



# The Effect of Bariatric Surgery on Asian Patients with Type 2 Diabetes Mellitus and Body Mass Index $< 30 \text{ kg/m}^2$ : a Systematic Review and Meta-analysis

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## Abstract

**Background** The effect of bariatric surgery on the glycemic control of patients with obesity and type 2 diabetes mellitus is obvious. However, the effect in patients with body mass index (BMI)  $< 30 \text{ kg/m}^2$  especially Asian population has not been widely reported and acknowledged.

**Methods** We performed a literature search in Medline, Embase, and the Cochrane Library from January 2000 to March 2018. All the studies involving the effect of bariatric surgery on patients with type 2 diabetes and BMI  $< 30 \text{ kg/m}^2$  from Asian countries or regions were included in this meta-analysis.

**Results** Twelve studies including 697 patients were examined in this meta-analysis. Clinical indexes in 6, 12, and 24 months follow-up were analyzed, respectively. BMI and waist circumference reduced by  $2.88 \text{ kg/m}^2$  and  $12.92 \text{ cm}$ , respectively, at 12 months postoperatively. There were reductions in fasting plasma glucose, 2-h postprandial plasma glucose, and glycated hemoglobin A1c at all the three time points after surgery,  $3.13 \text{ mmol/L}$ ,  $5.46 \text{ mmol/L}$ , and  $2.13\%$  at 6 months;  $3.22 \text{ mmol/L}$ ,  $6.46 \text{ mmol/L}$ , and  $2.38\%$  at 12 months;  $1.99 \text{ mmol/L}$ ,  $5.84 \text{ mmol/L}$ , and  $1.58\%$  at 2 years. Insulin only reduced by  $1.70 \mu\text{U/ml}$  at 12 months. C-peptide reduced by  $0.70 \text{ ng/ml}$  and  $0.40 \text{ ng/ml}$  at 6 months and 2 years. Bariatric surgery led to reduction in total cholesterol, triglyceride, and low-density lipoprotein cholesterol, while augment in high-density lipoprotein cholesterol at 6 and 12 months. Glucagon-like peptide 1 increased by  $2.48 \text{ pmol/L}$  and  $4.00 \text{ pmol/L}$  at half a year 1 year.

**Conclusions** Asian patients with type 2 diabetes and BMI  $< 30 \text{ kg/m}^2$  could achieve significant improvement in weight, glycemic control, lipid profiles, and  $\beta$ -cell function in short and medium terms after bariatric surgery, but long-term follow-up is necessary to evaluate the effectiveness.

**Keywords** Bariatric surgery · Type 2 diabetes · BMI  $< 30 \text{ kg/m}^2$

## Introduction

Diabetes mellitus is a global health issue. In 2015, the International Diabetes Federation (IDF) estimated that 1 in 11 adults aged 20–79 years had diabetes mellitus globally, about 415 million population. This estimate is predicted to rise to 642 million by 2040 [1]. The IDF reports that the countries with the highest number of death resulting from

diabetes are China, India, and Indonesia, all of which are Asian countries [2]. Over 90% of diabetes mellitus populations are type 2 diabetes mellitus (T2DM).

In Western countries, the relationship between T2DM and obesity is well acknowledged, as 90% of patients with T2DM are overweight or obese [3]. However, in Asian countries, patients with T2DM are at a lower BMI compared with Caucasian [4]. According to a recent survey by the Ministry of Health and Welfare of Korea, the mean body mass index (BMI) of patients with T2DM in Korea is  $24.9 \pm 3.3 \text{ kg/m}^2$  [5], while that in China is just  $24 \text{ kg/m}^2$  [6]. T2DM in Asian people is characterized by insulin resistance and deterioration in pancreatic islet cells function [7, 8].

According to the IDF, metabolic surgery is recommended for patients with T2DM and BMI  $> 35 \text{ kg/m}^2$ . Surgery should be considered as optional treatment for patients with T2DM

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and BMI 30–35 kg/m<sup>2</sup>. Considering the characteristics of Asian patients, the BMI threshold should be reduced by 2.5 kg/m<sup>2</sup> [9]. It is reported that the improvement of T2DM after metabolic surgery often occurs before any significant weight loss [10]. Therefore, the effectiveness of metabolic surgery to treat patients with T2DM and low BMI is of more and more interest. A meta-analysis was conducted to research clinical value of metabolic surgery on patients with T2DM and low BMI [11]; however, focusing on Asian population may be more valuable and significant.

In this study, we attempted to analyze the research on the effect of metabolic surgery on Asian patients with T2DM and BMI < 30 kg/m<sup>2</sup> so as to explore and identify whether metabolic surgery could be chosen to treat T2DM for Asian patients with BMI < 30 kg/m<sup>2</sup>.

## Methods

### Search Strategy

We performed a literature search in Medline, Embase, and the Cochrane Library from January 2000 to March 2018. The main search terms were as follows: “metabolic surgery or bariatric surgery or obesity surgery or Roux-en-Y or gastric bypass or sleeve gastrectomy or gastric banding or biliopancreatic diversion or duodenal-jejunal bypass or jejunoileal bypass” and “diabetes or diabetes mellitus or type 2 diabetes or T2DM” and “non-obese or overweight or low BMI or body mass index <30 kg/m<sup>2</sup> or normal weight.” We chose the research from Asian countries or regions and also manually screened the references from the included articles.

### Inclusion and Exclusion Criteria

The following criteria were used for inclusion: (1) patients with T2DM and baseline BMI < 30 kg/m<sup>2</sup> undergoing metabolic surgery; (2) studies that provided at least one of the outcomes of interest; (3) studies reported by the same institution, the most recent or the larger sample size study was included; (4) studies published in English. The exclusion criteria were as follows: (1) case reports, letters, comments, conference proceedings, review articles, meta-analyses, abstracts only; (2) lack of plasma glucose indices or the evaluation of glycemic improvement; (3) patients lost to follow-up. After removing excluded abstracts, the same criteria were used to screen the full text of the remaining articles.

### Data Extraction and Quality Assessment

Two reviewers independently extracted the data from the included studies, and discrepancies were resolved by a third investigator. Basic characteristics of each trial were as follows:

the first author, year of publication, country or region, study design, operation type, sample size, gender composition, mean age, diabetes duration, follow-up duration. The following indices were extracted at baseline and follow-up: body mass index (BMI), waist circumference, fasting plasma glucose (FPG), 2-h postprandial plasma glucose (2hPG), glycated hemoglobin A1c (HbA1c), fasting insulin, fasting C-peptide, homeostatic model of insulin resistance (HOMA-IR), total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-c), low-density lipoprotein cholesterol (LDL-c), and fasting glucagon-like peptide 1 (GLP-1). All relevant tables and figures were reviewed for exact data extraction.

Newcastle-Ottawa Scale was used to assess the quality and risk of bias, which consists of three factors: patient selection, comparability, and outcome. Funnel plots were used to estimate potential publication bias.

### Statistical Analysis

Analyses were conducted using the summarized data from the available studies with Review manager 5.3 software. The weighted mean difference (WMD) and 95% confidence intervals (CI) were used to assess the continuous data and statistical heterogeneity was tested by the chi-square test. If there was a significant heterogeneity among the included studies ( $P < 0.10$ ,  $I^2 > 50\%$ ), the random effects model should be used to calculate the WMD and 95% CI; otherwise, the fixed effects model is used. A  $P$  value < 0.05 was considered to be statistically significant. Publication bias analysis was performed using the software Stata, version 12.0.

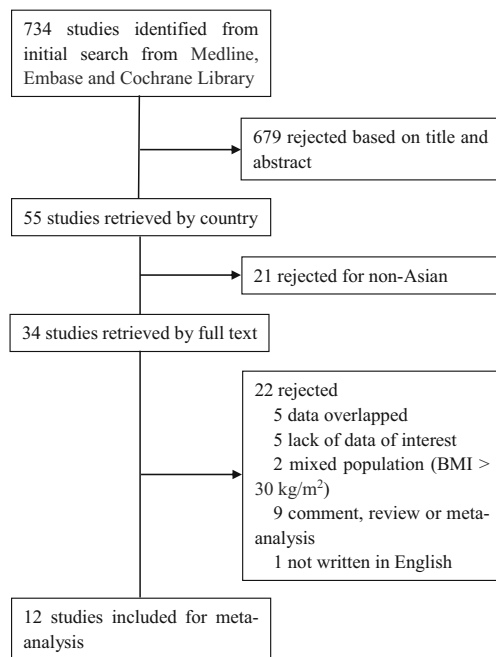
## Results

### Search Results

A flow diagram of the studies selection is provided in Fig. 1. The initial searches brought about 734 articles, of which 679 articles were rejected on the base of title and abstract. Of the remaining 55 articles, 21 were excluded for non-Asian papers. After a full-text review, 22 studies were rejected, of which 5 were replications of the same data, 5 were lack of adequate data, 2 had mixed population, 9 were comments, reviews, or meta-analyses, and 1 was not written in English. In total, 12 studies were included in final meta-analysis [12–23]. The basic characteristics of the included studies were showed in Table 1.

### Quality Assessment

The quality assessments of the included studies are showed in Table 2. As the included studies were not randomized



**Fig. 1** Study selection

controlled trials or even cohort studies, the quality was generally low. Inclusion criteria of patients in some studies were not BMI < 30 kg/m<sup>2</sup>, which may lack of representativeness.

## Systematic Review

The 12 studies were prospective or retrospective studies, involving 697 patients with T2DM, of which 8 from China, 2 from Taiwan, and 2 from Korea. Different kinds of surgical procedures were investigated: Roux-en-Y gastric bypass (RYGB) in ten studies, duodenojejunal bypass (DJB) in one,

sleeve gastrectomy (SG) in one, and single anastomosis gastric bypass (SAGB) in one study. The follow-up time ranged from 6 months to 3 years. One study had a 98.5% follow-up rate at 1 year after surgery, but got back to 100% at 3 years postoperatively [14]. One study had 48.4% follow-up rate at 1 year [16]. In another one, there were 37.8%, 62.2%, and 86.7% patients lost to follow-up at 12, 24, and 36 months, respectively, after surgery [18]. The other nine studies have a 100% follow-up rate.

## Meta-analyses

### BMI

Of all the articles, three studies reported mean changes in BMI at half a year after surgery. According to the WMD calculation, the BMI reduction was 3.92 kg/m<sup>2</sup> (95% CI 2.01–5.83 kg/m<sup>2</sup>,  $P < 0.0001$ ) (Fig. 2a). Changes in BMI at 1 year after surgery were pooled for nine studies, and the reduction was 2.88 kg/m<sup>2</sup> (95% CI 1.47–4.30 kg/m<sup>2</sup>,  $P < 0.0001$ ) (Fig. 2b). As the heterogeneity among studies was obvious ( $P < 0.00001$ ), the random effects model was applied in both analyses.

### Waist Circumference

There was no statistical significance in waist circumference changes at half a year after surgery ( $P = 0.16$ ) (Fig. 3a). Changes in waist circumference at 1 year after surgery were available for five studies. The reduction of waist circumference was 12.92 cm (95% CI 8.62–17.21 cm,  $P < 0.00001$ ) (Fig. 3b) in the random effects model.

**Table 1** Basic characteristics of the included studies

Included study	Region	Study design	Type of surgery	Sample size (male/female)	Mean age (years)	Diabetes duration (years)	Follow-up period (months)
Chen 2014 [12]	China	Retrospective	RYGB	35 (22/13)	45.3 ± 8.5	3.7 ± 2.4	12
Cui 2015 [13]	China	Retrospective	RYGB	58 (36/22)	48.5 ± 12.3	< 15	12
Di 2016 [14]	China	Retrospective	RYGB	66 (28/38)	50.4 ± 11.4	8.9 ± 5.2	36
Gong 2017 [15]	China	Prospective	RYGB	31 (14/17)	46.2 ± 11.1	8.3 ± 5.7	6
Heo 2013 [16]	Korea	Prospective	DJB	31 (19/12)	46.6 ± 7.7	8.3 ± 4.7	12
Ke 2017 [17]	China	Retrospective	RYGB	47 (26/21)	47.45 ± 8.69	5.58 ± 4.40	24
Kim 2014 [18]	Korea	Prospective	SAGB	172	46 ± 11	9.6 ± 5.2	36
Lee 2015 [19]	Taiwan	Prospective	GB/SG	80 (30/50)	47.7 ± 9.1	6.5 ± 5.1	12
Liang 2015 [20]	China	Prospective	RYGB	80 (37/43)	48.52	7	12
Malapan 2014 [21]	Taiwan	Prospective	RYGB	29 (13/16)	53	10.4	12
Wang 2016 [22]	China	Retrospective	RYGB	40 (25/15)	49.13 ± 8.15	5.82 ± 2.85	24
Yin 2014 [23]	China	Retrospective	RYGB	28 (8/20)	51.6	9.6	12

DJB duodenojejunal bypass, GB gastric bypass, RYGB Roux-en-Y gastric bypass, SAGB single anastomosis gastric bypass, SG sleeve gastrectomy

**Table 2** Quality assessment of the included studies for meta-analysis using Newcastle-Ottawa Scale (NOS)

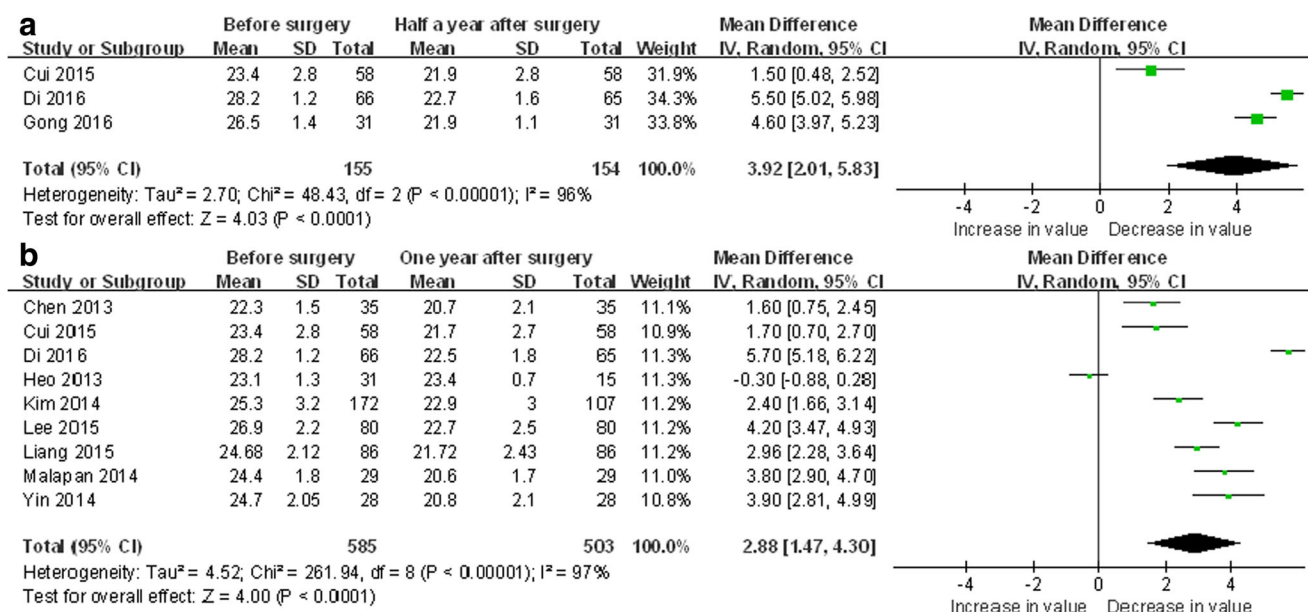
Studies	Selection			Comparability	Exposure		
	Representativeness of the patients	Ascertainment of exposure	Outcome not present at start		Assessment of outcome	Adequate follow-up period ( $\geq 1$ year)	Adequacy of follow-up
Chen 2014 [12]	No	Yes	Yes	Yes	Yes	Yes	Yes
Cui 2015 [13]	No	Yes	Yes	Yes	Yes	Yes	Yes
Di 2016 [14]	Yes	Yes	Yes	Yes	Yes	Yes	No
Gong 2017 [15]	No	Yes	Yes	Yes	Yes	No	Yes
Heo 2013 [16]	No	Yes	Yes	Yes	Yes	Yes	No
Ke 2017 [17]	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Kim 2014 [18]	Yes	Yes	Yes	Yes	Yes	Yes	No
Lee 2015 [19]	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Liang 2015 [20]	No	Yes	Yes	Yes	Yes	Yes	Yes
Malapan 2014 [21]	No	Yes	Yes	Yes	Yes	Yes	Yes
Wang 2016 [22]	No	Yes	Yes	Yes	Yes	Yes	Yes
Yin 2014 [23]	No	Yes	Yes	Yes	Yes	Yes	Yes

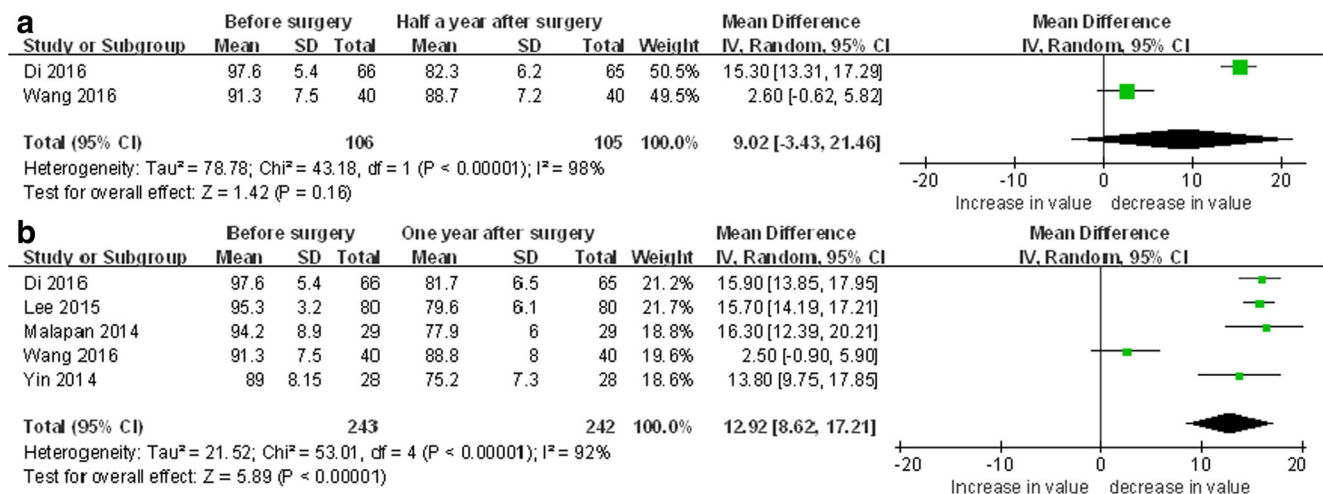
### Fasting Plasma Glucose

Of the 12 studies, several reported the changes of FPG at the three time points after surgery. The level of FPG decreased by 3.13 mmol/L (95% CI 1.62–4.65 mmol/L,  $P < 0.0001$ ) (Fig. 4a) at half a year after surgery, 3.22 mmol/L (95% CI 2.19–4.24 mmol/L,  $P < 0.00001$ ) (Fig. 4b) at 1 year after surgery, and 1.99 mmol/L (95% CI 1.16–2.82 mmol/L,  $P < 0.00001$ ) (Fig. 4c) at 2 years after surgery. The random effects model was used in these analyses.

### 2-h Postprandial Plasma Glucose

The level of 2hPG decreased by 5.46 mmol/L (95% CI 3.23–7.69 mmol/L,  $P < 0.00001$ ) (Fig. 5a) at half a year after surgery, 6.46 mmol/L (95% CI 4.54–8.39 mmol/L,  $P < 0.00001$ ) (Fig. 5b) at 1 year after surgery, and 5.84 mmol/L (95% CI 2.55–9.13 mmol/L,  $P = 0.0005$ ) (Fig. 5c) at 2 years after surgery. All three analyses were in the random effects model.

**Fig. 2** Forest plots of BMI changes after bariatric surgery: **a** half a year after surgery; **b** 1 year after surgery

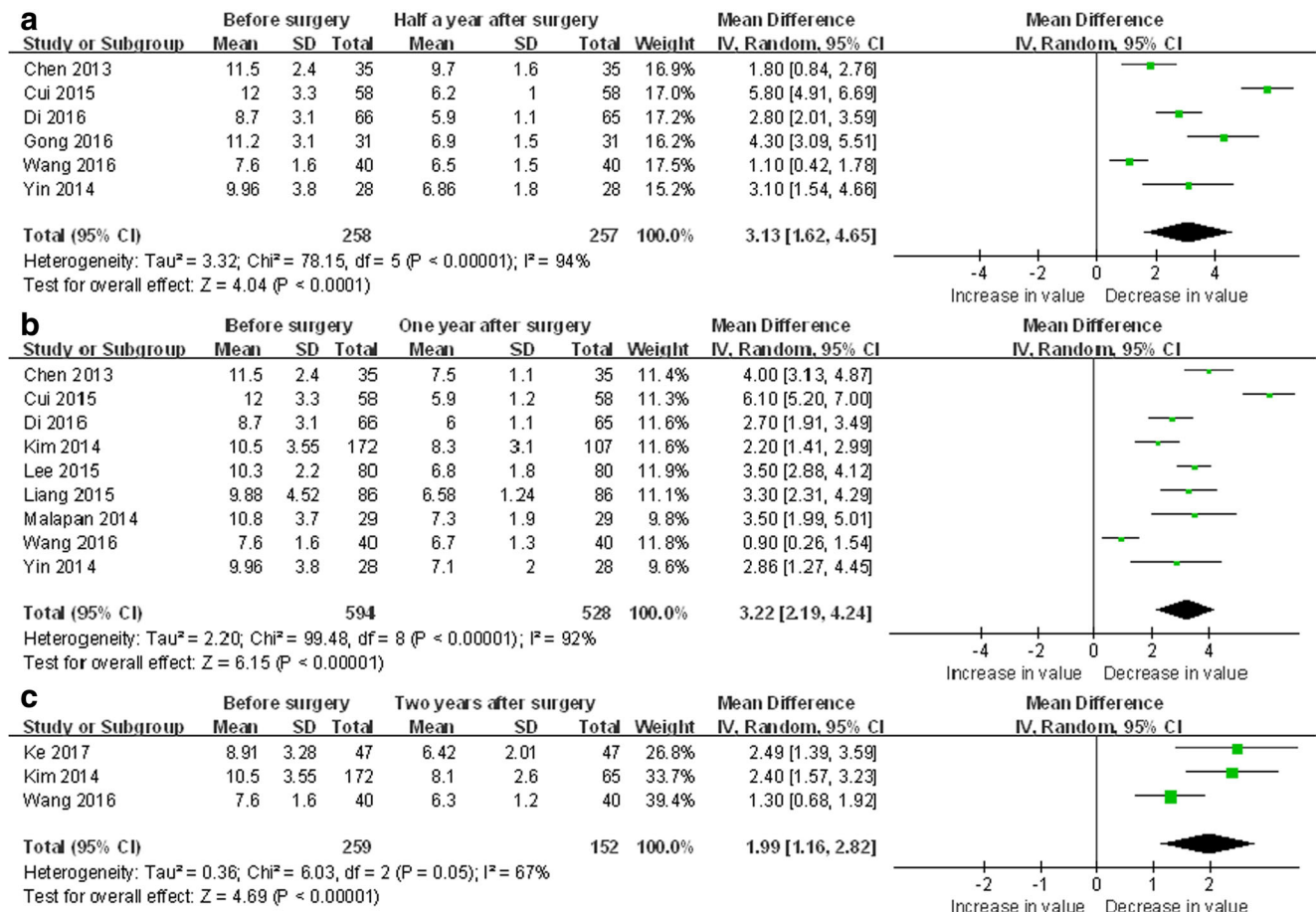


**Fig. 3** Forest plots of waist circumference changes after bariatric surgery: **a** half a year after surgery; **b** 1 year after surgery

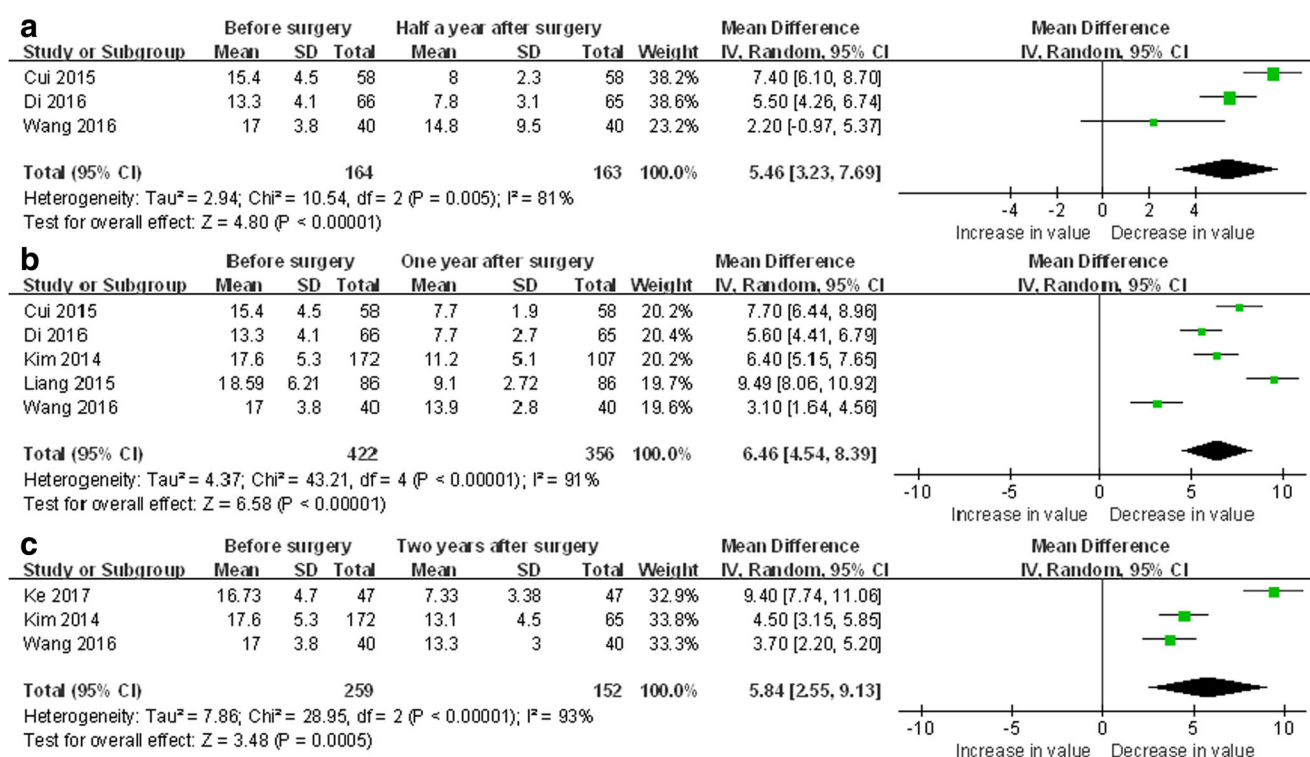
### HbA1c

As an important index to estimate the prognosis of T2DM, most articles reported the changes of HbA1c. The HbA1c reduction at half a year after surgery was 2.13% (95% CI

1.29–2.97%,  $P < 0.00001$ ) (Fig. 6a), 1 year after surgery was 2.38% (95% CI 1.75–3.01%,  $P < 0.00001$ ) (Fig. 6b), and 2 years after surgery was 1.58% (95% CI 0.59–2.57%,  $P = 0.002$ ) (Fig. 6c). After the heterogeneity test, the random effects model was used.



**Fig. 4** Forest plots of fasting plasma glucose changes after bariatric surgery: **a** half a year after surgery; **b** 1 year after surgery; **c** 2 years after surgery



**Fig. 5** Forest plots of 2-hour postprandial plasma glucose changes after bariatric surgery: **a** half a year after surgery; **b** 1 year after surgery; **c** 2 years after surgery

## Insulin

The reduction of insulin was  $1.70 \mu\text{U/ml}$  (95% CI  $0.62$ – $2.78 \mu\text{U/ml}$ ,  $P = 0.002$ ) (Fig. 7b) at 1 year after surgery in the fixed effects model. There was no statistical significance in changes at half a year ( $P = 0.08$ ) (Fig. 7a) and 2 years ( $P = 0.44$ ) (Fig. 7c) after surgery.

## C-peptide

The C-peptide reduction at half a year after surgery was  $0.70 \text{ ng/ml}$  (95% CI  $0.50$ – $0.89 \text{ ng/ml}$ ,  $P < 0.00001$ ) (Fig. 8a) and at 2 years after surgery was  $0.40 \text{ ng/ml}$  (95% CI  $0.13$ – $0.67 \text{ ng/ml}$ ,  $P = 0.004$ ) (Fig. 8c). Both of the analyses used the fixed effects model. However, the change of C-peptide at 1 year after surgery had no statistical significance ( $P = 0.17$ ) (Fig. 8b).

## HOMA-IR

According to the WMD calculation, there was no statistical significance in the changes of HOMA-IR within 2 years after surgery ( $P > 0.05$ ) (Fig. 9a–c).

## GLP-1

Of all the articles, several studies reported mean changes in fasting GLP-1. The level of GLP-1 increased by  $2.48 \text{ pmol/L}$

(95% CI  $1.25$ – $3.72 \text{ pmol/L}$ ,  $P < 0.0001$ ) at half a year after surgery in the random effects model (Fig. 10a), and increased by  $4.00 \text{ pmol/L}$  (95% CI  $1.55$ – $6.45 \text{ pmol/L}$ ,  $P = 0.001$ ) at 1 year after surgery in the random effects model (Fig. 10b).

## Lipid Metabolic Parameters

The lipid metabolic parameters are shown in Table 3. The total cholesterol, triglycerides, and LDL-C reduced by  $0.67 \text{ mmol/L}$  (95% CI  $0.19$ – $1.16 \text{ mmol/L}$ ,  $P = 0.007$ ),  $1.31 \text{ mmol/L}$  (95% CI  $0.76$ – $1.85 \text{ mmol/L}$ ,  $P < 0.00001$ ), and  $0.35 \text{ mmol/L}$  (95% CI  $0.06$ – $0.64 \text{ mmol/L}$ ,  $P = 0.02$ ), respectively, at half a year after surgery, and decreased by  $0.65 \text{ mmol/L}$  (95% CI  $0.47$ – $0.83 \text{ mmol/L}$ ,  $P < 0.00001$ ),  $1.07 \text{ mmol/L}$  (95% CI  $0.74$ – $1.39 \text{ mmol/L}$ ,  $P < 0.00001$ ), and  $0.42 \text{ mmol/L}$  (95% CI  $0.21$ – $0.64 \text{ mmol/L}$ ,  $P < 0.0001$ ), respectively, at 1 year after surgery. The level of HDL-C increased by  $0.08 \text{ mmol/L}$  (95% CI  $0.01$ – $0.14 \text{ mmol/L}$ ,  $P = 0.02$ ) at half a year after surgery in the fixed effects model, and increased by  $0.20 \text{ mmol/L}$  (95% CI  $0.10$ – $0.29 \text{ mmol/L}$ ,  $P < 0.0001$ ) at 1 year after surgery in the random effects model.

## Publication Bias

As HbA1c is the most important outcome of interest, Fig. 11 shows a funnel plot of the studies included in this meta-analysis that reported mean changes in HbA1c at year 1 visit.

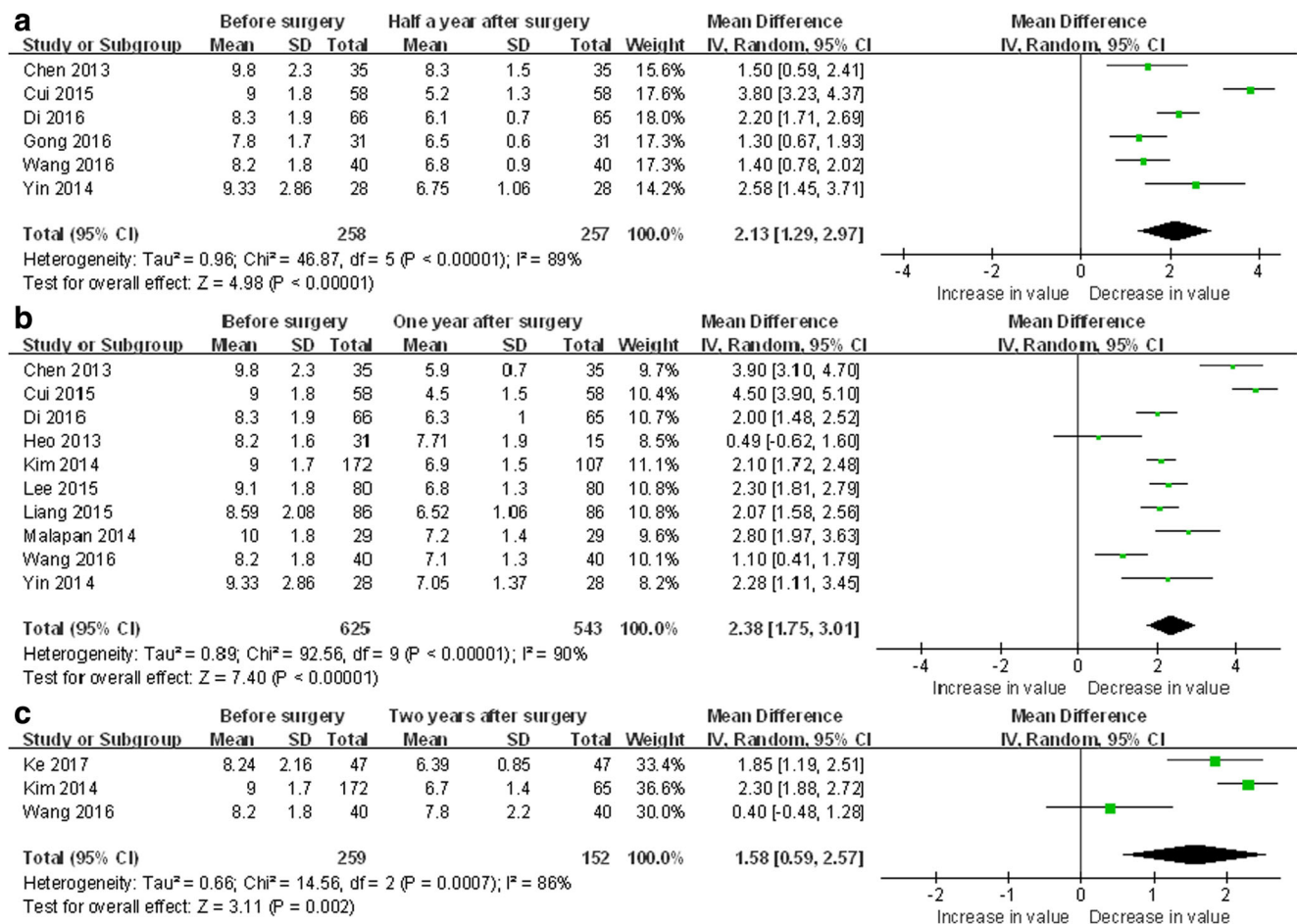


Fig. 6 Forest plots of HbA1c changes after bariatric surgery: **a** half a year after surgery; **b** 1 year after surgery; **c** 2 years after surgery

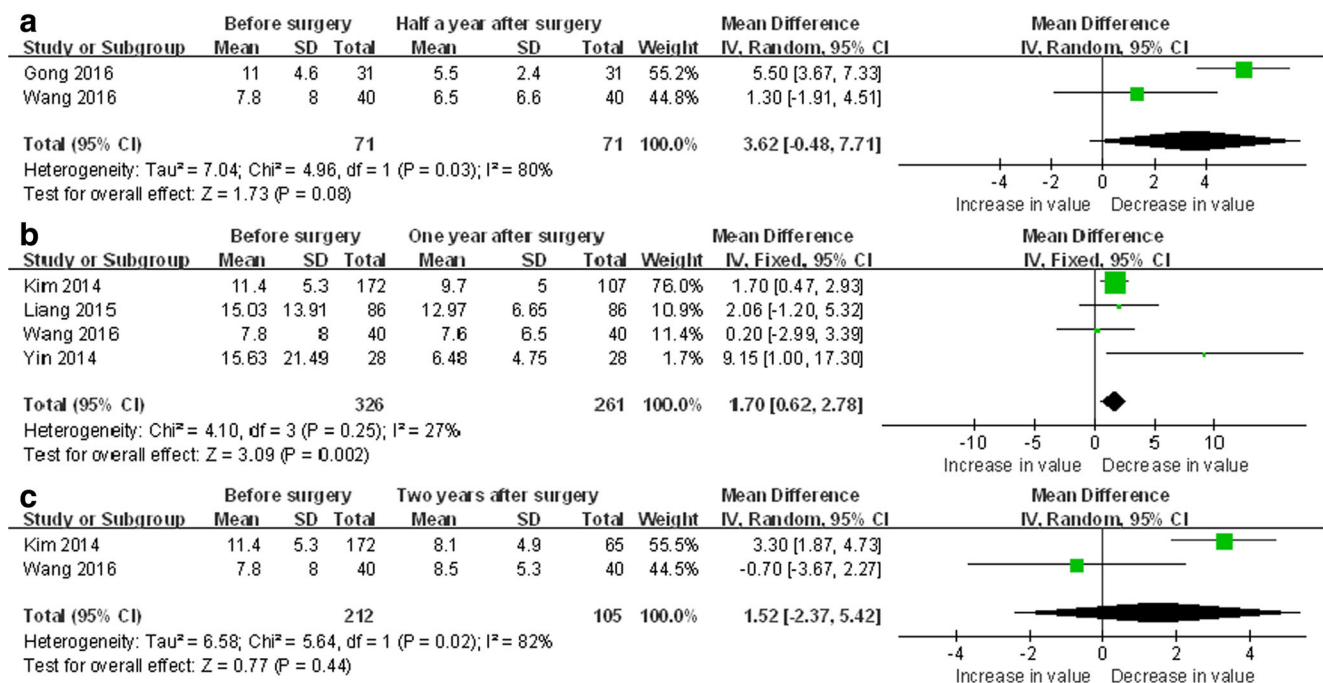
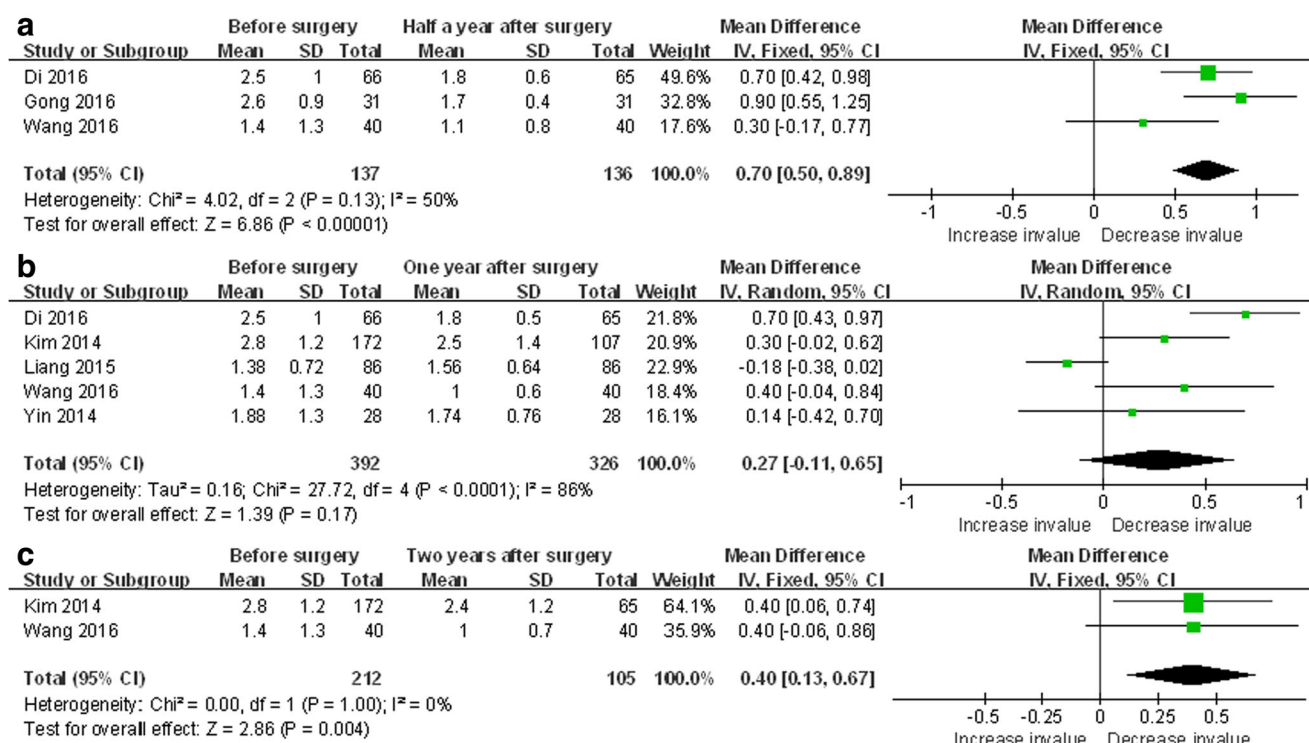


Fig. 7 Forest plots of insulin changes after bariatric surgery: **a** half a year after surgery; **b** 1 year after surgery; **c** 2 years after surgery



**Fig. 8** Forest plots of C-peptide changes after bariatric surgery: **a** half a year after surgery; **b** 1 year after surgery; **c** 2 years after surgery

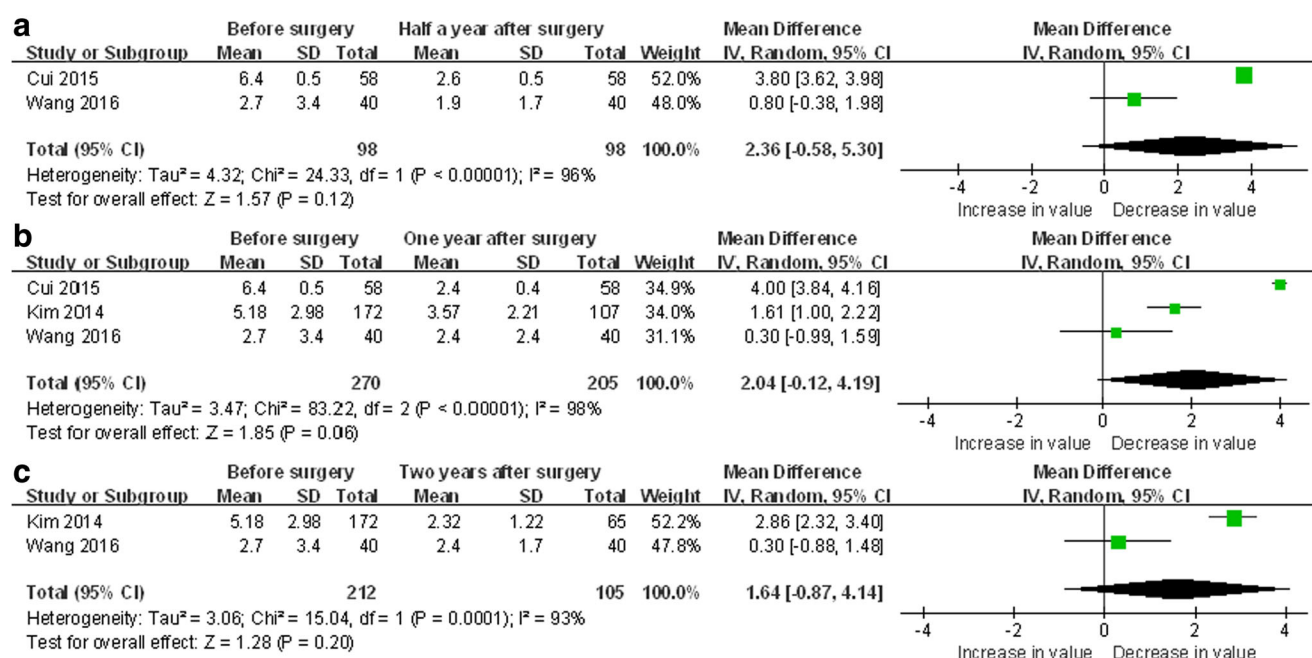
Not all studies lie inside the 95% CIs, indicating obvious publication bias.

## Discussion

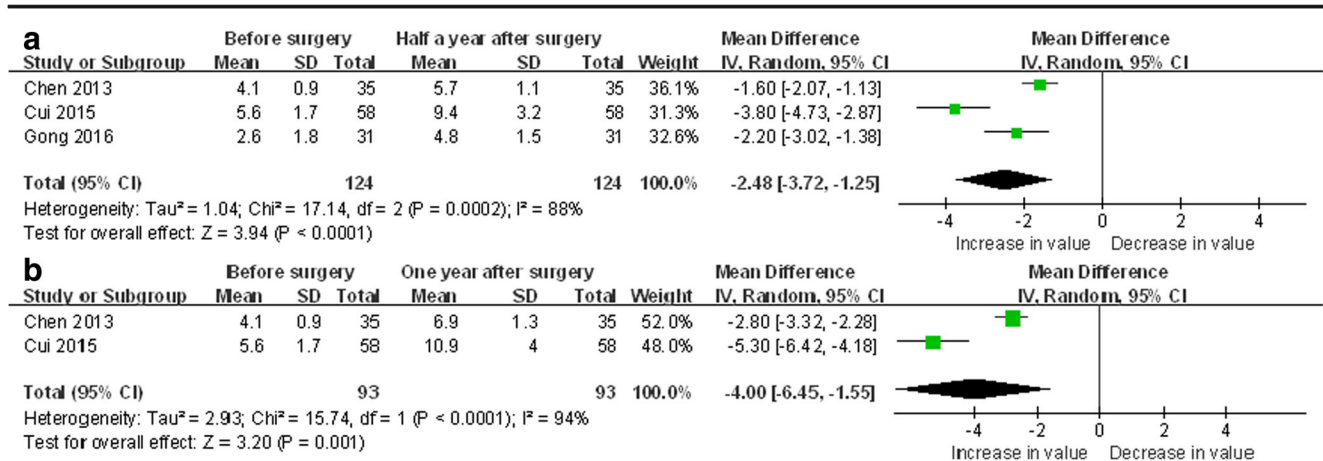
This meta-analysis of 6 prospective and 6 retrospective studies including 697 patients comparing the changes of indexes

before and after operation showed that bariatric surgery significantly reduced BMI, FPG, 2hPG, HbA1c, total cholesterol, triglycerides, and LDL-C while increased GLP-1 and HDL-c. We found no significant changes in waist circumference, insulin, C-peptide, and HOMA-IR at several time points after surgery.

T2DM is now one of the most important global health problems. More than 60% of the diabetes population comes



**Fig. 9** Forest plots of HOMA-IR changes after bariatric surgery: **a** half a year after surgery; **b** 1 year after surgery; **c** 2 years after surgery



**Fig. 10** Forest plots of GLP-1 changes after bariatric surgery: **a** half a year after surgery; **b** 1 year after surgery

from Asia and, at the same time, the incidence of T2DM is increasing more rapidly than that of other continents [8]. T2DM is a chronic disease characterized by insulin resistance and pancreatic islet dysfunction. As obesity is a well-known cause of insulin resistance, to maintain weight and diet balance is of importance, but with limited effect. In East Asians, the predominant pathogenic factor for T2DM patients with high BMI is insulin resistance, while  $\beta$ -cell dysfunction is predominant in patients with low BMI [24].

A large amount of studies have confirmed that bariatric surgery could not only treat morbid obesity, but also ameliorate blood glucose in patients with T2DM. A total of 1160 patients with obesity, of which 240 were diagnosed with T2DM, underwent laparoscopic gastric bypass surgery and 83% of these patients got improvement of blood glucose levels [25]. It was found that the remission of T2DM was 82%–98% in a retrospective analysis of 3568 patients with obesity treated with gastric bypass surgery [26]. A meta-

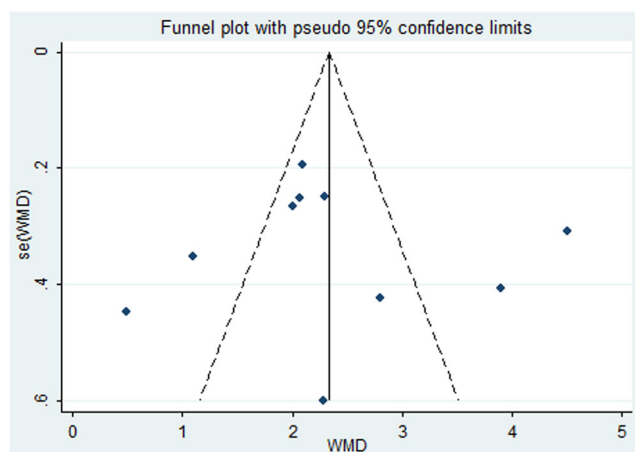
analysis of 22,094 cases showed that the long-term remission and improved glucose tolerance were 83.7% and 98.9%, respectively, of patients with obesity and T2DM [27]. The effectiveness of bariatric surgery on this population is worldwide acknowledged; however, whether this treatment is supposed to be recommended for non-obese patients with T2DM has not been universally recognized.

Compared with mildly obese and morbidly obese patients, the non-obese patients have a lower remission of T2DM. Lee et al. reported that non-obese ( $BMI < 30 \text{ kg/m}^2$ ), mild obese ( $BMI 30\text{--}35 \text{ kg/m}^2$ ), and morbid obese ( $BMI > 35 \text{ kg/m}^2$ ) T2DM patients who underwent bariatric surgery resulted in 25.0%, 49.5%, and 79.0% remission rate [19]. A systematic review reported that bariatric surgery is safe and effective in T2DM patients with a  $BMI < 35 \text{ kg/m}^2$ , as the remission rate was 85.3% [28]. However, among patients with a  $BMI < 30 \text{ kg/m}^2$ , 42.2%, 37%, and 37.2% patients achieved a HbA1c levels of  $< 6\%$ ,  $< 6.5\%$ , and  $< 7\%$ , respectively, during

**Table 3** Results of meta-analysis of lipid metabolic parameters

Outcomes of interest	Number of studies	Patients before surgery	Patients after surgery	WMD (95% CI)	P value	Study heterogeneity			
						$\chi^2$	df	$I^2$ , %	P value
Total cholesterol									
Half a year	2	106	105	0.67 (0.19–1.16)	0.007	3.41	1	71	0.06
One year	5	243	242	0.65 (0.47–0.83)	< 0.00001	5.57	4	28	0.23
Triglycerides									
Half a year	3	137	136	1.31 (0.76–1.85)	< 0.00001	0.49	2	0	0.78
One year	4	214	213	1.07 (0.74–1.39)	< 0.00001	5.96	3	50	0.11
HDL-C									
Half a year	3	137	136	− 0.08 (− 0.14 to − 0.01)	0.02	1.20	2	0	0.55
One year	5	243	242	− 0.20 (− 0.29 to − 0.10)	< 0.0001	9.94	4	60	0.04
LDL-C									
Half a year	3	137	136	0.35 (0.06–0.64)	0.02	5.34	2	63	0.07
One year	5	243	242	0.42 (0.21–0.64)	< 0.0001	7.78	4	49	0.10

*HDL-c* high-density lipoprotein cholesterol, *LDL-c* low-density lipoprotein cholesterol, *WMD* weighted mean difference, *df* degrees of freedom



**Fig. 11** Funnel plot for assessing publication bias. SE, standard error

short-term follow-up in another systematic review [11]. According to American Diabetes Association (ADA), the remission of T2DM was defined as a return to normal measures of glucose metabolism (HbA1c in the normal range, FPG < 5.6 mmol/L) at least 1 year without pharmacologic therapy or ongoing procedures [29]. The remission rate for bariatric surgery was lower with the new definition than with the previously used one [30]. Although the remission of T2DM standards was not exactly the same in above studies, BMI is also one of the important inclusion criteria for patients who would receive bariatric surgery. However, in Asian population, the percentage of T2DM patients with BMI  $\geq 35$  kg/m<sup>2</sup> is only 2%, and approximately 10% with BMI  $\geq 30$  kg/m<sup>2</sup> [31]. That is to say, just using BMI as a surgical standard for patients with T2DM may be a lack of practicability. Besides BMI, the assessment indicators including C-peptide and insulin resistance should be considered. Therefore, to find the potential effects of bariatric surgery on T2DM patients with normal BMI is of great significance for Asian population, which may finally break free the constraints of BMI standard for bariatric surgery.

It is necessary for both doctors and patients to identify the predictors of T2DM remission, so as to determine whether surgery is an effective measure to treat T2DM. In previous studies, four factors were reported to be independent predictors for glycemic control in non-obese Asian patients with T2DM following bariatric surgery, patient age, baseline BMI, fasting C-peptide, and disease duration [20, 32–34]. A multivariate analysis confirmed that ABCD score had significant predictive value on diabetes remission ( $P = 0.003$ ) [19]. Older age, lower BMI, lower baseline fasting C-peptide, and longer duration of T2DM reduce the likelihood of response to bariatric surgery. Although most studies demonstrated the importance of baseline BMI and weight loss on T2DM remission in non-obese patients, no relation between BMI and glycemic outcome was observed in several studies [20, 35]. C-peptide is a surrogate marker for insulin secretion and may reflect the

residual  $\beta$ -cell function [36, 37]. In terminal stage of T2DM,  $\beta$ -cell function is progressively destroyed and the C-peptide level becomes very low, which may be a contraindication for metabolic surgery. Aging and the duration of the disease reflect the natural process and deterioration of  $\beta$ -cell function [38]. Furthermore, individuals who underwent gastric bypass surgery got a higher remission rate of diabetes and lost more weight than other type of surgery [33]. Therefore, further research should be conducted to estimate these predictors for best selection for surgery, so as to change the guidelines for the treatment of patients with T2DM without the limitation of using BMI in the future.

This meta-analysis has several limitations. Our meta-analysis has a small number of studies, most of which have small sample sizes, and none of randomized controlled trials were included, so the quality was generally low. In addition, the effects of different types of surgery were not conducted sub-group analysis because of insufficient research. Further, heterogeneity was obvious in most analyses, and the pooled results in random effects model may be less convincing. Besides, as small number and insufficient test power of included studies, there was obvious publication bias. Lastly, individuals of Asian origin received bariatric surgery in the West have not been included in this meta-analysis.

## Conclusion

Based on the current meta-analysis, T2DM Asian patients with BMI < 30 kg/m<sup>2</sup> could achieve significant improvement in weight, glycemic control, lipid profiles, and  $\beta$ -cell function in short and medium terms after bariatric surgery. Bariatric surgery may be recommended for non-obese T2DM Asian patients, but long-term follow-up and randomized controlled trials are necessary to evaluate the effectiveness of bariatric surgery in such population.

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## Compliance with Ethical Standards

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

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