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ORIGINAL ARTICLE

Associations between basal metabolic rate and insulin resistance in non-diabetic obese adults: Evidence from NHANES 2011–2018

Hai Guo[1,2,3] · Dilihumaier Duolikun[1] · Qiaoling Yao[1,4,5]

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Abstract

Objective Skeletal muscle and adipocytes do not respond properly to normal levels of circulating insulin, representing the pathological condition known as insulin resistance (IR). This study aimed to evaluate the basal metabolic rate (BMR) in obese, non-diabetic adults and assess its potential relationship with laboratory indicators of IR.

Methods This cross-sectional retrospective study used data from the NHANES database 2011–2018. Obese (BMI ≥ 30 kg/m^2) adults aged 20 to 59 years without diabetes were eligible for inclusion. BMR was measured using the Mifflin-St Jeor equation. To calculate indicators of IR, NHANES laboratory values included fasting plasma glucose, fasting plasma insulin, and HbA1c. Univariate and multivariate logistic regression were performed to determine the associations between the study variables and prevalent BMR and IR.

Results A total of 1710 participants who met inclusion criteria were selected from the 2011–2018 NHANES database. Univariate analysis reveals significant associations between higher BMR and elevated fasting glucose, fasting insulin, and HOMA-IR ($\beta = 0.006$, 0.013, 0.004; $p < 0.001$, respectively). Multivariable analyses showed that BMR was significantly associated with fasting glucose, fasting insulin, and HOMA-IR ($\beta = 0.006$, 0.020, 0.005, respectively) but not to HbA1c.

Conclusions BMR is significantly associated with IR indicators in obese, non-diabetic US adults. These findings suggest that modifying BMR may help prevent IR deterioration in healthy obese populations. Future longitudinal studies are needed to confirm these findings and clarify the related physiological mechanisms.

Keywords Basal metabolic rate (BMR) · Insulin resistance (IR) · Obesity · Type 2 diabetes (T2DM) · National Health and Nutrition Examination Survey (NHANES)

Introduction

Insulin resistance (IR) is defined as a decrease in the response of tissue to insulin stimulation [1, 2]. As a result, IR is characterized by a decrease in glycogen synthesis, defective uptake and oxidation of glucose, and, to a limited extent, the ability to suppress lipid oxidation [3–5]. Many metabolic diseases, including type 2 diabetes mellitus (T2DM), in which the role of IR is critical, creating a state in which insulin-targeting tissues are less responsive to the physiological levels of insulin [2, 6]. Although the precise mechanisms of IR are not fully understood, oxidative stress, inflammation, insulin receptor mutations, endoplasmic reticulum stress, and mitochondrial dysfunction, all have been suggested [3, 7].

Obesity has become epidemic worldwide and is a major risk factor for health status, leading to increased morbidity and complications that impose enormous costs on affected

✉ Qiaoling Yao
ql.yao@hotmail.com

1 Department of Physiology, School of Basic Medical Sciences, Xinjiang Medical University, No.397, Xinyi Street, Urumqi 830011, Xinjiang, China

2 Department of Anesthesiology, The First Affiliated Hospital of Xinjiang Medical University, Urumqi, Xinjiang, China

3 Xinjiang Perioperative Organ Protection Laboratory (XJDX1411), Urumqi, Xinjiang, China

4 Xinjiang Key Laboratory of Molecular Biology for Endemic Diseases, Urumqi, Xinjiang, China

5 State Key Laboratory of Pathogenesis, Prevention and Treatment of High Incidence Diseases in Central Asian, Urumqi, Xinjiang, China

individuals, families, healthcare systems, and society as a whole [6–8]. Obesity has a profound effect on the biomolecular and functional properties of insulin-sensitive tissues such as adipose tissue, skeletal muscle, and liver tissue. Recent research has demonstrated that adenosine triphosphate (ATP) is a signal of energy surplus in the mechanism of obesity-associated insulin resistance [7]. Therefore, obesity is strongly associated with the development of insulin resistance, which plays a crucial role in the pathogenesis of obesity-associated cardiometabolic complications, such as the metabolic syndrome components, type 2 diabetes, and cardiovascular disease [8].

In the last few years, studies have reported energy expenditure as a component directly linked to T2DM, accompanied by noticeable increases in basal metabolic rate (BMR) or the resting metabolic rate (RMR) associated with the progression of IR [9, 10]. However, while increased BMR, obesity, and IR are recognized risk factors for T2DM, data are lacking regarding associations between BMR and indicators of IR in relatively healthy (non-T2DM) obese individuals [11, 12]. Early recognition and intervention may prevent IR deterioration and subsequent development of T2DM in high-risk individuals among the obese population [13]. This study aimed to evaluate BMR among non-diabetic, obese adults and to assess its potential relationship with laboratory indicators of IR.

Methods

Data source

The present study performed secondary analysis of data from The National Health and Nutrition Examination Survey (NHANES) database. NHANES data were collected by its administrative entity, the Centers for Disease Control and Prevention (CDC), National Center for Health Statistics (NCHS) in the USA (http://www.cdc.gov/nchs/nhanes/). The survey is designed to regularly evaluate the health and nutritional status of adults and children in 2-year cycles across the USA. It features a complex, multistage design to collect and analyze data representative of the national, non-institutionalized US population. The data are released for research purposes and the NCHS grants researcher permission to use the data upon request. Participants in NHANES complete a household interview and are invited to undergo an extensive examination in the NHANES mobile examination center (MEC), including a physical examination, specialized measurements, and laboratory tests. Evaluation of subjects within the NHANES database is considered to be reliable and multidimensional and can be equated to a population-level assessment [14].

Ethical considerations

The NCHS Research Ethics Review Board reviewed and approved NHANES, and all survey participants provided signed informed consent before participating. Therefore, no further ethical approval and informed consent was required to perform the secondary analyses undertaken in this manuscript. Please check the NHANES website for NCHS Research Ethics Review Board Approval (https://www.cdc.gov/nchs/nhanes/irba98.htm). Additionally, all NHANES data released by the NCHS are de-identified and the data remain anonymous during data analysis.

Study population

The present study extracted data from four released cycles of the US NHANES database (2011–2012, 2013–2014, 2015–2016, 2017–2018), covering 8 years. Adults aged 20–59 years who were obese (defined as BMI $\geq$ 30 kg/m^2) and without diabetes were eligible for inclusion. Exclusion criteria included a history of cancer, pregnancy, and incomplete data on insulin resistance and glucose homeostasis indicators, including missing data of fasting blood glucose, fasting insulin, and HbA1c. Participants with diabetes were identified through at least one of the following and were subsequently excluded from the study cohort: a positive response to questionnaires "Are you taking insulin?" "Did a doctor tell you, you have diabetes?" "Do you take pills to lower blood sugar?" or HbA1c $\geq$ 6.5%, fasting glucose $\geq$ 126 mg/dL, or glucose level $\geq$ 200 mg/dL in oral glucose tolerance test (OGTT) in the NHANES laboratory data [15].

Study variables

Measurement of indicators of IR and glucose homeostasis

Fasting plasma glucose, fasting plasma insulin, and HbA1c values were obtained through the NHANES laboratory data files. HOMA-IR, in particular, was used to assess IR based on fasting glucose and insulin concentrations and defined as fasting insulin (mU/mL) $\times$ fasting glucose (mg/dL)/405. Details and protocol requirements on the collection of laboratory parameters are documented on the NHANES website: https://wwwn.cdc.gov/Nchs/Nhanes/2011-2012/GLU_G.htm.

Measurement of BMR

BMR means the amount of energy utilized by a body in physical and psychological resting rate, after a night's sleep,

awake without any previous physical activity post-meal intake (10 h after last meal) and neutral environment [16]. BMR measurement requires strict controlling before and during the testing such as control of food intake, medication, physical activity, temperature, and time of day. These factors may limit the use of indirect calorimetry [17]. Due to these limitations, several prediction equations have been developed to determine BMR using body height, weight, sex, and other individual differences. Newer predictive such as Mifflin-St Jeor prediction equation proposed by Mifflin and St Jeor [18] is more accurate (73.4%) compared to indirect calorimetry and is routinely used in clinical practice and research.

In the present study, the basal metabolic rate (BMR) was calculated using the Mifflin-St Jeor equation. The ADA (American Dietetic Association) published a comparison of various equations in which the Mifflin-St Jeor was found to be the most accurate [18]. This predictive equation separates the calculation for men and women as follows:

Men : $10 \times \text{weight (kg)} + 6.25 \times \text{height (cm)} - 5 \times \text{age (y)} + 5$
Women : $10 \times \text{weight (kg)} + 6.25 \times \text{height (cm)} - 5 \times \text{age } (y) - 161.$

The body composition measurements were performed using whole-body dual-energy x-ray absorptiometry (DXA) exams (Hologic, Inc., Bedford, MA, USA), which provided values for total and regional fat mass and lean soft tissue mass. Appendicular skeletal muscle mass was defined as the sum of the lean soft tissue mass of both arms and legs. Visceral mass of fat inside the abdominal cavity was measured at the approximate interspace locations of L4 and L5 vertebra.

GFR was estimated from re-calibrated serum creatinine using the 4-variable Modification of Diet in Renal Disease (MDRD) Study equation. The IDMS-traceable MDRD Study equation was applied that uses standardized creatinine: $\text{GFR} = 175 \times (\text{standardized serum creatinine})^{-1.154} \times (\text{age})^{-0.203} \times 0.742$ (if the subject is a woman) $\times 1.212$ (if the subject is black). Estimated GFR was reported in ml/min/1.73 m^2.

Participants' smoking status was classified as non-smoker, former smoker, or current smoker as follows: a non-smoker was lifetime smoking of less than 100 cigarettes; a former smoker was lifetime smoking > 100 cigarettes but not currently a smoker; and a current smoker was lifetime smoking > 100 cigarettes and responded "yes" to the question "Do you smoke now?".

Alcohol consumption was defined by responses to the survey questions.

Hypertension was defined as those who responded "yes" to the questions: "Were you told on two or more different visits that you had hypertension, also called high blood pressure?" or "Because of your (high blood pressure/hypertension), have you ever been told to … take prescribed medicine?", or with average of three consecutive measures of systolic blood pressure ≥ 140 mmHg, or with average of three consecutive measures of diastolic blood pressure ≥ 90 mmHg.

Dyslipidemia was defined as the self-reported response "yes" to the question: "To lower your blood cholesterol, have you ever been told by a doctor or other health professional to take prescribed medicine?" or as total cholesterol > 240 mg/dL, an HDL-c level < 40 mg/dL, an LDL-c level ≥ 140 mg/dL, or triglyceride level ≥ 150 mg/dL.

Chronic respiratory tract disease was defined as having chronic bronchitis, emphysema, current asthma or allergic rhinitis in answers to the following questions: "Do you still… have chronic bronchitis?" "Has a doctor or other health professional ever told you that you… had emphysema?" "Do you still have asthma?" or "During the past 12 months, have you had an episode of hay fever?" Cardiovascular diseases were defined by positive responses to questions about physician diagnoses of myocardial infarction, angina, or coronary heart disease.

Sedentary time was assessed by NHANES base on each individual's daily hours of TV, video, or computer use according to the in-person interview and was divided into three different categories: < 3, 3–6, and ≥ 6 h.

Covariates

Demographic data including age, gender, race, family income-to-poverty ratio, and education level were obtained through in-person interviews conducted by trained interviewers using the Family and Sample Person Demographics questionnaires and the Computer-Assisted Personal Interviewing (CAPI) system (Confirmit Corp. New York, USA). Collected data were weighted according to the NHANES protocol. Body mass index (BMI) values were obtained from the NHANES examination measurements, calculated as body weight (kilograms) divided by height (meters squared). Body weight was measured using an electronic load cell scale, and standing height was measured using a fixed stadiometer. The amount of total energy intake was derived from the NHANES dietary interview estimating the types and amounts of foods and beverages consumed during the 24-h period prior to the interview.

Statistical analysis

NHANES uses a complex, multistage, probability sampling design to assure national representation, wherein sampling

weights (WTSAF2YR), pseudo-stratum (SDMVSTRA), and pseudo-cluster (SDMVPSU) provided by NHANES were applied in all analyses as guided by the NCHS [19, 20]. Weights are created in NHANES to account for the complex survey design (including oversampling), survey non-response, and post-stratification adjustment to match total population counts from the Census Bureau. A sample weight is assigned to each sample person. It is a measure of the number of people in the population represented by that sample person. Fasting insulin and fasting glucose are collected from those sample persons who were subsampled to fast before attending a morning MEC exam session and who actually fasted for at least 8.5 h before the blood draw. This group is approximately half the sample of those who were MEC examined. Therefore, we used the fasting subsample weights (WTSAF2YR). Categorical data was analyzed by PROC SURVEYFREQ statement presented as unweighted counts (weighted %). Continuous data was analyzed by PROC SURVEYREG statement and presented as mean and standard error (SE). Linear regression was conducted using the SURVEYREG statement to determine associations between study variables and fasting glucose, fasting insulin, HbA1c, and HOMA-IR.

Significant variables in univariate analysis were entered into multivariate models after adjusting for covariates. All statistical assessments were two sided and evaluated at the $p < 0.05$ level of significance. Statistical analyses were performed using SAS statistical software (version 9.4, SAS Inc., Cary, NC, USA).

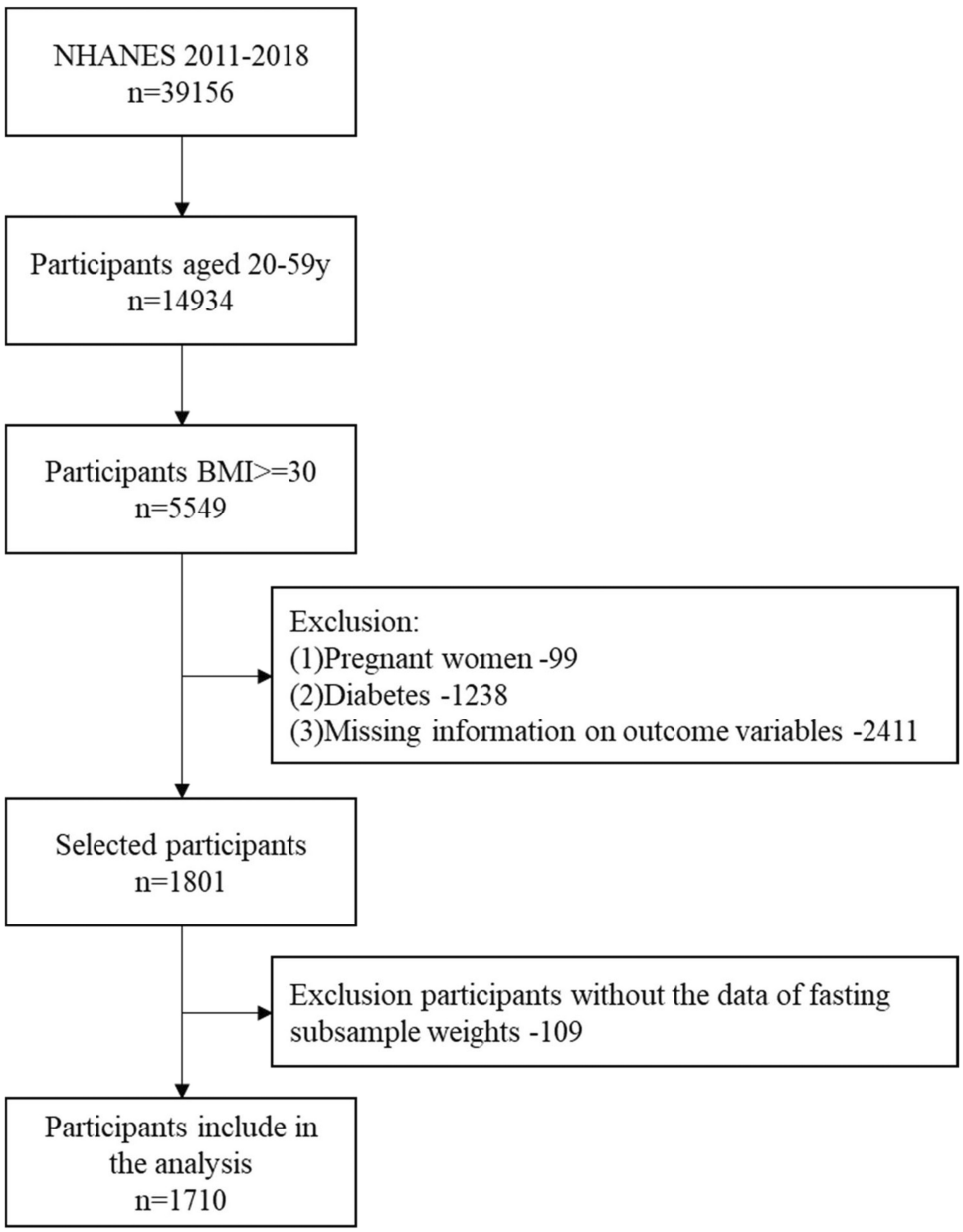

Fig. 1 Flow diagram of study sample selection

Results

Study population

From the original 39,156 subjects in NHANES 2011–2018, a total of 5549 participants aged 20–59 years with BMI ≥ 30 kg/m^2 were eligible for inclusion. After excluding pregnant women, individuals with confirmed diabetes, cancer history, or those who lacked complete information on fasting glucose, fasting insulin, HbA1c, or parameters to estimate HOMA-IR, 1801 subjects remained. Given that the parameters of insulin sensitivity were collected from subjects who were subsampled to fast before attending a morning NHANES MEC examination, data without the subsample weights were also excluded. Finally, 1710 participants were included in the subsequent analyses. The flow diagram of the study sample selection is presented in Fig. 1.

Table 1 Characteristics of non-diabetic obese adults 20–59 years in NHANES 2011–2018

	Overall (n = 1710)	Male (n = 747)	Female (n = 963)	p-value
Fasting glucose, mg/dL	100.4 ± 0.3	102.4 ± 0.4	98.6 ± 0.4	**< 0.001**
Fasting insulin, μU/L	17.1 ± 0.4	18.1 ± 0.6	16.2 ± 0.5	**0.009**
HbA1c, %	5.4 ± 0.01	5.4 ± 0.02	5.4 ± 0.01	0.059
HOMA-IR, μU/L* mmol/L	4.3 ± 0.1	4.6 ± 0.2	4.0 ± 0.1	**0.002**
BMR, kcal/day	1809.4 ± 9.0	2007.7 ± 12.4	1629.8 ± 8.6	**< 0.001**
Age, years	39.2 ± 0.4	38.8 ± 0.5	39.5 ± 0.5	0.251
Age, categories				
20–29	395 (23.4)	172 (22.1)	223 (24.5)	**0.042**
30–39	495 (28.9)	245 (31.3)	250 (26.8)	
40–49	446 (25.5)	193 (27.2)	253 (23.9)	
50–59	374 (22.3)	137 (19.5)	237 (24.9)	
BMI, kg/m^2	35.9 ± 0.2	34.9 ± 0.3	36.8 ± 0.3	**< 0.001**
Race				
Non-Hispanic White	607 (59.1)	293 (62.2)	314 (56.3)	**< 0.001**
Non-Hispanic Black	469 (15.2)	157 (11.0)	312 (18.9)	
Hispanic	177 (7.2)	79 (7.3)	98 (7.0)	
Others	457 (18.6)	218 (19.4)	239 (17.8)	
Smoking status				
Never	1041 (60.5)	415 (56.7)	626 (64.0)	**0.001**
Former	289 (19.6)	166 (24.6)	123 (15.2)	
Current	379 (19.8)	166 (18.7)	213 (20.8)	
Missing	1	0	1	
Energy intake, kcal/day	2252.8 ± 27.2	2574.1 ± 47.3	1956.8 ± 31.0	**< 0.001**
Visceral fat mass, kg	683.9 ± 8.6	693.5 ± 10.8	674.4 ± 12.4	0.220
Appendicular muscle mass	26,057.0 ± 244.8	30,979.0 ± 216.4	21,728.0 ± 190.2	**< 0.001**
CVD	66 (3.2)	24 (2.3)	42 (3.9)	0.075
Chronic respiratory tract disease	216 (11.2)	61 (7.0)	155 (14.9)	**< 0.001**
Hypertension	578 (32.9)	256 (34.7)	322 (31.2)	0.194
Dyslipidemia	690 (39.7)	345 (45.0)	345 (34.9)	**< 0.001**
eGFR	101.9 ± 0.8	99.4 ± 1.0	104.1 ± 1.2	**0.003**
Sedentary time, hours/day				
< 3	286 (31.4)	129 (31.3)	157 (31.6)	0.763
3–6	511 (53.9)	224 (55.1)	287 (52.9)	
6 +	147 (14.6)	64 (13.6)	83 (15.6)	
Missing	766	330	436	

Continuous data are presented as mean ± SE. Categorical data are presented as unweighted count (weighted %). Factors with significance ($p < 0.05$) are shown in bold

BMR basal metabolic rate, *BMI* body mass index, *CVD* cardiovascular disease, *HbA1c* glycated hemoglobin, *HOMA-IR* Homeostatic Model Assessment for Insulin Resistance

Characteristics of non-diabetic obese subjects

Mean age of the study population was 39.2 ± 0.4 years, most of whom were non-Hispanic White (59.1%) and non-smokers (60.5%)., Subjects' mean fasting glucose level was 100.4 ± 0.3 mg/dL, mean fasting insulin level was 17.1 ± 0.4 µU/L, mean HbA1c was 5.4% ± 0.01, and HOMA-IR was 4.3 ± 0.01. Males had a significantly higher mean fasting glucose, fasting insulin, and HOMA-IR, as well as BMR, total energy intake, and appendicular muscle mass than females. Although females had significantly higher mean BMI and eGFR values. Among comorbidities, 39.7% of the participants had dyslipidemia; a higher proportion of females had chronic respiratory tract disease than males (14.9% vs. 7.0%), whereas a higher proportion of males had dyslipidemia than females (45.0% vs. 34.9%) (Table 1).

Associations between BMR and indicators of IR and HbA1c

Univariate analysis revealed significant correlations between increased BMR and higher fasting glucose, fasting insulin, and HOMA-IR ($\beta = 0.006$, 0.013, 0.004, respectively; $p < 0.001$) but not with HbA1c (Table 2).

Table 2 Univariate analysis of associations between fasting glucose, fasting insulin, HbA1c, HOMA-IR, and study variables

Study variables	Fasting glucose (mg/dL)		Fasting insulin (µU/L)		HbA1c (%)		HOMA-IR	
	B ± SE	*p*-value	B ± SE	*p*-value	B ± SE	*p*-value	B ± SE	*p*-value
BMR, kcal/day	0.006 ± 0.001	**< 0.001**	0.013 ± 0.001	**< 0.001**	− 0.0001 ± 0.00003	0.105	0.004 ± 0.0004	**< 0.001**
Age, years	0.174 ± 0.023	**< 0.001**	− 0.142 ± 0.030	**< 0.001**	0.009 ± 0.001	**< 0.001**	− 0.028 ± 0.008	**0.001**
Age, categories								
20–29	Ref		Ref		Ref		Ref	
30–39	2.079 ± 0.074	**0.007**	− 2.605 ± 1.007	**0.012**	0.040 ± 0.024	0.094	**− 0.534** ± 0.274	0.056
40–49	4.579 ± 0.910	**< 0.001**	− 2.920 ± 1.082	**0.009**	0.174 ± 0.033	**< 0.001**	− 0.525 ± 0.300	0.085
50–59	4.863 ± 0.853	**< 0.001**	− 4.402 ± 0.969	**< 0.001**	0.254 ± 0.032	**< 0.001**	**− 0.884** ± 0.258	**0.001**
Gender								
Female	Ref		Ref		Ref		Ref	
Male	3.748 ± 0.553	**< 0.001**	1.918 ± 0.707	**0.009**	− 0.040 ± 0.021	0.059	0.631 ± 0.193	**0.002**
BMI, kg/m^2	0.186 ± 0.052	**0.001**	0.682 ± 0.081	**< 0.001**	0.009 ± 0.002	**< 0.001**	0.184 ± 0.022	**< 0.001**
Race								
Non-Hispanic White	Ref		Ref		Ref		Ref	
Non-Hispanic Black	− 1.996 ± 0.608	**0.002**	0.115 ± 0.929	0.902	0.181 ± 0.027	**< 0.001**	− 0.084 ± 0.250	0.737
Hispanic	− 0.532 ± 1.008	0.600	0.538 ± 1.193	0.654	0.031 ± 0.031	0.314	0.081 ± 0.313	0.798
Others	0.847 ± 0.707	0.235	2.985 ± 0.852	**0.001**	0.094 ± 0.026	**0.001**	**0.773** ± 0.233	**0.002**
Smoking status								
Never	Ref		Ref		Ref		Ref	
Former	2.180 ± 0.785	**0.007**	0.248 ± 0.832	0.766	0.012 ± 0.281	0.683	0.142 ± 0.228	0.536
Current	0.055 ± 0.760	0.943	− 0.001 ± 0.814	0.999	0.071 ± 0.028	**0.013**	− 0.015 ± 0.233	0.950
Energy intake, kcal/day	0.001 ± 0.0003	**0.011**	0.001 ± 0.0002	**< 0.001**	0.00002 ± 0.00001	**0.045**	0.0004 ± 0.0001	**< 0.001**
Visceral fat mass, kg	0.010 ± 0.001	**< 0.001**	0.012 ± 0.002	**< 0.001**	0.0002 ± 0.0001	**< 0.001**	0.003 ± 0.001	**< 0.001**
Appendicular muscle mass	0.0003 ± 0.0001	**< 0.001**	0.0004 ± 0.0001	**< 0.001**	0.000002 ± 0.000002	0.459	0.0001 ± 0.00001	**< 0.001**
CVD	3.457 ± 1.331	**0.012**	0.660 ± 1.408	0.641	0.062 ± 0.066	0.347	0.266 ± 0.366	0.471
Chronic respiratory tract disease	− 0.257 ± 0.925	0.782	0.447 ± 1.001	0.657	0.034 ± 0.029	0.250	0.108 ± 0.285	0.707
Hypertension	3.486 ± 0.560	**< 0.001**	1.725 ± 0.837	**0.043**	0.077 ± 0.025	**0.003**	0.598 ± 0.236	**0.014**
Dyslipidemia	2.142 ± 0.428	**< 0.001**	− 0.310 ± 0.651	0.636	0.126 ± 0.023	**< 0.001**	0.002 ± 0.177	0.989
eGFR	− 0.021 ± 0.001	0.084	0.054 ± 0.015	**0.001**	− 0.00002 ± 0.0004	0.969	0.012 ± 0.004	**0.004**
Sedentary time, h/day								
< 3	Ref		Ref		Ref		Ref	
3–6	0.059 ± 0.782	0.940	− 0.152 ± 1.306	0.908	− 0.004 ± 0.030	0.902	− 0.032 ± 0.331	0.923
6+	1.603 ± 1.343	0.237	3.887 ± 2.218	0.085	0.058 ± 0.044	0.195	1.095 ± 0.653	0.099

β were calculated with PROC SurveyReg statement. Variables with $p < 0.05$ in univariate analysis were adjusted in multivariate model. Factors with significance ($p < 0.05$) are shown in bold

BMR basal metabolic rate, *BMI* body mass index, *CVD* cardiovascular disease, *HbA1c* glycated hemoglobin, *HOMA-IR* Homeostatic Model Assessment for Insulin Resistance

Figure 2 shows the results of multivariable analyses. After adjusting for all significant variables in univariate analysis, BMR was not significantly associated with indicators of IR or HbA1c. However, while excluding BMI and appendicular muscle mass from the model, as shown in model 2, BMR was significantly and positively associated with fasting glucose, fasting insulin, and HOMA-IR ($\beta = 0.006$, 0.020, 0.005, respectively) but not with HbA1c (Fig. 2).

Discussion

The present study showed that independent of known risk factors such as age, BMI, energy intake, smoking, and visceral fat mass, BMR was positively associated with fasting plasma glucose, fasting insulin level, and HOMA-IR in obese US adults aged 20–59 without T2DM. In the last few years, emerging interest has been shown in estimated BMR and body composition parameters such as visceral fat mass or muscle mass as markers of metabolic status, which may better reflect the impact of obesity on the human body [21, 22]. Previous studies have suggested that RMR and body composition may be strong markers that represent the actual metabolic state in the pathophysiology of T2DM complications such as retinopathy [12] and neuropathy [13]. However, the role of BMR and insulin sensitivity in non-diabetic subjects has barely been evaluated.

Amaro-Gahete et al. [23] assessed the associations between BMR, basal nutrient oxidation, and IR in middle-aged adults, showing that BMR was not associated with IR, even while greater basal fat oxidation and lower basal carbohydrate oxidation are associated with improved insulin sensitivity. Additionally, Drabsch et al. [24] reported that RMR was positively associated with fat mass and BMI, and RMR was positively associated with HOMA-IR. Alawad et al. [10] presented additional research results, indicating that RMR is significantly higher in obese diabetic patients compared to obese non-diabetic patients, particularly in those with inadequate glycemic control. The present research results mirrored those of that study even though we focused on non-diabetic obese individuals. In contrast to the present findings, Maciak et al. [11] found an inverse correlation between genetically determined RMR and the development of IR in mice. To determine the cause of the differences, it may be necessary to compare the animal model to the actual human population. However, because IR in the animal model is induced by a high-fat diet, we have no comparable way to intentionally restrict the diet of human study participants. In addition, the present study does not include dietary intake as a covariate. A Spanish interventional study assessed whether RMR of obese patients changes under ketogenic diet. Those authors concluded that a very low–calorie ketogenic diet in obese subjects does not induce a reduction in RMR as expected, although a rapid and sustained weight and fat mass loss were observed. The authors documented that it was probably due to the preservation of lean mass [11]. Meanwhile, results of the present study revealed that BMR was associated with IR independently from the visceral fat mass, but when the appendicular muscle mass was adjusted, BMR seems no more correlate with IR. These findings together suggest that the interplay of fat mass, muscle mass, and BMR should be carefully considered when evaluating the efficacy of interventions for obese individuals [25].

Strengths and limitations

The main strength of the present study is that NHANES data are comprehensive and nationally representative, drawn from a large and diverse sample of participants of the US population.

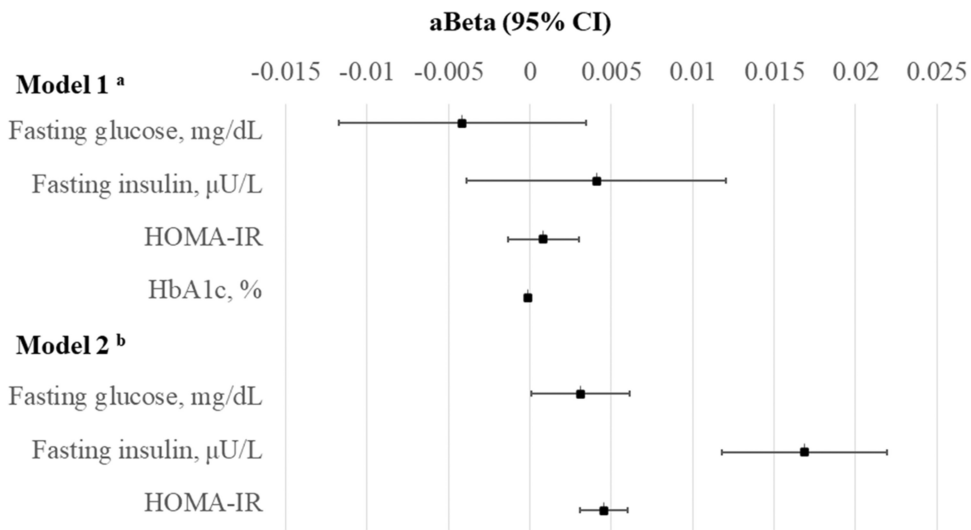

Fig. 2 The forest plot on associations between fasting glucose, fasting insulin, HbA1c, HOMA-IR, and BMR. Model 1 was adjusted with all variables significant in the univariate model. Model 2 was adjusted with variables significant in the univariate model excluding BMI, appendicular muscle mass. BMR, BMI, HbA1c, and HOMA-IR stand for basal metabolic rate, body mass index, glycated hemoglobin, and Homeostatic Model Assessment for Insulin Resistance, respectively

Therefore, the findings are likely generalizable to the overall US population. Also, demographics, lifestyle factors, and comorbidities were carefully controlled in regression analyses.

Nonetheless, the present study has several limitations. Firstly, the cross-sectional, retrospective design does not allow causal inferences to be made, and results may not be generalizable to other populations or geographic locations. Also, the cross-sectional design does not allow longitudinal assessment of variables since measures are collected by NHANES at only a single time point, which restricts long-term follow-up. Secondly, although known risk factors for IR were included in the analyses, other unknown confounders may still exist. Inaccurate reporting or recall bias may have occurred in face-to-face interviews of NHANES and self-reported questionnaires. Subjects were adults aged from 20 to 59 years old, and whether the findings apply to older adults (age 65 years and older) remains unclear. Sedentary behavior was assessed by NHANES questionnaires, not by objective measurement such as accelerometer and therefore could not be included in the analyses due to lack of data.

Conclusion

BMR is significantly associated with indicators of IR among non-diabetic obese adults in the USA. The clinical impact of this finding is that modifying BMR may have potential benefit in preventing deterioration of IR in an otherwise healthy obese population. Future longitudinal studies are warranted to confirm the findings of the present study and to understand the physiological mechanisms underlying the relationship between BMR and IR in this population.

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Data Availability The data that support the findings of this study are available from the corresponding author, Qiaoling Yao, upon reasonable request.

Declarations

Conflict of interest The authors declare no competing interests.

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