Roux-en-Y or Billroth II Reconstruction After Radical Distal Gastrectomy for Gastric Cancer

A Multicenter Randomized Controlled Trial

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Objective: The aim of the study was to compare the clinical symptoms between Billroth II (B-II) and Roux-en-Y (R-Y) reconstruction after distal subtotal gastrectomy (DG) for gastric cancer.

Background: Surgery is the mainstay of curative treatment for gastric cancer. The technique for reconstruction after DG remains controversial. Both B-II and R-Y are popular methods.

Methods: This is a prospective multicenter randomized controlled trial. From October 2008 to October 2014, 162 patients who underwent DG were randomly allocated to B-II (n = 81) and R-Y (n = 81) groups. The primary endpoint is Gastrointestinal (GI) Symptoms Score 1 year after surgery. We also compared the nutritional status, extent of gastritis on endoscopy, and quality of life after surgery between the 2 procedures at 1 year.

Results: Operative time was significantly shorter for B-II than for R-Y [mean difference 21.5 minutes, 95% confidence interval (95% CI) 3.8-39.3, P = 0.019]. The B-II and R-Y groups had a peri-operative morbidity of 28.4% and 33.8%, respectively (P = 0.500) and a 30-day mortality of 2.5% and 1.2%, respectively (P = 0.500). GI symptoms score did not differ between R-Y versus B-II reconstruction (mean difference -0.45, 95% CI -1.21 to 0.31, P = 0.232). R-Y resulted in a lower median endoscopic grade for gastritis versus B-II (mean difference -1.32, 95% CI -1.67 to -0.98, P < 0.001). We noted no difference in nutritional status (R-Y versus B-II mean difference -0.31, 95% CI -3.27 to 2.65, P = 0.837) and quality of life at 1 year between the 2 groups too.

Conclusion: Although BII is associated with a higher incidence of heartburn symptom and higher median endoscopic grade for gastritis, BII and RY are similar in terms of overall GI symptom score and nutritional status at 1 year after distal gastrectomy.

Keywords: Billroth II, radical distal gastrectomy reconstruction, Roux-en-Y

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astric cancer is the fourth most common malignancy and the third leading cause of cancer death worldwide.¹ Surgery is the mainstay of curative treatment. For most tumors affecting the distal part of the stomach, radical distal gastrectomy (DG) is the recommended operation.² However, the choice of reconstruction after DG remains controversial. Billroth I (B-I), Billroth II (B-II), and Roux-en-Y (R-Y) are all acceptable options.³ B-I gastroduodenostomy is a common reconstruction technique especially in Japan and Korea where the tumors are mostly diagnosed at an early stage. For most parts of the world, because the tumors are more locally advanced, B-II and R-Y gastrojejunostomy are more commonly performed. B-II is a simpler procedure to perform, but it is associated with bile reflux.⁴⁻⁶ R-Y is a more complex procedure with 2 anastomoses and it has its own specific complication such as Roux stasis syndrome.⁷⁻¹⁰ The R-Y technique was adapted to prevent bile reflux and comparative studies have shown that R-Y indeed causes less bile reflux than B-II or B-I reconstruction. However, the clinical significance of bile reflux remains elusive, as most patients may not experience any symptoms at all. Hence, both procedures are popular and the choice is often based on the surgeon's preference.

We conducted this multicenter randomized controlled trial (RCT) to compare B-II and R-Y reconstruction after DG for gastric cancer. Our primary endpoint is the severity of Gastrointestinal (GI) symptoms at 1 year after surgery. We also compared the 2 groups in terms of grades of gastritis on endoscopy, nutritional status, and quality of life (QOL) of the patients.

METHODS

Study Design

This is a multicenter prospective RCT conducted at specialized Upper Gastrointestinal (UGI) Surgery units at 4 tertiary hospitals in Singapore and Hong Kong. This study was approved by the Institutional Review Board of the respective institutions. Informed consent was obtained for all participants. This trial was registered at ClinicalTrials.gov (ID NCT01257711).

Patients

We included patients between ages of 21 and 80 years with histological diagnosis of gastric adenocarcinoma who underwent radical DG with curative intent. These patients were staged according to the American Joint Committee on Cancer (AJCC) 7th edition TNM staging for gastric cancer.¹¹ Pre-operative staging was done radiologically with a chest X-ray and a computerized tomography of the abdomen and pelvis. Routine pre-operative blood tests included

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complete blood count, renal profile, and liver function test. Patients who had previous gastrectomy, stomach, or small bowel surgery precluding construction of either form of anastomosis, radiological evidence of carcinomatosis, or who were admitted for emergency gastrectomy for complications related to the tumor, such as perforation, bleeding, and obstruction, were excluded.

Intervention

Patients were randomly allocated to R-Y or B-II reconstruction after DG for gastric cancer. Randomization was performed at the end of gastric resection to avoid dropout of patients with radiological locally advanced (T3 or T4) lesions for whom a diagnostic laparoscopy had to be performed first to exclude peritoneal metastases. DG and lymph node dissection were performed according to the guidelines published by the Japanese Gastric Cancer Association (JGCA).¹² All operations were performed by UGI surgeons who are specialized in gastric cancer surgery. The techniques of reconstruction were standardized throughout the participating institutions (Fig. 1). For B-II reconstruction, a loop of jejunum 10 to 15 cm distal to the duodenojejunal flexure was brought up to the remnant stomach in an isoperistaltic retrocolic or antecolic fashion. The anastomosis was constructed over either the anterior or posterior wall of stomach in a transverse plane at least 2 cm from the gastric remnant staple



Roux-en-Y method



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FIGURE 1. Reconstructive techniques.

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line. An enterotomy and a gastrostomy were created to allow for entry of linear cutting 60 to 75 mm stapler. The stapler entry point was closed with a hand-sewn suture by polydioxanone (PDS) 3/0 sutures. In cases of retrocolic approach, the mesenteric window was closed with nonabsorbable sutures.

For R-Y reconstruction, the jejunum was divided at 10 to 15 cm from the duodenojejunal flexure using a linear cutting 60 to 75 mm stapler. The distal jejunum was brought up in an iso-peristaltic retrocolic or antecolic fashion, and anastomosed to the posterior or anterior wall of stomach in a transverse plane at least 2 cm from the gastric remnant stapler line. An enterotomy and a gastrostomy were created to allow for the entry of linear cutting 60 to 75 mm stapler. The stapler entry point was closed in a single layer with PDS 3/0 sutures. A side-to-side jejuno-jejunal anastomosis was created 40 cm distal to the gastrojejunostomy using linear cutting 60 or 75 mm stapler. The stapler entry point was closed with PDS 3/0 sutures. The mesenteric windows were closed with nonabsorbable sutures.

Outcomes

Study participants were reviewed at 6 months and 1 year postoperatively. The primary outcome measure of the study was the GI Symptoms Score in patients who underwent R-Y and B-II reconstruction after 1 year. The GI Symptoms Score grades patients' symptoms of epigastric pain, heartburn, biliary vomiting, postprandial bloating, and nausea.¹³ Each of these 5 clinical symptoms was scaled from 0 to 5 points, and the grade of the GI Symptoms Score was based on the total score (from Grade 0 to Grade 4). The calculation of the GI Symptoms Score is illustrated in Annex 1, Supplemental data, http://links.lww.com/SLA/B204.

Secondary outcomes included nutritional status as measured by Nutritional Risk Index (NRI),^{14–17} degree of gastritis based on endoscopic and histological evaluation,¹⁸ and QOL was assessed with the European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire C30 (QLQ-C30).¹⁹ The calculation of NRI is shown in Annex 2, Supplemental datahttp://links.lww.com/SLA/B204. The classification of gastritis of gastric remnant is shown in Annex 3, Supplemental datahttp:// links.lww.com/SLA/B204.

Randomization

Once the patient met the inclusion/exclusion criteria, the patient was registered into the trial and informed consent was obtained. Study participants were randomized using a computer-generated list based on random permuted block with block size of 10, stratified by country. The allocation ratio was 1:1. After DG was performed, the trial coordinator revealed the randomization code to the surgeons who then completed the reconstruction according to the allocation.

Blinding

The nature of this study precluded blinding of either the operator or the patient. However, the research nurses who performed the interviews for patients (for both GI symptoms and QLQ-C30) and the clinicians who performed the follow-up endoscopy were blinded to the allocated group.

Sample Size Calculation

The sample size was calculated on the basis of the assumption that a reduction in GI symptoms score of 5 was clinically significant. With a 2-tailed α of 0.05, a power of 0.9, an allocation ratio of 1:1, 65 subjects on each arm were required (with a conservative SD of 10). In addition, allowing for an attrition rate of 20%, the total number of patients required in each arm is 80.

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REBUILD Trial CONSORT Flowchart



Statistical Methods

All statistical analyses were performed using SPSS 23.0 with statistical significance set at P < 0.05. Basic descriptive statistics for numerical variables were presented as mean \pm standard deviation

and n (%) for categorical variables. Differences in operating time between the 2 groups were analyzed using 2-sample t test when normality and homogeneity assumptions were satisfied. Otherwise, the Mann-Whitney U test was used. The differences in post-GI

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TABLE 1 Patient and Surgical Characteristics

	Billroth II N = 81	Roux-en-Y N = 81	
Age. vears*	62.0 ± 10.9	64.5 ± 10.9	
Sex	0210 ± 1010	0.110 ± 1015	
Male	46 (57%)	45 (56%)	
Female	35 (43%)	36 (44%)	
Ethnicity			
Chinese	70 (86%)	76 (94%)	
Malay	2 (3%)	3 (4%)	
Indian	4 (5%)	1 (1%)	
Others	5 (6%)	1 (1%)	
ASA classification			
Ι	15 (19%)	13 (16%)	
II	37 (46%)	50 (62%)	
III	29 (36%)	18 (22%)	
BMI, kg/m ²	23.3 ± 4.1	24.3 ± 4.2	
Neo-adjuvant chemotherapy	1 (1%)	2 (3%)	
Adjuvant therapy			
Chemotherapy	20 (25%)	23 (28%)	
Chemoradiotherapy	11 (14%)	8 (10%)	
Location of tumor			
Gastric body	33 (41%)	24 (30%)	
Antrum	51 (63%)	58 (72%)	
Pathological stage (AJCC 7th ed.)			
0	2	0	
1	27	25	
2	22	27	
3	26	26	
4	4	3	
Type of lymphadenectomy*			
D1	3 (4%)	1 (1%)	
D1+/D2	78 (96%)	80 (99%)	
Route of reconstruction			
Antecolic	69 (85%)	71 (88%)	
Retrocolic	12 (15%)	10 (12%)	
Location of gastric wall anastomosis			
Anterior	44 (54%)	47 (58%)	
Posterior	37 (46%)	34 (42%)	
Approach			
Laparoscopic	30 (37%)	36 (45%)	
Open	51 (63%)	44 (55%)	
*Values are mean \pm standard deviation.			

symptom scores, NRI, and QOL between the 2 groups were compared using linear regression adjusted for the pre scores. Chi-square or Fisher exact test was used to compare differences in 30-day morbidity and mortality rates. The analysis was performed on the basis of the principle of intention-to-treat.

RESULTS

The trial's CONSORT diagram is shown in Fig. 2. Between October 2008 and October 2014, a total of 164 patients were recruited for the trial. Two out of the 164 patients were noted to have advanced disease during surgery and a total gastrectomy had to be performed. They were excluded from the trial. The 162 remaining patients were allocated equally into each arm. There were 3 (1.9%) early postoperative (within 30 days) deaths, 2 in B-II group and 1 in R-Y group. The 2 patients in B-II passed away due to sudden cardiac arrest. In the R-Y group, 1 patient developed ischemia of the colon that required resection, but the patient subsequently died as a result of intra-abdominal sepsis. One hundred forty-one patients (87%) completed their 12 months follow-up study and were analyzed.

	Billroth II	Roux-en-Y	Р
Median time to resume soft diet, days*	5 (4-6)	5 (4-6)	0.331
Median total hospital stay, days*	9 (7–12)	8 (7–11)	0.259
Anastomotic leak	1 (1%)	2 (3%)	0.620
Delayed gastric emptying	11 (15%)	11 (14%)	0.537
Need for reoperation	3 (4%)	5 (6%)	0.360
Clavien classification			0.526
No morbidity	56 (69%)	51 (65%)	
Ι	11 (14%)	11 (14%)	
II	8 (10%)	6 (8%)	
III	4 (5%)	8 (10%)	
IV	0 (0%)	2 (3%)	
V	2 (3%)	1 (1%)	
30-day operative mortality	2 (2.5%)	1 (1.2%)	0.500

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Patient demographics and surgical details are summarized in Table 1. The characteristics of the 2 groups are similar. Operative time was significantly shorter for B-II (247.3 ± 56.7 minutes) than R-Y (269.5 ± 58.7 minutes, P = 0.015), with a mean difference of 21.5 minutes [95% confidence interval (95% CI) 3.8-39.3, P = 0.019]. The early postoperative outcomes were comparable between the 2 groups (Table 2). The overall postoperative morbidity (Clavien I and above complications) of B-II and R-Y were 28.4% and 33.8%, respectively (P = 0.500).

For GI Symptoms score, 57% and 62% of B-II and R-Y patients did not experience any symptoms. For the B-II group, 31% of patients had grade 1, 10% had grade 2, and 1.5% had grade 3 symptoms. For R-Y, 36% had grade 1, 3% had grade 2 and none had grade 3 symptoms (Fig. 3). None of the participants had grade 4 symptoms. In terms of overall GI Symptoms Score, there was no statistically significant difference between B-II



FIGURE 3. GI symptoms scores between the 2 groups.

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 (1.40 ± 2.50) and R-Y reconstruction $(0.97 \pm 1.70, P = 0.230)$, with a mean difference of -0.45 (95% CI -1.21 to 0.31, P = 0.232). Subgroup analysis of the individual symptom scores

found no difference between the 2 methods except for heartburn, which is more commonly reported by patients of B-II reconstruction (Fig. 4).

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TABLE 3. Endoscopic Assessment of Gastritis at Gastric Remnant

	Grade	Billroth II	Roux-en-Y
Endoscopic classification of inflammation	0	33	51
of the fermant stomach	1	20	12
	2	6	2
	3	5	2
	4	0	0
	5	0	1
	Not done	17	13

In terms of nutritional status, there was also no difference between the 2 methods (NRI of B-II 100.9 ± 7.6 vs R-Y 100.6 ± 8.3 , P = 0.84), with a mean difference of -0.31 (95% CI -3.27 to 2.65, P = 0.837) when comparing R-Y to B-II. The mean NRI for both groups fall into the well-nourished category.

For the degree of gastritis, patients with R-Y were found to have a lower median endoscopic grade for gastritis, with a mean difference of -1.32 (95% CI -1.67 to -0.98, P < 0.001). The incidence of the different grades of gastritis in each reconstruction arm noted on endoscopy is presented in Table 3. No significant differences were noted in the QOL after 1 year between the 2 groups when comparing domains measured with the EORTC QLQ-30, although there were some significant differences in within-group comparisons pre- and postoperation (Table 4, Supplemental data, http://links.lww.com/ SLA/B204). Both groups had an increase in Global Health scores, though only the R-Y group showed a significant within-group result (R-Y: 20%, P = 0.001; B-II: 6.7%, P = 0.490).

DISCUSSION

The results in this multicenter clinical trial show that there was no difference in terms of patient symptoms between R-Y and B-II reconstruction after distal gastrectomy 1 year after surgery. In addition, nutritional status and QOL were also similar between the 2 procedures, even though we found that gastritis was more prevalent on endoscopy among patients with B-II reconstruction.

Reconstruction method after a distal or subtotal gastrectomy is controversial. B-I, B-II, and R-Y techniques are all commonly performed in different parts of the world. B-I gastroduodenostomy is commonly done in Japan and Korea because most tumors diagnosed in these countries are early-stage. The anastomosis can be done with minimal tension. B-I is also more physiological, as it maintains a normal passage of food into the duodenum and it allows easy access to the bile duct.²⁰ For the rest of the world, where majority of gastric cancers diagnosed are more locally advanced and bulky, B-II and R-Y techniques are more commonly performed. B-II is a simple technique, but it is associated with bile reflux.⁴⁻⁶ Reflux gastritis is common and it may increase the risk of carcinogenesis at the gastric remnant.⁵ Addition of a Braun anastomosis has been described to reduce bile reflux, but its role remains uncertain.² R-Y technique, on the contrary, significantly reduces the risk of bile reflux.⁴⁻⁶ However, it is more complicated to perform with more anastomoses. It also increases the difficulty to assess the bile duct during endoscopic retrograde cholangiopancreaticogram (ERCP). In addition, some patients may develop delayed gastric emptying known as Roux stasis syndrome with functional obstruction of the Roux limb.^{7–10}

Our results show that even though B-II is associated with more reflux gastritis than R-Y, there are no differences clinically. These findings are similar to other studies in the literature.^{6,21,22} Lee et al²² compared B-I, B-II with Braun anastomosis and R-Y in patients after laparoscopic or open gastrectomy for cancer. Although there was significantly less reflux on endoscopy and isotope scan after R-Y, there was no difference in terms of patient symptoms and nutritional status among the 3 procedures.²² In a recent study from Japan comparing B-I and R-Y for gastric cancer, there was also no difference in terms of body weight and nutritional state even though there was more reflux gastritis in the B-I group.²³ Others also suggested that it is difficult to correlate endoscopic findings and symptoms in bile reflux after gastrectomy.^{24,25}

In our study, 14% of our patients developed delayed gastric emptying after R-Y, which was similar to B-II. It is characterized by nausea, vomiting, and abdominal pain after oral intake of food. Delayed gastric emptying after R-Y, or Roux stasis syndrome has been known to be prevalent in over 30% of patients in some studies.^{7–10} Gustavsson et al²⁶ suggested that a limb length of longer than 40 cm was associated with a higher risk of Roux stasis. In our study, the limb length was standardized at 40 cm. Hence, our incidence is low and is similar to other more recent studies.⁷

There are limitations in our study. One hundred forty-one patients (87%) completed follow-up at 1 year, translating to a lost-tofollow-up rate of 13%. Although this is within the attrition rate allowed for in our initial sample size calculation, these patients may introduce an inherent bias to our analysis. Eighteen percent of patients did not undergo follow-up endoscopy that may affect the true prevalence of gastritis in the gastric remnant. Finally, although there was no difference in terms of GI symptoms, nutrition, and QOL between the 2 procedures in 1 year, there may be advantages of R-Y over B-II in the long term. In a randomized study by Csendes et al²⁷ to compare B-II and R-Y in patients with duodenal ulcers with a mean follow-up of 15 years, patients with B-II experienced more GI symptoms and more reflux gastritis and Barrett esophagus on endoscopy. Histologically, atrophic gastritis and intestinal metaplasia were also more common after B-II. However, as the study populations were different from our study, whether the conclusion is the same for patients with gastric cancer is unknown. A long-term study is required to study these differences.

In conclusion, our randomized study showed that there was no difference in patient GI symptoms between B-II and R-Y reconstruction at 1 year even though reflux gastritis and heartburn symptom were more common after B-II. Nutrition status and QOL were also similar between the 2 techniques. B-II remains an acceptable method of reconstruction after distal gastrectomy for patients with gastric cancer.

REFERENCES

- 1. Ferro A, Peleteiro B, Malvezzi M, et al. Worldwide trends in gastric cancer mortality (1980-2011), with predictions to 2015, and incidence by subtype. *Eur J Cancer*. 2014;50:1330–1344.
- Kim JP. Current status of surgical treatment of gastric cancer. J Surg Oncol. 2002;79:79–80.
- Hirao M, Takiguchi S, Imamura H, et al., Osaka University Clinical Research Group for Gastroenterological Study. Comparison of Billroth I and Roux-en-Y reconstruction after distal gastrectomy for gastric cancer: one-year postoperative effects assessed by a multi-institutional RCT. *Ann Surg Oncol.* 2013;20: 1591–1597.
- Collard JM, Romagnoli R. Roux-en-Y jejuna loop and bile reflux. Am J Surg. 2000;179:298–303.
- Ma Z, Wang Z, Zhang J. Carcinogenicity of duodenogastric reflux juice in patients undergoing gastrectomy. *Zhonghua Wai Ke Za Zhi*. 2001;39:764–766.
- Montesani C, D'Amato A, Santella S, et al. Billroth I versus Billroth II versus Roux-en-Y after subtotal gastrectomy. Prospective randomized study. *Hep*atogastroenterology. 2002;49:1469–1473.
- Shimoda M, Kubota K, Katoh M, et al. Effect of Billroth II or Roux-en-Y reconstruction for the gastrojejunostomy on delayed gastric emptying after pancreaticoduodenectomy. *Ann Surg.* 2013;257:938–942.

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- Masui T, Kubora T, Nakanishi Y, et al. The flow angle beneath the gastrojejunostomy predicts delayed gastric emptying in Roux-en-Y reconstruction after distal gastrectomy. *Gastric Cancer*. 2011;15:281–286.
- Woodward A, Sillin LF, Wojtowycz AR, et al. Gastric stasis of solids after Roux gastrectomy: is the jejunal transaction important? *J Surg Res.* 1993;55: 317–322.
- Mathias JR, Fernandez A, Sninsky CA, et al. Nausea, vomiting, and abdominal pain after Roux-en-Y anastomosis: motility of the jejunal limb. *Gastroenterology*. 1985;88:101–107.
- Santiago JM, Sasako M, Osorio J. TNM-7th edition 2009 (UICC/AJCC) and Japanese classification 2010 in gastric cancer. Towards simplicity and standardization in the management of gastric cancer. *Cir Esp.* 2011;89: 275–281.
- Sano T, Aiko T. New Japanese classifications and treatment guidelines for gastric cancer: revision concepts and major revised points. *Gastric Cancer*. 2011;14:97–100.
- Chan DC, Fan YM, Lin CK, et al. Roux-en-Y reconstruction after distal gastrectomy to reduce enterogastric reflux and Helicobacter pylori infection. J Gastrointest Surg. 2007;11:1732–1740.
- Buzby GP, Knox LS, Crosby LO, et al. Study protocol: a randomized clinical trial of total parenteral nutrition in malnourished surgical patients. *Am J Clin Nutr.* 1988;47:366–381.
- Buzby GP, Williford WO, Peterson OL, et al. A randomized clinical trial of total parenteral nutrition in malnourished surgical patients: the rationale and impact of previous clinical trials and pilot study on protocol design. *Am J Clin Nutr.* 1988;47:357–365.
- Naber HJ, de Bree A, Schermer TRJ, et al. Specificity of indexes of malnutrition when applied to apparently healthy people: the effect of age. *Am J Clin Nutr.* 1997;65:1721–1725.
- 17. Abd-El-Gawad WM, Abou-Hashem RM, El Maraghy MO, et al. The validity of Geriatric Nutrition Risk Index: simple tool for prediction of nutritional-

related complication of hospitalized elderly patients. Comparison with Mini Nutritional Assessment. *Clin Nutr.* 2014;33:1108–1116.

- Dixon MF, Genta RM, Yardley JH, et al. Classification and grading of gastritis: the updated Sydney System. Am J Surg Pathol. 1996;20:1161–1181.
- Kyriaki M, Eleni T, Efi P, et al. The EORTC core quality of life questionnaire (QLQ-C30, version 3.0) in terminally ill cancer patients under palliative care: validity and reliability in a Hellenic sample. *Int J Cancer*. 2001;94:135–139.
- Kim BJ, O'Connell T. Gastroduodenostomy after gastric resection for cancer. Am Surg. 1999;65:905–907.
- Vogel SB, Drane WE, Woodward ER. Clinical and radionuclide evaluation of bile diversion by Braun enteroenterostomy: prevention and treatment of alkaline reflux gastritis. An alternative to Roux-en-Y diversion. *Ann Surg.* 1994;219:458–465.
- Lee MS, Ahn SH, Lee JH, et al. What is the best reconstruction after distal gastrectomy for gastric cancer? Surg Endosc. 2012;26:1539–1547.
- Hirao M, Takiguchi S, Imamura H, et al. Comparison of Billroth I and Rouxen-Y reconstruction after distal gastrectomy for gastric cancer: one-year postoperative effects assessed by a multi-institutional RCT. *Ann Surg Oncol.* 2013;20:1591–1597.
- Montesani C, DÁmato A, Santella S, et al. Billroth I vesus Billroth II versus Rou-en-Y after subtotal gastrectomy. Prospective randomized study. *Hepato*gastroenterology. 2002;49:1469–1473.
- Johnsson F, Joelsson B, Gudmundsson K, et al. Symptoms and endoscopic findings in the diagnosis of gastroesophageal reflux disease. Scand J Gastroenterol. 1987;22:714–718.
- Gustavsson S, Ilstrup DM, Morrison P, et al. Roux-Y stasis syndrome after gastrectomy. Am J Surg. 1988;155:490–494.
- Csendes A, Burgos AM, Smok G, et al. Latest results (12-21 years) of a prospective randomized study comparing Billroth II and Roux-en-Y anastomosis after a partial gastrectomy plus vagotomy in patients with duodenal ulcers. *Ann Surg.* 2009;249:189–194.