

Weight Regain Following Roux-en-Y Gastric Bypass: Etiology and Surgical Treatment

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ABSTRACT: The Roux-en-Y gastric bypass (RYGB) surgery helps patients achieve excellent excess weight loss, with subsequent improvement or resolution of co-morbidities. However, up to 20% of all RYGB patients, and 40% of the super morbidly obese, experience significant weight regain. The etiology of weight regain is multifactorial; hence, multidisciplinary management is mandatory. Revision options for failed conservative and medical management include resizing the restrictive component of the bypass or intensifying malabsorption. While improvement of restriction generally has limited efficacy, intensifying malabsorption achieves significant long-term excess weight loss. The optimal surgical option should be personalized, considering eating behavior and psychological issues, surgical anatomy of the bypass, and anesthetic and surgical risks.

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KEY WORDS: Roux-en-Y gastric bypass (RYGB), weight regain, etiology, revision, conversion

Metabolic and bariatric surgery is justified, provided that significant (> 50%) excess weight loss (EWL) and long-term (> 5 years) maintenance are achieved [1]. Accordingly, the Roux-en-Y gastric bypass (RYGB) is considered as the gold standard. The excellent EWL and subsequent improvement or resolution of co-morbidities outweighs the perioperative risks [2]. While the EWL stabilizes within 18–24 months, up to 20% of all RYGB patients and 40% of the super-morbidly obese experience significant weight regain (> 15% of maximal EWL) [3,4]. The focus of the current review is to examine the etiology of weight regain following RYGB and surgical treatment for failed conservative management.

Significant weight regain occurs in 20% of RYGB patients and is associated with relapse of co-morbidities and impaired quality of life

and deleterious lifestyle. Over the course of time, secondary alterations in the RYGB surgical anatomy might impair restriction or malabsorption and potentially lead to weight regain. For example, the development of a gastro-gastric fistula between the gastric pouch and remnant stomach impairs both restriction and malabsorption. This entity is rare, due to meticulous transection between the two gastric parts. We will not elaborate on this complication.

Restriction is related to the gastrojejunal complex (GJC) anatomy. Yimcharoen and colleagues [5] performed endoscopy at a mean interval of 6.9 years after RYGB on patients who experienced weight regain. They found a secondary dilated GJC anatomy in 71% of patients (i.e., dilated gastrojejunostomy [diameter > 2 cm], or dilated gastric pouch [length > 6 cm or width > 5 cm]), or both. Nevertheless, they did not find any significant correlation between the extent of dilatation and the total weight regain. Furthermore, in a meta-analysis, Jiang et al. [6] did not find a significant correlation between the primary anastomotic diameter and the EWL achieved after RYGB. Therefore, it is uncertain whether the GJC anatomy affects outcome.

Regarding malabsorption, Stefanidis and co-authors [7] examined whether the length of alimentary limb (range 40–250 cm) affected the EWL. Their review included four randomized controlled trials. A very modest short-term advantage for longer limb lengths was found only in super-morbidly obese patients.

However, the effect waned after 4 years. They concluded that the common channel length should be at focus when constructing the RYGB. A possible explanation for

the waning effect is adaptation of the small intestine over the course of time. In all, it remains controversial whether secondary alterations of the RYGB surgical anatomy lead to weight regain.

The RYGB alters the balance between gut hormones that stimulate appetite (e.g., ghrelin) and satiety (e.g., glucose-dependent insulinotropic peptide [GIP], glucagon-like peptide 1 [GLP-1]) [8]. Ghrelin levels decrease while GLP-1 levels increase, resulting in diminished hunger and early satiety. The new balance is disturbed in patients with weight regain as GIP and GLP-1 levels decrease after meal stimulation [9]. Hormonal changes after RYGB could also lead to recurrent postprandial hyper-insulinemic hypoglycemia due to hyper secretion of GIP

ETIOLOGY OF WEIGHT REGAIN

Etiology of weight regain following RYGB is multifactorial. Potential factors, besides genetics, include secondary altered surgical anatomy, altered metabolic and gut-hormonal balance,

and GLP-1 [10-12]. Consequently, patients might experience maladaptive eating behavior and weight regain.

Untreated or unrecognized pre-existing maladaptive eating behavior and psychiatric disorders predispose individuals to weight regain [13]. Not adhering to nutritional recommendations is another contributing factor [14-17]. Morbidly obese patients who do not pursue profound change of deleterious lifestyle, might “bypass the bypass”, and experience weight regain. Nutrition and psychological counseling are mandatory.

REVISION OPTIONS

Revision options include improvement of restriction or intensification of malabsorption [Table 1]. Comparing efficacy of the different revision options is difficult due to wide variance regarding the technique of revision, the time interval between RYGB and revision, and the reported data parameters (e.g., body mass index [BMI], EWL, total weight loss) [18]. Improving restriction can be performed by traditional surgery or endoluminal procedures. The latter are considered simpler and safer. Endoluminal procedures include sclerotherapy and tissue plication techniques using designated devices.

SCLEROTHERAPY

Sclerotherapy is performed by injecting sclerosant material (e.g., sodium murrhuate) into the gastrojejunal anastomotic rim to induce inducing scarring and narrowing. In a large retrospective study, Abu-Dayyeh and colleagues [19] reviewed the cases of 231 patients who underwent 575 sclerotherapy procedures after a mean 5.7-year interval following RYGB. Most patients (65%) needed several sessions. The mean BMI before RYGB was 50, median weight loss percentage (not EWL) was 39%, and median weight regain was 36%. Sclerotherapy resulted in an 18% reduction of the previous weight regain (i.e., mean 4.5 kg weight loss after 6 months). The intra- and post-procedure bleeding rates

were 2.4% and 0.2%, respectively. Small ulcers occurred in 1% of procedures. The authors also analyzed other studies, and found 82% weight regain stabilization (defined as weight decrease or gain of less than 2.27 kg from the pre-sclerotherapy weight). However, the mean weight loss was only 5.3 kg. The authors also stated that even though Catalano et al. [20] achieved mean weight loss of 20 kg after 18 months, their aggressive treatment resulted in 36% ulcer formation rate. Therefore, sclerotherapy is not an appealing option.

TRANS-ORAL OUTLET REDUCTION

Trans-oral outlet reduction (TORe) includes argon coagulation of the gastrojejunal anastomotic rim followed by tissue plication by full-thickness sutures. Vargas et al. [21] conducted a multi-center international study that included 130 patients. The mean post-RYGB EWL was 70%. Revision was performed at an 8.4-year interval. The mean prerevision BMI and weight regain

were 36.8 and 38.8% (24.6 kg), respectively. The achieved weight loss was 20% and 8 kg after 1 and 2 years, respectively. Major complications included esophageal tear that necessi-

Etiology is multifactorial; therefore, multidisciplinary management is mandatory. Revision procedures that improve restriction are generally ineffective, except for controversial salvage banding

tated endoscopic clipping (1%) and anastomotic stricture that required endoscopic dilatation (5%). In their meta-analysis, weight regain stabilization rate was 80–100%, and the short-term effect on weight regain was only 11–25%. Hence, TORe does not seem to be an attractive option.

ENDOSCOPIC GASTRIC PPLICATION AND RESTORATIVE OBESITY SURGERY ENDOSCOPIC

The endoscopic gastric plication (EGP) or restorative obesity surgery endoscopic (ROSE) procedures use designated device for gastric tissue plication and GJC resizing. Ong’uti et al. [22] stopped performing EGP because all patients (n=25) regained weight after 1 year and endoscopy revealed undone folds and disappearance of the tissue fasteners. Gallo and co-authors [23] achieved only 8% EWL after 1 year from ROSE. Most patients were lost to follow-up, yet reduction effect for both weight and GJC size were transitory. They discussed whether endoscopic revision of RYGB is a holy grail or epic fail.

TRADITIONAL OPEN GJC RECONSTRUCTION

Traditional open GJC reconstruction, reported by Mason et al. [24] in 1975, resulted in high postoperative morbidity. Laparoscopic procedures were developed with the intention of simplicity and safety.

LAPAROSCOPIC GASTROJEJUNAL SLEEVE REDUCTION

Parikh et al. [25] described the laparoscopic gastrojejunal sleeve reduction. Resection was performed over a 40F bugie, commencing at the jejunum, through the gastrojejunal anastomo-

Table 1. Roux-en-Y gastric bypass revision options for weight regain

Route	Restriction improvement	Malabsorption intensification
Endoluminal	Sclerotherapy Tissue plication techniques • TORe: trans oral outlet reduction • EGP: endoscopic gastric plication • ROSE: restorative obesity surgery endoscopic	None
Transabdominal	Open gastrojejunal complex reconstruction Laparoscopic • Gastrojejunal complex reconstruction • Gastrojejunal sleeve reduction • Gastric pouch resizing • Gastric pouch salvage banding	Conversion to distal gastric bypass reconstruction • Type I: long biliopancreatic limb (Sugerman [29]) • Type II: long alimentary limb (Brolin [30]) • Conversion to biliopancreatic diversion with duodenal switch

sis and gastric pouch, up to the left crust [Figure 1A]. Twelve patients underwent laparoscopic surgery, while two underwent urgent laparotomy due to RYGB complications. The pre-RYGB BMI, EWL, and pre-revision BMI were 46.8, 71.5%, and 35.5, respectively. Post-revision, the EWL was only 12.8% after 12 months. One patient needed endoscopic dilatation of the GJC. The authors concluded that the procedure was ineffective.

LAPAROSCOPIC GASTRIC POUCH RESIZING

Likewise, Iannelli et al. [26] performed laparoscopic gastric pouch resizing over a 34F bougie after a 49-month interval. Despite a high major complication rate (30%), the procedure was considered successful, resulting in 69% EWL. In fact, only seven patients had secondary pouch dilatation and the effect was rather small (EWL increased from 44 to 57%, BMI decrease by 3 points).

LAPAROSCOPIC RESECTION AND RECONSTRUCTION OF THE GJC

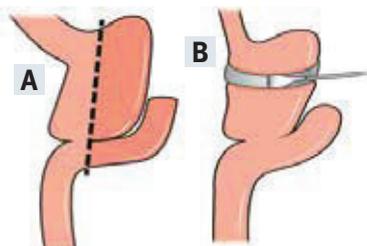
Hamdi et al. [27] performed laparoscopic resection and reconstruction of the GJC in 25 patients. The post-RYGB and pre-revision EWL were 69% and 40%, respectively. After revision, EWL was 64% and 43% at 1 and 2 years, respectively. Overall, resizing the GJC results in unsatisfactory and transient weight loss effect. This finding is in accordance with the impression of a non-significant correlation between the extent of GJC dilatation and weight regain.

GASTRIC POUCH SALVAGE BANDING

In a review of the literature, Vijgen et al. [28] found that most surgeons used an adjustable band for RYGB salvage, and few used a nonadjustable band. Band placement was distal to the esophago-gastric junction [Figure 1B], thus preserving the GJC anatomy. The authors found that the short-term effect was significant: 56–94% excess BMI loss (EBMIL) after 12–42 months in 94 patients. outcomes of gastric pouch salvage banding seem favorable. Unfortunately, the perioperative morbidity was high (17%) and mandated surgical intervention. Due to these risks and the disappointing long-term outcome as a primary procedure, the fate of salvage banding is questionable.

Figure 1. Illustration of surgical restriction improvement options

- [A] Illustration of gastrojejunal complex resizing
- [B] Illustration of gastric pouch salvage banding



Revision procedures that intensify malabsorption result in substantial and long-term excess weight loss, although it is technically demanding and entails the risk of significant protein-calorie malnutrition

Although improvement of restriction has overall limited efficacy, intensification of malabsorption seems favorable. Surgical procedures include RYGB conversion into distal gastric bypass or biliopancreatic diversion with duodenal switch (BPD/DS).

RYGB CONVERSION TO DISTAL GASTRIC BYPASS

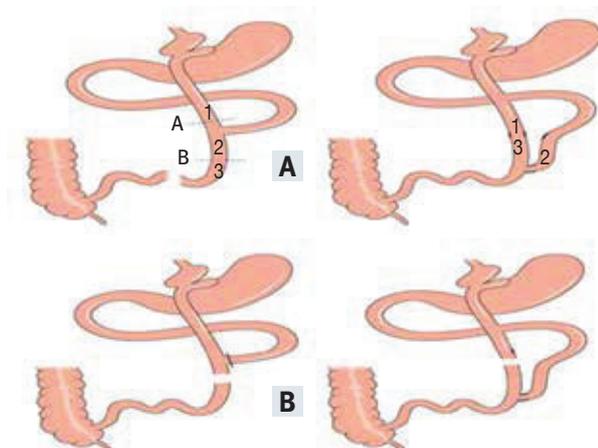
RYGB conversion to distal gastric bypass can be performed by distalization of the biliopancreatic limb (type I, Sugerma [29] or alimentary one (type II, Brolin [30]). Sugerma and colleagues [29] described RYGB conversion to type I distal gastric bypass [Figure 2A] as creating a very long biliopancreatic limb in super-morbidly obese patients. The alimentary limb was transected in close proximity to the jejunojunostomy and the ileum was transected 250 cm proximal to the ileocecal valve.

Two anastomoses were then performed: alimentary limb to the distal ileal stump and biliopancreatic limb to the terminal ileum, creating a 50 cm common channel. The first five patients developed severe protein calorie malnutrition (PCM) and required surgical revision to elongate the common channel. Two of them eventually died of hepatic failure. Consequently, the procedure

Figure 2. illustration of gastric bypass distalization

[A] Illustration of type I gastric bypass distalization. On the left, the dotted lines represent the staple line transecting the alimentary limb in close proximity to the jejunojunostomy (A) and the ileum 250 cm proximal to the ileocecal valve (B). On the right, anastomoses are performed between the stumps of the alimentary limb (1) and distal ileum (3), and between the stump of the biliopancreatic limb (2) and the ileum 150 cm from the ileocecal valve, creating a 145 cm alimentary limb and a 150 cm common channel

[B] Illustration of type II gastric bypass distalization. On the left, the dotted line represents the staple line transecting the biliopancreatic limb in close proximity to the jejunojunostomy. On the right, anastomosis is performed between the stump of the biliopancreatic limb and the ileum 75–100 cm from the ileocecal valve



was modified, creating a 150 cm common channel, and 145 cm alimentary limb. Twenty-two patients underwent the modified procedure, but 13% needed surgical revision due to severe PCM. There were no cases of mortality. The overall revision rate due to severe refractory PCM was 30%. Other early perioperative complications occurred in 48% of patients. The mean time interval between RYGB and revision was 5.6 years. The mean BMI decreased from 57 and 46 pre-RYGB and pre-revision to 37 and 32 after 1 and 5 years post-revision, respectively. The pre-revision EWL was 30% and increased to 61% and 69% after 1 and 5 years post-revision, respectively. Despite a high complication rate, the modified procedure seems very successful in terms of long-term EWL maintenance.

Brolin and Cody [30] described RYGB conversion to type II distal gastric bypass [Figure 2B] as creating a very long alimentary limb. This procedure was performed in 54 patients. Their primary bariatric surgery was RYGB (n=47), or pure restrictive operations (n=7). Almost all RYGB patients underwent con-

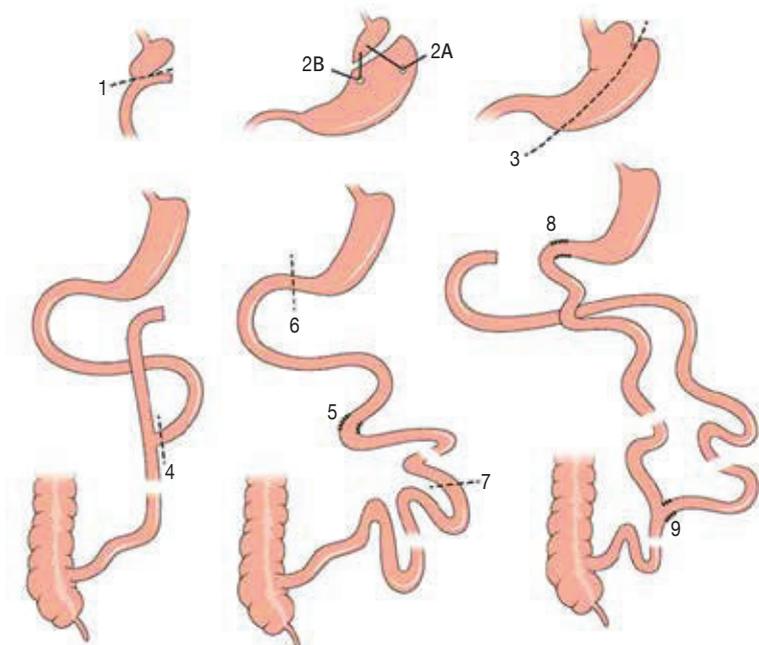
Revision should be personalized and consider eating behavior and psychological issues, surgical anatomy of the bypass, and anesthetic and surgical risks

comitant GJC revision. The biliopancreatic limb was transected from the jejunojejunostomy with anastomosis to the terminal ileum 75–100 cm proximal to the ileocecal valve. Early complication and mortality rates were 18% and 2%, respectively. PCM occurred in four patients (7.4%) and required revision, including common channel lengthening (n=2) or complete reversal to normal anatomy (n=1). The mean EWL after 1 year was 47.9%.

Buchwald and Oien [31] also described RYGB distalization in 53 patients after an interval of 10.8 years. They created a long biliopancreatic limb, 75–100 cm common channel, and alimentary limb of 75–100 cm (until 2011, and 250 cm thereafter [n=6]). The mean BMI pre-RYGB, at nadir, pre-revision, and 5 years post-revision were 54.3, 32.3, 47.2, and 31.4, respectively. Early (30-day) and late complication rates were 13.2% and 62.3%, respectively. Early and late mortality rates were 0% and 5.75%, respectively. TPN was required in 43.4%. Surgical revision due to severe PCM was needed in 26.4%. Revision included common channel lengthening (22.6%) or original RYGB anatomy restoration (3.8%). None of the six patients with 250 cm alimentary limb had significant complications or malnutrition.

It is difficult to compare the distalization types because of the insufficient number of cases for statistical analysis. Long-term EWL maintenance is achieved in both at a high cost of severe PCM, which often requires revision. Construction of a longer common channel is prudent. Lengths of 100–150 cm appear tolerable.

Figure 3. illustration of conversion to biliopancreatic diversion with duodenal switch. The gastrojejunostomy is divided (1), gastro-gastric anastomosis is created using a stapler (circular or linear) inserted through a gastrotomy on the greater curvature of the remnant (2A) or manually through a gastrotomy on the lesser curvature of the remnant (2B), and a sleeve gastrectomy is performed (3). The jejunojejunostomy is divided (4) and the proximal end of the roux limb is anastomosed to the distal end of the biliopancreatic limb (5), the duodenum is divided 5 cm distal to the pylorus (6), the ileum is transected proximal to the ileocecal valve (7) according to predetermined lengths of both alimentary limb and common channel. Duodeno-ileostomy (8) and ileo-ileostomy between the alimentary and biliopancreatic limbs (9) are created



RYGB CONVERSION TO BILIOPANCREATIC DIVERSION WITH DUODENAL SWITCH

RYGB conversion to biliopancreatic diversion with duodenal switch (BPD/DS) is technically challenging [Figure 3]. First, the gastrojejunostomy is divided. Gastro-gastric anastomosis is created between the gastric pouch and remnant stomach, followed by sleeve gastrectomy. Next, the jejunojejunostomy is divided and the proximal end of the roux limb is anastomosed to the distal end of the biliopancreatic limb or if the roux limb is short, it can be transected leaving the anastomosis intact. The duodenum is then divided 5 cm distal to the pylorus, and the ileum is transected proximal to the ileocecal valve according to predetermined lengths of both alimentary limb and common channel. Duodeno-ileostomy and ileo-ileostomy between the alimentary and biliopancreatic limbs are created [Figure 3].

Keshishian et al. [32] calculated the lengths of the alimentary limb and common channel as 35–45% and 8–12%, respectively, of the total small bowel length. They performed open conversion into BPD/DS in 47 patients. The primary bariatric surgery included vertical banding gastroplasty, RYGB, or both (n=16, n=26, n=5, respectively). Conversion was performed after an interval of 11.8 years. The EWL was 67% after 30 months. Their

study was skewed by confounding factors, including revision indication other than weight regain, and primary bariatric surgery other than RYGB. However, when analyzed separately, there was no statistical difference in outcome for the different primary surgeries. Postoperative complications included leakage from the gastric pouch (8.5%), which required surgical treatment in half of the patients, wound infection (2.1%), and hernia (2.1%). There were no cases of PCM.

Parikh et al. [33] created consistent lengths of both the alimentary limb and common channel, measuring 150 and 100 cm, respectively. They performed laparoscopic conversion into BPD/DS in 12 patients after 3.8 years interval from the primary RYGB or other previous surgical revision of the RYGB. One patient underwent open conversion into BPD/DS due to extensive adhesions from previous surgeries. The EWL was 63% after 11 months. Postoperative complications included gastro-gastrostomy stricture (33%), which required either a single endoscopic dilatation (75%) or laparoscopic revision (25%), wound complications (8%), and negative re-exploration for metabolic acidosis (8%). There were no cases of PCM.

RYGB conversion into BPD/DS is technically challenging. The two stages of the procedure (i.e., conversion into sleeve gastrectomy and construction of BPD/DS) can be performed either concomitantly or separately. Several technical methods have also been described for conversion into sleeve gastrectomy [34,35]. Construction of BPD/DS entails high complication rate; however, it achieves the best results so far regarding EWL and does not carry a risk for severe PCM.

SINGLE ANASTOMOSIS DUODENO-ILEAL SWITCH

Sanchez-Pernaute et al. [36] described a simpler modification of the original BPD/DS, the single anastomosis duodeno-ileal switch (SADIS). In SADIS, a formal sleeve gastrectomy is created, the duodenum is sectioned at the level of the gastroduodenal artery (i.e., 3 to 4 cm distal to the pylorus), and anastomosis is constructed between the proximal duodenum and the ileum, creating 200 to 300 cm common limb length [37]. SADIS seems safe as a primary bariatric procedure or for revision of sleeve gastrectomy with promising short-term outcome. However, its additive effect for weight regain following RYGB has not been reported yet.

CONCLUSIONS

Substantial weight regain occurs in up to 40% of RYGB patients within 10 years, which is usually associated with relapse of co-morbidities and impaired quality of life. Therefore, surgical treatment should be considered. The optimal surgical option should be planned individually, and should consider the patient's eating behavior (sweet-eater or large volume consumption), current RYGB surgical anatomy (evaluated by endoscopy and barium swallow study), and history of bariatric

surgeries. The general condition, medical history, and anesthetic and surgical risks should also be considered.

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References

- Scopinaro N, Gianetta E, Adami GF, et al. Biliopancreatic diversion for obesity at eighteen years. *Surgery* 1996; 119 (3): 261-8.
- Buchwald H, Avidor Y, Braunwald E, et al. Bariatric surgery: a systematic review and meta analysis. *JAMA* 2004; 292 (14): 1724-37.
- O'Brien PE, McPhail T, Chaston TB, Dixon JB. Systematic review of medium-term weight loss after bariatric operations. *Obes Surg* 2006; 16: 1032-40.
- Christou NV, Look D, MacLean LD. Weight gain after short- and long-limb gastric bypass in patients followed for longer than 10 years. *Ann Surg* 2006; 244 (5): 734-40.
- Yimcharoen P, Heneghan HM, Singh M, et al. Endoscopic findings and outcomes of revisional procedures for patients with weight recidivism after gastric bypass. *Surg Endosc* 2011; 25 (10): 3345-52.
- Jiang HP, Lin LL, Jiang X, Qiao HQ. Meta-analysis of hand-sewn versus mechanical gastrojejunal anastomosis during laparoscopic Roux-en-Y gastric bypass for morbid obesity. *Int J Surg* 2016; 32: 150-7.
- Stefanidis D, Kuwada TS, Gersin KS. The importance of the length of the limbs for gastric bypass patients—an evidence-based review. *Obes Surg* 2011; 21 (1): 119-24.
- Meek CL, Lewis HB, Reimann F, Gribble FM, Park AJ. The effect of bariatric surgery on gastrointestinal and pancreatic peptide hormones. *Peptides* 2016; 77: 28-37.
- Santo MA, Riccioppo D, Pajecki D, et al. Weight regain after gastric bypass: Influence of gut hormones. *Obes Surg* 2016; 26 (5): 919-25.
- Øhrstrøm CC, Worm D, Hansen DL. Postprandial hyperinsulinemic hypoglycemia after Roux-en-Y gastric bypass: an update. *Surg Obes Relat Dis* 2017; 13 (2): 345-51.
- Salehi M, Prigeon RL, D'Alessio DA. Gastric bypass surgery enhances glucagon-like peptide 1-stimulated postprandial insulin secretion in humans. *Diabetes* 2011; 60 (9): 2308-14.
- Roslin M, Damani T, Oren J, Andrews R, Yatco E, Shah P. Abnormal glucose tolerance testing following gastric bypass demonstrates reactive hypoglycemia. *Surg Endosc* 2011; 25 (6): 1926-32.
- Maleckas A, Gudaitytė R, Petereit R, Venclauskas L, Veličkienė D. Weight regain after gastric bypass: etiology and treatment options. *Gland Surg* 2016; 5 (6): 617-24.
- Sarwer DB, Wadden TA, Moore RH, et al. Preoperative eating behavior, postoperative dietary adherence, and weight loss after gastric bypass surgery. *Surg Obes Relat Dis* 2008; 4 (5): 640-6.
- Freire RH, Borges MC, Alvarez-Leite JI, Toulson Davisson Correia MI. Food quality, physical activity, and nutritional follow-up as determinant of weight regain after Roux-en-Y gastric bypass. *Nutrition* 2012; 28 (1): 53-8.
- Allied Health Sciences Section Ad Hoc Nutrition Committee, Aills L, Blankenship J, Buffington C, Furtado M, Parrott J. ASMBS Allied Health Nutritional Guidelines for the Surgical Weight Loss Patient. *Surg Obes Relat Dis* 2008; 4 (Suppl 5): S73-108.
- Zalesin KC, Franklin BA, Miller WM, et al. Preventing weight regain after bariatric surgery: an overview of lifestyle and psychosocial modulators. *Am J Lifestyle Med* 2010; 4 (2): 113-20.
- Tran DD, Nwokeabia ID, Purnell S, Zafar SN, Ortega G, Hughes K, et al. Revision of Roux-en-Y gastric bypass for weight regain: a systematic review of techniques and outcomes. *Obes Surg* 2016; 26 (7): 1627-34.
- Abu-Dayyeh BK, Jirapinyo P, Weitzner Z, et al. Endoscopic sclerotherapy for the treatment of weight regain after Roux-en-Y gastric bypass: outcomes, complications, and predictors of response in 575 procedures. *Gastrointest Endosc* 2012; 76 (2): 275-82.
- Catalano MF, Rudic G, Anderson AJ, Chua TY. Weight gain after bariatric surgery as a result of a large gastric stoma: endotherapy with sodium morrhuate may prevent the need for surgical revision. *Gastrointest Endosc* 2007; 66: 240-5.
- Vargas EJ, Bazerbachi F, Rizk M, et al. Transoral outlet reduction with full thickness endoscopic suturing for weight regain after gastric bypass: a large multicenter international experience and meta-analysis. *Surg Endosc* 2018; 32 (1): 252-9.

22. Ong'uti S, Ortega G, Onwugbuor M, Ivey G, Fullum T, Tran D. Effective weight loss management with endoscopic gastric plication using StomaphyX device: is it achievable? *Surg Obes Relat Dis* 2013; 9 (1): 1137.
23. Gallo AS, DuCoin CG, Berducci MA, et al. Endoscopic revision of gastric bypass: holy grail or epic fail? *Surg Endosc* 2016; 30 (9): 3922-7.
24. Mason EE, Printen KJ, Hartford CE, Boyd WC. Optimizing results of gastric bypass. *Ann Surg* 1975; 182 (4): 405-14.
25. Parikh M, Heacock L, Gagner M. Laparoscopic gastrojejunal sleeve reduction as a revision procedure for weight loss failure after Roux-en-Y gastric bypass. *Obes Surg* 2011; 21 (5): 6504.
26. Iannelli A, Schneck AS, Hébuterne X, Gugenheim J. Gastric pouch resizing for Roux-en-Y gastric bypass failure in patients with a dilated pouch. *Surg Obes Relat Dis* 2013; 9 (2): 260-7.
27. Hamdi A, Julien C, Brown P, et al. Midterm outcomes of revisional surgery for gastric pouch and gastrojejunal anastomotic enlargement in patients with weight regain after gastric bypass for morbid obesity. *Obes Surg* 2014; 24 (8): 1386-90.
28. Vijgen GH, Schouten R, Bouvy ND, Greve JW. Salvage banding for failed Roux-en-Y gastric bypass. *Surg Obes Relat Dis* 2012; 8 (6): 803-8.
29. Sugerman H, Kellum J, Demaria E. Conversion of proximal to distal gastric bypass for failed gastric bypass for superobesity. *J Gastrointest Surg* 1997; 1 (6): 51725.
30. Brolin R, Cody RP. Adding malabsorption for weight loss failure after gastric bypass. *Surg Endosc* 2007; 21 (11): 19246.
31. Buchwald H, Oien DM. Revision Roux-en-Y gastric bypass to biliopancreatic long-limb gastric bypass for inadequate weight response: case series and analysis. *Obes Surg* 2017; 27 (9): 22932302.
32. Keshishian A, Zahriya K, Hartoonian T, Ayagian C. Duodenal switch is a safe operation for patients who have failed other bariatric operations. *Obes Surg* 2004; 14 (9): 118792.
33. Parikh M, Pomp A, Gagner M. Laparoscopic conversion of failed gastric bypass to duodenal switch: technical considerations and preliminary outcomes. *Surg Obes Relat Dis* 2007; 3 (6): 6118.
34. Dapri G, Cadière GB, Himpens J. Laparoscopic conversion of Roux-en-Y gastric bypass to sleeve gastrectomy as first step of duodenal switch: technique and preliminary outcomes. *Obes Surg* 2011; 21 (4): 51723.
35. Lakdawala M, Limas P, Dhar S, et al. Laparoscopic revision of Roux-en-Y gastric bypass to sleeve gastrectomy: a ray of hope for failed Roux-en-Y gastric bypass. *Asian J Endosc Surg* 2016; 9 (2): 1227.
36. Sanchez-Pernaute A, Rubio Herrera MA, Perez-Aguirre E, et al. Proximal duodenal-ileal end-to-side bypass with sleeve gastrectomy: proposed technique. *Obes Surg* 2007; 17 (12): 16148.
37. Shoar S, Poliakin L, Rubenstein R, Saber AA. Single anastomosis duodeno-ileal switch (SADIS): a systematic review of efficacy and safety. *Obes Surg* 2018; 28 (1): 104-13.

Capsule

Spatial heterogeneity of the T cell receptor repertoire reflects the mutational landscape in lung cancer

Somatic mutations together with immunoediting drive extensive heterogeneity within non-small-cell lung cancer (NSCLC). Kroopa and colleagues examined heterogeneity of the T cell antigen receptor (TCR) repertoire. The number of TCR sequences selectively expanded in tumors varies within and between tumors and correlates with the number of nonsynonymous mutations. Expanded TCRs can be subdivided into TCRs found in all tumor regions (ubiquitous) and those present in a subset of regions (regional). The number of ubiquitous and regional TCRs correlates with the number of ubiquitous and regional nonsynonymous mutations,

respectively. Expanded TCRs form part of clusters of TCRs of similar sequence, suggestive of a spatially constrained antigen-driven process. CD8⁺ tumor-infiltrating lymphocytes harboring ubiquitous TCRs display a dysfunctional tissue-resident phenotype. Ubiquitous TCRs are preferentially detected in the blood at the time of tumor resection compared to routine follow-up. These findings highlight a noninvasive method to identify and track relevant tumor-reactive TCRs for use in adoptive T cell immunotherapy.

Nature Med 2019; 25: 1549

Eitan Israeli

Capsule

Single-cell immune landscape of human atherosclerotic plaques

Atherosclerosis is driven by multifaceted contributions of the immune system within the circulation and at vascular focal sites. However, specific characteristics of dysregulated immune cells within atherosclerotic lesions that lead to clinical events such as ischemic stroke or myocardial infarction are poorly understood. Using single-cell proteomic and transcriptomic analyses, Fernandez et al. uncovered distinct features of both T cells and macrophages in carotid artery plaques of patients with clinically symptomatic disease (recent stroke or transient ischemic attack) compared to asymptomatic disease (no recent stroke). Plaques from symptomatic patients were characterized by a distinct subset of CD4⁺ T cells and by T cells that were activated and differentiated. Moreover, some

T cell subsets in these plaques presented markers of T cell exhaustion. In addition, macrophages from these plaques contained alternatively activated phenotypes, including subsets associated with plaque vulnerability. In plaques from asymptomatic patients, T cells and macrophages were activated and displayed evidence of interleukin-1 β signaling. The identification of specific features of innate and adaptive immune cells in plaques that are associated with cerebrovascular events may enable the design of more precisely tailored cardiovascular immunotherapies.

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