Gastric cancer arising from the remnant stomach after distal gastrectomy: A review

Shinsuke Takeno, Tatsuya Hashimoto, Kenji Maki, Ryosuke Shibata, Hironari Shiwaku, Ippei Yamana, Risako Yamashita, Yuichi Yamashita

Department of Gastroenterological Surgery, Fukuoka University Faculty of Medicine, Fukuoka 814-0180, Japan

Author contributions: Takeno S designed and wrote this review article; Hashimoto T, Maki K, Shibata R, Shiwaku H, Yamana I and Yamashita R collected the references and analyzed those data in each section “Epidemiology”, “Effects of Reconstruction during Distal Gastrectomy on Carcinogenesis in the Remnant Stomach”, “Helicobacter pylori Infection”, “Epstein-Barr Virus Infection in the Remnant Stomach”, “Clinicopathological Characteristics” and “Endoscopic Treatment”; Yamashita Y directed and proofread this review article.

Correspondence to: Shinsuke Takeno, MD, PhD, Department of Gastroenterological Surgery, Fukuoka University Faculty of Medicine, Nanakuma 7-45-1, Johnan-ku, Fukuoka 814-0180, Japan. takeno@fukuoka-u.ac.jp

Received: October 25, 2013 Revised: January 22, 2014 Accepted: May 28, 2014 Published online: October 14, 2014

Abstract

Gastric stump carcinoma was initially reported by Balfour in 1922, and many reports of this disease have since been published. We herein review previous reports of gastric stump carcinoma with respect to epidemiology, carcinogenesis, Helicobacter pylori (H. pylori) infection, Epstein-Barr virus infection, clinicopathologic characteristics and endoscopic treatment. In particular, it is noteworthy that no prognostic differences are observed between gastric stump carcinoma and primary upper third gastric cancer. In addition, endoscopic submucosal dissection has recently been used to treat gastric stump carcinoma in the early stage. In contrast, many issues concerning gastric stump carcinoma remain to be clarified, including molecular biological characteristics and the carcinogenesis of H. pylori infection. We herein review the previous pertinent literature and summarize the characteristics of gastric stump carcinoma reported to date.

Key words: Remnant gastric cancer; Distal gastrectomy; Carcinogenesis; Helicobacter pylori; Endoscopic submucosal dissection

Core tip: Recent studies concerning gastric stump carcinoma were reviewed. Its carcinogenesis took more than 300 mo after distal gastrectomy for benign disease, in contrast to 100 mo for primary gastric cancer. Higher carcinogenetic risk was reported by molecular biological analysis in patients treated with Billroth II reconstruction than with Billroth I. Eradication of Helicobacter pylori in the remnant stomach improved the degree of inflammation and the pH level, and might prevent the development of carcinogenesis. Endoscopic treatment for gastric stump carcinoma has been recently reported, therefore, endoscopic surveillance should be repeated after distal gastrectomy.

INTRODUCTION

Gastric cancer is the second leading cause of cancer-related death in Asia and the fourth most common malignan-
cy worldwide\textsuperscript{[11,12]}. The five-year survival of patients with gastric cancer is estimated to be approximately 20\%, and it has been reported that only surgery, including lymphadenectomy, can provide curative effects\textsuperscript{[3,4]}. However, recent advances in early detection and the development of anticancer drugs have prolonged the prognosis\textsuperscript{[5,6]}.

Gastric stump carcinoma was originally defined as gastric cancer arising from the remnant stomach more than five years after distal gastrectomy for benign disease\textsuperscript{[7,8]}: The incidence of gastric stump carcinoma is estimated to be 1\%-2\%, according to the current literature\textsuperscript{[11,12]}. However, most cases of gastric cancer arising from the remnant stomach after distal gastrectomy involve a second primary gastric cancer, as the rate of gastrectomy against peptic ulcers has decreased for the last three decades due to the development of gastric acid inhibitor drugs and improvements in the prognosis of patients with gastric cancer, as described above\textsuperscript{[6,7,13]}. In addition, the development of endoscopic technology and periodical endoscopic surveillance has enabled clinicians to detect gastric cancer of the remnant stomach in the early stage, which may improve the unfavorable prognosis of patients with gastric stump carcinoma\textsuperscript{[13]}.

The characteristics of remnant gastric cancer may have changed from those previously reported in the literature. Therefore, we reviewed recent articles and attempted to clarify the modern characteristics, carcinogenesis, diagnosis and optimal treatment of remnant gastric cancer.

### EPIDEMIOLOGY

In 1922, Balfour first reported that, with respect to gastric cancer arising from the remnant stomach after surgery, the most important factor affecting life expectancy after surgery for gastric ulcers is the occurrence of gastric cancer, which accounts for approximately 40\% of the total number of deaths in this patient population\textsuperscript{[14]}. That series included gastric cancer as well as benign ulcers as the primary lesions and reported the incidence of remnant gastric cancer to be 3\% after resection of ulcerous lesions.

A population-based study of patients who underwent distal gastrectomy for benign disease was recently reported from Sweden. In that study, the incidence of remnant gastric cancer was 0.74\%, which is similar to the findings of previous reports\textsuperscript{[11,12,18]}. In addition, it is of interest that the incidence of gastric stump carcinoma is not higher than expected and increases only after more than 30 years after surgery for benign disease\textsuperscript{[15]}. Several reports have found that it takes more than 300 mo for gastric stump carcinoma to arise from the remnant stomach after distal gastrectomy for benign disease, in contrast to the approximately 100 mo observed following gastrectomy for primary gastric cancer (Tables 1 and 2\textsuperscript{[12,6-22]}).

### EFFECTS OF RECONSTRUCTION DURING DISTAL GASTRECTOMY ON CARCINOGENESIS IN THE REMNANT STOMACH

It has been reported that a reduction in the level of serum gastrin and gastroduodenal reflux are factors for carcinogenesis in the remnant stomach after distal gastrectomy. This finding has also been experimentally evaluated by Miwa et al\textsuperscript{[20]}. Billroth II reconstruction is more frequently associated with atrophic changes and an increased S phase cell count in the proliferative zone compared to that observed following treatment with Billroth I in the Wister rat model. In addition, it has been reported that intestinal metaplasia is rare. However, to the best of our knowledge, no clinical studies have compared the incidence of atrophic changes and intestinal metaplasia between patients treated with the Billroth I and II methods. The interval between primary distal gastrectomy and the diagnosis of stump carcinoma is significantly longer in patients treated with Billroth I reconstruction than in those treated with Billroth II reconstruction, according to a review of previous clinical retrospective studies\textsuperscript{[16-19,27,22]}.

In addition, there is a consensus that gastric stump carcinoma tends to arise from sites of anastomosis in patients treated with Billroth II reconstruction, in contrast to non-anastomotic sites in patients treated with

### Table 1 Interval between primary gastric cancer and gastric stump carcinoma

| Ref. | Previous disease (benign/malignancy) | Interval (mo) (all cases) | Interval (mo) (benign/malignancy) |
|------|-----------------------------------|--------------------------|----------------------------------|
| Kaneko et al\textsuperscript{[19]} 1998 | 21/22 | 180 | 288/118 |
| Takeno et al\textsuperscript{[18]} 2006 | 11/21 | 360/63 |
| Ohashi et al\textsuperscript{[23]} 2007 | 90 | |
| Ahn et al\textsuperscript{[24]} 2008 | 13/45 | 150 | 384/83 |
| Taniyama et al\textsuperscript{[25]} 2010 | 578/309 | 252 |
| Ojima et al\textsuperscript{[26]} 2010 | 17/21 | 180 | 264/108 |
| Komatsu et al\textsuperscript{[27]} 2012 | 19/14 | 240 | 360/144 |
| Li et al\textsuperscript{[28]} 2013 | 88/24 | 384/204 |

### Table 2 Interval and location of gastric stump carcinoma by reconstruction

| Ref. | Primary reconstruction | Interval (mo) | Location |
|------|------------------------|---------------|----------|
| Takeno et al\textsuperscript{[21]} 2006 | Billroth I/II | 21/11 | B-Ⅰ/II non/B-Ⅰ/II non |
| Ohashi et al\textsuperscript{[16]} 2007 | 71/28 | 7/64/5/23 |
| Ahn et al\textsuperscript{[20]} 2008 | 26/25 | 11/15/16/9 |
| Taniyama et al\textsuperscript{[25]} | 368/519 | 252/372 | 81/176/289/114 |
| 2010 | Komatsu et al\textsuperscript{[21]} | 16/16 | 144/384 |
| 2012 | Li et al\textsuperscript{[28]} 2013 | 42/70 | 19/23/45/25 |

B-Ⅰ: Billroth I ; B-Ⅱ: Billroth II ; ana: Anastomosis site; non: Non-anastomosis site.
Billroth I reconstruction, and that the incidence of gastric stump carcinoma is correlated with that of gastro-duodenal reflux, similar to that observed in experimental rat models\(^{16-19,21,22}\).

The condition of the remnant stomach mucosa after distal gastrectomy has been biologically examined at the molecular level. Tanigawa reported that the apoptotic index, p53 labeling index and Ki-67 labeling index are significantly higher in patients treated with Billroth II reconstruction than in those treated with Billroth I reconstruction\(^{28}\). In addition, Nakachi et al\(^{25}\) and Aya et al\(^{24}\) demonstrated a higher frequency of microsatellite instability in patients with gastric stump carcinoma (88.9%, 43%) than in those with primary upper third gastric carcinoma (20%, 6%). Furthermore, Aya reported a significantly higher frequency of microsatellite instability, as well as a higher frequency of both hMLH1 and hMSH2 inactivation, in patients treated with Billroth II reconstruction than in those treated with Billroth I reconstruction\(^{24}\).

Taking both clinicopathological and molecular biological changes into consideration, the Billroth I procedure is thus considered to be preferable to the Billroth II method, at least with respect to preventing the development of gastric stump carcinoma.

Roux-en-Y reconstruction has recently been adopted for reconstruction after distal gastrectomy to prevent gastro-duodenal reflux. The time for which the remnant gastric mucosa is exposed to bile reflux is shorter and the degree of remnant gastritis is more mild in patients treated with Roux-en-Y reconstruction than in those treated with Billroth II reconstruction\(^{27}\). Both the latest multi-institutional randomized controlled study and a meta-analysis support this finding, and it appears that a consensus has been reached on this issue\(^{28-30}\). No reports have thus far suggested that the incidence of gastric stump carcinoma is lower in patients treated with Roux-en-Y reconstruction than in those treated with Billroth I reconstruction. However, Roux-en-Y reconstruction is preferred from the viewpoint of reducing the incidence of gastro-duodenal reflux and remnant gastric mucosal injury related to gastric carcinogenesis.

**HELCOBACTER PYLORI INFECTION**

*Helicobacter pylori* (H. *pylori*) infection is a well-known major causative factor of carcinogenesis in the stomach. Nagahata reported that the rate of infection following gastrectomy gradually decreases over time. Recent studies have also examined the frequency of *H. pylori* infection in the remnant stomach after distal gastrectomy. The rate of infection ranges from 50% to 68.2% among all patients treated with distal gastrectomy, 55.6% to 72.2% among patients treated with Billroth I reconstruction and 58.3% to 66.7% among patients treated with Billroth II reconstruction (Table 3)\(^{[31-34]}\). Only one series has suggested the rate of infection to be lower in patients treated with the Roux-en-Y method, and further studies are thus required to clarify this issue\(^{[35]}\). It therefore appears that there are no significant differences between Billroth I and II reconstruction. Matsukura et al\(^{[35]}\) reported that eradication with dual and triple therapy is successful in 70% and 90% of *H. pylori* patients who undergo distal gastrectomy, respectively, and that the therapeutic efficacy is the same in patients treated with and without distal gastrectomy. It has also been demonstrated that the degree of inflammation improves and the pH level normalizes following eradication of *H. pylori* in the remnant stomach\(^{[36]}\). Therefore, treatment with eradication of *H. pylori* in the remnant stomach is recommended to prevent the development of gastric stump carcinoma, although no significant correlations have been reported between *H. pylori* infection and carcinogenesis in the remnant stomach.

**EPSTEIN-BARR VIRUS INFECTION IN THE REMNANT STOMACH**

Infection with the Epstein-Barr (EB) virus has been reported to be associated with various cancers, including stomach cancer. A few series have examined EB virus infection in patients with gastric stump carcinoma. According to these studies, the rate of infection ranges from 22.2% to 41.2% among all patients treated with distal gastrectomy, 0% to 12.5% among patients treated with Billroth I reconstruction and 30.4% to 58.3% among patients treated with Billroth II reconstruction (Table 4)\(^{[19,34,37]}\). Therefore, a higher rate of infection with the EB virus has been demonstrated in patients treated with Billroth II reconstruction.

In addition, EB-virus infection has been suggested to be correlated with the incidence of gastritis cystic polysposa and may also facilitate the development of *de novo* gastric stump carcinoma\(^{[17]}\).
Table 5  Clinicopathologic characteristics of gastric stump carcinoma

| Ref.                  | Patients age | pT (1/2/3/4)   | pN (positive/negative) | pM (positive/negative) | pStage | 5-yr survival |
|-----------------------|--------------|----------------|------------------------|------------------------|--------|---------------|
| Takeno et al[16,17], 2006 | 68.7         | 10/22 (1,2,3,4) | 12/20                  | 4/28                   | 21/11  | (1,2,3,4)    |
| Ohashi et al[18], 2007 | 67           | 67/16/6/17     | 13/84                  | 5/10                   | 77/62  | (1,2,3,4)    |
| Ahn et al[19], 2008   | 18/17/0/19   | 25/29          | 10/42                  |                        | 26/32  | (1,2,3,4)    |
| Ahn et al[20], 2008   | 58           | 15/31 (1,2,3,4) | 19/25                  | 17/41                  | 63.4%  | (3-yr)       |
| Tanigawa et al[21], 2010 | 68         | 315/245/197/130 | 534/327               | 26/661                 |        |               |
| Komatsu et al[22], 2012 | 68           | 10/22 (1,2,3,4) | 14/13                  |                        | 17/15  | (1,2,3,4)    |
| Li et al[23], 2013    | 1/3/44/64    | 66/46          | 31/81                  | 5/16/62/31             | 11%    |               |

Table 6  Clinicopathological comparison between primary upper third gastric cancer and gastric stump carcinoma

| Clinicopathologic characteristics | Ikeguchi et al[39], 1993 | P value | Chen et al[40], 1996 | P value | Newman et al[41], 1997 | P value | Komatsu et al[42], 2012 | P value |
|----------------------------------|--------------------------|---------|----------------------|---------|------------------------|---------|------------------------|---------|
| pT (1/2/3/4)                     | 63/15/157/31             | NS      | 5/30/88/20           | NS      | 11/15/46/7             | NS      | 69/75/54/9             | 0.07    |
| PUTGC                            | 4/3/7/6                  |         |                      |         | 7/6/11/1               | NS      | 10/10/7/6              |         |
| GSC                              |                          |         |                      |         | 69/75/54/9             | 0.07    |                       |         |
| pN (negative/positive)           |                          |         |                      |         | 0.07                   |         |                       |         |
| PUTGC                            | 99/167                   | NS      | 47/86                | NS      | 24/54                  | NS      | 118/89                | 0.7     |
| GSC                              | 11/9                     |         | 10/15                | NS      | 14/11                  | NS      | 20/13                 |         |
| M (negative/positive)            |                          |         |                      |         |                       |         |                       |         |
| PUTGC                            | 127/16                   | NS      | 20/5                 | NS      | Nov-68                 | NS      |                       |         |
| GSC                              | 20/5                     |         | 22/3                 | NS      |                       |         |                       |         |
| 5-yr survival                    |                          |         |                      |         |                       |         |                       |         |
| PUTGC                            | 62.1%                    | NS      | 25%                  | 0.31    | 37%                    | 0.1     | 63%                   | 0.67    |
| GSC                              | 52.5%                    |         | 46%                  |         |                       |         |                       |         |

PTUGC: Primary upper third gastric cancer; GSC: Gastric stump carcinoma; NS: Not significant.

**CLINICOPATHOLOGICAL CHARACTERISTICS**

The clinicopathological characteristics of gastric stump carcinoma have been analyzed in many reports, as summarized in Table 5[16-19,21,22,38]. For example, it has been reported that the prognosis of gastric stump carcinoma is unfavorable compared to that of primary gastric cancer, which may result from the more advanced stage of disease observed at diagnosis. There is currently no consensus regarding this issue based on a Japanese nationwide report of gastric cancer, although unevenness in the disease stage at diagnosis has been observed in various studies[39].

It has also been reported that there have been no remarkable changes in the number of gastric stump carcinoma patients with progressive tumor invasion. In contrast, the number of patients with progressive cancer invasion has been reported to gradually decrease in Japan since 1991, according to data for resected gastric cancer. Among patients with lymph node metastasis, there are no significant trends, as approximately half of all such patients were found to have node metastasis in a Japanese nationwide study and be negative for node metastasis in the previous literature regarding gastric stump carcinoma.

There have been several reports of prognostic analyses comparing gastric stump carcinoma and primary upper third gastric cancer[19-22] (Table 6). All such studies have suggested that there are no significant differences in either the prognosis or rate of progression between these two diseases. In contrast, it is of interest that gastric stump carcinoma exhibits a more favorable prognosis than primary upper third gastric cancer in patients with stage I or II disease and, inversely, a more unfavorable prognosis in patients with stage III or IV disease[40]. Concerning this result, Chen et al[20] reported that the left gastric artery is usually resected during distal gastrectomy, which may change the lymphatic flow and thereby influence the difference in prognosis observed in analyses of the cancer stage. Ikeguchi et al[39] also reported the incidence of jejuna mesenteric lymph node metastasis to be increased in patients with gastric stump carcinoma; these results may correlate with those of Chen. Controversially, Newman et al[41] reported that there are no prognostic differences between gastric stump carcinoma and upper third primary gastric cancer, even when the analysis is classified according to the cancer stage. Meta-analyses and/or multi-institutional randomized controlled studies with large series are therefore required to clarify these controversial results, although it may be difficult to conduct such studies due to the rarity of the disease.

**ENDOSCOPIC TREATMENT**

Previously, radical resection was the only curable treatment for gastric stump carcinoma, as observed in the setting of primary gastric cancer. However, advancements in endoscopic diagnosis and the popularization of periodic endoscopic screening after gastrectomy have enabled clinicians to detect gastric stump carcinoma at the early
stage. Hosokawa reported that 15 patients with gastric stump carcinoma were detected among 509 patients who underwent distal gastrectomy over more than 10 years, 12 of whom were diagnosed at an early stage, and concluded that endoscopic surveillance should be repeated every two to three years after distal gastrectomy²⁰¹. Similarly, several studies including small series of endoscopic treatment for gastric stump carcinoma have recently been reported, as summarized in Table 7. 𝑎– 𝑖.

Endoscopic submucosal dissection for gastric stump carcinoma (a (%))

| Ref.              | No. of ESD cases | En bloc resection | Complete resection | Mortality | Delayed bleeding | Perforation |
|-------------------|------------------|-------------------|--------------------|-----------|------------------|-------------|
| Takenaka et al²⁰⁰⁸ | 31               | 30 (97)           | 23 (74)            | 0         | 0                | 4 (13)      |
| Hirasaki et al²⁰⁰⁸| 17               | 17 (100)          | 14 (82)            | 0         | 3 (18)           | 0           |
| Lee et al²⁰¹⁰     | 13               | 13 (100)          | 12 (92.3)          | 0         | 0                | 0           |
| Nonaka et al²⁰¹³  | 139              | 131 (94)          | 118 (85)           | 0         | 2 (1.4)          | 2 (1.4)     |
| Tanaka et al²⁰¹³  | 33               | 33 (100)          | 31 (94)            | 0         | 1 (3)            | 3 (9)       |

ESD: Endoscopic submucosal dissection.

CONCLUSION

Clarifying the differences in the characteristics of gastric stump carcinoma and primary gastric cancer may enable clinicians to make an early diagnosis and improve clinical outcomes in patients with gastric stump carcinoma. In addition, multi-institutional analyses using large series may positively contribute to clarifying these issues.

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. Kamangar F, Dores GM, Anderson WF. Patterns of cancer incidence, mortality, and prevalence across five continents: defining priorities to reduce cancer disparities in different geographic regions of the world. J Clin Oncol 2006; 24: 2137-2150 [PMID: 16682732 DOI: 10.1200/JCO.2005.05.2308]

3. Kim JP, Lee JH, Kim SJ, Yu HJ, Yang HK. Clinicopathologic characteristics and prognostic factors in 10 783 patients with gastric cancer. Gastric Cancer 1998; 1: 125-133 [PMID: 9957069 DOI: 10.1007/BF012005006]

4. Hundahl SA, Phillips JL, Menck HR. The National Cancer Data Base Report on poor survival of U.S. gastric carcinoma patients treated with gastrectomy: Fifth Edition American Joint Committee on Cancer staging, proximal disease, and the “different disease” hypothesis. Cancer 2000; 88: 921-932 [PMID: 10679663 DOI: 10.1002/SIC.1097-0142(20000215)[4:921::AID-CNCR24]3.0.CO;2-S]

5. Miska S, Benhamiche AM, Jouve JL, Rat P, Faivre J. Prognostic factors after curative resection for gastric cancer. A population-based study. Eur J Cancer 2000; 36: 390-396 [PMID: 10708942 DOI: 10.1016/S0959-8049(99)00380-1]

6. Maruyama K, Kaminishi M, Hayashi K, Isobe Y, Honda I, Katal H, Araik, K, Kodera Y, Nashimoto A. Gastric cancer treated in 1991 in Japan: data analysis of nationwide registry. Gastric Cancer 2006; 9: 51-66 [PMID: 16767357 DOI: 10.1007/s10120-006-0370-y]

7. Sasaki M, Sakuramoto S, Katai H, Kinoshita T, Furukawa H, Yamaguchi T, Nashimoto A, Fujii M, Nakajima T, Ohashi Y. Five-year outcomes of a randomized phase III trial comparing adjuvant chemotherapy with S-1 versus surgery alone in stage II or III gastric cancer. J Clin Oncol 2011; 29: 4387-4393 [PMID: 22010012 DOI: 10.1200/JCO.2011.36.5908]

8. Pointer R, Schwab G, Königgräzer A, Bodner E, Schmid KW. Gastric stump cancer: etiopathological and clinical aspects. Endoscopy 1989; 21: 115-119 [PMID: 2743940 DOI: 10.1055/s-2007-1012917]

9. Safatle-Ribeiro AV, Ribeiro U, Reynolds JC. Gastric stump cancer: what is the risk? Dig Dis 1998; 16: 159-168 [PMID: 9618135 DOI: 10.1159/000016860]

10. Thorban S, Böttcher K, Ettner M, Roder JD, Busch R, Siewert JR. Prognostic factors in gastric stump carcinoma. Ann Surg 2000; 231: 188-194 [PMID: 10674609 DOI: 10.1097/00000658-20000200-00006]

11. Kodera Y, Yamamura Y, Torii A, Usaka K, Hirai T, Yasui K, Morimoto T, Kato T, Kito T. Incidence, diagnosis and significance of multiple gastric cancer. Br J Surg 1995; 82: 1540-1543 [PMID: 855813 DOI: 10.1002/bjs.1800821127]

12. Kaneko K, Kondo H, Saito D, Shirao K, Yamaguchi H, Yokota T, Yamao G, Sano T, Sasako M, Yoshida S. Early gastric stump cancer following distal gastrectomy. Gut 1998; 43: 342-344 [PMID: 9863478 DOI: 10.1136/gut.43.3.342]

13. Willje LH, Clark CG, Alexander-Williams J, Bell PR, Kennedy TL, Kirk RM, Mackay C. Effect of cimetidine on surgery for duodenal ulcer. Lancet 1981; 1: 1307-1308 [PMID: 6112617 DOI: 10.1016/S0140-6736(81)91082-7]

14. Balfour DC, Factors influencing the life expectancy of patients operated on for gastric ulcer. Ann Surg 1922; 76: 405-408 [PMID: 17864703 DOI: 10.1097/00000658-19220900-00004]

15. 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/jpc.27614]

16. Takeno S, Noguchi T, Kimura Y, Fujisawa S, Kubo N, Kawahara K. Early and late gastric cancer arising in the remnant stomach after distal gastrectomy. Eur J Surg Oncol 2006; 32: 1191-1194 [PMID: 16797159 DOI: 10.1016/j.ejso.2006.04.018]

17. Ohashi M, Katai H, Fukagawa T, Gotoda T, Sano T, Sasako
Comparison of Billroth I and Roux-en-Y reconstruction after distal gastrectomy for gastric cancer: one-year postoperative effects for a multi-institutional RCT. *Ann Surg Oncol* 2013; 20: 1591-1597 [DOI: 10.1245/s10434-012-2704-9]

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

Matsukura N, Tajiiri 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 [DOI: 10.1007/s10120-003-0234-7]

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 [DOI: 10.1007/s11605-005-1589-9]

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 Gastroenterol Surg* 2007; 11: 1732-1740 [DOI: 10.1007/s11605-007-0302-0]

Kato S, Matsukura N, Matsuda N, Tsuchiya S, Naito Z, Tajiiri T. Normalization of pH level and gastric mucosa after eradication of H. pylori in the remnant stomach. *J Gastroenterol Hepatol* 2008; 23 Suppl 2: S258-S261 [DOI: 19120008 [DOI: 10.1111/j.1440-1746.2008.05447.x]

Nishikawa J, Yanai H, Hirano A, Okamoto T, Nakamura H, Matsukawa K, Kawano T, Miura O, Okita K. High prevalence of Epstein-Barr virus in gastric remnant carcinoma after Billroth-II reconstruction. * scand J Gastroenterol* 2002; 37: 825-829 [DOI: 10.1080/gas.37.825.829]

Kaizaki Y, Hosokawa O, Sakurai S, Fukayama M. Epstein-Barr virus-associated gastric carcinoma in the remnant stomach: de novo and metachronous gastric remnant carcinoma. *J Gastroenterol* 2005; 40: 570-577 [DOI: 10.1007/s11605-005-1590-3]

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. *Ann J Surg* 2007; 194: 143-147 [DOI: 17681792 DOI: 10.1016/j.amjsurg.2006.10.034]

Ikeguchi M, Kondou A, Shibata H, Yamashiro T, Tsutisani S, Maeta M, Kaibara N. Clinicopathologic differences between carcinoma in the gastric remnant stump after distal partial gastrectomy with Billroth II reconstruction is associated with high-level microsatellite instability. *Anticancer Res* 2006; 26: 1403-1411 [PMID: 16619551]

Fukuhara K, Osugi H, Takada N, Takeamura M, Higashino M, Kinoshita H. Clinicopathologic characteristics of remnant gastric cancer after a distal gastrectomy. *J Gastrointest Surg* 2010; 14: 12370787 DOI: 10.1007/s00268-002-6363-z]

Fukuhara K, Osugi H, Takada N, Takeamura M, Higashino M, Kinoshita H. Clinicopathologic characteristics of remnant gastric cancer after a distal gastrectomy. *J Gastrointest Surg* 2010; 14: 12370787 DOI: 10.1007/s00268-002-6363-z]
Takeno S et al. Review of gastric stump carcinoma

guchi 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]

45 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]

46 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]

47 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]

48 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]
