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Effect of Preoperative Very Low-Calorie Diets on Hepatic Steatosis, Fibrosis, and Perioperative Outcomes of Bariatric Surgery

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Abstract

Introduction: Preoperative weight loss through a very low-calorie diet (VLCD) has been shown to reduce liver volume and technical difficulty in patients undergoing metabolic and bariatric surgery (MBS). However, the effect of preoperative VLCD on liver histology and other outcomes is not well demonstrated. Our study aimed to explore the effect of a 2-week preoperative VLCD, compared with no-dietary intervention, on hepatic steatosis, fibrosis, weight loss, and other postoperative outcomes of MBS.

Materials and Methods: This retrospective study was conducted at the Chulalongkorn Bariatric and Metabolic Institute, King Chulalongkorn Memorial Hospital, Bangkok, Thailand. The medical records of patients with severe obesity (body mass index ≥50 kg/m^2) attending the clinic from January 2005 to December 2020 were reviewed. Clinical data and laboratory investigations were collected at baseline and at each follow-up visit, up to 5 years postoperatively. Hepatic steatosis and fibrosis were assessed by liver biopsy intraoperatively.

Results: A total of 181 patients were included in this study. Preoperative VLCD was prescribed in 65 patients (VLCD group) and 116 patients received their usual diet (control group). Mean preoperative weight loss was 9.1 ± 6.1 kg in the VLCD group versus 0.0 ± 0.0 kg in the control group ($P = .000$). The VLCD group had significantly less number of patients with moderate and severe liver steatosis from the liver biopsy specimens (16.2% versus 46.3%; $P = .008$). However, there was no significant difference in fibrosis grade between those with VLCD and control (≥F2-fibrosis; 2.7% versus 7.5%; $P = .118$). Moreover, preoperative VLCD could reduce operating time in patients who underwent both laparoscopic Roux-en-Y gastric bypass (LRYGB; VLCD 163.4 ± 38.2 minutes versus control 215.1 ± 67.4 minute, $P = .000$) and laparoscopic sleeve gastrectomy (LSG; VLCD 110.8 ± 20.0 minutes versus control 131.0 ± 38.1 minutes, $P = .004$). During the 5-year follow-up, there were a significant difference of HbA1C between the VLCD and the control group (coefficient: −0.24 with 95% confidence interval [CI]: −0.44 to −0.04, $P = .019$), particularly in patients who underwent LRYGB (Coefficient: −0.26 with 95% CI: −0.49 to −0.03, $P = .028$), but not LSG. However, long-term weight loss outcomes and other biochemical outcomes were not different between the VLCD and the control group.

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Conclusion: Preoperative VLCD was associated with reduced liver steatosis and operative time in patients who underwent LRYGB and LSG. Moreover, preoperative VLCD significantly decreased HbA1C during a 5-year follow-up period. Therefore, it should be considered in patients with severe obesity, who will undergo MBS.

Keywords: nonalcoholic fatty liver disease, nonalcoholic steatohepatitis, hepatic steatosis, hepatic fibrosis, bariatric surgery, metabolic and bariatric surgery, very low-calorie diet

Introduction

Obesity is a major public health problem, and its prevalence has been increasing worldwide.[1,2] Obesity is linked to a range of health problems, including type 2 diabetes mellitus, hypertension, dyslipidemia, obstructive sleep apnea (OSA), and nonalcoholic fatty liver disease (NAFLD).[3] It has been estimated that the prevalence of NAFLD is as high as 95% in severely obese patients, compared to only 25%–30% in general population.[3] Metabolic and bariatric surgery (MBS) is the most effective treatment for severe obesity, resulting in significant, sustained weight loss and resolution of obesity-related complications.

However, excess body fat and enlarged liver may complicate the technical aspect of surgery and increase the risk of perioperative complications.[4] Preoperative weight loss before MBS has become of interest since it induces rapid weight loss, reduces liver volume, facilitates surgery, and may reduce perioperative complications. However, there has been no consensus of clear indication of preoperative weight loss in most recent guidelines.[4–6]

A very low-calorie diet (VLCD) is one of the most effective dietary interventions for weight loss, which restrict caloric intake to ≤800 kcal/day.[7] Nevertheless, there is currently no study that investigates the effects of preoperative VLCD on hepatic steatosis and fibrosis in patients who will undergo MBS. Moreover, the impact of preoperative weight loss, using VLCD, on long-term weight loss after MBS is still debatable[8–10] and there has been no consensus regarding the preoperative weight loss before MBS. Therefore, this study aimed to investigate the effects of preoperative VLCD, compared with no-dietary intervention, on liver histology, postoperative complications, and long-term weight loss outcomes in patients who underwent laparoscopic Roux-en-Y gastric bypass (LRYGB) or laparoscopic sleeve gastrectomy (LSG).

Materials and Methods

This study was conducted at the Chulalongkorn Bariatric and Metabolic Institute, King Chulalongkorn Memorial Hospital, Thai Red Cross Society, Bangkok, Thailand. After institutional review board approval was obtained, a retrospective review was conducted for all patients who attended the clinic from January 2005 to December 2020. Clinical data (age, sex, weight, height, and comorbid diseases) and laboratory investigations were collected at baseline and at each follow-up visit, up to 5 years postoperatively.

The patients were included if they were 18–65 years of age, body mass index (BMI) ≥50 kg/m^2, and underwent LRYGB or LSG. Exclusion criteria were patients who underwent revision surgery, patients with hepatitis B and C infection, significant alcohol consumption, and patients with eating disorders, psychiatric diseases, pregnancy, and lactation. Liver histology was assessed by liver biopsy intraoperatively. Primary outcomes were steatosis and fibrosis grade. Secondary outcomes were operative time, postoperative complications, length of hospital stays, weight loss outcomes, number of patients who achieved diabetes remission and biochemical changes after surgery.

At our institute, all obese patients with BMI ≥50 kg/m^2 were offered the in-hospital preoperative weight loss program. The patients were admitted to the hospital 2 weeks before surgery (VLCD group) and were prescribed an 800-kcal hospital diet with protein 100 g/day. The obese patients who were not willing to participate in the in-hospital preoperative weight loss program were considered the control group and were admitted to the hospital 1 day before surgery and consumed their usual diet. Excess weight loss is derived from the following formula: (weight loss/excess weight) × 100, where excess weight = preoperative weight – ideal body weight (IBW). BMI was calculated by weight (kilogram)/(height in meters)^2 and we use a BMI of 25 kg/m^2 in determining the IBW.

Statistical analysis

Continuous data were described as mean ± standard deviation, while categorical data were described as number (%). Comparison between groups is assessed by independent *t*-test for continuous variables and using chi-square (or Fisher exact test) for categorical variables.

Continuous data at each follow-up visits were analyzed with the linear mixed model. A 2-tailed $P < .05$ is considered significant. Data were analyzed as overall analysis and subgroup analysis stratified according to surgical type. The statistical package Stata/MP version 17 (StataCorp LLC, College Station, TX, USA) is used for statistical analysis.

Results

A total of 181 patients (56.4% male) were included in this study, 94 patients underwent LRYGB and 84 patients underwent LSG. The mean patients' age was 33.5 ± 10.0 years (range 23–43 years), and the mean preoperative BMI and weight were 60.0 ± 8.5 kg/m^2 and 168.7 ± 30.5 kg, respectively. Percentage of male was significant higher in patients who underwent LSG (LRYGB 46.8% versus LSG 66.7%, $P = .007$). Moreover, preoperative weight and BMI were significantly higher in patients who underwent LSG (LRYGB 159.0 ± 22.4 kg, 57.3 ± 6.2 kg/m^2 versus LSG 179.2 ± 34.5 kg, 62.9 ± 9.6 kg/m^2, $P < .001$). The number of comorbid diseases was not different between LRYGB and LSG.

Preoperative VLCD was prescribed in 65 patients (VLCD group) and 116 patients received their usual diet (control group). Baseline clinical characteristics and laboratory investigations were similar between the VLCD and the control group. (Tables 1 and 2). Mean preoperative weight loss was

Table 1. Baseline Characteristics of Study Participants

Variable	*Overall patients*			*Patients with LRYGB*			*Patients with LSG*		
	Control (N = 116)	*VLCD (N = 65)*	P	*Control (N = 46)*	*VLCD (N = 48)*	P	*Control (N = 70)*	*VLCD (N = 17)*	P
Age (years)	32.6 ± 9.6	35.1 ± 10.6	.113	33.0 ± 9.9	35.6 ± 10.4	.220	32.3 ± 9.5	33.6 ± 11.1	.640
Sex (Male), *n* (%)	68 (58.6)	34 (52.3)	.411	21 (45.7)	23 (47.9)	.826	47 (67.1)	11 (64.7)	.848
Weight (kg)	170.7 ± 31.4	165.1 ± 28.7	.243	158.2 ± 23.6	159.7 ± 21.5	.735	178.9 ± 33.2	180.1 ± 40.3	.894
BMI (kg/m^2)	60.6 ± 9.0	58.9 ± 7.3	.166	56.8 ± 6.2	57.8 ± 6.2	.423	63.1 ± 9.7	61.8 ± 9.5	.624
DM, *n* (%)									
IFG	12 (10.3)	11 (16.9)	.375	3 (6.5)	9 (18.8)	.138	9 (12.9)	2 (11.8)	.235
T2DM	45 (38.8)	26 (40)		23 (50)	17 (35.4)		22 (31.4)	9 (52.9)	
DM Med, *n* (%)									
GLP1RA	0	2 (3.4)	.093	0	2 (4.4)	.258	0	0	—
Insulin	2 (2.4)	1 (1.7)	.763	0	0		2 (3.7)	1 (7.1)	.577
DLP	60 (51.7)	34 (52.3)	.940	22 (47.8)	23 (47.9)	.993	38 (54.3)	11 (64.7)	.437
NAFLD, *n* (%)									
NAFL	48 (41.4)	31 (47.7)	.132	16 (50)	22 (51.2)	.539	32 (47.8)	9 (56.3)	.532
NASH	32 (27.6)	24 (36.9)		11 (34.4)	18 (41.8)		21 (31.3)	6 (37.5)	
HT, *n* (%)	81 (69.8)	46 (70.8)	.894	33 (71.7)	33 (68.8)	.751	48 (68.6)	13 (76.5)	.523
OSA, *n* (%)	105 (90.5)	61 (93.8)	.436	39 (84.8)	44 (91.7)	.299	66 (94.3)	17 (100.0)	.313
CAD, *n* (%)	1 (0.9)	0	.453	0	0	—	1 (1.4)	0	.620
PCOS, *n* (%)	6 (5.2)	5 (7.7)	.496	4 (8.7)	5 (10.4)	.777	2 (2.9)	0	.481
OA, *n* (%)	8 (6.9)	1 (1.5)	.112	4 (8.7)	1 (2.1)	.153	4 (5.7)	0	.313
TIA/CVA, *n* (%)	2 (1.7)	0	.287	1 (2.2)	0	.304	1 (1.4)	0	.620
GERD, *n* (%)	5 (4.3)	2 (3.1)	.680	2 (4.3)	2 (4.2)	.965	3 (4.3)	0	.385
CHF, *n* (%)	7 (6)	5 (7.7)	.667	2 (4.3)	2 (4.2)	.965	5 (7.1)	3 (17.6)	.179
Gout, *n* (%)	6 (5.2)	2 (3.1)	.511	3 (6.5)	2 (4.2)	.611	3 (4.3)	0	.385

Data were presented as mean ± SD and a number with percentage (%). $P < .05$ is considered significant.

BMI, body mass index; CAD, coronary artery disease; CHF, congestive heart failure. CVA, cerebrovascular accident; DLP, dyslipidemia; DM, diabetes mellitus; GERD, gastroesophageal reflux disease; GLP1RA, glucagon-like peptide-1 receptor agonist; HT, hypertension; IFG, impaired fasting glucose; NAFL, nonalcoholic fatty liver; NAFLD, nonalcoholic fatty liver disease; NASH, nonalcoholic steatohepatitis; LRYGB, laparoscopic Roux-en-Y gastric bypass; LSG, laparoscopic sleeve gastrectomy; OA, osteoarthritis; OSA, obstructive sleep apnea; PCOS, polycystic ovary syndrome; SD, standard deviation; T2DM, type 2 diabetes mellitus; TIA, transient ischemic attack; VLCD, very low-calorie diet.

9.1 ± 6.1 kg in the VLCD group compared to 0.0 ± 0.0 kg in the control group ($P < .001$). For patients who participated in the preoperative weight loss program, 63/65 patients (96.9%), 31/65 patients (47.7%), and 3/65 patients (4.6%) achieved at least 5%, 10%, and 15% weight loss, respectively. Moreover, preoperative VLCD significantly reduced fasting plasma glucose (FPG) before surgery ($P < .001$; Table 3).

A total of 104 patients underwent intraoperative liver biopsy; of these, 37 patients were in the VLCD group (37/65; 56.9%) and 67 were in the control group (67/116; 57.8%).

Table 2. Baseline Biochemical Data of Study Participants

Variable	*Overall patients*			*Patients with LRYGB*			*Patients with LSG*		
	Control (N = 116)	*VLCD (N = 65)*	P	*Control (N = 46)*	*VLCD (N = 48)*	P	*Control (N = 70)*	*VLCD (N = 17)*	P
HbA1C (%)	6.4 ± 1.0	6.2 ± 1.1	.332	6.4 ± 1.1	6.1 ± 1.0	.264	107.4 ± 25.4	111.7 ± 22.6	.536
FPG (mg/dL)	108.1 ± 29.6	106.8 ± 21.2	.757	109.3 ± 35.6	105.0 ± 20.7	.489	6.3 ± 1.0	6.4 ± 1.3	.875
TC (mg/dL)	192.8 ± 38.8	184.0 ± 38.0	.227	192.3 ± 41.1	182.7 ± 34.5	.335	193.1 ± 37.6	186.6 ± 45.7	.585
HDL-C (mg/dL)	43.0 ± 10.3	42.7 ± 9.2	.878	41.3 ± 9.2	42.8 ± 8.5	.511	44.0 ± 11.0	42.3 ± 11.2	.641
TG (mg/dL)	149.1 ± 71.5	127.5 ± 55.4	.084	138.1 ± 63.3	127.1 ± 55.3	.471	155.8 ± 76.0	128.6 ± 57.7	.220
LDL-C (mg/dL)	127.4 ± 41.8	121.6 ± 32.9	.434	128.6 ± 42.8	120.2 ± 30.8	.388	126.7 ± 41.7	125.0 ± 39.0	.899
AST (U/L)	28.4 ± 17.7	23.7 ± 12.6	.083	28.1 ± 15.5	22.7 ± 13.5	.100	28.6 ± 19.1	26.0 ± 10.3	.607
ALT (U/L)	40.7 ± 35.9	34.3 ± 25.6	.242	36.9 ± 22.4	33.8 ± 28.4	.579	43.1 ± 42.5	35.6 ± 17.6	.488
ALP (U/L)	73.8 ± 22.1	70.1 ± 16.2	.321	74.8 ± 20.1	70.0 ± 16.6	.294	73.1 ± 23.5	70.3 ± 15.7	.670
Plt (x $10^3/\mu$L)	300.1 ± 75.2	305.6 ± 83.7	.660	310.1 ± 76.5	308.2 ± 91.0	.915	293.6 ± 74.1	297.6 ± 58.1	.838
FIB-4 index	0.5 ± 0.3	0.6 ± 0.5	.540	0.5 ± 0.3	0.6 ± 0.6	.674	0.5 ± 0.3	0.5 ± 0.2	.998

Data were presented as mean ± SD. $P < .05$ is considered significant.

ALP, alkaline phosphatase; ALT, alanine transaminase; AST, aspartate transaminase; FIB-4 index, fibrosis-4 index; FPG, fasting plasma glucose; HbA1C, hemoglobin A1C; HDL, high-density lipoprotein cholesterol; kg, kilograms; kg/m^2, kilograms per meter squared; LDL, low-density lipoprotein cholesterol; LRYGB, laparoscopic Roux-en-Y gastric bypass; LSG, laparoscopic sleeve gastrectomy; mg/dL, milligram per deciliter; Plt, platelet; SD, standard deviation; TC, total cholesterol; TG, triglyceride; U/L, units per liter; μL, microliter; VLCD, very low-calorie diet.

Table 3. Weight Loss Response and Biochemical Data of Study Participants Before and After Preoperative Weight Loss Program Using Very Low-Calorie Diet

	Overall patients (N = 65)			*Patients with LRYGB (N = 48)*			*Patients with LSG (N = 17)*		
Variable	*Before VLCD*	*After VLCD*	P	*Before VLCD*	*After VLCD*	P	*Before VLCD*	*After VLCD*	P
Weight (Kg)	165.1 ± 28.7	156.1 ± 26.7	.000	159.8 ± 21.4	150.7 ± 19.9	.035	180.6 ± 40.5	169.1 ± 38.0	.399
BMI (Kg/m^2)	58.9 ± 7.3	55.7 ± 6.9	.000	57.8 ± 6.1	54.4 ± 5.9	.007	61.9 ± 9.5	58.1 ± 9.2	.242
FPG (mg/dL)	109.9 ± 21.8	98.2 ± 21.3	.000	104.9 ± 20.6	99.6 ± 22.0	.323	111.7 ± 22.6	98.4 ± 17.1	.181
AST (U/L)	24.1 ± 12.6	27.0 ± 13.0	.187	22.7 ± 13.5	25.3 ± 12.8	.391	26.0 ± 10.3	31.7 ± 12.3	.185
ALT (U/L)	34.6 ± 27.8	34.9 ± 22.6	.948	33.8 ± 28.4	31.0 ± 20.2	.619	35.6 ± 17.6	50.1 ± 25.3	.080
ALP (U/L)	68.4 ± 13.9	65.0 ± 15.8	.051	70.0 ± 16.6	66.3 ± 15.6	.365	70.3 ± 15.7	66.8 ± 15.9	.599

Data were presented as mean ± SD. $P < .05$ is considered significant.

ALP, alkaline phosphatase; ALT, alanine transaminase; AST, aspartate transaminase; BMI, body mass index; FPG, fasting plasma glucose; kg, kilograms; kg/m^2, kilograms per meter squared; LRYGB, laparoscopic Roux-en-Y gastric bypass; LSG, laparoscopic sleeve gastrectomy; mg/dL, milligram per deciliter; SD, standard deviation; U/L, units per liter; VLCD, very low-calorie diet.

A total of 84.6% (88/104) of patients had fatty liver, and liver fibrosis was detected in 29.8% (29/104) of the liver biopsy specimens. Hepatic steatosis grades were significantly different between the VLCD and the control group. The VLCD group had significantly less number of patients with moderate and severe liver steatosis, compared to those in the control group (16.2% versus 46.3%; $P = .008$). However, there was no significant difference in fibrosis grade between those in the VLCD and the control group (≥F2-fibrosis; 2.7% versus 7.5%; $P = .118$). In addition, when we stratified patients according to the surgical procedure (LRYGB versus LSG), there was no difference in the hepatic steatosis and liver fibrosis (Table 4).

Interestingly, preoperative VLCD significantly reduced operating time in patients who underwent both LRYGB (VLCD 163.4 ± 38.2 minutes versus control 215.1 ± 67.4 minutes, $P = .000$) and LSG (VLCD 110.8 ± 20.0 minutes versus control 131.0 ± 38.1 minutes, $P = .004$). However, there was no significant difference in the length of postoperative hospital stays between the groups regardless of the type of surgery. Also, early postoperative complications were similar between groups (Table 5).

The long-term weight loss outcomes and the number of patients who achieved diabetes remission, up to 5 years postoperative, were not different between the VLCD and the control group. Weight reduction was slightly greater in the VLCD group; however, it does not reach statistical difference (coefficient: -7.51 with 95% confidence interval [CI]: −16.29 to 1.27, $P = .094$; Fig. 1). Interestingly, during the 5-year follow-up, there were a significant difference of HbA1C between the VLCD and the control group (coefficient: −0.25 with 95% CI: −0.46 to −0.05, $P = .014$), particularly in patients who underwent LRYGB (coefficient: −0.28 with 95% CI: −0.52 to −0.47, $P = .019$), but not LSG (coefficient: 0.15 with 95% CI: −0.25 to 0.54, $P = .463$; Fig. 2). Others biochemical outcomes were not different between the VLCD and the control group.

Discussion

This study demonstrated that the 2-week VLCD led to a significant reduction of weight and FPG before the surgery. Moreover, preoperative VLCD significantly reduced moderate and severe liver steatosis and lowered operative time in

Table 4. Liver Histology of Study Participants

	Overall patients			*Patients with LRYGB*			*Patients with LSG*		
Variable	*Control (N = 67)*	*VLCD (N = 37)*	P	*Control (N = 21)*	*VLCD (N = 29)*	P	*Control (N = 46)*	*VLCD (N = 9)*	P
Hepatic steatosis									
Grade 0, <5%, *n* (%)	11 (16.4)	5 (13.5)	.008	4 (19.0)	3 (10.7)	.093	7 (15.2)	2 (22.2)	.217
Grade 1, mild 5%–33%, *n* (%)	25 (37.3)	26 (70.3)		8 (38.1)	20 (71.4)		17 (37.0)	6 (66.7)	
Grade 2, moderate >33%–66%, *n* (%)	16 (23.9)	4 (10.8)		3 (14.3)	3 (10.7)		13 (28.3)	1 (11.1)	
Grade 4, severe >66%, *n* (%)	15 (22.4)	2 (5.4)		6 (28.6)	2 (7.1)		9 (19.6)	0	
Hepatic fibrosis									
Grade 0, absent, *n* (%)	50 (74.6)	23 (62.2)	.189	17 (81.0)	18 (64.3)	.055	30 (73.2)	5 (55.6)	.332
Grade 1, perisinusoidal or periportal, *n* (%)	12 (17.9)	13 (35.1)		1 (4.8)	10 (32.1)		9 (22.0)	4 (44.4)	
Grade 2, perisinusoidal and portal/periportal, *n* (%)	3 (4.5)	1 (2.7)		1 (4.8)	1 (3.6)		2 (4.9)	0	
Grade 3, bridging fibrosis, *n* (%)	2 (3.0)	0		2 (9.5)	0		0	0	

Data were presented as a number with percentage (%). $P < .05$ is considered significant.

LRYGB, laparoscopic Roux-en-Y gastric bypass; LSG, laparoscopic sleeve gastrectomy; SD, standard deviation; VLCD, very low-calorie diet.

Table 5. Comparison of Immediate Postoperative Outcomes Between Control and Very Low-Calorie Diet Group

	Overall patients			*Patients with LRYGB*			*Patients with LSG*		
Variable	*Control (N = 116)*	*VLCD (N = 65)*	P	*Control (N = 46)*	*VLCD (N = 48)*	P	*Control (N = 70)*	*VLCD (N = 17)*	P
Operative time (minutes)	164.4 ± 66.0	149.7 ± 41.4	.068	215.1 ± 67.4	163.4 ± 38.2	.000	131.0 ± 38.1	110.8 ± 20.0	.004
Postoperative length of stay (days)	5.9 ± 3.2	6.51 ± 4.9	.346	6.4 ± 2.9	7.1 ± 5.3	.437	5.5 ± 3.4	5.0 ± 2.8	.501
Early postoperative complication, *n* (%)									
Extraluminal staple line bleeding	0	1 (1.5)	.180	0	1 (2.1)	.325	0	0	—
Intraluminal staple line bleeding	1 (0.9)	0	.453	1 (2.2)	0	.304	0	0	—
Staple line leakage	1 (0.9)	0	.453	0	0	—	1 (1.4%)	0	.620

Data were presented as mean ± SD and a number with percentage (%). $P < .05$ is considered significant.
LRYGB, laparoscopic Roux-en-Y gastric bypass; LSG, laparoscopic sleeve gastrectomy; SD, standard deviation; VLCD, very low-calorie diet.

patients who underwent either LRYGB or LSG. During the 5-year follow-up, there was a significant difference of HbA1C between the VLCD and the control group, particularly in patients undergoing LRYGB, but not LSG. However, long-term weight loss, number of patients who achieved diabetes remission, and other biochemical outcomes were not different between the VLCD and the control group.

In this study, the VLCD was the hospital diet containing 800 kcal and protein 100 g/day. The study diet was effective in terms of reducing preoperative weight and FPG. In clinical practice, VLCD can be prescribed as a nutritionally complete low-energy formula, total diet replacement, or standard diet. Both diets provide similar results in weight loss outcomes. Nevertheless, a standard diet may be better in terms of patients' compliance and tolerability.[11] Preoperative weight loss using VLCD, in patients who underwent MBS, could induce rapid weight loss, ranging from −2.8 to −14.8 kg, as well as a reduction in liver volume, visceral fat,[12] and total body fat.[13]

Short-term VLCD is safe and does not cause malnutrition or compromise immune function.[14,15] Nonetheless, VLCD may attenuate collagen synthesis without compromising wound healing.[16] Moreover, VLCD also induces loss of lean body mass, which may lower metabolic rate and have detrimental effect on long-term weight loss outcome. Therefore, VLCD containing high protein formula should be used to ensure that the patients will maintain their lean body mass during the rapid weight loss phase. In addition, hydration and electrolyte status should be monitored, as well as vitamin and mineral should be supplemented in all patients.

NAFLD is a major complication of obesity characterized by increased visceral fat, mainly in the liver's left lobe. Weight loss is the most effective treatment to reverse NAFLD. Previous studies indicated that weight reduction of at least 7% improved liver histology in patients with NALFD.[17] Moreover, preoperative VLCD is the effective treatment to induce rapid weight loss and reduce liver volume,[12,18] which facilitate the surgery and reduced surgeon's perceived complexity of the procedure.[19] Interestingly, our study demonstrated that preoperative VLCD could improve liver histology intraoperatively in obese patients who underwent MBS. However, a liver biopsy could not be performed before VLCD due to ethical concerns. Therefore, our study could not demonstrate the improvement of liver histology before and after weight loss intervention.

Our study revealed that preoperative VLCD significantly reduced the number of patients with moderate and severe hepatic steatosis, but it had no effect on hepatic fibrosis. Improvement of hepatic steatosis usually occurs more rapidly, while reversal of liver fibrosis usually requires at least several months to years.[20,21] Our finding confirmed the previous study demonstrating that preoperative weight loss significantly reduced hepatic steatosis, but it could not reverse hepatic fibrosis.[22]

Interestingly, preoperative VLCD significantly lowered operative time in patients who underwent either LRYGB or LSG. This implied that preoperative weight loss may reduce liver volume and facilitate the surgery. However, postoperative complications and length of hospital stay were not different between the VLCD and the control group. It might be explained by the fact that the operation was done by experienced surgeons and there were only a few complications in our study. Thus, we could not demonstrate the significant difference between groups. The finding was similar to the previous study, which indicated that preoperative weight loss resulted in the reduction of operative time in patients who underwent LRYGB without any effect on perioperative complications.[8]

The most obvious effect of VLCD is the significant and rapid weight loss, which leads to liver shrinkage[23,24] and improves the technical aspect of surgery. Nevertheless, it does not always translate to better postoperative outcomes. In our study, long-term weight loss, diabetes remission, and other biochemical outcomes were not different between the VLCD and the control group. Several studies revealed that preoperative weight loss had no effect on long-term weight loss outcomes[8,10] and the resolution of obesity-related complications.[8] However, our study showed that preoperative VLCD significantly reduced FPG before surgery. In addition, the A1C level significantly decreased during the 5-year follow-up period, particularly patients who underwent RYGB. Several studies indicated that preoperative glucose control might influence postoperative outcomes, not only

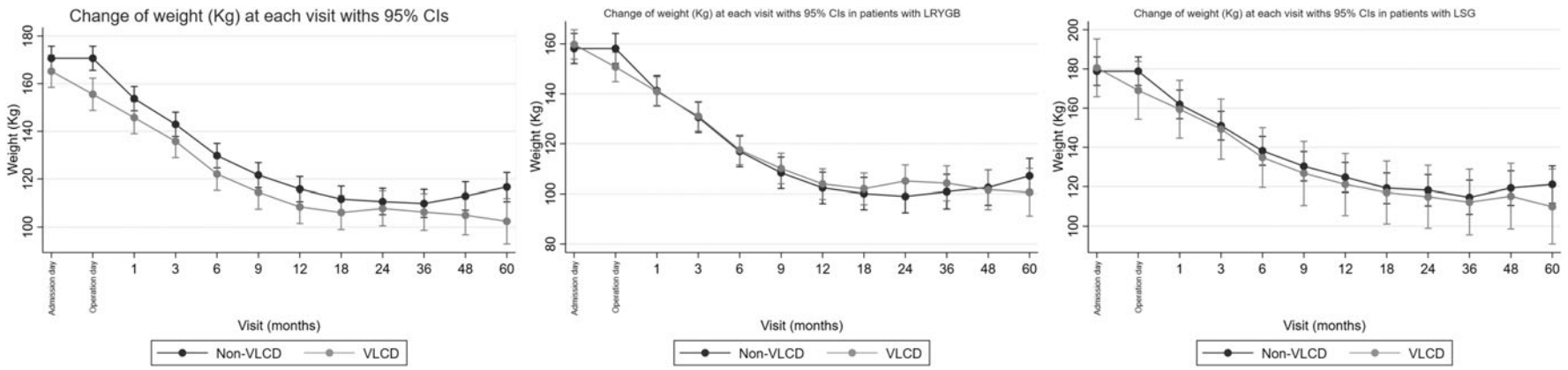

FIG. 1. Change of weight (Kg) at each visit with 95% CIs. CI, confidence interval.

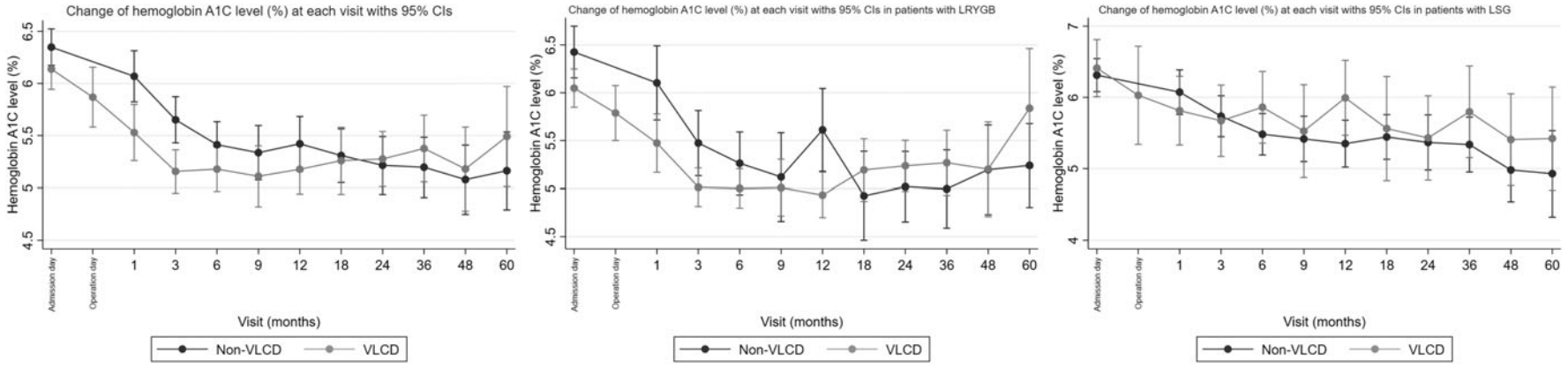

FIG. 2. Change of hemoglobin A1C level (%) at each visit with 95% CIs. CI, confidence interval.

glycemic control but also weight loss outcomes.[25] Therefore, intensive glucose control should be done preoperatively, particularly in people with diabetes, which may result in better long-term outcomes.[26]

The strength of the study is that we use liver biopsy to assess liver histology, which is the gold standard for diagnosis of NAFLD.[27] While comparing liver histology before and after a VLCD would be ideal, it would be challenging to achieve from a research standpoint. Moreover, our real-world evidence generated during clinical practice confirms the safety and effectiveness of using preoperative VLCD before MBS.

We acknowledge several limitations of this study. First, it was the retrospective study, so the patients were not randomized, which was prone to the potential confounders and bias. Second, the sample size of the study was small; thus, it limits the statistical power. Third, like other bariatric cohorts, there were high attrition rates in our study. The patients' compliances might influence the result of the study. Finally, patient-reported outcome measures were not collected in this study. Patients' perspectives on the tolerance of preoperative VLCD, the reasons for noncompliance, and other patient's lifestyle and eating habits that could influence long-term weight loss should be investigated in the future study.

Conclusion

This study demonstrated that preoperative VLCD led to a significant reduction of weight, and it was associated with reduced liver steatosis and operative time in patients who underwent MBS. Moreover, preoperative VLCD significantly decreased HbA1C during a 5-year follow-up period. Therefore, it should be considered in patients with severe obesity, who will undergo MBS.

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Authors' Contributions

A.K. designed the study, collected the data, performed the statistical analysis of data, wrote the article, and revised the article.

P.C.S. conceived the study, designed the study, performed the interpretation of data, wrote the article, provided critical comments, and revised the article.

P.B. performed the interpretation of data, provided critical comments, and revised the article.

S.R. performed the statistical analysis of data, provided critical comments, and revised the article.

S.T. performed the interpretation of data, provided critical comments, and revised the article.

S.U. conceived the study, designed the study, performed the interpretation of data, wrote the article, provided critical comments, and revised the article.

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