



Original Article

A favorable metabolic profile in metabolically healthy obesity is associated with physical activity level rather than abdominal fat volume in Japanese males

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Abstract. [Purpose] To determine the potential factors for difference in metabolic profiles between metabolically healthy obesity and metabolically unhealthy obesity, we investigated the difference in abdominal fat volume, metabolic characteristics, and physical activity levels between metabolically healthy obesity and metabolically unhealthy obesity identified with cardiovascular disease risk factors in Japanese males. [Participants and Methods] Of 305 volunteers recruited, 130 obese males (age: 46.9 ± 8.9 years; body mass index: 29.6 ± 3.5 kg/m²) met the criteria for the study. They were divided into two groups; metabolically healthy obesity and metabolically unhealthy obesity according to cardiovascular disease risk factors including low-density lipoprotein cholesterol. Abdominal fat volumes were measured using magnetic resonance imaging. Cardiovascular disease risk factors and metabolic characteristics were evaluated by blood pressure and blood parameters. Physical activity levels were measured using an accelerometer. [Results] Despite the fact that metabolically healthy obesity had a more favorable metabolic profile than the metabolically unhealthy obesity, no significant differences in visceral and subcutaneous fat volumes were found between the two groups. Moreover, the metabolically healthy obesity had a significantly greater physical activity expenditure and moderate-to-vigorous physical activity level than the metabolically unhealthy obesity. [Conclusion] A more favorable metabolic profile in metabolically healthy obesity may be associated with physical activity level rather than abdominal fat volumes in Japanese males.

Key words: Metabolically healthy obesity, Visceral fat, Moderate-to-vigorous physical activity

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INTRODUCTION

Obesity is often associated with all-cause mortality and the risk of metabolic abnormalities such as type 2 diabetes, hypertension, dyslipidemia, and coronary heart diseases¹⁾. However, some obese individuals do not have any metabolic abnormalities. Obesity without metabolic abnormalities is known as “metabolically healthy obesity (MHO)”²⁾.

Although there is no universal consensus on the definition of MHO²⁾, MHO individuals have less visceral fat (VF) area in comparison to individuals matched by age and body mass index (BMI)^{3–7)} and are more active⁸⁾ than metabolically unhealthy obesity (MUO) individuals. These findings are based on previous studies that compared between MHO and MUO identified with insulin sensitivity^{3–5, 7)} and metabolic syndrome components⁶⁾. However, to our knowledge, few studies have reported

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the comparisons between MHO and MUO identified with definitive cardiovascular diseases (CVD) risk factors, including low-density lipoprotein cholesterol (LDLC)⁹. As LDLC has been known as a primary risk factor of CVD^{1, 10}, the influence of LDLC on MHO and MUO should be taken into account. In addition, data on differences in abdominal fat “volume” between MHO and MUO are scarce. Assessment of the abdominal fat “area” using a single-slice image is less accurate¹¹, and quantification of abdominal fat distribution using multiple-slice image would be preferable. Moreover, the associations between abdominal fat volumes, metabolic profiles, and physical activity levels in MHO and MUO remain unclear.

The present study aimed to investigate the associations between abdominal fat volumes, metabolic characteristics, and physical activity levels in MHO and MUO, and determine the potential factors for difference in metabolic profiles between MHO and MUO. Therefore, we compared abdominal fat volumes, metabolic characteristics, and physical activity levels between MHO and MUO identified with CVD risk factors in Japanese males. It is important to investigate the morphological, physiological and life-related differences between MHO and MUO to elucidate the etiology of obesity-induced metabolic abnormalities.

PARTICIPANTS AND METHODS

Participants were recruited for the study of abdominal adiposity, which was conducted from 2009 to 2014. A total of 305 males were initially enrolled in the study. No participants had exercise training habits (≥ 2 sessions/week) over the past 1 year. Participants ($n=175$) were excluded from the present analysis, because their BMI values were not ≥ 25 kg/m² ($n=29$), abdominal fat contents were not measured using magnetic resonance imaging (MRI), and blood pressures were not measured ($n=78$), or they were receiving medications for high blood pressure, dyslipidemia, or hyperglycemia ($n=68$). Finally, we analyzed 130 participants (age: 46.8 ± 8.9 years, height: 171.6 ± 6.4 cm, weight: 87.2 ± 12.4 kg) in this study. The study conformed to the principles outlined in the Declaration of Helsinki and was approved by the ethics committee of the Comprehensive Human Sciences review board at the University of Tsukuba (approval number: 21-210, and 22-174). All participants provided written informed consent.

The MHO group consisted of obese males without CVD risk factors, whereas the MUO group consisted of obese males with one or more CVD risk factors. We defined obesity as a BMI ≥ 25 kg/m²¹²; CVD risk factors included systolic blood pressure ≥ 130 mmHg, diastolic blood pressure ≥ 85 mmHg, blood glucose (BG) level ≥ 110 mg/dL, high-density lipoprotein cholesterol (HDLC) level < 40 mg/dL, and triglycerides (TG) level ≥ 150 mg/dL, and LDLC level ≥ 140 mg/dL^{1, 10, 13}.

Height, weight, and waist circumference were measured¹⁴. Total body fat tissue mass (BFM) and lean tissue mass (LM) were assessed using dual-energy X-ray absorptiometry (Hologic, USA) with manufacturer-supplied software (version 1.35)¹⁵. However, we did not include 39 participants in the analysis data, because BFM and LM could not be measured. Abdominal fat volume and area were assessed using MRI (Siemens, Germany). The protocols and quantifications of the volume and area of the VF and subcutaneous fat (SF) were described previously^{11, 14}. Blood pressure was measured using a standard mercury sphygmomanometer. After 12 h of fasting, blood samples were collected to measure the total cholesterol (TC), HDLC, LDLC, TG, BG, insulin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and gamma-glutamyl transpeptidase (γ -GTP) levels. The homeostasis model assessment of insulin resistance (HOMA-IR) was calculated¹⁶. Peak oxygen uptake was determined using an incremental exercise protocol on a cycle ergometer using indirect calorimetry (Minato Medical Science, Japan)¹⁷. Physical activity energy expenditure (PAEE), light physical activity, and moderate-to-vigorous physical activity (MVPA) time were assessed with a uniaxial accelerometer (Suzuken Co. Ltd, Japan)¹⁸ for at least two consecutive weeks. The accelerometer data from participants who had worn the accelerometer for at least 10 h per day were considered in this study. The physical activity was categorized into one of nine levels (1.0–9.0) in the accelerometer¹⁸. Based on this, physical activity level from 1.0 to 3.0 and physical activity level from 4.0 to 9.0 were used as the light physical activity and MVPA, respectively. Energy intake was assessed using 3-day weighed dietary records with computer software (Excel Eiyo-kun, Kenpakusha, Japan).

The data are presented as mean \pm standard deviation. The Kolmogorov–Smirnov test was used to confirm normal distribution. The variables (TG, HOMA-IR, AST, ALT, and γ -GTP levels) were log-transformed because they were not normally distributed. An unpaired *t* test was used to compare the differences in all the parameters between MHO and MUO. Cohen’s *d* was calculated as the effect size (ES). Statistical analyses were performed using the SPSS version 24 software (IBM Corporation, USA). Statistical significance was set at $p < 0.05$.

RESULTS

Age, BMI, BFM, and LM did not significantly differ between the MHO and MUO groups ($p > 0.05$; ES: 0.17–0.35; Table 1), while weight was significantly higher in the MUO group than in the MHO group ($p = 0.042$; ES: 0.45).

The volumes and areas of VF and SF did not significantly differ between the two groups ($p > 0.05$; ES: 0.23–0.38; Table 1). Nevertheless, the blood pressure and most of the blood parameters (TC, HDLC, LDLC, TG, BG, insulin, AST, ALT, and γ -GTP levels, and HOMA-IR) in the MHO group were superior to those in the MUO group ($p < 0.05$; ES: 0.48–1.07; Table 1).

Energy, protein, fat, and carbohydrate intake did not differ between the MHO and MUO groups ($p > 0.05$). Conversely, PAEE and MVPA were significantly greater in the MHO group than in the MUO group ($p < 0.05$; ES: 0.92 and 1.04, respectively; Table 2).

Table 1. Characteristics, abdominal fat, and metabolic profiles in metabolically healthy obesity and metabolically unhealthy obesity

	MHO		MUO		p value	ES
	n	mean ± SD	n	mean ± SD		
Characteristics						
Age (years)	26	45.7 ± 8.7	104	47.2 ± 9.0	0.453	0.17
Height (cm)	26	170.1 ± 5.3	104	171.9 ± 6.6	0.194	0.28
Weight (kg)	26	82.8 ± 9.2	104	88.3 ± 12.9	0.042	0.45
BMI (kg/m ²)	26	28.6 ± 2.9	104	29.8 ± 3.6	0.111	0.35
BFM (kg) ^a	19	21.5 ± 4.9	72	22.7 ± 6.4	0.452	0.20
LM (kg) ^a	19	61.2 ± 7.2	72	63.8 ± 7.9	0.193	0.34
WC (cm)	26	98.8 ± 8.0	104	101.7 ± 8.3	0.115	0.35
Abdominal fat						
TF volume (cm ³)	26	7,929.4 ± 2,089.6	104	8,778.7 ± 2,560.1	0.120	0.35
VF volume (cm ³)	26	3,850.9 ± 1,318.9	104	4,172.4 ± 1,440.9	0.303	0.23
SF volume (cm ³)	26	4,078.4 ± 1,159.5	104	4,606.3 ± 1,668.1	0.130	0.34
VF area (cm ²)	26	141.8 ± 64.1	104	163.4 ± 55.6	0.088	0.38
SF area (cm ²)	26	242.0 ± 71.8	104	268.4 ± 90.4	0.168	0.31
Metabolic profiles						
SBP (mmHg)	26	115.5 ± 7.0	104	131.3 ± 16.1	<0.001	1.07
DBP (mmHg)	26	77.0 ± 5.9	104	88.8 ± 12.4	<0.001	1.04
TC (mg/dL)	26	191.3 ± 22.6	104	214.4 ± 34.0	<0.001	0.73
HDLC (mg/dL)	26	54.2 ± 10.6	104	48.4 ± 11.5	0.021	0.52
TG (mg/dL) ^b	26	1.97 ± 0.13	104	2.14 ± 0.23	<0.001	0.80
LDLC (mg/dL)	26	117.5 ± 16.3	104	134.5 ± 28.1	<0.001	0.65
BG (mg/dL)	26	89.9 ± 9.3	104	95.5 ± 9.5	0.008	0.60
HOMA-IR ^b	26	0.18 ± 0.22	104	0.30 ± 0.26	0.023	0.48
AST (IU/L) ^b	26	1.33 ± 0.11	104	1.40 ± 0.13	0.031	0.56
ALT (IU/L) ^b	26	1.40 ± 0.25	104	1.51 ± 0.21	0.034	0.51
γ-GTP (IU/L) ^b	26	1.48 ± 0.26	104	1.62 ± 0.25	0.011	0.56

^aThirty-nine participants were not included for missing data of dual-energy X-ray absorptiometry. ^blog-transformed. MHO: metabolically healthy obesity; MUO: metabolically unhealthy obesity; ES: effect size; BMI: body mass index; BFM: body fat tissue mass; LM: lean tissue mass; WC: waist circumference; TF: total fat; VF: visceral fat; SF: subcutaneous fat; SBP: systolic blood pressure; DBP: diastolic blood pressure; TC: total cholesterol; HDLC: high-density lipoprotein cholesterol; TG: triglyceride; LDLC: low-density lipoprotein cholesterol; BG: blood glucose; HOMA-IR: homeostasis model assessment of insulin resistance; AST: aspartate aminotransferase; ALT: alanine aminotransferase; γ-GTP: gamma-glutamyl transpeptidase.

The MHO group consisted of obese males without CVD risk factors, whereas the MUO group consisted of obese males with one or more CVD risk factors. Obesity was defined as a BMI ≥25 kg/m² ¹², CVD risk factors included SBP ≥130 mmHg, DBP ≥85 mmHg, BG level ≥110 mg/dL, HDLC level <40 mg/dL, and TG level ≥150 mg/dL, and LDLC level ≥140 mg/dL^{1, 10, 13}.

DISCUSSION

In the present study, we found no significant differences in abdominal fat volume between the MHO and MUO groups even though MHO had more favorable metabolic profiles. The MHO group had a significantly greater PAEE and MVPA than the MUO group. The favorable metabolic profiles of the MHO in the present study were partly attributed to the higher amount of physical activity of the participants with MHO. Physical activity, especially MVPA, can improve various health-related outcomes^{19, 20}. The 2008 Physical Activity Guidelines Advisory Committee Scientific Report concluded that the amount of MVPA per week is inversely associated with all-cause mortality, CVD mortality, and incidence of CVD²¹. In Japan, the Exercise and Physical Activity Guide for Health Promotion 2013 also reported that an increased amount of MVPA per week leads to a reduction in the risk of life-related diseases²². Therefore, high MVPA may contribute to the favorable metabolic profiles in MHO.

As several studies have reported differences in VF between MHO and MUO identified with insulin sensitivity^{3-5, 7}, the association between VF and IS should be apparent. However, when we identify MHO with CVD risk factors, the association between VAT and CVD risk factors would be obscure. Therefore, the differences in metabolic parameters between MHO and MUO identified with CVD risk factors cannot be necessarily explained only with VF. Adipogenesis/lipogenesis, adipocyte size, inflammation, and adipokines are known to be involved in the differences in metabolic parameters between MHO and

Table 2. Energy intake, physical activity energy expenditure, and aerobic capacity in metabolically healthy obesity and metabolically unhealthy obesity

	MHO		MUO		p value	ES
	n	mean \pm SD	n	mean \pm SD		
EI (kcal/day)	22	2,083.1 \pm 601.8	90	2,258.0 \pm 482.4	0.150	0.35
Protein (g/day)	22	77.3 \pm 27.1	90	79.6 \pm 18.1	0.705	0.12
Fat (g/day)	22	66.2 \pm 26.0	90	65.3 \pm 18.6	0.878	0.04
Carbohydrate (g/day)	22	282.9 \pm 83.4	90	307.6 \pm 82.9	0.215	0.30
EE (kcal/day)	21	2,556.1 \pm 323.4	84	2,429.7 \pm 284.4	0.079	0.44
PAEE (kcal/day)	21	428.2 \pm 200.2	84	289.5 \pm 138.8	<0.001	0.92
LPA (min/day)	19	811.9 \pm 288.9	70	816.8 \pm 329.0	0.953	0.02
MVPA (min/day)	19	65.2 \pm 26.4	70	41.8 \pm 21.7	<0.001	1.04
$\dot{V}O_2$ peak (mL/kg/min)	19	29.7 \pm 4.8	74	28.6 \pm 5.4	0.413	0.21

ES: effect size; EI: energy intake; EE: energy expenditure; PAEE: physical activity energy expenditure; LPA: light physical activity; MVPA: moderate-to-vigorous physical activity; $\dot{V}O_2$ peak: peak oxygen uptake

MUO²). These factors and physical activity may be associated with differences in metabolic parameters between MHO and MUO identified with CVD risk factors.

The associations between abdominal fat distribution and metabolic parameters may also be involved in ethnic differences. Japanese adults tend to have greater VF than SF compared to other ethnic populations²³). Therefore, the abdominal fat distributions in MHO and MUO may differ between Japanese males and other ethnic populations. Our findings provide a new insight into ethnic differences in the association between abdominal fat distribution and metabolic parameters in MHO and MUO. Moreover, in the present study, 20% of the participants were categorized as having MHO. According to data in Asia²⁴), the estimated prevalence of MHO with a BMI \geq 25 kg/m² and metabolic syndrome components ranged from 10.3 to 13.3%. Considering that MHO was defined on the basis of the definitive criteria of CVD risk factors in the present study, our results suggest that the prevalence of MHO is relatively higher and that MHO is not a rare phenotype in the Japanese population.

The strength of the present study is that we quantified the abdominal fat distribution using multiple-slice MRI, because single-slice imaging of abdominal fat is less accurate¹¹). Several previous studies reported a difference in the “VF area” between MHO and MUO³⁻⁷). In the present study, we found a tendency of difference in VF area (p=0.088), but VF volume did not differ between the MHO and MUO groups (p=0.303). This suggests that differences in abdominal fat area and volume must be interpreted with caution. Moreover, because the extent of the impact of each medication on abdominal fat and metabolic parameters cannot be quantified, we should avoid statistical adjustment. Therefore, we excluded data of participants taking medications from the analysis to eliminate the impact of each medication in the present study. However, the data were from a single community; therefore, the findings may not be simply generalized. In addition, the participants were middle-aged males; thus, our findings may not be applicable to females and older populations.

In conclusion, MHO had an abdominal fat distribution similar to that of MUO, despite having a more favorable metabolic profile. Moreover, PAEE and MVPA were greater in MHO than in MUO. These findings suggest that physical activity, with the exception of abdominal fat distribution, contribute to differences in metabolic profiles, to a greater extent, between MHO and MUO identified with CVD risk factors in Japanese males. Our findings highlight the importance of physical activity in preventing obesity-induced metabolic abnormalities.

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Conflict of interest

The authors declared that they have no competing interests.

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