

The Relationship Between Abdominal Body Composition and Metabolic Syndrome After a Weight Reduction Program in Adult Men with Obesity

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Chun-Cheng Liao^{1,2}
Wayne Huey-Herng Sheu³⁻⁵
Shih-Yi Lin^{4,6}
Wen-Jane Lee⁷
I-Te Lee^{3,4,8,9}

¹Department of Family Medicine, Taichung Armed Forces General Hospital, Taichung, Taiwan; ²School of Medicine, National Defense Medical Center, Taipei, Taiwan; ³Division of Endocrinology and Metabolism, Department of Internal Medicine, Taichung Veterans General Hospital, Taichung, Taiwan; ⁴School of Medicine, National Yang-Ming University, Taipei, Taiwan; ⁵Rong Hsing Research Center for Translational Medicine, College of Life Sciences, National Chung Hsing University, Taichung, Taiwan; ⁶Center for Geriatrics and Gerontology, Taichung Veterans General Hospital, Taichung, Taiwan; ⁷Department of Medical Research, Taichung Veterans General Hospital, Taichung, Taiwan; ⁸School of Medicine, Chung Shan Medical University, Taichung, Taiwan; ⁹College of Science, Tunghai University, Taichung City, Taiwan

Purpose: To assess the relationship between changes in abdominal adipose tissue and metabolic syndrome (MetS) in men with obesity after a weight reduction program (WRP).

Patients and Methods: Adult men with obesity and MetS were recruited for this prospective single-arm intervention study. Participants consumed an energy-restricted diet of 1200 kcal/day and performed 50-mins aerobic exercise daily for 12 weeks. Changes in the components of MetS were recorded. Changes in subcutaneous abdominal fat area (SAFA) and intra-abdominal fat area (IAFA) at the umbilicus level were determined using magnetic resonance imaging.

Results: A total of 30 men (mean age, 42.3 ± 10.0 years; body mass index, 33.7 ± 4.1 kg/m²) were included in this study. A moderate (8.0%) weight reduction occurred. Reversion of MetS was observed in 15 (50%) participants after the WRP. There was significant reduction in SAFA (68.3 ± 20.2 vs. 51.5 ± 18.6 cm²; $P < 0.001$) and IAFA (96.3 ± 15.6 vs. 86.0 ± 16.5 cm²; $P < 0.001$); the magnitude of reduction was greater for SAFA than for IAFA (-16.8 ± 7.7 vs. -10.3 ± 8.3 cm²; $P < 0.001$). Multivariate logistic regression analysis showed a reduction in IAFA to be an independent factor to decrease the risk of persistent MetS after WRP by adjustment for age, baseline IAFA, and change in SAFA (odds ratio = 0.25, 95% confidence interval: 0.07–0.95, $P = 0.041$). Reduction in SAFA was not significantly associated with the reversion of MetS ($P = 0.411$).

Conclusion: Reduction in IAFA via a 12-week WRP may help reverse MetS in men with obesity and MetS.

Keywords: body mass index, intra-abdominal fat, magnetic resonance imaging, metabolic syndrome, subcutaneous abdominal fat, visceral fat

Introduction

Obesity, characterized by an excessive proportion of body fat, is associated with chronic complications, including cardiovascular disease, type 2 diabetes mellitus, and cancer.¹ Obesity has become a growing health problem worldwide.²⁻⁴ Data from the Nutrition and Health Survey in Taiwan showed that the prevalence of obesity, defined by body mass index (BMI) ≥ 27 kg/m², was approximately 22.1% between 2013 and 2014.⁵

Abdominal obesity, characterized by increased waist circumference, is a relevant health issue.⁶⁻⁸ Generally, abdominal fat can be divided into subcutaneous and intra-abdominal fat.⁹ Although intra-abdominal fat, both visceral and retroperitoneal fat,

Correspondence: I-Te Lee
Division of Endocrinology and Metabolism, Department of Internal Medicine, Taichung Veterans General Hospital, 1650 Taiwan Boulevard, Sect. 4, Taichung 40705, Taiwan
Tel +886-4-23741300
Fax +886-4-23593662
Email itlee@vghtc.gov.tw

represents approximately 15% of the total body fat, it is closely associated with cardiovascular disease and mortality.¹⁰ Previous studies have indicated that intra-abdominal adipose tissue, but not subcutaneous abdominal one, is associated with insulin resistance and cardiovascular risks.⁶

Metabolic syndrome (MetS) comprises a cluster of abnormal components based on physiological, clinical, and metabolic factors that directly increase the risk of type 2 diabetes mellitus and cardiovascular morbidity and mortality.^{11–13} Abdominal obesity, one of the MetS components, should be considered a critical mechanism linking MetS and cardiovascular disease.¹⁴ Intra-abdominal fat has been reported as a long-term predictor of insulin resistance in a longitudinal observation.¹⁵

Physical activity along with restriction of energy intake is an effective first-line strategy to manage obesity.¹⁶ Weight reduction has been reported to improve cardiovascular risks in subjects with obesity after such a short-term intervention.^{17–19} A greater loss of subcutaneous fat than of visceral fat was observed in the whole body as well as abdominal area among the majority of weight reduction programs (WRP).²⁰ However, it is reported that visceral fat was a better predictor of insulin resistance, MetS, and mortality.^{21,22} We hypothesized that a reduction in visceral fat would have a stronger contribution to the improvement of MetS than a reduction in subcutaneous fat. Therefore, we assessed intra-abdominal fat area (IAFA) and subcutaneous abdominal fat area (SAFA) before and after WRP in men with obesity and MetS.

Materials and Methods

Participants

This prospective, single-arm interventional study was conducted at Taichung Veterans General Hospital in Taiwan. The inclusion criteria were (1) adult men, (2) age between 20 and 75 years, (3) MetS, and (4) BMI ≥ 27 kg/m², the cutoff for defining obesity in Taiwan.²³ The exclusion criteria were (1) current use of antidiabetic medications, medications for psychological disorders, and medications affecting body weight, such as systemic steroids; (2) changes in antihypertensive, lipid-lowering, or antiplatelet drugs within the past month; (3) endocrine diseases, such as thyroid or adrenal disorders; (4) acute or chronic kidney diseases with serum creatinine levels >200 μ mol/L; (5) severe systemic diseases, such as malignant or immune disorders; and (6) addiction to alcohol or drugs.

Weight Reduction Program

Participants enrolled in this study were required to decrease body weight via a 12-week program of intake restriction and exercise promotion. They were instructed by a dietitian to maintain a 1200 kcal/day diet, divided into 300 kcal at breakfast, 400 kcal at lunch, and 500 kcal at dinner. Participants were encouraged to undertake aerobic exercise for 50 mins daily. During the WRP, all subjects attended eight classes for the purpose of lifestyle training. The first three classes were held every week, and the others were held every 2 weeks. Each class included: anthropometric assessments by a study nurse; diet diaries reviewed by a registered dietitian; exercise target setting by a trained instructor; and group discussion among the participants, the dietitian, the cardiologist, and the endocrinologist. Following the class, subjects were required to attend a 50-min practice session for moderate-intensity aerobic exercise, which was provided by trained instructors in the presence of doctors.

A 10% reduction in basal body weight was suggested,^{24,25} and no medication changes were allowed during the study. The study was approved by the Institutional Review Board of Taichung Veterans General Hospital, and written informed consent was obtained by all participants. This study was conducted in accordance with the Declaration of Helsinki.

Measurements

Anthropometric parameters, blood pressure, fasting glucose, insulin, lipid profiles, abdominal fat content, and number of MetS components at baseline and at the end of the 12-week WRP were assessed. Height was measured (Pharmacia Taiwan Inc., Taipei, Taiwan) after participants had removed their shoes, and body weight (DETECTO, Cardinal Scale Manufacturing Co., Webb City, MO, USA) after they had taken off all heavy clothing. BMI was calculated as weight (kg) divided by height (m²). Waist circumference was measured midway between the lowest rib and iliac crest using a measuring tape (kp-1508, King Life, Taipei, Taiwan). Blood pressure was recorded in the sitting position using the DINAMAPTM Vital Signs Monitor (Model 1846 SX/P) after participants had rested for 10 mins; three readings were taken at intervals of 1 min and the average of the second and the third readings was registered. Blood samples were collected after an overnight fast. Fasting glucose and lipid levels were measured using commercial kits (Beckman Coulter, Fullerton,

CA, USA). Insulin was measured using commercial kits (Roche Diagnostics GmbH, Mannheim, Germany). The homeostasis model assessment of insulin resistance (HOMA-IR) index was calculated as fasting insulin (mg/dL) × fasting glucose (mmol/L)/405.²⁶ Adipose tissue depots were measured using magnetic resonance imaging (MRI) (Siemens Medical Systems, Iselin, NJ, USA), and dedicated software (Leonardo, Siemens Healthcare, Germany) was used to determine the IAFA and SAFA at the level of the umbilicus.²⁷ The IAFA/SAFA ratio (ISR) was calculated. We used the harmonized definition of MetS.²⁸ The criteria of abnormal components are as follows: (1) waist circumference ≥ 90 cm, (2) fasting glucose ≥ 100 mg/dL, (3) blood pressure $\geq 130/85$ mmHg, (4) triglycerides ≥ 150 mg/dL, and (5) high-density lipoprotein (HDL) cholesterol < 40 mg/dL. The number of MetS components was calculated as the sum of all abnormal components, and the definition of MetS was the number of MetS components ≥ 3 in each individual.

Statistical Analysis

Continuous variables were summarized as mean $\pm$ standard deviation and categorical variables as frequency and percentage. The normality of distribution of data was examined using the Kolmogorov–Smirnov test. The changes in parameters between baseline and the end of the WRP were examined using the Wilcoxon signed-rank test for continuous variables or the McNemar's test for categorical variables. The correlation was assessed using the Spearman correlation coefficient. Multivariate logistic analysis was used to identify the independent predictors for the reversion of MetS after the WRP. Two-sided $P < 0.05$ was taken to indicate statistical significance. SPSS 22.0 (IBM, Armonk, NY, USA) was used for statistical analysis.

Results

Out of the 40 candidates initially identified, six were excluded according to the criteria; another four dropped out of the study. Thus, a total of 30 participants completed the WRP and MRI assessments. The mean age was 42.3 ± 10.0 years, and an 8.0% weight reduction (from 98.3 ± 13.4 kg to 90.4 ± 14.2 kg, $P < 0.001$) was observed after the WRP. Table 1 shows the characteristics of the participants before and after the WRP. BMI and waist circumference were significantly decreased after the WRP (33.7 ± 4.1 vs. 31.0 ± 4.4 kg/m², $P < 0.001$; 109.7 ± 9.6 vs. 101.6 ± 10.8 cm, $P < 0.001$; respectively). Systolic and diastolic blood pressures were significantly decreased after the WRP

Table 1 Characteristics of All Participants Before and After the Weight Reduction Program

	Weight Reduction Program		P
	Before (n = 30)	After (n = 30)	
Age (years)	42.3 $\pm$ 10.0		
BMI (kg/m ²)	33.7 $\pm$ 4.1	31.0 $\pm$ 4.4	<0.001
Body weight (kg)	98.3 $\pm$ 13.4	90.4 $\pm$ 14.2	<0.001
Waist circumference (cm)	109.7 $\pm$ 9.6	101.6 $\pm$ 10.8	<0.001
Systolic BP (mmHg)	136.5 $\pm$ 17.1	121.5 $\pm$ 17.9	0.001
Diastolic BP (mmHg)	82.7 $\pm$ 11.1	73.8 $\pm$ 12.7	<0.001
Fasting glucose (mg/dL)	102.5 $\pm$ 15.7	96.9 $\pm$ 9.7	0.008
HDL cholesterol (mg/dL)	38.3 $\pm$ 7.0	41.9 $\pm$ 10.4	0.023
Triglycerides (mg/dL)	316.4 $\pm$ 485.2	201.9 $\pm$ 279.3	0.008
HOMA-IR	5.0 $\pm$ 3.2	3.1 $\pm$ 1.5	<0.001
Number of MetS components	3.8 $\pm$ 0.8	2.5 $\pm$ 1.5	<0.001
IAFA (cm ²)	96.3 $\pm$ 15.6	86.0 $\pm$ 16.5	<0.001
SAFA (cm ²)	68.3 $\pm$ 20.2	51.5 $\pm$ 18.6	<0.001
ISR	1.5 $\pm$ 0.4	1.8 $\pm$ 0.6	<0.001

Abbreviations: BMI, body mass index; BP, blood pressure; HDL, high-density lipoprotein; HOMA-IR, homeostatic model assessment of insulin resistance; IAFA, intra-abdominal fat area; ISR, intra-abdominal fat area/subcutaneous abdominal fat area ratio; MetS, metabolic syndrome; SAFA, subcutaneous abdominal fat area.

(136.5 ± 17.1 vs. 121.5 ± 17.9 mmHg, $P = 0.001$; 82.7 ± 11.1 vs. 73.8 ± 12.7 mmHg, $P < 0.001$; respectively). Plasma glucose was significantly decreased (102.5 ± 15.7 vs. 96.9 ± 9.7 mg/dL, $P = 0.008$). Fasting triglycerides and HDL cholesterol were significantly improved after the WRP (316.4 ± 485.2 vs. 201.9 ± 279.3 mg/dL, $P = 0.008$; 38.3 ± 7.0 vs. 41.9 ± 10.4 mg/dL, $P = 0.023$; respectively). The IAFA and SAFA were significantly decreased after the WRP (96.3 ± 15.6 vs. 86.0 ± 16.5 cm², $P < 0.001$; 68.3 ± 20.2 vs. 51.5 ± 18.6 cm², $P < 0.001$) respectively. There was a greater reduction in SAFA than in IAFA (-16.8 ± 7.7 vs. -10.3 ± 8.3 cm², $P < 0.001$)

At the end of the 12-week WRP, 15 (50%) participants had reversion of MetS and the other 15 (50%) participants had persistent MetS ($P < 0.001$ based on McNemar's test). The mean number of MetS components was significantly decreased in participants with reversion of MetS after the WRP (3.5 ± 0.7 vs. 1.3 ± 0.8 , $P < 0.001$) but not in those with persistent MetS (4.0 ± 0.8 vs. 3.7 ± 0.9 , $P = 0.262$; Table 2). BMI, IAFA, and SAFA were significantly decreased, and ISR was significantly increased in both groups. The reduction in IAFA was significantly greater in participants with the reversion of MetS than that in participants with persistent MetS (-14.2 ± 7.9 vs. -5.9 ± 6.3 cm², $P = 0.008$), but the reduction in SAFA was

Table 2 Comparison of Participants with Persistent MetS and Participants with Reversion of MetS After the Weight Reduction Program (WRP)

	Persistent MetS After WRP (n=15)	P*	Reversion of MetS After WRP (n=15)	P*	P [#]
Age (years)	45.2±10.6		41.5±9.2		0.312
BMI (kg/m ²)					
Baseline	32.5±3.2		33.9±4.6		0.358
Change	-2.2±1.3	<0.001	-3.4±1.5	<0.001	0.031
Waist circumference (cm)					
Baseline	108.9±7.6		108.1±10.3		0.817
Change	-8.6±5.3	<0.001	-9.3±6.3	<0.001	0.747
Systolic BP (mmHg)					
Baseline	137.1±16.5		135.8±18.2		0.835
Change	-8.2±17.1	0.085	-21.8±23.2	0.003	0.079
Diastolic BP (mmHg)					
Baseline	86.1±10.7		79.3±10.7		0.091
Change	-7.7±9.9	0.010	-10.1±9.8	0.001	0.510
Fasting glucose (mg/dL)					
Baseline	106.3±19.7		98.7±9.7		0.190
Change	-6.0±11.8	0.070	-5.1±9.8	0.061	0.829
HDL cholesterol (mg/dL)					
Baseline	37.3±5.5		39.3±8.3		0.428
Change	-2.2±4.9	0.105	9.3±6.5	<0.001	<0.001
Triglycerides (mg/dL)					
Baseline	438.7±671.3		194.2±70.8		0.172
Change	-141.1±307.1	0.097	-87.9±75.2	<0.001	0.520
HOMA-IR					
Baseline	5.2±2.2		4.9±4.0		0.800
Change	-1.8±3.4	0.001	-1.9±1.7	0.051	0.952
IAFA (cm ²)					
Baseline	91.4±10.4		100.6±18.3		0.426
Change	-5.9±6.3	0.008	-14.2±7.9	<0.001	0.008
SAFA (cm ²)					
Baseline	68.2±19.9		68.5±21.2		0.737
Change	-14.3±6.3	<0.001	-19.0±8.4	<0.001	0.117
ISR					
Baseline	1.6±0.5		1.5±0.4		0.894
Change	0.3±0.2	<0.001	0.4±0.4	0.008	0.521
Number of MetS components					
Baseline	4.0±0.8		3.5±0.7		0.120
Change	-0.3±0.9	0.262	-2.3±1.1	<0.001	<0.001

Notes: *P: significance of intra-group change before and after WRP. #P: significance of difference between the two groups.

Abbreviations: BMI, body mass index; BP, blood pressure; HDL, high-density lipoprotein; HOMA-IR, homeostasis model assessment of insulin resistance; IAFA, intra-abdominal fat area; ISR, intra-abdominal fat area/subcutaneous abdominal fat area ratio; MetS, metabolic syndrome; SAFA, subcutaneous abdominal fat area; WRP, weight reduction program.

comparable between the groups (-19.0 ± 8.4 vs. -14.3 ± 6.3 cm², $P = 0.117$). Among the MetS components, only the change in HDL cholesterol was significantly different between these two groups (9.3 ± 6.5 mg/dL in participants with MetS reversion vs. -2.2 ± 4.9 mg/dL in participants with persistent MetS, $P < 0.001$). A significantly inverse correlation was observed between changes in IAFA and HDL cholesterol (Spearman's correlation coefficient = -0.527 , $P = 0.006$; Table 3). Target weight reduction ($>10\%$ of baseline body weight) was achieved by only 9 (30%) of 30 participants. MetS reversion occurred in 2 of 9 participants who achieved target weight reduction and 13 of 21 participants who did not achieve target weight reduction ($P > 0.05$).

Multivariate logistic regression analysis estimated the association of multiple variables with persistent MetS after the WRP (Table 4). A reduction in IAFA was a significant factor to decrease the risk of persistent MetS after the WRP based on adjustments for age, SAFA change, and baseline IAFA (odds ratio = 0.25, 95% confidence interval: 0.07–0.95, $P = 0.041$). However, change in SAFA was not significantly associated with reversion to an absence of MetS in this logistic regression model ($P = 0.411$).

Discussion

The major finding was that IAFA reduction, but not SAFA reduction, was significantly associated with MetS reversion after the WRP. A previous cross-sectional study reported that visceral fat, but not subcutaneous fat, was associated with MetS.⁶ In a longitudinal study with 10-year follow-up, Tong et al²⁹ reported that baseline IAFA was predictive of the development of MetS in a 10-year observation. However, our strength in the present study is to demonstrate an independent association between IAFA reduction and MetS reversion via a WRP intervention in men with obesity and MetS. In the Multi-Ethnic Study of Atherosclerosis (MESA) study, Shah et al³⁰ also demonstrated that an increase in visceral fat, but not subcutaneous fat, was associated with a development of MetS in subjects without MetS at baseline. Park and Lee³¹ demonstrated that reduction in visceral fat was significantly correlated with the reduction of fasting blood glucose and triglyceride levels after WRP. These reports are in line with our findings indicating that the change in IAFA, instead of SAFA, was an important mechanism involved in MetS, even in the development of MetS during observation and the resolution of MetS in the WRP intervention.

Table 3 Correlation Between Changes in Body Fat and Changes in BMI, HOMA-IR and Components of Metabolic Syndrome

	IAFA	P	SAFA	P	ISR	P
BMI	0.577	0.002	0.705	<0.001	-0.263	0.194
HOMA-IR	-0.071	0.729	0.158	0.442	-0.226	0.267
Waist circumference	0.124	0.545	0.338	0.091	-0.454	0.020
Systolic BP	0.150	0.466	0.426	0.030	-0.114	0.578
Diastolic BP	-0.128	0.533	0.375	0.059	0.003	0.987
Fasting glucose	0.011	0.957	-0.123	0.549	-0.106	0.606
HDL cholesterol	-0.527	0.006	-0.156	0.446	-0.238	0.242
Triglycerides	0.481	0.013	0.195	0.341	-0.079	0.703

Abbreviations: BMI, body mass index; BP, blood pressure; HDL, high-density lipoprotein; HOMA-IR, homeostasis model assessment of insulin resistance; IAFA, intra-abdominal fat area; ISR, intra-abdominal fat area/subcutaneous abdominal fat area ratio; SAFA, subcutaneous abdominal fat area.

Table 4 Logistic Regression Analysis for the Effects of Associated Variables to Persistent Metabolic Syndrome After Weight Reduction Program

	Model 1		Model 2	
	Odds Ratio (95% CI)	P	Odds Ratio (95% CI)	P
Age	1.02 (0.94–1.12)	0.606	1.04 (0.94–1.15)	0.445
IAFA reduction	0.28 (0.09–0.89)	0.031	0.25 (0.07–0.95)	0.041
SAFA reduction	0.57 (0.17–1.93)	0.365	0.61 (0.19–1.97)	0.411
Baseline IAFA			0.41 (0.12–1.39)	0.152

Notes: All dependent variables were standardized after dividing by standard deviation. Model 1: Multivariate logistic regression analysis including age, IAFA reduction and SAFA reduction; Model 2: Multivariate logistic regression analysis including age, IAFA reduction, SAFA reduction, and baseline IAFA.

Abbreviations: IAFA, intra-abdominal fat area; CI, confidence interval; SAFA, subcutaneous abdominal fat area.

In the present study, the 12-week WRP produced a significant decrease in BMI and waist circumference. However, the target of 10% bodyweight reduction was not directly associated with the reversion of MetS. We found a greater reduction in SAFA than in IAFA in these participants with MetS. Consistent with our findings, a greater reduction in subcutaneous fat than in visceral fat was observed after lifestyle modification, weight-loss-promoting drugs, and bariatric surgery in a previous meta-analysis report.²⁰ However, it is well recognized that the accumulation of visceral fat has a stronger association with cardiovascular risks than subcutaneous fat.^{32,33} High expression of interleukin-6 and monocyte chemoattractant protein has been reported in visceral adipose tissue.^{34–36} Visceral fat situated close to the liver may deliver inflammatory factors to the liver through the portal vein and induce hepatic steatosis and dyslipidemia.^{37,38} Pontiroli et al³⁹ reported that reduction in visceral fat is more critical in cardiovascular prevention than that in subcutaneous fat after a bariatric restrictive surgery in patients with morbid obesity.

Weight reduction might lead to an improvement in inflammation and insulin resistance.⁴⁰ Chae et al⁴¹ reported that inflammatory cytokines and oxidative stress attenuated after a 3-year program of calorie restriction. It has been proven that a weight reduction can reduce the incidence of type 2 diabetes in the Diabetes Prevention Program,⁴² and that the change in MetS severity was a good predictor of type 2 diabetes and cardiovascular disease during the long-term follow-up.⁴³ In the present study, a significant reduction in insulin resistance and fasting plasma glucose level was observed after the WRP. The reduction in fasting glucose HOMA-IR was similar in participants with and without reversion of MetS. Visceral fat is known to be closely associated with insulin resistance, but recent reports suggest that subcutaneous fat may be also associated with insulin resistance in men. Our data suggest a general reduction in insulin resistance in all participants, but the reduction in HOMA-IR did not reach the statistical significance in a subgroup of participants with the reversion of MetS due to a wide variation in baseline HOMA-IR.⁴⁴

Weight reduction results in decreased catabolism and decreased secretion of HDL apolipoproteins.^{45,46} Therefore, improvement in the circulating level of HDL cholesterol is not as good as the improvement in other MetS components.⁴⁷ Interestingly, in the present study, reduction in IAFA was significantly correlated with an increase in HDL cholesterol,

and associated with a reversion of MetS via the improvement of the component of HDL cholesterol.

We recognize several limitations in the present study. First, because there were differences between the sexes in body fat distribution and the cutoff criteria for waist circumference and HDL cholesterol in MetS, we enrolled only male participants; our results may therefore not be applicable to women. Second, the sample size was relatively small, and we could not compare the effects of WRP on MetS in different age-group strata. Although MetS prevalence is correlated with age, the association between MetS and cardiovascular risk is noted across age strata.^{48,49} In the present study, the effect of IAFA reduction on MetS reversion was independent of age. Third, in order to keep all subjects in a similar lifestyle, we did not design a conventional treatment as controls, and we performed a fixed program regardless of participants' baseline conditions. Fourth, we only assessed MetS before and after the WRP but did not assess long-term outcomes.

Conclusion

Reduction in IAFA was an independent factor for improved MetS after a 12-week WRP in men with obesity and MetS at baseline. The magnitude of the IAFA reduction was less than that of SAFA, but the IAFA reduction contributed a significant effect on MetS reversion compared with SAFA. Further large-scale studies are warranted to investigate the long-term benefits of intra-abdominal fat reduction.

Abbreviations

BMI, body mass index; HDL, high-density lipoprotein; HOMA-IR, homeostasis model assessment of insulin resistance; IAFA, intra-abdominal fat area; ISR, intra-abdominal fat area/subcutaneous abdominal fat area ratio; MESA, multi-ethnic study of atherosclerosis; MetS, metabolic syndrome; MRI, magnetic resonance imaging; SAFA, subcutaneous abdominal fat area; WRP, weight reduction program.

Ethics Approval and Informed Consent

The study was approved by the Institutional Review Board of Taichung Veterans General Hospital, and written informed consent was obtained by all participants before the study procedures were performed.

Author Contributions

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declared no conflicts of interest in this work.

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