Endocrine (2019) 66:503–508
https://doi.org/10.1007/s12020-019-02092-8

ORIGINAL ARTICLE

Check for updates

Body muscle-to-fat ratio gender-specific cut-off values for impaired insulin sensitivity in patients with treatment-naïve type 2 diabetes mellitus

Noboru Kurinami[1] · Seigo Sugiyama[1,2] · Akira Yoshida[1] · Kunio Hieshima[1] · Fumio Miyamoto[1] · Keizo Kajiwara[1] · Katsunori Jinnouch[1] · Tomio Jinnouchi[1] · Hideaki Jinnouchi[1,3]

Received: 23 May 2019 / Accepted: 13 September 2019 / Published online: 19 October 2019

Abstract

Purpose We previously reported that the body muscle-to-fat ratio (BMFR), measured using bioelectrical impedance, significantly correlated with whole-body insulin sensitivity. We examined BMFR gender-specific cut-off values for impaired insulin sensitivity in treatment-naïve type 2 diabetes mellitus (T2DM) patients.

Methods Subjects included 101 untreated T2DM patients (male, 66; female, 35). We performed a hyperinsulinemic–euglycemic clamp examination to measure the steady-state glucose infusion rate (*M* value) as an indicator of whole-body insulin resistance. We defined the *M* value divided by the steady-state serum insulin value as the *M*/*I* value. We defined the existence of insulin resistance using an *M*/*I* ratio <9.0. The optimal cut-off value for BMFR was calculated by receiver operating characteristics (ROC) analysis.

Results The cut-off value of the BMFR for insulin resistance was 2.75 (area under the curve [AUC] = 0.83, sensitivity 75%, and specificity 76%, $P < 0.001$) for males and 1.65 (AUC = 0.87, sensitivity 84%, and specificity 81%, $P < 0.001$) for females. Simple linear regression analysis showed that BMFR was significantly correlated with the M/I value in both genders (males, $B = 0.77$, $P < 0.01$; females, $B = 0.83$, $P < 0.01$).

Conclusions BMFR cut-off values for impaired insulin sensitivity in treatment-naïve T2DM patients were 2.75 for males and 1.65 for females.

Keywords Diabetes mellitus · Insulin resistance · Obesity · Body muscle-to-fat ratio · Gender difference

Introduction

Obesity and fat deposition are closely involved in the pathogenesis of diabetes mellitus (DM) because of their effect on insulin resistance. The exacerbation of insulin resistance associated with excessive fat tissue deposition is the main condition of metabolic syndrome. It has been reported that metabolic syndrome increases the risk of cardiovascular disease and overall mortality by 1.53–2.18-fold and 1.27–1.60-fold, respectively [1–3]. Therefore, the assessment of insulin resistance is important in clinical practice. The hyperinsulinemic–euglycemic clamp test is the gold standard for evaluating insulin resistance; however, this method is complicated and not easy to perform in the daily clinical setting; a more practical index of insulin resistance is desired. Body composition analyzers (InBody) that perform bioelectrical impedance analysis (BIA) are used in clinical practice and research facilities worldwide. They provide a convenient, noninvasive, rapid (measurement time = 60 s) and simple to use method to calculate the body muscle-to-fat ratio (BMFR). In our previous study, we reported that the BMFR, measured by bioelectrical impedance with a hyperinsulinemic–euglycemic clamp, significantly correlated with whole body insulin sensitivity [4].

These authors contributed equally: Noboru Kurinami, Seigo Sugiyama

✉ Hideaki Jinnouchi
hideaki@jinnouchi.or.jp

[1] Diabetes Care Center, Jinnouchi Hospital, Kumamoto, Japan

[2] Division of Cardiovascular Medicine, Diabetes Care Center, Jinnouchi Hospital, Kumamoto, Japan

[3] Division of Preventive Cardiology, Department of Cardiovascular Medicine, Kumamoto University Hospital, Kumamoto, Japan

However, women store adipose tissue in subcutaneous areas compared with preferential visceral fat deposition in men [5]. Moreover, healthy women have more adipose mass and only two-thirds the skeletal muscles mass compared with men, so some factors that would be predicted to promote insulin resistance in women may be different in men [6]. We previously proposed that the BMFR cut-off value for insulin resistance was 2.40 in our total study population [4], but there remains a possibility that the cut-off value differs between genders.

In the current study, we hypothesized that the BMFR cut-off value for insulin resistance is different between men and women. We examined gender-specific BMFR cut-off values for impaired insulin sensitivity in patients with treatment-naïve type 2 DM (T2DM).

Methods

Subjects and protocol

All patients with untreated T2DM who visited the Diabetes Care Center at Jinnouchi Hospital between June 2014 and March 2019 were enrolled in this study. Those already being treated for diabetes, severe uncontrolled diabetes, diabetic ketoacidosis that needed immediate insulin treatment, or uncontrolled severe hypertension, and those who could not remain standing to have elementary body composition tests were excluded. Patients were examined using a hyperinsulinemic–euglycemic clamp to measure the steady-state glucose infusion rate (*M* value) as the reference indicator for insulin resistance. The *M* value was divided by the steady state serum insulin value (*I*), and the *M*/*I* value was compared with the elementary body composition and various clinical parameters. All tests were conducted within 1 week. Written informed consent was obtained from all patients. The study was conducted in accordance with the Declaration of Helsinki and the study protocol was approved by the Human Ethics Review Committee of Jinnouchi Hospital. This study was registered under the UMIN protocol registration system (ID: UMIN000033585).

Hyperinsulinemic–euglycemic clamp

Insulin sensitivity was evaluated using a hyperinsulinemic–euglycemic clamp with an artificial pancreas (Nikkiso STG-55, Tokyo, Japan), as reported previously [4, 7]. Insulin was administered as an intravenous loading dose (starting from 4.77 mU/kg/min that was gradually decreased to 1.67 mU/kg/min; under these conditions, the estimated plasma insulin concentration was about 100 mU/L) over 10 min followed by a continuous infusion at 1.5 mU/kg/min for 120 min. Plasma glucose concentrations were maintained at 5.5 mmol/L using a variable infusion of 10% glucose. Blood insulin concentration at steady state was measured when the hyperinsulinemic–euglycemic clamp examination was terminated (*I* value). Because of variations in the insulin clearance rate for each patient, the actual blood insulin concentrations during the hyperinsulinemic–euglycemic clamp test were different from the calculated insulin levels [8]. To correct for the effect of the variability in insulin concentrations among individual patients, we used the *M*/*I* value as an index of insulin sensitivity. This value indicates glucose use per 1 unit of blood insulin and it provides a good index that represents tissue insulin sensitivity, which reflects whole-body insulin resistance [9].

Measurement of body fat and muscle composition

We measured body composition, including body fat mass and body fat percentage, using the same method as described previously [10, 11]. Elementary body composition was measured using a direct segmental multifrequency bioelectrical impedance analyzer (InBody770; Biospace, Seoul, Korea), and we assessed total fat mass and body fat percentage. This analyzer processes 30 impedance measurements using six different frequencies (1, 5, 50, 250, 500, and 1000 kHz) at each of five body segments (right arm, left arm, trunk, right leg, and left leg), and 15 reactance measurements using tetrapolar eight-point tactile electrodes using three different frequencies (5, 50, and 250 kHz), at each of the five above-mentioned body segments [12, 13]. The BIA (InBody) used in this study has been shown to have a very good correlation regarding calculated body fat mass with gold standard measurement methods, such as the underwater weighing method, dual energy X-ray absorptiometry, and air displacement plethysmograph [14, 15].

Blood sampling and measurement of clinical parameters

Blood samples for HbA1c, fasting plasma glucose, fasting blood insulin, total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, triglycerides, and estimated glomerular filtration rate (eGFR) were collected from the antecubital vein and analyzed at the Jinnouchi Hospital laboratory. Body weight (kg), height (cm), and waist circumference (cm) were measured in the standing position and body mass index (BMI; kg/m^2) was calculated at the same time that body composition was measured.

Statistical analysis

The Shapiro–Wilk test was used to assess the normal distribution of continuous data. Data were expressed as the

mean ± standard deviation (SD). Data with skewed distributions were expressed as the median value with the interquartile range. Differences between two groups were tested using Fisher's exact test for categorical variables. Differences between continuous variables were analyzed using an unpaired *t*-test or the Mann–Whitney *U* test, as appropriate. A previous report demonstrated an *M* value of 5.7 as the cut-off for the presence of insulin resistance; [16] an *M*/*I* value of 9.0 was equivalent to the *M* value of 5.7 in our previous study [4]. Therefore, we defined a cut-off value of *M*/*I* <9.0 as indicating insulin resistance in receiver-operating characteristics (ROC) analyses. We used ROC curve analysis to calculate the area under the curve (AUC) and the cut-off value. The optimal BMFR cut-off value was calculated using the Youden index. $P < 0.05$ denoted statistical significance. Statistical analyses were performed using Statistical Package for Social Science (SPSS) version 23 (SPSS Inc., Tokyo, Japan).

Results

Subjects

A total of 105 patients with untreated T2 DM were enrolled and three patients (two with ketoacidosis, one in whom it was impossible to perform InBody770, and one with uncontrolled hypertension) were excluded. Table 1 shows the participants' baseline characteristics. All subjects had untreated T2DM and 54 patients (53.5%) demonstrated high levels of HbA1c > 8.4% (68 mmol/mol).

Results of body composition analysis

Analysis of elementary body composition using InBody770 showed that the total muscle quantity was 46.1 ± 10.2 kg, total fat quantity was 19.1 kg (range, 13.2–26.1 kg), body fat percentage was 28.6 ± 9.5%, and BMFR was 2.61 (range, 1.74–3.26). Body composition was compared by gender, and BMFR (male, 2.91 [range, 2.24–3.69] vs. female, 1.62 [range, 1.36–2.22], $P < 0.001$) and muscle quantity (males, 50.6 ± 8.6 kg vs. females, 37.6 ± 6.9 kg, $P < 0.001$) were significantly higher in the males compared with females. Body fat percentage was significantly higher in females compared with males (34.9 ± 10.2% vs. 25.1 ± 7.2%, respectively, $P < 0.001$).

Hyperinsulinemic–euglycemic clamp examination results

In the total population ($n = 101$), we measured *M* and *M*/*I* values by hyperinsulinemic–euglycemic clamp examination [*M*-value; 7.15 ± 2.99 mg m^{-2} min^{-1}, *M*/*I* value; 9.28 mg m^{-2} min^{-2} μIU^{-1} mL (range, 6.22–12.81 mg m^{-2} min^{-2} μIU^{-1} mL)]. Male patients in the insulin resistance group (*M*/*I* value < 9.0, $n = 28$) had significantly higher weight, BMI, waist circumference, body muscle quantity, body fat quantity, body fat percentage, fasting blood insulin, and triglycerides compared with the noninsulin resistance group (*M*/*I* value ≥9.0, $n = 38$) (Table 1). Men in the insulin resistance group showed significantly lower age, BMFR, and HDL-cholesterol levels compared with the noninsulin resistance group (Table 1). Females patients in the insulin resistance group (*M*/*I* value <9.0, $n = 19$) had significantly higher weight, BMI, waist circumference, body fat quantity, body fat percentage, and fasting blood insulin compared with the noninsulin resistance group (*M*/*I* value ≥9.0, $n = 16$) (Table 1). Women in the insulin resistance group showed a significantly lower BMFR compared with the noninsulin resistance group (Table 1).

Receiver operating characteristics analysis

Figure 1 shows the ROC analysis of the BMFR for insulin resistance. In males, the BMFR cut-off value for insulin resistance was 2.75 and the AUC was 0.83 (sensitivity 75% and specificity 76%, $P < 0.001$). In females, the BMFR cut-off value for insulin resistance was 1.65 and the AUC was 0.87 (sensitivity 84% and specificity 81%, $P < 0.001$).

Simple linear regression analysis between BMFR and *M*/*I* values

Because the ROC analysis showed that BMFR was significantly useful for making a clinical prediction for the presence of insulin resistance in treatment-naïve T2DM patients, we performed a simple linear regression analysis to obtain an approximate formula for the *M*/*I* ratio using BMFR.

The scatter plot by gender is shown in Fig. 2. In both genders, the BMFR showed a significant positive relationship with the *M*/*I* value (males, $B = 0.77$, $P < 0.001$; females, $B = 0.81$, $P < 0.001$). The approximate expression was as follows: *M*/*I* value = 3.65 × BMFR − 0.52 ($R^2 = 0.598$, $P < 0.001$) for males, and *M*/*I* value = 3.55 × BMFR + 2.22 ($R^2 = 0.695$, $P < 0.001$) for females.

Discussion

In this study, BMFR was significantly different between males and females among treatment-naïve T2DM patients. The BMFR cut-off value for the presence of insulin resistance was 1.65 and 2.75 for females and males, respectively.

In our previous study, we proposed that the BMFR cut-off value for insulin resistance was 2.40 in the overall

Table 1 Baseline clinical characteristics of the study subjects ($N = 101$)

	ALL	Male			Female		
		M/I < 9 ($n = 28$)	M/I ≥ 9 ($n = 38$)	*P* value	M/I < 9 ($n = 19$)	M/I ≥ 9 ($n = 16$)	*P* value
Male (%)	66 (65.3%)						
Age (years)	56.22 ± 13.35	50.14 ± 14.1	58.1 ± 11.84	0.0112	56.95 ± 13.93	60.63 ± 12.35	0.4188
Height (cm)	163.72 ± 9.25	170.07 ± 8.84	166.61 ± 6.4	0.0783	155.33 ± 6.07	155.62 ± 5.12	0.882
Weight (kg)	67.1 (55.5–77.5)	82.5 (69.35–93.5)	61.2 (54.2–72.3)	<0.001	68 (56.85–75.2)	51.5 (44.98–66.95)	0.0055
Muscle quantity (kg)	46.05 ± 10.15	55.21 ± 8.65	47.03 ± 6.84	<0.001	38.85 ± 7.73	36.01 ± 5.55	0.2298
Body fat quantity (kg)	19.1 (13.2–26.1)	24.05 (19.08–31.1)	14.6 (9.25–18.1)	<0.001	26.2 (22.1–34.7)	14.9 (9.68–23.1)	<0.001
BMI (kg/m^2)	24.9 (21.4–28.7)	27.95 (25.2–31.03)	22.4 (20.5–24.45)	<0.001	28.6 (24.4–31.4)	20.95 (18.63–26.73)	0.0014
Body fat percentage (%)	28.55 ± 9.54	29.84 ± 6.54	21.46 ± 5.84	<0.001	40.84 ± 5.61	27.88 ± 10.05	<0.001
Waist circumference (cm)	89.78 ± 13.95	98.2 ± 12.11	83.29 ± 9.04	<0.001	98.31 ± 13.95	79.55 ± 13.12	<0.001
BMFR	2.61 (1.74–3.26)	2.24 (1.84–2.77)	3.13 (2.77–4.72)	<0.001	1.47 (1.23–1.62)	2.44 (1.73–3.35)	<0.001
Hemoglobin A1c (%)	8.6 (7–11)	8.8 (7.08–10.78)	8.9 (7.25–11.05)	0.7551	8.4 (7.15–10.95)	7.7 (6.55–10.63)	0.6699
Hemoglobin A1c (mmol/mol)	70.4 (52.9–96.7)	72.7 (53.9–94.3)	73.8 (55.7–97.3)	0.7551	68.3 (54.6–96.2)	60.6 (48.1–92.7)	0.6699
Fasting plasma glucose (mg/dL)	153 (124–208)	151 (126–212)	163 (131.5–200)	0.909	149 (134.5–210)	122 (111.5–197.5)	0.3708
Fasting blood insulin (μU/mL)	5.4 (3.4–8)	7.65 (5.48–10.48)	3.7 (2.1–5.4)	<0.001	7.6 (6.15–12.7)	4.45 (3.4–5.55)	0.033
Total cholesterol (mg/dl)	205 (177–227)	205.5 (179.5–233.25)	198 (172.5–214.5)	0.1982	218 (200–237.5)	200.5 (171–221.75)	0.0743
HDL-cholesterol (mg/dL)	48 (41–57)	42 (35.75–48.25)	54 (44.5–59.5)	0.0014	49 (43.5–55)	57 (43.5–66.75)	0.1378
LDL-cholesterol (mg/dL)	130.27 ± 33.45	134.61 ± 39.8	127.28 ± 31.99	0.3385	139.89 ± 30.93	121.06 ± 26.68	0.065
Triglycerides (mg/dL)	111 (71–165)	150.5 (108.25–217.25)	96 (72.5–137.5)	0.0045	115 (103.5–179)	69 (60–98.75)	0.0811
eGFR (mL/min/1.73 m^2)	74.95 ± 17.02	72.97 ± 22.69	79.14 ± 15.63	0.278	71.89 ± 14.57	75.1 ± 15.65	0.5351

BMI body mass index, *BMFR* body muscle-to-fat ratio, *eGFR* estimated glomerular filtration rate, *HDL* high-density lipoprotein, *LDL* low-density lipoprotein

patient population with T2DM [4]. However, females generally have higher adipose mass and lower skeletal muscles mass compared with males [17]. The female gender has been suggested to have a favorable effect on glucose homeostasis, and available evidence from hyperinsulinemic–euglycemic clamp studies was summarized to delineate whether there is a gender difference in whole-body insulin sensitivity, and in particular in insulin-stimulated glucose uptake by skeletal muscle [18]. The Korea National Health Nutrition Examination Survey results reported that BMFR, calculated using bioelectrical impedance, is useful for predicting metabolic syndrome, and the cut-off values were 1.83 and 3.09 for females and males, respectively [19]. This indicates that the BMFR cut-off value was lower for females compared with males, which is similar to the results of this study.

The primary objective of this study was to calculate gender-specific cut-off values for the BMFR to predict the presence of insulin resistance. Insulin resistance is considered to be a main background mechanism of lifestyle diseases, such as hypertension and dyslipidemia, as well as T2DM. A simple diagnosis of insulin resistance using BMFR, as determined by bioelectrical impedance, is useful in daily clinical practice. Past studies showed that BMFR was also useful for predicting liver fat accumulation [20] and obstructive sleep apnea syndrome [21], which are obesity-related diseases. In addition, BMFR as an indicator of abnormal body composition and obesity could be a useful measure for insulin resistance-related diseases. In future studies, it will be important to examine whether BMFR provides a therapeutic target and prognostic indicator for various diseases caused by fat accumulation, as well as DM.

A limitation of this study was that the subjects were limited to patients with T2DM. To predict the presence of insulin resistance from the viewpoint of lifestyle-related disease prevention, it will be important to examine all populations, including healthy individuals.

In conclusion, BMFR cut-off values were 1.65 and 2.75 in females and males, respectively, for impaired insulin sensitivity in patients with treatment-naïve T2DM.

Acknowledgements We thank Jodi Smith and Charles Allan from Edanz Group (www.edanzediting.com/ac) for editing a draft of this paper.

Authors' contributions NK, SS, and HJ contributed to the analysis design, acquisition and interpretation of data, and reviewed/edited the paper. AY, KH, FM, KK, KJ, and TJ contributed to the interpretation of data and reviewed/edited the paper. All authors read and approved the final paper.

Compliance with ethical standards

Conflict of interest HJ has received honoraria from Novo Nordisk, Sanofi, AstraZeneca Pharmaceuticals, Astellas Pharma, Boehringer Ingelheim, Daiichi-Sankyo, Eli Lilly, Takeda, and Novartis Pharmaceuticals. SS has received honoraria from MSD, AstraZeneca Pharmaceuticals, Ono Pharmaceutical, Bayer Yakuhin, Ltd, and Novo Nordisk. The other authors declare that they have no conflict of interest.

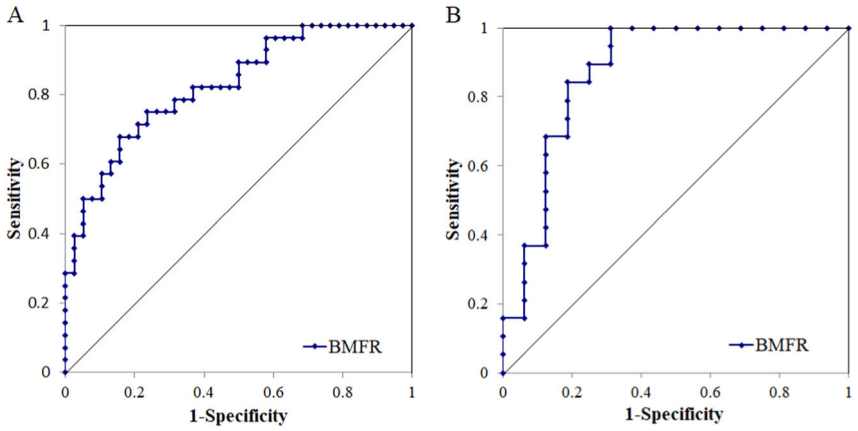

Fig. 1 Receiver operating characteristic curve analysis of BMFR for insulin resistance. **a** In males, the BMFR cut-off value for insulin resistance, defined as the optimal sensitivity and specificity of the ROC curve, was 2.75 (AUC, 0.83; standard error, 0.05; 95% confidence interval, 0.73–0.93; $P < 0.0001$). **b** In females, the BMFR cut-off value for insulin resistance, defined as the optimal sensitivity and specificity of the ROC curve, was 1.65 (AUC, 0.87; standard error, 0.07; 95% confidence interval, 0.74–1.00; $P < 0.0001$). AUC area under the curve, ROC receiver operating characteristic analysis, BMFR body muscle-to-fat ratio

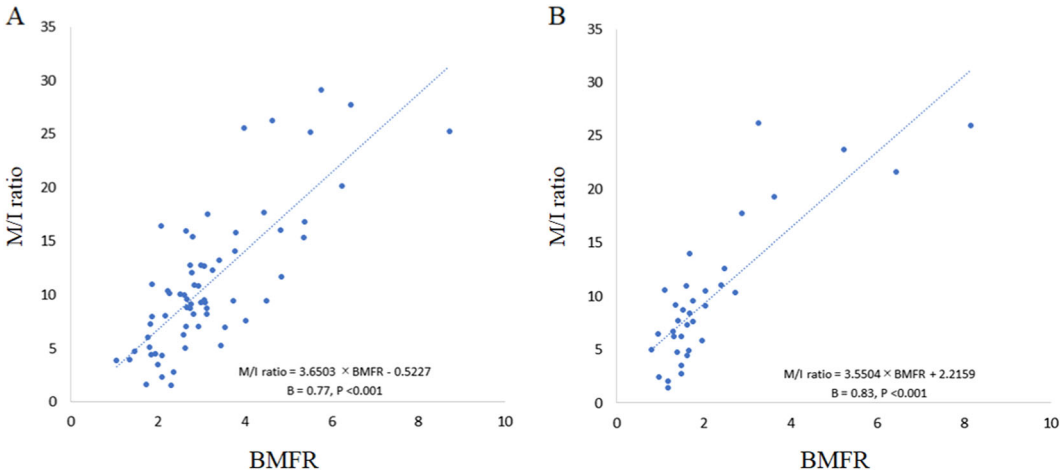

Fig. 2 Relationship between the M/I value and BMFR. **a** In males, the BMFR showed a significant negative relationship with the *M/I* value ($B = 0.77$, $P < 0.001$). **b** In females, the BMFR showed a significant negative relationship with the *M/I* value ($B = 0.83$, $P < 0.001$). BMFR body muscle-to-fat ratio

Ethical standards The article does not contain any studies with animals performed by any of the authors. The study received institutional ethical review and all participants provided informed consent. As such, this study conforms to the ethical standards of the Declaration of Helsinki.

Informed consent Informed consent was obtained from all individual participants included in the study.

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

References

1. E.S. Ford, Prevalence of the metabolic syndrome defined by the International Diabetes Federation among adults in the US. Diabetes Care **28**, 2745–2749 (2005)
2. A. Galassi, K. Reynolds, J. He, Metabolic syndrome and risk of cardiovascular disease: a meta-analysis. Am. J. Med. **119**, 812–819 (2006)
3. A.S. Gami, B.J. Witt, D.E. Howard, P.J. Erwin, L.A. Gami et al. Metabolic syndrome and risk of incident cardiovascular events and death: a systematic review and meta-analysis of longitudinal studies. J. Am. Coll. Cardiol. **49**, 403–414 (2007)

4. N. Kurinami, S. Sugiyama, A. Yoshida, K. Hieshima, F. Miyamoto et al. Correlation of body muscle/fat ratio with insulin sensitivity using hyperinsulinemic–euglycemic clamp in treatment-naïve type 2 diabetes mellitus. Diabetes Res. Clin. Pract. **120**, 65–72 (2016)
5. S. Kawanabe, Y. Nagai, Y. Nakamura, A. Nishine, T. Nakagawa et al. Association of the muscle/fat mass ratio with insulin resistance in gestational diabetes mellitus. Endocr. J. **66**, 75–80 (2019)
6. G. Enzi, M. Gasparo, P.R. Biondetti, D. Fiore, M. Semisa et al. Subcutaneous and visceral fat distribution according to sex, age, and overweight, evaluated by computed tomography. Am. J. Clin. Nutr. **44**, 739–746 (1986)
7. H. Jinnouchi, S. Sugiyama, K. Hieshima, N. Kurinami, K. Kajiwara et al. Liraglutide, a glucagon-like peptide-1 analog, increased insulin sensitivity assessed by hyperinsulinemic-euglycemic clamp examination in patients with uncontrolled type 2 diabetes mellitus. J. Diabetes Res. 706416 (2015). https://doi.org/10.1155/2015/706416.
8. H. Yki-Järvinen, V.A. Koivisto, Insulin sensitivity in newly diagnosed type 1 diabetics after ketoacidosis and after three months of insulin therapy. J. Clin. Endocrinol. Metab. **59**, 371–378 (1984)
9. R.A. DeFronzo, J.D. Tobin, R. Andres, Glucose clamp technique: a method for quantifying insulin secretion and resistance. Am. J. Physiol. **273**, E214–E223 (1979)
10. N. Kurinami, S. Sugiyama, H. Nishimura, A. Morita, A. Yoshida et al. Clinical factors associated with initial decrease in body-fat percentage induced by add-on sodium-glucose co-transporter 2 inhibitors in patients with type 2 diabetes mellitus. Clin. Drug Investig. **38**, 19–27 (2018)
11. N. Kurinami, S. Sugiyama, A. Yoshida, K. Hieshima, F. Miyamoto et al. Dapagliflozin significantly reduced liver fat accumulation associated with a decrease in abdominal subcutaneous fat in patients with inadequately controlled type 2 diabetes mellitus. Diabetes Res. Clin. Pract. **142**, 254–263 (2018)
12. K. Cha, G.M. Chertow, J. Gonzalez, J.M. Lazarus, D.W. Wilmore, Multifrequency bioelectrical impedance estimates the distribution of body water. J. Appl. Physiol. **79**, 1316–1319 (1995)
13. K. Cha, S. Shin, C. Shon, S. Choi, D.W. Wilmore, Evaluation of segmental bioelectrical impedance analysis (SIBA) for measuring muscle distribution. J. ICHPER SD **1**, 11–14 (1997)
14. A. Fürstenberg, A. Davenport, Comparison of multifrequency bioelectrical impedance analysis and dual-energy X-ray absorptiometry assessments in outpatient hemodialysis patients. Am. J. Kidney Dis. **57**, 123–129 (2011)
15. Q. Guo, C. Yi, J. Li, X. Wu, X. Yang et al. Prevalence and risk factors of fluid overload in Southern Chinese continuous ambulatory peritoneal dialysis patients. PLoS ONE **8**, e53294 (2013)
16. J. Cobb, W. Gall, K.P. Adam, P. Nakhle, E. Button et al. A novel fasting blood test for insulin resistance and prediabetes. J. Diabetes Sci. Technol. **7**, 100–110 (2013)
17. J.P. Frias, G.B. Macaraeg, J. Ofrecio, J.G. Yu, J.M. Olefsky et al. Decreased susceptibility to fatty acid-induced peripheral tissue insulin resistance in women. Diabetes **50**, 1344–1350 (2001)
18. A.M. Lundsgaard, B. Kiens, Gender differences in skeletal muscle substrate metabolism—molecular mechanisms and insulin sensitivity. Front. Endocrinol. **5**, 195 (2014)
19. J. Park, S. Kim, Validity of muscle-to-fat ratio as a predictor of adult metabolic syndrome. J. Phys. Ther. Sci. **28**, 1036–1045 (2016)
20. N. Kurinami, S. Sugiyama, M. Ayami, A. Yoshida, K. Hieshima et al. Ratio of muscle mass to fat mass assessed by bioelectrical impedance analysis is significantly correlated with liver fat accumulation in patients with type 2 diabetes mellitus. Diabetes Res. Clin. Pract. **139**, 122–130 (2018)
21. N. Kurinami, S. Sugiyama, H. Ijima, A. Yoshida, K. Hieshima et al. Clinical usefulness of the body muscle-to-fat ratio for screening obstructive sleep apnea syndrome in patients with inadequately controlled type 2 diabetes mellitus. Diabetes Res. Clin. Pract. **143**, 134–139 (2018)