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Peer Review of *World Journal of Diabetes*, Dimiter Avtanski, PhD, Director, Endocrine Research Laboratory, Friedman Diabetes Institute, Lenox Hill Hospital, New York, NY 10022, United States. davtanski@northwell.edu

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Guidelines and consensus: Jejunioileostomy for diabetes mellitus-surgical norms and expert consensus (2023 version)

Ji-Wei Shen, Chun-Yong Ji, Xue-Dong Fang, Bo Yang, Tian Zhang, Zheng-Cai Li, Hua-Zhi Li, Zhi-Yi Liu, Jun Tang, Chuan-Wen Liao, Ji-Zhou Lu, Xuan Yang, Xin-Guo Zhang

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Ji-Wei Shen, Department of General Surgery, Heilongjiang Provincial People's Hospital, Harbin 150036, Heilongjiang Province, China

Chun-Yong Ji, Department of General Surgery, Zhengzhou Central Hospital, Zhengzhou 450007, Henan Province, China

Xue-Dong Fang, Department of General Surgery, The Third Affiliated Hospital of Jilin University, Changchun 130033, Jilin Province, China

Bo Yang, Department of General Surgery, The Eighth Medical Center of the General Hospital of the People's Liberation Army, Beijing 100091, China

Tian Zhang, Department of General Surgery, 242 Affiliated Hospital of Shenyang Medical College, Shenyang 110034, Liaoning Province, China

Zheng-Cai Li, Department of General Surgery, Jingmen Petrochemical General Hospital in Hubei Province, Jingmen 448001, Hubei Province, China

Hua-Zhi Li, Department of General Surgery, Beijing Chuiyangliu Hospital Affiliated to Tsinghua University, Beijing 100022, China

Zhi-Yi Liu, Department of General Surgery, The Fourth Hospital of Jilin University, Changchun 130011, Jilin Province, China

Jun Tang, Department of General Surgery, The First People's Hospital of Xiangtan, Xiangtan 411101, Hunan Province, China

Chuan-Wen Liao, Department of General Surgery, Jiangxi First People's Hospital, Nanchang 332000, Jiangxi Province, China

Ji-Zhou Lu, Department of General Surgery, The Third People's Hospital of Gansu Province, Lanzhou 730020, Gansu Province, China

Xuan Yang, Department of General Thoracic Surgery, Liaoning Electric Power Center Hospital, Shenyang 110403, Liaoning Province, China

Xin-Guo Zhang, Department of General Surgery, The Third Medical Center of the General Hospital of the People's Liberation Army, Beijing 100039, China

Co-corresponding authors: Xuan Yang and Xin-Guo Zhang.

Corresponding author: Xin-Guo Zhang, MMed, Chief Doctor, Department of General Surgery, The Third Medical Center of the General Hospital of the People's Liberation Army, No. 69 Yongding Road, Haidian District, Beijing 100000, China.

13520495188@139.com

Abstract

Diabetes mellitus (DM) is a group of diseases characterized by high blood glucose caused by insufficient absolute or relative secretion of insulin. Once diagnosed, patients need long-term treatment with hypoglycemic drugs. Currently, the existing first-line hypoglycemic drugs do not provide effective treatment for DM and its complications. In the past, the first generation and the second generation of weight loss surgery, such as gastric bypass and sleeve gastric surgery, had strict body mass index requirements. Moreover, post-surgery, patients are prone to fluctuating hypoglycemia, gastroesophageal reflux, and dumping syndrome. Hence, the curative effect of this type of surgery was compromised to a certain extent. Jejunioileostomy is a third-generation surgery for patients with DM, which has been shown to improve glucose and lipid metabolism, without changing the original gastrointestinal tract structure. Different from previous weight loss surgeries, jejunioileostomy has been clinically observed to delay the development of DM-related complications. Additionally, the postoperative complications are mild and do not affect the patient's quality of life. Based on our clinical observations from multi-center large samples, our team developed a consensus on the operative period and perioperative management of jejunioileostomy as a reference for clinical researchers.

Key Words: Surgical; Diabetes; Weight loss surgery; Y-shaped anastomotic jejunal loops; Jejunioileostomy

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Core Tip: The surgical treatment of diabetes has evolved through three stages, shifting focus from weight-loss procedures to techniques that address insulin resistance and enhance glucagon-like peptide-1 (GLP-1) production. The most recent stage, jejunioileostomy, has been included in the national medical security. Unlike weight-loss surgeries which center around the stomach, diabetes surgeries aim to reduce insulin resistance and promote GLP-1 production, regardless of pre-surgery obesity status. Given the dissatisfaction rate with simple sleeve stomach surgeries, there's a growing trend to incorporate intestinal bypass. This consensus encapsulates expert opinions on various aspects of jejunioileostomy for diabetes treatment.

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INTRODUCTION

As a global chronic disease, diabetes mellitus (DM) seriously affects the quality of life of patients[1]. In recent years, surgical treatment options have garnered increasing attention. Of these, the side-to-side anastomosis of the empty ileum, an innovative surgical method, has shown remarkable effects in reducing blood sugar and improving islet function[2,3]. This study aimed to discuss the surgical norms and expert consensus of jejunioileostomy for DM, and provide a relevant reference for clinical research.

Surgical treatment of DM has been categorized into three generations. The first generation is the classic weight loss surgery, and in recent years, gastric bypass and sleeve stomach surgery have been relatively common. The second generation is gastric bypass surgery with appropriate enlargement of the gastric cavity, and precise calculations have been made for the two Y-shaped anastomotic jejunal loops. The third generation is jejunioileostomy, which has been included in the National Medical Security. From the second generation of surgery, there is a clear distinction between surgical treatment for DM and weight-loss surgery, especially at the molecular and biological levels and in terms of surgery design[4]. Weight loss surgery focuses on the stomach, and its molecular biology mechanism tends to change the levels of ghrelin and leptin, thereby achieving therapeutic effects[5]. In recent years, radiation intervention embolization of the left gastric artery for weight loss has also been developed based on this principle[6-8].

Combined with domestic research progress, our team summarized the design principle of the surgery as follows: (1) Reduce food-related stimulations on the "K" cells in the upper part of the jejunum, reducing cytokine secretion that promotes insulin resistance, thereby reducing the degree of insulin resistance in the body[9]. The second and third generations of surgery for diabetes have this effect; (2) Allow undigested food and wild-type digestive juices (such as bile) that are not fully mixed with food to enter the middle and lower digestive tracts earlier and more quickly, leading to

the large number of "L" cells present in this area to produce glucagon-like peptide-1 (GLP-1) and maintaining an elevated level in the body long-term[10-14]. This mechanism underpins the surgical treatment of DM and the associated key therapeutic effects. Notably, the surgical approaches that promote the elevation of GLP-1 are not dependent on the stomach including its size. Furthermore, whether the patient is obese before surgery or not, does not affect the surgical outcome[15,16]; and (3) In recent years, the role of the intestinal microbiota in the pathogenesis and treatment of DM has received extensive attention[17]. Jejunioleostomy may affect the host's metabolic status by altering the composition and metabolic activities of the intestinal microbiota[18]. Some studies have shown that after surgery, the number of beneficial bacteria in the gut increases and the number of harmful bacteria decreases. Additionally, the number of intestinal metabolites, such as short-chain fatty acids, also increases, which can help improve insulin sensitivity and lower blood sugar levels[19-21].

Surgical approaches that involve the stomach often damage the organ, resulting in varying degrees of postoperative malnutrition. Evidence suggests that the patient satisfaction rate (< 30%) of simple sleeve stomach surgery is not high, and the number of patients who are obese tends to increase. Overall, the long-term effects on T2DM has not been satisfactory. Consequently, in recent years, intestinal bypass has been performed together with sleeve stomach surgery including single port anastomosis of the residual stomach and jejunum, duodenal patency, and jejunal loop patency[22-24].

The following is a summary of the Special Committee on Operation Specifications and Expert Consensus of Jejunioleostomy for the Treatment of Diabetes Mellitus ".

JEJUNIOLEOSTOMY FOR DM - SURGICAL NORMS AND EXPERT CONSENSUS

Our recommendations include the indications and contraindications, preoperative evaluation and preparation, rational selection of surgical methods, postoperative complications and treatment, perioperative management, and other key points, based on the insights gained from each member unit, each having completed more than 20000 cases of jejunioleostomy for T2DM. The surgical treatment of DM in China began in 2004[25]. In previous studies, our team confirmed that jejunioleostomy has a definite hypoglycemic effect on patients with T2DM and no significant weight loss effect on patients within the normal weight range. In almost all treated patients, insulin and other hypoglycemic drugs were able to be reduced or even stopped[25]. Therefore, our team proposed the prospect of surgical T2DM treatment. We concluded that T2DM is a gastrointestinal disease that can be cured by surgery.

Surgical period management

Surgical indications: (1) Age \leq 70 years old; (2) Disease duration \leq 15 years (non-single item rejection); (3) Body mass index (BMI) \leq 32.5 kg/m²; (4) C-peptide release test showed a significant peak (more than twice the baseline value); (5) Fasting C-peptide value \geq 1/2 of the lower normal limit; (6) Of the 4 antibody tests for autoimmune diabetes (LADA), \leq 2 are positive; and (7) No serious comorbidities or complications affecting surgery.

For patients with insulin and C-peptide values between a quarter or half of the lower normal limit, surgery should be advised after careful evaluation. In particular, consider the patient's surgical intention.

Age, the course of illness, BMI, and the peak value of the C-peptide release test are references only, and not absolute indicators or contraindications. Those with positive LADA test results are no longer diagnosed as T2DM and the probability of long-term significant remission after surgery is reduced by 10%-40% (although most of these cases can also benefit from surgery). A comprehensive pre-surgical evaluation of both the advantages and disadvantages must be performed. Stringent selection of cases for treatment is advisable.

Surgical contraindications: (1) Type 1 diabetes beyond the honeymoon period. More than 95% of patients with type 1 diabetes have extremely low C-peptide values, thus surgery is contraindicated; (2) BMI \geq 32.5 kg/m². Interventional treatment *via* left gastric artery embolization is the first choice. After 2-4 weeks of weight loss, if the effect is still unsatisfactory or cannot be consolidated, jejunioleostomy for T2DM is the appropriate follow-up treatment; (3) C-peptide release test without a peak or reduced after glucose loading. When the tested patient exhibits high glucose inhibition, this test loses its clinical reference value; (4) After correcting for high glucose inhibition, the fasting C-peptide value should be less or equal to half of the lower normal limit; (5) Three to four diabetes autoimmunity antibody tests are positive; (6) Drug abuse, alcohol addiction, or uncontrollable mental illnesses; (7) Individuals with intellectual disabilities or immaturity, and those who cannot control their behaviors; (8) Those who have not received preoperative notification, without written informed consent, and patients with unrealistic surgical expectations; (9) Those who are unwilling to bear the potential risk of surgical complications; (10) Those who cannot cooperate or at risk of poor compliance with postoperative dietary and lifestyle changes; (11) Individuals with poor overall physical condition and/or difficulties tolerating general anesthesia or surgery; and (12) Coexisting conditions or comorbidities that are not effectively controlled and seriously impact health, such as coagulation disorders, thyroid dysfunction, malignant tumors, and cardiovascular and cerebrovascular diseases.

Perioperative management

Preoperative evaluation: (1) Documentation: Gender, age, course of illness, past and present medical history, diet and exercise status, complications, medication use, allergies, *etc.*; and (2) Physical examination: Body temperature, heart rate, blood pressure, BMI, skin changes, vision changes, limb changes, *etc.*

Preoperative examination items: (1) Routine examination: Blood routine, urine routine, major biochemical examination, coagulation function D-dimer; (2) T2DM-specific examination: Diabetes autoantibody, glycosylated hemoglobin, standard oral glucose tolerance test detection: Blood glucose (fasting, 30 points, 60 points, 120 points, 180 points after meal); Insulin release test (fasting, postprandial 30 points, 60 points, 120 points, 180 points); and C-peptide release test (fasting, postprandial 30 points, 60 points, 120 points, 180 points); and (3) Other auxiliary examinations: Electrocardiogram, ultrasound (liver, gallbladder, pancreas, spleen, vertebral artery, carotid artery, lower limb artery and vein), cardiac ultrasound (including EF value), chest and abdominal CT or plain film X-ray.

While conducting a detailed preoperative evaluation of the patient, special attention should be paid to blood sugar and blood pressure management, such as monitor fasting, pre-meal, 2-hour post-meal, and bedtime blood glucose levels. Use insulin or GLP-1-related preparations during the perioperative period to control blood glucose levels below 10 mmol/L and eliminate ketone bodies in blood and urine tests. If conditions permit the use of GLP-1-related drugs to control blood sugar before surgery, but blood sugar cannot be effectively controlled, it may be due to GLP-1 resistance, which predicts poor post-operative efficacy. For patients with concomitant hypertension, blood pressure should be dynamically monitored and relevant departments should be consulted to adjust the blood pressure to a safe surgical boundary. At the same time, maintain continuous communication with patients and their families, conduct pre-operative education, and sign informed consent forms for surgery and anesthesia.

Intraoperative management

Anesthesia management: (1) Oral hypoglycemic drugs should be discontinued during the perioperative period, and initiate insulin therapy or GLP-1-related preparations; and (2) Treatment measures, such as anesthesia maintenance, ventilation management, and fluid monitoring as per routine practices for anesthesia.

Intraoperative care: (1) The patient is lying flat on the operating bed in a 'big'- shaped position (The patient lies flat with his limbs spread out); (2) Position the head low and the feet elevated at 10 degrees. The patient should lie on the left side at 10 degrees. This position is convenient for intraoperative operation; (3) It is not necessary to insert a gastric or urinary tube; (4) For patients with hyperlipidemia and a history of thrombosis, it is recommended that anti-thrombotic pressure bands are placed on both lower limb pre-anesthesia and until 3 days after surgery, while also monitoring for D-dimer changes; and (5) Prevent the use of one dose of antibiotics, and instead administer antibiotics intravenously during anesthesia. If there is a possibility of contamination, such as excessive leakage of digestive fluid during surgery, an abdominal drainage tube can be left and antibiotics can continue to be used after surgery.

Recommended surgical techniques: (1) The surgeon stands between the patient's legs, with one surgical assistant on the left and one on the right side of the patient. It is also customary for the surgeon to stand on the left side of the patient and have two assistants switch positions; (2) Install a 1.0 cm television endoscope puncture device at the navel, a 0.5 cm puncture device to the left below the xiphoid process, a 0.5 cm puncture device at the midpoint of the line connecting the navel and the right anterior superior iliac spine, and a 1.2 cm puncture device at the midpoint of the line connecting the navel and the left anterior superior iliac spine. The placement of each puncture device can also be rearranged according to the surgeon's habits; (3) Abdominal exploration for intestinal adhesions and malrotation that may hinder surgical procedures. In females, observe to exclude polycystic ovaries; (4) Design of the jejunal anastomosis site and precisely recommended a length of 5000/20 (HOMA-IR+1) cm. The recommended length of 55 cm–120 cm should be roughly calculated. The more significant the insulin resistance, the shorter the intestinal loop should be; (5) Design of ileal anastomosis site. The recommended length of 5000/10 (BMI = 19) should be considered. The recommended length of 55 cm–120 cm should be roughly calculated. The higher the BMI index, the shorter the intestinal loop should be; (6) The sum of the lengths of the above two intestinal loops > 120 cm. Follow the principle of "distal to proximal, proximal to distal" for lateral anastomosis of the jejunum and ileum. Violating this principle will result in postoperative intestinal torsion or internal hernia. After the anastomosis, the two anastomotic intestinal loops will be sutured parallel up and down by 2 cm–3 cm to improve the compliance of the intestinal tract at the anastomotic site; (7) Kiss design. Aim for an anastomotic opening of 3.2 cm–6 cm. Use a cutting stapler to establish the anastomosis. Follow the longitudinal suture direction when suturing the intestinal wall incision of the insertion and cutting closure device. It is important to maintain the original design of the anastomotic site and avoid its shrinking, so that the compliance of the intestinal tract can be maintained. Manually suture the anastomosis. Care must be taken to ensure that the anastomosis is unobstructed to avoid intestinal stenosis; (8) Suture closure of the mesenteric foramen. The wide hiatus formed by tight suturing and anastomosis of the jejunum and ileum mesentery can prevent postoperative internal hernia. Suture with a 2-0 non absorbable barbed thread, fixing it to the retroperitoneum. During the process of suturing the mesenteric hiatus, if the suture needle puncture causes bleeding in the posterior abdominal wall and mesentery, tighten the suture or compress with a gauze strip to stop the bleeding. As long as there is no coagulation mechanism disorder found before surgery, there will be no bleeding or minimal bleeding, with no significant consequences; (9) Apply anti-adhesion preparations around the anastomotic site to prevent postoperative abdominal adhesions; and (10) Determine whether to place a drainage tube based on bleeding, exudation, and anastomotic conditions. A double anastomosis jejuniojejunostomy (the distal end of the ileum is anastomosed with the jejunum + the proximal end is anastomosed with the distal part of the ileum) was considered by the Special Committee. The T2DM treatment mechanism is the same as that of the conventional jejuniojejunostomy. A double anastomosis Jejunioileostomy could also be used for T2DM treatment.

Postoperative management: (1) Blood glucose management. Postoperative blood glucose control target is less than 10.0 mmol/L under any circumstances. To avoid hypoglycemia, optimize blood glucose monitoring using an automatic real-time blood glucose monitor; (2) Fluid replacement. The recommended fluid replacement volume for the first and second

24 hours after surgery is 1000 mL-1500 mL of colloidal solution, or 1500 mL of saline solution or equilibrium solution. Other liquids and intravenous nutrient solutions are not required; (3) Postoperative recovery. On the day of surgery, the patient should be able to sit up and get out of bed. On the first day after surgery, water and clear fluid can be consumed. On the second day after surgery, semi-liquid food can be consumed and the amount of intravenous fluid can be reduced. On the third day after surgery, a regular diet can be consumed and intravenous infusion should be stopped; (4) Blood pressure management. After surgery for T2DM, approximately 90% of patients with hypertension before surgery tend to return to normal due to the post-surgical increase in GLP-1, reducing the systemic smooth muscle tone. For patients with transient high blood pressure exceeding 180 mmHg after anesthesia, nitroglycerin intravenous infusion and other drugs should be used for blood pressure control. Cardiovascular physicians should also be consulted for medication guidance; and (5) Postoperative complications. With the continuous in-depth study of the mechanism of surgery for DM and the continuous summary of experience and lessons gained from clinical practice, the postoperative complications of jejunioleal anastomosis surgery for DM generally show a significant downward trend. The incidence rate of postoperative complications that require surgical or internal medicine intervention is approximately 15% of initial operation units, and less than 8% in units with surgical experience (> 60 cases). Adhesion and disruption of the gut microbiota after intra-abdominal surgery are common causes of postoperative complications.

Postoperative abdominal distention can be caused by slow recovery of gastrointestinal function, gastrointestinal autonomic nervous dysfunction caused by diabetes (diabetes gastroparesis), and obstruction of ileal input loop at the anastomosis caused by abdominal adhesion. Diffuse intestinal distension can be seen on X-rays. If it is not severe and the bowel sounds are weak, advise the patient to take medication, such as Simo Tang, a traditional Chinese medicine preparation for symptomatic relief. If mechanical intestinal obstruction occurs, whether it is due to intestinal adhesion, volvulus, or internal hernia, active surgical treatment should be taken. According to standardized surgical procedures, intestinal torsion and internal hernia are rare. Our committee has conducted barium meal imaging on more than 100 patients who have undergone surgery for more than six months. After oral barium meal administration for 12-24 hours, there is no residual barium agent in the small intestine, confirming the absence of internal circulation of intestinal contents in the small intestine.

Dysfunction of the gut microbiota after diarrhea surgery, obstruction of the jejunal output loop at the anastomotic site caused by abdominal adhesions, short jejunal and ileal loops used for anastomosis, and excessively wide anastomotic sites can all lead to postoperative diarrhea. If probiotics are ineffective or malnutrition is evident, minimally invasive intestinal reduction surgery can be performed. There are cases that suggest that T2DM can remain in remission 3-6 months after reduction surgery.

Abdominal pain

When the mesenteric hiatus is closed during surgery, it needs to be fixed and sutured with the posterior peritoneum. When suturing the posterior peritoneum, if the needle is inserted too shallow, there is a risk of postoperative tension loss and internal hernia. However, if the needle is inserted too deep, postoperative abdominal pain often occurs. In some cases, strong analgesics are needed. Usually, these types of patients can gradually improve before discharge or within one month after discharge. Do not suture the retroperitoneum due to abdominal pain.

Discharge and follow-up

Patients can be discharged within 4-7 days after surgery. Patients with postoperative blood glucose levels that do not meet the standard are recommended to take oral metformin as the first choice. Elderly patients can use GLP-1-related drugs (such as sitagliptin, exenatide, smeglutide, *etc*). Medications can be reduced or stopped after the pancreatic islets gradually proliferate after surgery.

All postoperative patients must be followed up short-term and long-term. Detailed follow-up data should be collected to evaluate the therapeutic effect and ensure a good long-term prognosis after surgery.

Recurrence

Postoperatively, patients with T2DM should maintain a healthy lifestyle. Patients should be supported by medical staff at local medical centers in a timely manner. For patients with postoperative high blood glucose recurrence, unhealthy lifestyle factors must be identified and addressed.

CONCLUSION

Jejunioileostomy, as an innovative surgical treatment for patients with DM. The surgical treatment has shown remarkable progress in recent years[26]. In the future, with further evidence from in-depth studies and explorations of the surgical mechanism, clinical efficacy, and safety, jejunioileostomy may play a more important role in the comprehensive treatment of patients with DM. Thanks to reviewer 2's comments, we added a summary section.

FOOTNOTES

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Country of origin: China

ORCID number: Xuan Yang 0009-0000-9673-2078.

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