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ORIGINAL CONTRIBUTIONS

Roux-en-Y Gastric Bypass for T2D Treatment in Chinese Patients with Low BMI: 5-Year Outcomes

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Abstract

Background RYGB was considered as an effective treatment for obese patients with T2D. However, 5-year outcomes including T2D remission after surgery have not been adequately studied in Chinese patients.

Objectives Our aim is to evaluate metabolic outcomes of RYGB in 5-year follow-up.

Methods We retrospectively divided 59 Chinese patients into two groups, namely BMI groups (group A: BMI < 28 kg/m^2; group B: BMI ≥ 28 kg/m^2) and A1C groups (group C: A1C < 7%; group D: A1C ≥ 7%). Their medical records were collected and cardiovascular risk and medications were evaluated in 5 years after RYGB.

Results Thirty patients were female (30/59, 50.85%). RYGB was performed laparoscopically without mortality or major complications. The mean BMI in 59 patients decreased from 30.89 ± 3.12 to 25.04 ± 3.48 in the fifth year. No one was lost to follow-up in 5 years. There were significant reductions in BMI, A1C, and oral medication or insulin in all groups. Diabetes remission rates in the first, third, and fifth years postoperation were 77.97, 61.02, and 49.15%. T2D relapse and requirement for antihypertensive agents increased in the third and fifth years. Larger quantity of subcutaneous fat area (SFA) and shorter duration of T2D preoperation were more likely to achieve remission of T2D postoperation.

Conclusions This study has confirmed that RYGB is an effective treatment for obese Chinese patients with T2D, resulting in diabetes remission, metabolic disorder control, and cardiovascular risk reduction.

Keywords Type 2 diabetes mellitus · Roux-en-Y gastric bypass · Obesity · Remission

Introduction

Type 2 diabetes mellitus (T2D) is a life-threatening disease that is highly prevalent. The number of people with T2D is estimated to rise from 382 million in 2013 to 592 million by 2035 [1]. In addition to medical and exercise therapy, bariatric surgery has recently become a popular therapeutic approach for patients with T2D and obesity. Indeed, half a million bariatric surgery procedures are now performed annually worldwide, and Roux-en-Y gastric bypass (RYGB) is the frequently performed surgical procedure in recent years. A number of conditions, including essential hypertension, diabetes, asthma, osteoarthritis, and hyperlipidemia, can be ameliorated or even resolved following bariatric surgery [2].

Recent statements from the Diabetic Surgery Summit have indicated that bariatric surgery should be performed in T2D patients with a body mass index (BMI) > 35 kg/m^2 and may be an option for T2D patients with a BMI 30–35 kg/m^2 and major co-morbidities [3]. However, the new guidelines in China state that bariatric surgery should be considered in T2D patients with a BMI ≥ 27.5 kg/m^2 [4], because in Asian populations, obesity is defined by a BMI ≥ 28 kg/m^2. However, the mechanism whereby bariatric surgery induces the remission of diabetes remains unclear. Our previous study provided evidence that T2D remission after bariatric surgery is influenced by T2D duration, BMI, and visceral fat volume in Chinese patients [5]. RYGB is an effective treatment for T2D patients, even those with a lower BMI, resulting in the remission of diabetes and better control of metabolic disorders, such that the 3-year cardiovascular risk is lower [6]. In the present study, we evaluated the prevalence of T2D remission after

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RYGB in Chinese patients with different levels of obesity and glycated hemoglobin (A1C).

Materials and Methods

Patients

We retrospectively reviewed the medical records of 59 patients who had undergone RYGB between February 2011 and May 2014. The Human Research Review Board of our institution approved the study and all patients provided their written informed consent. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Following the latest guidelines for metabolic surgery published by the Chinese Society for Metabolic and Bariatric Surgery, the inclusion criteria were (1) T2D duration ≤ 15 years, with adequate islet function defined as a fasting C-peptide during an oral glucose tolerance test (OGTT) of > 1 ng/mL and a ratio of peak-to-fasting blood glucose of > 2 ng/mL; (2) age 16–65 years; and (3) BMI 27.5–35 kg/m^2. Patients with established diagnoses of type 1 diabetes, latent autoimmune diabetes in adulthood, malignancy, debilitating disease, unresolved psychiatric illness, or substance abuse were excluded from the study.

Patients underwent standard RYGB, which included the creation of a 25–30-mL gastric pouch, a 100-cm biliopancreatic limb, and a 100-cm alimentary limb as described by Dixon et al. [7].

Definitions of Obesity and T2D

The diagnosis of T2D was made on the basis of the 1999 WHO criteria: a fasting plasma glucose ≥ 7.0 mmol/L and/or a 2-h plasma glucose during an OGTT ≥ 11.1 mmol/L. BMI was categorized according to standard Chinese guidelines [8] as follows: normal weight: BMI ≥ 18.5 and < 24 kg/m^2; overweight: BMI ≥ 24 and < 28 kg/m^2; and obesity: BMI ≥ 28 kg/m^2.

According to BMI and A1C, patients were divided into two groups: BMI groups (group A: BMI < 28 kg/m^2; group B: BMI ≥ 28 kg/m^2) and A1C groups (group C: A1C < 7%; group D: A1C ≥ 7%).

Remission of Diabetes, Hypertension, and Dyslipidemia

Diabetes complete remission was defined as glycated hemoglobin (A1C) level ≤ 6.5% for ≥ 1 year without active pharmacologic intervention in China [9], and partial remission was defined as A1C < 7.0%. Complete remission of hypertension was defined as a blood pressure < 120/80 mmHg without antihypertensive medication. Dyslipidemia remission was defined as normal lipid serum levels without medication.

Biochemical Measurements

Biochemical parameters were measured in serum samples obtained after an overnight fast. These were fasting glucose, postprandial glucose determined during an OGTT, fasting C-peptide, A1C, total cholesterol, triglyceride, high-density lipoprotein-cholesterol (HDL-c), and low-density lipoprotein-cholesterol (LDL-c). Cardiovascular risk was estimated using the total cholesterol-to-HDL-cholesterol ratio. Insulin resistance and β-cell function were assessed using the homeostasis model assessment of insulin resistance (HOMA-IR), which was calculated using the formula HOMA-IR (mIU/mmol/L^2) = fasting insulin (mIU/L) × fasting glucose (mmol/L)/22.5, and the homeostasis model assessment of β-cell function (HOMA-β), calculated using HOMA-β (%) = 20 × fasting insulin (mIU/L)/fasting glucose (mmol/L) − 3.5).

Subcutaneous fat area (SFA) was assessed using Philips Achieva 3.0-T magnetic resonance imaging (MRI) system (Philips Medical Systems, Eindhoven, The Netherlands) with standard array coils with the subject in the supine position. Breath-hold fast imaging with steady-state precession images were centered on the L4–L5 intervertebral disc using standard localizer images with the following parameters: TR = 4 ms, TE = 2 ms, number of slices = 12, slice thickness = 8 mm, image matrix = 256 × 256, and field-of-view = 500 × 500 mm. The four slices that were best aligned with the L4–L5 disc were analyzed using the SliceOmatic 5.0 software package (Escape Medical Viewer V3.2) to define SFA. SFA was measured by fitting a spline curve to points on the border of the subcutaneous and visceral regions [10]. Written informed consent including MRI scan for SFA calculating was obtained from all participants before starting the study.

Statistical Analysis

All statistical analyses were conducted using SPSS software (version 20.0; SPSS Inc., Armonk, NY, USA). One-way analysis of variance was used to compare values before and after the study. Contingency tables for categorical variables were analyzed using the Kruskal–Wallis test. Data are presented as the mean ± SD or median [interquartile range (IQR)]. Multiple stepwise logistic regression analysis was performed to assess the independent predictive effects of each variable on the prevalence of diabetes remission after surgery. The cut-off point for each predictor was evaluated using Youden's index and receiver operating characteristic (ROC) curves. $P < 0.05$ was accepted as indicating statistical significance.

Results

A total of 59 patients were studied (30 women [50.8%] and 29 men [49.2%]). RYGB was performed laparoscopically, without mortality or major complications. Severe malnutrition and vitamin deficiency were not observed during the 5-year follow-up period. The patients' baseline characteristics are shown in Table 1. However, age and T2D duration have statistically significant difference in groups A and B ($P < 0.01$).

Weight Loss

There were significant reductions in BMI, waist and hip circumferences, and waist-to-hip ratio following RYGB (Table 2). The BMI between groups A and B is significantly different statistically (Fig. 1). The total weight loss (TWL%) in the first, third, and fifth years after RYGB in group A was 19.17 ± 5.67, 18.36 ± 8.15, and 17.21 ± 7.84%. In group B, TWL% was 22.74 ± 7.03, 19.18 ± 7.27, and 19.26 ± 7.69%. However, there was no difference in BMI between groups C and D after RYGB.

Glycemic Control

The requirement for insulin was significantly lower in the first 3 years after RYGB in all the groups, and there was also a reduction in the requirement for oral medication (Table 3). The diabetes complete remission rates in the first, third, and fifth years after RYGB were 77.97, 61.02, and 49.15% in our study. Before surgery, the mean A1C in groups C and D was 6.3 ± 0.43 vs. 8.78 ± 1.67. The longer T2D duration, higher A1C value, and more insulin therapy (54.54%) were shown in group A before RYGB. The complete remission of diabetes in BMI groups and A1C groups were 18.18 vs. 56.25% and 80 vs. 33.33% in the fifth year after surgery. However, in the fifth year after surgery, the number of participants administering oral medication and insulin therapy increased, and some relapsed back into diabetes (A1C ≥ 7%).

A1C, fasting and postprandial glucose, fasting C-peptide, and fasting insulin concentrations were significantly reduced for the 3 years following surgery, with no differences among the groups. HOMA-IR and HOMA-β showed no significant changes in the 5 years following RYGB (Table 4).

Blood Pressure

Blood pressure decreased significantly following RYGB in all the groups. Although the baseline blood pressure in group B was a little higher than that in group A (133.1 ± 12.0 vs. 128.4 ± 12.0; $P > 0.05$), it decreased sharply after surgery and remained lower for the following 3 years. The same trends were identified for groups C and D.

The medication results being used by the participants are listed in Table 3. One year after surgery, the number of patients taking antihypertensive medication was significantly lower, and this remained true for the following 4 years. In the fifth year, the number of medications being used increased, but remained lower than at baseline. There were no significant differences between the BMI groups or the A1C groups.

Dyslipidemia

The total cholesterol, triglycerides, HDL-c, and LDL-c values are shown in Fig. 2 and Fig. 3. The baseline values of total

Table 1 Characteristics of the patients at baseline

Characteristic	Group A $N = 11$	Group B $N = 48$	P value	Group C $N = 20$	Group D $N = 39$	P' value
Age (years)	54.82 ± 8.83	47.77 ± 10.1	< 0.001	46.8 ± 11.04	50.26 ± 9.65	0.22
Female sex, no. (%)	7 (63.6)	23 (47.9)	0.347	8 (40)	22 (56.41)	0.233
T2DM duration (years)	10.64 ± 3.96	7.1 ± 4.55	0.021	6.01 ± 4.65	8.63 ± 4.42	0.042
History of hypertension, no. (%)	6 (54.54)	25 (52.08)	0.883	11 (55)	19 (48.71)	0.648
Weight (kg)	77.23 ± 4.06	88.2 ± 12.8	< 0.001	89.05 ± 13.22	84.67 ± 11.88	0.203
BMI (kg/m^2)	27.49 ± 0.32	31.67 ± 2.94	< 0.001	31.52 ± 2.94	30.57 ± 3.19	0.273
Waist circumference (cm)	96 ± 3.61	104.85 ± 9.7	< 0.001	106.35 ± 10.56	101.59 ± 8.64	0.069
Hip circumference (cm)	100 ± 4.69	107.1 ± 7.59	0.004	108.5 ± 8.07	104.38 ± 7.1	0.049
Waist–hip ratio	0.96 ± 0.04	0.98 ± 0.05	0.311	0.98 ± 0.06	0.97 ± 0.05	0.732
SBP (mmHg)	128.36 ± 12.03	133.08 ± 11.97	0.243	129.85 ± 10.48	133.41 ± 12.69	0.285
DBP (mmHg)	80 ± 6.65	84.02 ± 8.98	0.168	81.45 ± 9.3	84.21 ± 8.33	0.252

P values are for comparisons of groups A and B. P' values are for comparisons of groups C and D. Group A: BMI < 28 kg/m^2. Group B: BMI ≥ 28 kg/m^2. Group C: A1C < 7%. Group D: A1C ≥ 7%

BMI, body mass index; *HR*, heart rate; *SBP*, systolic blood pressure; *DBP*, diastolic blood pressure

Table 2 Anthropometric characteristics in 1, 3, and 5 years after surgery

Variable	BMI < 28	BMI ≥ 28	*P* value	A1C < 7	A1C ≥ 7	*P′* value
Weight (kg)						
1 year	62.67 ± 2.31**	68.2 ± 12.88**	0.005	65.01 ± 13.03**	67.57 ± 12.12**	0.231
3 years	64 ± 4.36**	70.56 ± 13.03**	0.049	71.53 ± 15.44**	69.42 ± 11.77**	0.331
5 years	64.5 ± 2.29**	72.58 ± 15.24**	0.078	69.5 ± 15.88**	70.29 ± 13.23**	0.748
BMI (kg/m^2)						
1 year	21.94 ± 1.3**	24.4 ± 3.01**	<0.001	23.33 ± 2.78**	24.32 ± 2.99**	0.231
3 years	21.65 ± 1.65**	25.42 ± 3.21**	0.003	25.11 ± 3.31**	24.49 ± 3.36**	0.562
5 years	22.76 ± 2.12	25.57 ± 3.53**	0.002	24.44 ± 3.68**	25.35 ± 3.38**	0.347
SFA (cm^2)						
Baseline	199.88 ± 44.3	299.71 ± 94.98	0.002	300.71 ± 104.97	272.22 ± 90.82	0.297
1 year	121.58 ± 47.37**	162.35 ± 82.97**	0.215	145.39 ± 87.74**	163.66 ± 74.41**	0.446
3 years	108.07 ± 55.51**	183.16 ± 69.74**	0.025	165.68 ± 91.48**	164.72 ± 58.81**	0.975
5 years	142.99 ± 84.89	190.33 ± 88.95**	0.242	143.83 ± 74.47**	202.78 ± 90.7**	0.064
Waist circumference (cm)						
1 year	80.5 ± 5.19**	86.7 ± 9.19**	0.008	84.2 ± 9.93**	86.36 ± 8.33**	0.389
3 years	81.75 ± 5.26**	90.09 ± 9.82**	0.026	90.63 ± 10.56**	87.3 ± 9.08**	0.280
5 years	84.68 ± 6.34**	89.84 ± 10.01**	0.110	86.53 ± 11.97**	90 ± 8.07**	0.200
Hip circumference (cm)						
1 year	90.4 ± 2.95**	95.65 ± 7.33**	0.001	94.4 ± 7.5**	94.89 ± 6.87**	0.806
3 years	90.25 ± 5.04**	98.11 ± 8.72**	0.019	98.44 ± 10.28**	95.59 ± 7.6**	0.305
5 years	93.86 ± 4.35**	97.09 ± 8.14**	0.211	96.21 ± 8.24**	96.59 ± 7.42**	0.861
Waist–hip ratio						
1 year	0.89 ± 0.04**	0.91 ± 0.05**	0.356	0.89 ± 0.05**	0.91 ± 0.05**	0.137
3 years	0.91 ± 0.04**	0.92 ± 0.05**	0.526	0.92 ± 0.05**	0.91 ± 0.05**	0.638
5 years	0.9 ± 0.05**	0.93 ± 0.07**	0.330	0.9 ± 0.07**	0.93 ± 0.07**	0.059
SBP (mmHg)						
1 year	125.78 ± 17.36	120.54 ± 10.99**	0.395	116.75 ± 11.11**	123.67 ± 12.21**	0.023
3 years	123 ± 8.82	126.86 ± 18.62	0.573	124.25 ± 15.11	127.26 ± 18.51	0.585
5 years	123.09 ± 12.51	124.48 ± 14.73**	0.774	121.26 ± 12.04*	125.68 ± 15.15*	0.273
DBP (mmHg)						
1 year	75 ± 7.45	76.74 ± 7.75**	0.520	73.95 ± 7.84**	77.81 ± 7.31**	0.071
3 years	78.13 ± 7.32	77.69 ± 8.91**	0.898	76.44 ± 7.9	78.56 ± 8.97*	0.439
5 years	76.09 ± 8.46	76.96 ± 9.87**	0.790	74.11 ± 9.92*	78.13 ± 9.19**	0.135

P values are for comparisons of groups A and B. *P′* values are for comparisons of groups C and D. Group A: BMI < 28 kg/m^2. Group B: BMI ≥ 28 kg/m^2. Group C: A1C < 7%. Group D: A1C ≥ 7%

BMI, body mass index; *HR*, heart rate; *SBP*, systolic blood pressure; *DBP*, diastolic blood pressure; *SFA*, subcutaneous fat area

*$P < 0.05$, **$P < 0.01$: compared to preoperation

cholesterol, triglycerides, HDL-c, and LDL-c values in groups A and B were 4.86 ± 1 vs. 4.9 ± 0.89, 2.52 ± 2.75 vs. 2.72 ± 3.07, 1 ± 0.27 vs. 1.02 ± 0.25, and 2.85 ± 0.92 vs. 2.84 ± 0.85. In groups C and D, these were 4.64 ± 0.82 vs. 5.02 ± 0.93, 2.16 ± 1.43 vs. 2.95 ± 3.52, 1 ± 0.23 vs. 1.03 ± 0.26, and 2.71 ± 0.86 vs. 2.91 ± 0.85. The cardiovascular risk scores decreased significantly in the all groups after surgery (Table 3). However, the cardiovascular risk of group A in the fifth year postoperation has no difference compared with preoperation ($P > 0.05$).

Factors Predictive of Diabetes Remission After RYGB

The multivariate analysis showed that patients who had a larger quantity of SFA and shorter duration of diabetes before surgery were more likely to achieve remission of their diabetes after RYGB. ROC analysis showed that the areas under the curve (AUCs) for SFA and duration of diabetes were 0.733 and 0.778, respectively. The cut-off point for SFA volume was 0.439, and that for the duration of diabetes was 0.447 (Fig. 4).

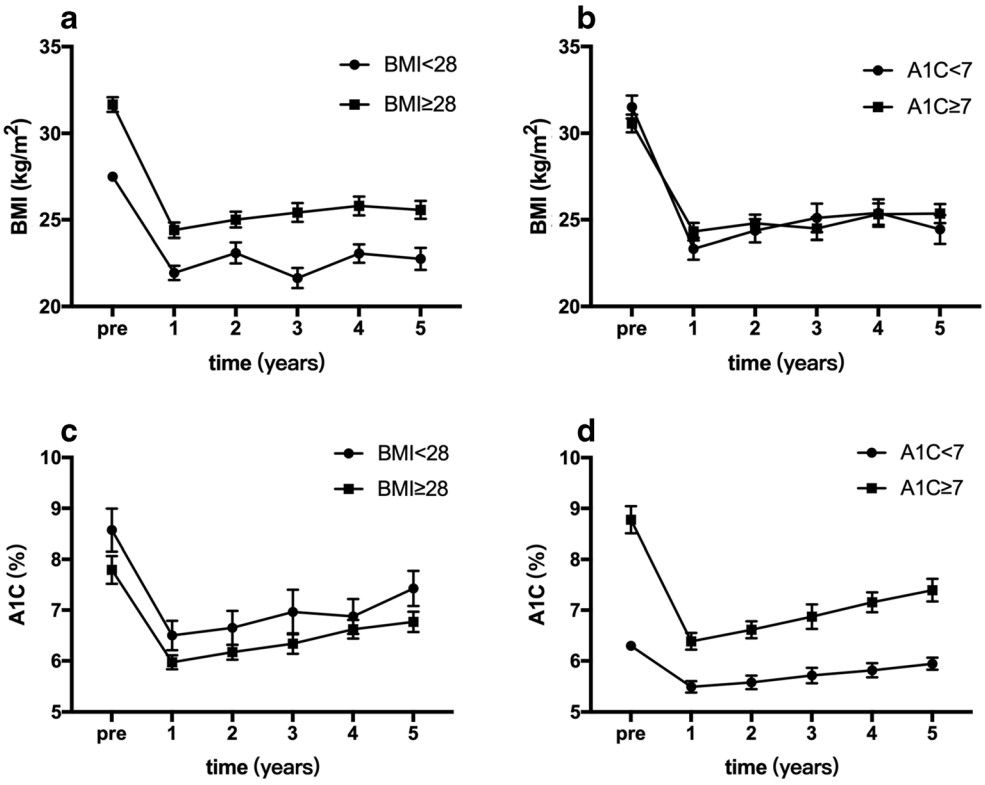

Fig. 1 A1C and BMI were decreased sharply after RYGB. BMI decreased and kept stable after surgery (**a**, **b**). In different BMI groups and A1C groups, A1C was decreased after surgery with an increasing trend in the 5-year follow-up (**c**, **d**)

Discussion

Few previous studies have determined the effects of RYGB over a 5-year period of follow-up in China. We designed the present study on the basis of the Chinese obesity guidelines [11], which differ slightly from the IDF standards [12]. We accordingly divided the participants into two BMI groups (groups A and B) to better represent the obesity status of these Chinese patients and two A1C groups (groups C and D). The A1C groups were designed on the basis of the standards of care for T2D in China. The latest surgical criteria published by the Chinese Society for Metabolic and Bariatric Surgery are also based on these guidelines.

The major cause of death in individuals with T2D is microvascular disease, the risk of which we assessed using the total cholesterol-to-HDL ratio and found it to be lower in all the groups after RYGB. However, the cardiovascular risk of group A in the fifth year postoperation has no decreasing trend significantly, owing to the limited sample size (only 11 patients in group A in Table 3). Analysis of blood pressure and the use of antihypertensive agents showed that RYGB ameliorates hypertension in T2D patients, and this effect was maintained for 5 years. This is important, because patients with poorly controlled T2D are at high risk of microvascular complications [13]. RYGB more effectively reduced SBP than DBP, which was not consistent with the findings of a previous study [14]. Most patients stopped using insulin until the fifth year following surgery, and there was only one patient in group A and none in group C using insulin in the fifth year. Overall, 8.5% of the participants required insulin to control their glycemia again. Similarly, the number of patients using antihypertensive drugs decreased after RYGB (to 2.6% for 1 year), but increased from the third year (to 20.3% in the fifth year).

Weight loss remains the primary outcome of interest after RYGB. All patients achieved significant weight loss in this study, while avoiding malnutrition and excessive weight loss. The BMI of group B (BMI > 28) was higher than that of group A (BMI < 28), both before and after surgery. Although the BMI of group A was lower than 28 kg/m^2, the patients were overweight (27.5 ± 0.3 kg/m^2). Our results also showed that there was no difference in BMI between groups C and D. The body mass of the participants was quite stable after the initial loss at the 3-year follow-up visit, but there was a small increase in the fifth year. Weight regain after RYGB has become a concern in recent years in China. Dayan et al. showed that significant weight regain occurred in 20% of RYGB patients and 40% of the super-morbidly obese experience significant weight regain (> 15% of maximal EWL) [15].

This study has confirmed that RYGB is an effective treatment for obese Chinese patients with T2D. There is a widespread interest in its effects on obesity-related co-morbidities, especially diabetes, hypertension, and hyperlipidemia. The diabetes complete remission rates in the first, third, and fifth years after RYGB were 76.27, 50.84, and 49.15% in our study. Almalki et al. reported that gastric bypass resulted in complete diabetes control in up to 62.0% of patients [16] Yu

Table 3 Metabolic syndrome and medication use at baseline and after surgery

Variable	Group A	Group B	Group C	Group D
Baseline				
Insulin therapy no./total no. (%)	6/11 (54.54)	19/48 (39.58)	5/20 (20)	20/39 (51.28)
OHGA no./total no. (%)	9/11 (81.81)	43/48 (89.58)	19/20 (95)	33/39 (84.61)
Antihypertensives no./total no. (%)	1/11 (9.09)	7/48 (14.58)	1/20 (5)	7/39 (17.95)
Cardiovascular risk	5.11 ± 1.6	5.03 ± 1.43	4.81 ± 1.11	5.16 ± 1.59
1 year				
Insulin therapy no. /total no (%)	2/11 (18.18)	2/48 (4.17)	1/20 (5)	3/39 (7.69)
OHGA no./total no. (%)	2/11 (18.18)	4/48 (8.33)	0/20 (0)	6/39 (15.38)
Antihypertensives no./total no. (%)	0/11 (0)	1/48 (0.02)	0/20 (0)	1/39 (2.56)
Cardiovascular risk	3.47 ± 0.55**	3.35 ± 0.77**	3.16 ± 0.61**	3.49 ± 0.78**
Diabetes remission no./total no. (%)	7/11 (63.64)	39/48 (81.25)	19/20 (95)	27/39 (69.23)
3 years				
Insulin therapy no./total no (%)	2/11 (18.18)	0/48 (0)	1/20 (5)	1/39 (2.56)
OHGA no./total no. (%)	2/11 (18.18)	7/48 (14.58)	0/20 (0)	9/39 (23.07)
Antihypertensives no./total no. (%)	0/11 (0)	4/48 (8.33)	2/20 (10)	2/39 (5.13)
Cardiovascular risk	3.31 ± 1.13**	3.44 ± 0.77**	3.39 ± 0.97**	3.44 ± 0.74**
Diabetes remission no./total no. (%)	4/11 (36.36)	32/48 (66.67)	18/20 (90)	18/39 (46.15)
5 years				
Insulin therapy no./total no. (%)	1/11 (9.09)	3/48 (6.25)	1/20 (6.25)	3/39 (7.69)
OHGA no./total no. (%)	6/11 (54.54)	11/48 (22.92)	3/20 (15)	14/39 (35.90)
Antihypertensives no./total no. (%)	1/11 (9.09)	11/48 (22.92)	4/20 (20)	8/39 (20.51)
Cardiovascular risk	4.22 ± 1.59	3.69 ± 0.94**	3.68 ± 1.02**	3.84 ± 1.14**
Diabetes remission no./total no. (%)	2/11 (18.18)	27/48 (56.25)	16/20 (80)	13/39 (33.33)

Cardiovascular risk calculated as the total cholesterol/HDL ratio. Group A: BMI < 28 kg/m^2. Group B: BMI ≥ 28 kg/m^2. Group C: A1C < 7%. Group D: A1C ≥ 7%

OHGA, oral hypoglycemic agents

*P < 0.05, **P < 0.01: compared to preoperation

and colleagues found that the 1-year remission rate was 73.5% [17]. This indicates that RYGB has a potent effect on obesity in combination with T2D. Furthermore, a 10-year survey showed that 58% of patients demonstrated diabetes remission after RYGB and their weight loss was significant and sustainable [18], and Kim et al. reported a 71% remission rate and a mean of 26 months after RYGB [19]. A1C in our study had decreased from 6.3 to 5.7% in group C and from 8.8 to 6.9% in group D at the 3-year follow-up visit; this was followed by a small increase in the fifth year after surgery. Taken together, these data indicate that gastrointestinal metabolic surgery, and RYGB in particular, is an effective treatment for obese patients with T2D.

In recent years, multivariate analyses have shown that BMI, T2D duration, and visceral fat volume are independent predictors of T2D remission after surgery [17, 18]. However, in the present study, we found that T2D duration and SFA have impacts on T2D remission rates post-RYGB. The area of subcutaneous in the T2D patients decreased substantially after surgery and then remained stable for the following 5 years. The reduction in SFA has previously been shown to be greater than that in visceral fat [20]. In addition, another study has shown that abdominal subcutaneous fat thickness is a reliable indicator of the severity of nonalcoholic fatty liver disease in obese patients [21]. Furthermore, after bariatric surgery, the reduction in subcutaneous fat cell volume is more strongly associated with the improvement in insulin sensitivity [22, 23], and some recent studies have shown that large subcutaneous fat cells may be associated with a higher risk of developing T2D [24, 25]. Therefore, the reduction in SFA following RYGB is likely to be associated with an increase in insulin sensitivity, an improvement in pancreatic islet function, and a reduction in A1C. However, the mechanisms whereby bariatric surgery alters fat distribution and glucose homeostasis remain unclear.

Older age, a longer history of T2D, and the use of insulin are all recognized as negative predictors of diabetes remission after metabolic surgery [26, 27]. A previous study also showed that a duration of T2D ≤ 4 years, an A1C ≤ 7.1%, and no requirement for insulin therapy were preoperative predictors of remission [28]. The significant reductions in C-peptide, insulin, HOMA-IR, and HOMA-β in the present study are indicative of an amelioration of insulin resistance, and these results are similar to those of

Table 4 Clinical parameters at baseline and after surgery

Variable	BMI < 28	BMI > 28	*P* value	A1C < 7	A1C ≥ 7	*P′* value
A1C (%)						
Baseline	8.57 ± 1.39	7.79 ± 1.88	0.200	6.3 ± 0.43	8.78 ± 1.67	< 0.001
1 year	6.5 ± 0.91**	5.97 ± 0.94**	0.110	5.49 ± 0.5**	6.39 ± 0.98**	< 0.001
3 years	6.96 ± 1.24*	6.34 ± 1.18**	0.191	5.71 ± 0.59**	6.87 ± 1.26**	< 0.001
5 years	7.43 ± 1.15*	6.77 ± 1.37**	0.147	5.95 ± 0.53*	7.39 ± 1.38**	< 0.001
hs-CRP (mg/L)						
Baseline	3.13 ± 2.86	2.73 ± 2.81	0.767	2.74 ± 2.52	2.81 ± 2.97	0.939
1 year	0.31 ± 0.17	1.81 ± 7.12	0.513	3.17 ± 10.91	0.68 ± 1.22**	0.347
3 years	1.24 ± 2.72	1.13 ± 2.31*	0.912	1.85 ± 3.37	0.71 ± 1.3**	0.213
5 years	1.23 ± 2.69	0.99 ± 2.19**	0.759	0.85 ± 1.37*	1.14 ± 2.64*	0.648
Fasting C-peptide (ng/mL)						
Baseline	2.17 ± 0.76	2.99 ± 1.46	0.077	3.03 ± 1.41	2.74 ± 1.39	0.445
1 year	1.62 ± 0.33**	1.94 ± 0.57**	0.100	1.79 ± 0.51**	1.93 ± 0.57**	0.366
3 years	1.41 ± 0.38*	2.01 ± 0.63**	0.020	1.86 ± 0.64**	1.94 ± 0.63**	0.715
5 years	1.87 ± 0.7	2.1 ± 0.73**	0.345	1.97 ± 0.74**	2.1 ± 0.72*	0.507
Fasting insulin						
Baseline	50.39 ± 100.9	20.78 ± 15.14	0.354	34.31 ± 73.92	22.19 ± 19.66	0.338
1 year	30.55 ± 71.25	6.21 ± 3.03**	0.308	16.79 ± 50.81	7.09 ± 4.48**	0.405
3 years	13.05 ± 14.51	6.96 ± 3.48**	0.276	8.11 ± 6.94	8.08 ± 7.35**	0.991
5 years	19.22 ± 26.89	7.98 ± 4.99**	0.197	10.48 ± 17.95	9.87 ± 9.46**	0.863
FBG (mmol/L)						
Baseline	8.51 ± 2.61	8.24 ± 2.21	0.733	6.73 ± 1.22	9.09 ± 2.27	< 0.001
1 year	6 ± 1.16*	5.73 ± 1.14**	0.813	5 ± 0.69**	6.21 ± 1.11**	< 0.001
3 years	6.4 ± 1.43	6.14 ± 1.73**	0.696	5.26 ± 1.03**	6.74 ± 1.74**	0.004
5 years	6.76 ± 1.66	6.57 ± 2.09**	0.779	5.41 ± 0.86**	7.21 ± 2.15**	< 0.001
PBG (mmol/L)						
Baseline	14.95 ± 3.59	12.93 ± 4.65	0.181	10.94 ± 3.19	14.51 ± 4.65	0.003
1 year	7.68 ± 2.81**	7.43 ± 2.91**	0.496	6.04 ± 2.15**	8.29 ± 2.93**	0.004
3 years	9.15 ± 3.02**	8.23 ± 3.38**	0.483	6.34 ± 2.22**	9.62 ± 3.25**	0.001
5 years	11.32 ± 3.24*	9.48 ± 3.83**	0.146	7.48 ± 3.1**	11.01 ± 3.54**	0.001
HOMA-β						
Baseline	50.2 (37.1–73.7)	76.7 (45.8–117.5)	0.727	88.9 (68.4–175.9)	58.1 (37.1–106.5)	0.268
1 year	65.7 (27.7–135.4)	58.0 (33.9–88.3)*	0.462	63.6 (52.7–157.1)	53.2 (29.7–75.5)	0.269
3 years	59.7 (35.3–111.5)	53.1 (29.9–98.4)	0.545	96.8 (53.1–135.9)	43.2 (26.8–84.7)	0.082
5 years	69.5 (30.4–89.9)	53.1 (30.8–84.5)	0.420	64.6 (41.8–120.7)	40.3 (28.8–78.0)	0.319
HOMA-IR						
Baseline	5.2 (2.5–17.0)	5.8 (4.0–9.4)	0.328	5.3 (3.8–6.7)	6.3 (3.6–10.8)	0.991
1 year	1.4 (1.1–4.9)	1.3 (0.9–2.0)**	0.281	1.0 (0.9–1.5)	1.4 (1.1–2.2)**	0.515
3 years	1.3 (1.1–4.7)	1.4 (1.2–2.4)**	0.294	1.3 (1.1–1.5)	1.8 (1.2–2.8)**	0.397
5 years	2.0 (1.5–6.0)	1.9 (1.3–2.6)**	0.167	1.5 (0.9–2.2)	2.1 (1.5–3.5)**	0.522

P values are for comparisons of groups A and B. *P′* values are for comparisons of groups C and D. Group A: BMI < 28 kg/m^2 . Group B: BMI ≥ 28 kg/m^2 . Group C: A1C < 7%. Group D: A1C ≥ 7%

FBG, fasting plasma glucose; *PBG*, postprandial glucose; *A1C*, hemoglobin A1c; *HOMA-IR*, homeostasis model assessment-insulin resistance; *HOMA-β*, homeostasis model assessment β-cell; *hs-CRP*, hypersensitive C-reactive protein

*$P < 0.05$, **$P < 0.01$: compared to preoperation

a previous 3-year follow-up study [10]. And some studies showed that preoperative fasting C-peptide could predict T2D remission in Chinese patients after RYGB [29, 30]. However, it is clear that the shorter the duration of T2D, the higher the rate of diabetes remission that will be achieved using RYGB.

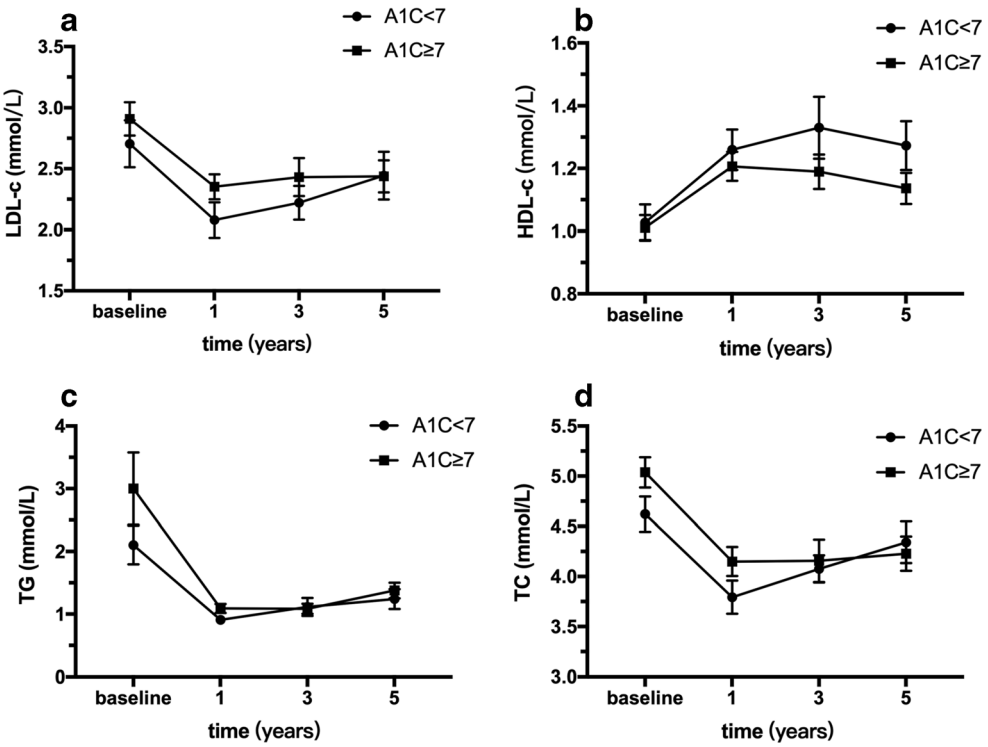

Fig. 2 **a**–**d** In the A1C groups, LDL-c, TG, and TC decreased significantly with increased HDL-c in 1, 3, and 5 years after RYGB. TC, total cholesterol; TG, total triglycerides; HDL-c, high-density lipoprotein-cholesterol; LDL-c, low-density lipoprotein-cholesterol

We found significant improvements in a number of metabolic parameters following RYGB. However, weight regain and recurrent hyperglycemia also occurred in some patients after several years. Indeed, a previous 10-year follow-up study showed that 9% of patients required revision surgery [18]. Fortunately, none of the patients in the present study required conversion, repair, or reversal surgery. Instead, poor diet or lifestyle may explain the longer-term failure of weight and diabetes control. Therefore, it is necessary to review current practice regarding the management of such patients over the long term, with a focus on maintaining improvement in glycemia and weight loss.

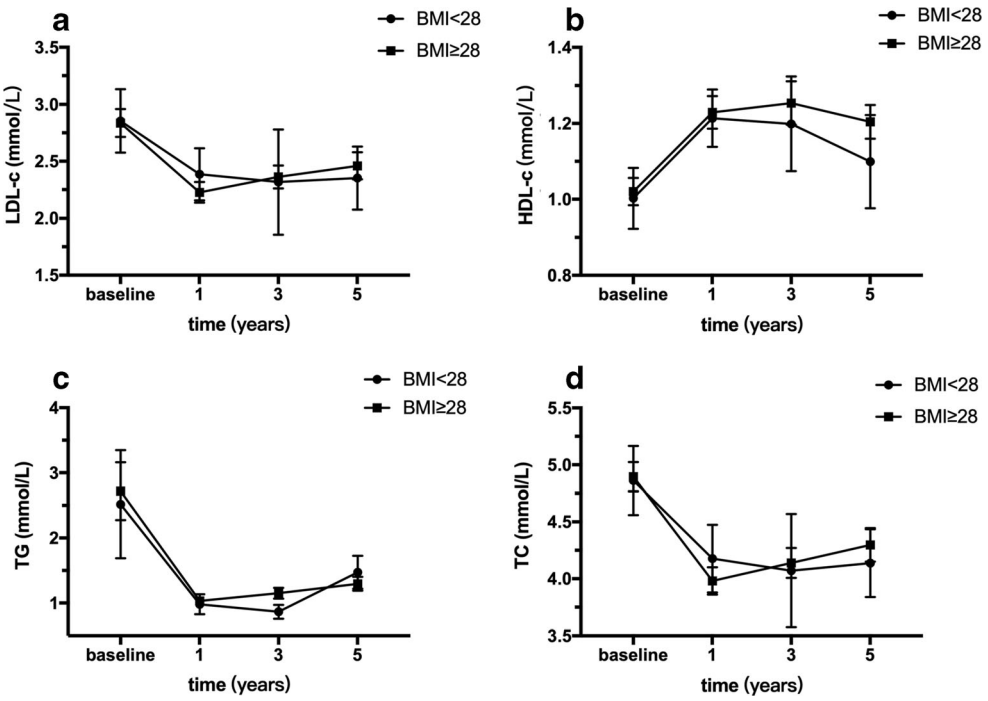

Fig. 3 **a**–**d** In the BMI groups, TG and TC decreased significantly with increased HDL-c in 1, 3, and 5 years after RYGB. TC, total cholesterol; TG, total triglycerides; HDL-c, high-density lipoprotein-cholesterol; LDL-c, low-density lipoprotein-cholesterol

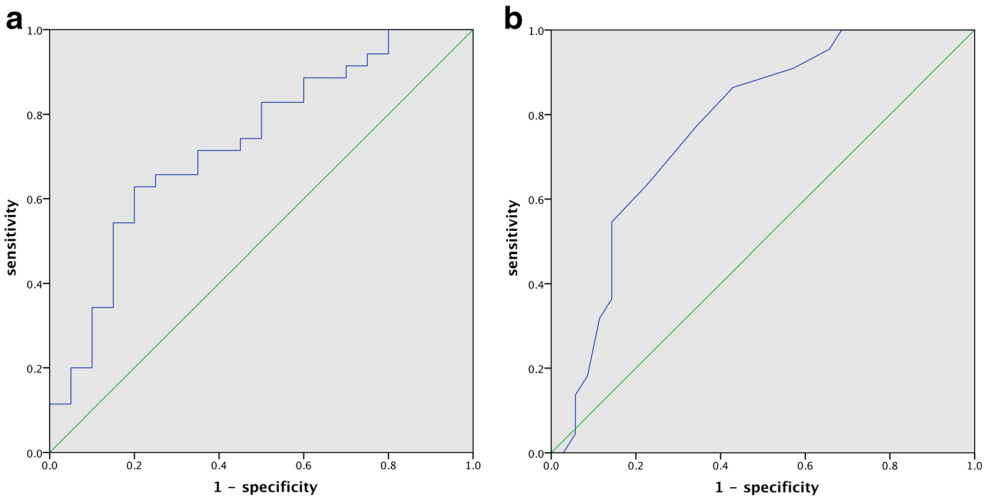

Fig. 4 Subcutaneous fat area (SFA) (**a**) and T2D duration (**b**) might have impacts on T2D remission post-RYGB. Area under the ROC curve for subcutaneous fat and T2D duration was 0.733 and 0.778 ($P = 0.008$ and $P = 0.002$). Their cut-off points were 0.439 and 0.447

In this 5-year study, patients with differing BMIs and A1C values all showed significant improvements in body mass, diabetes control, and metabolic outcomes, as shown previously [14, 18, 19]. However, T2D relapse and a requirement for antihypertensive agents increased between the third year and fifth year, which implies that blood pressure and glucose control should be carefully monitored as part of the long-term follow-up after RYGB. The present results also suggest that SFA volume and T2D duration prior to surgery are two important predictors of diabetes remission after metabolic surgery. By taking these factors into account, better follow-up care can be provided following bariatric surgery.

There were a number of limitations to the present study, including its retrospective design and the limited sample size. Patients that underwent RYGB were older and more likely to require insulin and/or multiple medications 5 years after surgery, which may have confounded the results. The limited duration of follow-up may also mean that a lower rate of diabetes relapse was recorded than if the cohort had been followed for longer. Future studies are needed containing larger numbers of patients who are followed for longer. Furthermore, we did not assess the quality of life of the patients, which has been assessed in some previous studies.

Conclusion

However, despite these limitations, we have presented clear evidence that RYGB is an effective treatment for T2D in Chinese patients. Diabetes and metabolic disorders remain under control in most patients 5 years after RYGB, which also reduces their cardiovascular risk. We have also shown that T2D duration and SFA of patients before surgery may also have an impact on their likelihood of remission. Therefore, we should select the patients who are most likely to benefit from surgery and provide focused follow-up assessments and treatment following surgery, because there was a trend for weight regain and diabetes relapse 5 years after RYGB.

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Compliance with Ethical Standards The Human Research Review Board of our institution approved the study and all patients provided their written informed consent. The study was conducted in accordance with the principles of the Declaration of Helsinki.

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

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