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Review Article

Effect of bariatric surgeries on Metabolic Rate, A Systematic Review and Meta-analyses.

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Abstract

Background and aims: We aimed to summarize earlier studies on the effects of different types of bariatric surgeries on resting metabolic rate (RMR), resting energy expenditure (REE), and basal metabolic rate (BMR). The aim of this study was to determine the effects of bariatric surgery on the pulmonary function in the morbid obese patients.

Methods: We searched PubMed, SCOPUS, Web of Science, and Cochrane from inception to October 2020 using relevant keywords.

Results: Overall 13 studies were included. Pooled effect size suggested a significant effect of bariatric surgeries on REE (Weighted mean difference (WMD): -360.11, 95% CI: -446.67, -273.55, $p < 0.0001$; $I2 = 69.6\%$), RMR (WMD: -228.05, 95% CI: -290.70, -165.41, $p < 0.0001$; $I2 = 0\%$), and BMR (WMD: -551.59 mg/dl, 95% CI: -696.25, -406.92, $p < 0.0001$; $I2 = 5.9\%$).

Conclusion: Taken together, the data suggest that bariatric surgeries have beneficial effects to reduce REE, RMR, and BMR.

Keywords: Bariatric surgeries, Metabolic rate, Obesity.

Introduction

Over-weight and obesity are global health problems with more than 1.9 billion individuals currently dealing with them (1). It has been proved that obesity is associated with major chronic diseases such as cancer, cardiovascular diseases, and diabetes (2-4). Morbid obesity, which is defined as having a BMI of 40 or more, or 35 or more and experiencing obesity-related health conditions, is a serious health complication that can interfere with basic physical functions such as breathing or walking (5). As conventional therapies such as restricted diet and changing lifestyle take time and are sometimes not entirely effective (6), new therapies such as bariatric surgeries have gained attention. Bariatric surgeries include a variety of procedures to lessen the intake of food by reducing the size of the stomach by a gastric band or by removing a portion of the stomach or reducing the small intestine. According to long-term studies, not only bariatric surgeries proved to be fairly successful in causing weight loss (7), but also they can help alleviate a variety of chronic diseases such as diabetes, hypertension, and sleep apnea (8-12). Although, they could cause some major side effects as they are aggressive procedures (13, 14), still, the accumulated evidence of the benefits of bariatric surgery has made it a therapy of choice for patients with severe obesity (15).

The long-term weight management is directly related to energy expenditure through metabolism (16). The metabolic rate represents the number of calories needed to maintain basic body functions. The metabolic rate is assessed by measuring the amount of heat produced by the subject's body. basal metabolic rate (BMR) and resting metabolic rate (RMR) are two different techniques used for this matter. Although the basics are the same, however, to measure BMR, subjects need to go through stricter conditions such as fasting and spending the night in the hospital to perform the test first thing in the morning, hence, BMR may be slightly more accurate (17). Metabolic rate is flexible and can be auto-adjusted in individuals when their calorie intake changes considerably (18) and could be one of the main reasons that conventional weight management programs fail in some cases (19) .

There have also been reports of weight regain in the individuals who went through bariatric surgeries (20). Whether or not the changes in metabolic rate are to blame or other variables (such as bad eating habits or sedentary lifestyle) is still unknown. Therefore, we conducted this comprehensive systematic review and meta-analysis of available prospective - non-randomized studies to investigate how REE, RMR, and BMR change after going through various types of bariatric surgeries and whether or not they could interfere with the process of weight loss.

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Methods

Study design: To perform this meta-analysis, Meta-analyses of Observational Studies in Epidemiology (MOOSE) statement guideline was used (21).

Search Strategy. A throughout search was conducted in PubMed/Medline, Scopus, Web of Science, and Cochrane from inception to October 2020. the merger of MeSH and non-MESH terms were as follows: ((“Gastric Bypass”[MeSH]) OR (“Gastric Bypass”[Title/Abstract]) OR ("Greenville Gastric Bypass"[MeSH]) OR (“Greenville Gastric Bypass”[Title/Abstract]) OR ("Bariatric Surgery"[MeSH]) OR (“Bariatric Surgery”[Title/Abstract]) OR ("Roux-en-Y Gastric Bypass"[Title/Abstract]) OR (“Roux-en-gastric bypass”[Title/Abstract]) OR (“RYGB”[Title/Abstract]) OR (“laproscopicRoux-en-gastric bypass”[Title/Abstract]) OR (LRYGB[Title/Abstract]) OR (Gastrojejunostomy[Title/Abstract]) OR (Gastrectomy[MeSH]) OR (Gastrectomy[Title/Abstract]) OR (“sleeve gastrectomy”[Title/Abstract]) OR (gastroplasty[Title/Abstract])) AND ((“resting metabolic rate”[Title/Abstract]) OR (“basal metabolism”[MeSH]) OR (“Basal Metabolic Rate”[Title/Abstract]) OR (“basal metabolism”[Title/Abstract]) OR (“RMR”[Title/Abstract]) OR (“REE”[Title/Abstract]) OR (BMR[Title/Abstract])). We hand searched all reference lists of eligible articles, related reviews, and meta-analyses as we did not want to miss any relevant studies. We did not include unpublished documents and grey literature like conference papers, theses, and patents. Our search was limited to English-language articles. Two independent researchers (ASh, ED) conducted the study searching and selection independently.

Eligibility criteria. The included studies in this meta-analysis were as follows: (1) all written in English (2) prospective cohort studies (3) only executed on adult population; ≥18 years-old (4) reported one of the following measures; REE, RMR and/or BMR (5) performed one of the common bariatric surgeries including Roux-EN-Y Gastric Bypass (RYGB), Laparoscopic adjustable gastric banding (LAGB), Sleeve gastrectomy (SG), and Vertical banded gastroplasty (VBG).

Articles were excluded if (1) obesity was not the reason of surgery (2) they were not prospective cohort studies, and (3) had lack of sufficient data for the outcomes of interest in individuals.

Data Extraction. Two independent researchers (ASh, ED) conducted the study selection independently whereas a chief investigator (LA) was also present to resolve any differences or controversies. In the case of data deficiency, we contacted the accountable author to acquire the required data. The following data were obtained from each study; first author’s name, year of publication, study location, study duration, gender, mean age and mean body mass index (BMI) of participants, study design, health status of study population, number of participants in each group, weight, REE, RMR and BMR before and after intervention, methods which were used for assessment of metabolic rate, surgery type, and follow up time .

Quality Assessment. Two authors independently assessed the quality of included studies by the Newcastle-Ottawa Quality Assessment Scale (NOS). This scale comprises of three quality factors: selection (maximum 4 stars), comparability (maximum 2 stars), and outcome (maximum 3 stars). A maximum of 9 stars represents the highest quality. A total score of 7 or more was considered to indicate high-quality studies (22).

Synthesis of results. Mean and standard deviation (SD) of RMR, REE, BMR or BEE were used for determination of side effects, otherwise standard errors (SE) were converted to SD according to the formula of $SE*\sqrt{n}$. This Meta-analysis was conducted to compare the pooled estimates of the metabolic rate before and after obesity surgeries. A fixed-effect model was used to combine the effect size of studies. In case of significant between-study heterogeneity, we conducted subgroup analysis based on participants’ gender, duration of follow-up, age, and the type of surgery they had gone through to detect possible sources of heterogeneity. Publication bias was assessed by Egger's test. We also performed a sensitivity analysis using a random-effects model in which each study was excluded to examine the influence of that study on the overall estimate. All statistical analyses were done using Stata software version 12 (StataCorp. College Station, Texas, USA). $P < 0.05$ was considered as statistically significant.

Results

Findings from Systematic Review

Study selection

Out of 507 provided articles in the initial search, 306 unduplicated studies screened for the title and abstract evaluation. Totally, 282 unrelated studies discarded due to the primary evaluation of inclusion criteria: Unrelated title (n = 272), non-English (n = 3), review articles (n = 7). Consequently, 11 studies excluded after full-text evaluation 1) publication that evaluate the effect of bariatric surgeries with a combination of other treatments (n=2), 2) studies which did not contain sufficient information (n= 9). Finally, 13 studies remained that met all our inclusion criteria. The flow diagram of the search process is depicted in Fig. 1.

Study Characteristics

Characteristics of included studies are summarized in Table 1. In total, 408 participants were recruited. Included studies were published between 1997 and 2018. The follow-up period ranged between 3 months to 30 months. The sample size of the included studies ranged from 5 to 103 male and females. All studies were prospective non-randomized. Selected studies enrolled subjects with diabetes (23) and patients suffering from obesity. Among 13 included studies, 6 carried out in the United States of America (USA) (24-29), two in France (30, 31), two in Brazil (32, 33), one in Switzerland (34), one in Italy (35) and one in Iran (36). Three studies enrolled only females (30, 31, 34) and the rest involved both genders (24-29, 32, 33, 35, 36). In addition, included studies enrolled patients with different baseline BMI; 4 studies carried out on subjects with a BMI between 40-45 kg/m2 (31, 33, 34, 36), 4 between 45-50 kg/m2 (24, 25, 27, 32), and 3 above 50 kg/m2 (26, 28, 29) and two studies didn't report baseline BMI (30, 35).

Findings from meta-analysis

Effect of bariatric surgery on BMR

The effect of bariatric surgery on BMR has been investigated in three studies involving 42 participants (26, 27, 35). Pooled effect size from the fixed-effects model showed that bariatric surgery significantly decreased BMR (WMD: -551.59 mg/dl, 95% CI: -696.25, -406.92, $p < 0.001$) without heterogeneity among studies ($I2 = 5.9\%$, $p = 0.000$) (Figure 2).

Effect of bariatric surgery on RMR

Overall analysis of bariatric surgery influence on the RMR presented in Figure 3. Combining 7 effect sizes through the fixed-effects model revealed a significant decreasing effect of bariatric surgeries on the RMR of 169 enrolled participants in five studies (24, 25, 30, 32, 33). (WMD: -228.05, 95% CI: -290.70, -165.41, $p < 0.001$) without significant heterogeneity among included studies ($I2 = 0\%$, $p = 0.912$).

Effect of bariatric surgery on REE

The effect of bariatric surgery on REE investigated in five studies with 197 participants (28, 29, 31, 34, 36). Pooled effect size revealed a decreasing effect of bariatric surgeries on the REE levels of participants (WMD: -360.11, 95% CI: -446.67, -273.55, $p < 0.001$) with significant heterogeneity among studies ($I2 = 69.6\%$, $p = 0.010$). Findings from subgroup analyses revealed that gender and follow-up duration, explained the between-study heterogeneity. We found that both participants under the age of 40 (WMD: -351.64, 95% CI: -375.92, -327.32, $p < 0.001$) and ≥ 40 (WMD: -357.85, 95% CI: -434.13, -281.57, $p < 0.001$) showed significant decreasing effect on REE. Among included studies, two of them carried out only on female participants; subgroup analysis revealed that the women group (WMD: -352.20, 95% CI: -375.90, -328.50, $p < 0.001$) and group of both sex (WMD: -352.50, 95% CI: -458.79, -246.20, $p < 0.001$) showed significant lowering effect on REE. We also stratified subjects based on follow-up duration in which both stratification showed significant lowering effect on REE.

The effect of bariatric surgeries on weight and BMI depicted in Figure 4. Overall analysis of 15 effect size showed the significant lowering effect of bariatric surgeries on both weight and BMI. We also conducted subgroup analysis based on age (<40 and ≥ 40 years old), sex, type of surgery, and follow-up duration. As shown in Table 2, findings of subgroup analysis revealed that follow-up duration and gender appear to be the source of heterogeneity for BMI. Weight and BMI were decreased significantly following bariatric surgeries in all subgroups.

Sensitivity analysis and publication bias

Sensitivity analysis based on a random-effect model showed that excluding any single study from the analysis did not significantly alter the pooled effect sizes. There was no evidence of publication bias for studies examining the effect of bariatric surgery on RMR (P= 0.756), REE (P= 0.935), BMI (P= 0.975) and weight (P= 0.891).

Table.1 baseline characteristics of included studies

Study	Year	Sex	Country	Mean age	n-1	n-2	FU	Surgery type	out-come	BMI 1	BMI 2	Quality assess-ment
Louis Flancbaum et al.	1997	M/F	USA	Nr	70	23	24	RYGB	REE	52 (10)	34 (8)	7
Bobbioni- harsch et al.	2000	F	Switzer-land	38/9	20	20	12	RYGB	REE	43.9 (1.3)	30.1 (1.2)	5
Sai Krupa Das et al.	2003	M/F	USA	39	36	30	14	GBP	REE	50.1 (9.3)	30.8 (5.7)	6
Muriel Coupaye et al.	2005	F	France	42/7	36	36	12	AGB	RMR	Nr	Nr	6
Daniel Gene Carey et al.	2006	M/F	USA	40/5	19	17	12	Various	BMR	48.7 (2.5)	30.8 (3.7)	6
Silvia Leite Faria et al.	2012	M/F	Brazil	38/2	46	46	6	RYGB	RMR	40.6 (4.6)	29 (4.1)	6
Giuseppe Benedetti et al.	2013	M/F	Italy	36/1	14	14	30	BPD	BMR	Nr	Nr	6
Motahareh Hasani et al.	2015	M/F	Iran	34	21	21	3	LGP	REE	41.4 (5.6)	32.7 (34.2)	7
Nancy F. Butte et al.	2015	M/F	USA	16/5	11	11	12	RYGB	BMR	57 (10.5)	40.1 (10.7)	6
Matthew G. Browning et al.	2016	M/F	USA	46/2	13	13	6	Various	RMR	46.4 (5.8)	36.8 (6.1)	5
Matthew G. Browning et al.	2016	M/F	USA	46/6	8	8	6	LRYGB	RMR	47.1 (6.8)	34.1 (5.6)	6
Matthew G. Browning et al.	2016	M/F	USA	45/4	5	5	6	LAGB	RMR	45.3 (4.2)	41.2 (4.3)	6
Arnaud Sans et al.	2017	F	France	40/6	103	103	12	LRYGB	REE	43.3 (4.9)	28.1 (4.7)	6
Bruce M. Wolfe et al.	2018	M/F	USA	46/3	25	16	24	Various	RMR	47.8 (5.2)	31.7 (9.2)	6
Robert de cleva et al.	2018	M/F	Brazil	38/9	45	45	6	RYGB	RMR	47.8 (4.9)	Nr	6

n-1 initial sample size, n-2 final sample size, FU follow-up in months, BMI 1 pre-operative body mass index, BMI 2 post-operative body mass index

M: male, F: female, Nr: not reported, RYGB: Roux-en-Y gastric bypass, AGB: adjustable gastric banding, BPD: Billopancreatic diversion, LGP: Laparoscopic gastric placation, GBP: gastric bypass, LAGB: Laparoscopic adjustable gastric banding, LRYGB: Laparoscopic Roux-en-Y gastric bypass, various: combination of procedures
All of the included studies were conducted as prospective non-randomized design.
BMI defined as mean (SD).

Table 2. Subgroup analyses for the effect of bariatric surgery on REE, weight, and BMI.

Sub-grouped by	No. of trials	WMD (95% CI)	P Value	I^2 (%)	P
REE					
Follow-up period					
≤ 12 months	3	-351.20 (-374.73, -327.66)	≤0.001	0	0.393
> 12 months	2	-381.17 (-506.80, -225.55)	≤0.001	91.1	0.001
Sex					
Women	2	-352.20 (-375.90, -328.50)	≤0.001	27.3	0.241
Both sex	3	-352.50 (-458.79, -246.20)	≤0.001	83.0	0.003
Age					
< 40	3	-351.64, (-375.92, -327.32)	≤0.001	72.1	0.028
≥ 40	2	-357.85, (-434.13, -281.57)	≤0.001	83.2	0.015
BMI					
Follow-up period					
≤ 12 months	11	-13.98 (-14.54, -13.41)	≤0.001	76.4	≤0.001
> 12 months	4	-17.50 (-19.66, -15.34)	≤0.001	0	0.475
Sex					
Women	3	-14.18 (-14.83, -13.53)	≤0.001	39.6	0.191
Both sex	12	-14.25 (-15.24, -13.26)	≤0.001	78.5	0.001
Age					
< 40	7	-13.68 (-14.35, -13.02)	≤0.001	61.6	0.016
≥ 40	8	-15.24 (-16.19, -14.30)	≤0.001	78.0	≤0.001
Type of surgery					
RYGB	3	-16.42 (-18.20, -14.65)	≤0.001	80.9	0.005
LAGB	8	-14.07 (-14.66, -13.48)	≤0.001	69.5	0.002
Various	2	-11.73 (-14.49, -8.98)	≤0.001	91.5	0.001
Weight					
Follow-up period					
≤ 12 months	11	-35.77 (-37.44, -34.10)	≤0.001	75.1	≤0.001
> 12 months	4	-46.55 (-51.98, -41.13)	≤0.001	71.6	0.014
Sex					
Women	3	-37.38 (-39.27, -35.49)	≤0.001	72.9	0.025
Both sex	12	-34.97 (-37.98, -31.96)	≤0.001	80.2	0.000
Age					
< 40	7	-36.35 (-38.27, -34.42)	≤0.001	83.7	≤0.001
≥ 40	8	-37.49 (-40.37, -34.62)	≤0.001	74.4	≤0.001
Type of surgery					
RYGB	3	-37.45 (-39.19, -35.71)	≤0.001	69.9	0.036
LAGB	8	-19.63 (-28.82, -10.44)	≤0.001	59.1	0.017
Various	2	-37.02 (-42.98, -31.07)	≤0.001	36.7	0.209

Abbreviations; BMI; body mass index, REE; resting energy expenditure.
Subgroup analysis by the type of surgeries was not performed, since not enough data was available to be differentiated by this variable.

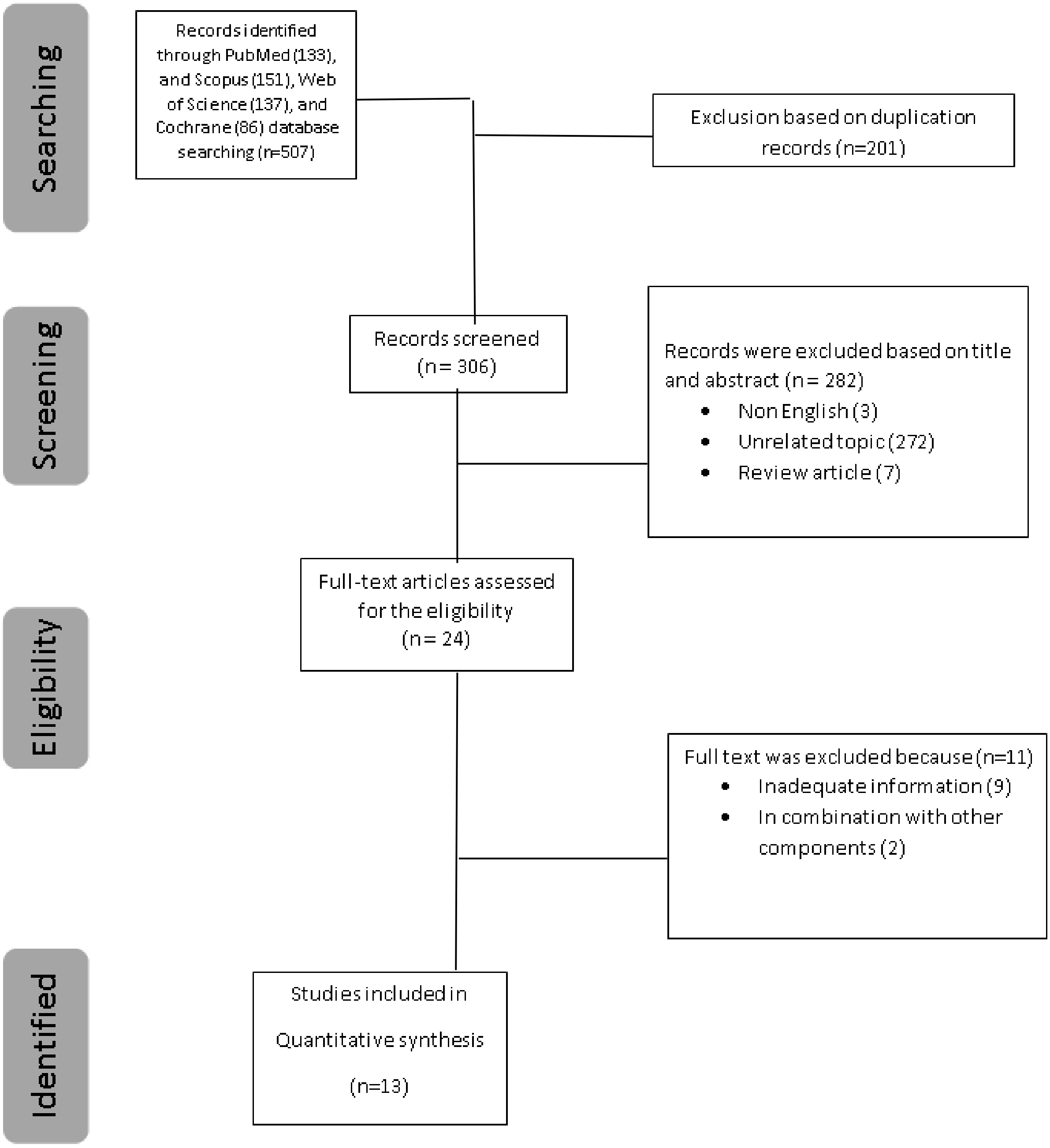

Figure 1. Study flow chart

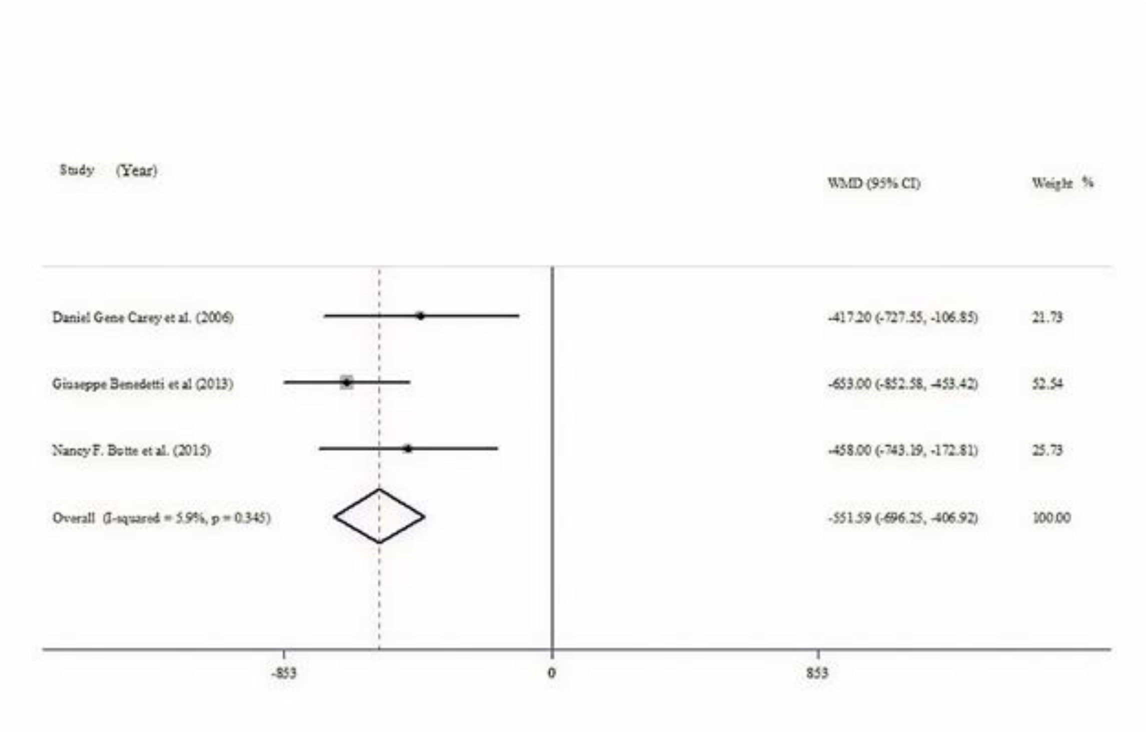

Figure 2. Forest plot displaying weighted mean difference and 95% confidence intervals for the impact of bariatric surgeries on BMR.

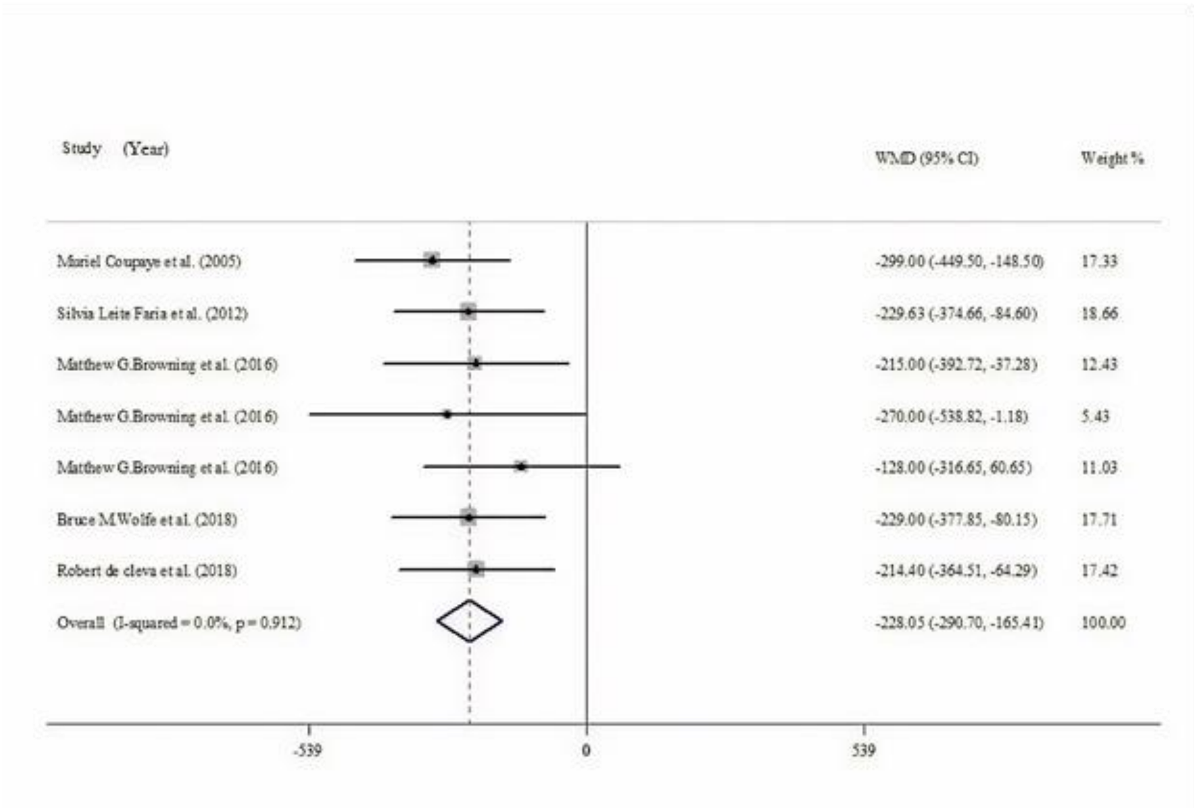

Figure 3. Forest plot displaying weighted mean difference and 95% confidence intervals for the impact of bariatric surgeries on RMR.

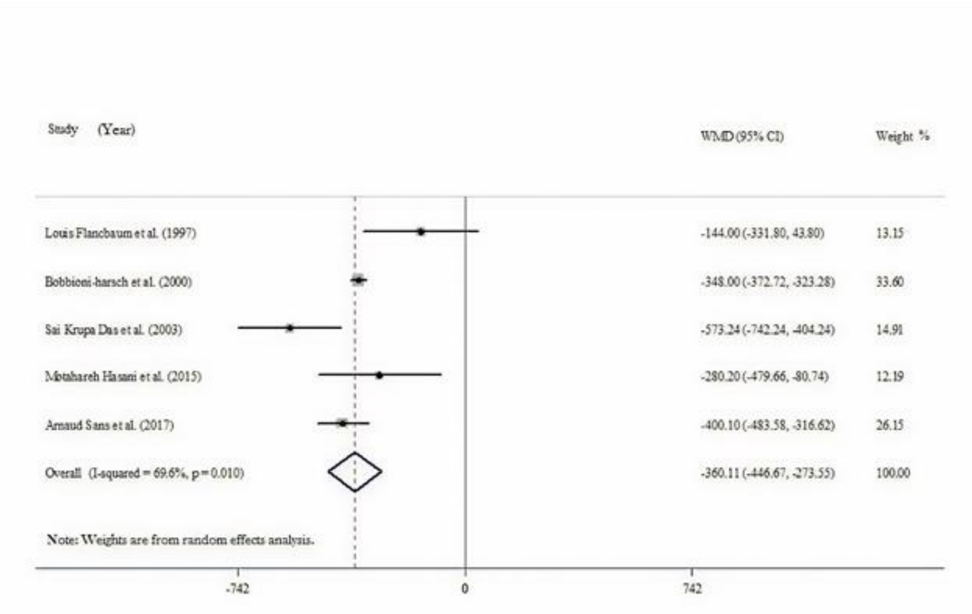

Figure 4. Forest plot displaying weighted mean difference and 95% confidence intervals for the impact of Bariatric Surgeries on REE.

Discussion

This is the first meta-analysis that studies the effect of various types of bariatric surgeries on BMR, RMR, and REE. We found that REE, RMR, and BMR were significantly reduced in individuals who went through different types of bariatric surgeries .

Based on what we have found, bariatric surgeries proved to have a continuous effect on reducing weight and BMI. Although several very-long-term surveys were in line with our findings (37-39), Christoe et al. reported significant weight regain following gastric bypass of a decade follow up (40). Moreover, Goyal et al. claimed that one-third of their participants have gained almost all the weight they had lost over the years (41). One study claimed that one year after surgery, weight regain begins to occur or weight loss halts (42). Bad eating habits or decreased metabolic rate (which is a result of altered body composition) are suggested as the possible factors for this event (43, 44). Whether or not the changes in metabolic rate is to blame has been a topic of discussion as the results are controversial. Faria et al. suggested that lower REE after surgery could be a possible factor for weight regain (45) whereas Cardeal et al. found no correlation between the decrease in REE and risk of weight regain after LRYGB (46). Though according to the articles included in this meta-analysis, weight and BMI of the individuals continued to drop remarkably in studies with a follow up more than 12 months. while several studies were in accordance with ours, Carey et al showed that the decrease in BMR stops most commonly 6 months after the surgery. They mentioned the role of age as a significant factor in this matter and pointed out that the decrease in REE in other studies might be due to the fact that they included senior individuals (47).

As it is known, changes in metabolic rate could play an important role in limiting weight loss or causing weight regain in the long-term (48). It is confirmed that weight loss leads to a decrease in metabolic rate, therefore, weight regain may happen (49). This phenomenon which is called adaptive thermogenesis forms a vicious cycle which leads to weight regain following conservative weight loss programs and is considered to be the main reason for their occasional ineffectiveness (50). Although the reduction of REE in patients who went through bariatric surgery is not as great as the ones who are only submitted to a restricted diet, it is still significant (51) .

The role of adaptive thermogenesis as one the main mechanisms leading to weight regain following bariatric surgery has recently been noted. Reduction of metabolic rate could be due to the loss of both lean body mass (LBM) and fat mass (FM) following bariatric surgeries. However, it should be kept in mind that the impact of these components differ as LBM is the main detriment of metabolic rate (48). Most people who go through bariatric surgeries have a BMI more than 45 Kg/m2 and therefore due to the higher FM: LBM ratio, it is safe to say that the drop of metabolic rate could mainly be due to the loss of FM and is independent of changes in LBM (52, 53). As Vaurs et al. reported, patients tend to lose only 30% of their LBM following bariatric surgeries, whereas the extent of FM loss is estimated to be 70% (54) .

It was evident in our study and several others that metabolic rate continues to drop as the individuals continue to lose their fat mass, but the decreased metabolic rate would not interfere with the process of weight loss (55). Some studies mentioned a new variable called weight-adjusted RMR to explain this matter. They showed that although both weight and metabolic rate continues to drop following surgery, however, the decrease in weight (which is mostly due to the loss of adipose tissue) is greater than metabolic rate (which is almost independent of FM), therefore, nearly after 6 months, weight-adjusted RMR starts increasing due to the decrease in FM: LBM ratio (56). Also, other alterations in the body that occur following bariatric surgeries, such as Changes in gut microbiota, escalating diet-induced thermogenesis, and altered levels of appetite-regulating hormones could be the contributing factors leading to the increase of weight-adjusted RMR (57-59). Peptide YY (PYY) and glucagon-like-peptide 1 (GLP-1) are the two hormones with anorectic properties that are elevated following bariatric surgeries, mainly due to the altered gastrointestinal anatomy and/or innervation (60). Apart from mentioned factors, some lifestyle modifications such as performing regular physical exercise or having better food choices can also have a major role in the increase of LBM compared with FM (54).

There are potential limitations existing in our study which should be considered. For one, none of the articles had followed its participants for more than 30 months which could have been of better help to achieve more detailed results. The absence of only men group is of notice since it would have given us a better view to evaluate the variable of sex in this study. In conclusion, we found that despite a significant decrease in metabolic rate, the participants continue to lose weight successfully.

Transparency Declaration :The lead author affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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