Early effect of bariatric surgery on urogenital function in morbidly obese men

Maha Aleid, PhD[1], Asif Muneer, BSc (Hons) MB, FRCSEd, FRCS(Eng), MD, FRCS(Urol)[2], Sara Renshaw, MBSS, MA(Cantab), MRCS, FHEA[2], Jason George, MBSS, MA(Cantab), MRCS, FHEA[2], Andrew Jenkinson, MBBS, MS, FRCS[2], Marco Adamo, MMBS[2], Mohamed Elkalaawy, MS, MD[2,3], Rachel L Batterham, MBBS, PhD[2,4], David J Ralph, BSc MS FRCS(Urol)[2], Majid Hashemi, MD, FRCS[2] and Selim Cellek[*], MD, PhD[5]

1. Cranfield University, Bedfordshire, MK43 0AL, UK
2. University College London Hospital, London, NW1 2BU, UK
3. University of Alexandria, Alexandria 21561, Egypt
4. University College London, London, WC1E 6JF, UK
5. Anglia Ruskin University, Essex, CM1 1SQ, UK

***Corresponding author:** Prof. Selim Cellek, Anglia Ruskin University, Faculty of Medical Science, Bishop Hall Lane, Chelmsford, Essex, CM1 1SQ, United Kingdom; selim.cellek@anglia.ac.uk

Running head: Early effect of bariatric surgery on ED and LUTS

Keywords: bariatric surgery, weight loss, erectile dysfunction, lower urinary tract symptoms, body mass index

Abstract:

Introduction: Obesity is an independent risk factor for erectile dysfunction (ED) and lower urinary tract symptoms (LUTS). Bariatric surgery has been shown to improve erectile function and urinary symptoms in previous medium to long term studies (3-12 months post-operative follow up).

The aim: is to investigate the early effect (1 month post-op) of bariatric surgery on ED and LUTS which has not previously been investigated.

Methods: Morbidly obese men (BMI >35 kg/m^2) undergoing bariatric surgery were asked to complete International Index of Erectile Function (IIEF) and International Prostate Symptom Score (IPSS) questionnaires before the surgery and 1, 3 and 6 months after the surgery.

Main outcome measure: The influence of bariatric surgery on urogenital function, BMI, fasting blood glucose (FBG) and HbA1C were analysed using parametric and non-parametric tests for paired samples.

Results: Out of 30 patients who have completed the study, 18 reported erectile dysfunction (ED; IIEF<25) and 14 reported moderate-severe LUTS (IPSS ≥8) before the operation. 12 patients had both ED and moderate-severe LUTS. IIEF, IPSS, BMI, percentage weight loss, FBG and HbA1c all improved significantly and rapidly after the bariatric surgery starting at the 1 month post-operative time point and continued to improve throughout the study in all patients with ED or moderate to severe LUTS.

Conclusions: This is the first study showing improvement in erectile and urinary function within 1 month after the bariatric surgery; an effect that was in parallel with glycaemic improvement and weight loss.

Introduction:

According to the World Health Organisation definition, overweight (BMI≥25 kg/m^2) and obesity (BMI≥30 kg/m^2) is an abnormal or excessive fat accumulation that may impair overall health [1,2] . With an increasing number of overweight or obese people globally, obesity has now been recognised as an epidemic affecting the health of populations mainly through obesity-related diseases such as Type 2 diabetes, cardiovascular diseases and stroke [1,3]. It is therefore not surprising that obesity has been identified as an independent risk factor for erectile dysfunction (ED) and lower urinary tract symptoms (LUTS) [4-8].

Corona et al. (2009) suggested that obesity is directly related to lower androgen levels in men who suffer from ED, and that obesity related comorbidities, particularly hypertension, are considered significant causes of arteriogenic obesity-related ED 9. The association between obesity and ED can be partly explained through increased levels of various pro-inflammatory cytokines in obese people [10]. These signs of inflammation have a strong connection with endothelial dysfunction, which is directly related to ED through the nitric oxide pathway [11]. Similarly LUTS has been suggested to be caused by microvascular dysfunction [12] which can be observed in obese men 13. Other hypotheses for LUTS in obesity are increased oestrogen to testosterone ratio [4], which may play a role in prostate tissue hyperplasia, increased prostate volumes [14] and increased sympathetic nervous system activity 15.

Weight loss either through non-surgical methods (i.e. diet, medication, exercise) or surgical methods (i.e. bariatric surgery) has been shown to improve both erectile [16,17] and urinary function [1618]. The improvement following bariatric surgery has been more effective and longer-lasting than the non-surgical approaches [17]. Previous studies on the effect of bariatric surgery on ED and LUTS have investigated time points 3-12 months and over after the surgery. Although all of these studies have shown a significant improvement in erectile [16,19,20,21,22] and urinary function [19,22] , the improvement was parallel to the weight loss. The patients had achieved significant weight loss while their urogenital function improved.

It is known that bariatric surgery can have an acute glycaemic effect: as short as 48 hours after the operation, the patients are known to have improved blood glucose levels [3,23,24,25]. Hence bariatric surgery has been coined as a "*surgical treatment for diabetes*" [26]. Although the exact mechanism of this phenomenon is currently unknown, this suggests that glycaemic improvement may potentially precede weight loss after the bariatric surgery in the early post-operative phase. We therefore assessed the urogenital function of morbidly obese men (BMI>35 kg/m^2 with obesity-related comorbidity) pre-operatively and at 1, 3 and 6 months after bariatric surgery.

Materials and Methods:

Patient selection: Male patients listed for bariatric surgery who had BMI >35 kg/m^2 with obesity-related comorbidity or BMI >40 kg/m^2 [2], age over 30 years (47.2 ±8.1) and were able to read and understand the questionnaires were included in the study from February 2013 to July 2015. Patients were excluded if they were not sexually active or were younger than 30 or older than 75. None of the patients were treated or had received prior treatment for ED or LUTS.

Data collection: The patients were given International Index of Erectile Function (IIEF) 27 and International Prostate Symptom Score (IPSS) 28 questionnaires to complete, their weight and height were measured and venous blood was drawn from the study participants following UCLH guidelines to measure fasting blood glucose (FBG) and glycated haemoglobin (HbA1c) concentrations were measured using hexokinase method and cation exchange chromatography respectively 1 month before the surgery and 1, 3 and 6 months after the surgery.

Data analysis: Statistical analysis was performed using the statistical software SPSS version 22 (SPSS Inc., Chicago, IL, USA) for Windows, to perform exploratory data analysis and produce descriptive statistics. Normal distribution was assessed using skewness test [29]. Non-normally distributed data are presented as median and interquartile range (IQR) while normally distributed data are presented as mean ± standard deviation. Non-parametric Wilcoxon signed rank test was used to compare repeated measurements between two time points for non-normally distributed data. Paired t-test was used to compare repeated measurements between two time points for normally distributed data. Mann Whitney U test was performed to compare the differences between the two groups for non-normally distributed data 29. Percentage of total weight loss (%TWL) was used in order to describe the weight loss after bariatric surgery [30].

Ethical considerations: The data was collected from a planned clinical audit at XXXXXXX. The project was approved by Ethics Committee of XXXXX University XXXXXX (XXXXXX 03.13 on 13th February 2013). Informed written consent was obtained from all patients.

Results:

Baseline characteristics: ED vs NO-ED

49 patients were initially assessed for the study, 14 of them withdrew from the study and 5 were found to be not sexually active. The remaining 30 patients that were included in the study were arbitrarily divided into NO-ED (IIEF erectile function domain score >25; n=12) and ED (IIEF erectile function domain score ≤25; n=18) groups. The baseline characteristics of the two groups are shown in Table 1. The IIEF scores in all domains were lower in ED group than NO-ED group. IPSS scores were higher in ED group than NO-ED group except in frequency, intermittency, strain and nocturia. There was no significant difference between the two groups in age, BMI, FBG and HbA1c (Table 1).

Baseline characteristics: No-Mild LUTS vs Moderate-Severe LUTS

When a similar analysis was performed based on their IPSS scores, the patients were arbitrarily divided into two groups: No LUTS or mild LUTS (NO-MILD LUTS group; total IPSS score < 8; n=16) and moderate or severe LUTS (MODERATE-SEVERE LUTS group; total IPSS score ≥ 8; n=14). The baseline characteristics of the two groups are shown in Table 2. The patients in MODERATE-SEVERE LUTS group were older and had lower scores in total IIEF, erectile function, intercourse satisfaction and overall satisfaction domains than NO-MILD LUTS group. In all IPSS domains MODERATE-SEVERE LUTS group had higher scores than NO-MILD LUTS groups. There was no significant difference between the two groups in BMI, FBG and HbA1c (Table 2).

Surgery types:

All patients underwent laparoscopic sleeve gastrectomy, laparoscopic gastric bypass or laparoscopic gastric band operations. There was no statistical difference between the ED or NO-ED groups with respect to the type of operation they received. Within the ED group 44.4%, 33.3% and 22.3% of patients received sleeve, bypass and band respectively. The percentages were 41.6%, 25.1% and 33.3% for sleeve, bypass and band respectively for the patients in NO-ED group (P=0.421). Similarly there was no difference between NO-MILD LUTS and MODERATE-SEVERE LUTS groups with respect to the type of operation they received (P=0.89). Within the NO-MILD LUTS group 43.8%, 31.3% and 25.0% of patients received sleeve, bypass and band respectively. The percentages were 42.9%, 28.6% and 28.6% for sleeve, bypass and band respectively for the patients in MODERATE-SEVERE LUTS group.

Effect of bariatric surgery on BMI and %TWL:

In both ED and NO-ED groups, a significant decrease in BMI (Figure 1A) and increase in %TWL (Figure 1B) was observed after the surgery. The weight loss reached statistical significance at 1 month and continued throughout to 6 months (Figure 1). There was no statistically significant difference between ED and NO-ED groups at any time points.

Similarly when the patients were divided into NO-MILD LUTS and MODERATE-SEVERE LUTS groups, a significant decrease in BMI (Figure 2A) and a significant increase in %TWL (Figure 2B) were observed after the surgery (P<0.01). The weight loss reached statistical significance at 1 month and continued throughout to 6 months (Figure 2). There was no statistically

significant difference between NO-MILD LUTS and MODERATE-SEVERE LUTS groups at any time points.

Effect of bariatric surgery on erectile function:

In the ED group, the surgery caused a significant increase in the total IIEF score at 3 months; the median of the baseline, 1, 3 and 6 months post-operation total IIEF scores were 35.0 , 39.0 , 60.0 and 66.5 respectively (1, 3 and 6 months significantly different from baseline, (P=0.02, P=0.001 and P<0.001 respectively; Figure 3A). The earliest increase within the domains was observed in erectile function and intercourse satisfaction domains starting at 1 month (Figure 3B and 3C). The increase in the other domains (orgasmic function, sexual desire and overall satisfaction) reached significance at 3 months and further increased at 6 months (Figure 3C).

In the NO-ED group, while patients started with high scores pre-operatively, the median of the total IIEF scores were 68.5 , 68.5 , 72.0 and 72.0 pre-operatively, 1, 3, and 6 month post-operatively respectively with no significant changes (Figure 3A). Although a decrease in erectile function domain score was observed at 1 month post-operatively (Supplementary Figure 1A), the change was not statistically significant. The only significant increase was observed in sexual desire and intercourse satisfaction domains at 6 months (Supplementary Figure 1B).

In the MODERATE-SEVERE LUTS group, the median of total IIEF scores were 32.5 , 32.0 , 59.0 and 66.0 at the baseline and 1, 3 and 6 months post-operatively respectively showing a significant increase at 3 and 6 months from baseline (P=0.003 and P=0.002 respectively; Supplementary Figure 2A). All domains showed a significant improvement after the surgery; erectile function, intercourse satisfaction and overall satisfaction improved at 1 month while the other domains reached significance at 3 months (Supplementary Figure 2B and 2C).

In the NO-MILD LUTS group, although total IIEF scores were high pre-operatively, a significant increase was still observed at 3 and 6 months post-operatively (the median of the total IIEF scores were 64.5 , 57.0 , 72.0 and 71.5 pre-operatively, 1, 3, and 6 month post-operatively respectively with significant changes at 3 and 6 months (P=0.02, P=0.015; Supplementary Figure 2A). The significant changes were observed in desire, intercourse satisfaction, orgasmic function and overall satisfaction domains at 6 months post-operative time points (Supplementary Figure 2B and 2C).

In overall, out of 18 patients with ED (total IIEF score <25) before the surgery, 4, 8 and 12 of them were re-classified as NO-ED at 1, 3 and 6 months post-operatively respectively.

Effect of bariatric surgery on urinary function:

In the ED group, a significant improvement in total IPSS score was observed: the median total IPSS scores were 12.5, 8.5, 4.0 and 2.0 for pre-operative and 1, 3 and 6 months post-operative time points (P=0.002, P=0.001 and P=0.001) respectively (Figure 4A). The improvements in frequency, intermittency, weak stream, nocturia and quality of life domain scores were observed at 1 month which further improved throughout the study. The decrease in urgency

and incomplete emptying domain scores reached significance at 3 months. There was no significant change in straining domain score throughout the study (Figure 4B).

In the NO-ED group, with most of the patients starting with near normal low scores, the only effects of surgery observed were a significant increase in quality of life domain score at 1 month which decreased back to normal at 3 months and a significant decrease in nocturia domain score at 6 months (Supplementary Figure 3).

In MODERATE-SEVERE LUTS group, a significant decrease in total IPSS score was observed: the total median scores were 14.5, 11.0, 7.0 and 2.5 for pre-operative and 1, 3 and 6 months post-operative time points respectively (P=0.001, P<0.001 and P<0.001; Figure 5A). Significant improvements in frequency, intermittency, weak stream and nocturia domains were observed at 1 month post-operatively while the other domains (incomplete emptying, urgency and quality of life) reached significance at 3 months (Figure 5B). In straining domain, a significant improvement was observed at 3 months which did not continue at 6 months (Figure 5B).

In NO-MILD LUTS group, the IPSS scores were low pre-operatively. A further decrease in total IPSS score was observed but this was not significant. Significant improvements in nocturia and urgency domains were observed at 3 and 6 months post-operative time points. There were no significant changes in any of the other domains at any time points (Supplementary Figure 4).

In overall, out of 14 patients with MODERATE-SEVERE LUTS (total IPSS score ≥8) before the surgery, 1, 7 and 9 of them were re-classified as NO-MILD LUTS at 1, 3 and 6 months post-operatively.

Effect of bariatric surgery on glycaemic indices:

At baseline, 7 (39%) and 11 (61%) patients with ED (n=18) had FBG and HbA1c levels above the normal range respectively (5.8 mmol/l and 42 mmol/mmol respectively). In NO-ED group (n=12) the number of patients above the normal range were 5 (42%) and 6 (50%) respectively; there was no statistical difference between the two groups (P>0.05). In both ED and NO-ED groups, a decrease in FBG and HbA1c concentrations was observed after the surgery starting at 1 month and with a further decrease throughout the study. The decrease in FBG reached significance at 1 month in ED group while at 6 months in NO-ED group. The decrease in HbA1c reached significance at 1 month in both ED and NO-ED groups (Figure 6A and 6B).

In both NO-MILD LUTS and MODERATE-SEVERE LUTS groups, a decrease in FBG and HbA1c concentrations was observed after the surgery starting at 1 month and with a further decrease throughout the study (Figure 7A and B).

Interestingly, although the decrease in HbA1c in ED or MODERATE-SEVERE LUTS groups was significant, it was not sufficient to bring the HbA1c levels below the recommended threshold (42 mmol/mmol). This was achieved in NO ED or NO-MILD LUTS groups (Figure 6B and 7B).

Discussion:

Bariatric surgery, whether gastric bypass or sleeve banding, resulted insignificant weight loss as early as 1 month in our study. By 6 months, all of the patients have almost reached 20-25% weight loss which is comparable to other studies with similar post-operative follow up duration [16,22,31,32,33].

Previous studies investigating the effect of bariatric surgery on erectile function have shown a significant improvement at the earliest time point of 12 months [16202122]. A longer study of 10 years has shown a decline in erectile function most probably due to ageing [34]. A recent study has shown a significant effect at 3 months [22]. The authors have demonstrated a significant improvement in all domains of IIEF questionnaire at 3 months post-operatively. This is in accordance with our findings where all of the domains reached significant improvement at 3 months. Interestingly at 1 month, only erectile function and intercourse satisfaction were significantly improved in our study.

Several studies suggested the reasons behind the improvement in sexual function after bariatric surgery; Mora and colleagues (2013) suggested that this was, due to the weight reduction occurring after bariatric surgery further than the parallel improvement in testosterone level and metabolic profiles such as insulin sensitivity, C-reactive protein and lipid profile 21. Reis et al suggested the role that oestrogens may play in erectile function since they show a significant increase in the hormone levels with BMI reduction following bariatric surgery 16. Another factor suggested for this improvement is the acute reduction of FBG 22.

A correlation of testosterone and other hormone levels to erectile function has been suggested by previous studies [3237]. According to Corona *et al.* (2016) meta-analysis shows that testosterone has a principal role in controlling male sexual desire and hormone replacement therapy can improve low desire and erectile dysfunction in hypogonadal individuals 38. Hormone levels were not measured in our study which should be highlighted as a limitation. Likely, the acute improvement in intercourse satisfaction after one month post-operative in our study might be due to psychosocial reasons, which may have improved after the weight loss [39,40]. Sexual desire was the least improved domain in our study. This can be explained by the effect of major surgery on the patient's overall wellbeing (i.e. patients may be feeling tired after the surgery hence not interested in sex).

Most of the previous studies investigating the effect of bariatric surgery on urinary function have focused on urinary incontinence and overactive bladder symptoms in women [4142]. The studies on bariatric surgery and LUTS in men are limited. A recent study looked into the IPSS scores of men at 6 weeks and 1 year following bariatric surgery. They found significant weight loss and improvement in urgency and frequency at 6 weeks [43]. Although we have observed significant improvement in frequency, intermittency, weak stream, nocturia and quality of life in 1 month after the surgery in ED group, the improvement in urgency did not reach significance until 3 months. This may be due to the difference in statistical methods employed in the two studies; furthermore Luke et al did not stratify their patients according to their IIEF scores. Nevertheless, the significant improvement in IPSS scores in ED group but not in NO-ED group which had near normal scores before the operation further highlights the

importance of the link between ED and LUTS and the necessity of investigating both erectile and urinary function together in men with obesity.

It was interesting to observe that fasting blood glucose and HbA1c levels were reduced significantly and rapidly after the bariatric surgery in all patients. Such an acute glycaemic improvement following bariatric surgery has been reported previously [2326]. We have observed in our study that the decrease in HbA1c levels in the patients with ED or MODERATE-SEVERE LUTS was not as dramatic as other patients. Although it is very difficult to draw any conclusions from such a small group of patients, this may be due the fact that these patients may have had high HbA1c levels longer than the others which may be one of the underlying causes of their urogenital dysfunction.

Several limitations to our study merit further discussion. The small sample size of the study groups might have overestimated the correlations between variables. Another important consideration is that the study patients may not be a random sample of the male morbidly obese population due to the lack of randomisation. However, the groups (ED vs NO-ED and NO-MILD LUTS vs MODERATE-SEVERE LUTS) were well matched for pre-operative patient characteristics. The lack of a control group in the study prevents the assessment of the prevalence of impaired sexual function in patients who did not undergo bariatric surgery over time. Moreover, it is known that serum testosterone and aromatase enzyme levels are crucial in determining erectile and urological function and that obesity can influence such levels [44]. Measurement of serum testosterone and aromatase levels at the same time points would add further to our understanding of the mechanism underlying the observed improvements in function.

Conclusions:

ED and LUTS are commonly observed in obese men. Bariatric surgery may possibly improve erectile and urinary function as well as glycaemic indices. Our study is the first study showing such improvement in both functions as early as 1 month following bariatric surgery.

Acknowledgements:

Maha Aleid was supported with a scholarship from King Faisal Specialist Hospital and Research Centre. Preliminary results from this study were presented at European Society for Sexual Medicine Congresses in 2015 and 2016.

References:

1. World Health Organisation. Obesity: preventing and managing the global epidemic. Technical Report Series- WHO 2000;894.
2. NICE. Obesity: identification, assessment and management, https://www.nice.org.uk/guidance/cg189/chapter/introduction ;2014 [accessed 03.05.2015].
3. Wickremesekera K, Miller G, DeSilva Naotunne T, Knowles G, Stubbs R.S. Loss of insulin resistance after Roux-en-Y gastric bypass surgery: A time course study. Obesity Surgery 2005;15:474-81.
4. Giovannucci E, Rimm E.B, Chute C.G, Kawachi I, Colditz G.A, Stampfer M.J, Willett W.C. Obesity and benign prostatic hyperplasia. American Journal of Epidemiology 1994;140:989-1002.
5. Esposito K, Giugliano D. Obesity, the metabolic syndrome, and sexual dysfunction. International Journal of Impotence Research 2005;17:391-8.
6. Kristal A.R, Arnold K.B, Schenk J.M, Neuhouser M.L, Weiss N, Goodman P, Antvelink C.M, Penson D.F, Thompson I.M. Race/ethnicity, obesity, health related behaviors and the risk of symptomatic benign prostatic hyperplasia: results from the prostate cancer prevention trial. The Journal of urology 2007;177:1395-400.
7. O'Brien P.E. 2010. Bariatric surgery: Mechanisms, indications and outcomes. Journal of gastroenterology and hepatology 2010;25:1358-65.
8. Lee R.K, Chung D, Chughtai B, Te A.E, Kaplan S.A. Central obesity as measured by waist circumference is predictive of severity of lower urinary tract symptoms. BJU international 2012;110:540-5.
9. Corona G, Mannucci E, Forti G, Maggi M. Hypogonadism, ED, metabolic syndrome and obesity: a pathological link supporting cardiovascular diseases. International journal of andrology 2009;32:587-98.
10. Traish A.M, Feeley R.J and Guay A. Mechanisms of obesity and related pathologies: Androgen deficiency and endothelial dysfunction may be the link between obesity and erectile dysfunction. FEBS Journal 2009;276:5755-67.
11. Hammoud A.O, Gibson M, Peterson C.M, Hamilton B.D, Carrell D.T. Obesity and male reproductive potential. Journal of andrology 2006;27:619-26.
12. Cellek S, Cameron N. E, Cotter M. A, Fry C. H, Ilo D. Microvascular dysfunction and efficacy of PDE5 inhibitors in BPH-LUTS. Nature Reviews Urology 2014;11:231-41.
13. Boillot A, Zoungas S, Mitchell P, Klein R, Klein B, Ikram M. K, Neubauer A. S. Obesity and the microvasculature: a systematic review and meta-analysis. PloS one 2013;8:e52708.
14. Muller R. L, Gerber L, Moreira D. M, Andriole G, Hamilton R. J, Fleshner N, Freedland S. J. Obesity is associated with increased prostate growth and attenuated prostate volume reduction by dutasteride. European urology 2013;63:1115-21.

15. Vignozzi L, Gacci M, Cellai I, Santi R, Corona G, Morelli A, Rastrelli G, Comeglio P, Sebastanelli A, Maneschi E, Nesi G. Fat boosts, while androgen receptor activation counteracts, BPH-associated prostate inflammation. The prostate 2013;73:789-800.
16. Reis L.O, Favaro W.J, Barreiro G.C, De Oliveira L.C, Chaim E.A, Fregonesi A, Ferreira U. Erectile dysfunction and hormonal imbalance in morbidly obese male is reversed after gastric bypass surgery: A prospective randomized controlled trial. International journal of andrology 2010;33:736-44.
17. Gloy V.L, Briel M, Bhatt D.L, Kashyap S.R, Schauer P.R, Mingrone G, Bucher H.C, Nordmann A.J. Bariatric surgery versus non-surgical treatment for obesity: a systematic review and meta-analysis of randomised controlled trials. BMJ (Clinical research edition) 2013;347:f5934.
18. Randall J, Slater M, Stewart A, Pugh G, Lewis K, Levy C, Alessandri-Gray P. The Effectiveness of Non-Surgical Weight Management Interventions for Obesity in the UK: A Review and Meta-Regression Analysis. Open Journal of Medical Psychology 2014;3:235.
19. Kuruba R, Almahmeed T, Martinez F, Torrella T.A, Haines K, Nelson L.G, Gallagher S.F, Murr M.M. Bariatric surgery improves urinary incontinence in morbidly obese individuals. Surgery for Obesity and Related Diseases 2007;3:586-90.
20. Dallal R.M, Chernoff A, O'Leary M.P, Smith J.A, Braverman J.D, Quebbemann B.B. Sexual Dysfunction Is Common in the Morbidly Obese Male and Improves after Gastric Bypass Surgery. Journal of the American College of Surgeons 2008;207:859-64.
21. Mora M, Aranda G.B, De Hollanda A, Flores L, Puig-Domingo M, Vidal J. Weight loss is a major contributor to improved sexual function after bariatric surgery. Surgical Endoscopy and Other Interventional Techniques 2013;27:3197-204.
22. Groutz A, Gordon D, Schachter P, Amir H, Shimonov M. Effects of bariatric surgery on male lower urinary tract symptoms and sexual function. Neurourology and urodynamics 2016.
23. Pournaras D.J, Osborne A, Hawkins S.C, Vincent R.P, Mahon D, Ewings P, Ghatei M.A, Bloom S.R, Welbourn R, Le Roux C.W. Remission of type 2 diabetes after gastric bypass and banding: Mechanisms and 2 year outcomes. Annals of Surgery 2010;252:966-71.
24. Rizzello M, Abbatini F, Casella G, Alessandri G, Fantini A, Leonetti F, Basso N. Early postoperative insulin-resistance changes after sleeve gastrectomy. Obesity Surgery 2010;20:50-5.
25. Basso N, Capoccia D, Rizzello M, Abbatini F, Mariani P, Maglio C, Coccia F, Borgonuovo G, De Luca M.L, Asprino R, Alessandri G, Casella G, Leonetti F. First-phase insulin secretion, insulin sensitivity, ghrelin, GLP-1, and PYY changes 72 h after sleeve gastrectomy in obese diabetic patients: The gastric hypothesis. Surgical Endoscopy and Other Interventional Techniques 2011;25: 3540-50.
26. Dixon J.B, Le Roux C.W, Rubino F, Zimmet P. Bariatric surgery for type 2 diabetes. The Lancet 2012a; 79:2300-11.
27. Rosen R.C, Riley A, Wagner G, Osterloh I.H, Kirkpatrick J, Mishra A. The international index of erectile function (IIEF): A multidimensional scale for assessment of erectile dysfunction. Urology 1997;49:822-30.

28. Plante M, Corcos J, Gregoire I, Belanger M.F, Brock G, Rossingol M. The International Prostate Symptom Score: Physician versus self- administration in the quantification of symptomatology. Urology 1996;47:326-8.
29. Groeneveld, RA, Meeden, G. Measuring skewness and kurtosis. The Statistician 1984, pp 391-399.
30. Sczepaniak J.P, Owens M.L, Shukla H, Perlegos J, Garner W. Comparability of weight loss reporting after gastric bypass and sleeve gastrectomy using BOLD data 2008–2011. Obesity Surgery 2015;25:788-95.
31. Anderson W.A, Greene G.W, Forse R.A, Apovian C.M, Istfan N.W. Weight loss and health outcomes in African Americans and whites after gastric bypass surgery. Obesity 2007;15:1455-63.
32. Montero P.N, Stefanidis D, Norton H.J, Gersin K, Kuwada T. Reported excess weight loss after bariatric surgery could vary significantly depending on calculation method: a plea for standardization. Surgery for Obesity and Related Diseases 2011;7:531-4.
33. Dixon J.B, Straznicky N.E, Lambert E.A, Schlaich M.P, Lambert G.W. Laparoscopic adjustable gastric banding and other devices for the management of obesity. Circulation 2012b;126:774-85.
34. Ranasinghe W.K.B, Wright T, Attia J, McElduff P, Doyle T, Bartholomew M, Hurley K, Persad R.A. Effects of bariatric surgery on urinary and sexual function. BJU international 2011;107:88-94.
35. Feldman H.A, Goldstein I, Hatzichristou D.G, Krane R.J, McKinlay J.B. Impotence and its medical and psychosocial correlates: results of the Massachusetts Male Aging Study. The Journal of urology 1994;151:54-61.
36. Feldman H.A, Longcope C, Derby C.A, Johannes C.B, Araujo A.B, Coviello A.D, Bremner W.J, McKinlay J.B. Age trends in the level of serum testosterone and other hormones in middle-aged men: longitudinal results from the Massachusetts male aging study. The Journal of Clinical Endocrinology & Metabolism 2002;87:589-98.
37. Isidori A.M, Giannetta E, Gianfrilli D, Greco E.A, Bonifacio V, Aversa A, Isidori A, Fabbri A, Lenzi A. Effects of testosterone on sexual function in men: results of a meta-analysis. Clinical endocrinology 2005;63:381-94.
38. Corona G, Isidori A.M, Aversa A, Burnett A.L, Maggi M. Endocrinologic Control of Men's Sexual Desire and Arousal/Erection. The journal of sexual medicine 2016;13: 317-37.
39. Sarwer D.B, Lavery M, Spitzer J.C. A review of the relationships between extreme obesity, quality of life, and sexual function. Obesity Surgery 2012;22:668-76.
40. Keddie A.M. Associations between severe obesity and depression: results from the National Health and Nutrition Examination Survey, 2005-2006. Preventing chronic disease 2011;8:A57.
41. Burgio K.L, Richter H.E, Clements R.H, Redden D.T, Goode P.S. Changes in urinary and fecal incontinence symptoms with weight loss surgery in morbidly obese women. Obstetrics and gynecology 2007;110:1034-40.
42. Laungani R.G, Seleno N, Carlin A.M. Effect of laparoscopic gastric bypass surgery on urinary incontinence in morbidly obese women. Surgery for Obesity and Related Diseases 2009;5:334-8.

43. Luke S, Addison B, Broughton K, Masters J, Stubbs R, Kennedy-Smith A. Effects of bariatric surgery on untreated lower urinary tract symptoms: a prospective multicentre cohort study. BJU international 2015;115:466-72.
44. Cohen P. The hypogonadal–obesity cycle: role of aromatase in modulating the testosterone–estradiol shunt–a major factor in the genesis of morbid obesity. Medical hypotheses 1999;52:49-51.

Table 1: Baseline characteristics of the patients before the bariatric surgery

	ED Group (n=18)	NO-ED Group (n=12)	Statistical difference
Age (years)	48.9 ± 7.0	44.1 ± 6.9	P=0.12
Height (m)	1.8 (1.7, 2.0)	1.8 (1.6, 1.9)	P=0.94
Weight (kg)	147.1 (94.8, 232.5)	143.9 (107.9, 230.1)	P=0.71
BMI (kg/m^2)	46.8 (37.9, 61.9)	47.8 (37.1, 69.5)	P=0.09
FBG (mmol/l)	5.3 (4.6, 8.3)	5.4 (4.4, 14.9)	P=0.07
HbA1c (mmol/mol)	43.5 (37.0, 58.0)	44.0 (32.0, 95.0)	P=0.09
IIEF total score	35.0 (13.0, 64.0)	68.5 (51.0, 74.0)	**P=0.03**
IIEF EF domain	13.0 (2.0, 25.0)	29.0 (27.0, 30.0)	**P=0.02**
IIEF OF domain	8.0 (1.0, 10.0)	10.0 (6.0, 10.0)	**P=0.02**
IIEF SD domain	6.0 (2.0, 8.0)	8.5 (4.0, 10.0)	**P=0.004**
IIEF IS domain	6.0 (0.0, 13.0)	12.5 (6.0, 15.0)	**P=0.002**
IIEF OS domain	5.5 (2.0, 10.0)	9.0 (4.0, 10.0)	**P=0.001**
IPSS total score	12.5 (0.0, 28.0)	4.5 (1.0, 14.0)	**P=0.01**
IPSS IE	1.5 (0.0, 5.0)	0.0 (0.0, 2.0)	**P=0.02**
IPSS Freq	2.0 (0.0, 5.0)	0.5 (0.0, 5.0)	P=0.08
IPSS Intermit	1.5 (0.0, 5.0)	0.0 (0.0, 4.0)	P=0.09
IPSS Urgency	2.0 (0.0, 5.0)	0.0 (0.0, 3.0)	**P=0.01**
IPSS Weak stream	1.0 (0.0, 2.0)	0.0 (0.0, 2.0)	**P=0.01**
IPSS Strain	0.0 (0.0, 2.0)	0.0 (0.0, 1.0)	P=0.98
IPSS Nocturia	1.0 (0.0, 5.0)	1.0 (0.0, 3.0)	P=0.92
IPSS QoL	12.5 (0.0, 28.0)	4.5 (1.0, 14.0)	**P=0.002**

(EF: erectile function; OF: orgasmic function; SD: sexual desire; IS: intercourse satisfaction; OS: overall satisfaction; IE: incomplete emptying; Freq: frequency; Intermit: intermittency; Strain: straining; QoL: quality of life).

Table 2: Baseline characteristics of NO-MILD LUTS vs MODERATE-SEVERE LUTS

	NO-MILD LUTS Group (n=16)	MODERATE-SEVERE LUTS Group (n=14)	Statistical difference
Age (years)	46.1 ± 7.0	49.1 ± 9.8	**P=0.03**
Height (m)	1.8 (1.64, 2.01)	1.8 (1.7, 1.94)	P=0.35
Weight (kg)	147.5 (94.8, 230.1)	149.3 (112.1, 232.5)	P=0.73
BMI (kg/m^2)	47.5 (37.9, 69.5)	45.0 (37.9, 69.5)	P=1.0
FBG (mmol/l)	5.3 (4.5, 14.9)	5.4 (4.7, 8.3)	P=0.73
HbA1c (mmol/mol)	44.5 (39.0, 56.0)	43.5 (37.0, 58.0)	P=0.94
IIEF total score	64.0 (13.0, 74.0)	32.5 (23.0, 62.0)	**p<0.01**
IIEF EF domain	28.0 (2.0, 30.0)	17.7 (14.6, 20.2)	**p=0.03**
IIEF OF domain	10.0 (1.0, 10.0)	7.6 (6.3, 8.4)	P=0.06
IIEF SD domain	7.8 (7.3, 8.9)	6.9 (6.0, 8.6)	P=0.05
IIEF IS domain	12.0 (0.0, 15.0)	6.4 (5.5, 8.0)	**P=0.04**
IIEF OS domain	8.6 (7.5, 9.0)	6.4 (4.6, 7.4)	**p<0.01**
IPSS total score	3.2 (1.7, 3.8)	12.7 (12.4, 15.7)	**p<0.01**
IPSS IE	0.0 (0.0, 1.0)	3.5 (0.0, 5.0)	**P=0.01**
IPSS Freq	0.0 (0.0, 4.0)	3.0 (1.0, 5.0)	**P=0.002**
IPSS Intermit	0.0 (0.0, 2.0)	2.0 (0.0, 5.0)	**P=0.01**
IPSS Urgency	0.0 (0.0, 3.0)	2.0 (0.0, 5.0)	**P=0.01**
IPSS Weak stream	0.0 (0.0, 2.0)	2.0 (1.0, 5.0)	**p<0.01**
IPSS Strain	0.0 (0.0, 1.0)	1.0 (0.0, 2.0)	**P=0.02**
IPSS Nocturia	1.0 (0.0, 3.0)	2.0 (0.0, 5.0)	**P=0.02**
IPSS QoL	1.5 (0.0, 3.0)	3.5 (2.0, 6.0)	**p<0.01**

(EF: erectile function; OF: orgasmic function; SD: sexual desire; IS: intercourse satisfaction; OS: overall satisfaction; IE: incomplete emptying; Freq: frequency; Intermit: intermittency; Strain: straining; QoL: quality of life).

Figure Legends:

Figure 1: The effect of bariatric surgery on BMI (**A**) of patients with ED (circles) and NO-ED (squares) at 1 month pre-op, 1 month post-op, 3 months post-op and 6 months post-op. *Significantly different from pre-op NO-ED (P<0.002); **significantly different from pre-op ED (P<0.001). The effect of bariatric surgery on %TWL (**B**) of patients with ED (circles) and NO-ED (squares) at day of surgery, 1 month post-op, 3 months post-op and 6 months post-op. *Significantly different from day of surgery NO-ED (P<0.002); **significantly different from day of surgery ED (P<0.001).

Figure 2: The effect of bariatric surgery on BMI (**A**) of patients with NO-MILD LUTS (circles) and MODERATE-SEVERE LUTS (squares) at 1 month pre-op, 1 month post-op, 3 months post-op and 6 months post-op. A significant decrease in BMI at 1 month post-op (**A**) and increase in %TWL (**B**) was observed after the surgery in NO-MILD LUTS and MODERATE-SEVERE LUTS. The weight loss reached statistical significance at 1 month post-op and continued throughout to 6 months post-op (*P<0.01 and **P<0.001) respectively. There was no difference between NO-MILD LUTS and MODERATE-SEVERE LUTS groups at any time points (P=0.925).

Figure 3: The effect of bariatric surgery on total IIEF scores **(A)** of patients with ED (circles) and NO-ED (squares) at 1 month pre-op, 1 month post-op, 3 months post-op and 6 months post-op. *Significantly different from pre-op ED at 1, 3 and 6 months post-op (P=0.02, *=0.001 and P<0.001 respectively); **significantly different from pre-op NO-ED at 6 months post-op (P=0.013). Erectile function domain (**B**) and orgasmic function, sexual desire, intercourse satisfaction and overall satisfaction domains (**C**) of patients with ED at pre-op, 1 month post-op, 3 months post-op and 6 months post-op. *Erectile function and intercourse satisfaction domains significantly different from pre-op (P<0.02 and P<0.004 respectively); **sexual desire domain significantly different from pre-op (P<0.002); ***orgasmic function domain significantly different from pre-op (P<0.004).

Figure 4: The effect of bariatric surgery on IPSS total score in ED (circles) and NO-ED (squares) groups at 1 month pre-op, 1 month post-op, 3 months post-op and 6 months post-op. **A**: The improvements in IPSS total score in ED group was observed at 1 month which further improved throughout the study; *significantly different from pre-op ED at 1, 3 and 6 months post-op (P=0.02, P=0.001 and P<0.001 respectively). No significant change was observed in NO-ED group throughout the study (P=0.928, P=0.179 and P=0.107 respectively). **B:** The effect of bariatric surgery on IPSS domains scores in ED group only. Please see Supplementary Figure 3 for NO-ED group. The improvements in frequency, intermittency, weak stream, nocturia and quality of life domain scores were observed at 1 month post-op (*P=0.01, *P=0.008, *P=0.005, *P=0.024 and *P=0.001 respectively) and further improved throughout the study. The decrease in urgency and incomplete emptying domain scores reached significance at 3 months post-op (**P=0.023 and **P=0.007 respectively). There was no significant change in straining domain score throughout the study (P=0.81)

Figure 5: The effect of bariatric surgery on IPSS total score in MODERATE-SEVERE LUTS (squares) and NO-MILD LUTS (circles) groups (**A**): The improvements in IPSS total score in

MODERATE-SEVERE LUTS was observed at 1 month which further improved throughout the study (*P=0.02, *P=0.001 and *P=0.001 respectively). No significant improvement observed in NO-MILD LUTS group throughout the study (P=0.833, P=0.241 and P=0.138 respectively). The effect of bariatric surgery on IPSS domains scores in MODERATE-SEVERE LUTS group only. For NO-MILD LUTS results please see Supplementary Figure 4. Significant improvements in frequency, intermittency, weak stream and nocturia domains were observed at 1, 3 and 6 months post-operative time points (P=0.04, P=0.017 and P=0.002) (P=0.02, P=0.016 and P=0.01) (P=0.008, P=0.007 and P=0.002) (P=0.004, P=0.006 and P=0.002) respectively. A significant improvement in IPSS- straining at 3 months post-op was observed but did not continue to 6 months post-op (**P=0.033, P=0.154 respectively).

Figure 6: The effect of bariatric surgery on fasting blood glucose concentrations (FBG, **A**) and glycated haemoglobin concentrations (HbA1c, **B**) in ED (circles) and NO-ED (squares) groups. The decrease in FBG levels reached significance at 1 months post-op in ED group (*P<0.001) and at 6 months post-op in NO-ED group (**P=0.047). The decrease in HbA1c levels reached significance at 1 month pre-op in both ED (*P<0.001) and NO-ED groups (**P<0.004). The upper limits of the normal range (FBG 5.8 mmol/l and HbA1c 42 mmol/mmol) are shown with broken lines.

Figure 7: The effect of bariatric surgery on fasting blood glucose concentrations (FBG, **A**) and glycated haemoglobin concentrations (HbA1c, **B**) in NO-MILD LUTS (circles) and MODERATE-SEVERE LUTS (squares) groups. The decrease in FBG levels reached significance at 1 months post-op in both groups (**A**; *P<0.005, **P<0.003). The decrease in HbA1c levels reached significance at 1 month pre-op in both NO-MILD LUTS group (*P<0.001) and MODERATE-SEVERE LUTS groups (**P<0.003). The upper limits of the normal range (FBG 5.8 mmol/l and HbA1c 42 mmol/mmol) are shown with broken lines.

Supplementary Figure Legends:

Supplementary Figure 1:

The effect of bariatric surgery on IIEF domains scores in NO-ED group: Erectile function domain (**A**) and orgasmic function, sexual desire, intercourse satisfaction and overall satisfaction domains (**B**) of patients with NO-ED at 1 month pre-op, 1 month post-op, 3 months post-op and 6 months post-op. *Sexual desire and intercourse satisfaction domains significantly different from pre-op (P<0.02 and P<0.01 respectively).

Supplementary Figure 2:

The effect of bariatric surgery on IIEF total scores (**A**) and erectile function domain (**B**) and the remaining individual domain scores (**C**) in MODERATE-SEVERE LUTS (squares) and NO-MILD LUTS (circles) groups: **A:** The total IIEF scores increased significantly after the surgery at 3 months and 6 months post-op in both groups (*P<0.002 in NO-MILD LUTS and **P<0.003 in MODERATE-SEVERE LUTS). **B**: Erectile function domain scores remained high in NO-MILD LUTS group throughout the study while increased significantly in MODERATE-SEVERE LUTS group

from 1 month post-op onwards (**P<0.05 vs pre-op). **C:** Intercourse satisfaction and orgasmic function domains showed significant increase at 1 month post-op MODERATE-SEVERE LUTS group while the remaining domains improved at 6 months post-op (*P<0.05). In NO-MILD LUTS group, only significant increase was observed in desire, intercourse satisfaction, orgasmic function and overall satisfaction domains at 6 months (**P<0.05).

Supplementary Figure 3:

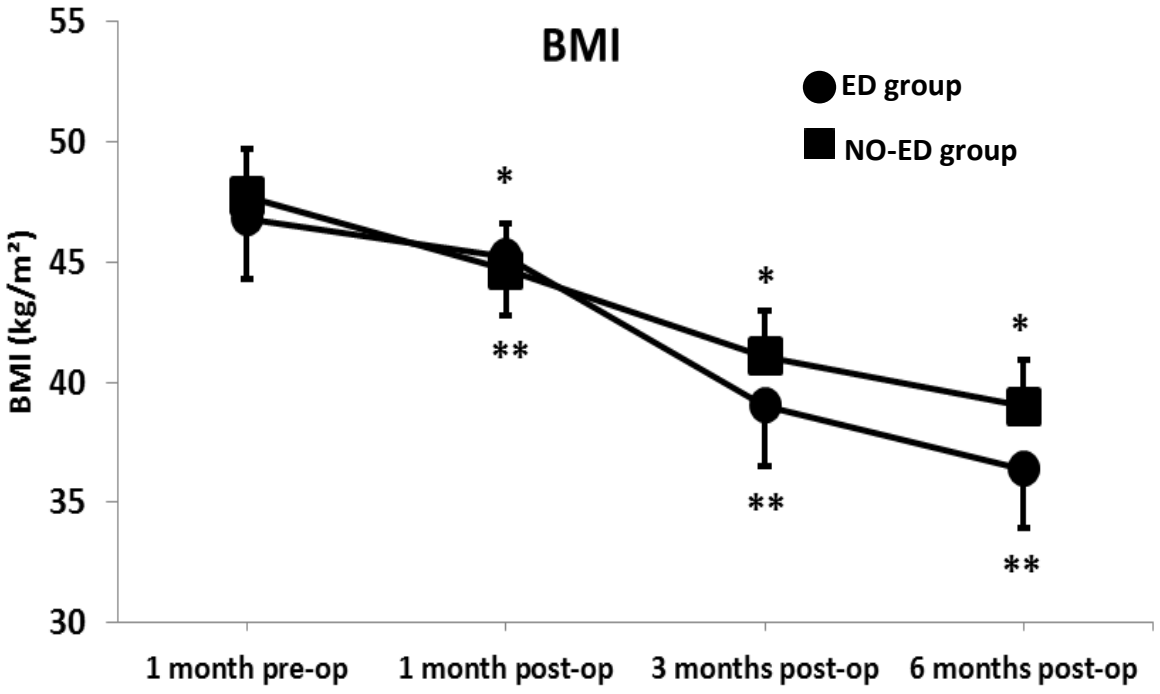
In the NO-ED group there was a significant increase in quality of life domain score at 1 month post-op compared to 1 month pre-op; this effect was not observed at 3 months post-op or 6 months post-op (*P=0.046 at 1 month post-op vs pre-op). A significant decrease in nocturia at 6 months post-op compared to 1 month pre-op (**P=0.027) was observed.

Supplementary Figure 4:

In the NO-MILD LUTS group a significant improvement in nocturia and urgency domains was observed at 3 and 6 months post-operative time points (*P=0.035, *P=0.046) and (**P=0.031, **P=0.041) respectively.

FIGURE 1

A


BMI
ED group
NO-ED group
BMI (kg/m²)
55
50
45
40
35
30
*
**
*
**
*
**
1 month pre-op
1 month post-op
3 months post-op
6 months post-op

B

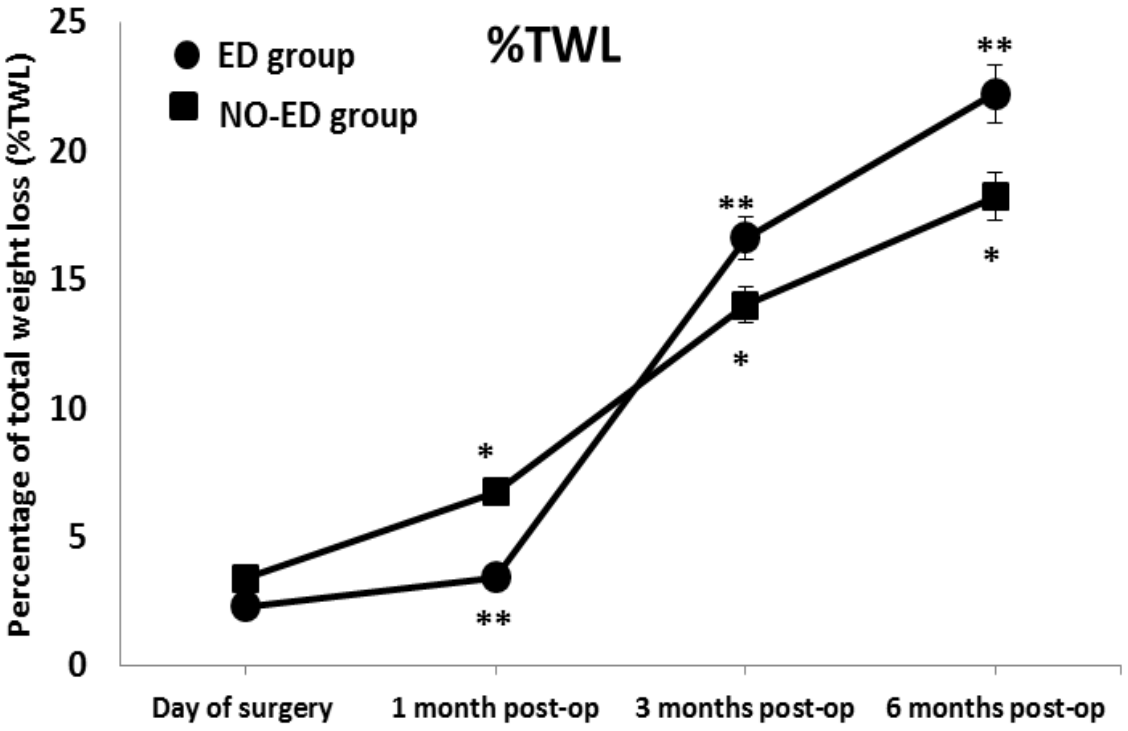
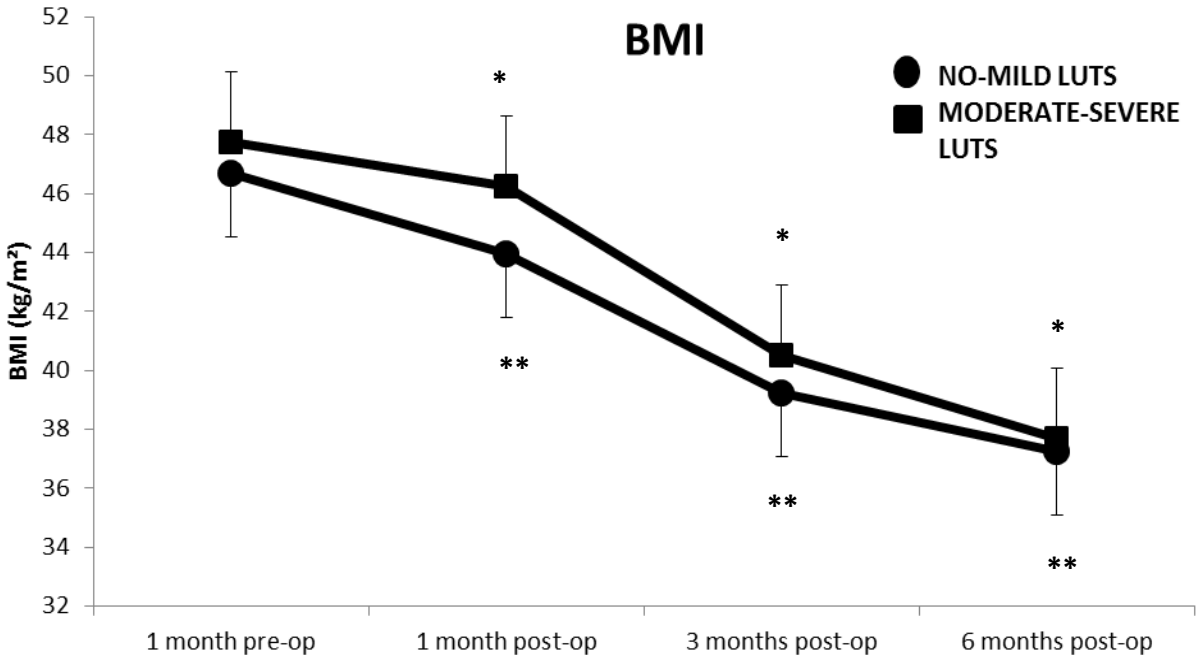

%TWL
ED group
NO-ED group
Percentage of total weight loss (%TWL)
25
20
15
10
5
0
*
**
**
*
**
*
Day of surgery
1 month post-op
3 months post-op
6 months post-op

FIGURE 2

A


BMI
NO-MILD LUTS
MODERATE-SEVERE LUTS
BMI (kg/m²)
52
50
48
46
44
42
40
38
36
34
32
*
**
1 month pre-op
1 month post-op
3 months post-op
6 months post-op

B

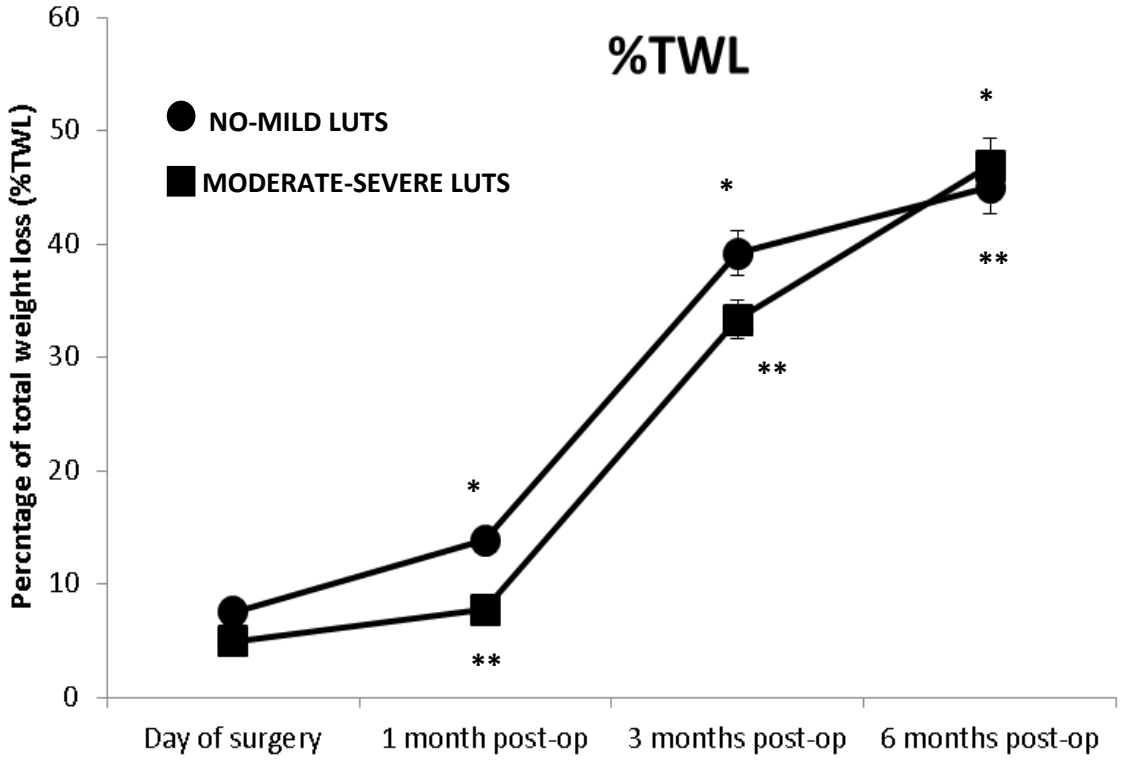
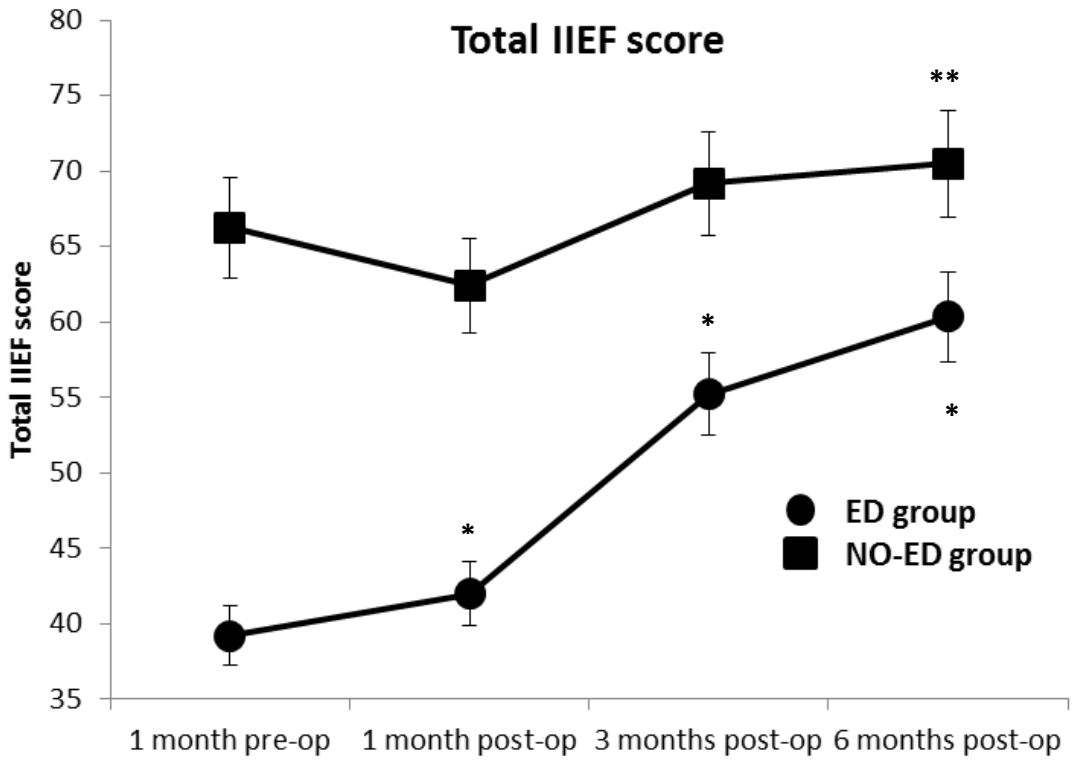
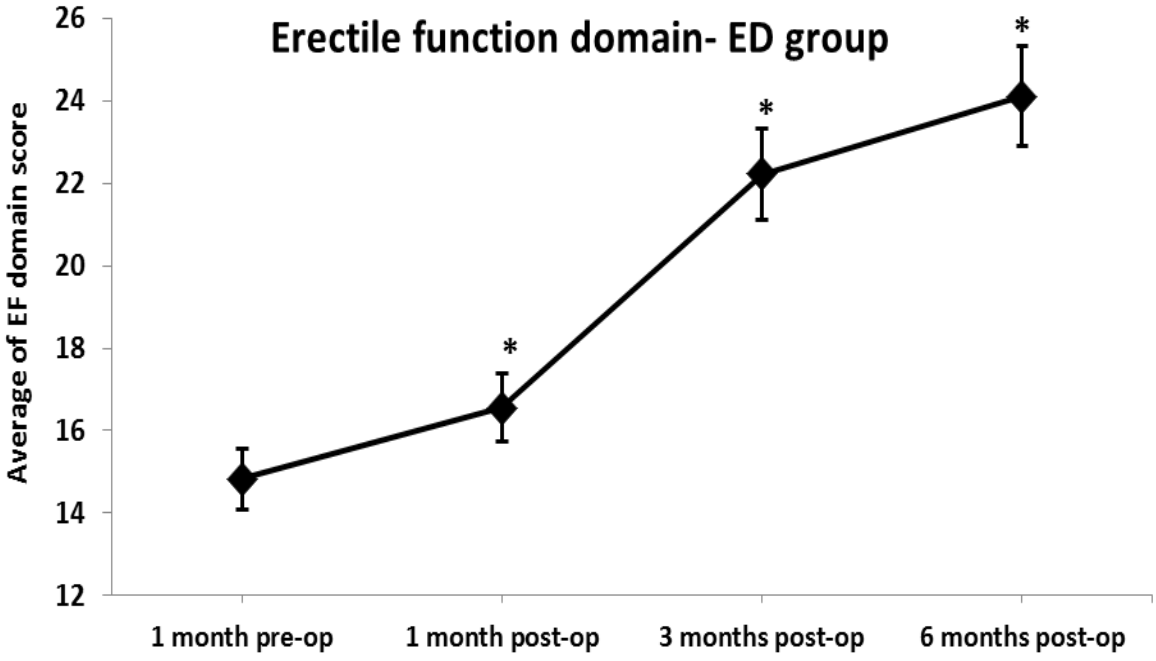

%TWL
NO-MILD LUTS
MODERATE-SEVERE LUTS
Percntage of total weight loss (%TWL)
60
50
40
30
20
10
0
*
**
Day of surgery
1 month post-op
3 months post-op
6 months post-op

FIGURE 3

A


Total IIEF score
Total IIEF score
80
75
70
65
60
55
50
45
40
35
1 month pre-op
1 month post-op
3 months post-op
6 months post-op
ED group
NO-ED group
*
*
*
**

B


Erectile function domain- ED group
Average of EF domain score
26
24
22
20
18
16
14
12
1 month pre-op
1 month post-op
3 months post-op
6 months post-op
*
*
*

C

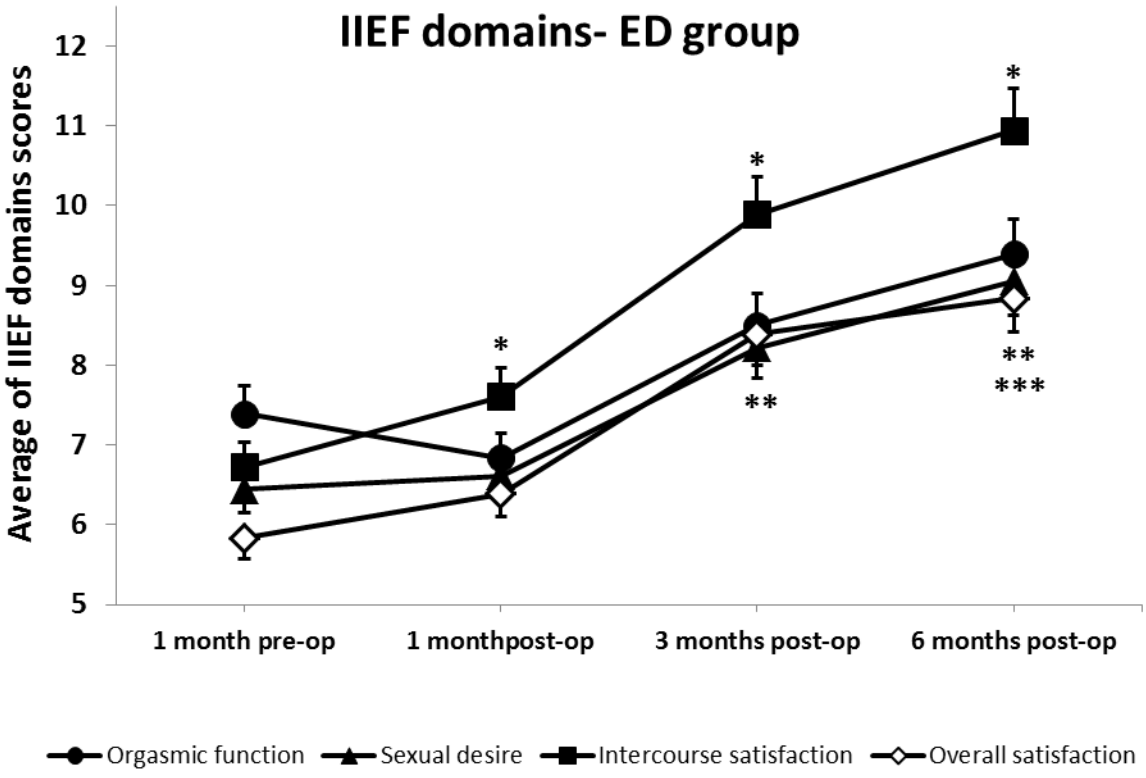
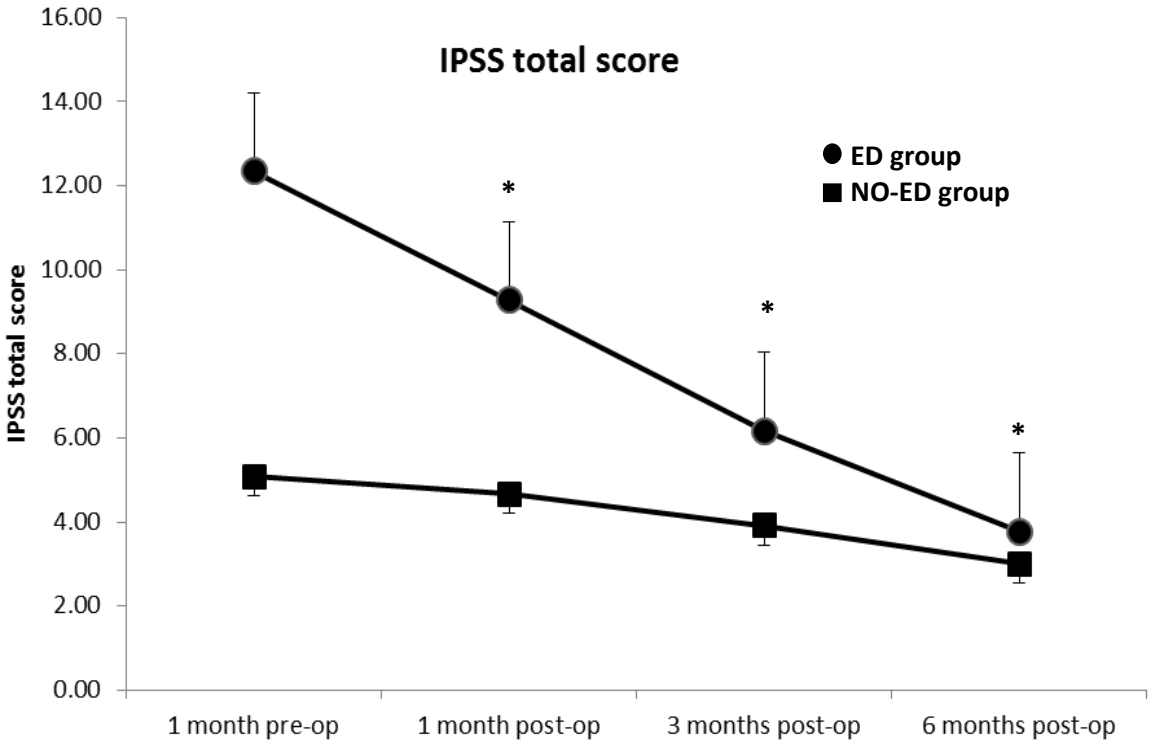

IIEF domains- ED group
Average of IIEF domains scores
12
11
10
9
8
7
6
5
*
*
*
**
**
***
1 month pre-op
1 monthpost-op
3 months post-op
6 months post-op
Orgasmic function
Sexual desire
Intercourse satisfaction
Overall satisfaction

FIGURE 4

A


IPSS total score
ED group
NO-ED group
IPSS total score
16.00
14.00
12.00
10.00
8.00
6.00
4.00
2.00
0.00
*
*
*
1 month pre-op
1 month post-op
3 months post-op
6 months post-op

B

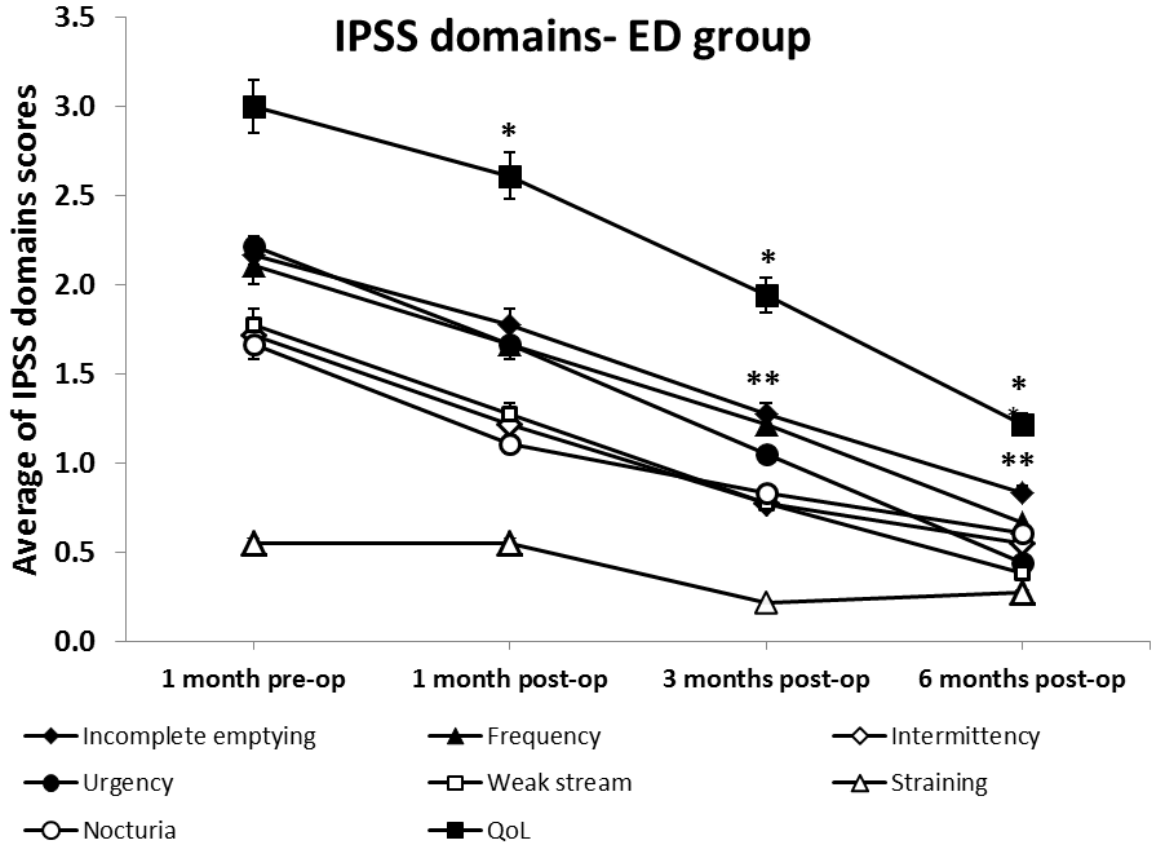
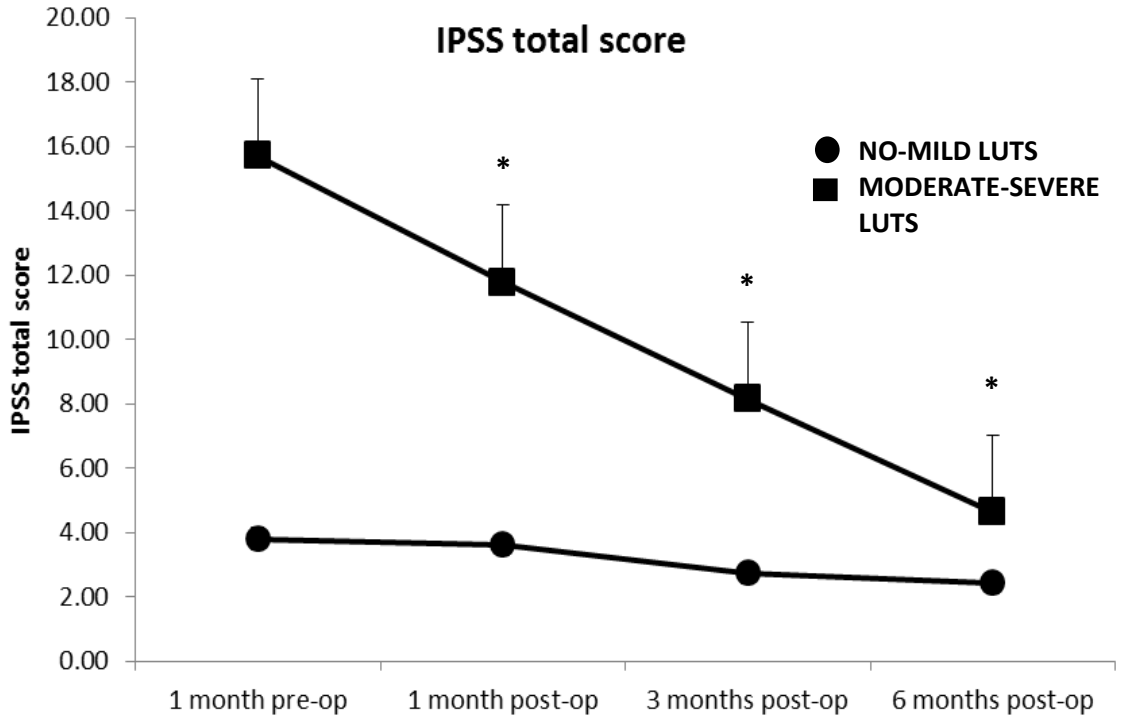

IPSS domains- ED group
Average of IPSS domains scores
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
*
*
**
*
**
1 month pre-op
1 month post-op
3 months post-op
6 months post-op
Incomplete emptying
Frequency
Intermittency
Urgency
Weak stream
Straining
Nocturia
QoL

FIGURE 5

A


IPSS total score
IPSS total score
20.00
18.00
16.00
14.00
12.00
10.00
8.00
6.00
4.00
2.00
0.00
NO-MILD LUTS
MODERATE-SEVERE LUTS
*
*
*
1 month pre-op
1 month post-op
3 months post-op
6 months post-op

B

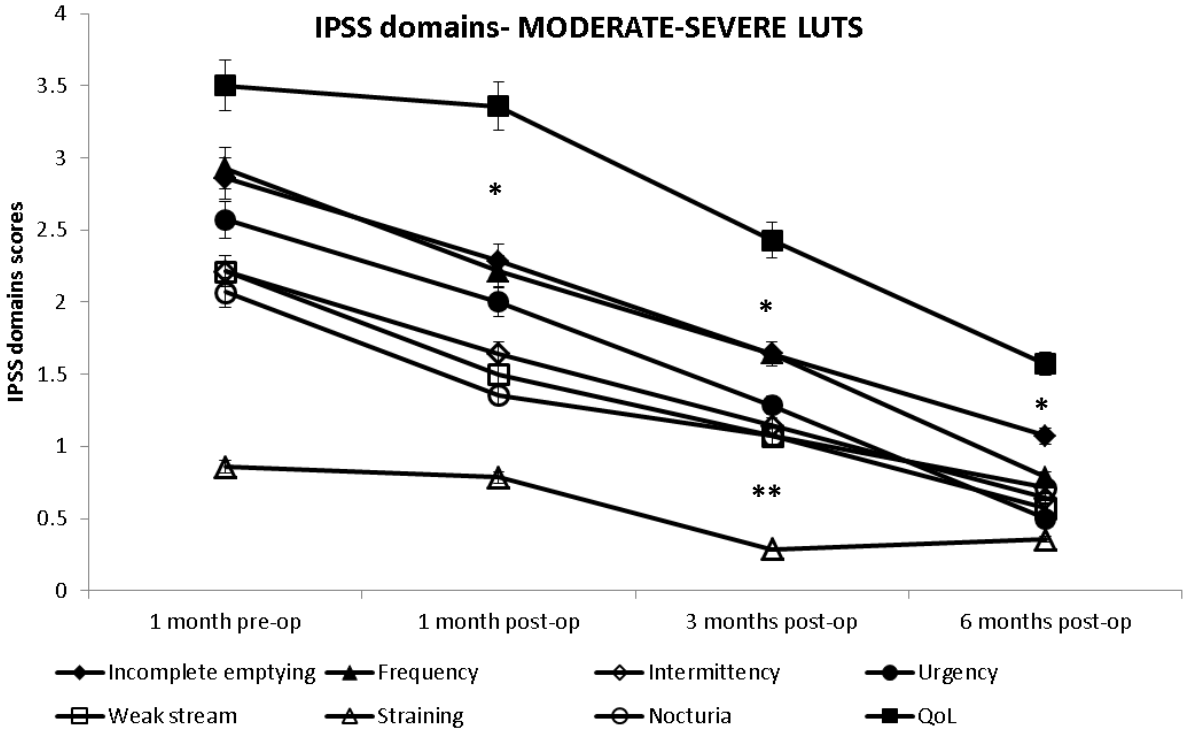
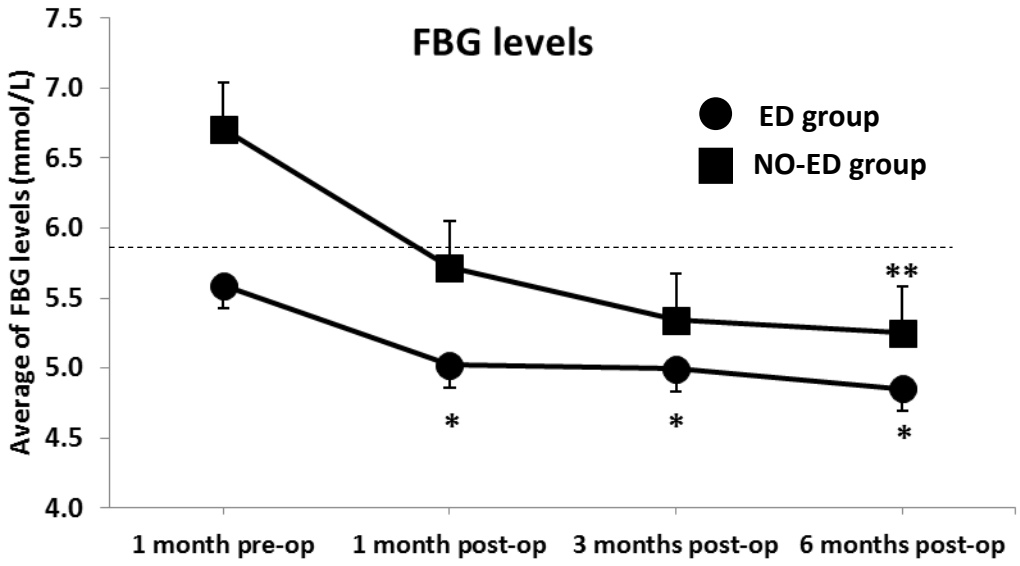

IPSS domains- MODERATE-SEVERE LUTS
IPSS domains scores
4
3.5
3
2.5
2
1.5
1
0.5
0
*
*
*
**
1 month pre-op
1 month post-op
3 months post-op
6 months post-op
Incomplete emptying
Frequency
Intermittency
Urgency
Weak stream
Straining
Nocturia
QoL

FIGURE 6

A


FBG levels
Average of FBG levels (mmol/L)
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
ED group
NO-ED group
**
*
*
*
1 month pre-op
1 month post-op
3 months post-op
6 months post-op

B

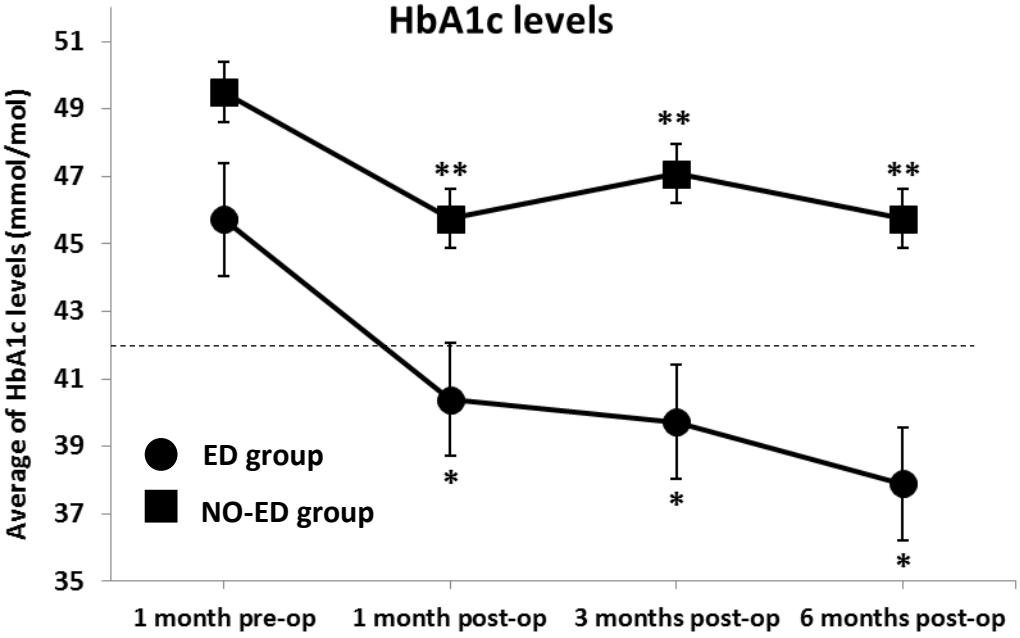
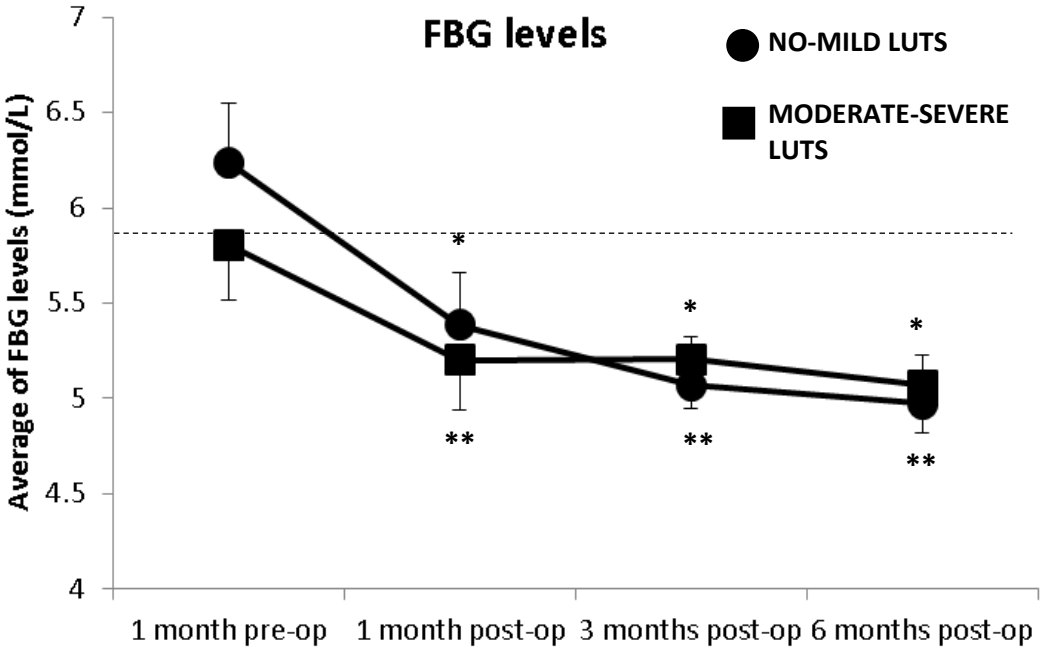
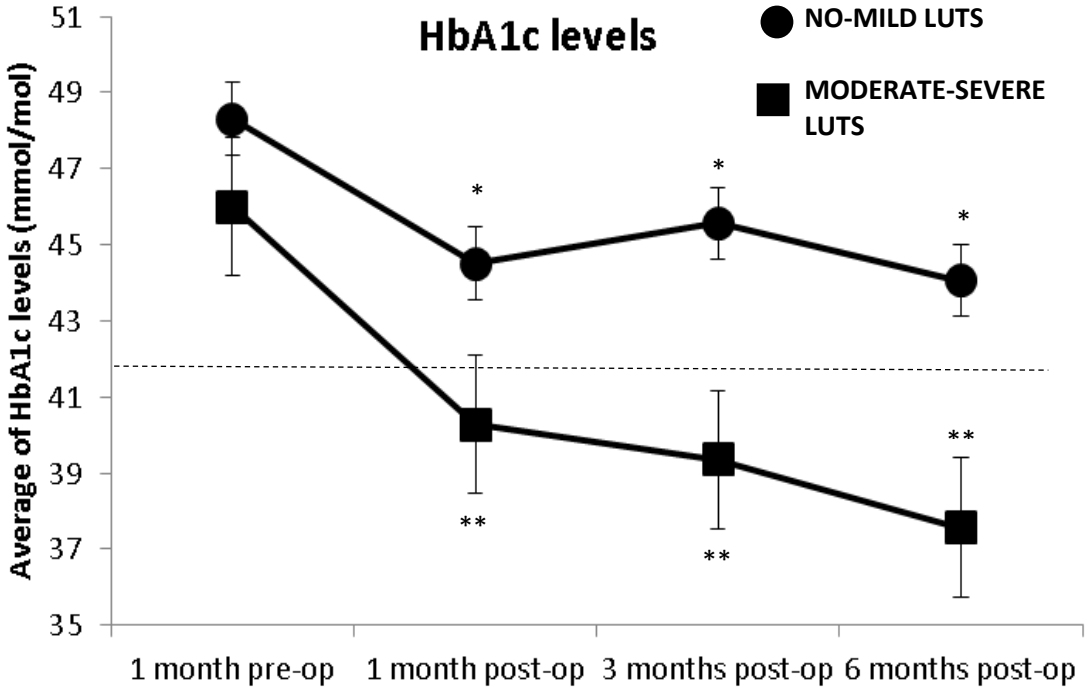

HbA1c levels
Average of HbA1c levels (mmol/mol)
51
49
47
45
43
41
39
37
35
**
**
**
*
*
*
ED group
NO-ED group
1 month pre-op
1 month post-op
3 months post-op
6 months post-op

FIGURE 7

A

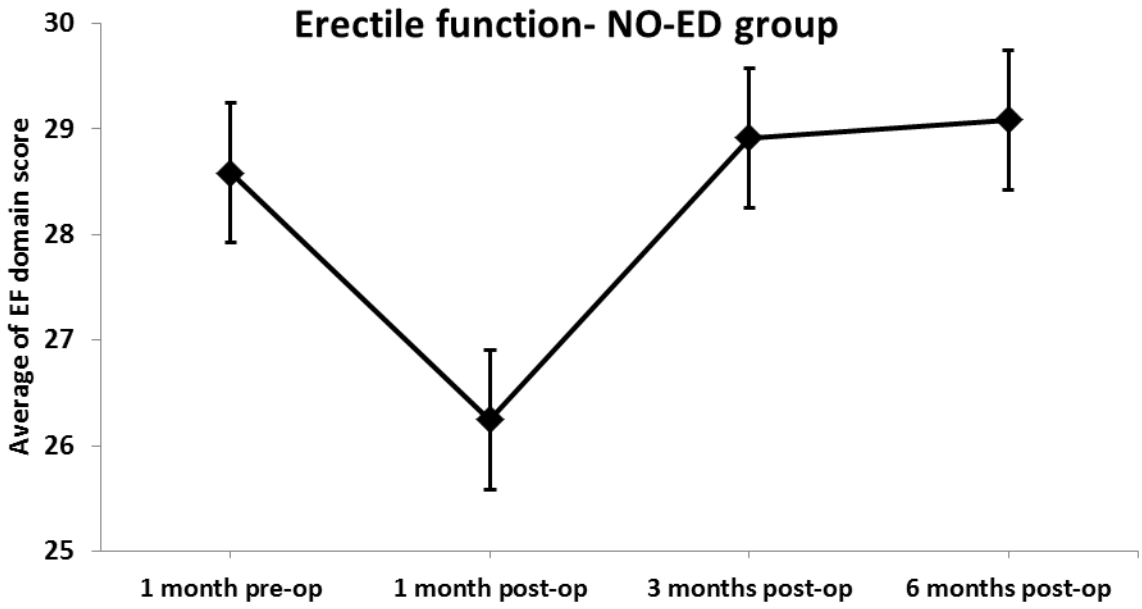

FBG levels
NO-MILD LUTS
MODERATE-SEVERE LUTS
Average of FBG levels (mmol/L)
7
6.5
6
5.5
5
4.5
4
*
**
*
**
*
**
1 month pre-op
1 month post-op
3 months post-op
6 months post-op

B

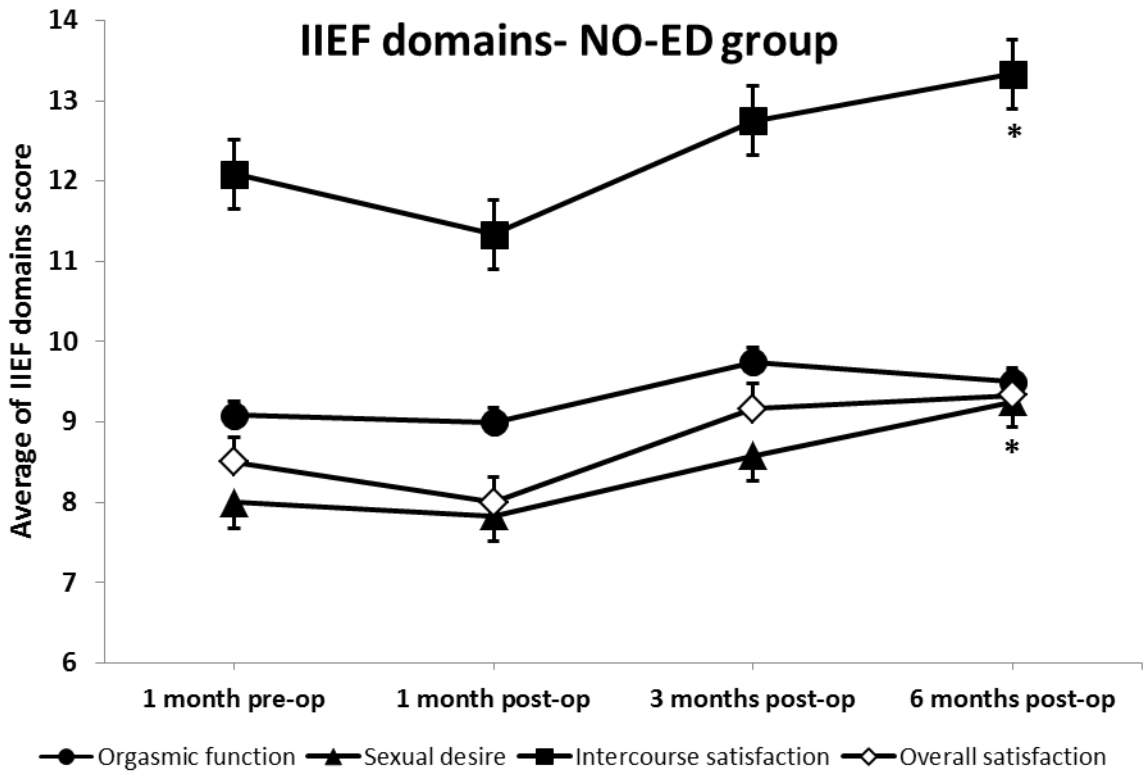

HbA1c levels
NO-MILD LUTS
MODERATE-SEVERE LUTS
Average of HbA1c levels (mmol/mol)
51
49
47
45
43
41
39
37
35
*
**
*
**
*
**
1 month pre-op
1 month post-op
3 months post-op
6 months post-op

Supplementary Figures:

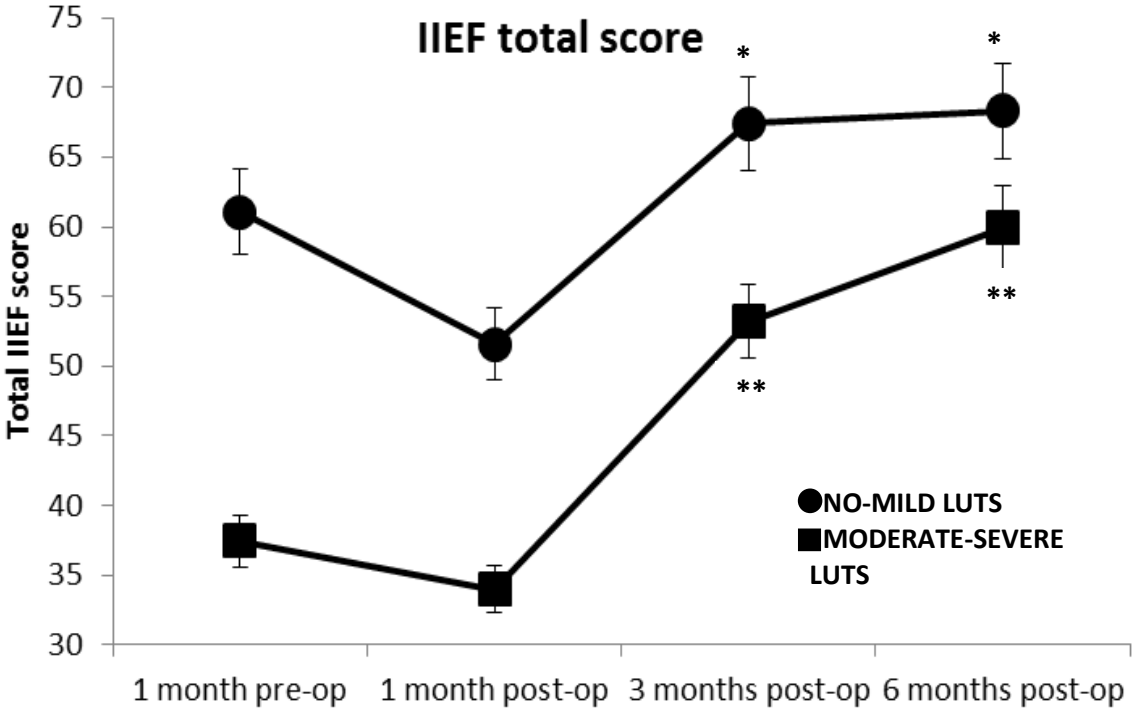
Supplementary Figure 1A



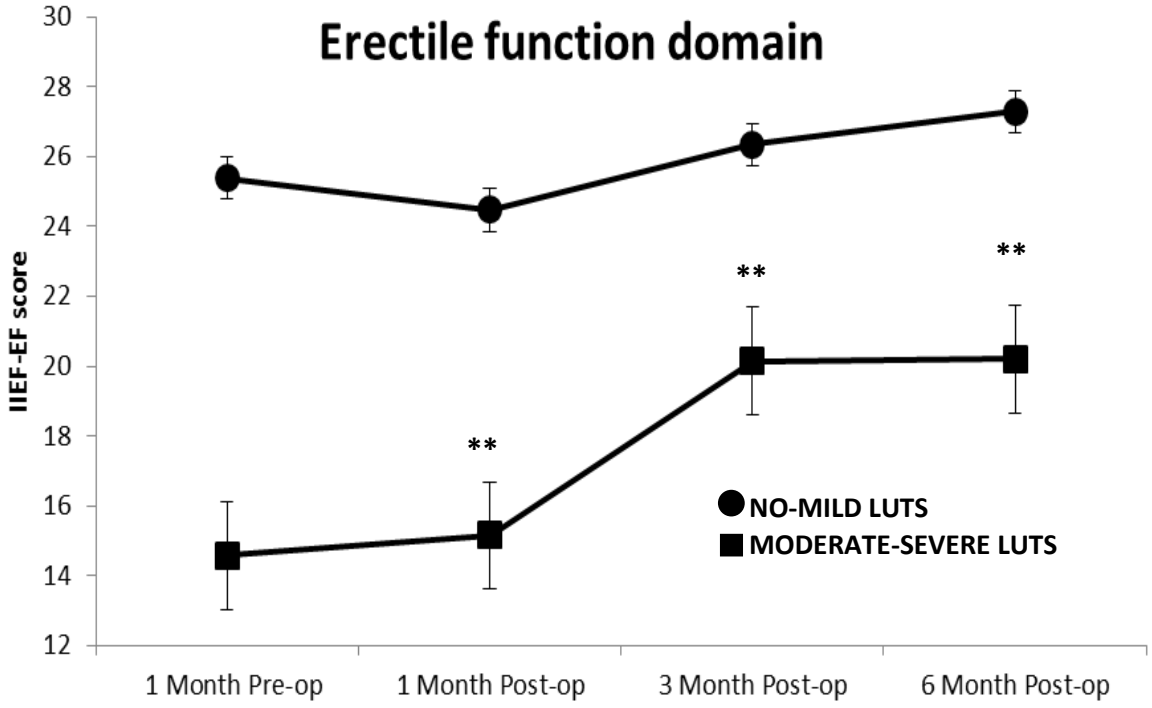
Supplementary Figure 1B



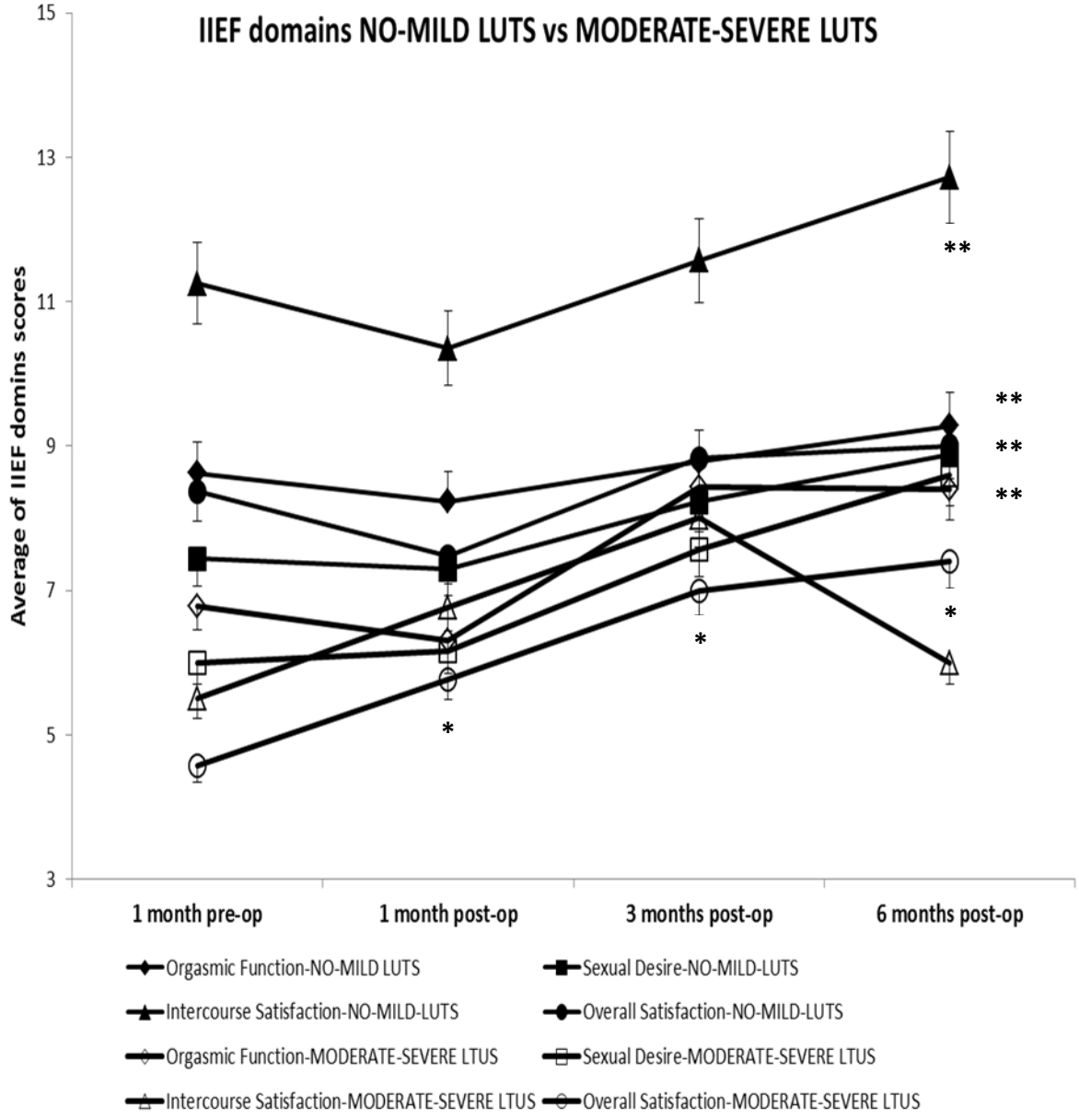
Supplementary Figure 2A



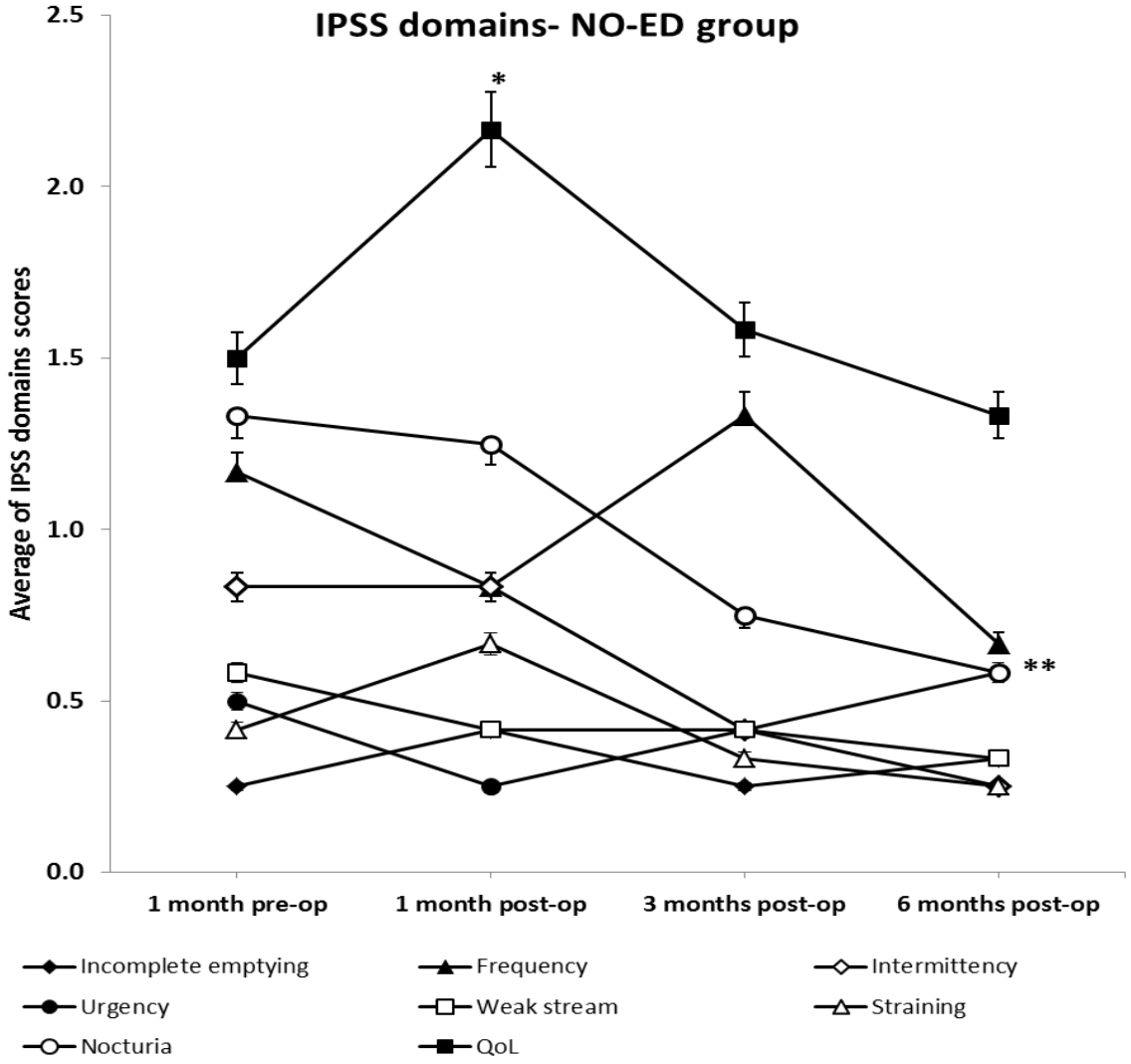
Supplementary Figure 2B



Supplementary Figure 2C



Supplementary Figure 3



Supplementary Figure 4