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위절제 범위 및 장문합 길이에 따른 당뇨 조절
효과 및 기전에 관한 동물실험

**Effect and mechanisms of diabetes resolution
according to the range of gastric resection and the
length of anastomosis in animal model**

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허 연 주

Abstract

Effect and mechanisms of diabetes resolution according to the range of gastric resection and the length of anastomosis in animal model

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Purpose The aim of this study was to examine the effect and mechanism of roux-en Y resectional gastric bypass (RYGB) on improvement of diabetes according to the length of anastomosis and the range of gastric resection in animal model.

Methods Sprague-Dawley rats were induced to obese glucose intolerance via high fat diet for 3 months. They were underwent long-limb RYGB (conventional RYGB, cRYGB) which was about 95% gastric resection with 15cm of roux-limb and 40cm of biliopancreatic (BP) limb (n = 9), short-limb RYGB which was about 95% gastric resection with 8cm of roux-limb and 4cm of BP limb (sRYGB) (n=9), fundus-sparing RYGB which was about 70% gastric resection with 8cm of roux-limb and 4cm of BP limb (fRYGB) (n=9) or sham operation (n = 9). After 6 weeks, oral glucose tolerance tests (OGTT) were performed, and gut hormone which can contribute to the obese diabetes

including insulin, glucagon-like peptide-1 (GLP-1), glucose-dependent insulinotropic peptide (GIP), and ghrelin were analyzed.

Results In sRYGB group, there was no difference in food intake compared with cRYGB group, but improvement of hyperglycemia was not shown. The cRYGB group showed significantly decreased food intake, body weight, and random glucose ($p < 0.05$). In the cRYGB and sRYGB groups, glucose was significantly steeply increased till 30 min and insulin was sharply increased till 30 min without significance during OGTT. Total GLP-1 was higher at 30 min in the cRYGB than other groups without significance. fRYGB group showed similar change of body weight and random glucose compared with sham group and showed slowly increased pattern in OGTT and GLP-1 and lowest peak point in insulin and GIP due to time-lag caused by gastric stasis.

Conclusion We could identify that long-limb roux-en Y bypass with 95% gastric resection was needed to achieve not only the loss of body weight, but also improvement of diabetes through this experiment. This could be related with increase of GLP-1.

Keywords: Roux-en-Y gastric bypass, Rats, Sprague-Dawley, glucagon-like peptide-1, glucose-dependent insulinotropic peptide, ghrelin

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INTRODUCTION

Gastric cancer is one of the significant global health problems. It is the fifth most common cancer and third leading cause of cancer-related death worldwide [1]. In Korea, the proportion of EGC was markedly increased owing to widespread of health screening and diagnostic tools [2]. According to improvement of treatment result for EGC, concern of treatment of EGC reached to not only better survival but also improvement of quality of life.

The prevalence of diabetes mellitus (DM) is rapidly increasing as a consequence of aging population, urbanization in the wake of rapid industrialization, and lifestyle changes [3]. DM presently affects more than 285 million people worldwide, a number expected to be 439 million with increase of 54% in 2030 [4]. In Korea, diabetes mellitus ranked in 6th in the statistics of mortality for 2014, and the ratio is 20.7 persons per 100,000 [5]. Until now, there is no absolute treatment for complete remission, and complication risk increased when disease period is getting longer, so that the importance of diabetes is very serious. In the early period, the purpose of bariatric surgery was weight loss, however, nowadays it is used for the most effective treatment modality for diabetes [6] and obesity [7]. Mingrone et al.[8] reported that bariatric surgery induced remission of diabetes in the 70-80% of obese patients with diabetes, therefore meaning of bariatric surgery is extended to metabolic surgery.

Meanwhile, according to the study which was conducted to investigate DM resolution after gastrectomy in gastric cancer patients, many gastric cancer patients with DM who received a gastrectomy showed remission (19.7%) or improvement(37.1%) of DM [9]. The degree and consistency of improvement of diabetes after gastrectomy in gastric cancer is relatively lower than that after bariatric-metabolic surgery.

Therefore, we assume that modification of gastric cancer surgery to bariatric-metabolic surgery including the length of roux limb makes it possible to cure not only gastric cancer but also diabetes.

Especially, the mechanism of the remission of diabetes by the most typical bariatric-metabolic surgery, roux-en Y gastric bypass, is not clear, however several possible mechanisms are reported; (1) decrease of food intake due to decrease of gastric volume and loss of appetite, (2) foregut hypothesis that this results induced by effects of bypass the 98% of stomach, duodenum, and proximal jejunum, (3) hindgut hypothesis that this results induced by gastrointestinal hormone surge from food reached to distal jejunum quickly [10].

In this study, we performed several kinds of roux-en Y gastric bypass (RYGB) surgery in hyperglycemic rats to investigate the effect and mechanism of RYGB on improvement of diabetes according to the length of anastomosis and the range of gastric resection.

MATERIALS AND METHODS

Animals and Diet

Male Sprague-Dawley (SD) rats who were 4 weeks of age were purchased from Orient Bio Inc. (Sunnam, Korea). They were fed 60% high fat rat diet (Central Lab. Animal Inc., Seoul, Korea) and water *ad libitum* at the Seoul National University Hospital Biomedical Research Institute. All animal procedures were approved by the Institutional Animal Care and Use Committee (IACUC) of Seoul National University (IACUC approval no. 14-0179).

Experimental Protocol

After the rats were acclimated for 1 week, food intake, weight and random glucose were measured. After 3 months of high fat diet, induced glucose intolerance was confirmed through intraperitoneal glucose tolerance test (IPGTT). According to glucose level and body weight, the hyperglycemia-induced rats evenly underwent one of the following operations with same mean glucose level in the all groups: 1) long-limb RYGB (cRYGB) (n=9), 2) short-limb RYGB (sRYGB) (n=9), 3) fundus-sparing RYGB (fRYGB) (n=9), or 4) sham operation (controls, n=9). All groups were also fed the same type of diet after operations. In all groups, postoperative measurements of random glucose were performed at 4th, 5th, and 6th weeks for a total follow-up of 7th

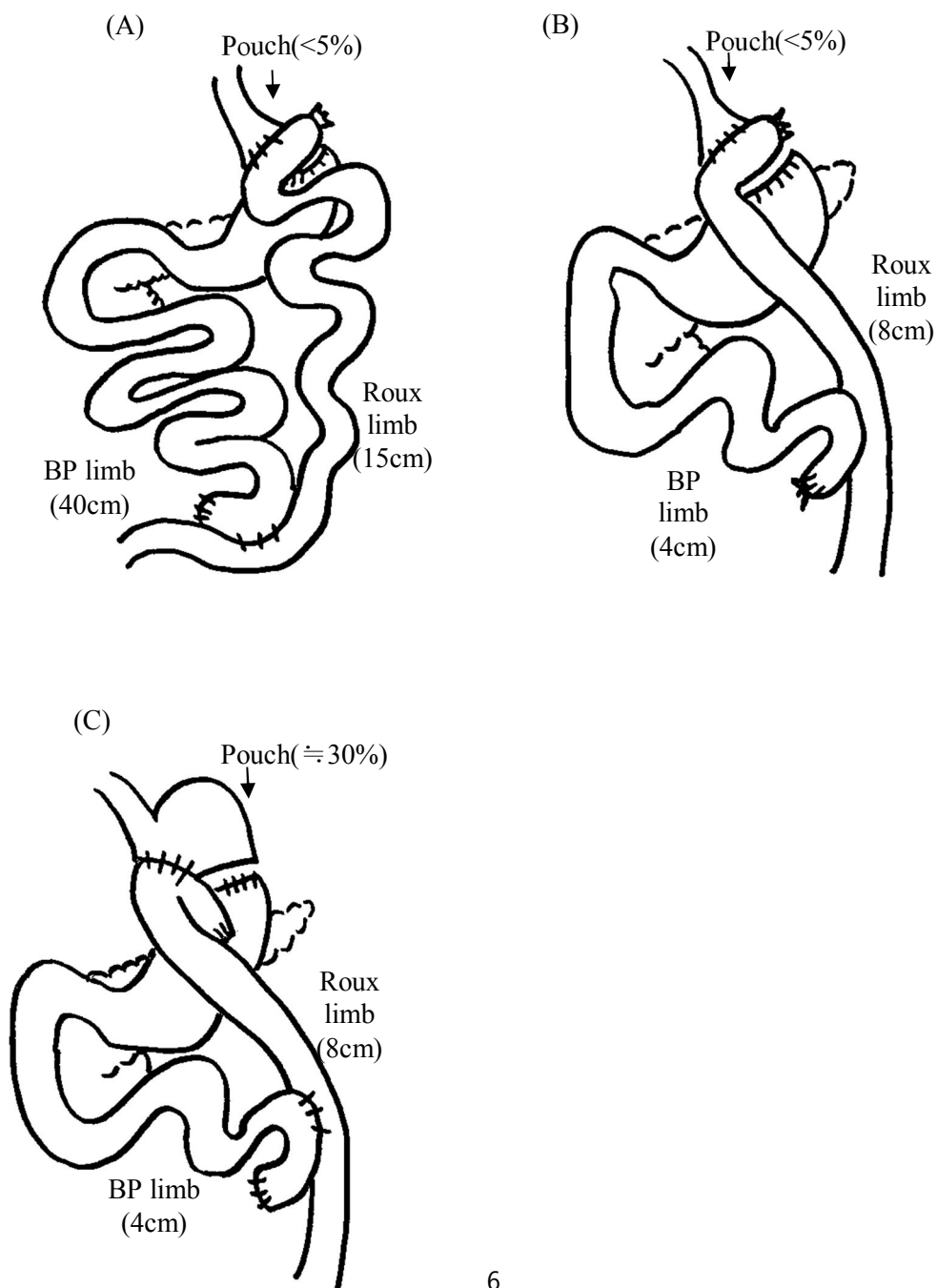
weeks. Oral glucose tolerance was measured at 7th weeks after surgery. Plasma insulin, glucagon-like peptide-1 (GLP-1), glucose-dependent-insulinotropic peptide (GIP), and ghrelin were measured during oral glucose tolerance test (OGTT). After OGTT, the rats were sacrificed.

Interventions: surgical techniques (Fig. 1)

After overnight fasting, operations were performed under general anesthesia with 2% isoflurane. Cefazolin (30 mg/kg) was injected subcutaneously immediately before laparotomy as a prophylactic antibiotic. After midline laparotomy, jejunum was divided at 40 cm from treiz ligament in cRYGB and 4cm from treiz ligament in sRYGB and fRYGB. Both ends were ligated with vicryl 5-0. side-to-side jejuno-jejunostomy was done with 6-0 monocryl interrupted suture at 15cm of roux limb in cRYGB, 8cm in sRYGB and fRYGB. Stomach was divided just below GE junction in cRYGB and sRYGB. In fRYGB, proximal resection of stomach was performed below fundus for saving it. Distal part of divided stomach (about 95% in cRYGB and sRYGB and about 70% in fRYGB) was closed by 5-0 vicryl running suture. End-to-side gastro-jejunostomy was done with 6-0 monocryl interrupted suture. For sham operations, just whole abdomen manual exploration was performed. Fascia and skin were closed two layer using 3-0 vicryl. Normal saline (5cc) was administered subcutaneously after surgery for hydration. Meloxicam (2 mg/kg) was administered intramuscularly for pain control. Water was given

since postoperatively 1st day. On postoperatively 2nd day, high fat diet and water were given ad libitum.

Figure 1. Surgical procedure. (A) Conventional RYGB, (B) Short-limb RYGB, (C) Fundus-sparing RYGB



Measurements

Weight and food intake were measured once a week measured by an electrical scale (A&D, Tokyo, Japan) for the following period after surgery. For random blood glucose, blood was collected from tail vein and the glucose levels were measured by glucometer (OneTouch Ultra; LifeScan, Milpitas, CA, USA).

For IPGTT, after 24 hours of fasting, a dose of 0.5 UI/kg zoletil (Actrapid®, Novo Nordisk, Boulogne-Billancourt, France) was injected intramuscularly after general anesthesia with 2% isoflurane. Blood glucose was measured baseline, 30, 60, and 120 minutes after the administration of 20% of dextrose solution (1 g/kg) by intraperitoneal injection. Blood was obtained as described before and analyzed using a glucometer.

For OGTT, after 24 hours of fasting, a dose of 0.5 UI/kg zoletil (Actrapid®, Novo Nordisk, Boulogne-Billancourt, France) was injected intramuscularly after general anesthesia with 2% isoflurane. Blood glucose was measured baseline, 30, 60, and 120 minutes after the administration of 20% of dextrose solution (1 g/kg) by oral gavage. Blood was obtained as described before and analyzed using a glucometer. Sampling was done as for other tests at baseline, 30, 60, 90, and 120 minutes. For plasma hormones measurements, blood from the tail of rats was collected in EDTA tubes containing aprotinin (500 kallikrein inhibitory units/ml of blood). After centrifugation at 1500 g at 4°C for 20 minutes, plasma was immediately separated and stored at -80°C until

analyzed. Rat radioimmunoassay kits were used for measurement of insulin, total glucose-dependent insulintrophic peptide (GIP) (Milliplex Map rat metabolic magnetic bead panel kit (No. RMHMG-84K, Millipore, USA)), total glucagon-like peptide-1 (GLP-1) (No. EZGLP1T-36K, Millipore, USA) and ghrelin (No. EZRGRT-91K, Millipore, USA).

Statistical Analysis

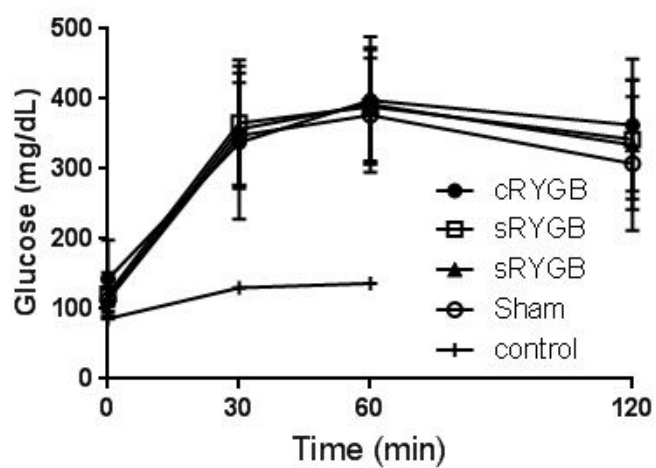
Data are expressed as mean \pm standard error of the mean (SEM). Serial data of body weights, food intake, glucose, and hormone levels were analyzed by two-way repeated measures ANOVA with Bonferroni *post hoc* test and the Mann-whitney U test as appropriate. Areas under curve (AUC) were calculated by trapezoidal integration. AUCs of glucose and hormone levels were analyzed by Mann-Whitney U test. Statistical analysis was performed using Prism 5.0 (GraphPad, San Diego, CA, USA) and SPSS version 21.0 software (SPSS, Chicago, IL, USA). P values 0.05 were considered to be statistically significant.

RESULTS

Before treatments, there were no significant differences between groups in terms of weight, average diet and random glucose (Table 1). The mortality rate was 13.9% (5/36). According to results from IPGTT, we confirmed that glucose intolerance was induced and we divided as 4 groups. There were no differences in glucose level among 4 groups retrospectively (Fig. 2).

Table 1. Preoperative Data					
	cRYGB (n=9)	sRYGB (n=9)	fRYGB (n=9)	Sham (n=9)	p-value
Initial body weight (g)	159.7±8.6	159.1±3.8	160.9±5.9	158.8±6.7	0.907
Body weight after high fat diet for 3 months (g)	624.0±62.0	619.8±58.2	643.4±82.8	619.3±55.5	0.949
Average diet (g/week)	131.4±12.0	134.6±13.6	134.3±16.2	134.4±10.0	0.845
Random glucose (mg/dL)	122.6±13.3	114.2±11.0	112.8±9.9	114.6±13.6	0.324

Figure 2. The result of intraperitoneal glucose tolerance test



+ control : normal chow diet for 3 months

Random glucose

cRYGB reduced random plasma glucose levels. Mean plasma glucose 7th weeks postoperatively was 92.3 ± 20.6 mg/dL, whereas mean preoperative values were 122.7 ± 13.3 mg/dL ($P=0.020$). The other groups did not significantly change blood glucose levels. And level of glucose remained consistently lowest in the cRYGB group through the entire follow-up period (Fig. 3 (A)).

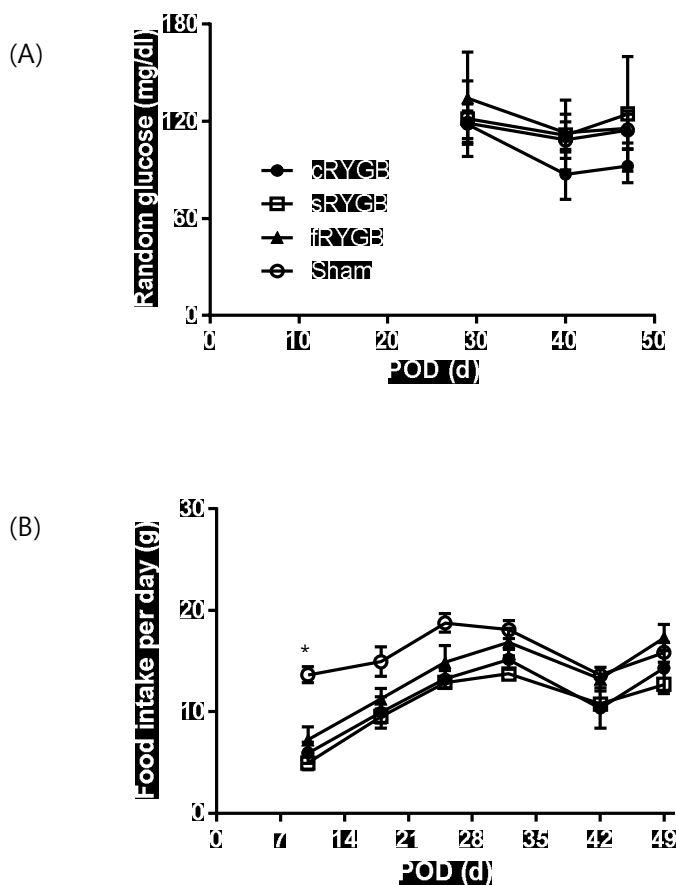
Weight loss and Food Intake

In cRYGB and sRYGB, body weight was gradually decreased. However, sham and fRYGB showed the increasing tendency of body weight similarly. After 2 weeks postoperatively, there was significant difference in body weight between cRYGB and fRYGB groups ($P=0.038$). In cRYGB and sRYGB, however, the gap of body weight was getting bigger after 4 weeks postoperatively, so that cRYGB showed the lowest body weight on postoperative 7th week without significance ($p=0.066$) (Fig. 3 (B)).

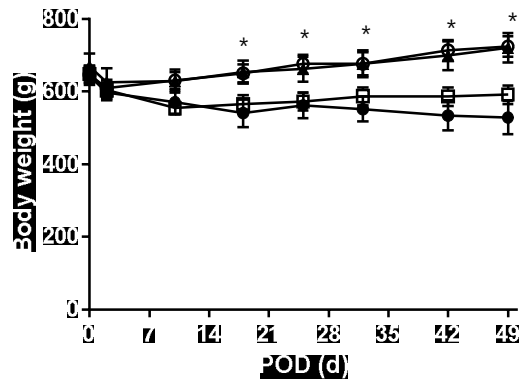
3 RY groups showed less amount of food intake than sham group at immediate postoperative period ($p<0.001$), and amount of food intake was gradually increased according to the time. Despite the fact that cRYGB group showed lower plasma glucose than other groups, there were no significant differences in average daily food intake between cRYGB and other groups

($p=0.224$ in cRYGB vs. sRYGB; $p=0.445$ in cRYGB vs. fRYGB; $p=0.689$ in cRYGB vs. sham). Meanwhile, sRYGB group showed significantly less amount of food intake per day than fRYGB ($p=0.001$) (Fig. 3 (C)).

Figure 3. Random glucose levels (A), 24 hour food intake (B), and body weights (C). Data are shown as the mean \pm standard error of the mean (SEM). Filled circle, cRYGB ;white square, sRYGB ; filled triangle, fRYGB ; white circles, sham group. * $P < 0.05$ when cRYGB group was compared to the sham group using a two-way repeated measures ANOVA with a Bonferroni post hoc test.



(C)



OGTT

In OGTT, glucose levels were steeply increased until 30 minute in cRYGB and sRYGB. However, fRYGB showed gradually increase pattern (Fig. 4(A)). Meanwhile, AUC of glucose until 30 minute was similar between cRYGB and sRYGB groups (not shown).

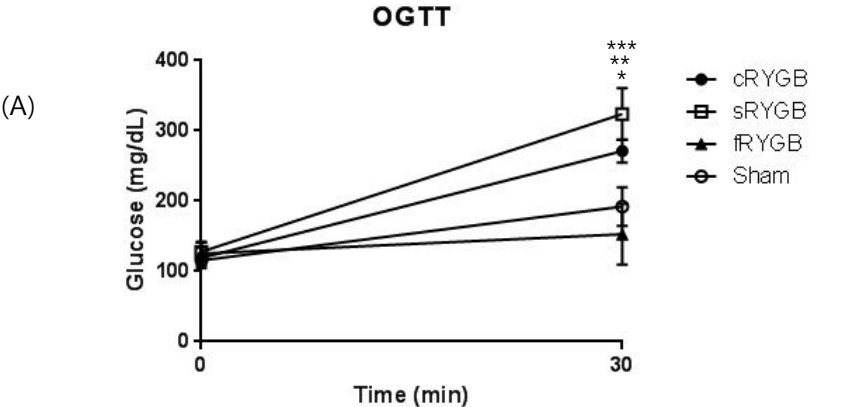
Hormones Measurements

During OGTT, insulin level was steeply increased until 30 minute, however, there was no significant difference. cRYGB, sRYGB and sham groups showed increase pattern similarly, but in fRYGB groups, insulin level did not increase (Fig. 4 (B)).

In GLP-1, cRYGB showed steeply increase pattern until 30 minute. There were no big changes in sRYGB, fRYGB and sham groups (Fig. 5 (A)). Especially, AUC of GLP-1 until 30 minute was different between cRYGB and sRYGB groups, and cRYGB were significantly higher than sRYGB group ($p=0.002$) (Fig. 5 (B)). Moreover, % increase until 30 minutes was significantly higher in cRYGB than sRYGB ($p=0.036$) (Fig. 5 (C)).

In GIP, there was significant difference at baseline (Fig. 6 (A)). cRYGB group always showed the highest level among all groups from baseline to 30 minutes. Therefore, AUC of GIP until 30 minutes showed highest tendency in the cRYGB without significance (Fig. 6 (B)).

Figure 4. Plasma levels of glucose (A) and insulin (B) during OGTT. Filled circle, cRYGB ; white square, sRYGB ; filled triangle, fRYGB ; white circles, sham group. *, **, *** $P < 0.05$ using Mann-Whitney U test.



*, cRYGB vs. sham ; **, sRYGB vs. fRYGB; ***, sRYGB vs. sham

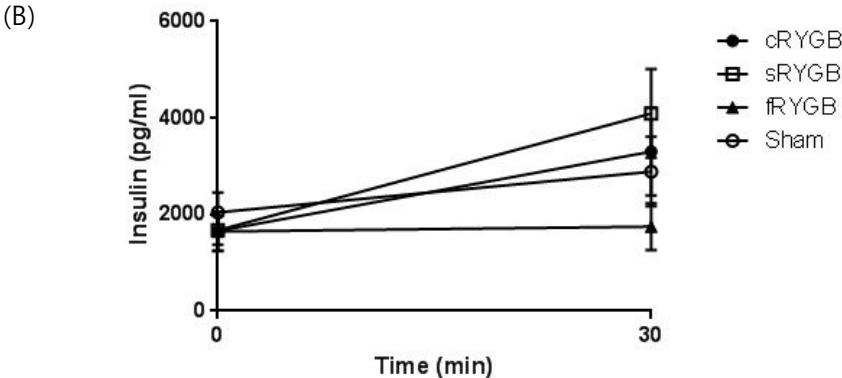
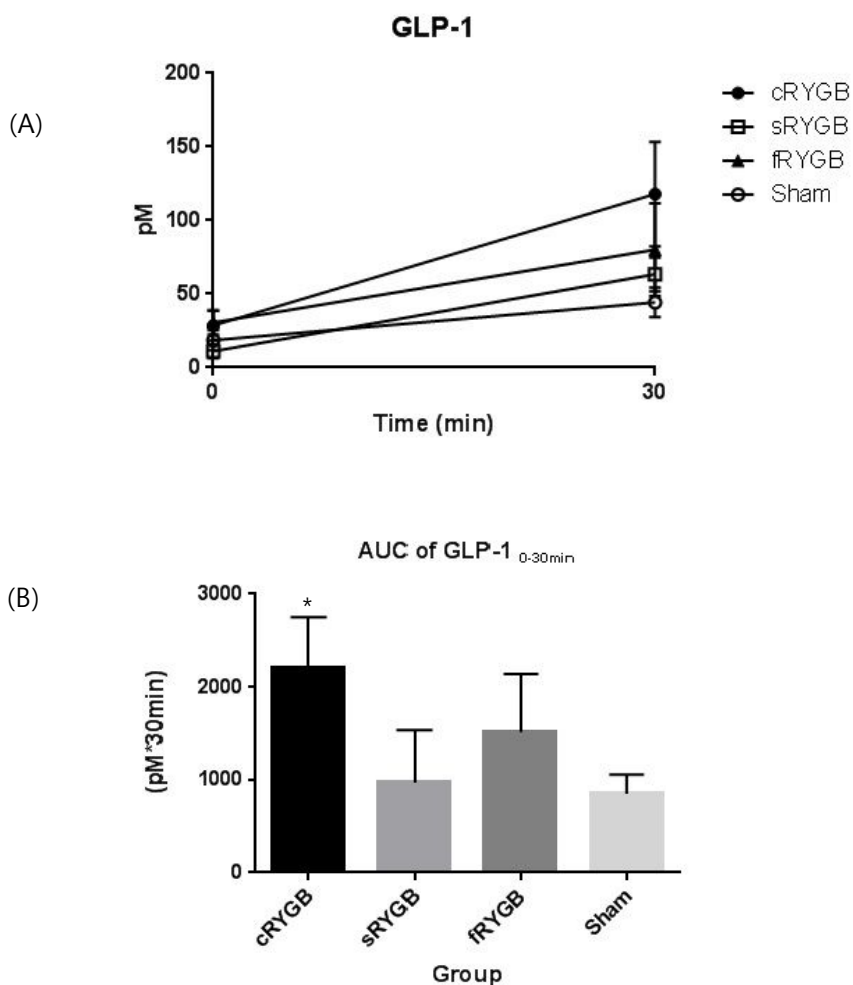
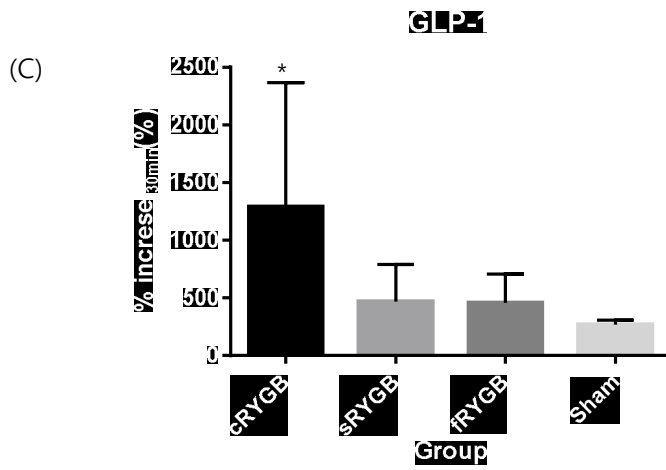


Figure 5. Plasma levels of total GLP-1 (A), 30min AUC of GLP-1 (B), and 30min % increase of GLP-1 (C) during OGTT. Data are shown as the mean \pm SEM. Filled circle, cRYGB ;white square, sRYGB ; filled triangle, fRYGB ; white circles, sham group. *, $P < 0.05$ using Mann-Whitney U test.

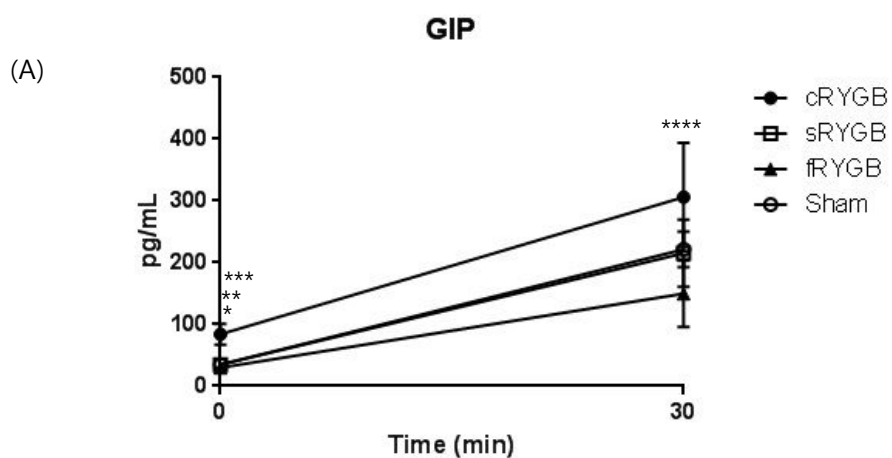


* cRYGB vs. sRYGB



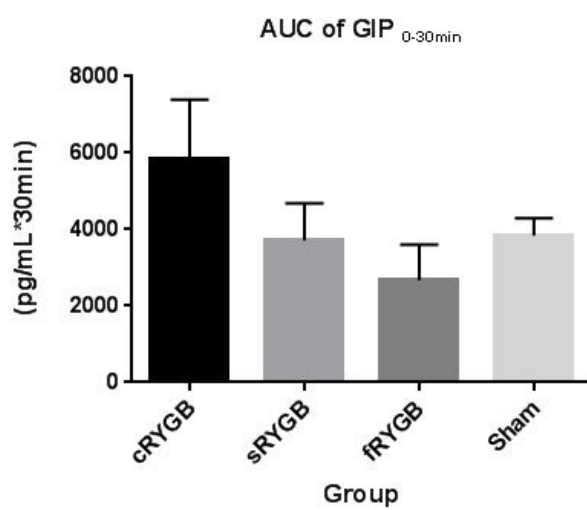
* cRYGB vs. sRYGB

Figure 6. Plasma levels of total GIP (A) and 30 min AUC of GIP (B) during OGTT. Data are shown as the mean \pm SEM. Filled circle, cRYGB ;white square, sRYGB ; filled triangle, fRYGB ; white circles, sham group. *, **, ***, **** $P < 0.05$ when compared to the sham group using a two-way repeated measures ANOVA with a Bonferroni post hoc test.



*, cRYGB vs. sRYGB ; **, cRYGB vs. fRYGB ; ***, cRYGB vs. sham ;
****, sRYGB vs. sham

(B)



DISCUSSION

Our findings demonstrate that the RYGB improves glucose intolerance and obesity in an animal model of obese diabetes. Our study allows several considerations. The effect on glucose metabolism seems to be induced by not only secondary to weight loss according to food restriction but also other factors. Indeed, in terms of the length of anastomosis, cRYGB showed similar food intake, but body weight loss was bigger and random glucose level was lower compared to sRYGB. In terms of extent of resection, sRYGB showed lower food intake, and body weight loss was bigger and random glucose level was similar compared to fRYGB. Obviously, the lower food ingestion was shown in cRYGB, sRYGB and fRYGB showed relatively higher food ingestion and showed higher random glucose level. It is well known that improvement of glucose metabolism occurred just after bariatric-metabolic surgery before weight loss. The one of those mechanisms was reported that postoperatively low calorie intake cause improvement of hyperglycemia in early phase [11, 12]. Both RYGB and gastric band induce rapid decrease of food intake immediately postoperative period, however, only RYGB showed rapid decrease of blood glucose level [13, 14]. Therefore, improvement of diabetes after RYGB was explained by not only weight loss but also other factors.

The mechanism of the remission of diabetes by the most typical bariatric-metabolic surgery, roux-en Y gastric bypass, is not clear. However, several possible mechanisms are reported; (1) decrease of food intake due to decrease of gastric volume and loss of appetite, (2) foregut hypothesis that this results induced by effects of bypass the 95% of stomach, duodenum, and proximal jejunum, (3) hindgut hypothesis that this results induced by gastrointestinal hormone surge from food reached to distal jejunum quickly [10]. Foregut theory is that abnormal functional change on duodenum and proximal jejunum makes anti-incretin to release, and induced abnormality of glucose metabolism in patients with diabetes, so that if this part is bypassed by surgery, improvement of diabetes can achieve [15]. Hindgut theory is that un-chymed food stimulated distal small bowel, so that increased incretin secretion makes improvement of glucose metabolism [16]. Incretin is a kind of hormone which was 'INtestin seCRETion INSulin' named by La Barre at 1929 [17]. That hormone stimulates the secretion of pancreatic insulin according to the food intake. GIP and GLP-1 are typical incretins in human, and they make proliferation of pancreatic B cell and increase of insulin secretion. In distal small bowel, there are L-cells which secretes GLP-1, peptide YY (PYY) which suppresses the appetite and OXM oxyntomodulin (OXM) which delays the gastric emptying time and lower secretion of gastric juice, and so on. Hindgut theory is that undigested food stimulates L-cells in distal small bowel, so that increase of incretin induces improvement of glucose metabolism.

However, the mechanism after bariatric-metabolic surgery cannot be explained only single theory, and foregut and hindgut theories are not opposing but complementary theory accounts improvement of glucose.

For the bariatric/metabolic bypass surgery, the long limb bypass is chosen and in that case, the range of BP limb is 30-70 cm and the range of roux limb is 75-150 cm. From our pilot study, the whole length of small intestine in rats was around 1m. We decided the length of intestinal limbs according to reported articles of long-limb bypass surgery for rats [18-20] and similar ratio with bariatric/metabolic surgery for human. In typical gastric cancer surgery, BP limb makes as short as possible for preventing for A-loop syndrome and roux limb also makes as short as possible for increase of absorption of nourishment. In contrast, BP limb and roux limb were made long enough for maximizing the metabolic effect in standard bariatric-metabolic surgery. In this study, sRYGB which is mimicking for total gastrectomy (TG) showed weight loss, but improvement of glucose was not shown. fRYGB which is mimicking for subtotal gastrectomy (STG) for gastric cancer did not show neither weight loss nor improvement of glucose. Only cRYGB group showed satisfactory weight loss and improvement of glucose. According to the previous reports, the rate of remission after gastric cancer surgery including TG and STG is very low [21, 22]. There were attempts to adapt long limb RYGB to overcome the limitations. Orci L et al. reported that longer Roux-limb might only be efficient in super obese patients [23]. Meanwhile, there could be anatomical

problems including roux stasis and nutritional problems including vitamin and trace element deficiencies [24]. However, Kim et al. reported that there was no roux stasis syndrome, anemia and hypoalbuminemia after gastrectomy for gastric cancer with long limb Roux-en Y reconstruction in the pilot study [25]. According to these previous studies and our results, gastric cancer surgery with long-limb RYGB is feasible and seems to be effective for improvement of diabetes.

About that mechanism, we analyzed the hormone during OGTT. According to the hormone analysis, baseline GIP was significantly higher at baseline and continuously maintained in most high level in cRYGB group. In terms of GLP-1, its % increase till 30 minutes was significantly highest in cRYGB. GIP enhances glucose-dependent insulin secretion from pancreatic b-cells and increases glucagon secretion from pancreatic a-cells [26, 27]. GIP does not inhibit gastric emptying and has no effect on appetite/satiety. In patients with type 2 diabetes, GIP loses its insulinotropic activity, while it preserves its glucagonotropic activity [26, 27]. In contrast, GLP-1 increases glucose-dependent insulin secretion and decreases glucagon secretion in both normal subjects and type 2 diabetes patients [27, 28]. GLP-1 decelerates gastric emptying, decreases appetite and increases satiety [27, 28]. Rapid increase of GLP-1 and continuous secretion of GIP seems to influence on improvement of glucose metabolism.

There are several limitations in this study. Most important thing is the vague OGTT result. The sampling was very difficult process when we performed the OGTT. In rats, sampling from tail was firstly chosen, then sampling from cutting and squeezing the tail was performed. Finally, the sampling was performed via heart puncture in 120 minutes. These processes were inevitable because whole amount of blood in rats are very limited. Thus, these very stressful situation and sampling underwent other site are seemed to cause unstable OGTT results. Thus, we showed the only immediate response till 30 minutes. And there are no models of long-limb fundus sparing procedure and the control group for normal chow diet. If there were these models, we could make the clear study design and reasonable evidences. Lastly, we explained the fRYGB group showed delayed gastric emptying. However, we did not present the actual evidence including pathologic changes. In the future, standardized sampling protocol, more detailed study design, and histological reviews are needed.

CONCLUSION

We could identify that long-limb roux-en Y bypass with 95% gastric resection was needed to achieve not only the loss of body weight, but also improvement of diabetes through this experiment. This could be related with rapid increase of GLP-1. This result could be adapted in gastric cancer patients with obese diabetes.

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국문초록

목적 본 연구의 목적은 동물모델에서 위절제 범위 및 장문합 길이에 따른 당뇨 조절 효과 및 기전을 알아봄으로써 궁극적으로 당뇨를 동반한 위암 환자에서의 변형 위절제술의 가능성을 평가해 보고자 함이다.

방법. Sprague-Dawley 쥐에게 3 개월 간 고지방식이를 통해 비만형 포도당 불내성을 유발하였다. 총 네 그룹으로 나누어 1) 95%의 위절제 및 roux-limb(15cm), 담체 limb(40cm)에 문합을 시행한 원거리 루와이 위공장문합술(long-limb RYGB, conventional RYGB, cRYGB) (n = 9), 2) 95%의 위절제 및 roux-limb(8cm), 담체 limb(4cm)에 문합을 시행한 단거리 루와이 위공장문합술(short-limb RYGB, sRYGB) (n=9), 3) 70%의 위절제 및 roux-limb(8cm), 담체 limb(4cm)에 문합을 시행한 기저부 보존 단거리 위공장문합술(fundus-sparing RYGB, fRYGB) (n=9) 또는 4) 가짜 수술 (sham operation) (n = 9)을 시행하였다. 수술 후 6 주 뒤, 경구 당부하 검사를 시행하였고, 비만형 당뇨에 영향을 주는 장관 호르몬인 인슐린, 글루카곤-유사 펩티드-1 (GLP-1), 포도당-의존성 인슐린 펩티드 (GIP)와 그렐린을 분석하였다.

결과. sRYGB 군에서는 cRYGB 군과 비교하였을 때 섭취량은 차이가 없었으나 고혈당의 호전은 보이지 않았다. cRYGB 군은 통계학적으로 유의하게 섭취량 감소, 체중감소, 혈당 감소를 보였다 ($p<0.05$). 경구 당부하 검사를 하는 동안 cRYGB 와 sRYGB 군에서, 통계적으로 유의하게 혈당이 30 분까지 급격하게 증가하였고, 인슐린은 30 분까지 급격하게 증가하였으나 통계적 유의성은 없었다. 총 GLP-1 은 cRYGB 군에서 30 분에서 다른 군에 비해 높은 경향을 보였다. fRYGB 군은 가짜 수술군과 유사한 체중 변화와 혈당 변화를 보였고, 경구 당부하 검사와 GLP-1 은 서서히 지속적으로 증가하는 모습을 보였으며, 인슐린과 GIP 는 음식물의 위 배출 지연에 기인한 것으로 추정되는 낮은 최고점을 보였다.

결론. 본 연구에서 체중 감소 뿐만 아니라 당뇨의 호전을 이루기 위해서는 95%의 위 절제를 동반한 원거리 루와이 위공장문합술을 시행해야 함을 알 수 있었다. 이는 글루카곤 유사 펩티드-1 의 급격한 증가와 관련되었을 것으로 추정된다.

주요어 : 루와이 위 우회술, 쥐, Sprague-Dawley, 글루카곤 유사

펩티드-1, 포도당-의존성 인슐린 펩티드, 그렐린

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