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Resting energy expenditure and insulin resitance in obese patients, differences in women and men

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Abstract. – *Background and Objective:* **There is little research about the relation of REE and insulin resistance with gender. The aim of our work was to study gender differences in REE and insulin resistance in obese patients.**

Research Methods and Procedures: **A population of 131 obesity patients was analyzed in a prospective way. The following variables were specifically recorded: age, smoking habit, drinking habit, weight, body mass index (BMI), waist circumference, and waist-hip ratio. Blood pressure, basal glucose, insulin, fibrinogen, and C-reactive protein. HOMA was calculated. An indirect calorimetry, tetrapolar electrical bioimpedance and a serial assessment of nutritional intake with 3 days written food records were performed.**

Results: **The mean age was 31.7 ± 9.2 years and the mean BMI 34.4 ± 5.3. Cardiovascular risk factors were similar in both groups. Anthropometric measurements showed an average waist circunference (107.8 ± 16.1 cm), waist-to hip ratio (0.93 ± 0.11), and average weight (94.8 ± 20.2 kg). Bipolar body electrical bioimpedance showed the next data; fat free mass (55.2 ± 17.1 kg) and fat mass (35.7 ± 12.3 kg). Indirect calorimetry showed higher resting metabolic rate (REE) in males (2001.7 ± 443 Kcal/day vs. 1774.7 ± 344 Kcal/day; $p < 0.05$). REE corrected by fat free mass was similar (male 34.2 ± 17 Kcal/day/kg vs female 39 ± 11.6 Kcal/day/kg; ns). Nutritional intake and HOMA were similar in males and females. In the multivariate analysis with a dependent variable (RMR), the fat free mass remained in the male model (F = 18.5; $p < 0.05$), with an increase of 17.8 (CI95%:9.1-26.2) kcal/day with each 1 kg of fat free mass adjusted by age. In the female model, the fat free mass remained in the model (F = 1 2.5; $p < 0.05$), with an increase of 15.2 (CI95%:6.3-24.2) kcal/day with each 1 kg of fat free mass adjusted by age.**

Conclusion: **REE was higher in males than females, with a higher influence of fat free mass in males than females. No association between insulin resistance and REE was detected.**

Key Words:

Energy expenditure, Obesity, Sex Interaction, Women.

Introduction

Obesity is associated with insulin resistance, which is an important threat to adult health, and is belevied to underlie type 2 diabetes mellitus and cardiovascular disease[1]. However, insulin resistance (resistance to insulin-stimulated glucose uptake) can precede the onset of diabetes mellitus.

Obesity is a multifactorial problem, but there is different evidence about the roles of resting energy expenditure (REE) in its development[2]. REE is one of the many factors that could influence weight and thereby modulate insulin resistance. Some authors have found[3] REE to be an independent determinant of insulin sensitivity in patients with type 2 diabetes. Aerobic activity[4] and dietary composition are reported to influence REE[5], but fat free mass remained the principal determinant of REE. The organs (e.g. kidney, lungs, heart, brain and digestive tract) togheter contribute around 60% to the energy expended by fat free mass, and muscle is responsible for the remaining 40%[6]. REE was shown to be significantly higher in adult men than in women, irrespective of differences in body composition and aerobic fitness[7]. When sex differences were found, their implications were not explored, and there is little research about the contributions of REE to insulin resistance independent of body composition.

The aim of our work was to study gender differences in REE and insulin resistance.

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Subjects and Methods

Subjects

A population of 131 obesity non diabetic outpatients (BMI 30-40) was analyzed in a prospective way. The following variables were specifically recorded: age, smoking habit, weight, and body mass index (BMI).

Procedure

All patients with a 2 weeks weight-stabilization period before recruitment were enrolled. Weight, blood pressure, basal glucose, insulin, fibrinogen, and c-reactive protein blood levels were measured.

Assays

Plasma glucose levels were determined by using an automated glucose oxidase method (Glucose analyser 2, Beckman Instruments, Fullerton, California).Insulin was measured by enzymatic colorimetry (Insulin, WAKO Pure-Chemical Industries, Osaka, Japan) and the homeostasis model assessment for insulin sensitivity (HOMA) was calculated using these values[8]. Cortisol was measured by immunoturbimetry (Roche Diagnostcis GmbH, Mannheim, Germany).

C reactive protein CRP (c-reactive protein) was measured by immunoturbimetry (Roche Diagnostcis GmbH, Mannheim, Germany), analytical sensivity 0.5 mg/dl.

Fibrinogen was determined by a functional quantitative assay according to the method of Clauss[9]

Blood pressure was measured twice after a 10 minutes rest with a random zero mercury sphygmomanometer, and averaged.

Indirect Calorimetry

Indirect calorimetry (MedGem;Health Tech, Golden, USA) was performed in a standard way (fasting conditions and 8 hours of previous resting). Resting metabolic rate (Kcal/day) and oxygen consumption (ml/min) were calculated[10].

Anthropometric Measurements

Body weight was measured to an accuracy of 0.5 kg and body mass index computed as body weight/(height^2). Waist (narrowest diameter between xiphoid process and iliac crest) and hip (widest diameter over greater trochanters) circumferences to derive waist-to hip ratio (WHR) were measured, too. Tetrapolar body electrical bioimpedance was used to determine body composition[11]. An electric current of 0.8 mA and 50 kHz was produced by a calibrated signal generator (Biodynamics Model 310e, Seattle, WA, USA) and applied to the skin using adhesive electrodes placed on right-side limbs. Resistance and reactance were used to calculate total body water, fat and fat-free mass.

Dietary Intake

Patients received prospective serial assessment of nutritional intake with 3 days written food records. All enrolled subjects received instruction to record their daily dietary intake for three days including a weekend day. Handling of the dietary data was by means of a personal computer equipped with personal software, incorporating use of food scales and models to enhance portion size accuracy. Records were reviewed by a registered dietitian and analyzed with a computer-based data evaluation system. National composition food tables were used as reference[12]. Drinking and smoking habit were recorded as dicotomic variables. Regular aerobic physical activity was mantained during the period study (2-3 hours per week).

Statistical Analysis

The results were expressed as average ± standard deviation. The distribution of variables was analyzed with Kolmogorov-Smirnov test. Quantitative variables with normal distribution were analyzed with a two-tailed, paired Student's-t test and ANOVA test. Non-parametric variables were analyzed with the U-Mann and K-Kruskal tests. Qualitative variables were analyzed with the chi-square test, with Yates correction as necessary, and Fisher's test. A multiple regression model (step by step) was used to study the dependent variable RMR. A *p*-value under 0.05 was considered statistically significant.

Results

One hundred and thirty-one patients gave informed consent and were enrolled in the study. The mean age was 31.7 ± 9.2 years and the mean BMI 34.4 ± 5.3. Baseline characteristics of patients were presented in Table I. Cardiovascular risk factors were similar in both groups.

Table I. Clinical and epidemiological characteristics of study population.

Characteritics	Male (n = 63)	Female (n = 68)	p
Age(years)	32.9 ± 15.5	29.2 ± 8.6	Ns
BMI(kg/m^2)	36.1 ± 5.8	33.1 ± 4.4	< 0.05
Systolic BP (mmHg)	135.1 ± 13.2	130.1 ± 11.9	Ns
Dyastolic BP (mmHg)	80.5 ± 9.1	75.9 ± 9.5	Ns
Glucose (mg/dl)	97.5 ± 9.8	93.6 ± 9.2	Ns
Insulin (mUI/L)	18.7 ± 14.2	14.9 ± 9.6	Ns
HOMA	2.94 ± 2.4	2.1 ± 1.2	Ns
CRP (mg/dl)	3.3 ± 3.1	3.9 ± 3.2	Ns
Fibrinogen (mg/dl)	391.7 ± 104	420.2 ± 61.9	Ns

BP: Blood pressure. CRP: c reactive protein. HOMA: Homeostatic model assessment.

All subjects were weight stable during the 2 weeks period preceding the study (body weight change, 0.26 ± 0.12 kg). Anthropometric measurements showed an average waist circunference (107.8 ± 16.1 cm), waist-to hip ratio (0.93 ± 0.11 cm), and average weight (94.8 ± 20.2 kg). Tetrapolar body electrical bioimpedance showed the next data; fat free mass (55.2 ± 17.1 Kg) and fat mass (35.7 ± 12.3 kg). Table II shows differences between sexs.

Indirect calorimetry showed higher resting metabolic rate (REE) in males (2001.7 ± 443 kcal/day vs. 1774.7 ± 344 kcal/day; $p < 0.05$) and oxygen consumption (284.7 ± 63.9 ml/min. vs. 255.9 ± 49.9 ml/min.; $p < 0.05$). REE corrected by fat free mass was similar (34.2 ± 17 Kcal/day/kg vs 39 ± 11.6 Kcal/day/kg;ns).

Serial assessment of nutritional intake with 3 days written food records did not showed differences; a calory intake of (1789.6 ± 561 kcal/day vs. 1750.5 ± 672 kcal/day; $p < 0.05$), a carbohydrate intake of (175 ± 82 g/day vs. 179.7 ± 92 g/day; ns), a fat intake of (79.4 ± 24.8 g/day vs. 79.2 ± 30.7 g/day; ns) and a protein intake of (86.7 ± 21.4 g/day vs. 79.4 ± 28.2 g/day). Smoking habit was higher in males (18.5% vs 3.4%; $p < 0.05$), drinking habit was similar in both sexs (3,7% vs 3,4%; ns) and regular exercise was similar (11.1% vs 13.8%; $p < 0.05$).

In male patients, correlation analysis showed a significant correlation among REE and the independent variables; weight (r = 0.7; $p < 0.05$), BMI (r = 0.5; $p < 0.05$), waist circumference (r = 0.6; $p < 0.05$), waist-hip ratio (r = 0.6; $p < 0.05$) and fat free mass (r = 0.7; $p < 0.05$). No correlations were detected with glucose, insulin, HOMA and dietary intakes. These associations disappeared with the correction of REE by fat free mass. Corrected RMR was associated with fat free mass (r = 0,7; $p < 0.05$).

In female patients, correlation analysis showed a significant correlation among REE and the independent variables; weight (r = 0.7; $p < 0.05$), waist circumference (r = 0.5; $p < 0.05$), waist-hip ratio (r = 0.4; $p < 0.05$) and fat free mass (r = 0.6; $p < 0.05$). No correlations were detected with glucose, insulin and HOMA and dietary intakes. Only corrected RMR was associated with fat free mass (r = 0.6; $p < 0.05$).

In the multivariate analysis with a dependent variable (RMR), the fat free mass remained in the male model (F = 18.5; $p < 0.05$), with an increase of 17.8 (CI95%:9.1-26.2) Kcal/day with each 1 kg of fat free mass adjusted by age. In the female model, the fat free mass remained in the

Table II. Anthropometric characteristics by sex.

Characteritics	Male (n = 63)	Female (n = 68)	p
Fat free mass (kg)	65.8 ± 17.1	45.3 ± 12.2	< 0.05
Fat mass (kg)	32.3 ± 12.1	39.3 ± 11.6	< 0.05
Waist circunference	112.8 ± 17.3	103.6 ± 13.9	< 0.05
Waist to hip ratio	0.96 ± 0.1	0.90 ± 0.1	< 0.05

model (F = 12.5; $p < 0.05$), with an increase of 15.2 (CI95%:6.3-24.2) Kcal/day with each 1 kg of fat free mass adjusted by age

Discussion

The major finding of this study was that REE of our obese subjects was higher in males than females and this difference disappeared with the fat free mass correction.

In adults, it was suggested that the greater thermogenic effect of androgens compared with estrogens might also contribute to the sex difference in metabolic rate[13]. Some authors[14] found an independent effect of sex on REE. Perhaps, the REE measurements in that study were not carried out in the fasting state and incorporated the unpredictable energy cost of meal-induced thermogenesis. In our study, patients were in a fasting state for at least 8 hs., minimizing this effect.

In some studies[15], dietary composition was shown to affect REE and this item was assessed here by a 3 days written food records. No food component intake in the present study was significantly associated with REE. In our study, physical activity could not explain the sex difference in REE, because males had similar activity than females.

The sex difference in REE without corrected by fat free mass that was observed might, therefore, predispose females to obesity more than the males, and the obesity epidemic is known to affect females more than males[16]. Buchholtz et al[17] had similar results that us.

In some studies relations between insulin sensivity and resting thermogenesis was detected[18]. In patients with liver cirrhosis, higher than normal resting expenditure energy was associated with insulin resistance regardless of diabetes[19-20]. Our data did not detect this association, previously studies were performed with different populations such as cirrhotic patients[21], pregnant women[22], and diabetic patients[23]. Our patients had obesity without diabetes mellitus, perhaps a low insulin resistance such as detected in our patients, it is not enough to influence in energy expenditure.

In multivariant analysis, male sex produce a higher increase with each kg of fat free mass than female sex, a clear interaction was detected in these two models. In fact, specific equations must take sex into account to predict adequately[24].

In conclusion, REE was higher in males than females, with a higher influence of fat free mass in males than females. No association between insulin resistance and REE was detected.

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