

A study on clinicopathological features and prognostic factors of patients with upper gastric cancer and middle and lower gastric cancer.

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Abstract

Objective: To compare the difference on clinicopathological features and prognostic factors in patients with upper gastric cancer and middle and lower gastric cancer.

Methods: 168 cases of gastric cancer patients treated in our hospital from January 2010 to March 2013 were enrolled as the research objects. All of these patients have complete data and were confirmed by pathology and classified into stages I-III period, with 90 cases of upper gastric cancer and 78 cases of middle and lower gastric cancer respectively. Of the 168 cases, 150 cases (89.3%) underwent R0 treatment (no residue under microscope after resection), 18 cases (10.7%) underwent R1 treatment (microscopic residual) and 152 cases (90.5%) underwent D2 (radical type II) perigastric lymph node dissection treatment.

Results: There were no significant differences on TNM stage, operation modes, the number of dissected lymph nodes and postoperative complications between the upper gastric cancer group and middle and lower gastric cancer group ($P>0.05$). There were significant differences on preoperative complications and postoperative adjuvant chemotherapy between the upper gastric cancer group and middle and lower gastric cancer group ($P<0.05$). 3 y Overall Survival (OS) and Progression-Free Survival (PFS) in the upper gastric cancer group were 35.6% (32/90 cases) and 47.8% (43/90) ($P=0.026$), and 43.6% (34/78 cases) and 51.3% (40/78) respectively in middle and lower gastric cancer group ($P=0.035$). Logistic regression analysis showed that risk factors affecting the prognosis of upper gastric cancer were preoperative complications and postoperative adjuvant chemotherapy, while the risk factors affecting the prognosis of middle and lower gastric cancer were TNM staging, preoperative complications and postoperative adjuvant chemotherapy. By the last follow-up on March 31, 2017, 51 of 90 (56.7%) patients with upper gastric cancer and 34 of 78 (43.6%) patients with middle and lower gastric cancer died respectively ($P<0.05$).

Conclusion: There were significant differences on the clinical pathological features and prognosis between patients with upper gastric cancer and middle and lower gastric cancer patients, it is of great guiding significance to know the pathological features of cancer in different parts, it can provide individualized treatment options for patients and improve the prognosis of patients.

Keywords: Gastric cancer, Upper gastric cancer, Middle and lower gastric cancer, Pathological features, Prognostic factors.

Accepted on October 30, 2017

Introduction

Gastric cancer is one of the most common malignant tumors, and its fatality rate ranks the third [1] of all malignant tumors. China is the main country of gastric cancer in Asia, accounting for 42.6% of the patients the entire world and the incidence of elderly gastric cancer in China has increased significantly in recent years. Despite the significant progress of gastric cancer treatment (such as surgery, radiotherapy, chemotherapy and targeted therapy) in recent years, the 5 y survival rate is only 20%-30%, which was closely related to the high malignancy and biological complexity of gastric cancer [2]. Upper gastric

cancer mainly includes lesions at the junction and the fundus of the stomach, and upper gastric cancer is usually diagnosed in the advanced stage. Due to complexed lymphatic drainage in this area and the specific operation methods which involves thoracotomy, gastrointestinal anastomosis of esophagus and diaphragm, abdominal blood vessels and lymph node removal, the efficacy of treatment is often poor [3]. Previous studies have shown that [4], upper gastric cancer has unique epidemiological and biological characteristics, and surgical treatment is different from the middle and lower gastric cancer. It was also reported that [5], compared with middle and lower gastric cancer, there were more male patients than female

patients with upper gastric cancer. Upper gastric cancer is often a late disease with low survival rate and is pathologically characterized by diffuse growth and low grade. Relevant data show that [6,7] the prognosis of gastric cancer is not only closely related to the treatment methods, biological behaviors and clinical pathological features, but also affected by gross type, invasion depth, lymph node metastasis and infiltration growth types and types of gastric cancer serosal surface. At present, there are few reports about the differences of prognostic factors between upper gastric cancer and middle and lower gastric cancer. Our previous studies have shown that the prognosis of upper gastric cancer may be poor. Therefore, this study further compared the clinicopathological features, prognosis and prognostic factors between patients with upper gastric cancer and middle and lower gastric cancer.

Data and Methods

General data

168 cases of gastric cancer patients treated in our hospital from January 2010 to March 2013 were enrolled as the research objects. All of these patients have complete data and were confirmed by pathology and classified into stages I-III period. General data were as follows: 116 males and 52 females; aged 28 to 76 y old with a mean age (64.7 ± 1.5 y); 132 cases of adenocarcinoma, 34 cases of signet ring cell carcinoma and 2 cases of adenosquamous carcinoma; 90 cases of upper gastric cancer and 78 cases of middle and lower gastric cancer. All patients routinely underwent gastroscopy, upper abdominal CT, chest X-ray, ultrasound examination of neck and other staging examinations, and were confirmed no distant metastasis. Electrocardiogram, blood routine, liver and kidney function examination were routinely performed before operation and chemotherapy. There were clear indications for surgery treatment and postoperative adjuvant chemotherapy, and all the patients were informed before the treatment and signed consents.

Treatment modes

Of 168 patients with gastric cancer, 150 (89.3%) underwent R₀ treatment, 18 (10.7%) underwent R₁ treatment, and 152 (90.5%) underwent D₂ peri-gastric lymph node dissection treatment. The number of dissected perigastric lymph nodes was 3 to 50, and the median was 20. Among these patients, 74.4% (125/168) patients underwent >15 lymph nodes dissection. The number of positive lymph nodes was 0-38, and the median was 6. 64 cases (38.1%) underwent adjuvant chemotherapy for 1-8 cycles, with a median of 4 cycles.

Follow up

All patients were reexamined every 3 months within 2 y after the first course of treatment, and every 6 months within 3 to 5 y. Routine examination included physical examination, routine blood test, liver and kidney function and imaging examinations. Patients were followed by telephone. The primary endpoints were Overall Survival (OS) and Progression

Free Survival (PFS). The causes of death were defined as cancer related deaths, cancer treatment related deaths and comorbidities related deaths.

Statistical analysis

SPSS 21 statistical software was adopted for analysis. Comparisons on the rate differences between the two groups were conducted using the Chi-square test. Survival rates were analysed using Kaplan-Meier. Survival difference between the groups was compared using log-rank test. Multivariate analysis was analysed using Logistic regression analysis. $P < 0.05$ means a significant difference.

Results

Comparisons on basic clinical characteristics between upper gastric cancer and middle and lower gastric cancer

There were no significant differences on basic clinical characteristics of sex, age, size of cancer and so on between the upper gastric cancer group and middle and lower gastric cancer group ($P > 0.05$, Table 1).

Table 1. Comparisons on basic clinical characteristics between upper gastric cancer and middle and lower gastric cancer.

Basic clinical characteristics	Upper gastric cancer (n=90)	Middle and lower gastric cancer (n=78)	P
Sex			0.095
Male	62	44	
Female	28	34	
Age (y)	63.9 ± 1.4	65.1 ± 1.7	0.264
Size of cancer			0.899
<5 cm	72	63	
≥ 5 cm	18	15	
Growth pattern			0.131
Clumps growth	9	16	
Nests growth	29	19	
Diffuse growth	52	43	
Depth of invasion			0.127
T1	9	12	
T2	21	26	
T3	60	40	
Pathological classification			0.306
Glandular cancer	70	62	
Signet ring cell carcinoma	19	15	

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Gland scale cancer	0	2
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Comparisons on clinicopathological features and treatment modes between upper gastric cancer and middle and lower gastric cancer

There were no significant differences on TNM stage, operation modes, the number of dissected lymph nodes and postoperative complications between the upper gastric cancer group and middle and lower gastric cancer group ($P>0.05$). There were significant differences on preoperative complications and postoperative adjuvant chemotherapy between the upper gastric cancer group and middle and lower gastric cancer group ($P<0.05$, Table 2).

Table 2. Comparisons on clinicopathological features between upper gastric cancer and middle and lower gastric cancer.

Clinicopathological features	Upper gastric cancer (n=90)	Lower gastric cancer (n=78)	χ^2	P
TNM staging			0.672	0.731
I-II	30	38		
III	60	40		
Preoperative complications				
Yes	46	30	12.518	0.000
No	44	48		
Operation modes 1				0.606
R ₀	80	70		
R ₁	10	8		
Operation modes 2			1.084	0.472
D ₀ /D ₁	8	4		
D ₂	82	74		

Table 3. Multivariate analysis of prognostic factors between patients with upper gastric cancer and middle and lower gastric cancer.

Cancer site	B	SE	Wald χ^2	OR (95% CI)	P
Upper gastric cancer					
TNM staging	0.234	0.502	0.308	1.344	0.604
(I+II vs. III)				(0.501-3.154)	
Preoperative complications	2.057	0.535	13.608	7.509	<0.001
(No vs. Yes)				(2.682-22.146)	
Postoperative adjuvant chemotherapy	0.724	0.261	6.703	1.744	0.018
(No vs. Yes)				(1.563-2.951)	
Lower gastric cancer					
TNM staging	0.416	0.065	29.182	1.686	0
(I+II vs. III)				(0.957-4.132)	

Dissected lymph nodes			0.103	0.146
<15	20	23		
≥ 15	70	55		
Postoperative complications			0.455	0.593
Yes	9	6		
No	81	72		
Postoperative adjuvant chemotherapy			10.169	0.007
Yes	50	14		
No	40	64		

Comparisons on prognosis between patients with upper gastric cancer and middle and lower gastric cancer

By the last follow-up, the total follow-up was 1 to 40 months with a median follow-up of 24.5 months. 3 y OS and PFS in patients with upper gastric cancer were 35.6% (32/90 cases) and 47.8% (43/90), respectively ($P=0.026$), and 43.6% (34/78 cases) and 51.3% (40/78 cases) in middle and lower gastric cancer patients ($P=0.035$).

Multivariate analysis of prognostic factors between patients with upper gastric cancer and middle and lower gastric cancer

Logistic regression analysis showed that risk factors affecting the prognosis of upper gastric cancer were preoperative complications and postoperative adjuvant chemotherapy, while the risk factors affecting the prognosis of middle and lower gastric cancer were TNM staging, preoperative complications and postoperative adjuvant chemotherapy (Table 3).

Preoperative complications	-1.232	0.504	6.612	0.255	0.017
(No vs. Yes)				(0.091-0.741)	
Postoperative adjuvant chemotherapy	1.406	0.603	7.115	4.026	0.006
(No vs. Yes)				(1.539-13.425)	

Comparisons on death causes in patients with upper gastric cancer and middle and lower gastric cancer

By the last follow-up on March 31, 2017, 51 of 90 (56.7%) patients with upper gastric cancer and 34 of 78 (43.6%) patients with middle and lower gastric cancer died respectively

($P < 0.05$). Among these deaths, cancer related death was 44 and 32 cases respectively in the two groups, while cancer treatment or complication related death was 7 and 2 cases respectively (Table 4).

Table 4. Comparisons on death causes in patients with upper gastric cancer and middle and lower gastric cancer.

Death causes	Death in upper gastric cancer (n=51)	Death in middle and lower gastric cancer (n=34)	χ^2	P
Cancer related deaths	44	32	5.127	0.032
Treatment or comorbidities related deaths	7	2	6.046	0.024
Pulmonary infection	2	0		
Cardiovascular accident	2	0		
Anastomotic bleeding	1	1		
Intestinal obstruction	1	0		
Anastomotic obstruction	1	1		

Summary

There were no significant differences on TNM stage, operation modes, the number of dissected lymph nodes and postoperative complications between the upper gastric cancer group and middle and lower gastric cancer group ($P > 0.05$). There were significant differences on preoperative complications and postoperative adjuvant chemotherapy between the upper gastric cancer group and middle and lower gastric cancer group ($P < 0.05$). 3 y OS and PFS in the upper gastric cancer group were 35.6% (32/90 cases) and 47.8% (43/90) ($P = 0.026$), and 43.6% (34/78 cases) and 51.3% (40/78) respectively in middle and lower gastric cancer group ($P = 0.035$). Logistic regression analysis showed that risk factors affecting the prognosis of upper gastric cancer were preoperative complications and postoperative adjuvant chemotherapy, while the risk factors affecting the prognosis of middle and lower gastric cancer were TNM staging, preoperative complications and postoperative adjuvant chemotherapy. By the last follow-up on March 31, 2017, 51 of 90 (56.7%) patients with upper gastric cancer and 34 of 78 (43.6%) patients with middle and lower gastric cancer died respectively ($P < 0.05$).

Discussion

From the etiological perspective, gastric cancer is the result of many factors, the pathogenesis involves changes in genetics of many genes and pathways and epigenetic changes, and it shows different trends in various clinical stages. In China, the

incidence and mortality of gastric cancer are at the forefront of malignant tumors. Although some progress has been made in the basic and clinical research of gastric cancer in recent decades, the diagnosis and treatment of gastric cancer is still not optimistic, the 5 y overall survival rate is still low. Most of the gastric cancer is already in the middle and late stage when diagnosed, about 60% of patients still have the recurrence and metastasis even comprehensive treatment based on surgery treatment has been performed [8,9].

Previous studies have confirmed that [10], the site of gastric cancer is an independent prognostic factor. In this study, we analysed clinical data of patients with upper gastric cancer and middle and lower gastric cancer to investigate the pathological features of cancer at different parts and to investigate the clinical significance of the differences, which has important significance in the individual treatment for gastric cancer. Some scholars [11] have found that the proportion of male gastric cancer patients is significantly higher than that of female, and the age composition of gastric cancer is the least in young people and the most in the elderly, which is basically consistent with the results of this study.

The biology of tumor is an important basis for the occurrence, development and clinical pathological characteristics, reflecting the nature or malignant degree of a tumor [12]. The biological behaviors of gastric cancer in different stages are significantly different. The results of this study showed that there were no significant differences on TNM stage, operation

modes, the number of dissected lymph nodes and postoperative complications between the upper gastric cancer group and middle and lower gastric cancer group ($P>0.05$). There were significant differences on preoperative complications and postoperative adjuvant chemotherapy between the upper gastric cancer group and middle and lower gastric cancer group ($P<0.05$). It is suggested that there are significant differences in preoperative complications and postoperative adjuvant chemotherapy and other clinical pathological features between upper gastric cancer and middle and lower gastric cancer.

The incidence of upper gastric cancer is increasing in recent years. Studies have shown that [13-15] upper gastric cancer is difficult to be detected in early stage, and is characterized by low degree of differentiation, high degree of malignancy, wide invasion and other pathological features. The prognosis is significantly worse than the middle and lower gastric cancer. The results of this study showed that the 3 y OS and PFS of patients with upper gastric cancer were significantly lower than those of patients with middle and lower gastric cancer ($P<0.05$). The main reason of the worse prognosis of patients with upper gastric cancer is that the early symptoms are not obvious, the related lesions mostly grow infiltratively or even spread directly, causing more extensive and subtle lymph node metastasis. Special anatomic sites and more residual cancer can also lead to the result. Logistic regression analysis showed that risk factors affecting the prognosis of upper gastric cancer were preoperative complications and postoperative adjuvant chemotherapy, while the risk factors affecting the prognosis of middle and lower gastric cancer were TNM staging, preoperative complications and postoperative adjuvant chemotherapy. It is suggested that there may be some differences in the clinical prognostic factors between upper gastric cancer and middle and middle and lower gastric cancer. From the statistical results, we speculated that the upper gastric cancer is characterized by low differentiation, late clinical stage, deep invasion and extensive lymph node metastasis. These clinical features determine their prognosis. To improve the early diagnosis rate of gastric cancer, and to follow the standard radical operation standard actively, it is helpful to improve the curative effect of gastric cancer by comprehensive treatment based on operation.

In summary, there were significant differences on the clinical pathological features and prognosis between patients with upper gastric cancer and patients with middle and lower gastric cancer, it is of great guiding significance to know the pathological features of cancer in different parts, it can provide individualized treatment options for patients and improve the prognosis of patients. As our study is retrospective and the sample size was relatively small, there may be some bias in the study, and a prospective study with larger sample size is needed to confirm the findings.

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