The Remission of Type 2 Diabetes Mellitus in Chinese Patients After Metabolic Surgery and Its Preoperative Contributing Factors: A Cohort Study

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Research

Keywords: Diabetes Mellitus, Obesity, Metabolic Surgery, Contributing Factors

DOI: https://doi.org/10.21203/rs.3.rs-555035/v1

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Abstract

**Background and Objective:** Existing data about the contributing factors of operative effect for type 2 diabetes mellitus (T2DM) are still limited in Chinese patients, especially about preoperative blood routine and biochemical indexes. We evaluated a prospective cohort of T2DM patients in early and middle stage with obesity to assess the post-operative prognosis and investigate its contributing factors.

**Methods:** Adult T2DM participants in early and middle stage with obesity were enrolled and received metabolic surgery. Clinical data such as age, sex, baseline body mass index, percentage excess weight loss, glycemia range and drug consumption were collected and analyzed. Patients were managed by a multi-disciplinary team and followed up for 12 months. Complete remission was defined as HbA1c < 6.0%, fasting glucose < 5.6 mmol/l, without pharmacological intervention for at least 3 months.

**Results:** In this study, a total of 96 T2DM patients with metabolic surgery were included. Among them, 61 (63.54%) patients had complete remission and 85 (88.50%) had post-operative partial remission after a 12-month clinical follow-up. Only 1 patient was reported to have an anastomotic leak; no surgical mortality during the follow-up. According to the complete remission or not, the patients were divided into two groups. There were significant differences on stroke history, fasting blood sugar and white blood cell between them. Furthermore, in multivariable analyses models, preoperative triglyceride (adjusted OR, 0.585; 95%CI, 0.418-0.819; p<0.01) and preoperative lymphocyte count (adjusted OR, 2.647; 95%CI, 1.141-6.142; p < 0.05) was significantly associated with complete remission of T2DM.

**Conclusion:** Our data suggest that T2DM patients with lower triglyceride and higher lymphocyte count tended to achieve post-operative remission. Preoperative evaluation of lipid metabolism and immune function may be helpful for the evaluation of prognosis of metabolic surgery.

Introduction

As a traditionally intractable chronic medical condition, the medical management of type 2 diabetes mellitus (T2DM) typically consists of lifestyle modifications and specific glucose-lowering medications(1, 2). Most patients benefit from these conservative approaches in a short term, however, persistent clinical remission and its associated metabolic improvement is rarely achieved(2, 3). At the same time, the pharmacotherapy of T2DM is often oriented towards managing only hyperglycemia, rather than the disease's numerous metabolic disorders(4).

The pathogenesis of insulin resistance and T2DM is closely related to overall and visceral adiposity(5, 6). The remarkable effects of metabolic surgery regarding metabolic amelioration and therapeutic modality for T2DM have gradually gathered attention(7). In a large sample study, a considerable number of patients (75%) achieved remission of T2DM after two years' surgery(8). Furthermore, the remission and weight loss were accompanied by a regression of microalbuminuria and a lower incidence of vascular complications(9). However, existing data about the contributing factors of operative effect, especially about preoperative blood routine and biochemical indexes, are still limited.

In this cohort study, the demographic and clinical characteristics of T2DM patients with obesity receiving metabolic surgery were collected. Meanwhile, the correlations between preoperative indicators and prognosis were examined in a 12-month follow-up.

Methods

**Study Population**

We conducted a prospective single-cohort study of T2DM individuals who received metabolic surgery in the First Affiliated Hospital of Soochow University between January 2013 and July 2018. T2DM was defined as 1) using of diabetes medication; 2) fasting whole blood glucose ≥ 7.0 mmol/L and/or random whole blood glucose ≥ 11.1 mmol/L; 3) patients according to national or local patient registers with diabetes. Diagnosis and classification of T2DM was based on the criteria established by the American Diabetes Association(10). Diabetic patients were managed by a multi-disciplinary team included endocrinologist and general surgeon. The exclusion criteria were as follows: 1) patients were younger than 18 years old or older than 65 years old; 2) patients with a body mass index (BMI) ≤ 32 kg/m²; 3) patients with history of previous metabolic surgery; 4) patients with type 1 diabetes or poor beta-cell function (diagnosed anti-GAD or islet-cell auto-antibodies, insulin use for more than ten years, fasting C-peptide < 1 ng/ml, or unresponsive to a stimulus test); 5) patients with end organ damage; 6) patients with pregnancy; 7) patients had a history of infection within 2 weeks before admission that was defined as fever(T ≥ 38°C) and at least one other typical symptoms (cough, rhinitis, hoarseness, sneezing, or vomiting); 8) patients had a history of alcoholic cirrhosis, hematomatological diseases, autoimmune diseases, or treatment with immunosuppressive agents.

All participants accepted nutritional, psychological and endocrinological assessments. Diabetic patients with obesity were eligible for the study if they had a BMI>32 kg/m² and/or poorly controlled T2DM after 6 months of nutrition intervention and hypoglycemic treatment. All post-operative patients received the same medical advice and treatment, including reasonable diet, effective blood pressure control and inactive hypoglycemic therapy (monotherapy or off medication).

**Surgical Procedures**

Surgical procedures included the following two types of metabolic procedures: (1) laparoscopic Roux-en-Y gastric bypass (LRYGB); (2) laparoscopic sleeve gastrectomy (LSG). Procedure would be selected after a comprehensive pre-operative conference with the multi-disciplinary team. All procedures were performed by the same experienced surgical team. Briefly, we used a standard 5-port laparoscopic technique. The LRYGB operation involves an antecolic, antegastric Roux limb, a 100-cm bilo-pancreatic limb, and a 100-cm alimentary limb. The gastric pouch was approximately 30 ml, and the gastrojejunostomy was created by a stapler technique with an anastomosis 1.0-1.5 cm in diameter. LSG was performed by creating a sleeve gastrectomy over a 36Fr bougie and
leaving a 4-6 cm long antrum. Thromboembolic prophylaxis consisted of perioperative pneumatic compression and low-molecular weight heparin (4000 U) during anesthetic induction.

**Clinical Information Collection**

Demographics were collected through electronic patient records and administrative databases. Patients’ body weight was measured in light clothing without shoes to the nearest 0.1 kg, and body height was measured to the nearest 0.1 cm. BMI was calculated as weight in kilograms divided by height in meters squared. Complete blood cell counts and blood biochemical parameters, including the individual components of glycemic control (levels of serum glucose, HbA1c levels), were assessed preoperatively. Peripheral venous blood samples were collected on the morning of the second day after admission with an overnight fasting.

**Outcome Variables**

The primary outcome was the complete remission of T2DM at post-operative 12 months. Other outcomes were partial remission of T2DM at post-operative 12 months, percentage excess weight loss (%EWL) at post-operative 6 months (good outcome: >50%), and %EWL at post-operative 12 months (good outcome: >50%). Complete remission was defined as achieving glycaemia below the diabetic range (HbA1c in the normal range [< 6.0%], fasting glucose < 5.6 mmol/l) without pharmacological intervention for at least 3 months. Partial remission was defined as sub-diabetic hyperglycaemia (HbA1C not diagnostic of diabetes [< 6.5%], fasting glucose 100-125 mg/dl [5.6-6.9 mmol/l]) without pharmacological intervention for at least 3 months. Diabetic patients were managed by a multidisciplinary team, but each patient was followed by the case manager. First clinical evaluation was performed 1 week after discharge. Then clinical and laboratory evaluation (fasting glucose, glycosylated hemoglobin and blood count) were performed at post-operative 3, 6, 9, and 12 months.

**Data Analyses**

Continuous variables were analyzed as mean and standard deviation or the median and interquartile range while categorical variables were analyzed as frequency and percentage, properly. Student’s t-test, Mann-Whitney U test or Chi-square test was used to assessed differences among variables. Pearson’s correlation coefficients were calculated to assess the relationship between the variables. Logistic regression analysis was used to find contributing factors which associated with remission of T2DM in patients receiving metabolic surgery. Models were built for groups of confounding factors: Model 1 was adjusted for demographics; Model 2 was adjusted for model 1 covariates and medical history of stroke and hypertension; and Model 3 additionally for baseline blood routine, biochemical indexes and BMI. Considering the correlation among smoking status, alcohol consumption and gender in China, we did not bring them into the adjustment factors at the same time. The level of significance for these descriptive comparisons was established at 0.05 for two-sided hypothesis testing. Statistical analysis was performed in SPSS 25.0.

**Results**

**Participants and Descriptive Characteristics**

The initial sample included 429 patients with diabetes. Only 104 T2DM patients with obesity were recruited. A 12-month clinical follow-up was performed. Eight patients were lost (8/104, 7.7%) and 96 participants (60 LRYGB and 36 LSG) finally formed the basis of this report. Only 1 patient was reported to have an anastomotic leak; no surgical mortality during the follow-up. As the number of participants with severe postoperative complications and death was very small, no useful separate analysis could be made. Patient selection is illustrated in Fig. 1.

Among all subjects, 45.8% were male (44/96); the age was 36.0 (30.0, 45.0) years old; 28 (29.2%) patients had a smoking history; 83 (86.5%) had a hypertension history; and 6 (6.3%) had a stroke history. Baseline white blood cell (WBC) was 8.13 ± 2.16 × 10⁹/L; lymphocyte count was 1.90 (1.53, 2.32) × 10⁹/L; total cholesterol (TC) was 4.73 ± 0.95 in mmol/L; triglyceride (TG) was 1.99 (1.37, 2.98) in mmol/L; and fasting blood sugar (FBS) was 8.19 (6.38, 10.87) in mmol/L; preoperative BMI was 39.25 (34.4, 44.75). Among them, 61 (63.54%) patients had complete remission at post-operative 12 months; and 11.5% patients did not achieve post-operative remission. Meanwhile, %EWL at post-operative 6 months was 66.45 (56.35, 73.18); %EWL at post-operative 12 months was 72.65 (66.98, 81.05). Patient characteristics were shown in Table 1.
Table 1
The characteristics of patients receiving surgical T2DM treatment

| Characteristics                        | Patients (N = 96) |
|----------------------------------------|------------------|
| Demographics and medical history       |                  |
| Age in years, median (IQR)             | 36 (30, 45)      |
| Male, n (%)                            | 44 (45.8)        |
| Smoking status, n (%)                  | 28 (29.2)        |
| Alcohol consumption, n (%)             | 20 (20.8)        |
| Hypertension, n (%)                    | 83 (86.5)        |
| Stroke history, n (%)                  | 6 (6.3)          |
| Hyperlipidemia, n (%)                  | 80 (83.3)        |
| Clinical features                      |                  |
| Surgical procedure                     |                  |
| LRYGB, n (%)                           | 60 (62.5)        |
| LSG, n (%)                             | 36 (37.5)        |
| Preoperative BMI, median (IQR)         | 39.25 (34.4, 44.75) |
| Preoperative FBG in mmol/l, median (IQR)| 8.19 (6.38, 10.87) |
| Preoperative WBC in ×10^9 /L, mean ± SD | 8.13 ± 2.16      |
| Preoperative N in ×10^9 /L, median (IQR)| 5.91 (4.79, 7.40) |
| Preoperative L in ×10^9 /L, median (IQR)| 1.90 (1.53, 2.32) |
| Preoperative M in ×10^9 /L, median (IQR)| 0.59 (0.43, 0.76) |
| Preoperative RDW (%), median (IQR)     | 12.90 (12.50, 13.60) |
| Preoperative creatinine in µmol/L, median (IQR) | 54.20 (46.00, 66.88) |
| Preoperative TC in mmol/L, mean ± SD   | 4.73 ± 0.95      |
| Preoperative TG in mmol/L, median (IQR)| 1.99 (1.37, 2.98) |
| Outcomes                               |                  |
| complete remission at 12 months after operation, n (%) | 61 (63.5) |
| partial remission at 12-months after operation, n (%) | 85 (88.5) |
| %EWL at 6-months after operation, median (IQR) | 66.45 (56.35, 73.18) |
| %EWL at 12-months after operation, median (IQR) | 72.65 (66.98, 81.05) |

Abbreviations: IQR, interquartile range; BMI, body mass index; FGB, fasting blood glucose; TC, total cholesterol; TG, triglyceride; %EWL, percentage excess weight loss.

Comparison Of Clinical Characteristics In Patients Receiving Metabolic Surgery

According to the remission of T2DM or not, these participants were divided into two groups: the complete post-operative remission group with 61 patients and the non-complete post-operative remission group with 35 patients. Statistical analysis indicated that there were significant differences on stroke history, baseline WBC and FBS (P < 0.05); However, there was no difference on age, gender, smoking, drinking, hypertension, hyperlipidemia, surgical procedure, baseline TC, TG, BMI or other factors between two groups (P > 0.05, Table 2).
Table 2
Comparison of descriptive characteristics between groups of patients with complete remission or not

| Characteristics | complete remission (N = 61) | Non-complete remission (N = 35) | P value |
|-----------------|-----------------------------|---------------------------------|---------|
| Demographics and medical history | | | |
| Age in years, median (IQR) | 37 (28.5, 46.5) | 35 (30, 42) | 0.994 |
| Male, n (%) | 27 (44.3) | 17 (48.6) | 0.683 |
| Smoking status, n (%) | 17 (27.9) | 11 (31.4) | 0.712 |
| Alcohol consumption, n (%) | 12 (19.7) | 8 (22.9) | 0.711 |
| Hypertension, n (%) | 53 (86.9) | 30 (85.7) | 1.000 |
| Stroke history, n (%) | 1 (1.6) | 5 (14.3) | 0.023 |
| Hyperlipidemia, n (%) | 50 (82.0) | 30 (85.7) | 0.635 |
| Clinical features | | | |
| Surgical procedure | | | |
| LRYGB, n (%) | 26 (72.2) | 10 (27.8) | 0.171 |
| LSG, n (%) | 35 (58.3) | 25 (41.7) | 0.255 |
| Preoperative BMI, median (IQR) | 39.30 (34.95, 45.30) | 39.1 (33.7, 42.7) | < 0.001 |
| Preoperative FBG in mmol/l, median (IQR) | 6.79 (5.45, 8.65) | 11.18 (8.64, 13.62) | < 0.001 |
| Preoperative WBC in ×10^9/L, mean ± SD | 8.47 ± 2.39 | 7.53 ± 1.53 | 0.021 |
| Preoperative N in ×10^9/L, median (IQR) | 5.01 (3.59, 6.25) | 4.57 (3.39, 5.26) | 0.092 |
| Preoperative L in ×10^9/L, median (IQR) | 2.46 (2.02, 2.94) | 2.41 (2.00, 2.89) | 0.532 |
| Preoperative M in ×10^9/L, median (IQR) | 0.45 (0.35, 0.59) | 0.42 (0.37, 0.56) | 0.678 |
| Preoperative RDW (%), median (IQR) | 13.00 (12.45, 13.55) | 12.8 (12.5, 13.6) | 0.873 |
| Preoperative creatinine in µmol/L, median (IQR) | 57.00 (46.00, 69.60) | 52.00 (46.00, 60.00) | 0.107 |
| Preoperative TC in mmol/L, mean ± SD | 4.66 ± 0.85 | 4.87 ± 1.11 | 0.295 |
| Preoperative TG in mmol/L, median (IQR) | 1.86 (1.35, 2.86) | 2.33 (1.66, 3.83) | 0.060 |

Furthermore, we calculated the correlation coefficients between age, gender, smoking, drinking, hypertension, coronary disease, stroke history, BMI, blood biochemical criterions, complete remission and partial remission at post-operative 12 months, %EWL at post-operative 6 months, and %EWL at post-operative 12 months. Observed correlation coefficients: r = 0.405 between preoperative BMI and WBC (p < 0.01); r = 0.220 between preoperative TG and partial post-operative remission (p < 0.05); r = −0.251 between stroke history and complete post-operative remission (p < 0.05); r = 0.286 between %EWL at post-operative 12 months and complete post-operative remission. Post-operative remission had weak but significant correlations with stroke history, preoperative TG, and %EWL at post-operative 12 months (Table 3).
Contributing Factors Associated With Prognosis In Postoperative T2DM Patients

Univariate and multivariable logistic regression analyses were used to identify the risk factors associated with prognosis in postoperative T2DM patients. In the demographic-adjusted Model (Model 1), only preoperative FBS was significantly associated with all four prognoses. After further adjustment for medical history of patients in Model 2, baseline WBC was associated with complete post-operative remission of T2DM at post-operative 12 months (adjusted OR, 1.283; 95%CI, 1.006–1.637; p < 0.05) (Table 4).
Table 4
Logistic regression analysis of contributing factors associated with prognosis in patients receiving surgical T2DM treatment

| Factor                        | Total (N = 96) | Univariate OR       | Multivariate OR      |
|-------------------------------|----------------|---------------------|----------------------|
| Complete remission at 12-months| 61 (63.5)     | 0.574 (0.455–0.723)** | 0.569 (0.451–0.718)*** |
| **Model 1**                   |                |                     |                      |
| Preoperative FBG              | 1.270 (1.008–1.600)* | 1.283 (1.006–1.637)* |
| **Model 2**                   |                |                     |                      |
| Preoperative WBC              | 1.036 (0.972–1.104) | 1.026 (0.937–1.123) |
| Preoperative BMI              | 1.356 (0.745–2.470)* | 2.647 (1.411–6.142)* |
| Preoperative lymphocyte count | 0.789 (0.508–1.226) | 0.592 (0.339–1.035) |
| Preoperative TC               | 0.757 (0.590–0.971)* | 0.585 (0.418–0.819)** |
| Partial remission at 12-months| 85 (88.5)      | 0.785 (0.664–0.928)** | 0.774 (0.649–0.924)** |
| **Model 1**                   |                |                     |                      |
| Preoperative WBC              | 1.248 (0.876–1.779) | 1.350 (0.898–2.029) |
| **Model 2**                   |                |                     |                      |
| Preoperative BMI              | 1.115 (0.983–1.266) | 1.515 (1.022–2.244)* |
| Preoperative lymphocyte count | 1.512 (0.581–3.939) | 6.718 (0.772–58.462) |
| Preoperative TC               | 1.030 (0.530–2.002) | 2.155 (0.600–7.738) |
| Preoperative TG               | 0.596 (0.434–0.820)** | 0.323 (0.141–0.737)** |
| %EWL at 6-months              | 80 (83.3)      | 0.798 (0.685–0.930)** | 0.796 (0.680–0.931)** |
| **Model 1**                   |                |                     |                      |
| Preoperative WBC              | 1.157 (0.870–1.539) | 1.173 (0.872–1.577) |
| **Model 2**                   |                |                     |                      |
| Preoperative BMI              | 0.992 (0.919–1.072) | 0.998 (0.902–1.105) |
| Preoperative lymphocyte count | 2.113 (0.871–5.130) | 3.603 (1.230–10.556)* |
| Preoperative TC               | 0.774 (0.444–1.348) | 0.662 (0.332–1.320) |
| Preoperative TG               | 1.017 (0.774–1.336) | 0.994 (0.700–1.412) |
| %EWL at 12-months             | 86 (89.6)      | 0.761 (0.637–0.908)** | 0.754 (0.623–0.913)** |
| **Model 1**                   |                |                     |                      |
| Preoperative WBC              | 1.510 (0.994–2.295) | 1.485 (0.970–2.275) |

***p < 0.001. **p < 0.01. *p < 0.05.

Model 1: demographics-adjusted
Model 2: additionally adjusted for medical history of stroke and hypertension
Model 3: additionally adjusted for preoperative BMI, preoperative lymphocyte count, preoperative creatinine, preoperative TC, preoperative TG, preoperative platelet
based on 96 patients
In the fully adjusted model(Model 3), after additional adjustment for the preoperative blood biochemical criterions and BMI, our results indicated that preoperative TG (adjusted OR, 0.585; 95%CI, 0.418–0.819; p < 0.01) and preoperative lymphocyte count (adjusted OR, 2.647; 95%CI, 1.141–6.142; p < 0.05) was associated with complete remission of T2DM at post-operative 12 months. At the same time, preoperative TG (adjusted OR, 0.323; 95%CI, 0.141–0.737; p < 0.01) and preoperative BMI (adjusted OR, 1.515; 95%CI, 1.022–2.244; p < 0.05) was associated with partial remission of T2DM at post-operative 12 months. Preoperative lymphocyte count (adjusted OR, 3.603; 95%CI, 1.230-10.556; p < 0.05) was associated with %EWL at post-operative 6 months; Preoperative TC (adjusted OR, 0.370; 95%CI, 0.150–0.913; p < 0.05) was associated with %EWL at post-operative 12 months. However, baseline WBC, neutrophil count and monocyte count showed no association with prognosis in post-operative T2DM patients in the fully adjusted models (Table 4).

### Discussion

In our study, the operative effect in T2DM patients with obesity as well as preoperative blood biochemical indexes were analyzed. Our results showed that patients with lower preoperative TG levels were more likely to have post-operative remission of T2DM. In addition, preoperative lymphocyte count was also associated with complete post-operative remission of T2DM and %EWL in short term after operation. To our knowledge, this study was the first time to analyze the relationship between the preoperative blood biochemical indexes and post-operative remission of T2DM in metabolic surgery.

The underlying mechanism for diabetes remission after metabolic surgery is intriguing and weight loss is the most essential part of the treatment, even in non-obese patients(11, 12). Abnormal lipid metabolism is a chronic and progressive disease. Previous studies found a bimodal adipocyte distribution in morbidly obese individuals: hypertrophy of the larger adipocyte population and higher proportion of very small adipocytes(13). Large adipocyte size may reduce adipose tissue acyl-CoA synthetase and diacylglycerol acyltransferase activities, suggesting lower capacity for fatty acid storage(14). Meanwhile, hypertrophic remodeling of white adipose tissues is associated with adipose tissue dysfunction and lean organs, especially heart and liver, overexposure to circulating triglycerides (TG), ultimately leading to insulin resistance and metabolic diseases(13, 15, 16). Hepatic TG accumulation and hepatic insulin resistance may play an important role in impaired inhibition of gluconeogenesis(17). Previous study had shown that metabolic surgery improves fatty liver and hepatic insulin sensitivity, and reduces expression of pancreatic markers associated with diabetes(18). Moreover, glycerol fluxes remained unchanged one week after RYGB, but a significant decrease 1 year after surgery(19, 20). Although we could not find any evidence to show the effect metabolic surgery on lipid tolerance, these results underscore the importance of impaired glycerol metabolic regulation for fasting glucose levels.

In the present study, we observed lower preoperative TG levels in complete remission group. Moreover, preoperative TG was independently associated with post-operative remission of T2DM after excluding effects of confounding. However, it is difficult to determine the causal relationship between preoperative TG, abnormal lipid metabolism and T2DM on the available evidence. We can only preliminarily infer that low preoperative TG may indicate mild lipid metabolism abnormality or short duration, and it may predict the post-operative remission of T2DM, independently of traditional risk factors.

Obesity is a condition that is associated with low grade inflammation due to hypertrophy and hyperplasia of adipose tissues(21, 22). Immune cells are not only the key players in inducing low grade chronic inflammation in obesity and also are main factor responsible for pathogenesis of insulin resistance resulting Type 2 diabetes(22). Our data suggested that higher preoperative lymphocyte count was related with post-operative complete remission and short-term %EWL. Recently studies suggested that lymphocytes were involved into the pathogenesis of obesity that associated insulin resistance(23-25).

Meanwhile, cytokines secretion from lymphocytes were involved directly in recruitment and phenotypic switch of other immune cells(26, 27). The biomarkers of inflammation trigger inflammatory pathways in liver cells resulting in insulin insensitivity(28). There is a significant change in number of some lymphocyte subsets like NKT cells, Th1 cells and Th2 cells during obesity(29). Higher preoperative lymphocyte count may indicate a stronger immune response in obesity(28-30). However, the precise roles of lymphocyte subsets in obesity are still unclear and needed to be further investigated.

Our data should be interpreted with some caution due to limitations of the study. Since the participants in this study were recruited only from one clinical unit, there may have retrospective bias inherent due to the insufficient sample size. We used definitions of post-operative complete and partial remission similar to ADA consensus statement, but not identical(31). Considering that the general lack of regular physical examination in Chinese patients may lead to the undetected T2DM, we did not include the duration of DM into variables. The study is observational in nature. We can’t prove the causal relationship among
preoperative TG, lymphocyte count and post-operative remission of T2DM. Moreover, we did not assess lipid metabolism at follow-up time points. The exact clinical relevance needs to be further studied.

**Conclusion**

Our data indicated that most T2DM patients benefited from metabolic surgery. Preoperative TG and lymphocyte count were independently associated with post-operative complete remission of T2DM. Preoperative evaluation of lipid metabolism and immune function may be used to evaluate the prognosis of metabolic surgery and avoid unnecessary operation.

**Abbreviations**

T2DM, type 2 diabetes mellitus; BMI, body mass index; LRYGB, Roux-en-Y gastric bypass; LSG, laparoscopic sleeve gastrectomy; %EWL, percentage excess weight loss; IQR, interquartile range; TC, total cholesterol; TG, triglyceride; WBC, white blood cell; FBS, fasting blood sugar.

**Declarations**

**Acknowledgments**

We would like to thank Prof. Xingshun Xu for valuable comments on this manuscript.

**Funding**

This work was supported by the grants from Priority Academic Program Development of Jiangsu Higher Education Institutions (20KJB320021) and Province Science and Technology Program of Jiangsu (BL2014048).

**Ethics approval and consent to participate**

This study involving human participants were reviewed and approved by the Institutional Review Board of The First Affiliated Hospital of Soochow University. The procedures used in this study adhere to the tenets of the Declaration of Helsinki. The experiments comply with the current laws of the country in which they were performed. All patients gave informed consent.

**Consent for publication**

Not applicable.

**Conflict of interest**

On behalf of all authors, the corresponding author states that there is no conflict of interest.

**Availability of data and materials**

The original data that support the findings of this study are available from the corresponding author but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request.

**Authors' contributions**

YY, LN, and JN designed the study. YY, LN, LM, RW, ST, ZM, and BS evaluated the subjects and collected the data. LY and YY analyzed the data. YY, LN and LM wrote the initial draft, with BS and JN participating in revising the manuscript.

**References**

1. Sapra A, Bhandari P. Diabetes Mellitus. StatPearls. Treasure Island (FL) 2021.
2. Stark Casagrande S, Fradkin JE, Saydah SH, Rust KF, Cowie CC. The prevalence of meeting A1C, blood pressure, and LDL goals among people with diabetes, 1988-2010. Diabetes Care. 2013;36(8):2271-9.
3. Shubrook JH, Chen W, Lim A. Evidence for the Prevention of Type 2 Diabetes Mellitus. J Am Osteopath Assoc. 2018;118(11):730-7.
4. Padhi S, Nayak AK, Behera A. Type II diabetes mellitus: a review on recent drug based therapeutics. Biomed Pharmacother. 2020;131:110708.
5. Freeman AM, Pennings N. Insulin Resistance. StatPearls. Treasure Island (FL) 2021.
6. Bellou V, Belbasis L, Tzoulaki I, Evangelou E. Risk factors for type 2 diabetes mellitus: An exposure-wide umbrella review of meta-analyses. PLoS One. 2018;13(3):e0194127.
7. Shah A, Laferrere B. Diabetes after Bariatric Surgery. Can J Diabetes. 2017;41(4):401-6.
8. Adams TD, Davidson LE, Litwin SE, Kolotkin RL, LaMonte MJ, Pendleton RC, et al. Health benefits of gastric bypass surgery after 6 years. JAMA. 2012;308(11):1122-31.
9. Burggraaf B, Castro Cabezas M. Interventions in type 2 diabetes mellitus and cardiovascular mortality-An overview of clinical trials. Eur J Intern Med. 2017;42:1-15.
10. American Diabetes A. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2019. Diabetes Care. 2019;42(Suppl 1):S13-S28.

11. Lee WJ, Almulaifi A, Chong K, Chen SC, Tsou JJ, Ser KH, et al. The Effect and Predictive Score of Gastric Bypass and Sleeve Gastrectomy on Type 2 Diabetes Mellitus Patients with BMI < 30 kg/m(2). Obes Surg. 2015;25(10):1772-8.

12. Affinati AH, Esfandiar NH, Oral EA, Kraftson AT. Bariatric Surgery in the Treatment of Type 2 Diabetes. Curr Diab Rep. 2019;19(12):156.

13. Grenier-Larouche T, Carreau AM, Golen A, Frisch F, Biertho L, Marceau S, et al. Fatty Acid Metabolic Remodeling During Type 2 Diabetes Remission After Bariatric Surgery. Diabetes. 2017;66(11):2743-55.

14. Hames KC, Koutsari C, Santosia S, Bush NC, Jensen MD. Adipose tissue fatty acid storage factors: effects of depot, sex and fat cell size. Int J Obes (Lond). 2015;39(6):884-7.

15. Kunach M, Noll C, Phoenix S, Guerin B, Baillargeon JP, Turcotte EE, et al. Effect of Sex and Impaired Glucose Tolerance on Organ-Specific Dietary Fatty Acid Metabolism in Humans. Diabetes. 2015;64(7):2432-41.

16. Walker RE, Ford JL, Boston RC, Savinova OV, Harris WS, Green MH, et al. Trafficking of nonesterified fatty acids in insulin resistance and relationship to dysglycemia. Am J Physiol Endocrinol Metab. 2020;318(3):E392-E404.

17. Jin ES, Szuszkiewicz-Garcia M, Browning JD, Baxter JD, Abate N, Malloy CR. Influence of liver triglycerides on suppression of glucose production by insulin in men. J Clin Endocrinol Metab. 2015;100(1):235-43.

18. Abu-Gazala S, Horwitz E, Ben-Haroush Schyr R, Bardugo A, Israeli H, Hijia A, et al. Sleeve Gastrectomy Improves Glycemia Independent of Weight Loss by Restoring Hepatic Insulin Sensitivity. Diabetes. 2018;67(6):1079-85.

19. Camasta S, Gastaldelli A, Mari A, Bonuccelli S, Scartabelli G, Frascerra S, et al. Early and longer term effects of gastric bypass surgery on tissue-specific insulin sensitivity and beta cell function in morbidly obese patients with and without type 2 diabetes. Diabetologia. 2011;54(8):2093-102.

20. Gastaldelli A, Iaconelli A, Gaggini M, Magnone MC, Veneziani A, Rubino F, et al. Short-term Effects of Laparoscopic Adjustable Gastric Banding Versus Roux-en-Y Gastric Bypass. Diabetes Care. 2016;39(11):1925-31.

21. Hotamisligil GS. Inflammation, metaflammation and immunometabolic disorders. Nature. 2017;542(7640):177-85.

22. Asghar A, Sheikh N. Role of immune cells in obesity induced low grade inflammation and insulin resistance. Cell Immunol. 2017;315:18-26.

23. Courtier J, Nuoto-Antar AM, Agarwal N, Wilkerson GK, Saha P, Kulkarni V, et al. Lymphocytes upregulate CD36 in adipose tissue and liver. Adipocyte. 2019;8(1):154-63.

24. Hong CP, Park A, Yang BG, Yun CH, Kwak MJ, Lee GW, et al. Gut-Specific Delivery of T-Helper 17 Cells Reduces Obesity and Insulin Resistance in Mice. Gastroenterology. 2017;152(8):1998-2010.

25. McLaughlin T, Liu LF, Lamendola C, Shen L, Morton J, Rivas H, et al. T-cell profile in adipose tissue is associated with insulin resistance and systemic inflammation in humans. Arterioscler Thromb Vasc Biol. 2014;34(12):2637-43.

26. Harmon DB, Sriakulapu P, Kaplan JL, Oldham SN, McSkimming C, Garmey JC, et al. Protective Role for B-1b B Cells and IgM in Obesity-Associated Inflammation, Glucose Intolerance, and Insulin Resistance. Arterioscler Thromb Vasc Biol. 2016;36(4):682-91.

27. McLaughlin T, Ackerman SE, Shen L, Engleman E. Role of innate and adaptive immunity in obesity-associated metabolic disease. J Clin Invest. 2017;127(1):5-13.

28. Ringses R, Eder K, Mooren FC, Kruger K. Metabolic signals and innate immune activation in obesity and exercise. Exerc Immunol Rev. 2015;21:58-68.

29. Liu L, Hu J, Wang Y, Lei H, Xu D. The role and research progress of the balance and interaction between regulatory T cells and other immune cells in obesity with insulin resistance. Adipocyte. 2021;10(1):66-79.

30. Cohen S, Danzaki K, Maclver NJ. Nutritional effects on T-cell immunometabolism. Eur J Immunol. 2017;47(2):225-35.

31. Buse JB, Caprio S, Cerfalu WT, Ceriello A, Del Prato S, Inzucchi SE, et al. How do we define cure of diabetes? Diabetes Care. 2009;32(11):2133-5.

**Figures**
The initial sample included 429 patients with diabetes. Only 104 T2DM patients with obesity were recruited. A 12-month clinical follow-up was performed. Eight patients were lost (8/104, 7.7%) and 96 participants (60 LRYGB and 36 LSG) finally formed the basis of this report. Only 1 patient was reported to have an anastomotic leak; no surgical mortality during the follow-up. As the number of participants with severe postoperative complications and death was very small, no useful separate analysis could be made. Patient selection is illustrated in Figure 1.