

Is There a Role for Palliative Gastrectomy in Patients with Stage IV Gastric Cancer?

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Abstract

Patients with metastatic gastric cancer are currently not considered operative candidates and are most often offered systemic therapy. Palliative resection of the primary tumor has been considered irrelevant to the outcome and has been recommended only for palliation of symptoms. We have examined the role of palliative gastrectomy and its impact on survival in patients with stage IV gastric cancer at initial diagnosis between 1990 and 2000. A total of 105 patients with stage IV disease were identified during this period; 81 of them (77.1%) had no resection, and 24 (22.9%) underwent palliative gastric resection. Mean survival in those without resection who received chemotherapy (with or without radiation) treatment was 5.9 months (95% confidence interval 4.2–7.6). For those with resection and adjuvant therapy, mean survival time was 16.3 months (95% confidence interval 4.3–28.8 months). Kaplan-Meier survival analysis showed significantly better survival in those with resection and adjuvant therapy (log-rank test, $P = 0.01$). Mortality and morbidity rates associated with palliative resection were 8.7% and 33.3%, respectively, which did not differ statistically from the 3.7% and 25.3% in patients who underwent curative gastrectomy during same period of time. However, the length of hospitalization (22 versus 16 days) was significantly higher compared with those without stage IV disease. These data suggest that palliative resection combined with adjuvant therapy may improve survival in a selected group of patients with stage IV gastric cancer. Palliative gastrectomy plus systemic therapy should be compared with systemic therapy alone in a randomized trial.

The incidence of gastric cancer has decreased in the United States and worldwide. There were 22,710 new cases of gastric carcinoma in United States in year 2003.¹ Because a screening program is not cost effective, most patients with gastric cancer present at an advanced stage.

Surgical resection remains the main curative treatment for gastric cancer. Although the role of palliative gastrectomy in patients with advanced gastric cancer is unclear, several studies have suggested that resection may provide

some survival benefit.^{2–5} However, the extended survival after palliative gastrectomy in other studies was associated with significant postoperative morbidity, prolonged hospital stay, and poor quality of life.^{6–8} The aims of palliative resection are to enable oral food intake by improving obstructive symptoms, bleeding, or pain. The aim of the present study was to evaluate patient outcome after palliative gastric resection for metastatic gastric cancer.

PATIENTS AND METHODS

Between 1990 and 2000, 210 cases of histologically proven gastric adenocarcinoma were identified. Of those

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210 patients, 104 (49.5%) underwent gastric resection. Stage IV gastric cancer was defined based on American Joint Commission on Cancer (AJCC, 6th edition), as M₁ or T₄N₁₋₃M₀.⁹

This study was approved by the Institutional Review Board of each participating institution individually. All patients were treated at the University of Kentucky, University of Tennessee, or Providence Hospital, Southfield, Michigan. Because of the small number of patients, no comparison was made of institutional difference in outcome or survival.

This is retrospective analysis of 105 patients with stage IV disease identified during this period; 81 (77.1%) received either no operation or a bypass procedures with or without adjuvant treatment, and 24 (22.9%) underwent palliative gastric resection (Table 1). The patients were divided into four groups based on treatment (Table 1). The indications for palliative gastrectomy were judged individually by attending surgeons based on patients' general health, performance status, symptoms, extent of disease, and feasibility of resection.

Patient clinicopathological features, extent of disease, survival, operative mortality and morbidity, length of hospitalization, and readmissions were recorded. Hospital mortality was defined as death within 30 days or during the hospital stay.

For descriptive statistics and survival analyses the SPSS PC software was applied. The independent Students' *t*-test was used to test the differences between groups, and the chi-squared test of association was used for categorical data. The Mann-Whitney *U*-test was used for length of hospitalization comparison. Cumulative survival rates were calculated according to the Kaplan-Meier analysis. Survival differences were compared using log-rank test; *P* values less than 0.05 were considered statistically significant.

RESULTS

This series consists of 105 patients with stage IV gastric adenocarcinoma. Of these 105 patients, 24 (22.9%) underwent resection and 81 (77.1%) did not. The characteristics of patients are shown in Tables 2 and 3. In the non-resection group, 34 (41.9%) received adjuvant therapy and 47 (58.1%) received no treatment.

The mortality after palliative gastrectomy and laparotomy/bypass was 8.3% (2/24) and 8.5% (3/35) respectively. Because of the retrospective nature of this study, complete information on performance status was not available. In addition, because some of the patients did

Table 1.
Treatment groups.

Resection (n = 24)
Group 1: Resection with adjuvant therapy (n = 12)
Group 2: Resection alone (n = 12)
No Resection (n = 81)
Group 3: Chemotherapy with/without radiation (n = 34)
Group 4: No treatment (n = 47)

not received any treatment or resection, the clinicopathological features of some of the tumors were based on CT or endoscopy findings.

The mean survival in patients who had palliative gastrectomy (13.2 months) was longer than in patients who underwent no resection (5.5 months), 2-year survival for the two groups was 25% and 0, respectively. The 5-year survival in the resection group was 5%. There was a significant difference in survival between patients treated with and without gastrectomy (Fig. 1). The mean survival of the patients with stage IV gastric cancer based on treatment modality is shown in Table 4 and Figure 2.

A statistically significant survival advantage was present comparing those patients who had resection plus adjuvant therapy with other groups (log-rank test, *P* = 0.014). However, the survival rates in groups 2, 3, and 4 were not statistically significant. Most of the chemotherapy regimens that patients received were 5-FU (5-fluorouracil) based. No specific protocol was followed for chemotherapy regimen, and the dose and duration of the regimen was based on the opinion of the medical oncologist in each case.

The mean survival among patients who underwent palliative gastrectomy for T₄, N₁₋₃, M₀ disease (n = 5) and M₁ disease with (n = 17) distant metastasis was 14.4 months (3.6–25.1, 95% confidence interval) and 11.2 months (3.5–18.9, 95% confidence interval), respectively. As shown in Figure 3, this was not statistically significant (log-rank test. *P* = 0.37). The patients who did not have distant metastasis were classified as stage IV, based on AJCC, 6th edition, as having T₄, N₁₋₃, M₀ disease. T₄ indicates tumor invading adjacent structures such as pancreas, colon, or spleen. Although these patients have M₀ disease, their survival rate is comparable with that of patients with M₁ disease, as shown in Figure 3.

Table 5 and Figure 4 show survival of patients who had distant metastasis (M₁) base on treatment modality.

As shown in Figure 4, group 1 patients (resection plus adjuvant therapy) had a significant survival advantage

Table 2.
Patients with stage IV gastric carcinoma.

Variable	Surgery group (n = 24)	Non-surgical group (n = 81)	P Value
M/F ratio	14/10	50/31	0.79
Age (mean)	57	62	0.74
Distant metastasis	18 (75%)	62 (76.5%)	0.77
Adjuvant treatment	12 (50.0%)	34 (41.9%)	0.52
Laparotomy (by-pass)	NA	35 (43.2%)	NA
Mean survival (CI*)	13.2 (5.6–20.8)	5.5 (3.8–7.3)	0.006

*95% confidence interval.

Table 3.
Clinicopathological characteristics of the patients with palliative gastrectomy.

Variable	Resected cases (n = 24)	Non-resected cases (n = 81)	P Value
Location of tumor			
Upper third	7 (29.2%)	25 (30.8%)	0.8
Middle third	4 (16.7%)	15 (18.5%)	
Lower third	7 (29.2%)	19 (23.5%)	
Diffuse	6 (25%)	22 (27.2%)	
Tumor size			
> 5 cm	18 (66.7%)		
< 5 cm	6 (33.3%)		
Gross pathology (Borrmann's classification)			
Polypoid	9 (37%)		
Ulcerative	6 (25%)		
Ulceroinfiltrative	3 (12.5%)		
Infiltrative	6 (25%)		
Histology			0.9
Intestinal type	9 (37.5%)	27 (33.3%)	
Diffuse type	15 (62.5%)	54 (66.7%)	
Grade (differentiation)			
Well	0	0	0.7
Moderately	1 (4.2%)	10 (12.3%)	
Poor	23 (95.8%)	71 (87.7%)	
Signet cell	11 (45.8%)	40 (49.3%)	0.9
Depth of invasion (T) ^b			
T1	0		
T2	0		
T3	8 (33.3%)		
T4	16 (66.7%)		
Lymphovascular invasion	15 (62.5%)		
Nodal status ^b			
N0	1 (4.2%)		
N1	12 (50%)		
N2	6 (25%)		
N3	5 (20.8%)		
Operation			
Subtotal gastrectomy	10 (41.7%)		
Total gastrectomy	4 (16.6%)		
Multiorgan resection	10 (41.7%)		
Site of distant metastasis ^a			
Liver	5 (27.7%)	30 (37.1%)	0.7
Distant nodes	12 (66.6%)	20 (22.7%)	
Adrenal gland	2 (11.1%)	–	
Ovary	4 (22.2%)	22 (27.2%)	
Peritoneum	9 (50%)	35 (43.2%)	

^aSome patients had more than one site.

^bBased on AJCC Cancer Staging Manual, 6th edition.

When complete data were not available for comparison, the area is left blank.

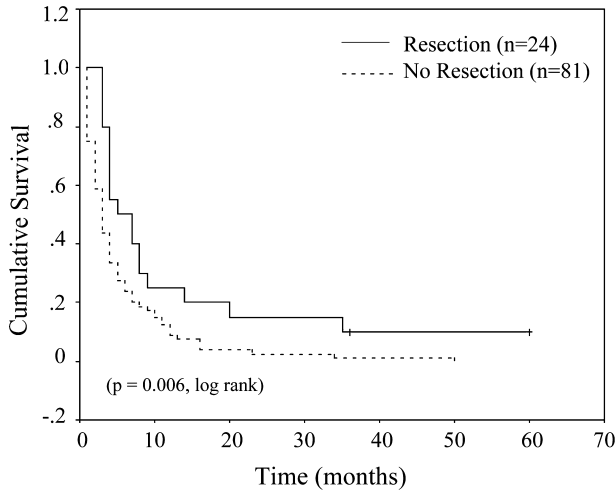


Figure 1. Survival of patients with stage IV gastric cancer with and without palliative resection.

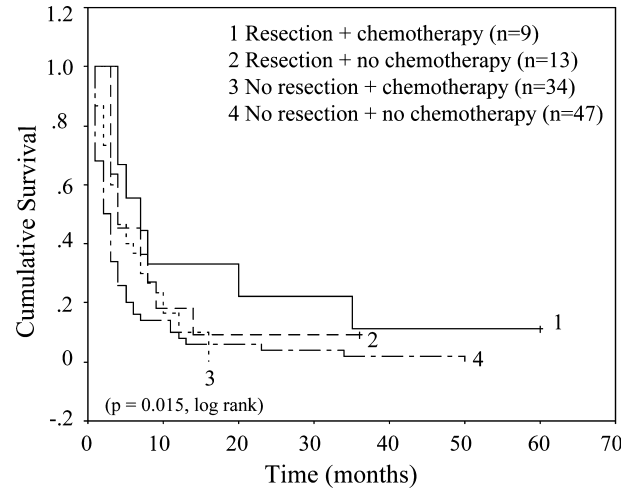


Figure 2. Survival of patients with stage IV gastric cancer based on treatment modality.

Table 4.

Patients overall survival based on treatments modality.

Treatment modality (number of patients)	Mean survival (months)	95% confidence interval (months)
Group 1 Resection + adjuvant therapy (n = 9)	16.3	4.3–28.2
Group 2 Resection alone (n = 13)	8.5	3–14
Group 3 Chemotherapy with or without radiation (n = 34)	5.9	4.2–7
Group 4 No treatment (n = 47)	5.2	2.8–7.6

over the other three groups (log-rank test, $P = 0.02$). The survival rates in groups 2, 3, and 4 were not different.

Mortality, morbidity, length of hospitalization, and readmissions in patients who underwent palliative gastrectomy for stage IV gastric cancer compared to patient outcomes in patients who underwent curative gastrectomy during the same period are shown in Table 6.

DISCUSSION

In the countries where screening for gastric cancer is not routine, this disease is often far advanced at the time of diagnosis. Except for early gastric cancer, patient survival is poor. Based on surveillance, epidemiology, and end results (SEER) data, the average survival for patients with stage IV gastric cancer is 16 weeks, with only 25% living 34 weeks or longer.¹⁰ Alternatively,

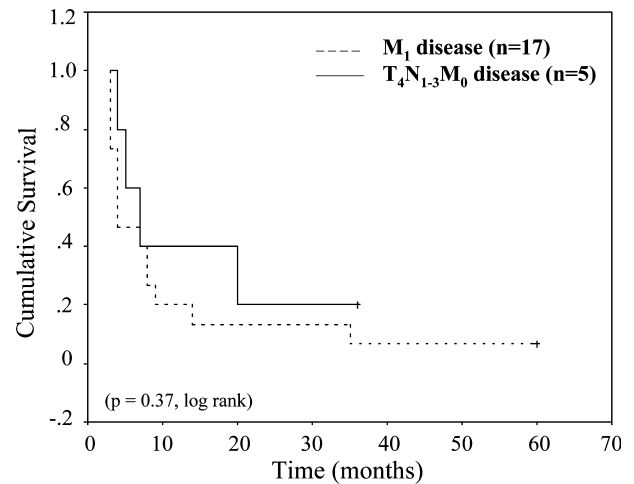


Figure 3. Survival in patients with stage IV gastric cancer who underwent palliative gastrectomy in the presence or absence of distant metastasis.

gastric cancer response to conventional chemotherapy is poor, especially in patients reported in Western studies.^{11,12} Glimelius *et al.*, randomized 61 patients with advanced gastric cancer to receive either chemotherapy plus supportive care or supportive care only. Overall survival was longer in the chemotherapy group (median 8 months versus 5 months), although the difference was not statistically significant ($P = 0.12$).¹³ In our series, the mean survival in the patients who only received adjuvant therapy was 5.9 months compare to 5.2 months in those with no treatment.

Radical resection is the primary treatment for gastric cancer, but for patients with advanced or metastatic disease the benefit of resection is unclear. The role of palliative gastrectomy in patients with metastatic gastric

Table 5.

Survival in patients with distant metastasis (M₁, excluding T₄N₁₋₃, M₀) based on treatment modality.

Treatment modality (number of patients)	Mean survival (months)	95% confidence interval (months)
Group 1 Resection + adjuvant therapy (n = 5)	22.2	2.7–41.6
Group 2 Resection alone (n = 12)	5.8	3.5–8
Group 3 Chemotherapy with or without radiation (n = 34)	6.3	4.1–8.4
Group 4 No treatment (n = 47)	4.8	2.1–7.5

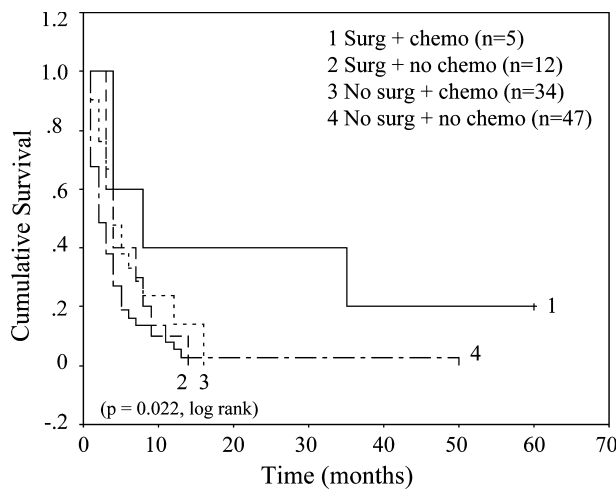


Figure 4. Survival, based on treatment modality, of patients with stage IV gastric cancer who had distant metastasis.

cancer is matter of debate and controversy. Although some studies have shown that palliative gastrectomy is associated with survival benefit,^{2-5,14-18} other studies show that there is no role for palliative gastrectomy in patients with stage IV gastric cancer.⁶⁻⁸

The rationale for offering palliative gastrectomy to patients with stage IV gastric carcinoma is that primary tumor will result in gastric obstruction, perforation, bleeding, or debilitating ascites. Resection should therefore be associated with removal of gross disease with the goal to improve function and quality of life by removing a bulky symptomatic tumor. However, if a significant proportion of the tumor load is removed (cytoreduction surgery), perhaps the disease may be more responsive to adjuvant treatment.¹⁹ In theory, if the majority of the tumor can be debulked safely in combination with chemotherapy and radiation, the results may improve. It is clear that volume and tumor burden reduction diminishes the metabolic

Table 6.

Early outcome in patients who underwent palliative versus curative gastrectomy.

Variable	Palliative (n = 24)	Curative (n = 80)	P Value
Mortality	2 (8.3%)	3 (3.7%)	0.7
Sepsis, MOF	2		
ARDS	1	0	
MI	0	1	
Morbidity	8 (33.3%)	20 (25%)	0.5
Anastomotic leak, IA	3	2	
Wound infection	1	5	
RF	1	4	
Pneumonia	1	3	
SBO	1	3	
EC fistula	0	2	
Sepsis		1	1
Readmissions	11 (45.8%)	22 (27.5%)	0.1
Mean length of stay (range)	22 (9–55)	16 (4–40)	0.001

ARDS: adult respiratory distress syndrome, EC: enterocutaneous, IA: intra-abdominal abscess, MI: myocardial infarction, MOF: multiple organ failure, RF: respiratory failure, SBO: small bowel obstruction.

demands made on the patient by the tumor. In addition, because the tumor itself can produce immunosuppressive cytokine, reducing the tumor burden may also have an immunologic benefit.²⁰

In our study, the overall survival of patients who were treated with multimodality approach (surgery plus adjuvant treatment) was far better than for those who were not (Table 3 and Figure 2), which supports the above argument. Alternatively, the survival advantage of palliative gastrectomy was also seen in patients with distant metastasis (Figure 4). Fujisaki *et al.*,²¹ have shown that gastric resection and degree of hepatic involvement are the only prognostic factors that predict survival in gastric cancer with concomitant liver metastases. Our earlier studies support this concept.^{16,17} However, Chow *et al.*,¹⁸ found that palliative gastrectomy did not improve survival in patients with gastric cancer and liver metastases.

Despite the survival advantage of palliative gastrectomy, some studies show high mortality and morbidity associated with the operation.^{6-8,14} In a Dutch Gastric Cancer Trial, 285 (26%) of 1078 randomized patients were classified as noncurative at laparotomy, and 156 patients had a palliative resection.¹⁴ The overall median survival of patients who underwent palliative resection was 8.1 months compared to 5.4 months in patients who had no resection ($P < 0.001$). However, the morbidity (38% versus 12%) and length of hospitalization (15 versus 10 day) was significantly higher in the resection group. Recently, progress in anesthesia and surgical

techniques has significantly reduced the risk associated with radical surgical procedures. In our study the mortality and morbidity of palliative gastrectomy was 8.7% and 33.3%, respectively, which was not statistically different from mortality and morbidity of curative gastrectomy. However, length of hospitalization was significantly greater (22 versus 16 days). Owing to the nature of the study, no information on quality of life was available.

We believe that selection of appropriate patients with stage IV gastric cancer for resection is the key. These patients might be individuals with acceptable performance status, in whom resection of the tumor is technically feasible despite the fact that they might have metastatic disease. Removing the primary tumor might reduce tumor burden and leave the patients more responsive to adjuvant modalities.^{23–25} Recently, there have been multiple trials which show an improvement in outcome when treating patients with metastatic gastric cancer with chemotherapy.^{26–29}

Our findings showed that even in stage IV gastric cancer, palliative gastrectomy might be associated with survival advantage in selected group of patients, especially if combined with adjuvant therapy as part of multimodality treatment. As long as the primary tumor can be removed with reasonable risk of mortality and morbidity, every attempt should be made to resect the tumor.³⁰ Leaving the tumor not only involves high risk of poor oral intake, pain, obstruction, and bleeding, it also greatly decreases the likelihood of a response to adjuvant treatment.

ACKNOWLEDGEMENTS

The authors thank Catherine Lobocki, M.S., for help in statistical analysis.

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