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BRIEF ARTICLE

Factors predicting survival in patients with proximal gastric carcinoma involving the esophagus

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Abstract

AIM: To investigate the clinicopathologic features which predict surgical overall survival in patients with proximal gastric carcinoma involving the esophagus (PGCE).

METHODS: Electronic pathology database established in the Department of Pathology of the Nanjing Drum Tower Hospital was searched for consecutive resection cases of proximal gastric carcinoma over the period from May 2004 through July 2009. Each retrieved pathology report was reviewed and the cases with tumors crossing the gastroesophageal junction line were selected as PGCE. Each tumor was re-staged, following the guidelines on esophageal adenocarcinoma, according to the 7th edition of the American Joint Commission on Cancer Staging Manual. All histology slides were studied along with the pathology report for a retrospective analysis of 13 clinicopathologic features, i.e., age, gender, *Helicobacter pylori* (*H. pylori*) infection, surgical modality, Siewert type, tumor Bormann's type, size, differentiation, histology type, surgical margin, lymphovascular and perineural invasion, and pathologic stage in relation to survival after surgical resection. Prognostic factors for overall survival were assessed with uni- and multi-variate analyses.

RESULTS: Patients' mean age was 65 years (range: 47-90 years). The male: female ratio was 3.3. The 1-, 3- and 5-year overall survival rates were 87%, 61% and 32%, respectively. By univariate analysis, age, male gender, *H. pylori*, tumor Bormann's type, size, histology type, surgical modality, positive surgical margin, lymphovascular invasion, and pT stage were not predictive for overall survival; in contrast, perineural invasion (P = 0.003), poor differentiation (P = 0.0003), > 15 total lymph nodes retrieved (P = 0.008), positive lymph nodes (P = 0.001), and distant metastasis (P = 0.005) predicted poor post-operative overall survival. Celiac axis nodal metastasis was associated with significantly worse overall survival (P = 0.007). By multivariate analysis, ⩾ 16 positive nodes (P = 0.018), lymph node ratio > 0.2 (P = 0.003), and overall pathologic stage (P

= 0.002) were independent predictors for poor overall survival after resection.

CONCLUSION: Patients with PGCE showed worse overall survival in elderly, high nodal burden and advanced pathologic stage. This cancer may be more accurately staged as gastric, than esophageal, cancer.

Key words: Cancer; Esophagus; Gastroesophageal junction; Staging; Stomach

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INTRODUCTION

Carcinoma in the gastroesophageal junction (GEJ) region can be sub-grouped by the Siewert classification system into 3 types on the basis of the distance between tumor epicenter and the GEJ line[1,2]. Type I carcinomas are centered in the distal esophagus, 1-5 cm above the GEJ. They arise largely from Barrett's esophagus (BE), may or may not invade the GEJ, and are commonly reported as Barrett's adenocarcinoma. Type Ⅱ tumors straddle the GEJ line and are believed to be true GEJ cancers with epicenter within 1 cm above and 2 cm below the GEJ. Type Ⅲ tumors are sub-cardial gastric cancers with epicenter 2-5 cm below the GEJ that is crossed as they grow proximally.

Although the Siewert classification system has been widely used internationally, its prognostic value has been challenged[3-5]. In Asian countries, type I GEJ cancer is rare and types Ⅱ and Ⅲ carcinomas behave similarly[5,6]. In China, almost all GEJ carcinomas arise in the proximal stomach with a stable or slightly increased incidence in recent years[7-10]. In our most recent study comparing clinicopathologic features of GEJ cancer between Chinese patients treated in Nanjing, China, and American patients treated in Boston, the United States, we showed that almost all GEJ cancers in Chinese patients were Siewert types Ⅱ and Ⅲ tumors[11], unlike those seen in American patients in which the distribution of these three types of tumors was almost evenly[12]. Their tumors were not BE-related, but associated with proximal gastritis with *Helicobacter pylori* (*H. pylori*) infection and a better overall survival rate, despite a larger tumor size and more advanced pathologic stages at diagnosis[11]. Surprisingly, the studies on factors predicting post-operative overall survival in Chinese patients with proximal gastric carcinoma involving the esophagus (PGCE) are scarce. The purpose of the present study was to investigate clinicopathologic features that may predict overall survival after surgical resection in Chinese patients with PGCE who were treated at a single high-volume tertiary medical center in Nanjing, China.

MATERIALS AND METHODS

Selection of patients

A total of 177 consecutive resection cases of histopathologically confirmed proximal gastric carcinoma were identified through a search of the computerized pathology database established in the Department of Pathology of the Nanjing Drum Tower Hospital in Nanjing, China, over the period from May 2004 through July 2009. Each pathology report was reviewed (by Huang Q) for cases with tumors crossing the GEJ line. Inclusion criteria were: (1) a tumor with epicenter in the proximal stomach within 5 cm below the GEJ and invading into the distal esophagus, which corresponded to Siewert types Ⅱ and Ⅲ tumors; (2) no chemotherapy or radiation therapy before the surgical resection; and (3) the availability of follow-up information through telephone interviews (by Feng AN) to the patient or family members. Exclusion criteria consisted of: (1) the tumor not crossing the GEJ; and (2) the patient lost to follow-up. Following a standard comprehensive surgical pathology processing protocol, all resection specimens were evaluated for the Bormann's gross type and surgical margins. The GEJ line, defined by the proximal end of gastric longitudinal mucosal folds, was evaluated in each case. The tumor epicenter location and its distance from the GEJ were recorded. The number of overall survival months after surgery was calculated until May 2010, based on whether the patient was alive or had died of any cause. For all selected patients, medical records and pathology reports were re-evaluated for demographic and clinicopathologic information, tumor stage, surgical approach (total or partial gastrectomy or Ivor-Lewis procedure), completeness of resection, and histopathology of the tumor. The study protocol was approved by the Medical Ethics Committee of the Nanjing Drum Tower Hospital in Nanjing, China.

Tumor staging

All tumors were staged with the esophageal cancer staging criteria, according to the 7th edition of the American Joint Commission on Cancer Staging Manual (AJCC 7)[13]. The status of regional involved lymph nodes in the para-distal esophageal, para-cardial and peri-gastric regions was determined microscopically. The lymph nodes in the celiac axis region, including the left gastric artery, celiac artery, hepatic and splenic hila, *etc*., were identified by the surgeon during the operation, submitted as separate specimens and examined microscopically. Lymph node metastasis was determined by the routine histological examination. In this study, since PGCE was classified as GEJ cancer

and staged as esophageal cancer, metastases to celiac axis regional nodes were considered as distant metastasis[13,14].

The proximal, distal and radial margins of resection were routinely inked for microscopic examination and classified as negative or positive if there was histological evidence of carcinoma present at, or within 1 mm of the inked resection edge. Lymphovascular and peri-neural invasion was assessed microscopically on routine histology sections. Suspected distant tumor metastasis in the liver or other organs detected and biopsied intraoperatively was confirmed microscopically.

Statistical analysis

All patients' demographic and tumor gross characteristics were considered categorical variables except for age, overall survival month, number of lymph nodes retrieved and number of lymph nodes involved, which were classified as continuous variables. All statistical analysis was carried out (by Shi J) using the SPSS software (SPSS Inc., version 15.0, Chicago, IL, United States). Specific comparison between groups was performed using χ^2 and Student *t* tests. Patient overall survival rates after surgical resection were estimated with the Kaplan-Meier method and the log rank test. The patients who were alive at the last follow-up were censored for calculation of the overall survival rates. Cox multivariate proportional hazards regression models were used to assess the overall survival power of these parameters. The *P* value of < 0.05 was considered statistically significant.

RESULTS

Clinicopathologic characteristics

A total of 142 cases were eligible for this study. The patients' demographics, clinicopathologic characteristics, and the results of univariate overall survival analysis were shown in Table 1. Most (82%) tumors were type Ⅱ of the Siewert classification, while there was no type Ⅰ tumor in this cohort. The mean patient age was 65 years (range: 47-90). The male-female ratio was 3.3. The number of months of patient follow-up after surgical resection was 29 ± 17 mo (mean ± SD, range: 1-70 mo). By the time of the last follow-up, 58 (41%) patients had died and the remaining survivors were censored. Overall, the 1-, 3- and 5-year overall survival rates were 87%, 61% and 36%, respectively. Among the demographic and pathologic variables, perineural invasion and poor tumor differentiation were associated with worse overall survival (Table 1). None of the surgical modalities were found significant for overall survival prediction. The status of *H. pylori* infection, tumor gross type, gender, age, tumor size, lymphovascular invasion, and even positive surgical margins were not significant for overall survival prediction by univariate analysis.

Pathologic staging

Following the AJCC 7 staging guidelines, the vast majorities (88%) of tumors were skewed to pT3 and only a few staged at pT1 ($n = 4$), pT2 ($n = 12$) and pT4 ($n = 1$). The pT stage was found not to be a relevant factor for overall survival prediction. In contrast, positive lymph node metastasis were detected in 106 (75%) cases and significantly associated with worse overall survival (Table 2). Twelve of 142 patients (8%) had distant metastasis at the time of operation and showed significantly worse overall survival.

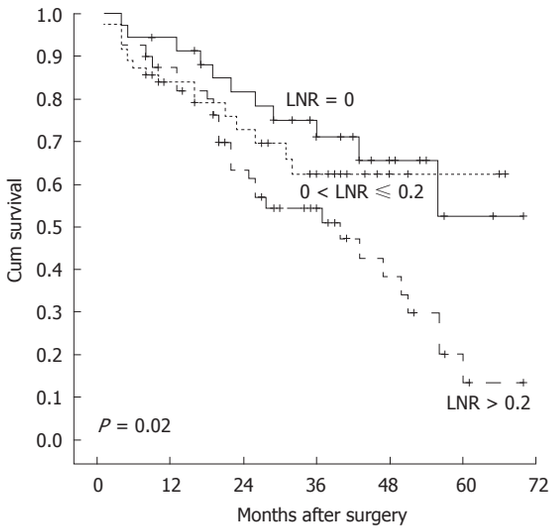

Figure 1 Kaplan-Meier overall survival curves of patients stratified by various lymph node ratios. The difference in overall survival among lymph node ratio (LNR) groups was statistically significant.

Lymph node status with overall survival

The mean number of lymph nodes retrieved per case was 21 (range: 4-66). The presence of lymph node metastasis was found in 106 (75%) cases. There were 12 patients (8%) with cancer metastasis in celiac axis lymph nodes, which significantly predicted worse overall survival by univariate analysis (Table 2). There was a statistically significant overall survival difference between patients with a total number of retrieved lymph nodes ≤ 15 and ≥ 16 (Table 2). The numbers of positive lymph nodes more than 7 and 16 were worse overall survival predictors. The ratio of the number of positive nodes to the total number of nodes retrieved, i.e., the lymph node ratio, was significantly associated with worse overall survival (Tables 2 and 3, Figure 1).

Significance of the lymph node ratio on overall survival

Among 3 different lymph node ratio groups, the lymph node ratios were significantly associated with the worse overall survival (Tables 2 and 3). The overall survival status was better illustrated on a Kaplan-Meier plot among groups with lymph node ratios > 0.2, compared to that with the ratio ≤ 0.2 (Figure 1). We found that the relative risk for poor overall survival was 37-fold when the lymph node ratio was over 0.4 and 75-fold when over 0.5, compared with the ratio at 0.

Independent factors predicting overall survival retained at multivariate analysis

By multivariate analysis, over 16 positive lymph nodes per

Table 1 Demographic, clinical, and pathological features predicting overall survival in patients with proximal gastric carcinoma involving esophagus

Characteristics	Number of patients (%)	Months after surgery (mean ± SD)	*P* value	1-yr survival %	3-yr survival %	5-yr survival %
Age (yr)			0.108			
< 70	97 (68.3)	30 ± 17		91.1	65.3	40.1
⩾ 70	45 (31.7)	27 ± 19		77.0	49.3	17.3
Gender			0.594			
Male	109 (76.8)	28 ± 17		71.1	61.1	23.1
Female	33 (23.2)	30 ± 18		88.3	60.1	48.1
Helicobacter pylori infection			0.400			
Negative	80 (56.3)	30 ± 18		87.3	67.6	29.4
Positive	62 (43.7)	27 ± 17		87.1	50.8	32.3
Surgical modality			0.950			
Partial gastrectomy	112 (78.9)	29 ± 18		85.7	68.6	35.1
Total gastrectomy	21 (14.8)	28 ± 18		76.2	65.3	0.0
Ivor-Lewis procedure	9 (6.3)	29 ± 17		89.2	60.6	34.3
Siewert type			0.444			
Type Ⅱ	116 (81.7)	29 ± 17		86.8	63.8	27.2
Type Ⅲ	26 (18.3)	33 ± 19		88.5	50.2	40.2
Bormann's type			0.380			
Polypoid	2 (1.4)	27 ± 26		100.0	50.1	50.1
Fungating	17 (12.0)	34 ± 20		83.3	70.9	53.2
Ulcerated	96 (67.6)	28 ± 17		88.0	56.3	26.8
Flat	27 (19.0)	26 ± 18		86.5	66.6	29.6
Tumor size (cm)			0.087			
< 3	19 (13.4)	30 ± 17		87.0	72.1	17.2
3.1-7.9	112 (78.9)	30 ± 17		89.7	61.5	38.5
> 8	11 (7.7)	18 ± 15		63.6	26.5	0.0
Surgical margin			0.165			
Negative	126 (88.7)	30 ± 17		88.8	60.6	30.1
Positive	16 (11.3)	23 ± 19		74.5	66.2	33.1
Lymphovascular invasion			0.050			
Negative	56 (39.4)	33 ± 18		90.9	65.6	31.2
Positive	86 (60.6)	27 ± 17		84.	57.6	31.7
Perineural invasion			0.003			
Negative	55 (38.7)	35 ± 18		92.7	63.4	41.3
Positive	87 (61.3)	26 ± 17		83.6	59.4	19.3
Tumor differentiation			0.0003			
Well	1 (0.7)	57		100.0	100.0	100.0
Moderately	70 (49.3)	34 ± 17		95.2	69.3	44.2
Poorly	70 (49.3)	24 ± 16		81.3	52.7	11.3
Undifferentiated	1 (0.7)	4		0.0	0.0	0.0
Tumor histopathology			0.548			
Adenocarcinoma (nitric oxide synthase)	112 (78.9)	31 ± 17		89.6	71.0	34.2
Adenocarcinoma with micropapillary feature	24 (16.9)	24 ± 10		100	0.0	0.0
Adenosquamous carcinoma	9 (6.3)	28 ± 15		88.9	33.3	0.0
Mucinous carcinoma	9 (6.3)	24 ± 14		88.9	30.5	30.5
Signet ring cell carcinoma	23 (16.2)	23 ± 19		69.3	58.5	39.0
Carcinoma with neuroendocrine features	7 (4.9)	28 ± 17		100.0	50.0	25.0
Carcinoma with mixed types	37 (26.1)	24 ± 13		86.3	50.1	50.1
Pathologic T stage			0.400			
1A	2	38 ± 27		100.0	50.0	50.0
1B	2	47 ± 3		100.0	100.0	100.0
2	12	27 ± 17		83.3	72.9	54.7
3	125	29 ± 17		87.0	59.8	29.2
4A	0	0		-	-	-
4B	1	18		100.0	0.0	0.0
Pathologic N stage			0.001			
0	36	35 ± 17		94.4	72.0	53.5
1	22	32 ± 17		91.3	70.1	70.1
2	35	30 ± 17		85.3	64.7	15.9
3A	35	25 ± 17		85.3	57.4	14.4
3B	14	15 ± 9		70.7	41.3	10.3
Pathologic M stage			0.005			
M0	130	28 ± 18		88.3	64.5	32.5
M1	12	12 ± 4		75.0	13.1	13.1
Overall stage			0.012			
1A	4	42 ± 16		100.0	75.0	75.0
1B	7	30 ± 15		100.0	100.0	100.0
2A	26	34 ± 19		88.5	63.0	42.0
2B	26	32 ± 17		84.6	66.8	60.7
3A	29	31 ± 17		93.1	72.6	19.8
3B	29	27 ± 18		86.2	62.9	15.3
3C	9	18 ± 10		76.2	15.2	15.2
4	12	16 ± 9		75.0	13.1	13.1

Table 2 Univariate analysis of overall survival in patients with lymph node metastasis

Characteristic	No. of patients (%)	Overall survival			
		HR	95% CI[1]		*P* value
Celiac axis lymph node					
Negative	130 (92)	1.00			
Positive	12 (8)	3.33	1.40	7.95	0.007
Perineural invasion					
Negative	55 (38.7)	1.00			
Positive	87 (61.3)	1.48	0.54	4.11	0.447
Number of nodes retrieved/case					
10	21 (15)	1.00			
⩾ 11	121 (85)	1.48	0.72	3.06	0.290
⩽ 15	46 (32)	1.00			
⩾ 16	96 (68)	2.29	1.24	4.22	0.008
⩽ 23	100 (70)	1.00			
⩾ 24	42 (30)	1.15	0.65	2.03	0.627
Number of positive nodes/case					
⩽ 6	58 (41)	1.00			
⩾ 7	48 (34)	1.72	1.20	2.46	0.003
⩽ 15	92 (65)	1.00			
⩾ 16	14 (10)	2.30	1.40	3.77	0.001
Lymph node ratio					
0	36 (25)	1.00			
⩽ 0.2	40 (28)	1.34	0.61	2.97	0.467
> 0.2	66 (46)	2.28	1.15	4.51	0.018

[1]Hazards ratios (HR), 95% confidence interval (CI) and *P* values for post-operative time to recurrence and overall survival were adjusted according to important clinical characteristics. Survival time was defined as the period from the surgical treatment to endpoint of follow-up.

Table 3 Independent overall survival predictors retained by multivariate analysis

Factor	No. of patients	Multivariate analysis			
		HR	95% CI		*P* value
Celiac axis lymph node		Compared to pN0			
Negative	130				
Positive	12	1.76	0.68	4.57	0.246
Number of positive nodes/case		Compared to pN0			
$LN^+ \geqslant 7$	48	1.34	0.6	2.96	0.467
$LN^+ \geqslant 16$	14	2.77	1.15	4.51	0.018
Lymph node ratio		Compared to pN0			
⩽ 0.2	40	3.8	1.28	11.26	0.016
> 0.2	66	7.79	2.05	29.57	0.003
Overall stage pIV		Compared to pI			
	12	18.43	2.27	145.62	0.002
Tumor differentiation		Compared to well differentiated			
poorly differentiated	70	1.42	0.79	2.55	0.243

LN: Lymph node; HR: Hazards ratio; CI: Confidence interval.

case, lymph node ratio > 0.2, and the overall pathologic stage were found to be independent factors for predicting worse surgical overall survival (Table 3).

DISCUSSION

In this study, the factors predicting overall surgical survival in Chinese patients with PGCE are similar to those of gastric cancers but different from those of GEJ cancers reported in patients from Western countries[15-18]. We show that in Chinese patients, type I GEJ carcinomas remain vanishingly rare and PGCE tumors are mostly as type Ⅱ and some as type Ⅲ GEJ cancers. The factors predicting surgical overall survival are comparable to those reported in Japan[6] and China Taiwan[5]. Importantly, nodal burden in PGCE correlates highly with post-operative overall survival, as seen in gastric cancer. Nodal metastasis in the celiac axis region is a significant predictor of worse overall survival. Finally, the independent risk factors for worse overall survival in our patients include tumor metastasis in more than 16 nodes, the lymph node ratio > 0.2, distant metastasis, and overall pathologic stage; in contrast, the prognostic factors, such as > 70 years, BE, the male gender, tumor histology type, the surgical resection method, and even positive resection margin, *etc*., are not significant for predicting overall survival in Chinese patients with PGCE, which are predictive in type I GEJ carcinomas in Western patients[15,19], probably because of the rarity of the type I GEJ carcinomas in Chinse patients. Our results would impact upon surgical management of Chinese patients with PGCE, if confirmed in a larger prospective trial(s).

Accurate GEJ cancer staging is difficult. The AJCC 7 staging system requires the use of the esophageal scheme for pathologic staging of this group of cancers, regardless of the location of tumor epicenters. This new mandate is controversial. In a recent study, we showed that PGCE staged with the gastric cancer staging rules was better stratified, especially for the pN and pⅢ stages, compared to the use of the esophageal scheme that showed an erroneously better overall survival in the patients staged at pⅢA than those at pⅠA and pⅡB[20]. The results shown in this study further substantiate the above conclusion and lent support to the contention that the current AJCC 7 cancer staging system for GEJ cancer needs to be modified when applied to Chinese patients with PGCE.

Lymph node metastasis in gastric cancer has been shown to be more significant in predicting overall survival than tumor invasion depth.This concept was confirmed in this study. For instance, we found no significant differences in overall survival among patients with different pT stages by either univariate or multivariate analysis. In contrast, the number of positive lymph nodes dictated patient overall survival[16]. Furthermore, the total number of nodes retrieved (> 15) had a significant overall survival predictive value, as suggested by others[17]. This may have resulted in a more precise evaluation of positive nodes and thus more accurate pN staging. In the current series, the overall survival was significantly worse in the patients with considerable nodal burden such as more than 7 positive nodes and higher lymph node ratios. Apparently, a rich lymphatic network in the GEJ region, and/or protein lytic enzymes secreted by neoplastic cells, may facilitate the lymphatic dissemination of neoplastic cells to intra-abdominal nodes[16,21]. It was reported that even for pT1b GEJ cancers, 30% of cases with positive

nodes had a 5-year overall survival rate of only 33%[18]. Moreover, patients with primary tumors in the middle to lower esophagus and the proximal stomach were found to have nodal diseases within the abdomen at rates of as high as 45% to 93%[22,23]. Taken together, our data emphasize the important overall survival predictive value for a thorough abdominal nodal dissection in Chinese patients with PGCE[21].

The significance of the ratio between involved and retrieved lymph nodes for overall survival prediction has not been described in patients with PGCE. Our results add into a growing body of evidence for the value of a lymph node ratio in predicting overall survival of patients with PGCE. In the late 1990s, Siewert *et al*[24] published their findings of prognostic significance of the lymph node ratio in gastric cancer in a large German cohort of 1654 cases. Their conclusion was repeatedly confirmed by the studies in gastric cancer patients in Japan[25,26], China Taiwan[5], mainland China[27,28], South Korea[29], Spain[30] and Italy[31]. The advantage of the use of this parameter in patients with PGCE lies upon its ease to use, irrespective of the surgical methods used by different surgeons and various types of resection specimens from different patients[24]. In reality, the number of retrieved lymph nodes is largely influenced by the extent of lymph node dissection by different surgeons, whose nodal dissection skills vary[32,33]. It was reported that patients with a lymph node ratio smaller than 0.2 had a better overall survival rate[33,34], which is also our experience. As the lymph node ratio increases, so is the increased relative risk of poor overall survival. Our data show that in patients with PGCE, the lymph node ratio could be used clinically as a powerful overall survival predictor.

The significance of metastatic nodal disease in the celiac axis region in patients with GEJ cancers for overall survival prediction remains obscure due to limited studies in the literature[18,21]. When nodal metastasis is discovered in this region, some studies classify it as a pM1a disease of distal esophageal or GEJ cancers[14], according to the 6th AJCC cancer staging system. The overall survival predictive value of positive celiac lymph nodes in proximal gastric cancer stays controversial[18,35-37]. It was reported that the patients with undetected celiac nodal disease at the time of surgical resection were subsequently found to have celiac nodal involvement with overall survival similar to that of patients with stage Ⅲ disease[21]. In our previous[28] and current studies on PGCE, nodal disease in the celiac axis region was also an important overall survival predictor by univariate analysis, which, however, did not reach a statistically significant level by multivariate analysis, probably due to the small sample size. Nevertheless, it appears that the site of nodal disease may be as important as the number of nodal metastasis in predicting overall survival for patients with PGCE.

The major limitations of this study are several. First, the sample size of the current cohort was relatively small and most cancer cases were advanced and staged at pⅢ. There were only a few cases staged at p Ⅰ or pⅣ, which might have contributed to the lack of significance for the tumor pT stage in overall survival prediction. Second, the patient follow-up was carried out by telephone interview only. This might have invited inaccurate and biased results. At present, an accurate electronic patient medical record system has not been established in China and the government death record of citizens is not available to the public. Therefore, telephone interview has been the primary tool to collect the overall survival information. Finally, because of the retrospective nature of the study, the methods for surgical resection, lymph node retrieval, and specimen dissection were not standardized, which might have caused inconsistent nodal retrieval results. However, in over 75% of cases in this study, the number of lymph nodes retrieved per case was over 21. Therefore, the overall data quality should be reasonably solid and reliable.

In conclusions, PGCE, like gastric cancer, has similar overall survival after resection in patients with no or minimal nodal burden in this cohort of consecutively treated Chinese patients. However, the elderly patients over 70 years and those with considerable nodal diseases including celiac nodal metastasis, distant metastasis, and advanced summary pathologic stage fare worse in overall survival after resection. Application of the AJCC 7 esophageal staging scheme to PGCE may be less accurate in predicting overall survival than applying the gastric staging scheme[20]. Because of the small sample size and a single institution experience, further larger, prospective studies are required to validate our findings in the Chinese patient population.

COMMENTS

Background

In China, almost all gastroesophageal junction (GEJ) carcinomas arise in the proximal stomach with a stable or slightly increased incidence in recent years. In our most recent study comparing clinicopathologic features of GEJ cancer between Chinese patients treated in Nanjing, China, and American patients treated in Boston, the United States, the authors showed that GEJ cancers in Chinese patients were unlike those seen in American patients. However, the studies on factors predicting post-operative overall survival in Chinese patients with proximal gastric carcinoma involving the esophagus (PGCE) are scarce.

Research frontiers

The purpose of the present study was to investigate clinicopathologic features that may predict overall survival after surgical resection in Chinese patients with PGCE who were treated at a single high-volume tertiary medical center in Nanjing, China.

Innovations and breakthroughs

In this study, the factors predicting overall surgical survival in Chinese patients with PGCE are similar to those of gastric cancers but different from those of GEJ cancers reported in patients from Western countries. The authors show that in Chinese patients, type Ⅰ GEJ carcinomas remain vanishingly rare and PGCE tumors are mostly as Siewert type Ⅱ and some as type Ⅲ GEJ cancers. The factors predicting surgical overall survival are comparable to those reported in Japan and Taiwan. Importantly, nodal burden in PGCE correlates highly with post-operative overall survival, as seen in gastric cancer. Nodal metastasis in the celiac axis region is a significant predictor of worse overall survival. Finally, the independent risk factors for worse overall survival in our patients include tumor metastasis in more than 16 nodes, the lymph node ratio > 0.2, distant metastasis and overall pathologic stage; in contrast, the prognostic factors, such as > 70 years, Barrett's esophagus, the male gender, tumor histology type, the surgical resection method, and even positive resection margin, *etc.*, are not significant for predicting overall survival in Chinese patients

with PGCE, which are predictive in Siewert type Ⅰ GEJ carcinomas in Western patients, probably because of the rarity of the Siewert type Ⅰ GEJ carcinomas in Chinse patients.

Applications

Their results would impact upon surgical management of Chinese patients with PGCE, if confirmed in a larger prospective trial(s). The authors suggest that the GEJ cancer in Chinese patients be treated as gastric cancer.

Peer review

This study was designed as the next step to examine the clinicopathologic features that may predict survival after surgical resection of proximal gastric carcinoma, keeping in mind that this tumor type is rare in Chinese patients. The manuscript is well written and methodology is accurately described. By multivariate analysis, > 16 positive nodes, lymph node ratio > 0.2, distant metastasis and summary pathologic stage were found to be independent predictors for poor survival. The authors stress that the lymph node ratio could be used as a reliable survival predictor, as this parameter is not influenced by the surgical methods and the number of retrieved lymph nodes.

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