Significant Improvement of Erectile Function after Roux-en-Y Gastric Bypass Surgery in Obese Chinese Men with Erectile Dysfunction

Li Kun · Zhang Pin · Di Jianzhong · Han Xiaodong · Yu Haoyong · Bao Yuqian · Zhang Hongwei

Abstract

Background We aimed to examine the effect of Roux-en-Y gastric bypass surgery (RYGB) on erectile dysfunction (ED), cavernosal morphological vasculopathy, and carotid wall alterations in severely obese Chinese men.

Methods We performed a retrospective cohort study of 39 obese men with ED who underwent RYGB between 2011 and 2012. Erectile function was assessed by the International Index of Erectile Function-5 (IIEF-5) before and 1 year after surgery. Intima-media thickness of carotid and cavernosal arteries and cavernosal peak systolic velocity (PSV) were investigated by color Doppler ultrasound. Endothelial function was assessed with the L-arginine test.

Results Eighteen (46.2 %) men had cavernosal vasculopathy and 21 (53.8 %) had carotid vasculopathy before surgery, and these proportions decreased to 15.4 % and 23.1 % after surgery, respectively. There was a significant improvement in carotid and cavernosal intima-media thickness postoperatively. IIEF-5 (17.3 to 23.8, $P<0.05$), PSV (23 to 37, $P<0.05$), and endothelial scores (6.1 to 8.2, $P<0.05$) were all improved after RYGB. The increase in endothelial function scores was positively associated with changes in pre- to postoperative IIEF-5 scores ($r=0.438$, $P=0.017$). Younger age, being married, and lower preoperative IIEF-5 scores were independently related to greater improvement in erectile function.

Conclusions ED can be relieved after RYGB in obese Chinese patients, accompanied by the improvement of cavernosal morphological vasculopathy and carotid wall alterations. Changes in endothelial function may contribute to this improvement, while preoperative body mass index and the amount of weight loss do not.

Keywords Erectile dysfunction · Gastric bypass surgery · Endothelial function · Obesity · Weight loss

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Introduction

Erectile dysfunction (ED) is defined as the persistent inability to attain and maintain an erection that is sufficient to permit satisfactory sexual intercourse [1]. Several epidemiological studies have reported that a high prevalence of ED affected over 150 million men worldwide in 1995. This prevalence will reach 322 million by 2025 according to the Massachusetts Male Aging Study, with the largest projected increase in Africa, Asia, and South America [2].

ED is common in obese males. Obesity increases the risk of ED in individuals by 1.3 times and 79 % of the men suffering from ED are overweight [3]. Several studies have shown that development of ED is closely associated with diabetes, hyperlipidemia, hypertension, and metabolic syndrome [4–6]. ED is also significantly and independently associated with an increased risk of cardiovascular disease, coronary heart disease, stroke, and all-cause mortality, which indicates that ED is a warning sign of these diseases [4, 6–8]. Penile vascular impairment is one of the most important reasons for ED, and increased mean carotid artery intima-media thickness (IMT) is regarded as a predominant predictive factor of cardiovascular diseases and atherosclerosis [9]. A previous study suggested that patients with ED and metabolic syndrome have

a higher prevalence of cavernosal vasculopathy and peripheral vascular alterations [10].

Currently, the growing consensus for treatment of ED favors bariatric surgery [11–13], which achieves substantial weight loss, significantly improves metabolic syndrome, and relieves type 2 diabetes [14, 15]. Furthermore, findings of several studies have shown that ED is reversed after gastric bypass surgery [16].

This study aimed to determine whether ED, cavernosal vasculopathy, and peripheral vascular alterations are improved after Roux-en-Y gastric bypass surgery (RYGB) in Chinese patients with ED. Furthermore, we examined which factors might contribute to the improvement of erectile function and which factors were independently related to a greater postoperative improvement in the International Index of Erectile Function-5 (IIEF-5) scores.

Materials and Methods

Participants and Procedures

Patients in our study were recruited from the Sixth People's Hospital Affiliated to Shanghai Jiao Tong University between 2011 and 2012. A total of 121 men had RYGB during this period. They all completed the IIEF-5 questionnaire prior to RYGB.

The inclusion criteria comprised patients in the Obesity Clinic of our hospital whose IIEF-5 score was less than 21, those who were 18–65 years old, and those who were candidates for RYGB. The exclusion criteria were men with scrotal trauma, corporal fibrosis, a history of pelvic surgery, use of phosphodiesterase type-5 inhibitors, or taking hormone replacement therapy. Of 53 patients enrolled in our study, 11 refused to participate and 3 complained of sexual inactivity during the past 4 weeks. Those 14 patients were excluded from our study and 39 participants remained (Fig. 1).

We performed a retrospective cohort study of 39 men who had completed a series of questionnaires and measurements, including clinical and ultrasound parameters before surgery and 1 year after surgery. All of the tests mentioned above were routine during the follow-up period and the results were available in hospital files.

Methods

Biochemical and hormonal parameters were evaluated by obtaining blood samples from all of the participants after an overnight fast. Samples were obtained 7 days before assessment of the IIEF-5. Biochemical parameters included plasma glucose levels, lipid profile (total cholesterol, high-density lipoprotein cholesterol, and triglyceride levels), and C-reactive protein (CRP) levels. Lipid profiles were determined
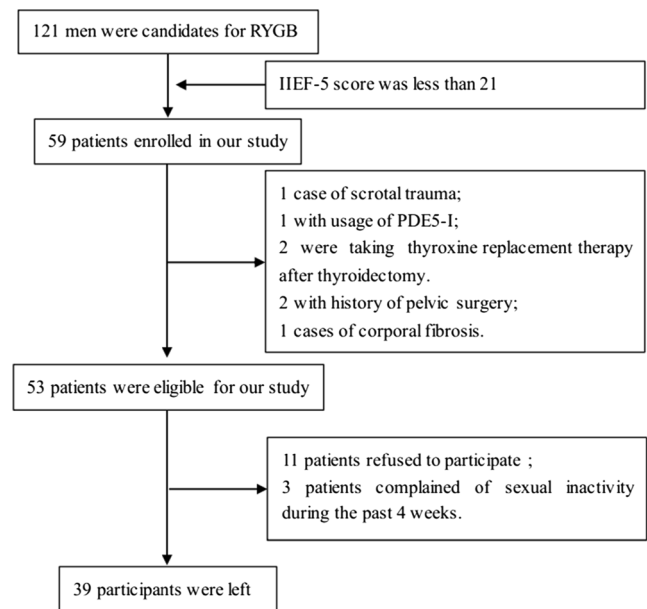

Fig. 1 Flow chart to show how the patients with erectile dysfunction were chosen

by standard enzymatic methods (Hitachi 747 analyzer, Castle Hill, NSW, Australia). CRP levels were assayed by the particle-enhanced immunoturbidimetric analyzer (Roche Diagnostics, Mannheim, Germany). In addition, we measured testosterone levels by using an electrochemiluminescence immunoassay (Roche Diagnostics).

Anthropometric evaluations consisted of assessments of body weight, height, and waist circumference (WC). Weight was measured by using an electronic scale (accuracy=0.1 kg) with the participant in barefoot and wearing light clothes. Height was determined by using a fixed wall stadiometer (accuracy=0.5 cm). WC was measured with a standard, flexible, inelastic measuring tape (accuracy=0.5 cm) at the level of the iliac crest. Body mass index (BMI) was calculated as weight/height^2.

Five-item Version of the International Index of Erectile Function

Containing only 5 questions, each item on a 5-point scale (1–5), the IIEF-5 is an abridged IIEF, and is a useful subjective diagnostic tool for ED [9, 17]. The sum scores of all items are used to evaluate penile erectile function. A score of 0 refers to low erectile function, whereas a score of 5 indicates the best functional status. The total scores of the questionnaire survey range from 1 to 25, and the optimal cutoff of the scores for erectile function is 21. A man who scores more than 21 points is considered to have normal erectile function, otherwise, he is regarded as having ED. Based on the IIEF-5 scores, penile erectile function can be divided into 5 categories: severe ED (1–7), moderate ED (8–11), mild to moderate ED (12–16), mild ED (17–21), and normal erectile function (22–25).

Color Doppler Ultrasound Examination

All of the participants were measured by a high-resolution echo-color-Doppler (Aplio XV Toshiba, Tokyo, Japan) equipped with a multi-frequency linear probe by the same doctor who was blinded to the patients. Cavernosal peak systolic velocity (PSV), IMT, and carotid arterial IMT were measured [9]. Penile and carotid vasculopathy were classified [18].

Endothelial Function Testing

Endothelial function was evaluated by the L-arginine test, as previously described [19, 20]. Esposito designed a score in which platelet aggregation and blood pressure responses to L-arginine (3 g i.v.) are summed. This provides a score ranging from 0 to 10 points, which indicates maximal impairment of endothelial function and normal endothelial function, respectively [21].

Demographic Characteristics, History of Health, Current Medication, and Alcohol and Tobacco Consumption

Demographic data such as age, marital status, and educational level were collected via questionnaire. The Health History Checklist was used for assessing the participants' health condition. This list included (1) whether the participants had been currently diagnosed with certain disorders (e.g., hypertension, diabetes, dyslipidemia, and metabolic syndrome), (2) whether they had experienced spinal cord injury, radical pelvic surgery, scrotal trauma, cavernous fibrosis, or prostatic disease, and (3) whether they had taken phosphodiesterase type 5 inhibitors or any other hormone replacement therapy. Finally, the names of medications, and the frequency of alcohol drinking and smoking were recorded.

Statistical Analysis

We performed statistical analysis using SPSS version 20.0. The preoperative and postoperative characteristics of obese men with ED were compared by using paired samples t tests. Changes in cavernosal or carotid vasculopathy were calculated by McNemar's chi square test. Correlations between clinical parameters and IIEF-5 were analyzed by partial correlation analysis. Multivariate predictors of pre- to postoperative changes in IIEF-5 scores were conducted by stepwise regression analysis. Demographic (age, marital, and education status), preoperative variables (BMI and IIEF-5 score), and postoperative weight loss were entered in this procedure.

Statistical significance was defined as $P < 0.05$. Data are presented as the mean value±SD.

Results

Demographic Characteristics

The study comprised 39 obese men with ED whose mean age was 45.2 years (range, 25–65 years) and the mean initial BMI was 41.2 kg/m^2 (range, 36–59 kg/m^2). One year after the operation, the mean BMI decreased from 41.2 to 32.1 kg/m^2 and mean waist circumference decreased from 138.4 to 102.7 cm ($P < 0.05$) (Table 1).

Participants were predominantly married (84.6 %) and over half (53.8 %) of them had at least a 4-year college degree. The most commonly reported health conditions preoperatively were diabetes (100 %), hypertension (76.9 %), hyperlipidemia (69.2 %), and metabolic syndrome (59 %). Slightly less than half (46.2 %) of the participants drank more than 1 alcoholic drink per week and nearly a quarter of those (25.6 %) had smoked more than 25 pack-years (Table 2).

Medication Use

Medications that were most commonly taken preoperatively were statins (74.4 %), antihypertensives (76.9 %), oral diabetes medication (43.6 %), insulin (66.7 %), antiarrhythmics (41 %), and anti-reflux medication (15.4 %) (Table 2). The data of medication use at baseline and 1 year after surgery are shown in Table 3. A total of 43.5 % of participants no longer required any class of medication 1 year after surgery, 61.5 % no longer required any class of diabetes medication 1 year after surgery, 46.6 % no longer required any class of hypertension medication 1 year after surgery, and 74.2 % no longer required any class of hyperlipidemia medication 1 year after surgery (Table 3).

Clinical and Ultrasound Parameters, and ED

Fasting blood glucose, total cholesterol, and triglyceride levels were significantly decreased after surgery compared with before surgery ($P < 0.05$). High-density lipoprotein cholesterol levels were markedly increased postoperatively compared with preoperatively ($P < 0.05$, Table 1). There was a trend for a decrease in serum CRP levels in obese men with ED postoperatively compared with preoperatively, ($P = 0.329$). Testosterone levels were moderately elevated after surgery compared with before surgery ($P = 0.052$).

Baseline IIEF-5 scores before the operation were less than 21 points. The mean postoperative IIEF-5 score increased from 17.3 points before surgery to 23.8 points after surgery ($P < 0.05$). PSV and endothelial function scores were significantly increased postoperatively compared with preoperatively ($P < 0.05$). Furthermore, cavernosal and carotid IMT were decreased ($P < 0.05$), as well as cavernosal and carotid

Table 1 Changes in clinical and ultrasound parameters of the participants before and 1 year after surgery[a]

Variable	Pre-GB	Post-GB	P value
BMI (kg/m^2)	41.2±8.5	32.1±7.3	0.013
WC (cm)	138.4±16.3	102.7±8.1	0.021
FBG (ng/dL)	118.3±17.6	93.6±9.8	0.000
Serum lipids (mg/dL)			
Total cholesterol	186±35	164±29	0.006
Triglycerides	175.2±26.6	98.7±19.2	0.000
HDL cholesterol	42.3±7.9	59.4±8.2	0.03
Testosterone (nmol/L)	13.2±2.6	16.4±3.2	0.052
CRP (mg/l)	1.1±0.3	0.9±0.4	0.329
Endothelial function scores	6.1±2.1	8.2±2.3	0.008
IIEF-5	17.3±5.5	23.8±6.1	0.004
PSV	23±8.4	37±11.6	0.002
IMT cavernosal (mm)	0.33±0.03	0.18±0.02	0.018
IMT carotid (mm)	0.97±0.19	0.72±0.23	0.026
Cavernosal vasculopathy (%)	46.2 (18)	15.4 (6)	0.000
Carotid vasculopathy (%)	53.8 (21)	23.1 (9)	0.000

BMI body mass index, *WC* waist circumference, *FBG* fasting blood glucose, *CRP* C-reactive protein, *HDL cholesterol* high-density lipoprotein cholesterol, *IIEF-5* international index of erectile function, *PSV* peak systolic velocity, *IMT* intima-media thickness

vasculopathy, postoperatively compared with preoperatively (P<0.05).

We also examined changes in the IIEF-5 score and clinical parameters pre- to postoperatively by multivariate correlation analysis (Table 4). We found that the increase in IIEF-5 scores after surgery was positively associated with the improvement of endothelial function (r=0.438, P=0.017).

The results of multivariate regression analysis are shown in Table 5. Being married, having younger age, and having lower preoperative IIEF-5 scores were independently correlated with a greater improvement in IIEF-5 scores postoperatively.

Discussion

The prevalence of ED in patients with metabolic syndrome is directly proportional to the number of metabolic syndrome components [22], with approximately 20, 30, and 35 % of patients with ED having 3, 4, or 5 components of metabolic syndrome, respectively. In addition, subsequent studies have indicated that WC, hypertension, high cholesterol levels, diabetes, and advanced age are all increased with the risk of ED [23, 24]. Several studies have provided evidence that bariatric surgery may play an essential role in the improvement of ED. In our study, we found that IIEF-5 scores were increased after gastric bypass surgery in obese Chinese patients with ED. Cavernosal morphological vasculopathy and carotid wall

Table 2 Preoperative characteristics of the participants

Age (M±SD years)	45.2±12.3
BMI (M±SD kg/m^2)	41.2±8.5
Marital status (%, n)	
Married	84.6 (33)
Divorced	0
Single	15.4 (6)
Education (%, n)	
<4 years college	46.2 (18)
≥4 years college	53.8 (21)
Frequently reported health conditions (%, n)	
Metabolic syndrome (%)	59 (23)
Arterial hypertension (%)	76.9 (30)
Diabetes or glycemia >100 mg/dL (%)	100 (39)
HDL <40 mg/dL (%)	53.8 (21)
Triglycerides >150 mg/dL (%)	69.2 (27)
Current alcohol use (%, n)	
Never	5.1 (2)
<1 drink/week	48.7 (19)
≥1 drink/week	46.2 (18)
Smoking (%, n)	
Never	51.3 (20)
Smoker (<25 pack-years)	23.1 (9)
Smoker (≥25 pack-years)	25.6 (10)
Frequently reported medications (%, n)	
Anti-reflux	15.4 (6)
Anti-hypertensives	76.9 (30)
Anti-arrhythmics	41 (16)
Statins	74.4 (29)
Oral diabetes medications	43.6 (17)
Insulin	66.7 (26)

alterations were decreased after surgery. We also found that the improvement in endothelial function might have contributed to this positive effect. Additionally, younger age, being married, and lower preoperative IIEF-5 scores were independently correlated with greater postoperative improvement in IIEF-5 scores.

Ethnicity is regarded as a factor that affects sexual function [25, 26]. However, previous studies that reported a positive effect of bariatric surgery on erectile function were primarily conducted in Western individuals [27–29]. Whether these results are also present in Chinese patients is unknown. This study has provided preliminary evidence that indicates that there are similar improvements in Chinese men with ED after surgery.

Penile vascular impairment, which is the predominant reason for ED, is diagnosed by PSV and cavernosal arterial morphology (IMT ≥0.3 mm or presence of plaques) [30], which are directly related to peripheral vasculopathy and the severity of cardiovascular risk factors [31].

Table 3 Medication use at baseline and at 1 year after surgery

Medications	Preoperation	Postoperation
No. of any class of medications		
≥4 medications	15	3
3 medications	21	6
2 medications	19	10
1 medication	2	9
Not taking any class of medication	0	17
Diabetes medications		
≥2 medications	7	2
1 medication	10	7
Insulin—no. of patients	26	4
Not taking this class of medication	0	24
Hypertension medications		
≥2 medications	8	2
1 medication	22	14
Not taking this class of medication	9	23
Hyperlipidemia medications		
≥2 medications	6	0
1 medication	25	8
Not taking this class of medication	8	31
Any medication		
≥2 medications	3	1
1 medication	16	6
Not taking this class of medication	20	32

43.5 % no longer required any class of medication 1 year after surgery, 61.5 % no longer required any class of diabetes medication 1 year after surgery, 46.6 % no longer required any class of hypertension medication 1 year after surgery, and 74.2 % no longer required any class of hyperlipidemia medication 1 year after surgery

Table 4 Multivariate correlations between changes in IIEF-5 scores and clinical parameters pre- to postoperatively

Variable	r	P
WC	−0.104	0.234
BMI	−0.274	0.151
Triglycerides	−0.038	0.842
HDL cholesterol	0.077	0.691
FBG	−0.291	0.127
CRP	−0.356	0.064
Testosterone	0.199	0.132
Endothelial score	0.438	0.017

Furthermore, an increased mean carotid artery IMT is a good predictive parameter of generalized atherosclerosis and cardiovascular disease, and does correlate with erectile function [9]. There is a higher prevalence of cavernosal vasculopathy or plaques in patients with ED and metabolic syndrome compared with ED patients without metabolic syndrome. Our study found that with the improvement of ED and metabolic syndrome, the incidence of cavernosal morphological vasculopathy and carotid wall alterations decreased and PSV improved.

Several studies have shown that sexual function can be improved after gastric bypass surgery. Dallal et al. found that half of ED patients no longer required treatment with medications, which might have a close relationship with the improvement of obesity-related ED [29]. Moreover, Reis et al. pointed out that surgery-induced weight loss and increased testosterone levels could justify an improvement of erectile function [27]. However, in our study, we found that improved endothelial function might have a close correlation with reversed ED. Multifactorial

mechanisms may be involved in surgery-associated improvement of ED.

Endothelial dysfunction and abnormalities of the vasodilator system play an important part in the pathophysiology of ED. Vascular disease of penile arteries is the most common cause of ED, accounting for up to 80 % of cases [32, 33]. Endothelial dysfunction prevents the smooth muscle cells lining the arterioles from relaxing, which inhibits vasodilatation [34]. In addition, impairment of endothelial-dependent vasodilatation, which causes atherosclerosis of arteries, leads to flow-limiting stenosis of the penile artery. Adequate cavernous flow is indispensable to achieve an erection, while flow-limiting stenosis of the penile artery may prevent an adequate arterial supply, thus causing ED. In our study, we found an improvement in PSV and endothelial function scores in patients with ED after surgery, which might explain the reversal of ED.

Interestingly, our findings indicated that the improvement of ED in Chinese men undergoing bariatric surgery may be independent of BMI and weight loss. Therefore, further studies are needed to evaluate the extent of postoperative changes in correlated variables, including neurogenic endocrinological and psychogenic factors, which may account for these improvements. Additionally, drugs, including antihypertensives, antiarrhythmics, and statins, are frequently associated with ED [24, 35]. There was a high rate of frequent use of medication in our study. Medication use decreased and 43.5 % of the patients completely stopped taking drugs postoperatively

Table 5 Predictors of pre- to postoperative changes in IIEF-5 scores

Variable	Standardized β	t	P value
Age (<40 years)	−0.322	−3.132	0.008
Marital status (married)	0.243	2.023	0.042
Education status	−0.143	−1.362	0.234
Preoperative BMI	0.092	0.923	0.332
Preoperative IIEF-5 scores	−0.654	−6.381	<0.001*
% EWL	−0.168	−1.487	0.213

% EWL % excess weight loss

*Model: $R^2 = 0.62$, $P < 0.001$

(Table 3). Therefore, further investigation in larger samples is required to examine the effects of discontinued use of medication after surgery.

Several studies have shown that the development of ED is closely associated with diabetes, hyperlipidemia, hypertension, and metabolic syndrome [4–6]. In our patients, there was a high prevalence of diabetes, hypertension, dyslipidemia, and metabolic syndrome before the operation. After surgery, 61.5 % of diabetic patients, 46.6 % of hypertensive patients, and 74.2 % of dyslipidemia patients no longer required treatment. Whether short-term remission of these long-standing comorbidities postoperatively can improve erectile function is still unclear.

Findings from recent studies have indicated that lifestyle significantly affects ED [36], including smoking and alcohol use. Guay et al. reported that cessation of smoking can considerably and rapidly improve erectile function in individuals with a smoking history of at least 30 pack-years [37]. In addition, a 2011 meta-analysis suggested that lifestyle changes and a reduction in cardiovascular risk factors could greatly contribute to the improvement of erectile function [38]. In our study, almost half of the patients had a history of tobacco and alcohol abuse. Some people succeeded in quitting smoking and drinking, but others renewed tobacco and alcohol use postoperatively. Controlling these two factors is difficult. Therefore, we did not take these two factors into account in our statistical model. More comprehensive studies regarding the influence of lifestyle modifications on ED are required.

While ED was improved after RYGB, as well as cavernosal and carotid vasculopathy, the statistical power was limited by the small number of RYGB individuals. As noted above, a more comprehensive study of predictors of the improvement in ED in the Chinese population is required. Information is also required on whether short-term remission of comorbidities and lifestyle modifications after RYGB might account for these improvements. Consequently, future studies need to examine whether these improvements persist over time after stabilizing or regaining weight.

In summary, our study was the first to examine changes in ED in obese Chinese men with ED after gastric bypass surgery. This study shows that IIEF-5 scores, cavernosal morphological vasculopathy, and carotid wall alterations are improved after RYGB. The improvement in endothelial function might explain the reversed ED. In addition, younger age, being married, and lower preoperative IIEF-5 scores are independently related to greater postoperative improvement in IIEF-5 scores. A more comprehensive study is required to determine whether physiological, medical, lifestyle, and psychosocial elements play an important role, and if these improvements are sustained over time.

Conflict of Interest The authors declare that they have no conflicts of interest.

Ethical Approval For this type of study (retrospective study) formal consent is not required.

Informed Consent Informed consent was obtained from all individual participants included in the study.

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