



Changes in Energy Expenditure of Patients with Obesity Following Bariatric Surgery: a Systematic Review of Prospective Studies and Meta-analysis

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Abstract

We herein summarize the available literature on the effects of bariatric surgery (BS) on energy expenditure in individuals with obesity. We conducted a systematic literature review, and 35 prospective studies met our inclusion criteria. The findings indicate that BS contributes to increased diet-induced thermogenesis (DIT) and decreased total energy expenditure (TEE) and resting energy expenditure (REE) in patients with obesity. The meta-analysis demonstrated a significant decrease in TEE and REE within 6 months following BS. With the sustained decrease in REE, there was no further decrease in TEE between the 6- and 12-month follow-up. Increased DIT might explain the variance between the patterns of REE and TEE change. The postoperative decrease in REE/FFM and increase in REE/BW were observed. The changes in substrate utilization might be consistent with the change in the respiration quotient postoperatively.

Keywords Bariatric surgery · Energy metabolism · Diet-induced thermogenesis (DIT) · Respiration quotient (RQ) · Substrate oxidation

Introduction

Obesity and obesity-related complications have been regarded as the main causes of adverse health risks. The increasing prevalence of obesity has been confirmed as a major public health concern. The Global Burden of Disease study revealed that 603.7 million adults and 107.7 million children were diagnosed with obesity in its analysis of 195 countries including more than 68.5 million people in 2015 [1]. Bariatric surgery

(BS) has been approved as an effective treatment that achieves sustained reduction of body weight (BW), which may result from changes in the energy balance after surgery.

Changes in various components of energy expenditure, such as resting energy expenditure (REE), diet-induced thermogenesis (DIT), and physical activity (PA), may influence the long-term maintenance of weight loss after BS. REE represents the energy that maintains the basic energy requirements of daily life, which comprises two thirds of total energy expenditure (TEE). Notably, an excessive decline in REE is a major determinant of weight regain, and increased REE/BW is a strong predictor of excess weight loss after BS [2, 3]. DIT is the energy produced during food digestion and absorption. It is defined as an increase of the REE after food consumption, which represents 10% to 15% of the TEE. A low DIT also contributes to weight gain and obesity [4]. The respiration quotient (RQ) is applied to estimate the utilization of substrates by an organism. If the RQ approaches 0.7, it indicates that the organism mainly uses fat oxidation, and the closer it gets to 1.0, the greater the tendency for carbohydrate oxidation.

Given the importance of energy expenditure for weight control and changes in energy expenditure that result from altered BW following BS, we investigated how energy

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metabolism changes in individuals with obesity who have undergone BS.

Materials and Methods

Study Design

This systematic review and meta-analysis was conducted according to the Cochrane Handbook for Systematic Reviews of Interventions [5] and is presented based on the Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines [6].

Search Strategy

Eligible studies were trials reporting changes in the energy expenditure of patients with obesity following BS. Only full reports published in the English language were considered. The measure of effect of treatment was, in the whole sample and within each group of patients, the change of energy expenditure. Retrieval of studies was based on MEDLINE, EMBASE, Web of Science, and the Cochrane Central Register of Controlled Trials (CENTRAL) in The Cochrane Library from inception until 30 June 2018 with the combination of the following terms: (“energy metabolism” OR “energy requirements” OR “resting energy expenditure” OR “basal metabolic rate” OR “total energy expenditure” OR “indirect calorimetry” OR “diet-induced thermogenesis” OR “physical activity level”) AND (“bariatric surgery” OR “Roux-en-Y” OR “gastric bypass” OR “sleeve gastrectomy” OR “gastroplasty” OR “biliopancreatic diversion” OR “adjustable gastric banding”). A manual search was also performed on reference lists from articles, reviews, editorials, and proceedings of international congresses. Decisions on which trials to include were made by the authors (authors 1, 2, 3, and 4) in an unblinded manner.

Inclusion and Exclusion Criteria

Two reviewers independently screened all abstracts and selected articles for the meta-analysis if they met all of the following criteria: (1) described randomized controlled trials or prospective studies, (2) were written in the English language, (3) were conducted on human subjects, and (4) described changes in energy expenditure of patients with obesity following BS. For studies without the required outcomes, the author(s) were contacted via e-mail for more relevant information, if necessary. In studies that analyzed multiple interventions, only data associated with BS were considered for inclusion. The exclusion criteria were (1) observational studies including cohort, cross-sectional, and case-control studies and (2) reviews, comments, case reports, abstracts, animal studies, and unpublished studies.

Primary Outcomes

The main outcomes were the changes of TEE, REE (including the resting and basal metabolic rate), REE/BW, REE/fat-free mass (FFM), PA, DIT, RQ, and substrate oxidation after BS. To evaluate the energy-sparing phenomenon, we analyzed findings from studies that compared measured REE and REE values predicted from linear regression equations before and after BS.

Data Extraction

Two investigators independently reviewed the abstracts of all citations. Data verifications between the two authors were performed to ensure reliability and completeness after all abstracts were reviewed. The inclusion criteria were applied to all identified studies independently. Different decisions were resolved by consensus. The full texts of potentially relevant articles identified through other sources were retrieved. If multiple articles from the same study were searched, only the article with the longest follow-up period was included. Data regarding the research design, type of surgery, participant characteristics, study duration, and outcomes were independently extracted. We contacted the authors for the primary reports of the unpublished data. If the authors did not reply, the available data were used for our analyses.

Methodological Quality Assessment

We used the nine-point Newcastle–Ottawa Scale to assess the study quality for all included observational studies [7]. We arbitrarily classified quality as high (score of 7–9) or low (score of 0–3). We excluded studies from our meta-analysis if they had poor quality. Discrepant opinions between authors were resolved to reach a consensus.

Statistical Analysis

The data were pooled using RevMan 5.0 software (The Nordic Cochrane Centre, Copenhagen, Denmark) and STATA/SE version 15 (Stata Corp, College Station, TX, USA). For each study, we calculated the mean difference (MD) with 95% confidence interval (CI) for continuous data. A random-effects model (DerSimonian–Laird method) was used when significant heterogeneity was detected between studies ($P < 0.10$; $I^2 > 50\%$). Otherwise, a fixed-effects model (Mantel–Haenszel test) was used. Subgroup analyses were performed by type BS (Roux-en-Y gastric bypass [RYGB] and other types of BS) and follow-up period (6 months and 12 months). A sensitivity analysis was performed to assess the stability of the meta-analysis results. Publication bias was assessed by the Egger’s test and represented graphically by funnel plots.

Results

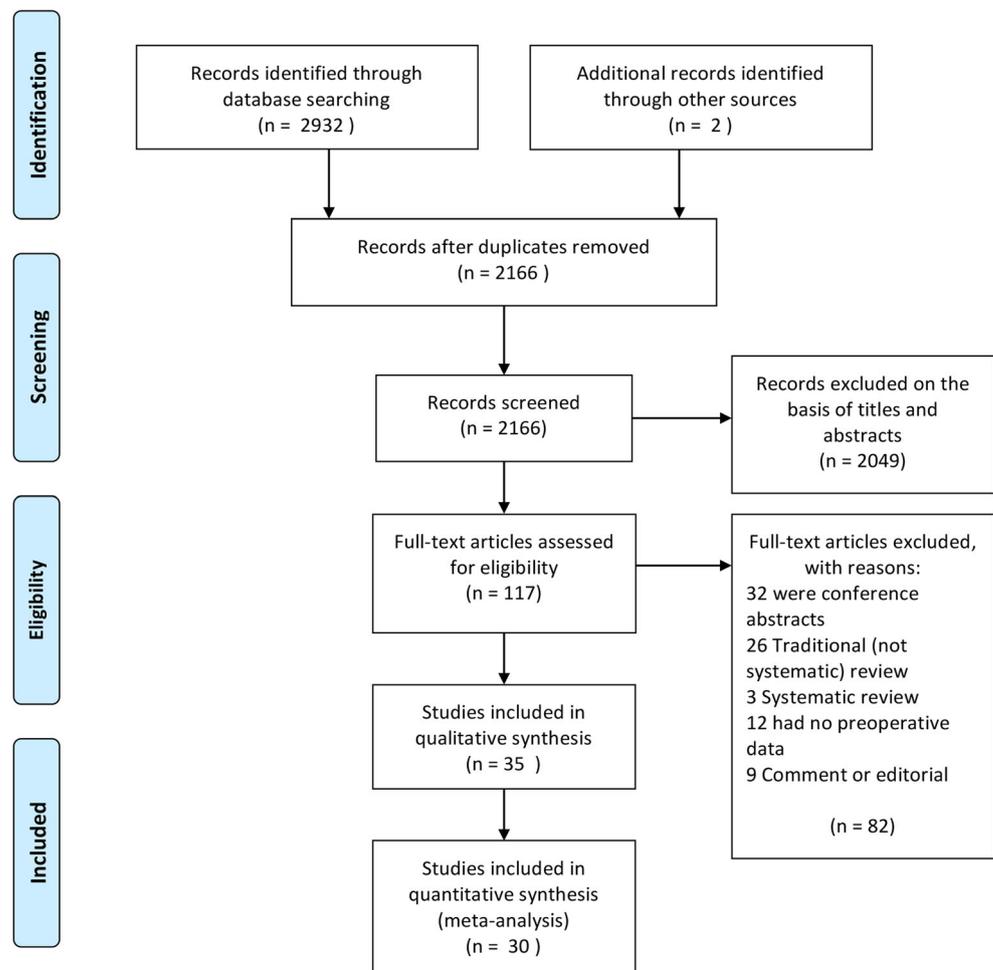
Description of Included Studies

After excluding duplicate results, the initial search included 2166 articles. In total, 2131 articles were excluded because 2049 were off the topic after scanning the title and/or the abstract, 32 were conference abstracts, 26 were traditional (not systematic) reviews, 3 were systematic reviews, 12 had no preoperative data, and 9 were comments or editorials. Thus, 35 articles were included in our systematic review, and 30 studies involving 1233 patients were included in the meta-analysis (Fig. 1). The characteristics of the studies are outlined in Tables 1 and 2.

Quality Assessment of Included Studies

The total score of the Newcastle Ottawa scale ranged from 4 to 8. None of the studies had low quality (total score of < 3); thus, none were excluded from the meta-analysis.

Fig. 1 Flow diagram of the selection process. RCT, randomized controlled trial



Changes in TEE, REE, REE/FFM, and REE/BW

TEE

The change in TEE between the preoperative period and follow-up was reported in six studies [22, 29, 33, 38, 40, 41]. Compared with the preoperative value, the TEE was significantly lower at 2, 6, and 12 months postoperatively (preop and 2-mo MD 342.53, 95% CI 287.38–397.67, $P < 0.001$, $I^2 = 79%$; preop and 6-mo MD 699.72, 95% CI 574.43–825.01, $P < 0.001$, $I^2 = 0%$; preop and 12-mo MD 537.80, 95% CI 480.95–594.64, $P < 0.001$, $I^2 = 77%$) (Fig. 2). In addition, the TEE at 6 months was significantly lower than that at 2 months after BS (MD 154.14, 95% CI 104.43–203.84, $P < 0.001$, $I^2 = 4%$) (Fig. 2). However, there was no significant difference in the TEE between 6 and 12 months after BS (MD – 34.80, 95% CI – 129.21 to 59.61, $P = 0.72$, $I^2 = 34%$) (Fig. 2).

REE

Eight trials [9, 13, 17, 21, 29, 30, 33, 34] reported the changes in REE at 3 months or < 3 months after BS. The meta-analysis

Table 1 Study details and patient demographics

Included trials (country)	Type of study	No. of patients (female)	Age (years)	Baseline BMI or BW	Assessment periods (follow-up)
Busetto 1995 [8] (Italy)	Prospective study	12 (12)	35.8 ± 8.1 years	46.9 ± 6.8 kg/m ²	6 months
Flancbaum 1997 [9] (USA)	Prospective study	70 (59)	NR	52 ± 10 kg/m ²	6 weeks, 3, 6, 12, 18, and 24 months
Flancbaum 1998 [10] (USA)	Prospective study	60 (51)	Mean age of 39 years	51.5 ± 10 kg/m ²	6 weeks, 3, 6, 12, 18, and 24 months
Van Gemert 1998 [11] (Netherlands)	Prospective study	6 (1)	28 ± 7 years	48.1 ± 7.0 kg/m ²	3, 6, and 12 months
Benedetti 2000 [12] (Italy)	Prospective study	14 (9)	36.1 ± 1.62 years	132.6 ± 18.90 kg	30 months
Bobbioni-Harsch 2000 [13] (Switzerland)	Prospective study	20 (20)	38.9 ± 2.5 years	43.9 ± 1.3 kg/m ²	3, 6, and 12 months
Van Gemert 2000 [14] (Netherlands)	Prospective study	8 (7)	24–60 years	47.88 ± 7.03 kg/m ²	3, 12 months
Das 2003 [15] (England)	Prospective study	30 (24)	39.0 ± 9.6 years	50.1 ± 9.3 kg/m ²	14 ± 2 months
Coupaye 2005 [16] (France)	Prospective study	36 (36)	42.7 ± 8.7 years	47.2 ± 8.5 kg/m ²	12 months
Carey 2006 [17] (USA)	Prospective study	19 (14)	40.5 ± 10.2 years	48.7 ± 2.5 kg/m ²	1, 3, 6, and 12 months
Galtier 2006 [18] (France)	Prospective study	73 (73)	39.1 ± 10.4 years	44.3 ± 7.0 kg/m ²	13.3 ± 6.0 months
Olbers 2006 [19] (Sweden)	RCT	LGBP, n = 37 LVBG, n = 46	RYGB: 37.4 ± 0.4 years VGB: 37.4 ± 0.5 years	RYGB: 42.3 ± 4.5 kg/m ² VGB: 42.6 ± 4.2 kg/m ²	12 months
Carrasco 2007 [20] (Chile)	Prospective study	38 (34)	36.3 ± 10.5 years	44.0 ± 4.5 kg/m ²	6 months
Castro 2008 [21] (Brazil)	Prospective study	21 (21)	38.86 ± 6.49 years	47.31 ± 5.81 kg/m ²	3 months
Tamboli 2010 [22] (USA)	Prospective study	29 (25)	43.8 ± 9.6 years	46.3 ± 5.5 kg/m ²	6, 12 months
Faria 2012 [2] (Brazil)	Prospective study	46 (43)	38.24 ± 10.89 years	40.63 ± 4.64 kg/m ²	12.41 ± 6.54 months
Iesari 2013 [23] (USA)	Prospective study	6 (4)	41.2 ± 11.8 years	49.7 ± 9.1 kg/m ²	6 months
Iannelli 2013 [24] (France)	Prospective study	RYGB: 30 (24) SG: 30 (22)	RYGBP: 38.4 ± 10.0 years SG: 37.8 ± 9.5 years	RYGB: 49.1 ± 5.0 kg/m ² SG: 49.1 ± 4.8 kg/m ²	12 months
Faria 2014 [25] (Brazil)	Prospective study	13 (11)	39.5 ± 7.0 years	40.6 ± 3.0 kg/m ²	12 months
Iannelli 2014 [26] (France)	Prospective study	115 (115)	39.9 ± 10 years	44.6 ± 5.2 kg/m ²	12 months
Knuth 2014 [27] (USA)	Prospective study	13 (9)	39 ± 9 years	47.0 ± 7.6 kg/m ²	6, 12 months
Rabl 2014 [28] (USA)	Prospective study	RYGB: 12 (9) AGB: 8 (7)	RYGB: 47.4 ± 8.7 years AGB: 49.0 ± 10.7 years	RYGB: 48.4 ± 6.8 kg/m ² AGB: 44.3 ± 5.0 kg/m ²	14 days, 6 months
Butte 2015 [29] (USA)	Prospective study	11 (8)	16.5 ± 0.8 years	44 ± 19 kg	1.5, 6, and 12 months
Hasani 2015 [30] (Iran)	Prospective study	21 (NR)	34 ± 8 years	41.45 ± 5.68 kg/m ²	3 months
Werling [31] 2015 (Sweden)	Prospective study	6 (6)	NR	41.4 kg/m ²	10 days, 3 and 20 months
Schneider 2016 [32] (Switzerland)	RCT	RYGB: 19 (16) SG: 23 (20)	RYGB: 40.3 ± 10.9 years SG: 41.2 ± 10.4 years	RYGB: 44.4 ± 6.3 kg/m ² SG: 43.4 ± 5.9 kg/m ²	17 ± 5.6 months
Tam 2016 [33] (Australia)	Prospective study	RYGB: 5 (5) SG: 9 (7) LAGB: 7 (7)	RYGB: 49 ± 5 years SG: 42 ± 4 years LAGB: 48 ± 5 years	RYGB: 45.1 ± 2.5 kg/m ² SG: 49.9 ± 3.4 kg/m ² LAGB: 43.1 ± 1.8 kg/m ²	8 weeks, 12 months
Tam 2016 [34] (Australia)	Prospective study	Band: 8 (7) SG: 14 (11)	Band: 53 ± 9 years SG: 39.9 ± 12.2 years	Band: 42.0 ± 5.1 kg/m ²	6 weeks and 3, 6, 12, and 24 months

Table 1 (continued)

Included trials (country)	Type of study	No. of patients (female)	Age (years)	Baseline BMI or BW	Assessment periods (follow-up)
Browning 2017 [35] (USA)	Prospective study	RYGB: 13 (8)	RYGB: 47.8 ± 7.7 years	SG: 41.6 ± 7.4 kg/m ² RYGB: 45.2 ± 5.1 kg/m ² RYGB: 47.1 ± 6.8 kg/m ² AGB: 45.3 ± 4.2 kg/m ²	6 months
Moehlecke 2017 [36] (Brazil)	Prospective study	30 (25)	43 ± 12 years	49 ± 9 kg/m ²	6 months
Bettini 2018 [37] (Italy)	Prospective study	154 (98)	45.1 ± 11.6 years	45.5 ± 7.2 kg/m ²	12 months
Clewa 2018 [3] (Brazil)	Prospective study	54	38.9 ± 9.4 years	47.8 ± 4.9 kg/m ²	6 months
Ravelli 2018 [38] (Brazil)	Prospective study	20 (20)	29.4 ± 5.1 years	44.9 ± 2.5 kg/m ²	6, 12 months
Wilms [39] 2018 (Switzerland)	Prospective study	233 (175)	40.3 ± 11.1 years	45.9 ± 6.45 kg/m ²	12 months
Wolfe 2018 [40] (USA)	Prospective study	16 (14)	46.3 ± 11.2 years	47.8 ± 5.2 kg/m ²	6, 24 months

LGBP laparoscopic Roux-en-Y gastric bypass surgery, *LVBG* laparoscopic vertical banded gastroplasty, *LAGB* laparoscopic adjustable silicone gastric banding, *VBG* vertical banded gastroplasty, *BMI*/body mass index, *BW* body weight, *RYGB* Roux-en-Y gastric bypass, *SG* sleeve gastrectomy, *AGB* adjusted gastric band, *Band* gastric band, *RCT* randomized controlled trial, *NR* not reported

revealed a significant reduction in REE at ≤ 3 months after RYGB and other types of BS (MD 240.88, 95% CI 218.21–263.56, $P < 0.001$, $I^2 = 0\%$; MD 159.41, 95% CI 112.64–206.18, $P < 0.001$, $I^2 = 11\%$, respectively) (Figs. 3 and 4). In 12 studies that reported 6-month outcomes [3, 9, 13, 17, 20, 27–29, 34, 36, 40–42], the meta-analysis revealed a significant reduction in REE at 6 months after RYGB and other types of BS (MD 381.76, 95% CI 337.31–426.21, $P < 0.001$, $I^2 = 48\%$; MD 76.87, 95% CI 28.37–125.38, $P = 0.002$, $I^2 = 28\%$, respectively) (Figs. 3 and 4). Likewise, the results from 15 studies [2, 9, 12, 13, 17, 24–27, 29, 33, 34, 37, 39, 40] showed a statistically significant decrease in REE 12 months after RYGB and other types of BS (MD 387.74, 95% CI 369.12–406.37, $P < 0.001$, $I^2 = 82\%$; MD 363.87, 95% CI 327.22–400.52, $P < 0.001$, $I^2 = 87\%$, respectively) (Figs. 3 and 4). The changes in REE between 3, 6, and 12 months after BS were reported in seven studies [9, 13, 17, 27, 29, 34, 40]. A sustained decrease in REE after gastric bypass surgery was observed at 3, 6, and 12 months of follow-up (3-mo and 6-mo MD 52.01, 95% CI 30.79–73.23, $P < 0.001$, $I^2 = 22\%$; 6-mo and 12-mo MD 57.6, 95% CI 38.14–77.07, $P < 0.001$, $I^2 = 12\%$; 3-mo and 12-mo MD 115.06, 95% CI 95.05–135.07, $P < 0.001$, $I^2 = 1\%$) (Fig. 3). Compared with the 3-month outcomes, there was a statistically significant decrease in REE at both 6 and 12 months after other types of BS (MD 84.39, 95% CI 31.48–137.31, $P = 0.002$, $I^2 = 0\%$; MD 86.00, 95% CI 48.09–123.91, $P < 0.001$, $I^2 = 0\%$, respectively) (Fig. 4). There was no significant difference in the change in REE between 6 and 12 months after other types of BS (MD –5.04, 95% CI –49.11 to 39.03, $P = 0.82$, $I^2 = 0\%$) (Fig. 4).

REE/FFM and REE/BW

REE/BW was reported in nine studies [2, 3, 18, 25, 28, 30, 32, 36, 37] and REE/FFM in five studies [16, 20, 28, 30, 37]. There was a significant increase in REE/BW after RYGB and other types of BS (MD –2.44, 95% CI –2.81 to –2.06, $P < 0.001$, $I^2 = 34\%$; MD –1.21, 95% CI –1.75 to –0.67, $P < 0.001$, $I^2 = 0\%$, respectively) (Fig. 5). REE/FFM decreased significantly after BS (MD 3.97, 95% CI 3.20–4.73, $P < 0.001$, $I^2 = 38\%$) (Fig. 5).

Differences in Measured REE and Predicted REE Using Linear Regression

There was no significant difference between predicted REE and measured REE before the operation, without evidence of statistical heterogeneity (MD 0.82, 95% CI –25.47 to –27.11, $P = 0.95$, $I^2 = 0\%$) (Fig. 6). However, compared with the predicted REE, the measured REE decreased significantly at 3, 6, and 12 months after RYGB and other types of BS (MD –109.09, 95% CI –127.85 to –90.32, $P < 0.001$; MD –88.35, 95% CI –105.73 to –70.97, $P < 0.001$; MD –

Table 2 Study details (population and invention)

Included trials (country)	Population (obesity or diabetes or metabolic syndrome)	Inventions (surgery)	Inventions (food energy intake postoperatively)	EE measure methods	Parameters
Busetto 1995 [8] (Italy)	12 premenopausal women (all patients exclude endocrine disease)	ASGB	After surgery, a diet was arranged to fit a 24-h energy introduction of 2.5MJ (40% protein, 25% fat, 35% carbohydrate)	Indirect calorimetry	RMR(MJ/d)
Flancaum 1997 [9] (USA)	BMI ranged between 40 and 80 kg/m ² ; none were found to be hypothyroid.	RYGB	3-day standardized food logs and 24-h recall	Indirect calorimetry; pREE based on Harris–Benedict (HB) equation	MREE; pREE; RQ
Flancaum 1998 [10] (USA)	clinically severe obesity (BMI > 40 kg/m ² or BMI > 35 kg/m ² with severe comorbid conditions)	RYGB	3-day standardized food logs and 24-h recall	Indirect calorimetry; pREE based on Harris–Benedict (HB) equation	MREE; pREE; HB
Van Gemert 1998 [11] (Netherlands)	Clinically severe obesity	VBG	Maintain their normal diet for at least 3 days prior to the experiment	SMRm measured in respiration chamber; pSMR based on FFM and FM using a linear regression formula	pSMR; mSMR
Benedetti 2000 [12] (Italy)	All obese patients had diabetes mellitus prior to surgery. None of the women examined had menstrual flow, and they were studied in the follicular phase of the menstrual cycle.	BPD	The nutrient content of food was derived from computerized tables.	Indirect calorimetry; pBMR based on the Harris–Benedict (HB) equation	BMR, pBMR-HB npRQ; substrate oxidation; PA
Bobbiomi-Harsch 2000 [13] (Switzerland)	Morbid obesity	RYGB	Each patient was instructed to fulfill a food record during 3 days before each visit.	Indirect calorimetry; pREE based on FFM using a linear regression formula	mREE, pREE substrate oxidation rates
Van Gemert 2000 [14] (Netherlands)	Morbidly obese patients with no obesity-related comorbidities (diabetes or cardiovascular disease), and no medication was used.	VBG	Patients were instructed to keep their normal dietary habits for at least 3 days prior to the experiment.	Doubly labeled water method; respiration chamber; PAI = TEE/SMR	TEE; SMR; RQ; NSMR; PAI; substrate metabolism
Das 2003 [15] (England)	Morbid obese patients with no diabetes, cancer, coronary heart disease, endocrine disorders, or other acute or chronic diseases. Individuals also could be excluded if they were using medication known to influence energy expenditure	RYGB;	TEF was measured for 4 h after the consumption of 400 mL of a mixed liquid meal	15-day doubly labeled water; indirect calorimetry; PAL values = TEE/REE; self-reported activity questionnaires	TEE; REE; AEE; NREE; TEF; RQ; PPRQ; PAL
Coupaye 2005 [16]	Obese patients	LAGB	NR	Indirect calorimetry	RMR
Carey 2006 [17] (USA)	Of the 14 female subjects, 6 were in the early phase and 5 were in the late phase of the menstrual cycle, with 3 subjects being postmenopausal. Of the 19 patients, 4 were diagnosed with arthritis, 11 hypertension, 7 hyperlipidemia, 5 T2DM, 4 low-back problems, 1 claudication, and 1 sleep apnea.	16 LRYGB, 2 open RYGB, 1 LAGB	NR	VO2000 Portable Measurement System	BMR; BMR/LBW
Galtier 2006 [18] (France)	Of 73 obese nondiabetic women, 10 were postmenopausal; severe obesity (BMI > 40 kg/m ² or BMI > 35 kg/m ² with severe comorbid conditions)	AGB	Patients were asked to refrain from strenuous exercise and to maintain their usual intake of caffeinated beverages during the 3 days preceding the measurements	Indirect calorimetry; pRMR based on body weight, height, age, and sex using a linear regression formula	RMR; pRMR RMR/FFM; RMR/BW; RQ; substrate oxidation
Olbets 2006 [19] (Sweden)	LGBP, n = 37 LVBG, n = 46	RYGB and AGB	The Swedish Obese Subjects study questionnaire was used for dietary assessment.	Indirect calorimetry	BMR
Carasco 2007 [20] (Chile)	BMI ≥ 40 kg/m ² or BMI ≥ 35 kg/m ² with comorbidities; 15 hypertension, 7 T2DM, 5	RYGB	Patients were interviewed by a dietitian who conducted a food frequency	Indirect calorimetry	REE REE/FFM RQ

Table 2 (continued)

Included trials (country)	Population (obesity or diabetes or metabolic syndrome)	Inventions (surgery)	Inventions (food energy intake postoperatively)	EE measure methods	Parameters
Castro 2008 [21] (Brazil)	glucose intolerance, 19 dyslipidemia, 21 arthropathy BMI ≥ 40 kg/m ² ; 14 hypertension, 7 T2DM, 6 asthma, and 1 hiatal hernia Patients with thyroid disorders were excluded.	RYGB	questionnaire, and 3-day records were filled NR	Indirect calorimetry	% fat oxidation REE REE/BW npRQ
Tamboli 2010 [22] (USA)	29 subjects with extreme obesity (13 T2DM). Exclusion criteria included a history of type 1 diabetes, current use of oral anticoagulants, intercurrent infection, a prior gastric operation, or a positive pregnancy test.	RYGB	Each patient was counseled by a bariatric registered dietitian to consume a balanced, postgastroectomy diet of 900–1000 kcal/day and was encouraged to exercise, postoperatively.	A whole-room indirect calorimeter	TEE, kcal/day sleepEE, kcal/day Total RQ Sleep RQ Nonprotein RQ Substrate oxidation
Faria 2012 [2] (Brazil)	Inclusion criteria included a preoperative BMI of > 35 kg/m ² and age range of 20 to 65 years; Exclusion criteria included untreated thyroid disease, fever and the presence of infection, and currently taking any medications that enhance EE.	RYGB	NR	Indirect calorimetry	REE REE/BW
Iesari 2013 [23] (USA)	BMI of > 40 kg/m ² None of the patients had diabetes mellitus or any other endocrine or nonendocrine disease.	BPD	During the day spent in the calorimetric chamber, the patients performed physical exercise at 16:00 by walking for 30 min up a 10% gradient at a constant speed of 3 km/h. All subjects were given a diet of 30 kcal/kg of fat-free mass (kg FFM) consisting of 55% carbohydrate, 30% fat, and 15% protein. This amount was divided as follows: 20% at breakfast, 40% at lunch, 10% as an afternoon snack, and 30% at dinner.	1 day in the indirect calorimetry chamber.	REE; TEE; PA Exercise, kcal/day Exercise, kcal/30 min DIT (% of meal)
Iannelli 2013 [24] (France)	15 patients in the LSG group (50%) and 14 (46.7%) in the RYGB group fulfilled the MetS criteria before surgery; Exclusion criteria were the following: patients with a history of inflammatory disease.	RYGBP, SG	NR	Indirect calorimetry	REE
Faria 2014 [25] (Brazil)	The inclusion criteria were as follows: BMI > 40 kg/m ² or BMI > 35 kg/m ² with associated comorbidities and age > 18 years. Exclusion criteria were the following: age > 65 years, severe heart or respiratory problems, breastfeeding, apparent infection, or fever.	RYGB	For the determination of DIT, patients were offered a standard mixed meal of 200 mL of coconut water and a chicken salad sandwich on whole wheat bread, which contained 270 kcal (62% carbohydrates, 12% proteins, and 26% lipids). Patients were counseled to meet a daily consumption of 70 g of protein or 1.5 g/kg of ideal body weight	Indirect calorimetry	RQ-fasting RQ-postprandial Δ RQ REE, kcal/day REE/BW, DIT DIT/BW REE
Iannelli 2014 [26] (France)	Only Caucasian premenopausal women (at least 10 menstrual periods in the previous year, the last one less than 60 days before inclusion in	RYGB		Indirect calorimetry	

Table 2 (continued)

Included trials (country)	Population (obesity or diabetes or metabolic syndrome)	Inventions (surgery)	Inventions (food energy intake postoperatively)	EE measure methods	Parameters
Knauth 2014 [27] (USA)	the study) under 50 years of age were studied. Exclusion criteria were the following: patients with alcohol abuse and a history of inflammatory disease. BMI > 40 kg/m ²	RYGB	They were counseled to transition from a liquid diet to a balanced diet of 900–1000 kcal/day containing 70 g of protein and were encouraged to exercise postoperatively.	Indirect calorimetry pRMR based on FFM, FM, age, and group using a linear regression formula	mREE pRMR
Rabl 2014 [28] (USA)	Inclusion criteria included morbidly obese nondiabetic patients; Exclusion criteria included previous weight loss surgery, foregut and/or hindgut surgery, and diagnosis of endocrine or chronic renal disease	RYGB, AGB	During the 14-day outpatient period, they consumed a standardized low-calorie diet—800 kcal/day (25% carbohydrate, 48% protein, and 27% fat).	Indirect calorimetry	REE REE/BW REE/LBM
Butte 2015 [29] (USA)	Inclusion criteria were Tanner stage IV or V and BMI > 50 kg/m ² or BMI > 40 kg/m ² with comorbidities. Exclusion criteria included a positive urine pregnancy test and serious psychiatric or cognitive disorders.	RYGB	Food intake was provided as three meals and two snacks with a macronutrient composition consisting of 30% protein, 25% fat, and 45% carbohydrate. Food intake was offered at 1.2 times basal metabolic rate (BMR) predicted for obese adolescents at baseline and at 600, 1100, and 1400 kcal/day at 1.5, 6, and 12 months postbaseline, respectively.	24-h calorimetry	TEE Nonprotein EE BMR Sleeping EE Activity EE (AEE) PAL RQ Substrate utilization
Hasami 2015 [30] (Iran)	Inclusion criteria included morbidly obese patients who underwent to surgery had BMI > 40 kg/m ² . Exclusion criteria included history or current psychological conditions that influence on perception of surgery or postoperative assessment and recommendations, history of type 1 and 2 diabetes, prior gastric operation, positive test of pregnancy, cancer, and current use of oral anticoagulants.	Laparoscopic gastric placcation surgery	NR	Indirect calorimetry pREE based on the Harris–Benedict (HB) equation	mREE pREE REE/BW REE/FFM REE/FM
Werling 2015 [31] (Sweden)	Patients were not prescribed any pre-surgical weight loss diet but were weight stable for at least 3 months prior to the study. Patients were free from comorbidities and medication, and were nonsmokers. Study participants were invited to study visits during the same phase of the menstrual period	RYGB	During the stay in the chamber at visit 2, standardized liquid meals containing 200 kcal each were served as lunch (13.30 h), dinner (18.00 h), evening snack (21.00 h), and breakfast 08.40 h in the morning second day of the study visit. During visit 3, semiliquid meals were served in the chamber, containing 250 kcal at lunch (13.30 h), 300 kcal	Indirect calorimetry in a metabolic chamber	TEE BMR MAT PA RQ

Table 2 (continued)

Included trials (country)	Population (obesity or diabetes or metabolic syndrome)	Inventions (surgery)	Inventions (food energy intake postoperatively)	EE measure methods	Parameters
Schneider 2016 [32] (Switzerland)	Inclusion criteria included morbidly obese patients (BMI > 40 or > 35 kg/m ²) with the presence of at least 1 comorbidity, aged between 18 and 65 years, and failure of conservative treatment over 2 years. Exclusion criteria were severe symptomatic gastroesophageal reflux disease (GERD) despite medication, large hiatal hernia, expected dense adhesions at the level of the small bowel, the need for endoscopic follow-up of the duodenum, and patients with inflammatory bowel disease.	RYGB SG	at dinner (18.00 h), 200 kcal as evening snack (21.00 h), and 300 kcal at breakfast 08.40 h in the morning of the second day of the study visit. During visit 4 in the chamber, the patients received four meals consisting of a 400-kcal fixed lunch at 13.30, a 600-kcal fixed dinner at 18.00, one 120-kcal fixed evening snack at 21.00, and a 400-kcal fixed breakfast the following morning at 08.40. The standard dinner consisted of meat balls and mashed potatoes (600 kcal with 13 E% protein, 41 E% carbohydrate, 46 E% fat)	Indirect calorimetry	REE; fat and carbohydrate oxidation
Tam 2016 [33] (Australia)	The inclusion criteria were as follows: BMI > 40 kg/m ² or BMI > 35 kg/m ² with associated comorbidities. Exclusion criteria were participants who had diabetes diagnosed more than 5 years ago or had previous malabsorptive or restrictive surgery, a history of inflammatory intestinal disease, psychiatric conditions, or the use of medications that affect weight or metabolic rate were excluded.	RYGB SG LAGB	Three meals and one snack were provided at scheduled intervals, and participants were instructed to eat all their food within 30 min. The food intake in the chamber during the week 8 assessment was provided at 890 kcal/day for all subjects.	Metabolic chamber indirect calorimetry predicted EE based on FFM, FM, and sex using a linear regression formula	mTEE pTEE mSleepEE pSleepEE REE %Activity/day Spontaneous physical activity
Tam 2016 [34] (Australia)	Inclusion criteria were a BMI > 35 kg/m ² , age between 18 and 65 years, ability to give informed consent, an absence of previous bariatric or gastric surgery, and agreement to use effective contraception and avoid getting pregnant during the trial	Band SG RYGB	Patients had been on a 2-week commercially available very-low-energy diet (VLCD) and postoperatively were on a medically and dietitian-supervised hypocaloric diet typical for postsurgery patients	Indirect calorimetry pREE based on FFM, age, and sex using a linear regression formula	mREE pREE
Browning 2017 [35] (USA)	Inclusion criteria included morbidly obese nondiabetic patients;	RYGB, AGB	NR	Indirect calorimetry pREE based on FFM, FM, age, and sex using a linear regression formula	mREE pREE

Table 2 (continued)

Included trials (country)	Population (obesity or diabetes or metabolic syndrome)	Inventions (surgery)	Inventions (food energy intake postoperatively)	EE measure methods	Parameters
Moshlecke 2017 [36] (Brazil)	<p>Exclusion criteria included previous weight loss surgery, foregut and/or hindgut surgery, and diagnosis of endocrine or chronic renal disease</p> <p>Eligible participants were ≥ 18 years old with a BMI > 40 kg/m² (or BMI > 35 kg/m² with at least 1 obesity-related comorbidity). Patients with impaired thyroid function or cancer were excluded.</p>	RYGB	NR	Indirect calorimetry; Pedometer; International Physical Activity Questionnaire (IPAQ-LF)	REE REE/BW REE/FFM
Bettini 2018 [37] (Italy)	<p>The inclusion criteria were as follows: BMI > 40 kg/m² (or BMI > 35 kg/m² with associated comorbidities). Exclusion criteria for this study were diagnosis of cancer in the previous 5 years, baseline or current insulin therapy, thyroid hormones imbalance, presence of infections or chronic inflammatory diseases, abuse of caffeine (more than three coffee/day), and use of weight-loss drugs and other drugs that could interact with REE.</p>	SG	<p>After surgery, patients received a nutritional plan (balanced hypocaloric diet providing an energy deficit of around 500 kcal per day with about 25–30% of energy from fat, 50–55% from carbohydrates, and 20% from protein) and physical activity prescriptions (at least 150 min per week of moderate intensity physical activity).</p>	Indirect calorimetry	REE REE/BW REE/FFM
Clewa 2018 [3] (Brazil)	<p>The inclusion criteria were as follows: BMI > 40 kg/m² or BMI > 35 kg/m² with associated comorbidities. Patients with a pacemaker, acute or chronic disease (congestive heart failure, chronic renal failure, and liver failure) associated with excessive water retention, treatment with steroid medication for any reason, or use of artificial devices (orthosis or prosthesis) or who did not agree to participate in this study were excluded.</p>	Bariatric surgery	NR	Indirect calorimetry	RMR RMR/BW
Ravelli 2018 [38] (Brazil)	<p>The inclusion criteria were: age between 20 and 45 years, fertile, and a body mass index between a BMI of 40 and 50 kg/m². Participants were excluded who presented with edema or diseases that might have caused alterations in the energy metabolism and who used medicines which cause metabolic and absorptive alterations. BMI > 35 kg/m²</p>	RYGB	NR	DLW; Triaxial accelerometer; pREE based on the Harris–Benedict (HB) equation	TEE MET pREE
Wilms 2018 [39] (Switzerland)	<p>BMI > 35 kg/m²</p>	RYGB	NR	Indirect calorimetry	mREE
Wolfe 2018 [40] (USA)	<p>The inclusion criteria were at least 18 years old and no prior bariatric surgery. Exclusion criteria were pregnant, reversal, conversions, inactivations, and death.</p>	<p>14 RYGB 1 AGB 1 BPD with a duodenal switch</p>	<p>LABS patients followed best practice guidelines for postbariatric-surgery care, which included education regarding the composition and energy content of their diets and calcium,</p>	<p>pREE based on FFM, FM, age, sex, and height using a regression formula DLW; indirect calorimetry</p>	<p>pREE RQ TDEE</p>

RQ

Changes in the RQ were reported in nine studies [8, 9, 15, 20–22, 25, 29, 39]. Compared with baseline, the RQ decreased significantly at 6 months [8, 9, 20–22, 25, 29] (MD 0.04, 95% CI 0.03–0.05, $P < 0.001$, $I^2 = 0\%$) (Supplement 1), while no significant difference was observed at 12 months [9, 15, 22, 25, 29, 39], with evidence of statistical heterogeneity (MD 0.00, 95% CI -0.00 to 0.01, $P = 0.31$, $I^2 = 92\%$) (Supplementary Fig. 1).

Sensitivity Analysis and Publication Bias

The studies included in the meta-analysis of REE, TEE, and RQ at 12 months following surgery showed considerable statistical heterogeneity. A sensitivity analysis was performed to evaluate the stability of the results. None of the results were significantly altered, indicating that our results were robust (Supplementary Fig. 2). Because publication bias can affect the results of meta-analyses, we attempted to evaluate this potential publication bias by using funnel plot analysis and Egger’s test. The funnel

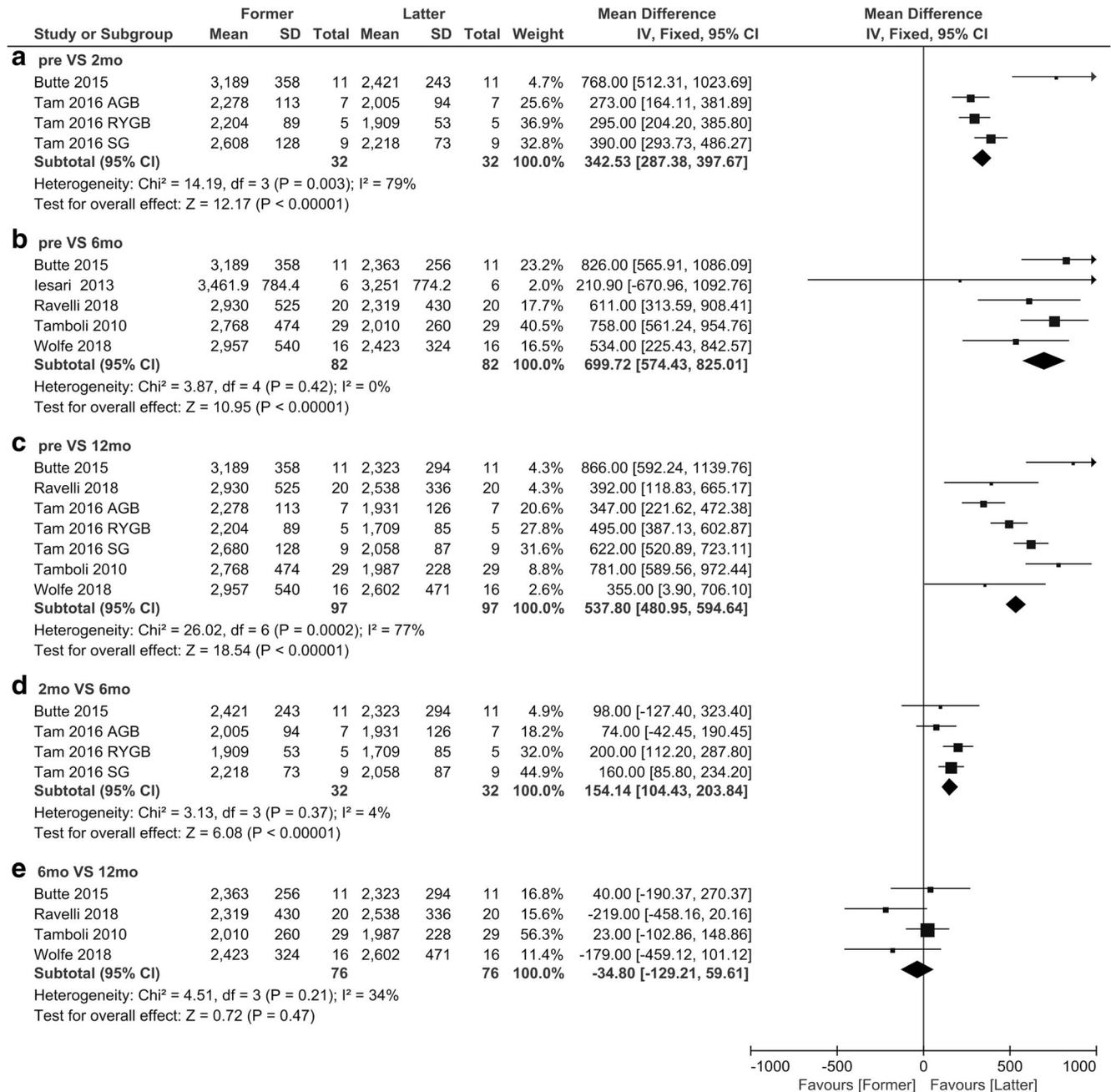


Fig. 2 Forest plot comparing TEE preoperatively and 2, 6, and 12 months after all types of bariatric surgeries. TEE, total energy expenditure

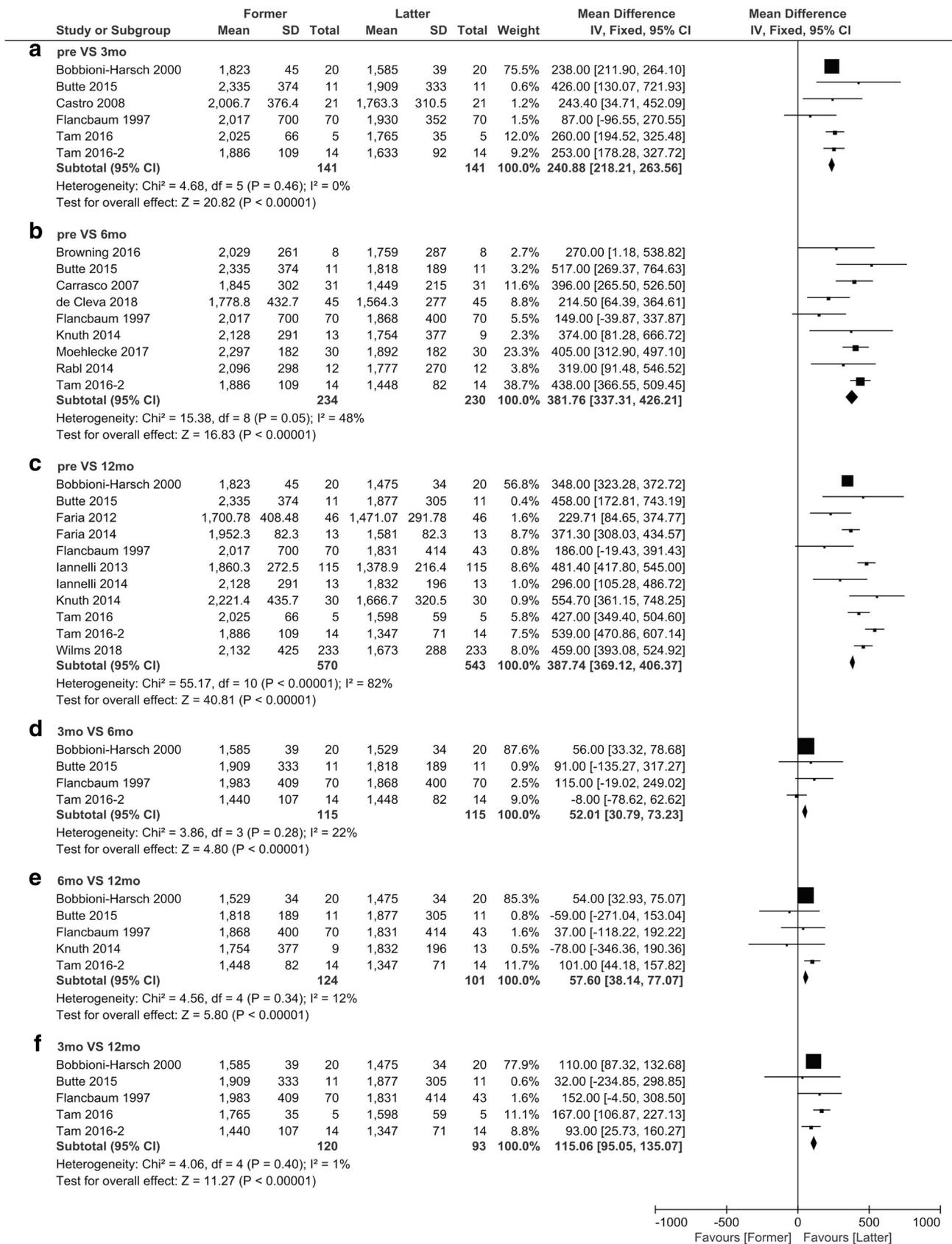


Fig. 3 Forest plot comparing REE preoperatively and 3, 6, and 12 months after RYGB. REE, resting energy expenditure; RYGB, Roux-en-Y gastric bypass

plots for studies that evaluated REE, TEE, and RQ suggested a symmetric distribution of studies around the effect size, and Egger's test confirmed the lack of publication bias except for REE/FFM ($P = 0.033$) (Supplementary Fig. 3).

Discussion

BS can result in substantial weight loss in patients with obesity, and the long-term durability of weight loss is proven to be superior to lifestyle and nonsurgical treatments [10, 11]. The total BW is composed of the FFM and fat mass (FM), which are both determinants of REE. Most studies have shown a post-BS decrease in REE that had been predicted by a decrease in both FFM and FM [3, 19, 39]. In our review, we found a statistically significant decrease in REE at 3, 6, and 12 months following BS, which is consistent with the most substantial changes in BW and body composition in the first year after surgery. Moreover, the decrease in TEE is proportional to the weight change within 6 months after surgery, and there is no further change in TEE with ongoing weight loss.

Although all organs and tissues are metabolically active, large differences in REE exist between organs and tissues. Among organs comprising the FFM, the heart and kidneys have the highest REE (440 kcal/kg/day), closely followed by the brain and liver (200 kcal/kg/day). In contrast, adipose tissue (4.5 kcal/kg/day) and skeletal muscle (13 kcal/kg/day) have lower metabolic rates [35]. Individuals with obesity have a larger FM but also a larger FFM than do individuals without obesity [35]. During the dramatic weight-loss phase in the first postoperative year, the substantial weight loss consists of a reduction in low-metabolic FM; only a small part of the weight loss is the result of thermogenically active FFM, mainly due to the reduction in skeletal muscle [43]. When we evaluated REE in relation to BW and FFM utilizing both ratio-based methods, our findings indicated that the REE/FFM ratio decreased after BS, while the REE/BW ratio increased. The postoperative decrease in REE/FFM may be attributed to the decline in FFM metabolism, and the increase in REE/BW may be the result of the substantial loss of metabolically inert FM.

Interestingly, reductions in REE measured by indirect calorimetry were greater than the predicted REE using linear regression (from FFM and FM). In other words, REE prediction equations overestimated REE after weight loss [27, 44]. In our study, we also confirmed that the measured REE was less than the predicted REE at 3, 6, and 12 months after BS. The mechanism of this energy-sparing phenomenon is not clear. One of the main reasons might be that almost half of the studies involving predicted REE [9, 12, 30, 38, 45] used the Harris–Benedict (HB) formula, which is not an appropriate formula for patients with obesity. In addition, several studies proposed many explanations. One assumption is that the

sympathetic nervous system activity could be blunted by the decreases in circulating leptin and thyroid hormones, which seem to be responsible for the energy-sparing phenomenon [46, 47]. Several studies have suggested that replacement of plasma leptin to pre-weight loss levels reverses this phenomenon, perhaps through alterations in mitochondrial content and/or coupling [48, 49] and maintenance of thyroid hormone concentrations [50]. An alternative explanation for this is that early starvation, decreased insulin secretion, and an increased free water clearance rate are closely associated with this phenomenon [51]. The decline in FFM metabolism, which might be caused by starvation-induced decreases in the heart rate and glomerular filtration rate and increased hepatic gluconeogenesis, also adds to the explanation of the energy-sparing phenomenon after BS. In support of this concept, we confirmed that the degree of the energy-sparing phenomenon was beyond the expected effect of the FM and FFM loss on REE.

The decrease in TEE does not appear to follow the same pattern of the REE change after BS. Our review showed that a sustained decline in REE was observed until 1 year following surgery, while there was no significant difference in the value of TEE between 6 and 12 months postoperatively. One possible explanation for this is the change in PA and DIT. However, most studies indicated no significant differences in PA after surgery [14, 15, 31, 33, 38]. Thus, we concluded that increased absolute and weight-adjusted DIT might explain the variance in the patterns of REE and TEE change.

Anatomical changes after BS lead to a wide range of endocrine, metabolic, and ecologic changes that influence central neuroendocrine signaling related to the energy expenditure balance after food ingestion. Postprandial release of biliary acid and gut hormones and changes in the gut microbiota composition have been proposed to contribute to the increase in DIT observed after BS, especially RYGB. Intestinal mucosal hyperplasia and hypertrophy have been confirmed after RYGB [52]. Cell turnover is upregulated after surgery by flattened and broadened villi, reduced epithelial surface area, and increased cell proliferation, which could increase diet-induced energy expenditure [31, 53]. Moreover, enhanced DIT after meals might be partly explained by small bowel mucosal hypertrophy [54, 55]. All of these well-documented postoperative changes may together and collectively influence TEE [56–59].

We demonstrated that carbohydrate and fat utilization returned to the preoperative levels or even reversed in the weight stable phase despite an increase in fat utilization and a decrease in carbohydrate utilization within 1.5 to 6 months after surgery. Such changes might be consistent with the fact that the RQ decreased significantly at 6 months while no significant difference was observed between baseline and 12 months. A negative energy balance caused by very-low-calorie diets might result in a shift toward increased fat oxidation. In other words, when patients eat a low-carbohydrate diet early postoperatively, increased fat utilization is mainly due to

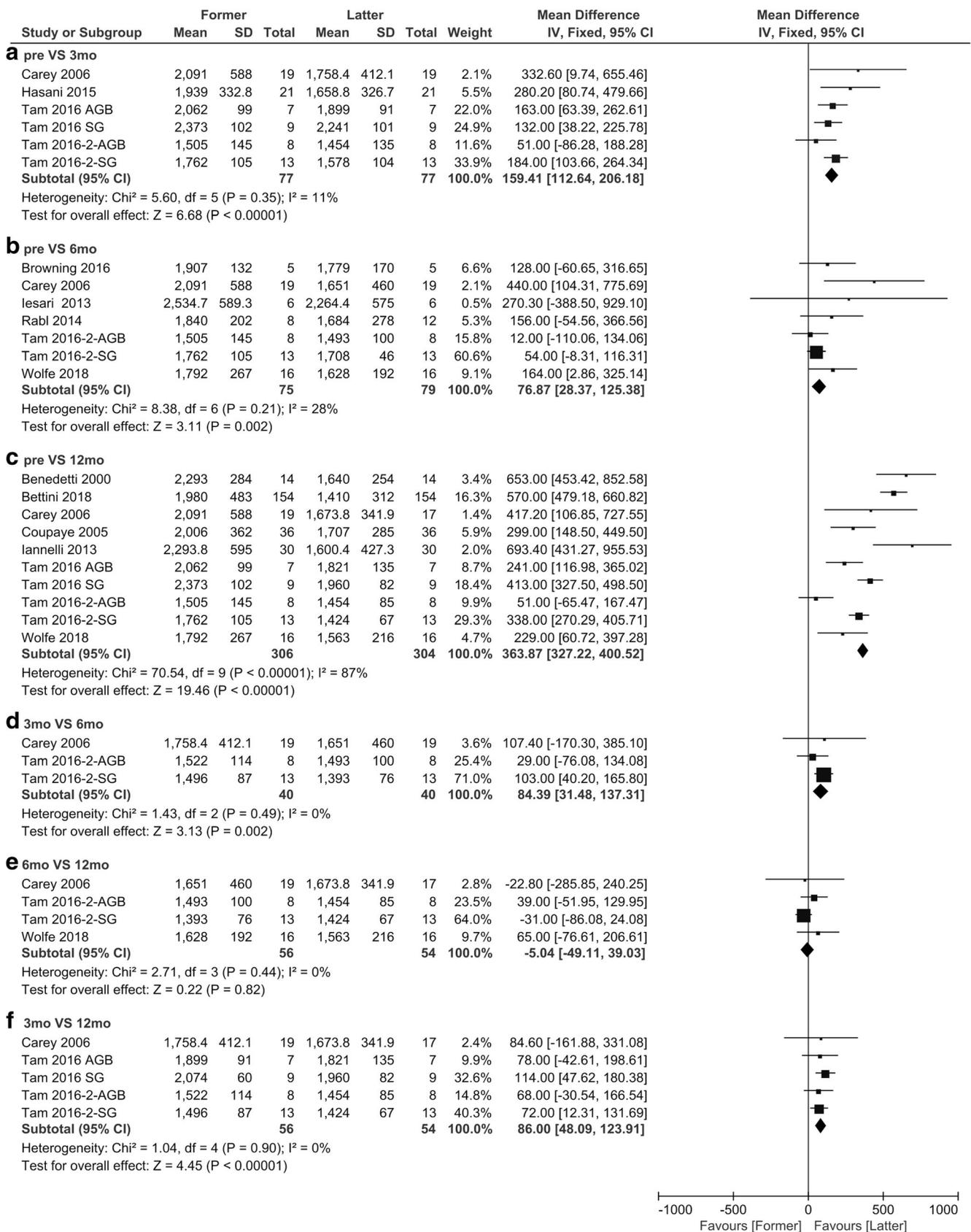


Fig. 4 Forest plot comparing REE preoperatively and 3, 6, and 12 months after bariatric surgeries other than RYGB. REE, resting energy expenditure

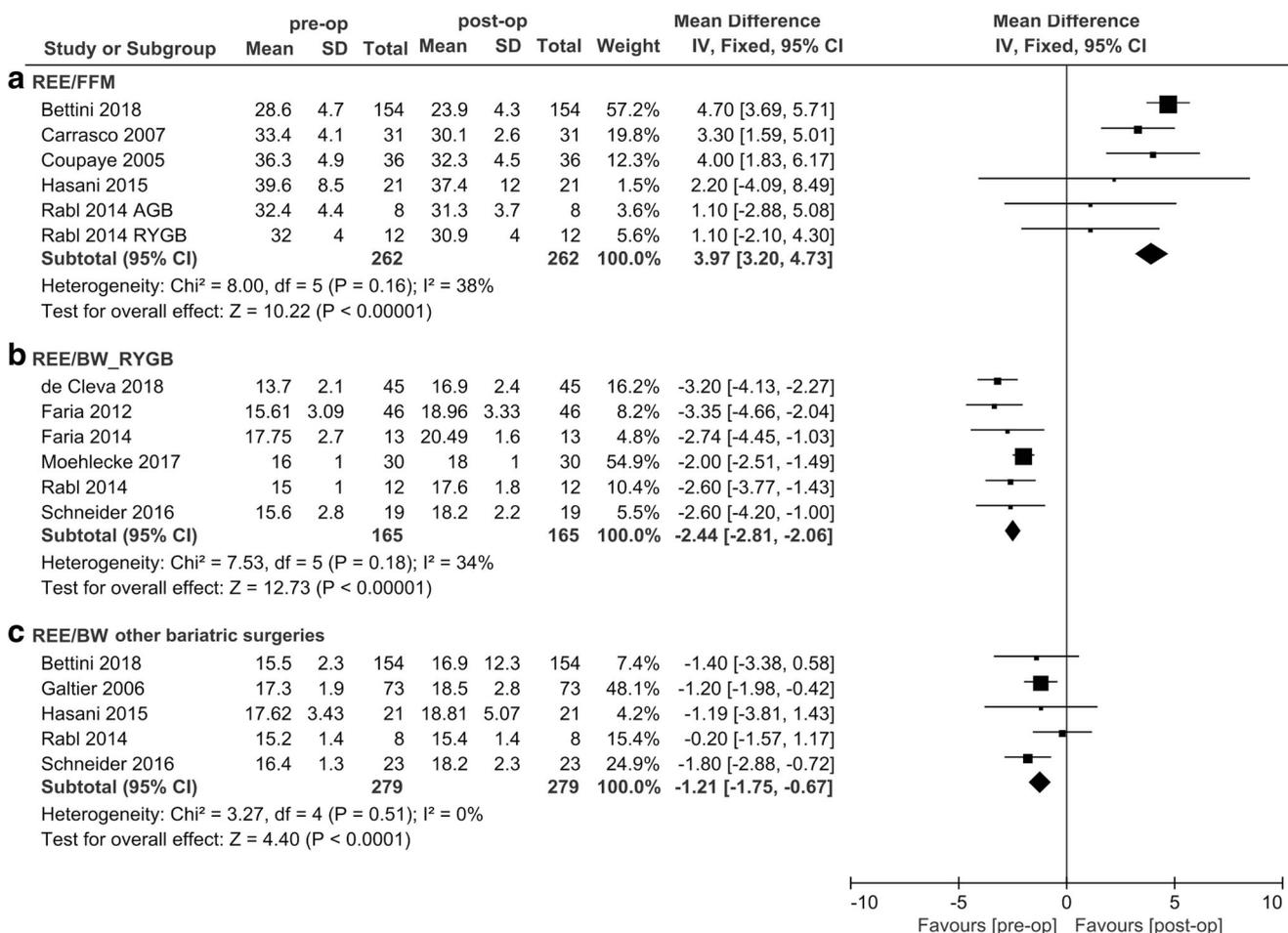


Fig. 5 Forest plot comparing REE/FFM and REE/BW between the preoperative and postoperative periods. REE, resting energy expenditure; FFM, fat-free mass; BW, body weight

a shift from the use of energy intake to the use of endogenous fat reserves for fuel. In addition, an increase in fat mobilization with a decrease in fat intake contributes to massive loss of adipose tissue [29]. Considering that the changes in diet and weight appear to have stabilized at 12 months after surgery, carbohydrate and fat utilization returned to the preoperative levels.

Both lean body mass and protein oxidation decrease during the semi-starvation phase. Thus, a protein-sparing mechanism that does not totally prevent loss of FFM during this period is likely to exist. Our review suggests the occurrence of a steady decrease in protein oxidation that lasts until weight stabilization. Therefore, it is reasonable to presume that decreased protein oxidation is not only due to semi-starvation but is primarily due to the inability of patients to consume some protein-rich foods, such as meat, after BS. These results emphasize the need for nutritional assessment and support of individuals with obesity after BS, especially during the phase of rapid weight loss.

The heterogeneity among studies analyzing REE, RQ, and TEE was statistically significant. We performed a sensitivity

analysis for these heterogeneities, and the results suggested that our results were robust. We believed that the observed heterogeneity in our meta-analysis was mainly attributed to differences in population, duration of obesity, study design, sample size, or comorbidities.

Our review has some strengths and limitations. The strengths include the comprehensive search method, data extraction, and study quality assessment performed by two independent reviewers. Some limitations of the current meta-analysis should be acknowledged. First, although comprehensive search strategies were implemented, this systematic review is inevitably subject to publication bias. Second, because the number of studies included in the meta-analysis was relatively small, some of the subgroup analyses were difficult to implement. Third, the methodological differences in the assessment of energy expenditure may have introduced bias. We acknowledge that the gold standard technique for measurement of energy expenditure in free-living circumstances (the double-labeled water technique) has been used in a limited number of studies. Because individuals with large differences in weight have different REE results in absolute terms,

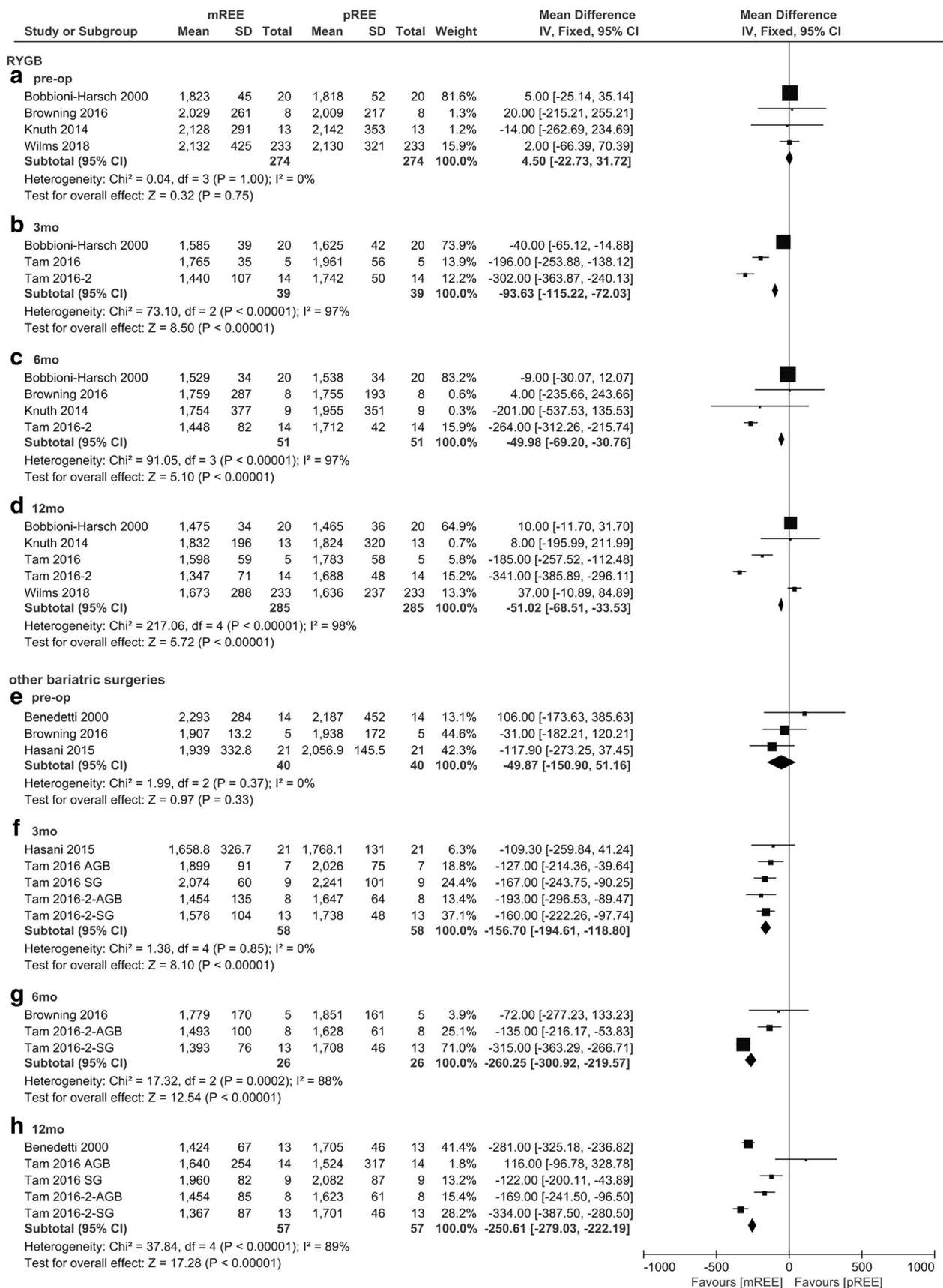


Fig. 6 Forest plot comparing mREE and pREE at baseline and 3, 6, and 12 months postoperatively. mREE, measured resting energy expenditure

normalizing REE for total BW or FFM might be a good method to explore the relationship between REE and body composition. However, when adjusting for muscle mass, there is an important bias among the methods usually used to assess body composition among the obese population. Fourth, changes in energy metabolism after BS may be exaggerated or underestimated by inadequate control of confounders, especially highly variable methods in how body composition was assessed and the populations from which the REE prediction equations were derived. Although most studies excluded some factors that can affect energy metabolism, unknown confounders may partly explain the observed outcomes. Therefore, a more precise analysis should be conducted if individual data are available; this would allow for adjustment by other covariates, including age, sex, race, medication situation, smoking status, drinking status, and obesity-related complications. Finally, most studies included in the review had only 1- to 12-month follow-up periods, but weight gain after BS always occurs 1 year postoperatively. Therefore, a large prospective trial with long-term outcomes must be performed.

Conclusions

We found a statistically significant decrease in REE at 3, 6, and 12 months following BS, which is consistent with the most substantial changes in BW and composition in the first year after surgery. Moreover, the decrease in TEE was proportional to the weight change within 6 months after surgery, and no further change in TEE occurred with ongoing weight loss. The increased absolute and weight-adjusted DIT might explain the variance between the patterns of REE and TEE changes. The postoperative decrease in REE/FFM may be attributed to the decline in FFM metabolism. The increase in REE/BW may be the result of the substantial loss of metabolically inert FM. Carbohydrate and fat utilization returned to the preoperative levels or even reversed in the weight stable phase despite an increase in fat utilization and a decrease in carbohydrate utilization within 1.5 to 6 months after surgery. Such a change might be consistent with the fact that the RQ decreased significantly at 6 months while no significant difference was observed between baseline and 12 months. However, most studies included in the review had only 1- to 12-month follow-up periods despite the fact that weight gain after BS always occurs 1 year later. Therefore, a large prospective trial with long-term outcomes must be performed.

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflicts of interest.

Ethical Statement For this type of study (systematic review and meta-analysis), formal consent is not required.

Informed Consent Statement Informed consent was obtained from all individual participants included in the study.

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