0.047	0.176	0.591**	0.032	0.290	0.381	0.141
ΔLDL-cholesterol (mg/dL)	−0.007	0.143	0.129	0.070	0.151	0.168	−0.030	−0.036
ΔHDL-cholesterol (mg/dL)	0.042	−0.699**	−0.567**	−0.160	−0.720**	−0.554**	0.491*	−0.622**

Notes: *$P < 0.05$; **$P < 0.01$. Patients receiving lipid-lowering drugs were excluded from the analysis related to lipid profiles, as were patients receiving antihypertensive drugs from the analyses related to blood pressure.
Abbreviations: VAT, visceral adipose tissue; SAT, subcutaneous adipose tissue; TAT, total adipose tissue; V/S ratio, the ratio of visceral adipose tissue area to subcutaneous adipose tissue area; WC, waist circumference; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

measurement of abdominal fat compared with CT, although it is more expensive.[36]

Finally, the lack of an HCD group as a control may be considered a limitation, although our study aimed to evaluate preferential abdominal fat loss induced by LCDs.

Can preferential VAT loss be achieved with moderate LCDs?

Most HCD intervention studies examining abdominal fat loss demonstrated absolute VAT and SAT loss in both sexes, as well as a reduction in weight.[24–29,37,38] Our moderate LCD also significantly decreased absolute VAT and SAT and resulted in weight loss. These results agree with the results of an HCD intervention study involving non-obese Japanese patients with diabetes whose BMIs were similar to those of our patients.[38] In terms of the percentage of abdominal fat loss, Chaston and Dixon reported that HCDs resulted in 8.3%–50% VAT loss and 2.6%–41% SAT loss in obese subjects with BMIs ranging from 26 to 40.[18] Our moderate LCD also resulted in a 14.2% VAT loss in men and an 18.9% VAT loss in women, as well as a 9.0% SAT loss in men and an 8.8% SAT loss in women. These results suggest that the efficacy of moderate LCDs on absolute changes, and on changes in the percentage of abdominal fat loss, is comparable to that of HCDs.

Regarding the preferential loss of VAT or SAT, many HCD intervention studies have reported equivocal and inconsistent results. These inconsistencies may be due to the variable intervention period, sex differences and the use of 2 methods (% loss or ratio) to assess changes in VAT and SAT. Some studies were conducted for approximately 3 months in women only,[24] and another was conducted for 4 weeks in men and women.[19] Several studies used V/S to assess preferential abdominal fat loss,[19,24,27,29,37] whereas another used the percentage of loss.[18] The variety of study designs makes it difficult to compare results between studies. In addition, only a few of the HCD intervention studies used a 6-month study period or examined the sex difference.[25,37] Collectively, there is no compelling evidence of preferential VAT loss resulting from intervention with HCDs in either women or men.[18]

In contrast, our 6-month moderate LCD intervention study demonstrates that VAT and SAT significantly decreased in both sexes. Furthermore, %ΔVAT was greater than %ΔSAT in men and women, but the difference did not achieve statistical significance in men. One possible reason for this discrepancy between men and women is that, compared with SAT loss, VAT loss may occur earlier in men.[18] A study with an intermediate time point may have been able to detect the VAT loss, as well as a decrease in HbA_{1c} levels and BMI, in men. Earlier CT assessment of the changes in abdominal fat distribution may be warranted to evaluate preferential abdominal fat loss.

The correlation between abdominal fat distribution and cardiovascular risk factors

LCDs induce a decrease in FBG in conjunction with a decrease in serum TG levels and an increase in serum HDL-C levels, which are characteristic of the differences between LCDs and HCDs.[1–5] This study demonstrates the correlations of changes in abdominal fat distribution with ΔFBG, ΔHDL-C, and ΔTG in women. Our results suggest that the major benefit of moderate LCDs is abdominal fat loss in patients with T2DM who have higher serum TG levels and/ or lower serum HDL-C levels.

Although numerous HCD intervention studies have been conducted, relatively little is known about the correlations between %ΔVAT or %ΔSAT and changes in cardiovascular risk factors in patients on HCDs. One researcher has described correlations between ΔVAT and ΔTG, as well as ΔV/S and ΔFBG.[27] Others have described correlations between ΔVAT and ΔFBG, Δinsulin and either Δtotal cholesterol or ΔLDL-C and ΔSAT and either Δtotal cholesterol or ΔLDL-C.[28] The inconsistent results from the serum lipid profiles seem to be due to the high-carbohydrate conditions.

We focused on which adipose tissues contribute more to changes in cardiovascular risk factors. Concerning the above 3 cardiovascular risk factors, %ΔSAT was correlated with two (ΔFBG and ΔHDL-C) of the factors, while %ΔVAT was correlated with one (ΔTG). Taking into consideration the recent reviews that describe no compelling evidence of weight loss due to intervention with HCDs and/or exercise that targets preferential VAT loss,[18] our study may provide evidence that SAT increases cardiovascular risk to the same extent as VAT in women.

Conclusion

A significant decrease in absolute VAT and SAT in men and women with good glycemic and BMI control, as well as a tapering off of sulfonylurea use and the improvement of the serum lipids profiles, can be achieved with the a moderate LCD. Significant preferential VAT loss was achieved in women, and VAT loss was greater than SAT loss in both men and women, although the difference was not statistically significant in men. Concomitantly, significant correlations of %ΔSAT with ΔHDL, as well as ΔFBG and %ΔVAT with ΔTG were observed in women. We suggest that the moderate LCD may be effective for preferential VAT loss in patients with T2DM who have lower serum HDL-C and/or higher serum TG levels, and that both VAT and SAT may influence CRFs in female patients with T2DM who are following a moderate LCD.

However, we did not find a significant association between abdominal fat loss and changes in cardiovascular risk factors in men. Further detailed studies with intermediate assessments are required to clarify the relationship between preferential abdominal fat loss and changes in cardiovascular risk factors.

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Disclosure

The authors declare that they have no competing interests.

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