



Thyroid function post-bariatric surgery: an updated systematic review and meta-analysis

Niloofer Seighali^{1,2,3} · Alireza Khodayari Javazm^{2,3} · Sina Kazemian³ · Mohammadhasan Matin⁴ · Hedi Soltani⁴ · Mahya Beikmohammadi⁴ · Amirhossein Mehrpour⁴ · Mahmood Bakhtiyari⁵

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Abstract

This systematic review and meta-analysis aim to comprehensively assess the effect of bariatric surgery on thyroid function. A search of PubMed, Web of Science, and Scopus databases was performed until 19 November 2024. Sixty-seven studies with 8,754 total patients included in our analysis showed a significant decrease in pooled standard mean differences (SMD) of serum TSH, total T3, and free T3 levels post operation (p -value < 0.05). Our analysis showed a significant marginal decrease in total T4 level by subgroup analysis in overall region and surgery (p -value < 0.05) whereas free T4 didn't change significantly (p -value > 0.05). Subgroup analyses, meta-regression, and publication bias analysis were done. Based on this meta-analysis, significant reduction of TSH, marginally total T4, Total T3, and free T3 levels, as well as non-significant change of FT4 are expected following bariatric surgery.

Key Points

- Bariatric surgery significantly reduces serum TSH, Total T3, and free T3 levels.
- Total T4 shows a marginal decrease, while free T4 remains largely unchanged.
- 67 studies with 8754 total patients included in analysis.
- Subgroup analysis, meta-regression, and publication bias analyses support the robustness of these findings.

Keywords Bariatric surgery · Thyroid function · T4 · Obesity · Meta-analysis

✉ Niloofer Seighali
niloofarseighali@gmail.com

✉ Alireza Khodayari Javazm
khodayarialireza499@gmail.com

Sina Kazemian
Dr.sinakazemian@gmail.com

Mohammadhasan Matin
m.h.matin2561@gmail.com

Hedi Soltani
Hedi77st@gmail.com

Mahya Beikmohammadi
mahya.beikmohamadi@gmail.com

Amirhossein Mehrpour
amir.mehrpourr@gmail.com

Mahmood Bakhtiyari
Mahmood.bakhtiyari@ymail.com

¹ Non-Communicable Disease Research Center, Alborz University of Medical Sciences, Karaj, Islamic Republic of Iran

² Cardiovascular Research Center, Alborz University of Medical Sciences, Karaj, Islamic Republic of Iran

³ Tehran Heart Center, Cardiovascular Disease Research Institute, Tehran University of Medical Science, Tehran, Islamic Republic of Iran

⁴ Student Research Committee, School of Medicine, Alborz University of Medical Sciences, Karaj, Islamic Republic of Iran

⁵ Department of Community Medicine, School of Community Medicine, Alborz University of Medical Sciences, Karaj, Islamic Republic of Iran

Abbreviations

TSH	thyroid stimulating hormone
T4	thyroxine
T3	triiodothyronine
SG	sleeve gastrectomy
RYGB	Roux-en-Y gastric bypass
GB	gastric banding
BPD	Bilio-pancreatic diversion

Introduction

Thyroid hormones play a major role in energy balance and they determine how much energy the body burns; therefore, changes in thyroid activity can increase the likelihood of weight gain and various metabolic disorders [1]. Body weight is associated with thyroid-stimulating hormone (TSH) and thyroid hormones such as T4 [2]. Individuals with morbid obesity have a high rate of both overt and sub-clinical hypothyroidism [3]. Obesity has become a major global health problem because its prevalence has increased and it has well-known effects on health [4]. Moreover, thyroid disorders can increase the risk of developing other serious diseases such as cardiovascular diseases [5], Type 2 diabetes mellitus [6], and cancers [7].

An effective option for reducing weight and the risk of obesity-related diseases is bariatric surgery [8]. Studies have shown that bariatric surgery can increase life expectancy compared to medical therapy, however, the mortality rate of individuals with obesity is still greater than the general population [9]. Currently, most of the weight loss surgeries around the world are sleeve gastrectomy or Roux-en-Y gastric bypass [10].

The impact of bariatric surgery on thyroid function after the operation is still not certain. Some previous studies found significant decreases in TSH and T4 levels after bariatric surgery [11], some found elevated TSH [12], while others reported no significant changes in thyroid function tests [13]. A 36-month follow-up of 117 patients with obesity who underwent laparoscopic Roux-en-Y gastric bypass in a retrospective study determined free thyroxine (FT4) and free triiodothyronine (FT3) levels decreased post-surgery while thyroid-stimulating hormone (TSH) levels remained unchanged [14]. In contrast with the mentioned study, another study published in 2017 evaluated 16 patients with obesity and euthyroid thyroid function before and after laparoscopic sleeve gastrectomy. The result showed a reduction in TSH levels, while FT4 and FT3 levels remained stable [15]. Furthermore, a previous meta-analysis conducted in 2017 including 24 studies demonstrated a significant reduction in TSH, FT3, and T3 levels. However, FT4, T4, and rT3 levels were not

significantly changed postoperatively [16]. Since more than forty studies with controversies in the effect of bariatric surgeries on thyroid function have been published after 2017, an updated meta-analysis is needed. Therefore, this meta-analysis aims to evaluate some controversial aspects of the relationship between bariatric surgery and thyroid function in patients with obesity.

Materials & Methods

This systematic review was conducted by Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [17]. our study has been registered at PROSPERO with the following registration code: (provided in the cover letter).

Search Strategy

We performed a comprehensive search in PubMed, Web of Science, and Scopus up to 19 November 2024, using the search syntax with the combination of following key terms: (“bariatric surgery”) AND (“thyroid” OR “hypothyroidism” OR “hyperthyroidism” OR “TSH” OR “triiodothyronine” OR “thyroxine”) AND (obese), alongside with their equivalent MESH terms, without no restriction in our search results (Supplementary file, Table S2).

Eligibility Criteria

Two-step screening was performed by two reviewers (A.K. and M.M.). Discrepancies were resolved by the third reviewer (N.S.). Studies met the following criteria: (1) Population: patients with obesity (BMI > 30) with any pre-operation thyroid function; (2) Assessment: any type of bariatric surgery, like: sleeve gastrectomy (LSG), Roux-en-Y gastric bypass (RYGB), gastric banding (GB), biliopancreatic diversion (BPD), etc.; (3) Comparison: not applicable; (4) Outcome: serum levels of TSH, free and total T3, free and total T4, BMI and fat mass; (5) Type of Study: all types of original studies. There was no restriction on the language and date of the published report. Case report studies, studies with fewer than 20 participants, case series, studies with a population in which patients had a BMI < 30, review studies, meta-analyses, letter-to-editor articles, and commentary studies without any relevant data were excluded. Four independent authors (A.K., M.M., H.S., M.B.) extracted data on study characteristics such as Author, year, population, total patients, country, region, design, follow-up duration, serum levels of TSH, free and total T4, free and total T3, BMI, fat mass, age, and the female ratio onto a dedicated excel

spreadsheet. Discrepancies were resolved through discussion and mutual consensus.

Quality Assessment

The quality of the included studies was evaluated by four reviewers (A.K., M.M., H.S., M.B.) independently using the modified version of the Newcastle–Ottawa Quality Assessment [18]. We deleted the item “Selection of non-exposed cohort” because it was not applicable for included cohort studies without control groups. The studies with 6 or more yeses are rated as “Good”, 4–5 as “Fair”, and with 3 or fewer as “Poor” quality reports. Any disagreements in the quality assessment were resolved through discussion with the fifth author (N.S.).

Statistical Analysis

All analyses were performed using the meta, metafor, and ggplot2 packages in R version 4.2.1 (The R Foundation, Vienna, Austria). Statistical significance was determined at a two-sided *P*-value threshold of <0.05 . We synthesized data by calculating effect sizes using standard mean differences (SMD) for all outcomes. We then used random-effects models to pool the standard mean differences (SMD).

To assess how serum levels of thyroid hormones differ post-operation in different periods, we pooled SMDs using a random-effects model across 3 distinct time intervals: “first 6 months,” “1 year,” and “over 1 year to the latest follow-up available in each study.” Additionally, subgroup analysis was done by categorizing studies based on pre-operation thyroid function. We included all types of pre-operation thyroid function and classified studies in subgroups of euthyroid, hypothyroid, and the mixed group (in which studies didn’t separate their population by the subgroup)). We didn’t have any hyperthyroidism population in the included studies; thus, this subgroup was excluded from analysis spontaneously. Subgroup analysis by surgery type (RYGB, SG, GB, BPD, Mixed), and their region (Europe, North America, South America, Asia, and Africa) were done, too. Outcomes for the subgroups are considered as the latest follow-up.

To assess heterogeneity, we utilized the Cochrane *Q*-test and *I*² statistic, considering *I*² values as high if higher than 75. Furthermore, we examined the modifying effect of factors such as baseline BMI, age, and percentage of female participants through conducting a meta-regression analysis. The results of the meta-regression were visualized using bubble plots. To evaluation of potential publication bias, we used visual inspection of symmetry in comparison-adjusted funnel plots.

Results

Characteristics of Included Studies

Based on our systematic search, we retrieved 1610 records. After removing duplicates, title, and abstract screening was done on 1488 remnant articles. Overall, 67 articles with 8754 total patients (5959 female (68.1%)) with a mean BMI of 44.53 and a mean age of 40.08 ± 8.49 years were included in our analysis (Fig. 1). The median follow-up duration of included studies was 12 months (range: 1–96 months, IQR: 6–12 months). Studies with BMI < 30 like Di et al., 2016 [19] were excluded. A population of 34 studies (50.7%) were euthyroid in pre-operation state, versus 11 studies (16.4%) were hypothyroidism, and the remnant 12 studies (17.9%) were mixed in thyroid function pre-surgery. 21 studies done Sleeve gastrectomy (SG) [20–40], 13 studies Roux-en-Y gastric bypass (RYGB) [14, 41–52], 2 studies Biliopancreatic diversion (BPD) [53, 54], 2 studies were Gastric banding (GB) [55, 56], the remnant 28 studies were in mixed types, and type of surgery of one of the studies wasn’t mentioned in the full text [57]. Region distributions of studies were in order: Asia (34 studies), Europe (21 studies), North America (6 studies), South America (3 studies), Africa (3 studies). Additional characteristic data of each included study is provided in Table 1.

The assessment of the risk of bias for included studies using the quality assessment checklist based on the Newcastle–Ottawa Scale showed there were 61 studies with good [14, 20–25, 27–31, 33–56, 58–60, 62–80, 82, 84, 85], and 6 with fair methodological quality [26, 32, 57, 61, 81, 83]. Detailed characteristics of each study and its quality assessment are provided in supplementary material (Supplementary material, Table S3).

TSH Level

Sixty-one studies were incorporated in the meta-analysis of TSH level. Pooled data by the time of assessed TSH level, showed that the serum TSH level decreased significantly after 6 to 12 months post bariatric surgery (SMD = -1.28 , 95%CI [-1.97 , -0.59], *p*-value = 0.00027 and SMD = -1.32 , 95%CI [-2.23 , -0.32], *p*-value = 0.0045, respectively) (Fig. S50 and Fig. 2. A, respectively). No significant change in serum TSH levels was observed beyond 12 months post-surgery (SMD = -0.67 , 95% CI [-1.43 , 0.08], *P*-value = 0.080) (Fig. 2. B). Based on the subgroup analysis, RYGB and SG surgery significantly decrease TSH levels compared to other types of surgeries (SMD = -0.51 , 95% CI [-0.80 , -0.22], *P*-value = 0.00056 and SMD = -2.40 , 95% CI [-4.06 ,

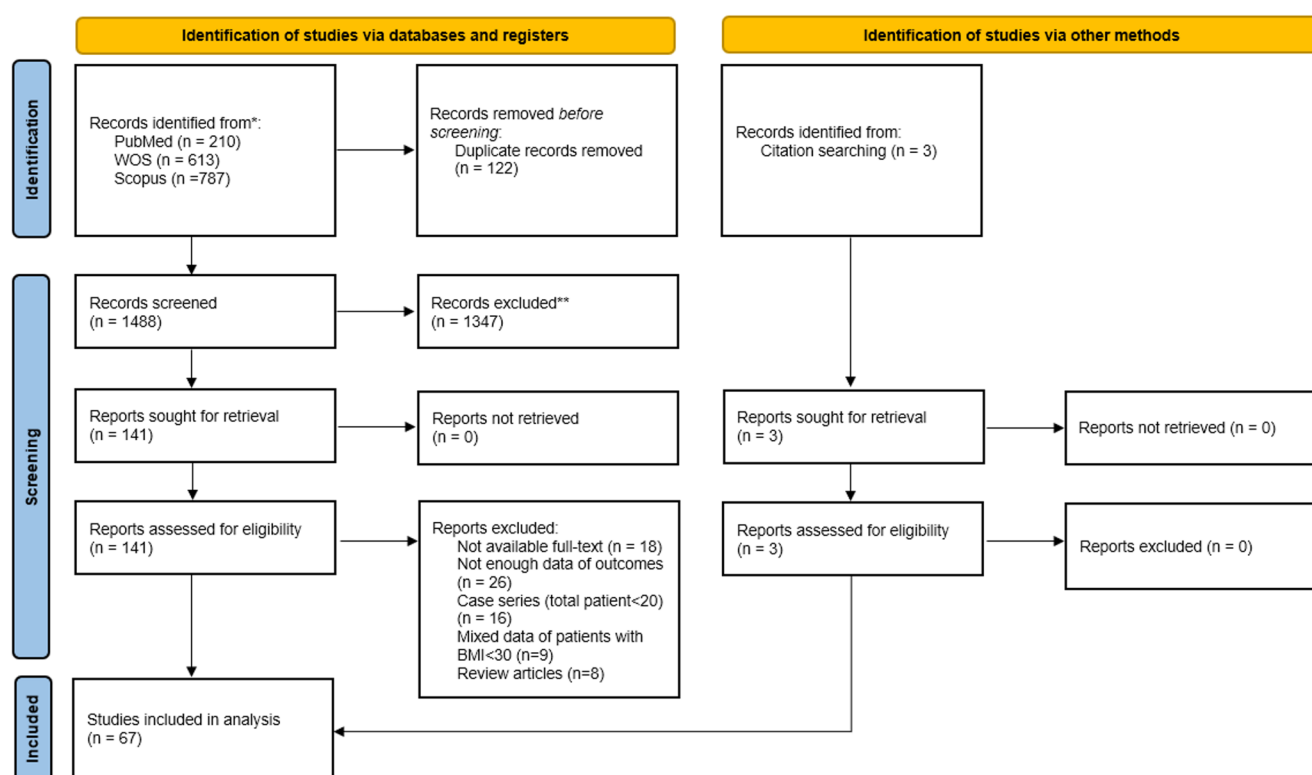


Fig. 1 PRISMA flow diagram

−0.75], P -value=0.0046) (Supplemental material. Figure S1). Other subgroup analysis based on region and pre-operation thyroid function provided in Supplemental material, Table S4.

Total T4 Level

Pooled data of ten studies incorporated in this analysis show no significant decrease of serum total T4 levels after bariatric surgery (p -value>0.05) based on follow-up and surgery types (Fig. 3 and Figure S49. A, respectively). However, the overall result by surgery and region (Figure S49.B) subgroups was statistically significant in decrease of total T4 post operation (p -value<0.05). By the way, other subgroup analysis based on region and surgery type provided in Supplemental material, Table S4.

Free T4 Level

Pooled data of forty-two included studies in this analysis showed bariatric surgery didn't have a significant effect on the serum-free T4 levels in none of the 6 months, 12 months, and over 12 months (p -value>0.1) (Fig. S50 and Fig. 4), respectively). All subgroups showed nonsignificant results (p -value>0.05) (Supplemental material. Table S4).

Total T3 Analysis

Eleven studies were incorporated in the analysis of total T3 levels demonstrating a significant decrease in serum-free T3 levels in 6-month and 1-year follow-ups (SMD=−0.66, 95% CI [−1.02, −0.30], p -value<0.001, and SMD=−1.09, 95% CI [−1.91, −0.28], p -value<0.01, respectively) (Fig. 5). Subgroup analysis by the type of surgery showed RYGB significantly decreased the serum level of total T3 significantly with low heterogeneity in studies (I^2 =13.7%, SMD=−0.93, 95%CI [−1.15, −0.71], p -value<0.0001) (Supplemental material. Figure S7). Results of other subgroup analysis is provided in Supplemental material.

Free T3 Level

Twenty-four studies were incorporated in the meta-analysis of the free T3 level. Analysis showed a significant decrease in post-surgery free T3 after 6 months and 12 months against the levels beyond 12 months (p -value>0.01 vs. p -value>0.05) (Fig. 6). Also, most of the subgroups such as BPD, RYGB, Europe, Asia, and euthyroid subgroups showed a significant decrease in free T3 after surgery (p -value<0.01) (Supplemental material. Figure S10–12).

Table 1 Characteristics of included studies

Study ID	Country	Region	Design	Total Number	Follow-up Duration (month)	Age (mean±SD)	Female(%)	Mean Baseline BMI	Pre-operation Thyroid Function	Surgery Type
Alagna, et al., 2003 [53]	Italy	Europe	Prospective	38	12	N/A	68.42	47.02	Euthyroid	Bilio-Pancreatic Diversion
Dittmar, et al., 2003 [56]	Germany	Europe	Prospective	26	17	39±9.38	69.23	48.1	Euthyroid	Gastric Banding
Moulin, et al., 2005 [49]	Brazil	South America	Prospective	72	12	39.6±9.8	86.11	53	Mixed	Roux-en-Y Gastric Bypass
Chikunguwo, et al., 2007 [28]	USA	North America	Retrospective	86	12	N/A	79.06	49	Euthyroid	Sleeve Gastrectomy
Komer, et al., 2009 [58]	USA	North America	Prospective	43	13	46±2.3	81.39	45.56	Euthyroid	Mixed
Nannipieri, et al., 2009 [50]	Italy	Europe	Prospective	27	12	45.68±5.49	77.77	45	N/A	Roux-en-Y Gastric Bypass
Vila, et al., 2009 [51]	Austria	Europe	Prospective	28	14	N/A	57.14	48.2	Euthyroid	Roux-en-Y Gastric Bypass
Dall'Asta, et al., 2010 [55]	USA	North America	Retrospective	258	24	41.1±0.66	83.72	44.1	Euthyroid	Gastric Banding
Gniuli, et al., 2010 [54]	Italy	Europe	Retrospective	45	24	43±10	66.66	50.28	Mixed	Bilio-Pancreatic Diversion
Janković, et al., 2012 [59]	Austria	Europe	Retrospective	433	12	41±12	75.98	47	Mixed	Mixed
MacCuish, et al., 2012 [48]	UK	Europe	Retrospective	55	24	46.5±1.38	76.36	48.08	Euthyroid	Roux-en-Y Gastric Bypass
Gkotsina, et al., 2013 [31]	Greece	Europe	Retrospective	32	1	33.36±6.4	N/A	42.12	N/A	Sleeve Gastrectomy
Lips, et al., 2013 [46]	Netherlands	Europe	Retrospective	31	3	49.4±0.6	100	43.9	Euthyroid	Roux-en-Y Gastric Bypass
Abu-Ghanem, et al., 2014 [40]	Israel	Asia	Prospective	38	12	39.7±1.97	73.68	42.4	Euthyroid	Sleeve Gastrectomy
Hasani, et al., 2015 [57]	Iran	Asia	Prospective	21	3	34±8	90.47619048	41.45	Euthyroid	N/A
Janssen, et al., 2015 [44]	Netherlands	Europe	Retrospective	503	12	43±12	N/A	N/A	Mixed	Roux-en-Y Gastric Bypass
Vaurs, et al., 2015 [60]	France	Europe	Prospective	114	12	39.6±11.7	81.57	43.3	Euthyroid	Mixed
Fierabracci, et al., 2016 [61]	Italy	Europe	Retrospective	93	28	48±9	96.77	45.9	Hypothyroidism	Mixed
Bawahab, et al., 2017 [24]	Saudi Arabia	Asia	Prospective	50	12	N/A	80	42	N/A	Sleeve Gastrectomy
Ferrannini, et al., 2017 [41]	Italy	Europe	Prospective	25	12	43±8	72	N/A	Euthyroid	Roux-en-Y Gastric Bypass
Liu, et al., 2017 [47]	China	Asia	Retrospective	81	6	47.78±11.44	58.02	30.82	Euthyroid	Roux-en-Y Gastric Bypass
Zendel, et al., 2017 [62]	Israel	Asia	Retrospective	93	12	46.6±11.2	91.39	43.7	Hypothyroidism	Mixed
Zhang, et al., 2017 [14]	China	Asia	Retrospective	117	36	47.3±11.8	52.99	31.1	Euthyroid	Roux-en-Y Gastric Bypass
Matute, et al., 2018 [63]	USA	North America	Retrospective	35	12	47.7±12.45	82.85	N/A	N/A	Mixed

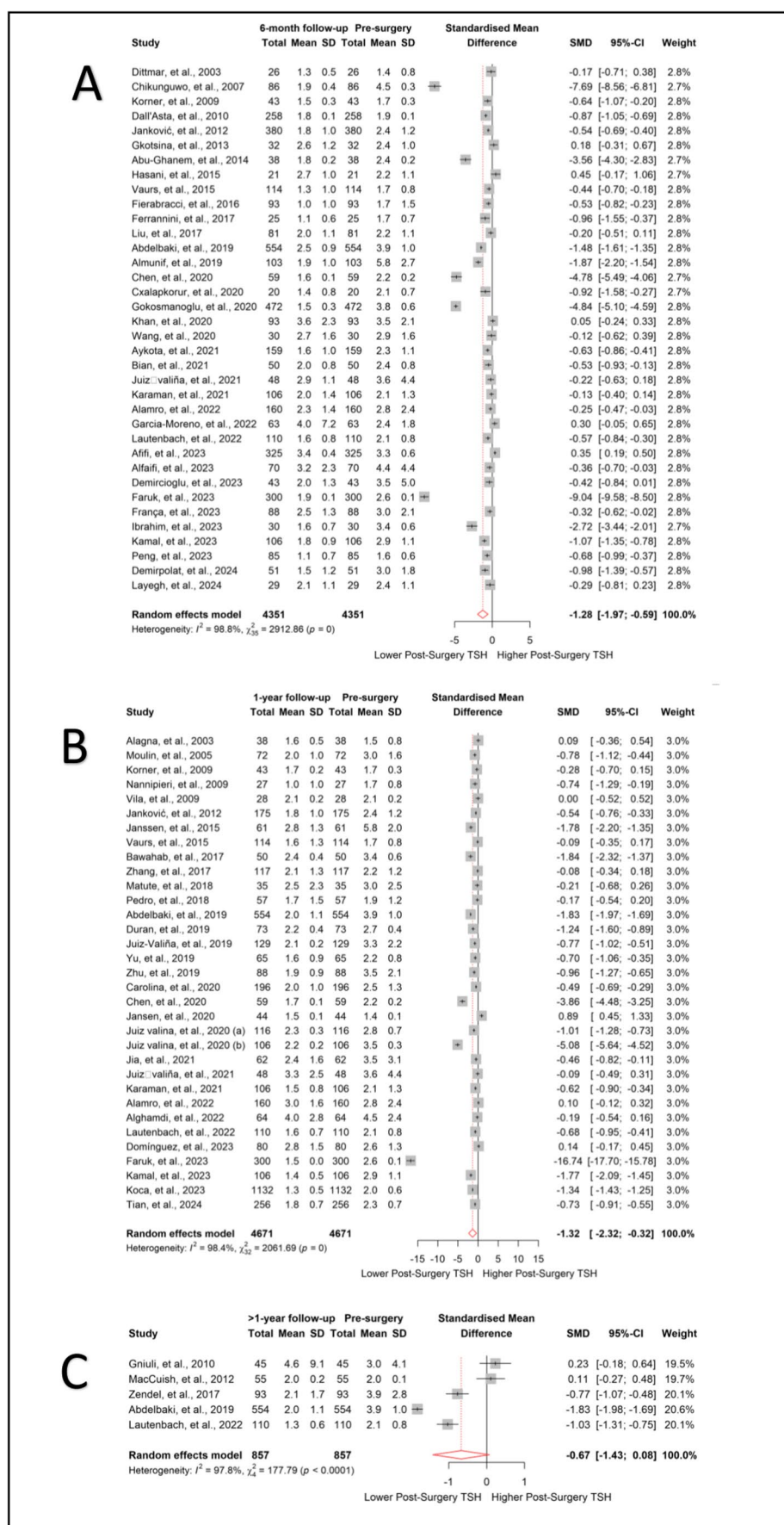
Table 1 (continued)

Study ID	Country	Region	Design	Total Number	Follow-up Duration (month)	Age (mean±SD)	Female(%)	Mean Baseline BMI	Pre-operation Thyroid Function	Surgery Type
Pedro, et al., 2018 [64]	Portugal	Europe	Retrospective	57	12	47±10	92.98	44.2	Hypothyroidism	Mixed
Rudnicki, et al., 2018 [65]	Israel	Asia	Retrospective	90	11	44.9±12.35	80	43.8	Hypothyroidism	Mixed
Abdelbaki, et al., 2019 [20]	Egypt	Africa	Prospective	554	18	41±12	77.61	45	Mixed	Sleeve Gastrectomy
Almunif, et al., 2019 [22]	Saudi Arabia	Asia	Retrospective	103	86	N/A	74.75	46.49	Hypothyroidism	Sleeve Gastrectomy
Duran, et al., 2019 [66]	Turkey	Asia	Prospective	73	12	41.5±9.6	80.82	47.9	N/A	Mixed
Juiz-Valiña, et al., 2019 [67]	Spain	Europe	Retrospective	129	12	46.6±0.8	71.31	49.3	Euthyroid	Mixed
Xia, et al., 2019 [68]	China	Asia	Prospective	101	6	33.4±11.8	56.43	42.1	Euthyroid	Mixed
Yu, et al., 2019 [52]	China	Asia	Retrospective	65	12	39.9±10.3	52.30	32.5	Euthyroid	Roux-en-Y Gastric Bypass
Zhu, et al., 2019 [39]	China	Asia	Retrospective	88	12	30.7±9.55	56.81	40.08	Mixed	Sleeve Gastrectomy
Carolina, et al., 2020 [43]	Brazil	South America	Retrospective	215	24	36.2±9.7	75.81	40.2	Mixed	Roux-en-Y Gastric Bypass
Chen, et al., 2020 [27]	China	Asia	Prospective	59	12	30.7±1.3	38.98	40.2	Euthyroid	Sleeve Gastrectomy
Cxalapkorur, et al., 2020 [26]	Turkey	Asia	Prospective	20	3	40.15±7	100	46.95	N/A	Sleeve Gastrectomy
Gokosmanoglu, et al., 2020 [69]	Turkey	Asia	Prospective	472	6	41	63.98	52.5	Euthyroid	Mixed
Jansen, et al., 2020 [70]	Norway	Europe	Prospective	44	12	N/A	54.54	N/A	Euthyroid	Mixed
Juiz valina, et al., 2020 (a) [71]	Spain	Europe	Prospective	116	12	45.2	83.62	47.86	Euthyroid	Mixed
Juiz valina, et al., 2020 (b) [72]	Spain	Europe	Retrospective	106	12	47.5±0.9	78.30	49.8	Euthyroid	Mixed
Khan, et al., 2020 [73]	India	Asia	Retrospective	93	29.8	42.2±10.4	87.09	47.8	Hypothyroidism	Mixed
Wang, et al., 2020 [38]	China	Asia	Prospective	30	6	33.16±11.03	43.33	38.97	Euthyroid	Sleeve Gastrectomy
Aykota, et al., 2021 [23]	Turkey	Asia	Retrospective	159	6	34.18±10.01	78.61	43.2	Euthyroid	Sleeve Gastrectomy
Bian, et al., 2021 [74]	China	Asia	Retrospective	50	6	27.6±6.2	64	40.7	Euthyroid	Mixed
Jia, et al., 2021 [33]	China	Asia	Retrospective	62	36	32.38±10.11	58.06	39.75	Mixed	Sleeve Gastrectomy
Juiz-Valiña, et al., 2021 [75]	Spain	Europe	Retrospective	48	12	46.17±10.11	93.75	46.89	Hypothyroidism	Mixed
Karaman, et al., 2021 [35]	Turkey	Asia	Prospective	106	12	36.44±11.31	81.13	46.9	Euthyroid	Sleeve Gastrectomy
Najjari, et al., 2021 [76]	Iran	Asia	Retrospective	281	6	43.78±10.49	13.16	43.45	Hypothyroidism	Mixed
Alamro, et al., 2022 [77]	Saudi Arabia	Asia	Retrospective	160	12	41.9±10.6	59.37	48.8	Mixed	Mixed
Alghamdi, et al., 2022 [21]	Saudi Arabia	Asia	Retrospective	64	12	11.2±2.3	53.12	44.94	N/A	Sleeve Gastrectomy
Garcia-Moreno, et al., 2022 [78]	Spain	Europe	Retrospective	63	24	48.78±10.8	92.06	44.63	Hypothyroidism	Mixed
Lautenbach, et al., 2022 [79]	Germany	Europe	Retrospective	135	96	42.1±10.6	68.88	50.8	Euthyroid	Mixed
Ma, et al., 2022 [36]	China	Asia	Prospective	244	12	31.2±10	79.50	41.74	Mixed	Sleeve Gastrectomy
Affifi, et al., 2023 [80]	Egypt	Africa	Retrospective	325	6	47±4.49	70.15	40.59	Mixed	Mixed
Alfaifi, et al., 2023 [81]	Saudi Arabia	Asia	Retrospective	70	N/A	N/A	84.28	N/A	Hypothyroidism	Mixed

Table 1 (continued)

Study ID	Country	Region	Design	Total Number	Follow-up Duration (month)	Age (mean±SD)	Female(%)	Mean Baseline BMI	Pre-operation Thyroid Function	Surgery Type
Demircioglu, et al., 2023 [29]	Turkey	Asia	Prospective	43	6	36.97±11.21	74.41	43.93	Mixed	Sleeve Gastrectomy
Domínguez, et al., 2023 [82]	USA	North America	Retrospective	80	12	42.8±12.9	67.5	39.4	Euthyroid	Mixed
Faruk, et al., 2023 [25]	Turkey	Asia	Retrospective	300	12	34.92±10.57	79.66	45.72	Euthyroid	Sleeve Gastrectomy
França, et al., 2023 [42]	Brazil	South America	Prospective	88	12	40.53	61.36	43.95	Euthyroid	Roux-en-Y gastric bypass (RYGB)
Ibrahim, et al., 2023 [32]	Iraq	Asia	Prospective	30	3	N/A	N/A	51.32	N/A	Sleeve Gastrectomy
Kamal, et al., 2023 [34]	Egypt	Africa	Prospective	106	12	42±6.1	88.67	50.85	N/A	Sleeve Gastrectomy
Koca, et al., 2023 [37]	Turkey	Asia	Retrospective	1137	12	39	82.93	45.91	N/A	Sleeve Gastrectomy
Peng, et al., 2023 [83]	USA	North America	Prospective	85	3	40.4±11.2	85.88	44	Euthyroid	Mixed
Demirpolat, et al., 2024 [30]	Turkey	Asia	Retrospective	51	6	41	90.19	45.1	Hypothyroidism	Sleeve Gastrectomy
Layegh, et al., 2024 [45]	Iran	Asia	Retrospective	29	3	38.52±8.57	62.06	45.93	Euthyroid	Roux-en-Y Gastric Bypass
Tian, et al., 2024 [84]	China	Asia	Prospective	256	12	35	53.12	38.37	Euthyroid	Mixed
Wang, et al., 2024 [85]	China	Asia	Prospective	23	6	28.71±10.35	56.52	46.15	Euthyroid	Mixed

Fig. 2 Serum TSH levels after bariatric surgery (A) 1-year follow-up and, (B) over 1-year follow-up



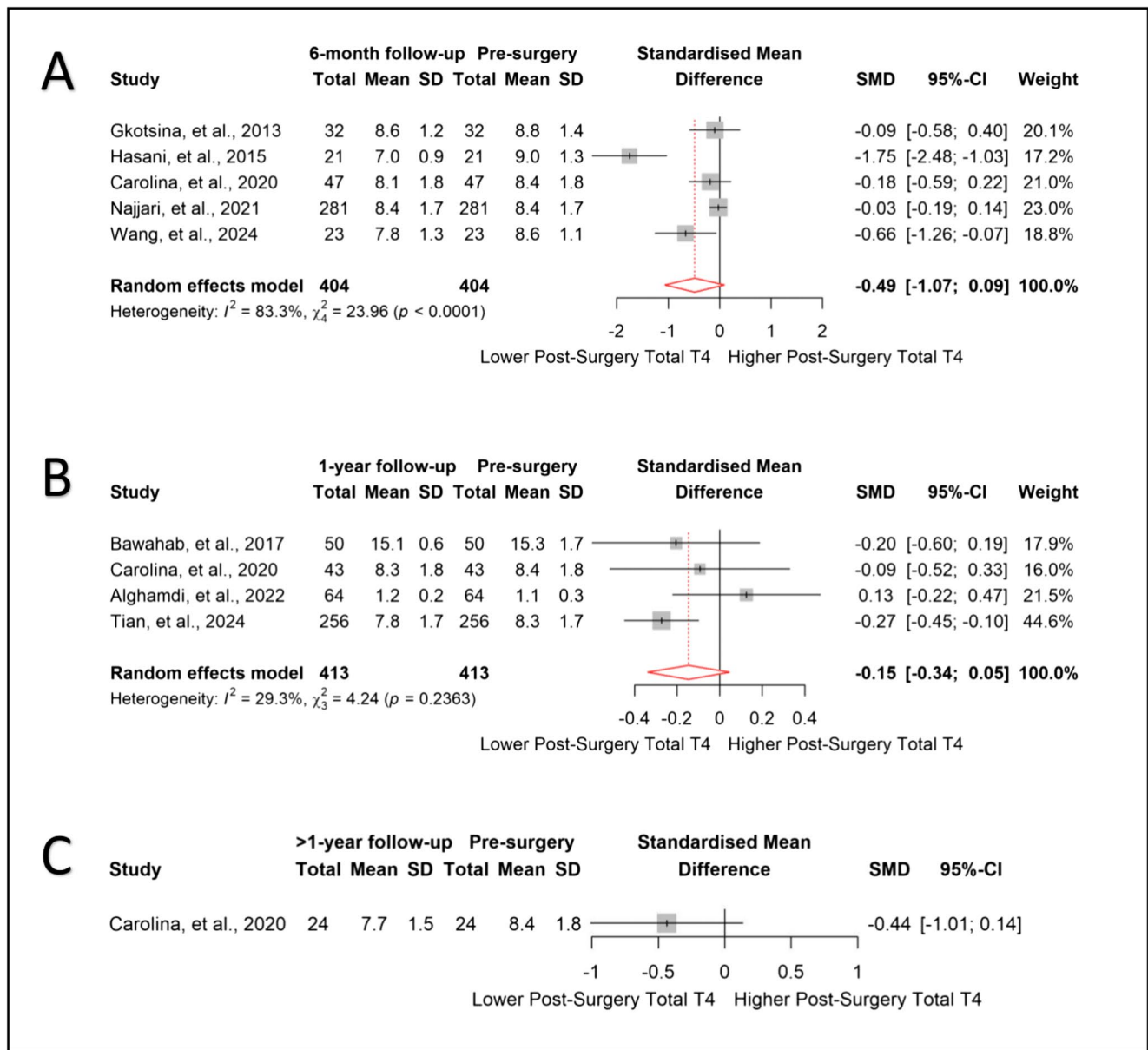


Fig. 3 Serum total T4 levels after bariatric surgery (A) 6-month follow-up, (B) 1-year follow-up and, (C) over 1-year follow-up

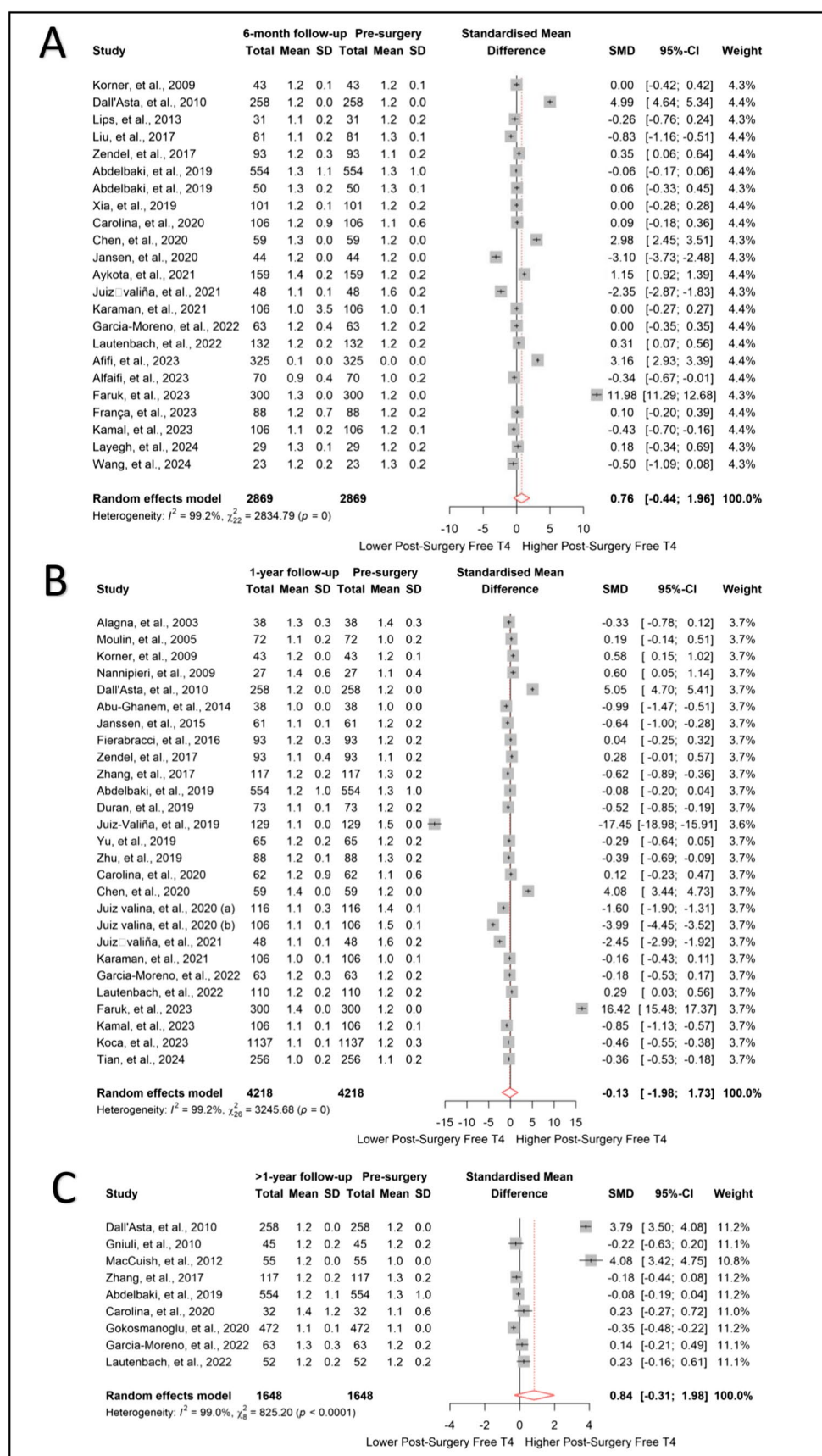
Fat-Mass Analysis

Analysis including 11 studies, showed a significant decrease in fat mass post-surgery (SMD=-3.6, 95%CI [-6.36, -0.84], p -value=0.00739) (Supplemental material. Figure S13). Subgroup analysis showed a significant decrease in heterogeneity by the BPD surgery ($I^2=36.3\%$) and Asia region ($I^2=0\%$) compared to the other groups (Supplemental material. Figure S14-16).

BMI Analysis

Fifty-two studies included in the analysis of BMI demonstrated that the BMI of patients with obesity decreased significantly after bariatric surgery (SMD=-4.08, 95%CI [-5.29, -2.88], p -value ≈ 0) (Supplemental material. Figure S17). All the subgroups showed a significant decrease in BMI (p -value <0.05) except GB (p -value=0.249) (Supplemental material. Figure S18-20).

Fig. 4 Serum free T4 levels after bariatric surgery (A) 1-year follow-up, and (B) over 1-year follow-up



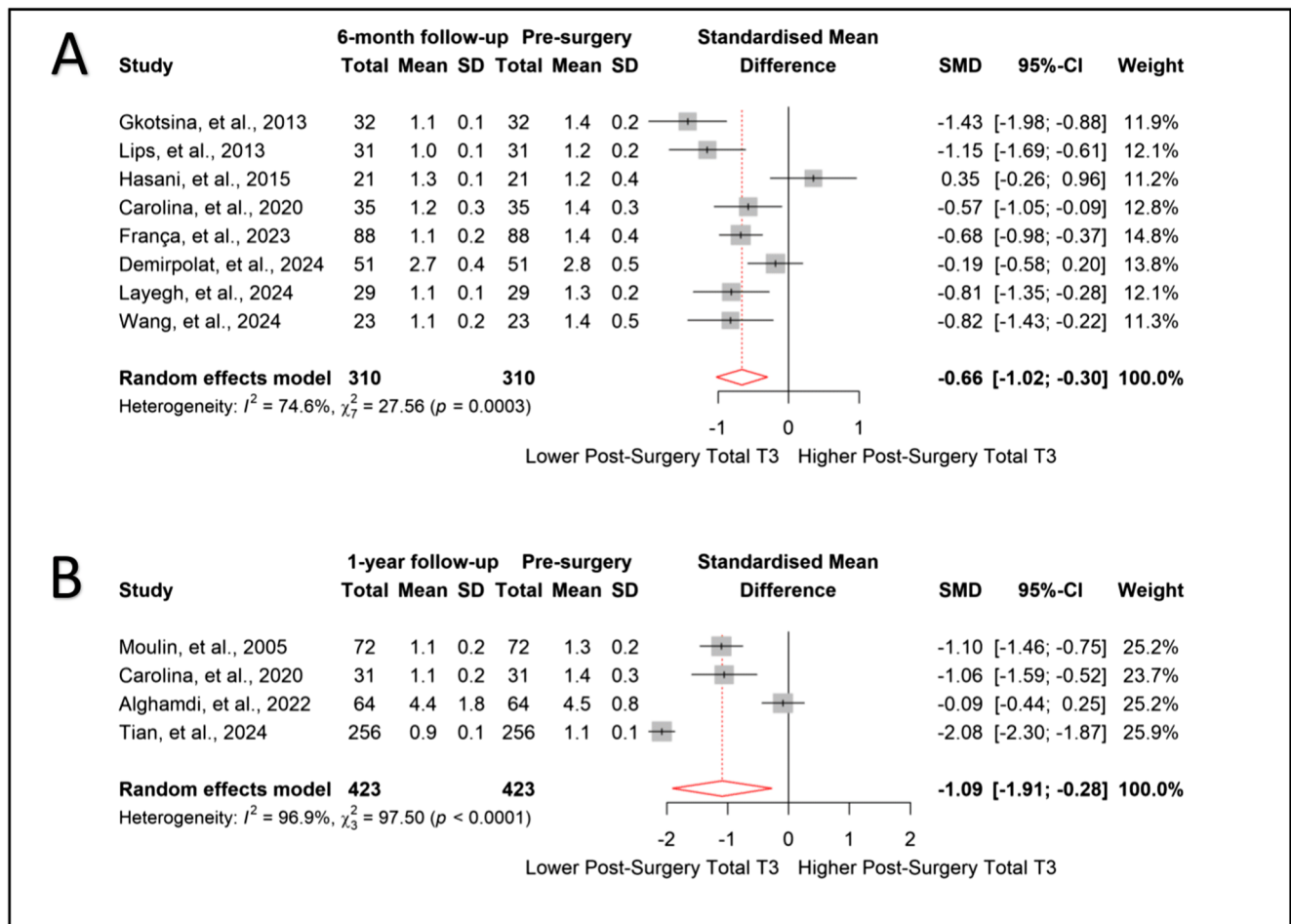


Fig. 5 Serum total T3 levels after bariatric surgery (A) 6-month follow-up, and (B) 1-year follow-up

Meta-Regression

Meta-regression analysis showed significant modifying effects of mean age on TSH and free T4, baseline BMI on TSH, and inverse correlation of female ratio with total T4 levels (Supplemental material Figure S21, S27, S22, and S26, respectively). The analysis demonstrated that younger individuals may experience higher TSH decrease post-operation, and conversely (p -value=0.01, $I^2=98.49\%$, B-cox=0.07). Also, patients with higher baseline BMI over 30 may show a larger decrease in TSH changes post-bariatric surgery (p -value=0.003, $I^2=98.39\%$, b-cox= -0.09). It should be noted that as the regression line crossed the SMD line (=0) around the BMI of 31, in patients with lower BMI, TSH may be increased but as we included the patients with BMI>30 other studies are needed to assess this hypothesis. Furthermore, a higher female ratio may result in lower serum total T4 level (higher decrease) (p -value=0.046). Also, our analysis shows that as the age increases till the point around 42 years, the free t4 level shows a lower increase; but over

the age of 42 years, patients may experience more decrease in free T4 levels (p -value<0.0001) (Supplemental material Figure S27). Moreover, analysis revealed that as the age increases after the point around 34 years, fat mass decreases larger (p -value=0.016) (Supplemental material Figure S39, Table S5).

Overall Publication Bias

Upon reviewing the funnel plots no significant publication bias was found across outcomes, except for BMI and free T3 (Supplemental material Figure S48 and S45, respectively). For these outcomes, funnel plots showed visible asymmetries (Egger's test p -value=0.022 and 0.0003, respectively) with the concentration on left-sided negative SMDs. This indicates potential publication bias with the presence of a small study effect. Notably, publication bias for fat mass was found statistically non-significant but it is marginal and considered probable publication bias (Egger test p -value=0.056).

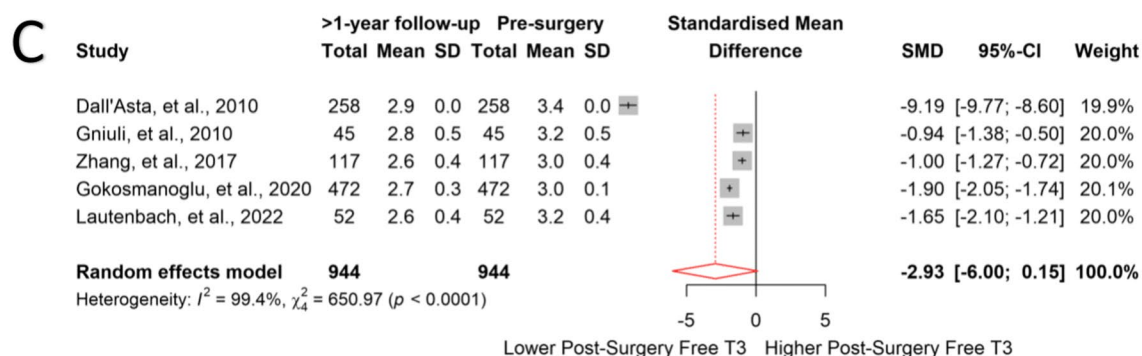
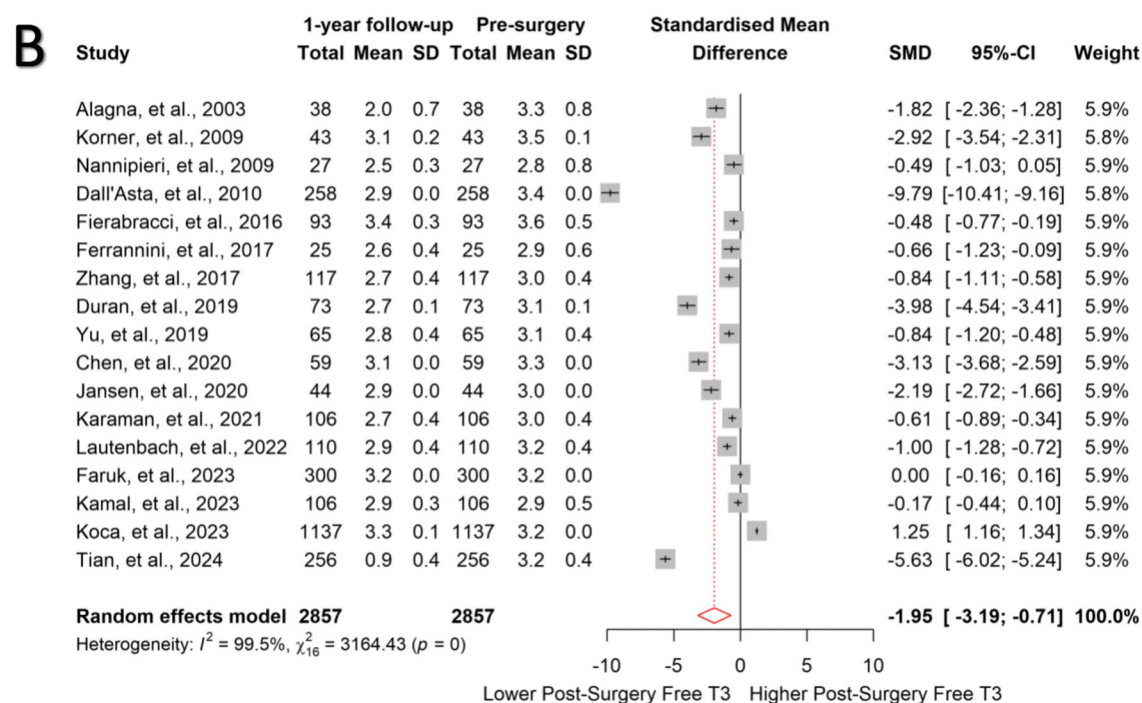
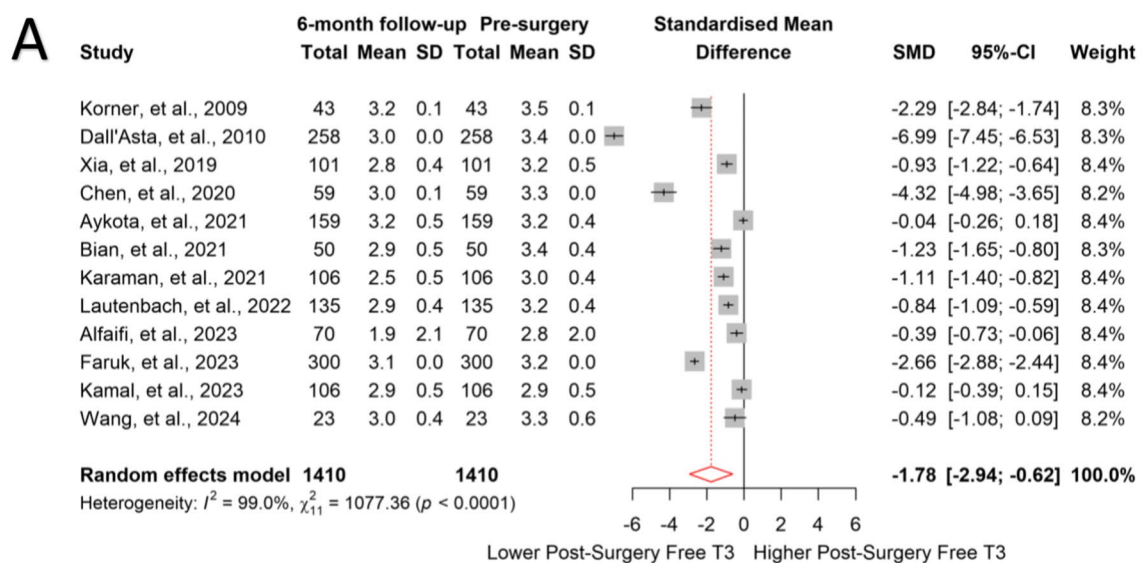


Fig. 6 Serum free T3 levels after bariatric surgery (A) 6-month follow-up, (B) 1-year follow-up, and, (C) over 1-year follow-up

Discussion

The impact of bariatric surgery on weight loss and obesity-related diseases such as metabolic syndrome has recently garnered significant attention. The effect of obesity on thyroid hormones, as an important determinant in metabolism, indicates the elevation of TSH and T3 concentrations [86, 87]. The responsible mechanism consists of [1] peripheral thyroid hormone resistance due to the downregulation of thyroid hormone receptors, and [2] activation of the hypothalamus-pituitary-thyroid (HPT) axis due to elevation of the leptin [50, 88, 89]. Several studies have evaluated the changes in thyroid hormone profile following bariatric surgery. The current meta-analysis has been conducted to evaluate the association between bariatric surgery and thyroid function tests. We investigated a significant decrease in TSH, T3, and FT3 concentrations, whereas FT4 and T4 levels didn't demonstrate significant alternation after bariatric surgery.

Weight loss caused by modifying lifestyle can also decrease TSH levels [90]. Our study demonstrated reduced serum TSH levels, especially after 6 to 12 months post-bariatric surgery. The majority of the studies revealed similar results. A study by Dall'Asta et al. reported no alternation in post-operative TSH level [55] and a study by MacCuish et al. reported steady TSH after surgery [48]. The decrease in TSH levels mostly occurred in Asian, patients undergoing SG surgery, and euthyroid individuals. The variations between studies may arise from different surgical type, characteristics, ethical, and genetically features of case and control groups, and power of the study. TSH exhibits seasonal and circadian variations, which should be considered when interpreting results [91–94].

Although an association between bariatric surgery and alternations in thyroid function has been reported in this study, the main causes and responsible mechanisms remain unclear. A significant decrease in leptin levels due to a reduction in adipose tissue, suppresses the HPT axis and peripheral T4 to T3 conversion, leading to reduced TSH and thyroid hormone levels. As adipose tissue acts as an endocrine organ, its reduction alters circulating adipokines, particularly leptin that is known to stimulate hypothalamic TRH secretion. The postoperative fall in leptin may therefore lead to lower TSH output, consistent with the reductions observed in this analysis [95–97]. Associated weight loss also reverses obesity-induced downregulation of TSH receptor expression, which decreases peripheral thyroid hormone resistance [50]. Additionally, increased growth hormone levels post-surgery regulate the HPT axis, leading to lowered TSH levels [39, 98]. The obesity-related systemic inflammation reduces after

weight loss which makes the TSH concentration decrease and improves thyroid hormone function and sensitivity [39]. Furthermore, bariatric surgery suppresses B and T lymphocyte activation, reducing thyroid autoimmune antibodies and inflammatory cytokines, which may inhibit the destruction of the thyroid gland and excessive hormone release [68]. Modifying the glycemic and lipid profiles caused by bariatric surgery has also been effective in thyroid hormone levels [27, 99, 100]. A recent study has reported a positive correlation between serum ghrelin levels and TSH levels which demonstrated that the reduction in ghrelin due to RYGB and SG surgery types may contribute to the decrease in TSH levels [101]. Moreover, alterations in nutrient absorption and hepatic metabolism could influence peripheral thyroid hormone conversion. The reduction in FT3 may indicate diminished type 1 and type 2 deiodinase activity, limiting T4-to-T3 conversion and reflecting a new energy-conserving state during rapid metabolic adaptation [102].

A recent systematic review and meta-analysis including 24 studies concluded that bariatric surgery in patients with obesity causes a decrease in serum TSH, FT3, and T3 levels, whereas T4, FT4, and rT3 levels did not change post-operative [16]. Some also report reduced levothyroxine requirements after surgery in hypothyroid individuals. However, the mentioned study has limitations, we included 67 studies with the total population of 8,754 patients to update and overcome the limitations as it was possible.

Our findings emphasize the importance of considering and monitoring the postoperative hormonal changes, as these alternations necessitate levothyroxine dose adjustments due to malabsorption after bariatrics surgery and further reductions in BMI and lean body mass which is the primary determinant. Clinically, results suggest that postoperative reductions in thyroid hormone levels might represent a physiological adjustment rather than true hypothyroidism. The concurrent improvement in thyroid function among patients with preexisting subclinical or overt hypothyroidism supports the hypothesis that excess adiposity exerts a reversible strain on the HPT axis.

Our research is updated and provides an extensive search of databases to gather a comprehensive collection of studies on this topic. This study had limitations that need to be considered in the analysis of future studies to achieve more accurate results. Thyroid-associated antibodies such as TPOAb and TgAb, were not analyzed and evaluated in this study due to lack of enough data. Some of the subgroups are imbalanced in the region of the included studies, and a small number of individuals undergoing BPD and GB compared with other types of surgery. Heterogeneity among studies from differences in surgical techniques, follow-up duration, and baseline thyroid status limits the generalizability of the pooled estimates.

Conclusion

In conclusion, bariatric surgery has an important impact on thyroid hormone levels and reduces TSH, total T3, free T3, and marginally total T4 serum levels. This effect is attributed to the age, sex, region, surgery type, baseline BMI, and pre-operative thyroid function, emphasizing the importance of monitoring patients' post-operation for changes in thyroid hormones and the management of thyroid function, especially in patients with previous hypothyroidism and using levothyroxine. The included studies had heterogeneity in their design, follow-up times, and patient profiles, such as pre-operation thyroid function, which may have contributed to some variability in the results. In addition, we were unable to evaluate thyroid antibodies, which could have provided more insight into autoimmune factors. Future well-designed studies with longer follow-up and antibody measurements are needed to better understand how bariatric surgery affects thyroid function over time.

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Declarations

Ethics Approval and Consent to Participate Not applicable.

Consent for Publication Not applicable.

Competing interests The authors declare no competing interests.

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