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ABOUT COVER

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AIMS AND SCOPE

The primary aim of *World Journal of Diabetes* (*WJD*, *World J Diabetes*) is to provide scholars and readers from various fields of diabetes with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJD mainly publishes articles reporting research results and findings obtained in the field of diabetes and covering a wide range of topics including risk factors for diabetes, diabetes complications, experimental diabetes mellitus, type 1 diabetes mellitus, type 2 diabetes mellitus, gestational diabetes, diabetic angiopathies, diabetic cardiomyopathies, diabetic coma, diabetic ketoacidosis, diabetic nephropathies, diabetic neuropathies, Donohue syndrome, fetal macrosomia, and prediabetic state.

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ORIGINAL ARTICLE

Retrospective Study

Clinical study on the effect of jejunoileal side-to-side anastomosis on metabolic parameters in patients with type 2 diabetes

Ji-Kui Wang, Di Zhang, Jin-Feng Wang, Wan-Lin Lu, Jing-Yuan Wang, Shi-Feng Liang, Ran Liu, Jing-Xin Jiang, Hong-Tao Li, Xuan Yang

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Abstract

BACKGROUND

At present, the existing internal medicine drug treatment can alleviate the high glucose toxicity of patients to a certain extent, to explore the efficacy of laparoscopic jejunoileal side to side anastomosis in the treatment of type 2 diabetes, the report is as follows.

AIM

To investigate the effect of jejunoileal side-to-side anastomosis on metabolic parameters in patients with type 2 diabetes mellitus (T2DM).

METHODS

We retrospectively analyzed the clinical data of 78 patients with T2DM who were treated *via* jejunoileal lateral anastomosis. Metabolic indicators were collected preoperatively, as well as at 3 and 6 months postoperative. The metabolic indicators analyzed included body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP), fasting blood glucose (FBG), 2-hour blood glucose (PBG), glycated hemoglobin (HbA1c), fasting C-peptide, 2-hour C-peptide (PCP), fasting insulin (Fins), 2-hour insulin (Pins), insulin resistance index (HOMA-IR), β Cellular function index (HOMA-β), alanine aminotransferase, aspartate aminotransferase, serum total cholesterol (TC), low-density lipoprotein cholesterol (L DL-C), triglycerides (TG), high-density lipoprotein, and uric acid (UA) levels.

RESULTS

SBP, DBP, PBG, HbA1c, LDL-C, and TG were all significantly lower 3 months postoperative *vs* preoperative values; body weight, BMI, SBP, DBP, FBG, PBG, HbA1c, TC, TG, UA, and HOMA-IR values were all significantly lower 6 months postoperative *vs* at 3 months; and PCP, Fins, Pins, and HOMA-β were all significantly higher 6 months postoperative *vs* at 3 months (all $P < 0.05$).

CONCLUSION

Side-to-side anastomosis of the jejunum and ileum can effectively treat T2DM and improve the metabolic index levels associated with it.

Key Words: Metabolic diseases; Type 2 diabetes; Jejunoileal side-to-side anastomosis; Glycolipid metabolism; Islet function

Core Tip: This study investigates the impact of jejunal ileal side to side anastomosis on metabolic parameters in patients with type 2 diabetes. The procedure showed significant improvements in patients' metabolic indicators such as body mass index, blood pressure, blood glucose, insulin resistance index, and cholesterol levels at 3 and 6 months post-surgery. This suggests that jejunal ileal side to side anastomosis could be an effective treatment for managing type 2 diabetes and improving metabolic health.

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INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a metabolic disease characterized by abnormally high blood glucose levels. Recent changes in lifestyles and dietary structures at societal levels have resulted in an increasing incidence of T2DM year over year, making the disease a global public health concern[1,2]. Insulin resistance and impaired pancreatic beta cell function represent the main routes of pathogenesis for this disease[3]. Existing internal medicine drug treatments can alleviate the toxicity of excessively high blood glucose levels to a certain extent in patients with T2DM; however, these patients often require costly lifelong medication. Many patients have poor compliance, as long-term follow-up observations have shown that the blood sugar control compliance rate is < 60%[4,5]. As the disease progresses, most patients experience complications such as enlarged blood vessels and microvasculature that can significantly impact their quality of life and expected lifespan[6]. Patients with T2DM often have abnormal levels of metabolic indicators such as blood lipids and uric acid (UA), which can exacerbate the occurrence and development of T2DM-related complications, as well as worsen the patient's hyperglycemic state[7]. Treatment is often difficult and shows poor efficacy. Laparoscopic jejunoileal lateral anastomosis, however, can promote the secretion of larger amounts of glucagon-like peptide-1 by intestinal L cells. This can then promote the proliferation of pancreatic islet cells, reduce insulin resistance, and effectively control disorders of glucose and lipid metabolism. To compensate for the shortcomings of internal medicine for the treatment of T2DM, laparoscopic jejunal-ileal lateral anastomosis has been increasingly performed in clinical practices and has generally achieved good results. This study was approved by the ethics committee of our hospital, which allowed access to the clinical data of patients with T2DM. We used these to compare relevant metabolic indicators preoperative to those at 3 and 6 months postoperative, to explore the efficacy of laparoscopic jejunoileal side-to-side anastomosis for the treatment of T2DM.

MATERIALS AND METHOD

Research objective

We retrospectively analyzed the clinical data of patients who underwent laparoscopic jejunoileal anastomosis at the General Thoracic Surgery Ward of Liaoning Electric Power Center Hospital between 2020-2023.

Our inclusion criteria were: (1) Age ≤ 75 years old; (2) Body mass index (BMI) ≤ 32.5 kg/m^2; (3) C-peptide release test results showing a significantly high peak of > 2 × the baseline value; (4) Fasting C-peptide (FCP) value of ≥ 1/2 of the lower limit of the normal range; (5) A negative diabetes autoimmune antibody test (LADA) result; and (6) No serious comorbidities or complications affecting surgical candidacy.

The exclusion criteria were: (1) Diabetes hyperosmolar coma or diabetes ketoacidosis and other diabetes-related acute complications within the preceding three months; (2) Recent experience of severe infections, surgeries, or trauma, or being in an exceptional physical state such as pregnancy, breastfeeding, or under 18 years of age; (3) Use of antibiotics over the preceding 6 months; and (4) Prior history of serious liver function damage, cardiovascular and cerebrovascular diseases, infectious diseases, malignant tumors, or kidney disease.

The study's protocol was approved by the hospital's ethics committee (approval number: LNDLYY-2023-PXWK-001). All of the participants understood the nature and purpose of the study and signed an informed consent form. This study included 78 patients: 40 males and 38 females, aged 30-67 years, with a median age of 52.5 years.

Methods

Surgical methods: Following the successful induction of general anesthesia, each patient was placed in the supine position to undergo routine abdominal disinfection and draping. An incision approximately 1 cm in length was made at the lower edge of the navel, and a pneumoperitoneum needle was used to puncture the abdomen to establish a pneumoperitoneum. The intra-abdominal pressure was maintained at 13 mmHg, and a 10 mm trocar needle was used to perform a puncture, through which the laparoscopic lens was inserted. Cannulas were inserted 5, 12, and 5 mm down the rib margin of the left clavicle and at the bilateral Maxwell points. The intestinal wall was opened with an electric hook at the marking points of the jejunum and ileum (selected based on the patient's BMI and C-peptide value), after which a 45 # cutting stapler was placed into the jejunal and ileal lumens on both sides to stimulate anastomosis. An absorbable barbed wire was used to suture the entire layer to the nearby muscular layer, and a non-absorbable barbed wire was used to suture the mesentery.

Data collection: Follow-up was conducted through in-person outpatient visits, as well as *via* telephone and WeChat interviews, mainly for the purposes of assessing metabolic indicators at 3 and 6 months postoperative.

(1) The general items and glucose metabolic indicators measured included: Height and weight to calculate BMI [BMI = weight/height^2 (kg/m^2)]; morning systolic blood pressure (SBP) and diastolic blood pressure (DBP); 5 mL of venous blood on an empty stomach (*i.e.*, after fasting for 8-10 hours), oral glucose tolerance test to measure fasting blood glucose (FBG), 2-hour blood glucose (PBG), and glycated hemoglobin (HbA1c); C-peptide release experiment to measure FCP and 2-hour C-peptide (PCP); insulin release experiment to measure fasting insulin (Fins) and 2-hour insulin (Pins); insulin resistance index (HOMA-IR = FBG × Fins)/22.5), and β Cellular function index = 20 × Fins/[FBG-3.5]); and (2) Patient levels of the following indicators related to lipid and purine metabolism were also collected: Alanine aminotransferase (ALT), aspartate aminotransferase (AST), serum total cholesterol (TC), low-density lipoprotein cholesterol (LDL), triglycerides (TG), high-density lipoprotein (HDL), and UA.

Statistical analysis

SPSS 23.0 statistical software was used to process the data, and continuous variables with normal distributions were represented as means ± SD. Single-factor analysis of variance was used for inter-data comparisons. Non-normally distributed continuous variables were represented as medians and interquartile ranges. Statistical significance was set at $P < 0.05$.

RESULTS

Comparison of weight loss effects, as well as blood pressure and blood glucose indicators among the patients

We compared weight loss, blood pressure, and blood glucose indicator changes among patients. In the patients we observed, SBP, DBP, PBG, and HbA1c levels were lower at 3 and 6 months postoperative than those at preoperative. The patient's body weight, BMI and FBG at 6 months postoperative were lower than those at 3 months postoperative and preoperative. The differences were statistically significant 6 months postoperative 3 months postoperative (all $P < 0.05$; Table 1).

Comparison of pancreatic islet function indicators among patients

When we compared the patients' pancreatic islet functions and homeostatic indexes, we found no statistically significant differences between the preoperative and 3 months postoperative values. However, their 6 months postoperative tests showed higher PCP Fins, Pins, and HOMA-β values compared to their 3-month postoperative and preoperative but in HOMA-IR is the opposite result 3 months postoperative (all $P < 0.05$; Table 2).

Comparison of lipid and purine metabolic indicators among the patients

In our comparison of lipid and purine metabolic indicators among the patients. LDL-C and TG levels were lower at 3 months postoperative *vs* preoperative baselines; TC values were lower at 6 months postoperative *vs* preoperative values; and TG and UA values were lower at 6 months postoperative *vs* 3 months postoperative (all $P < 0.05$). There was no statistically significant difference in LDL-C levels at 6 months *vs* 3 months postoperative (Table 3).

Table 1 Comparison of weight loss effects, as well as blood pressure and blood glucose indicators among the patients (*n* = 78)

Time	Weight (kg)	BMI (kg/m²)	SBP (mmHg)	DBP (mmHg)	FBG (mmol/L)	PBG (mmol/L)	HbA1c (%)
Preoperative	69.5 ± 6.8	24.3 ± 2.3	150.9 ± 10.2	110.2 ± 9.2	10.5 ± 2.7	17.8 ± 2.6	9.2 ± 0.9
3 months postoperative	69.2 ± 6.1	24.1 ± 2.4	141.4 ± 8.2[a]	98.6 ± 8.1[a]	10.1 ± 1.6	12.8 ± 2.1[a]	8.1 ± 0.7[a]
6 months postoperative	67.4 ± 7.2[a,b]	23.1 ± 2.5[a,b]	135.2 ± 9.4[b]	86.4 ± 8.6[b]	7.2 ± 1.1[a,b]	9.8 ± 2.3[b]	7.1 ± 0.6[b]

[a]$P < 0.05$ *vs* preoperative value.
[b]$P < 0.05$ *vs* 3 months postoperative value.
BMI: Body mass index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; FBG: Fasting blood glucose; PBG: Postprandial blood glucose; HbA1c: Hemoglobin A1c.

Table 2 Comparison of pancreatic islet function indicators among patients (*n* = 78)

Time	FCP (ng/mL)	PCP (ng/mL)	Fins (uIU/mL)	Pins (uIU/mL)	HOMA-IR	HOMA-β
Preoperative	1.1 ± 0.3	2.9 ± 0.4	16.8 ± 2.7	27.7 ± 3.6	7.7 ± 1.8	35.5 ± 5.2
3 months postoperative	1.1 ± 0.2	2.9 ± 0.5	16.9 ± 2.9	28.1 ± 2.7	7.9 ± 1.9	35.9 ± 4.9
6 months postoperative	1.2 ± 0.2	3.6 ± 0.4[a,b]	19.1 ± 2.3[a,b]	36.4 ± 2.9[a,b]	6.1 ± 0.8[a,b]	39.2 ± 4.1[a,b]

[a]$P < 0.05$ *vs* preoperative value.
[b]$P < 0.05$ *vs* 3 months postoperative value.
HOMA-β: β Cellular function index; FCP: Fasting c-peptide; PCP: Postprandial c-peptide; Fins: Fasting insulin; Pins: Postprandial insulin; HOMA-IR: Homeostasis model assessment of insulin resistance.

Table 3 Comparison of lipid and purine metabolic indicators among the patients (*n* = 78)

Time	ALT (U/L)	AST (U/L)	TC (mmol/L)	LDL-C (mmol/L)	TG (mmol/L)	HDL-C (mmol/L)	UA (μmol/L)
Preoperative	37. 1 ± 4.1	25.8 ± 3.6	5.2 ± 0.8	3.4 ± 0.7	4.2 ± 0.9	0.9 ± 0.08	410. 9 ± 35.1
3 months postoperative	38. 2 ± 3.1	24.6 ± 2.9	5.3 ± 0.7	2.6 ± 0.4[a]	2.7 ± 0.5[a]	1.0 ± 0.09	405. 2 ± 30.4
6 months postoperative	38. 9 ± 3.7	25.4 ± 2.2	4.2 ± 0.3[a,b]	2.5 ± 0.6[a]	2.0 ± 0.3[b]	1.0 ± 0.07	345. 2 ± 28.2[a,b]

[a]$P < 0.05$ *vs* preoperative value.
[b]$P < 0.05$ *vs* 3 months postoperative value.
ALT: Alanine transaminase; AST: Aspartate aminotransferase; TC: Total cholesterol; LDL-C: Low density lipoprotein cholesterol; TG: Triglyceride; HDL-C: High density lipoprotein cholesterol; UA: Uric acid.

DISCUSSION

T2DM and its complications have high incidence and mortality rates, which significantly threaten both physical and mental health in patients with the condition-which currently represents a major global public health concern[8]. Controlling T2DM and the lipid and purine metabolic disorders that accompany it has become an urgent medical goal in China, as well as worldwide. Currently, the traditional treatment for T2DM is based on internal medicine and includes oral medications, insulin, and enterotropin[9,10]. Considering the recently demonstrated effectiveness of hypoglycemic treatments in China, the HbA1c compliance rate is < 60% and poor patient compliance represents the main reason for inadequate blood sugar control[11]. Based on our previous research experience and results, there are several major reasons for poor treatment compliance in patients with T2DM: The associated drugs must be taken for life, some hypoglycemic drugs must be taken 2-3 times a day, and some of the drugs carry significant gastrointestinal side effects. Owing to their limited curative effects, many patients require a combination of medications, which typically increases the incidence of missed medications. Hypoglycemic drugs are expensive and, when combined with other medications for treating T2DM-associated complications, many patients are unable to survive very long with the condition. If abnormal blood glucose and lipid levels are not fully regulated significant fluctuations can result in a loss of confidence in treatment approaches. Considering these factors and difficulties, internal medicine-based treatments for T2DM may represent an ineffective route.

Traditional metabolic surgeries used to treat T2DM generally include laparoscopic Roux-en-Y gastric bypass surgery, laparoscopic sleeve gastrectomy, laparoscopic adjustable gastric band surgery, and biliary pancreatic bypass duodenal transposition surgery, among many others. Studies have shown that these surgeries can improve glucose and lipid metabolism in patients[12], but may also carry certain risks such as gastric emptying disorders, dumping syndrome, intestinal hernia, insulinoma, malnutrition, and residual gastric cancer[13-15]. Recently, laparoscopic jejunal-ileal side-to-side anastomosis has emerged as a viable treatment option for patients with T2DM who have normal or relatively high BMI. This surgery can effectively reduce blood sugar levels, delay diabetic complications, reduce the risk of gastrectomy or open placement, and alleviate T2DM. As was mentioned earlier, laparoscopic jejunoileal lateral anastomosis involves diversion of the jejunum and ileum, allowing partially undigested food and digestive fluid to quickly reach the distal ileum and colon, stimulating the production of glucagon-like peptide 1 (GLP-1) by L cells at the ileum's terminus to achieve the goal of controlling blood sugar and improving metabolism.

Recently, several metabolic factors have been shown to be closely associated with T2DM. This study retrospectively analyzed data from 78 patients who underwent laparoscopic jejunostomy at our hospital, measured their preoperative and postoperative glucose, lipid, and purine metabolic indicators, and explored the impacts of the surgery. In terms of glucose metabolism and blood pressure, we observed a decrease in PBG and HbA1c levels at 3 months postoperative *vs* preoperative values, and a decrease in body weight at 6 months postoperative. BMI, SBP, DBP, FBG, PBG, and HbA1c levels were all reduced at 6 months postoperative *vs* 3 months. We observed no statistically significant differences in pancreatic islet function in the patients at 3 months postoperative *vs* preoperatively; however, we did find significant differences in PCP Fins, Pins, and HOMA-β at 6 months postoperative, indicating that pancreatic function began to recover around 6 months after the procedure. As pancreatic function gradually recovered, metabolic indicators improved, and insulin resistance and secretion abnormalities also improved accordingly. The reason for this is considered to be the increased secretion of GLP-1 as a result of the surgery, which in turn promotes the proliferation and differentiation of pancreatic β cells, inhibits their apoptosis, and regulates the blood glucose levels of patients with T2DM based on blood glucose concentration. It also reduces insulin resistance, promotes satiety, and achieves the therapeutic effects of reducing blood sugar, weight, and blood pressure[16-18]. This is consistent with the physiological mechanisms of GLP-1 in the human body that have been previously reported worldwide.

Studies have shown that ALT and AST levels are directly related to the onset and development of T2DM, and thus represent independent risk factors for the condition. In the early stages of diabetes, an increase in transaminase often means that a patient's glucose tolerance becomes impaired[19-21]. With the aggravation of abnormal glucose metabolism, transaminase levels then continue to increase. Inflammatory reactions occur in the body during the state of hyperglycemia, and the resultant liver damage can directly damage the function of pancreatic islet β cells. This causes or promotes the progression of diabetes, indicating that the risk of T2DM is closely related to the increase of transaminase [22]. In this study, we assessed and compared the preoperative and postoperative transaminase levels of our patients. As we found no significant differences in these levels in our cohort, we considered that this may be associated with our mean BMI of < 25 kg/m^2. In future studies, the sample size should be increased to include patients with T2DM and central obesity, to further explore this notion.

Patients with T2DM often exhibit abnormal lipid metabolism and hyperuricemia. Among the enrolled population in this study, the main symptoms were elevated HDL levels and hypertriglyceridemia, with varying degrees of hyperuricemia[23]. Elevated triglyceride and lipid levels may damage the function of pancreatic islets *via* lipid toxicity, whereas elevated HDL and LDL levels, as well as hyperuricemia, are significantly related to the occurrence and development of T2DM-associated atherosclerosis[24,25]. In this study, we observed a 3-month postoperative decrease in LDL-C and TG levels *vs* preoperative ones. At 6 months postoperative, we observed significantly lower TC, TG, and UA levels compared to the 3-month postoperative values. This indicated that lateral jejunoileal anastomosis surgery can benefit patients in terms of blood lipid levels around 3 months after the procedure, and significant improvements in blood lipid and UA levels may be expected at 6 months postoperative. Based on these results, we hypothesize that these changes are related to GLP-1 improving blood lipid levels by increasing liver lipase levels[26,27], downregulating receptor signaling mediated by the muscle thermogenic sympathetic nervous system[28], and directly controlling peripheral lipid metabolism through the central nervous system[29-33].

Postscript

Traditional surgical treatments are more suitable for patients with simple obesity. Studies have shown that traditional metabolic surgeries can alleviate metabolic disorders in patients and, to some extent, compensate for the shortcomings of oral treatment drugs in such patients[12]. However, results in patients with T2DM with normal BMI were normal. For patients with complex obesity such as centripetal obesity caused by Cushing's syndrome, surgery cannot resolve the patient's obesity and should instead aim to treat the primary disease.

CONCLUSION

Laparoscopic jejunoileal anastomosis improved glucose, lipid, and purine metabolism, as well as other related indicators in our cohort of patients with T2DM. In addition to reducing blood sugar, this procedure may provide comprehensive benefits in terms of lipid and purine metabolism, as well as blood pressure and body weight control. By stimulating the secretion of endogenous GLP-1, the pathological and physiological mechanisms of insulin resistance and its insufficient secretion are fundamentally improved in patients with T2DM, thus avoiding the postoperative complications often associated with traditional weight loss surgeries. In future studies, as the number of follow-up cases increases and the sample size expands, we aim to enroll more patients with T2DM in order to further observe the long-term efficacy of laparoscopic jejunoileal anastomosis and provide a theoretical basis for the surgical treatment of T2DM.

FOOTNOTES

Author contributions: Wang JK and Zhang D searched data, organized information, and drafted the manuscript; Wang JF, Lu WL, Wang JY, Liang SF, Liu R and Jiang JX screening and sorting information; Yang X and Li HT inspiration, editing and critically revising the manuscript for intellectual content. Wang JK and Zhang D contributed equally to this work as co-first authors. At the beginning of the study, Li HT as the decision maker, and Yang X, the corresponding author, jointly formulated the research plan and carried out the experimental design. Then, in the ethics link, Li HT completed the writing of the ethics document and cooperated with the ethics committee of my unit to conduct the ethical review until the ethics was passed, laying a foundation for the smooth progress of this research. In the process of data analysis, the author Li HT participated in data statistics and data proofreading. In the process of manuscript revision, author Li HT was able to cooperate with corresponding author Yang X to respond to the valuable questions raised by reviewers, correct and proofread the manuscript, process the revision and resubmit the revised manuscript until the manuscript was accepted. Considering the contribution of the author Li HT in this manuscript, the team decided to change the author ranking of Li HT from the first author to the co-corresponding author after collective discussion.

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