### **ORIGINAL CONTRIBUTIONS**





# Systematic Review and Meta-Analysis of the Impact of Bariatric Surgery on Lower Urinary Tract Symptoms in Males

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### Abstract

**Background** Obesity is a chronic disease with multisystem morbidity. There are multiple studies reporting the effect of bariatric surgery on cardiovascular and metabolic disease, but few examine its impact on lower urinary tract symptoms. This article aims to perform a systematic review with meta-analysis, to determine the effects of bariatric surgery on lower urinary tract symptoms in male patients.

**Methods** Medline, Embase, conference proceedings, and reference lists were searched for studies reporting the quantitative measurement of lower urinary tract symptoms score pre- and postweight loss surgery. The primary outcome was International Prostate Symptom Score (IPSS) before and after bariatric surgery. Secondary outcomes were changed in body mass index (BMI) and total body weight (TBW). Weighted mean differences (MD) were calculated for continuous outcomes.

**Results** Seven studies were included in the analysis of 334 patients undergoing bariatric surgery. Mean study follow-up was between 3 and 36 months. IPSS score ranged from 3-12.7 preoperatively and 1.9-6.9 postoperatively. There was a statistically significant improvement in the IPSS score following bariatric surgery (MD 2.82, 95% CI 0.96 to 4.69, p=0.003). Bariatric surgery also resulted in statistically significant reduction of BMI and TBW.

**Conclusion** Bariatric surgery produces a significant improvement on lower urinary tract symptoms in men with obesity. This may be due to improvement of insulin sensitivity, testosterone levels or lipid profile associated with weight loss.

Keywords LUTS · Bariatric surgery · IPSS · Meta-analysis

# Introduction

Obesity is a chronic disease with multisystem morbidity [1]. It is increasingly prevalent across all age groups and especially

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in the Western population leading to considerable increases in healthcare expenditure [2]. The urinary effects of obesity have been reported in multiple studies, which link increasing body mass index (BMI) with incontinence and lower urinary tract symptoms (LUTS) such as poor flow, frequency, urgency, nocturia, incomplete bladder emptying and intermittency [3] [4] [5].

LUTS are a significant burden on healthcare resources, with an estimated \$4bn spent annually in the United States on the management of benign prostatic hyperplasia (BPH), a key cause of LUTS [6]. There is an independent association with increasing BMI and LUTS in males [4] [7]. Conservative interventions to reduce weight in mildly overweight males has been shown to reduce LUTS [8]. Bariatric surgery has been demonstrated to reduce urinary incontinence in female patients [9]. There are only a few studies in men that examine either the LUTS symptom burden in the prebariatric surgery population or the impact of bariatric surgery on LUTS.

This article aims to perform a systematic review with metaanalysis to determine the effects of bariatric surgery on LUTS in men.

# Methods

A systematic review was completed to evaluate the impact of bariatric surgery on lower urinary tract symptoms in male patients. This article is reported according to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) statement [10].

# Search Strategy

A comprehensive electronic search was performed using Medline and Embase databases from 1966 to December 2020. The search strategy included the terms 'bariatric surgery', 'obesity surgery', 'bariatrics', 'LUTS', 'lower urinary tract symptoms', 'males', 'male' and 'men', which were used in combination with the Boolean operators AND or OR. Additionally, the literature search was complemented by a hand-search of published abstracts from meetings of the International Federation for the Surgery of Obesity and Metabolic disorders from 2012 to 2020, the British Obesity and Metabolic Surgery Society Annual meeting from 2010 to 2020, and the American Society for Metabolic and Bariatric Surgery from 2013 to 2020. Furthermore, the references of all included studies were searched for any additional relevant citations.

#### **Selection Criteria**

Two authors (IS and ACC) independently screened the abstracts of identified papers and determined eligibility for inclusion in the meta-analysis. Studies were selected if they only included patients above the age of 18, where the primary outcome was lower urinary tract symptoms (LUTS) in male patients before and after bariatric surgery assessed using the International Prostate Symptom Score (IPSS) questionnaire [11]. The questionnaire assesses for incomplete emptying, frequency, intermittency, urgency, weak stream, and straining. Patients are then classified into one of the three groups based on the total IPSS score: 0-7 mildly symptomatic, 8-19 moderately symptomatic, and 20-35 severely symptomatic. Disparities were resolved by the wider authorship team. Exclusion criteria included non-English studies where no translation was available, duplicate studies, studies including only female population or studies with LUTS measurement other than IPSS questionnaire. Full-text articles of all selected abstracts were further reviewed by two reviewers (IS and ACC) using the same criteria, and disputes were resolved by a senior reviewer. Included studies were then assessed for methodological quality and bias using the MINORS tool for nonrandomized studies [12].

## **Data Extraction**

Data was extracted from the selected studies by one reviewer (IS) and then checked for accuracy by second reviewer (ACC). The primary outcome was mean change in LUTS score as measured by the IPSS questionnaire before and after bariatric surgery. The questionnaire was first developed by the American Urological Association [11], and subsequently accepted as an internationally validated tool for the assessment of LUTS. It is considered to be reliable, sensitive, and responsive [13] [14]. Secondary outcomes comprised BMI and Total Body Weight (TBW) in kilograms. The following patient characteristics were assessed: age, pre- and postoperative BMI, TBW and IPSS total score.

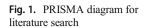
# **Statistical Analysis**

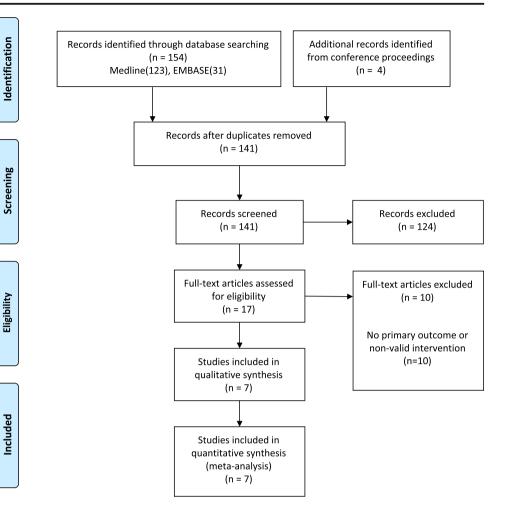
All categorical variables were reported as frequencies or percentages, and continuous data was expressed as mean  $\pm$  standard deviation. Where studies had outcomes reported as a median rather than a mean value, medians were used in the statistical analysis. Meta-analysis was performed for outcomes related to lower urinary tract symptoms in male patients before and after weight loss surgery. Outcomes were assessed using weighted mean difference (MD). The estimated size-effects were calculated using the Revman 5.4 software (Review Manager (RevMan) [Computer program]. Version 5.4, The Cochrane Collaboration, 2020). Where data was not available in the article or from the authors, the Cochrane methods for missing data were followed [15]. All pooled outcome measures were determined using the DerSimonian and Laird's random-effects model [16]. Heterogeneity in the results of the studies was assessed using a chi-square test of heterogeneity (significance level p < 0.1) and the I<sup>2</sup> measure of inconsistency [17].

# Results

# **Study Selection**

The search generated a total of 158 articles. A total of 17 articles were duplicates and therefore removed (Fig. 1). After assessment, seven articles met the inclusion criteria and were considered for systematic review and included in





the meta-analysis. All included articles reported on cohort studies.

### **Basic Demographics**

A total of seven studies [18] [19] [20] [21] [22] [23] [24] provided data on 334 male patients (Table 1). The mean age was 43.9 years and the mean follow up was 15.9 months. The bariatric surgery techniques used across the studies included: sleeve gastrectomy (196 patients), Roux-en-Y gastric bypass (92), and sleeve gastrectomy with duodeno-jejunal bypass [19]. The reported procedure types in Aleid et al. study [18] were laparoscopic sleeve gastrectomy, gastric bypass, and gastric band but no number per procedure was recorded. A total of 23 out of 70 patients were men in Luke et al.'s included cohort [21] but the numbers and types of procedures (mixture of sleeve gastrectomy and bypass procedure) was not clear from the manuscript. The pre-operative mean BMI for the total study population was

44.4 kg/m2. The preoperative mean IPSS score was 6.78.

## **Quality Assessment of Included Studies**

Studies were assessed for bias and methodological quality using the MINORS criteria (Table 2). All studies were graded as low-moderate in quality.

### Outcomes

#### Change in IPSS

All seven studies [18] [19] [20] [21] [22] [23] [24] used IPSS for the quantitative assessment of lower urinary tract symptoms in men before and after bariatric surgery. IPSS score ranged from 3 to 12.7 preoperatively and 1.9 to 6.9 postoperatively. LUTS demonstrated statistically significant improvement following weight loss surgery (Fig. 2) (MD 2.82, 95% CI 0.96 to 4.69,

Table 1	Details of th	Table 1Details of the studies included in the meta-analysis	led in the	meta-analysis							
Studies	Year of Study publication period		Country	Country Study type	Number Age of (mea patients +/- S	Age (mean +/- SD)	Operations performed	Number of patients followed Longest for postoperative assessment follow-up (months)	Longest follow-up (months)	Mean preoperative BMI (+/-SD)	Mean postoperative BMI (+/-SD)
Liu	2020	2012–2019 China		Prospective cohort study	143	43 +/- 10.4	Sleeve gastrectomy, gastric bypass	70 (15 lost to follow-up, remainder not at 3 years postoperative)	36	39.1 +/- 5.2 31.5 +/- 4.9	31.5 +/- 4.9
Fujisaki	2019	2013-2014 Japan		Retrospective cohort study	45	40 (26 73)	Gastric bypass, sleeve gastrectomy, sleeve gastrectomy with duodenoieiunal bypass	45	12	40.8 (28.3–77.2)	29.1
Aleid	2017	2013–2015 United King dom	э.	Prospective cohort study	14	49.1 +/- 9.8	Ľ	14	6	45 (37.9–69.5) 37.5 +/- 7.1	37.5 +/- 7.1
Uruc	2016	2014-2015 Turkey		Prospective cohort study	22	34.59 +/- 8.1	Laparoscopic sleeve gastrectomy	22	11	49.57 +/- 6.2 38.98 +/- 5.5	38.98 +/- 5.5
Groutz	2016	Not Is reported	Israel	Prospective cohort study	53	39 +/- 12.5	Laparoscopic sleeve gastrectomy	44 (12 excluded for no LUTS)	3	42.8+/-5.3	31.3 +/- 5.4
Luke	2014	2009–2011 New Ze nd	New Zeala- nd		23	49.06 +/- 9.7	Laparoscopic and open gastric bypass, laparoscopic sleeve gastrectomy	23	12	46.04+/-6.6	33.24
Ranasinghe 2010	le 2010	2001–2009 <i>i</i>	Australia	2001–2009 Australia Retrospective cohort study	34	52.8 +/- 9.3	52.8 +/- Laparoscopic gastric bypass 9.3	34	31.8	47.3+/-12.7	38.4+/-6.2

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Table 2.Assessment ofMINORS criteria

Criteria	Study						
	Ranasinghe 2010	Luke 2014	Groutz 2016	Uruc 2016	Aleid 2017	Fujisaki 2019	Liu 2020
A clearly stated aim	2	2	2	2	2	2	2
Inclusion of consecutive patients	2	2	2	2	2	2	2
Prospective data collection	1	2	2	2	2	1	2
Endpoint appropriate to the study	2	2	2	2	2	2	2
Unbiased assessment of the study endpoint	1	1	1	1	1	1	1
Follow up period appropriate to the aim of the study	2	2	1	2	2	2	2
Loss of follow up less than 5%	1	1	0	0	1	0	1
Prospective calculation of study size	0	0	0	0	0	0	2
An adequate control group	0	0	0	0	0	0	0
Contemporary groups	0	0	0	0	0	0	0
Baseline equivalence of groups	0	0	0	0	0	0	0
Adequate statistical analysis	2	2	2	2	2	2	2
Total	13	14	12	13	14	12	16

0, not reported; 1, reported but inadequate; 2, reported and adequate

p=0.003). Heterogeneity between studies was high (I<sup>2</sup> = 89%) and statistically significant (p<0.00001).

#### Mean BMI Change

There was statistically significant reduction in mean BMI following bariatric surgery (Fig. 3) (MD 9.41, 95% CI 7.67 to 11.15, p<0.00001). Heterogeneity was moderate (I<sup>2</sup> = 58%) and statistically significant (p=0.03).

#### Mean TBW Change

Four of the studies [21] [22] [23] [24] included in the metaanalysis reported change in the mean TBW. TBW was shown to be statistically significantly lower after bariatric surgery (Fig. 4) (MD 28.33, 95% CI 21.10 to 35.57, p<0.00001). Heterogeneity was moderate (I<sup>2</sup> = 54%) and statistically significant (p=0.09).

# Discussion

This study reports the first meta-analysis of the impact of bariatric surgery on lower urinary tract symptoms in men. Seven studies were included reporting on 334 male patients who underwent a range of bariatric procedures such as Rouxen-Y gastric bypass, sleeve gastrectomy, sleeve gastrectomy with duodenojejunal bypass, and gastric band. All studies used the internationally validated IPSS questionnaire for the assessment of lower urinary tract symptoms in men meaning that the assessments are robust and uniform across the total study population and can be directly applicable to a wider population.

This meta-analysis demonstrated a statistically significant improvement in LUTS following bariatric surgery in male patients with obesity. The observed mean change in IPSS was 2.82 points. Barry and colleagues reported that the minimal clinically perceptible change in IPSS score is 3.1 points;

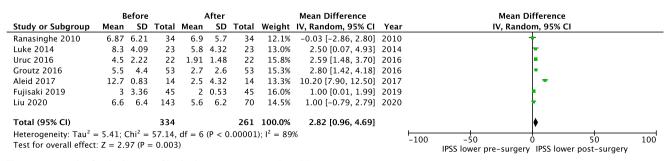


Fig. 2. Forest plot for the impact of bariatric surgery on LUTS (IPSS score)

Before bariatric surgery				After bariatric surgery			Mean Difference		Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDEFG
Uruc 2016 49.57 6.21 22 38.98 5.51 22								10.59 [7.12, 14.06]	-	
Ranasinghe 2010	47.3	12.67	34	38.4	6.18	34	9.2%	8.90 [4.16, 13.64]	+	
Luke 2014	46.04	6.63	23	38.24	5.81	23	12.8%	7.80 [4.20, 11.40]	· · · · · · · · · · · · · · · · · · ·	
Liu 2020	39.1	5.2	143	31.5	4.9	143	25.3%	7.60 [6.43, 8.77]		
Groutz 2016	42.8	5.3	53	31.3	5.4	53	20.5%	11.50 [9.46, 13.54]		
Fujisaki 2019	40.8	12.23	45	29.1	5.81	45	11.5%	11.70 [7.74, 15.66]	+	
Aleid 2017	45	7.9	14	37.5	7.1	14	7.3%	7.50 [1.94, 13.06]		
Total (95% CI)			334			334	100.0%	9.41 [7.67, 11.15]	•	
Heterogeneity: $Tau^2 = 2.76$ ; $Chi^2 = 14.38$ , $df = 6$ (P = 0.03); $l^2 = 58\%$ Test for overall effect: Z = 10.61 (P < 0.0001)										
BMI lower pre-surgery BMI lower post-surgery										surgery

Fig. 3. Forest plot for the impact of bariatric surgery on BMI

however, this was considered to be strongly influenced by the baseline IPSS score [25]. Men who had a baseline score of less than 20 rated their lower urinary tract symptoms as slightly improved when the mean difference was 2 points, whereas men with a baseline score of 20 or above required mean reduction of IPSS score with 6 points to achieve similar improvement of symptoms.

The link between obesity and lower urinary tract symptoms in males has been demonstrated in multiple studies [4] [26] [27] [28]. Some authors suggest a strong association between waist circumference, high BMI, metabolic syndrome and BPH [4] [26]. One potential mechanism is a faster rate of BPH progression due to elevated insulin levels in patients with type 2 diabetes, raised BMI and waist circumference [26]. Another explanatory mechanism may be that weight loss reduces urinary frequency and volume through improved kidney function [29]. Alternatively, Zuchetto et al. propose a theory that BPH in men with obesity is a consequence of obesity-related hormonal changes including increase of oestrogens and decrease of testosterone levels as a result of peripheral aromatisation of androgens in the adipose tissue [28]. A fourth potential etiology of the development or worsening of lower urinary tract symptoms in obesity is atherosclerotic disease in the presence of metabolic syndrome. This could lead to ischemia-related changes such as fibrosis which may cause bladder dysfunction [30] [31]. Prospective studies incorporating objective urodynamic measures and correlating these to postoperative weight loss would additionally assist with determining mechanisms of symptomatic improvement.

The mechanisms through which bariatric surgery leads to improvement of voiding function are not completely known. Other weight loss lifestyle modifications such as healthy diet and increased physical activity, are also likely to improve LUTS in patients with obesity. Khoo et al. report that an 8week low-calorie diet led to significant alleviation of LUTS and improved sexual function in 68 men with obesity. This was also associated with improved plasma testosterone levels and insulin sensitivity [9]. However, bariatric surgery is the most effective way of weight loss, reduction in BMI, and waist circumference, and also treatment of other obesityrelated comorbidities [32] [33]. Addressing the forementioned potential pathophysiological mechanisms of development of lower urinary tract symptoms in obesity could lead to their improvement as demonstrated in our meta-analysis.

This study's findings should be considered in light of its limitations. Despite a comprehensive search, the literature surrounding this topic is limited. This current study identified only seven studies which met the inclusion criteria and were included in the final meta-analysis. This may limit the generalisability of the findings of this study. However, the use of an internationally validated questionnaire to assess the primary study outcome may counteract this. While IPSS is validated and accepted for measurement of LUTS, it does not fully assess all urinary symptoms which may impact quality of life including not capturing stress incontinence [34]. The mean follow-up was 15.9 months with three studies [18] [19] [22] which had less than 12-month follow-up. This may be insufficient time to observe the durability of LUTS improvement and long-term effects of bariatric surgery, particularly as maximal weight loss occurs around two years following bariatric surgery [35]. Loss to follow-up was only described in two of the studies [19] [24], with one of those reporting on different numbers of patients at the baseline and 3-year postoperative assessment [19]. None of the included studies complemented the IPSS assessment with a more objective urological functional assessment such as urinary flow rate or bladder residual volume measurement. Furthermore, the quality of the selected studies which was assessed using the

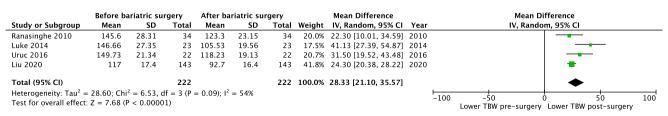


Fig. 4 Forest plot for the impact of bariatric surgery on total body weight

MINORS criteria was low-moderate with relatively small sample size and retrospective data collection. Finally, none of the studies had a comparator group of only lifestyle modifications, nor subgroup analysis performed to compare results depending on type of bariatric procedure.

Regardless of these limitations, this study is a thorough analysis which confirms that bariatric surgery produces a significant improvement on lower urinary tract symptoms in men with obesity. Greater clarification could be offered by larger age- and LUTS severity-stratified prospective studies with complementary objective urodynamic physiological assessments. Further studies are necessary to investigate in detail the pathophysiological mechanisms, including prostate volume and function, through which lower urinary tract symptoms develop in male patients with obesity, and their improvement following weight loss surgery.

Author Contribution IS, ACC, WH, and CP were involved in research design. IS, ACC, and RCN were involved in data acquisition. All authors were involved in data interpretation, production of the manuscript, and critical revisions. All authors approved the final submitted manuscript.

#### Declarations

**Ethical Approval** This study was a systematic review of published research; therefore, no ethical or governance approvals were required.

Conflict of Interest The authors declare no competing interests.

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