

RESEARCH ARTICLE

Factors Predicting Survival of Patients with Gastric Cancer

Wen-Li Lin¹, Jia-Ling Sun^{2*}, Shu-Chan Chang¹, Pei-Hua Wu¹, Wen-Tsung Huang³, Chao-Jung Tsao³

Abstract

Background: Gastric cancer is one of the most common causes of cancer death in Taiwan. The literature has previously shown that age, tumor site, T categories, and number of metastatic nodes significantly affect prognosis. The aim of this study was to determine the long-term survival of patients with gastric cancer, as well as the effect of particular prognostic factors on survival. **Materials and Methods:** This was a survival analysis study with retrospective design. We reviewed the records of 64 patients with adenocarcinoma of the stomach who had undergone gastrectomy with curative intent between 2009 and 2012 at a teaching hospital in southern Taiwan. Data extracted from patient documents included age, gender distribution, tumor location, and pathological grading. **Results:** The median follow-up time was 4 years, and there were 31 deaths attributed to gastric cancer. Kaplan-Meier analysis revealed that retrieval of less than 15 lymph nodes from a patient was a significant predictor of survival. A significant predictor of poorer survival was higher pathological grading. **Conclusions:** Our results indicate that the number of lymph nodes retrieved and pathological grading could be viewed as crucial prognostic factors affecting the survival of individuals with gastric cancer.

Keywords: Gastric cancer - metastatic lymph nodes - survival - Taiwan

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Introduction

Cancer is an important global health issue and gastric cancer is one of the most important diseases affected health in the world wide. Gastric cancer has a poor prognosis (Zare et al., 2013; Calik et al., 2014; Etemadi et al., 2014). In 2011, gastric cancer was the seventh most prevalent form of cancer in Taiwan. The new cases of gastric cancer were 4.13% of totally new cases and 5.38% died of gastric cancer in 2011 (Health Promotion Administration Ministry of Health and Welfare, 2014). In that year, a total of 3,824 individuals were newly diagnosed with gastric cancer while 2,288 died from it (Ministry of Health and Welfare, 2013; Health Promotion Administration Ministry of Health and Welfare, 2014).

The number of lymph nodes removed from a patient comprise one of the most important prognostic indicators of gastric cancer, and the seventh edition of the tumor, lymph node, metastasis (TNM) staging system increased the required number of examined lymph nodes in gastric cancer from 15 to 16 (Son et al., 2012; Zhang et al., 2012). The number of lymph node removed is an independent prognostic factor regardless of the number of lymph nodes actually examined. In predicting the prognosis of gastric cancer, lymph node metastasis is an important prognostic indicator for patients with radically resected gastric cancer

(Alatengbaolide et al., 2013). The only way to cure patients with advanced gastric cancer is by gastrectomy with adequate regional lymph node dissection, although this has only recently been implemented as the standard of care in Western countries (de Steur et al., 2013).

The previous studies shown that age, tumor location, T categories, number of metastatic nodes, and N ratio significantly affect prognosis, with number of metastatic lymph node being an independent prognostic factor regardless of the examined number of lymph nodes (Alatengbaolide et al., 2013; Zare et al., 2013; Calik et al., 2014). Stephens et al. (2005) study reported that symptoms which may suggest gastric cancer like dyspepsia and/or epigastric pain, weight loss was the most common alarm symptom, present in 50.8% of patients, and cumulative survival rate at 5 years was 38% for patients without alarm symptoms versus 15 % for those with alarm symptoms.

Histopathology is the most common method for diagnosing and following the progression of gastric cancer, and it has been reported that the risk of death is increased significantly among patients with poorly differentiated or moderately differentiated cancer in terms of histological grade (Zhu et al., 2011; Calik et al., 2014). While gastric cancer is one of the most common causes of cancer death in Taiwan; however, there have been no previous studies on survival and predictive factors for

¹Cancer Center, ³Department of Hematology and Oncology, Chi Mei Medical Center, Liouying, ²Department of Nursing, Yuanpei University, Hsinchu, Taiwan *For Correspondence: ling5966@yahoo.com.tw

gastric cancer. Therefore, the aims of this study were to determine effect of prognostic factors on survival rates of gastric cancer according to sex, age, tumor location, pathological grading, number of lymph nodes removed, and symptoms.

Materials and Methods

Design

This retrospective study was conducted using data from 2009 to 2012.

Subjects

We retrospectively reviewed 64 consecutive patients diagnosed with adenocarcinoma of the stomach who had undergone gastrectomy with curative resection (R0) at a single medical center in southern Taiwan. Any patient with microscopic positive margins, with tumor extension within 5 mm of resected margins (R1 resection), or with grossly positive resected margins or residual disease after resection (R2 resection), as well as those receiving neoadjuvant concurrent chemo-radiotherapy or neoadjuvant chemotherapy, were all excluded from the study in order to exclude the effects of such treatments on their lymph nodes. The follow-up time for patients, meanwhile, was continued until December 31, 2013.

Data Collection

Collected data included sex, age, tumor location, pathological grading, number of lymph nodes removed, and symptoms. Patients were categorized into two groups based on their cancer stage; those with stages I and II were considered to have local gastric cancer, while those with higher stages (III and IV) were considered to have metastatic disease. Follow-up time was defined as the interval between diagnosis time and the time of death or last contact with the patient or patient's family members. Survival was defined as the time from diagnosis to date of death or last follow up for censored patient.

Analysis

All data were analyzed using SPSS 19.0 software. For statistical analyses, categorical variables are reported as continuous variables with a mean and standard deviation (SD). Continuous variables with a non-normal distribution are reported in terms of the median. The Kaplan-Meier method was used to assess the impact of different categorical predictors on patients' survival. Differences in the distribution of events between categorical variables were evaluated using the log-rank test. Categorical variables showing significant association with patient survival were then placed in a multivariate Cox regression model in order to calculate adjusted hazard ratios along with their 95% confidence interval. The differences between groups were considered significant when the relevant *p* value was less than or equal to 0.05.

Results

Subject Characteristics

A total of 64 patients were included in the study,

Table 1. Baseline Characteristics of Patients (N=64)

Items	Number	%
Sex		
Male	39	60.9
Female	25	39.1
Age		
<50	12	19
50~59	6	9.3
60~69	1	1.5
70~79	18	28
>80	27	42.2
Location		
Distal	6	9.4
Unspecified	9	14.1
Proximal	49	76.5
Pathological grading		
Well differentiated	1	1.5
Moderate differentiated	6	9.4
Poorly differentiated	57	89.1
Number of lymph nodes removed		
<15	38	59.3
≥15	26	40.7
Symptoms		
Abdomen pain	59	92.2
Weight loss	61	95.3
Stage		
I/II	27	42.2
III/IV	37	57.8

including 39 men (60.9%) and 25 women (39.1%) (male/female = 1.56). The mean age of the patients was 64.4±12.4 years (62.8±13 in men and 66.9±11 in women (*p*=0.315)). At clinical presentation, weight loss was the most prevalent complaint; overall, 61 out of 64 patients (95.3%) reported this symptom at the time of diagnosis. Baseline characteristics of study participants are presented in Table 1.

For 38 patients (59.3%), the number of lymph nodes removed was <15, while the number of lymph nodes removed was ≥15 for 26 patients (40.7%). Most lesions were located at the proximal portion of the stomach (76.5%). Regarding disease severity, 7 patients (10.9%) were categorized in the low grade group, while 57 patients (89.1%) were classified in high grade group. The median follow-up time was 4 years.

Effects of Different Factors on Survival of Patients with Gastric Cancer

There were 31 deaths attributed to gastric cancer in the study. The results were analyzed by Kaplan-Meier test (Table 2). Kaplan-Meier analysis revealed that a patient's tumor grade (*p*=0.004) was a significant predictor of survival. A significant predictor of survival, was the number of lymph nodes removed (*p*=0.05). A lower number of lymph nodes removed was showed a predictor for poorer survival.

Cox-proportional Regression Model for Grade and Number of Lymph Nodes Removed

The Cox-proportional regression model was used to calculate HRs (95% CI) in terms of the tumor grade and number of lymph nodes removed. The results are presented in Table 3. Both tumor grade and number of lymph

Table 2. Effects of Factors on Survival of Gastric Cancer Patients (N=64)

Items	Event/Total	p
Sex		0.315
Male	17/39	
Female	14/25	
Age		0.908
<50	6/12	
50~59	3/6	
60~69	0/1	
70~79	9/18	
>80	13/27	
Location		0.871
Distal	4/6	
Unspecified	4/9	
Proximal	23/49	
Pathological grading		0.004*
Well differentiated	1/1	
Moderate differentiated	1/6	
Poorly differentiated	29/57	
Number of lymph nodes removed		0.05*
<15	21/38	
≥15	10/26	
Abdomen pain		0.201
No	4/5	
Yes	27/59	
Weight loss		0.338
No	2/3	
Yes	29/61	
Stage		0.06
I/II	8/27	
III/IV	23/37	

*p<0.05

Table 3. Cox-proportional Regression Model for Factors Predicting (N=64)

Items	Hazard Ratio	95% CI		p
		Lower	Upper	
Pathological grading				
Well differentiated	1			
Moderate differentiated	0.335	0.045	2.519	0.288
Poorly differentiated	8.549	0.991	73.723	0.05*
Number of lymph nodes removed				
≥15	1			
<15	2.751	1.22	6.203	0.015*

*p<0.05

nodes removed were significantly associated with poorer survival. A high grade tumor was associated with an HR (95% CI) of 8.549 (0.991-73.723) compared with a low grade tumor. Similarly, numbers of retrieved lymph nodes less than 15 were associated with higher risk of death. HR (95%CI) for numbers of retrieved lymph nodes less than 15 was 2.751 (1.220-6.203) compared with numbers of retrieved lymph nodes more than 15 (Table 3).

Discussion

Among Taiwanese gastric cancer patients, the median age of gastric cancer diagnosis has previously been reported to be 65 years (Taiwan Cancer Registry, 2013); in our data, the median age was 66 years. In our study, the most prevalent clinical presentation was weight loss. Similar to literature, weight loss and persistent vomiting were the most sensitive predictors of gastric cancer

(Stephens et al., 2005). The impacts of several factors including sex, age, tumor location, pathological grading, number of lymph nodes removed, and symptoms on the survival were investigated in order to identify determinant variables. In our study, high grade tumors and numbers of retrieved lymph nodes less than 15 were significantly associated with poorer survival. Similar to a recent study, patients had the risk of death was found to be significantly increased among patients with poorly differentiated or moderately differentiated cancer in terms of histological grade (Zhu et al., 2011; Zhang et al., 2012; Calik et al., 2014). Furthermore, in our data, high grade tumors were associated with an HR (95% CI) of 8.549 (p=0.05) compared with low grade tumor.

In the previous literature, the number of resected lymph nodes has been reported to determine the prognosis of gastric cancer, and an association between an adequate number of lymph nodes and improved overall survival has likewise been reported (Lee et al., 2001; Smith et al., 2005; Coburn et al., 2006). Our results are in accordance with previous reports in that a significant improvement in survival was noted for patients with 15 or more lymph nodes resected. Specifically, average survival improved from 25 months to 42 months among patients treated with an extended resection, and in gastric cancer, a minimum harvest of 15 lymph nodes is recommended (Volpe et al., 2000), as this is also considered an indicator of quality of care in gastric surgery (Shen et al., 2007). We believe that there is a real enhancement in survival for gastric cancer patients when more than 15 lymph nodes are identified in the resected specimen. Similar to our previous study, numbers of retrieved lymph nodes less than 15 were associated with an HR (95% CI) of 2.751 (p=0.015) compared with numbers of retrieved lymph nodes more than 15. This gives us a good reason to strive for a surgical resection with adequate lymph node removal when it is performed with a curative intent.

In conclusion, the number of lymph nodes removed is thus an important prognostic factor for gastric cancer. This will require vigilant training of the next generation of surgeons as well as prudent referral of patients with the diagnosis of gastric cancer to experienced surgeons. Further research workup is therefore mandatory to develop a more accurate staging policy to subcategorize gastric cancer, especially for patients with an inadequate number of lymph nodes retrieved.

References

- Alatengbaolide, Lin D, Li Y, et al (2013). Lymph node ratio is an independent prognostic factor in gastric cancer after curative resection (R0) regardless of the examined number of lymph nodes. *Am J Clin Oncol*, **36**, 325-30.
- Calik M, Calik I, Demirci1 E, Altun E et al (2014). Goseki grade and tumour location influence survival of patients with gastric cancer. *Asian Pac J Cancer Prev*, **15**, 1429-34.
- Coburn NG, Swallow CJ, Kiss A, Law C (2006). Significant regional variation in adequacy of lymph node assessment and survival in gastric cancer. *Cancer*, **107**, 2143-51.
- de Steur WO, Dikken JL, Hartgrink HH (2013). Lymph node dissection in resectable advanced gastric cancer. *Dig Surg*, **30**, 96-103.

- Etemadi M, Pourian M, Shakib A et al (2014). A registry program for familial gastric cancer patients referred to cancer institute of Iran. *Asian Pac J Cancer Prev*, **15**, 2124-44.
- Health Promotion Administration Ministry of Health and Welfare (Taiwan). (2014). Cancer registry annual report, 2011, Taiwan.
- Lee HK, Yang HK, Kim WH et al (2001). Influence of the number of lymph nodes examined on staging of gastric cancer. *Br J Surg*, **88**, 1408-12.
- Ministry of Health and Welfare (2013, July 17th). Top ten cancer report of prevalence and incident (Accessed on May 21, 2014).
- Son T, Hyung WJ, Lee JH et al (2012). Clinical implication of an insufficient number of examined lymph nodes after curative resection for gastric cancer. *Cancer*, **118**, 4687-93.
- Stephens MR, Lewis WG, White S et al (2005). Prognostic significance of alarm symptoms in patients with gastric cancer. *Br J Surg*, **92**, 840-6.
- Smith DD, Schwarz RR, Schwarz RE (2005). Impact of total lymph node count on staging and survival after gastrectomy for gastric cancer: Data from a large US-population database. *J Clin Oncol*, **23**, 7114-24.
- Shen JY, Kim S, Cheong JH et al (2007). The impact of total retrieved lymph nodes on staging and survival of patients with pT3 gastric cancer. *Cancer*, **110**, 745-51.
- Taiwan Cancer Registry (2013). Analysis of 2007-2011 new diagnosed survival rates of Top 10 cancer in 2012.
- Volpe CM, Driscoll DL, Douglass HO (2010). Outcome of patients with proximal gastric cancer depends on extent of resection and number of resected lymph nodes. *Ann Surg Oncol*, **7**, 139-44.
- Zare A, Mahmoodi M, Mohammad K, et al (2013). Survival analysis of patients with gastric cancer undergoing surgery at the Iran Cancer Institute: a method based on multi-state models. *Asian Pac J Cancer Prev*, **14**, 6369-73.
- Zhang, YF, Shi J, Yu HP et al (2012). Factors predicting survival in patients with proximal gastric carcinoma involving the esophagus. *World J Gastroenterol*, **18**, 3602-9.
- Zhu HP, Xia X, Yu CH et al (2011). Application of Weibull model for survival of patients with gastric cancer. *BMC Gastroenterol*, **11**, 1-6.