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REVIEW ARTICLE

Effect of Bariatric Surgery on Serum Inflammatory Factors of Obese Patients: a Systematic Review and Meta-Analysis

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Abstract

Obesity is one of the main causes of inflammation. Previous studies have reported inconclusive results regarding the effect of bariatric surgery on inflammatory markers. This systematic review and meta-analysis is aimed at describing the effect of bariatric surgery on C-reactive protein (CRP), interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α). PubMed/Medline and Scopus were systematically searched for all eligible studies from inception to June 2018. Results are expressed as weighted mean difference (MD) with 95% confidence intervals (CI) using a random effects model. Overall, 116 studies which evaluated serum CRP, IL-6, and TNF-α after bariatric surgery were included. Pooled effect size showed significant reduction in serum CRP (− 5.30 mg/l, 95% CI − 5.46, − 5.15, $P < 0.001$), IL-6 (− 0.58 pg/ml, 95% CI − 0.64, − 0.53, $P < 0.001$), and TNF-α (− 0.20 pg/ml, 95% CI − 0.39, − 0.02, $P = 0.031$) with significant heterogeneity across studies (> 95% for all factors). Bariatric surgery significantly lowered inflammatory factors; however, baseline BMI, follow-up duration and type of surgery could impact the extent of observed effects.

Keywords Bariatric surgery · C-reactive protein · Interleukin 6 · Tumor necrosis factor-α · Meta-analysis

Introduction

Nowadays, it is not obscure to anyone that obesity has become a major problem in both developed and developing countries [1]. Not only it could lead to major chronic diseases like cancer and CVD [2] but also it has a negative effect on individuals' self-esteem which could lead to severe depression [3]. The detrimental effect of obesity on mental and physical performance lead to make people, even slightly overweight ones, to consider losing weight. Since the traditional recommendations such as following a strict diet or a hardcore exercise program have failed to be completely effective [4], people have been looking for a new easier way to get rid of all the fat mass.

Bariatric surgery is one of the new methods that has recently come to spotlight since it has been proven successful in losing weight [5]. Moreover, long-term studies proved it useful for curing a variety of diseases such as diabetes and CVD [6]. However, it cannot be expected to be without adverse effects as it is a completely aggressive surgery. Metabolic bone disease, development of gallstones, hyperoxaluria and deficiency of iron, vitamin B12, fat-soluble vitamins, thiamine, and folate are a number of common complaints that have been seen in the patients who went under this procedure [7–11].

Inflammation is a normal process in which the body responses to everyday diseases and injuries [12]. Therefore, it is considered an essential tool for the body to mend a destructed tissue and to recover after a disease. However, chronic inflammation suits the body for the potential diseases such as hay fever, atherosclerosis, rheumatoid arthritis, diabetes, and even cancer [13–18]. Recent studies have suggested a

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link between obesity and inflammation, as increased mass of adipose tissue may activate the immune process in white adipose tissue (WAT) and liver and immune cells [19]. WAT is the source of some pro-inflammatory cytokines such as tumor necrosis factor alpha (TNF-α) and interleukin-6 (IL-6), which both could be regarded as indicators of inflammation [20]. Interleukin 6 can also regulate C-reactive protein secretion which is an acute phase protein, and its serum level increases during inflammation; thus, it can also be a good marker of inflammation [21]. These three markers are considered the most important pro-inflammatory cytokines.

Previous studies exploring the impact of bariatric surgery on serum levels of IL-6, TNF-α, and CRP, as the most important biomarkers for inflammation, have reported inconclusive results. The controversy among the literatures might be due to differences in the obesity surgery, baseline weight, or follow-up period. Accordingly, the present systematic review and meta-analysis was performed to resolve these inconsistencies and to report pooled analysis for the effect of bariatric surgery on serum levels of IL-6, TNF-α, and CRP based on bassline body mass index, surgery type, and follow-up duration.

Methods

To perform this meta-analysis, the Preferred Reporting Items of Systematic Reviews and Meta-Analyses (PRISMA) statement guideline was used [22].

Search Strategy

A throughout search was conducted in PubMed/Medline and Scopus from inception to June 2018. The MeSH and non-MeSH terms were as follows: "bariatric surgery", "Roux-en-gastric bypass", "RYGB", "Laparoscopic Roux-en-gastric bypass", "LRYGB", "gastric bypass", "GB", "sleeve gastrectomy", "SG", "laparoscopic sleeve gastrectomy", "Billopancreatic Diversion", "BPD", "adjustable gastric banding", "AGB" "vertical banded gastroplasty", "VBG" AND "CRP", "C-Reactive Protein", "High Sensitive C-Reactive Protein", "hs-CRP", "Tumor Necrosis Factor-alpha", "TNF-α", "Interleukin-6", "IL-6".We hand searched all reference lists of eligible articles, related reviews, and meta-analyses as we did not want to miss any relevant studies. We did not include unpublished documents and gray literature like conference papers, theses, and patents.

Eligibility Criteria

Studies were included in this meta-analyses if they met the following criteria: (1) all were written in English; (2) were randomized or non-randomized trial studies; (3) only executed on human, (4) reported baseline BMI and at least one of the following measures: CRP, IL-6, and TNF-α; (5) performed one of the common bariatric surgery (RYGB, SG, VBG, AGB,BPD); (6) executed on patients with a BMI higher than 40 or 35 with at least one comorbidity (such as atherosclerosis, diabetes, and asthma). Articles were excluded if (1) the subjects had a BMI less than 35, (2) obesity was not the reason of surgery, and (3) had lack of sufficient data for the outcomes of interest in individuals. All editorials, reviews, letters to editors, conference papers, animal studies, and molecular studies were excluded. Totally in our initial search, we found 1163 papers. After removing duplicates, 1001 abstracts were selected for a more detailed review; subsequently, 863 studies were excluded due to following reasons: unrelated topic (667), inadequate information (177), non-English (3), animal studies (8), and review article (8). At last, 138 citations remained after screening for titles and abstracts. After full-text evaluation, 22 other studies were also excluded: (1) publication that evaluated the effect of bariatric surgery with combination of other treatments ($n = 2$), (2) papers which had the same database ($n = 4$) and, (3) studies that enough information was not stated in them ($n = 16$). After scrutinizing the full-text papers and based on our inclusion criteria, 114 prospective and 2 retrospective studies were chosen for the systematic review, and none of our included studies were excluded from the meta-analysis. PRISMA flow diagram of search process is depicted in Fig. 1.

Data Extraction

Two independent researchers (M. A., A. Sh.) did the study selection, whereas a chief investigator (Sh.A.) was also present to resolve any differences or controversies. In case of data deficiency, we contacted the corresponding author to acquire the necessary data. The following data were obtained from each study: first author's name; year of publication; study location; study duration; age and gender of participants; mean and SD of serum levels of CRP, IL-6, and TNF-α; study design; health status of study population; number of participants in each groups; BMI before and after intervention; just if all individuals had the same disease, it was mentioned. If the mean inflammatory factors were not reported in the control group, it was considered a study without a control group.

Assessment of Study Quality

Two authors independently assessed the quality of the included studies by the Newcastle-Ottawa Quality Assessment Scale (NOS). This scale comprised three quality factors: selection (maximum 4 stars), comparability (maximum 2 stars), and outcome (maximum 3 stars). A maximum of 9 stars represents

the highest quality. A total score of 7 or more was considered to indicate high-quality studies [23, 24].

Statistical Analysis

Mean difference was used as the effect size and a random effects model was utilized for the meta-analysis [25]. Using random-effects model, effect sizes were acquired as weighted mean difference (WMD) and 95% CI by the DerSimonian-Laird method. A test for heterogeneity was performed (using Q statistic and I^2) [26]. The subgroup analysis was conducted to find out possible sources of heterogeneity among included studies. A meta-regression analysis was performed to investigate whether participant baseline BMI and also duration of follow-up could explain heterogeneity across studies and also affect the measured effect size. Covariates for the meta-regression analysis were defined according to the results of the subgroup analysis and evidence-based knowledge. Publication bias was investigated by visual inspection of the funnel plot as well as by using the Egger's regression method. We used the sensitivity analysis to assess the effect of each study on the overall effect size by removing each study in turn. All statistical analyses were carried out using Stata MP V.14.0.

Results

Findings from Systematic Review

Characteristics of eligible studies are summarized in Table 1. The articles had been published between 2001 and 2017. The sample size of the included studies was between 5 and 765 participants (total sample size of studies ($n = 8084$). The control group was followed up only in four studies [27–30]. Across included studies, five were carried out in patient with diabetes [31–35], one study in patients with insulin resistance [36], one study in patients with asthma [37], two in metabolic syndrome [38, 39], one in atherosclerosis [40], and one in patients with Crohn's disease [41]. Twenty-two studies were just done on females [39, 42–62], one study on males [61], and the rest of the included studies were conducted on both genders [27–38, 40, 41, 63–142]. We considered all of the included studies for meta-analysis.

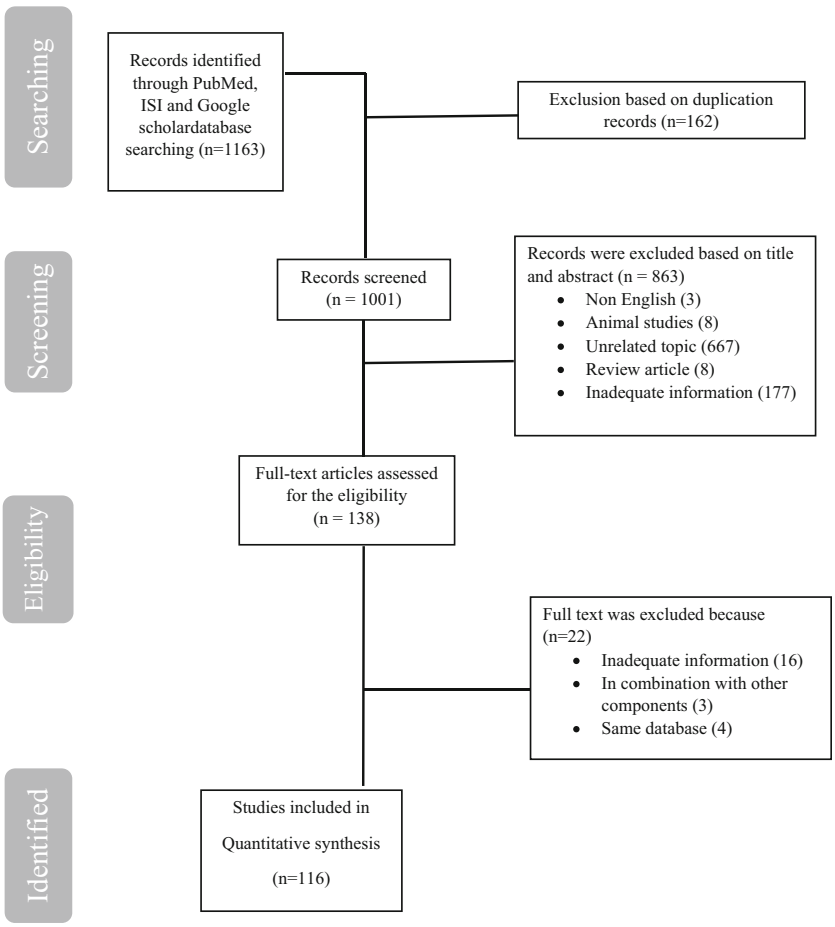

Fig. 1 PRISMA study flow chart

Table 1 Characteristics of included studies in the meta-analysis

Study(disease)/year	Sex	*N*1	*N*2	FU	Surgery	Type	BMI1	BMI2	Age	Country	NO-scale
CRP											
Pardina/2012	Both	34	34	12 M	RYGB	PNR	48.8	30.9	(21–61)	Spain	7
Komorowski (METs)/2011	Both	28	28	48 M	VBG	PNR	45.8	28.2	43.7 ± 10	Poland	5
Miller/2011	Both	15	15	6 M	RYGB	PNR	55.1	40.5	45.9 ± 8.9	USA	6
Pallayova/2011	Both	23	23	12 M	Various	PNR	52.3	35.7	41.9 ± 8.6	USA	6
Tussing-Humphreys/2011	W	17	17	6 M	Various	PNR	46.6	37.6	Nr	USA	7
Kopp/2006	W	43	43	17 M	VBG	PNR	48	33	41 ± 7	Austria	6
Bueter/2010	Nr	13	13	1 M	AGB	PNR	Nr	Nr	Nr	Germany	5
Bueter/2010	Nr	10	10	1 M	RYGB	PNR	Nr	Nr	Nr	Germany	5
Bueter/2010	Nr	11	11	1 M	SG	PNR	Nr	nr	Nr	Germany	5
Bueter/2010	Both	34	34	1 M	Various	PNR	44.6	41.4	40.2 ± 1.1	Germany	5
Vazquez/2006	Both	26	26	4 M	Various	PNR	46.2	36.7	39 ± 10	Spain	6
Tussing-Humphreys/2010	W	20	20	6 M	Various	PNR	47.5	39.5	35.5 ± 7.2	USA	6
Tschoner/2011	Both	36	36	18 M	Various	PNR	42.9	33.9	(21–53)	Austria	6
Sainsbury/2008	Both	26	26	6 M	RYGB	PNR	54.4	41.8	(31–60)	UK	7
Van De Sande-Lee/2011	Both	13	13	8 M	RYGB	PNR	39.1	28.1	34.0 ± 10	Brazil	7
Ress/2010	Both	32	32	18 M	AGB	PNR	42.6	33.1	34.6 ± 8.7	Austria	6
Perez-Romero/2010	Both	96	96	24 M	RYGB	PNR	53	31.8	41.6 ± 9.6	Spain	6
Hakaem/2009	Both	61	61	12 M	SG	PNR	47.5	30.5	Nr	Saudi Arabia	6
Agrawal/2009	Both	62	62	14.8 M	RYGB	Retro	49.8	34.1	46	USA	6
Hakaem/2009	Both	29	29	6 M	SG	PNR	50.9	35.1	32.7 ± 10.2	Saudi Arabia	6
Manco/2006	W	10	10	36 M	BPD	PNR	42	32	38 ± 13	Italy	6
Chen/2009	Both	640	640	12 M	Various	PNR	41.2	29.1	31.3 ± 8.9	China	6
Gannage–Yared/2008	Both	106	106	6 M	Various	PNR	40.6	31.1	36.7 ± 10.2	Lebanon	7
Lin/2007	W	28	28	6 M	RYGB	PNR	48.2	35.5	36 ± 11.7	USA	6
Lin (Atherosclerosis)/2007	Both	69	69	6 M	VBG	PNR	39.0	32.8	34.0 ± 9.9	Taiwan	5
Geloneze (gly/gly PM)/2012	Both	26	26	12 M	RYGB	PNR	45	28	37.2 ± 10.7	Brazil	5
Geloneze (gly/Ser PM)/2012	Both	29	29	12 M	RYGB	PNR	44	28	37.2 ± 9.4	Brazil	5
Wong/2011	Both	37	37	9 M	SG	PNR	46	33	46 ± 13	Austria	6
Boesing/2010	Both	20	20	6 M	RYGB	PNR	48.1	34.9	38.8 ± 11.1	Brazil	7
Lima (METs)/2010	W	19	19	1 M	RYGB	PNR	45.5	40.5	35.3 ± 6.7	Brazil	5
Woodard/2010	Both	765	765	12 M	RYGB	PNR	47.4	31.4	43.8	USA	6
Rd/2010	Both	73	73	12 M	AGB	PNR	44.4	35.3	46.6	USA	6
Swarbrick/2008	W	19	19	1 M	RYGB	PNR	45.6	30.8	40.6 ± 1.8	USA	5
Carroll/2009	Both	34	34	6 M	AGB	PNR	43.4	37.4	Nr	USA	9
		C(17)	C(17)				C(22.3)	C(22.3)			
Chacon/2008	W	61	61	6 M	RYGB	PNR	47.5	33.4	43.0 + −8.9	Spain	6
Zagorski/2005	Both	20	20	6 M	RYGB	PNR	44.5	31.5	33.9	USA	6
Broch/2010	W	63	63	12 M	RYGB	PNR	49.7	32.1	45.0 ± 9.3	Spain	6
Schaller/2009	W	31	31	18 M	RYGB	PNR	46.2	33.1	41 ± 11	Austria	6
Botella-Carretero/2007	W	33	33	14 M	Various	PNR	49.8	34.3	38 ± 10	Spain	6
Moschen/2011	Both	21	21	6 M	AGB	PNR	43.1	34.9	36.9	Austria	6
Simon/2009	W	77	77	6 M	RYGB	PNR	49.1	31.7	45.5 ± 9.6	Spain	6
Shimizu/2017	Both	10	10	6 M	SG	PNR	40.9	30.8	48.8 ± 2.7	Japan	6
Thoni/2017	Both	20	20	12 M	AGB	PNR	43.5	35.8	(27–41)	Austria	6
Alilia/2018	W	157	157	12 M	Various	PNR	46.4	32.3	36.2 ± 9.3	France	6
Alilia/2018	W	135	135	12 M	Various	PNR	48.3	35.3	48.0 ± 10.3	France	6
Lambert/2018	Both	109	109	12 M	Various	PNR	38.8	27.0	(18–60)	Brazil	6
Magro (Crohn's disease)/2017	Both	11	10	12 M	RYGB	PNR	46.3	32.1	(18–65)	Brazil	5
Park/2017	Both	43	43	6 M	RYGB	PNR	36.9	29.5	(26–45)	South Korea	6
Randell/2018	Both	197	197	12 M	SG	PNR	49.0	35.7	(22–70)	Canada	6
Blum/2012	W	73	73	3 M	Various	PNR	44.1	34.9	39.8 ± 11.9	Israel	6
Blum/2012	M	29	29	3 M	Various	PNR	42.5	34.9	43.0 ± 13.0	Israel	6
Cugno/2012	W	25	25	12 M	AGB	PNR	42.7	34.9	40.6 ± 8.7	Italy	6
Brethauer/2011	Both	15	12	6 M	RYGB	PNR	48.9	35.4	49.2 ± 10.4	USA	6
Capuron/2011	W	101	70	12 M	RYGB	PNR	47.4	32.2	37.8 ± 11.2	France	6
Iannelli/2010	Both	12	12	6 M	RYGB	PNR	51	37.5	35.7 ± 8.6	France	6
Iannelli/2010	Both	10	10	6 M	SG	PNR	51.4	40	39.3 ± 8.9	France	6
Richette/2011	Both	140	44	6 M	Various	PNR	50.7	40.4	44 ± 10.3	France	6
Tamboli/2011	Both	8	8	12 M	RYGB	PNR	46.3	31.1	40 ± 11	USA	6
Boulet/2012	Both	12	10	12 M	Various	PNR	51.2	34.4	41 ± 10	Canada	9
		C(11)	C(10)				C(45.7)	C(43.4)	Nr		
Cintra/2012	W	40	40	16 M	RYGB	PNR	55.7	31.9	40.1 ± 8.0	Brazil	6
Ramsey/2013	Both	431	299	11 M	RYGB	PNR	47.6	Nr	44.3	USA	6

Table 1 (continued)

Study(disease)/year	Sex	*N*1	*N*2	FU	Surgery	Type	BMI1	BMI2	Age	Country	NO-scale
Garrido-Sanchez/2012	Both	18	18	3 M	BPD	PNR	50.5	42.07	40.6 ± 10.3	Spain	6
Garrido-Sanchez/2012	Both	13	13	3 M	SG	PNR	48.0	40.03	43 ± 11.0	Spain	6
Illan-Gomez/2012	W	60	60	12 M	RYGB	PNR	47.6	30.50	40.3 ± 10.8	Spain	7
Lammert/2012	Both	30	30	11 M	Various	PNR	48.9	35.5	45.3 ± 11.2	Germany	6
Nerla/2012	Both	50 C(20)	50 C(20)	3 M	Various	PNR	47.1 C(46)	36.8 C(46.2)	38 ± 9 C(41 ± 11)	Italy	7
Saleh/2012	Both	47	47	6 M	RYGB	PNR	47.1	31.6	41	Brazil	6
Cheng (type 2 DM)/2013	Both	14	14	12 M	RYGB	PNR	47	36	52 ± 13	USA	5
Dillard/2013	Both	13	11	12 M	RYGB	PR	42.3	36.6	(27–68)	Poland	6
Gjessing/2013	Both	138	118	12 M	SG	PNR	44.3	30.5	43 ± 12.5	Norway	6
Iannelli/2013	Both	30	30	12 M	RYGB	PNR	49.1	32.5	35.7 ± 8.6	France	6
Iannelli/2013	Both	30	30	12 M	SG	PNR	49.1	34.7	39.3 ± 8.9	France	6
Jimenez (insulin-S)/2013	Both	52	52	12 M	Various	Retro	44.7	29.6	43.9 ± 12.8	USA	6
Jimenez (insulin-R)/2013	Both	52	52	12 M	Various	Retro	44.9	29.1	43.7 ± 12.0	USA	5
Maymo-Masip/2013	Both	23	23	6 M	Various	PNR	56	43	40.2 ± 10	Spain	7
Nijhawan/2013	Both	20	20	12 M	Various	PNR	51.9	46.0	41	USA	6
Ruiz-Tovar/2013	Both	40	40	12 M	SG	PNR	51.9	27.6	43.2 ± 10.2	USA	6
Sdralis/2013	Both	14	12	12 M	SG	PR	41.9	24.6	31.8 ± 7.6	USA	6
Werling/2013	Both	63	63	15 M	RYGB	PNR	43.7	29.2	43 ± 15.3	Sweden	6
Arismendi/2014	Both	129	129	12 M	Various	PNR	46	30	46 ± 12	Spain	7
Auguet/2014	W	30	30	12 M	Various	PNR	46.5	32.5	47.2 ± 8.9	Spain	7
De moura-Grec/2014	Both	90	59	6 M	RYGB	PNR	49.3	35.32	38.4 ± 10.9	Brazil	7
Flores/2014	Both	32	32	12 M	Various	PNR	45	31	53 ± 9	USA	6
Iaffaldano/2014	Both	20	20	36 M	AGB	PNR	41.5	29.9	37	Italy	6
Knosgaard/2014	Both	20	20	3 M	RYGB	PNR	43.0	34.3	41.2 ± 11	Denmark	6
Mallipedhi/2013	Both	22	22	6 M	SG	PNR	50.1	39.6	48 ± 7	USA	6
Santos/2014	Both	46	46	3 M	RYGB	PNR	43.1	37.3	40.5 ± 10.3	Portugal	6
Torriani/2014	Both	21	21	12 M	RYGB	PNR	43	30	45 ± 14	USA	6
Yang/2014	Both	178	178	12 M	Various	PNR	42.0	28.6	36.2 ± 12.1	Taiwan	6
Yang/2014	Both	47	47	12 M	RYGB	PNR	42.7	28.6	33.2 ± 9.4	Taiwan	6
Yang/2014	Both	32	32	12 M	SG	PNR	42.4	28.7	33.9 ± 9.4	Taiwan	6
Chalut-Carpentier/2014	Both	38	27	6 M	RYGB	PNR	45.5	33.6	43 ± 9	USA	6
Sales-Peres/2015	Both	50	50	12 M	RYGB	PNR	49.6	32.2	38.9 ± 10.1	Brazil	6
Galanakis/2015	Both	38	38	12 M	Various	PNR	43.6	32.8	35.7 ± 10	Greece	6
Hawkins/2015	Both	77	77	12 M	Various	PNR	46.7	30.5	43.4 ± 10.6	USA	6
Montecucco/2015	Both	11	11	12 M	RYGB	PNR	43.3	27.9	35 ± 7.3	Switzerland	6
Netto/2015	Both	41	39	6 M	RYGB	PNR	44.6	31.6	39.4 ± 10.9	USA	6
Oliveria/2015	Both	25	25	6 M	RYGB	PNR	49.7	33.4	39.2 ± 8.07	Brazil	6
Sparks/2015	Both	53	53	12 M	Various	PNR	47.8	32.6	47.9 ± 10.5	USA	6
Van Huisstede (asthma)/2014	Both	27	27	12 M	Various	PNR	45.1	31.3	(19–48)	Netherlands	5
Van Huisstede/2014	Both	39	39	12 M	Various	PNR	43.1	29.3	(18–50)	Netherlands	6
Campello/2016	Both	20	20	12 M	SG	PNR	47.5	34.8	43 ± 12	Italy	6
Illan Gomez/2016	Both	79	79	12 M	RYGB	PNR	47.5	30.1	38.5 ± 10.0	Spain	7
Lips (type 2 DM)/2016	Both	27	27	3 M	RYGB	PNR	42.0	34.7	56 ± 6	Netherlands	6
Richette/2016	Both	154	154	6 M	Various	PNR	47.8	36.4	41.0 ± 12.3	France	6
Santilli/2016	Both	12	12	12 M	AGB	PNR	43.7	34.7	(27–50)	Italy	6
Shih/2015	Both	69	69	12 M	Various	PNR	42.3	27.2	30.2 ± 1.0	Taiwan	6
Shih (DM)/2015	Both	24	24	12 M	Various	PNR	41.4	28.6	34.0 ± 1.4	Taiwan	5
Belligoli/2017	Both	197	180	12 M	SG	PNR	47.4	32.7	43 ± 11	USA	6
Faver/2017	Both	175	175	12 M	Various	PNR	44	29	41 ± 11	France	6
Garrido-sanchez/2016	Both	20	20	3 M	RYGB	PNR	49.5	40.0	48.8 ± 8.8	Spain	6
Garrido-sanchez (type2 DM)/2016	Both	23	23	3 M	RYGB	PNR	49.4	41.2	51.2 ± 9.5	Spain	5
Gesquiere/2017	Both	54	42	12 M	RYGB	PNR	40.5	27.4	48	Belgium	6
Johansson/2017	Both	124	124	12 M	RYGB	PNR	43.5	31.1	43.2 ± 11.6	Sweden	6
Jurets/2017	Both	31	31	12 M	Various	PNR	46.1	31.1	42 ± 12	Austria	7
Parreno Caparros/2017	Both	68	68	12 M	RYGB	PNR	48.2	30.7	39.5 ± 10.1	Spain	7
Sans/2017	Both	103	103	12 M	RYGB	PNR	43.3	28.1	40.6 ± 11.2	France	6
IL-6											
Miller/2011	Both	15	15	6 M	RYGB	PNR	55.1	40.5	45.9 ± 8.9	USA	6
Pallayova/2011	Both	23	23	12 M	Various	PNR	52.3	35.7	41.9 ± 8.6	USA	6
De Luis/2010	Both	32	32	12 M	BPD	PNR	50.2	34.2	43.9 ± 6.9	Spain	6
De Luis/2010	Both	9	9	12 M	BPD	PNR	50.1	35.8	42.4 ± 7.7	Spain	6
Tussing-Humphreys/2011	W	17	17	6 M	Various	PNR	46.6	37.6	Nr	USA	7
Kopp/2006	W	43	43	17 M	VBG	PNR	48	33	41 ± 7	Austria	6

Table 1 (continued)

Study(disease)/year	Sex	*N*1	*N*2	FU	Surgery	Type	BMI1	BMI2	Age	Country	NO-scale
Vazquez/2006	Both	26	26	4 M	Various	PNR	46.2	36.7	39 ± 10	Spain	6
Tussing-Humphreys/2010	W	20	20	6 M	Various	PNR	47.5	39.5	35.5 ± 7.2	USA	6
Maruna/2001	Both	18	18	3D	AGB	PNR	46.1	Nr	(34–51)	Czech Republic	6
Tschoner/2011	Both	36	36	18 M	Various	PNR	42.95	33.97	(21–53)	Austria	6
Sainsbury/2008	Both	26	26	6 M	RYGB	PNR	54.4	41.8	(31–60)	UK	7
Van De Sande-Lee/2011	Both	13	13	8 M	RYGB	PNR	39.1	28.1	34.0 ± 10	Brazil	7
Perez-Romero/2010	Both	96	96	24 M	RYGB	PNR	53	31.8	41.6 ± 9.6	Spain	7
Manco/2006	W	10	10	36 M	BPD	PNR	42	32	38 ± 13	Italy	6
Lin/2007	Both	28	28	6 M	RYGB	PNR	48.2	35.5	36 ± 11.7	USA	6
Geloneze (gly/gly PM)/2012	Both	26	26	12 M	RYGB	PNR	45	28	37.2 ± 10.7	Brazil	5
Geloneze (gly/ser PM)/2012	Both	29	29	12 M	RYGB	PNR	44	28	37.2 ± 9.4	Brazil	5
Di Renzo/2011	Both	62	62	6 M	AGB	PNR	44.9	39.5	43.3 ± 10.7	Italy	6
Lima (METs)/2010	W	19	19	1 M	RYGB	PNR	45.5	40.5	35.3 ± 6.7	Brazil	5
Swarbrick/2008	W	19	19	1 M	RYGB	PNR	45.6	30.8	40.6 ± 1.8	USA	5
Chacon/2008	W	61	61	6 M	RYGB	PNR	47.5	33.4	43.0 ± 8.9	Spain	6
Shimizu/2017	Both	10	10	6 M	SG	PNR	40.9	30.8	48.8 ± 2.7	Japan	6
Capuron/2011	W	101	70	12 M	RYGB	PNR	47.4	32.2	37.8 ± 11.2	France	6
Chung/2011	Both	20	20	1D	RYBG	PNR	43.0	Nr	28.0 ± 7.0	South Korea	6
Marantos/2011	W	20	20	12 M	Various	PNR	41.4	31.05	(24–48)	Greece	7
Richette/2011	Both	140	44	6 M	Various	PNR	50.7	40.4	44 ± 10.3	France	6
Tamboli/2011	Both	8	8	12 M	RYGB	PNR	46.3	31.1	40 ± 11	USA	6
Ueda/2011	Both	14	14	7D	RYGB	PNR	50.8	49.5	40 ± 10	USA	5
Illan-Gomez/2012	W	60	60	12 M	RYGB	PNR	47.65	30.50	40.3 ± 10.8	Spain	7
Lammert/2012	Both	30	30	11 M	Various	PNR	48.9	35.5	45.3 ± 11.2	Germany	6
Dillard/2013	Both	13	11	12 M	RYGB	PR	42.3	36.6	(27–68)	Poland	6
Lips/2013	Both	32	31	3 M	RYGB	PNR	44.2	37.1	Nr	Netherlands	7
Lips (DM)/2013	Both	30	27	3 M	RYGB	PNR	43.5	36.1	Nr	Netherlands	6
Lips/2013	Both	62	58	3 M	RYGB	PNR	43.9	36.6	49.4 ± 0.6	Netherlands	7
Maymo-Masip/2013	Both	23	23	6 M	Various	PNR	56	43	40.2 ± 10	Spain	7
Sdralis/2013	Both	14	12	12 M	SG	PR	41.9	24.6	31.8 ± 7.6	USA	6
Silva-Nunes/2013	W	21	21	6 M	Various	PNR	46.5	39.2	34.2 ± 8.4	Portugal	7
Mallipedhi/2013	Both	22	22	6 M	SG	PNR	50.1	39.6	48 ± 7	USA	6
Nestvold/2014	Both	97	97	12 M	Various	PNR	46.8	23	(26–61)	Norway	7
Netto/2015	Both	41	39	6 M	RYGB	PNR	44.6	31.6	39.4 ± 10.9	USA	6
Van Huisstede (asthma)/2014	Both	27	27	12 M	Various	PNR	45.1	31.3	(19–48)	Netherlands	5
Van Huisstede/2014	Both	39	39	12 M	Various	PNR	43.1	29.3	(18–50)	Netherlands	6
Campello/2016	Both	20	20	12 M	SG	PNR	47.5	34.8	43 ± 12	Italy	6
Illan Gomez/2016	Both	79	79	12 M	RYGB	PNR	47.5	30.1	38.5 ± 10.0	Spain	7
Kelly/2016	Both	39	39	12 M	Various	PNR	51.0	34.7	16.5 ± 1.6	USA	6
Kelly/2016	Both	13	13	12 M	RYGB	PNR	58.7	46.8	16.5 ± 1.6	USA	6
Lips (DM 2)/2016	Both	27	27	3 M	RYGB	PNR	42.0	34.7	56 ± 6	Netherlands	6
Richette/2016	Both	154	154	6 M	Various	PNR	47.8	36.4	41.0 ± 12.3	France	6
Shih/2015	Both	69	69	12 M	Various	PNR	42.3	27.2	30.2 ± 1.0	Taiwan	6
Shih (DM)/2015	Both	24	24	12 M	Various	PNR	41.4	28.6	34.0 ± 1.4	Taiwan	5
Belligoli/2017	Both	197	180	12 M	SG	PNR	47.4	32.7	43 ± 11	USA	6
Farey/2016	Both	15	15	3 M	SG	PNR	42.3	35.3	50.9 ± 11.9	Australia	6
Jurets/2017	Both	31	31	12 M	Various	PNR	46.1	31.1	42 ± 12	Austria	7
Parreno Caparros/2017	Both	68	68	12 M	RYGB	PNR	48.2	30.7	39.5 ± 10.1	Spain	7
Schamtz/2016	Both	20 C(20)	20 C(20)	12 M	RYGB	PNR	43.0 C(46.2)	27.3 C(48.3)	36.7 ± 10.5 C(39.2 ± 12.4)	Brazil	9
Schamtz (DM)/2016	Both	20 C(20)	20 C(20)	12 M	RYGB	PNR	43.4 C(46.2)	25.4 C(48.3)	52.0 ± 10.7 C(39.2 ± 12.4)	Brazil	8
TNF-α											
Miller/2011	Both	15	15	6 M	RYGB	PNR	55.1	40.5	45.9 ± 8.9	USA	6
Pallayova/2011	Both	23	23	12 M	Various	PNR	52.3	35.7	41.9 ± 8.6	USA	6
DeLuis/2010	Both	32	32	12 M	BPD	PNR	50.2	34.2	43.9 ± 6.9	Spain	6
DeLuis/2010	Both	9	9	12 M	BPD	PNR	50.1	35.8	42.4 ± 7.7	Spain	6
Kopp/2006	W	43	43	17 M	VBG	PNR	48	33	41 ± 7	Austria	6
Vazquez/2006	Both	26	26	4 M	Various	PNR	46.2	36.7	39 ± 10	Spain	6
Maruna/2001	Both	18	18	3D	AGB	PNR	46.1	Nr	(34–51)	Czech Republic	6
Tschoner/2011	Both	36	36	18 M	Various	PNR	42.9	33.9	(21–53)	Austria	6
Sainsbury/2008	Both	26	26	6 M	RYGB	PNR	54.4	41.8	(31–60)	UK	7
Van De Sande-Lee/2011	Both	13	13	8 M	RYGB	PNR	39.1	28.1	34.0 ± 10	Brazil	7
Perez-Romero/2010	Both	96	96	24 M	RYGB	PNR	53	31.8	41.6 ± 9.6	Spain	7

Table 1 (continued)

Study(disease)/year	Sex	*N*1	*N*2	FU	Surgery	Type	BMI1	BMI2	Age	Country	NO-scale
Manco/2006	W	10	10	36 M	BPD	PNR	42	32	38 ± 13	Italy	6
Shimizu/2017	Both	10	10	6 M	SG	PNR	40.9	30.8	48.8 ± 2.7	Japan	6
Appachi/2011	Both	160	45	6 M	Various	PNR	50.1	38.9	49 ± 10	USA	6
Chung/2011	Both	20	20	1D	RYBG	PNR	43.0	Nr	28.0 ± 7.0	South Korea	6
Huang/2011	Both	13	12	6 M	RYGB	PNR	47.4	35.4	48.5 ± 3	USA	6
Tamboli/2011	Both	8	8	12 M	RYGB	PNR	46.3	31.1	40 ± 11	USA	6
Illan-Gomez/2012	w	60	60	12 M	RYGB	PNR	47.6	30.5	40.3 ± 10.8	Spain	7
Lammert/2012	Both	30	30	11 M	Various	PNR	48.9	35.5	45.3 ± 11.2	Germany	6
Dillard/2013	Both	13	11	12 M	RYGB	PR	42.3	36.6	(27–68)	Poland	6
Lips/2013	Both	32	31	3 M	RYGB	PNR	44.2	37.1	Nr	Netherlands	7
Lips(DM)/2013	Both	30	27	3 M	RYGB	PNR	43.5	36.1	Nr	Netherlands	6
Lips/2013	Both	62	58	3 M	RYGB	PNR	43.9	36.6	49.4 ± 0.6	Netherlands	7
Maymo- Masip/2013	Both	23	23	6 M	Various	PNR	56	43	40.2 ± 10	Spain	7
Sdralis/2013	Both	14	12	12 M	SG	PR	41.9	24.6	31.85 ± 7.62	USA	6
Silva-Nunes/2013	w	21	21	6 M	Various	PNR	46.5	39.2	34.2 ± 8.4	Portugal	7
Nestvold/2014	Both	97	97	12 M	Various	PNR	46.8	23	(26–61)	Norway	7
Netto/2015	Both	41	39	6 M	RYGB	PNR	44.6	31.6	39.4 ± 10.9	USA	6
Van Huisstede (asthma)/2014	Both	27	27	12 M	Various	PNR	45.1	31.3	(19–48)	Netherlands	5
Van Huisstede/2014	Both	39	39	12 M	Various	PNR	43.1	29.3	(18–50)	Netherlands	6
Campello/2016	Both	20	20	12 M	SG	PNR	47.5	34.8	43 ± 12	Italy	6
Lips (DM 2) /2016	Both	27	27	3 M	RYGB	PNR	42.0	34.7	56 ± 6	Netherlands	6
Sams/2016	Both	20	8	6 M	RYGB	PNR	47.2	34.5	37.2 ± 11.6	USA	6
Sams/2016	Both	5	2	6 M	AGB	PNR	48.3	44.3	38.3 ± 12.9	USA	6
Belligoli/2017	Both	197	180	12 M	SG	PNR	47.4	32.7	43 ± 11	USA	6
Farey/2016	Both	15	15	3 M	SG	PNR	42.3	35.3	50.9 ± 11.9	Australia	6
Jurets/2017	Both	31	31	12 M	Various	PNR	46.1	31.1	42 ± 12	Austria	7
Schamtz/2016	Both	20 C(20)	20 C(20)	12 M	RYGB	PNR	43.0 C(46.2)	27.3 C(48.3)	36.7 ± 10.5 C(39.2 ± 12.4)	Brazil	9
Schamtz(DM)/2016	Both	20 C(20)	20 C(20)	12 M	RYGB	PNR		25.4 C(48.3)	52.0 ± 10.7 C(39.2 ± 12.4)	Brazil	8

Study(disease)/year first author and year of study,, *M* men, *W* women, *N1* initial sample size, *N2* final sample size, *FU* follow-up in months (M) and days (D), *Surgery* type of bariatric surgery performed, *Type* study design, *PNR* prospective non-randomized, *R* randomized, *Retro* retrospective, *BMI1* pre-operative BMI, *BMI2* post-operative BMI, *AGE* defined as mean ± SD or (age interval), *Nr* not reported, *C* control group, *NO-scale* Newcastle Ottawa Scale, *RYGB* Roux-en-Y gastric bypass, *AGB* adjustable gastric banding, *SG* sleeve gastrectomy, *BPD* biliopancreatic diversion, Various combination of procedures, *VBG* vertical banded gastroplasty, *METs* metabolic syndrome, *insulin-R* insulin resistance, *PM* polymorphism, *gly* glycine, *ser* serine

Findings from Meta-Analysis

Bariatric Surgery and CRP

Among included studies which evaluated CRP as an outcome measure, BMI decreased significantly in patients following bariatric surgery (Supplemental Fig. 1). Overall, subgroup analysis (based on type of surgery) on the CRP changes after bariatric surgery was presented in Fig. 2. Combining 121 effect sizes revealed a significant decreasing effect of bariatric surgeries on the CRP levels of participants (WMD − 5.30, 95% CI − 5.46, − 5.15, $P < 0.001$). In addition, a between-study heterogeneity was found (I^2 = 100%; $P_{\text{heterogeneity}} < 0.001$).

Furthermore, in subgroup analysis, a significant effect of various types of bariatric surgeries on the CRP levels except the BPD type was found. In addition, we found a decreasing effect of bariatric surgeries on the CRP levels of participants after different follow-up durations including less than 3 months, 6 months, 12 months, or more than 12 months follow-up duration; however, there was not any significant effect of bariatric surgeries on the CRP levels of participants after 3 months' follow-up duration. In addition, it has been shown significant increasing effect of bariatric surgeries on the CRP levels for studies which were conducted among individuals with a baseline BMI < 40 kg/m^2 or > 50 kg/m2 (Table 2).

Bariatric Surgery and IL-6

Among included studies which investigated IL-6 as an outcome measure, BMI decreased significantly following bariatric surgery (Supplemental Fig. 2). Pooled effect size from random effect revealed that the IL-6 serum level decreased significantly following bariatric surgery (WMD − 0.58, 95% CI − 0.64, − 0.53), with significant heterogeneity among studies (I^2 97.7%, $P < 0.001$) (Fig. 3). Findings of subgroup analysis revealed a significant effect of different types of bariatric surgeries including RYGB, BPD, and other miscellaneous types on the IL-6 levels of individuals. According to these

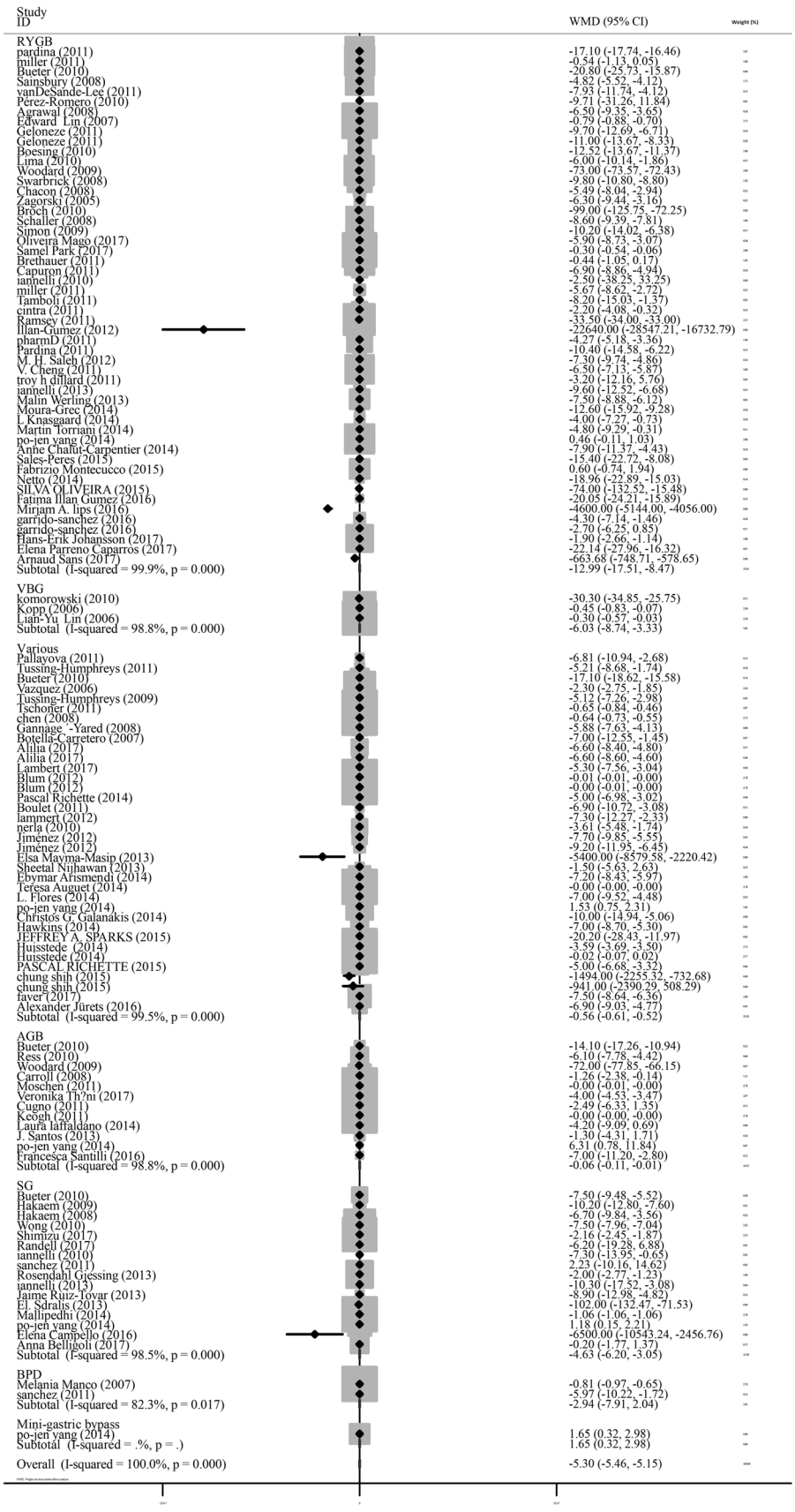

Fig. 2 Overall subgroup analysis (based on type of surgery) on the CRP changes after bariatric surgery

analyses, we found a significant inverse influence of bariatric surgeries on IL-6 concentration for studies with 6 months and more duration of follow-up. In addition, a significant decreasing effect of bariatric surgeries on the IL-6 levels for studies which were conducted among individuals with a baseline BMI < 40 kg/m^2 or > 50 kg/m2 was observed (Table 2).

Bariatric Surgery and TNF-α

Among included studies which studied the effect of bariatric surgery on TNF-α, BMI decreased significantly following bariatric surgery (Supplemental Fig. 3). The influence of bariatric surgeries on TNF-α concentration was indicated in Fig. 4. Thirty-nine effect sizes were pooled and an inverse influence in this regard was found (WMD − 0.20 95% CI − 0.39, − 0.02, $P = 0.031$), with significant heterogeneity among studies (I^2 95.4%, $P < 0.001$). Findings of subgroup analysis showed no significant effect of different types of bariatric surgeries on the TNF-α levels. We found a significant inverse influence of bariatric surgeries on TNF-α concentration for studies with 12 months' follow-up; however, there was not any significant increasing effect of bariatric surgeries on the TNF-α levels after other follow-up durations. In addition, a significant decreasing effect of bariatric surgeries on the TNF-α levels was found for studies which were conducted among individuals with a baseline BMI < 40 kg/m^2 and ≥ 45 to > 50 kg/m^2 (Table 2).

Meta Regression Analysis

Meta-regression analysis indicated no linear relationship of baseline BMI with the absolute changes in CRP serum level, IL-6, and TNF-α. Moreover, no significant associations with follow-up duration and CRP, IL-6 and TNF-α were found, although a potential reducing trend of serum CRP was observed with follow-up duration and baseline BMI (Supplemental Fig. 4 and 5).

Publication Bias and Sensitivity Analysis

Sensitivity analysis was performed to assess the influence of each study on the pooled result (WMD) by removing each study in turn. Sensitivity analysis indicated that the result was not excessively influenced by any of the individual studies. There was no evidence of publication bias for studies investigating the effect of bariatric surgery on CRP (Egger's $P = 0.29$) and TNF-α (Egger's $P = 0.21$) based on Egger's test and by visual inspection of funnel plots (Supplemental Fig. 6); however, funnel plot and egger's linear test indicated significant publication bias among studies which evaluated the effect of bariatric surgery on IL-6 ($P < 0.001$) (Supplemental Fig. 6).

Discussion

Findings from our systematic review and meta-analysis indicate a significant reduction in the levels of various inflammatory cytokines including CRP, IL-6, and TNF-α as the most commonly measured inflammatory factors in bariatric surgery researches.

Obesity is associated with a moderate and chronic increase in such inflammatory factors which are hypothesized to decrease after bariatric surgeries [20, 21]. The results of this meta-analysis are in line with other studies looking at the effects of bariatric surgery on inflammatory factors. For instance, an earlier pooled analysis of cohort studies found a decreasing effect of bariatric surgeries on levels of CRP and IL-6 [143]. However, it must be noted that previous meta-analysis included only forty-eight studies. In the present study, 116 unique studies were included. A previous meta-analysis showed that only CRP and IL-6 decreased following bariatric surgery but TNF-α remained unchanged; in contrast, we showed that apart from CRP and IL-6, TNF-α also decreased significantly following bariatric surgery, which could be an important new finding in this field.

In the current study, we found significant effects of different bariatric surgeries on levels of CRP and IL-6 and TNF-α. These observed findings are in line with prior studies, which have illustrated an inverse effect of medical or dietary weight loss on obesity-induced inflammatory status. For instance, Heilbronn et al. observed that energy restriction and weight loss with very-low-fat diets reduce C-reactive protein concentrations among obese women [144]. Previous meta-analysis stated that the change in TNF-α after bariatric surgery was not significant. However, the correlation of TNF-α reduction and decrease in body mass index (BMI) varied among these studies. Bastard et al found that dietary methods of weight loss can reduce the levels of all three inflammatory markers including CRP, IL-6, and TNF-α [145], which is in line with our study. However, another randomized clinical trial has not indicated any significant attenuation of inflammation after neither medical nor dietary weight loss [88]. Also, data from a previous meta-analysis revealed a beneficial effect of low-fat diets [146] and exercise training on CRP levels regardless of the age or sex of the individuals [147]. Furthermore, animal and human studies have shown that bariatric surgeries might have a significant effect on both the adipose tissue inflammation and weight loss [148].

Although the biologic mechanisms by which bariatric surgery resolves inflammatory conditions are mostly unknown, weight loss followed by the surgery has been shown as one of the most important mechanisms that explain the reduction in levels of inflammatory factors [149]. Moreover, the correlation to other variables is inconsistent across bariatric surgery studies, including weight loss, blood pressure reduction, and change in lipids [150]. Probably, the major factor is the reduction of adipocyte mass through bariatric surgeries which is the

Table 2 Subgroup analyses for the effect of bariatric surgery on CRP, IL-6, and TNF-α concentrations

Subgrouped by	No. of trials	WMD[a] (95% CI)	*P* value[b]	I^2 (%)[c]	P^d
CRP					
Type of surgery					
RYGB	52	− 12.99 (− 17.51 to − 8.47)	≤ 0.001	99.9	≤ 0.001
VBG	3	− 6.3 (− 8.74 to − 3.33)	≤ 0.001	98.8	≤ 0.001
Various	36	− 0.56 (− 0.61 to − 0.52)	≤ 0.001	99.5	≤ 0.001
AGB	12	− 0.06 (− 0.11 to − 0.01)	0.02	98.8	≤ 0.001
SG	16	− 4.63 (− 6.20 to − 3.05)	≤ 0.001	98.5	≤ 0.001
BPD	2	− 2.94 (− 7.91 to − 2.04)	0.24	82.3	0.01
Follow-up period					
< 3 months	6	− 12.40 (− 16.24, − 8.56)	≤ 0.001	95.1	≤ 0.001
3 month	10	− 0.01 (− 0.04, 0.03)	0.64	97.1	≤ 0.001
6 month	30	− 3.18 (− 3.58, − 2.78)	≤ 0.001	100.0	≤ 0.001
12 months	62	− 3.09 (− 3.17, − 3.02)	≤ 0.001	99.9	≤ 0.001
> 12 month	12	− 5.37 (− 6.69, − 4.05)	≤ 0.001	98.4	≤ 0.001
Baseline BMI					
< 40 kg/m^2	4	− 1.29 (− 2.21, − 0.37)	0.006	91.2	≤ 0.001
40 to < 45 kg/m^2	43	− 0.14 (− 0.17, − 0.11)	≤ 0.001	98.7	≤ 0.001
≥ 45 to < 50 kg/m^2	55	− 10.22 (− 12.14, − 8.29)	≤ 0.001	99.9	≤ 0.001
> 50 kg/m^2	17	− 4.31 (− 5.61, − 3.00)	≤ 0.001	93.6	≤ 0.001
IL-6					
Type of surgery					
RYGB	27	− 1.07 (− 1.29, − 0.86)	≤ 0.001	97.8	≤ 0.001
Various	17	− 1.38 (− 2.42, − 0.35)	0.009	96.7	≤ 0.001
AGB	2	40.87 (− 46.80, 128.55)	0.36	93.3	≤ 0.001
SG	6	0.07 (− 0.75, 0.89)	0.86	79.4	≤ 0.001
BPD	3	− 1.03 (− 2.05, − 0.01)	0.04	68.1	0.04
Follow-up period					
< 3 months	4	7.28 (− 1.22, 15.78)	0.09	96.3	≤ 0.001
3 month	5	− 0.26 (− 0.66, 0.15)	0.21	79.6	0.001
6 month	14	− 0.24 (− 0.29, − 0.19)	≤ 0.001	97.9	≤ 0.001
12 months	26	− 2.06 (− 3.00, − 1.11)	≤ 0.001	95.8	≤ 0.001
> 12 month	4	− 1.30 (− 2.53, − 0.07)	0.03	95.4	≤ 0.001
Baseline BMI					
< 40 kg/m^2	1	− 17.80 (− 24.35, − 11.25)	≤ 0.001	–	–
40 to < 45 kg/m^2	20	− 1.37 (− 2.21, − 0.53)	0.001	98.5	≤ 0.001
≥ 45 to < 50 kg/m^2	23	− 0.86 (− 0.99, − 0.73)	≤ 0.001	96.9	≤ 0.001
> 50 kg/m^2	13	− 1.00 (− 1.76, − 0.24)	0.01	96.5	≤ 0.001
TNF-alpha					
Type of surgery					
RYGB	19	− 0.26 (− 0.73, 0.21)	0.27	96.3	≤ 0.001
Various	10	− 0.09 (− 0.43, 0.25)	0.61	89.7	≤ 0.001
AGB	2	24.47 (− 24.98, 73.92)	0.33	97.3	≤ 0.001
SG	5	− 0.54 (− 1.21, 0.13)	0.11	56.2	0.058
BPD	3	− 1.75 (− 5.93, 2.44)	0.41	96.3	≤ 0.001
Follow-up period					
< 3 months	2	24.58 (− 24.64, 73.81)	0.32	97.2	≤ 0.001
3 month	5	0.60 (− 0.50, 1.70)	0.28	82.2	≤ 0.001
6 month	11	− 0.16 (− 0.51, 0.19)	0.36	97.0	≤ 0.001
12 months	16	− 1.67 (− 2.70, − 0.64)	0.001	94.6	≤ 0.001
> 12 month	4	− 0.01 (− 0.04, 0.02)	0.60	0.00	0.49
Baseline BMI					
< 40 kg/m^2	1	− 13.20 (− 20.93, − 5.47)	0.001	–	–
40 to < 45 kg/m^2	15	− 0.60 (− 1.51, 0.31)	0.19	95.4	≤ 0.001
≥ 45 to < 50 kg/m^2	15	− 0.41 (− 0.68, − 0.13)	0.004	93.1	≤ 0.001
> 50 kg/m^2	9	− 0.30 (− 0.79, 0.18)	0.22	96.7	≤ 0.001

[a] Effect size was expressed as weighted mean difference

[b] For meta-analysis: $P < 0.05$ was considered to be a significant effect of bariatric surgery on inflammatory markers index by using a random-effects model

[c] The I^2 statistic was calculated by using Cochran's test, and $I^2 > 50\%$ was considered to indicate significant heterogeneity across studies

[d] P value for I^2

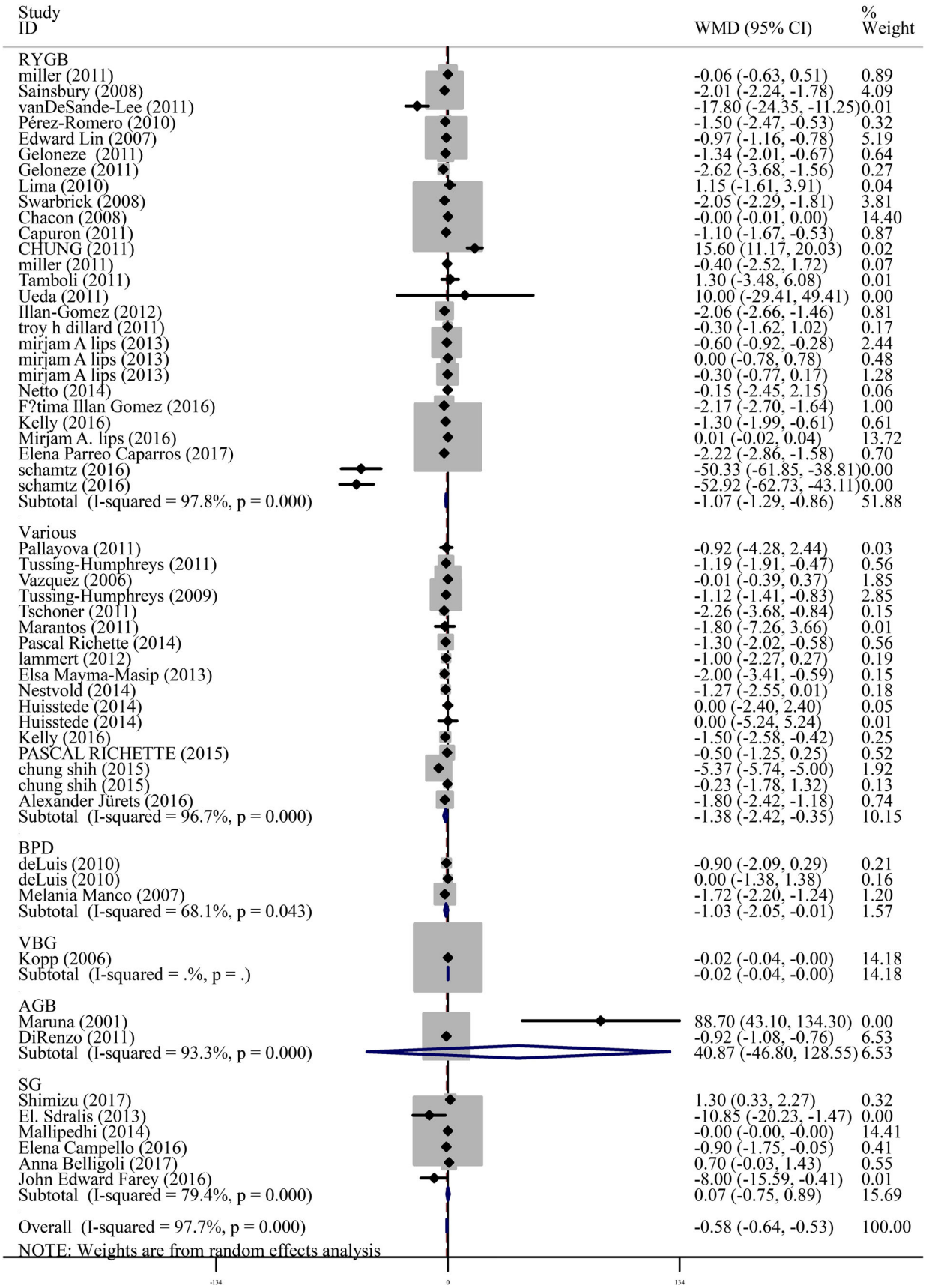

Fig. 3 Findings of subgroup analysis of different types of bariatric surgeries for IL-6

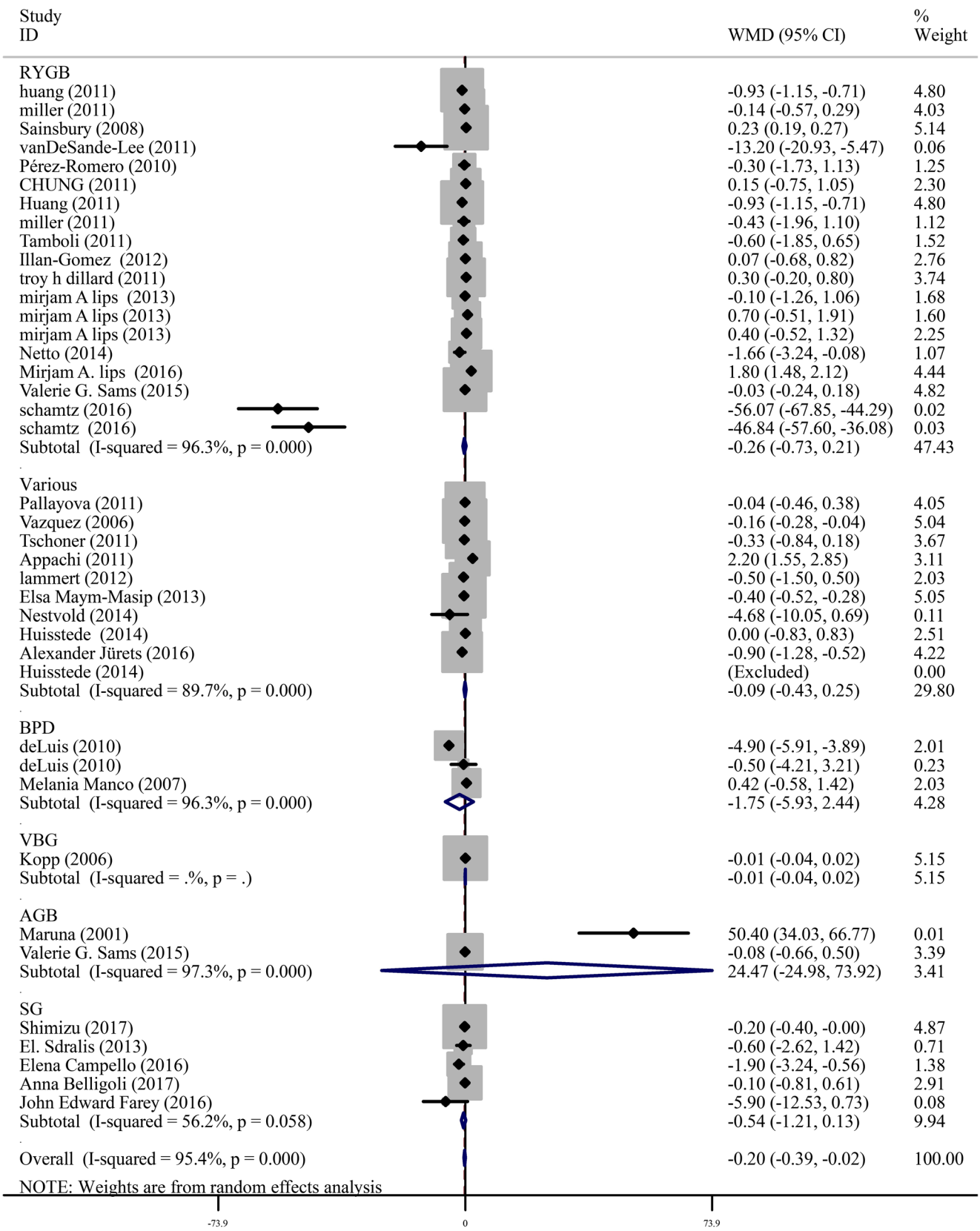

Fig. 4 The influence of bariatric surgeries on TNF-α concentration

mechanism responsible for the decline in inflammation state [149]. Thus, it would be expected that inflammatory markers would decrease linearly as BMI decreased. Perhaps, some other mechanism other than decreased BMI and fat mass, such as decreased caloric intake, decreased nutrient absorption, or decreased need for detoxification of ingested substances by the liver, may contribute to this reduction.

Inflammation is a highly significant risk factor for both morbidity and mortality. Inflammation is a highly significant risk factor for both morbidity and mortality [151]. It is well-identified that long-term inflammation is associated with the increase risk of a vast number of chronic disease such as mood disorders [152], atherosclerosis, and coronary artery disease [153], neurodegenerative diseases [154], cancers [155], chronic obstructive pulmonary disease [156], hypertension [157], and diabetes [158]. Overall, our study showed a beneficial effect of bariatric surgery on inflammatory factors which may provide a protective effect against a number of metabolic health conditions of obesity, including diabetes, cardiovascular disease, and cancer as they all are associated with inflammation.

This meta-analysis has several strengths, such as this is the newest available data to show the effect of weight loss via various bariatric surgeries on the obesity-associated chronic inflammation. However, controversy between present study and previous meta-analysis could be due to fewer included studies in the previous meta-analysis, which can impact the pooled effect size.

In conclusion, findings from this meta-analysis of clinical trial studies suggested that bariatric surgeries might cause a significant reduction in the levels of various inflammatory markers including CRP, IL-6, and TNF-α.

Compliance with Ethical Standards

Ethical issues (including plagiarism, misconduct, data fabrication, falsification, double publication or submission, redundancy) have been completely observed by the authors.

Conflict of Interest All authors declare that they have no conflict of interest.

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