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Original Article

INSUFFICIENT LOSS OF WEIGHT AND/OR ABSENCE OF DM2 REMISSION AFTER ROUX-EN-Y GASTRIC BYPASS: FACTORS THAT MAY INFLUENCE THE UNSATISFACTORY RESULTS

Perda insuficiente de peso e ou ausência de remissão da diabete melito tipo 2 após a derivação gástrica em Y-de-Roux: fatores que podem influenciar os resultados insatisfatórios

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Study conducted at the Department of Obesity and Related Diseases, University Hospital, Federal University of Rio Grande do Norte, Natal, Brazil.

ABSTRACT - ***Background*** - Roux-en-Y gastric by-pass is considered one of the most effective treatments for maintaining long-term weight loss. However, it is associated to failures manifested by the inability to maintain weight loss, weight gain or poor glycemic control. ***Objective*** - Study the possible factors that influence weight loss failure and/or DM2 remission. ***Methods*** - Case-control study of 159 patients submitted to gastric by-pass two or more years postoperatively. Twenty-four individuals with unsatisfactory weight loss and/or DM2 remission were selected as cases and 24 with satisfactory weight loss and/or absence of DM2 remission as controls, matched for age and postoperative time. ***Results*** - Of the 24 cases and controls evaluated, the percentage weight gain was 19.32% and 8.68%, percentage DM2 remission 26.6% and 87.5% and percentage DM2 recurrence 6.6% and 0.0%, respectively. Cases and controls exhibited mean maximum preoperative BMI of 53.50±12.24 kg/m2 and 48.77±5.19 kg/m2, respectively. These values were statistically significant in terms of poor weight management or failed surgery. ***Conclusion*** - Patients with elevated initial maximum BMI (≥ 50kg/m2) displayed higher weight loss failure rates. Food intolerance and socioeconomic differences are considered factors in weight gain.

HEADINGS - Obesity. Gastric bypass. Diabetes mellitus. Heredity.

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RESUMO - ***Racional*** - A derivação gastrojejunal em Y-de-Roux é considerada um dos tratamentos mais eficientes para a manutenção de peso a longo prazo; porém, está associada à falhas manifestadas por impossibilidade de manutenção ou reganho de peso e descontrole glicêmico. ***Objetivo*** - Estudar os possíveis fatores que influenciam na falha do controle de peso e ou remissão da DM2. ***Métodos*** - Estudo do tipo caso-controle, com 159 pacientes submetidos ao bypass gástrico com dois anos ou mais de pós-operatório, sendo selecionados para casos 24 pacientes com perda ponderal insatisfatória e ou ausência de remissão da DM2 e para controle 24 pacientes com perda ponderal satisfatória e ou remissão do DM2, pareados por idade e tempo de pós-operatório. ***Resultados*** - Dos 24 casos e 24 controles avaliados, o percentual de reganho de peso foi de 19,32% e 8,68% e o percentual de remissão da DM2 foi de 26,6% e 87,5% assim como o percentual de recorrência da DM2 foi de 6,6% e 0,0% para casos e controles. Observando o IMC máximo pré-operatório, os casos apresentaram em média 53,50±12,24 kg/m2 e controles 48,77±5,19 kg/m2 sendo que o IMC máximo anterior ao bypass gástrico foi estatisticamente significativo no que se refere à falha no controle de peso ou insucesso da operação. ***Conclusão*** - Pacientes com IMC máximo inicial elevado (≥ 50kg/m2) apresentaram maior índice de falha na perda ponderal. A intolerância alimentar e diferenças socioeconômicas são consideradas fatores de reganho de peso.

DESCRITORES - Obesidade. Derivação Gástrica. Diabetes Mellitus. Hereditariedade

INTRODUCTION

The physiopathology of morbid obesity is complex and not restricted exclusively to excessive calorie intake. Genetic, physical, physiological and behavioral factors interact in the weight gain process. Furthermore, the easy access to inexpensive high-calorie foods contributes to weight gain, especially among low-income populations[23].

Obesity, considered a worldwide epidemic, is associated to other comorbidities, including cardiovascular diseases and type 2 diabetes mellitus (DM2). Individuals with body mass index (BMI) of 35 Kg/m^2 have a 2.5-fold higher risk than those with BMI between 20 and 25 Kg/m^2, while for those with BMI > 40 Kg/m^2 the risk is 10 times greater[24].

Obese individuals may be predisposed to the development of DM2 due to insulin resistance, glucose intolerance and pancreatic beta cell failure, whose prevalence has been increasing in recent years. BMI, the dominant risk factor for diabetes, is the primary and most harmful comorbidity of obesity[7,8,11,12,20].

The popularization of obesity surgery has made it possible to assess its results in diabetic patients. Bariatric surgery has shown a significant improvement or even long-term resolution of diabetes. It is also known that the impact of the operation on DM2 is significantly higher in patients with shorter disease duration and those using less medication, particularly insulin[19].

A retrospective study conducted in Virginia, USA assessed 177 diabetic and obese patients submitted to Y-en-Roux gastric by-pass with postoperative time greater than five years (maximum 16 years). DM2 was resolved in 89% of the individuals in the first five years; however, 43% experienced a relapse in glycemic control[1,17]. A 10-year follow-up study that assessed patients submitted to Y-en-Roux gastric surgery showed that peak weight loss occurred between 18 and 24 months, where morbidly obese (but not super obese) individuals lost up to 91.8% of body weight[6]. However, significant failure rates were observed (characterized as maintaining BMI > 35 Kg/m^2), mainly in the super obese population. In five years, 18% of patients did not maintain BMI below 35 Kg/m^2 (9% of morbidly obese and 43% of super obese), whereas after 10 years, the failure rate was 35% (20% of morbid obese and 58% of super obese)[6].

Among the risk factors that can lead to weight gain are super obesity and postoperative follow-up, as well as patients compromised by faulty recommendations[4,17].

Literature studies regarding the influence of socioeconomic factors on weight regain after gastric by-pass showed no significant relationship for this factor, despite the difficulties of underprivileged classes in acquiring healthy foods and undergoing suitable postoperative follow-up[10,15,26].

This study aimed at investigating weight loss failure (insufficient weight loss) and/or lack of DM2 remission in patients submitted to Y-en-Roux gastric bypass within the previous two years, and verify the association between failed surgery and the study variables.

METHODS

The research was approved by the institutional Research Ethics Committee, under protocol 601/11 and informed consent was obtained from all participants. This case-control study, conducted in 2011, assessed 159 patients of both sexes, aged between 20 and 65 years, submitted to Y-en-Roux gastric bypass, two or more years postoperatively, at the Department of Obesity Surgery and Related Diseases of Onofre Lopes University Hospital, belonging to the Federal University of Rio Grande do Norte, Natal, Brazil.

Cases consisted of 24 patients with unsatisfactory weight loss (excess weight loss < 50%; current BMI > 35 Kg/m^2, weight regain ≥ 50%) and/or absence of DM2 remission (continued use of antidiabetic drugs; HbA1c > 7; fasting glycemia > 110 mg/dl; postprandial glycemia > 180 mg/dl). Controls were composed of 24 patients with satisfactory weight loss (excess weight loss > 50%; current BMI < 35 Kg/m^2; weight regain ≤ 50%), and/or DM2 remission (non-use of antidiabetic drugs; HbA1c < 7, fasting glycemia< 110 mg/dl; postprandial glycemia < 180 mg/dl), matched for age and postoperative time.

The survey was conducted using medical records, nursing reports, directed interviews, as well as physical and laboratory assessment.

The study variables were age, postoperative time, gender, locality of residence (urban or rural), marital status (with or without a partner), schooling, preoperative BMI, percentage DM2 remission, presence of DM2, weight loss with calculation of minimum postoperative BMI and two years postoperatively, percentage regain of lost weight and laboratory results of routine preoperative examinations[21,22].

Patients with BMI ≥40.0 were classified as severely or grade III obese, while those with BMI ≥50.0 were considered super obese[5].

Blood pressure was measured after 5 minutes' rest using a stethoscope and sphygmomanometer with obese cuff and the patient in the sitting position[9]. Individuals with a history of hypertensive disease, those exhibiting systolic blood pressure

greater than or equal to 140 mmHg or diastolic blood pressure greater than or equal to 90 mmHg, and those who were using antihypertensives were considered hypertensive.

Brazilian Bariatric and Metabolic Surgery recommendations were used to assess the percentage regain of lost weight[22].

The results of routine postoperative laboratory examinations (fasting and postprandial glycemia, HbA1c, total cholesterol, HDL-c, LDL-c, triglycerides, basal insulin, Ht, Hb, AST, ALT, ferritin, vitamin D and vitamin B12) were recorded.

According to I Brazilian Guidelines on Diagnosis and Treatment of Metabolic Syndrome, patients exhibiting fasting glycemia of 126 mg/dl (two samples from different day), glycemia of 200 mg/dl after the oral tolerance test with 75 g of glucose, or those using medication to treat DM2 were considered to have type 2 diabetes mellitus. Glycemia was measured by blood sample, using a biochemical analyzer[21].

For this study, patients with previous diagnosis of dyslipidemia and those who reported using statins before by-pass were considered dyslipidemic[22].

With respect to food-related signs, gagging was defined as discomfort while swallowing, followed or not by vomiting, generally related to mastication and swallowing.

Statistical analysis

Descriptive analysis of study variables was conducted to determine their relative and absolute distribution in table and graph form. Chi-square and Fisher's exact tests were used to verify the association between variables. Odds ratio was calculated using 95% confidence intervals, with their values adjusted by multiple logistic regression (variables with $p < 0.25$ were selected). The student's t-test was used to compare the means of the two groups. Statistical analysis was carried out using SPSS 17.0 software, considering a significance level of 5%.

RESULTS

Of the 159 patients with two or more years of follow-up, 48 were selected and reassessed (24 cases and 24 controls), matched for age and postoperative time. Mean age was 44.58±11.81 years for cases and 41.38±9.89 years for controls; postoperative time was 42.08±11.44 months for cases and 42.00±15.04 for controls; mean initial BMI (preoperative) was 53.50±12.24 kg/m^2 for cases and 48.77±5.19 kg/m^2 for controls; the mean percentage regain of lost weight was 19.32±17.76 for cases and 8.68±9.84 for controls and the percentage absence of DM2 remission was 71.43% for cases and 12.5% for controls.

In relation to the other clinical-laboratory variables, cases exhibited 15.08 ± 3.32 mg/dl more total cholesterol than controls ($p = 0.046$), 139.83 ± 2.33 pg/ml less vitamin B12 ($p < 0.045$) and 1.24 ± 0.17 uUI/ml less basal insulin ($p < 0.016$) (Table 1).

TABLE 1 - Mean and standard deviation of laboratory examination results two years after gastric by-pass for cases and controls

Laboratory Examinations	Case (n=24)	Control (n=24)	p
Fasting glycemia	106,25±49,50	85,2±9,85	0,052
Postprandial glycemia	122,23±52,02	104,27±15,57	0,117
HbA1c	5,24±1,04	4,98±0,70	0,305
Total cholesterol	175,41±27,04	160,33±23,72	0,046
HDL	52,38±10,45	52,58±9,16	0,942
Triglycerides	104,13±42,12	104,92±27,73	0,939
Hematocrit	37,51±4,65	37,94±4,07	0,735
Hemoglobin	12,40±1,39	12,61±1,68	0,624
AST/TGO	25,83±11,31	27,88±9,27	0,498
ALT/TGP	25,71±12,46	25,96±7,82	0,934
Ferritina	59,38±55,25	102,18±93,93	0,061
VitD	31,92±14,05	32,61±5,12	0,823
VitB12	412,06±236,73	551,89±234,40	0,045
Insulina basal	3,57±1,64	4,81±1,81	0,016

$p \leq 0.05$ – statistically significant difference – student's t-test

There was no statistically significant difference in the percentages of patients according to study group (cases or controls) and the variables gender, locality of residence, marital status and schooling (chi-squared, p=0.245/ 0.768) (Table 2).

TABLE 2 - Number and percentage of patients according to study group and sociodemographic variables

Variables	Case (n=24)		Control (n=24)		p	OR (IC95%)
	Nº.	%	Nº.	%		
Sex						
Female	22	91,7	18	75,0	(1)0,245	3,67 0,55 – 30,26
Male	2	8,3	6	25,0		
Locality of residence						
Capital	16	66,7	19	79,2	(2)0,330	0,53 0,12 – 2,28
Interior	8	33,3	5	20,8		
Situação conjugal						
Com companheiro	15	62,5	14	58,3	(2)0,768	1,19 0,32 – 4,45
Sem companheiro	9	37,5	10	41,7		
Escolaridade						
Até fundamental	10	41,7	9	37,5	(2)0,768	1,19 0,62 – 1,93
Média ou superior	14	58,3	15	62,5		

$p \leq 0.05$ – $p \leq 0.05$ – statistically significant difference; (1) Fisher's exact test; (2) Chi-squared.

Logistic regression analysis (Table 3) revealed that systemic blood pressure and family history, DM2 and family history, gagging, gender and dyslipidemia exhibited no statistically significant association with gastric by-pass failure. On the other hand, maximum BMI (preoperative) showed a statistically significant association with the procedure (p=0.047).

TABLE 3 – Multiple logistic regression according to the variables included (n=48)

Variables	Adjusted OR	IC 95%	p
Systemic blood pressure	1,29	0,17 – 9,95	0,805
DM 2	1,42	0,14 – 14,24	0,767
Gagging	0,74	0,11 – 4,77	0,748
Family history of DM2	2,36	0,27 – 20,77	0,438
Gender	5,50	0,56 – 54,26	0,145
Dyslipidemia	17,99	0,93 – 347,23	0,056
Family history of hypertension	11,87	0,95 – 148,68	0,055
Maximum BMI	1,13	1,01 – 1,28	**0,047**

$p \leq 0.05$ – statistically significant association with gastric by-pass failure

DISCUSSION

Some of the by-pass patients did not obtain satisfactory results in terms of weight loss and maintenance or DM2 management. With respect to weight regain, other studies showed that it occurs in 63.6% of patients undergoing this operation, varying according to postoperative time and initial BMI postoperative follow-up is the most important factor in this regain[17]. Lack of weight management is also related to super obesity[4].

The absence of DM2 remission can vary from 11% to 43%; recurrence may be related to a number of factors, such as time since DM2 diagnosis[5,25,27] and lower BMI[9,13]. This range of results shows the need to intensify studies in order to determine the cause of failure, improve techniques and increase the success rate.

Routine laboratory examinations showed a significant difference for cases and controls with respect to total cholesterol, vitamin B12 and basal insulin, but it cannot be confirmed whether they are predictive factors for treatment failure. Meta-analysis to judge the effectiveness of the technique in terms of hyperlipidemias demonstrated that the initial total cholesterol of 307 mg/dl decreased by an average of 33.2 mg/dl[4] after surgery.

These results corroborate those obtained in a retrospective study conducted in Campinas, Brazil with 386 patients exhibiting the same conditions as those described here. Individuals with DM2 (undergoing remission or not) showed similar levels of total cholesterol and basal insulin. As observed in the present study, basal insulin was significantly lower in patients with DM2 remission[16].

It was also observed that mean vitamin B12 levels were higher than 200 pg/ml, which was within recommended parameters[18]. However, literature findings show a deficiency of vitamin B12, among others, after gastric by-pass, possibly related to altered absorption, poor food quality, reduced intake and intolerance[2,18].

In relation to sociodemographic variables, there was no significant difference between cases and controls. With respect to gender, similar findings were obtained in meta-analyses conducted in 2004 and 2009, with greater frequency in women (72.6% and 79.6%, respectively[3,4]).

Socioeconomic status, analyzed by schooling level, showed a predominance of secondary or university education in both cases and controls, but with no significant difference. This is in accordance with literature studies, which revealed no difference between weight loss and socioeconomic levels[1,15,26].

On the other hand, a study on food intolerance with 47 patients submitted to this operation in Natal, Brazil showed that socioeconomic level is significantly related to the degree of food intolerance[14].

Logistic regression demonstrated that maximum BMI before by-pass was statistically significant in terms of poor weight management or failed surgery. This same finding was observed in Canada, showing that patients with elevated initial maximum BMI (≥ 50kg/m^2), exhibited a higher weight loss failure rate, reaching 58% in those with more than ten years postoperative follow-up[6].

On the other hand, a retrospective study carried out at Columbia University with 42 diabetic patients at least three years after surgery, showed that patients with higher preoperative BMI exhibited better DM2 remission results, but the percentage of weight regain was inversely proportional for the groups with and without DM2 remission (37.7% and 15.4%[9], respectively.

CONCLUSION

Maximum BMI showed an association with gastric by-pass failure, that is, heavier patients were more likely to experience poor weight and DM2 management postoperatively. Food intolerance and socioeconomic differences were considered factors for weight regain.

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