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Mouse Models of Bariatric Surgery

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Abstract

Morbid obesity is linked to increased incidences of glucose intolerance, Type 2 diabetes mellitus, cardiovascular diseases, various forms of liver disease, and specific forms of cancer. Treatment of obesity by lifestyle modifications (i.e. changes in diet and exercise) and drug therapy is generally ineffective. Bariatric surgery is currently the most effective means of treating obesity and related disorders. We as well as others have developed surgical procedures for application to genetic mouse models that mimic an array of human bariatric surgical procedures used in the treatment of obesity. The application of bariatric surgery to genetic mouse models will broaden our understanding of the role of the gut in metabolic disease. Models that have been developed include gastric banding, sleeve gastrectomy (SG), Roux-en-Y gastric bypass (RYGB) with a complete exclusion of the stomach, duodenal-jejunal bypass (DJB) and biliopancreatic diversion (BPD). The detailed methods of these procedures are provided.

Keywords

Bariatric surgery; gastric banding; sleeve gastrectomy; Roux-en-Y gastric bypass; duodenal-jejunal bypass; biliopancreatic diversion; mice

INTRODUCTION

Obesity is linked to increased incidences of insulin resistance, Type 2 diabetes mellitus (T2DM), cardiovascular diseases, various forms of liver disease and specific forms of cancer. Based on the nutrient pass patterns, bariatric surgery is divided into two classes: restrictive procedures, *e.g.* gastric banding and sleeve gastrectomy (SG), and bypass

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procedures, *e.g.* Roux-en-Y gastric bypass (RYGB), duodenal-jejunal bypass (DJB) and biliopancreatic diversion (BPD). Although restrictive and bypass procedures both produce significantly more weight loss and improvement in diabetes than pharmacological approaches (Cunneen, 2008; Phillips et al., 2009), bariatric surgeries differ in their efficacy towards amelioration of morbid obesity, clinical symptoms of T2DM, and risk factors for cardiovascular disease.

Currently, bariatric surgeries are amongst the most effective and sustainable approaches for the treatment of obesity and diabetes. Restriction of nutrient intake has been considered as a contribution to the beneficial effects of bariatric surgery. However, mechanisms beyond nutrient restriction and malabsorption are poorly understood. While the reliable way to obtain research data concerning the mechanisms of bariatric surgery is to study humans, numerous barriers prevent mechanistic studies in human subjects. Surgical procedures and patient populations vary and make well-controlled experiments impossible. Therefore, animal models allow the testing of putative mechanisms whereby surgical procedures lead to decreases in food intake and gastrointestinal absorption, and affect the regulation of metabolism, hormone action and inflammatory responses. Moreover, gene transfected and knockout mice are currently available, which are able to allow us to test molecular and cellular events induced by bariatric surgery, which would provide insight into the pathogenesis of insulin resistance and diabetes

The Vanderbilt Mouse Metabolic Phenotyping Center (MMPC) has provided a platform for development of mouse bariatric surgery models. These mouse surgical models include gastric banding, SG, RYGB, DJB and BPD. These models provide unique opportunities to understand the mechanisms associated with the beneficial effects of bariatric surgery in the treatment of morbid obesity, diabetes, and cardiovascular disease and from which we can gain valuable insight into gut physiology and the pathogenesis of insulin resistance and cardiovascular disease. The use of these procedures in the mouse will provide clinicians with better guidance in proper selection of surgical procedures to apply to obese patients. A major objective in the application of bariatric surgery to mutant mouse models is to develop candidate pharmaceutical targets that would reproduce effects of bariatric surgery and eliminate the need for invasive procedures. The aim of the following is to describe surgical procedures developed in the Vanderbilt MMPC that are designed to mimic bariatric surgical procedures used in patients.

Mouse selection: general surgical considerations

To develop the surgical models and characterize the primary metabolic effects of bariatric surgery we have utilized high-fat induced obese (DIO) mice and genetically obese mice. DIO mice (C57BL/6) are created by feeding a high fat diet (60% fat, Bio-Serv, Frenchtown, NJ) for 12 weeks, beginning at 6 weeks of age. Compared with lean mice fed a chow diet, the mice fed a high-fat diet show a gradually increased body weight, adiposity, plasma insulin and leptin, impaired glucose tolerance and insulin resistance. However, this dietary regimen does not result in β -cell failure or insulin-deficient diabetes. C57BL/KsJ background leptin receptor-deficient C57BL/KsJ-db/db (BKS-db) mice are obese and have uncontrolled increases in blood sugar and develop severe depletion of pancreatic β -cells and

diabetes with aging (Kodama et al., 1994a; Mao et al., 2006). Pre-diabetic BKS-db mice fed a chow show early metabolic derangements and insulin resistance before the onset of β -cell failure (Baetens et al., 1978; Goren et al., 2004). Elevation of plasma insulin begins at two weeks of age and elevation of blood glucose occurs at 8 weeks of age. Plasma insulin levels are decreased by 40% and 80% at 8 and 12 weeks of age, respectively. Adult or diabetic BKS-db mice with a regular chow reveal significant reduction of beta-cell mass at 14 weeks of age.. This depletion in β -cells results in decreased plasma insulin levels and uncontrolled hyperglycemia (Guedes et al., 2011). Another polygenic model of severe obesity, New Zealand Obese (NZO) mice, develops insulin-deficient diabetes in 40% of males (Harrison and Itin, 1979; Kodama et al., 1994b; Kodama et al., 1994c). High fat-diet can accelerate progression to overt diabetes, and our results show that high fat diet (60% fat) induces insulin-deficient diabetes with a 100% of prevalence in NZO males (unpublished data). T2DM results from a combination of genetic and environmental factors and is increasingly attributed to environmental factors, particular HFD, thus the NZO mouse model provides a clinically relevant approach to define whether genetic and HFD-mediated diabetes can be prevented by bariatric surgery.

All experiments involving animals must be approved by the Institutional Animal Care and Use Committee (IACUC).

The protocols within this manuscript require thorough familiarity with small animal survival surgery. It is neither possible nor practical to describe every specific action required for surgical procedures, and therefore, the information provided here is meant for use only by qualified animal surgeons.

BASIC PROTOCOL 1: GENERAL PROCEDURES AND CARE

Introduction

The steps below comprise the fundamental procedures required for downstream surgeries presented in Basic Protocol 2-5, as well as the alternate protocol. Therefore, please refer to this Basic Protocol as a starting point for specific bariatric surgeries. Likewise, the Materials list presented here applies to subsequent surgical techniques; there may be additional materials required for specific procedures, and these are listed where appropriate.

Materials

Animals

These surgical procedures have been developed for mice. In general, animals exhibiting obesity are utilized for these purposes. Genetically modified strains that are prone to develop obesity or obesity induced by feeding a high fat diet may be used for these procedures. The idiosyncrasy of each model whether genetically modified or dietary induced will need to be considered in performing these procedures.

Instrumentation/Equipment

Surgical microscope

Rodent anesthetic induction chamber Anesthesia machine modified for rodent surgery
Water circulated heating pad and pump
Surgical instruments including, forceps, scissors, needle holders and retractors

Sutures and Surgical Supplies

9-0 sutures monofilament nylon with 3/8 inch taper-point needle
5-0 sutures, polyglactin 910
4-0 sutures monofilament nylon
Surgical gloves
Surgical mask and gown
1-cc syringe
2 × 2 inch cotton gauze
Cotton tips

Chemicals and Pharmaceuticals

Chlorhexidine 2% scrub
Chlorhexidine 2% solution
Povidone iodine
Physiological saline: 0.9% (w/v) NaCl
Isoflurane
Oxygen
Buprenorphine

Presurgical preparation and procedures: surgical instrumentation and

materials—1. Fine microsurgical instruments are required for these procedures. The surgical instruments include scissors, forceps, clamps, needle holders and retractors of the appropriate size and design for the delicate gastric and intestinal incisions and suturing techniques.

2. Instruments are manually or ultrasonically cleaned thoroughly and sterilized prior to use and packaged or wrapped to prevent contamination and damage.

3. Gastrointestinal (GI) anastomosis is performed using 9-0 nylon monofilament. These sutures employ the use of a 3/8 inch taper-point needle.

Animal considerations pre-surgery—4. Mice are housed at 23°C on a 07:00-19:00 light cycle, with access to water and food *ad libitum*.

5. Animals are fasted for 4 to 6 hours prior to the surgery.

Anesthesia—6. All surgeries are performed under general anesthesia. Induction is achieved in an anesthetic chamber and the anesthetic plane is maintained by delivering the isoflurane plus O₂ through a cone placed around the mouse's nose.

The animal remains in a surgical plane of anesthesia throughout the procedure. The animal's vital signs are monitored throughout surgery, including respiratory rate, response to noxious stimulus, and spontaneous movement.

7. Following induction of anesthesia the animals are placed on a water-circulated heating pad to assist in the maintenance of body temperature.

Analgesia—8. Pre-emptive analgesia is administered at this time. Analgesics are administered (Buprenorphine; 0.05 mg per mouse, subcutaneous) 10 minutes prior to the incision. This is followed by a second dose 6-12 hours later, then as needed by evidence of clinical signs of pain.

Clinical signs can include; depression, anorexia, vocalization, hunched posture, chewing, etc. (Schuler et al., 2009). Recovery and post-operative observations are continuous until the mice are ambulatory.

9. The abdominal area is shaved and the skin is washed three consecutive times with 2% chlorhexidine diacetate scrub and rinsed chlorhexidine diacetate solution.

10. The surgical site is then coated with povidone iodine solution. The preparative solutions are maintained at 39°C to assist in maintenance of body temperature.

11. Following the preparative procedures the animal is transferred to a water-circulated heating pad located in the surgical operating field and the animal is positioned and the surgical operating scope is focused.

General procedures—12. Using scissors, make an incision extending from the xiphoid process to the lower abdominal area; this permits exposure of the esophagus, stomach, and small bowel.

13. Abdominal closure is achieved with 5-0 polyclactin sutures on a taper point needle using and interrupted pattern.

14. Skin closure is performed in the same fashion using 4 - 0 nylon monofilament.

15. Upon general closure subcutaneous saline (0.5 ml) is administered for fluid maintenance and analgesics are administered.

Post-surgery recovery—16. The animals are recovered on a water-circulated heating pad and observed continuously until ambulatory. Food and water are provided *ad libitum* upon return to housing.

17. Shama surgical procedures are performed in parallel with the bariatric procedures. One ml saline is injected subcutaneously immediately, post-surgery.

Monitoring during the immediate post-operative period is performed until the animal has regained the ability to ambulate.

18. Daily examination and dietary intake, body weight, fasting blood glucose assessments are performed, post-surgery.

BASIC PROTOCOL 2: GASTRIC BANDING

Introduction

Gastric banding is a gastric restrictive procedure. In the humans, this procedure is created by placing an adjustable band 2cm below the gastroesophageal junction to create a small proximal gastric pouch, and the stomach and duodenum remain in the GI tract. Anatomically, the mouse does not permit the creation of a small gastric pouch as performed in the human; however, this procedure does result in a restrictive nutrient intake. This procedure involves the placement of a restrictive suture cuff around the gastroesophageal junction. The steps below assume that the procedures for pre-surgery preparation detailed in Basic Protocol 1 have already been implemented, and that the general surgical guidelines and post-surgery recovery considerations will be followed.

Materials

Refer to Basic Protocol 1

Elastic thermoplastic polyurethane cord (gastric banding material) Beadalon Inc. (Valley Township, PA).

Steps

1. The gastroesophageal junction is isolated and an elastic silicon rubber string (0.23 mm O.D.) is placed around the gastroesophageal junction and the stomach and duodenum remain in the digestive continuity of the GI tract (Troy et al., 2008).
2. The ends of the string are tied together to form an elastic circular band with the tension of the band adjusted such that the expansion capacity of the gastroesophageal junction is restricted as food passes into the stomach (Figure 1).

The banding procedure is relatively simple to perform however; it is difficult to define the tension (diameter) of the lower esophagus in mice. The utility of this procedure in the mouse has thus far been quite limited. In a cohort of twelve gastric banding-treated mice ($n = 12$), none died during surgery or in the immediate post-operative period, 4 mice died within one month post-surgery and necropsy revealed that the band's tension was too restrictive. Another 4 mice failed to lose weight due to ineffective banding (Yin et al., 2011). The remaining 4 animals demonstrated weight reductions similar to those in the bypass procedures.

BASIC PROTOCOL 3: SLEEVE GASTRECTOMY (SG)

Introduction

SG or vertical sleeve gastrectomy (VSG) is a surgical procedure that maintains gastric and duodenal continuity in the GI tract, however the procedure eliminates the greater curvature of the stomach. SG in humans has shown promising results with respect to obesity and diabetes improvement (Lakdawala et al., 2009; Videla et al., 2009). Diabetes is resolved in more than 70% of patients (Buchwald and Scopinaro, 2009; Silecchia et al., 2006). The results from a group in the United Kingdom revealed an improvement in their diabetes in 95% of patients who had laparoscopic SG vs. 50% of patients who had laparoscopic adjustable gastric banding follow-up at 13 months (Gan et al., 2007).

Materials

See Basic Protocol 1

Steps

1. The procedure in the mouse, as in humans, involves the transection and excision of more than 80% of the stomach (Gan et al., 2007). Following anesthetic induction and stabilization the animal's abdomen is shaved and aseptically prepared.
2. A midline incision is performed at the xiphoid process and extended to the lower abdominal providing exposure to the entire splanchnic bed.
3. Gentle retraction of stomach provides exposure to the lower portion of the esophagus and entire stomach. The gastrosplenic ligamentum and vessels are ligated and cut.

After the stomach is completely isolated, a clamp is placed on the stomach 0.8cm to the curvature ventriculi minor curve of the stomach. The transection extends from the upper-most part of the forestomach to the lower portion of the greater curvature, essentially excising the greater curvature of the stomach. The resected stomach is removed from the abdominal cavity.

4. The remaining stomach is approximated and uninterrupted sutured using 9 - 0 nylon monofilament sutures (Ethicon, Figure 2a and 2b).

Our surgical success rate for this procedure was 100% (n = 14) and the clinical observations demonstrated improvements insulin resistance in the short term (4 weeks). Thus, SG represents a reliable gastric restrictive procedure that can be performed in mice and replicates the procedures performed in humans. This procedure can be performed alone or in combination with other bariatric surgery, such as DJB and BPD.

BASIC PROTOCOL 4: ROUX-EN-Y GASTRIC BYPASS (RYGB)

Introduction

RYGB is a bypass procedure that results in nutrient bypass of the stomach, duodenum and the proximal portion of the jejunum. In humans the procedure entails the creation of a small pouch of proximal stomach (30 ml) in continuity with the mid to distal jejunum, thus isolating the majority of the stomach, duodenum and the proximal jejunum from the GI tract. The stomach of the mouse is comprised of a proximal non-glandular forestomach and a distal glandular portion and the gastroesophageal junction of the mouse is located in a central portion of the lesser curvature and thus presents a significant surgical challenge in attempting to replicate the procedure performed in humans. Consequently, we developed a procedure similar to the RYGB performed in humans, with a side-to-side anastomosis of the jejunum was performed with the lower portion of the esophagus.

Materials

See Basic Protocol 1

1. Following anesthetic induction and stabilization the animal's abdomen is shaved and aseptically prepared.
2. A midline incision is performed at the xiphoid process and extended to the lower abdominal providing exposure to the entire splanchnic bed.
3. Gentle retraction of stomach provides exposure to the middle and lower portion of the esophagus and entire stomach.
4. The paraesophageal vessels are separated. A suture is placed at the point between the esophagus and the fundus immediately distal to the esophageal-jejunal anastomosis.
5. An incision is made on the esophagus above the suture, and the distal jejunum is anastomosed to the esophagus by uninterrupted sutures with 9-0 suture (Ethicon).

The distances of jejuno-jejunostomy to the Ligament of Treitz and the site of the esophageal-jejunostomy are 4 cm and 6 cm, respectively (Figure 3a and 3b).

6. The jejuno-jejunostomy is performed using a side to side anastomosis and the terminal end of the transected jejunum is oversewn. The surgical success rate is 80%.

This procedural caveat differs from the RYGB procedure performed in humans in which the fundus of the stomach is preserved. However, this model provides an approach to study role of the stomach in the pathogenesis of insulin resistance and obesity related diabetes.

BASIC PROTOCOL 5: DUODENAL-JEJUNAL BYPASS (DJB)

Introduction

DJB is an experimental surgical technique created by Rubino et al. (Rubino and Marescaux, 2004), where the stomach remains a part of the GI tract and the duodenum is excluded from GI continuity. This procedure can be used to investigate whether the control of diabetes is a secondary outcome from the treatment of obesity or a direct result of the duodenal-jejunal exclusion.

Materials

See Basic Protocol 1

Steps

1. The procedure in the mouse involves an anastomosis of the jejunum to the duodenum after transection at the site of the pylorus (Figure 4a and 4b) (Lan et al., 2010; Rubino et al., 2006). Following anesthetic induction and stabilization the animal's abdomen is shaved and aseptically prepared.
2. A midline incision is performed at the xiphoid process and extended to the lower abdominal providing exposure to the stomach, duodenum and proximal jejunum.
3. After isolation of the pylorus and duodenum, the duodenum is transected immediate distal to the pylorus.
4. The transected jejunum is then anastomosed to the remaining duodenum at the pyloric junction in an end-to-side fashion.

The distances of jejuno-jejunostomy to the Ligament of Treitz and the site of the duodenal-jejunal anastomoses are 4 cm and 6 cm, respectively.

5. The jejuno-jejunostomy is performed using a side to side anastomosis and the terminal end of the transected duodenum and jejunum is oversewn.
6. The procedures are performed using 9 - 0 monofilament nylon.

The surgical success rate is ~ 80%. A recent report in humans suggests that a simple bypass of the duodenum and jejunum (DJB) without gastric bypass is not able to improve insulin resistance (Kindel et al., 2011). Our unpublished results suggest that RYGB, but not DJB, delayed disease progression to insulin-deficient diabetes in a polygenic model (New Zealand Obese, NZO). More studies are required to test the important role of stomach exclusion in improving insulin resistance and preventing T2DM associated with the foregut bypass.

ALTERNATE PROTOCOL: BILIOPANCREATIC DIVERSION

Introduction

A variation of this procedure is the biliopancreatic diversion (BPD), a foregut bypass procedure for the treatment of Class 3 morbid obesity (BMI > 45), and it allows food to

bypass the duodenum, jejunum and part of ileum. Existing clinical results suggest that BPD is extremely effective in ameliorating diabetes, resulting in normoglycemia and increased insulin sensitivity in over 90% of patients up to 20 years post-surgery (Scopinaro et al., 2005).

Materials

See Basic Protocol 1

Steps

1. The BPD procedure isolates the duodenum and pancreas from the GI tract and involves the transection of the jejunum 4 cm distal to the ligament of Trietz with the surgical anastomosis of the distal jejunum to the stomach.
2. The proximal jejunal segment is anastomosed to the ileum in a side-to-side fashion 10 cm proximal to the ileum-ascending colon junction.
3. In the mouse the proximal duodenum is ligated at the pyloric-duodenal junction using 6-0 silk, but not transected.

This procedure isolates the duodenum, most of the jejunum and pancreatic secretion from the GI tract.

Our data show that the surgical success rate is 90% (9/10), whereas most of the mice 89% (8/9) undergoing BPD procedure died of severe malnutrition within 4 to 8 weeks (Yin et al., 2011). A modification of the BPD procedure in the mouse entails the anastomosis of the distal jejunum to the duodenum instead of the anastomosis of the distal jejunum to the stomach, as described in the DJB procedure; this requires an additional jejuno-ileal anastomosis.

COMMENTARY

Background Information

Obesity is an epidemic that has been described as the greatest current threat to human health. Its contribution to health care costs has increased exponentially (Buchwald et al., 2004; Skopkova et al., 2007). Lifestyle intervention and pharmaceutical therapies have had minimal success in maintaining clinically relevant weight loss. Bariatric surgery is the most effective therapy for morbid obesity and among the most effective therapies for the comorbidities of obesity (Goldfine et al., 2009; Saber et al., 2008). Beneficial effects of bariatric surgery besides weight loss, include reduced insulin resistance and decreased risk factors for cardiovascular disease (Goldfine et al., 2009). The effects of bariatric surgery exceed the anticipated effects of mechanical manipulation of gut nutrient passage and have positive clinical effects that are independent of weight loss. This has resulted in the development and application of bariatric surgery procedures for the treatment of morbid obesity or for the treatment of milder obesity with associated pathology (Goldfine et al., 2009; Kadera et al., 2009; Keating et al., 2009; Kral and Naslund, 2007; Wong and Marwick, 2007). As a consequence of the effectiveness of bariatric surgery, the number of

bariatric surgery procedures has steadily risen during the past 20 years. The broad beneficial effects of bariatric surgery have led to great interest in understanding the role of the gut in health and disease.

Critical Parameters

When applying mouse bariatric surgery for the study of human bariatric surgery mechanisms, it is critical to remember that mouse models cannot completely reflect the bariatric surgery procedures performed in humans. For example, our mouse RYGB model completely excludes the stomach, whereas the clinical gastric bypass procedure preserves a pouch so that the stomach is not completely bypassed. We have recently developed another gastric bypass procedure in which a very small pouch is created thus mimicking the clinical scenario. This model is currently under investigation.

Complications—The potential problems include short-term and long-term complications. Immediate surgical complications include:

Anastomotic leaks: Anastomosis leak usually occurs in the foregut bypass procedures, including DJB, RYGB and BDP, within two days post-surgery due to inadequate tissue healing. The incidence of this complication is 5% in the foregut bypass procedures. Anastomotic leaks can occur at the sites of gastro-jejunal, jejuno-jejunal, duodenal-jejunal and ileo-jejunal anastomoses. Mice with this complication die a few days following surgery. Practices that can reduce the incidence of this complication include gentle manipulation of the gut tissues and use of appropriate surgical instruments, especially clamps for gut anastomosis. Suturing techniques with appropriate suture to tissue tension are critically important.

Bleeding: GI bleeding is an unusual complication in mouse bariatric surgery procedures but can originate at anastomotic sites. The incidence of bleeding is usually less than 1% in these bariatric surgery procedures. The clinical signs and symptoms of bleeding is almost impossible to detect and the mouse with GI bleeding typically dies within 24 hours post-surgery. Accurate suturing and gentle tissue manipulation are required throughout the entire surgical procedure.

Infection: Intra-abdominal infection is a potential complication in bariatric surgery procedures (5%). Strict attention to aseptic technique is required to prevent contamination of the abdominal cavity and the transected and anastomotic sites.

Long-term complications include nutritional deficiencies (Xanthakos, 2009; Xanthakos and Inge, 2006). Anemia occurs in the foregut bypass mice; potential causes include: (i) the duodenum and proximal jejunum are the sites of iron absorption and are excluded in gastric bypass procedures; and (ii) the hypo-acidic environment after RYGB decreases the bioavailability of oral iron as well as optimal function of iron transport (von Drygalski and Andris, 2009). Mice undergoing foregut bypass that do not receive iron supplementation will die 8-16 weeks post-operatively due to iron deficient anemia. Dextran iron solution (10mg/kg, i.m.) is administered at two weeks following bariatric surgery and every two weeks thereafter. Other nutritional complications include deficiency of vitamin B12, low

folate and calcium (Toh et al., 2009; Xanthakos, 2009; Xanthakos and Inge, 2006); these have not been observed to cause clinical disease post operatively. However, subtle changes, as a result of these deficiencies, have not been thoroughly investigated in all surgical models.

Euthanasia: Animals with severe malnutrition, depression, anorexia, vocalization, hunched posture, chewing, and lack of response to eye blink are humanely euthanized. Loss of >20% lean mass, such as severe malnutrition, is included as an endpoint for euthanasia. The IACUC and the Panel on Euthanasia of the American Veterinary Medicine Association have approved the method of euthanasia.

Anticipated Results

Surgical success rate will be expected to be over 80% and preventable complications less than 20% after intentional training. A successful gastric bypass procedure will improve insulin resistance and prevent overt diabetes in more than 80% of DIO and genetic obese mice.

Time Considerations

All mouse bariatric surgeries would be accomplished within one hour.

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Figure 1.
Gastric banding. 1a. Gastric banding figure. 1b. The photo of gastric banding.

Figure 2. Sleeve gastrectomy. 2a. Sleeve gastrectomy figure. . The stomach is exposed and approximately 80% of stomach is removed (the forestomach and 70% of the granular stomach). . 2b. The photo of Sleeve gastrectomy.

Figure 3.

Roux-en-Y gastric bypass (RYGB). 3a. The figure of RYGB with complete exclusion of the stomach. The mouse RYGB involves the anastomosis between the esophagus and the jejunum, which is different from the RYGB procedure performed in humans that creates a stomach pouch out of a small portion of the stomach and attaching it directly to the small intestine. The mouse RYGB bypasses the whole stomach and duodenum. E-J, esophago-jejunal anastomosis; J-J, jejuno-jejunal anastomosis. Sleeve gastrectomy figure. The whole forestomach and 70% of the granular stomach are removed. 3b. The photo of RYGB.

Figure 4. Duodenal-jejunal bypass (DJB). 4a. The figure of DJB. DJB consists of a stomach-preserving bypass of the duodenum and a short segment of the proximal jejunum. The distal jejunum is anastomosed to the proximal duodenum. D-J, duodenal-jejunal anastomosis; J-J, jejuno-jejunal anastomosis. 4b. The photo of DJB.