#### REVIEW





# Bariatric Surgery Does Not Improve Semen Quality: Evidence from a Meta-analysis

Zhiguang Gao<sup>1</sup> · Yuzhi Liang<sup>2</sup> · Sen Yang<sup>1,4</sup> · Tao Zhang<sup>1</sup> · Zuyuan Gong<sup>1</sup> · Min Li<sup>1</sup> · Jingge Yang<sup>3</sup>

Received: 23 November 2021 / Revised: 31 December 2021 / Accepted: 13 January 2022 / Published online: 10 February 2022 © The Author(s), under exclusive licence to Springer Science+Business Media, LLC, part of Springer Nature 2022

## Abstract

The meta-analysis aimed to explore the possible relationship between bariatric surgery and semen quality. PubMed, EMBASE, and CENTRAL were searched from database inception through October 28, 2021. Articles were eligible for inclusion if they evaluated the impact pre- and post-bariatric surgery on semen parameters. A total of 9 studies with 218 patients were found. The mean preoperative age distribution of the patients included centralized from 18 to 50 years, and the mean pre-op BMI ranged from 36.7 to 70.5 kg/m<sup>2</sup>. The follow-up period ranged from 6 to 24 months. The results revealed that bariatric surgery had no significant effect on sperm volume, concentration, total count, morphology, total motility, progressive motility, viability, semen pH, and semen leukocytes. Bariatric surgery does not improve semen quality in obese males.

Keywords Bariatric Surgery · Semen Quality · Sperm · Obesity · Meta-Analysis

Zhiguang Gao, Yuzhi Liang and Sen Yang contributed equally to this work.

#### **Key Points**

1. Bariatric surgery did not change sperm volume, concentration, and total count.

2. There were no changes in sperm morphology, motility, and viability after bariatric surgery.

3. Semen pH and leukocytes remained unchanged following bariatric surgery.

4. Bariatric surgery does not improve semen quality in obese men.

☐ Jingge Yang dukeyjg@126.com

> Zhiguang Gao gaozhiguangscholar@dingtalk.com

Yuzhi Liang 297227216@qq.com

Sen Yang 326285114@qq.com

Tao Zhang 1184069367@qq.com

Zuyuan Gong 55917590@qq.com

Min Li drlimin@yahoo.com

# Introduction

Obesity has a significant and increasing impact on people's good health. As a chronic disease, obesity carries with it numerous health-related consequences, including reproductive abnormality [1, 2]. In men, it is estimated that a 10-kg weight gain may reduce fertility by about 10% [3, 4]. There have been several investigations reporting abnormalities in semen parameters associated with increased body weight [5, 6], and an increased prevalence of azoospermia or oligozoospermia is demonstrated among obese male patients [7, 8].

- <sup>1</sup> Department of Gastrointestinal Surgery, the affiliated Dongguan Shilong People's Hospital of Southern Medical University, Dongguan 523320, China
- <sup>2</sup> Department of Medical Imaging, the affiliated Dongguan Shilong People's Hospital of Southern Medical University, Dongguan 523320, China
- <sup>3</sup> Guangdong Medical University, Zhanjiang, Guangdong Province, China
- <sup>4</sup> Department of Gastrointestinal Surgery, First Affiliated Hospital of Jinan University, 613 Huangpu Avenue West, Guangzhou 510630, Guangdong Province, China

Bariatric surgery has proven to be an effective treatment strategy in treating obesity and improving associated comorbidities. At present, the most commonly conducted bariatric surgical procedures are Roux-en-Y gastric bypass (RYGB) and sleeve gastrectomy (SG). Several studies have investigated the changes in semen parameters in patients with obesity after bariatric surgery, reporting controversial results. Some reported no alteration in sperm volume, total count, morphology, and the total and progressive motility after SG [9], some found elevated sperm volume and viability but no alteration in concentration, total count, morphology, and the total and progressive motility after RYGB [10], while others observed a severe worsening of semen parameters after bariatric surgery [11, 12].

Previous meta-analysis by Wei et al. including 6 articles indicated that RYGB significantly increased sperm volume, while SG elevated normal morphology rate; however, sperm concentration and the percentage of progressive motility remained unchanged after surgery [13]. Deficiently, this study had a small sample size (n = 90) and included two case reports with a sample size of less than 4, so the results should be treated with caution. Subsequently, another metaanalysis conducted by Lee Y et al. in exploring the effect of bariatric surgery on male sexual function mentioned that bariatric surgery did not affect male sperm quality, but this result was not the primary outcome of the study [14]. In addition, these reviews did not investigate the changes in total sperm count, sperm viability, semen pH, and semen leukocytes. Recently, Wood et al. found that, despite no statistical changes in sperm volume, morphology, and motility after RYGB, sperm concentration and total count reduced notably [15]. Nevertheless, the latest research showed that bariatric surgery led to a significant improvement in sperm volume, concentration, progressively motile sperm count, and morphology [16].

Based on these different pieces of evidence, it is hard for us to draw a conclusion about the exact relationship between bariatric surgery and semen quality. Therefore, this study aimed to make a meta-analysis regarding the impact of bariatric surgery on semen quality.

## Methods

## Search Strategy

A comprehensive literature search was conducted in October 2021 adhering to the Preferred Reporting items for Systematic Reviews and Meta-Analyses (PRISMA) [17] using the databases PubMed, EMBASE, and the Cochrane Central Register of Controlled Trials (CENTRAL) for articles published in English that included the terms "bariatric surgery," "metabolic surgery," "obesity surgery," "weight loss surgery," "sleeve gastrectomy," "gastric bypass," "gastric banding," "duodenojejunal bypass," "biliopancreatic diversion," "sperm," "semen," and "reproductive function." The search was conducted in October 2021 and was not limited to any date range. The references of identified articles and reviews were also searched manually to ensure that other relevant articles were not missed.

## **Inclusion and Exclusion Criteria**

Inclusion criteria were as follows: (1) obese subjects with BMI > 30 kg/m<sup>2</sup>; (2) provided the pre- and postoperative data of semen analysis (e.g., sperm volume, concentration, total count, % normal morphology, % progressive motility, % total motility, % sperm viability, and semen pH and leukocytes). No available data, animal studies, case reports (n < 3), comments, letters, conference abstracts, reviews, and meta-analyses were excluded. If similar studies used data from overlapping populations, only the study with the most information was included, and others were excluded. As for the missing data, we would contact the authors by email for complete information if possible.

## **Selection Process and Data Abstraction**

Three reviewers independently screened the titles, abstracts, and full text according to the inclusion and exclusion criteria and extracted the corresponding data to fill in a pre-specified form. Final discrepancies were resolved by discussion. The following data were extracted: the first author, publication year, country, study design, type of bariatric surgery, number of study participants, mean age at the time of surgery, length of follow-up, preoperative mean BMI, and outcome indicators.

## **Outcomes Assessed and Risk of Bias Assessment**

The primary outcomes were sperm quality. In this study, meta-analyses were conducted on the nine domains of sperm quality, which included sperm volume (ml), sperm concentration ( $10^6/ml$ ), total sperm count ( $10^6$ ), % total motility, % normal morphology, % progressive motility, % sperm viability, semen pH, and semen leukocytes ( $10^6/ml$ ). Secondary outcomes were sex hormones (total testosterone (TT), estradiol (E2), and sex hormone–binding globulin (SHBG)). The quality of included studies was evaluated by the Methodological Index for Non-Randomized Studies (MINORS) [18].

## **Statistical Analysis**

In this study, the standardized mean difference (SMD) with 95% confidence intervals (CIs) was calculated for continuous variables. Mean and standard deviation (SD) was calculated for studies that reported median (minimum, maximum) using the computing method proposed by Wan et al [19]. For data shown as median (interquartile range, IQR), the following calculation formula was used: mean = median, SD=IQR/1.35, according to the Cochrane handbook of systematic reviews of interventions. Assessment of heterogeneity was completed using the inconsistency  $(I^2)$  statistic, with a significance threshold of  $I^2 > 50 \%$  [20]. If the  $I^2$  statistic was significant, a random effect model was used to estimate pooled effect size. Otherwise, a fixed effect model would be employed. Sensitivity and subgroup analyses were performed if necessary and feasible. The one-study-out method was used for sensitivity analyses, and subgroup analyses were performed based on whether or not data was shown as median (interquartile range) (yes vs. no), type of surgery (RYGB vs. SG vs. RYGB/SG), and follow-up duration ( $\geq$ 12 months vs. < 12 months). Publication bias was assessed by the Egger test for the included studies  $\geq 6$ . A p value < 0.05 was defined as statistical significance. All statistical

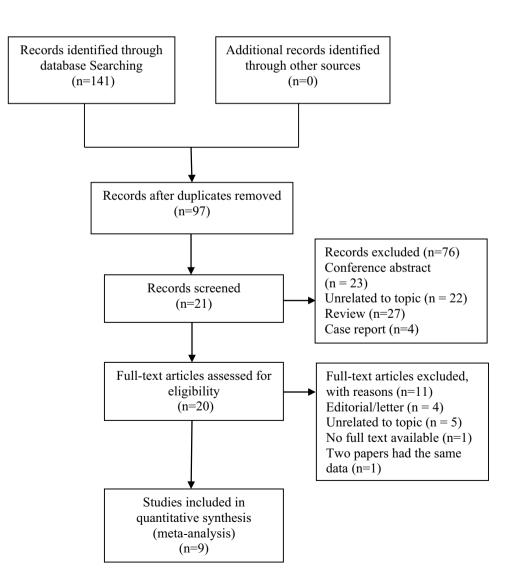
Fig. 1 Flow diagram of study selection

analysis and meta-analysis were performed on Review Manager (RevMan version 5.3) and Stata (version 12.0).

## Results

## **Literature Retrieval Results and Basic Characteristics**

The flow diagram outlining the search process is shown in Figure 1. A total of 141 potential articles were identified. After removing duplicates and reviewing titles, abstracts, and full text, 10 publications were identified for eligibility of inclusion criterion [9, 10, 15, 16, 21–26]. Thereinto, two papers had the same first author with the same semen analysis data [21, 22], and one of them was included for analysis [22]. Hence, the remaining 9 articles with a total of 218 patients were included in the meta-analysis [9, 10, 15, 16, 22–26]. Quality assessment of the included studies is presented in Table 2.



Study characteristics of included studies are presented in Table 1. The average preoperative age distribution centralized from 18 to 50 years and the mean pre-op BMI ranged from 36.7 to 70.5 kg/m<sup>2</sup>. The types of data expression were not completely consistent among these studies. Seven adopted means  $\pm$  SD, one used median (interquartile range), and one employed median (minimum, maximum). Also, different types of bariatric procedures included Roux-en-Y gastric bypass (RYGB; 4 studies), sleeve gastrectomy (SG; 2 studies), and RYGB/SG (3 studies). The follow-up period ranged from 6 to 24 months (Table 2).

## **Primary Outcome**

#### **Sperm Volume**

Nine trials documented the sperm volume before and after bariatric surgery. Significant heterogeneity was observed among studies ( $I^2 = 81\%$ ). The random effects model showed that there was no significant change in sperm volume after surgery (SMD = -0.34, 95% CI -0.86 to 0.18, p= 0.20) (Fig. 2a). As shown in Table 3, subgroup analysis did not resolve heterogeneity, but the pooled results showed that RYGB had a positive effect on sperm volume increase. Additionally, one study removal sensitivity analysis did not change the overall summary result. No significant publication bias was found with the Egger test (p = 0.216).

Table 1 Study characteristics

#### **Sperm Concentration**

Seven studies reported preoperative and postoperative sperm concentration. Heterogeneity was considered borderline to be statistically significant ( $I^2 = 62\%$ ). The random effects model showed that there was no relationship between bariatric surgery and sperm concentration (SMD = -0.17, 95% CI -0.60 to 0.25, p = 0.43) (Fig. 2b). Subgroup analysis could not explain the source of heterogeneity. In sensitivity analysis, the pooled estimate remained stable after omitting any one of the studies in turn. Nevertheless,  $I^2$  decreased from 62 to 0% after excluding the study by Velotti et al. [16]. No significant publication bias was seen using the Egger test (p = 0.674).

## **Total Sperm Count**

Five studies examined the effect of bariatric surgery on total sperm count. Because of the presence of heterogeneity ( $I^2 = 75\%$ ), the random effects model was used to pool result and showed that total sperm count did not change significantly after surgery (SMD = 0.21, 95% CI -0.27 to 0.70, p = 0.39) (Fig. 2c). The pooled estimate remained statistically significant regardless of which studies were excluded. Publication bias was not detected because the number of included studies was less than 6.

Study	Country	Study design	Surgery	n	Mean age	Follow- up (months)	Pre-BMI (mean $\pm$ SD) (kg/m <sup>2</sup> )	Outcome indicators
Calderón 2019* [21]	Spain	Prospective	LRYGB LSG	20	50±10	24	41±10	SV <sup>A</sup> , SC, semen pH, TM, PM, SVB, NM
Calderón 2020* [22]	Spain	Prospective	LRYGB LSG	20	50±10	24	41 <u>±</u> 10	SV <sup>A</sup> , SC, semen pH, TM, PM, SVB, NM
Carette 2019 [23]	France	Prospective	RYGB SG	46	38.9 <u>±</u> 7.9	12	44.1±5.5	SV, TSC, TM, SVB, NM
El Bardisi 2016 [9]	Egypt	Prospective	SG	46	36.8± 3.38	12	$70.5 \pm 12.02$	SV <sup>B</sup> , TSC <sup>B</sup> , TM <sup>B</sup> , NM <sup>B</sup> , PM <sup>B</sup>
Fariello 2021 [24]	Brazil	Prospective	RYGB	15	20-50	12	45.7 <u>±</u> 8.3	SV, SC, TSC, NM, PM,
Legro 2015 [25]	USA	Prospective	RYGB	6	18-40	12	48 <u>+</u> 7	SV, SC, TM, NM
Reis 2012 [26]	Brazil	Prospective	GB	10	$41.7 \pm 10.8$	24	36.7±11.5	SV, SC, TM, NM, SVB, semen pH, LK
Samavat 2018 [10]	Italy	Prospective	LRYGB	23	NR	6	45.8 ± 7.4	SV, SC, TSC, SVB, NM, TM, PM, semen pH
Velotti 2021 [16]	Italy	Prospective	LSG	35	36.40±5.17	6	39.56±1.51	SV, SC, NM, PM
Wood 2020 [15]	Brazil	Prospective	RYGB VG	18	39.0 (16.0)	6	43.9 (11.6)	SV <sup>A</sup> , SC <sup>A</sup> , TM <sup>A</sup> , TSC <sup>A</sup> , PM <sup>A</sup> , NM <sup>A</sup> , LK <sup>A</sup>

*NR* not reported, *RYGB* roux-en-Y gastric bypass, *LSG* laparoscopic sleeve gastrectomy, *SG* sleeve gastrectomy, *GB* gastric bypass, *VG* vertical sleeve gastrectomy *BMI* body mass index, *SV* sperm volume (ml), *SC* sperm concentration ( $10^6$  /ml), *TM* total motility (%), *PM* progressive motility (%), *SVB* sperm viability (%), *NM* normal morphology (%), *TSC* total sperm count ( $10^6$  /ml), *LK* leukocyte ( $10^6$ /ml)

\*These two papers had the same first author with the same semen analysis data, and we included the later one for analysis

<sup>A</sup>Data was shown as medians (interquartile range)

<sup>B</sup>Data was shown as medians (minimum, maximum)

Study	A stated aim of the study	Inclusion of consecutive patients	Prospective collection of data	Endpoints appropriate to the study aim	Unbiased assessment of the study endpoint	Follow-up period appropriate to the aim of the study	Loss to follow-up not exceeding 5%	Prospective calculation of the study size	Total
Calderón 2020 [22]	2	2	2	2	2	2	2	0	14
Carette 2019 [23]	2	2	2	2	2	2	2	0	14
El Bardisi 2016 [9]	2	2	2	2	2	2	2	0	14
Fariello 2021 [24]	2	2	2	2	2	2	2	0	14
Legro 2015 [25]	2	1	2	2	2	2	2	0	13
Reis 2012 [26]	2	2	2	2	2	2	2	0	14
Samavat 2018 [10]	2	2	2	2	2	2	2	0	14
Velotti 2021 [16]	2	2	2	2	2	2	2	0	14
Wood 2020 [15]	2	2	2	2	2	2	2	0	14

The items are scored 0 (not reported), 1 (reported but inadequate), or 2 (reported and adequate). The global ideal score being 16 for non-comparative studies

#### Semen Total Motility and Progressive Motility

Seven trials were included in the meta-analysis of sperm total motility. No significant heterogeneity was seen between studies ( $I^2 = 9\%$ ), so the fixed effect model was used to pool result and showed that bariatric surgery did not affect the sperm total motility (SMD = 0.15, 95% CI -0.07 to 0.36, p = 0.18) (Fig. 2d). When any one of the studies was excluded, the pooled results did not change significantly. Pooled analyses were also performed in six enrolled articles with the evaluation of seminal progressive motility. Meta-analysis showed that no homogeneity existed ( $I^2 = 78\%$ ) and indicated that there was no statistical change in sperm progressive motility after the bariatric surgery intervention (SMD = -0.41, 95% CI -0.91to 0.08, p = 0.10) (Fig. 2e). In the subgroup analysis, the outcomes showed that progressive motility after bariatric surgery remained stable regardless of follow-up duration  $(12 \ge \text{months or} < 12 \text{ months})$  and type of bariatric surgery (RYGB or SG). When omitting any one study out in turn, the pooled estimate was remarkably changed. The p values of the Egger test for sperm total motility (p =0.268) and progressive motility (p = 0.599) suggested that there was no significant publication bias.

#### Normal Morphology

Data on sperm normal morphology was presented in nine articles. Based on the random effects model ( $I^2$ =83%), the analysis of data from these articles presented no differences in the percentage of normal morphology before and after surgery (SMD = -0.31, 95% CI -0.80 to 0.19, p = 0.22) (Fig. 2f). Subgroup analysis did not address heterogeneity, but the results showed that, regardless of follow-up duration, neither RYGB nor SG had any effect on the normal

morphology rate. Sensitivity analysis using the one-studyout method yielded similar results. Publication bias was not found (Egger, p = 0.480).

#### Sperm Viability, Semen pH, and Semen Leukocytes

Information about sperm viability, semen pH, and semen leukocytes in the obese individuals pre- and post-surgery was available in 4, 3, and 2 studies, respectively.  $I^2$  was 64%, 87%, and not applicable, respectively. The random effects models showed bariatric surgery did not result in significant variation in sperm viability (SMD = -0.28, 95% CI -0.57 to 0.00, p = 0.05) (Fig. 2g), semen pH (SMD = -0.18, 95% CI -1.32 to 0.97, p = 0.76) (Fig. 2h), and semen leukocytes (SMD = -0.17, 95% CI -0.85 to 0.50, p = 0.61) (Fig. 2i).

#### Secondary Outcomes

#### Sex Hormones

From 9 studies included, 7 studies reported TT (n = 138), 7 for E2 (n = 138), and 5 for SHBG (n = 82). Both TT and SHBG levels were significantly increased after bariatric surgery (SMD = -1.15, 95% CI -1.86 to -0.44, p = 0.001 and SMD = -1.49, 95% CI -1.84 to -1.13, p < 0.00001, respectively). In contrast, E2 levels were significantly decreased after surgery (SMD = 0.74, 95% CI 0.07 to 1.40, p = 0.03).

## Discussion

Obesity has many ramifications upon people's life; one growing area of concern is that of reproductive capacity. Excessive weight gain had a positive correlation with sperm

Fig. 2 Forest plot of the effect of bariatric surgery on semen quality. a Semen volume. b Sperm concentration. c Total sperm count. d Total motility. e Progressive motility. f Normal morphology. g Sperm viability. h Semen pH. i Semen leukocytes

а	preoperat			perative			Std. Mean Difference	Std. Mean Difference
Study or Subgroup Calderón 2020	Mean SD 2.5 0.74	Total 20	Mean 2.3	SD T 1.33	otal 20	Weight 11.6%	IV, Random, 95% CI 0.18 [-0.44, 0.80]	IV, Random, 95% Cl
Carette 2019	2.75 1.26	46	2.71	1.22	46	13.5%	0.03 [-0.38, 0.44]	+
El Bardisi 2016	5.13 3.27	46	3.33	1.74	46	13.4%	0.68 [0.26, 1.10]	=
Fariello 2021 Legro 2015	2 1.1 2.1 1.1	15 6	3	0.7	15 6	10.2%	-1.06 [-1.83, -0.28] 0.03 [-1.11, 1.16]	
Reis 2012	2.9 0.8	10	4.1	0.8	10	8.2%	-1.44 [-2.44, -0.43]	
Samavat 2018	2.2 1.3	23	2.8	1.4	23	11.9%	-0.44 [-1.02, 0.15]	-
/elotti 2021 Nood 2020	2.25 0.93 1.5 0.59	35 17	2.8 1.2	0.85 0.74	35 17	12.9% 11.0%	-0.61 [-1.09, -0.13] 0.44 [-0.24, 1.12]	
fotal (95% CI)		218			218	100.0%	-0.19 [-0.62, 0.23]	•
Heterogeneity: Tau <sup>2</sup> : Test for overall effect			'= 8 (P <	< 0.0001)	;  ² =	77%		-4 -2 0 2 4 Favours [Increased] Favours [Decreased]
b	preoperat			operative			Std. Mean Difference	Std. Mean Difference
Study or Subgroup Calderón 2020	Mean SD 18 69	Total 20	Mean 12	<u>SD T</u> 38	otal 20	Weight 15.9%	IV, Random, 95% Cl 0.11 [-0.51, 0.73]	IV, Random, 95% Cl
Fariello 2021	42 48.4	15	60.7	39	15	14.1%	-0.41 [-1.14, 0.31]	
Legro 2015 Reis 2012	65 73 78.7 58.6	6 10	99 104	148 66.5	6 10	8.8% 11.8%	-0.27 [-1.41, 0.87] -0.39 [-1.27, 0.50]	
Samavat 2018	83 100	23	55	63	23	16.5%	0.33 [-0.25, 0.91]	
/elotti 2021 Nood 2020	6.47 3.96 72.5 81.5	35 17	10.9 47	5.24 49.8	35 17	18.0% 14.9%	-0.94 [-1.44, -0.45] 0.37 [-0.31, 1.05]	
Fotal (95% CI)	12.0 01.0	126				100.0%	-0.17 [-0.60, 0.25]	
Heterogeneity: Tau <sup>2</sup> :		5.97, df	= 6 (P =				-0.17 [-0.00, 0.25]	-4 -2 0 2 4
Test for overall effect	: Z = 0.79 (P = 1	).43)						Favours [Increased] Favours [Decreased]
C Study or Subgroup	pretoperat Mean SD		post Mean	toperativ SD	e Total	Weight	Std. Mean Difference IV, Random, 95% Cl	Std. Mean Difference IV, Random, 95% Cl
Carette 2019	177.7 177.7	46	108.2	92.9	46	23.1%	0.49 [0.07, 0.90]	IV, Naturall, 95% CI
El Bardisi 2016	37 32.26		35.6	28.87	46	23.2%	0.05 [-0.36, 0.45]	
Fariello 2021 Samavat 2018	101.8 139.1 130 150	15	181.2	121.5	15 23		-0.59 [-1.33, 0.14] -0.10 [-0.68, 0.48]	
Wood 2020	122.8 98.9		17	59.8	17	16.8%	1.26 [0.52, 2.01]	
Total (95% CI)		147				100.0%	0.21 [-0.27, 0.70]	· · · · · · · · · · · · · · · · · · ·
Heterogeneity: Tau <sup>2</sup> = Test for overall effect:			= 4 (P =	0.003); P	*= 75	%		-4 -2 0 2 4 Favours [Increased] Favours [Decreased]
	preoperat		pact	lonerate			Std. Mean Difference	Favours (Increased) Favours (Decreased)
d Study or Subgroup	Mean SD	Total	Mean		Total		IV, Fixed, 95% Cl	Std. Mean Difference IV, Fixed, 95% Cl
Calderón 2020 Carette 2019	35 35 35 12.6		35 31.8	50 12	20 46	12.1%	0.00 [-0.62, 0.62] 0.26 [-0.15, 0.67]	
El Bardisi 2016	40.25 21.43	46	34.25	16.47	46	27.4%	0.31 [-0.10, 0.72]	-
Legro 2015	46 25		55	28	6	3.6%	-0.31 [-1.45, 0.83]	
Reis 2012 Samavat 2018	34 8.9 48.7 19.3		36 55.2	8.5 20.6	10 23	6.0% 13.7%	-0.22 [-1.10, 0.66] -0.32 [-0.90, 0.26]	
Wood 2020	64.5 18.5		52	21.5	17	9.8%	0.61 [-0.08, 1.30]	+
Total (95% CI)		168			168	100.0%	0.15 [-0.07, 0.36]	· · · •
Heterogeneity: Chi <sup>2</sup> = Test for overall effect:			l <sup>2</sup> = 9%					-4 -2 0 2 4
								Favours [Increased] Favours [Decreased]
e Study or Subgroup	preoperat Mean SD			toperativ SD		Waista	Std. Mean Difference	Std. Mean Difference
Study or Subgroup Calderón 2020	Mean SD 20 30		Mean 25	35	Total 20		-0.15 [-0.77, 0.47]	IV, Random, 95% CI
El Bardisi 2016	22.5 15.79	46	23.25	15.11	46	19.2%	-0.05 [-0.46, 0.36]	+
Fariello 2021 Samavat 2018	43.1 11.9 38.9 19.7		59.2 43	8.4 21.1	15		-1.52 [-2.35, -0.69] -0.20 [-0.78, 0.38]	
Velotti 2021	13.84 8.37	35	23.29	9.09	35	18.0%	-1.07 [-1.57, -0.57]	
Wood 2020	39 21.5	17	31	23.7	17	15.7%	0.35 [-0.33, 1.02]	
Total (95% CI) Heterogeneity: Tau <sup>2</sup> =	: 0.30: Chi <sup>2</sup> = ?	156 2.37. df	= 5 (P -	0.0004>		100.0% 8%	-0.41 [-0.91, 0.08]	<b></b>
Test for overall effect			- 0 -					-4 -2 0 2 4 Favours (Increased) Favours (Decreased)
f	preoperat	ive	post	toperativ	е		Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean SD	Total	Mean	SD	Total		IV, Random, 95% Cl	IV, Random, 95% Cl
Calderón 2020 Carette 2019	2 4		2 14.1	4 8.5	20 46	11.7%	0.00 [-0.62, 0.62] 0.15 [-0.26, 0.56]	Ŧ
El Bardisi 2016	56.5 22.56	46	67.5	22.56	46	13.1%	-0.48 [-0.90, -0.07]	+
Fariello 2021	4.9 1.4		9.5 7	1.6	15		-2.98 [-4.06, -1.90]	
Legro 2015 Reis 2012	10 8 8.2 4		11	11 2.6	6 10		0.29 [-0.85, 1.43] -0.79 [-1.71, 0.12]	
Samavat 2018	8.5 7.8	23	5	4.6	23	11.9%	0.54 [-0.05, 1.13]	-
/elotti 2021 Nood 2020	2.34 1.11 3 1.5	35 17	3	0.94 2.22	35 17	12.7% 11.3%	-0.63 [-1.12, -0.15] 0.52 [-0.17, 1.20]	
Total (95% CI)		218				100.0%	-0.31 [-0.80, 0.19]	•
Heterogeneity: Tau <sup>2</sup> =		6.08, df	= 8 (P <	0.00001;			-oro ( [-oroo) or [5]	-4 -2 0 2 4
Test for overall effect	Z = 1.22 (P = 0	.22)						Favours [Increased] Favours [Decreased]
g	preoperat	ve	posto	operative			Std. Mean Difference	Std. Mean Difference
Study or Subgroup Calderón 2020		Total 20	Mean 10			Weight 21.4%	IV, Fixed, 95% Cl 0.00 (-0.62, 0.62)	IV, Fixed, 95% Cl
Carette 2019	56.7 14.6	43	59.7	5 15.7	43	45.8%	-0.20 [-0.62, 0.62]	
Reis 2012 Samavat 2018	73.8 6.5 68.6 13.4	10 23	73	17.1	10 23	10.7%	0.06 [-0.82, 0.94] -0.90 [-1.51, -0.29]	
	00.0 13.4		1 3.3	10.3				
Fotal (95% CI) Heterogeneity: Chi² =	5.45, df = 3 (P	96 = 0.14)	;   <sup>2</sup> = 45	%	96	100.0%	-0.28 [-0.57, 0.00]	<u> </u>
Test for overall effect								-4 -2 0 2 4 Favours [Increased] Favours [Decreased]
h Study of Substant	preoperati			operative			Std. Mean Difference	Std. Mean Difference
Study or Subgroup Calderón 2020	Mean SD 8.1 0.2	Total 20	Mean 8.3	SD T 0.3	otal 20	Weight 49.3%	IV, Random, 95% CI -0.77 [-1.41, -0.12]	IV, Random, 95% Cl
	8 0	10	8	0	10		Not estimable	L
	7.65 0.21	23	7.57	0.18	23	50.7%	0.40 [-0.18, 0.99]	Γ
Reis 2012 Samavat 2018		53	1 /P -	0 0001- 12		100.0% %	-0.18 [-1.32, 0.97]	<b>+</b> ++
Samavat 2018 Total (95% Cl)	- 0.50: 01:2 - 0		- i (P'=)	o.008); f*	- 90	N		-10 -5 0 5 10 Favours [Increased] Favours [Decreased]
Samavat 2018								area histored i aroun [bourdabu]
Samavat 2018 Total (95% CI) Heterogeneity: Tau <sup>2</sup> :								
Samavat 2018 Total (95% CI) Heterogeneity: Tau <sup>2</sup> :	Z = 0.30 (P = ) preoperati	0.76) we		perative			Std. Mean Difference	Std. Mean Difference
Samavat 2018 Fotal (95% CI) Heterogeneity: Tau <sup>2</sup> : Test for overall effect <b>i</b> Study or Subgroup	Z = 0.30 (P = ) preoperati Mean SD	0.76) ve Total	Mean	SD T	otal	Weight	IV, Random, 95% Cl	Std. Mean Difference IV, Random, 95% Cl
Samavat 2018 Total (95% CI) Heterogeneity: Tau <sup>2</sup> : Test for overall effect <b>i</b> Study or Subgroup Reis 2012	Z = 0.30 (P = 1 preoperati <u>Mean SD</u> 0 0	0.76) we <u>Total</u> 10	Mean 0	SD T(	otal 10	Weight	IV, Random, 95% CI Not estimable	
Samavat 2018 Total (95% CI) Heterogeneity: Tau <sup>a</sup> : Test for overall effect <b>i</b> Study or Subgroup Reis 2012 Wood 2020	Z = 0.30 (P = 1 preoperati <u>Mean SD</u> 0 0	0.76) we <u>Total</u> 10 17	Mean 0	SD T	otal 10 17	Weight 100.0%	IV, Random, 95% CI Not estimable -0.17 [-0.85, 0.50]	
Samavat 2018 Total (95% CI) Heterogeneity: Tau <sup>2</sup> : Test for overall effect <b>i</b> Study or Subgroup Reis 2012	Z = 0.30 (P = 1 preoperati <u>Mean SD</u> 0 0 2 9.3	0.76) we <u>Total</u> 10	Mean 0	SD T(	otal 10	Weight	IV, Random, 95% CI Not estimable	

 Table 3
 Subgroup analyses of sperm volume, sperm concentration, total sperm count, normal morphology, progressive motility, and sperm viability

Subgroup	No. of studies	No. of partici- pants	Pooled SMD (95% CI)	$I^{2}(\%)$	P value
Sperm volume					
Data expressed as median (interquartile range)					
Yes	2	37	0.30 [-0.16, 0.76]	0	0.20
No	7	181	-0.34 [-0.86, 0.18]	81	0.20
Follow-up time					
$\geq 12$ months	6	143	-0.18 [-0.76, 0.40]	80	0.54
< 12 months	3	75	-0.24 [-0.83, 0.35]	68	0.43
Bariatric surgery					
RYGB and SG	3	83	0.15 [-0.16, 0.45]	0	0.34
RYGB	4	54	-0.72 [-1.28, -0.16]	44	0.01
SG	2	81	0.04 [-1.23, 1.31]	94	0.95
Sperm concentration					
Data expressed as median (interquartile range)					
Yes	1	27	0.37 [-0.31, 1.05]	-	0.29
No	6	109	-0.27 [-0.72, 0.19]	61	0.25
Follow-up time					
$\geq$ 12 months	5	74	-0.03 [-0.35, 0.30]	0	0.88
< 12 months	2	52	-0.31 [-1.59, 0.98]	89	0.64
Bariatric surgery					
RYGB and SG	2	37	0.23 [-0.23, 0.68]	0	0.33
RYGB	4	54	-0.09 [-0.49, 0.32]	9	0.67
SG	1	35	-0.94 [-1.44, -0.45]	-	0.0002
Total sperm count	•	50	01911[1111, 0110]		0.0002
Data expressed as median (interquartile range)					
Yes	1	17	1.26 [0.52, 2.01]	_	0.0009
No	4	130	0.03 [-0.37, 0.43]	59	0.88
Follow-up time		100		0,7	0.00
$\geq 12$ months	3	107	0.05 [-0.47, 0.58]	70	0.85
< 12 months	2	40	0.56 [-0.78, 1.90]	88	0.41
Bariatric surgery	-	10	0.00[ 0.70, 1.90]	00	0.11
RYGB and SG	2	63	0.81 [0.06, 1.56]	69	0.03
RYGB	2	38	-0.29 [-0.76, 0.18]	6	0.22
SG	1	46	0.05 [-0.36, 0.45]	-	0.83
Normal morphology	1	10	0.05 [ 0.50, 0.15]		0.05
Data expressed as median (interquartile range)					
Yes	1	17	0.52 [-0.17, 1.20]	_	0.14
No	8	201	-0.41 [-0.94, 0.11]	83	0.12
Follow-up time	0	201	0.41[ 0.74, 0.11]	05	0.12
$\geq$ 12 months	6	143	-2.12 [-4.95, 0.70]	78	0.14
< 12 months	3	75	-2.12[-4.95, 0.70] 0.62[-1.16, 2.41]	80	0.14
Bariatric surgery	5	15	0.02 [-1.10, 2.41]	80	0.49
RYGB and SG	3	83	0.84 [-0.24, 1.92]	0	0.13
RYGB	3 4	83 54	-1.14 [-5.19, 2.92]	0 84	0.13
SG	4 2	34 81	-4.76 [-14.68, 5.15]	84 79	0.38
Progressive motility	2	01		17	0.55
Data expressed as median (interquartile range)					
Yes	1	17	8.00 [-7.21, 23.21]		0.3
No	5	17	-0.55[-1.08, -0.02]	- 77	0.5

#### Table 3 (continued)

Subgroup	No. of studies	No. of partici- pants	Pooled SMD (95% CI)	$I^{2}(\%)$	P value			
Follow-up time		·						
$\geq 12$ months	3	81	-0.51 [-1.29, 0.28]	80	0.20			
< 12 months	3	75	-0.33 [-1.15, 0.49]	83	0.43			
Bariatric surgery								
RYGB and SG	2	37	0.08 [-0.41, 0.56]	10	0.75			
RYGB	2	38	-0.83 [-2.12, 0.47]	85	0.21			
SG	2	81	-0.55 [-1.55, 0.45]	90	0.28			

quality damage that could contribute to infertility. In the present study, we found that only a small proportion of obese males had a normal baseline semen analysis, which suggests that increased body weight may have a significant impact on sperm quality impairment. With regard to this aspect, Hofny et al. [27] found that BMI was positively related to abnormal sperm morphology and negatively to sperm concentration and motility in obese fertile and infertile men. Hammiche et al. [28] confirmed that obesity was negatively associated with sperm concentration, total motile sperm count, and ejaculate volume. Belloc et al. [5] observed BMI inversely correlated with sperm volume, concentration, and progressive motility. Besides, other investigators also demonstrated a negative relationship between BMI and sperm counts [8].

The underlying mechanism between obesity and impaired sperm quality remains unclear, and several main reasons may account for it. First, it is the alteration in hormonal levels. The hormonal profiles in obese men were often characterized by increased estrogen levels and decreased testosterone and inhibin B levels, which deleteriously affect spermatogenesis via hypothalamic-pituitary-gonadal (HPG) axis [29]. Furthermore, hyperinsulinemia related to insulin resistance and decreased sex hormone-binding globulin (SHBG) level may also play a role [29, 30]. Second, inflammatory mediators and adipokines can bring harm to human sperm. Several various inflammatory mediators (e.g., TNF- $\alpha$ , IL-1, and IL-6) secreted from excess white adipose tissue have a toxic effect on sperm function [30, 31]. Adipose tissue can also secrete a mass of adipokines such as leptin. Elevated leptin levels and leptin resistance occurred in patients with obesity are detrimental to sperm formation [30, 31]. In addition, these adipokines induce the production of reactive oxygen species (ROS), generating a process known as oxidative stress (OS). Third, ROS excessive production is known to have negative effects on male fertility [30, 32, 33]. Another noteworthy reason is the increased scrotal temperature. Spermatogenesis is a temperature-sensitive process. The accumulation of suprapubic and inner thigh fat can increase the local testicular temperature to levels affecting sperm production [29–31].

In the present study, the most comprehensive meta-analysis on the effects of bariatric surgery on semen quality in men with obesity was conducted. However, the results showed that no significant improvement or deterioration in semen quality was found. In agreement with our results, El Bardisi et al. [9] reported 46 male individuals studied before and 1 year after SG surgery whose sperm parameters remained stable after the procedure. Legro et al. [25] did not find any correlations between semen variations and weight loss experienced by the 6 subjects who underwent RYGB in a 12-month followup study. Similarly, Reis et al. [26] observed no changes in sperm quality 24 months after RYGB. Besides, sperm concentration, total count, motility, or normal morphology rate did not show any difference in the subgroup analysis.

All the patients included were submitted to SG or RYGB in the current study. SG and RYGB could improve insulin resistance [34], decrease estrogen concentrations, and elevate SHBG, testosterone, and inhibin B levels [22, 35]. Surgery-induced weight loss could result in an improvement of the chronic proinflammatory state, OS, and leptin resistance [36, 37]. Furthermore, the scrotal temperature might be better regulated after excessive weight loss. Although surgery could lead to these favorable changes, no significant improvement in sperm quality was observed. Therefore, other factors, including energy imbalance, smoking, sedentarism, environmental factors, and toxin accumulation [30, 32, 38, 39], might take responsibility for the lack of improvement of semen quality after bariatric surgery. Moreover, the results of our subgroup analysis for RYGB found significantly increased sperm volume after surgery. This may be explained by the little effect of these factors that did not get affected by bariatric surgery and many benefits brought by surgery mentioned earlier. Due to the small patient samples in this subgroup, these pooled estimates should be cautiously treated. To date, the exact cause is unclear, and our greatest concern is that a decline in semen quality due to obesity may be an irreversible event that cannot be improved by surgically induced weight loss. For obese people with a high risk of infertility or sperm impairment, undergoing bariatric surgery early may be a favorable decision.

In the sperm concentration analysis, heterogeneity was derived from the article focusing on patients with idiopathic infertility [16]. This indicated that different study populations were likely to be the main reason for heterogeneity. According to sperm concentration, patients can be classified into three categories: oligospermia, azoospermia, and normal semen. Because the different populations were analyzed separately in a very small percentage of included studies, subgroup analyses by types of study populations were not performed. In terms of this aspect, El Bardisi et al. [9] reported that sperm parameters improved in oligospermia patients who underwent SG, and sperm reappeared in the ejaculate of six previously azoospermic patients. However, Carette et al. [23] found that the prevalence of oligozoospermia raised from 17.4 to 21.7% after RYGB and SG. Likewise, Wood et al. [15] concluded the prevalence of both oligospermic patients and severe oligospermia patients after bariatric surgery was higher than before surgery; moreover, 2 patients developed azoospermia after surgery. Nevertheless, our meta-analysis results showed no significant changes in oligospermia (SMD = 0.78, 95% CI 0.26 to 2.36, p = 0.67) and azoospermia (SMD = 0.97, 95%) CI 0.09 to 9.99, p = 0.98) after bariatric surgery.

This meta-analysis was not without limitations. First, it is a small sample study. Only 9 researches with 218 patients were included. Furthermore, heterogeneity between included studies was high for all outcomes except sperm total motility and sperm viability. This heterogeneity may be because of the varying patient populations. Future research should take the different study populations into account. Another limitation is that most of the studies are observational with no comparators. They are of suboptimal quality relative to experimental studies.

# Conclusion

Based on the currently available evidence, bariatric surgery does not improve semen quality in obese males. Randomized prospective studies with larger samples and longer follow-up are needed to confirm these findings.

**Funding** This work received financial support from the Natural Science Foundation of Guangdong Province (no. 2017A030313855), Dongguan Science and Technology of Social Development Program (no. 20211800902451 and 202050715024111) and Chongqing Natural Science Foundation Project (cstc2021jcyj-msxmX0036).

## Declarations

Ethics Approval For this type of study, formal consent is not required.

Informed Consent Informed consent does not apply.

Conflict of Interest The authors declare no competing interests.

## References

- Pfeifer S, Fossum G, Pisarska M, et al. Obesity and reproduction: a committee opinion. Fertil Steril. 2015;104:1116–26. https://doi. org/10.1016/j.fertnstert.2015.08.018.
- Preiss K, Brennan L, Clarke D. A systematic review of variables associated with the relationship between obesity and depression[J]. Obes Rev. 2013;14(11):906–18.
- Sallmén M, Sandler DP, Hoppin JA, et al. Reduced fertility among overweight and obese men. Epidemiology. 2006;17(5):520–3.
- Cortese S, Cuzzolaro M, Maffeis C, et al. [Depressive symptoms and low self-esteem in obese children and adolescents]. [J]. Minerva Pediatrica. 2005;57(2):65.
- Belloc S, Cohen-Bacrie M, Amar E, et al. High body mass index has a deleterious effect on semen parameters except morphology: results from a large cohort study. Fertil Steril. 2014 Nov;102(5):1268–73. https://doi.org/10.1016/j.fertnstert.2014. 07.1212.
- Ramaraju GA, Teppala S, Prathigudupu K, et al. Association between obesity and sperm quality. Andrologia. 2018;50(3) https://doi.org/10.1111/and.12888.
- Sermondade N, Faure C, Fezeu L, et al. Obesity and increased risk for oligozoospermia and azoospermia. Arch Intern Med. 2012;172(5):440–2. https://doi.org/10.1001/archinternmed.2011. 1382.
- Sermondade N, Faure C, Fezeu L, et al. BMI in relation to sperm count: an updated systematic review and collaborative meta-analysis. Hum Reprod Update. 2013;19(3):221–31. https://doi.org/10. 1093/humupd/dms050.
- El Bardisi H, Majzoub A, Arafa M, et al. Effect of bariatric surgery on semen parameters and sex hormone concentrations: a prospective study. Reprod Biomed Online. 2016;33(5):606–11. https://doi.org/10.1016/j.rbmo.2016.08.008.
- Samavat J, Cantini G, Lotti F, et al. Massive weight loss obtained by bariatric surgery affects semen quality in morbid male obesity: a preliminary prospective double-armed study. Obes Surg. 2018;28(1):69–76. https://doi.org/10.1007/s11695-017-2802-7.
- Lazaros L, Hatzi E, Markoula S, et al. Dramatic reduction in sperm parameters following bariatric surgery: report of two cases. Andrologia. 2012;44(6):428–32. https://doi.org/10.1111/j.1439-0272.2012.01300.x.
- Sermondade N, Massin N, Boitrelle F, et al. Sperm parameters and male fertility after bariatric surgery: three case series. Reprod Biomed Online. 2012;24(2):206–10. https://doi.org/10.1016/j. rbmo.2011.10.014.
- Wei Y, Chen Q, Qian W. Effect of bariatric surgery on semen parameters: a systematic review and meta-analysis. Med Sci Monit Basic Res. 2018;24:188–97. https://doi.org/10.12659/ MSMBR.910862.
- Lee Y, Dang JT, Switzer N, et al. Impact of bariatric surgery on male sex hormones and sperm quality: a systematic review and meta-analysis. Obes Surg. 2019;29(1):334–46. https://doi.org/10. 1007/s11695-018-3557-5.
- Wood GJA, Tiseo BC, Paluello DV, et al. Bariatric surgery impact on reproductive hormones, semen analysis, and sperm DNA fragmentation in men with severe obesity: prospective study. Obes Surg. 2020;30(12):4840–51. https://doi.org/10.1007/ s11695-020-04851-3.
- Velotti N, Elisa De Palma FD, Sosa Fernandez LM, et al. Effect of bariatric surgery on in vitro fertilization in infertile men with obesity. Surg Obes Relat Dis. 2021;17(10):1752–9. https://doi. org/10.1016/j.soard.2021.07.007.

- Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Int J Surg. 2010;8(5):336–41.
- Lim K, Nini E, Forestier D, et al. Methodological index for nonrandomized studies (MINORS): development and validation of a new instrument. ANZ J Surg. 2015;73(9):712–6.
- 19. Wan X, Wang W, Liu J, et al. Estimating the sample mean and standard deviation from the sample size, median, range, and/ or interquartile range. BMC Med Res Methodol. 2014;14:135. https://doi.org/10.1186/1471-2288-14-135.
- Higgins JP, Thompson SG. Quantifying heterogeneity in a metaanalysis. Stat Med. 2002;21(11):1539–58. https://doi.org/10.1002/ sim.1186.
- Calderón B, Gómez-Martín JM, Cuadrado-Ayuso M, et al. Circulating zinc and copper levels are associated with sperm quality in obese men after metabolic surgery: a pilot study. Nutrients. 2020;12(11):3354. https://doi.org/10.3390/nu12113354.
- Calderón B, Huerta L, Galindo J, et al. Lack of improvement of sperm characteristics in obese males after obesity surgery despite the beneficial changes observed in reproductive hormones. Obes Surg. 2019;29(7):2045–50. https://doi.org/10.1007/ s11695-019-03798-4.
- 23. Carette C, Levy R, Eustache F, et al. Changes in total sperm count after gastric bypass and sleeve gastrectomy: the BARIASPERM prospective study. Surg Obes Relat Dis. 2019;15(8):1271–9. https://doi.org/10.1016/j.soard.2019.04.019.
- Fariello RM, de Carvalho RC, Spaine DM, et al. Analysis of the functional aspects of sperm and testicular oxidative stress in individuals undergoing metabolic surgery. Obes Surg. 2021 Jul;31(7):2887–95. https://doi.org/10.1007/s11695-021-05350-9.
- Legro RS, Kunselman AR, Meadows JW, et al. Time-related increase in urinary testosterone levels and stable semen analysis parameters after bariatric surgery in men. Reprod Biomed Online. 2015;30(2):150–6. https://doi.org/10.1016/j.rbmo.2014.10.014.
- Reis LO, Zani EL, Saad RD, et al. Bariatric surgery does not interfere with sperm quality--a preliminary long-term study. Reprod Sci. 2012;19(10):1057-1062. https://doi.org/10.1177/1933719112 440747.
- Hofny ER, Ali ME, Abdel-Hafez HZ, et al. Semen parameters and hormonal profile in obese fertile and infertile males. Fertil Steril. 2010;94(2):581–4. https://doi.org/10.1016/j.fertnstert.2009.03. 085.
- Hammiche F, Laven JS, Twigt JM, et al. Body mass index and central adiposity are associated with sperm quality in men of subfertile couples. Hum Reprod. 2012;27(8):2365–72. https://doi.org/ 10.1093/humrep/des177.

- Hammoud AO, Gibson M, Peterson CM, et al. Impact of male obesity on infertility: a critical review of the current literature. Fertil Steril. 2008;90(4):897–904. https://doi.org/10.1016/j.fertn stert.2008.08.026.
- Mintziori G, Nigdelis MP, Mathew H, et al. The effect of excess body fat on female and male reproduction. Metabolism. 2020;107:154193. https://doi.org/10.1016/j.metabol.2020.154193.
- Bellastella G, Menafra D, Puliani G, et al. How much does obesity affect the male reproductive function? Int J Obes Suppl. 2019;9(1):50–64. https://doi.org/10.1038/s41367-019-0008-2.
- Rosenblatt A, Faintuch J, Cecconello I. Abnormalities of reproductive function in male obesity before and after bariatric surgerya comprehensive review. Obes Surg. 2015;25(7):1281–92. https:// doi.org/10.1007/s11695-015-1663-1.
- Shukla KK, Mahdi AA, Mishra V, et al. Withania somnifera improves semen quality by combating oxidative stress and cell death and improving essential metal concentrations. Reprod Biomed Online. 2011;22(5):421–7. https://doi.org/10.1016/j. rbmo.2011.01.010.
- Rao RS, Yanagisawa R, Kini S. Insulin resistance and bariatric surgery. Obes Rev. 2012;13(4):316–28. https://doi.org/10.1111/j. 1467-789X.2011.00955.x.
- Pellitero S, Olaizola I, Alastrue A, et al. Hypogonadotropic hypogonadism in morbidly obese males is reversed after bariatric surgery. Obes Surg. 2012;22(12):1835–42. https://doi.org/10.1007/ s11695-012-0734-9.
- Min T, Prior SL, Dunseath G, et al. Temporal effects of bariatric surgery on adipokines, inflammation and oxidative stress in subjects with impaired glucose homeostasis at 4 years of follow-up. Obes Surg. 2020;30(5):1712–8. https://doi.org/10.1007/s11695-019-04377-3.
- Terra X, Auguet T, Guiu-Jurado E, et al. Long-term changes in leptin, chemerin and ghrelin levels following different bariatric surgery procedures: Roux-en-Y gastric bypass and sleeve gastrectomy. Obes Surg. 2013;23(11):1790–8. https://doi.org/10.1007/ s11695-013-1033-9.
- Sepaniak S, Forges T, Gerard H, et al. The influence of cigarette smoking on human sperm quality and DNA fragmentation. Toxicology. 2006;223(1-2):54–60. https://doi.org/10.1016/j.tox.2006. 03.001.
- Magnusdottir EV, Thorsteinsson T, Thorsteinsdottir S, et al. Persistent organochlorines, sedentary occupation, obesity and human male subfertility. Hum Reprod. 2005;20(1):208–15.

**Publisher's Note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.