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► To cite this version:

Claire Carette, Rachel Lévy, Florence Eustache, Gabriel Baron, Muriel Coupaye, et al.. Changes in total sperm count after gastric bypass and sleeve gastrectomy: the BARIASPERM prospective study. *Surgery for Obesity and Related Diseases*, 2019, 15 (8), pp.1271-1279. 10.1016/j.soard.2019.04.019 . hal-03040814

HAL Id: hal-03040814

<https://hal.science/hal-03040814>

Submitted on 20 Jul 2022

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Changes in total sperm count after gastric bypass and sleeve gastrectomy: the BARIASPERM prospective study

Running title: Sperm alterations with bariatric surgery

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**Changes in total sperm count after gastric bypass and sleeve gastrectomy: the
BARIASPERM prospective study**

Running title: Sperm alterations with bariatric surgery

5 Abstract

Background: The massive weight loss induced by bariatric surgery is associated with major benefits but the effect on semen variables is still uncertain.

Objectives: To explore semen modifications with gastric bypass (GB) and sleeve gastrectomy (SG).

10 Setting: Five French University Hospitals

Methods: Male candidates for bariatric surgery with no history of infertility were recruited in this controlled prospective study. Sperm characteristics were collected before surgery then six months and up to 12 months after surgery.

Results: Forty-six adult men who underwent GB (n = 20) or SG (n = 26) were included. Total sperm count (TSC) tended to be lower at 6 months and showed a significant decrease at 12 months in both surgery groups -69.5 millions (-96.8 to -42.2 millions ; $p = 0.0021$). TSC at 12 months relative to baseline was -41.4 millions ($p = 0.0391$) following GB and -91.1 millions ($p = 0.0080$) following SG. This was counterbalanced by an associated resolution of hypogonadism and decrease of DNA fragmentation in most patients with time after surgery.

20 Conclusion: Improvement in some semen variables after bariatric surgery observed in 3 previous studies is in contrast to the lower mean total sperm count found in this study at one

year. The possible reversibility of this effect at long-term and the impact of surgery on fertility both remain unknown.

25 **Key words:** Sperm count, bariatric surgery, gastric bypass, sleeve gastrectomy, fertility

Introduction

Bariatric surgery has become a widespread treatment option for patients with severe obesity, involving > 550,000 operations/year worldwide, with North America, Brazil and France being the 3 leading countries (1). The most commonly performed procedures are sleeve gastrectomy (SG) and gastric bypass (GB). Bariatric surgery improves conditions that cause infertility in women, such as polycystic ovarian syndrome (PCOS) and insulin resistance, and there are also some reports of an improvement in menstrual patterns and spontaneous fertility rates (2). Obesity also negatively influences semen quality in men (3). Campbell et al. showed that male obesity is associated with an increased percentage of abnormal sperm with low mitochondrial membrane potentials, increased sperm DNA fragmentation and abnormal morphology; and also, an increased risk of non-viable pregnancies (4). Several mechanisms may contribute to quantitative and qualitative changes in sperm, such as alterations in hormones, oxidative stress and epigenetics (5). Sperm from obese men used for *in-vitro* fertilisation or intra cytoplasmic sperm injection has been associated with a greater number of pregnancy losses, and less chance of a live birth; however, there is also contradictory data (6). There are few studies addressing whether weight loss might restore fertility in men (7). Studies in mice provide evidence that sperm variables could be improved by a switch from a high-fat to a low-fat diet, an effect also enhanced by exercise (8). A pilot study found that weight loss induced by lifestyle modifications may potentially lead to improvements in semen quality; 43 obese men were included in a 14-week weight loss programme with median weight loss of 15% (9). Whether the improvement in semen quality is a result of the reduction in body weight per se or other factors related to an improved lifestyle remains unknown. In addition, lifestyle modifications are rarely sufficient to achieve significant weight loss of 10 - 15 %, and regaining weight is a common issue to tackle in the long run.

The massive and rapid weight loss obtained by bariatric surgery is associated with

major metabolic benefits but the effect on semen and fertility is open to debate. Initially, bariatric surgery was described as beneficial because of the resolution of male obesity-associated secondary hypogonadism (MOSH), as was observed for PCOS in female (10). In men, weight loss following bariatric surgery is expected to increase testosterone levels, restore reproductive function and improve the chances of fertility. Unfortunately, few studies have assessed the hormonal and clinical variables of fertility in relation to surgical weight loss. A few case series have reported alterations of sperm quality after bariatric surgery, stimulating interest in this crucial issue. This is especially the case as mean age for bariatric surgery in male patients is about 40 years old, a common age for fathering children in most countries (11,12). One randomized study did not show sperm quality changes in 10 patients who had GB versus controls who did not have surgery (13). Another recent prospective study showed an improvement of semen variables in 23 patients who underwent GB versus 8 controls (14), while a larger prospective study of 46 patients who had SG showed a significant increase in sperm concentration, but only in men with preoperative azoospermia and oligospermia (15). BARIASPERM is the first prospective study addressing sperm count changes in both GB and SG patients, without a history of infertility, through examination of semen before surgery and at 6 and 12 months post-operation.

Materials and Methods

Study design and patients

BARIASPERM was a French multicentre observational and controlled prospective study. Male candidates for bariatric surgery (GB and SG) were recruited in five University Hospital centres; none had a history of infertility. Sperm characteristics were studied before and after surgery. The protocol was approved by the local ethics committee (CPP2012-08-01) and all participants gave written informed consent. This trial was registered with

clinicaltrials.gov (NCT01842295). Inclusion criteria were men of reproductive age (18 - 50 years) with a body mass index (BMI) $\geq 40 \text{ kg/m}^2$ or 35 kg/m^2 and, at least one obesity comorbidity, as recommended by French guidelines for candidates for bariatric surgery (16). All participants were included after approval of the bariatric surgery project. The exclusion criteria were known history of infertility with or without sperm alterations or refusal to participate.

Anthropometric variables were obtained according to a standardised protocol. Biochemical tests included Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) calculations, lipid profiles, inflammation and metabolic variables (ferritin, interleukin-6, tumour necrosis factor-alpha, C-reactive protein, leptin and adiponectin), prokineticine 2 (PK2), sex hormone assays (follicle stimulating hormone, luteinizing hormone, oestradiol, total testosterone, bioavailable testosterone and sex hormone-binding globulin; SHBG), oxidative stress markers (superoxide dismutase and glutathione peroxidase), nutritional markers (vitamins A, B and E) and pollutants (dioxins and polychlorinated biphenyls). In addition, questionnaires were used to investigate nutritional intakes (food frequency questionnaire), libido (International Index of Erectile Function; IIEF5), tobacco, quality of life (36-Item Short Form Health Survey; SF-36) and physical activity (International Physical Activity Questionnaire; IPAQ).

Semen analysis

Sperm samples were collected at the laboratory after 3–5 days of sexual abstinence. After semen liquefaction, semen analysis was performed according to World Health Organization guidelines (WHO, 2010), assessing semen volume, sperm concentration, and sperm motility. From this data, total sperm counts (TSC) were calculated. The percentage of morphologically normal spermatozoa was assessed according to the modified classification of David (17).

Determination of sperm DNA integrity

To evaluate sperm nuclear DNA integrity, the terminal uridine nick-end labelling (TUNEL) assay was performed on semen samples using the In Situ Cell Death Detection Kit (Roche Applied Science, Penzberg, Germany). After trypsinization, spermatozoa were fixed in Carnoy's solution (2:1 methanol/acetic acid) and stored at -20°C. Spermatozoon pellets were permeabilized for 20 minutes with 0.1% Triton X-100 in sodium citrate solution and washed with phosphate buffer saline (PBS). Then cells were incubated with fluorescein isothiocyanate (FITC)-labelled dUTP and terminal deoxyribonucleotidyl transferase (TdT; TUNEL solution). The positive control sample was treated with 100 µl of DNase (0.5 mM) for 1 hour at 37°C before incubation with TUNEL solution; while for the negative control TdT was omitted. Cells were then washed twice in PBS and spread over slides. Slides were dried at room temperature in the dark and 4',6-diamidino-2-phenylindole (DAPI) solution was added. Slides were examined using fluorescence microscopy. The total sperm DNA fragmentation rate was calculated as the number of FITC-positive cells from the total number of sperm nuclei (labelled with DAPI); at least 200 spermatozoa were counted. For each sample the analysis was performed twice by 2 investigators blinded to the surgical association of the material and its temporal characteristics.

Outcomes

The primary outcome for the study was the variation of TSC from just prior to (baseline) and 6 months after surgery. Secondary outcomes were analysed at both 6 and 12 months after the operation assessing the impact of the surgery on various anthropometric and biological variables (vitamins, metabolic, hormonal and pollutants). In addition, the type of surgery

technique was correlated with the variation of TSC. Changes in lifestyle (diet, physical activity and tobacco consumption) were also evaluated at baseline and 6 months after surgery.

Statistical analysis

A paired t test, with adjustment on the mean-centered baseline value to enhance power, was used to compare the mean of quantitative outcomes between baseline and after surgery (18). McNemar's test (or Bowker's test for symmetry, when appropriate) was used to compare qualitative paired data. For secondary outcomes, Hochberg adjustment for multiple comparisons was used to maintain the overall type 1 error rate at 5%. An adjusted $p < 0.05$ was considered statistically different. Statistical analysis was performed using SAS software, version 9.3 (SAS Institute Inc., Cary, N.C.) and R software (version 3.4.1).

Results

Of 147 adult men listed for bariatric surgery, 71 were excluded or unreachable, 24 refused to participate, and 52 were accepted into the study (Figure 1). Of these 52, 2 patients were excluded by investigator decision, 3 patients were unable to provide a sperm sample and 1 was lost to follow-up. The remaining 46 patients completed the study, undergoing bariatric surgery of either GB ($n = 20$) or SG ($n = 26$), with post-operative follow-up of 1 year. Participants mean age and BMI were $38.9 (\pm 7.9)$ years old and $44.1 (\pm 5.5) \text{ kg/m}^2$, respectively (Table 1). As expected, bariatric surgery resulted in a substantial decrease in BMI by 6 and 12 months post-surgery, of $-10.9 (-10.0 \text{ to } -11.8)$ and $-12.7 (-11.6 \text{ to } -13.8) \text{ kg/m}^2$, respectively (Table 2). TSCs had decreased by 6 months and were significantly lower at 12 months for both the GB and SG groups, at $-69.5 \times 10^6 (-42.2 \times 10^6 \text{ to } -96.8 \times 10^6; p = 0.0021)$; changes for individual surgery procedures were $-41.4 \times 10^6 (-17.0 \times 10^6 \text{ to } -65.8 \times 10^6; p = 0.0391)$ and $-91.1 \times 10^6 (-45.8 \times 10^6 \text{ to } -136.5 \times 10^6; p = 0.0080)$ for GB and SG, respectively. At baseline,

8 patients (17.4 %) presented with oligozoospermia, i.e. $< 15 \times 10^6$ sperm per ml. At 6 and 12 months, a slight increased number of patients presented with oligozoospermia (21.7 % for both time points); some patients showed improvement in the number of spermatozoa per ml and others deteriorated with time (Table 3). The percentage of normal spermatozoa decreased from 15.4% (± 8.7) at baseline to 12.4% (± 6.4) at 12 months, a 3.0% decrease ($4.8 - 1.1\%$; $p = 0.0416$). The percentage of partial and total fragmentation of DNA determined in 33 patients also showed a significant decrease at 12 months of 1.1%, ($0.5 - 1.7\%$; $p = 0.0021$) and 2.2% ($1.1 - 3.4\%$; $p = 0.0095$), respectively. Values of semen volume (ml), and spermatozoa motility (%) and vitality (%) were not modified.

We were not able to show any correlation between variations in TSC and BMI, either at 6 or at 12 months post-surgery (Fig. 2). As expected, we found an increase in total testosterone and SHBG with time after surgery (Fig. 3). Interestingly the presence of MOSH defined by total testosterone < 10.5 nmol/L (23/46 patients i.e. 50% at baseline) decreased massively with time after surgery, with 4/46 and 1/46 patients with the condition at 6 and 12 months, respectively. In addition, metabolic and inflammatory variables improved with time post-surgery; whereas, insulin, HOMA-IR and leptin decreased with weight loss (Fig. 3). No correlation was found between vitamin or pollutant levels in blood at each time point and the primary outcome (data not shown).

Discussion

Our study showed that total sperm count was decreased at 12 months after bariatric surgery in patients with no history of infertility, despite improvements of total testosterone and SHBG levels. Deterioration of sperm quality occurred even in the absence of a previous history of infertility, in a cohort of patients in whom < 20 % presented with oligozoospermia at baseline. These results were consistent with the deleterious consequences on sperm variables previously suggested for bariatric surgery in a few alarming case reports (19–21). However,

175 the effects of bariatric surgery on semen quality are still controversial (22). Only 3 previous
prospective studies addressed this important question with opposite results. One study showed
no deterioration among sperm variables when comparing 10 patients who underwent GB with
20 month follow-up versus controls, despite a massive weight loss in the intervention group
(13). They reported no change in median sperm concentration in the control group (40.6×10^6
180 $\pm 29.8 \times 10^6/\text{ml}$) and a non-significant improvement was seen in the surgery group ($100.4 \times$
 $10^6 \pm 66.5 \times 10^6/\text{ml}$). One could argue that the number of patients in each group ($n = 10$) was
insufficient to demonstrate any significant effect; moreover, median sperm concentrations
were different between the surgery and control groups at baseline, with $78.7 \times 10^6 \pm 58.6 \times$
 $10^6/\text{ml}$ and $40.3 \times 10^6 \pm 33.7 \times 10^6/\text{ml}$, respectively. Samavat et al. designed a prospective
185 study of 31 morbidly obese men undergoing GB ($n = 23$) versus an unbalanced non-surgery
group ($n = 8$), assessing sperm variables at baseline and 6 months (14). They showed a similar
positive trend in the total sperm number in the surgery group, though only the increase in
semen volume and viability was statistically significant (increases of 0.6 ml and 10 %,
respectively; $p < 0.05$). As in the first study of Reis et al., total sperm count and concentration
190 seem to be higher in the surgery group than in the group not operated on, even at baseline
(mean sperm concentration of 83.0×10^6 , $\pm 100.0 \times 10^6/\text{ml}$ and 16.0×10^6 , $\pm 19.0 \times 10^6/\text{ml}$,
respectively). El Bardisi et al. have conducted a prospective study of 46 infertile patients who
underwent SG showing a significant increase in sperm concentration, but only in men with
preoperative azoospermia and oligozoospermia (15). This last study design was completely
195 different owing to a history of infertility among participants (median years of infertility of 3.8
years, 1.4 - 5.9). Median TSC was low preoperatively (2.5×10^6 , 0 - $143 \times 10^6/\text{ml}$) and
postoperatively (7.2×10^6 , 0 - $128 \times 10^6/\text{ml}$) with non-significant improvement across the
group of 46 patients. While we also showed major improvement of MOSH as assessed by
total testosterone levels, TCS was altered significantly at 12 months postoperatively in our

200 prospective controlled study.

The exclusion of patients with a history of infertility was a major difference with the previous prospective studies. Indeed, our population presented high semen quality at baseline compared to the other studies previously mentioned and if it has been demonstrated that bariatric surgery and the obtained massive weight loss ameliorate seminal variables in patients with reduced semen quality, bariatric surgery was not expected to decrease these variables starting from a seminal healthy population. Table 3 reported data on the only eight oligozoospermic patients present in our cohort where normalization of sperm count was evident in 4 and 5 of them respectively at 6 and 12 months after bariatric surgery. These last results are consistent with the previous data including those from El Bardisi et al. who described a significant increase in semen variables, including sperm count, only in those with reduced semen quality at baseline (oligozoospermic or azospermic). In contrast, Table 3 will also show that a number of patients with normal baseline TCS will present oligospermia at 6 and 12 month after surgery (n=6 and 7/38 respectively). Because the study was limited to 1 year, we did not assess whether the effects of the weight loss from bariatric surgery on semen variables were reversible long-term. Furthermore, the ultimate effect on male fertility remains unknown and difficult to predict with the apparent paradoxical situation of worsening TSC postoperatively, but resolution of MOSH and decreased fragmentation of spermatozoa DNA.

MOSH has been found in approximately 40 – 60% of severely obese male candidates for bariatric surgery, which leads to complete resolution in many patients (23,24). Correlations between testosterone levels and semen alterations are not clear; a prevalence of 62 % of sperm variables abnormalities has been shown in 31 patients with moderate to severe obesity, but the frequencies of low total or free testosterone values were similar in patients with abnormal and normal semen (24). This was consistent with our findings that showed in our 50% of included patients with hypogonadism at baseline, a reversibility of hypogonadism

225 with massive weight loss at 6 and 12 months but no correlations with sperm quality improvement. Finally we did not find any significant change in libido assessed by IIEF5 at 6 months although, in a larger observational cohort, half of men experienced clinically meaningful improvements in sexual functioning one year after bariatric surgery (25).

In agreement with our results, El Bardisi et al. did not find any positive correlation
230 between semen changes and the extent of weight loss experienced by the 46 patients who underwent SG (15). Samavat et al. showed a significant correlation between changes in sperm number and BMI for 23 patients who underwent GB, but looking back to the Figure 1 of this original article, we found that the correlation was carried strongly by only two patients (14). Our study was designed to investigate semen changes after the two main types of bariatric
235 surgery (SG and GB) and did not show any differences in the sperm consequences of the 2 types of procedures. On the other hand, given the presence of oligospermia cases that have appeared de novo in post-surgery (Table 3), the average age of the patients who are candidates for bariatric surgery and the frequency of difficulties to conceive for a non-negligible number of couples suffering from obesity, consultation specialized in fertility
240 disorders with the idea of performing a sperm count with cryopreservation for later use might be systematically proposed.

Finally all the published results, including ours, suffer from a main limitation concerning the number of participants. We could argue that this is probably driven by the fact that a vast majority of operated patients are women (>80% in France) and that sperm
245 collection is restrictive.

Conclusions

Improvement in some semen variables after bariatric surgery observed in 3 previous studies is in contrast to the lower mean total sperm count found in this study at one year The possible

250 reversibility of this effect at long-term and the impact of surgery on fertility both remain
unknown.

Authors' role

255 SC who was the grant holder and chief investigator, contributed to study design and
implementation, and wrote the protocol. RL and PR contributed to study design. GB was
responsible for the statistical analysis plan and provided statistical analysis. CC wrote the first
draft of the manuscript. All authors have read and approved the final report.

Acknowledgements

The study was funded by a grant from Programme Hospitalier de Recherche Clinique –
PHRC 2011 (Ministère de la Santé, N° AOM 11193). The sponsor was Assistance Publique –
Hôpitaux de Paris (Délégation à la Recherche Clinique et à l'innovation). We are indebted to
Pr Jean-Marc Treluyer and the staff of the Clinical Research Department (Unité de Recherche
265 Clinique "Paris Cochin") for their valuable technical and logistical support. We would like to
thanks Myriam Benarroch and Celine Faure for their logistical support during the study.

Funding

The BARIASPERM study was funded by the French National Programme Hospitalier de
270 Recherche Clinique – PHRC 2011 (Ministère de la Santé, N° AOM 11193).

Conflict of interest

SC holds shares of MyGoodLife. For the remaining authors none were declared.

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Tables

355 Three tables have been uploaded as separate documents.

Figure legends

Figure 1: Flowchart of the BARIASPERM study

Figure 2: Absence of significant correlations between total sperm count (TSC) and body
360 mass index (BMI) changes between inclusion and 6 months (M6) and 12 months (M12)
postoperatively.

Figure 3: Changes in sexual and metabolic hormones

Figure 1: Flowchart of the BARIASPERM study

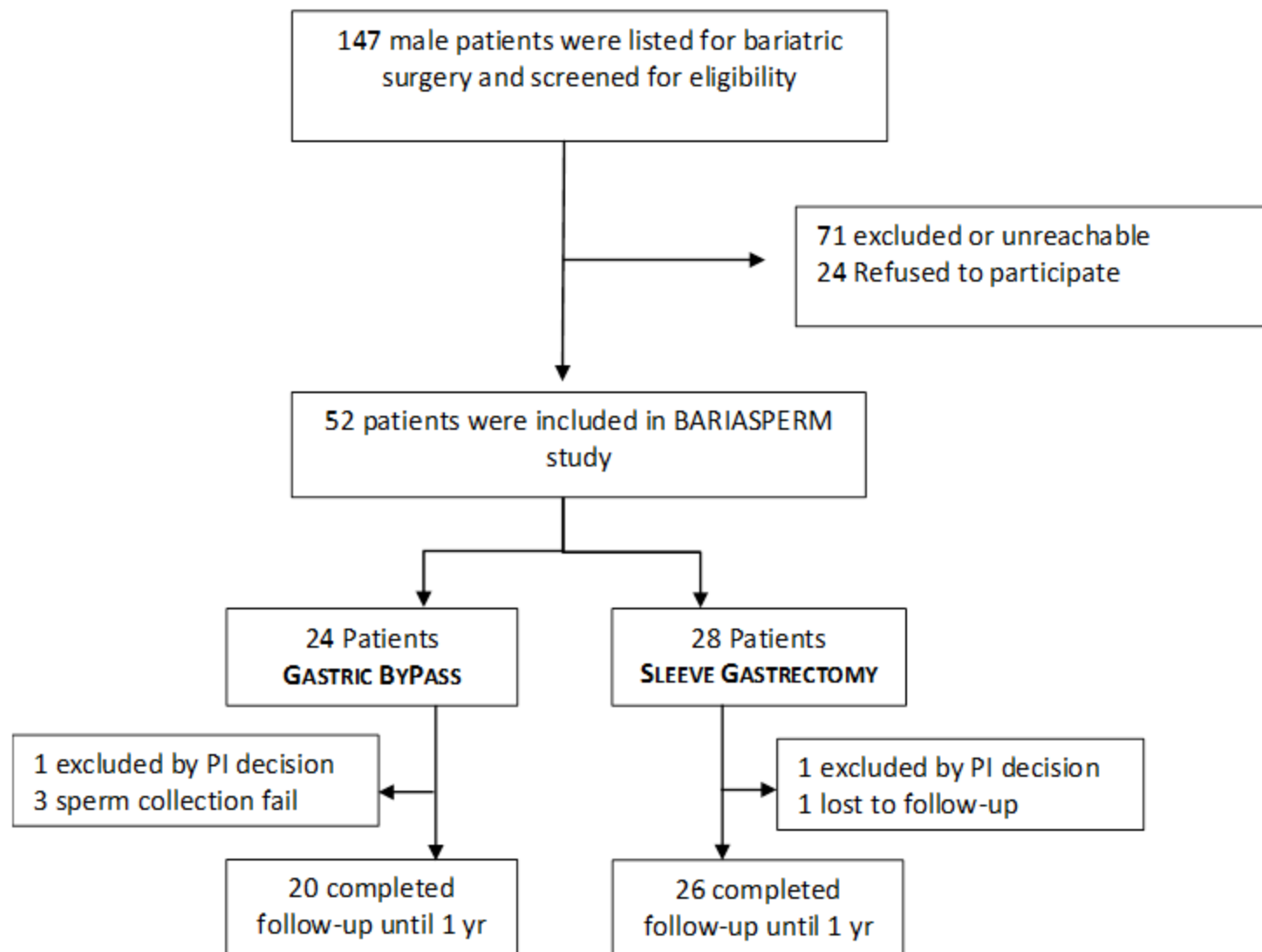
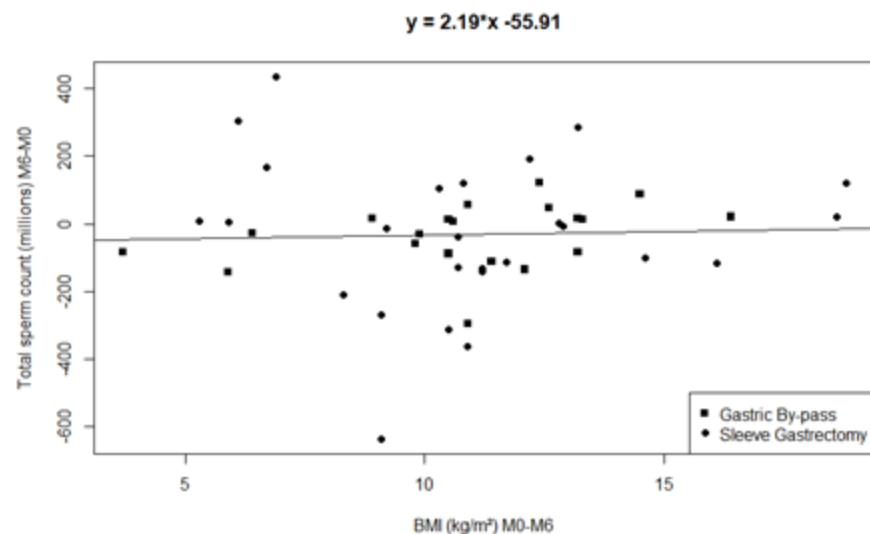
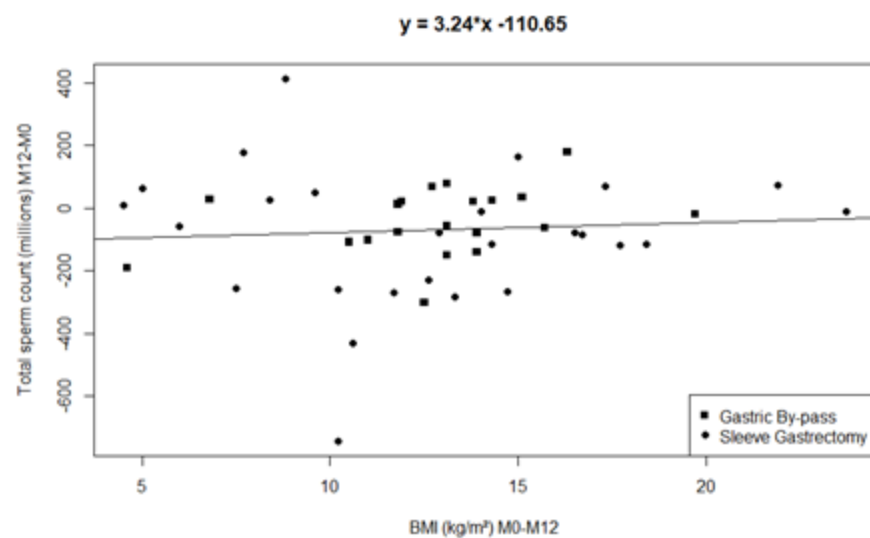


Figure 2: Absence of significant correlations between total sperm count (TSC) and body mass index (BMI) changes between inclusion and 6 months (M6) and 12 months (M12) postoperatively.

M6 : $R^2=0.00$, $p=0.79$



M12 : $R^2=0.00$, $p=0.62$



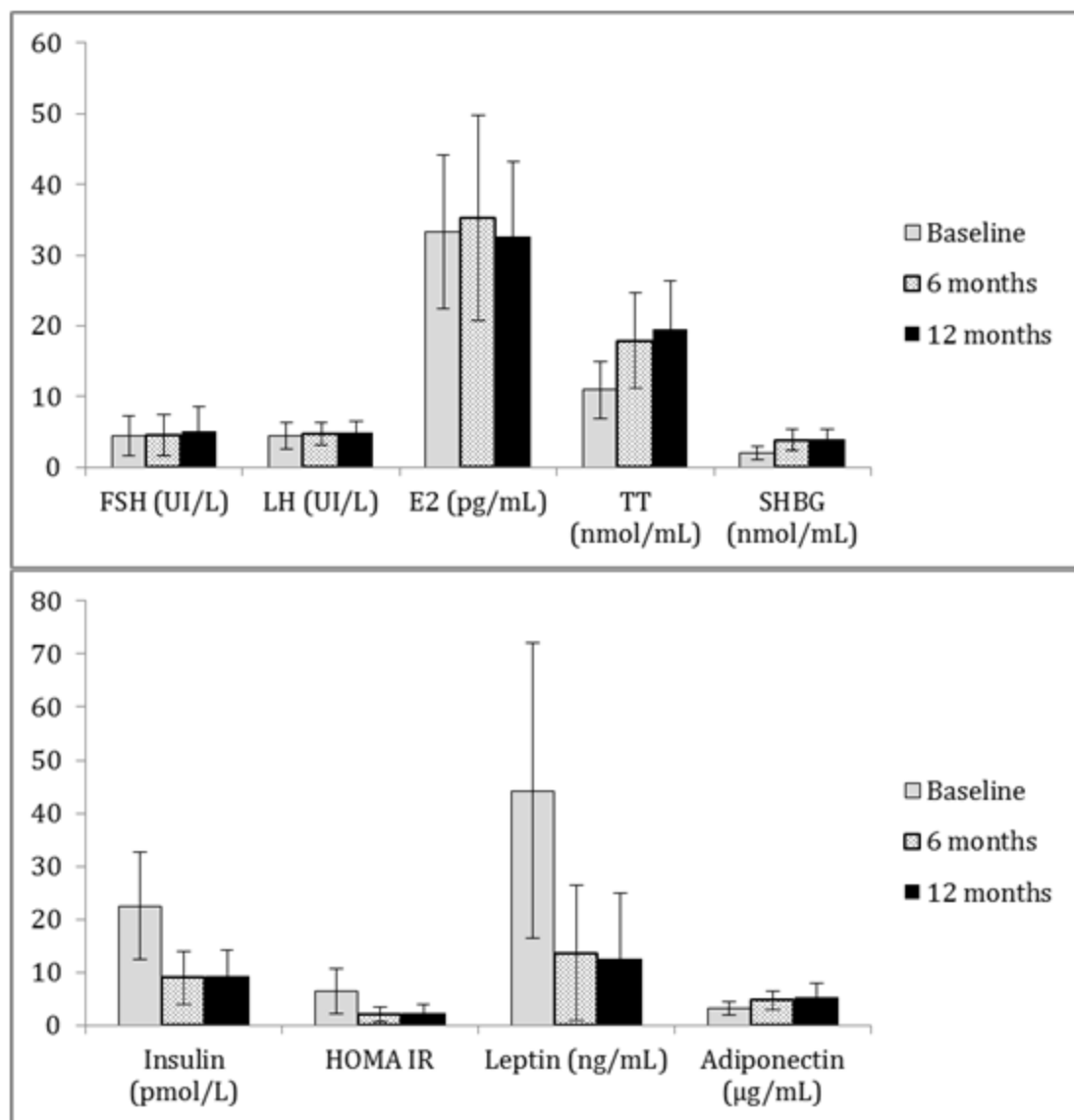


Figure 3: Changes in sexual and metabolic hormones with time after bariatric surgery.

Table 1: Preoperative anthropometric and biological characteristics of the 46 study completers

Characteristics at inclusion	Surgery group		Both groups (n=46)
	Gastric By-pass (n=20)	Sleeve Gastrectomy (n=26)	
Anthropometrics measures, mean (SD)			
Age, years	41.7 (6.9)	36.8 (8.0)	38.9 (7.9)
Weight, kg [Range]	138.4 (18.2) [106-178]	141.8 (23.5) [106-192]	140.3 (21.2) [106-192]
BMI, kg/m²	44.1 (4.9)	44.1 (6.0)	44.1 (5.5)
Waist circumference, cm [Range]	140.1 (12.1) [117-158]	137.5 (15.0) [113-171]	138.6 (13.8) [113-171]
Systolic blood pressure, mm Hg	131.6 (16.2)	135.0 (14.8)	133.6 (15.3)
Diastolic blood pressure, mm Hg	83.0 (13.6)	90.5 (14.6)	87.3 (14.5)
Fasting Laboratory values, mean (SD)			
Total cholesterol, mmol/L	4.9 (0.9)	5.1 (1.0)	5.0 (0.9)
LDL cholesterol, mmol/L	3.1 (0.8)	3.2 (0.8)	3.2 (0.8)
HDL cholesterol, mmol/L	1.2 (0.4)	1.0 (0.2)	1.1 (0.3)
Triglycerides, mmol/L	1.4 (0.6)	2.0 (0.8)	1.7 (0.8)
Glucose, mmol/L	6.0 (2.1)	6.1 (1.7)	6.1 (1.8)
Insulin, pmol/L	21.8 (8.2)	23.1 (11.5)	22.5 (10.1)
HOMA-IR	6.4 (4.7)	6.4 (4.0)	6.4 (4.3)

Abbreviations: BMI = Body Mass Index; HOMA-IR: Homeostatic model assessment of insulin resistance; SD: Standard Deviation.

Table 2: Changes in the seminal, anthropometric and lifestyle habits parameters with bariatric surgery after 6 and 12 months of follow-up compared to inclusion

Criteria	N	Baseline	6 months	12 months	6 months - Baseline (CI95%)*	p value	Adjusted p value **	12 months – baseline (CI95%)*	p value	Adjusted p value **
Total sperm count (10 ⁶)*, mean (SD)	46	177.7 (177.7)	145.7 (130.6)	108.2 (92.9)	-32.1 (-68.8;4.7)+++	0.0856		-69.5 (-96.8;-42.2)	<0.0001	0.0021
Total sperm count - GB patients (10 ⁶)*, mean (SD)	20	119.6 (107.5)	86.7 (68.4)	78.2 (51.8)	-32.9 (-61.8;-4.0)	0.0278	0.4170	-41.4 (-65.8;-17.0)	0.0022	0.0391
Total sperm count - SG patients (10 ⁶)*, mean (SD)	26	222.5 (208.0)	191.0 (149.1)	131.3 (110.5)	-31.4 (-91.4;28.5)	0.2900	0.9354	-91.1 (-136.5;-45.8)	0.0004	0.0080
Volume (ml), mean (SD)	46	2.75 (1.26)	2.73 (1.45)	2.71 (1.22)	-0.01 (-0.37;0.35)	0.9354	0.9354	-0.04 (-0.37;0.29)	0.8047	0.9354
Motility (%), mean (SD)	46	35.0 (12.6)	33.1 (12.4)	31.8 (12.0)	-2.0 (-5.2;-1.3)	0.2304	0.9354	-3.3 (-6.7;0.1)	0.0592	0.7696
Vitality (%), mean (SD)	43	56.7 (14.6)	60.0 (14.8)	59.7 (15.7)	3.3 (-0.5;7.1)	0.0833	0.9354	3.0 (-1.3;7.4)	0.1683	0.9354
Partial fragmentation of DNA (%),mean (SD)	33	4.6 (4.2)	4.3 (2.4)	3.5 (1.8)	-0.3 (-1.1;0.5)	0.4727	0.9354	-1.1 (-1.7;-0.5)	<0.0001	0.0021
Total fragmentation of DNA (%),mean (SD)	33	9.9 (6.3)	8.3 (5.7)	7.7 (3.5)	-1.6 (-3.5;0.3)	0.1022	0.9354	-2.2 (-3.4;-1.1)	0.0005	0.0095
Typic sperm (%), mean (SD)	43	15.4 (8.7)	14.1 (8.5)	12.4 (6.4)	-1.3 (-3.9;1.3)	0.3112	0.9354	-3.0 (-4.8;-1.1)	0.0026	0.0416
Weight (kg)**, mean (SD)	46	140.4 (21.8)	105.8 (19.6)	100.1 (19.5)	-34.7 (-37.5;-31.8)	<0.0001	0.0021	-40.3 (-44.0;-36.7)	<0.0001	0.0021
BMI (kg/m ²)**, mean (SD)	46	44.1 (5.7)	33.2 (5.4)	31.4 (5.3)	-10.9 (-11.8;-10.0)	<0.0001	0.0021	-12.7 (-13.8;-11.6)	<0.0001	0.0021
Waist Circumference (cm), mean (SD)	46	138.6 (13.8)	111.7 (16.0)	107.9 (15.5)	-26.9 (-29.8;-24.1)	<0.0001	0.0021	-30.7 (-33.9;-27.5)	<0.0001	0.0021
Hip Circumference (cm), mean (SD)	46	128.6 (13.3)	107.9 (14.1)	104.5 (13.0)	-30.7 (-23.0;-18.4)	<0.0001	0.0021	-24.1 (-26.6;-21.6)	<0.0001	0.0021
IPAQ: Physical activity, n (%)	38			-	-	0.0394	0.5516	-	-	-
Low		16 (42.1)	7 (18.4)							
Middle		16 (42.1)	16 (42.1)							
High		6 (15.8)	15 (39.5)							
IIEF5 (5-25)***, mean (SD)	44	20.4 (4.4)	20.5 (6.2)	-	0.1 (-1.0;1.3)	0.8152	0.9354	-	-	-
Tobacco, n (%)	46			-	-	0.7212	0.9354	-	-	-
Never smoked		7 (15.2)	6 (13.0)							
Ex-smoker		17 (37.0)	17 (37.0)							
Smoker		22 (47.8)	23 (50.0)							
Expired CO (ppm), mean (SD)	28	5.8 (4.6)	7.3 (10.0)	-	1.5 (-1.9;4.8)	0.3757	0.9354	-	-	-

Abbreviations: SD: Standard Deviation; CI: Confidence Interval ; GB: Gastric bypass; SG: Sleeve gastrectomy; BMI: Body Mass Index; IPAQ International Physical Activity Questionnaire; IIEF5: International Index of Erectile Function Questionnaire; CO : Carbon Monoxyde.

*For quantitative variables only

**Adjusted p values (Hochberg adjustment). An adjusted p <0.05 was considered statistically different

+++Primary outcome

*Total sperm counts (TSC) = Number of spermatozoa (in millions) per ml x volume (ml)

**Measured value (handled by reported value if missing data)

***Only patients with IIEF5 > 4

Table 3: Percentage of patients presenting with oligospermia at inclusion compared to 6 and 12 months postoperatively. Oligospermia is defined by sperm concentration less than 15 millions per ml (World Health Organization 2010). The 10 patients with oligospermia at 6 and 12 months were not the very same patients.

		Inclusion	6 months		12 months	
			Oligospermia	Normal	Oligospermia	Normal
Inclusion	Oligospermia	8 (17.4%)	4	4	3	5
	Normal	38	6	32	7	31
	Total	46	10 (21.7%)	36	10 (21.7%)	36