

Survival of D1 versus D2 Gastrectomy for Patients with Gastric Cancer in Srinagarind Hospital

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Background: Gastric cancer is the second leading cause of cancer death and the fourth most common cancer worldwide. For patients considered curable, surgery is the main curative treatment. There is controversy regarding extensiveness of lymph node dissection between D1, limited to the perigastric nodes, and D2, extended to regional lymph nodes outside the perigastric area.

Objective: The objective of the present study was to compare the survival rate of patients that underwent D1 and D2 gastrectomy at Srinagarind Hospital.

Materials and Methods: The present research was a retrospective cohort study. The inclusion criterion was all resectable gastric cancer patients that underwent gastrectomy with lymphadenectomy for curative intention at Srinagarind Hospital between January 2010 and December 2014. The primary outcome was the survival rate of patients with D1 and D2 gastrectomy.

Results: Seventy-four eligible patients were included. The overall 5-year and median survival time of all recruited patients in the present study were 17.4% (95% CI 5.9 to 28.9) and 584 days (95% CI 446 to 722) with comparable survival between D1 and D2 group. There were 10 cases (13.51%) of morbidity such as bile leakage, wound infection, pancreatic fistula, upper gastrointestinal bleeding, and re-operation from postoperative bleeding. There was one case (1.35%) of postoperative mortality. Postoperative complications and mortality of D1 and D2 group did not differ significantly ($p=0.20$).

Conclusion: No difference was found in the survival and complication between D1 and D2 gastrectomy at Srinagarind Hospital.

Keywords: Gastric cancer, D1 gastrectomy, D2 gastrectomy, Survival, Morbidity, Mortality

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Gastric cancer is the second leading cause of cancer death and the fourth most common cancer worldwide⁽¹⁾. Early gastric cancer has no associated symptoms. Most symptoms of gastric cancer, such as gastric outlet obstruction, hematemesis, weight loss, and palpable abdominal masses, reflect advanced stages of the disease⁽²⁾. The extension of disease frequently reveals lymph node, peritoneum, and liver metastases. The prognosis and treatment options depend on the stage of the cancer⁽³⁾. For patients considered curable, surgery is the main curative treatment. There is controversy regarding the extensiveness of lymph node dissection between D1, limited to the perigastric nodes, and D2, extended to regional lymph nodes outside the perigastric area⁽⁴⁾. Many studies revealed that D2 group had significantly better survival with less morbidity and mortality⁽⁵⁻⁷⁾, while some studies

showed disadvantage of D2 gastrectomy^(4,8). In high-incidence countries, such as Japan and South Korea, D2 lymphadenectomy is the most commonly performed lymphadenectomy. Less extensive lymphadenectomies are often performed in lower-incidence countries such as the United States⁽⁹⁾.

In Thailand, the incidence of gastric cancer in men and women is 4.1/100,000 and 2.5/100,000, respectively⁽¹⁾. Surgical treatment with radical gastrectomy in combination with lymphadenectomy is standard, but the extension of lymph node dissection is still controversial.

The objective of the present study was to compare the survival rate of patients that underwent D1 and D2 gastrectomy at Srinagarind Hospital.

Materials and Methods

The present study was a retrospective observational trial, which was approved by the Khon Kaen University Human Ethics Committee in Human Research (HE591176). Requirement for informed consent from

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Table 1. Patient demographic and clinical data

	D1 (n = 49)	D2 (n = 25)	p-value
Sex, n			
Male:female	32:17	15:10	0.66
Age (years)			0.30
Mean ± SD	57±10.4	59.2±8	
Median (range)	58 (35 to 81)	62 (42 to 75)	
Location of tumor, n (%)			0.44
Upper	10 (20.4)	5 (20.0)	
Middle	3 (6.1)	4 (16.0)	
Lower	9 (18.4)	6 (24.0)	
More than one	27 (55.1)	10 (40.0)	
Macroscopic finding, n (%)			0.54
Non-scirrhus	18 (36.7)	11 (44.0)	
Scirrhus	31 (63.3)	14 (56.0)	
Histologic grade, n (%)			0.94
Well or moderately differentiated	22 (44.9)	11 (44.0)	
Poorly differentiated	27 (55.1)	14 (56.0)	
T-category, n (%)			0.86
T1	1 (2.0)	1 (4.0)	
T2	2 (4.1)	2 (8.0)	
T3	17 (34.7)	8 (32.0)	
T4	29 (59.2)	14 (56.0)	
N-category, n (%)			0.36
N0	11 (22.4)	6 (24.0)	
N1	7 (14.3)	6 (24.0)	
N2	14 (28.6)	9 (36.0)	
N3	17 (34.7)	4 (16.0)	
M-category, n (%)			0.34
M0	49 (100)	24 (96.0)	
M1	0 (0.0)	1 (4.0)	
Stage, n (%)			0.41
I	2 (4.1)	2 (8.0)	
II	11 (22.5)	3 (16.0)	
III	35 (71.4)	18 (72.0)	
IV	1 (2.0)	2 (4.0)	
Harvested node			0.024
Mean ± SD	12.2±7.3	16.9±10.0	
Median (range)	11 (2 to 35)	15 (4 to 41)	
Positive node			0.10
Mean ± SD	6.3±6.4	4.0±5.2	
Median (range)	4 (0 to 22)	3 (0 to 19)	

D1 = D1 gastrectomy; D2 = D2 gastrectomy; SD = standard deviation

the patient was waived since patient confidentiality protection had been guaranteed. The data extracting sheet did not have the name of the patient but was tagged by a unique study number.

The inclusion criteria were all resectable gastric cancer patients that underwent gastrectomy with lymphadenectomy for curative intent. The exclusion criteria were cases of advanced or unresectable gastric cancer. The primary outcome was survival of patients with D1 and D2 gastrectomy. All patients were

Table 2. Surgical data and outcomes

	D1 (n = 49)	D2 (n = 25)	p-value
Type of gastrectomy, n (%)			0.99
Distal	26 (53.1)	13 (52.0)	
Total	21 (42.8)	11 (44.0)	
Proximal	2 (4.1)	1 (4.0)	
Margin, n (%)			0.28
R0	38 (77.6)	22 (88.0)	
R1	11 (22.4)	3 (12.0)	
Operative time (minutes)			<0.001
Mean	173.2±63.8	254.6±55.2	
Median (range)	160 (50 to 360)	240 (165 to 360)	
Operative blood loss (mL)			0.96
Mean ± SD	359.0±287.9	363.2±361.9	
Median (range)	250 (20 to 1,400)	200 (100 to 1,700)	

D1 = D1 gastrectomy; D2 = D2 gastrectomy; SD = standard deviation

managed perioperatively by experienced surgeons under standard protocol of the institute. The choice of type of operation depended on each surgeon's preference and experience. The authors reviewed all eligible medical records of Srinagarind Hospital between January 2010 and December 2014. The extracted data comprised all patient clinical data as well as the date of operation and death.

Statistical analysis

Continuous data were presented as mean ± standard deviation (SD) and compared using unpaired t-test or Mann-Whitney U test. Categorical data were presented as number (%) and analyzed using Pearson's Chi-square or Fisher's exact test. Overall survival was assessed using the Kaplan-Meier analysis with log-rank test. A p-value of less than 0.05 was considered statistically significant. All calculations were performed using SPSS for Windows version 16.0 (SPSS Inc., Chicago, IL, USA).

Results

Seventy-four cases were recruited, with 49 cases (66.2%) that underwent D1 and 25 cases (33.8%) that underwent D2 gastrectomy. Both groups had comparable clinical data regarding demographic, location of tumor, macroscopic finding, histologic grade, T-category, N-category, M-category, stage, and positive node, but the D2 group had a higher number of harvested node (Table 1). As for surgical data, they were comparable type of gastrectomy, margin, and operative blood loss but the D2 group had longer operative time (Table 2). Due to institutional limitation, the surgeons did not perform peritoneal washing during surgery.

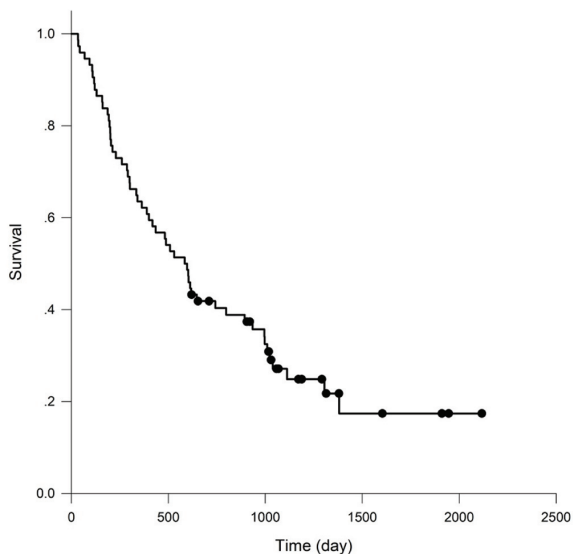


Figure 1. Overall survival curve of all gastrectomy patients.

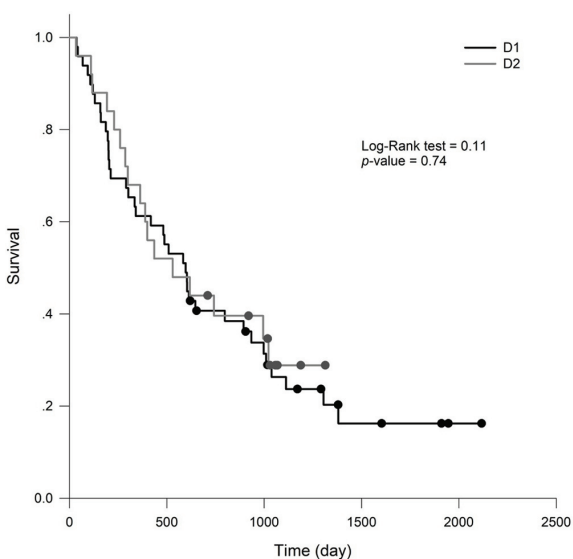


Figure 2. Survival curves of D1 and D2 gastrectomy patients.

Survival

The survival curve of all patients in the present study is shown in Figure 1. The overall 5-year and median survival time of all recruited patients were 17.4% (95% CI 5.9 to 28.9) and 584 days (95% CI 446 to 722), respectively. Based on the Kaplan-Meier method with Log-Rank test, both D1 and D2 group had comparable survival rate ($p=0.74$) (Figure 2). The 1-year, 3-year, 5-year, and median survival time of D1 and D2 group are presented in Table 3.

Table 3. Survival data of D1 and D2 gastrectomy

Survival	D1 (n = 49)	D2 (n = 25)
1-year survival (%) (95% CI)	61.2 (47.5 to 74.9)	64.0 (45.2 to 82.8)
3-year survival (%) (95% CI)	26.3 (13.4 to 39.2)	28.9 (9.9 to 47.9)
5-year survival (%) (95% CI)	16.2 (4.1 to 28.3)	N/A
Median survival time (days) (95% CI)	597 (437 to 756)	530 (174 to 885)

D1 = D1 gastrectomy; D2 = D2 gastrectomy; CI = confidence interval

Table 4. Postoperative complications

Complications	D1 (n = 49)	D2 (n = 25)	Total (n = 74)
Bile leakage	2 (4.1)	1 (4.0)	3 (4.1)
Wound infection	3 (6.1)	1 (4.0)	4 (5.4)
Pancreatic fistula	1 (2.0)	0 (0.0)	1 (1.4)
Upper GI bleeding	1 (2.0)	0 (0.0)	1 (1.4)
Re-operation (postoperative bleeding)	0 (0.0)	1 (4.0)	1 (1.4)
Death	0 (0.0)	1 (4.0)	1 (1.4)
Total	7 (14.3)	4 (16.0)	11 (14.9)

D1 = D1 gastrectomy; D2 = D2 gastrectomy; GI = gastrointestinal
 p -value = 0.20

Morbidity and mortality

Overall, there were 10 cases (13.6%) of morbidity i.e., bile leakage, wound infection, pancreatic fistula, upper gastrointestinal bleeding, and re-operation from postoperative bleeding. There was one case (1.4%) of postoperative mortality. Postoperative complications and mortality of D1 and D2 group did not differ significantly ($p=0.20$) (Table 4).

Discussion

Surgery is the main curative treatment for gastric cancer. The prognosis and treatment options depend on the stage of the cancer. The two most-used classifications are the Classification of Japanese Gastric Carcinoma Association (JGCA)⁽¹⁰⁾ and TNM classification of the American Joint Committee on Cancer (AJCC)⁽³⁾. The results of classification of patients in the present study using these two classifications were similar. Most of the patients had advanced disease, with 76% at TNM stage III and IV and 77% with nodal metastasis. One patient had distant metastasis to the liver. Potentially, curative resection was performed for all patients.

The aim of gastrectomy in cases of gastric cancer is microscopically complete resection (R0 resection), starting with freeing the tumor at the proximal, distal, and radial margin in gastrectomy, and then followed by adequate lymphadenectomy. Generally,

the margin in gastrectomy must be at least 3 to 5 cm. For the adequate lymphadenectomy, at least 15 nodes according to the National Comprehensive Network (NCCN) Guideline⁽¹¹⁾, or 16 nodes according to the JGCA Guideline^(2,10) must be performed. However, one study suggested that a lymphadenectomy of at least 25 lymph nodes was associated with the best long term results⁽⁶⁾. In the present study, the average number of lymph nodes dissected in each group was slightly different, with 12.2 (range 2 to 35) being dissected in the D1 gastrectomy group, and 16.9 (range 4 to 41) in the D2 gastrectomy group. These data are important because the number of dissected nodes is considered a marker of quality for D2 gastrectomy.

The present study showed the overall 5-year survival was 17.4% (95% CI 5.9 to 28.9), which is lower than other studies⁽¹²⁻¹⁶⁾. The survival rate depends on the expertise of the surgeon and the regimen of chemotherapy. In high-incidence country like Japan, the standard operation for gastric cancer is a radical D2 resection, with a reported operative mortality of 1.9% or less and overall 5-year survival rates of 59.4% for patients with curative surgery at the Cancer Institute Hospital, Tokyo⁽¹⁷⁾. In Thailand, a 10-year period study of D2 gastrectomy from Ramathibodi Hospital reported the 5-year survival rate of 59%⁽¹⁸⁾. Another study in early gastric cancer patients from Siriraj Hospital reported no mortality during the mean follow-up period of 30.53 months⁽¹⁹⁾. The difference in survival is partly due to the fact that most of the patients in the present study had reached advanced stages of the disease, while in the aforementioned studies, most patients were at early stages. In addition, the present institute's financial restriction led to the limited quantity of standard adjuvant therapy. Another factor is that our surgeons have less experience. With additional practice, we expect the survival rate in this group of patients to increase.

The survival rate of patients that underwent D1 and D2 gastrectomy in the present study was not significantly different. The present study result is different from most retrospective studies in Japan^(5,12,17,20) as well as in some non-Japanese centers^(13-15,21,22) that showed favorable result of D2 gastrectomy. However, the present result is in accordance with some prospective randomized comparison of D1 versus D2 resection recruiting 267 and 400 patients that showed no difference in the overall 5-year survival between the two arms^(16,23). Therefore, the choice of surgery between D1 and D2 should be based mainly on perioperative surgical risk of the patient rather than the expected result.

The overall morbidity rate in the present study was 13.6%, which is lower than many studies^(4,8,24) and similar to one study⁽²³⁾. There was no significant difference in morbidity between D1 and D2 group, which is similar with some studies^(23,25) but different from many studies that revealed that D2 resection caused more morbidity^(4,8). There was only one case with mortality (1.4%) in the present study, which is lower than most studies^(4,8,23,24). These findings reflect the high quality of perioperative patient management of the present institute.

Limitation

Since this was a retrospective study, there were some inaccuracy of medical records and the inconsistency of protocol of treatment of each patient, e.g., different regimen of chemotherapy. There may be additional uncontrolled confounding factors among groups. Further studies using prospective randomized trials are suggested.

Conclusion

The overall 5-year and the median survival time of all recruited patients in the present study were 17.4% (95% CI 5.9 to 28.9) and 584 days (95% CI 446 to 722) with comparable survival between D1 and D2 group. There were 10 cases (13.51%) of morbidity i.e., bile leakage, wound infection, pancreatic fistula, upper gastrointestinal bleeding, and re-operation from postoperative bleeding. There was one case (1.35%) of postoperative mortality. Postoperative complications and mortality of D1 and D2 group did not differ significantly ($p=0.20$).

What is already known on this topic?

The main curative treatment for curable gastric cancer is surgery. There is still controversy regarding the extensiveness of lymph node dissection between D1, limited to the perigastric nodes, and D2, extended to regional lymph nodes outside the perigastric area. There is also inconsistency with the results of D1 versus D2 regarding survival of the patients.

What this study adds?

The present study reveals that survival of the patients with D1 and D2 gastrectomy at Srinagarind Hospital was comparable with a low incidence of postoperative morbidity and mortality. Therefore, the choice of surgery between D1 and D2 should be based mainly on perioperative surgical risk of the patient rather than the expected result. The 5-year

survival in this study was lower than many studies due to differences in experience of the surgeons and the chemotherapy protocol.

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Potential conflicts of interest

The authors declare no conflict of interest.

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