Resectable Gastric Cancer: Operative Mortality and Survival Analysis

Chia-Siu Wang, MD; Chin-Chuan Hsieh, MD; Tzu-Chieh Chao, MD; Yi-Yin Jan, MD; Long-Bin Jeng, MD; Tsann-Long Hwang, MD; Min-Fu Chen, MD; Pang-Chi Chen[1], MD; Jen-Shi Chen[2], MD; Swei Hsueh[3], MD

Background: This study evaluated the survival outcome and determined the prognostic factors for gastric cancer patients who underwent gastric resection in the past 6 years.

Methods: Between 1994 and 2000, a total of 1322 patients with gastric cancer who underwent gastric resection in our hospital comprised the study subjects. Their mean age was 61.1 (range, 14-92) years. There were 865 male and 457 female patients. Total gastrectomy was performed in 389 (29.4%) and distal gastrectomy in 933 patients. Curative resection was performed in 961, and palliative resection in 361 patients. A D2 or greater lymphadenectomy was required for curative resection. Patients received postoperative chemotherapy if they underwent palliative resection.

Results: Early or pT1 gastric cancer accounted for 17.7% and lymph node metastasis for 62.1% of all resected cases. The overall operative mortality and morbidity rates were 3.3% and 18.0%, respectively . The operative mortality for palliative total gastrectomy was particularly high (8.5%). The overall cumulative 5-year survival rate of all resected patients was 45.6%, and it was 57.0% after curative resection. Multivariate analysis revealed that lymph node metastasis, serosal invasion, peritoneal seeding, positive resection margin, liver metastasis, old age, tumor size, and lymphatic invasion were independent prognostic factors.

Conclusion: The most important prognostic factors for survival were lymph node metastasis, serosal invasion, peritoneal seeding, positive resection margin, liver metastasis, old age, tumor size, and lymphatic invasion. The operative mortality and survival outcome of our gastric cancer patients after gastric resection compared favorably with those of other series in other countries.
(Chang Gung Med J 2002;25:216-27)

Key words: **gastric cancer, gastrectomy, operative mortality, prognostic analysis.**

Gastric cancer is the fourth leading cause of cancer-related death in Taiwan. The incidence and mortality rate of gastric cancer have gradually decreased over the past 5 decades.[1,2] Surgery

The contents of this paper were presented at the 4th Annual Terry Fox International Cancer Symposium (on Gastric Cancer), at Chang Gung Memorial Hospital, Kweishan, Taoyuan, Taiwan, on October 21, 2000.

From the Departments of General Surgery, [1]Department Gastroenterology, [2]Department Hematology-Oncology, [3]Department Pathology, Chang Gung Memorial Hospital, Taipei.

Received: Oct. 18, 2001; Accepted: Nov. 29, 2001

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

remains the mainstay of treatment for gastric cancer. Curative resection without residual tumors is the key to long-term survival.[3] To improve the quality of treatment, a protocol, consisting of diagnostic work-up, surgery, pathological studies, and postoperative care, was developed in 1994 by all people involved in gastric cancer treatment in our hospital. Definitions of terms in this protocol followed the pTNM (pathological tumor-node-metastasis) classification of the International Union Against Cancer (Union Internacional Contra la Cancer, UICC) and the Japanese General Rules for Gastric Cancer Study.[4,5] A Japanese-style lymph node dissection was adopted for curative resection.[6,7] Information and follow-up data on registered patients were recorded into database files. This study was designed to evaluate the outcome of our patients after gastric resection and to determine the prognostic factors for their survival.

METHODS

Between 1994 and 2000, a total of 1486 patients with gastric cancer was operated on in Chang Gung Memorial Hospital, Taipei. Operations consisted of gastric resection in 1322 patients and non-resection procedures in the other 164 patients. Those who underwent gastric resection (n = 1322), were our subjects of study. The mean age was 61.1 ¡ 13 years, while the median age was 63.4 (range, 14-92) years. There were 865 male and 457 female patients with a gender ratio at 1.89.

Surgery

Whenever feasible, gastric resection was the choice of treatment for gastric cancer. The location of the tumor within the stomach determined the extent of gastric resection: tumors in the upper 1/3 were treated with total gastrectomy; tumors in the body of the stomach were treated with either total gastrectomy or distal gastrectomy; and tumors in the distal 1/3 of the stomach were treated with distal gastrectomy. A curative resection was defined by the intent of the surgeon to excise all macroscopic disease with tumor-free histologic margins. The resection included not only the cancer and surrounding normal stomach, but also the greater and lesser omenta and perigastric lymph nodes en bloc.[5] An extended or D2 lymphadenectomy was required to remove lymph nodes from around the stomach and those along the hepatic, splenic, and celiac arteries (the anatomic N2 level in the Japanese system).[5-7] Intraoperative frozen sectioning was routinely performed to ensure a tumor-free margin. A distal pancreaticosplenectomy was not routinely performed, except when there was direct invasion into the body or tail of the pancreas or to the spleen. In cases with incurable factors like peritoneal seeding, widespread lymph node metastasis, or liver metastasis, a palliative operation with or without gastric resection was performed. Palliative resection might allow for positive resection margins and did not require a systemic lymphadenectomy. Due to differences in treatment modes, patients were divided into curative and palliative groups.

Postoperative chemotherapy

Postoperative chemotherapy was used for patients who had undergone palliative resection if they consented and their performance status was less than or equal to 3 according to the scoring system of the Eastern Cooperative Oncology Group (ECOG). The therapy commenced within 1 month of the operation. The chemotherapy was categorized into 5-fluorouracil (5-FU)- and cisplatin-based regimens. The most frequently used regimen was a combination of 2600 mg/m^2 of 5-FU and 150 mg of 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.[8] The chemotherapy was repeated every 8 weeks until disease progression or unacceptable toxicity was encountered or the patient refused further treatment.

Adjuvant chemotherapy was conducted for stage II or III patients within 1 month after curative resection. Patients received a 4-drug combination regimen, in which 450 mg/m^2 of 5-FU was administered in an intravenous bolus on days 1 and 8; 150 mg/m^2 of leucovorin in an intravenous infusion on days 1 and 8; 40 mg/m^2 of epirubicin in an intravenous bolus on day 1; and 50 mg/m^2 of cisplatin in an intravenous infusion on day 1. The treatment was given in 4-week cycles for a total of 6 cycles. Thereafter, patients received oral tegafur (a derivative of 5-FU) daily for the following 1-2 years.

Because of unsatisfactory results (data not shown), this regimen was replaced after October 1999 with Grau's mitomycin-based regimen, in which 10 mg/m^2 of mitomycin was administered intravenously on day 1 and then oral tegafur was given for 5 weeks in a 6-week cycle for a total of 4 cycles.[9]

Variables studied

The study items included age, gender, tumor location, tumor size, gross (Borrmann) type, depth of invasion, resection margin, histologic type, lymph node metastasis, vascular invasion, lymphatic invasion, perineural invasion, and tumor markers. Resected specimens were studied pathologically according to the criteria described in the Japanese General Rules for Gastric Cancer Study.[5] The staging system followed UICC's pTNM classification for gastric cancer.[4] The histologic features were classified into 2 types: (1) differentiated or intestinal, consisting of papillary and/or tubular adenocarcinoma, and (2) undifferentiated or diffuse, consisting of poorly differentiated adenocarcinoma, signet-ring cell carcinoma, and/or mucinous adenocarcinoma.[10]

Tumor markers, including serum CEA, CA199, and CA125, were examined preoperatively in patients. The cut-off points for normal serum levels were 5 U/dl for CEA and 37 U/dl for CA199 and CA125.

Postoperative events recorded during hospitalization were used to determine the morbidity and mortality for each group. Operative mortality was defined as death during the same admission period. After discharge, all patients received periodic follow-up study at the outpatient department, or by means of telephone or mailed questionnaires, until the time of this study or the patient died.

Statistical analysis

Cumulative survival curves were calculated according to Kaplan and Meier's method. The end point in the analysis was cancer-related death. The cumulative 5-year survival rate was calculated to express survival. The median survival time and 95% confidence interval were also calculated. In the univariate analysis, the log-rank test was used to assess statistical differences between groups. In the multivariate analysis, the Cox proportional hazard model was used as a general model to determine the independent factors.

RESULTS

Demographics of patients

Operations included a subtotal gastrectomy in 933 (including Billroth I in 225 and Billroth II in 708) and a total gastrectomy in 389 (29.4%) patients. According to the UICC's classification of residual tumors,[4] R0 (no residual tumor or curative resection) was achieved in 961 (72.7%), R1 (microscopic residual tumor) in 104 (7.9%), and R2 (macroscopic residual tumor) in 257 patients (19.4%). Combining R1 and R2, a total of 525 patients (37.3%) was classified as the palliative group, however patients in R1 had undergone a curative attempt during the operation. The reasons for patients being categorized into R1 included positive resection margins in 85 (81.7%) and/or distant lymph node metastasis in 49 (47.1%). Of patients categorized as R2, 49 (19.1%) had liver metastasis, 181 (70.4%) had peritoneal spread, 25 (9.7%) had distant lymph node metastasis, 67 (26.5%) had incomplete resection of a T4 tumor, and 65 (25.4%) had positive resection margins.

Cancer locations in 1322 resected cases included the upper 1/3 in 280 (21.2%), the middle 1/3 in 298 (22.5%), the lower 1/3 in 725 (54.8%), and the entire stomach in 19 (1.4%) patients.

Mean tumor size (maximal diameter) was 4.7 ¡ 2.9 cm or a median of 4.0 (range, 0.1-24) cm. The gross morphology was distributed as Borrmann 0 (early cancer or early-simulated cancer) in 240, Borrmann 1 in 64, Borrmann 2 in 120, Borrmann 3 in 656, Borrmann 4 in 174, and unclassified in 68 patients. These could also be summarized into 2 types: localized type (Borrmann 0-2) in 424 and infiltrative type (Borrmann 3-4) in 898 patients.

Histologically, lesions consisted of papillary type in 9 (0.7%), well-differentiated tubular type (tub1) in 150 (11.3%), moderately differentiated tubular type (tub 2) in 421 (31.8%), poorly differentiated type (por) in 506 (38.3%), signet-ring cell type (sig) in 203 (15.4%), and mucinous type (muc) in 33 (2.5%) patients. The histologic type could also be divided into the differentiated (intestinal) type in 577 (43.6%) and undifferentiated (diffuse) type in 745 (56.4%) patients.

The depth of invasion was T1 in 234 (17.7%), T2 in 177 (13.4%), T3 in 757 (57.3%), and T4 in 154 (11.6%) patients. Invasion depth could also be divid-

ed into serosa-invading tumor (T3 or T4) in 911 and serosa-free tumor (T1 or T2) in 411 cases. The incidence of so-called 'early gastric cancer', defined as a T1 tumor regardless of lymph node status, accounted for 17.7% of our resected cases. Among them, cancer was confined to the mucosa in 128 and to the submucosa in 106 patients.

Lymph node metastasis occurred in 821 (62.1%) patients. According to the Japanese classification (anatomical stations), lymph node metastasis was classified as n1 in 496 (37.5%), n2 in 274 (20.7%), n3 in 35 (2.6%), and n4 in 16 (1.2%) patients.[5] According to the 1997 UICC lymph node classification (number of positive lymph nodes), lymph node metastasis was classified as N1 (number=1-6) in 409 (30.9%), N2 (number = 6-15) in 257 (19.4%), and N3 (number > 15) in 155 (11.7%) patients.[4]

Microscopically, vascular invasion was detected in 221(16.7%), lymphatic invasion in 676 (51.1%), and perineural invasion in 510 (38.6%) cases.

The resection margin was positive in 150 (11.3%) patients with involvement of the proximal margin in 88 (6.6%) and the distal margin in 76 (5.7%). Both proximal and distal margins were positive in 14 patients. This accounted for 9.8% of our patients undergoing a curative attempt and 25.6% of those having palliative surgery.

Distant metastasis occurred in 250 patients. These included peritoneal seeding in 181, liver metastasis in 49, and distant lymph node metastasis in 56 patients.

Among the 1322 resected cases, the stage distribution was IA in 202 (15.3%), IB in 132 (10.0%), II in 195 (14.8%), IIIA in 243 (18.4%), IIIB in 135 (10.2%), and IV in 415 (31.4%) patients.

Serum CEA level was checked in almost all patients before the gastrectomy, while serum CA19.9 and CA125 were examined in a portion (n = 398) of patients. Abnormal elevation of serum tumor markers was noted in 22.2% of patients for CEA, 21.7% for CA19.9, and 14.6% for CA125. A higher tumor stage was closely associated with a greater percentage of patients with abnormal elevation of any serum tumor marker ($p < 0.0001$). Patients with normal serum CEA survived longer than those with elevated serum CEA ($p < 0.0001$) (Fig.1).

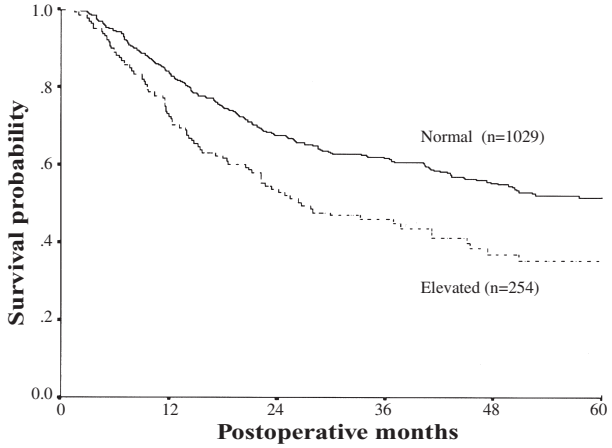

Fig. 1 Kaplan-Meier survival curves of patients divided into normal and elevated serum CEA groups before the operation (log rank $p < 0.0001$). A normal serum CEA level is < 5 U/dl.

Operative morbidity and mortality

There were 238 patients (18.0%) who experienced complications after the operation. Table 1 lists postoperative complications of gastrectomy in both curative and palliative groups. Palliative surgery had a greater complication rate than did curative resection (23.3% vs. 16.0%, $p = 0.002$). Anastomotic leakage and intra-abdominal abscess were the 2 major complications. The incidence of anastomotic leakage and other minor complications was significantly greater in patients after palliative resection,

Table 1. Comparison of Postoperative Complications between Curative and Palliative Gastrectomies in 1322 Gastric Cancer Patients

Complication	Type of resection		*p*
	Curative	Palliative	
No. of patients	961	361	
Morbidity, no.(%)	154 (16.0)	84 (23.3)	0.002
Anastomotic leakage	36 (3.8)	35 (9.7)	< 0.001
Postoperative bleeding	4 (0.4)	4 (1.1)	0.148
Intra-abdominal abscess	42 (4.4)	18 (5.0)	0.631
Wound infection	22 (2.3)	15 (4.2)	0.067
Gastric stasis	13 (1.4)	5 (1.4)	0.964
Cardiopulmonary	22 (2.3)	7 (1.9)	0.699
Pancreatitis	6 (0.6)	6 (1.7)	0.076
Intestinal obstruction	6 (0.6)	2 (0.5)	0.883
Others†	43 (4.5)	31 (8.6)	0.004

†Others: minor complications including urinary tract infection, prolonged fever, deep vein thrombosis, stroke, etc.

Table 2. Operative Mortality of Distal and Total Gastrectomies in 1322 Gastric Cancer Patients

Type of resection	Curative		Palliative		*p*
	Mortality	no. (%)	Mortality	no. (%)	
Distal gastrectomy	709	15 (2.3)	220	8 (3.6)	0.205
Total gastrectomy	252	9 (3.6)	141	12 (8.5)	0.037
Total	961	24 (2.5)	361	20 (5.5)	0.006

especially total gastrectomy.

There were a total of 44 operative deaths with an overall operative mortality rate of 3.3% in our patients. When patients were divided into curative and palliative groups, the palliative groups had a greater operative mortality (5.5% vs. 2.5%, $p=0.006$). There was no difference in operative mortality between curative and palliative distal gastrectomies ($p=0.205$), but there was a significant difference between curative and palliative total gastrectomies ($p=0.037$) (Table 2). As to the extent of resection, the operative mortality for total gastrectomy was significantly greater than that for distal gastrectomy (2.5% vs. 5.3%, $p=0.008$). It was worthwhile noting that the operative mortality for palliative total gastrectomy (8.5%) was particularly higher than those for curative distal gastrectomy (2.3%), palliative distal gastrectomy (3.6%), and curative total gastrectomy (3.6%) ($p<0.001$, $p=0.048$, and $p=0.037$, respectively).

Combined pancreaticosplenectomy resulted in 2 surgical deaths (12.5%) following R2 resection (n=16), however there were none following R0 (n=22) or R1 (n=4) resections ($p=0.182$).

Risk factors for surgical mortality

The surgical mortality of our patients was closely correlated with associated medical diseases ($p=0.019$), residual tumor classification ($p=0.017$), pathological staging ($p=0.013$), peritoneal seeding ($p=0.001$), total gastrectomy ($p=0.024$), and very old age (≥ 80 years) ($p<0.001$). It was inversely correlated with lymph node dissection ($p=0.046$). 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 determinant risk factors for operative mortality of gastric resection were peritoneal seeding, severe medical disease, and very old age (with risk ratios of 3.39, 2.05, and 1.87, respectively).

Survival outcome

The median follow-up duration of survivors was 42.8 months. The overall cumulative 5-year survival rate of our 1322 patients with gastric resection was 45.6%, and median survival time was 47.2 (95% CI: 39.5-55.2) months, while it was 57% after curative resection. It was 14.2% (median survival time: 19.1 months) and 14.4% (median survival time: 10.8 months) for palliative R1 and R2 resection, respectively (log rank $p=0.0098$).

The cumulative 5-year survival rate was 51.8% after distal gastrectomy. The cumulative 5-year survival rate and median survival time were 30.8% and 19.5 (95% CI: 15.1-23.9) months, respectively, after total gastrectomy (log rank $p<0.0001$). In patients with curative resection, the cumulative 5-year

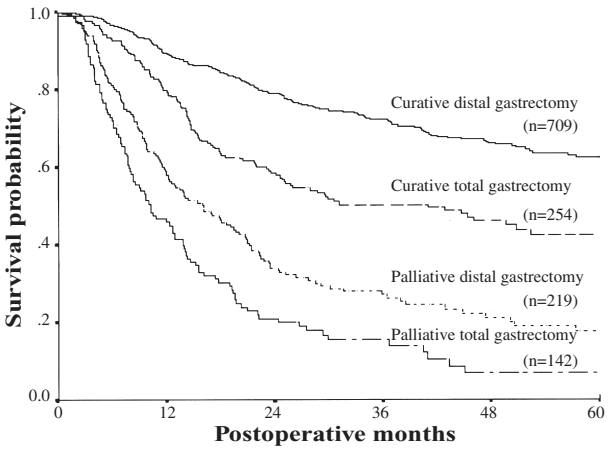

Fig. 2 Kaplan-Meier survival curves of patients following different types of gastric resection (log rank $p=0.0005$ between palliative distal gastrectomy and palliative total gastrectomy; log rank $p<0.0001$ for all other pairwise comparisons).

survival rate and median survival time were 62.1%, and 59.7 (95% CI: 51.0-68.4) months, respectively after distal gastrectomy, while they were 42.6% and 41.0 (95% CI: 25.7-56.4) months, after total gastrectomy (log rank $p < 0.0001$) (Fig. 2).

Of the 361 patients who underwent palliative resection, 158 patients (43.8%) received postoperative chemotherapy. The median survival time of patients with chemotherapy was 17.4 (95% CI: 14.0-20.8) months, while the median survival time of those without chemotherapy was 9.6 (95% CI: 7.6-11.6) months with a significant difference (log rank $p = 0.011$)

Prognostic factor analysis

Table 3 shows the results of univariate analysis

Table 3. Survival Data and Univariate Analysis of Prognostic Factors in 1322 Gastrectomized Patients with Gastric Cancer

Variable	No.	5-yr survival rate	Median survival time (95%CI)	Log-rank *p*
Age (yr)				
< 70	968	48.86	56.53 (44.69-68.37)	0.0002
≥ 70	354	36.62	30.10 (20.54-39.66)	
Gender				
male	967	45.72	44.67 (33.54-55.79)	0.6460
female	519	45.02	50.33 (38.27-62.39)	
Location				
upper 1/3	280	29.26	19.23 (13.92-24.55)	< 0.0001
middle 1/3	298	52.50	75.13 (37.95-112.32)	
lower 1/3	725	50.04	60.63 (NA)	
entire	19	8.82	13.40 (6.72-20.08)	
Borrmann classification				
Type 0-II	424	71.42	NA	< 0.0001
Type III-IV	898	32.31	25.03 (20.83-29.24)	
Tumor size (cm)				
< 4.0	562	66.32	NA	< 0.0001
≥ 4.0	760	29.33	21.07 (18.56-23.57)	
Depth of invasion				
pT1	234	91.56	NA	< 0.0001
pT2	177	75.76	NA	
pT3	757	30.00	24.60 (21.38-27.82)	
pT4	154	16.75	12.53 (9.30-15.76)	
Gastrectomy				
distal	933	51.78	71.17 (NA)	< 0.0001
total	389	30.80	19.47 (15.07-23.86)	
Histologic type				
differentiated.	577	55.53	71.17 (NA)	< 0.0001
undifferentiated	745	38.05	29.77 (23.01-36.52)	
Lymph node metastasis (no. of positive lymph nodes) (UICC, 1997)				
pN0 (0)	501	80.36	N.A.	< 0.0001
pN1 (1-6)	409	37.63	33.33 (25.08-41.59)	
pN2 (7-15)	257	12.88	17.73 (13.92-21.55)	
pN3 (> 15)	155	6.47	11.53 (8.44-14.63)	
Distant metastasis				
pM0	1072	52.30	71.03 (NA)	< 0.0001
pM1	250	14.64	10.80 (9.02-12.58)	

Table 3. Survival Data and Univariate Analysis of Prognostic Factors in 1322 Gastrectomized Patients with Gastric Cancer ***(Continued)***

Variable	No.	5-yr survival rate	Median survival time (95%CI)	Log-rank *p*
Peritoneal seeding				
negative	1141	50.18	60.63 (49.74-71.52)	< 0.0001
positive	181	14.16	10.77 (8.94-12.59)	
Liver metastasis				
negative	1273	47.02	50.33 (40.67-60.00)	< 0.0001
positive	49	0.0	11.30 (7.59-15.01)	
Vascular invasion				
negative	1101	50.66	61.80 (50.90-72.70)	< 0.0001
positive	221	18.69	14.70 (11.80-17.60)	
Lymphatic invasion				
negative	646	68.48	NA	< 0.0001
positive	676	23.03	19.70 (17.58-21.82)	
Perineural invasion				
negative	1812	58.26	NA	< 0.0001
positive	510	23.29	19.70 (17.25-22.15)	
Resection margin				
negative	1272	50.57	61.80 (50.61-72.99)	< 0.0001
positive	150	8.82	13.47 (11.60-15.33)	
Serum CEA level				
normal (≤ 5 U/dl)	1029	51.64	71.03 (NA)	< 0.0001
elevated (> 5 U/dl)	293	35.31	26.67 (14.97-38.36)	
Residual tumor classification				
R0	961	57.0	NA	< 0.0001
R1	104	14.17	19.07 (15.07-23.07)	
R2	257	14.39	10.77 (9.03-12.51)	
Pathologic stage				
IA	202	94.39	NA	< 0.0001
IB	132	84.56	NA	
II	195	63.35	NA	
IIIA	243	37.97	32.83 (22.11-43.56)	
IIIB	135	15.75	22.13 (16.78-27.49)	
IV	415	14.77	12.87 (11.23-14.50)	

NA: not available or computable.

of prognostic factors in our patients. Significant prognostic factors included age ($p = 0.0002$), tumor location, tumor size, gross type, histologic type, depth of invasion, lymph node metastasis and peritoneal seeding, liver metastasis, resection margin, vascular invasion, lymphatic invasion, perineural invasion, pathologic stage (Fig. 3), type of gastrectomy, and preoperative serum CEA level (Fig. 1) ($p < 0.0001$).

Multivariate analysis was further performed using the Cox regression method on the prognostic factors which were significant in the univariate analysis. The most important prognostic factors, identified by multivariate analysis, were lymph node metastasis, serosal invasion, peritoneal seeding, positive resection margin, liver metastasis, old age, tumor size, and lymphatic invasion (Table 4). Tumor location, histologic type, vascular invasion, gross type, and serum CEA turned out to be factors of no significance in the multivariate analysis.

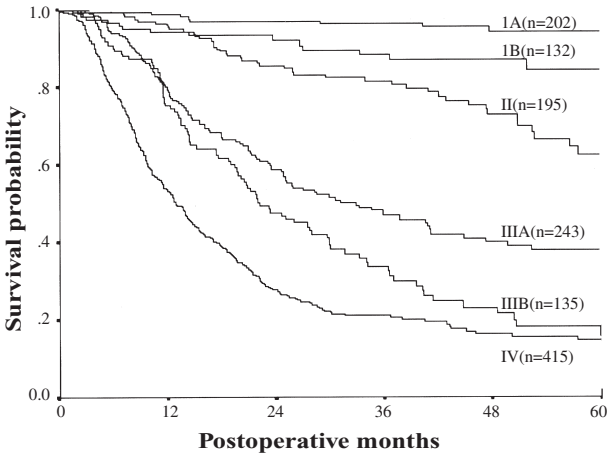

Fig. 3 Kaplan-Meier survival curves for patients according to UICC's pTMN classification (1997 edition) for gastric cancer (log rank $p < 0.0001$).

Table 4. Most-important Prognostic Factors Determined by Multivariate Analysis in 1322 Gastrectomized Patients with Gastric Cancer

Variable	Risk ratio	95% confidence interval	*p*
Lymph node metastasis (positive vs. negative)	1.62	1.51-1.72	< 0.0001
Depth of invasion (pT3-4/pT1-2)	3.30	2.94-3.66	< 0.0001
Peritoneal seeding (positive vs. negative)	1.74	1.53-1.96	< 0.0001
Resection margins (positive vs. negative)	1.71	1.49-1.93	< 0.0001
Liver metastasis (positive vs. negative)	2.25	1.90-2.60	< 0.0001
Size (cm) (≥ 4 vs. < 4)	1.45	1.24-1.67	0.0006
Age (yr) (≥ 70 vs. < 70)	1.30	1.11-1.49	0.0065
Lymphatic invasion (positive vs. negative)	1.36	1.13-1.60	0.0107

DISCUSSION

A curative resection with no residual tumors has been recognized as the key factor in reducing locoregional recurrence and improving survival of patients with gastric cancer.[7,11,12] A D2 gastrectomy is advocated as the golden standard for radical treatment of gastric cancer by Japanese surgeons.[6,7] We have adopted D2 lymphadenectomy since the 1980s. However, results from the application of D2 lymphadenectomy in the West are controversial. Recently data from a number of non-Japanese series have shown the safety and survival benefit of D2 gastrectomy, especially for stage II or IIIA patients.[13-17] Although there were unfavorable results in some randomized control studies,[18,19] it is commonly accepted as the treatment of choice for gastric cancer.[11,20,21]

Mortality and morbidity rates of curative resection vary among authors and procedures, ranging 0%-13% and 13%-59%, respectively, for D2 gastrectomy.[22,23] Our mortality rate (3.3%) for curative gastrectomy was comparable to those of other series. Mortality and morbidity rates of a total gastrectomy were higher than those after distal gastrectomy, due to wider tissue dissection and the risk of leakage from esophagojejunal anastomosis.[22,24] A combined resection of the distal pancreas and spleen was reported to be responsible for postoperative complications with a total gastrectomy.[25] The operative mortality of palliative total gastrectomy was particularly high in our own and in other series, mostly due to the debilitated general condition of patients and advanced stage of disease.[26,27] We suggest that total gastrectomy be replaced with non-resection procedures in patients with high-risk factors, such as severe medical diseases, extensive peritoneal seeding, and old age.

Overall survival rates for gastric cancer after curative resection vary in a wide range among different countries.[1] Generally, Japanese series have better survival than do non-Japanese ones (60.5% vs. 39.4%), largely because Japanese patients are operated on at an earlier stage. The overall 5-year survival rate after curative resection was 57% in our series which compares favorably with survival rates reported in other series (Japan, 60%; Germany, 46%; US, 36%-46%; Italy 54.9%), being especially near that of Japanese series.[28] The survival rate for gastric cancer patients has been improving over the past 30 years.[1,2] Earlier diagnosis, curative surgery, and better perioperative care have all contributed to the

improvement.

The survival of gastric cancer patients postoperatively is influenced by prognostic factors in 3 main categories: tumor, treatment, and host. Among tumor-related factors, the status of UICC's TNM (depth of invasion, lymph node metastasis, and distant metastasis) and stage are well recognized as essential predictors for the prognosis. The prognostic significance of other tumor-related factors, including tumor size, gross type, tumor location, histologic type, vascular invasion, lymphatic invasion, and perineural invasion, is inconsistent among different series.[11,12,29-32] With respect to host-related factors, old age and male gender are regarded as potential risk factors in some series.[31,33] Among treatment-related factors, UICC's residual tumor classification or surgical curability is a well-established risk factor for recurrence. Positive resection margin is 1 of the important unfavorable prognostic factors for survival.[12] A positive impact of radical lymph node dissection on the prognosis is supported by most series.[11,29,30] Some reports have listed surgical complications and blood transfusions as unfavorable prognostic factors.[11,34]

Complete resection of all macroscopic and microscopic tumors remains the primary mode of gastric cancer treatment. However, a substantial portion of patients with gastric cancer will die of recurrent or metastatic disease even after curative resection. Additional modes of treatment, such as chemotherapy, radiotherapy, and immunotherapy, are required as additive or adjuvant therapies. The role of adjuvant chemotherapy remains controversial due to conflicting results between Japan and Western countries. Adjuvant chemotherapy has been advocated as a routine multimodality therapy for locally advanced gastric cancer in Japan.[35] It is not recommended except for clinical trial in Western countries.[36] However, a recent meta-analysis of randomized studies of adjuvant chemotherapy from Western countries showed a borderline favorable result.[37] Currently, we are carrying out a clinical trial of adjuvant chemotherapy with a mitomycin-based regimen according to Graus and most Japanese series.[9,35]

Early aggressive chemotherapy is recommended for patients who have undergone palliative resection.[38] A regimen, consisting of weekly high-dose 5-fluorouracil and leucovorin infusions, has been selected for our patients following palliative resection.[8] In a phase II prospective trial, this regimen could achieve a 33.3% partial response rate, in addition to having acceptable toxicity.[8] In this study, the 5-FU-based regimens were demonstrated to offer significant survival benefits for patients following palliative resection.

The incidence rate of early gastric cancer was 17.7% in our resected patients, being intermediate between those in Japan (25%-60%) and in Western countries (2%-15%).[39] The use of mass surveys has partially contributed to an earlier diagnosis of gastric cancer in Japan. Cost-effective considerations could be a reason not to undertake a mass survey in Taiwan, because Taiwan is not a high-incidence area for gastric cancer. The prognosis of early (pT1) gastric cancer is excellent with 5-year survival rates over 90% after gastrectomy, but not in patients with lymph node metastasis.[40] As an alternative to gastrectomy, less-invasive techniques, including endoscopic mucosal resection and a laparoscopic approach, are currently practiced in our patients with early gastric cancer. These techniques can avoid operative risks and side effects of gastrectomy, which might be overtreatment for some patients with early gastric cancer.

Serum CEA and CA19.9 are the tumor markers most frequently measured preoperatively in patients with gastric cancer. Positive rates of preoperative serum CEA and CA19.9 were 22.2% and 21.7%, respectively, in our patients. Neither are useful tools for mass screening or early detection of gastric cancer in the general population. Nevertheless, preoperative serum CEA or CA19.9 level is a good prognostic indicator for gastric cancer.[41] Elevation of preoperative serum CEA was associated with a later stage of gastric cancer, and also a shorter survival in our patients.[42]

Great efforts have been made to improve the quality of treatment for gastric cancer in our hospital. This initial report shows that results of operative mortality and survival outcome in our patients compare favorably with those of other series. With the aim of a 0 mortality rate, we have been more careful in case selection and preoperative preparation of patients for extensive procedures. To improve patient survival, we have conducted trials of more-radical surgery such as D4 lymphadenectomy (para-

aortic lymph node dissection), and more-effective adjuvant therapies. Basic research is also ongoing along with investigations of clinical medicines to promote better treatments. We hope to find new tumor markers and effective treatments that might offer a cure for gastric cancer.

Acknowledgments

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

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可切除的胃癌：手術死亡率和存活預後的分析

王嘉修 謝清川 趙子傑 詹益銀 鄭隆賓 黃燦龍 陳敏夫 陳邦基[1]
陳仁熙[2] 薛 綏[3]

背 景：本文旨在評估本院近六年來胃癌切除手術的成績，存活分析並判定重要的預後因子。

方 法：於1994年和2000年期間，本院共有1,322胃癌病人接受胃切除手術。平均年齡是61.1歲(差距，14-92)。包括865位男性和457位女性。施行全胃切除術有389 (29.4%) 位，遠端胃切除術有933位。其中根治切除者961位，緩解切除者361位。根治切除術必須包含D2或更高層次淋巴結的廓清術。緩解手術的病人術後給予化學治療。

結 果：早期 (pT1) 胃癌佔總切除例的17.7%，而淋巴結轉移佔62.1%。胃切除術的總死亡率和併發症率分別是3.3%和18.0%，兩者於緩解切除術都高過根治切除。各種手術中以緩解性的全胃切除術術死率特別高 (8.5%)。全部病人的五年累積存活率是45.6%，其中根治切除者達57.0%。多變數分析發現影響存活最重要的預後因子包括淋巴結轉移、胃壁漿膜的侵犯、腹膜播種、切離斷端陽性、肝臟轉移、高齡、腫瘤大小和淋巴管的侵襲。

結 論：最重要的預後因子包括淋巴結轉移、胃壁漿膜的侵犯、腹膜播種、切離斷端陽性、肝臟轉移、高齡、腫瘤大小和淋巴管的侵襲。本院近六年來胃癌病人胃切除手術的死亡率和五年累積存活率和世界上其他系列的成績較佳者相類似。

(長庚醫誌 2002;25:216-27)

關鍵字：胃癌，胃切除手術，手術死亡率，預後分析。

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