**Name of journal:** ***World Journal of Gastroenterology***

**ESPS Manuscript NO: 19004**

**Manuscript type: TOPIC HIGHLIGHT**

**2016 Gastric Cancer: Global view**

**Current status in remnant gastric cancer after distal gastrectomy**

Ohira M *et al*. Current status in remnant gastric cancer

Masaichi Ohira, Takahiro Toyokawa, Katsunobu, Sakurai, Naoshi Kubo, Hiroaki Tanaka, Kazuya Muguruma, Masakazu Yashiro, Naoyoshi Onoda, Kosei Hirakawa

**Masaichi Ohira, Takahiro Toyokawa, Katsunobu, Sakurai, Naoshi Kubo, Hiroaki Tanaka, Kazuya Muguruma, Masakazu Yashiro, Naoyoshi Onoda, Kosei Hirakawa,** Department of Surgical Oncology, Osaka City University Graduate School of Medicine, Osaka 545-8585, Japan

**Author contributions**: Ohira M and Toyokawa T contributed equally to prepare this manuscript; Ohira M and Toyokawa T wrote the manuscript; Ohira M, Toyokawa T and Onoda N designed the review; Sakurai K, Kubo N and Tanaka H collected the references and analyzed data; Ohira M, Toyokawa T and Muguruma K contributed drafting of manuscript; Onoda N and Hirakawa K revised the manuscript critically; all authors read and approved the final manuscript.

**Conflict-of-interest statement:** All authors have no conflicts of interest or financial ties to disclose.

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**Correspondence to: Naoyoshi Onoda, MD, PhD, Associate Professor,** Department of Surgical Oncology, Osaka City University Graduate School of Medicine 1-4-3 Asahimachi, Abeno-ku, Osaka 545-8585, Japan. nonoda@med.osaka-cu.ac.jp

**Telephone:** +81-6-66453838

**Fax:** +81-6-66466450

**Received:** April 28, 2015

**Peer-review started:** May 6, 2015

**First decision:** August 25, 2015

**Revised:** November 9, 2015

**Accepted:** December 12, 2015

**Article in press:**

**Published online:**

**Abstract**

Remnant gastric cancer (RGC) and gastric stump cancer after distal gastrectomy (DG) are recognized as the same clinical entity. In this review, the current knowledges as well as the non-settled issues of RGC are presented. Duodenogastric reflux and denervation of the gastric mucosa are considered as the two main factors responsible for the development of RGC after benign disease. On the other hand, some precancerous circumstances which already have existed at the time of initial surgery, such as atrophic gastritis and intestinal metaplasia, are the main factors associated with RGC after gastric cancer. Although eradication of *Helicobacter pylori* (*H. pylori*) in remnant stomach is promising, it is still uncertain whether it can reduce the risk of carcinogenesis. Periodic endoscopic surveillance after DG was reported useful in detecting RGC at an early stage, which offers a chance to undergo minimally invasive endoscopic treatment or laparoscopic surgery and leads to an improved prognosis in RGC patients. Future challenges may be expected to elucidate the benefit of eradication of *H. pylori* in the remnant stomach if it could reduce the risk for RGC, to build an optimal endoscopic surveillance strategy after DG by stratifying the risk for development of RGC, and to develop a specific staging system for RGC for the standardization of the treatment by prospecting the prognosis.

**Key words**: remnant gastric cancer; *Helicobacter pylori*; endoscopic treatment; surveillance; laparoscopic surgery

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**Core tip:** There seemed two different categories of remnant gastric cancer. One develops at the stomal area following distal gastrectomy for benign disease after a long latency period, caused by the duodenogastric reflux. The other develops in the remnant stomach following gastric cancer surgery during the follow-up period, correlated with *Helicobacter pylori*. Early detection and aggressive surgical approach are essential to improve the prognosis. A specific staging system should be necessary to predict the prognosis. Minimally invasive treatments, such as endoscopic or laparoscopic surgery, have been applied recently.

Ohira M, Toyokawa T, Sakurai K, Kubo N, Tanaka H, Muguruma K, Yashiro M, Onoda N, Hirakawa K. Current status in remnant gastric cancer after distal gastrectomy. *World J Gastroenterol* 2015; In press

**Introduction**

Gastric cancer is the fourth most common malignancy. Although the prognosis of gastric cancer has improved notably because of progress in diagnosis and treatment, it remains the second leading cause of cancer-related mortality worldwide[1]. Remnant gastric cancer (RGC) after distal gastrectomy (DG) has been reported to account for 1%-8% of all gastric cancers[2,3]. RGC and gastric stump cancer are recognized as the same clinical entity, where gastric cancer develops in the stump or in the remnant stomach following a gastrectomy irrespective of the histology of the primary lesion (benign or malignant). Since Balfour first described RGC in 1922[4], many studies of RGC have been reported by various researchers. As possible important factors for the pathogenesis for RGC, duodenogastric reflux and *Helicobacter pylori (H. pylori)* infection, both of them are associated with chronic gastritis, have been investigated.

In comparison with primary gastric cancer, RGC has commonly been diagnosed at an advanced stage, resulting in a low rate of curative resection and a poor prognosis[5-7]. However, recently, the incidence and etiology of RGC have been changing, because of the decrease in the opportunity to undergo gastrectomy for benign disease, early detection and the stomach-preserved treatment of the initial gastric cancer, and improvement of the outcomes in patients with gastric cancer. Furthermore, recent advances in diagnostic and therapeutic techniques have contributed to early detection and the minimally invasive treatment of RGC.

The aim of this review is to provide an overview of the current knowledge and issues related to RGC based on the recent literature.

**PATHOGENESIS OF REMNANT GASTRIC CANCER**

From the clinical observations, cancer in the remnant stomach could be classified into several categories: cancer newly developed in the remnant stomach (newly developed RGC); cancer remaining in the remnant stomach after the initial gastric surgery (remaining RGC); metachronously developed gastric cancer; and recurrent cancer in the remnant stomach[8]. It is considered that the mechanism of carcinogenesis in RGC after DG differs between the cause of initial operation; benign disease or gastric cancer.

***Initial disease***

Experimental studies have demonstrated that the risk for gastric cancer is higher in the remnant stomach than in the normal gastric mucosa[9-11], but epidemiological studies have not reported definitive conclusions. In prospective cohort studies, some reports from Western countries have shown that remnant stomach after DG for peptic ulcer disease had a higher risk for gastric cancer[12-14], whereas reports from Japan have shown the opposite result[15,16]. This discrepancy could result from the difference in the rate of incidence of primary gastric cancer in the general population; Japan has one of the highest incidences of primary gastric cancer in the world[17].

Some authors have investigated RGC after DG for benign disease in order to elucidate the development of newly developed RGC. It has been reported that the two main factors responsible for environmental changes affecting remnant gastric mucosa after gastrectomy are chronic damage attributed to duodenogastric reflux and denervation of the gastric mucosa[9-11,18]. Miwa *et al*[19] showed that duodenogastric reflux had potent carcinogenic activities in the rat. Kaminishi *et al*[10] demonstrated that denervation of the gastric mucosa promoted carcinogenesis in the remnant stomach using a rat model.

Because of the improvement of drug therapy for duodenal and gastric ulcers, gastrectomy for benign disease has decreased over the last 2 decades. Still, this type of RGC has not decreased due to the long latency period required for carcinogenesis after initial surgery. In contrast, RGC after DG for gastric cancer has become more common. Hosokawa *et al*[20] reported that the cumulative risk of developing RGC in patients who underwent DG after early gastric cancer was 2.4% at 5 years and 6.1% at 10 years. Similarly, Morgagni *et al*[21] reported that the cumulative risk of RGC in patients who underwent DG after early gastric cancer was 2.6% at 10 years, 3.2% at 15 years, and 4% at 20 years.

Several studies have demonstrated the clinicopathological differences between RGC after benign disease and that after gastric cancer[3,8,22-31] (Table 1). In these studies, compared with Billroth-I (B-I) reconstruction, RGC was observed more frequently at the anastomotic site in Billroth-II (B-II) reconstruction. The probable reason for this difference is that the anastomotic site is continuously bathed with duodenogastric reflux, resulting in mucosal inflammation and regeneration after B-II reconstruction. The average interval between initial DG and the second surgery for RGC is reported to be 22-34.6 years for benign disease and 6.8-18.8 years for gastric cancer. This long interval for the development of RGC in the benign group is thought to be attributed to the chronic stimulation by duodenogastric reflux. Successive activation of cellular proliferation in the anastomotic site has been demonstrated. The reason for the shorter interval for RGC after DG for gastric cancer is that patients already have some precancerous lesions, such as atrophic gastritis and intestinal metaplasia, and they are followed-up closely with endoscopic examination[32].

***Reconstruction method***

B-II reconstruction is generally considered to have a higher risk of newly developed RGC than B-I reconstruction, because a significant association between B-II reconstruction and RGC after DG for benign disease has been demonstrated. However, Tanigawa *et al*[33] and Leo *et al*[31] noted that B-II reconstruction was performed more often in DG for peptic ulcer disease until the late 1980s in Japan and Italy. Although there have been some reports that showed a higher risk of newly developed RGC after DG for peptic ulcer disease in B-II reconstruction than in B-I reconstruction[13,34], a meta-analysis[35] and a recent large population-based study from Sweden[36] demonstrated that type of reconstruction did not affect the risk of newly developed RGC. From these findings, whether B-II reconstruction results in a higher risk of newly developed RGC than B-I reconstruction remains uncertain.

***H. pylori infection***

In primary gastric cancer, it has been generally accepted that *H. pylori* infection is the definite carcinogen for gastric cancer[37-39], and *H. pylori* eradication therapy can reduce the prevalence of gastric cancer[40]. However, the significance of *H. pylori* infection in the development of RGC for patients after DG remains controversial.

The rate of *H. pylori* infection in the remnant stomach has been reported to have a broad range (17.4%-68.2%)[41-49], which is lower than in the non-operated stomach. Although it has been reported that spontaneous regression of *H. pylori* is rare under normal circumstances, several researchers have demonstrated that spontaneous regression of *H. pylori* has been observed with time after operation, regardless of the initial disease for DG[41,48,50]. We previously demonstrated that the prevalence of *H. pylori* infection was significantly lower in patients with severe duodenogastric reflux than in those without duodenogastric reflux[41]. Although significant differences were not shown in any study, there seems to be a trend for a lower *H. pylori* prevalence in B-II reconstruction than in B-I reconstruction. Duodenogastric reflux is considered a possible factor that inhibits the growth of *H. pylori*. On the other hand, Nakagawara *et al*[51] and Chan *et al*[46] demonstrated that the prevalence of *H. pylori* was significantly lower in R-Y reconstruction than in B-II reconstruction, even though duodenogastric reflux was observed significantly less in R-Y reconstruction. These reports may indicate there are factors other than duodenogastric reflux that inhibit the growth of *H. pylori* in the remnant stomach.

Similar to patients with peptic ulcer disease, the success rate of *H. pylori* eradication using triple therapy in remnant stomach has been reported to be around 90%[42,52,53] (Table 2). In a randomized, controlled trial, Kim *et al*[53] demonstrated not only that the efficacy of preoperative and postoperative proton pump inhibitor-based eradication therapies was not significantly different in patients undergoing DG for gastric cancer, but also that neither the type of reconstruction method nor the presence of duodenogastric reflux in the remnant stomach affected its efficacy. There is evidence that *H. pylori* infection is a cause of chronic atrophic gastritis and intestinal metaplasia, which are considered possible precancerous conditions for gastric cancer[38,54]. Several authors[41,49,55] reported that chronic and active mucosal inflammation was closely associated with *H. pylori* infection in the remnant stomach. It was demonstrated that eradication of *H. pylori* infection in the remnant stomach improved the degree of chronic active gastritis[42,52,56]. Given these reports, the eradication of *H. pylori* infection in the remnant stomach may prevent the development of RGC after DG. We have suggested that young patients with mild atrophic gastritis and without duodenogastric reflux may be the best candidates for *H. pylori* eradication therapy, because they had the highest probability of *H. pylori* colonization in the remnant stomach[41,52]. However, it is still uncertain whether eradication of *H. pylori* in remnant stomach can reduce the risk of carcinogenesis. Further prospective, large studies are needed to elucidate the efficacy of *H. pylori* eradication therapy for the prevention of RGC in patients who undergo DG.

**THE DIFFERENCE BETWEEN REMNANT GASTRIC CANCER AND PRIMARY PROXIMAL GASTRIC CANCER**

In several studies, the clinicopathological features of RGC have been compared with those of primary proximal gastric cancer (PPGC) because of the similar anatomical location. It has been demonstrated that the male-to-female ratio was significantly higher for RGC than for PPGC[8,22,57,58]. The reason for the male dominance is that male patients have a higher risk for both gastroduodenal ulcer and gastric cancer[30,31].

It has been reported that RGC has unique patterns of lymph node metastasis compared with PPGC. In PPGC, the main lymphatic flow drains to the lymph nodes along the celiac artery through the lymph nodes at the lesser curvature, the left gastric artery, and the right side of the cardia. In RGC, it has been considered that the characteristics of lymph node metastases are different from PPGC because abnormal lymphatic formation is induced as a result of cutting off these lymphatic pathways at the initial surgery[31]. Furthermore, Tokunaga *et al*[30] mentioned that altered lymphatic drainage after DG may affect the long-term survival of RGC patients with advanced stage disease. Previous studies have investigated the incidence of lymph node metastasis focusing on around the splenic artery, in the splenic hilum, at the lower mediastinum, and in the jejunal mesentery[8,24,31,57,59-63] (Table 3). Some authors demonstrated a higher incidence of lymph node metastasis around the splenic artery, in the splenic hilum, and at the lower mediastinum in RGC; therefore, lymphadenectomy of these regions is recommended for curative surgery. In patients with previous B-II reconstruction, the rate of lymph node metastases in the jejunal mesentery has been reported to be 10.0%-67% (Table 3). Thorban *et al*[57] reported that RGC patients with lymph node metastases in the jejunal mesentery had a poor prognosis, with a median survival time (MST) of 13.2 months. Similarly, Leo *et al*[31] reported that RGC patients with lymph node metastases in the jejunal mesentery had worse outcomes than those with metastases in other lymph node stations. Therefore, jejunal mesentery lymph node dissection including the origins of each involved jejunal artery is recommended for RGC patients with previous B-II reconstruction. However, the details of the spread of lymph node metastases in RGC patients are still uncertain, because the number of patients examined in these studies was too small.

Adhesions caused by prior surgery, especially for malignant disease because of lymph node dissection, lead to a higher rate of adjacent organ resections in comparison with primary gastric cancer to achieve curative resection[3,8,24,57,63]. Prior studies reported the poor prognosis of patients with RGC[5,6]. However, as shown in Table 4, most recent studies, except the study by Tokunaga *et al*[30], have reported that RGC had equivalent survival compared with PPGC, regardless of stage[3,8,22,24,30,57,63].

**ENDOSCOPIC SURVEILLANCE**

Recent advances in endoscopic diagnostic techniques have led to more frequent detection of early RGC after DG. Early detection is essential not only to improve the prognosis of RGC, but also to offer a chance for endoscopic treatment. For early detection of RGC, some authors have reported the importance of periodic follow-up endoscopy after gastrectomy[20,21,32,64]. Komatsu *et al*[28] reported that the duration of follow-up was significantly associated with the stage of RGC progression. An *et al*[22] reported that the prognosis of 7 patients with RGC diagnosed at annual examination was excellent, with a 5-year survival of 100% without recurrence. Thus, early detection by periodic endoscopic examination may lead to a better prognosis.

The optimal period and interval of endoscopic surveillance to detect RGC at an early stage have not been determined. In patients who undergo DG for gastric cancer, endoscopic surveillance is considered mainly to detect remaining and metachronous gastric cancer. Hosokawa *et al*[20] noted that periodic endoscopic examinations to detect RGC at an early stage are recommended at intervals of 2-3 years, because, among 15 patients examined at an interval of no more than 2 years, RGC was detected at an early stage in 12 patients (80%). Ohashi *et al*[23] and Ojima *et al*[27] recommended annual endoscopic surveillance from 1 year after DG for gastric cancer to at least 10 years. On the other hand, because the risk of newly developed RGC after gastrectomy for benign disease is thought to be increased from more than 20 years, annual endoscopic screening is recommended to start at least 15-20 years after gastrectomy for benign disease and continue for as long as the patients can receive treatment for RGC[24,57,64].

**OPTIMAL TREATMENT**

The mainstay of treatment for RGC patients is radical surgical resection. R0 resection is an important prognostic factor in RGC, as well as conventional gastric cancer[3,25,29,57]. As some authors have recommended, although R0 resection with an aggressive surgical approach is technically difficult in RGC patients, it might contribute to improving the long-term outcome.

In most studies, the UICC classification was used to determine the N stage in RGC patients, regardless of the initial reconstruction method and the previous disease. However, the number of retrieved lymph nodes is expected to be insufficient to determine the N stage in some RGC patients, especially those with previous malignant disease, which may lead to uncertain staging. Indeed, some authors showed that the total number of retrieved lymph nodes and the perigastric lymph node metastasis rate were lower than for PPGC[3,8,58,63]. Li *et al*[62] and Costa-Pinho *et al*[58] reported that the N stage of the 7th edition of the TNM staging system was not suitable for predicting the outcomes of RGC patients. Therefore, it may be one of the future challenges to create a specific staging system for RGC.

***Endoscopic intervention***

Endoscopic submucosal dissection (ESD) has been widely accepted as the standard treatment for early gastric cancer patients without potential risk of lymph node metastasis, because ESD is less invasive than surgery and provides better quality of life. Surgical resection for RGC has been reported to have a relatively high postoperative morbidity rate and a high adjacent organ resection rate, so ESD is an attractive treatment. However, it is considered challenging to perform ESD for early RGC, because performing ESD is technically difficult due to the limited space within which to manipulate and the existence of staples or severe fibrosis around the anastomosis and suture line. Recently, several retrospective studies of ESD for RGC have been reported[65-71] (Table 5). According to these studies, the en bloc resection rate and the complete resection rate were reported to be 91%-100% and 74%-94%, respectively. Lee *et al*[68] demonstrated that there were no significant differences between RGC and upper-third gastric cancer in the complete resection rate of ESD, whereas Takenaka *et al*[65] reported that, when the lesion was located on or not on the suture line, the complete resection rates were 58% and 84%, respectively. With regard to complications, the perforation and bleeding rates were reported to be 0%-17.7% and 0%-17.6%, respectively. The occurrence of perforation was reported to be significantly higher for RGC than for non-remnant gastric cancer[65], and Tanaka *et al*[71] demonstrated that the occurrence of perforation was significantly more frequent in anastomotic sites (27.3%) than in non-anastomotic sites (0%).

Although the indications for ESD for primary gastric cancer were similar to those of early RGC in previous studies[65-71], there has been only one report assessing whether the same indication for ESD for primary gastric cancer can be applied to RGC. Choi *et al*[72] reviewed 17 surgically resected patients who were possible candidates for ESD for RGC, and they demonstrated that they had no evidence of lymph node metastasis. There is only one study of long-term outcomes after ESD for RGC, in which Nonaka *et al*[70] reported that the cause-specific survival rate was 100% during the median follow-up period of 4.5 years. Further studies are required to confirm the indications and oncological feasibility of ESD for RGC.

***Laparoscopic surgery***

Laparoscopic surgery for gastric cancer has been widely accepted because of several advantages, such as less postoperative pain, reduced blood loss, earlier recovery, fewer complications, and shorter hospitalization[73-75]. However, because adhesions and anatomical alterations due to previous gastrectomy make laparoscopic surgery complicated and difficult, laparoscopic total gastrectomy has not generally been considered to be indicated in patients with RGC in the early era of laparoscopic surgery. Recently, five studies, including small series of laparoscopic total gastrectomy for RGC compared with open gastrectomy, have been reported[76-80] (Table 6). All studies showed a longer operation time for laparoscopic surgery. On the other hand, four of five studies, except Son *et al*[80], showed less blood loss, more retrieved lymph nodes, shorter time to first flatus, and a lower complication rate in laparoscopic surgery. In the study reported by Son *et al*[80], there were 8 cases (47.1%) of open conversion, for which the most common reason was the presence of severe adhesions after gastrectomy for malignant disease. Although the follow-up time was short in each study, all three studies that assessed survival demonstrated that the 5-year survival rate was similar between laparoscopic surgery and open surgery[77,78,80]. Because the size of each study was small, multicenter studies should be considered to confirm the advantages of laparoscopic gastrectomy for RGC.

**CONCLUSION**

In conclusion, there are two different diseases included in the category of RGC. One is RGC that develops at the stomal area of the remnant stomach following DG for benign disease. The lesion commonly develops after a long latency period, possibly influenced by the successive activation of cellular proliferation with the duodenogastric reflux. The other is RGC that develops in the atrophic mucosa of the remnant stomach following DG for gastric cancer. The lesion could be found during the follow-up period by periodic endoscopic examination and might be in line with the carcinogenic pathway of the initial gastric cancer correlated to *H. pylori*. There is no guideline to indicate the standardized stratification method or to suggest the possible optimal treatment strategy for RGC. Still, it is obvious that the prognosis of patients with gastric cancer depends on the stage, which is determined by the T and N categories, and that early detection and an aggressive surgical approach to achieve R0 resection are essential to improve the prognosis of RGC patients. Recent advances in endoscopic interventions or laparoscopic surgery may provide patients with a better quality of life after minimally invasive treatments.

**References**

1 **Ferlay J**, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *Int J Cancer* 2010; **127**: 2893-2917 [PMID: 21351269 DOI: 10.1002/ijc.25516]

2 **Sinning C**, Schaefer N, Standop J, Hirner A, Wolff M. Gastric stump carcinoma - epidemiology and current concepts in pathogenesis and treatment. *Eur J Surg Oncol* 2007; **33**: 133-139 [PMID: 17071041 DOI: 10.1016/j.ejso.2006.09.006]

3 **Mezhir JJ**, Gonen M, Ammori JB, Strong VE, Brennan MF, Coit DG. Treatment and outcome of patients with gastric remnant cancer after resection for peptic ulcer disease. *Ann Surg Oncol* 2011; **18**: 670-676 [PMID: 21063791 DOI: 10.1245/s10434-010-1425-1]

4 **Balfour DC**. Factors influencing the life expectancy of patients operated on for gastric ulcer. *Ann Surg* 1922; **76**: 405-408 [PMID: 17864703 DOI: 10.1097/00000658-192209000-00014]

5 **Orlando R 3rd**, Welch JP. Carcinoma of the stomach after gastric operation. *Am J Surg* 1981; **141**: 487-491 [PMID: 6164300 DOI: 10.1016/0002-9610(81)90145-8]

6 **Ovaska JT**, Havia TV, Kujari HP. Retrospective analysis of gastric stump carcinoma patients treated during 1946-1981. *Acta Chir Scand* 1986; **152**: 199-204 [PMID: 3716739]

7 **Kodera Y**, Yamamura Y, Torii A, Uesaka K, Hirai T, Yasui K, Morimoto T, Kato T, Kito T. Gastric stump carcinoma after partial gastrectomy for benign gastric lesion: what is feasible as standard surgical treatment? *J Surg Oncol* 1996; **63**: 119-124 [PMID: 8888805 DOI: 10.1002/(SICI)1096-9098(199610)63:2<119::AID-JSO9>3.0.CO;2-H]

8 **Tanigawa N**, Nomura E, Niki M, Shinohara H, Nishiguchi K, Okuzawa M, Toyoda M, Morita S. Clinical study to identify specific characteristics of cancer newly developed in the remnant stomach. *Gastric Cancer* 2002; **5**: 23-28 [PMID: 12021856 DOI: 10.1007/s101200200003]

9 **Kondo K**, Kojima H, Akiyama S, Ito K, Takagi H. Pathogenesis of adenocarcinoma induced by gastrojejunostomy in Wistar rats: role of duodenogastric reflux. *Carcinogenesis* 1995; **16**: 1747-1751 [PMID: 7634399 DOI: 10.1093/carcin/16.8.1747]

10 **Kaminishi M**, Shimizu N, Shiomoyama S, Yamaguchi H, Ogawa T, Sakai S, Kuramoto S, Oohara T. Etiology of gastric remnant cancer with special reference to the effects of denervation of the gastric mucosa. *Cancer* 1995; **75**: 1490-1496 [PMID: 7889480 DOI: 10.1002/1097-0142(19950315)75:6+<1490::AID-CNCR2820751518>3.0.CO;2-3]

11 **Kaminishi M**, Shimizu N, Shimoyama S, Yamaguchi H, Tsuji E, Aoki F, Nomura S, Yoshikawa A, Kuramoto S, Oohara T, Inada K, Tatematsu M. Denervation promotes the development of cancer-related lesions in the gastric remnant. *J Clin Gastroenterol* 1997; **25 Suppl 1**: S129-S134 [PMID: 9479639 DOI: 10.1097/00004836-199700001-00022]

12 **Viste A**, Bjørnestad E, Opheim P, Skarstein A, Thunold J, Hartveit F, Eide GE, Eide TJ, Søreide O. Risk of carcinoma following gastric operations for benign disease. A historical cohort study of 3470 patients. *Lancet* 1986; **2**: 502-505 [PMID: 2875248 DOI: 10.1016/S0140-6736(86)90368-5]

13 **Caygill CP**, Hill MJ, Kirkham JS, Northfield TC. Mortality from gastric cancer following gastric surgery for peptic ulcer. *Lancet* 1986; **1**: 929-931 [PMID: 2871238 DOI: 10.1016/S0140-6736(86)91041-X]

14 **Toftgaard C**. Gastric cancer after peptic ulcer surgery. A historic prospective cohort investigation. *Ann Surg* 1989; **210**: 159-164 [PMID: 2757419 DOI: 10.1097/00000658-198908000-00004]

15 **Tokudome S**, Kono S, Ikeda M, Kuratsune M, Sano C, Inokuchi K, Kodama Y, Ichimiya H, Nakayama F, Kaibara N. A prospective study on primary gastric stump cancer following partial gastrectomy for benign gastroduodenal diseases. *Cancer Res* 1984; **44**: 2208-2212 [PMID: 6713408]

16 **Asano A**, Mizuno S, Sasaki R, Aoki K, Yokoyama H, Yokoyama Y. The long-term prognosis of patients gastrectomized for benign gastroduodenal diseases. *Jpn J Cancer Res* 1987; **78**: 337-348 [PMID: 3108214]

17 **Sowa M**, Onoda N, Nakanishi I, Maeda K, Yoshikawa K, Kato Y, Chung YS. Early stage carcinoma of the gastric remnant in Japan. *Anticancer Res* 1993; **13**: 1835-1838 [PMID: 8267389]

18 **Kondo K**. Duodenogastric reflux and gastric stump carcinoma. *Gastric Cancer* 2002; **5**: 16-22 [PMID: 12021855 DOI: 10.1007/s101200200002]

19 **Miwa K**, Hasegawa H, Fujimura T, Matsumoto H, Miyata R, Kosaka T, Miyazaki I, Hattori T. Duodenal reflux through the pylorus induces gastric adenocarcinoma in the rat. *Carcinogenesis* 1992; **13**: 2313-2316 [PMID: 1473239 DOI: 10.1093/carcin/13.12.2313]

20 **Hosokawa O**, Kaizaki Y, Watanabe K, Hattori M, Douden K, Hayashi H, Maeda S. Endoscopic surveillance for gastric remnant cancer after early cancer surgery. *Endoscopy* 2002; **34**: 469-473 [PMID: 12048630 DOI: 10.1055/s-2002-32007]

21 **Morgagni P**, Gardini A, Marrelli D, Vittimberga G, Marchet A, de Manzoni G, Di Cosmo MA, Rossi GM, Garcea D, Roviello F. Gastric stump carcinoma after distal subtotal gastrectomy for early gastric cancer: experience of 541 patients with long-term follow-up. *Am J Surg* 2015; **209**: 1063-1068 [PMID: 25218580 DOI: 10.1016/j.amjsurg.2014.06.021]

22 **An JY**, Choi MG, Noh JH, Sohn TS, Kim S. The outcome of patients with remnant primary gastric cancer compared with those having upper one-third gastric cancer. *Am J Surg* 2007; **194**: 143-147 [PMID: 17618792 DOI: 10.1016/j.amjsurg.2006.10.034]

23 **Ohashi M**, Katai H, Fukagawa T, Gotoda T, Sano T, Sasako M. Cancer of the gastric stump following distal gastrectomy for cancer. *Br J Surg* 2007; **94**: 92-95 [PMID: 17054314 DOI: 10.1002/bjs.5538]

24 **Schaefer N**, Sinning C, Standop J, Overhaus M, Hirner A, Wolff M. Treatment and prognosis of gastric stump carcinoma in comparison with primary proximal gastric cancer. *Am J Surg* 2007; **194**: 63-67 [PMID: 17560911]

25 **Ahn HS**, Kim JW, Yoo MW, Park do J, Lee HJ, Lee KU, Yang HK. Clinicopathological features and surgical outcomes of patients with remnant gastric cancer after a distal gastrectomy. *Ann Surg Oncol* 2008; **15**: 1632-1639 [PMID: 18379851 DOI: 10.1245/s10434-008-9871-8]

26 **Firat O**, Guler A, Sozbilen M, [Ersin S](http://www.ncbi.nlm.nih.gov/pubmed/?term=Ersin%20S%5BAuthor%5D&cauthor=true&cauthor_uid=18607624), [Kaplan H](http://www.ncbi.nlm.nih.gov/pubmed/?term=Kaplan%20H%5BAuthor%5D&cauthor=true&cauthor_uid=18607624). Gastric remnant cancer: an old problem with novel concerns. *Langenbecks Arch Surg* 2009; **394**: 93-97 [PMID:18607624 DOI: 10.1007/s00423-008-0382-7]

27 **Ojima T**, Iwahashi M, Nakamori M, Nakamura M, Naka T, Katsuda M, Iida T, Tsuji T, Hayata K, Takifuji K, Yamaue H. Clinicopathological characteristics of remnant gastric cancer after a distal gastrectomy. *J Gastrointest Surg* 2010; **14**: 277-281 [PMID: 19911236 DOI: 10.1007/s11605-009-1090-5]

28 **Komatsu S**, Ichikawa D, Okamoto K, Ikoma D, Tsujiura M, Nishimura Y, Murayama Y, Shiozaki A, Ikoma H, Kuriu Y, Nakanishi M, Fujiwara H, Ochiai T, Kokuba Y, Otsuji E. Progression of remnant gastric cancer is associated with duration of follow-up following distal gastrectomy. *World J Gastroenterol* 2012; **18**: 2832-2836 [PMID: 22719193 DOI: 10.3748/wjg.v18.i22.2832]

29 **Li F**, Zhang R, Liang H, Zhao J, Liu H, Quan J, Wang X, Xue Q. A retrospective clinicopathologic study of remnant gastric cancer after distal gastrectomy. *Am J Clin Oncol* 2013; **36**: 244-249 [PMID: 22495457 DOI: 10.1097/COC.0b013e3182467ebd]

30 **Tokunaga M**, Sano T, Ohyama S, Hiki N, Fukunaga T, Yamada K, Yamaguchi T. Clinicopathological characteristics and survival difference between gastric stump carcinoma and primary upper third gastric cancer. *J Gastrointest Surg* 2013; **17**: 313-318 [PMID: 23233273 DOI: 10.1007/s11605-012-2114-0]

31 **Di Leo A**, Pedrazzani C, Bencivenga M, Coniglio A, Rosa F, Morgani P, Marrelli D, Marchet A, Cozzaglio L, Giacopuzzi S, Tiberio GA, Doglietto GB, Vittimberga G, Roviello F, Ricci F. Gastric stump cancer after distal gastrectomy for benign disease: clinicopathological features and surgical outcomes. *Ann Surg Oncol* 2014; **21**: 2594-2600 [PMID: 24639193 DOI: 10.1245/s10434-014-3633-6]

32 **Sowa M**, Kato Y, Onoda N, Kubo T, Maekawa H, Yoshikawa K, Nishimura M, Nakanishi I, Chung YS. Early cancer of the gastric remnant with special reference to the importance of follow-up of gastrectomized patients. *Eur J Surg Oncol* 1993; **19**: 43-49 [PMID: 8436240]

33 **Tanigawa N**, Nomura E, Lee SW, Kaminishi M, Sugiyama M, Aikou T, Kitajima M. Current state of gastric stump carcinoma in Japan: based on the results of a nationwide survey. *World J Surg* 2010; **34**: 1540-1547 [PMID: 20182716 DOI: 10.1007/s00268-010-0505-5]

34 **Lundegårdh G**, Adami HO, Helmick C, Zack M, Meirik O. Stomach cancer after partial gastrectomy for benign ulcer disease. *N Engl J Med* 1988; **319**: 195-200 [PMID: 3393171 DOI: 10.1056/NEJM198807283190402]

35 **Tersmette AC**, Offerhaus GJ, Tersmette KW, Giardiello FM, Moore GW, Tytgat GN, Vandenbroucke JP. Meta-analysis of the risk of gastric stump cancer: detection of high risk patient subsets for stomach cancer after remote partial gastrectomy for benign conditions. *Cancer Res* 1990; **50**: 6486-6489 [PMID: 2145061]

36 **Lagergren J**, Lindam A, Mason RM. Gastric stump cancer after distal gastrectomy for benign gastric ulcer in a population-based study. *Int J Cancer* 2012; **131**: E1048-E1052 [PMID: 22532306 DOI: 10.1002/ijc.27614]

37 **Nomura A**, Stemmermann GN, Chyou PH, Kato I, Perez-Perez GI, Blaser MJ. Helicobacter pylori infection and gastric carcinoma among Japanese Americans in Hawaii. *N Engl J Med* 1991; **325**: 1132-1136 [PMID: 1891021 DOI: 10.1056/NEJM199110173251604]

38 **Parsonnet J**, Friedman GD, Vandersteen DP, Chang Y, Vogelman JH, Orentreich N, Sibley RK. Helicobacter pylori infection and the risk of gastric carcinoma. *N Engl J Med* 1991; **325**: 1127-1131 [PMID: 1891020 DOI: 10.1056/NEJM199110173251603]

39 **Uemura N**, Okamoto S, Yamamoto S, Matsumura N, Yamaguchi S, Yamakido M, Taniyama K, Sasaki N, Schlemper RJ. Helicobacter pylori infection and the development of gastric cancer. *N Engl J Med* 2001; **345**: 784-789 [PMID: 11556297 DOI: 10.1056/NEJMoa001999]

40 **Fukase K**, Kato M, Kikuchi S, Inoue K, Uemura N, Okamoto S, Terao S, Amagai K, Hayashi S, Asaka M. Effect of eradication of Helicobacter pylori on incidence of metachronous gastric carcinoma after endoscopic resection of early gastric cancer: an open-label, randomised controlled trial. *Lancet* 2008; **372**: 392-397 [PMID: 18675689 DOI: 10.1016/S0140-6736(08)61159-9]

41 **Onoda N**, Maeda K, Sawada T, Wakasa K, Arakawa T, Chung KH. Prevalence of Helicobacter pylori infection in gastric remnant after distal gastrectomy for primary gastric cancer. *Gastric Cancer* 2001; **4**: 87-92 [PMID: 11706766 DOI: 10.1007/PL00011729]

42 **Matsukura N**, Tajiri T, Kato S, Togashi A, Masuda G, Fujita I, Tokunaga A, Yamada N. Helicobacter pylori eradication therapy for the remnant stomach after gastrectomy. *Gastric Cancer* 2003; **6**: 100-107 [PMID: 12861401]

43 **Kirsch C**, Madisch A, Piehler P, Bayerdorffer E, Stolte M, Miehlke S. Helicobacter pylori in gastric corpus of patients 20 years after partial gastric resection. *World J Gastroenterol* 2004; **10**: 2557-2559 [PMID: 15300905 DOI: 10.3748/wjg.v10.i17.2557 ]

44 **Abe H**, Murakami K, Satoh S, Sato R, Kodama M, Arita T, Fujioka T. Influence of bile reflux and Helicobacter pylori infection on gastritis in the remnant gastric mucosa after distal gastrectomy. *J Gastroenterol* 2005; **40**: 563-569 [PMID: 16007389 DOI: 10.1007/s00535-005-1589-9]

45 **Giuliani A**, Caporale A, Demoro M, Benvenuto E, Scarpini M, Spada S, Angelico F. Gastric cancer precursor lesions and Helicobacter pylori infection in patients with partial gastrectomy for peptic ulcer. *World J Surg* 2005; **29**: 1127-1130 [PMID: 16096865 DOI: 10.1007/s00268-005-7713-4]

46 **Chan DC**, Fan YM, Lin CK, Chen CJ, Chen CY, Chao YC. Roux-en-Y reconstruction after distal gastrectomy to reduce enterogastric reflux and Helicobacter pylori infection. *J Gastrointest Surg* 2007; **11**: 1732-1740 [PMID: 17876675 DOI: 10.1007/s11605-007-0302-0]

47 **Li XB**, Lu H, Chen HM, Chen XY, Ge ZZ. Role of bile reflux and Helicobacter pylori infection on inflammation of gastric remnant after distal gastrectomy. *J Dig Dis* 2008; **9**: 208-212 [PMID: 18959592 DOI: 10.1111/j.1751-2980.2008.00348.x]

48 **Bair MJ**, Wu MS, Chang WH, Shih SC, Wang TE, Chen CJ, Lin CC, Liu CY, Chen MJ. Spontaneous clearance of Helicobacter pylori colonization in patients with partial gastrectomy: correlates with operative procedures and duration after operation. *J Formos Med Assoc* 2009; **108**: 13-19 [PMID: 19181603 DOI: 10.1016/S0929-6646(09)60027-9]

49 **Giuliani A**, Galati G, Demoro M, Scimò M, Pecorella I, Basso L. Screening of Helicobacter pylori infection after gastrectomy for cancer or peptic ulcer: results of a cohort study. *Arch Surg* 2010; **145**: 962-967 [PMID: 20956764 DOI: 10.1001/archsurg.2010.211]

50 **Nagahata Y**, Kawakita N, Azumi Y, Numata N, Yano M, Saitoh Y. Etiological involvement of Helicobacter pylori in "reflux" gastritis after gastrectomy. *Am J Gastroenterol* 1996; **91**: 2130-2134 [PMID: 8855735]

51 **Nakagawara H**, Miwa K, Nakamura S, Hattori T. Duodenogastric reflux sustains Helicobacter pylori infection in the gastric stump. *Scand J Gastroenterol* 2003; **38**: 931-937 [PMID: 14531528 DOI: 10.1080/00365520310005163]

52 **Onoda N**, Katsuragi K, Sawada T, Maeda K, Mino A, Ohira M, Ishikawa T, Wakasa K, Hirakawa K. Efficacy of Helicobacter pylori eradication on the chronic mucosal inflammation of the remnant stomach after distal gastrectomy for early gastric cancer. *J Exp Clin Cancer Res* 2005; **24**: 515-521 [PMID: 16471313]

53 **Kim CG**, Song HJ, Kook MC, [Hong EK](http://www.ncbi.nlm.nih.gov/pubmed/?term=Hong%20EK%5BAuthor%5D&cauthor=true&cauthor_uid=17714557), [Park S](http://www.ncbi.nlm.nih.gov/pubmed/?term=Park%20S%5BAuthor%5D&cauthor=true&cauthor_uid=17714557), [Lee JY](http://www.ncbi.nlm.nih.gov/pubmed/?term=Lee%20JY%5BAuthor%5D&cauthor=true&cauthor_uid=17714557), [Lee JH](http://www.ncbi.nlm.nih.gov/pubmed/?term=Lee%20JH%5BAuthor%5D&cauthor=true&cauthor_uid=17714557), [Ryu KW](http://www.ncbi.nlm.nih.gov/pubmed/?term=Ryu%20KW%5BAuthor%5D&cauthor=true&cauthor_uid=17714557), [Kim YW](http://www.ncbi.nlm.nih.gov/pubmed/?term=Kim%20YW%5BAuthor%5D&cauthor=true&cauthor_uid=17714557), [Bae JM](http://www.ncbi.nlm.nih.gov/pubmed/?term=Bae%20JM%5BAuthor%5D&cauthor=true&cauthor_uid=17714557), [Choi IJ](http://www.ncbi.nlm.nih.gov/pubmed/?term=Choi%20IJ%5BAuthor%5D&cauthor=true&cauthor_uid=17714557). Preoperative versus postoperative Helicobacter pylori eradication therapy in gastric cancer patients: a randomized trial. *Am J Gastroenterol* 2008; **103**: 48-54 [PMID:17714557 DOI: 10.1111/j.1572-0241.2007.01482.x]

54 **Forman D**, Newell DG, Fullerton F, Yarnell JW, Stacey AR, Wald N, Sitas F. Association between infection with Helicobacter pylori and risk of gastric cancer: evidence from a prospective investigation. *BMJ* 1991; **302**: 1302-1305 [PMID: 2059685 DOI: 10.1136/bmj.302.6788.1302]

55 **Lee Y**, Tokunaga A, Tajiri T, Masuda G, Okuda T, Fujita I, Kiyama T, Yoshiyuki T, Kato S, Matsukura N, Yamada N. Inflammation of the gastric remnant after gastrectomy: mucosal erythema is associated with bile reflux and inflammatory cellular infiltration is associated with Helicobacter pylori infection. *J Gastroenterol* 2004; **39**: 520-526 [PMID: 15235868 DOI: 10.1007/s00535-003-1337-y]

56 **Hamaguchi K**, Ogawa K, Katsube T, [Konno S](http://www.ncbi.nlm.nih.gov/pubmed/?term=Konno%20S%5BAuthor%5D&cauthor=true&cauthor_uid=14767774), [Aiba M](http://www.ncbi.nlm.nih.gov/pubmed/?term=Aiba%20M%5BAuthor%5D&cauthor=true&cauthor_uid=14767774). Does eradication of Helicobacter pylori reduce the risk of carcinogenesis in the residual stomach after gastrectomy for early gastric cancer? Comparison of mucosal lesions in the residual stomach before and after Helicobacter pylori eradication. *Langenbecks Arch Surg* 2004; **389**: 83-91 [PMID:14767774 DOI: 10.1007/s00423-003-0451-x]

57 **Thorban S**, Böttcher K, Etter M, Roder JD, Busch R, Siewert JR. Prognostic factors in gastric stump carcinoma. *Ann Surg* 2000; **231**: 188-194 [PMID: 10674609 DOI: 10.1097/00000658-200002000-00006]

58 **Costa-Pinho A**, Pinto-de-Sousa J, Barbosa J, Costa-Maia J. Gastric stump cancer: more than just another proximal gastric cancer and demanding a more suitable TNM staging system. *Biomed Res Int* 2013; **2013**: 781896 [PMID: 24151622 DOI: 10.1155/2013/781896]

59 **Sasako M**, Maruyama K, Kinoshita T, Okabayashi K. Surgical treatment of carcinoma of the gastric stump. *Br J Surg* 1991; **78**: 822-824 [PMID: 1873711 DOI: 10.1002/bjs.1800780718]

60 **Ikeguchi M**, Kondou A, Shibata S, Yamashiro H, Tsujitani S, Maeta M, Kaibara N. Clinicopathologic differences between carcinoma in the gastric remnant stump after distal partial gastrectomy for benign gastroduodenal lesions and primary carcinoma in the upper third of the stomach. *Cancer* 1994; **73**: 15-21 [PMID: 8275417 DOI: 10.1002/1097-0142(19940101)73:1<15::AID-CNCR2820730105>3.0.CO;2-J]

61 **Han SL**, Hua YW, Wang CH, Ji SQ, Zhuang J. Metastatic pattern of lymph node and surgery for gastric stump cancer. *J Surg Oncol* 2003; **82**: 241-246 [PMID: 12672008]

62 **Li F**, Zhang R, Liang H, Liu H, Quan J, Zhao J. The pattern of lymph node metastasis and the suitability of 7th UICC N stage in predicting prognosis of remnant gastric cancer. *J Cancer Res Clin Oncol* 2012; **138**: 111-117 [PMID: 22048654 DOI: 10.1007/s00432-011-1034-9]

63 **Komatsu S**, Ichikawa D, Okamoto K, Ikoma D, Tsujiura M, Shiozaki A, Fujiwara H, Murayama Y, Kuriu Y, Ikoma H, Nakanishi M, Ochiai T, Kokuba Y, Otsuji E. Differences of the lymphatic distribution and surgical outcomes between remnant gastric cancers and primary proximal gastric cancers. *J Gastrointest Surg* 2012; **16**: 503-508 [PMID: 22215245 DOI: 10.1007/s11605-011-1804-3]

64 **Greene FL**. Management of gastric remnant carcinoma based on the results of a 15-year endoscopic screening program. *Ann Surg* 1996; **223**: 701-76; discussion 701-76; [PMID: 8645043 DOI: 10.1097/00000658-199606000-00008]

65 **Takenaka R**, Kawahara Y, Okada H, Tsuzuki T, Yagi S, Kato J, Ohara N, Yoshino T, Imagawa A, Fujiki S, Takata R, Nakagawa M, Mizuno M, Inaba T, Toyokawa T, Sakaguchi K. Endoscopic submucosal dissection for cancers of the remnant stomach after distal gastrectomy. *Gastrointest Endosc* 2008; **67**: 359-363 [PMID: 18226704 DOI: 10.1016/j.gie.2007.10.021]

66 **Hirasaki S**, Kanzaki H, Matsubara M, Fujita K, Matsumura S, Suzuki S. Treatment of gastric remnant cancer post distal gastrectomy by endoscopic submucosal dissection using an insulation-tipped diathermic knife. *World J Gastroenterol* 2008; **14**: 2550-2555 [PMID: 18442204 DOI: 10.3748/wjg.14.2550]

67 **Hoteya S**, Iizuka T, Kikuchi D, Yahagi N. Clinical advantages of endoscopic submucosal dissection for gastric cancers in remnant stomach surpass conventional endoscopic mucosal resection. *Dig Endosc* 2010; **22**: 17-20 [PMID: 20078659 DOI: 10.1111/j.1443-1661.2009.00912.x]

68 **Lee JY**, Choi IJ, Cho SJ, Kim CG, Kook MC, Lee JH, Ryu KW, Kim YW. Endoscopic submucosal dissection for metachronous tumor in the remnant stomach after distal gastrectomy. *Surg Endosc* 2010; **24**: 1360-1366 [PMID: 19997930 DOI: 10.1007/s00464-009-0779-6]

69 **Nishide N**, Ono H, Kakushima N, Takizawa K, Tanaka M, Matsubayashi H, Yamaguchi Y. Clinical outcomes of endoscopic submucosal dissection for early gastric cancer in remnant stomach or gastric tube. *Endoscopy* 2012; **44**: 577-583 [PMID: 22402983 DOI: 10.1055/s-0031-1291712]

70 **Nonaka S**, Oda I, Makazu M, Haruyama S, Abe S, Suzuki H, Yoshinaga S, Nakajima T, Kushima R, Saito Y. Endoscopic submucosal dissection for early gastric cancer in the remnant stomach after gastrectomy. *Gastrointest Endosc* 2013; **78**: 63-72 [PMID: 23566640 DOI: 10.1016/j.gie.2013.02.006]

71 **Tanaka S**, Toyonaga T, Morita Y, Fujita T, Yoshizaki T, Kawara F, Wakahara C, Obata D, Sakai A, Ishida T, Ikehara N, Azuma T. Endoscopic submucosal dissection for early gastric cancer in anastomosis site after distal gastrectomy. *Gastric Cancer* 2014; **17**: 371-376 [PMID: 23868403 DOI: 10.1007/s10120-013-0283-5]

72 **Choi YY**, Kwon IG, Lee SK, Kim HK, An JY, Kim HI, Cheong JH, Mliwa RT, Shin SK, Lee YC, Hyung WJ, Noh SH. Can we apply the same indication of endoscopic submucosal dissection for primary gastric cancer to remnant gastric cancer? *Gastric Cancer* 2014; **17**: 310-315 [PMID: 23695167 DOI: 10.1007/s10120-013-0265-7]

73 **Xiong JJ**, Nunes QM, Huang W, Tan CL, Ke NW, Xie SM, Ran X, Zhang H, Chen YH, Liu XB. Laparoscopic vs open total gastrectomy for gastric cancer: a meta-analysis. *World J Gastroenterol* 2013; **19**: 8114-8132 [PMID: 24307808 DOI: 10.3748/wjg.v19.i44.8114]

74 **Chen K**, Xu XW, Zhang RC, Pan Y, Wu D, Mou YP. Systematic review and meta-analysis of laparoscopy-assisted and open total gastrectomy for gastric cancer. *World J Gastroenterol* 2013; **19**: 5365-5376 [PMID: 23983442 DOI: 10.3748/wjg.v19.i32.5365]

75 **El-Sedfy A**, Brar SS, Coburn NG. Current role of minimally invasive approaches in the treatment of early gastric cancer. *World J Gastroenterol* 2014; **20**: 3880-3888 [PMID: 24833843 DOI: 10.3748/wjg.v20.i14.3880]

76 **Kim HS**, Kim BS, Lee IS, Lee S, Yook JH, Kim BS. Laparoscopic gastrectomy in patients with previous gastrectomy for gastric cancer: a report of 17 cases. *Surg Laparosc Endosc Percutan Tech* 2014; **24**: 177-182 [PMID: 24686356 DOI: 10.1097/SLE.0b013e31828f6bfb]

77 **Kwon IG**, Cho I, Guner A, Choi YY, Shin HB, Kim HI, An JY, Cheong JH, Noh SH, Hyung WJ. Minimally invasive surgery for remnant gastric cancer: a comparison with open surgery. *Surg Endosc* 2014; **28**: 2452-2458 [PMID: 24622766 DOI: 10.1007/s00464-014-3496-8]

78 **Nagai E**, Nakata K, Ohuchida K, Miyasaka Y, Shimizu S, Tanaka M. Laparoscopic total gastrectomy for remnant gastric cancer: feasibility study. *Surg Endosc* 2014; **28**: 289-296 [PMID: 24013469 DOI: 10.1007/s00464-013-3186-y]

79 **Tsunoda S**, Okabe H, Tanaka E, [Hisamori S](http://www.ncbi.nlm.nih.gov/pubmed/?term=Hisamori%20S%5BAuthor%5D&cauthor=true&cauthor_uid=25503677), [Harigai M](http://www.ncbi.nlm.nih.gov/pubmed/?term=Harigai%20M%5BAuthor%5D&cauthor=true&cauthor_uid=25503677), [Murakami K](http://www.ncbi.nlm.nih.gov/pubmed/?term=Murakami%20K%5BAuthor%5D&cauthor=true&cauthor_uid=25503677), [Sakai Y](http://www.ncbi.nlm.nih.gov/pubmed/?term=Sakai%20Y%5BAuthor%5D&cauthor=true&cauthor_uid=25503677). Laparoscopic gastrectomy for remnant gastric cancer: a comprehensive review and case series. *Gastric Cancer* 2014; Epub ahead of print [PMID: 25503677 DOI: 10.1007/s10120-014-0451-2]

80 **Son SY**, Lee CM, Jung DH, Lee JH, Ahn SH, Park do J, Kim HH. Laparoscopic completion total gastrectomy for remnant gastric cancer: a single-institution experience. *Gastric Cancer* 2015; **18**: 177-182 [PMID: 24477417 DOI: 10.1007/s10120-014-0339-1]

**P-Reviewer:** Huang CM **S-Editor:** Gong ZM

**L-Editor:** **E-Editor:**

**Table 1 Initial reconstruction, interval, and location of remnant gastric cancer based on primary disease**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Ref.** | **Primary disease** | **No. of patients** | **Initial reconstruction****(B-I/B-II/R-Y)** | **Interval (yr)** | **Location (Stomal/non-stomal)** |
| Tanigawa *et al*[8] 2002 | benign | 20 | 7/13 | 25.8 | 8/12 |
| cancer | 27 | 18/9 | 10.6 | 3/24 |
|  |  |  |  |  |  |
| An *et al*[22] 2007 | benign | 25 | - | 28.6 | 16/9 |
| cancer | 13 | - | 18.8 | 7/6 |
|  |  |  |  |  |  |
| Ohashi *et al*[23] 2007 | cancer | 108 | 71/281 | 7.5 | 14/94 |
|  |  |  |  |  |  |
| Schaefer *et al*[24] 2007 | benign | 19 | 1/18 | 34 | 11/8 |
|  |  |  |  |  |  |
| Ahn *et al*[25] 2008 | benign | 13 | 0/13 | 32.4 | 12/1 |
| cancer | 45 | 6/381 | 6.8 | 23/21 |
|  |  |  |  |  |  |
| Firat *et al*[26] 2009 | benign | 26 | 0/26 | 32 | 16/10 |
|  |  |  |  |  |  |
| Ojima *et al*[27] 2010 | benign | 17 | 12/5 | 22 | 8/9 |
| cancer | 21 | 16/5 | 9 | 2/19 |
|  |  |  |  |  |  |
| Mezhir *et al*[3] 2011 | benign | 105 | B-II: 97 | 32 | 72/33 |
|  |  |  |  |  |  |
| Komatsu *et al*[28] 2012 | benign | 19 | 4/15 | 30 | 9/10 |
| cancer | 14 | 12/11 | 12 | 2/12 |
|  |  |  |  |  |  |
| Li *et al*[29] 2013 | benign | 88 | 28/60 | 32.1 | 55/33 |
| cancer | 24 | 14/10 | 16.8 | 9/15 |
|  |  |  |  |  |  |
| Tokunaga *et al*[30] 2013 | benign | 89 | 23/66 | 31.0 | 46/43 |
| cancer | 78 | 59/171 | 9.4 | 13/65 |
|  |  |  |  |  |  |
| Leo *et al*[31] 2014 | benign | 176 | 10/167 | 34.6 | 71/105 |

1remining cases were reconstructed by Roux-en-Y, Stomal: anastomotic site, non-stomal: non-anastomotic site. B-I: Billroth-I; B-II: Billroth-II; R-Y: Roux-en-Y.

**Table 2 The success rate of *Helicobacter pylori* eradication therapy in remnant stomach**

|  |  |  |  |
| --- | --- | --- | --- |
| **Ref.** | **No. of patients** | **Regimen of eradication** | **Success rate,*****n* (%)** |
| Matsukura *et al*[42] 2003 | 20 | Dual therapy | 14 (70.0) |
| lansoprazole 60 mg, AMPC 1500 mg for 2 wk |
| 20 | Triple therapy | 18 (90.0) |
| lansoprazole 60 mg, AMPC 1500 mg, CAM 800 mg daily for 1 wk |
| Onoda *et al*[52] 2005 | 33 | Triple therapy | 30 (90.9) |
| rabeprazole 20 mg, AMPC 1500 mg, CAM 800 mg daily for 1 wk |
| Kim *et al*[53] 2008 | 61 | Triple therapy | 53 (86.9) |
| rabeprazole 20 mg, AMPC 2000 mg, CAM 1000 mg daily for 1 wk |

AMPC: amoxicillin; CAM: clarithromycin.**Table 3 The incidence of lymph node metastases of remnant gastric cancer and primary proximal gastric cancer in the splenic hilar region, around the splenic artery, in the lower mediastinum, and in the jejunal mesentery**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Ref.** | **No. of patients** | **Splenic hilar****(No. 10)** | **Splenic artery****(No. 11)** | **Lower mediastinum** | **Jejunal mesentery lymph node metastases** |
| **No. 110** | **No. 111** |
| Sasako *et al*[59]1991 | RGC | 52 | 15.2% | 23.5% | - | - | 15.2% |
| PPGC | 656 | 10.4% | 10.4% | - | - | - |
| Ikeguchi *et al*[60] 1994 | RGC | 20 | 0% | 25.0% | - | - | 10.0% |
| PPGC | 266 | 11.3% | 15.4% | - | - | - |
| Thorban *et al*[57] 2000 | RGC | 47 | - | - | - | - | 31.9% |
| PPGC | 498 | - | - | - | - | - |
| Tanigawa *et al*[8] 2002 | RGC | 32 | 8.3% | 9.1% | - | 50.0% | 60.0% |
| PPGC | 310 | 16.7% | 21.7% | - | 6.7% | - |
| Han *et al*[61] 2003 | RGC | 67 | 60.0% | 72.3% | - | 50.0% | 16.7% |
| PPGC | - | - | - | - | - | - |
| Schaefer *et al*[24] 2007 | RGC | 19 | - | - | - | - | 22.2% |
| PPGC | 194 | - | - | - | - | - |
| Li *et al*[62] 2012 | RGC | 83 | 21.4% | 14.2% | 33.3% | 33.3% | 54.5% |
| PPGC | 300 | 36.4% | 16.7% | 13.6% | 13.0% | - |
| Komatsu *et al*[63] 2012 | RGC | 33 | 12.1% | - | - | - | 67% |
| PPGC | 207 | 6.8% | - | - | - | - |
| Leo *et al*[31] 2014 | RGC | 176 | 10.0% | 7.1% | - | - | 46.4% |
| PPGC | - | - | - | - | - | - |

RGC: remnant gastric cancer; PPGC: primary proximal gastric cancer.

**Table 4 Comparison of operative outcomes between remnant gastric cancer and primary proximal gastric cancer**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Ref.** | **No. of patients** | **R0 resection rate (%)** | **Adjacent organ resection rate** | **Prognosis after curative resection** |
| Thorban *et al*[57] 2000 | RGC | 50 | 85.1 | colon: 19.1%, pancreas: 6.4%, liver: 8.5% | MST: 30.9 mo |
| PPGC | 516 | 73.9 | colon: 0%, pancreas: 2.8%, liver: 4.9% | MST: 32.1 mo |
| Tanigawa *et al*[8] 2002 | RGC | 47 | 68.1 | 68.1% | 5-yr OS: 56% |
| PPGC | 310 | - | - | 5-yr OS: 53% |
| An et al[22] 2007 | RGC | 38 | 92.1 | - | 5-yr OS: 54% |
| PPGC | 794 | 86.4 | - | 5-yr OS: 63% |
| Schaefer *et al*[24] 2007 | RGC | 19 | - | colon: 5.3%, pancreas: 10.5%, liver: 5.3% | 5-yr OS: 71% |
| PPGC | 194 | - | - | 5-yr OS: 48% |
| Mezhir *et al*[3] 2011 | RGC | 105 | 60.0 | colon: 10.1%, pancreas or liver: 5.8% | 5-yr OS: 53% |
| PPGC | 2099 | - | - | unknown |
| Komatsu *et al*[63] 2012 | RGC | 33 | 78.8 | colon: 6.1%, pancreas: 12.2%, liver: 6.1% | unknown |
| PPGC | 207 | - | colon: 2.9%, pancreas: 4.3%, liver: 1.9% | unknown |
| Tokunaga *et al*[30] 2013 | RGC | 167 | 88.0 | - | 5-yr OS: 54% |
| PPGC | 755 | 93.8 | - | 5-yr OS: 78% |

RGC: remnant gastric cancer; PPGC: primary proximal gastric cancer; MST: median survival time; OS: overall survival.

**Table 5 Clinical outcomes of endoscopic submucosal dissection for remnant gastric cancer *n* (%)**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Ref.** | **No. of ESD****lesions** | **No. of lesions located on the suture line** | **En bloc resection rate**  | **Complete resection rate** | **Complications** |
| **Perforation** | **Bleeding** |
| Takenaka *et al*[65] 2008 | 31 | 12 (38.7) | 30 (96.8) | 23 (74.2) | 4 (12.9) | 0 |
| Hirasaki *et al*[66] 2008 | 17 | - | 17 (100) | 14 (82.4) | 0 | 3 (17.6) |
| Hoteya *et al*[67] 2010 | 401 | - | - | 38 (95.0) | 1 (2.5) | 2 (5.0) |
| Lee *et a*l[68] 2010 | 13 | 6 (46.2) | 13 (100) | 11 (84.6) | 0 | 0 |
| Nishide *et al*[69] 2012 | 622 | 29 (46.8) | 59 (95.2) | 53 (85.5) | 11 (17.7) | 5 (8.2) |
| Nonaka *et al*[70] 2013 | 94 | - | 86 (91.5) | 77 (81.9) | 2 (2.1) | 2 (2.1) |
| Tanaka *et al*[71] 2014 | 33 | 11 (33.3) | 33 (100) | 31 (93.9) | 3 (9.1) | 1 (3.0) |

1including 9 patients of gastric tube cancer after esophagectomy; 2including 14 patients of gastric tube cancer after esophagectomy. ESD: endoscopic submucosal dissection.

**Table 6 Clinical outcomes of laparoscopic surgery for remnant gastric cancer**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Ref.** | **Type of****procedure** | **No. of****patients** | **Operation time (min)** | **Blood loss (ml)** | **Conversion to open surgery** | **No. of retrieved****lymph nodes** | **Complication rate (%)** | **5-yr OS (%)** |
| Kim *et al*[76] 2014 | Lap | 171 | 197 | - | 0% | 12.9 | 23.5 | - |
| Open | 50 | 149 | - | - | - | 30.0 | - |
| Kwon *et al*[77] 2014 | Lap | 182 | 266 | 182 | 5.6% | 8 | 33.3 | 100 |
| Open | 58 | 203 | 193 | - | 7 | 44.8 | 94.9 |
| Nagai *et al*[78] 2014 | Lap | 12 | 362 | 69 | 0% | 23.7 | 0 | 77.8 |
| Open | 10 | 271 | 746 | - | 15.9 | 20.0 | 72.9 |
| Tsunoda *et al*[79] 2014 | Lap | 10 | 325 | 55 | 0% | 22 | 10.0 | - |
| Open | 6 | 289 | 893 | - | 7 | 33.3 | - |
| Son *et al*[80] 2015 | Lap | 17 | 234 | 228 | 47.1% | 18.8 | 35.3 | 67 |
| Open | 17 | 170 | 184 | - | 22.3 | 29.4 | 60.3 |

1including 10 cases of distal gastrectomy; 2including 8 cases of robotic surgery. OS: overall survival.