Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy Dovepress
open access to scientific and medical research

Open Access Full Text Article

REVIEW

Research Progress of Duodenal-Jejunal Bypass Liner in the Treatment of Obesity and Type 2 Diabetes Mellitus

Ji-Hua Chen[1,2,*], Zi-Han Yu[1,2,*], Qin-Ling Fei Liu[1,2], Qing-Guo Meng[1,2], Xin Chen[1,2]

[1]Department of Gastroenterology and Hepatology, Tianjin Medical University General Hospital, Tianjin, People's Republic of China; [2]Tianjin Institute of Digestive Disease, Tianjin Medical University General Hospital, Tianjin, People's Republic of China

*These authors contributed equally to this work

Correspondence: Xin Chen, Department of Gastroenterology and Hepatology, Tianjin Medical University General Hospital, Tianjin, People's Republic of China, Email xchen03@tmu.edu.cn

Abstract: With the development of economy and improvement of people's living standards, the incidence of obesity and type 2 diabetes mellitus (T2DM) has increased significantly and obesity has also become one of the most important risk factors of T2DM. In light of these trends, there have been many ways to take effect in losing weight. However, they also have corresponding deficiencies including inapparent curative effect, complex and incomplete reversible procedures and severe complications. Duodenal-Jejunal Bypass Liner (DJBL), which mimics Roux-en-Y gastric bypass (RYGB), is proved to play a key role in weight loss and control of T2DM. DJBL is reversible, less invasive and is more suitable for the treatment of obesity and T2DM, which is associated with multiple mechanisms, including incretin effect, gastric emptying mechanism, bile acid regulation, intestinal microbiota, inflammatory reaction mechanism and neural mechanism. In our review, we aimed to elaborate DJBL's clinical efficacy, safety and mechanisms in detail.

Keywords: duodenal-jejunal bypass liner, obesity, type 2 diabetes mellitus, Roux-en-Y gastric bypass

Background

With the development of the economy and the improvement of people's standard of living, the incidence of obesity and type 2 diabetes mellitus (T2DM) has risen sharply and has become a worldwide public health problem. Several data have shown that the number of obese people in the world has almost tripled since 1975, with up to 39% of people aged 18 among them, overweight and obese people accounting for 13%.[1] Meanwhile, 10% of adults (20–79 years old) have developed diabetes mellitus which is the ninth leading cause of death worldwide, most of which are related to T2DM.[2,3] Obesity is one of the most important risk factors for T2DM; thus, the control of obesity is greatly critical for human health.

At present, there are several ways to lose weight, including diet, exercise, acupuncture, drugs and surgery. However, the first three methods are time-consuming and it is easy for patients to regain their weight. Meanwhile, bariatric surgeries, such as sleeve gastrectomy and Roux-en-Y gastric bypass (RYGB), also play important roles in the treatment of obesity and T2DM. However, the surgical procedure is complicated, invasive, incompletely reversible and has complications involving marginal ulcers, internal hernias, dumping syndrome, malnutrition, vitamin deficiencies and a high risk of postoperative gastroesophageal reflux disease.[4] Therefore, duodenal-jejunal bypass liner (DJBL), a novel bariatric technique that mimics RYGB surgery and covers the same duodenal-jejunal part of the gut was developed to make up for these shortcomings. And, as a reversible treatment, DJBL has become a hotspot in the treatment of obesity and T2DM. Hence, our article aims to review the clinical efficacy, safety and mechanism of DJBL.

Received: 14 July 2022
Accepted: 19 October 2022
Published: 28 October 2022

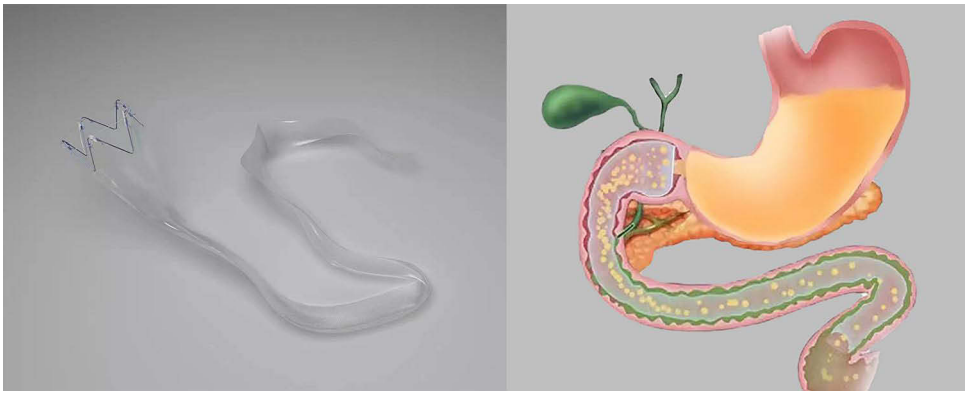

Figure 1 The duodenal-jejunal bypass liner (left)—and in situ (right) (Supported by Tongee Medical Technology Co. Ltd).

Duodenal-Jejunal Bypass Liner (DJBL)

Duodenal-jejunal bypass liner is an endoscopic reversible duodenal jejunal bypass technology invented by GI Dynamics in 2008 based on the RYGB principle, which is mainly used to treat obesity and T2DM.[5] In addition, DJBL consists of a nitinol anchor and a 60 cm impermeable liner made of fluoropolymer. It can be placed in the duodenum under an endoscope, and the anchor is fixed to the intestinal wall of the duodenal bulb by the small barbs that grasp the intestinal mucosa. Then, the inner edge of the anchor is provided with a thin line connecting to the fixed point for later removal of the device. The liner covers all of the duodena and is distally located to the proximal jejunum (Figure 1).

Moreover, DJBL forms a duodenojejunal bypass by lining the mucosa proximal to the small intestine. The ingested nutrients descend directly into the stomach and then pass through the liner into the proximal jejunum. Meanwhile, pancreatic fluid and bile are naturally secreted, thus flowing downwards between the liner and the intestinal wall, and mixed with the digesta in the jejunum distal to the DJBL.

Clinical Efficacy of DJBL

To date, various studies have been conducted worldwide on the clinical value of DJBL, including prospective, open-label studies and clinical randomised trials (Tables 1 and 2).

Table 1 Clinical Efficacy of DJBL: Prospective, Open-Label Trial

Study	Number of Cases (T2DM in Brackets)	Pre-DJBL BMI (kg/m^2)	Baseline HbA1c	Study Duration (Weeks)	Post-DJBL EWL (%)	Post-DJBL Weight Loss (kg)	Post-DJBL HbA1c	Post-DJBL Fasting Blood Glucose
Leonardo Rodriguez-Grunert et al 2008[6]	12(4)	43	-	12	23.6	-	HbA1c decreased in 3 patients (< 5%)	Four patients returned to normal fasting blood glucose
Eduardo G.H et al 2012[7]	22(22)	44.8±7.4	8.9%±1.7%	52	39.0±3.9	-	Down by 2.1%±0.3%	Down by 30.3±10.2 mg/dL
Charlotte de Jonge et al 2013[8]	17(17)	30–50	8.4%±0.2%	24	-	12.7±1.3	7.0%±0.2%	Down by 3.0mmol/L
Bark Betzel et al 2017[9]	185(185)	35.1±4.3	67 mmol/mol	46±15	46±18	12.8±8.0	61 mmol/mol	-
Liat Deutsch et al 2018[10]	39(39)	37.5±5.0	7.2%	39	15.1%±6.0% (TBWL%)	18.6	6.3%	-

Abbreviations: BMI, body mass index; EWL, excess weight loss; TBWL, total body weight loss; HbA1c, hemoglobin A1c; -, not listed.

Table 2 Clinical Efficacy of DJBL: Randomized Controlled Trial

Study	Number of Cases	Pre-DJBL BMI (kg/m^2)	Pre-DJBL HbA1c	Study Duration (Weeks)	Body Weight Change (kg)	BMI Decrease (kg/m^2)	Post-DJBL EWL (%)	Post-DJBL HbA1c
M. Tarnoff et al 2009[11]	25(versus 14 diet control)	42.0±5.1 device 40.0±3.5 in control	-	12	10.3±3.2 device 2.6±3.5 in control	-	22.0% device 5.0% in control	-
Keith S. Gersin et al 2010[12]	13(versus 24 sham control)	46.0 device 46.0 in control	-	12	8.2±1.3 device 2.1±1.1 in control	-	11.9%±1.4% device 2.7%±2.0% in control	-
Ruben Schouten et al 2010[13]	26(versus 11 diet control)	48.9 device 47.4 in control	8.8% device 7.3% in control	13	-	5.5 device 1.9 in control	19.0% device; 6.9% in control	7.7% device 6.9% in control
Parviez Koehestanie et al 2014[14]	34(versus 39 diet control)	34.6 device; 36.8 in control	8.3% device 8.3% in control	26	10.6 device; 5.3 in control	3.3 device 1.8 in control	32.0% device; 16.4% in control	7.0% device 7.9% in control

Abbreviations: BMI, body mass index; EWL, excess weight loss; HbA1c, hemoglobin A1c; -, not listed.

Based on the data, DJBL has significant effects on body weight, blood glucose and Hemoglobin A1c (HbA1c) in obese patients with T2DM. In the clinical randomised trial study of Koehestanie et al,[14] a total of 34 patients received DJBL implantation (device group) and 39 patients belonged to the dietary control group (control group). The baseline BMIs of the device group and control group were 34.6 kg/m^2 and 36.8 kg/m^2, respectively, and the baseline HbA1c was 8.3%. After 26 weeks, the body weight of the device group decreased by 10.6 kg and that of the control group by 5.3 ($P < 0.05$). Correspondingly, the mean EWL of the device group was 32.0%, whereas that of the control group was 16.4% ($P < 0.05$) and the BMI decreased by 3.3 kg/m^2 and 1.8 kg/m^2 ($P < 0.05$), respectively. Not only was the body weight lost but also the blood glucose improved. Meanwhile, HbA1c in the device group and the control group decreased by 1.3% and 0.4%, respectively ($P < 0.05$), and the use of hypoglycemic drugs also decreased. In addition, Obermayer et al[15] found that DJBL can improve insulin sensitivity in obese patients with T2DM.

At present, the treatment duration of DJBL is suggested to be limited to 1 year. Recently, some studies explored the long-term treatment effect of DJBL. In their experiment, the treatment time was extended to 24 months. The results showed that 44 subjects completed the 12-month follow-up; however, only 24 subjects completed the 24-month follow-up because of complications, such as DJBL anchor perforation and device obstruction. During the follow-ups, the subjects' weight continued to decline and their blood glucose levels were improved.[16] Hence, DJBL implantation contributes to weight loss and blood glucose control, and the best result was acquired when it is about 12 months after implantation. As the treatment time is prolonged, the incidence of complications will also greatly increase.

In addition to the effects of weight loss and glucose reduction, other studies have reported that DJBL can reduce blood pressure, hsCRP, lipoprotein-associated phospholipase A2, small dense lipoprotein fraction LDL-4, total cholesterol, LDL-c and other cardiovascular risk biomarkers.[17–19] Meanwhile, DJBL can improve liver fibrosis, and prevent or even reverse the progression of non-alcoholic fatty liver disease (NAFLD) in patients with T2DM and non-diabetic.[20] However, there are still few studies on DJBL in the treatment of NAFLD, and it is necessary to carry out more animal and clinical trials to investigate the efficacy of DJBL.

Mechanisms of DJBL

Obesity is a major factor contributing to the development of glucose intolerance and T2DM, and RYGB is considered to be one of the most effective treatments to reduce body weight and improve glucose metabolism. Hence, there are numerous studies on the mechanisms of RYGB, including its effects on the incretin effect, gastric emptying, bile acids, the nervous system and intestinal microorganisms.[21,22] DJBL mimics the duodenojejunal bypass portion of RYGB to exert weight loss and hypoglycemic effects. Therefore, the mechanisms of DJBL are similar to RYGB. Herein, the mechanisms of DJBL are summarised as follows:

Mechanism of Incretin

Incretins are gut hormones that potentiate insulin secretion after meal ingestion in a glucose-dependent manner.[23] The insulin secretory response of incretins, called the incretin effect, accounts for at least 50% of the total insulin secreted after oral glucose.[24] Moreover, incretins mainly include glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP). Meanwhile, GIP is a polypeptide secreted by mucosal κ cells in the duodenum and proximal jejunum during food stimulation. Thus, it can promote insulin synthesis and secretion, but it can cause insulin resistance and hyperglycemia to develop T2DM. Furthermore, GLP-1 is a peptide secreted by distal small intestinal epithelial L cells, which can promote β cell proliferation, stimulate insulin synthesis and secretion, inhibit glucagon secretion and promote glycogen synthesis and lipolysis. GLP-1 can also slow down gastrointestinal movement and increase satiety.[25] In T2DM, the function of the distal small intestine secreting GLP-1 is impaired and the β cells are damaged, ultimately affecting insulin secretion and body metabolism. In addition, DJBL affects the secretion of GLP-1 and GIP through both foregut and hindgut mechanisms, hence, losing weight and improving glucose metabolism.

In animal experiments, Shuang et al[26] implanted DJBL into diabetic rats. After 12 weeks, the GLP-1 level in plasma and distal ileum of the rats in the device group was significantly higher than that in the control group, meanwhile, the number of GLP-1 positive cells in the distal ileum of the device group was also higher than that in the control group. The same results were found in other clinical studies. de Jonge et al[8] implanted DJBL in 17 obese patients with T2DM. After 24 weeks, the weight of patients was significantly reduced, blood glucose was also rapidly controlled, the level of GLP-1 after a meal increased and the GIP level decreased. Then, after DJBL implantation, when food passes through the duodenum and proximal jejunum, it does not directly contact the intestinal wall; hence, it cannot stimulate mucosal κ cells to secrete GIP, thereby resulting in the decrease of GIP concentration. Digesta quickly enters the distal part of the small intestine, stimulates L cells to secrete GLP-1 and causes the concentration of GLP-1 to rise, which affects the body's metabolism and promotes weight loss and blood glucose improvement.

Although the increase of GLP-1 in patients after DJBL implantation is a key factor mediating weight loss and blood glucose improvement,[27] the level of GLP-1 has not increased or even decreased after DJBL implantation, since the patients' weight loss and blood glucose have improved.[28,29] Therefore, multicentre and larger sample size clinical studies are needed to further explore the effects of GLP-1 after DJBL implantation.

Gastric Emptying Mechanism

Ghrelin is a peptide produced in the stomach, mainly secreted by P/D1 cells at the bottom of the human stomach and the pancreas ε cells to stimulate starvation. Meanwhile, peptide YY (PYY) is an intestinal anorexic hormone, which is mainly secreted by the ileum and colon. Thus, it can inhibit gastrointestinal emptying and increase satiety. In a study on RYGB, the level of PYY increased, whereas the level of ghrelin decreased, the sense of satiety significantly increased and the food intake decreased.[21] However, it is not the same in obese patients with T2DM implanted with DJBL. After DJBL implantation, an increase in PYY concentration was observed in patients.[29] Together, PYY and GLP-1 delay gastric emptying, enhance the sense of satiety and decrease the level of ghrelin, thereby leading to hunger reduction, thus suppressing appetite and reducing weight. However, different from RYGB, the fasting ghrelin levels increased after DJBL implantation in some patients.[28,29] In addition, the elevation of ghrelin could be explained by the reduced food intake that is prescribed by the dietary guidelines that accompany the placement of the DJBL.[28] However, another study showed that the DJBL procedure resulted in a temporary increase in mean fasting ghrelin concentrations which ended

after 12 months in lower levels.[30] Meanwhile, although DJBL implantation delayed gastric emptying, it was not associated with weight loss and improvement in T2DM.[31]

Bile Acid Regulation

Bile acid is an agonist of cell membrane G protein-coupled receptor TGR5, which in turn promotes the release of GLP-1 and PYY, thereby resulting in increased insulin and decreased glucose levels.[21] Meanwhile, CCK is a peptide hormone released by intestinal mucosal I cells. It can mediate gallbladder contraction, Oddi sphincter relaxation and release bile acids through CCK1R. After RYGB, the concentration of total bile acids in patients increases significantly ($P < 0.05$).[32] DJBL, as an alternative therapy for RYGB, has been proven to increase the bile acid concentration in obese patients with T2DM and GLP-1 secretion through bile acids and improve glucose metabolism.[29] This may be explained that the implantation of DJBL leads to bile descending between the liner and the intestinal wall to the distal L cells. Undiluted bile acids may enhance the stimulation of the L cell TGR5 receptor, thereby resulting in increased GLP-1 release. In addition, bile acids can also bind farnesoid X receptor (FXR), which can induce ileal cells to secrete fibroblast growth factor (FGF) 19. Herein, FGF19 is an endocrine hormone that is mostly secreted from ileal enterocytes. Moreover, FGF19 can regulate the growth of organs and tissues, bile acid synthesis, fatty acid oxidation, glucose metabolism and mitochondrial functions.[33] The study by Kaválková et al[34] showed that the FGF19 in the serum of obese patients with T2DM remarkably increased after implantation of DJBL. However, in the study of van Nierop et al,[35] there was no significant change in serum FGF19 level after DJBL implantation. At present, there are still few studies on the effect of DJBL on the bile acid-FXR-FGF19 axis. Whether DJBL implantation affects FGF19 still needs more studies to verify.

Intestinal Microbiota

The intestinal microbiota is classified as the total collection of microbial organisms (bacteria and microbes) within the gastrointestinal tract. It contains tens of trillions of microorganisms, including at least 1000 different species of known bacteria.[36] Therefore, maintaining intestinal microbiota homeostasis is essential for health. Disruption of intestinal microbiota homeostasis—called dysbiosis—has been associated with type 2 diabetes mellitus, obesity, inflammatory bowel disease and irritable bowel syndrome.[37] Meanwhile, in healthy adults, both Firmicutes and Bacteroidetes are the main components of gut bacteria, accounting for more than 90%. However, compared with the lean control group, the proportion of Firmicutes in obese people increases, and the proportion of Bacteroidetes and bacterial diversity decreases.[38] After RYGB, this trend was reversed, that is, the proportion of Firmicutes decreased and the proportion of Bacteroidetes increased after RYGB.[39] In addition, the proportion of Proteobacteria and Verrucomicrobiota increases after RYGB, and these changes may be related to the reduction of inflammation and significant weight loss.[40] The intestinal microbiota is closely associated with bile acids. The increase of Bacteroidetes can promote the passage of primary bile acids through 7 α- Hydroxylase which is converted to secondary bile acids, thus leading to more GIP and GLP-1 release. The concentration of secondary bile acids has certain antibacterial properties, and the increase in its concentration in turn affects the composition of intestinal microbiota.[22,41] Simultaneously, the intestinal microbiota is also affected by intestinal pH value. After RYGB, gastric acid secretion decreased, gastrointestinal pH changed and then affected the composition of intestinal microbiota.[21] de Jonge et al[42] detected the changes in intestinal microbiota in 17 obese patients with T2DM after implantation of DJBL and found that the abundance of Proteobacteria and Firmicutes greatly increased, and the diversity of intestinal microbiota also increased. However, this result is not completely consistent with those after RYGB implantation, but there are relatively few studies on the changes in intestinal microbiota after DJBL implantation. Hence, whether or not the changes are consistent with RYGB still needs further research.

Inflammatory Reaction Mechanism

White adipose tissue has the function of secreting adipokines and cytokines. Obesity leads to the phenotypic transformation of white adipose tissue, which is characterised by inflammatory and dysfunctional adipocytes. Mast adipocytes and tissue-resident immune cells undergo phenotypic changes, stop secreting anti-inflammatory and protective cytokines and start secreting chemokines, such as C-C chemokine receptor type 2 (CCR2), monocyte chemoattractant protein (MCP)

and semaphorin 3A (SEMA3A), thus increasing the secretion of local and systemic inflammatory factors (such as TNF-α, IL-1, IL-6). Meanwhile, inflammatory adipokines and cytokines in turn induce peripheral insulin resistance.[43] There are essential changes in adipokines and inflammatory factors in patients after RYGB, such as IL-6, IL-8, TGF-β, CRP and leptin decreased, while adiponectin increased.[44–46] However, in the study of de Jonge et al[47] it was found that after implantation of DJBL, the inflammatory factors in patients did not decrease. On the contrary, TNF- α and IL-6 levels increased. However, the study still has some limitations because of the small sample size; thus, it still needs to be further demonstrated by clinical trials with a larger number of samples.

Neural Mechanism

The vagal afferent fibres of the stomach and proximal small intestinal mucosa are so sensitive to mechanical stretch that they can detect the volume of ingested food. After an RYGB operation, some branches of the vagus nerve are cut off and the transmission of signals including intestinal hormones (such as ghrelin) can be impaired, which can reduce the hedonic behaviour related to eating delicious and high-calorie food, thus reducing food intake.[21] Accordingly, it is speculated that DJBL implantation may reduce the excitability of the vagus nerve to food intake; however, its specific mechanism remains to be investigated.

Adverse Events of DJBL

As an emerging technique for reducing weight and improving glucose metabolism, DJBL is reversible and less invasive. It has increasingly become a major treatment option for obese patients with T2DM. Given this, its security has also drawn more and more attention.

Betzel et al[48] systematically summarised DJBL-related adverse events (AEs). The results showed that 1056 cases were extracted from the data, and a total of 891 AEs occurred, of which 75.8%, 20.5% and 3.7% were mild, moderate and severe, respectively. There were no fatal cases reported. A total of 255 patients (24.1%) removed the device early. Mild AEs mainly included nausea, vomiting, anchor ulceration and so on. Meanwhile, moderate AEs included mucosal laceration of the oesophagus or oral cavity, anchor-related AEs, such as migration, ulceration and perforation, liner-related AEs, containing obstruction, eversion, inflammation/infectious AES, involving pancreatitis, cholecystitis and cholangitis. Severe AEs (SAEs) were composed of liver abscesses, gastrointestinal haemorrhages, oesophageal perforation and so on. In addition, there are some metabolic diseases related to AEs, covering hypoglycaemia, lipid metabolism disorder and so on. The US Food and Drug Administration (FDA) stopped its clinical trial in 2015 because of the risk of liver abscess after DJBL implantation.[17] However, up to now, the cause of liver abscesses is unclear, and it is speculated that it may be related to ascending cholangitis.[49]

Future Prospects

Weight and blood glucose can be significantly improved after DJBL implantation; however, weight and blood glucose tend to rebound after explantation of the DJBL.[50,51] In the follow-up of 59 obese patients with T2DM after explantation of the DJBL, Betzel et al[51] found that after 1 year of explantation, the body weight of patients were elevated but still below the baseline level, while their HbA1c were elevated and above the baseline level. In addition to the rebound of body weight and blood glucose, AEs caused by DJBL also restrict its further use, thus containing the high incidence of ulceration and perforation at the anchor site and the unclear occurrence of SAE such as liver abscess. Furthermore, the treatment time of DJBL is limited to 1 year for now because of the increasing incidence of AEs with the extensive treatment time. Therefore, there is still much room for further improvement of DJBL. For patients whose weight and blood glucose bounced back after explantation of the DJBL, reimplantation in a short term should be considered.[52] After implantation of the DJBL, when weight loss and blood glucose improvement reached the platform stage, adding other endoscopic weight loss technologies is advisable, covering gastric balloons to enhance the therapeutic effect.[53,54] Moreover, it is necessary to improve the anchor to mitigate damage to the intestinal wall of the anchor site. Simultaneously, the DJBL should be upgraded to prolong the service time of the device and provide longer-term treatment for patients. Hence, it is also urgently essential to explore the causes of SAEs, enhance device performance

and promote the wide application of DJBL. Finally, more animal experiments and clinical trials are needed to further carry out to clarify the functions of DJBL.

Conclusion

DJBL, as a simulation device for RYGB, is mainly used to treat patients with T2DM and obesity. Its advantage is reversible and less invasive, however, its development has been restricted because of the high incidence of AEs and SAEs. Therefore, in this review, we expound on the clinical efficacy, mechanism of action and adverse events of DJBL to provide references for further clinical application. In the existing two domestic DJBL clinical trials, our research group found that after DJBL implantation, the weight, blood glucose and HbA1c levels of the patients decreased significantly, and the fatty liver was improved. Herein, one patient with a long-term menstrual disorder returned to the normal menstrual cycle. Although the incidence of SAEs currently affects the widespread use of DJBL, it is believed that DJBL can be a better treatment choice for more patients with obesity and T2DM with the improvement of its safety and tolerability, and can play a crucial part in the fields of obesity-related metabolic diseases.

Abbreviations

Kg, kilogram; hsCRP, high-sensitivity C-reactive protein; LDL, low-density lipoprotein; CCK, cholecystokinin; TGR, Takeda G-protein-coupled receptor; TNF, tumour necrosis factor alpha; IL, interleukin; TGF, transforming growth factor.

Ethical Approval and Informed Consent Statement

Formal consent is not required for this type of study. Therefore, informed consent does not apply.

Author Contributions

H.-J.C. was responsible for the conception, design and writing of this article. H.-Z.Y. was responsible for the conception and substantial revision of this article. F.-L.Q.L. was responsible for the conception and critical review of this article. G.-Q.M. was responsible for the conception and critical review of this article. X.C. was responsible for the conception, design, critical review and substantial revision of this article. All authors have agreed on the journal to which the article will be submitted. All authors have reviewed and agreed on all versions of the article before submission, during revision, the final version accepted for publication and any significant changes introduced at the proofing stage. All authors agree to take responsibility and are accountable for the contents of the article.

Funding

This review was supported by the Science and Technology Program of Tianjin (No.21JCQNJC00990).

Disclosure

The authors declare that they have no conflict of interest.

References

1. World Health Organization. *Obesity and Overweight*. World Health Organization; 2021.
2. International Diabetes Federation (IDF). *IDF Diabetes Atlas 2021*. International Diabetes Federation (IDF); 2021.
3. World Health Organization. *The Top 10 Causes of Death*. World Health Organization; 2020.
4. Chen G, Zhang GX, Peng BQ, Cheng Z, Du X. Roux-En-Y gastric bypass versus sleeve gastrectomy plus procedures for treatment of morbid obesity: systematic review and meta-analysis. *Obes Surg*. 2021;31(7):3303–3311. doi:10.1007/s11695-021-05456-0
5. Fishman E, Melanson D, Lamport R, Levine A. A novel endoscopic delivery system for placement of a duodenal-jejunal implant for the treatment of obesity and type 2 diabetes. *Annu Int Conf IEEE Eng Med Biol Soc*. 2008;2008:2501–2503. doi:10.1109/IEMBS.2008.4649708
6. Rodriguez-Grunert L, Galvao Neto MP, Alamo M, Ramos AC, Baez PB, Tarnoff M. First human experience with endoscopically delivered and retrieved duodenal-jejunal bypass sleeve. *Surg Obes Relat Dis*. 2008;4(1):55–59. doi:10.1016/j.soard.2007.07.012
7. de Moura EG, Martins BC, Lopes GS, et al. Metabolic improvements in obese type 2 diabetes subjects implanted for 1 year with an endoscopically deployed duodenal-jejunal bypass liner. *Diabetes Technol Ther*. 2012;14(2):183–189. doi:10.1089/dia.2011.0152
8. de Jonge C, Rensen SS, Verdam FJ, et al. Endoscopic duodenal-jejunal bypass liner rapidly improves type 2 diabetes. *Obes Surg*. 2013;23(9):1354–1360. doi:10.1007/s11695-013-0921-3

9. Betzel B, Homan J, Aarts EO, et al. Weight reduction and improvement in diabetes by the duodenal-jejunal bypass liner: a 198 patient cohort study. *Surg Endosc*. 2017;31(7):2881–2891. doi:10.1007/s00464-016-5299-6
10. Deutsch L, Ben Haim L, Sofer Y, Gluck N, Santo E, Fishman S. Long-term effects of proximal small bowel exclusion by duodenal-jejunal bypass liner on weight reduction and glycemic control in diabetic patients. *Surg Obes Relat Dis*. 2018;14(10):1561–1569. doi:10.1016/j.soard.2018.07.022
11. Tarnoff M, Rodriguez L, Escalona A, et al. Open label, prospective, randomized controlled trial of an endoscopic duodenal-jejunal bypass sleeve versus low calorie diet for pre-operative weight loss in bariatric surgery. *Surg Endosc*. 2009;23(3):650–656. doi:10.1007/s00464-008-0125-4
12. Gersin KS, Rothstein RI, Rosenthal RJ, et al. Open-label, sham-controlled trial of an endoscopic duodenojejunal bypass liner for preoperative weight loss in bariatric surgery candidates. *Gastrointest Endosc*. 2010;71(6):976–982. doi:10.1016/j.gie.2009.11.051
13. Schouten R, Rijs CS, Bouvy ND, et al. A multicenter, randomized efficacy study of the EndoBarrier Gastrointestinal Liner for presurgical weight loss prior to bariatric surgery. *Ann Surg*. 2010;251(2):236–243. doi:10.1097/SLA.0b013e3181bdfbff
14. Koehestanie P, de Jonge C, Berends FJ, Janssen IM, Bouvy ND, Greve JW. The effect of the endoscopic duodenal-jejunal bypass liner on obesity and type 2 diabetes mellitus, a multicenter randomized controlled trial. *Ann Surg*. 2014;260(6):984–992. doi:10.1097/SLA.0000000000000794
15. Obermayer A, Tripolt NJ, Aziz F, et al. EndoBarrier™ implantation rapidly improves insulin sensitivity in obese individuals with type 2 diabetes mellitus. *Biomolecules*. 2021;11(4):574. doi:10.3390/biom11040574
16. Betzel B, Cooiman MI, Aarts EO, et al. Clinical follow-up on weight loss, glycemic control, and safety aspects of 24 months of duodenal-jejunal bypass liner implantation. *Surg Endosc*. 2020;34(1):209–215. doi:10.1007/s00464-019-06752-8
17. Laubner K, Riedel N, Fink K, et al. Comparative efficacy and safety of the duodenal-jejunal bypass liner in obese patients with type 2 diabetes mellitus: a case control study. *Diabetes Obes Metab*. 2018;20(8):1868–1877. doi:10.1111/dom.13300
18. Roehlen N, Laubner K, Bettinger D, et al. Duodenal-Jejunal Bypass Liner (DJBL) improves cardiovascular risk biomarkers and predicted 4-year risk of major CV events in patients with type 2 diabetes and metabolic syndrome. *Obes Surg*. 2020;30(4):1200–1210. doi:10.1007/s11695-019-04324-2
19. Glaysher MA, Ward J, Aldhwayan M, et al. The effect of a duodenal-jejunal bypass liner on lipid profile and blood concentrations of long chain polyunsaturated fatty acids. *Clin Nutr*. 2021;40(4):2343–2354. doi:10.1016/j.clnu.2020.10.026
20. Patel SR, Hakim D, Mason J, Hakim N. The duodenal-jejunal bypass sleeve (EndoBarrier Gastrointestinal Liner) for weight loss and treatment of type 2 diabetes. *Surg Obes Relat Dis*. 2013;9(3):482–484. doi:10.1016/j.soard.2013.01.015
21. Abdeen G, le Roux CW. Mechanism underlying the weight loss and complications of Roux-en-Y gastric bypass. review. *Obes Surg*. 2016;26(2):410–421. doi:10.1007/s11695-015-1945-7
22. Aron-Wisnewsky J, Doré J, Clement K. The importance of the gut microbiota after bariatric surgery. *Nat Rev Gastroenterol Hepatol*. 2012;9(10):590–598. doi:10.1038/nrgastro.2012.161
23. Campbell JE, Drucker DJ. Pharmacology, physiology, and mechanisms of incretin hormone action. *Cell Metab*. 2013;17(6):819–837. doi:10.1016/j.cmet.2013.04.008
24. Kim W, Egan JM. The role of incretins in glucose homeostasis and diabetes treatment. *Pharmacol Rev*. 2008;60(4):470–512. doi:10.1124/pr.108.000604
25. Patriti A, Facchiano E, Sanna A, Gullà N, Donini A. The enteroinsular axis and the recovery from type 2 diabetes after bariatric surgery. *Obes Surg*. 2004;14(6):840–848. doi:10.1381/0960892041590818
26. Shuang J, Zhang Y, Ma L, et al. Relief of diabetes by duodenal-jejunal bypass sleeve implantation in the high-fat diet and streptozotocin-induced diabetic rat model is associated with an increase in GLP-1 levels and the number of GLP-1-positive cells. *Exp Ther Med*. 2015;10(4):1355–1363. doi:10.3892/etm.2015.2669
27. Rohde U, Federspiel CA, Vilmann P, et al. The impact of EndoBarrier gastrointestinal liner in obese patients with normal glucose tolerance and in patients with type 2 diabetes. *Diabetes Obes Metab*. 2017;19(2):189–199. doi:10.1111/dom.12800
28. Koehestanie P, Dogan K, Berends F, et al. Duodenal-jejunal bypass liner implantation provokes rapid weight loss and improved glycemic control, accompanied by elevated fasting ghrelin levels. *Endosc Int Open*. 2014;2(1):E21–7. doi:10.1055/s-0034-1365222
29. Vilarrasa N, de Gordejuela AG, Casajoana A, et al. Endobarrier® in grade I obese patients with long-standing type 2 diabetes: role of gastrointestinal hormones in glucose metabolism. *Obes Surg*. 2017;27(3):569–577. doi:10.1007/s11695-016-2311-0
30. Stratmann B, Krepak Y, Schiffer E, et al. Beneficial metabolic effects of duodenal jejunal bypass liner for the treatment of adipose patients with type 2 diabetes mellitus: analysis of responders and non-responders. *Horm Metab Res*. 2016;48(10):630–637. doi:10.1055/s-0042-115175
31. de Moura EG, Lopes GS, Martins BC, et al. Effects of duodenal-jejunal bypass liner (EndoBarrier®) on gastric emptying in obese and type 2 diabetic patients. *Obes Surg*. 2015;25(9):1618–1625. doi:10.1007/s11695-015-1594-x
32. Pournaras DJ, Glicksman C, Vincent RP, et al. The role of bile after Roux-en-Y gastric bypass in promoting weight loss and improving glycaemic control. *Endocrinology*. 2012;153(8):3613–3619. doi:10.1210/en.2011-2145
33. Guo A, Li K, Tian HC, et al. FGF19 protects skeletal muscle against obesity-induced muscle atrophy, metabolic derangement and abnormal irisin levels via the AMPK/SIRT-1/PGC-α pathway. *J Cell Mol Med*. 2021;25(7):3585–3600. doi:10.1111/jcmm.16448
34. Kaválková P, Mráz M, Trachta P, et al. Endocrine effects of duodenal-jejunal exclusion in obese patients with type 2 diabetes mellitus. *J Endocrinol*. 2016;231(1):11–22. doi:10.1530/JOE-16-0206
35. van Nierop FS, de Jonge C, Kulik W, et al. Duodenal-jejunal lining increases postprandial unconjugated bile acid responses and disrupts the bile acid-FXR-FGF19 axis in humans. *Metabolism*. 2019;93:25–32. doi:10.1016/j.metabol.2018.12.009
36. Ley RE, Hamady M, Lozupone C, et al. Evolution of mammals and their gut microbes. *Science*. 2008;320(5883):1647–1651. doi:10.1126/science.1155725
37. Engen PA, Green SJ, Voigt RM, Forsyth CB, Keshavarzian A. The gastrointestinal microbiome: alcohol effects on the composition of intestinal microbiota. *Alcohol Res*. 2015;37(2):223–236.
38. Ley RE, Turnbaugh PJ, Klein S, Gordon JI. Microbial ecology: human gut microbes associated with obesity. *Nature*. 2006;444(7122):1022–1023. doi:10.1038/4441022a
39. Koulas SG, Stefanou CK, Stefanou SK, et al. Gut microbiota in patients with morbid obesity before and after bariatric surgery: a ten-year review study (2009–2019). *Obes Surg*. 2021;31(1):317–326. doi:10.1007/s11695-020-05074-2
40. Dang JT, Mocanu V, Park H, et al. Roux-en-Y gastric bypass and sleeve gastrectomy induce substantial and persistent changes in microbial communities and metabolic pathways. *Gut Microbes*. 2022;14(1):2050636. doi:10.1080/19490976.2022.2050636

41. Li JV, Ashrafian H, Bueter M, et al. Metabolic surgery profoundly influences gut microbial-host metabolic cross-talk. *Gut*. 2011;60(9):1214–1223. doi:10.1136/gut.2010.234708
42. de Jonge C, Fuentes S, Zoetendal EG, et al. Metabolic improvement in obese patients after duodenal-jejunal exclusion is associated with intestinal microbiota composition changes. *Int J Obes*. 2019;43(12):2509–2517. doi:10.1038/s41366-019-0336-x
43. Kawai T, Autieri MV, Scalia R. Adipose tissue inflammation and metabolic dysfunction in obesity. *Am J Physiol Cell Physiol*. 2021;320(3):C375–C391. doi:10.1152/ajpcell.00379.2020
44. Lindegaard KK, Jorgensen NB, Just R, Heegaard PM, Madsbad S. Effects of Roux-en-Y gastric bypass on fasting and postprandial inflammation-related parameters in obese subjects with normal glucose tolerance and in obese subjects with type 2 diabetes. *Diabetol Metab Syndr*. 2015;7:12. doi:10.1186/s13098-015-0012-9
45. Kelly AS, Ryder JR, Marlatt KL, Rudser KD, Jenkins T, Inge TH. Changes in inflammation, oxidative stress and adipokines following bariatric surgery among adolescents with severe obesity. *Int J Obes*. 2016;40(2):275–280. doi:10.1038/ijo.2015.174
46. Agrawal V, Krause KR, Chengelis DL, Zalesin KC, Rocher LL, McCullough PA. Relation between degree of weight loss after bariatric surgery and reduction in albuminuria and C-reactive protein. *Surg Obes Relat Dis*. 2009;5(1):20–26. doi:10.1016/j.soard.2008.07.011
47. de Jonge C, Rensen SS, D'Agnolo HM, Bouvy ND, Buurman WA, Greve JW. Six months of treatment with the endoscopic duodenal-jejunal bypass liner does not lead to decreased systemic inflammation in obese patients with type 2 diabetes. *Obes Surg*. 2014;24(2):337–341. doi:10.1007/s11695-013-1154-1
48. Betzel B, Drenth JPH, Siersema PD. Adverse events of the duodenal-jejunal bypass liner: a systematic review. *Obes Surg*. 2018;28(11):3669–3677. doi:10.1007/s11695-018-3441-3
49. Maggi U, Formiga A, Lauro R. Hepatic abscess as a complication of duodenal-jejunal bypass sleeve system and review of the literature. *Surg Obes Relat Dis*. 2016;12(5):e47–e50. doi:10.1016/j.soard.2016.02.018
50. Riedel N, Laubner K, Lautenbach A, et al. Trends in BMI, glycemic control and obesity-associated comorbidities after explantation of the Duodenal-Jejunal Bypass Liner (DJBL). *Obes Surg*. 2018;28(8):2187–2196. doi:10.1007/s11695-018-3144-9
51. Betzel B, Koehestanie P, Homan J, et al. Changes in glycemic control and body weight after explantation of the duodenal-jejunal bypass liner. *Gastrointest Endosc*. 2017;85(2):409–415. doi:10.1016/j.gie.2016.07.027
52. Leventi E, Günthert SJ, Stier C, Staikov P, Stein J, Farrag K. Is early reimplantation of the duodenal-jejunal bypass liner viable? *Obes Surg*. 2019;29(5):1690–1693. doi:10.1007/s11695-019-03758-y
53. Sartoretto A, Marinos G, Sui Z. Concurrent placements of a duodenal-jejunal bypass liner and an intragastric balloon among severely obese patients: a case series. *ACG Case Rep J*. 2019;6(6):e00101. doi:10.14309/crj.0000000000000101
54. Ghoz H, Jaruvongvanich V, Matar R, et al. A preclinical animal study of combined intragastric balloon and duodenal-jejunal bypass liner for obesity and metabolic disease. *Clin Transl Gastroenterol*. 2020;11(9):e00234. doi:10.14309/ctg.0000000000000234