Introduction

Which is better survival of gastric cancer patients with Billroth I or Billroth II reconstruction after distal gastrectomy? This question remains unanswered and is both old and new among gastric surgeons. The advantages of Billroth I may be depended on the restoration of a physiological digestive tract circuit and only one anastomotic portion, but the procedure is technically more difficult than that of Billroth II for anastomotic tension. However, for the reason of restoring digestive tract continuity, this procedure is a standard operation for trainee surgeons for gastric cancer in Japan, but not in Western countries\(^1\). Therefore, at present, we undertake gastric resection with Billroth I reconstruction. However, when leakage occurs, there are severe problems in the clinical setting. Contrary to Billroth I reconstruction, Billroth II gastrojejunostomy is an easier technique for a trainee surgeon, because of the easier tensionless anastomosis and lower incidences of bile reflux and reflux esophagitis after gastrectomy. In general, a physiological digestive tract circuit is the most important value for cancer patients in Japan, while an easier technique with lesser postoperative morbidity is important for surgeons in Western countries.

Although surgeons undertake gastric resection for long-term good quality of life of patients and all surgeons and patients wish for long-term survival postoperatively, there are very few reports about the long-term effects of the resection status, type of reconstruction, or jejunal pouch formation on the greater than 10-year outcomes. This represents one of the fundamental problems in gastric surgery, together with that of duodenal passage advantages or disadvantages. Although many patients have received these procedures to date in Japan as well as worldwide, surgeons have published few reports for the results of reconstruction after gastrectomy, as reviewed and summarized by Piessen et al\(^1\), for reconstruction after gastrectomy.

Abstract

Background: The question in the title remains unanswered and also is both old and new among gastric surgeons. Although there have been many reports about the early-stage quality of life and postoperative morbidity, they have failed to conclude about the advantages of these two reconstructions after distal gastrectomy. In this study, we summarized more than 30 years of experience and evaluated whether the Billroth I or Billroth II reconstruction procedure is better for patient survival after distal gastrectomy.

Methods: From January 1977 to August 2005, a total of 1410 gastric cancer patients underwent distal gastrectomy with Billroth I \((n=1184)\) or Billroth II \((n=226)\) reconstruction in the Department of Gastroenterological Surgery, Tokai University. The 10- and 20-year follow-up cases numbered 980 (82.8\%) and 692 (58.4\%) for Billroth I, and 213 (94.2\%) and 195 (86.3\%) for Billroth II as of September 2009, respectively. Among them, 1015 patients (72.0\%) received curative resection and were followed to evaluate the types of recurrence.

Results: In the patients with Billroth I and Billroth II, the 5-, 10-, 15-, and 20-year survival rates were 77.4\%, 66.6\%, 56.0\%, and 45.7\%, and 39.7\%, 32.8\%, 25.9\%, and 19.6\%, respectively \((P<0.0001; \text{relative risk, 2.683; 95\% confidence interval, 2.261–3.183})\). The patients in stages IA and IIA showed significantly better survival with Billroth I than with Billroth II. The patients with Billroth II \(10/86, 11.6\%\) showed significantly higher hematogenous recurrence than those with Billroth I \(41/929, 4.4\%\).

Conclusions: If gastric cancer patients must receive distal gastrectomy, we recommend they receive Billroth I reconstruction.

Key Words: Gastric cancer, long-term survival, Billroth I and Billroth II reconstruction, distal gastrectomy

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We wonder whether surgeons have been under the false impression that there is no significant evidence regarding differences in survival between Billroth I and Billroth II because there are no definite high-quality controlled study reports about the long-term survival. Although this matter should still be discussed in the gastric surgical world, several reconstruction techniques are continuing to be performed. Almost all studies have focused on the early stage of patient satisfactory outcomes, such as nutritional status and quality of life, and keeping postoperative morbidity as low as possible, rather than on patient survival.

In this study, we summarized over 30 years of experience in the Department of Gastroenterological Surgery, Tokai University, and evaluated which procedure of Billroth I or Billroth II reconstruction is better for patient survival after distal gastrectomy.

**Materials and methods**

From January 1977 to August 2005, a total of 1410 gastric cancer patients underwent distal gastrectomy with Billroth I (n=1184) or Billroth II (n=226) reconstruction in the Department of Gastroenterological Surgery, Tokai University. Our department introduced the resident system from the beginning. After an attending doctor (a chief resident) gave information about the operative methods as well as the advantages or disadvantages of these two reconstructions to a patient admitted to our Department for treatment of gastric cancer, the patient was allowed to select one of the reconstruction procedures. As a result, almost all of the patients selected the physiological digestive tract circuit benefit associated with the Billroth I procedure.

The 10- and 20-year follow-up cases numbered 980 (82.8%) and 692 (58.4%) for Billroth I, and 213 (94.2%) and 195 (86.3%) for Billroth II as of September 2009, respectively. There were 987 men and 423 women, and the average age was 60.0 years (range, 21–91). The background characteristics of the patients in each group are summarized in Table 1. Among them, 1015 patients (72.0%) received curative resection and were followed to evaluate the types of recurrence. The types of recurrence at first diagnosis were divided into four groups: peritoneal, hematogenous (including liver, lung, and bone metastasis), lymphatic, and locoregional recurrence. The patients were routinely followed by an echogram and a blood test each year, and a CT scan was performed when the need arose.

Postoperative adjuvant therapy consisted of PSK, F, FPSK, MMC, MF, and MFPSK therapies. These therapies were designated as familial therapies for gastric cancers under the social insurance system in Japan. PSK therapy consisted of oral administration of 3.0 g/day after gastrectomy for >1 year. F therapy consisted of oral administration of fluoropyrimidines after gastrectomy for >1 year, namely 5-fluorouracil 150 mg/day, Tegafur 600 mg/day or UFT 600 mg/day, which all had a final active substance of 5-fluorouracil. MMC therapy consisted of intravenous injection of MMC 20 mg intraoperatively and/or 10 mg on postoperative day 1. FPSK therapy consisted of F+PSK therapy. MF therapy consisted of MMC+F therapy. MFPSK therapy consisted of MMC+F+PSK therapy.

All statistical analyses were carried out using SPSS software version 18 (SPSS Inc., Chicago, IL). A $\chi^2$-square test was used to compare the prevalences in patients. Differences were considered significant when $P<0.05$. The survival period of cancer patients was defined as the interval from gastrectomy to death, with data regarding survivors censored at the last follow-up (September 2010). Survival curves were calculated using the Kaplan–Meier product-limit estimate and differences in survival were assessed by the log-rank test and Cox univariate analyses with the relative risk (RR) and 95% confidence interval (95% CI).

**Results**

There were significant differences between patients with Billroth I and Billroth II for sex (males, 71.4% vs. 62.8%), tumor advancement, and number of lymph nodes examined (88.5% vs. 65.7%) (Table 1). Thirteen patients with Billroth II (9 cases) and Billroth I (4 cases) were died within 30-days, and 433 gastric cancer death (294 or 139 respectively), 57 other cancer death (45 or 12 respectively) and 212 non-cancer death (190 or 22 respectively) after gastrectomy as of September 2009.

In patients with Billroth I and Billroth II, the 5-, 10-, 15-, and 20-year survival rates were 77.4%, 66.6%, 56.0%, and 45.7%, and 39.7%, 32.8%, 25.9%, and 19.6%, respectively ($P<0.0001$; RR, 2.683; 95%CI, 2.261–3.183).

Fig. 1 shows the survival curves of patients who underwent distal gastrectomy with Billroth I and Billroth II according to the pTNM stage Ver. 4 classification. There were significant differences for stage I and stage IV patients who underwent distal gastrectomy with Billroth I and Billroth II (log-rank test, $P=0.034$ and $P<0.001$, respectively). Table 2 summarizes the results of the Cox univariate analyses according to the pTNM stages.

Table 3 shows the types of recurrence in 1015 patients with curative resection. There was significantly higher hematogenous recurrence in patients with Billroth II reconstruction (10/86, 11.6%) than in those with Billroth I reconstruction (41/929, 4.4%) ($P=0.003$, RR=2.85 (95% CI, 1.374-5.913)). There were no significant differences in residual gastric cancer incidence after operation between Billroth I and Billroth II, 2.0% (24/1183) and 1.3% (3/227), respectively. And also there were no significant differences in double cancer incidence after operation.
Table 1. Characteristics of the patients

| Billroth I | Billroth II | Total | p value |
|-----------|-------------|-------|---------|
| Gender | | | |
| F | 339 | 84 | 423 | | | |
| M | 845 | 142 | 987 | p=0.01 |
| Age | | | | |
| <64 | 728 | 130 | 858 | | | |
| 65- | 456 | 96 | 552 | ns | | |
| Depth of Cancer | | | | |
| t1-t2 m | 398 | 25 | 423 | | | |
| sm | 327 | 38 | 365 | | | |
| pm | 212 | 20 | 141 | | | |
| t3-t4 ss | 136 | 41 | 177 | | | |
| se | 126 | 73 | 199 | | | |
| si, sei | 3 | 15 | 18 | p<0.001 |
| unknown\textsuperscript{a} | 73 | 14 | 87 | | | |
| Lymph node metastasis | | | | |
| (-) | 796 | 77 | 873 | | | |
| (+) | 315 | 128 | 443 | p<0.001 |
| unknown\textsuperscript{a} | 73 | 21 | 94 | | | |
| pTNM stage (Ver. 4) | | | | |
| stage I A | 675 | 56 | 731 | | | |
| IB | 190 | 19 | 209 | | | |
| II | 125 | 23 | 148 | | | |
| IIIA | 78 | 22 | 100 | | | |
| IIIB | 19 | 6 | 25 | | | |
| IV | 97 | 100 | 197 | p<0.001 |
| Histology | | | | |
| diff\textsuperscript{b} | 703 | 128 | 831 | | | |
| undiff\textsuperscript{c} | 481 | 98 | 579 | ns | | |
| No. of lymph nodes examined | | | | |
| 1-14 | 123 | 71 | 194 | | | |
| 15- | 942 | 136 | 1078 | p<0.001 |
| unknown\textsuperscript{a} | 119 | 19 | 138 | | | |
| Within 30-days death | | | | |
| | 7 | 6 | 13 | ns | | |
| Double Cancer after distal gastrectomy | | | | |
| (+) | 475 | 100 | 575 | p<0.001 |
| (-) | 526 | 46 | 572 | | | |
| unknown\textsuperscript{a} | 183 | 80 | 263 | | | |
| Total | 1184 | 226 | 1410 | | | |

\textsuperscript{a}; Could not be evaluated because of lack of data or stage IV.

b; papillary adenocarcinoma and well- and moderately differentiated adenocarcinoma.
c; poorly differentiated adenocarcinoma including signet ring cell carcinoma, mucinous adenocarcinoma and undifferentiated adenocarcinoma.
d; Could not be evaluated because of lack of data.
m; tumor invades mucosa, sm; tumor invades submucosa, pm; tumor invades muscularis propria, ss; tumor invades subserosa, se; tumor penetrates serosa, and si, sei; tumor invades adjacent structures.

Table 2. Results of the Cox univariate analyses in patients who underwent distal gastrectomy with Billroth I vs. Billroth II according to the pTNM stage classification.

| pTNM stage | p-value | RR 95\%CI |
|------------|---------|-----------|
| IA | 0.035 | 1.497 1.029 2.177 |
| IB | 0.719 | 0.885 0.453 1.726 |
| II | 0.104 | 1.518 0.918 2.511 |
| IIIA | 0.341 | 1.334 0.737 2.415 |
| IIIB | 0.597 | 1.293 0.499 3.349 |
| IV | 0.000 | 1.975 1.464 2.664 |

RR; Relative risk

Table 3. Recurrence in 1015 patients with curative operation and types of recurrence.

| Recurrence | Billroth I | Billroth II | Total | p-value |
|------------|-----------|-------------|-------|---------|
| (-) | 857 | 71 | 928 | | | |
| (+) | 72(7.8\%) | 15(17.4\%) | 87 | P=0.002 |
| Peritoneal\textsuperscript{*} | | | | |
| (-) | 894 | 80 | 974 | | | |
| (+) | 35(3.8\%) | 6(7.0\%) | 41 | NS | | |
| Hematogenous\textsuperscript{*} | | | | |
| (-) | 888 | 76 | 964 | | | |
| (+) | 41(4.4\%) | 10(11.6\%) | 51 | P=0.003 |
| Lymphatic\textsuperscript{*} | | | | |
| (-) | 907 | 83 | 990 | | | |
| (+) | 22(2.4\%) | 3(3.5\%) | 25 | NS | | |
| Locoregional\textsuperscript{*} | | | | |
| (-) | 927 | 86 | 1013 | | | |
| (+) | 2(0.2\%) | 0 | 2 | NS | | |
| Total | 929 | 86 | 1015 | | | |

\textsuperscript{*}; duplication (+)
between Billroth I and Billroth II, 12.7% (150/1183) and 12.8% (29/227), respectively.

In patients who received postoperative adjuvant therapy, those without adjuvant therapy, and unknown group by using Cox univariate analysis, there were significant differences between the patients with Billroth I and Billroth II (P<0.001, RR=2.417, and 95%CI=1.888–3.095, P<0.001, RR=3.221, and 95%CI=2.228–4.656, and P<0.001, RR=2.038, and 95%CI=1.469–2.826, respectively). Fig. 2 shows the survival curves of pTNM stage IV patients who did not receive adjuvant therapy (A), those who received adjuvant therapy (B), and unknown group (C). There were significant differences between patients with Billroth I and Billroth II in these groups (log rank test, P=0.001, P=0.008, and P=0.023, respectively). Fig. 3 shows that stage IV patients with Billroth II (B) showed significant differences between those with and without adjuvant therapy, but not those with Billroth I (A) (P<0.001, RR=2.980, and 95%CI=1.658–5.354).

Table 4 shows the result of multivariate analysis according to all death by using 7 variables such as age (-64 vs. 65-), tumor depth (t1,t2 vs. t3,4), reconstruction (Billroth I vs. Billroth II), Lymph node metastasis (n(-) vs. n(+)), gender (female vs. male), histology (differentiated type vs. undifferentiated type), and adjuvant therapy ((-) vs. (+)). Age, tumor depth, reconstruction, Lymph node metastasis, and gender showed significant prognostic variables. The analysis was performed for the early period after gastrectomy, the focus was on morbidity and quality of life of patients rather than on their survival.

In this study, we showed a better survival benefit for patients in stages IA and IV who received Billroth I compared with those who received Billroth II. The result from the analysis of Cox multivariate analysis showed that reconstruction was a significant prognostic variable in the case of gastric cancer death, but not in the case of non-cancer death. This result indicates the correlation between duodenal passage and non-duodenal passage with the recurrence of the tumor. The results of this study indicate several important matters. If surgeons desire long-term patient survival, all data about gastric cancer in each institute and hospital need to be re-evaluated for the survival and duodenal passage advantages, with lesser gastric resection, as well as pouch formation in the future.

There are also no previous reports about the recurrence type, indication of adjuvant therapy, and Billroth I or Billroth II after distal gastrectomy. In this study, we supposed that non-duodenal passage reconstruction happened to cause the higher hematogenous recurrence and that patients without duodenal passage reconstruction and received postoperative adjuvant therapy were shown more effective than those with duodenal passage reconstruction.

In conclusion, patients in stages IA and IV with Billroth I after gastrectomy showed significantly better survival than those with Billroth II. Patients with Billroth II showed significantly higher hematogenous recurrence than those with Billroth I. Therefore, if gastric cancer patients must receive distal gastrectomy, we recommend they undergo duodenal passage reconstruction using the Billroth I procedure.
Table 4. Results of Cox multivariate analysis according to all death by using 7 variables.

| Variable                              | p value | R   | 95% CI lower | 95% CI upper |
|---------------------------------------|---------|-----|--------------|--------------|
| Age (-64 vs. 65-)                     | <0.001  | 3.622 | 2.972        | 4.413        |
| Tumor depth (t1,2 vs t3,4)            | <0.001  | 2.685 | 2.136        | 3.375        |
| Reconstruction (B1 vs B2)             | <0.001  | 2.215 | 1.780        | 2.757        |
| Lymph node metastasis (n(-) vs n(+)) | <0.001  | 2.130 | 1.723        | 2.632        |
| Gender (Female vs. Male)              | NS      | 1.433 | 1.170        | 1.755        |
| Histology (diff. vs. undiff.)         | NS      | 1.073 | 0.885        | 1.302        |
| Adjuvant Therapy ((-) vs (+))         | NS      | 0.912 | 0.740        | 1.123        |

RR: Relative risk

Table 5. Result of Cox multivariate analysis according to the cause of death by using 7 variables.

| Cause of death | Variable                              | p value | R   | 95% CI lower | 95% CI upper |
|---------------|---------------------------------------|---------|-----|--------------|--------------|
| Gastric cancer death | Age (-64 vs. 65-)                     | NS      | 1.235 | 0.965        | 1.580        |
| Other cancer death | Tumor depth (t1,2 vs t3,4)            | <0.001  | 2.722 | 1.724        | 2.994        |
| Non-cancer death | Reconstruction (B1 vs B2)             | 0.03    | 1.356 | 1.029        | 1.786        |
|                | Lymph node metastasis (n(-) vs n(+)) | <0.001  | 2.519 | 1.882        | 3.371        |
|                | Gender (Female vs. Male)              | NS      | 1.028 | 0.796        | 1.329        |
|                | Histology (diff. vs. undiff.)         | 0.012   | 0.739 | 0.583        | 0.937        |
|                | Adjuvant Therapy ((-) vs (+))         | NS      | 1.128 | 0.834        | 1.524        |
|                | Age (-64 vs. 65-)                     | 0.009   | 3.265 | 1.336        | 7.983        |
|                | Tumor depth (t1,2 vs t3,4)            | NS      | 0.212 | 0.033        | 1.363        |
|                | Reconstruction (B1 vs B2)             | NS      | 0.708 | 0.207        | 2.419        |
|                | Lymph node metastasis (n(-) vs n(+)) | NS      | 2.271 | 0.970        | 5.319        |
|                | Gender (Female vs. Male)              | NS      | 1.141 | 0.375        | 3.467        |
|                | Histology (diff. vs. undiff.)         | NS      | 0.549 | 0.182        | 1.660        |
|                | Adjuvant Therapy ((-) vs (+))         | NS      | 0.02    | 3.080        | 1.195        |

RR: Relative risk

Fig. 2. Survival curves of pTNM stage IV patients. Patients who did not receive postoperative adjuvant therapy (A), those who received postoperative adjuvant therapy (B), and unknown group (C). Solid line indicates patients with Billroth I and dotted line indicates those with Billroth II.

Fig. 3. Survival curves of pTNM stage IV patients who underwent distal gastrectomy with Billroth I, and those with Billroth II. Patients who underwent distal gastrectomy with Billroth I (A), and those with Billroth II (B). Solid line indicates patients receiving postoperative adjuvant therapy, dotted line indicates those receiving no postoperative adjuvant therapy, and thin solid line indicates unknown group.
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