

Benefits of Palliative Surgery for Far-Advanced Gastric Cancer

Chia-Siu Wang, MD; Tzu-Chieh Chao, MD; Yi-Yin Jan, MD; Long-Bin Jeng, MD;
Tsann-Long Hwang, MD; Miin-Fu Chen, MD

Background: The optimum strategy for palliative surgery in gastric cancer patients remains undetermined.

Methods: In total, 525 patients who had undergone palliative surgery between 1994 and 2000 were evaluated in terms of operative mortality, survival, and palliative effect. Patients were grouped according to the UICC's classification of residual tumors (R) after the operation: microscopic residual tumor (R1) (N=104) and macroscopic residual tumor (R2) (N=421). Gastric resection was performed in all R1 patients and in 257 of the R2 patients. Non-resection procedures were performed in 164 of the R2 patients, including gastrojejunostomies in 64, gastrostomies in 17, jejunostomies in 60, and laparotomies only in 23.

Results: The operative mortality did not significantly differ among R1 distal gastrectomies (4.5%), R2 distal gastrectomies (3.3%), and R1 total gastrectomies (2.9%) ($p=0.919$). R2 total gastrectomies showed a particularly higher operative mortality (10.9%) than did the other resection procedures. The survival time and palliative duration were significantly longer in patients after palliative resection than after non-resection operations. Postoperative chemotherapy prolonged the survival time of patients after palliative surgery.

Conclusion: R1 or R2 distal gastrectomies and R1 total gastrectomies have benefits of survival prolongation and symptomatic palliation. However, the use of a total gastrectomy in R2 patients must be selectively reserved for far-advanced cases, otherwise it should be replaced with less-invasive procedures to avoid a high operative mortality rate. Postoperative chemotherapy is useful for prolonging survival time.
(*Chang Gung Med J* 2002;25:792-802)

Key words: gastric cancer, palliative surgery, total gastrectomy.

Palliative or noncurative surgery is defined by the presence of any gross or microscopic residual tumors remaining postoperatively regardless of whether the surgical attempt was originally palliative or curative. It is indicated for far-advanced cases,

and less often for debilitated or very old patients. The proportion of palliative surgeries among gastric cancer operations is decreasing due to advancements in early detection and the availability of more-radical techniques.⁽¹⁾ Nevertheless, they account for more

Presentation: A portion of the contents of this paper were presented at the 38th World Congress of Surgery of the International Society of Surgery/Societe Internationale de Chirurgie (ISS/SIC) in Viena, Austria during International Surgical Week ISW99, August 17, 1999.

From the Department of General Surgery, Chang Gung Memorial Hospital, Taipei; Chang Gung University, Taoyuan.

Received: Jun. 10, 2002; Accepted: Sep. 3, 2002

Address for reprints: Dr. Chia-Siu Wang, Department of General Surgery, Chang Gung Memorial Hospital. 6, West Chia-Pu Road, Putzi City, Chiayi, Taiwan 613, R.O.C. Tel.: 886-5-3621000 ext. 2752; Fax: 886-5-3623002; E-mail: wangcs@cgmh.org.tw

than 30% of gastric cancer surgeries in non-Japanese series.⁽¹⁻⁴⁾

The purposes of palliative surgery differ from those of curative surgery. It is practiced mainly for symptomatic palliation of obstruction, bleeding, or pain of gastric cancer.^(5,6) It does not aim to cure and is not for long-term survival, but for limited survival benefits. The surgical risks of palliative surgery are high, because the general condition of patients may be quite deteriorated in the later stages of gastric cancer.⁽⁷⁾ The decision-making process for palliative surgery should consider not only the benefits of palliation and the survival time, but also the operative risks.

The optimum strategy for palliative surgery with gastric cancer remains undetermined. A controversial issue is whether a total gastrectomy is a worthwhile palliative treatment.^(7,8) Furthermore, the rationales of aggressive procedures, such as an extended lymphadenectomy and resection of metastatic foci in the liver or peritoneum, have recently been discussed.^(9,10) Another issue of concern is how long a gastrojejunostomy can serve its bypass function for patients with obstruction.^(11,12) In this article, we evaluate the clinical benefits of palliative surgery for our gastric cancer patients.

METHODS

Between 1994 and 2000, a total of 1486 patients was operated on for primary gastric cancer in Chang Gung Memorial Hospital, Taipei. According to the UICC's classification of residual tumors,⁽¹³⁾ surgery with no residual tumors (R0) or curative resection was achieved in 961 (64.7%) patients. Surgery with microscopic residual tumors (R1) was performed in 104 (7.0%), and surgery with macroscopic residual tumors (R2) in 421 (28.3%). For this study, we enrolled 522 (35.3%) patients who had received palliative surgery (R1 or R2). The reasons for R1 included positive resection margins in 85 (81.7%), and/or distant lymph node metastasis in 49 (47.1%). The R2 surgeries were further subgrouped into resection (R2-A) in 257 (17.3%) patients and non-resection (R2-B) in 164 (11.0%) patients. R2-A patients had liver metastasis in 49 (19.1%), peritoneal seeding in 181 (70.4%), distant lymph node metastasis in 25 (9.7%), a residual T4 tumor in 67 (26.5%), and positive resection margins in 65 (25.4%). Finally,

the reasons for R2-B included liver metastasis in 28 (17.1%), peritoneal seeding in 87 (53.0%), and an unresectable T4 tumor in 125 (76.2%).

Surgery

Whenever feasible, gastric resection was our first choice of treatment for patients with gastric cancer. A curative (R0) resection was defined as the surgeon's intent to excise all macroscopic disease, leaving all histologic margins free of tumors. The resection included not only the cancer and surrounding normal stomach, but also the greater and lesser omenta and perigastric lymph nodes en bloc. An extended lymphadenectomy was required to remove lymph nodes around the stomach and those along the hepatic, splenic, and celiac arteries (the anatomic N2 level in the Japanese system).⁽¹⁴⁾ The R1 resection operation was initially performed the same as for an R0 resection with a curative intent. However, because of technical difficulties, no further resection, such as a pancreaticoduodenectomy or subtotal esophagectomy, was conducted to gain a free margin. For palliative purposes, a systemic lymphadenectomy was not required in R2 resections. Non-resection operations consisted of gastrojejunostomies (N=64), gastrostomies (N=17), jejunostomies, (N=60), and laparotomies only (N=23). Gastrostomies and jejunostomies were studied as a group, which together were classified as an intubation operation.

The location of the tumor within the stomach determined the extent of gastric resection: tumors in the upper third were treated with a total gastrectomy; tumors in the body of the stomach were treated with either a total gastrectomy or distal gastrectomy; and tumors in the distal third of the stomach were treated with a distal gastrectomy. For a T4 tumor, combined resection of the invaded neighboring organs such as the transverse colon or the liver was performed. A distal pancreaticosplenectomy was not routinely performed, except when there was direct invasion into the body or tail of the pancreas or spleen.

Variables studied

Resected specimens were studied pathologically according to the criteria described in the Japanese General Rules for Gastric Cancer Study⁽¹³⁾ and the UICC's pTNM classification.⁽¹⁴⁾ The study items included age, gender, tumor location, tumor size, gross (Borrmann) type, wall invasion, resection mar-

gin, histologic type, lymph node metastasis, vascular invasion, lymphatic invasion, and perineural invasion. The histologic features were classified into 2 types: 1) differentiated or intestinal type, consisting of papillary and/or tubular adenocarcinomas, and 2) undifferentiated or diffuse type, consisting of poorly differentiated, signet-ring cell, and/or mucinous adenocarcinomas.

The postoperative events registered during hospitalization were used to determine morbidity and mortality. Operative mortality was defined as death during the same admission period. After discharge, all patients were receiving periodic follow-up study in the outpatient department until the time of this writing, or until their death. The palliative effect was expressed as 'the duration of palliation', and was defined as the period in which symptoms were relieved and during which parenteral fluid or nutritional therapy was not required.⁽¹¹⁾

Postoperative chemotherapy

Chemotherapy was performed if the patient consented, and the performance status was less than or equal to 3 in the scoring system of the Eastern Cooperative Oncology Group. Therapy commenced within 1 month of the operation. Chemotherapy could be categorized into 5-fluorouracil (5-FU)-based and cisplatin-based regimens. The most frequently used regimen was a combination of 2600 mg/m² 5-FU and 150 mg leucovorin, which were infused simultaneously through a portable pump over a 24-h period once a week for 6 weeks with a 2-week break prior to repetition of treatment.⁽¹⁵⁾ Chemotherapy was repeated every 8 weeks until disease progression, unacceptable toxicity, or patient refusal.

Statistical analysis

When appropriate, the Mann-Whitney U test or Fisher's exact test was used for between-group comparisons. Logistic regression was used to identify which of the clinicopathological variables were associated with operative mortality after gastric resection. Follow-up was carried out until December 2001 or until the patient expired. The survival of patients was expressed by median survival times and 95% confidence intervals (CIs). The cancer-specific survival outcome was expressed by applying the

Kaplan-Meier method for all patients excluding those who died immediately after surgery. The log-rank test was used to compare the prognostic significance of individual variables on survival and the duration of palliation. A *p* value of < 0.05 was considered statistically significant. In pairwise multiple comparisons, however, the significance level, α , was adjusted to avoid a type I error and to retain an overall significance level of 0.05 by using the Bonferroni correction, where the adjusted α level was equal to 0.05 divided by the number of tests or comparisons. The adjusted α level is noted in the text wherever necessary.

RESULTS

Demographics of patients

The median age of all 1486 patients was 63.4 years, and the gender ratio (male: female) was 1.9 : 1; both parameters were very similar among the R0, R1, and R2 groups (*p*=0.826 and *p*=0.654, respectively). Table 1 presents a comparison of the clinicopathological characteristics of the 3 groups which underwent gastric resection. R2 patients without gastric resection (R2-B) were not included, for there were no surgical specimens for histopathological study. Compared to the R0 group, both the R1 and R2 groups presented a bigger tumor size, a greater percentage of upper-third location, grossly infiltrative type (Borrmann type 3 and 4), histologically undifferentiated type, vascular invasion, lymphatic invasion, and perineural invasions (*p*<0.001 for all, except for the percentage of upper location, *p*=0.001). The percentage of serosal invasion and lymph node metastasis was greater in the R1 and R2 than in the R0 group (*p*<0.001). The proportion of total gastrectomies was 26.2% and 32.7% for the R0 and R1 groups, while it was 41.6% for the R2 group (*p*<0.001). Combined spleen and/or pancreas resection was performed more frequently in the R1 and R2 than in the R0 group (25.8% and 25.9% vs. 13.7%, *p*<0.001). It was a concomitant procedure in 53.4% of patients that underwent a total gastrectomy.

Postoperative complications

Table 2 lists postoperative complications of gastrectomies in the curative group and the 3 palliative groups. The morbidity rate was significantly greater

Table 1. Comparison of Clinicopathological Characteristics of the 3 Groups (R0, R1, and R2) Who Underwent Gastric Resection According to the UICC's Residual Tumor Classification

| Variable | Group | | | <i>p</i> |
|-----------------------------|-------------|-----------|------------|----------|
| | R0 | R1 | R2 | |
| No. of patients | 961 | 104 | 257 | |
| Age (yr), median | 63.4 | 64.3 | 63.2 | 0.826 |
| Gender | | | | |
| Male | 624 | 69 | 172 | 0.654 |
| Female | 337 | 35 | 85 | |
| Associated medical diseases | | | | |
| Yes | 739 | 78 | 198 | 0.544 |
| No | 222 (23.1) | 26 (25.0) | 49 (19.1) | |
| Location in stomach | | | | |
| Proximal | 181 (18.8)* | 26 (25.2) | 73 (28.4) | 0.001 |
| Middle | 219 | 19 | 60 | |
| Distal | 551 | 58 | 116 | |
| Entire | 10 | 1 | 8 | |
| Tumor size (cm) | | | | |
| Median | 3.5 | 5 | 6 | < 0.001 |
| (interquartile) | (2-5.5) | (4-7) | (4-8) | |
| Gross type (Borrmann type) | | | | |
| I, II | 391 | 16 | 41 | < 0.001 |
| III, IV | 570 (59.3) | 88 (84.6) | 216 (83.9) | |
| Histologic type | | | | |
| Differentiated | 466 | 31 | 80 | < 0.001 |
| Undifferentiated | 495 (51.5) | 73 (70.2) | 177 (68.9) | |
| Serosal invasion | | | | |
| No | 400 | 5 | 6 | < 0.001 |
| Yes | 561 (58.4) | 99 (95.2) | 251 (97.7) | |
| Lymph node metastasis | | | | |
| No | 458 | 13 | 30 | < 0.001 |
| Yes | 503 (52.3) | 91(87.5) | 227 (88.3) | |
| Gastrectomy | | | | |
| Total | 249 (25.9) | 34 (32.7) | 106 (41.2) | < 0.001 |
| Billroth I | 197 (21.5) | 10 (9.6) | 18 (7.0) | |
| Billroth II | 515 | 60 | 133 | |
| Vascular invasion | | | | |
| No | 860 | 88 | 153 | < 0.001 |
| Yes | 101 (10.5) | 16 (15.4) | 104 (40.4) | |
| Lymphatic invasion | | | | |
| No | 566 | 31 | 49 | < 0.001 |
| Yes | 395 (41.1) | 73 (70.2) | 208 (80.9) | |
| Perineural invasion | | | | |
| No | 665 | 41 | 106 | < 0.001 |
| Yes | 296 (30.8) | 63 (60.6) | 151 (58.8) | |
| Resection margin | | | | |
| Negative | 961 | 19 | 192 | < 0.001 |
| Positive | 0 (0.0) | 85 (81.7) | 65 (25.3) | |
| Liver metastasis | | | | |
| No | 961 | 104 | 208 | < 0.001 |
| Yes | 0 (0.0) | 0 (0.0) | 49 (19.1) | |
| Peritoneal seeding | | | | |
| No | 961 | 104 | 76 | < 0.001 |
| Yes | 0 (0.0) | 0 (0.0) | 181 (70.4) | |

* No. of patients (percentage).

Abbreviations: R0: no residual tumor; R1: microscopic residual tumor; R2: macroscopic residual tumor.

for patients after palliative surgery than after curative surgery (23.3% vs. 16.0%, $p=0.002$). However there were no differences among the 3 groups (R1, R2-A, and R2-B) of patients after palliative surgery ($p=0.675$). Anastomotic leakage and an intra-abdominal abscess were the 2 major complications after gastric resection. The incidence of anastomotic leakage was significantly greater in patients after palliative resection, especially total gastrectomies. The incidence of postoperative gastric stasis was especially greater in patients after gastrojejunostomies ($p<0.001$). The non-resection group had a higher incidence of postoperative bowel obstruction ($p=0.002$) due to progressive peritoneal carcinomatosis.

Operative mortality

Table 3 shows the operative mortality following various surgical procedures stratified by the UICC's residual tumor classification. The operative mortalities for R1 resection, and R2 resection and non-resection were 3.8%, 6.2%, and 17.1%, respectively, with significant difference among them ($p<0.0001$). The operative mortality did not significantly differ among R1 distal gastrectomies (4.5%), R2 distal gastrectomies (3.3%), and R1 total gastrectomies (2.9%) ($p=0.919$). However, R2 total gastrectomies showed a particularly higher operative mortality (10.9%) than other resection procedures ($p=0.00382$). Combined pancreaticosplenectomies resulted in 2 surgical deaths (12.5%) following R2 resection (N=16), however there were no deaths following R0 (N=22) or R1 (N=4) resections ($p=0.182$).

Mortality rates of the non-resection group were 23.4%, 10.9%, and 10.5%, respectively, after intubation surgery, gastrojejunostomies, and laparotomies only. The major cause of hospital deaths for the non-resection group was downhill progression of the disease, in contrast to surgical complications, mainly anastomotic leakage, for the resection group.

Risk factors for operative mortality with gastric resection

The surgical mortality of our patients (R0, R1, and R2, N=1322) who underwent gastric resection was closely related to severe medical diseases (presence/absence) ($p=0.019$), residual tumor classifica-

Table 2. Postoperative Complications of Gastric Cancer Surgery According to the UICC's Residual Tumor Classification

| Complication | Surgery in residual tumor classification | | | | <i>p</i> |
|-------------------------|--|-----------|-----------|-----------|----------|
| | R0 | R1 | R2-A | R2-B | |
| No. of patients | 961 | 104 | 257 | 164 | |
| Morbidity, no.(%) | 154 (16.0) | 21 (20.2) | 63 (24.5) | 39 (23.8) | 0.004 |
| Anastomotic leakage | 36 (3.8) | 6 (5.8) | 29 (11.3) | 3 (4.7*) | < 0.001 |
| Postoperative bleeding | 4 (0.4) | 0 (0.0) | 4 (1.6) | 3 (1.8) | 0.068 |
| Intra-abdominal abscess | 42 (4.4) | 6 (5.8) | 12 (4.7) | 3 (1.8) | 0.376 |
| Wound infection | 22 (2.3) | 4 (3.8) | 11 (4.3) | 6 (3.7) | 0.298 |
| Gastric stasis | 13 (1.4) | 2 (1.9) | 3 (1.2) | 9 (14.1*) | < 0.001 |
| Cardiopulmonary | 22 (2.3) | 2 (1.9) | 5 (1.9) | 10 (6.1) | 0.032 |
| Pancreatitis | 6 (0.6) | 2 (1.9) | 4 (1.6) | 0 (0.0) | 0.161 |
| Intestinal obstruction | 6 (0.6) | 0 (0.0) | 2 (0.8) | 6 (3.7) | 0.002 |
| Others# | 43 (4.5) | 11 (10.6) | 21 (8.2) | 10 (6.1) | 0.017 |

* Among those undergoing gastrojejunostomy bypass (n = 64).

Others: urinary tract infection, prolonged fever, deep vein thrombosis, stroke, etc.

Abbreviations: R0: no residual tumor; R1: microscopic residual tumor; R2: macroscopic residual tumor; -A: resection; -B: non-resection.

Table 3. Operative Mortality of Various Surgical Procedures in Patients Grouped According to the UICC's Residual Tumor Classification

| Group | No. | Mortality, no. (%) |
|--------------------|-----|--------------------|
| R0 | 961 | 24 (2.5) |
| Distal gastrectomy | 709 | 15 (2.3) |
| Total gastrectomy | 252 | 9 (3.6) |
| R1 | 104 | 4 (3.8) |
| Distal gastrectomy | 70 | 3 (4.5) |
| Total gastrectomy | 34 | 1 (2.9) |
| R2-resection | 257 | 16 (6.2) |
| Distal gastrectomy | 150 | 5 (3.3) |
| Total gastrectomy | 107 | 11 (10.3) |
| R2-non-resection | 164 | 28 (17.1) |
| Gastrojejunostomy | 64 | 7 (10.9) |
| Intubation | 77 | 18 (23.4) |
| Laparotomy alone | 26 | 3 (11.5) |

Abbreviations: R0: no residual tumor; R1: microscopic residual tumor; R2: macroscopic residual tumor.

Table 4. Logistic Regression Analysis of the Most Important Risk Factors for Operative Mortality with Gastric Resection (N = 1322)

| Variable | Risk ratio | 95% CI* | <i>p</i> |
|----------------------|------------|-------------|----------|
| Peritoneal seeding | 3.39 | (2.81-3.97) | < 0.0001 |
| Old age (≥ 80 years) | 1.87 | (1.52-2.22) | 0.0005 |
| Medical diseases | 2.05 | (1.52-2.58) | 0.0081 |

Abbreviations: CI: confidence interval.

tion (R0, R1, or R2) ($p=0.017$), pathological stage (stage III, IV/stage I, II) ($p=0.013$), peritoneal seeding (presence/absence) ($p=0.001$), extent of resection (total gastrectomy/distal gastrectomy) ($p=0.024$), and very old age (≥ 80 years/ < 80 years) ($p<0.001$). It was inversely correlated with lymph node dissection (yes/no) ($p=0.046$). It was not correlated to tumor location, tumor size, gross type, serosal invasion, lymph node metastasis, positive margin, or combined resection of adjacent organs. Logistic regression analysis revealed that the most important risk factors for operative mortality with gastric resection were peritoneal seeding, severe medical disease, and very old age (risk ratios of 3.39, 2.05, and 1.87, respectively) (Table 4).

The three most important risk factors were compared in the 4 groups of patients undergoing resection and included an R1 distal gastrectomy, R2 distal gastrectomy, R1 total gastrectomy, and R2 total gastrectomy. There were no significant differences in the proportions of very old patients or severe medical diseases in the 4 groups ($p=0.939$ and $p=0.309$, respectively). A significantly higher proportion of peritoneal seeding was noted in the group with R2 total gastrectomies than in the other 3 groups ($p<0.001$).

Survival outcomes

Figure 1 illustrates the cumulative survival curves of the 4 groups of patients according to the

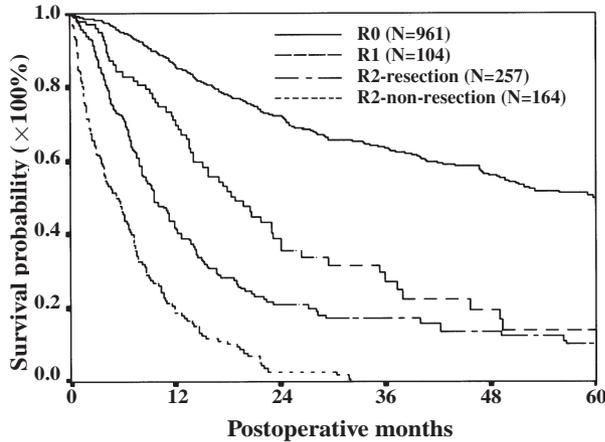


Fig. 1 Cumulative survival curves of patients grouped according to the UICC's residual tumor classification (log-rank $p < 0.0001$ for R1 or R2 resection or R2 non-resection vs. R0; log-rank $p < 0.0001$ for R2 non-resection vs. R1; log-rank $p = 0.0004$ for R2 resection vs. R1).

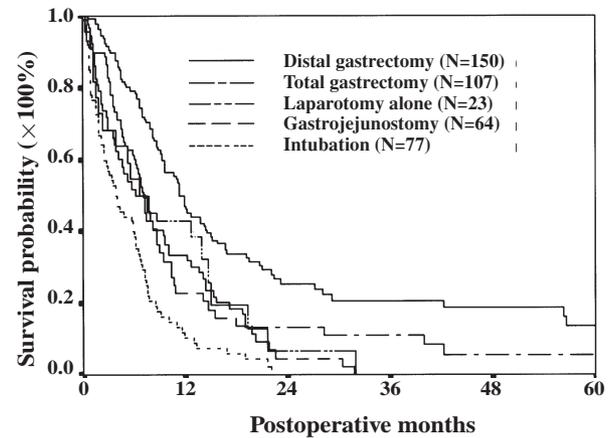


Fig. 2 Cumulative survival curves of patients after different palliative operations. The survival time after distal gastrectomies was significantly longer than that for any of the other palliative procedures. The survival time after intubation was significantly shorter than that after any other palliative procedure. The survival time for a total gastrectomy did not significantly differ from that of a gastrojejunostomy or a laparotomy only.

residual tumor classification. For the R1, R2-A, and R2-B groups, the median survival times were 18.8 (95% CI, 13.9-23.7), 9.5 (95% CI, 7.7-11.4), and 5.3 months (95% CI, 3.7-6.9), respectively, whereas for the R0 group it was 59.7 months (95% CI, 51.7-67.7). Differences in survival rates between any 2 of the 4 groups were statistically significant (log-rank $p < 0.0001$, R1 or R2-A or R2-B vs. R0; log-rank $p < 0.0001$, R2-B vs. R1; log-rank $p = 0.0004$, R2-A vs. R1; Bonferroni's adjusted α level = 0.0167).

Figure 2 illustrates survival curves of patients after palliative surgery. The median survival times after distal gastrectomies and total gastrectomies were 11.3 (95% CI, 9.6-13.0) and 7.1 months (95% CI, 6.0-8.2), respectively. Median survival times after gastrojejunostomies, intubation, and laparotomies only were 6.2 (95% CI, 3.5-8.9), 3.8 (95% CI, 2.1-5.5), and 6.6 months (95% CI, 3.0-10.2), respectively. Patients who underwent distal gastrectomies survived significantly longer than those who had total gastrectomies, laparotomies only, or intubation procedures (log-rank $p = 0.0006$, < 0.0001 , and < 0.0001 , respectively), and nonsignificantly longer than those who had gastrojejunostomies (log-rank $p = 0.014$; Bonferroni's adjusted α level = 0.0125). Survival times of patients did not differ among total

gastrectomies, gastrojejunostomies, and laparotomies only (total gastrectomies vs. gastrojejunostomies, log-rank $p = 0.125$; total gastrectomies vs. laparotomies only, log-rank $p = 0.722$; gastrojejunostomies vs. laparotomies only, log-rank $p = 0.454$). The survival time after intubation was significantly shorter than those after distal gastrectomies or total gastrectomies (log-rank $p < 0.0001$ and $= 0.0001$, respectively), but non-significantly shorter than those of gastrojejunostomies or laparotomies only (log-rank $p = 0.019$ and $= 0.021$, respectively; Bonferroni's adjusted α level = 0.0125).

The median survival time of patients with liver metastasis (N = 77) was 6.9 months (95% CI, 4.6-9.2). Among them, patients (N = 49) who underwent gastric resection survived longer than those (N = 28) who underwent non-resection operations (median survival time: 11.1 vs. 4.0 months, log-rank $p < 0.0001$). Combined resection of liver metastasis (N = 19) did not offer a longer survival time than leaving the liver metastasis alone (N = 58) (median survival time: 12.6 vs. 11.1 months, log-rank $p = 0.577$). The median survival time of patients

with peritoneal seeding (N=258) was 7.5 months (95% CI, 6.3-8.7). Patients with peritoneal seeding survived longer after gastric resection (N=181) than did those after non-resection operations (N=77) (median survival time: 9.5 vs. 4.3 months, respectively, log-rank $p < 0.0001$).

Survival benefits of chemotherapy

Fifty-six (53.8%) R1 patients, 102 (39.7%) R2-A patients, and 42 (25.6%) R2-B patients received postoperative chemotherapy. Figure 3 illustrates the cumulative survival curves of patients who underwent palliative surgery with or without postoperative chemotherapy. The median survival time of patients who received postoperative chemotherapy was 14.1 months (95% CI, 12.2-16.0), in contrast to 6.7 months (95% CI, 5.5-7.9) for those who did not (log-rank $p < 0.0001$). If stratified into R1, R2A, and R2B, patients who received postoperative chemotherapy survived significantly longer than those who did not (log-rank $p = 0.010$ for R1, $p < 0.0001$ for R2-A, and $p = 0.002$ for R2-B).

Duration of palliation

Regarding the duration of palliation, the median time was 3.6 months (95% CI, 0.4-6.8) in the gastrojejunostomy group and 1.2 months (95% CI, 0.3-3.4) in the intubation group (log-rank $p = 0.054$). The

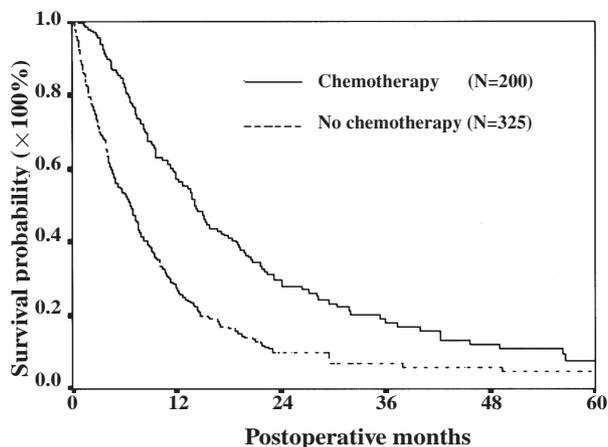


Fig. 3 Cumulative survival curves of patients who did and those who did not receive postoperative chemotherapy after palliative surgery (log-rank $p < 0.0001$).

median durations of palliation after distal and total gastrectomies were 8.9 (95% CI, 7.0-10.8) and 4.9 months (95% CI, 3.9-5.9), respectively (long-rank $p = 0.170$). The median duration of palliation after distal gastrectomies was significantly longer than that after any non-resection procedures (log-rank $p < 0.0001$). Total gastrectomies had no significant palliative benefits compared to gastrojejunostomies (log-rank $p = 0.054$).

DISCUSSION

In the UICC's TNM classification for gastric cancer, a residual tumor or tumor load after gastric surgery is also listed as 1 of the determinant predictors of survival.⁽¹⁶⁾ After palliative surgery, patients with microscopic residual tumors survived longer than those with macroscopic residual tumors. It is well recognized that palliative resection produces a longer survival than non-resection surgery.^(6,17-19) Patients survived longer after a gastrojejunostomy or a laparotomy only compared to those who had intubation surgery in other and our own series,^(6,7,17) because intubation surgery is usually performed on patients in a later stage such as those with extensive peritoneal carcinomatosis. However some series failed to show any differences in survival between the two.^(12,19)

Symptomatic palliation or quality of life is as an important survival benefit as operative safety in selecting surgical procedures for patients with far-advanced gastric cancer.⁽¹²⁾ Resection is currently accepted as the most effective procedure for symptomatic palliation.⁽⁵⁻⁷⁾ The palliative effect after gastric resection endured longer than that after non-resectional procedures.⁽¹²⁾ Whenever feasible, gastric resection should be the first choice. Our study supports distal gastrectomy being the best palliative surgery, but it is indicated only for cancers of the distal stomach.

Non-resectional surgery provides only very limited palliation. Gastric outlet obstruction is the most frequent indication for non-resection procedures. A gastrojejunostomy can effectively relieve the obstruction, allowing resumption of an oral diet following the operation. However, some do not consider it satisfactory palliation, because the bypass function can not be maintained as long as patients will

survive.⁽¹¹⁾ Therefore, it is not recommended whenever gastric resection is feasible.^(6,7,11) Intubation is the operation of last choice for gastric outlet obstruction.⁽⁶⁾ The feeding function of a jejunostomy can be maintained for only 1.4 months on average, which is too short to render it a worthwhile palliative procedure.

Postoperative gastric stasis following a gastrojejunostomy occurred in a high percentage (14.1%) of patients, most of whom had risk factors like a history of chronic obstruction or malnutrition before the operation.⁽²⁰⁾ A temporal feeding jejunostomy should be added for cases of chronic gastric outlet obstruction. It can serve as a feeding port for enteral nutrition, once gastric stasis develops.

The mortality and morbidity rates of palliative surgery were significantly greater than those following curative resection in other and our own studies.^(6,7,21) Anastomotic leakage is the main cause of operative mortality following gastric resection, whereas disease progression is the most common cause of hospital death following non-resection procedures. For cancers of the distal stomach, a bypass or gastrojejunostomy can be performed to avoid the mortality and morbidity of a gastrectomy in high-risk patients. However, for cancers of the proximal third of the stomach, a bypass operation is seldom performed to take the place of a total gastrectomy for high-risk patients. In the R2-resection group, the percentage of patients with total gastrectomies (41.6%) was much higher than that in the R0 (26.2%) or R1 group (32.7%). This may explain why R2 total gastrectomies had a particularly higher operative mortality than did R1 and R2 distal gastrectomies or R1 total gastrectomies in this series.

From logistic regression analysis, we identified peritoneal seeding, very old age (> 80 years), and severe medical diseases as the most important risk factors influencing the operative mortality of patients who underwent gastric resection (Table 4). The proportion of patients of a very old age or with severe medical diseases did not differ in gastrectomized patients of the various residual tumor groups. However, a higher proportion of peritoneal seeding was particularly noted in patients receiving R2 total gastrectomies. This provides another reason for the high mortality of R2 total gastrectomies among our patients.

Some clinicians disapprove of a total gastrectomy as a palliative procedure due to its high operative mortality and short survival times.^(22,23) However, several recent reports did not oppose the use of a palliative total gastrectomy, suggesting that it is a relatively safe procedure compared to a distal gastrectomy.^(7,8,19) Nevertheless, it is generally recognized that, for a better postoperative quality of life and nutritional status, total gastrectomies should not be performed in principle for all cases except for cancers of the proximal third of the stomach. The selection of a total gastrectomy must be stringent for R2 patients. We suggest that a total gastrectomy is an acceptable operation for R1 patients with cancers of the proximal third of the stomach, while it should be done selectively for R2 patients because of the high operative mortality. For R2 patients, a gastrectomy is not the only method of treatment for proximal-third cancers; instead, other treatment modalities such as trans-endoscopic stenting, laser therapy, and brachytherapy might be safer alternatives.^(24,25)

Postoperative residual or occult tumor cells may continue to grow in patients following palliative surgery. Early aggressive chemotherapy is recommended for these patients.^(26,27) A regimen, consisting of a weekly high-dose 5-FU and LV infusion, originally recommended for colon cancer, has been tried in our hospital.^(15,28) The result of a phase II prospective trial revealed a partial response in 33.3% of 37 patients, in addition to an acceptable toxicity even in patients with a relatively poor performance status.⁽¹⁵⁾ In this study, postoperative chemotherapy was demonstrated capable of improving the survival of incurable patients regardless of whether gastric resection was performed or not.

Recently some more-aggressive operations have been advocated for patients with distant metastasis to the para-aortic lymph nodes, liver, or peritoneum.^(9,29) Para-aortic lymph node dissection prolonged the survival of patients if the number of metastatic para-aortic lymph nodes was ≤ 3 .⁽²⁹⁾ A combined hepatectomy for liver metastasis prolonged the survival time of patients with liver metastasis confined to 1 lobe.⁽¹⁸⁾ For patients with peritoneal seeding, a 5-year survival of 24% was observed in a clinical trial (N = 14) that utilized an extensive peritonectomy and perioperative intraperitoneal chemotherapy, in addition to an extended gastrectomy.^(10,30) For far-advanced

cases, radical or aggressive surgery would certainly increase postoperative mortality and morbidity. Therefore, in the decision-making process for these aggressive operations, one must consider not only the survival benefits, but also the surgical risks and postoperative quality of life.

Acknowledgments

The authors would like to thank the Cancer Unit of Chang Gung Memorial Hospital, Taipei, Taiwan for financially supporting this research. Dr Ting-Chang Chang's contribution to the statistical analysis is also highly appreciated.

REFERENCES

1. Akoh JA, Macintyre IMC. Improving survival in gastric cancer: review of 5-year survival rates in English language publications from 1970. *Br J Surg* 1992;79:293-9.
2. Wanebo HJ, Kenedy BJ, Chmiel J, Steele G, Winchester D, Osteen R. Cancer of the stomach: a patient care study by the American College of Surgeons. *Ann Surg* 1993; 218:583-92.
3. Siewert JR, Bottcher K, Stein HJ, Roder JD, and the German Gastric Cancer Study Group. Relevant prognostic factors in gastric cancer: ten-year results of the German gastric cancer study. *Ann Surg* 1998;228:449-61.
4. Wang, CS, Hsieh CC, Chao TC, Jan YY, Jeng LB, Hwang TL, Chen MF, Chen PC, Chen JS, Hsueh S. Resectable gastric cancer: operative mortality and survival analysis. *Chang Gung Med J* 2002;25:216-27.
5. Ekblom GA, Gleysteen JJ. Gastric malignancy: resection for palliation. *Surgery* 1980;88:476-81.
6. Hallissey MT, Allum WH, Roginski C, Fielding JW. Palliative surgery for gastric cancer. *Cancer* 1988;62:440-4.
7. Haugstvedt T. Benefit of resection in palliative surgery. *Dig Surg* 1994;11:121-5.
8. Monson JRT, Donohue JH, McIlrath DC, Farnell MB, Ilstrup DM. Total gastrectomy for advanced cancer: a worthwhile palliative procedure. *Cancer* 1991;68:1863-8.
9. Kikuchi S, Tsukamoto H, Mieno H, Sato K, Kobayashi N, Shimao H, Sakakibara Y, Hiki Y, Kabita A. Results of resection of gastric cancer with distant metastasis. *Hepato-Gastroenterol* 1998;45:592-6.
10. Yonemura Y, Fujimura T, Fushida S, Fujita H, Bando E, Nishimura G, Miwa K, Endou Y, Tanaka M, Sasaki T. A new surgical approach (peritonectomy) for the treatment of peritoneal dissemination. *Hepato-Gastroenterol* 1999; 46:601-9.
11. Kikuchi S, Tsutumi O, Kobayashi N, Tsukamoto H, Shimao H, Sakakibara Y, Hiki Y, Kakita A. Does gastrojejunostomy for unresectable cancer of the gastric antrum offer satisfactory palliation? *Hepato-Gastroenterol* 1999; 46:584-7.
12. Ouchi K, Sugawara T, Ono H, Fujiya T, Kamiyama Y, Kakugawa Y, Mikuni J, Yamanami H. Therapeutic significance of palliative operations for gastric cancer for survival and quality of life. *J Surg Oncology* 1998;69:41-4.
13. Sobin LH, Wittekind CH, UICC. TNM classification of malignant tumors. 5th ed. Heidelberg, Springer-Verlag: UICC, International Union Against Cancer, 1997.
14. Japanese Research Society For Gastric Cancer. Japanese classification of gastric carcinoma. First English edition, Kanehara & Co, LTD. Tokyo 1995.
15. Lin YC, Liu HE, Wang CH, Wang HM, Yang TS, Liao CT, Chen JS. Clinical benefit and response in patients with gastric cancer to weekly 24-hour infusion of high-dose 5-fluorouracil (5-FU) and leucovorin (LV). *Anticancer Res* 1999;19:5615-20.
16. Bonenkamp JJ, Sassako M, Hermans J, van de Velde CJ. Tumor load and surgical palliation in gastric cancer. *Hepato-Gastroenterol* 2001;48:1219-21.
17. Crookes PF, Incarbone R, Peters JH, Engle S, Bremner CG, DeMeester TR. A selective therapeutic approach to gastric cancer in a large public hospital. *Am J Surg* 1995; 170:602-5.
18. Kakeji Y, Maehara Y, Tomoda M, Kabashima A, Ohmori M, Oda S, Ohno S, Sugimachi K. Long term survival of patients with stage IV gastric cancer. *Cancer* 1998;82: 2307-11.
19. Doglietto BG, Pacelli F, Caprino P, Alfieri S, Carriero C, Malerba M, Crucitti F. Palliative surgery for far-advanced gastric cancer: a retrospective study on 305 consecutive patients. *Am Surg* 1999;36:352-5.
20. Bar-Natan M, Larson GM, Stephens G, Massey T. Delayed gastric emptying after gastric surgery. *Am J Surg* 1996;172:24-8.
21. Wang CS, Chao TC, Hsueh S, Jeng LB, Jan YY, Chen SC, Hwang TL, Chen MF. Proximal third gastric adenocarcinoma: results of total gastrectomy by general surgeons and analysis of prognostic factors. *J Surg Assoc ROC* 1996;29:382-90.
22. ReMine WH. Palliative operations for incurable gastric cancer. *World J Surg* 1979;3:721-9.
23. Lawrence W. Jr, McNeer G. The effectiveness of surgery for palliation of incurable gastric cancer. *Cancer* 1958; 11:28-32.
24. Siersema PD, Schrauwen SL, van Blankenstein M, Steyerberg EW, van der Gaast A, Tilanus HW, Dees J, Rotterdam Esophageal Tumor Study Group. Self-expanding metal stents for complicated and recurrent esophago-gastric cancer. *Gastrointest Endosc* 2001;54:579-86.
25. Spencer GM, Thorpe SM, Blackman GM, Solano J, Tobias JS, Lovat LB, Bown SG. Laser augmented by brachytherapy versus laser alone in the palliation of adenocarcinoma of the esophagus and cardia: a randomized

- study. *Gut* 2002;50:224-7.
26. Maehara Y, Sugimachi K, Akagi M, Kakegawa T, Shimazu H, Tomita M. Early postoperative chemotherapy following noncurative resection for patients with advanced gastric cancer. *Br J Cancer* 1992;65:413-6.
 27. Hanazaki K, Mochizuki Y, Machida T, Yokoyama H, Sodeyama H, Sode Y, Wakabayashi M, Kawamura N, Miyazaki T. Postoperative chemotherapy in non-curative gastrectomy for advanced gastric cancer. *Hepato-Gastroenterol* 1999;46:1238-43.
 28. Ardalan B, Chua L, Tian EM, Reddy R, Sridhar K, Benedetto P, Richman S, Legaspi A, Waldman S, Morrell L, Feun L, Savaraj N, Livinstone A. A phase II study of weekly 24-hour infusion with high dose 5-fluorouracil with leucovorin in colorectal carcinoma. *J Clin Oncol* 1991;19:625-30.
 29. Kunisaki C, Shimad H, Yamaoka H, Takahashi M, Okuno K, Akiyama H, Nomura M, Moriwaki Y. Indications for paraaortic lymph node dissection in gastric cancer patients with paraaortic lymph node involvement. *Hepato-Gastroenterol* 2000;47:586-9.
 30. Sugarbaker PH, Yonemura Y. Palliation with a glimmer of hope: management of respectable gastric cancer with peritoneal carcinomatosis. *Hepato-Gastroenterol* 2001; 48:1238-47.

晚期胃癌的緩解性手術之效益

王嘉修 趙子傑 詹益銀 鄭隆賓 黃燦龍 陳敏夫

背景：針對晚期胃癌病人的緩解性外科治療，最完善的策略迄今尚未有定論。

方法：於1994和2000年間總共有525位晚期胃癌病人接受緩解性外科治療。本文旨在分析此類手術的危險性、存活、和緩解效果等各方面的優劣點，評估其效益。依據UICC有關術後殘餘腫瘤(R)的分類法：顯微的殘餘腫瘤(R1)有104人，和肉眼的殘餘腫瘤(R2)有421人。所有R1病人和257位R2病人施行胃切除術。非切除手術共施行於164位R2病人，包括：胃空腸吻合術(N = 64)，胃造瘻術(N = 17)，空腸造瘻術(N = 60)，和單開腹(N = 23)。

結果：R1遠端胃切除術，R2遠端胃切除術，和R1全胃切除術的手術死亡率分別是4.5%，3.3%，和2.9%，其間並無明顯差別。R2全胃切除手術之手術死亡率(10.9%)特別的高出以上各種切除手術。除了R2全胃切除手術外，各種緩解性切除後的存活時間和有效緩解期都比非切除手術長久。緩解手術以後化學治療有延命的效果。

結論：對於晚期胃癌病人，R1或R2遠端胃切除術或R1全胃切除術具有延命或緩解症候的效果。但是施行R2全胃切除術必須做有選擇性的決定，或考慮以其他比較不侵襲的治療方法來取代以減低手術死亡率。緩解手術以後化學治療也有延命的好處。
(長庚醫誌 2002;25:792-802)

關鍵字：胃癌，緩解手術，全胃切除術。