

Prospective Observational Longitudinal Study Evaluating Erectile Dysfunction in 50 Type 2 Diabetic Patients with BMI Below 35 Kg/m² Submitted to Ileal Interposition Associated to Sleeve Gastrectomy



Ricardo Alexandre Fernandes Ferro^{1*}, Áureo Ludovico de Paula², Sérgio Vencio³, Rafael Caiado-Vencio⁴, Marco Antônio Gonçalves Rodrigues⁵ and Marco Túlio Costa Diniz⁵

¹School of Health Sciences, Brasília, Brazil

²Department of Surgery, Hospital de Especialidades, Brazil

³Federal University of Goiás, Brazil

⁴Pontifical Catholic University of Goiás, Brazil

⁵Department of Surgery, Federal University of Minas Gerais, Brazil

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***Corresponding author:** Ricardo Alexandre Fernandes Ferro, School of Health Sciences, Brasília, SQSW 303, Bloco G/306, Sudoeste, Brasília-DF, CEP: 70.673-307, Brazil, Email: ricardo.ferrobsb@yahoo.com.br

Abstract

Background: Erectile dysfunction (ED) is a mistreated and neglected complication that affects 35%-75% of males with type 2 diabetes (T2DM) leading to worsening quality of life and interpersonal relations. Males with T2DM develop ED 5-10 years earlier than non-diabetics.

Methods: This was a prospective, longitudinal and observational study including 50 consecutive male patients with T2DM and a body mass index (BMI) <35Kg/m² who underwent laparoscopic ileal interposition associated to sleeve gastrectomy (II-SG).

Objectives: Observe the ED prevalence before and after 12 months of II-SG evaluated by a questionnaire. Evaluate global sexual function 12 months after the procedure and compare with initial parameters. Analyze if diabetes duration was an interfering factor in sexual function improvement 12 months after the surgery.

Results: Mean age was 54.4 years (37-69). Mean diabetes duration was 12, 1 years (05-23 years). Mean HbA1c was 8, 8 % (7, 5-10, 5%). After 12 months, we observed a significant improvement in glycemic control, dyslipidemia, blood pressure and a reduction in the use of insulin and anti-diabetic agents (p<0.05). Erectile dysfunction, sexual intercourse satisfaction, orgasmic function, sexual desire and overall sexual life satisfaction were improved (p<0.05). ED prevalence was 78% before and 46% after the procedure. More than 15 years of diagnosis was a bad predictor for ED improvement.

Conclusion: Ileal Interposition associated to sleeve gastrectomy, significantly improved erectile function, satisfaction with sexual intercourse, orgasmic function, sexual desire and sexual life of patients with type 2 diabetes 1 year after the surgery.

Keywords: Erectile and sexual dysfunction; Type 2 diabetes; Ileal interposition

Abbreviations: ED: Erectile Dysfunction; T2DM: Type 2 Diabetes; BMI: Body Mass Index; II-SG: Ileal Interposition Associated to Sleeve Gastrectomy; HbA1c: Glycated Hemoglobin; ADA: American Diabetes Association; IIEF: International Index of Erectile Function Questionnaire; IBM: International Business Machines; SPSS: Statistical Package for Social Sciences

Introduction

Diabetes mellitus type 2 (T2DM) is a chronic metabolic disorder with a dramatically increasing prevalence. T2DM stems from a progressive insulin secretory defect on the background of insulin resistance. Prolonged insufficient metabolic control

with constantly elevated HbA1c levels inevitably leads to complications, most commonly to diabetic nephropathy, diabetic retinopathy, diabetic neuropathy, and macrovascular problems [1].

Modern anti-glycemic agents and life style modifications can lead to metabolic control, but a long-lasting effect still needs to be proven. Erectile dysfunction is a chronic complication presented in a wide range (35-75%) in T2DM male patients, usually 5-10 years earlier than non-diabetic males [2]. Relaxation of the smooth muscles of the venous (cavernous) sinusoids is the final erection mechanism and having sinusoids endothelium integrity is vital for the process. On the other hand, endothelium injury is present in the vast majority organic causes of ED [3]. Obesity, dyslipidemia and diabetes are independent risk factors for cardiovascular disease and also constitute major risk factors for ED, where sinusoids endothelium injury is an indicative of developing atherosclerosis [4]. In the very obese patient with type 2 diabetes, bariatric surgery appears to be a treatment modality that is both highly effective and increasingly attractive [5]. On the other hand, in the most frequent kind of type 2 diabetes, i.e., the hyperglycaemia surfacing after the fourth decade of life in moderately obese subjects, is a progressive disease, and resolution, whether spontaneous or by treatment, is rare. This discrepancy in outcome is irrefutable and unaccounted for [6].

One potential explanation is that the hyperglycaemia of morbid obesity has a different pathogenesis from the hyperglycaemia of the moderately obese or lean diabetic. Another possibility is that bariatric surgery per se interferes with glucose metabolism in ways that none of the other antidiabetic treatments does. The available evidence, if limited and non-homogeneous, suggests that at least some of the antidiabetic effect of bariatric surgery may be independent of the induced weight loss [7].

De Paula et al. had shown that in type 2 diabetic patients with a BMI below 35 kg/m², ileal interposition associated to sleeve gastrectomy (II-SG) is an effective, safe and long-lasting procedure reaching normal levels of blood glucose, HbA_{1c}, lipid profile and blood pressure in 86% of patients without any anti-diabetic agents [8,9]. In this prospective, longitudinal and observational study we observed the ED prevalence before and after 12 months of II-SG evaluated by a questionnaire, evaluate global sexual function 12 months after the procedure and compare with initial parameters and analyze if diabetes duration was an interfering factor in sexual function improvement 12 months after the surgery.

Methods

This was a prospective, longitudinal and observational study with a mean follow up of 12 months designed to evaluate ED in T2DM patients.

Study population

The study included 50 consecutive male patients with type 2 diabetes (diagnosed according to the revised ADA criteria) and a body mass index (BMI) <35kg/m², who underwent laparoscopic ileal interposition associated to sleeve gastrectomy (II-SG). Mean age was 54.4 years (37-69). Smoking was present in 12% of the

patients. Mean diabetes duration was 12, 1 years (05-25 years). Patients were invited to participate the study and respond a questionnaire in the pre- and postoperative period. All subjects gave written informed consent to the study, and the protocol was approved by the ethics committee of the hospital and referenced by the consolidated note from Plataforma Brasil/Ministério da Saúde.

Surgical procedure

The surgical procedure was performed by laparoscopy. II-SG started with division of the jejunum 20cm bellow the Treitz ligament using a linear stapler. An ileal segment of 200cm was removed 30cm proximally to the ileocecal valve, and interposed peristaltically up into the jejunum. The anastomoses were performed functionally side by side. The intestinal measurements were performed with traction along the antimesenteric border using a 10cm atraumatic gasper. The sleeve gastrectomy was performed after devascularization of the greater curvature using the ultrasonic scalpel. A 36-French Fouchet orogastric calibration tube was placed along the lesser curvature toward the pylorus. The gastric resection was performed starting at the antrum and continuing up to the angle of His using a linear stapler; the staple line was covered by an invaginating suture [10].

Inclusion criteria : All subjects had had type 2 diabetes for at least 3 years but none had had major upper abdominal surgery; active sexual life in the last four weeks preceding the procedure; hbA_{1c} above 7% in the last three months; documentation of HbA_{1c} exceeding 7.5% for at least 3 months; stable weight, defined as no significant change (>3%) over the 3 months before enrollment; evidence of stable treatment with oral hypoglycemic therapy or insulin for at least 12 months; BMI less than 35 kg/m².

Exclusion criteria : Elderly patients (>70years); Type 1 diabetes (Positive anti GAD and anti-IA-2 auto-antibodies); previous major upper abdominal surgery; pregnancy; malignant or debilitating diseases; severe pulmonary or cardiac diseases, severe renal disease (glomerular filtration rate <30ml/min); use of appetite suppressant medication, eating disorder such as bulimia or binge eating; obesity due to any other endocrine disorder; users of penile prosthesis; use of PDE5 inhibitor medication or any other kind of ED treatment in the last 4 weeks before the procedure; hormonal replacement therapy with testosterone or any other medication that interferes in the steroid hormone laboratory dosage in the last three months before the surgery.

Questionnaire: A standardized questionnaire was applied in 56 T2DM patients in the preoperative period and in 50 after 12 months of follow-up. In 6 patients, we were unable to apply the questionnaire in the appropriate period. This was a discreet procedure conducted by the same investigator in the day before the surgery and after 12 months when a clinical and laboratory evaluation were performed. The International Index of Erectile

Function Questionnaire (IIEF) was used to classify the sexual dysfunction level [11].

Statistical Analysis

All analyses were performed using the International Business Machines (IBM) Statistical Package for Social Sciences (SPSS) Advanced Statistics version 17.084. Some results were analyzed based on their frequency distribution. The chi-square test (χ^2) with Yates correction in contingency tables was used to analyze associations between two variables. When the sample size was too small, resulting in expected values lower than five in one or more blanks, we applied the Fisher's exact test. P values are two-sided and $p < 0.05$ was accepted as statistically significant. Analysis of variance was used to compare means and the Kruskal-Wallis test for comparison of medians.

To analyze the effects of the surgical procedure were employed variables change before and after the procedure, using the McNemar test. For running the test, two conditions must be satisfied: the measurement scale needs to be nominal and with two measures. Another condition to be satisfied is data independence and parity, in other words, data must belong to the same individual, in this study represented by the patient before and after surgery, each patient being independent of each other, so the conditions for the test were met.

To analyze the IIEF variables preoperatively and 12 months later the nonparametric Wilcoxon test was used. In order to reach a significance of 95%, the minimum number of patients enrolled were 21. This means that the number collected from 56 patients before and 50 patients later caters perfectly for scientific and statistical analysis. To quantify the reliability degree between some preoperative and postoperative assessments Kappa coefficient was employed. Kappa values vary depending on the degree of concordance.

Kappa values	Degree of concordance
0-0, 20	Weak
0, 21-0, 40	Considerable
0, 41-0, 60	Moderate
0, 61-0, 80	Substantial
0, 81-1, 00	Almost complete

Results

In this prospective, longitudinal observational study, 50 male with T2DM were evaluated pre and 12 month post Ileal interposition associated with sleeve gastrectomy, showing significant improvement in Erection hardness grading scale (EHGS) and International Index of Erectile Function (IIEF). Before the procedure all patients used antidiabetic oral drugs and/or insulin. However, after 12 months, it was restricted to only 10% of them. The same reduction was observed in relation to the use of antihypertensive drugs ($p < 0.05$). All

procedures were performed laparoscopically, and there was no mortality. Preoperatively, dyslipidemia was diagnosed in 91.6% of the patients. Arterial hypertension was observed in 75%, nephropathy in 33.3%, retinopathy in 20.8%, neuropathy in 33.3% and coronary artery disease in 33.3% of the patients.

There was a significant decrease ($p < 0.05$) in serum total cholesterol, LDL- cholesterol, triglycerides, fasting glucose, postprandial glucose, hemoglobin A1c, insulin, HOMA-IR and microalbuminuria. The variables creatinine clearance and serum HDL- cholesterol showed significant increase ($p < 0.05$).

Evaluation of erectile function before and 12 months after surgery

Erection hardness grading scale (EHGS) provides evaluation of penile rigidity using a four-grade scale, where score of 1 indicates that the penis is larger than normal, but not hard; 2 means the penis is hard, but not hard enough for penetration, 3 means the penis is hard enough for penetration but not completely hard, and 4 indicates that the penis is completely hard and fully rigid. Before surgery, 22% of patients were able to make vaginal penetration (EHGS 3-4). After 12 months of operation, this number increase to 54% ($p < 0,05$). Before the operation, 34% of patients were scale-graded as 1 and after the intervention this rate decreased to 14% ($p < 0,05$). After 12 months of operation, the number of patients scale-graded 3 doubled and tripled in grade 4. In both cases the differences were significant ($p < 0.05$). Such observations can be translated by the IIEF.

Evaluating the data of the International Index of Erectile Function Questionnaire obtained in the study, it was concluded that there was an improvement in erectile function score given by the erection, when comparing the results observed in the pre-and postoperative II-SG. This difference was significant ($p < 0.05$). The same was found regarding satisfaction with sexual intercourse, the orgasmic function, sexual desire and overall sexual experience.

Assessment of satisfaction with sexual intercourse before and 12 months after surgery

24% of patients had satisfactory level before the operation, with scores less than 10. This rate increased to 62% in the evaluation performed 12 months after surgery ($p < 0.01$).

Evaluation of orgasmic function before and 12 months after surgery

The orgasmic function before and after surgery showed significant improvement ($p < 0.05$), with 50% of patients reporting maximum score postoperatively, while only 6% reached initially.

Evaluation of sexual desire before and 12 months after surgery

While only 26% of patients had satisfactory sexual desire (score less than seven) before the intervention, 96% of them

reached these levels in the analysis 12 months after the procedure ($p < 0.001$).

Assessment of overall satisfaction with the sexual act of the couple before and 12 months after surgery

Regarding overall satisfaction with sexual intercourse the couple, initially 32% of patients had adequate index of satisfaction (score equal to or above seven). After 12 months, 62% of them reached adequate levels of satisfaction ($p < 0.05$).

Evaluation of the total international index of erectile function score before and 12 months after surgery

The IIEF score can range from 5 to 75 points. We observed a significant improvement. Before the operation, 32% of patients scored 30 points. In the second evaluation, the figure was 6% ($p < 0.01$). On the other hand, 40% of patients had a score equal to or greater than 40 in the preoperative evaluation and this index increased to 74% after 12 months of operation ($p < 0.05$).

Correlation of chronological parameters and laboratory with the spheres of sexual function before and 12 months after surgery

Correlating diabetes duration with improved sexual function 12 months after surgery shows that patients who did not had significant improvement in the IIEF and EHGS parameters were those who had more time to diagnosis (more than 180 months). These bad-responder group includes 10% of the patients who maintained the use of antidiabetic medication 12 months after surgery. Among the 25 patients with scores below 10 in the requirement satisfaction with sexual intercourse after 12 months of II-SG were all those more than 15 years of diabetes diagnosis. The same can be said for orgasmic function, sexual desire and overall satisfaction with sexual intercourse.

Discussion

In this report of 12 months follow-up of 50 consecutive type 2 diabetic patients with BMI < 35 submitted to laparoscopic ileal interposition associated with a sleeve gastrectomy, we showed that 89.9% had HbA1c below 7% without antidiabetic medication. Using IIEF we evaluated the five main spheres of human sexual function, namely, erectile function, satisfaction with sexual intercourse, orgasmic function, sexual desire and overall satisfaction with sexual function. IIEF has been used widely and universally by medical literature and it becomes possible to compare the results of this study with other published or which may be realized [12].

In this study, the prevalence of ED in T2DM was 78% applying the IIEF. According to Ferrini & cols, it is estimated that by the time a man is in his 40's, he has about a 40% chance of having some form of ED and this prevalence increases about 10% per decade thereafter [13]. There was no significant reduction in BMI before and after the surgical procedure, which reinforces the thesis that the weight loss is not the main mechanism in metabolic improvement observed in T2DM

patients undergoing procedures such as ileal interposition [14]. The metabolic results found in this study are in agreement with other previously published papers using the same technique-ileal Interposition associated with Sleeve Gastrectomy [15,16]. Before surgery, all patients used oral antidiabetic drugs and/or exogenous insulin, and even then, all had HbA1c above 7%. So, they were outside the therapeutic goal (HbA1c < 7%) established by recognized international organizations. Twelve months after surgery, 90% of patients had HbA1c below 7% without the use of any antidiabetic medication. Midterm results of this procedure shown similar results and we hypothesized that sustained weight loss associated with better insulin sensitivity and continuous after-meal GLP-1 secretion may be the reason [17].

T2DM patients normally have decreased HDL-cholesterol, elevated triglycerides and LDL-cholesterol. After 12 months of surgery we observed normalization of HDL-cholesterol, LDL-cholesterol and triglycerides, with a significant difference compared to preoperative period. The obtained control of dyslipidemia in patients of the current study may have contributed to the improvement in sexual function [18]. It reinforces the data of several authors demonstrating that lipemic control is extremely important for endothelial dysfunction improvement, including erectile dysfunction. Dyslipidemia leads to a decreased production of nitric oxide (NO) and/or decreased NO dependent muscle relaxation. This may explain why even young dyslipidemic individuals have a higher prevalence of ED [19].

In this study, we were able to show 78% of patients with inability to vaginal penetration (EHGS 1 and 2) before surgery. After 12 months, 46% of patients still EHGS 1 and 2. Analyzing EHGS and IIEF compiled data we observed a significant difference between the findings pre- and postoperatively ($p < 0.05$) in all spheres of sexuality analyzed by the test, i.e., erectile function, satisfaction with sexual intercourse, orgasmic function, sexual desire and overall satisfaction with sex life. Patients with uncontrolled DM present with lower rates of NO intracavernous synthesis. It is possible that the metabolic control obtained by II-SG may have improved NO synthesis and thereby favored erectile function. One of the weaknesses of this study is that we were unable to access this data. The number of patients and time of follow-up also account for [20].

Even though there has been no significant reduction in BMI, the observed weight loss, especially abdominal/visceral fat, may have contributed to the improvement in sexual function. Visceral fat can convert testosterone hormone (predominantly male) in estradiol hormone (predominantly female) and the first is essential for all sexual spheres. It is known that plasma concentration of testosterone is inversely proportional to BMI and DM2 patients may show a reduction in free testosterone [21]. Patients who did not show significant improvement in some spheres were precisely those who had diabetes duration over 15 years. These patients probably had micro and macrovascular

irreversible injuries. Thus, even with the improvement of virtually all metabolic parameters following II-SG, these patients did not achieve the degree of improvement in all sexual spheres experienced by those with shorter disease.

Normal sexual function requires complex interaction between vascular, neurologic, hormonal and psychological systems [22]. It is possible that, in addition to metabolic control provided by the surgical procedure, other factors may contribute to the improvement in the sexual life of these patients. After II-SG most of them do not require everyday measurements of blood glucose, antidiabetic, antihypertensive and lipid lowering medications. This improves quality of life, triggers more willingness to work capacity, to sexual activity and physical activity.

Conclusion

The incidence of erectile dysfunction in patients with type 2 diabetes mellitus was 78% before surgery and 46% after 12 months. After 12 months postoperatively, significant improvement in erectile function, satisfaction with sexual intercourse, orgasmic function, sexual desire and sexual life of patients were seen.

Patients with diabetes duration over 15 years had lower responses in controlling diabetes mellitus and sexual dysfunction.

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