

Clinicopathological Analysis as Predictive Factors for Recurrence in Early Gastric Cancer

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OBJECTIVE To identify clinicopathological characteristics as predictive factors for recurrence in early gastric cancer (EGC), and to determine which lesions should be removed by gastrectomy by means other than endoscopic mucosal resection (EMR).

METHODS Data from 249 patients with EGC were collected and the relationship between their clinicopathological characteristics and postoperative recurrence was retrospectively analyzed by univariate analysis.

RESULTS Of the 249 patients after gastrectomy, 19 cases (7.6%) experienced a recurrence. The postoperative recurrence rate was 18.9% (7/37) in patients with lymph node metastasis, and 5.7% (12/212) in those without. Lymph node metastases were found to be significantly related to recurrence in EGC ($P = 0.005$).

CONCLUSION Lymph node metastases were the only predictive factor for recurrence in EGC. However, this was not the determining factor for performing gastrectomy rather than EMR. Although after gastrectomy with lymphadenectomy of EGC, patients with lymph node metastasis should be considered as candidates for adjuvant treatment. For lymph-node metastatic EGCs, adjuvant therapy is recommended following gastrectomy with lymphadenectomy.

KEY WORDS: early gastric cancer, recurrence, lymph node metastasis, endoscopic mucosal resection.

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Introduction

Early gastric cancer (EGC) has been defined as a gastric carcinoma in which the invasion is confined to the mucosa or submucosa, regardless of the presence of lymph node metastasis^[1]. The apparent incidence of EGC has been increasing because of advances in diagnostic procedures^[2]. EGC has a favorable prognosis after gastrectomy with lymph node dissection. However, excessive gastrectomy and lymphadenectomy may affect perioperative morbidity and mortality^[3]. Therefore, minimally invasive treatment such as endoscopic mucosal resection (EMR) has been considered to be an appropriate option for EGC patients.

It has been reported that recurrence of EGC occurred in some patients after gastrectomy with lymphadenectomy^[4]. However, little has been known in terms of the incidence rate and the predictive factors for recurrence, because of the relatively low incidence of recurrence after gastrectomy with lymphadenectomy for EGC.

Thus, in our study we retrospectively analyzed the clinicopathological characteristics for recurrence of EGC by reviewing cases, in order to identify predictive risk factors of recurrence and identify lesions that are candidates for gastrectomy rather than EMR.

Patients and Methods

Patients

A total of 249 patients with EGC underwent surgery in the Department of Oncology, First Affiliated Hospital of China Medical University, Shenyang, from 1990 through 2006. The criteria used for inclusion in this study were as follows: *i*) D1 or above lymph node dissections had been performed. *ii*) Recurrence of the tumor was confirmed by physical findings, radiological imaging, endoscopic examination with biopsy, and surgery. There were 178 male and 71 female patients, with an average age of 54.8 years (range 19–84 years). Among the 249 cases on which gastrectomy was performed with lymphadenectomy, 19 patients had recurrence of EGC.

Reference standard

The tumor location, macroscopic type, and histological type were based on the Japanese Classification of Gas-

tric Carcinoma^[5]. The histological type included differentiated and undifferentiated types. Macroscopic types included the following: protruded (type I), superficial elevated (type IIa), flat (IIb), superficial depressed (type IIc), and excavated (type III).

Statistical analysis

All data were analyzed using SPSS15.0 statistical software. The clinicopathological parameters between patients with and without recurrence were determined by the χ^2 test. A *P* value of less than 0.05 was considered as a significant difference.

Results

Clinicopathological characteristics related to the recurrence

The relationship among various clinicopathological characteristics and recurrence was analyzed by the χ^2 test (Table 1). Lymph node metastasis was significantly associated with a higher rate of recurrence (*P* = 0.005). However, no significant relationship was found between recurrence and sex, age, tumor location, macroscopic type, tumor size, tumor depth, or histologic type.

Recurrence in EGC

Of the 249 patients with EGC, 19 cases (7.6%) had a postoperative recurrence. The relationship between the only risk factor and recurrence was studied. The recurrence rate was 18.9% (7/37) in patients with lymph node metastasis, and 5.7% (12/212) in those without.

Discussion

Although the prognosis of EGC is excellent, a small but definite number of postoperative recurrences have been reported. The recurrence rate of EGC treated by gastrectomy has been reported to vary from 1.4% to 6.4%^[6,7]. In our study, the recurrence rate for gastrectomy with lymphadenectomy was 7.6%.

The risk factors related to recurrence of EGC have been discussed in several articles^[8]. Ichiyoshi et al.^[9] reported that the elevated type, and positive lymph nodes were significantly associated with a high risk of recurrence. Shiozawa et al.^[6] considered some other factors, such as submucosal invasion, a gross appearance of IIa + IIc type and a tumor size > 40 mm. However, in our study, lymph node metastases were the only significant predictive factor for the recurrence of EGC using univariate analysis. Lymph node metastases have been repeatedly proposed as one of the most important predictive factors in many studies^[10,11], which are similar to our results. The postoperative recurrence rate with and without lymph node metastasis, was 18.9% and 5.7% respectively.

Excessive gastrectomy and lymphadenectomy may

Table 1. Univariate analysis of factors associated with recurrence in EGC (cases).

Characteristic	Recurrence		Recurrence rate (%)	<i>P</i> value
	Positive	Negative		
Sex				NS
Male	14	164	7.9	
Female	5	66	7.0	
Age, years				NS
< 60	8	135	5.6	
≥ 60	11	95	10.4	
Location				NS
Upper	2	18	10.0	
Middle	4	28	12.5	
Lower	13	184	6.6	
Tumor size				NS
≤ 2 cm	5	106	4.5	
> 2 cm	14	124	10.1	
Macroscopic type				NS
I	1	7	12.9	
II	13	175	6.9	
III	5	48	9.4	
Histological type				NS
Differentiated	10	138	6.8	
Undifferentiated	9	92	8.9	
Tumor depth				NS
Mucosa	9	107	7.8	
Submucosa	10	123	7.5	
Lymph node metastasis				0.005
Negative	12	200	18.9	
Positive	7	30	5.7	

NS: not significant

affect perioperative morbidity and mortality. We have to look to improving post-operative function and quality of life after gastric cancer surgery without adversely affecting long term outcome^[12]. Therefore, minimally invasive treatments such as EMR are considered to be appropriate options for EGC patients. However, current application of EMR is limited to indications^[13]. Thus, we sought to expand the use of EMR to EGC by retrospectively examining recurring EGC to determine predictive factors for recurrence.

In our study, univariate analysis demonstrated that the presence of lymph node metastasis was the only predictive factor for recurrence. Although lymph node metastases seem to identify a high-risk population that perhaps should not be offered EMR, this can be determined only after gastrectomy with lymphadenectomy. Thus, these pathological features are not useful in EMR. Based on our finding, there were no proper predictive factors to determine EGC cases with a high risk of recurrence or preoperatively determine which operation (gastrectomy with lymphadenectomy or EMR) should be performed.

The application of adjuvant chemotherapy for lymph node metastatic EGCs has been a controversial issue. Sano et al.^[14] recommended that adjuvant chemotherapy for EGC with lymph node metastasis is not recommended, because of its low incidence of recurrence, but Maehara et al.^[15] supported adjuvant chemotherapy because of the high susceptibility of cancer cells within lymph nodes to chemotherapeutic agents. In our study, the postoperative recurrence rate was 18.9% in patients with lymph node metastasis, and 5.7% in those without. This result suggests that EGC with lymph node metastasis could be considered in a high risk individual who is a good candidate for adjuvant treatment such as chemotherapy.

In conclusion, lymph node metastases were the only predictive factor for recurrence. However, this cannot be confirmed before surgery or EMR. This pathologic factor was not useful to identify patients at high risk for recurrence who should be offered gastrectomy rather than EMR. Although after gastrectomy with lymphadenectomy for EGC, patients with lymph node metastasis should be considered as candidates for adjuvant treatment.

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