Randomized controlled trial of uncut Roux-en-Y vs Billroth II reconstruction after distal gastrectomy for gastric cancer: Which technique is better for avoiding biliary reflux and gastritis?

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AIM
To identify which technique is better for avoiding biliary reflux and gastritis between uncut Roux-en-Y and Billroth II reconstruction.

METHODS
A total of 158 patients who underwent laparoscopy-assisted distal gastrectomy for gastric cancer at the First Hospital of Jilin University (Changchun, China) between February 2015 and February 2016 were randomized into two groups: uncut Roux-en-Y (group U) and Billroth II reconstruction.
II group (group B). Postoperative complications and relevant clinical data were compared between the two groups.

RESULTS
According to the randomization table, each group included 79 patients. There was no significant difference in postoperative complications between groups U and B (7.6% vs 10.1%, P = 0.576). During the postoperative period, group U stomach pH values were lower than 7 and group B pH values were higher than 7. After 1 year of follow-up, group B presented a higher incidence of biliary reflux and alkaline gastritis. However, histopathology did not show a significant difference in gastritis diagnosis (P = 0.278), and the amount of residual food and gain of weight between the groups were also not significantly different. At 3 mo there was no evidence of partial recanalization of uncut staple line, but at 1 year the incidence was 13%.

CONCLUSION
Compared with Billroth II reconstruction, uncut Roux-en-Y reconstruction is secure and feasible, and can effectively reduce the incidence of alkaline reflux, residual gastritis, and heartburn. Despite the incidence of recanalization, uncut Roux-en-Y should be widely applied.

Key words: Gastric cancer; Uncut Roux-en-Y; Billroth II; Bile reflux; Alkaline gastritis

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Core tip: Because of the challenge of recanalization, the uncut Roux-en-Y reconstruction is still controversial and needs further study. This study is the first randomized controlled trial concentrating on uncut Roux-en-Y vs Billroth II reconstruction after distal gastrectomy for gastric cancer. This study aimed to compare uncut Roux-en-Y and Billroth II reconstruction in terms of postoperative complications, including biliary reflux and gastritis. Despite the incidence of recanalization, uncut Roux-en-Y reconstruction is secure and feasible, and can effectively reduce the incidence of alkaline reflux, residual gastritis, and heartburn.

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MATERIALS AND METHODS
This is a randomized controlled trial which was evaluated and approved by the ethics committee at our institution, and registered in clinicaltrials.gov with the number NCT02694081. Between February 2015 and February 2016, a total of 158 patients with gastric cancer treated at the First Hospital of Jilin University (Changchun, China), who met the inclusion criteria and provided informed consent, were randomized into one of two groups: uncut Roux-en-Y group (group U) or Billroth II group (group B). Randomization was done after laparoscopic exploration with the randomization table, which was produced using SPSS v18.0 for Windows software by the Division of Clinical Research at our hospital. Patients as well as investigators (assessing outcomes and analyzing data) were masked. The inclusion criteria were: (1) distal gastric cancer diagnosed by endoscopy, CT scan, and pathology study; (2) patients who underwent LADG; and (3) age between 18 and 75 years. The exclusion criteria were: (1) late-stage gastric carcinoma or pyloric obstruction; (2) preoperative esophageal reflux symptoms, esophagitis, or hiatal hernia; and (3) systemic disease including diabetes, severe chronic lung disease, cirrhosis, or esophageal varices.

All included patients underwent LADG with D2 lymphadenectomy, which was performed by the same surgical team. For reconstruction, a 5-cm mini-laparotomy was made to complete a delta-shaped Billroth II anastomosis using a 80 mm linear stapler[27]. In the uncut Roux-en-Y group, gastrojejunostomy was performed at 25 cm distal to the Treitz ligament, and jejunum-jejunum anastomosis at 40 cm from the afferent limb. The blade of the linear stapler (Covidien GIA8038S, Medtronic, Minneapolis, MN, the United States of America) was removed to perform the uncut procedure of the afferent jejunal limb, 5 cm proximal to the gastrojejunostomy in the jejunum (Figure 1A and B).

During the postoperative period, omeprazole 40 mg was given to all patients twice a day. Ambulation was encouraged from the first day after operation, and the nasogastric tube was kept in place for 5 d. All patients

INTRODUCTION
There remains no clear consensus regarding the preferred reconstructive surgical procedure after laparoscopy-assisted distal gastrectomy (LADG) for gastric cancer[1,2]. Compared with Japan[3] and Korea[4], early gastric cancer only accounts for a small percentage in China, and most gastric cancer cases are found in advanced stages at the initial diagnosis. It is inappropriate for surgeons to perform Billroth I anastomosis after subtotal gastrectomy. In 2005, Uyama first combined LADG with uncut Roux-en-Y reconstruction; however, its use remains controversial[5,6]. In our department, we usually prefer Billroth II and uncut Roux-en-Y reconstruction.

The current study aimed to compare these two reconstruction techniques in terms of postoperative complications, including biliary reflux and gastritis.

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a small amount of lymphocytes and transparent microscopic field (Figure 3A); grade 1, intermediate between grades 0 and 2 (Figure 3B); and grade 2, acute inflammation with fully infiltrated tissue by lymphocytes or inflammatory cells (Figure 3C).

**Statistical analysis**
All statistical analyses were performed using SPSS v18.0 for Windows software. Continuous variables are expressed as mean and SD and compared by Student’s t-test. Categorical variables were analyzed by Pearson χ² test. The pH variables were compared by repeated measures analysis of variance. A two-tailed P value < 0.05 was considered statistically significant.

**RESULTS**
According to the randomization table, each group included 79 patients. Baseline data are shown in Table 1. There were no significant difference in gender or pathological data (P > 0.05), but the average age of group U patients was older than group B patients (58.0 ± 11.4 vs 61.8 ± 11.4 years, P = 0.030). The surgical time was slightly longer in group U (154.8 ± 17.8 vs 145.5 ± 15.1 mins, P = 0.001), but there was no difference in blood loss (74.1 ± 26.7 vs 74.0 ± 36.6 mL, P > 0.05).

There was no significant difference in postoperative complications between the two groups (7.6% vs 10.1%, P = 0.576). One patient in each group underwent reoperation because of intra-abdominal bleeding. In group U, a patient with ileus required reoperation after 1 mo of conservative treatment. In group B, a patient received emergency endoscopy to insert a stomach tube into the afferent loop to release pressure due to A-loop syndrome. For both groups, no gastroparesis syndrome was found during the postoperative period (Table 2).

According to the Clavien-Dindo classification for surgical complications[9], in group U grade I complications were recorded in 3.8%, grade II in 1.3%, and grade IIIb in 2.5% of the cases. In group B grade I complications were recorded in 3.8%, grade II in 2.5%, grade IIIa in 1.3%, and grade IIIb in 2.5% of the cases. There was still no significant difference between the two groups (P = 0.954).

The stomach pH was lower in group U patients, with a significant statistical difference (P < 0.05) (Table 3). During the postoperative period, all stomach pH values in group U patients were below 7.00. Conversely, all stomach pH values in group B patients were higher than 7.00 (Figure 4).

Three months later, regarding the postoperative esophagogastro-duodenal series after 30 min, a higher ratio of full emptying was seen in group B patients (88.2% vs 76.6%, P = 0.061), but with no statistical significance.

At the end of the 1-year follow-up period, three patients in group U and one patient in group B were...
U (55.1%). However, the result of biopsy showed no significant difference (63.8% vs 70.8%, \( P = 0.278 \)), but the linear-by-linear association was significant (\( P_{\text{trend}} = 0.015 \)). Besides, there was no significant difference for the incidence of diarrhea, residual food, or gain of weight between the two groups (Table 4).

**DISCUSSION**

In 1988, uncut Roux-en-Y reconstruction was first...
Our study showed there was no significant difference in the percentage of residual gastritis reported by Stiegman and Goff. Some studies over the years have confirmed that this reconstruction can preserve myoneural continuity to eliminate Roux stasis syndrome. Because uncut Roux-en-Y is a modification of Billroth II reconstruction, it makes sense to compare Billroth II and uncut Roux-en-Y to determine the better procedure after LADG.

Our study showed there was no significant difference for the incidence of postoperative complications between the two groups (7.6% vs 10.1%, P > 0.05). Moreover, for the severity of postoperative complications, according to the Clavien-Dindo classification of surgical complications, there was no significant difference (P = 0.954). A-loop syndrome does not occur in the uncut Roux-en-Y group, and the incidence of duodenal stump leakage was lower than that of the Billroth II group. The reason for this may be that the Braun anastomosis effectively relieves the pressure of the afferent loop, but more cases should be included to confirm this difference.

For biliary reflux, during the postoperative period, all group U pH values were lower than 7.00, thus representing an acidic stomach environment. In group B patients, all pH values were higher than 7.00, representing an alkaline stomach environment with alkaline reflux, which can be considered an important risk factor for gastric stump cancer (Figure 2). In addition, according to patient outcomes at the 1-year follow-up, the bile reflux incidence in group B patients was significantly higher than that in group U (P = 0.000). However, the incidence of bile reflux in group U patients was 60.9%, which is higher than the equivalent statistic in Park and Kim’s report (less than 30%) (Figure 2). There are two main reasons that can explain these data. On one hand, the incidence of partial recanalization reached 13.0%. In this study, for partial recanalization, all those cases were first observed by endoscopy, and the result would be confirmed by esophagogastroduodenal series if there was doubt. Recanalization eventually allowed bile access to the gastric remnant. On the other hand, for some other cases, the bile reflux happened through the efferent loop, and a small amount of bile was usually found in the bottom of residual stomach with no overflow (grade 1).

Regarding gastritis, the incidence in group B patients (72.2%) was significantly higher than that in group U patients (55.1%), with a higher incidence of heartburn in group B patients as well (23.6%). These results allow us to conclude that uncut Roux-en-Y can reduce the occurrence of residual gastritis and heartburn proportion in Billroth II reconstruction. However, the biopsy results showed no significant difference between the two groups (P = 0.278).

We draw two conclusions from these results. First, the pattern of bile reflux is different. The majority of group U patients were classified into grade 2 (58.3%), but perhaps it depends not only on the amount but also on the pattern of biliary reflux. Second, the follow-up time was too short to show differences in the percentage of residual gastritis on biopsy, so the linear-by-linear association P value was also calculated. The result showed a significant difference.

![Figure 4: Perioperative potential of hydrogen (pH) in the stomach of the patients.](https://example.com/figure4.png)
difference ($P_{\text{end}} = 0.015$), meaning that the severity of residual gastritis for group B was worse than that for group U on biopsy.

For residual food, there was no significant difference between the two groups (11.6% vs 4.2%, $P > 0.05$). For gastrointestinal anastomosis of both procedures, the stoma was extensive along the greater curvature. No gastrointestinal anastomosis syndrome was found during follow-up, which is perhaps related to myoneural continuity. At 3-mo follow-up, the incidence of full emptying at 30 min reached 76.6% and 88.2% in group U and B patients, respectively (Table 4). As a result, no retention of afferent loop stump was found during the follow-up, and the incidence of residual food was lower than that in other studies\cite{4,10}.

This study adopted body weight change to evaluate postoperative nutritional status of patients, and 1 year later, the weight change values of group U and group B patients were -0.04 ± 3.6 kg and -0.18 ± 3.8 kg, respectively, with no significant difference. Moreover, there was no significant difference in survival rates of group U and group B patients after 1 year (90.79% vs 92.31%, respectively; $P > 0.05$).

In conclusion, the uncoc Roux-en-Y Y digestiv reconstruction procedure is secure and feasible. Moreover, it can effectively reduce the incidence of alkaline reflux, residual gastritis, and heartburn seen in classical Billroth II procedure. Besides, the uncoc technique still needs improvement so that the risk of staple line dehiscence is minimized, with a longer follow-up period to reevaluate the exact risk. Despite the incidence of recanalization\cite{17,21}, uncoc Roux-en-Y should be widely applied.

**COMMENTS**

**Background**

In 1988, uncoc Roux-en-Y reconstruction was first reported by Stiegman and Goff. Some studies over the years have confirmed that this reconstruction can preserve myoneural continuity to eliminate Roux stasis syndrome. However, because of the challenge of recanalization, the uncoc Roux-en-Y is still controversial and really needs further study. Since uncoc Roux-en-Y is a modification of Billroth II reconstruction, it makes sense to compare Billroth II and uncoc Roux-en-Y to determine the better procedure after laparoscopy-assisted distal gastrectomy (LADG).

**Research frontiers**

Compared with Japan and Korea, early gastric cancer only accounts for a small percentage in China, and most gastric cancer cases are found in advanced stages at the initial diagnosis. It is inappropriate for surgeons to perform Billroth I anastomosis after subtotal gastrectomy. In 2005, Uyama first combined LADG with uncoc Roux-en-Y reconstruction, and since then it has been the hotspot for many years. However, its use remains controversial. Some surgeons believe that it is better than Billroth II and uncoc Roux-en-Y reconstructions, while others do not.

**Innovations and breakthroughs**

This study is the first randomized controlled trial concentrating on uncoc Roux-en-Y vs Billroth II reconstruction after distal gastrectomy for gastric cancer. It aimed to compare uncoc Roux-en-Y and Billroth II reconstruction in terms of postoperative complications, including biliary reflux and gastritis. Despite the incidence of recanalization, uncoc Roux-en-Y reconstruction is secure and feasible, and can effectively reduce the incidence of alkaline reflux, residual gastritis, and heartburn.

**Applications**

There remains no clear consensus regarding the preferred reconstructive surgical procedure after LADG for gastric cancer. In this study, uncoc Roux-en-Y reconstruction is secure and feasible, and can effectively reduce the incidence of alkaline reflux, residual gastritis, and heartburn. Therefore, uncoc Roux-en-Y should be widely applied in the future. Besides, the uncoc technique still needs improvement so that the risk of staple line dehiscence is minimized, with a longer follow-up period to reevaluate the exact risk.

**Peer-review**

Interesting comparison of two techniques of postgastrectomy reconstruction.

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