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Effect of bariatric surgery on atherogenicity and insulin resistance in patients with obesity class II: a prospective study

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ABSTRACT

Objective Enormous efforts have been made to evaluate reliable, simple and practical indicators for predicting patients at risk of progression of cardiovascular disease events, whereby bariatric surgery has remained understudied. Thus, we performed this study to assess the effect of bariatric surgery procedures on atherogenicity and insulin resistance indicators.

Design Cohort study.

Setting, participants and outcome measures Four hundred and forty-three class II obese (severely obese) patients who underwent sleeve gastrectomy, Roux-en-Y gastric bypass, or one anastomosis gastric bypass were followed up for 12 months after surgery. Atherosclerosis-related indicators were evaluated at baseline, as well as 6 and 12 months after surgery.

Results Atherogenic index of plasma, lipoprotein combine index, atherogenic coefficient, cholesterol index, Castelli's risk indices I and II, and triglyceride to high-density lipoprotein-cholesterol ratio (p<0.01) improved after 12 months. Additionally, bariatric surgery yielded a significantly reduced triglyceride glucose index. There was no significant difference between procedures in terms of indicators. The Spearman correlation test showed a significant inverse correlation between weight plus fat mass and atherosclerosis-related indicators as well as a positive correlation between percentage of excess weight loss and these indicators.

Conclusions This study demonstrated three bariatric surgery procedures' ability to improve atherogenicity and insulin resistance in patients with obesity class II. The anti-atherogenicity effects can be partly assigned to the reduction of body weight and adipose tissue. Nevertheless, further studies with larger sample sizes and longer follow-ups are required to confirm our results.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ Our study is a large prospective study of patients undergoing bariatric surgery.
- ⇒ The included patients were followed for a relatively long period.
- ⇒ Simple and practical indicators were used for evaluating the impact of bariatric surgery on atherogenicity and insulin resistance.
- ⇒ Lack of a not matched control group was a limitation of our study.
- ⇒ The other limitation was lack of randomisation.

INTRODUCTION

Obesity, characterised by increased fat mass (FM) percentage, is a multifactorial chronic disease that has become epidemic worldwide.[1 2] Ample evidence has shown that obesity is responsible for massive economic and psychosocial burden on the healthcare system and is widely considered a leading public health concern; thus, it is essential to provide effective interventions for controlling and managing obesity as well as related consequences.[2–4] Due to the high prevalence of metabolic abnormalities, especially atherogenic dyslipidaemia, insulin resistance, chronic inflammation and hypertension, obesity is known as one of the substantial risk factors for increased cardiovascular disease (CVD) morbidity and mortality.[5 6]

Accumulated evidence suggests that obesity might be linked to elevated concentrations of atherogenic particles such as small, dense low-density lipoprotein cholesterol (sdLDL-C), apo-β, etc, causing higher risk of premature atherosclerosis and ensuing mortality.[7 8] There is a growing trend toward severe atherosclerosis in obese patients; however, the conventional lipid profile cannot reflect accurate information on prognosis, initiation and severity of atherosclerosis.[9 10] Thus, it is critical in clinical settings to detect and use indicators that are more practical and effective in predicting atherosclerosis when compared with traditional ones even when other indicators are within the normal range.[9 11] Recently, studies have offered several new indicators

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such as ATS-related indicators including the atherogenic index of plasma (AIP), triglyceride glucose (TyG) index, lipoprotein combine index (LCI), atherogenic coefficient (AC), cholesterol index (CHOLINDEX), Castelli's risk indices I and II (CRI-I and CRI-II), and triglyceride (TG) to high-density lipoprotein-cholesterol (HDL-C) ratio, which can predict the risk of CVD among the high-risk population.[11–14] It is also acknowledged that these indicators potentially reflect low-density lipoprotein-cholesterol (LDL-C) and sdLDL-C levels as well as progression of atherosclerosis and CVD events.[9 13–15] Evidence has shown that sdLDL-C particles are more atherogenic in comparison to larger LDL-C, since they have a high ability to penetrate the arterial wall, lower tendency to LDL-C receptors, lower resistance to oxidative stress and longer half-life.[16] In addition, these particles are associated with higher risk of obesity, type 2 diabetes mellitus and CVD.[17] Thus, evaluation of sdLDL-C might be useful in clinical practice, but it is not cost effective and may represent some technical limitations.[13]

Bariatric surgery is the most effective and enduring therapy for treatment of patients with obesity class II (severely obese); unlike other interventions, it is a promising option in clinical practice because of achieving and maintaining weight loss as well as treatment of related comorbidities in the long-term including atherogenic dyslipidaemia and insulin resistance, and improving endothelial dysfunction.[8 18 19]

Given the strong association between obesity and atherosclerosis-related risk factors such as atherogenic dyslipidaemia and insulin resistance, and due to the remarkable effects of bariatric surgery on these risk factors, we decided to evaluate the effect of bariatric surgery on atherogenicity and insulin resistance. Second, this study wanted to explore the impact of bariatric surgery procedures on atherosclerosis-related indicators 12 months after-surgery in patients with severe obesity. Finally, we aimed to assess whether these possible effects of bariatric surgery were correlated to weight loss.

METHODS

Initially, 443 patients with obesity class II who underwent bariatric surgery in Taleghani hospital (Shahid Beheshti University of Medical Sciences (SBMU), Tehran, Iran) were included in this cohort study. Table 1 reports the inclusion criteria which required class II obese patients aged between 18 and 55 years, having a body mass index (BMI) of 35–55 kg/m^2, and having undergone a sleeve gastrectomy (SG), Roux-en-Y gastric bypass (RYGB) or one anastomosis gastric bypass (OAGB) for the first time. Patients were excluded because of unwillingness to participate, adherence to a specific diet, having a history of experiencing CVD events, liver diseases, renal disorders, cancer, infectious diseases, immunity disorders, type 1 diabetes, any inflammatory diseases and pregnancy. Additionally, taking herbal medicine, anti-inflammatory drugs (corticosteroids and non-steroidal anti-inflammatory drugs such as ibuprofen, naproxen, diclofenac and celecoxib), medications that are known to impact lipids such as Statins, Fibrate, Orlistat, glucagon-like peptide-1 agonist therapy (GLP-1A) and hypoglycaemic agents like SGLT2 sodium-glucose co-transporters-2 inhibitors, dipeptidyl peptidase-4 inhibitor, GLP-1A, insulin, metformin and drinking alcohol for more than 30 g/day, were considered as exclusion criteria.

Table 1 Inclusion and exclusion criteria for participants in this study

Inclusion criteria	Exclusion criteria
Class II obese patients	Declined to participate
Aged between 18 and 55 years old	Adherence to a specific diet
Having a BMI of 35–55 kg/m^2	History of CVD events
Undergoing a sleeve gastrectomy, Roux-en-Y gastric bypass or one anastomosis gastric bypass	Liver diseases, renal disorders, cancer and type 1 diabetes mellitus
	Infectious diseases, immunity diseases, any inflammatory diseases
	Pregnancy
	Taking herbal medicine, anti-inflammatory drugs (NSAIDs, corticosteroids), insulin therapy

BMI, body mass index; CVD, cardiovascular disease; NSAIDs, non-steroidal anti-inflammatory drugs.

In this study, all patients who met the inclusion criteria were assessed by a medical team educated for bariatric surgery, including a surgeon, endocrinologist and nutritionist at baseline, as well as 6 and 12 months following bariatric surgery. According to the American Society for Metabolic and Bariatric Surgery guidelines, a trained nutritionist planned diets and educated patients on nutritional recommendations. They were advised by the trained nutritionist to follow a high protein, low-calorie liquid diet (600–800 kcal/day) for the first month after surgery and to add solid foods into their diet gradually. Thus, the caloric intake of patients increased to 800–1000 kcal/day and 1000–1200 kcal/day in the second and third months after bariatric surgery, respectively. For physical activity, the patients were advised and educated to start walking at a low speed and to increase their speed to the threshold limit gradually, according to the American College of Sports Medicine. Accordingly, the participants were asked to perform physical activity for 150–200 min/week for 3–5 days/week in the second-month postsurgery.

Anthropometric indices and body composition

The body weight, FM and fat-free mass (FFM) were measured to the nearest 0.1 kg using an InBody 370 body impedance analyzer (Biospace America). Accordingly, the patients were asked to keep fasted for at least 4–5 hours, avoid alcohol for a minimum of 24 hours, avoid exercise for more than 12 hours, maintain balanced hydration, lie down for at least 5 min before measurement, wear light clothes and take off their shoes. Their

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height was recorded to the nearest 0.5 cm via a stadiometer (Seca, Hamburg, Germany). Calculation of BMI was performed based on weight (in kilograms) to height (in square metre) ratio. The percentage of excess weight loss (%EWL) and percentage of total weight loss (%TWL) were defined using the following formulas:

%EWL=[(initial weight (kilograms)−weight on follow-up (kilograms))/(initial weight (kilograms)−ideal weight (kilograms)]×100.

%TWL=[(initial weight (kilograms)−weight on follow-up (kilograms))/(initial weight (kilograms))]×100.

Determination of the atherogenicity and insulin resistance indices

Fasting blood was obtained at the baseline, as well as 6 and 12 months after bariatric surgery. Biochemical indices were determined at the beginning and end of the study. Total cholesterol (TC), LDL-C, HDL-C and TG were assessed using Pars Azmoon kits (Pars Azmoon Kit). Serum glucose concentration was evaluated using the glucose oxidase method. The atherosclerosis-related indicators were assessed using fasting blood glucose and lipid profile components, including LDL-C, HDL-C, TC and TG. The following formulas were applied for atherogenicity and insulin resistance evaluation in class II obese patients who underwent surgery.

$$\text{CRII} = \frac{\text{Total cholesterol}\left(\frac{\text{mmol}}{\text{L}}\right)}{\text{HDL}-\text{C}\left(\frac{\text{mmol}}{\text{L}}\right)}$$

$$\text{CRI}-\text{II} = \frac{\text{LDL}-\text{C}\left(\frac{\text{mmol}}{\text{L}}\right)}{\text{HDL}-\text{C}\left(\frac{\text{mmol}}{\text{L}}\right)}$$

$$\text{Triglyceride to HDL}-\text{C ratio} = \frac{\text{Triglyceride}\left(\frac{\text{mmol}}{\text{L}}\right)}{\text{HDL}-\text{C}\left(\frac{\text{mmol}}{\text{L}}\right)}$$

$$\text{TyGindex} = \text{Ln}\left(\frac{\text{Fasting triglycerides}\left(\frac{\text{mg}}{\text{dl}}\right)\times\text{fasting glucose}\left(\frac{\text{mg}}{\text{dl}}\right)}{2}\right)$$

please correct this phrase: TyG index

$$\text{AC} = \frac{\text{Total cholesterol}\left(\frac{\text{mmol}}{\text{L}}\right)-\text{HDL}-\text{C}\left(\frac{\text{mmol}}{\text{L}}\right)}{\text{HDL}-\text{C}\left(\frac{\text{mmol}}{\text{L}}\right)}$$

$$\text{AIP} = \text{Log}_{10}\left(\frac{\text{Triglycerides}\left(\frac{\text{mmol}}{\text{L}}\right)}{\text{HDL}-\text{C}\left(\frac{\text{mmol}}{\text{L}}\right)}\right)$$

$$\text{LCI} = \frac{\text{Total cholesterol}\left(\frac{\text{mmol}}{\text{L}}\right)\times\text{triglycerides}\left(\frac{\text{mmol}}{\text{L}}\right)\times\text{LDL}-\text{C}\left(\frac{\text{mmol}}{\text{L}}\right)}{\text{HDL}-\text{C}\left(\frac{\text{mmol}}{\text{L}}\right)}$$

$$\text{CHOLINDEX} = \frac{\text{LDL}-\text{C}\left(\frac{\text{mmol}}{\text{L}}\right)-\text{HDL}-\text{C}\left(\frac{\text{mmol}}{\text{L}}\right)}{\text{HDL}-\text{C}\left(\frac{\text{mmol}}{\text{L}}\right)}$$

Statistical analysis

We used the statistical package for social sciences software V.20 (SPSS) for statistical analysis. The Kolmogorov-Smirnov test was used to determine the normal distribution of continuous variables (p>0.05). According to the normality of the data distribution, the results were described as mean±SD for continuous variables and as numbers and percentages (%) for categorical variables. The differences in characteristics between participants in three bariatric surgery procedures were examined using a one-way analysis of variance (ANOVA) test for continuous variables and a χ^2 test for categorical variables. Post-hoc (Bonferroni) analyses were performed to analyse the mean differences in continuous variables across three bariatric surgery procedures. To account for multiple testing for three bariatric surgery procedures, findings were considered statistically significant if they passed the Bonferroni cut-off of p<0.017 (α 0.05/3). One-way repeated measure ANOVA was used to compare differences of atherosclerosis-related indicators by the time points, at baseline, after 6 months and after 12 months of bariatric surgery procedures. Bivariate correlations were assessed with Spearman's rho correlation coefficient to examine the correlation between changes of %EWL, weight, FM and changes of atherosclerosis-related indicators over 12-month follow-up. A p value of <0.05 was considered as the level of significance for correlations.

Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

RESULTS

From June 2015 to October 2020, 443 (361 women and 82 men) obese patients who underwent bariatric surgery were recruited with a mean±SD age of 41.69±11.29 and a mean±SD weight of 120.17±17.77. Table 2 lists the characteristics of participants at baseline. Among these patients, 225 (50.7%) patients underwent SG, 90 (20.3%) underwent RYGB and 128 (28.9 %) underwent OAGB. At baseline, patients who underwent SG had a lower body weight, BMI, FM and FFM compared with the other procedures (p value <0.017).

After surgery, %TWL was 32.4%, and their BMI and FM significantly decreased at 6 months, with this reduction lasting for 12 months (table 3). FM declined after 6 and 12 months following bariatric surgery, where this reduction was higher in RYGB (32.97±9.19) and OAGB (30.93±7.69) than in SG (26.80±7.86). According to table 4, the mean weight, and BMI were significantly improved in RYGB and OAGB compared with the SG at 12 months. %TWL was significantly higher in RYGB compared with the SG. Additionally, %EWL significantly difference between OAGB and SG. RYGB did not show significant changes compared with OAGB at 12 months in terms of anthropometric indices. The anthropometric and body composition results indicated the effectiveness of SG, RYGB and OAGB in weight loss of patients with obesity class II.

The biochemical parameters in each time is presented in online supplemental table 1. There is no significant difference between the three procedures in atherosclerosis-related indicators at baseline, including CRI-I, CRI-II, TG to HDL-C ratio, TyG index, AIP, LCI, CHOLINDEX and AC. These indicators significantly improved during 6 and 12 months postsurgery (table 3). Improvements in atherosclerosis-related indicators were different at 12 months compared with 6 months after surgery. It was further observed that after 12 months, surgery could reduce the mean of CRI-I (3.20±0.79), CRI-II (1.81±0.63), TG to HDL-C ratio (0.80±0.32), TyG index (8.32±0.30), AIP (0.23±0.15), LCI (9.17±6.56), CHOLINDEX

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Table 2 Baseline characteristics of participations

Variable	SG	RYGB	OAGB	P value
Sex male	32 (%14.2)	17 (%18.88)	33 (%25)	0.027
Age	41.44±11.91	43.11±9.57	41.12±11.19	0.398
Height	1.62±0.08	1.63±0.09	1.64±0.09	0.130
Weight	116.74±15.98*	125.96±19.97	122±17.90	<0.001
BMI (kg/m^2)	44.23±4.24*	46.78±4.53	45.09±4.35†	<0.001
FM	56.85±9.49*	60.68±11.71	59.35±9.87	0.004
FFM	59.89±11.27*	65.27±12.89	62.64±12.77	0.001
CRI-I	4.23±1.16	4.13±1.17	4.28±1.26	0.651
CRI-II	2.35±0.82	2.31±0.80	2.44±0.90	0.496
TG to HDL-C ratio	1.47±0.78	1.40±0.68	1.52±0.84	0.541
TyG index	8.95±0.56	8.89±0.53	8.95±0.50	0.659
AIP	0.47±0.22	0.45±0.22	0.48±0.22	0.640
LCI	21.85±17.96	19.86±15.26	22.83±16.85	0.448
CHOLINDEX	1.35±0.82	1.31±0.80	1.44±0.90	0.496
AC	3.23±1.16	3.13±1.16	3.28±1.26	0.651

Data are means±SD for quantitative variables and frequency (%) for qualitative variables.
Analysis of variance for quantitative variables, χ^2 for qualitative variables.
P<0.017 were considered statistically significant after the Bonferroni correction.
*Significant difference between SG compared with RYGB.
†Significant difference between RYGB to OAGB.
‡Significant difference between SG compared with OAGB.
AC, atherogenic coefficient; AIP, atherogenic index of plasma; BMI, body mass index; CHOLINDEX, cholesterol index; CRI-I, castelli risk index-I; CRI-II, castelli risk index-II; FFM, fat free mass; FM, fat mass; HDL-C, high-density lipoprotein-cholesterol; LCI, lipoprotein combine index; OAGB, one anastomosis gastric bypass; RYGB, roux-en-Y gastric bypass; SG, sleeve gastrectomy; TG, triglyceride; TyG, triglyceride glucose.

(0.81±0.63) and AC (2.20±0.79) compared with the baseline (p<0.001). Note that there has been no significant difference between procedures in terms of these indicators (table 4). According to the present results, bariatric surgery is considered as an effective strategy for improving atherosclerosis in patients with obesity class II. The mean±SD difference between baseline and 12 months after bariatric surgery values for each procedure is shown in online supplemental table 2.

Table 3 Mean±SD from baseline and multiple follow-ups in the characteristic

	Time (months)			
Variable	0	6	12	P value*
Weight	120.17±17.77	87.83±12.42	81.04±11.47	<0.001
BMI (kg/m^2)	45.01±4.43	32.93±3.29	30.39±3.12	<0.001
Fat mass (kg)	58.37±10.19	34.89±8.55	29.08±8.15	<0.001
FFM (kg)	61.79±12.23	52.93±10.14	51.96±9.45	<0.001
TWL (%)	–	26.77±4.85	32.40±5.73	<0.001
EWL (%)	–	61.37±11.74	74.04±13.06	<0.001
CRI-I	4.22±1.18	3.77±0.98	3.20±0.79	<0.001
CRI-II	2.36±0.83	2.15±0.74	1.81±0.63	<0.001
TG to HDL-C ratio	1.47±0.78	1.02±0.51	0.80±0.32	<0.001
TyG index	8.94±0.53	8.51±0.39	8.32±0.30	<0.001
AIP	0.46±0.22	0.32±0.17	0.23±0.15	<0.001
LCI	21.71±17.13	13.72±9.26	9.17±6.56	<0.001
CHOLINDEX	1.36±0.83	1.15±0.74	0.81±0.63	<0.001
AC	3.22±1.18	2.77±0.98	2.20±0.79	<0.001

*One-way repeated measure analysis of variance was used to compare differences of variables by the three time points.
AC, atherogenic coefficient; AIP, atherogenic index of plasma; BMI, body mass index; CHOLINDEX, cholesterol index; CRI-I, castelli risk index-I; CRI-II, castelli risk index-II; EWL, Excess weight loss; FFM, fat free mass; FM, Fat mass; HDL-C, high-density lipoprotein-cholesterol; LCI, lipoprotein combine index; TG, triglyceride; TWL, total weight loss; TyG, triglyceride glucose.

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Table 4 Comparison of indicators between SG, RYGB and OAGB over 12-month follow-up

Variable	SG vs RYGB	SG vs OAGB	RYGB vs OAGB	P value (SG vs RYGB)	P value (SG vs OAGB)	P value (RYGB vs OAGB)	P value*
Weight	6.41±1.27	4.65±1.12	−1.76±1.40	<0.001†	<0.001‡	0.63	<0.001
BMI (kg/m^2)	2.10±0.41	1.36±0.36	−0.74±0.45	<0.001†	0.001‡	0.31	<0.001
FM (kg)	6.16±1.01	4.12±0.89	−2.03±1.11	<0.001†	<0.001‡	0.21	<0.001
FFM (kg)	0.14±0.76	0.52±0.67	0.37±0.84	0.85	0.44	0.65	0.740
TWL (%)	−2.54±0.70	−0.89±0.62	1.64±0.77	0.001†	0.39	0.10	0.002
EWL (%)	−1.88±1.61	−4.10±1.43	−2.22±1.78	0.73	0.013‡	0.64	0.017
CRI-I	−0.01±0.15	0.07±0.13	0.09±0.16	0.99	0.92	0.92	0.804
CRI-II	−0.05±0.11	0.08±0.10	0.13±0.12	0.95	0.81	0.63	0.544
TG to HDL-C ratio	−0.03±0.08	0.08±0.07	0.11±0.09	0.97	0.66	0.54	0.428
TyG index	−0.02±0.05	0.00±0.05	0.03±0.06	0.97	0.99	0.94	0.876
AIP	−0.00±0.02	0.02±0.02	0.02±0.02	0.99	0.59	0.74	0.491
LCI	−1.68±2.04	0.76±1.81	2.45±2.25	0.79	0.96	0.62	0.546
CHOLINDEX	−0.05±0.11	0.08±0.10	0.13±0.12	0.95	0.81	0.64	0.544
AC	−0.01±0.15	0.08±0.14	0.10±0.17	0.99	0.92	0.92	0.804

Data are means±SD.
P<0.017 were considered statistically significant after the Bonferroni correction.
*Analysis of variance was used to compare changes between groups.
†Significant difference between SG compared with RYGB.
‡Significant difference between SG compared with OAGB.
§Significant difference between RYGB to OAGB.
AC, Atherogenic coefficient; AIP, atherogenic index of plasma; BMI, body mass index; CHOLINDEX, cholesterol index; CRI-I, Castelli risk index-I; CRI-II, Castelli risk index-II; EWL, excess weight loss; FFM, free fat mass; FM, fat mass; HDL-C, high-density lipoprotein-cholesterol; LCI, lipoprotein combine index; OAGB, one anastomosis gastric bypass; RYGB, roux-en-Y gastric bypass; SG, sleeve gastrectomy; TG, triglyceride; TWL, total weight loss; TyG, triglyceride glucose.

The Pearson correlation test was performed on the total population to confirm the robustness of the observed changes and to define the parameters on which they depend. Table 5 presents the correlation between mean changes of %EWL, weight, plus FM and mean changes of atherosclerosis-related indicators. The inverse correlations were demonstrated between mean changes of %EWL and mean changes of CR-I, CRI-II, AIP, LCI, CHOLINDEX and AC. Mean weight changes had a correlation with CR-I, CRI-II, AIP, LCI and CHOLINDEX. Also, there was a correlation between mean changes of FM with CR-I, CRI-II, AIP, LCI, CHOLINDEX and AC. In SG, atherosclerosis-related indicators had a significant correlation with mean weight changes (except TG to HDL-C ratio), FM (except TG to HDL-C ratio and CRI-II) and %EWL (except TG to HDL-C ratio and TyG). In RYGB, a significant correlation between CRI-II, TG to HDL-C ratio, LCI, CHOLINDEX with FM was observed. Also, there was a correlation between CRI-II, LCI and CHOLINDEX with %EWL. In OAGB, CRI-II and CHOLINDEX were correlated with mean weight changes and FM (online supplemental table 3). These results partially indicate a correlation between weight loss and reduction of FM combined with an improvement of atherosclerosis-related indicators.

Table 5 Correlation between %EWL, weight and fat mass with atherosclerosis-related indicators over 12-month follow-up

	Weight		FM		%EWL	
Variable	Rho	P value	Rho	P value	Rho	P value
CRI-I	0.119	0.012	0.156	0.001	−0.124	0.009
CRI-II	0.144	0.002	0.181	0.000	−0.171	0.000
TG to HDL-C ratio	0.086	0.070	0.086	0.070	−0.071	0.136
TyG	0.087	0.066	0.065	0.172	−0.056	0.235
AIP	0.103	0.030	0.116	0.015	−0.109	0.022
LCI	0.120	0.011	0.116	0.014	−0.130	0.006
CHOLINDEX	0.144	0.002	0.181	0.000	−0.171	0.000
AC	0.012	0.119	0.156	0.001	−0.124	0.009

Spearman's rho correlation coefficient was used to evaluate the correlation between variables.
AC, atherogenic coefficient; AIP, atherogenic index of plasma; CHOLINDEX, cholesterol index; EWL, excess weight loss; FM, fat mass; HDL-C, high-density lipoprotein-cholesterol; LCI, lipoprotein combine index; TG, triglyceride; TyG, triglyceride glucose.

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DISCUSSION

Obesity is considered a pivotal risk factor and contributes to increased CVD morbidity and mortality. Previous studies have indicated that obesity may be involved in the initiation and progression of atherosclerosis because of changes in the structure and function of arteries.[20 21] We have found that bariatric surgery can considerably improve cardiometabolic health in patients with obesity class II through beneficial effects on atherogenicity and insulin resistance. In other words, the findings of this study demonstrated that all three bariatric surgery procedures can reduce the risk of cardiovascular complications by improving insulin sensitivity and reducing associated risk factors. In recent years, many researchers have made many attempts to detect more practical surrogate markers for sdLDL-C.[22 23] However, this feasible measure describes balance between anti-atherogenic and pro-atherogenic lipoproteins, patient's response to medications, and better prognosis of atherosclerosis than traditional lipid indicators in the clinical setting.[7 24] According to interesting evidence these indicators could diagnose at risk patients, especially when LDL-C level is in the normal range.[7] Therefore, it is essential to evaluate the risk of CVD beyond the routine parameters in clinical practice, particularly because there is a limitation to the commercial kit to assess sdLDL and other atherogenic particles.[7 15]

Although medical therapy using various lowering LDL-C agents including statin and non-statin drugs regimen remains the critical cornerstone of CVD risk prevention in dyslipidaemia management in high-risk patients with excess body weight, It is well documented that surgery-induced weight loss can play a crucial role in improving obesity-related metabolic abnormalities in severely obese patients failed to achieve their treatment goals using recommended medical therapy.[25 26] No similar study investigated the effect of various bariatric surgery procedures on the atherosclerosis-related indicators. Nevertheless, the present study results are in line with previous findings in similar studies, which have evaluated the effects of bariatric surgery on glucose hemostasis and conventional lipid profile, and demonstrated the hypoglycaemic and hypolipidemic properties of bariatric surgery. A study indicated that atherogenicity improved 12 months after bariatric surgery through reducing apo B-containing lipoproteins and activity of lipoprotein-associated phospholipase A2, oxLDL-C (oxidised LDL-C) and elevating HDL-2 concentration.[27] A similar study found that the anti-atherogenic effects of bariatric surgery emerged with the increase of greater HDL-C and reduction of smaller HDL-C and oxLDL-C/LDL-C ratio after 13 months.[16] In addition, a meta-analysis of 11 studies indicated that bariatric surgery could significantly improve oxLDL-C concentration, with this improvement being correlated with BMI changes.[28] Recently, in another study, the potential effect of bariatric surgery on preventing or slowing down the onset of atherosclerosis was highlighted by improvements in endothelial dysfunction, chronic inflammation and reduction of endothelium-adhesion molecules after 12 months.[29]

Early diagnosis of atherosclerosis in the subclinical stage is crucial to evaluate the need for a medical therapy. Recently, studies have proposed that AIP may be a better indicator compared with plasma lipoprotein profile to assess the risk of atherosclerosis.[30 31] AIP could be considered as an indicator of arteries health through the factors associated with stiffness, including inflammation and oxidative stress, phenotypical changes in the smooth muscle, and extracellular matrix formation.[32 33] AIP has been known as an indicator for predicting coronary artery disease, mortality and CVD events, showing an inverse relationship with the size of LDL-C particles and a direct relationship with sdLDL-C.[33–35] Thus, AIP is an available and reliable indicator for the efficiency of anti-atherogenic interventions and the prediction of the risk of developing atherosclerosis as well as CVD among at-risk patients.[15 23 32] The current study showed that AIP improved significantly 12 months after bariatric surgery, suggesting an improvement in the health of vessels in patients with obesity class II. Further, this improvement did not differ between the three procedures and was indeed independent of the type of procedure. In line with this study, a clinical trial study performed on 34 class II obese patients with or without diabetes found that SG caused considerable improvement in AIP in both groups of patients.[36] They proposed AIP as a valid and reliable indicator for CVD risk among patients with obesity class II.[36]

Other markers associated with atherosclerosis, including LCI, AC, CHOLINDEX, CRI-I, CRI-II and TG to HDL-C ratio showed significant improvements at the end of the study compared with the baseline. In other words, this study suggests that bariatric surgery procedures could attenuate the atherogenic processes in patients with class II obesity by reducing oxidative stress, improving glucose metabolism and atherogenic dyslipidaemia, thereby lowering the risk of atherosclerosis and CVD events. Note that the effect of weight loss on adipose tissue could be a fundamental mechanism for explaining the anti-atherogenic effects of bariatric surgery:

1. Bariatric surgery reduces the secretion of inflammatory cytokines from the adipose tissue. It also promotes the production of antioxidant enzymes, including paraoxonase-1 and catalase, thereby suppressing reactive oxygen species (ROS) production available for oxidation of sdLDL-C.[37 38]
2. Bariatric surgery improves qualitative features of LDL-C particles to non-atherogenic phenotype in patients with obesity. It decreases influx of FFAs to the liver, considerably reducing the generation of larger very low- density lipoprotein-cholesterol (VLDL-C) rich in TG, while elevating the apoE-contain in VLDL-C particles which produces larger LDL-C.[39 40] It lowers the free cholesterol and free cholesterol/esterified cholesterol ratio in LDL-C lipoproteins and consequently reduces the generation of sdLDL-C and oxLDL-C.[29]

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3. Evidence has suggested that patients after bariatric surgery experience HDL-C remodelling toward healthier HDL-C particles and a distinct trend toward more prominent size and increased serum concentration of HDL-C particles, which are protective against atherogenicity.[41–44]

Insulin resistance is a significant risk factor for atherosclerosis since it is associated with endothelial dysfunction, inflammation and oxidative stress.[45] Various techniques have been used to evaluate insulin resistance; however, the gold standard method is hyperinsulinaemic-euglycaemic (HE) clamp technique.[46] Nevertheless, this technique is costly, laborious and unsuitable for routine assessments in clinical practice. Recently, the TyG index has been proposed for insulin resistance, which has sensitivity of 96.5% and specificity of 85.0% to diagnosis of insulin resistance compared with the HE clamp.[46] It is obtained from serum TG and FBS concentrations, and is strongly associated with increased risk of metabolic syndrome, arterial stiffness, atherosclerosis and CVD.[45] Compared with the Homeostatic Model Assessment for Insulin Resistance, it has high sensitivity for diagnosing insulin resistance and can be used as a favourable surrogate of it.[45 47 48] Accordingly, in this study, a significant improvement was observed in the TyG index 12 months postsurgery, indicating a reduction in insulin resistance. Thus, we deduced that bariatric surgery could potentially lower the risk of atherosclerosis in class II obese patients. In line with our findings, Zhang *et al* conducted a study on 57 non-diabetic women who underwent bariatric surgery to assess insulin resistance. They found that the lipoprotein insulin resistance score, calculated using lipoproteins levels, improved significantly 12 months after RYGB and SG.[49] Similar to our study, this improvement was independent of bariatric surgery procedures.[49] The mechanisms involved in the bariatric surgery effect on insulin resistance have not been precisely understood, but it is considered multifactorial.[50] The impact of the bariatric surgery-induced weight loss on adipose tissue modulates adipose tissue lipolysis and reduces circulation of FFAs, resulting in enhanced insulin sensitivity. Further, it may recover the insulin signalling pathway and boost insulin sensitivity due to enhancing the expression of the genes involved in the insulin pathway, such as glucose transporter type 4, and reducing chronic inflammation.[51]

The current study evaluated the effect of bariatric surgery on atherosclerosis-associated indicators with a large sample size, which presents new knowledge about the risk of atherosclerosis in class II obese patients. Nevertheless, this study had several limitations. First, there was no matched control group that did not undergo surgery, which could provide precise conclusions from our findings. Second, direct measurement of arterial stiffness and endothelial function markers could provide a better understanding of the importance of atherosclerosis-related indicators on the health of vessels following surgery. Finally, the patients were not recruited randomly for each procedure, which explains the significant weight difference at the baseline.

Conclusion

This study demonstrated the ability of three bariatric surgery procedures in improving atherogenicity and insulin resistance in patients with obesity class II. This reduction of atherogenicity appeared based on improvements in atherosclerosis-associated indicators, including AIP, TyG index, LCI, AC, CHOLINDEX, CRI-I, CRI-II and TG to HDL-C ratio 12 months post-bariatric surgery. Although the effects of surgery are multifactorial, in this study, the anti-atherogenicity effects can be partly assigned to reducing weight and adipose tissue. Nevertheless, to confirm our results and to explore the main mechanisms implicated in the anti-atherogenic activity of bariatric surgery, further studies with larger sample sizes and longer follow-ups are required.

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