

Original Article

Effects of bariatric surgery on male sperm parameters and lower urinary tract symptoms: a systematic review and meta-analysis

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Abstract: There is an emerging awareness of obese characteristics in males correlating with sperm parameters and lower urinary tract symptoms (LUTS). Bariatric surgery (BS) has become a valid treatment for morbid obesity, achieving great weight loss results recently. The aim of this study was to investigate differences in male sperm parameters and LUTS, before and after BS. Embase, the Cochrane Library, and PubMed databases, along with references from relevant articles, were searched between January 2001 and March 2018. The current meta-analysis was conducted to investigate the alteration tendency of sperm parameters and LUTS after BS. A total of 6 studies were included in the meta-analysis. No significant improvements were observed regarding sperm motility ($P = 0.74$), sperm concentrations ($P = 0.57$), and normal morphology rates ($P = 0.21$), after BS, except for sperm volume ($P = 0.01$). International Prostate Symptom Scores (IPSS) ($P < 0.00001$) in post-operative groups were significantly lower than those in pre-operative groups. BS is an effective means of treatment for obesity, improving LUTS for males. However, the effects of BS on sperm parameters appear to be limited.

Keywords: Obesity, bariatric surgery, sperm parameters, lower urinary tract symptoms

Introduction

Obesity has become one of the most important health problems, worldwide. It has been associated with multiple physical comorbidities, including hypertension, diabetes, insulin resistance, cardiovascular disease, cancer, and musculoskeletal disease [1-3]. The prevalence of obesity has nearly doubled over the past three decades [4, 5]. According to data presented by the World Health Organization (WHO) in 2015, the amount of overweight adults has reached 1.9 billion, in which 600 million were marked as obese [6]. Recently, important aspects of obesity-related comorbidities, such as sex hormone disorders, infertility, sexual dysfunction, and LUTS, have been paid more attention in the obesity field.

Conservative weight-loss programs, including lifestyle modification and pharmacotherapy, can achieve limited effects [3, 7, 8] or even present

a relapse course [8]. Acquiring significant weight loss and resolving obesity-related comorbidities satisfactorily, BS has emerged. It has become the most effective treatment for morbid obesity [7, 8]. This may be because of different social pressures to gain normal weight between men and women. Only 20% of patients undergoing BS were men [9]. This may be the reason why studies are lacking regarding changes in male sexual function, sperm parameters, and LUTS, before and after surgery.

Post-operative LUTS, assessed by IPSS, seems to be well-relieved [3, 5, 10, 11]. However, studies concerning the association between BS and LUTS in men have been limited. Three studies revealed no significant improvements achieved in semen parameters after BS [4, 12, 13]. Severe worsening of sperm parameters was presented in two case reports [14, 15]. Because of the contradictory phenomenon mentioned above, the current systematic review was con-

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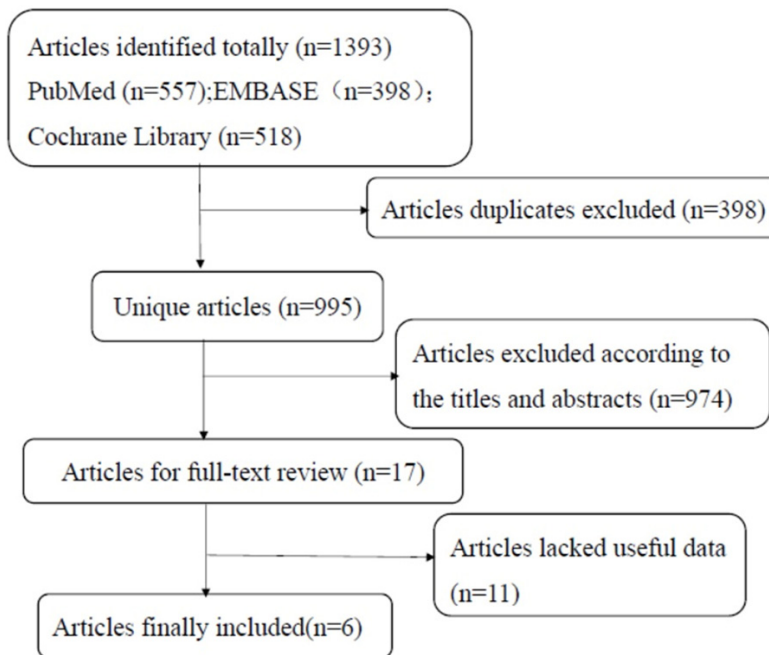


Figure 1. Flow diagram of study selection.

ducted, aiming to investigate the alteration tendency of sperm parameters and LUTS after BS.

Materials and methods

Search strategy

To systematically review the effects of BS on semen parameters and LUTS in obese men, an electronic search of Embase, the Cochrane Library, and PubMed databases was carried out from January 2001 to March 2018. The following search terms were used: Obesity, bariatric surgery, weight loss surgery, sperm, semen, LUTS, and IPSS. The following limits were applied: Humans, gender (male). There were no limitations on language. This systematic review was performed in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [16].

Study selection

Two authors (ZY, JJC) separately reviewed records to select studies reporting the effectiveness of bariatric surgery on sperm parameters and LUTS in morbidly obese men. Any discrepancies were resolved by open discussion. Reference lists of included studies were checked, manually, identifying further studies. Indications for bariatric surgery included men with morbid obesity with a BMI of 35-40 kg/m², obe-

sity-related comorbidities, or a BMI > 40 mg/m² [17]. Primary outcomes included International Prostate Symptoms Scores (IPSS) and semen analysis. Questionnaires concerning IPSS were used to assess LUTS. Conference abstracts and articles without full texts were excluded because of limited data. Articles with unavailable data were excluded. If the results of the same population were reported more than one time, only the most recent and most complete data was included.

Data extraction

Data was extracted, independently, by two authors (ZY, JJC) using a standard form. These two reviewers

discussed any discrepancies. If unresolved, they consulted with a third reviewer (HW) for a final decision. The following data was extracted: Number of enrolled patients, country, year, patient characteristics (the mean age, BMI), semen parameters, scores of IPSS, before and after surgery. All collected data was recorded in an electronic database.

Quality assessment

Included papers were distinguished according to the 2011 Oxford Centre for Evidence-Based Medicine (OCEBM) levels of evidence [18] for therapy studies. Levels of evidence were divided into five degrees in OCEBM: 1) Studies defined as systematic reviews of randomized controlled trials (RCT) or n-of-1 trials; 2) Studies defined as RCT or observational studies with significant effects; 3) Non-RCT/follow-up studies; 4) Studies, such as case series, case-controls, or historically controlled; and 5) Mechanism-based reasoning studies.

Data synthesis and analysis

The current study estimated mean differences (MD) with 95% CIs for continuous outcomes pooled across studies. Inconsistency was quantified using the I² statistic. Heterogeneity is considered significant if I² > 50% [19]. A fixed-effects models was used for meta-analyses of

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Table 1. Characteristics of the 6 included studies

Study	Year	Country	Sample size	Age (M/R, y)	Q	Semen (Y/N)	Pre-BMI	Study design
Groutz A	2016	Israel	39	40.7	IIEF	N	42.8	Prospective, case series
			41	40	IPSS	N	42.2	
Ranasinghe WK	2011	Australia	34	52.8	IIEF, IPSS	N	47.3	Retrospective, cohort study
El Bardisi H	2016	USA	46	29-44	/	Y	71.4	Prospective, case series
Uruc F	2016	Turkey	22	34.59	IPSS	N	49.57	Prospective, case series
Legro RS	2015	USA	6	18-40	/	Y	48	Prospective, case series
Reis LO	2012	Brazil	10	36.7	IIEF-5	Y	55.7	Prospective, comparative study

M: Mean, R: Range, y: year, Q: Questionnaire, Y: Yes, N: No, Pre-BMI: Preoperative body mass index. IIEF: International index of erectile function, IPSS: International prostate symptom score.

Table 2. Parameters presented by 6 included studies before and after BS

Study	Time	Sperm parameters				
		V	M	C	Vi	nM
El Bardisi H	B	2.5/2.8	33/18.4	2.5/27.8		63/19.4
	y 1	2.0/1.5	32/11.4	7.2/24.9		85/19.4
Legro RS	B	2.1/1.1	46/25	65/73		10/8
	1 m	2.7/1.3	44/9	23/28		13/15
	3 m	3.0/1.2	55/16	30/28		13/11
	6 m	2.4/0.9	48/23	50/63		8/9
	y 1	2.0/2.0	55/28	99/148		7/11
Reis LO	B	2.9/0.8	34.0/8.9	78.7/58.6	73.8/6.5	8.2/4.0
	y 2	4.1/0.8	36.0/8.5	104.0/66.5	71.7/7.6	11.0/2.6
Study	Groutz A		Ranasinghe WK		Uruc F	
	B	3 m	B	PO	B	PO
IPSS	5.5/4.4	2.7/2.6	6.87/6.21	6.90/5.70	4.5/2.22	1.91/1.48

All parameters in Table 2 are presented as mean/standard deviation. V: sperm volume (ml), M: motility (%), C: concentration ($10^6/ml$), Vi: vitality, nM: Normal morphology (%), y: year, m: month, PO: Post-operation (The certain time was not mentioned). IPSS: International prostate symptom score.

cases lacking heterogeneity. In cases of heterogeneity, a random-effects model was used. Two-sided $P < 0.05$ indicates statistical significance for all analysis outcomes. Comparative effects were analyzed using the traditional pairwise meta-analysis method, applying Cochrane Collaboration review manager software (RevMan v.5.3.0).

Results

Description of studies

A total of 1,393 articles were identified through the present search strategy. According to titles and abstracts, 17 studies were included and underwent full text reviews. Only six studies [2-5, 12, 13] were suitable and finally included in the meta-analysis, after excluding another 11 inappropriate articles (Figure 1). Chara-

cteristics of all suitable studies are shown in Table 1. Primary results are listed in Table 2.

According to 2011 OC-EBM levels of evidence [18], two studies were defined as prospective comparative studies, reaching level 3, and four studies were defined as prospective case series, reaching level 4.

Sperm parameters

Sperm parameters from 62 patients were collected from three articles [4, 12, 13] (Figure 2). Based on the current meta-analysis, no significant improvements were observed regarding sperm motility (MD 0.80, 95% CI [-3.88, 5.47], $P = 0.74$) (Figure 2B), sperm concentrations (MD 2.95, 95% CI [-7.22, 13.13], $P = 0.57$) (Figure 2C), and normal morphology rates (MD 4.07, 95% CI [-1.60, 6.54], $P = 0.001$) (Figure 2D) after BS, except for sperm volume (MD 0.54, 95% CI [0.11, 0.96], $P = 0.01$) (Figure 2A). Because of a lack of data concerning sperm vitality, this parameter was not analyzed. Heterogeneity was detected in the results of normal morphology rates ($I^2 = 79\%$). Sensitivity analysis (data not shown) revealed that El Bardisi H's study obviously influenced results. It was hypothesized that the reason this study resulted in heterogeneity was the bigger sample size, compared to other studies. This study was excluded from the review, repeating the test through a random-effects model. Results

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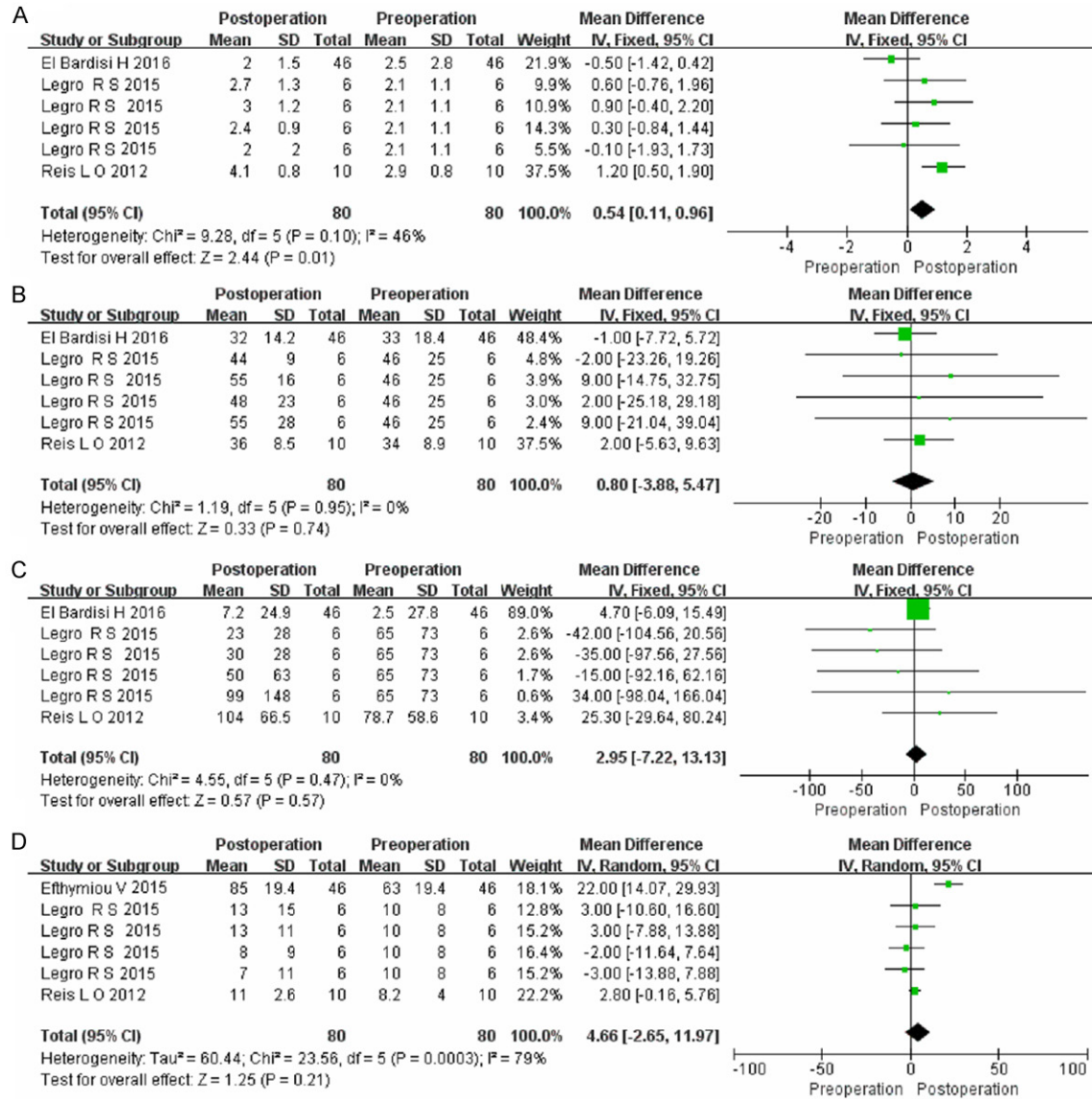


Figure 2. Forest plot of sperm parameters before and after BS. A. Sperm volume. B. Sperm motility. C. Sperm concentration. D. Sperm normal morphology rate.

were MD = 2.14, 95% CI [-0.47, 4.74] and P = 0.11 in normal morphology rates (Figure 3).

Lower urinary tract symptoms

LUTS was assessed by IPSS. Three articles [2, 3, 5] were obtained, including 97 patients (Figure 4). The current study only analyzed total IPSS scores because of a lack of specific data for every item. Total IPSS scores (MD -2.41, 95% CI [-3.27, -1.55], P < 0.00001) were significantly higher after BS. No obvious heterogeneity was observed.

Discussion

The association between obesity and male infertility has been thought to be caused by endocrine dysregulation, environmental toxins accumulating in adipose tissue, increased scrotal temperatures, altered sexual health, and genetic abnormalities [4, 13], contributing to abnormal sperm production. Recent studies have underlined the impact of obesity and weight loss surgery on sperm parameters [4, 12, 13]. However, data regarding the effects of

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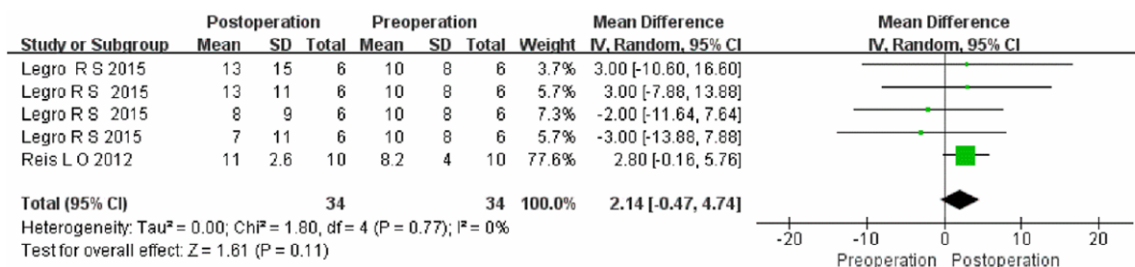


Figure 3. Forest plot of sperm normal morphology rates after BS, excluding El Bardisi H's study.

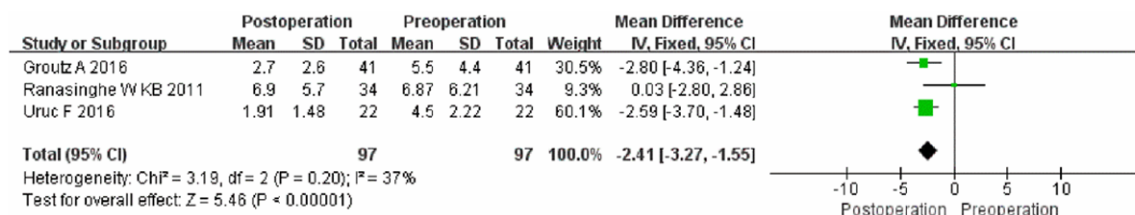


Figure 4. Forest plot of total IPSS before and after BS.

weight loss surgery on sperm parameters has been limited.

In the current meta-analysis, no significant improvements were observed regarding sperm motility, sperm concentrations, and normal morphology rates after BS, except for sperm volume. Effects of BS on sperm parameters appear to be limited. Unfortunately, this study did not include sperm vitality because of a lack of data.

In contrast, dramatic reductions in sperm parameters were observed in two case reports [14, 15]. Sermondade N [14] reported a case series of three male patients that underwent rapid and major weight loss following BS. Severe worsening of semen parameters was observed during the months after bariatric surgery, including extreme asthenospermia. However, azoospermia was not observed. Alterations in spermatogenesis in one patient were reversible two years after surgery. Two out of the three couples obtained pregnancies with treatment of intracytoplasmic sperm injections with fresh spermatozoa. In Lazaros L' study [15], they observed a marked reduction of sperm parameters in two patients in a period of twelve to eighteen months after surgery. Reduction of sperm parameters may be attributed to nutrient alterations, such as low carotenoid, pre-albumin levels, vitamin deficiencies (like vitamin A, D, B12, and so on) and trace

element depletion (like altered zinc concentrations). These may result in spermatogenesis arrest and testicular degeneration [14, 15].

Studies have shown that obese men have larger prostates that can cause LUTS [20]. The mechanism may be an increase of estrogen/testosterone that originates from testosterone turning into estrogens in the adipose tissue of obese males [21]. In addition, due to fat accumulation, intra-abdominal and intravesical pressure is increased. The pelvic base muscle is weakened. Thus, LUTS is triggered [5]. Increased sympathetic nervous system activity in obese men may be another reason leading to LUTS [22]. Weight loss has shown to improve female urinary symptoms [23]. However, studies involving weight loss surgery and LUTS in obese man have been limited. The current study analyzed the association between BS and LUTS in obese men. Because of a lack of specific data of every item, the current study only analyzed total symptom scores. Total IPSS scores were significantly higher after BS. However, contrary to present results, one article [2] showed no improvements in urinary incontinence with weight loss after BS.

Published data has revealed that BS not only contributes to significant and long-term weight loss but also resolves or improves multiple obesity-related comorbidities, including diabetes mellitus, hypertension, and cardiovascular dis-

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ease, as well as significantly reducing drug use and costs [24]. A decrease in fat mass after weight loss might also decrease fat accumulation in the abdomen, thighs, and scrotum. This may result in a decrease of testicular temperature, promoting spermatogenesis [25].

A former meta-analysis [26] suggested significant increases in plasma sex hormone-binding globulin (SHBG) and total testosterone (TT) after weight loss diet. In addition, they also found body weight loss was associated with a decrease in estradiol and an increase in androgen and gonadotropins levels. Multiple regression analysis showed that the degree of body weight loss was the best determinant of TT rise.

Obesity-related male sexual dysfunction and LUTS can be reversed due to improvements in physical comorbidities, sex hormone disorders, and a decrease in fat mass after BS. However, no significant improvements regarding sperm parameters, except for sperm volume, were shown in the current cumulative analysis. This could be attributed to short-term nutrient alterations after surgery. Thus, more studies with long-term follow-ups should be conducted.

There were some limitations to this systematic review and meta-analysis: 1) Data from most studies was not suitable for meta-analysis. Thus, only 6 articles were included. Sample sizes included into this study were also limited; 2) Because of limited articles and sample sizes, this study did not perform subgroup analysis and regression analysis; 3) One included article was a retrospective study, allowing for recall bias. The use of questionnaires, based on subjective assessment, may have introduced influencing factors, such as individual patient satisfaction with the surgery.

Conclusion

BS was shown to be an effective means of treatment for obesity, helping patients lose weight and improving male LUTS. However, the effects of BS on sperm parameters appear to be limited. Data regarding changes in sperm parameters and LUTS, before and after BS, are also limited. More controlled studies with long-term follow-ups should be conducted, confirming present conclusions.

Disclosure of conflict of interest

None.

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