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´´Júlio de Mesquita Filho´´

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Alterações do nível de atividade física e composição corporal após cirurgia bariátrica

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RESUMO

A obesidade é caracterizada pelo excesso de gordura corporal e é considerada um importante fator de risco para doenças cardiometabólicas. Dentre as estratégias para o tratamento, principalmente da obesidade mórbida, a cirurgia bariátrica apresenta resultados significativos na redução da massa corporal e controle das comorbidades associadas. Por outro lado, observa-se que nem todos os pacientes submetidos à cirurgia atingem redução significativa da massa corporal e/ou manutenção desta ao longo do tempo. Investigar os fatores envolvidos no comportamento da massa corporal após cirurgia bariátrica se faz importante para melhorar a efetividade do tratamento da obesidade mórbida. O presente trabalho tem como foco as atividades físicas e composição corporal e consiste na apresentação de três estudos. O primeiro estudo teve como objetivo avaliar as alterações das atividades físicas e composição corporal seis e doze meses após cirurgia bariátrica. Trinta e quatro mulheres submetidas à cirurgia de derivação gástrica em Y de Roux (DGYR) completaram o estudo. As atividades físicas foram mensuradas diretamente por meio de um acelerômetro tri-axial, antes e após seis e doze meses da cirurgia. A composição corporal foi estimada por bioimpedância multifrequencial nos mesmos períodos. O percentual de tempo gasto em atividades físicas moderada-vigorosa (AFMV) aumentou significativamente do período pré para 6 meses após cirurgia, entretanto, não foi observada diferença em 12 meses. Alterações não significativas foram detectadas para as outras variáveis de atividade física. O percentual de sujeitos que atingiram ≥ 150 min de AFMV por semana foi de 5,9%, 11,8% e 14,7%, para o período pré, 6 e 12 meses após a cirurgia, respectivamente. A análise de regressão multivariada sugeriu que as atividades sedentárias determinaram a perda de massa magra nos períodos de seis meses (β = -0,333; IC95% = -0,649; 0,003) e doze meses (β = -0,510; 95 % CI = -0,867, -0,154) após a cirurgia. Os achados do primeiro estudo indicam o percentual gasto em AFMV aumentou 6 meses após cirurgia DGYR, mas esta alteração não foi mantida em 12 meses. Apesar da considerável perda de massa corporal após cirurgia, a maioria dos sujeitos foram classificados como fisicamente inativos e não foi observada alteração do comportamento sedentário. Esses dados reforçam a importância de orientar os pacientes bariátricos para aumentar o nível de atividade física no período pós-operatório. O objetivo do segundo estudo foi comparar o consumo de oxigênio em repouso mensurado por calorimetria indireta com os resultados obtidos por fórmulas preditivas. Participaram do estudo 40 mulheres obesas na fila de espera para a cirurgia bariátrica. As fórmulas preditivas utilizadas foram: MIfflin-St Jeor (MSJ), *Female Brazilian Population* (FBP), Henry & Rees (HR), Harris-Benedict (HB), Schofield (S) e World Health Organization (WHO). O valor médio de consumo de oxigênio foi 2,27 ± 0,024 $ml \cdot kg^{-1} \cdot min^{-1}$, e o valor médio de taxa metabólica de repouso foi 0,66 ± 0,07 $kcal \cdot kg^{-1} \cdot h^{-1}$. Os valores mensurados de consumo de oxigênio e a taxa metabólica de repouso foram 35,14 ± 7,10 e 33,62 ± 7,46%, respectivamente, menor que o valor padrão de 1MET (3,5 $ml \cdot kg^{-1} \cdot min^{-1}$ e 1 $kcal \cdot kg^{-1} \cdot h^{-1}$, respectivamente). As equações de MSJ e

FBP apresentaram maior índice de predição a nível individual (entre ± 10% da medida mensurada) para estimar o consumo de oxigênio de repouso e a taxa metabólica de repouso. Os achados do segundo estudo indicaram que, em mulheres obesas, o valor padrão de 1MET superestimou o gasto energético de repouso relativo. A correção do valor de 1MET pelas fórmulas preditivas (MSJ e FBP) favorecem uma melhor estimativa do gasto energético das atividades físicas em mulheres na fila de espera para a cirurgia bariátrica. O terceiro estudo teve como objetivo avaliar a influência do polimorfismo *ACTN3 R577X* com as alterações da composição corporal após a cirurgia bariátrica. Quarenta mulheres participaram deste estudo. A composição corporal foi estimada por meio de bioimpedância multifrequencial nos períodos pré, seis, doze e vinte e quatro meses após a cirurgia DGYR. Os resultados indicaram que o percentual de alteração da massa corporal e massa de gordura foram significativamente maior para as pacientes com o genótipo XX comparado com o genótipo RX/RR, sem diferença significativa para a perda de massa magra livre de gordura. Os achados do terceiro estudo indicaram que mulheres obesas com o genótipo XX tiveram alterações mais positivas na composição corporal após a cirurgia DGYR.

Palavras-chave: Derivação gástrica em Y de Roux. Acelerômetro. Gasto energético. Polimorfismo. Bioimpedância.

ABSTRACT

Obesity is characterized by excess body fat and is considered an important risk factor for cardiometabolic diseases. Among treatment strategies, mainly for morbid obesity, bariatric surgery exhibits significant outcomes by reducing body mass and controlling associated comorbidities. On the other hand, it has been observed that not all patients undergoing this surgery achieve significant body mass reduction and/or maintenance over time. The assessment of factors involved in body mass evolution after bariatric surgery is important for improving the effectiveness of the treatment of morbid obesity. The present research focused on physical activities and body composition, and consists of the presentation of three studies. The goal of the first study was to assess changes in physical activities and body composition six and twelve months after bariatric surgery. Thirty-four women undergoing Roux-en-Y gastric bypass surgery completed the study. Physical activities were directly measured using a tri-axial accelerometer before and six and twelve months after the surgery. Body composition was estimated by multifrequency bioimpedance during the same periods. The percent time spent in moderate-to-vigorous physical activity (MVPA) changed significantly from pre- to 6 months post-surgery; however, no difference was observed at 12 months. No significant changes was detected for others physical activities variables. The percentage of subjects achieving ≥ 150 min per week of MVPA in bout ≥ 10 min was 5.9%, 11.8%, and 14.7%, for pre, 6 and 12 months post-surgery, respectively. Multivariable regression analysis suggest that the percent time spent in sedentary activity determined fat-free mass loss (%) at 6-months (β = -0.323; 95% CI = -0.649, 0.003) and 12 months (β = -0.510; 95% CI = -0.867, -0.154) post-surgery. The findings of the first study indicated that MVPA increased 6 months post-RYGB surgery, but this change was not maintained at 12-months. Despite the considerable body mass loss post-surgery, the majority of subjects was classified as physically inactive and did not change sedentary behavior. These data reinforce the importance to guide bariatric patients in order to increase the physical activity level in the postoperative period. The goal of the second study was to compare the resting oxygen consumption measured by indirect calorimetry with the results obtained by predictive formulas. Forty obese women on the waiting list for bariatric surgery. The predictive formulas used were: Mifflin-St Jeor (MSJ), Female Brazilian Population (FBP), Henry & Rees (HR), Harris-Benedict (HB), Schofield (S) and World Health Organization (WHO). The mean value of oxygen consumption was 2.27 ± 0.024 ml·kg^{-1}·min^{-1}, and the mean value of resting metabolic rate was 0.66 ± 0.07 kcal·kg^{-1}·h^{-1}. The measured values of oxygen consumption and resting metabolic rate were 35.14 ± 7.10 and 33.62 ± 7.46%, respectively, lower than the 1MET standard value (3.5 ml·kg^{-1}·min^{-1} and 1 kcal·kg^{-1}h^{-1}, respectively). The MSJ and FBP equations showed higher prediction at individual level (within ± 10% of the measurement) to estimate resting oxygen consumption and resting metabolic rate. The findings of the second study indicated that, in obese women, the

1MET standard value overestimated the relative resting energy expenditure. The correction of the 1MET value by predictive formulas (MSJ and FBP) promote a better estimation of energy expenditure by physical activities in women on the waiting list for bariatric surgery. The goal of the third study was to assess the influence of *ACTN3 R577X* polymorphism on body composition changes after bariatric surgery. Body composition was estimated by multifrequency bioimpedance pre, six, twelve and twenty-four months after RYGB surgery. The results indicated that the percentage of changes in body mass and fat mass were significantly higher for patients with XX genotype compared to RX/RR genotype, with no significant difference for fat-free mass loss. The findings of the third study indicated that obese women with XX genotype exhibited more positive changes in body composition after RYGB surgery.

Keywords: Roux-en-Y gastric bypass. Accelerometer. Energy expenditure. Polymorphism. Bioimpedance.

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SUMÁRIO

1. INTRODUÇÃO

A obesidade tem sido caracterizada como epidemia mundial e considerada um problema de saúde pública. O desenvolvimento da obesidade possui etiologia multifatorial, envolvendo uma complexa interação entre fatores genéticos e ambientais.[1,2] Especificamente, hábitos alimentares inadequados, associados com estilo de vida sedentário, influenciam no desequilíbrio entre o gasto e consumo energético que, a longo prazo, é responsável pelo acúmulo excessivo de gordura corporal.[3,4]

Considerada um importante fator de risco para o desenvolvimento de diversas doenças cardiometabólicas,[5] a obesidade mórbida reduz consideravelmente a qualidade e expectativa de vida.[6,7]

O tratamento da obesidade e das alterações metabólicas associadas deve ser pautado na redução da massa adiposa (tecido alvo). Nesse sentido, a realização regular de exercícios físicos, em associação com dietas hipocalóricas, é recomendada e reconhecida como tratamento não medicamentoso no controle da obesidade.[8]

Por outro lado, essas intervenções comportamentais apresentam baixa adesão em adultos com obesidade mórbida, resultando em baixa eficácia na redução significativa da massa corporal e reganho ao longo do tempo.[9]

Entre os aspectos que contribuem com o reganho da massa corporal perdida inicialmente, observa-se: baixa adesão do tratamento (dieta e/ou exercício físico) ao longo do tempo; redução da taxa metabólica de repouso; e adaptações fisiológicas relacionadas ao aumento do apetite,[10,11] Desta forma, devido à incapacidade de manter a redução da massa corporal por métodos tradicionais, a cirurgia bariátrica é reconhecida como um método invasivo, porém efetivo, para induzir redução significativa da massa corporal a longo prazo.[9] Nesse contexto, a cirurgia bariátrica é recomendada para indivíduos obesos que não obtiveram sucesso por métodos não invasivos (e.g., dietas e exercícios físicos) e possuem índice de massa corporal (IMC) superior a 40 kg/m^2 ou superior a 35 kg/m^2 com comorbidades associadas.[12]

Dentre os resultados obtidos pelo procedimento cirúrgico, observa-se que, além da diminuição significativa da massa corporal, alguns estudos reportam reduções de aspectos inflamatórios sistêmicos,[13,14] melhora da sensibilidade à insulina,[15,16] da hipertensão arterial sistêmica[17,18,19] e da hiperlipidemia.[17,18]

Por outro lado, observa-se que nem todos os pacientes submetidos ao procedimento cirúrgico atingem redução significativa da massa corporal e/ou manutenção desta ao longo do tempo.[20,21] Entre os possíveis fatores que contribuem para a recuperação da massa corporal, alterações anatômicas (dilatação gástrica e gastrojejunal) e psicofisiológicas podem ocorrer após a cirurgia, favorecendo o aumento da ingestão de alimentos.[22] Portanto, a abordagem interdisciplinar desempenha um papel fundamental para a saúde do paciente e no sucesso da cirurgia bariátrica ao longo do tempo.

Entre as alterações comportamentais que devem ser abordadas durante o período pós-operatório, sugere-se o aumento do nível de atividade física, o qual pode contribuir para a efetividade da cirurgia e aumentar a qualidade de vida do paciente.[23]

Nesse contexto, dois artigos de revisão sistemática indicaram uma positiva associação entre o aumento das atividades físicas e a redução da massa corporal no período pós-operatório.[24, 25] Em adição, pacientes que apresentavam aumento do nível de atividade física após cirurgia bariátrica relataram melhor qualidade de vida,[26] saúde mental e menores sintomas depressivos.[27] No entanto, é importante ressaltar que grande parte desses estudos[24-27] utilizaram questionários de autorrelato para determinar o nível de atividade física.[24-27]

Questionários de autorrelato exigem grande subjetividade em relação à intensidade da atividade física realizada e o viés nas respostas são limitações desses métodos.[28] em especial para a população obesa.[29]

Nesse sentido, Bond et al.[30] compararam as alterações das atividades físicas de intensidade moderada/vigorosa antes e seis meses após cirurgia bariátrica utilizando um questionário de autorrelato (*Paffenbarger Physical Activity Questionnaire*) com os dados obtidos por meio do acelerômetro tri-axial. Os resultados obtidos pelo questionário mostraram um aumento de cinco vezes para atividades físicas com intensidade moderada/vigorosa após a cirurgia. Por outro lado, não foi observada alteração das atividades físicas com intensidade moderada/vigorosa pelo acelerômetro.[30] Estes resultados indicam que os pacientes bariátricos podem superestimar o nível de atividade física quando respondem questionários de autorrelato. Desta forma, os resultados obtidos por meio deste método devem ser interpretados com cautela.

Acelerômetro bi- e tri-axial captura aceleração do movimento corporal, em dois e três eixos, respectivamente, e permite quantificar a frequência, duração e intensidade das atividades físicas realizadas.[31] Assim, medidas objetivas (como acelerômetro) são importantes para esclarecer a influência das atividades físicas sobre o resultado da cirurgia bariátrica.

Estudos utilizando acelerômetro mostraram que pacientes na lista de espera para a cirurgia bariátrica apresentavam baixo nível de atividade física.[32, 33] Além disso, estudos indicaram não alteração do nível de atividade física no períodos de três,[34] seis[30,34] e nove meses[35] após cirurgia bariátrica.

Em relação aos resultados da cirurgia, Josbeno et al. [36] investigaram indivíduos em diferentes períodos de pós-operatório (2, 3, 4 e 5 anos). Os autores apontaram uma positiva associação entre atividades físicas com intensidade moderada/vigorosa e o percentual da perda do excesso de peso (% PEP). Estes dados indicam que o aumento do nível de atividade física pode contribuir para o aumento da taxa de sucesso da cirurgia bariátrica.

O presente estudo representa uma continuidade das nossas pesquisas. O foco principal foi investigar os aspectos envolvidos no comportamento da massa corporal e sua relação com o consumo alimentar, metabolismo energético, marcadores hormonais/inflamatórios sistêmicos e genéticos em mulheres com obesidade mórbida que foram submetidas à cirurgia de derivação gástrica em Y de Roux.

Neste estudo, debruçamos na importância do nível de atividade física e genética nas alterações da composição corporal. Considerando que o número de cirurgias bariátricas aumentou consideravelmente nos últimos anos, fatores que influenciam nos resultados da cirurgia são temas importantes para a abordagem do paciente bariátrico pela equipe multidisciplinar.

Portanto, o objetivo geral deste estudo foi avaliar a influência da cirurgia de derivação gástrica em y de Roux (DGYR) em mulheres nas alterações das atividades físicas e composição corporal após seis e doze meses do tratamento cirúrgico.

No presente trabalho são apresentados três artigos. No primeiro artigo objetivou-se investigar a influência da cirurgia DGYR nas alterações do nível de atividade física e composição corporal em mulheres obesas. No segundo artigo foi investigada a relação entre o consumo de oxigênio de repouso mensurado por calorimetria indireta e os resultados obtidos em fórmulas preditivas em mulheres obesas na lista de espera para a cirurgia bariátrica. O terceiro artigo teve como objetivo investigar a influência de um polimorfismo *ACTN3 R577X* (rs1815739) nas alterações da composição corporal após cirurgia DGYR em mulheres obesas.

Capítulo 1.

Physical activity and body composition changes after Roux-Y gastric bypass surgery

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ABSTRACT

This study aimed to determine the physical activity level preoperatively and at 6 and 12 months postoperatively among female patients who underwent bariatric surgery, and to investigate its relationship with body composition changes. Thirty-four women who had Roux-Y gastric bypass (RYGB) surgery completed the study. Physical activity was measured objectively for 7 consecutive days by using an Actigraph GT3X+ accelerometer. Body composition was estimated by using multifrequency bioimpedance analysis. The percentage of time spent in moderate-to-vigorous physical activity (MVPA) changed significantly from preoperatively to 6 months postoperatively (median 2.3% [interquartile range, IQR: 1.9–3.5] vs. 3.4% [IQR: 2.4–4.7); however, no difference was observed at 12 months (3.2% [IQR: 2.0–4.1]). No significant changes ($p > 0.05$) were detected for other physical activity variables. The percentage of subjects achieving ≥150 min/week of MVPA in bouts of ≥10 min was 5.9%, 11.8%, and 14.7% preoperatively, 6 months postoperatively, and 12 months postoperatively, respectively. Multivariable regression analysis suggested that the percentage of time spent in sedentary activity was associated with fat-free mass loss (%) at 6 months (β = -0.323; 95% confidence interval [CI] = -0.649 to 0.003) and 12 months (β = -0.510; 95% CI = -0.867 to -0.154) postoperatively. In conclusion, the overall MVPA increased at 6 months post-RYGB surgery; however, this change was not maintained at 12 months. Despite the considerable body mass loss postoperatively, most of the subjects were classified as being physically inactive and did not change their sedentary behavior. These findings indicate that female patients undergoing bariatric surgery should be encouraged to increase their physical activity level post-RYGB surgery.

Keywords: physical activity, accelerometer, body composition, bariatric surgery

INTRODUCTION

Physical inactivity is a term used to indicate failure to achieve the recommended minimum moderate-to-vigorous physical activity (MVPA) for developing and maintaining physical fitness and health [1, 2]. In this context, important research associations have recommended the practice of achieving a minimum of 150 min/week of MVPA accumulated in bouts of ≥10 min [3-6].

Another important variable is sedentary behavior, which is characterized as any activity during waking hours that results in low energy expenditure (<1.5 metabolic equivalents [METs]) while in a sitting or reclining posture [1]. In general, physical inactivity and sedentary behavior are independent risk factors that may be associated with the development of noncommunicable chronic diseases [2] and should be monitored in clinical practice.

Concerning patients undergoing bariatric surgery, a meta-analysis study reported an association between the increase of physical activity level and body mass loss after the surgery [7,8]. Additionally, bariatric patients who became more physically active after the surgery showed improved quality of life parameters [9], mental health, and depressive symptoms [10].

Although the available evidence indicates a positive relationship between physical activity level and body mass loss after bariatric surgery, an important limitation of these related studies [7-10] was the use of self-report questionnaires to assess physical activity levels. In this context, Bond et al. [11] compared the changes in MVPA intensity between before and 6 months after the operation, by using a self-report questionnaire (Paffenbarger Physical Activity Questionnaire) and a triaxial accelerometer. The results obtained by the questionnaire showed a fivefold increase in MVPA; however, no difference was detected with the accelerometer [11]. These contradictory results indicate that bariatric patients can overreport physical activities, and that results from studies that use self-report questionnaires should be interpreted with caution.

Given the importance of physical activity level for health outcomes and surgical success, more valid methods for objectively measuring the intensity of physical activities are necessary. A triaxial accelerometer measures body movement acceleration in three axes (vertical, horizontal right to left, and horizontal front to back planes), and allows quantifying the frequency, duration, and intensity of physical activities. This direct assessment provides a more accurate and reliable tool for monitoring physical activity levels [12].

Although the importance of physical activity in reducing the risk factors for chronic diseases and improving physical and psychological conditions has been previously established [2, 5], obese subjects have reported several barriers (internal and external) to performing regular physical activity and becoming physically active owing to their excess body mass [13].

The main aim of this study was to verify if bariatric surgery per se and the standard care after surgery would result in a decrease of sedentary behavior and increase of MVPA. Additionally, this study aimed to verify if any physical activity variable could be better associated with the attenuation of fat-free mass loss and an increase of body fat loss in the postoperative period. Therefore, in this study, we determined the physical activity level among female bariatric patients preoperatively and postoperatively (6 and 12 months), and investigated its relationship with body composition changes.

METHODS

Subjects

Forty-two female candidates for bariatric surgery volunteered to participate in this study and signed an informed consent form for participation. The inclusion criteria were as follows: (a) age between 20 and 40 years and (b) body mass index (BMI) ≥40 kg/m^2. The non-inclusion criteria were as follows: presence of (a) joint and muscular limitations, (b) diseases that affect functional capacity, or (c) genetic syndromes associated with obesity. All patients were recruited from the same bariatric center in Piracicaba (São Paulo), Brazil (from January through February 2014), and data collection was completed in November 2015. All subjects underwent Roux-Y gastric bypass (RYGB) surgery performed by the same medical staff (from August through November 2014). This study was approved by the local research ethics committee (protocol no. 74/13).

Study Design

This prospective study was designed to compare the preoperative and 6 and 12 months postoperative changes in physical activity level and body composition in female bariatric patients. To this end, each subject was instructed to wear a triaxial accelerometer during 7 consecutive days (5 weekdays and 2 weekend days) in the preoperative (~2 months before) and 6 and 12 months post-RYGB surgery periods. Additionally, body composition parameters were estimated by using multifrequency bioimpedance analysis in the same periods.

Physical Activity Assessment

Physical activities were monitored by using a triaxial accelerometer. The device (GT3X+ model; ActiGraph, Pensacola, FL, USA) was calibrated for each subject by using ActiLife 6 software (ActiGraph, Pensacola, FL, USA) according to the manufacturer's instructions. The device (~27 g; 3.8 × 3.7 × 1.8 cm) was attached to the waist (right side) by using an elastic belt. The subjects were instructed to engage in their normal physical activity routine while wearing the device, and to remove it only during bathing and physical activities involving water. The data collected by the accelerometer were transferred to and analyzed with ActiLife 6 software. A minimum of 10 h of wear time per day was required to validate the data. Nonwearing time was excluded from analyses. Sedentary activities were considered as activities with ≤100 counts/min; light activity, between 101 and 1952 counts/min; and MVPA ≥1953 counts/min [14].

Body Composition

Body composition was estimated by using a vertical bioimpedance analyzer. The equipment (InBody 230; BioSpace, Seoul, Korea) uses multifrequency bioelectrical impedance on eight tactile points. The measurements were conducted with subjects wearing light clothing and without shoes and socks. The tests for preoperative and postoperative analyses were conducted in the morning at the same time of the day in a temperature-controlled (24°C) room.

The following instructions were provided to the subjects before the assessments: (a) to fast and (b) not drink water 3 h before the test; (c) to not take diuretics 24 h before the test; (d) to not perform physical exercises 24 h before the test; (e) to not take a bath in the morning; (f) to urinate and/or defecate at least 30 min before the test; and (g) to not wear metal accessories (e.g., earrings and watches) during the evaluation [15].

Statistical Analysis

The Friedman repeated-measures test was used to compare the preoperative and postoperative (6 and 12 months) physical activity level and body composition changes. When a significant interaction effect was found, a Dunn post hoc test was performed. The interaction between study variables, by using body composition (percentage changes of body mass, fat mass, and fat-free mass) as the dependent variable, was assessed by means of multivariate linear regression tests. The significance level adopted was $p \leq 0.05$. Data were expressed as median and interquartile range (IQR: 25th–75th percentile).

RESULTS

Figure 1 illustrates the flowchart of the study. A total of 42 patients were eligible for and agreed to participate in this study. At 6 months after surgery, two patients dropped out. Two patients at 6 months and three patients at 12 months after surgery did not properly use the accelerometer, and their data were excluded from the analyses.

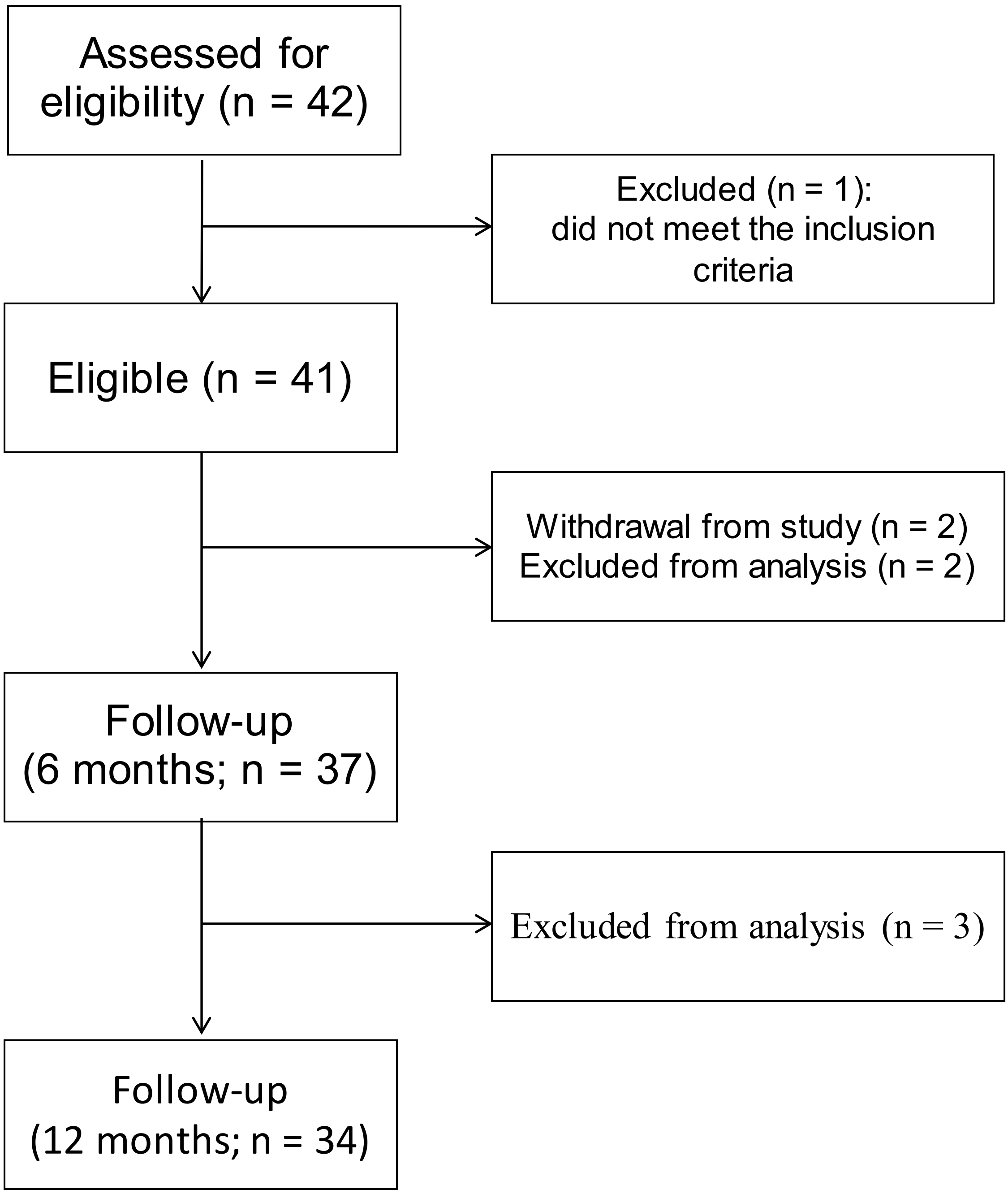

Figure 1: flowchart of the study

The subjects had a median age of 31.56 (26.25–36.75) years; height, 1.59 (1.55–1.63) m; and BMI, 44.43 (41.90–46.44) kg/m^2 before the surgery. Table 1 shows the preoperative and 6 and 12 months postoperative body composition parameters. Significant decreases (p < 0.001) were evident for body mass, fat mass, and fat-free mass at 6 and 12 months after surgery, compared with the preoperative values. Significant decreases (p < 0.001) were found in body mass and fat mass, in the comparison between 6 and 12 months after surgery. However, no difference (p > 0.05) was detected for fat-free mass between 6 and 12 months after RYGB.

The median daily were time (accelerometer) values were 1210.0 min/day (1166.0–1247.0) preoperatively, 1183 min/day (1119.0–1241.0) at 6 months postoperatively, and 1160.0 min/day (1103.0–1227.0) at 12 months postoperatively (p = 0.08).

No significant differences were found between the preoperative and postoperative values for the variables step count (p = 0.57), percentages of time spent in sedentary activity (p = 0.81), percentages of time spent in light activity (p = 0.28), sedentary bouts of ≥30 min/day (p = 0.24), MVPA in bouts of ≥10 min/day (p = 0.64), and in MVPA in bouts of ≥10 min/week (p = 0.47).

The post hoc test indicated significant increases in the percentage of time spent in MVPA at 6 months postoperatively compared with the preoperative values (p < 0.05); however, no significant difference (p > 0.05) was observed at 12 months postoperatively (Table 2).

The percentage of subjects achieving ≥150 min/week of MVPA in bouts of ≥10 min was 5.9%, 11.8%, and 14.7% preoperatively, 6 months postoperatively, and 12 months postoperatively, respectively. The percentage of subjects who did not perform any single MVPA in bouts of ≥10 min was 52.9%, 41.2%, and 47.1% preoperatively, 6 months postoperatively, and 12 months postoperatively, respectively.

Table 1. Body composition variables pre- and post-RYGB surgery

Variables	Preoperative	6 Months	12 Months	6-Month changes (%)	12-Month changes (%)
Body mass (kg)	111.0 (103.6 to 121.3)	78.5* (74.2 to 91.0)	73.8*# (66.2 to 84.9)	-27.7 (-29.2 to -26.5)	-33.4 (-36.5 to -29.6)
Fat mass (kg)	57.9 (54.5 to 64.2)	33.2* (29.0 to 38.1)	27.0*# (23.6 to 33.6)	-44.6 (-47.9 to -39.4)	-52.4 (-57.6 to -47.0)
Fat-free mass (kg)	51.5 (49.6 to 56.6)	46.5* (44.7 to 49.6)	46.8* (44.1 to 50.5)	-10.9 (-12.5 to -8.0)	-10.9 (-14.0 to -8.5)

* $p < 0.001$ compared with preoperative values. # $p < 0.001$ compared with 6-month values. RYGB, Roux-Y gastric bypass.

Table 2. Physical activity levels pre- and post-RYGB surgery

Variables	Preoperative	6 Months	12 Months
Step count (per day)	7553.5 (5379.0–8901.0)	8090.5 (6285.0–9480.0)	8039.5 (5970.0–9590.0)
Sedentary activity (%)	77.0 (72.5–81.1)	77.0 (72.1–80.8)	77.8 (73.2–79.9)
Light activity (%)	20.0 (17.0–24.6)	19.1 (16.8–23.4)	19.8 (16.6–22.5)
MVPA (%)	2.3 (1.9–3.5)	3.4 (2.4–4.7)*	3.2 (2.0–4.1)
MVPA in bouts of ≥10 min/week	0.0 (0.0–23.0)	19.0 (0.0–72.0)	15.5 (0.0–78.0)
MVPA in bouts of ≥10 min/day	0.0 (0.0–3.3)	2.7 (0.0–9.4)	0.9 (0.0–10.3)
Sedentary activity in bouts of ≥30 min/day	163.7 (140.2–207.9)	189.9 (156.8–220.1)	172.3 (147.7–198.9)

Data are expressed as median (interquartile range). RYGB, Roux-Y gastric bypass; MVPA, moderate-to-vigorous physical activities. * $p < 0.05$ compared with preoperative values.

Multivariate regression analysis suggested that sedentary activity was associated with fat-free mass loss (%) at 6 months (-0.323; 95% confidence interval [CI] = -0.649 to 0.003) and 12 months (β = -0.510; 95% CI = -0.867 to -0.154) after RYGB surgery. Additionally, there was a significant association of light physical activity (β = 0.642; 95% CI = -0.239 to 1.045) and sedentary activity in bouts of >30 min (β = -0.052; 95% CI = -0.098 to -0.007) with fat-free mass loss at 12 months. MVPA was associated with fat-free mass loss at 6 months (β = 1.714; 95% CI = 0.422 to 3.006) after RYGB surgery (table 3 and 4).

Table 3. Associations between body composition changes and physical activity level at 6 months after RYGB surgery.

	Body mass loss (%)	**Fat-free mass loss (%)**	**Fat mass loss (%)**
Sedentary activity (%)	-0.046 (-0.446 to 0.352)	**-0.323 (-0.649 to 0.003)***	-0.052 (-0.546 to 0.442)
Light activity (%)	0.054 (-0.406 to 0.515)	0.291 (-0.095 to 0.677)	0.104 (-0.464 to 0.672)
MVPA (%)	0.148 (-1.508 to 1.803)	**1.714 (0.422 to 3.006)**$^{\#}$	-0.333 (-2.378 to 1.712)
MVPA in bouts of ≥10 min/day	-0.056 (-0.271 to 0.159)	0.066 (-0.120 to 0.253)	-0.021 (-0.288 to 0.246)
Sedentary in bouts of ≥30 min/day	0.021 (-0.019 to 0.062)	-0.015 (-0.051 to 0.020)	0.031 (-0.019 to 0.081)

Multiple regression analysis adjusted for baseline body mass index and age. Data are expressed as unstandardized regression coefficients (β) with 95% confidence intervals in parentheses. RYGB, Roux-Y gastric bypass; MVPA, moderate-to-vigorous physical activity. * $p > 0.05$; # $p > 0.01$.

Table 4. Associations between body composition changes and physical activity level at 12 months after RYGB surgery.

	Body mass loss (%)	Fat-free mass loss (%)	Fat mass loss (%)
Sedentary activity (%)	-0.233 (-0.755 to 0.289)	**-0.510 (-0.867 to -0.154)***	-0.073 (-0.779 to 0.633)
Light activity (%)	0.540 (-0.039 to 1.120)	**0.642 (0.239 to 1.045)#**	0.423 (-0.381 to 1.227)
MVPA (%)	-1.424 (-2.961 to 0.113)	0.178 (-1.063 to 1.419)	-1.849 (-3.909 to 0.211)
MVPA in bouts of ≥10 min (day)	-0.101 (-0.284 to 0.082)	0.020 (-0.122 to 0.163)	-0.143 (-0.387 to 0.101)
Sedentary in bouts of ≥30 min (day)	-0.025 (-0.090 to 0.039)	**-0.052 (-0.098 to -0.007)***	0.014 (-0.073 to 0.100)

Multiple regression analysis adjusted for baseline body mass index and age. Data are expressed as unstandardized regression coefficients (β) with 95% confidence intervals in parentheses. RYGB, Roux-Y gastric bypass; MVPA, moderate-to-vigorous physical activity.

* $p > 0.05$; # $p > 0.01$.

DISCUSSION

This study aimed to investigate the preoperative and 6 and 12 months postoperative changes in physical activity level among female bariatric patients, and to investigate the relationship between body composition changes and triaxial accelerometer variables. The main findings were as follows: (a) the percentage of time spent for MVPA increased only at 6 months postoperatively; (b) most of the subjects were classified as being physically inactive both before and after surgery; (c) no changes in sedentary behavior was observed in the postoperative period; and (c) sedentary activity was inversely associated with fat-free mass loss at 6 and 12 months after surgery.

Bariatric surgery is recognized as an effective method for the treatment of morbid obesity, and its success is often indicated by the percentage of excess weight loss (%EWL) [16]. On the other hand, the ideal body mass reduction must be associated with fat mass loss and maintenance of fat-free mass, an important parameter that can be assessed with bioimpedance analysis. In our study, accentuated body mass reduction was evident during the postoperative period (6 and 12 months), with higher percentage changes in fat mass (median values of -44.28% and -52.33%, respectively) than fat-free mass (median values of -11.11% and -10.88%, respectively) (Table 1). These data show that fat mass loss was the major contributor to body mass reduction, showing a positive effectiveness on body composition during 6 and 12 months post-RYGB surgery.

Concerning physical activity changes, in our study, the percentage of time spent in MVPA increased from preoperatively to 6 months postoperatively; however, this change was not evident at 12 months after surgery. Furthermore, no significant changes were observed from preoperatively to 6 and 12 months postoperatively for the following variables: time spent in sedentary activity, time spent in light activity, MVPA in bouts of ≥10 min (per day or week), and in sedentary activity in bouts of ≥30 min (per day) (Table 2).

An important aspect that needs to be highlighted is the MVPA recommendation (≥150 min/week) for developing and maintaining physical fitness and health [3-6]. In this study, the percentage of subjects achieving ≥150 min/week of MVPA in bouts of ≥10 min was 5.9% (two subjects) in the preoperative period. The current results are consistent with those of Bond et al. [17] and King et al. [18], who reported percentages of 4.5% and 3.4% among American women with obesity in the waiting list for bariatric surgery. However, the current study data are lower than those of other studies in European women with obesity that report percentages of 18% [19] and 14.2% [20] in the preoperative period. The differences among studies may be due to distinct environmental and cultural characteristics among countries and regions.

Nevertheless, these related studies [18-20] showed no significant changes in accumulated MVPA (in bouts of ≥10 min) per week in the postoperative period, indicating that most bariatric patients remain physically inactive after the surgery. Indeed, the current results showed that only 11.8% (four subjects) and 14.7% (five subjects) met the MVPA recommendations at 6 and 12 months after surgery, respectively.

Moreover, in our study, half of the subjects did not perform any single MVPA in bouts of ≥10 min in the preoperative period (52.9%), with no substantial changes at 6 months (41.2%) and 12 months (47.1%) postoperatively. These data are comparable to the results of other studies [17, 21] that report that most bariatric patients did not accumulate any MVPA in continuous bouts of ≥10 min.

Concerning sedentary behavior, there are no specific recommendations and threshold values in the literature. In this study, the female bariatric patients spent a higher proportion of time in sedentary activities before and after surgery (median values ~77%), and no significant changes were observed in sedentary activities in bouts of ≥30 min. Our results are in line with those of other studies that indicate that bariatric patients spent a major proportion of daytime hours in sedentary activities (>70%), with no significant change after surgery [19, 22, 23].

Therefore, the considerable body mass loss observed during the short-term periods (6 and 12 months) after bariatric surgery is not a determining factor for increase in MVPA in bouts of ≥10 min and decrease in sedentary behavior. Thus, behavioral interventions to increase the physical activity level should be considered. In this context, recent randomized controlled trial studies indicated that face-to-face physical activity counseling was an effective method for increasing daily bouts of MVPA among candidates for bariatric surgery [24, 25], and these changes are maintained at 6 months after surgery [25].

Some studies [9, 26, 27] indicated a positive association between MVPA assessed by using self-report physical activity questionnaires and body mass loss after bariatric surgery. On the other hand, in bariatric patients, these data cannot be considered conclusive once self-report physical activity questionnaires were not in agreement with accelerometer data [11, 28]. The first evidence to show an interaction between physical activity assessed by using an accelerometer and body mass loss after bariatric surgery was provided by Josbeno et al. [29]. In their study, the authors investigated subjects who had undergone RYGB surgery, at different times after the surgery (2, 3, 4, and 5 years). Their results indicated that MVPA was related ($r = 0.44$)

to the %EWL, and subjects that accumulated >150 min/week of MVPA had greater %EWL than physically inactive subjects [29].

In the current study, regression analysis demonstrated that the percentage of time spent in sedentary activity and MVPA was associated with fat-free mass loss at 6 months after surgery. In addition, the percentage of time spent in sedentary activity, light activity, and sedentary activity in bouts of ≥30 min was associated with fat-free mass loss at 12 months after surgery. No significant values were observed when body mass loss or body fat mass loss was used as a dependent variable (Tables 3 and 4).

These findings suggest that replacing the time spent on sedentary activities (<1.5 METs) with MVPA (>3.0 METs) and light physical activities (1.5–2.99 METs) in the postoperative period may be a strategy to induce positive changes in body composition for female bariatric patients, and this result warrants further investigation.

The major strength of this study lies in the facts that the physical activity level was assessed by using a triaxial accelerometer, the patients underwent the same surgical procedure (RYGB surgery, performed by the same medical staff), and the patients received the same counseling about nutrition and physical activity before and after surgery from the same interdisciplinary team. On the other hand, some limitations of this study need to be addressed. First, a small sample size was investigated. Second, body composition was estimated by using a double-indirect method (bioelectrical impedance analysis). Although the multifrequency bioimpedance technique is a valid method for assessing body composition [30], it is not as accurate as more sophisticated methods such as dual-energy x-ray absorptiometry.

In conclusion, the overall MVPA increased at 6 months post-RYGB surgery; however, this change was not maintained at 12 months. Despite the considerable body mass loss after surgery, most of the subjects were classified as being physically inactive and did not change their sedentary behavior. These findings indicate that female bariatric patients should be encouraged to increase their physical activity level post-RYGB surgery.

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Capítulo 2.

PREDICTIVE EQUATIONS AND METABOLIC EQUIVALENT (MET) AMONG FEMALE BARIATRIC SURGICAL CANDIDATES: ONE SIZE DOES NOT FIT ALL

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ABSTRACT

One metabolic equivalent (1MET) is expressed in standard values of 3.5 $ml \cdot kg^{-1} \cdot min^{-1}$ or 1 $kcal \cdot kg^{-1} \cdot h^{-1}$. Recent studies have suggested the correction of the 1MET standard value by the Harris–Benedict equation to provide more accurate values. On the other hand, controversies also exist between predictive equations to estimate resting metabolic rate (RMR), particularly in morbidly obese individuals. This study aimed to measure resting oxygen uptake (VO_2) and determined RMR by indirect calorimetry, and the results of women on the waiting list for bariatric surgery were compared using six predictive equations. Forty morbidly obese women from Brazil participated in this study. The predictive equations used to estimate RMR were as follows: Mifflin–St Jeor (MSJ), Female Brazilian Population (FBP), Henry & Rees (HR), Harris–Benedict (HB), Schofield (S), and World Health Organization (WHO). The resting VO_2 mean value was 2.27 ± 0.24 $ml \cdot kg^{-1} \cdot min^{-1}$, and the mean RMR was 0.66 ± 0.07 $kcal \cdot kg^{-1} \cdot h^{-1}$. The measured resting VO_2 and RMR were 35.14 ± 7.10 and 33.62 ± 7.46%, respectively, lower than the 1MET standard value (3.5 $ml \cdot kg^{-1} \cdot min^{-1}$ and 1 $kcal \cdot kg^{-1} \cdot h^{-1}$). The MSJ and FBP equations presented a higher index of accuracy predictions at the individual level (within ± 10% measured) to estimate resting VO_2 and RMR ($kcal \cdot kg^{-1} \cdot h^{-1}$). In conclusion, the 1MET standard value overestimates the measured resting VO_2 and RMR values and is not applicable to women bariatric surgical candidates. The predictive equations of MSJ and FPB were the most accurate for the estimation of resting VO_2 and RMR.

Keywords: morbid obesity, energy expenditure, indirect calorimetry, resting metabolic rate

INTRODUCTION

The determination of energy expenditure is an important variable for nutrition sciences, as the control of energy balance (intake and expenditure) is crucial in the prevention and treatment of obesity. In this context, indirect calorimetry is a widely used method to estimate energy metabolism. From the analysis of expired gases, it is possible to determine energy expenditure at rest and during physical activities [1].

However, the use of this sophisticated equipment is restricted, due to the high cost and size, and requires specialized professionals to manipulate it. On the other hand, in clinical practice, resting metabolic rate (RMR) and physical activities energy expenditure is commonly estimated from predictive equations and self-reported questionnaires, respectively.

With respect to physical activities, the energy expenditure estimation is based on the metabolic equivalent (MET) method, which represents the number of times that oxygen uptake (VO_2) is increased in comparison to the rest values [2-4]. In this context, 1MET represents the average rate of VO_2 at rest, which is expressed by the standard value of 3.5 $ml \cdot kg^{-1} \cdot min^{-1}$ and is approximately equal to 1 $kcal \cdot kg^{-1} \cdot h^{-1}$ [3]. Although it is commonly accepted and applied in adults, the exact origin of the standard resting VO_2 value is unknown. It is speculated that the 1MET value was determined from the VO_2 measurement of a healthy man (40 years old and body mass approximately 70 kg), sitting at rest [5].

In contrast, several studies demonstrated significant lower resting VO_2 values in different populations [6-11], raising questions about the use of a universal value for all adults. A review by McMurray et al. [12] indicates that the measurement of RMR is highly variable, and that it typically has a lower value (0.86 $kcal \cdot kg^{-1} \cdot h^{-1}$) than the standard 1MET value (1.00 $kcal \cdot kg^{-1} \cdot h^{-1}$). Furthermore, the authors reported that RMR is higher in men than in women, decrease with increasing age, and is lower in obese subjects (BMI > 30 kg/m^2) than eutrophic subjects [12]. Thus, using the 1MET standard value may underestimate the energy expenditure calculated based on this methodology, particularly in morbidly obese women.

Considering more accurate estimates, several studies [6, 11] have suggested a correction to the 1MET value based on the Harris–Benedict (HB) equation [correct 1MET = 3.5 ÷ predicted value by HB equation (ml·kg^{-1}·min^{-1})] to provide a more individualized and accurate method to estimate energy expenditure. However, several of the predictive equations presented in the literature to estimate RMR give divergent results, and there is a lack of consensus regarding the identity of the most accurate equation [13-15], particularly for obese individuals [14]. It has been suggested that the predictive equation used to estimate RMR should be selected according to the population characteristics.

Currently, the worldwide increase in obesity is characterized as epidemic, is associated with several comorbidities (e.g., hypertension, dyslipidemia, insulin resistance, heart disease, and some cancers), and is thus considered to be a public health problem [16, 17]. The variables sleeping metabolic rate, RMR, thermic effect of food, physical activity and recovery from physical activity must be considered to determine the total daily energy expenditure of an individual [18]. The accuracy in the estimation of these metabolic variables can aid the planning of nutrition interventions and physical training programs for body mass loss in morbidly obese subjects.

Therefore, in this study, we aimed to measure resting VO_2 and determine RMR by indirect calorimetry and then compare this with the results of six predictive equations using women on the waiting list for bariatric surgery as subjects. We hypothesized that the 1MET standard value (3.5 ml·kg^{-1}·min^{-1} and 1 kcal·kg^{-1}·h^{-1})

overestimates the measured resting VO_2 and RMR for morbidly obese women. In addition, although it is known that predictive equations can present divergent results, we considered that some could provide a better estimate of resting VO_2 and RMR than the 1MET standard value.

METHODS

Subjects

In total, 40 Brazilian women volunteered to participate in this study. The eligible criteria for participation were: (a) to be in post-menarche and pre-menopause period; (b) to be aged between 20 and 40 years; and (c) to have a body mass index (BMI) ≥ 40 kg/m^2. The non-inclusion criteria were as follows: (a) having thyroid disease; (b) having diabetes mellitus; and (c) to be using medication that could alter cardiovascular function and/or resting metabolic rate. All volunteers were candidates for bariatric surgical and signed an informed consent form after being instructed about research procedures. This study was approved by the local Research Ethics Committee (protocol number: 74/13) and was in accordance with the Helsinki Declaration.

Experimental Procedures

This cross-sectional study was designed to compare direct measurements (indirect calorimetry) with estimated values from predictive equations for female candidates for bariatric surgery. To this end, each subject visited the laboratory twice. In the first visit, the subjects were familiarized with the equipment and received verbal instructions about the experimental procedures. In the second visit, the evaluation was conducted. Resting parameters were measured by indirect calorimetry to determine oxygen uptake (VO_2) and carbon dioxide production (VCO_2).

The body composition was assessed by multifrequency bioelectrical impedance. The tests were conducted in a quiet, dimly lit room, with a relative humidity of 40–60% and a temperature of 23–25°C. The estimation of RMR (kcal/day) was assessed by the predictive equations of Harris and Benedict (HB) [19], FAO/WHO/UNU (WHO) [20], Schofield (S) [21], Miffilin–St Jeor (MSJ) [22], Henry and Rees (HR) [23] and Female Brazilian Population (FBP) [24], as shown in Table 1. In addition, resting VO_2 was estimated using the six predictive equations results, as shown below:

$$Kcal \cdot day^{-1} \text{ (estimate value)} \div 1440 = kcal \cdot min^{-1}$$

$$kcal \cdot min^{-1} \div 5 = L \cdot min^{-1}$$

$$L \cdot min^{-1} \div [\text{body mass (kg)}] \times 1000 = ml \cdot kg^{-1} \cdot min^{-1}$$

The RMR in $kcal \cdot kg^{-1} \cdot h^{-1}$ was also estimated as shown below:

$$Kcal \cdot day^{-1} \text{ (estimate value)} \div 24 = kcal \cdot h^{-1}$$

$$kcal \cdot h^{-1} \div [\text{body mass (kg)}] = kcal \cdot kg^{-1} \cdot h^{-1}$$

Table 1: Predictive equations for resting metabolic rate

References	**Equations**
Harris–Benedict [19]	RMR (kcal·day^{-1}) = 666 + 9.6 × body mass (kg) + 1.8 × height (cm) − 4.7 × age (y)
FAO/WHO/UNU [20] - 18–30 y	RMR (kcal·day^{-1}) = 14.5 × body mass (kg) + 465
FAO/WHO/UNU [20] - 30–60 y	RMR (kcal·day^{-1}) = 8.7 × body mass (kg) + 829
Schofield [21] - 18–30 y	RMR (kcal·day^{-1}) = [0.062 × body mass (kg) + 2.036] × 239
Schofield [21] - 30–60 y	RMR (kcal·day^{-1}) = [0.034 × body mass (kg) + 3.538] × 239
Miffilin–St Jeor [22]	RMR (kcal·day^{-1}) = 9.99 × body mass (kg) + 6.25 × height (cm) − 4.92 × age (y) – 161
Henry & Ree [23]	RMR (kcal·day^{-1}) = [0.048 × body mass (kg) + 2.562] × 239
Female Brazilian Population Rodrigues et al. [24]	RMR (kcal·day^{-1}) = 172.19 + 10.93 × body mass (kg) + 3.10 × height (cm) − 2.55 × age (y)

Legend: RMR: resting metabolic rate

Indirect Calorimetry

The subjects were asked not to perform physical activities and to abstain from nicotine, alcohol, and caffeine for a period of 24 h prior to the indirect calorimetry measurement. In addition, the subjects were instructed to travel to the laboratory by car after 8 h of sleep and fasting [10]. To determine RMR, we used an indirect calorimeter CCM Express (MedGraphics, St. Paul, USA). Initially, the flow was calibrated by a 3-liter syringe, according to the manufacturer's instructions. The equipment was calibrated for each evaluation using standard known gas concentrations: reference (21% O_2 and 79% N_2) and calibration (12% O_2, 5.09% CO_2, and 82.91% N_2).

In brief, the subjects were acclimated to the assessment apparatus during 10 min and after the exhaled gases were measured until an apparent VO_2 steady state had been achieved (change <10%) after 30 min of measurement. For analysis, we used the average values (VO_2 and VCO_2) during a 3-5 min steady-state period [25]. The RMR was calculated according to the formula [26]:

$$RMR = [(3.9 \times O_2) + (1.1 \times VCO_2)] \times 1440$$

During the evaluation, the subjects remained in the supine position, awake, and emotionally undisturbed. They were instructed not to talk, perform body movements, and avoid sneezing and coughing. The measurements were performed between 08:00 and 11:00 AM.

Body Composition

Body composition was determined by bioimpedance. The measurements were conducted in an InBody 230 analyzer (Biospace, Seoul, Korea). The equipment uses multifrequency impedance with an eight-point tactile electrode. In brief, the subjects were instructed to stand on the equipment and properly position their feet in the electrodes to determine body mass. After the initial measurement, the subjects positioned their hands in tactile electrodes for impedance measurements.

The subjects were instructed to: a) fast overnight; b) not drink water during the 3 h before the test; c) not use diuretics medicine during the 24 h before the test; d) not perform physical exercises during the 24 h before the test; e) not take a bath in the morning before the test; f) go to the bathroom (to urinate or defecate) at least 30 min before the test; and g) not wear metal accessories (e.g., earrings and watches) [27]. During evaluation, the subjects wore light clothing without shoes or socks.

Statistical Analysis

Comparisons between the indirect calorimetry and predictive equations were performed by applying a Kruskal–Wallis test followed by Dunn’s post hoc test. The prediction was considered to be accurate when the predicted value from the equation was between 90 and 110% of the value measured by indirect calorimetry; a predicted value below 90% was considered to be an underestimate; and a predicted value above 110% was considered to be an over estimate. The percentage of subjects for whom an RMR value was obtained from predicted equations that was within 10% of the measured value was used as an index of accuracy on an individual level. The mean difference and percentage between predicted equations and the measured values (bias) was considered as an index of accuracy on a group level. The significance level adopted was $p < 0.05$. The data are expressed as mean ± standard deviation (SD).

Results

Table 2 shows values for subject's characteristics, body composition, resting VO_2, VCO_2, and RMR. All subjects were classified as morbidly obese, presenting a BMI >40 kg/m^2 and a body fat percentage >50%. For resting VO_2, values were in the range of 1.89–2.92 ml·kg^{-1}·min^{-1} among subjects, with a mean value of 2.27 ± 0.24 ml·kg^{-1}·min^{-1}. For RMR (kcal·kg^{-1}·h^{-1}), values were in the range of 0.55–0.86 kcal·kg^{-1}·h^{-1}, with a mean value of 0.66 ± 0.07 kcal·kg^{-1}·h^{-1}. The measured resting VO_2 and RMR values were 35.14 ± 7.10 and 33.62 ± 7.47% less than the 1MET standard value (3.5 ml·kg^{-1}·min^{-1} and 1.0 kcal·kg^{-1}·h^{-1}), respectively.

Table 2. Subject's characteristics, body composition, and ventilatory variables

Variables	Mean	SD	Minimum	Median	Maximum
Age (y)	31.47	5.49	22.00	30.5	40.00
Body Mass (kg)	111.81	11.51	93.00	110.90	139.70
Height (cm)	159.91	4.98	152.00	171.00	160.35
BMI (kg·m$^{2-1}$)	43.89	2.81	40.00	43.55	50.00
Fat Mass (kg)	58.37	6.57	43.40	57.85	74.50
Body Fat (%)	52.19	1.98	46.80	52.25	55.60
Fat-free Mass (kg)	53.37	5.23	45.90	52.40	67.30
Skeletal Muscle Mass (kg)	30.01	3.17	25.3	29.40	38.20
Body Water (kg)	39.22	3.84	33.70	38.45	49.50
VO_2 (l·min^{-1})	0.25	0.03	0.21	0.24	0.35
VCO_2 (l·min^{-1})	0.22	0.03	0.18	0.21	0.32
VO_2 (ml·kg^{-1}·min^{-1})	2.27	0.24	1.89	2.23	2.92
RMR (kcal·kg^{-1}·h^{-1})	0.66	0.07	0.55	0.65	0.86

BMI: body mass index; VO_2: oxygen consumption; VCO_2: carbon dioxide production; RMR: resting metabolic rate.

Table 3 shows the values in kcal·day^{-1} for RMR measured by indirect calorimetry and predictive equations. The MSJ (mean difference 21.57 kcal·day^{-1}) and FBP (mean difference 31.53 kcal·day^{-1}) equations estimated the closest values for RMR at the group level. In addition, the index of accuracy predictions on an individual level was higher for the MSJ (60%) and FBP (60%) equations, while the WHO equation (42.5%) obtained the lowest index of accuracy prediction.

Table 3. Resting metabolic rate by indirect calorimetry and predictive equations.

	RMR (kcal·day^{-1})	Mean Difference	Mean Difference (%)	Accuracy Predictions (%)	Over Predictions (%)	Under Predictions (%)
IC	1780.66 ± 237.55	----	---	---	---	---
MSJ	1802.23 ± 141.29	21.57 ± 200.33	2.28 ± 10.59	60.00	25.00	15.00
FBP	1812.19 ± 137.16	31.53 ± 198.73	2.86 ± 10.56	60.00	25.00	15.00
HR	1876.93 ± 128.87^{a,b,c}	96.27 ± 217.23	6.68 ± 11.65	57.50	32.50	10.00
HB	1874.69 ± 119.39^{a,b,c}	94.03 ± 199.63	6.49 ± 10.89	52.50	37.50	10.00
S	1928.45 ± 220.81^{a,b}	147.78 ± 255.12	9.38 ± 13.87	50.00	42.50	7.50
WHO	1943.76 ± 217.90^{a,b,c}	162.81 ± 225.39	10.07 ± 12.29	42.50	50.00	7.50

RMR = resting metabolic rate; IC = indirect calorimetry; MSJ = Mifflin–St Jeor; FBP = Female Brazilian Population; HR = Henry and Ree; HB = Harris and Benedict; S = Schofield; and WHO = World Health Organization. [a]Significant difference ($p < 0.001$) compared to IC. [b]Significant difference ($p < 0.001$) compared to MSJ; [c]Significant difference ($p < 0.001$) compared to FBP.

Table 4 shows the measured resting VO_2 and that estimated by the predictive equations. No differences were observed between the measured and estimated resting VO_2 ($ml \cdot kg^{-1} \cdot min^{-1}$) for the MSJ and FBP equations. The index of accuracy predictions on an individual level were higher for the FBP (72.5%) and MSJ (67.5%) equations.

Table 5 shows the measured RMR in $kcal \cdot kg^{-1} \cdot h^{-1}$, and the value estimated by the predictive equations. No differences were observed between the measured and estimated RMR for the MSJ and FBP equations. The index of accuracy predictions on an individual level were also higher when using the MSJ (60%) and FBP (57.5%) equations. The WHO equations provided a lower index of accuracy predictions for resting VO_2 and RMR.

Table 4. Resting oxygen uptake by indirect calorimetry and predictive equations.

	Resting VO_2 (mL/kg/min)	Mean Difference	Difference (%)	Accuracy Predictions (%)	Over Predictions (%)	Under Predictions (%)
IC	2.21 ± 0.29	---	---			
MSJ	2.24 ± 0.06	−0.02 ± 0.24	−0.08 ± 10.09	67.50	12.50	20.00
FBP	2.25 ± 0.06	−0.01 ± 0.24	0.43 ± 10.04	72.50	12.50	15.00
HR	2.33 ± 0.10[a,b,c]	0.07 ± 0.26	4.21 ± 11.11	52.50	32.50	15.00
HB	2.33 ± 0.09[a,b,c]	0.06 ± 0.24	3.98 ± 10.33	55.00	30.00	15.00
S	2.42 ± 0.25[a,b]	0.13 ± 0.31	6.81 ± 13.39	52.50	40.00	12.50
WHO	2.46 ± 0.21[a,b,c]	0.15 ± 0.27	7.52 ± 11.90	47.50	40.00	7.50

IC = indirect calorimetry; MSJ = Mifflin–St Jeor; FBP = Female Brazilian Population; HR = Henry and Ree; HB = Harris and Benedict; S = Schofield; and WHO = World Health Organization. [a]Significant difference ($p = 0.001$) compared to IC. [b]Significant difference ($p = 0.001$) compared to MSJ; c Significant difference ($p = 0.001$) compared to FBP.

Table 5. Resting metabolic rate (kcal/kg/h) by indirect calorimetry and predictive equations.

	RMR (kcal/kg/h)	Mean Difference	Difference (%)	Accuracy Predictions (%)	Over Predictions (%)	Under Predictions (%)
IC	0.66 ± 0.07	---	---			
MSJ	0.67 ± 0.02	−0.02 ± 0.24	2.48 ± 10.80	60.00	25.00	15.00
FBP	0.68 ± 0.02	−0.01 ± 0.24	3.13 ± 10.79	57.50	27.50	15.00
HR	0.70 ± 0.03[a,b,c]	0.07 ± 0.26	6.92 ± 11.80	52.50	37.50	10.00
HB	0.70 ± 0.03[a,b,c]	0.06 ± 0.24	6.76 ± 11.02	52.50	37.50	10.00
S	0.72 ± 0.08[a,b]	0.13 ± 0.31	9.66 ± 14.31	47.50	45.00	7.50
WHO	0.73 ± 0.07[a,b,c]	0.15 ± 0.27	10.28 ± 12.75	40.00	52.50	7.50

RMR = resting metabolic rate; IC = indirect calorimetry; MSJ = Mifflin–St Jeor; FBP = Female Brazilian Population; HR = Henry and Ree; HB = Harris and Benedict; S = Schofield; and WHO = World Health Organization. [a]Significant difference ($p = 0.001$) compared to IC. [b]Significant difference ($p = 0.001$) compared to MSJ; c Significant difference ($p = 0.001$) compared to FBP.

DISCUSSION

The accurate estimation of RMR and physical activity energy expenditure is important in the determination of total energy expenditure and to guide the clinical practice when treating morbidly obese patients. In this study, we measured the resting VO_2 and RMR of female candidates for bariatric surgery by indirect calorimetry and compared the measured values with those obtained from six predictive equations.

The main findings were: a) the measured resting VO_2 and RMR values were lower than the 1MET standard value; b) the MSJ and BFP equations presented higher indexes of accuracy to estimate RMR and resting VO_2 values; and c) the WHO equation presented the lowest index of accuracy in the estimation of RMR and resting VO_2 values. These results confirm our initial hypothesis that the 1MET standard value overestimates the measured resting VO_2 from morbidly obese women and provide further evidence that the MSJ and BFP equations more accurately correct the 1MET value than the HB and other predictive equations.

The estimated energy expenditure from physical activities is commonly based on the MET method. The Compendium of Physical Activities was created to standardize MET units from different physical activities, and, when not measured, the standard values of 3.5 $ml \cdot kg^{-1} \cdot min^{-1}$ or 1 $kcal \cdot kg^{-1} \cdot h^{-1}$ are adopted as references (1MET) [2-4]. Our data shows that resting the VO_2 in female candidates for bariatric surgery was smaller than the 1MET standard value, with a mean value of 2.27 ± 0.24 $ml \cdot kg^{-1} \cdot min^{-1}$ (Table 1). In agreement with the current results, Wilms et al. [28] reported that the measured resting VO_2 was 2.47 ± 0.33 $ml \cdot kg^{-1} \cdot min^{-1}$ for overweight to morbidly obese women. In addition, in Wilms et al.'s study, the resting VO_2 values progressively decreased with increasing BMI [28], which reinforces the notion that the level of obesity has an influence on the resting parameters.

Obesity can be defined as the excessive accumulation of adipose mass, which is considered a tissue metabolically less active than other organs and tissues [such as brain, heart, liver, kidney skeletal muscle, and residual mass ($kcal \cdot kg^{-1} \cdot h^{-1}$)] in humans [29]. A multiple regression analysis conducted by Byrne et al. [6] showed that fat mass was the strongest predictor (59%) of the variability in resting VO_2 values in a large cohort of adults who were heterogeneous in age (18–74 y) and body composition (2.7–50.4 % body fat). These data show that an excess of body fat mass is associated with a lower resting VO_2 when the values are expressed relative to the total body mass ($ml \cdot kg^{-1} \cdot min^{-1}$).

An overestimation of resting VO_2 and RMR per total body mass, as indicated in the current study (33–35%), may lead to errors in the estimation of energy expenditure and compromise dietary interventions to control body mass loss. It is important to highlight that preoperative body mass loss is recommended to bariatric patients, as this can reduce operative time, hospital stay, and the morbidity rate [30]. Thus, a precise estimation of energy expenditure is necessary to guide behavioral interventions for patients on the waiting list for bariatric surgery.

A number of studies also indicate lower resting VO_2 values (ranging from 2.5 to 3.3 $ml \cdot kg^{-1} \cdot min^{-1}$) than the standard 1MET value in apparently healthy adults [6, 10, 11], the elderly [7, 9], and cardiac patients [8], and the findings of the current study show that this also applies to morbidly obese women. These data indicate that one standard value should not be used to characterize women on the waiting list for bariatric surgery. To estimate the energy expenditure from physical activities using the MET method among female bariatric patients, it is better to consider the mean standard value of 0.66 $kcal \cdot kg^{-1} \cdot h^{-1}$ rather than the standard value of 1.0 $kcal \cdot kg^{-1} \cdot h^{-1}$, as reported in the current study. On the other hand, our data suggest that predictive equations would be the most appropriate strategy to estimate the resting VO_2 and RMR relative to the total body mass.

The RMR is considered to be the major contributor (non-athletic subjects) of total daily energy expenditure, and predictive equations are the most used method in clinical practice. In our study, the MSJ and FBP equations were found to be the best at predicting RMR at group level compared with the results from indirect calorimetry (Table 3). In addition, the indexes of accuracy predictions on the individual level also indicate that the MSJ and FPB equations were the most accurate. These results are in agreement with Frankenfield et al. [14], who reported that the MSJ was the best equation to estimate RMR (within ± 10% measured) in obese adults. Furthermore, a systematic review study confirmed that the MSJ equation can be used to estimate RMR within 10% of the value measured via indirect calorimetry for healthy obese adults [31].

Studies [6, 11] have indicated positive results by correction of the 1MET value by the HB equation. In this context, Byrney et al. [6] measured energy expenditure during walking on a treadmill (5.6 km/h) and observed that the energy expenditure was 22% higher than that predicted by the MET standard method in overweight subjects. In contrast, the authors observed that the difference was reduced through 1 MET correction [6]. These data indicate that appropriate correction factors can allow a better estimation of energy expenditure from physical activities. In the present study, we expand these findings, showing that the selection of appropriate predictive equations improves the estimation of resting VO_2 and RMR per total body mass (Tables 4 and 5). Our data show that the use of the MSJ and FPB equations allows a better estimation of RMR values for Brazilian women who are on waiting list for bariatric surgery.

In conclusion, the standard 1MET value overestimates the measured resting VO_2 and RMR per total body mass and is not applicable to women bariatric surgical candidates. The predictive equations of MSJ and FBP were the most accurate in estimating the resting VO_2 and RMR values. Therefore, our findings suggest that it is necessary to identify the best predictive equation to correct the 1MET standard value.

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Capítulo 3.

Influence of *ACTN3 R577X* polymorphism in body composition changes after RYGB surgery among obese women: preliminary findings

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ABSTRACT

This study aimed to investigate the relationship between *ACTN3* R577X (rs1815739) polymorphism with body composition changes after Roux-en-Y gastric bypass (RYGB) surgery. Forty obese women participated in this study. The body composition was estimated by multifrequency bioimpedance analysis before surgery and at 6, 12, and 24 months postsurgery. Our results indicate that the percentage changes in body mass and body fat mass were significantly higher for XX than RX/RR genotypes, with no significant difference observed in the fat-free mass. Therefore, bariatric female patients with XX genotype from *ACTN3 R577X* polymorphism experienced more positive body composition changes after RYGB surgery.

Keywords: gene polymorphism, body composition, bariatric surgery.

1. Introduction

At present, bariatric surgery is the most effective treatment for severe obesity, resulting in prolonged long-term body mass loss, remission of obesity-related comorbidities, and decrease in mortality [1]; however, the results of bariatric surgery on body mass loss vary between subjects, and body mass regain is observed in a certain portion of the population [2]. Thus, the predicted factors associated with the treatment failure can suggest better strategies postsurgery.

Some studies estimated that the obesity phenotype is strongly influenced by genetic factors, with a high heritability on individual measures of body mass index (BMI) and body fat mass [3,4]. Therefore, the variability in body composition changes postbariatric surgery may also be associated in parts by genetic traits. In this context, some studies indicate that certain single-nucleotide polymorphisms (SNPs) are related to the bariatric surgery outcomes [5,6]. Herein, the present study will argue that *ACTN3 R577X* polymorphism can influence the magnitude of body composition changes in obese women postbariatric surgery.

An SNP (rs1815739) in exon 16 of the *ACTN3* gene (C→T transition at position 1747) results in a premature stop codon (replacement of arginine [R] with a premature stop codon [X] at amino acid position 577) and complete deficiency of the alpha-actin-3 protein in XX genotype subjects, which is present in approximately 16% of the population worldwide [7,8]. The alpha-actin-3 is a structural protein present in the sarcomere of fast-twitch muscle fibers. Despite no association of alpha-actinin-3 deficiency with any disease phenotype, some studies suggested lower muscle strength/power capacity and higher endurance performance in athletes [9].

Recent evidence indicates that the alpha-actinin-3 has a role in muscle cells metabolism, and the protein deficiency results in a shift from anaerobic phenotype toward oxidative phenotype [8]. Thus, due to an increase in the aerobic metabolic efficiency, we hypothesized that XX genotype subjects (protein deficiency) could have higher body composition changes postbariatric surgery. The purpose of this study was to investigate the relationship between *ACTN3* R577X (rs1815739) polymorphism and body composition changes after Roux-en-Y gastric bypass (RYGB) surgery.

2. Material and methods

2.1 Subjects

Forty obese women (aged 22–40 years; BMI 40–63 kg/m^2) undergoing RYGB surgery volunteered to participate in this study. The inclusion criteria for participation in this study included: (a) being female; (b) aged between 20 and 40 years; (c) BMI higher than 40 kg/m^2; and (d) registered on the waiting line for bariatric surgery. The exclusion criteria were: (a) having genetic syndromes associated with obesity; (b) hypothyroidism; and (c) infection with human immunodeficiency virus (HIV).

All subjects signed a free-and-informed consent form after being briefed on the research procedures. This study was submitted and approved by the local Research Ethics Committee (protocol 74/13).

2.2 Study design

A prospective study was designed to examine the association of *ACTN3 R577X* polymorphism with pre- to postoperative (%) body composition changes after RYGB surgery in a sample of Brazilian women.

Blood samples (~4 mL) were collected into vacutainer tubes containing EDTA in the preoperatory period for genotype analysis. Bioimpedance analyzes were assessed before surgery and at 6, 12, and 24 months after RYGB surgery. The same medical staff performed the RYGB surgeries and the patients were counseled regarding nutrition and physical activities by the same interdisciplinary team (usual care of bariatric clinic).

2.3 Genotyping

Genomic DNA was isolated from whole blood samples using the QIAamp DNA Blood Mini Kit (Quiagen). Genotyping was conducted using TaqMan universal PCR master mix (Applied Biosystems, Foster City, CA, USA) and TaqMan SNP Genotyping Assay (ID: C__590093_1_). The real-time polymerase chain reaction (RT-PCR) was processed in ABI 7500 fast equipment (Applied Biosystems, Foster City, CA, USA). All genotyping was analyzed in duplicate and 10% of the samples were randomly reanalyzed for quality control by an independent technician.

2.4 Body composition

Body composition was estimated by a vertical bioimpedance analyzer (InBody 230, BioSpace, Seoul, Korea), that uses multifrequency bioelectrical impedance on eight tactile-points. All the analyses were tested at a fixed time in the morning, in a temperature-controlled room (24°C). Standard instructions were provided to subjects prior to the assessments [10].

2.5 Statistical analyzes

The agreement of genotype frequencies with Hardy–Weinberg equilibrium expectations was tested by chi-square test. Independent t-test was used to compare the data (percentage changes) between XX and RX/RR genotypes (recessive model). For nonparametric data, the Mann–Whitney U-test was used. The significance level adopted was $p < 0.05$. Data were expressed as mean ± standard deviation.

3. Results

Thirteen subjects at 24 months postsurgery did not return to the bariatric clinic and, thus, could not be subjected to the bioimpedance analysis. Genotype frequencies were 14 (35%), 15 (37.5%), and 11 (27.5%) for RR, RX, and XX genotypes for *ACTN3 R557X* polymorphism, respectively, at 6 and 12 months postsurgery and 11 (33.33%), 14 (42.42%), and 8 (24.24%) for RR, RX, and XX genotypes, respectively, at 24 months postsurgery. Genotype distribution of *ACTN3 R577X* polymorphism was within the expectations of the Hardy–Weinberg equilibrium ($p > 0.05$).

No significant differences in age (XX = 33.4 ± 4.7 vs. RX/RR = 30.2 ± 5.2 years), body mass (XX = 113.2 ± 19.9 vs. RX/RR = 113.7 ± 10.8 kg), BMI (XX = 44.5 ± 6.7 vs. RX/RR = 44.5 ± 2.7 kg/m^2), body fat mass (XX = 56.3 ± 7.5 vs. RX/RR = 59.7 ± 5.9 kg), and fat-free mass (XX = 52.4 ± 5.9 vs. 53.9 RX/RR = 53.9 ± 5.3 kg) were evident between XX and RX/RR genotype in the preoperatory period.

Table 1 summarizes the body composition changes observed postsurgery according to the XX and RX/RR genotypes of *ACTN3 R577X* polymorphism. Our results indicate that obese women with XX genotype had higher ($p < 0.05$) percentage of changes (pre- to postsurgery) in body mass, and body fat mass than RX/RR genotypes at 6 and 12 months after RYGB surgery.

At 24 months postsurgery, the percentage of changes in body mass were also significantly higher for XX than RX/RR genotypes. Fat mass loss approached near significance value ($p = 0.08$) at 24 months postsurgery between genotypes (XX vs. RX/RR). The changes in fat-free mass did not differ ($p > 0.05$) between XX and RX/RR genotypes during the study period.

Table 1. Body composition changes in XX and RX/RR genotypes

	6 months postsurgery			12 months postsurgery			24 months postsurgery		
Variables	**XX (*n* = 11)**	**RX/RR (*n* = 28)**	***p*-value**	**XX (*n* = 11)**	**RX/RR (*n* = 29)**	***p*-value**	**XX (*n* = 8)**	**RR/RX (*n* = 19)**	***p*-value**
Body mass changes (%)	−32.6 ± 6.6	−26.2 ± 4.2	**0.005#**	−39.5 ± 6.8	−31.1 ± 5.5	**0.000**	−37.6 ± 7.8	−31.1 ± 6.8	**0.030**
Body fat mass changes (%)	−49.1 ± 7.4	−40.5 ± 7.5	**0.002**	−61.5 ± 9.9	−49.5 ± 9.7	**0.001**	−55.4 ± 10.6	−47.8 ± 10.4	0.082
Fat-free mass changes (%)	−11.0 ± 4.1	−10.4 ± 4.8	0.704	−12.3 ± 5.6	−10.8 ± 4.7	0.303#	−12.1 ± 4.9	−12.3 ± 5.7	0.946

#data compared by Mann–Whitney test. Data are expressed as mean ± standard deviation

4. Discussion

This study investigated the influence of *ACTN3 R577X* polymorphism on body compositions changes after RYGB surgery. The main findings were: (a) women with XX genotype presented higher body mass loss at 6, 12, and 24 months postsurgery; (b) XX genotype presented higher body fat mass loss at 6 and 12 months postsurgery; (c) there was no significant difference in body fat-free mass loss at 6, 12, and 24 months between XX and RX/RR genotypes. These preliminary findings confirm our initial hypothesis and provide new evidence that *ACTN3 R577X* polymorphism can modulate the body mass loss and body composition response of obese women subjected to RYGB surgery.

The knowledge of polymorphism genes that may be related to responsiveness during body mass loss process might be essential in identifying subjects at a higher risk of body mass loss failure. In this study, the presurgery body composition parameters were not different between XX and RX/RR genotypes; however, postsurgery, the changes of body composition were more evident to subjects with alpha-actinin-3 deficiency (XX genotypes), suggesting that *ACTN3 R577X* polymorphism influences the responsiveness.

The effect of alpha-actinin-3 deficiency on muscle fiber phenotype has been investigated in animal models. Actn3 knockout mice (model that mimics the human XX genotype) shows higher oxidative/mitochondrial activity in fast-twitch muscles, and enhanced endurance during exercise performance compared to the wild-type mice [11,12]. In addition, other evidence indicates that *ACTN3 R577X* polymorphism may be also associated with the skeletal muscle fiber type composition, with XX genotype subjects exhibiting a higher proportion of slow-twitch muscle fibers compared with RX and RR genotypes. [13].

Investigating molecular mechanisms, Seto et al. [14] observed that the skeletal muscle deficient of alpha-actinin-3 enhance calcineurin signaling pathway in both mice (knockout) and humans (XX genotype); therefore, it should be associated with a shift toward a more oxidative phenotype and in the determination of muscle fiber type.

These changes in skeletal muscle fiber metabolism, raise the possibility that higher oxidative phenotype can modulate responsiveness during body mass loss process. Corroborating with this idea, Tanner et al. [15] reported a strong relationship (*r* = 72) between the percentage of slow-twitch muscle fibers (type I) and the percentage of excess weight loss, at 12 months after gastric bypass surgery.

Skeletal muscles represent 35–45% of the total body mass and play a key role in whole-body energy metabolism. Thus, skeletal muscle fiber type proportion (oxidative or glycolytic phenotype) is relevant, and genetic traits have substantial influence in muscle fiber composition [16]. Our data suggested that patients with R allele carriers should be efficiently monitored in the postoperatory period.

Limitations of our study included a small sample size and a relatively high rate of loss at 24 months follow-up. In addition, skeletal muscle biopsy analysis could provide insight on the oxidative capacity and fiber type composition among the genotypes. Furthermore, studies with higher number of subjects are required to confirm these preliminary findings on *ACTN3 R577X* polymorphism.

5. Conclusion

In conclusion, bariatric female patients with XX genotype from *ACTN3 R577X* polymorphism experienced a higher percentage of changes in body mass and body fat mass during the first 2 years after RYGB surgery.

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4. CONSIDERAÇÕES FINAIS

A presente tese de doutorado apresenta três linhas de investigações, com o foco principal investigar a relação da obesidade mórbida e cirurgia bariátrica com a variáveis: atividades físicas, gasto energético em repouso e variabilidade genética.

<u>Primeiro Estudo:</u>

Considerada como a quarta principal causa de mortalidade global [(37)], estima-se que a inatividade física causa entre 6-10% das principais doenças crônicas não transmissíveis (doença cardíaca coronariana [7%], diabetes do tipo 2 [10%], câncer de mama e cólon [10%]), representando um fator de risco semelhante ao tabagismo e obesidade [(38)]. Em adição, estudos recentes mostram que o comportamento sedentário é um fator de risco para doenças cardio-metabólicas, independente do consumo de álcool, tabagismo e da inatividade física [(39)].

Considerando que as alterações hormonais, fisiológicas e entre outras, promovida cirurgia bariátrica, favorece a mudança do estilo de vida. A abordagem da equipe multidisciplinar em relação as atividades físicas ao paciente bariátrico é fundamental não só para evitar o reganho de massa corporal ao longo do tempo pós-cirurgia, mas para prevenir o desenvolvimento de doenças crônicas associadas a inatividade física e ao comportamento sedentário. Neste contexto, a principal questão do primeiro estudo foi verificar se a redução do excesso de massa corporal pela cirurgia bariátrica e o tratamento padrão pós-operatório, favorece na redução da inatividade física e comportamento sedentário.

Nossos resultados indicaram que o percentual de tempo gasto em atividades físicas com intensidade moderada-vigorosa (AFMV) aumentou seis meses após a cirurgia DGYR, mas esta alteração não foi mantida no período de doze meses. Apesar da considerável redução da massa corporal, a cirurgia bariátrica não influenciou as alterações sobre comportamento sedentário, sendo que a maioria dos pacientes foram classificados como fisicamente inativos antes e após-cirurgia. Em adição, foi verificado que o percentual de tempo gasto em atividades sedentárias determinaram negativamente as alterações sobre o conteúdo de massa magra livre de gordura. Estes dados reforçam a importância de orientar os pacientes bariátricos sobre o aumento do nível atividade física após a cirurgia.

Segundo Estudo:

A estimativa do gasto energético em repouso e atividades físicas é fundamental na elaboração de dietas e no controle do balanço energético (gasto vs. ingestão) para os pacientes que estão na lista de espera para a cirurgia bariátrica. Nesse mesmo sentido, a redução da massa corporal (> 5%) no período pré-operatório é recomendada para reduzir o risco cirúrgico e o tempo de internação (recuperação) [40]. O equivalente metabólico (MET) é uma metodologia simples para a determinação do gasto em atividades físicas na prática clínica. No entanto, estudos recentes sugerem que a correção do valor padrão de 1 MET por meio da equação de Harris-Benedict (3,5 [mL/kg/min] ÷ taxa metabólica de repouso estimada [mL/kg/min]) fornece uma estimativa mais individualizada e precisa do gasto energético mensurado diretamente [41, 42].

Por outro lado, várias equações preditivas são apresentadas na literatura para estimar a taxa metabólica de repouso, com resultados divergentes entre os estudos, fator que é dependente da característica da população avaliada [43]. Neste contexto, a principal questão do segundo estudo foi verificar entre diferentes equações preditivas, qual resultaria numa melhor estimativa da taxa metabólica de repouso (mL/kg/min), e indicar a equação mais adequada para a correção do valor padrão de 1MET em mulheres obesas.

Os resultados indicaram que o valor padrão de 1MET superestimou os valores de consumo de oxigênio e a taxa metabólica de repouso em mulheres obesas na fila de espera para a cirurgia bariátrica. Na comparação dos dados obtidos por calorimetria indireta com seis fórmulas preditivas, nosso estudo aponta duas fórmulas com maior capacidade de predição, i.e., *MIfflin-St Jeor* e *Female Brazilian Population*. Desta forma, a correção do valores de 1MET pela as fórmulas preditivas indicadas em nosso estudo, favorece uma melhor estimativa do gasto energético das atividades físicas realizadas por mulheres obesas.

<u>Terceiro Estudo:</u>

A responsividade frente a determinado tratamento vem sendo investigado por estudo estudos de associação genética. Por se tratar de um polimorfismo que resulta em *stop* códon prematuro, o polimorfismo *ACTN3* R577X resulta na ausência da proteína alfa-actinina-3 em indivíduos como o genótipo XX (44). Evidências indicam que a deficiência da proteína alfa-actinina-3 resulta na alteração do fenótipo muscular (anaeróbio para oxidativo) (44). Neste contexto, devido ao aumento da eficiência aeróbia muscular, hipotetizamos que pacientes bariátricos do genótipo XX, poderiam ter maiores alterações do conteúdo de gordura corporal após a cirurgia bariátrica.

No terceiro estudo, verificamos que o polimorfismo (rs1815739) do gene *ACTN3 R577X* esteve associado com as alterações na composição corporal nos períodos de seis, doze e vinte e quatro meses após cirurgia DGYR em mulheres obesas. Em específico, pacientes com o genótipo XX apresentam maiores reduções de massa corporal e massa de gordura corporal.

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