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ORIGINAL CONTRIBUTIONS

Cost-Utility of Laparoscopic Roux-en-Y Gastric Bypass in Chinese Patients with Type 2 Diabetes and Obesity with a BMI ≥ 27.5 kg/m2: a Multi-Center Study with a 4-Year Follow-Up of Surgical Cohort

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Abstract

Objectives To find whether Laparoscopic Roux-en-Y gastric bypass (RYGB) surgery was cost effective compared to conventional medical management (CMM) in Chinese patients with type 2 Diabetes(T2D) and obesity with a body mass index (BMI) ≥27.5 kg/m^2 in four years.

Methods A total of 106 obese T2D individuals who underwent RYGB and 106 T2D patients treated with CMM were enrolled from three academic medical centers. Total health related costs, Glycated Hemoglobin A1c (A1C) and BMI was recorded. Cost-Utility Analysis (CUA) was used. Utility values according to results of A1c were obtained from published studies.

Results Improvements were observed in A1C (8.6% at baseline to 6.2% in the first year, $p < 0.001$) and BMI (30.7 kg/m^2 at baseline to 24.3 kg/m^2 in the first year, $p < 0.001$), and the effect lasted for 4 years after RYGB. In the CMM group, A1C fluctuated in four years. The health utility for RYGB group scores 3.756, whereas CMM group scores 3.594 in four years. The total healthcare costs decreased sharply from the second year after RYGB ($8,483 [¥52,596] in the first year to $672[¥4,164] in the second year, $p < 0.001$) and maintained for 3 years. In the CMM group, the total healthcare costs changed without significance. RYGB costs US$19,359 (¥125,836) per quality-adjusted life years (QALY) gained (incremental cost-utility ratio [ICUR]) compared to CMM, which was lower than a willingness-to-pay (WTP) of $20,277/QALY.

Conclusions Compared to CMM, RYGB is cost-effective for Chinese patients with type 2 diabetes and obesity 4 years after operation.

Keywords Cost-utility analysis (CUA) · Quality-adjusted life years (QALY); roux-en-Y gastric bypass (RYGB) · Body mass index (BMI) · Glycated hemoglobin A1c (A1C) · Total healthcare costs · Type 2 diabetes(T2D) · Obesity

Introduction

In recent decades, the incidence of type 2 diabetes (T2D) has rapidly increased. T2D and its complications have become leading public health challenges in China [1]. In the causes of T2D, obesity is an important risk factor. Individuals with T2D and obesity are prone to increase consumption of total healthcare compared to normal individuals. Healthcare cost

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associated with diabetes in China has rocketed from 2.2 billion Chinese Yuan(CNY¥) in 1993 to 200 billion in 2007 and is forecasted to exceed 360 billion RMB by 2030 without adjustment for inflation [2, 3].

Bariatric surgery such as Roux-en-Y gastric bypass surgery (RYGB) may be more effective than medical and lifestyle interventions for the most severe form of obesity to have major and sustainable weight loss [4, 5]. Long-term follow-up observation of RYGB has confirmed that 30%~47% patients with T2D and obesity have achieved complete remission of T2D [6–8]. In addition, RYGB improves chronic obstructive pulmonary disease, cardiovascular disease, other respiratory diseases, musculoskeletal and connective tissue disorders, and mental disorders [9], resulting in a reduced consumption of related therapies [10].

However, the ability of bariatric surgery to significantly reduce expenditures to save costs remains controversial due to the high surgery-related costs (US $25,000 to $30,000) [11, 12]. Due to the remission of diabetes, we assumed that RYGB may have a more positive economic effect on patients with T2D and obesity.

Among patients with diabetes, only 25.8% (95% confidence interval, 95% CI, 24.9%–26.8%) received treatment (conventional medical management [CMM]) for diabetes, and only 39.7% (95% CI, 37.6%–41.8%) of those treated had adequate glycemic control in the Chinese adult population [13]. Uncontrolled glycemia in T2D developed diabetic complications which increase economic burden either for individuals or the society.

In our multicenter study, cost utility analysis (CUA) was used to find whether RYGB may be cost-effective compared to control group treated with CMM in terms of T2D and obesity in four years. To our knowledge, this is the first study to calculate the cost-effectiveness of RYGB versus CMM in T2D Patients in China.

Materials and Methods

A total of 106 obese T2D individuals who underwent RYGB from February 2011 to November 2013 and 106 T2D patients treated with CMM were enrolled from three academic medical centers. Follow-up visits were scheduled at 1, 3, 6 months (M) and yearly (Y) after surgery, until 4 years post-RYGB whereas 1, 2, 3 and 4 years after recruitment in CMM group. The follow-up visits were with a tolerance of ±30 days in all participants. The Ethics Committee of Shanghai Jiaotong University affiliated No. 6 Hospital, The Second Affiliated Hospital & Yuying Children's Hospital of Wenzhou Medical University and Shanghai Sixth People's Hospital East Affiliated to Shanghai University of Medicine & Health Sciences all approved the study (ChiCTR1800016455) and all subjects gave written informed consent.

The inclusion criteria for RYGB group included: 1) T2D duration≤15 years with adequate islet function: a fasting C-peptide >1 ng/mL and a ratio of peak to fasting by the oral glucose tolerance test >2; 2) age 18–65 years; and 3) Body mass index (BMI) ≥27.5 kg/m^2 and poorly controlled T2D combined with more than 2 symptoms of metabolic syndrome.

The inclusion criteria for CMM group included: 1) poorly controlled T2D, Glycated Hemoglobin A1c (A1C) matched with patients included in RYGB group; and 2) age 18–65 years, age and gender matched with patients included in RYGB group.

Patients with established diagnoses of type 1 diabetes(T1D), latent autoimmune diabetes in adulthood, malignancy, debilitating disease, unresolved psychiatric illness, substance abuse, or patients with an intention of pregnancy were excluded from the study. The patients who originally scheduled to follow up yet received treatment elsewhere were excluded from the study.

All the patients had complete clinical data including age, sex, weight (WT), BMI, glycated hemoglobin A1c (A1C) and biochemical variables in our database. The percentage of excess weight loss (%EWL) was calculated using the formula: (WT before – WT after) *100/ (WT before ideal body WT). Ideal body WT = WT corresponding to a BMI of 24 kg/m^2.

All patients in our study have comprehensive assessment of glucose and lipid metabolism disorders, urinary albumin/creatinine ratio (UACR) and estimated glomerular filtration rate (estimated GFR, eGFR), microvascular and macrovascular diabetic complications once a year and all patients received treatment strategy for diabetes and diabetic complications at visits. In addition, postoperative data regarding patient levels of folic acid, vitamin B12, serum iron, parathyroid hormone (PTH) and 25-hydroxy vitamin D [25(OH)D] were collected as indices of anemic and hypo calcemic status [14]. T2D treatments concluded oral antidiabetic therapy and/or insulin and/or glucagon-like peptide 1 receptor agonists (GLP-1 RA).

Laparoscopic RYGB Procedure

All obese patients with T2DM underwent RYGB, performed laparoscopically by a single surgeon using a standardized technique as previously reported [15]. A 25 ml gastric pouch was divided from the distal remnant. The biliopancreatic and alimentary limbs were 100-120 cm in length.

Health Utility

Changes in A1C levels are likely to affect Health-Related Quality of Life (HRQoL) for patients with T2D because of short-term impact and long-term diabetes complications [16, 17] . Since the individuals HRQoL descriptions are not available, CUA can be performed on the basis of published mean preference-based scores for the condition in question [18]. There is currently a lack of utility data for A1C of T2D, meaning that economic evaluation had to rely on a combination of type 1 and type 2 diabetes utilities, despite differences between the conditions and populations, or type 1 diabetes-specific utilities derived from different instruments. There existed the relationship between A1C and health utility, which were derived using the US time trade off valuation of the EQ-5D, for T1D. The utility values (1% increase in A1C was associated with a disutility of −0.027 [95% CI -0.049, −0.006]) for association between A1C and health utility in T1D when adjusted EQ-5D disutility estimates with A1C as continuous predictor from least squares regression(Adjusting for demographics, medications, and diagnosis codes) [19]. Then, we used this health utility score as an alternative. A utility value was assigned to each A1C, and utility differences for the relevant A1C were calculated. Adjusted association between A1C and EQ-5D health utility for study participants was mean estimated EQ-5D scores 0.955 by absolute A1C level 6% (5.5% to 6.4%),0.927 by 7% (6.5 to 7.4%), 0.900 by 8% (7.5 to 8.4%), 0.873 by 9% (8.5 to 9.4%) and 0.845 by 10% (9.5% to 10.4%). The number of Quality-Adjusted Life Years (QALYs) associated with the intervention (RYGB or CMM) is calculated by weighting the time spent in each state of A1C identified by the corresponding preference-based utility score [20].

Healthcare Costs

We selected patients who were only treated in our hospitals, and the cost information was obtained through computer systems. China has a complex public sponsored insurance system with private payers in the mix two. We recorded the actual and direct costs to deliver medical care, whether or not it was paid by public health insurance or patients themselves. Costs were recorded including drugs, medical tests (including blood glucose test strip) and consulting fee. All examination and treatment costs for diabetes and non-diabetes was included in total healthcare cost. The costs were estimated in both Chinese Yuan (¥) and US Dollars ($) with an exchange rate of 6.2 Chinese Yuan per one US Dollar according to the exchange rate in 2013.

Statistical Analysis

Data on normally distributed variables were expressed as means ± standard deviations and data on skewed variables were expressed as medians [with interquartile ranges (IQR)]. Differences in BMI and A1C 1, 2, 3, and 4 years after recruitment were compared with those at baseline. BMI and A1C were also compared between RYGB group and CMM group. Changes in [1] the total costs, [2] the medication costs, [3] the medical tests, and [4] the consulting fee 1, 2, 3, and 4 years after recruitment were recorded in both RYGB group and CMM group.

ICUR is defined by the difference in cost between RYGB and CMM, divided by the difference in their utility in four years.

Two-way ANOVA and chi-square tests were used. All reported *P*-values are two-tailed, and statistical significance was set at $p < 0.05$.

Statistical analyses were performed using SPSS 20.0 (SPSS, Chicago, IL, USA).

Willingness-to-Pay (WTP)

The ICER/ICUR denotes how much payment is required for one additional year of (quality-weighted) life and is compared with a pre-determined WTP threshold that differs by publication, society, economic system, time period, and other factors. Comparison of the ICER/ICUR with the WTP threshold concludes whether or not the intervention is deemed "cost-effective" [21]. The commonly cited $50,000 per QALY gained and the WHO criteria of 3-times the gross domestic product per capita ($20,277 in our study) per disability-adjusted life-year [22]. We chose a WHO's lower threshold that a WTP of 3 times the GDP per capita per QALY gained in this study, which is more convincing to test whether metabolic surgery is cost-effective.

Results

In RYGB group, complete data were available for 89 of the 106 patients (84.0%) at the 1-month follow-up, for 84 patients (79.2%) at the 3-month, for 84 patients (79.2%) at the 6-month, for 95 patients (89.6%) at the 1-year, for 74 patients (69.8%) at the 2-year, for 80 patients (75.5%) at the 3-year, and for 92 patients (86.8%) at the 4-year. Complete data were available for 88 of 106 patients (83.0%) at the 1-year follow-up, for 77 patients (72.6%) at the 2-year, for 79 patients (74.5%) at the 3-year, and for 68 patients (64.2%) at the 4-year in CMM group.

There was significant difference between the RYGB patients and the controls in terms of duration of T2D(Year), weight, BMI, Fasting C-peptide(ng/dL) and percentage of hypertension and Cardiovascular disease (Table 1). No statistically significant difference was found in A1C (%), fasting plasma glucose(mmol/L) and percentage of dyslipidemia (Table 1).

In RYGB group, BMI gradually decreased from 30.7 ± 3.0 kg/m^2 to 24.3 ± 2.4 kg/m^2 ($t = 10.061$ $p < 0.001$) one year after surgery and then stabilized during the next 3 years (Table 2). The percentage of excess weight loss (%EWL) was 50.2% (±26.5) at the 1-month follow-up, 78.2%(±39.7)

Table 1 Characteristics of the study cohort at baseline

Patients characteristics	RYGB Group	CMM Group	P value
Total	106	106	–
Male, *n* (%)	42 (39.6%)	42 (39.6%)	–
Age (year), mean ± SD	49.0 ± 11.1	49.6 ± 12.4	0.838
Duration of T2D(Year), mean ± SD	8.0 ± 4.8	4.3 ± 2.8	<0.001
Waist circumference (cm), mean ± SD			
Male	108.3 ± 11.1	89.6 ± 10.6	<0.001
Female	102.9 ± 9.8	86.7 ± 11.1	<0.001
Weight (kg), mean ± SD	94.1 ± 24.2	69.4 ± 13.9	<0.001
BMI (kg/m^2), mean ± SD	30.7 ± 3.0	24.8 ± 3.8	<0.001
A1C(%), mean ± SD	8.6 ± 2.1	8.5 ± 2.3	0.883
Fasting plasma glucose(mmol/L), mean ± SD	8.8 ± 2.8	8.1 ± 2.5	0.632
2hPG (mmol/L), mean ± SD	13.6 ± 4.2	13.6 ± 4.7	0.785
Fasting C-peptide(ng/dL), mean ± SD	2.5 ± 1.2	1.7 ± 1.2	<0.001
2 h C-peptide(ng/dL), mean ± SD	6.1 ± 3.2	5.2 ± 3.3	0.180
Hypertension *n* (%)	28(26.4%)	42(39.6%)	<0.001
SBP (mmHg), mean ± SD	132 ± 15	128 ± 16	0.298
DBP (mmHg), mean ± SD	84 ± 11	81 ± 10	0.421
Dyslipidemia *n* (%)	68(64.2%)	60(56.6%)	0.473
TC(mmol/L), mean ± SD	5.0 ± 1.2	4.9 ± 1.2	0.893
TG(mmol/L), median(IQR)	1.7(1.3~2.5)	1.4(1.0~2.1)	0.441
HDL-c(mmol/L), mean ± SD	1.0 ± 0.2	1.1 ± 0.3	0.550
LDL-c(mmol/L), mean ± SD	3.0 ± 0.9	3.2 ± 1.0	0.658
Cardiovascular disease *n* (%)	18(17.0%)	10(9.4%)	<0.001

RYGB, Roux-en-Y gastric bypass; CMM, conventional medical management; BMI, body mass index; A1C, Glycated Hemoglobin A1c; T2D, type 2 diabetes mellitus

This table shows the mean age, glycemic control (A1C), fasting plasma glucose and BMI at baseline for all patients who received the RYGB and a comparison group, composed of those in the patients who took CMM. The RYGB and CMM groups had similar age, A1C and fasting plasma glucose at baseline

at the 3-month, 94.8% (±45.6) at the 6-month, 102.8% (±49.6) at the 1-year, 99.6% (±57.2) at the 2-year, 94.5% (±51.8) at the 3-year, and 94.1% (±50.2) at the 4-year.

In CMM group, no statistically significant difference was found in BMI in the four years ($F = 0.340$, $p = 0.\ 712$, Table 3).

In RYGB group, A1C gradually decreased during the first year post-RYGB and then stabilized for the next 3 years (Table 2). A1C decreased from 8.6 ± 2.1% before surgery to 6.2 ± 1.0% ($t = 6.972$, $p < 0.001$) one year after surgery and kept lower compared with A1C at baseline. Remission after RYGB is clinically defined as a A1C <6.5% and no medications at 1 year post-operation [23]. Accordingly, we calculated the remission rate by total number of people who falls into the remission definition divided by the total number of people who underwent RYGB procedure. As a result, we observed a remission rate at 75.8%(72/95)1 year post-op, 64.9%(48/74)2 year post-op, 58.8%(47/80)3 year post-op, and 46.7%(43/92) 4 years post-op accordingly. And it is similar to those demonstrated in previous works. Furthermore, the reduction of BMI was in line with a significant improvement or normalization of A1C during follow-up.

In CMM group, A1C at 1, 2, 3 and 4 years after recruitment was 7.6 ± 2.1%, 8.1 ± 2.5%, 7.7 ± 2.6% and 8.3 ± 2.8%,

Table 2 BMI, A1C and health utility in RYGB group

Category	Baseline	3-Months	6-Months	1-Year	2-Years	3-Years	4-Years	Total
BMI (kg/m^2)	30.7 ± 3.0	25.6 ± 2.8	24.6 ± 2.5	24.3 ± 2.4	24.5 ± 2.6	24.6 ± 2.5	25.2 ± 2.6	-
A1C (%)	8.6 ± 2.1	6.2 ± 1.0	6.1 ± 0.8	6.2 ± 1.0	6.3 ± 1.0	6.3 ± 1.1	6.6 ± 1.1	–
Health utility, mean (95%CI)	0.891 (0.880–0.902)	0.944 (0.937–0.950)	0.947 (0.941–0.951)	0.944 (0.936–0.949)	0.941 (0.933–0.947)	0.937 (0.927–0.946)	0.933 (0.921–0.942)	3.756 (3.744–3.767)

Table 3 BMI, A1C and health utility in CMM group

Category	Baseline	1-Year	2-Years	3-Years	4-Years	Total
BMI (kg/m^2), mean ± SD	24.8 ± 3.8	25.2 ± 3.2	25.1 ± 2.7	24.9 ± 3.4	25.0 ± 3.7	–
A1C (%), mean ± SD	8.5 ± 2.3	7.6 ± 2.1	8.1 ± 2.5	7.7 ± 2.6	8.3 ± 2.8	–
Health utility, mean(95%CI)	0.890(0.878–0.907)	0.909(0.897–0.925)	0.892(0.882–0.912)	0.903(0.879–0.922)	0.890(0.872–0.923)	3.594(3.580–3.608)

RYGB, Roux-en-Y gastric bypass; CMM, conventional medical management; BMI, body mass index; A1C, Glycated Hemoglobin A1c

Table 2 and Table 3 showed the mean BMI, mean A1C and corresponding utility at baseline, and the changes in A1C and utility for all patients who received the RYGB and a comparison group, Difference of QALY between RYGB and CMM was 0.162

respectively(8.5% at baseline vs. 8.3% in the fourth year, t = 0.566, p =0. 572, Table 3).

According to association between glycated hemoglobin and health utility for Type 1 diabetes, we computed the health utility for study participants as Tables 2 and 3. The RYGB group scores 3.756(95%CI3.744–3.767) on the quality-adjusted life years (QALY) utility scale, whereas the CMM group scores 3.594(95%CI 3.580–3.608) in the four years. The difference in utility between RYGB and CMM in four years was 0.162.

In RYGB group, four patients (3.8%) developed complication of late acute cholecystitis after RYGB, and they underwent cholecystectomy. In CMM group, three patients were implanted with 7 cardiac stents for coronary heart disease and two patients underwent subtotal thyroidectomy for thyroid papillary carcinoma. There were no deaths. All related cost was calculated into the total healthcare cost.

A significant increment was observed in the total healthcare costs (including costs for RYGB procedure) in the first year post-surgery in RYGB group compared with CMM group($8,483 ± 3,181 (¥52,596 ± 19,723) in RYGB vs. $ 1,995 ± 380(¥12,371 ± 2,356) in CMM, t = 30.503,p < 0.001,Table 4). However, A significant reduction was observed in the total healthcare costs as early as the second year post-surgery and onwards ($8,483 ± 3,181 (¥52,596 ± 19,723) in the first year to $672 ± 163(¥4,164 ± 1,008) in the second year, t = 33.688,P < 0.001, Table 4) in RYGB group. In the CMM group, the total healthcare costs($1,995 ± 380 [¥12,371 ± 2,356] in the first year vs. $1,976 ± 363[¥12,252 ± 2,248] in the fourth year, t = 0.511, p = 0.611, Table 4) changed with no significance in the four years (F = 0.809, p = 0.812, Table 4).

The main reason for the reduction in RYGB group was the mean medication costs and medical tests costs. Compared with CMM group, the mean annual medication costs per patient in RYGB group was significantly lower ($92 [41~170]¥573 [252~1,054] in RYGB versus $215 [165~316]¥1334 [1,020~1,961] in CMM, p < 0.001) at the first year, and further over time to reach four years post-recruitment (Table 4). Our study was conducted in patients with type 2 diabetes mellitus complicated with obesity, so the most significant reduction in the mean medication costs was concerned with T2D treatments. Indeed, in RYGB group, the proportion of T2D patients receiving hypoglycemic drugs at baseline was 93.4%, and reduced respectively to 7.9%, 9.5%, 10.7%, 12.6%, 12.2%,16.2%and 17.4% respectively after 1,3,6 months, 1, 2, 3and 4 years after RYGB (Fig. 1a). Meanwhile, in CMM group, all of patients receiving antihyperglycemic drugs at baseline, and no significant difference was observed at 1, 2, 3and 4 years after the recruitment (Fig. 1b).

Although we observed a downward trend in consultancy fees in RYGB group, it accounted for only a small portion of the total healthcare cost in both groups.

Moreover, the mean costs of RYGB procedure and immediate post-surgery medication use or early surgery-related complications treatment were $7,924 ± 1,330 (¥49,126 ± 8,248) in RYGB group. It accounted for a large portion of the total cost of the first year after RYGB.

RYGB costs US$19,359 (¥125,836) per QALY gained (Incremental Cost-Utility Ratio [ICUR]) compared to CMM in Chinese patients with T2D and obesity, which was lower than a willingness-to-pay (WTP) of $20,277/QALY(3 times the GDP per capita of¥41,908 [$6,759] in 2013 from National Bureau of Statistics of China).

Discussion

In our multicenter study, we focused both on the total healthcare costs four years, and the improvement of glycemic control of T2D. A significant reduction in the A1C and BMI was observed in RYGB group as early as one-month post-surgery and onwards, while a significant reduction in the global costs in the second-year post-surgery and onwards. For RYGB vs. CMM, the ICUR was US$19,359 (¥125,836) per QALY gained, which was lower than a WTP of $20,277/QALY, indicating that RYGB in Chinese patients with type 2 diabetes and obesity is cost-effective; it is more costly than no surgery however it markedly improved quality of life. Previous cost-benefit assessments show that cost-effectiveness - but not cost savings - for bariatric procedures

Table 4 Mean annual cost per patient in RYGB group and CMM group

Category	1-Year RYGB	1-Year CMM	2-Years RYGB	2-Years CMM	3-Years RYGB	3-Years CMM	4-Years RYGB	4-Years CMM
Total healthcare cost($,¥), mean ± SD	$8,483 ± 3,181 ¥52,596 ± 19,723	$1,995 ± 380 ¥12,371 ± 2,356	$672 ± 163 ¥4,164 ± 1,008	$1,884 ± 379 ¥11,680 ± 2,350	$938 ± 425 ¥5,817 ± 2,633	$2,060 ± 382 ¥12,770 ± 2,368	$1,046 ± 328 ¥6,487 ± 2,036	$1,976 ± 363 ¥12,252 ± 2,248
Medication cost ($,¥), median(IQR)	$92(41~170) ¥573(252~1,054)	$215(165~316) ¥1,334(1,020~1,961)	$60(37~84) ¥372(227~518)	$205(170~258) ¥1,268(1,053~1,598)	$82(38~125) ¥507(238~776)	$226(192~277) ¥1,400(1,189~1,716)	$108(76~130) ¥669(472~803)	$218(168~285) ¥1,354(1,044~1,768)
Cost for T2D($,¥), median(IQR)	$51(13~77) ¥317 (79~476)	$161(132~205) ¥1,001(821~1,271)	$37(7~56) ¥227 (43~349)	$172(144~213) ¥1,065(894~1,321	$56(19~81) ¥348 (118~501)	$187(157~233) ¥1,162(973~1,445)	$98(48~132) ¥609 (298~816)	$188(159~232) ¥1,164(983~1,436)
Cost for Medical tests($,¥), mean ± SD	$529 ± 91 ¥3,277 ± 567	$1,561 ± 301 ¥9,676 ± 1,866	$566 ± 120 ¥3,509 ± 745	$1,455 ± 294 ¥9,019 ± 1,820	$754 ± 270 ¥4,673 ± 1,672	$1,599 ± 301 ¥9,912 ± 1,868	$813 ± 223 ¥5,043 ± 1,382	$1,527 ± 283 ¥9,466 ± 1,755
Consulting fee($,¥), median(IQR)	$48(35~56) ¥298 (220~350)	$116(82~166) ¥718(510~1,031)	$39(32~43) ¥240 (196~269)	$119(82~173) ¥735(509~1,074)	$56(41~66) ¥347 (253~410)	$123(89~174) ¥761(550~1,078)	$70(55~80) ¥433 (338~496)	$122(87~176) ¥759(537~1,093)

RYGB, Roux-en-Y gastric bypass; CMM, conventional medical management; T2D, type 2 diabetes mellitus; IQR, interquartile range (25th–75th)

This table shows the changes in Total healthcare cost, Medication cost, Cost for T2D, Cost for Medical tests and Consulting fee 4 years after the recruitment, for all patients who received the RYGB and CMM. The *P* value between the RYGB and CMM was all < 0.01

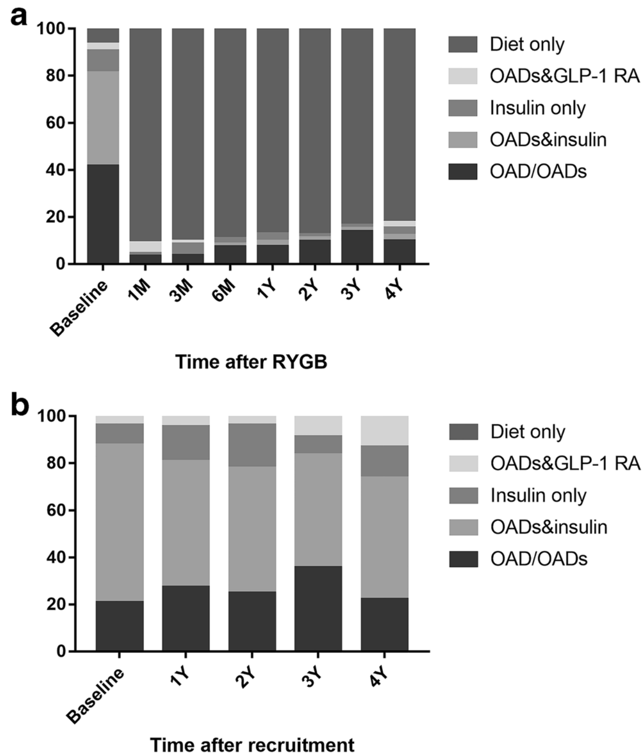

Fig. 1 a. Percentage of hypoglycemic agents before and after RYGB. b. Percentage of hypoglycemic agents before and after recruitment in CMM group. RYGB, Roux-en-Y gastric bypass; CMM, conventional medical management; OAD, Oral antidiabetic drugs; GLP-1 RA, Glucagon-like peptide 1 receptor agonists

compared with usual medical care or intensive lifestyles [24, 25].

Patients in the RYGB group underwent metabolic surgery, were followed up and took all treatments at the enrolling centers. Considering the collection of cost information through computer systems, we selected patients who were only treated all the time in our hospitals. The CMM group included T2DM patients who were enrolled in the same period and matched age, gender and A1C with RYGB groups, regardless of weight.

The marked reduction in BMI and A1C were observed in RYGB group in our study, which was consistent with previous studies. The complete remission rate of T2D is 64.9%~75% in RYGB [6–8]. T2D remission and obesity improvement at our centers has previously been described [26] and were in line with the results in this surgical cohort.

CUA was used to find the cost effectiveness of RYGB against CMM after four years. To our knowledge, only few previous studies have analyzed the relationship between A1C change and short-term effects on HRQoL in T2D [17, 18, 27]. Peyrot et al. [27] found that a change in A1C of −1.20% was associated with an improvement in health utility (measured by the EQ-5D) of 0.03 (95% CI 0.00, 0.07) in adults with T2D. Similarly, Martin Ridderstråle found the utility results associated with A1C change was 0.033,0.034 and 0.025 per percentage point for the patients with T2D in UK, Denmark and Sweden, respectively [17]. There only existed the relationship between A1C and health utility, which were derived using the US time trade off valuation of the EQ-5D, for T1D [19]. Predicted mean utility (EQ-5D scores) across varying levels of A1C (i.e., 6–10%), suggesting that higher levels of A1C are associated with decrements in utility following adjustment for diabetes-related complications, medications, and demographics [19]. In our study, the RYGB group scores 3.756 on the QALY utility scale, whereas the CMM group scores 3.594 in the four years. RYGB significantly improve the control of plasma glucose and lead to a small level of increase in the QALY gained against CMM. Because we should recommend the patients with T2D and morbid obesity to receive bariatric surgery as a priority treatment, we could not find a matched morbid obese group which had similar BMI to the RYGB group. Then we choose a matched T2D group which had similar A1C to the RYGB group. Therefore, the utility values were obtained according to results of A1C, not to BMI. Considering the improvement in obesity, the utility values of the RYGB group may be much higher than the utility values calculated only by A1C.

Because of direct costs on RYGB procedure in the RYGB group, total healthcare costs were high in the first year, however, they sharply decreased in the second year and sustained up to the fourth year in our surgical cohort. Meanwhile, in the CMM group, there were no significant difference in total healthcare costs among four years. Neovius M [28] studied 4044 Swedish obese subjects and found that compared with controls, surgically treated patients used more inpatient and nonprimary outpatient care during the first 6-year period after undergoing bariatric surgery but from years 7 through 20 drug costs were lower for surgery patients than for control patients. Of note, multiple surgery techniques such as Lap Band and vertical gastroplasty, gastric bypass and sleeve gastrectomy were included. The Swedish Obese Subjects study contained only 13% underwent gastric bypass [28]. We deliberately chose to limit our analysis on the impact of RYGB only, and all T2D patients, since different bariatric surgery techniques induce different metabolic results and result in variable healthcare associated costs. According to the comparison results of BMI, A1C and medical expenditure in RYGB group and CMM group, we identified that RYGB for patients with T2D and obesity probably have greater potential for health improvements and cost effective in the long term. However, it should be pointed out that direct cost of surgery procedure in China are much lower than that in the United States and European countries. RYGB costs $25 000 to $30 000 for the surgical admission (including the cost of the procedure and immediate preoperative, intraoperative, and postoperative services) in USA [11, 12], which was nearly three times higher than that in our cohort($7,924 ± 1,330 [¥49,126 ± 8,248]). Mean cost of RYGB procedures were £7100 in UK [29], which was also higher than that in our cohort. Our research is then more likely to conclude that RYGB has economic effective, because the cost of surgery procedure is lower. Borisenko O et al. found that bariatric surgery methods were cost-effective at 10 years post-surgery and cost-saving over the lifetime of the Belgian patient cohort [30]. Over the 10-year horizon, compared to CMM, bariatric surgery led to a cost increment of €9,386 and 1.6 additional QALY (€5,966/QALY), leading to 4.4 QALY gains and €300/patient average cost savings over lifetime in Spain [31]. Based on consensus at the World Health Organization (WHO), current benchmarks for cost-effectiveness thresholds have commonly been cited as approximately 1–3 times the per capita GDP of the country per additional QALY. In our study, we estimate that ICUR was less than the WTP within 4 years for RYGB patients. When the effect on obesity and T2D maintained for a longer time, we may then expect more cost effective to continue.

The main reason for the reduction was the mean medication costs and medical tests costs. And the marked cost reduction in T2D medication was observed to decrease 1-year post-RYGB in our surgical cohort and was one of the main causes of lower medication cost, which is in line with previous pharmaco-economic studies. Schauer PR [7] studied that oral antidiabetic agents and insulin therapy decreased by 80 and 79% 4 years post-RYGB in 191 diabetic patients. Segal JB et al. [32] found that in 6,235 patients after bariatric surgery, by 12 months after surgery, medication use for diabetes had also declined by 76%. In our RYGB group, the reduction of T2D treatment is in line with a significant improvement or normalization of A1C during follow-up. However, we had not separately reported medication use for other obesity-associated conditions such as hypertension, and hyperlipidemia. In another study, it was shown that one year after surgery, medication use for hypertension, and hyperlipidemia decreased promptly by 51%, and 59%, respectively [32].

However, our study presents some limitations. Firstly, the utility values according to results of A1C were derived using the US time trade off valuation of the EQ-5D for Type 1 Diabetes(T1D) and were assumed change linearly as A1C. Secondly, in the present study, we decided to focused on total healthcare costs and did not separately calculate the drugs costs to treat hypertension, dyslipidemia (statins or fibrates) and cardiovascular disease (CVD), although the major driver of diabetes costs is the treatment of the related vascular complications [33]. Thirdly, no adjustment for inflation has been made. The costing year might affect the results of the analysis; however, we believe that inflation does not affect the results significantly because of the inflation rate is not high in China (2.65% in 2012, 2.62% in 2013, 1.99% in 2014 and 1.44% in 2015 through comparison to 2011). Fourthly, due to fluctuations in blood glucose, the QALY values cannot be always accurate in reflecting annual glycemic control, so there may be some degree of overestimation or underestimation. To generalize our findings, the results need to be verified in a larger sample population with post-RYBG candidates.

Conclusion

Our study showed RYBG induces a significant reduction of total costs, as early as 2nd-year post-RYGB, compared to CMM. According to results of A1C, we obtained utility values higher in RYGB group than that in CMM group (3.756 vs. 3.594). In this study, the ICUR of RYGB referent to control CMM was $19,359(¥125,836)/QALY, which was lower than a WTP of $20,277/QALY. Hence, RYGB is estimated to be a cost-effective treatment for patients with T2D and obesity compared with other commonly available therapies in China; it is more costly however it markedly improved quality of life.

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Compliance with Ethical Standards

Conflict of Interest The authors have no conflicts of interest to declare.

Statement of Informed Consent Informed consent was obtained from all individual participants included in the study.

Statement of Human Rights This study was approved by the Ethics Committee of the Shanghai Jiao Tong University Affiliated Sixth People's Hospital and complied with the Declaration of Helsinki.

References

1. Ma RCW. Epidemiology of diabetes and diabetic complications in China. Diabetologia. 2018;1
2. Wang W, McGreevey WP, Fu C, et al. Type 2 diabetes mellitus in China: a preventable economic burden. Am J Manag Care. 2009;15(9):593–601.
3. Yang W, Zhao W, Xiao J, et al. Medical care and payment for diabetes in China: enormous threat and great opportunity. PLoS One. 2012;7(9):e39513.
4. Buchwald H, Avidor Y, Braunwald E, et al. Bariatric surgery: a systematic review and meta-analysis. Jama. 2004;292(14):1724–37.
5. Sjostrom L, Peltonen M, Jacobson P, et al. Bariatric surgery and long-term cardiovascular events. Jama. 2012;307(1):56–65.
6. Arterburn DE, Bogart A, Sherwood NE, et al. A multisite study of long-term remission and relapse of type 2 diabetes mellitus following gastric bypass. Obes Surg. 2013;23(1):93–102.
7. Schauer PR, Bhatt DL, Kirwan JP, et al. Bariatric surgery versus intensive medical therapy for diabetes - 5-year outcomes. N Engl J Med. 2017;376(7):641–51.
8. Mingrone G, Panunzi S, De Gaetano A, et al. Bariatric-metabolic surgery versus conventional medical treatment in obese patients with type 2 diabetes: 5 year follow-up of an open-label, single-centre, randomised controlled trial. Lancet (London, England). 2015;386(9997):964–73.
9. Suter M, Donadini A, Romy S, et al. Laparoscopic roux-en-Y gastric bypass: significant long-term weight loss, improvement of obesity-related comorbidities and quality of life. Ann Surg. 2011;254(2):267–73.
10. Hoerger TJ, Zhang P, Segel JE, et al. Cost-effectiveness of bariatric surgery for severely obese adults with diabetes. Diabetes Care. 2010;33(9):1933–9.
11. Weiner JP, Goodwin SM, Chang HY, et al. Impact of bariatric surgery on health care costs of obese persons: a 6-year follow-up of surgical and comparison cohorts using health plan data. JAMA Surg. 2013;148(6):555–62.
12. Makary MA, Clark JM, Shore AD, et al. Medication utilization and annual health care costs in patients with type 2 diabetes mellitus before and after bariatric surgery. Arch Surg (Chicago, Ill : 1960). 2010;145(8):726–31.
13. Xu Y, Wang L, He J, et al. Prevalence and control of diabetes in Chinese adults. Jama. 2013;310(9):948–59.
14. Rubino F, Nathan DM, Eckel RH, et al. Metabolic surgery in the treatment algorithm for type 2 diabetes: a joint statement by international diabetes organizations. Obes Surg. 2017;27(1):2–21.
15. Yu H, Di J, Bao Y, et al. Visceral fat area as a new predictor of short-term diabetes remission after roux-en-Y gastric bypass surgery in Chinese patients with a body mass index less than 35 kg/m2. Surg Obes Relat Dis. 2015;11(1):6–11.
16. Selvin E, Marinopoulos S, Berkenblit G, et al. Meta-analysis: glycosylated hemoglobin and cardiovascular disease in diabetes mellitus. Ann Intern Med. 2004;141(6):421–31.
17. Ridderstrale M, Evans LM, Jensen HH, et al. Estimating the impact of changes in HbA1c, body weight and insulin injection regimen on health related quality-of-life: a time trade off study. Health Qual Life Outcomes. 2016;14:13.
18. Dyer MT, Goldsmith KA, Sharples LS, et al. A review of health utilities using the EQ-5D in studies of cardiovascular disease. Health Qual Life Outcomes. 2010;8:13.
19. McQueen RB, Ellis SL, Maahs DM, et al. Association between glycated hemoglobin and health utility for type 1 diabetes. Patient. 2014;7(2):197–205.
20. Assessment DoEaPH. Choices in methods for economic evaluation. 2012.
21. Verma V, Sprave T, Haque W, et al. A systematic review of the cost and cost-effectiveness studies of immune checkpoint inhibitors. J Immunother Cancer. 2018;6(1):128.
22. Murray CJ, Evans DB, Acharya A, et al. Development of WHO guidelines on generalized cost-effectiveness analysis. Health Econ. 2000;9(3):235–51.
23. Buse JB, Caprio S, Cefalu WT, et al. How do we define cure of diabetes? Diabetes Care. 2009;32(11):2133–5.
24. Picot J, Jones J, Colquitt JL, et al. Weight loss surgery for mild to moderate obesity: a systematic review and economic evaluation. Obes Surg. 2012;22(9):1496–506.
25. Padwal R, Klarenbach S, Wiebe N, et al. Bariatric surgery: a systematic review of the clinical and economic evidence. J Gen Intern Med. 2011;26(10):1183–94.

26. Di J, Zhang H, Yu H, et al. Effect of roux-en-Y gastric bypass on the remission of type 2 diabetes: a 3-year study in Chinese patients with a BMI <30 kg/m(2). Surg Obes Relat Dis. 2016;12(7):1357–63.
27. Peyrot M, Rubin RR, Chen X, et al. Associations between improved glucose control and patient-reported outcomes after initiation of insulin pump therapy in patients with type 2 diabetes mellitus. Diabetes Technol Ther. 2011;13(4):471–6.
28. Neovius M, Narbro K, Keating C, et al. Health care use during 20 years following bariatric surgery. JAMA. 2012;308(11):1132–41.
29. Panca M, Viner RM, White B, et al. Cost-effectiveness of bariatric surgery in adolescents with severe obesity in the UK. Clin Obes. 2018;8(2):105–13.
30. Borisenko O, Lukyanov V, Debergh I, et al. Cost-effectiveness analysis of bariatric surgery for morbid obesity in Belgium. J Med Econ. 2018;21(4):365–73.
31. Sanchez-Santos R, Padin EM, Adam D, et al. Bariatric surgery versus conservative management for morbidly obese patients in Spain: a cost-effectiveness analysis. Exp Rev Pharmacoecon Outcomes Res. 2018;18(3):305–14.
32. Segal JB, Clark JM, Shore AD, et al. Prompt reduction in use of medications for comorbid conditions after bariatric surgery. Obes Surg. 2009;19(12):1646–56.
33. Ogurtsova K, da Rocha Fernandes JD, Huang Y, et al. IDF diabetes atlas: global estimates for the prevalence of diabetes for 2015 and 2040. Diabetes Res Clin Pract. 2017;128:40–50.