

The magnitude and progress of lean body mass, fat-free mass, and skeletal muscle mass loss following bariatric surgery: A systematic review and meta-analysis

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Summary

Postbariatric loss of muscle tissue could negatively affect long-term health due to its role in various bodily processes, such as metabolism and functional capacity. This meta-analysis aimed to unravel time-dependent changes in the magnitude and progress of lean body mass (LBM), fat-free mass (FFM), and skeletal muscle mass (SMM) loss following bariatric surgery. A systematic literature search was conducted in Pubmed, Embase, and Web of Science. Fifty-nine studies assessed LBM ($n = 37$), FFM ($n = 20$), or SMM ($n = 3$) preoperatively and ≥ 1 time points postsurgery. Random-effects meta-analyses were performed to determine pooled loss per outcome parameter and follow-up time point. At 12-month postsurgery, pooled LBM loss was -8.13 kg [95%CI -9.01 ; -7.26]. FFM loss and SMM loss were -8.23 kg [95%CI -10.74 ; -5.73] and -3.18 kg [95%CI -5.64 ; -0.71], respectively. About 55% of 12-month LBM loss occurred within 3-month postsurgery, followed by a more gradual decrease up to 12 months. Similar patterns were seen for FFM and SMM. In conclusion, >8 kg of LBM and FFM loss was observed within 1-year postsurgery. LBM, FFM, and SMM were predominantly lost within 3-month postsurgery, highlighting that interventions to mitigate such losses should be implemented perioperatively.

KEYWORDS

bariatric surgery, fat-free mass, lean body mass, skeletal muscle mass

1 | INTRODUCTION

Bariatric surgery induces an average weight loss of 32% of preoperative weight within two years postsurgery.¹ This weight loss does not only exclusively consists of fat mass loss but also includes loss of muscle mass.^{2,3} Muscle mass can be expressed by various terms, such as fat-free mass (FFM), lean body mass (LBM), and skeletal muscle mass

(SMM). These terms should not be used interchangeably, since the exact components are different (see Figure 1). A two-compartment model divides the body into fat mass and FFM, in which FFM contains bone tissue, water, organ tissue, and the skeletal muscles. LBM, as measured by three-compartment models, is defined as total body mass minus fat mass and bone mineral content. SMM only contains the dry weight of skeletal muscles and is estimated via segmental

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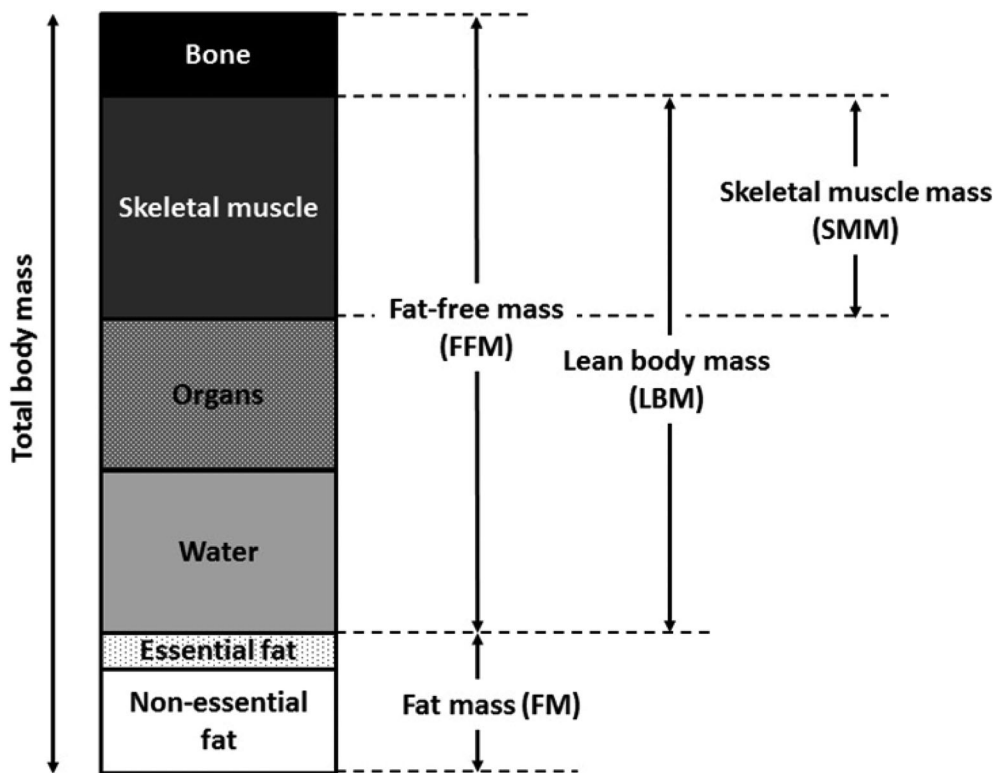


FIGURE 1 The components of fat-free mass, lean body mass, and skeletal muscle mass according to the definitions used by magnetic resonance imaging (MRI), dual energy X-ray absorptiometry (DXA), or computed tomography (CT) scans. Please note that proportions of the components are an approximation; exact proportions may vary across individuals

analysis of muscle volume by whole body MRI. Because skeletal muscle tissue is the main component of LBM and FFM, they are often used as a surrogate marker for SMM.

Muscle tissue is essential for a healthy metabolism, bone (re) modeling, thermoregulation, and preservation of functional capacity and can also function as a storage for glycogen, fat, and protein.⁴ A substantial loss of muscle tissue can, therefore, result in a decreased basal metabolism, functional impairment, and poorer quality of life.⁵⁻⁷ Furthermore, recent findings suggest that postbariatric FFM loss plays a role in energy balance regulation by increasing appetite, which may ultimately lead to weight regain.⁸⁻¹⁰ Therefore, loss of muscle tissue may negatively impact the long-term success of bariatric surgery. Previous studies suggested that muscle tissue is predominantly lost within 6 months postbariatric surgery.^{2,11} However, the exact amounts of loss that can be expected in each postoperative phase remain unclear. This makes it difficult for clinicians to recognize excessive amounts of LBM, FFM, and SMM loss. More insight into the expected ranges of postbariatric LBM, FFM, and SMM loss could help to identify patients who may benefit from additional care on muscle mass preservation. Furthermore, more insight into the time-dependent progress of LBM, FFM, and SMM loss will help to define the most optimal time window to counteract such loss in these patients.

Computed tomography (CT) and magnetic resonance imaging (MRI) are the gold standards to assess body composition *in vivo*, because they are not affected by hydration status.¹² Likewise, dual energy X-ray absorptiometry (DXA) is considered a good alternative to evaluate body composition, because of its high precision and reproducibility.¹³ However, postbariatric studies that use DXA, CT, or MRI have either small sample sizes or few longitudinal measurements, making it difficult

to determine the magnitude and progress of muscle mass loss over time. Combining findings from these studies may yield information on the expected ranges of postbariatric muscle mass loss over time. Therefore, the present systematic review and meta-analysis aimed to unravel time-dependent changes in the magnitude and progress of LBM, FFM, and SMM loss measured by DXA, CT or MRI following bariatric surgery.

2 | METHODS

2.1 | Search strategy

This systematic review was registered in PROSPERO (number CRD42020150511) and performed using the Preferred Reporting Items for Systematic reviews and Meta-Analysis statement 2015 (PRISMA). The databases of PubMed, Embase, and Web of Science were systematically searched for eligible articles up to March 15, 2021. The following search strategy was used: Bariatric surgery AND (DXA OR ((CT OR MRI) AND (Lean mass OR FFM OR Muscle mass))). The extensive search strategy with adaptations for each database is added in supporting information Table S1.

2.2 | Definitions of body composition parameters

This study included three body composition parameters: LBM, FFM, and SMM. Since these terms cannot be used interchangeably due to differences in components (see Figure 1), all analyses were performed for LBM, FFM and SMM separately.

2.3 | Study selection

Three reviewers independently screened all titles and abstracts for eligibility. Thereafter, the same three reviewers assessed the remaining studies in full text to determine whether the study could be included in our meta-analysis. Studies were deemed eligible if they conformed to the predetermined inclusion and exclusion criteria (Table 1). First, all subjects should be ≥ 18 years old, have a BMI ≥ 35 kg/m², and have undergone a bariatric procedure. Bariatric procedures included Roux-en-Y gastric bypass surgery (RYGB), sleeve gastrectomy (SG), biliopancreatic diversion (BPD), and adjustable gastric band procedures. Studies with temporary restrictive procedures (e.g., intragastric balloon) were excluded. Furthermore, studies that used ≥ 1 of the following outcomes—amount (kg) of LBM, FFM, or SMM measured with whole body DXA, CT, or MRI—were included. Studies with other measurement techniques; segmental analysis of DXA, CT, and MRI; or studies that exclusively reported outcomes relative to body weight (e.g., %FFM) were excluded. Finally, studies required longitudinal data on body composition with one preoperative measurement and at least one postoperative measurement. Small ranges in postoperative measurement were allowed; however, studies with >3 -month difference within one postoperative measurement point (e.g., mean follow-up: 18 months [range 12 to 24 months]) were also excluded. When separate studies had overlapping study populations, only the study with most observations was included. In case of more than one outcome measure within overlapping populations (e.g., Study 1: FFM ($n = 30$) and Study 2: FFM ($n = 25$) and SMM ($n = 25$)), the secondary outcome of the study with less observations was also included. Disagreement between reviewers was resolved through consensus.

2.4 | Data extraction

Data were extracted with the use of a predetermined data extraction file. One reviewer recorded all pre-operative and postoperative data on LBM, FFM, and SMM and corresponding standard deviations (SD) or standard error of the mean (SEM). Furthermore, other information was extracted, including year of publication; country; age; sex; preoperative BMI; preoperative LBM, FFM, or SMM mass; type of surgery; and weight loss per time point. In eight studies, data on body composition or weight loss were reported in figures; therefore, data were extracted using GetData Graph Digitizer software (version 2.26). When viable information was missing, data were requested from the authors by email ($n = 24$ studies; authors provided requested information in $n = 5$ studies).

2.5 | Assessment of risk of bias in included studies

The reporting quality of each included study was assessed using the STROBE Statement,¹⁴ which facilitates critical appraisal and interpretation of observational research. The checklist consists of 22 items relating to title, abstract, introduction, methods, and results and

TABLE 1 Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
<i>Population</i>	
- Human subjects	- Animal studies
- Bariatric procedure (including RYGB, SG, BPD, adjustable gastric banding, gastric bypass)	- Gastrectomy for other medical reasons (not focused on weight loss)
- All subjects ≥ 18 years old	- Abdominal liposuction
- Mean BMI ≥ 35 kg/m ²	- Other severe diseases: cancer, lung diseases, kidney diseases, gastrointestinal diseases, cardiovascular diseases or immunodeficiency diseases (except for obesity-related diseases such as diabetes mellitus type 2, hypertension, arthrosis and sleep apnoea)
<i>Study design</i>	
- Observational studies	- Cross-sectional studies
- Longitudinal measurements (including a preoperative measurement and ≥ 1 postoperative measurement)	- Review articles
- Control groups of randomized controlled trials	- Intervention groups of randomized controlled trials
	- Ranges >3 months within one postoperative measurement point
<i>Measurements</i>	
- Whole body DXA scan	- BIA
- Whole body CT	- Bod Pod
- Whole body MRI	
<i>Outcome</i>	
- Lean body mass / lean mass /lean tissue	- %FFM (percentage of body weight)
- Fat-free mass	
- Skeletal muscle mass/ muscle mass	
<i>Other</i>	
- English language	- Abstract only
- Full text available	- Conference proceedings
	- Study protocols
	- Letter to the editor
	- Case reports

Abbreviations: BIA, bioelectrical impedance analysis; BMI, body mass index; BPD, biliopancreatic diversion; CT, computed tomography; DXA, dual energy X-ray absorptiometry; FFM, fat-free mass; MRI, magnetic resonance imaging; RYGB, Roux-en-Y gastric bypass; SG, sleeve gastrectomy.

discussion sections of articles. A total of 34 points could be received; however, not all items were applicable in every study. Therefore, quality scores were calculated both as total of points and as

percentage of the applicable items. Subsequently, total scores were divided into three categories: <60%, 60–80%, and ≥80%.

2.6 | Data synthesis

Follow-up time points were divided into five categories: <3-month, ≥3- to <6-month, ≥6- to 9-month, 12-month, and 18- to ≤36-month postsurgery. If two follow-up measurements of one study fell within one time category (e.g., both 24- and 36-month postsurgery), only the first time point was included in the meta-analysis. In studies with multiple study arms (e.g., Roux-en-Y gastric bypass vs. SG), all study arms were separately included in statistical analyses. Since loss of muscle tissue is highly dependent on weight loss, the proportional loss within total weight loss (= %loss/WL) was estimated. First, study-specific % loss/WL was calculated at each time point, by dividing the mean LBM, FFM or SMM loss by the mean weight loss times 100. Then, a weight factor was applied based on the sample size of each study. Subsequently, the weighted average %loss/WL was calculated per time point. Although the %loss/WL is not suitable for meta-analysis since group level calculations may not reflect individual results and group level SEs are lacking, this outcome gives insight into the relative amount of postbariatric LBM, FFM, and SMM loss.

2.7 | Statistical analysis

A random-effects model (specified *a priori*) was used to account for possible heterogeneity between studies and to determine the overall effect (i.e., amounts of LBM loss, FFM loss, and SMM loss in kilograms). For each outcome measure, a meta-analysis was performed to estimate the pooled effect size per follow-up visit in terms of the mean difference with its corresponding 95%CI. Furthermore, Cochrane's Q statistic and I^2 were calculated to assess the degree of heterogeneity across studies. Whereas the Q statistic indicates significant heterogeneity at $P < 0.10$, the I^2 characteristic reflects the percentage of the observed between-study variability. An $I^2 > 50\%$ is considered as substantial heterogeneity.¹⁵ Forest plots were generated to illustrate the study-specific effect sizes with 95%CI. For the subanalysis, type of surgery was added to the model as additional fixed effect to determine the difference in LBM, FFM, and SMM loss between procedures, adjusted for time. Studies that included ≥2 procedures but did not distinguish their results for each type were excluded. Mean differences with respect to the reference group with corresponding 95%CI were determined for all possible comparisons. Additionally, forest plots for LBM, FFM, and SMM loss per bariatric procedure were generated, in which either the 12-month timepoint or the latest available timepoint was included per study. Finally, potential differences in proportional loss (= %loss/WL) between procedures were assessed by a one-way ANOVA. Statistical analyses were performed using R Statistical Software (version 3.6.2), and the script was added as a supporting information. Statistical significance was assumed at $P < 0.05$.

3 | RESULTS

The systematic search resulted in 302 eligible articles in PubMed, 507 articles in Embase, and 315 articles in Web of Science. After removal of duplicates and elimination based on the selection criteria, 59 studies were included in risk and bias assessment and quantitative analyses (Figure 2), with 37 studies assessing LBM,^{11,16–51} 20 studies assessing FFM^{22,25,52–70}, and 3 studies assessing SMM.^{71–73} The subanalysis on type of surgery was performed on 52 studies. Included studies were published from 2000 to 2021.

3.1 | Cohort characteristics

An overview of general characteristics of the included studies is displayed in Table 2. In total, data were aggregated from 2270 individuals with a mean BMI of 44.2 kg/m² (range 37.79 to 51.20 kg/m²). Mean LBM was 58.2 kg (range 49 to 69 kg), mean FFM was 63.1 kg (range 55 to 89 kg), and mean SMM was 27.1 kg (range 22 to 37 kg). Main continent of origin of the studies was Europe ($n = 38$), followed by North America ($n = 12$), Asia ($n = 5$), South America ($n = 3$), and Australia ($n = 1$). In 35 studies both sexes were included, whereas 22 studies exclusively included females. Most studies included only one type of surgery: RYGB ($n = 27$), adjustable gastric band ($n = 6$), SG ($n = 7$), BPD ($n = 5$), whereas 14 studies examined the effect of ≥2 procedures. Outcomes were predominantly measured by DXA ($n = 56$), whereas only three studies used MRI.

3.2 | Quality assessment of reporting

Fifty-nine studies were included for risk and bias assessment. The mean ± SD score on the STROBE checklist was 24.3 ± 2.4, reflecting 80.0 ± 7.7% of the maximal achievable score. One study scored below <60%, 26 studies scored between 60% and 80%, and 32 studies scored >80% (supporting information Figure S1). A sensitivity analysis of our main outcome measures after exclusion of the study with a score <60% did not yield different results. Study-specific STROBE scores were included in supporting information Table S2.

3.3 | Magnitude and progress of muscle mass loss

LBM loss, FFM loss, and SMM loss were displayed in forest plots (Figures 3–5, respectively). At 12-month postsurgery, meta-analyses showed pooled losses of –8.13 kg LBM [95%CI –7.26; –9.01], –8.23 kg FFM [95%CI –5.73; –10.74], and –3.18 kg SMM [95%CI –0.71; –5.64]. Although absolute SMM loss is lower compared with LBM and FFM loss, relative SMM loss with respect to preoperative SMM was equal to relative FFM and LBM loss (SMM: 13% vs. FFM 13% vs. 13% LBM). The estimated proportional loss with respect to weight loss at 12-month postsurgery was comparable with 23.4%, 20.8%, and 8.2% loss/WL for LBM, FFM, and SMM,

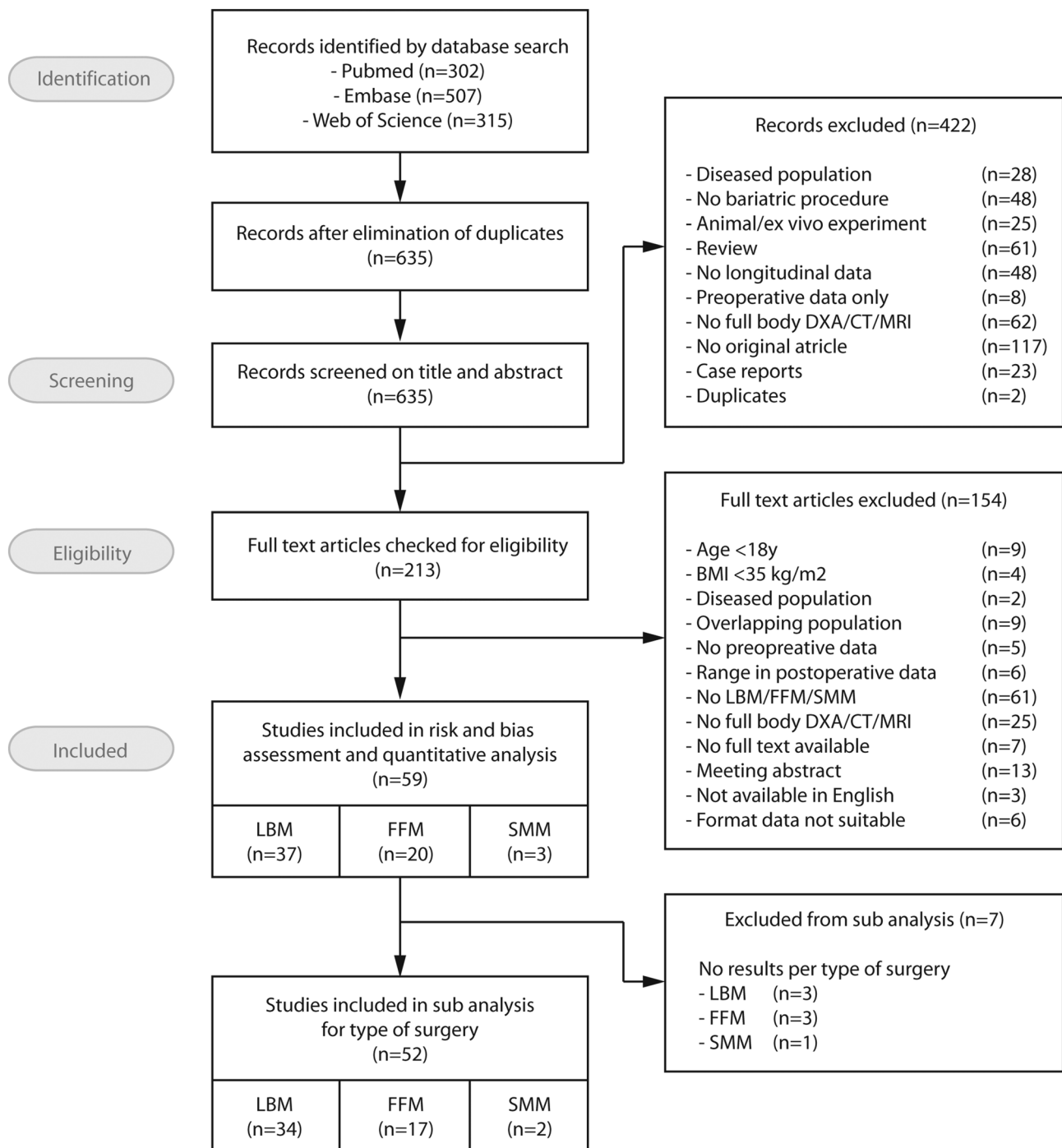


FIGURE 2 Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) flowchart of search strategy outcomes and screening process. CT, computed Tomography; DXA, dual energy X-ray absorptiometry; FFM, fat-free mass; LBM, lean body mass; MRI, magnetic resonance imaging; SMM, skeletal muscle mass

respectively. The studies ($n = 8$) that assessed LBM both at 12 and 18–36 months showed a mean loss of -1.29 ± 1.0 kg LBM between these timepoints, suggesting a more stabilized LBM after 12 months. On the contrary, all studies showed greatest declines in LBM, FFM, and SMM between the preoperative and first follow-up measurement, after which a more gradual decrease occurred. Patients lost -4.45 kg LBM [95%CI -6.21 ; -2.70] within 3-month

postsurgery, accounting for 55% of the 12-month LBM loss. A similar pattern was seen for FFM, in which the FFM loss within <3 months (-4.25 kg [95%CI -6.30 to -2.20]) reflected 52% of 12-month FFM loss and SMM loss at 3–6 months (-2.10 kg [95% CI -4.22 to 0.02]) reflected 66% of 12-month SMM loss. Study-specific changes in LBM, FFM, and SMM over time are displayed in supporting information Figure S2.

TABLE 2 Study characteristics of the included studies (n = 59)

Study	Country	N	Sex (M/F)	Age (years)	BMI (kg/m ²)	Muscle mass (kg)	Surgery type	Timepoints	Methods	Outcome
Arhire (2018)	Romania	75	13/62	42.1 ± 11.5	45.15 ± 6.78	65.58 ± 12.42	SG	pre, 6 months, 12 months	DXA	LBM
Bazzocchi (2015)	Italy	41	0/41	40.6 ± 10.0	42.6 ± 6.6	53.37 ± 11.15	RYGB	pre, 3 months, 6 months, 12 months	DXA	LBM
Beckman (2017)	USA	32	0/32	47 ± 12	48 ± 7	61 ± 10	RYGB	pre, 6–9 months, 12 months	DXA	LBM
Bellicha (2019)	France	45	0/45	43 [38–51]	42.6 [40.0–45.5]	56.4 [51.8–61.2]	RYGB	pre, 6 months	DXA	LBM
Blom-Høgestøl (2020)	Norway	34	13/21	45.2 ± 9.7	40.9 ± 3.5	61.1 ± 11.2	RYGB	pre, 12 months	DXA	LBM
Bojsen-Møller (2015)	Denmark	9	3/6	32 [29–46]	39.2 (35.2, 43.3)	64 (57, 71)	RYGB	pre, 3 months	DXA	FFM
Brzozowska (2020)	Australia	39	12/27	RYGB: 51.1 ± 7.6 SG: 51 ± 11BAND: 42.3 ± 13.1	RYGB: 42.3 ± 7.7SG: 42.6 ± 5.3BAND: 37.3 ± 4.5	RYGB: 56.1 ± 11SG: 59.7 ± 8.1BAND: 51.3 ± 6.7	RYGB (n = 7), SG (n = 21), BAND (n = 11)	Pre, 6 months, 12 months, 24 months, 36 months	DXA	LBM
Busetto (2000)	Italy	6	0/6	38 to 42	42.6 ± 1.1	65.4 ± 1.3	BAND	pre, 8 weeks, 24 weeks	MRI	FFM
Calleja-Fernández (2015)	Spain	46	7/39	45.43 ± 9.56	45.77 ± 5.10	LBM: 53.13 ± 9.30 FFM: 56.27 ± 8.58	BPD	pre, 12 months	DXA	LBM, FFM
Carrasco (2009)	Chile	42	0/42	37.7 ± 9.6	45.0 ± 4.3	58.9 ± 5.8	RYGB	pre, 6 months, 12 months	DXA	FFM
Chen (2021)	China	49	29/20	28 [23.5–35.0]	40.0 ± 5.4	60.7 ± 11.9	SG	Pre, 6 months, 12 months	DXA	LBM
Ciangura (2010)	France	42	0/42	39.5 ± 11.6	44.6 ± 6.1	61.5 ± 7.8	RYGB	pre, 3 months, 6 months, 12 months	DXA	LBM
Clements (2011)	USA	16	1/15	46 ± 7.5	43.6 ± 4.2	54 ± 8.1	RYGB	pre, 2 weeks, 8 weeks	DXA	LBM
Cole (2017)	USA	5	0/5	47.2 ± 10.9	48.8 ± 9.7	LBM: 63.5 ± 13.2FFM: 66.4 ± 13.9	RYGB	pre, 6 weeks, 6 months, 12 months, 9y	DXA	LBM, FFM
Coupaye (2005)	France	36	0/36	42.7 ± 8.7	47.2 ± 8.5	54.4 ± 7.1	BAND	pre, 12 months	DXA	LBM
Coupaye (2007)	France	32	0/32	42.6 ± 8.4	45.5 ± 6.4	25.7 ± 4.6	BAND	pre, 12 months	DXA	SMM
Davidson (2018)	USA	93	14/79	44.2 ± 11.6	Male: 44.7 ± 4.1Female: 45.7 ± 4.1	RYGB: 25.3 ± 3.3SG: 28.6 ± 4.8BAND: 23.6 ± 4.0	RYGB (n = 72), SG (n = 11), BAND (n = 10)	pre, 12 months, 24 months, 60 months	MRI	SMM

TABLE 2 (Continued)

Study	Country	N	Sex (M/F)	Age (years)	BMI (kg/m ²)	Muscle mass (kg)	Surgery type	Timepoints	Methods	Outcome
Diniz-Sousa (2020)	Portugal	20	4/16	46.5 ± 8.5	46.1 ± 4.2	53 (51.7, 54.5)	RYGB, SG	Pre, 1 month, 6 months, 12 months	DXA	LBM
Faucher (2019)	France	279	64/215	G1: 63.7 ± 2.7G2: 42.6 ± 9.7	G1: 44.5 ± 5.1 G2: 44.2 ± 5.4	G1: 58.6 ± 9.4G2: 61.4 ± 10.9	RYGB, SG	pre, 3 months, 6 months, 12 months	DXA	LBM
Favre (2018)	Switzerland	44	0/44	G1: 37.2 ± 9.5 G2: 38.5 ± 11.2 G3: 44.9 ± 3.8	G1: 42.5 ± 4.4G2: 41.7 ± 3.5G3: 39.9 ± 6.4	G1: 49.08 ± 6.96G2: 50.46 ± 6.92G3: 56.22 ± 5.57	RYGB	pre, 12 months	DXA	LBM
Fjeldborg (2015)	Denmark	31	12/19	43.9 ± 7.7	42.3 ± 4.7	67.1 ± 12.8	RYGB	pre, 12 months	DXA	LBM
Garrapa (2005)	Italy	15	4/11	32.5 ± 3.8	42.2 ± 0.9	55.98 (3.02)	BAND	pre, 6 months	DXA	FFM
Hayashi (2017)	Japan	14	4/10	G1: 43.3 ± 7.3G2: 64.6 ± 0.5	G1: 45.1 ± 7.5G2: 43.2 ± 4.8	G1: 63.4 ± 10.8G2: 37.9 ± 32.9	SG	pre 12 months	DXA	LBM
Hirsch (2020)	USA	21	NR	43.7 ± 10.7	51.2 ± 13.7	59.4 ± 9.2	RYGB, SG	Pre, 3 weeks, 12 weeks, 24 weeks	DXA	FFM
Jacobsen (2013)	Denmark	12	3/9	NR	39.2 ± 1.8	NR	RYGB	pre, 3 months	DXA	FFM
Johnson (2017)	USA	25	0/25	48 ± 10	46.6 ± 6.8	52.3 ± 11.6	RYGB	pre, 6 months, 12 months	DXA	FFM
Jorsal (2020)	Denmark	20	5/15	47 [39–50]	43.4 [39.7–47.0]	57.4 [52.2–66.4]	RYGB	Pre, 3 months	DXA	FFM
Kayser (2017)	France	59	0/59	RYGB: 37.3 ± 1.9BAND: 34.5 ± 1.6	RYGB: 46.5 ± 1.0BAND: 43.6 ± 0.7	RYGB: 58.9 (1.2)BAND: 55.5 (1.4)	RYGB (n = 37), BAND (n = 22)	pre, 1 month, 3 months	DXA	FFM
Kennigott (2019)	Germany	31	13/18	46.4 ± 9.7	45.2 ± 6.5	22.5 ± 4.7	RYGB (n = 11), SG (n = 20)	pre, 3 months, 12 months	MRI	SMM
Khoo (2014)	USA	30	10/20	49.6 ± 1.4	43.4 ± 0.8	63.0 ± 20.5	RYGB	pre, 6 months, 12 months	DXA	FFM
Kim (2020)	USA	44	10/34	45 ± 12	44 ± 7	62 ± 12	RYGB	pre, 6 months	DXA	LBM
Legro (2012)	USA	29	0/29	34.5 ± 4.3	49 ± 7	57 ± 5	RYGB	pre, 1 month, 3 months, 6 months, 12 months, 24 months	DXA	LBM
Lubrano (2004)	Italy	45	17/28	19 to 49	47.7 ± 6.4	62.3 ± 11.1	RYGB	pre, 1 month, 3 months, 6 months, 9 months, 12 months, 24 months, 36 months	DXA	LBM
Maimoun (2019)	France	30	5/25	40.9 ± 15.1	41.9 ± 4.5	59.8 ± 8.9	SG	pre, 1 months, 12 months	DXA	LBM

(Continues)

TABLE 2 (Continued)

Study	Country	N	Sex (M/F)	Age (years)	BMI (kg/m ²)	Muscle mass (kg)	Surgery type	Timepoints	Methods	Outcome
Marengo (2017)	Spain	38	0/38	46.3 ± 8.2	42.91 ± 3.62	54.97 ± 4.83	RYGB	pre, 12 months, 36 months	DXA	LBM
Matos (2020)	Brazil	17	0/17	41.2 ± 11	42.0 ± 3.6	57.2 ± 11.1	RYGB	Pre, 6 months	DXA	LBM
Mingrone (2002)	Italy	46	15/31	30 to 45	Male: 48.0 ± 5.4 Female: 48.3 ± 6.3	Male: 88.7 ± 8.1 Female: 59.3 ± 5.6	BPD	pre, 12 months	DXA	FFM
Moehlecke (2017)	Brazil	30	5/25	43 ± 12	49 (9)	80 (4)	RYGB	pre, 6 months	DXA	FFM
Moizé (2013)	Spain	50	9/41	RYGB: 43.0 ± 2.0 SG: 45.0 ± 2.9	RYGB: 45.5 ± 0.6 SG: 47.2 ± 1.0	RYGB: 53.5 (1.6) SG: 59.6 (2.2)	RYGB (n = 25), SG (n = 25)	pre, 4 months, 12 months	DXA	LBM
Nielsen (2021)	Denmark	41	6/35	39.6 ± 9.5	40.8 ± 1.2	68.0 (1.4)	RYGB, SG	Pre, 6 months, 18 months	DXA	FFM
Oibers (2006)	Sweden	83	NR	NR	RYGB: 42.3 ± 4.5 BAND: 42.6 ± 4.2	RYGB: 54.9 ± 8.9 BAND: 56.3 ± 9.1	RYGB (n = 37), BAND (n = 46)	pre, 12 months	DXA	LBM
Oppert (2018)	France	22	0/22	43.9 ± 10.7	43.6 ± 6.2	55.6 ± 8.4	RYGB	pre, 6 months	DXA	LBM
Rabl (2014)	USA	20	4/16	RYGB: 47.4 ± 8.7 BAND: 49.0 ± 10.7	RYGB: 48.4 ± 6.8 BAND: 44.3 ± 5.0	RYGB: 61.9 ± 15.4 BAND: 59.0 ± 7.6	RYGB, BAND	pre, 2 weeks, 6 months	DXA	LBM
Raffaelli (2015)	Italy	8	0/8	34 ± 4	51.2 ± 7.95	68.47 ± 21.26	BPD	pre, 6 months	DXA	FFM
Sajoux (2019)	Spain	39	2/37	40.8 ± 10.4	45.6 ± 6.2	56.7 ± 9.9	RYGB (n = 15), BPD (n = 15), SG (n = 19)	pre, 2-3 months, 4-6 months	DXA	FFM
Savastano (2010)	Italy	45	0/45	35.3 ± 9.1	42.1 ± 4.1	60.1 ± 6.1	BAND	pre, 6 months, 12 months	DXA	FFM
Sergi (2003)	Italy	6	0/6	38 to 42	42.8 ± 1.0	55.2 ± 2.4	BAND	pre, 2 months, 6 months	DXA	FFM
Tacchino (2003)	Italy	101	0/101	41 ± 8	45.5 ± 7.7	58.0 ± 6.6	BPD	pre, 2 months, 6 months, 12 months, 24 months	DXA	LBM
Talalaj (2020)	Poland	155	38/117	42.0 ± 10.5	43.9 ± 5.6	64.5 ± 10.6	SG	pre, 12 months	DXA	LBM
Tamboli (2010)	USA	29	4/25	43.8 ± 9.6	46.3 ± 5.5	62.9 ± 10.2	RYGB	pre, 6 months, 12 months	DXA	LBM
Tan (2016)	Singapore	22	6/13	40.6 ± 2.1	38.8 ± 1.3	56.56 (2.23)	RYGB (n = 10), SG (n = 12)	pre, 12 months	DXA	FFM

TABLE 2 (Continued)

Study	Country	N	Sex (M/F)	Age (years)	BMI (kg/m ²)	Muscle mass (kg)	Surgery type	Timepoints	Methods	Outcome
Turcotte (2019)	Canada	16	5/11	41.6 ± 8.8	49.4 ± 5.6	69.5 ± 16.1	BPD	pre, 3 months, 12 months	DXA	FFM
Vatier (2012)	France	86	19/67	42.3 ± 10.3	48.1 ± 5.9	68.8 ± 12.8	RYGB	pre, 6 months, 12 months	DXA	LBM
Vaurs (2015)	France	114	21/93	39.6 ± 11.7	43.3 ± 5.4	57.0 ± 10.5	RYGB (n = 70), SG (n = 44)	pre, 3 months, 12 months	DXA	LBM
Vilarrasa (2011)	Spain	59	0/59	46.0 ± 8.2	43.9 ± 4.2	54.1 ± 5.5	RYGB	pre, 12 months, 36 months	DXA	LBM
Von Scholten (2017)	Denmark	19	5/14	40 ± 9.3	41 ± 6	66.2 ± 12.2	RYGB	pre, 6 months	DXA	LBM
Werling (2015)	Sweden	6	0/6	41.1 (28.8 to 50)	41.4 (39.1 to 44.8)	55.9 (47.5 to 59.3)	RYGB	pre, 10 days, 3 months, 20 months	DXA	LBM
Zhang X (2018)	China	128	48/80	32.23 ± 10.52	39.66 ± 6.23	56.20 ± 11.81	SG	pre, 6 months	DXA	LBM
Zhang Y (2017)	China	37	18/19	G1: 42.71 ± 14.13G2: 29.04 ± 5.85	G1: 37.79 ± 4.87G2: 40.56 ± 4.54	G1: 55.29 ± 11.02G2: 62.92 ± 12.12	SG	pre, 3 months	DXA	LBM

Note: Data are displayed as mean ± SD, mean (SE), median [IQR 25%–75%], mean (LCI, UCI), or as (minimum to maximum).

Abbreviations: BAND, adjustable gastric banding; BPD, biliopancreatic diversion; DXA, dual-energy x-ray absorptiometry; FFM, fat-free mass; G1/G2/G3, group 1, 2, or 3 (when data are split based on patient characteristics); LBM, lean body mass; MRI, magnetic resonance imaging; NR, not reported; RYGB, Roux-en-Y gastric bypass; SG, sleeve Gastrectomy; SMIM, skeletal muscle mass.

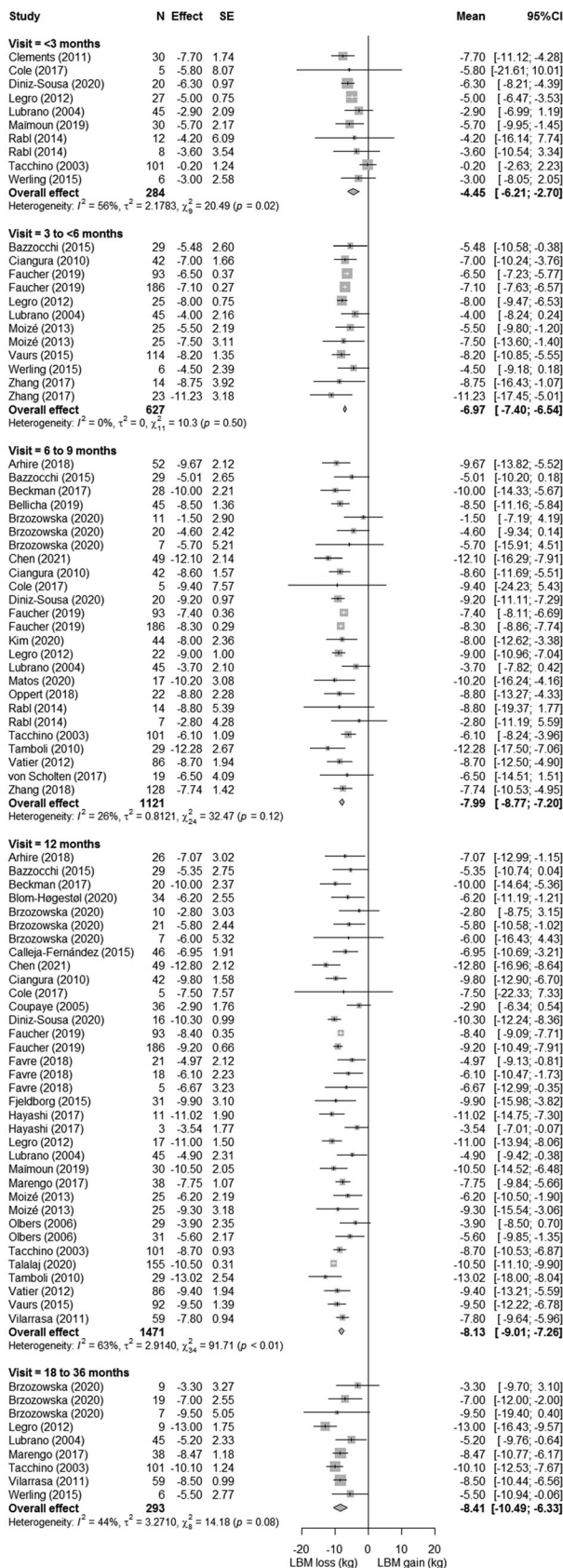
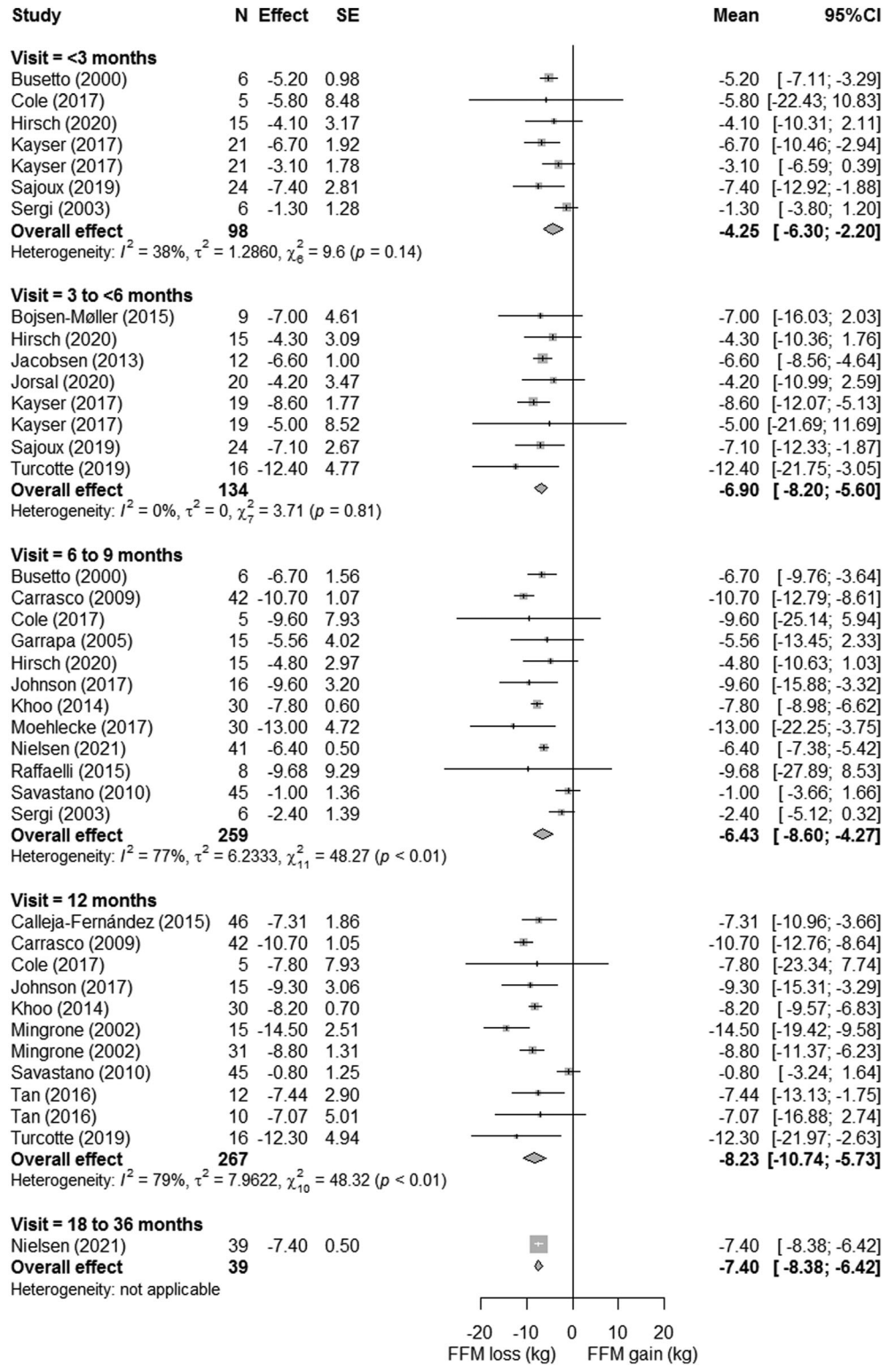


FIGURE 3 Forest plots of lean body mass loss with respect to preoperative measures. The effect size (mean difference between preoperative and postoperative measure) and 95% confidence interval for individual studies and the pooled estimate per time point are depicted. Mean follow-up time was 1.1 ± 0.6 months for <3 months, 3.2 ± 0.4 months for 3 to 6 months, 6.1 ± 0.3 months for 6 to 9 months, 12 ± 0 months for 12 months, and 26.2 ± 5.7 months for 18 to 36 months

FIGURE 4 Forest plots of fat-free mass loss with respect to preoperative measures. The effect size (mean difference between preoperative and postoperative measure) and 95% confidence interval for individual studies and the pooled estimate per time point are depicted. Mean follow-up time was 1.5 ± 0.8 months for <3 months, 3.3 ± 0.7 months for 3 to 6 months, 6 ± 0 months for 6 to 9 months, 12 ± 0 months for 12 months, and 18 ± 0 months for 18 to 36 months



3.4 | Muscle mass loss per surgery type

Forest plots of LBM, FFM, and SMM loss per bariatric procedure were displayed in supporting information Figures S3–S5. The comparison of LBM, FFM, and SMM loss between different types of surgery adjusted for time is illustrated in Figure 6. Adjustable gastric band procedures showed a lower LBM loss of -3.1 kg [95%CI -5.9, -0.3],

-4.2 kg [95%CI -6.6, -1.8], and -5.5 kg [95%CI -8.1, -2.9] compared with BPD, RYGB, and SG procedures, respectively (all $P < 0.05$). Similar effects were seen for FFM and SMM, in which the adjustable gastric band showed significantly smaller decreases in FFM compared with RYGB and BPD and smaller decreases in SMM with respect to RYGB and SG. However, the procedures induced differences in total body weight loss as well, in which the greatest weight loss was found

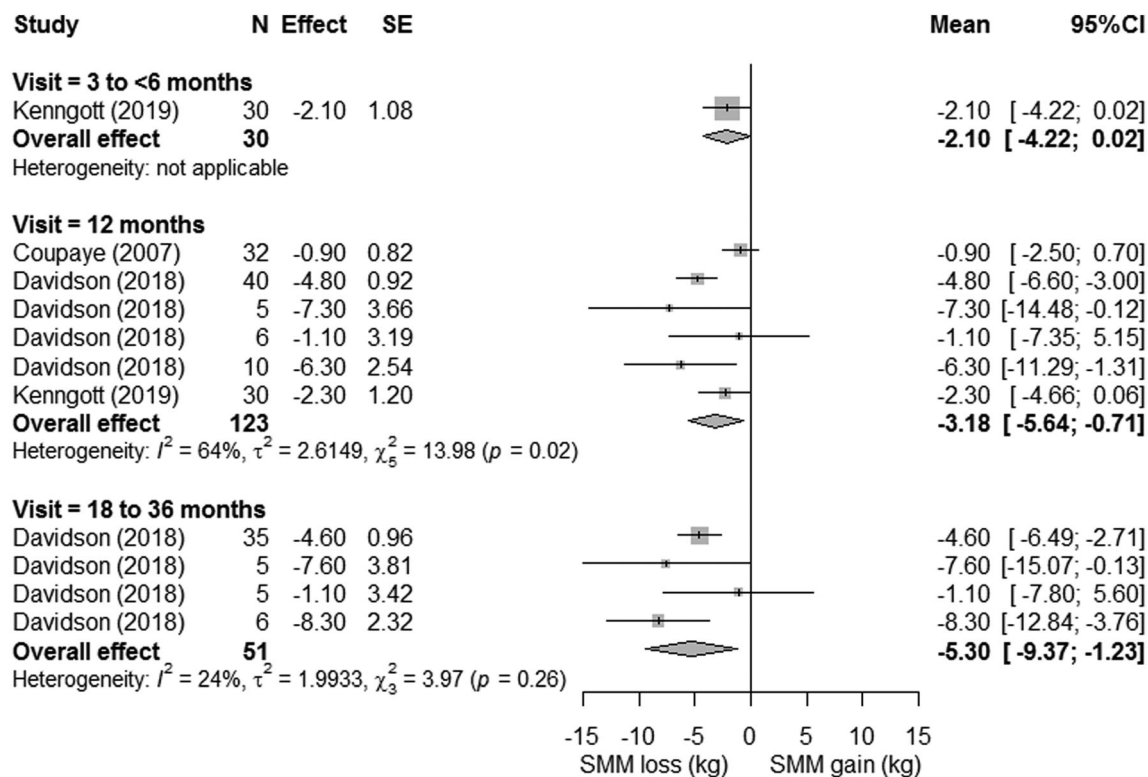


FIGURE 5 Forest plots of skeletal muscle mass loss with respect to preoperative measures. The effect size (mean difference between preoperative and postoperative measure) and 95% confidence interval for individual studies and the pooled estimate per time point are depicted. Mean follow-up time was 3 ± 0 months for 3 to 6 months, 12 ± 0 months for 12 months, and 24 ± 0 months for 18 to 36 months

for BPD (43.5 ± 9.8 kg), followed by RYGB (38.6 ± 5.2 kg), SG (33.2 ± 6.1 kg) and BAND (22.4 ± 6.1 kg). When considering LBM, FFM, and SMM loss with respect to total body weight loss, no significant differences in the proportional loss were observed across bariatric surgery types (supporting information Figure S6).

3.5 | Heterogeneity

At 12-month postsurgery, substantial heterogeneity in the amount of LBM, FFM, and SMM loss was observed across studies (supporting information Figure S7). For LBM, this resulted in a pooled effect range from -2.8 to -13.0 kg ($I^2 = 63\%$; $Q = 91.71$; $P < 0.01$). Likewise, large pooled effect ranges were found for FFM (range -0.8 to -14.5 kg; $I^2 = 77\%$; $Q = 48.32$; $P < 0.01$) and SMM (range -0.9 to -7.3 kg; $I^2 = 64\%$; $Q = 13.98$; $P = 0.02$). Furthermore, the relatively large standard errors and 95% CIs of individual studies suggest some heterogeneity in LBM, FFM, and SMM loss within studies as well.

4 | DISCUSSION

The present work is the first meta-analysis to assess the magnitude and progress of postbariatric LBM, FFM, and SMM loss and the impact of different bariatric procedures on such losses. We found a

considerable loss of LBM and FFM at 12-month postsurgery, which was predominantly lost within 3-month postsurgery and continuously decreases up to 6 months. Substantial heterogeneity was present across studies, which highlights the need for personalized care among postbariatric patients. Furthermore, these findings suggest that perioperative care programs should actively monitor changes in body composition and that interventions to limit muscle mass loss should start immediately after (or even before) surgery.

A previous review on changes in FFM during weight loss showed FFM losses of 17.5% to 31.3% of total weight loss after bariatric surgery, dependent on the procedure. However, only 16 studies were available at the time and no pooled meta-analysis, adjustments for time of follow-up, or statistical tests between procedures could be performed. Our meta-analysis demonstrated over 8-kg FFM and LBM loss within 1-year postbariatric surgery, which reflected 21% and 22% of total body weight loss, respectively. In comparison, weight loss by a 12-week low-caloric diet of 800–1000 kcal/day resulted in 1.5-kg FFM loss (16% loss/WL), whereas another 12-week isocaloric diet with 25% restriction of habitual diet resulted in 2.1-kg LBM loss (23% loss/WL).^{71,72} Although bariatric surgery induced greater amounts of FFM and LBM loss, proportional loss is quite similar to dietary interventions on the long term. This suggests a strong relation between weight loss and FFM or LBM loss, in which higher weight loss automatically results in greater FFM or LBM loss. However, higher proportional FFM losses of 30–33%loss/WL are observed within

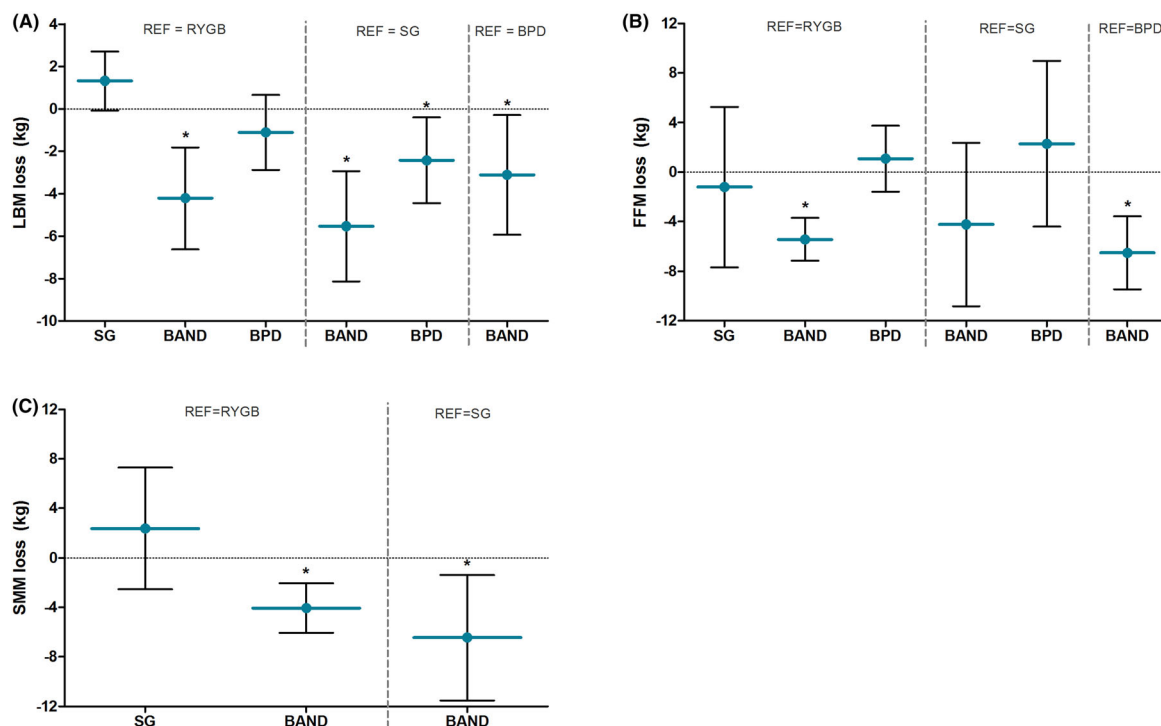


FIGURE 6 Differences in lean body mass loss (A), fat-free mass loss (B), and skeletal muscle mass loss (C) in kilograms between bariatric procedures adjusted for time-effects. Blue horizontal lines reflect the mean difference with respect to the reference group, and the error bars reflect the corresponding lower and upper limit of the 95%CI. A positive value on the y-axis reflects a greater loss compared with the reference group, whereas a negative value reflects a smaller loss than the reference group. BAND, adjustable gastric band operation; BPD, biliopancreatic diversion; RYGB, Roux-en-Y Gastric bypass; SG, sleeve gastrectomy; * $P < 0.05$ with respect to reference group

3-month postbariatric surgery, which suggests that excessive FFM loss predominantly occurs shortly after surgery.

Although benefits of weight loss may outweigh the burden of muscle mass loss in the early-postoperative phase, excessive loss of muscle tissue may particularly be detrimental on the long term, because of its role in various bodily processes, such as functional capacity, bone strength, and metabolic health. A previous meta-analysis showed a decline of -1.95 kcal in resting energy expenditure (REE) per kg FFM loss after bariatric surgery.⁷⁴ This decline in REE after bariatric surgery is greater than REE declines by dietary interventions,⁷⁵ but this difference was annulled by adjusting for changes in body composition. Still, 29% of bariatric patients showed greater declines in REE than can be explained by changes in body composition, which is indicative of adaptive thermogenesis.⁷⁵ This may be caused by altered metabolic activity of fat mass and vital organs.^{76,77} A lower REE is not necessarily problematic, since REE was found to regulate energy intake and appetite control in weight-stable subjects.⁷⁸ However, this relation between weight loss associated REE and energy intake and appetite control has not been confirmed for patients with severe obesity. Moreover, recent findings suggest that a higher proportional FFM loss during weight loss may enhance the drive to eat,¹⁰ which could still predispose weight regain and thus comprise long-term treatment outcomes. Moreover, predictive score of sarcopenia (i.e., degenerative loss of muscle strength, muscle quantity and quality, and low physical performance that occurs with aging

or immobility) based on sex-specific SMM index increased from 8% to 32% within 1-year postbariatric surgery.⁷⁹ When accompanied by muscle strength loss, this would increase the risk for frailty, functional disability, mortality, and cardiometabolic diseases.^{80,81} Co-existence of sarcopenia and obesity (i.e., sarcopenic obesity) is considered even more harmful, since the negative effects of low SMM and high fat mass may potentiate each other.⁸² For this reason, it would be valuable to include clinical outcomes, such as physical rehabilitation, muscle strength, and muscle function to determine the impact of bariatric surgery on long-term health.

The first postoperative weeks are most crucial to limit LBM and FFM loss, since $>50\%$ of the total loss occurs within 3-month post-surgery. This rapid loss shortly after surgery is probably multifactorial. First, dietary protein intake is found to decrease to approximately 30 g/day at 1 month postsurgery.^{83,84} This decrease in protein intake is likely caused by an overall restriction in dietary intake (i.e., only 500–800 kcal/day), which makes it difficult to achieve the recommended postbariatric protein intake of at least 60 g/day or 1.1 g/kg ideal body weight.⁸⁵ Second, muscle protein synthesis (MPS) functions via a dose–response relationship with protein intake, at which a dose of 20–40 g/meal leads to the most optimal response.⁸⁶ However, these larger portion sizes are not well tolerated by postbariatric patients, potentially leading to suboptimal anabolic responses. Third, the body does not store protein, despite its essential function throughout various bodily structures and processes. For this

reason, a regular and sufficient protein intake is required. However, in periods of protein deprivation (such as first postoperative weeks), unused muscle tissue is broken down to compensate for caloric restriction and to acquire amino acids for other processes.⁸⁷ Fourth, periods of muscle unloading are known to cause loss of muscle tissue, which is likely to occur as clinical guidelines discourage exercise (except walking and daily life activities) and prohibit lifting weight up to six weeks postbariatric surgery.⁸⁵ Together, these factors make postbariatric patients very susceptible for large amounts of muscle mass loss in the acute postoperative phase.

Our data present substantial heterogeneity in the magnitude of LBM, FFM, and SMM loss across studies. The subanalysis regarding bariatric procedures suggests that heterogeneity is mainly driven by type of surgery, in which adjustable gastric band procedures induced approximately 3 to 6 kg less LBM and FFM loss compared with other bariatric procedures. Nevertheless, weight loss is also lower after adjustable gastric band surgery.⁸⁸ Proportional loss was similar across procedures, which suggests that no bariatric procedure is more detrimental for LBM, FFM, or SMM than others. Furthermore, variation in magnitude of weight loss may also cause heterogeneity between and within studies. This hypothesis was confirmed by strong correlations between weight loss and LBM loss ($N = 73$, $r = 0.655$, $P < 0.001$), FFM loss ($N = 31$, $r = 0.639$, $P < 0.001$), and SMM loss ($N = 9$, $r = 0.854$, $P = 0.003$). Future studies are therefore encouraged to report proportional LBM, FFM, or SMM loss, in order to compare loss of muscle tissue between individuals. Other preoperative factors are known to affect postbariatric muscle mass loss, such as body composition, gender, ethnicity, age, thyroid function and prevalence of diabetes, and growth hormone deficiency.^{2,89-92} Postoperative factors such as protein intake and exercise levels may also contribute to the interindividual variation that was observed.⁹³ It is likely that the observed residual heterogeneity is caused by a combination of preoperative and postoperative factors. Unfortunately, we could not untangle their individual contributions due to the absence of this information in included studies and lack of stratified analyses. We therefore recommend future studies to consider these parameters in their analyses and perform stratified analyses to elucidate the exact impact of these factors on muscle mass loss. Taken together, the heterogeneity between and within studies calls for a more personalized approach in the battle against postbariatric LBM, FFM, and SMM loss.

In conjunction with the recognition of muscle mass loss as unfavorable consequence of bariatric surgery is enhancing, the research on this topic is expanding as well. Studies aiming for muscle mass preservation mainly focus on protein intake and (resistance) exercise, because of their essential role in protein synthesis. Whereas protein supplementation and exercise are often proposed as potential interventions, evidence of their effectiveness in muscle mass preservation during postbariatric weight loss is still scarce. Protein is known to increase satiety and enhance weight loss,^{94,95} but additional protein intake via supplementation or high-protein diets does not preserve LBM loss.⁹⁶ Likewise, studies incorporating (resistance) exercise training in postbariatric care show inconclusive results on muscle mass

loss.^{97,98} As both sufficient protein and exercise levels are required to optimally stimulate MPS, studies with combined approaches are warranted. Furthermore, certain other topics should be further addressed in future research. First, segmental analyses of postbariatric muscle mass should be performed to examine the impact of regional losses on health risks. Second, it should be determined how much of the FFM loss consists of preoperative excess fat mass and excess FFM.⁹⁹ Third, the magnitude of muscle tissue loss at which long-term health substantially decreases should be further addressed in order to develop evidence-based guidelines for clinical practice. Finally, there is evidence that muscle myostatin expression (i.e., a muscle growth inhibitor) is declined after bariatric surgery, suggesting that myostatin might be a natural regulator of muscle size in conditions of caloric restriction.^{100,101} It is however unknown to which extent changes in myostatin contribute to muscle mass preservation.

One limitation of this meta-analysis is that studies rarely report their exact definition of FFM or LBM and that DXA algorithms used to quantify body composition parameters were lacking. Due to interchangeable use of FFM and LBM, it could be possible that some data were stratified incorrectly. On the other hand, we were primarily interested in time-dependent within-study comparisons, so outcomes are likely less affected by this limitation. More clarity about underlying algorithms in DXA and more precise definitions of LBM and FFM could improve generalizability and harmonization of findings in future studies and meta-analyses.

5 | CONCLUSION

In conclusion, bariatric surgery induces 8 kg of LBM loss within 1-year postsurgery. The most optimal time window to intervene are the first weeks postsurgery, since 55% of LBM loss is lost within 3 months. Although adjustable gastric band procedures showed less absolute LBM, FFM, and SMM loss, proportional loss was similar compared with other procedures. Future studies should focus on identifying patients with high risk for excessive loss of muscle tissue and on optimization of protein intake (e.g., protein source, timing, and tolerance) and exercise guidelines (e.g., type, volume, intensity and tolerance) in the first postoperative months. These insights could support the development of evidence-based guidelines to limit postbariatric muscle mass loss, with feasible and effective interventions specifically for the bariatric population.

CONFLICT OF INTEREST

No conflict of interest was declared.

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SUPPORTING INFORMATION

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