Laparoscopic gastrectomy for early gastric cancer and the risk factors of lymph node metastasis

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Abstract

Objective: Lymph node metastasis (LNM) is one of the important prognostic factors of early gastric cancer (EGC). Moreover, LNM is also important when choosing therapeutic intervention for EGC patients. The purpose of this study is to explore the risk factors of LNM in EGC and to discuss the corresponding treatment.

Design: We retrospectively reviewed the medical records of 253 patients with EGC who underwent surgical therapy in our department between 2012 and 2015. Univariate analysis and Multivariate Cox regression were used to evaluate the independent risk factors of LNM.

Results: LNM was present in 38 cases among 253 patients (15%). Univariate analysis showed an obvious correlation between LNM and tumour location, tumour size, depth of invasion, morphological classification, gross type of the lesion and venous invasion. Multivariate analysis indicated that poorly differentiated carcinoma, submucosal cancer, tumour size ≥2 cm and venous invasion were the independent risk factors for LNM.

Conclusion: Tumour size, depth of invasion, morphological classification and blood vessel invasion were predictive risk factors for LNM in EGC. We propose that EGC patients with those risk factors should be accepted gastrectomy with LN dissection.

Keywords: Early gastric cancer, laparoscopic surgery, lymph node metastasis

INTRODUCTION

The concept of early gastric cancer (EGC) was first put forward in 1962 and was defined as a lesion confined to the mucosa or the submucosa which was regardless of the presence of regional lymph node metastases (LNM).[1-3] The overall 5 years survival rate in EGC patients after radical gastrectomy is >90%, while decreased 70%-80% 5 years survival rate in those patients after the same operation with the presence of LNM.[4,5] Thus, LNM is considered as one of the most important prognostic factors in EGC.[6] At present, radical gastrectomy is the best choice for treating EGC with LNM, including open gastrectomy and laparoscopic gastrectomy.[6,7] Compared with open gastrectomy, laparoscopic surgery has the advantages of small trauma, quick recovery and short hospitalisation time. With the advancement of endoscopic technology,
some minimally invasive techniques such as endoscopic submucosal dissection (ESD) have been introduced and gradually recognised as a safe and effective choice for EGC treatment.\[8,9\] However, in the early stage of gastric cancer, LNM could be present in some cases, and the LN dissection was not possible in the ESD process, which limited the application of EGC therapy.\[10\] Therefore, the evaluation of LNM is very important in the treatment of EGC and even determines the treatment modality.

In this study, 253 patients with EGC who accepted surgical treatment in our hospital between 2012 and 2015 were enrolled to assess the risk factors of LNM. In addition, the number of LNs in the open surgery group and the laparoscopic surgery group were compared to find the better surgical methods for LN dissection.

**MATERIALS AND METHODS**

**Patients**

The study protocol was approved by the Institutional Review Board of Qilu Hospital of Shandong University, Shandong Province, China. A total of 253 patients with EGC who underwent laparoscopic gastrectomy or open gastrectomy with lymphadenectomy in the Department of Gastrointestinal Surgery, Qilu Hospital of Shandong University between January 2012 and December 2015, were enrolled in this study. EGC was confirmed according to the histologic results after surgery, and the Japanese Classification of Gastric Cancer was used to designate the gross type of the tumour. Laparoscopic surgery or open gastrectomy was performed according to patient’s general condition and will.

Inclusion criterion: EGC; patients are willing to accept laparoscopic surgery, and the body could tolerate the general anaesthesia and carbon dioxide pneumoperitoneum. Exclusion criterion: the laparoscopic group excluded the bad pre-operative cardiopulmonary function which could not tolerate carbon dioxide pneumoperitoneum, and the post-operative pathology proved to be the advanced gastric cancer.

**Surgery**

Open gastrectomy patients were prepared in the supine position, and upper abdominal midline incision about 15 cm was used. Patients underwent laparoscopic surgery were placed in the supine position with the legs apart. The surgeon stood on the patient’s left side, with the first assistant on the patient’s right, and the camera operator stood between the patient’s legs. After the division of ligaments and dissection of LNs, an upper abdominal midline incision about 6 cm was used for specimen removal and gastrointestinal reconstruction. All patients underwent radical gastrectomy which was defined as the radical resection of tumour with LN dissection. Both the surgical procedure and the extent of LN dissection were in strict accordance with the Japanese gastric cancer treatment guidelines.\[11\] Among all the patients, 20 cases underwent proximal gastrectomy, 215 cases of distal gastrectomy and 18 cases of total gastrectomy. In distal gastrectomy, the No. 1, 3, 4sb, 4d, 5, 6, 7, 8a, 9, 11p, 12a group of LNs were dissected before performing tumour resection and Billroth I or Billroth II digestive tract reconstruction. Proximal gastrectomy involved in the dissection of No. 1, 2, 3, 4sa, 4sb, 7, 8a, 9, 11p group of LNs and esophagogastric anastomosis. Moreover, the total gastrectomy with D2 LN dissection including tumour resection, Roux-en-Y anastomosis and dissection of No. 1, 2, 3, 4sa, 4sb, 4d, 5, 6, 7, 8a, 9, 10, 11p, 11d, 12a group of LNs.

**Clinical observation**

Enrolled factors included: age (<60 years or ≥60 years), sex, tumour size (<2 cm or ≥2 cm), tumour location (upper third, middle third or lower third), gross type of the lesion (elevated, depressed, at or flat), depth of invasion (mucosal or submucosal), lymphatic-vascular involvement (present or absent) and histological type (differentiated or undifferentiated). The evaluation of these factors was in accordance with the Japanese Classification of Gastric Carcinoma established by the Japanese Research Society for Gastric Cancer.\[11\]

**Statistical analysis**

All numerical results were expressed as mean ± standard deviation. The cumulative incidence of LNM was calculated by the Kaplan–Meier method. All statistically significant variables in univariate analysis were entered into the multivariate Cox regression analysis. The comparisons between two groups were analysed by independent sample t-test, and categorical variables were assessed by the Chi-square test. P < 0.05 was considered statistically significant. All statistical analyses were performed with SPSS, Version 17.0 (SPSS, Chicago, IL, USA).

**RESULTS**

**Risk factors related to lymph node metastasis**

A total of 253 cases were enrolled in this study, and characteristics of patients are shown in Table 1. 38 out of 253 cases (15%) had LNM. Several factors were observed to analyse the risk factors of LNM. In univariate analysis, tumour location, tumour size, depth of invasion, gross type of lesion, vascular invasion and histological type
were associated with LNM. Sex and age had no significant correlation with LNM [Table 1]. Multivariate logistic regression analysis revealed that poorly undifferentiated carcinoma, submucosal cancer, venous invasion and tumour size ≥2 cm were the independent risk factors for LNM [Table 2 and Figure 1].

**Rates of lymph node metastasis in early gastric cancer**

Among the EGC patients with LNM, the numbers of the cases with tumour located in the upper third (n = 20), the middle third (n = 31) and the lower third (n = 202) part of the stomach were 1 (5%), 9 (29%) and 28 (13.9%), respectively [Figure 2a]. Among the patients with mucosal (n = 120) and submucosal (n = 133) gastric cancer, the numbers of cases with LNM were 6 (5%) and 32 (24%), respectively [Figure 2b]. Among the patients with tumour ≥2 cm and <2 cm in size, the numbers of the cases with LNM were 27 (21.2%) and 11 (8.7%), respectively [Figure 2c]. LNM was present in 11 (7.9%) cases with differentiated gastric cancer (n = 138) and in 27 (23.4%) cases with undifferentiated gastric cancer (n = 115) [Figure 2d]. In gastric cancer patients with (n = 11) and without (n = 242) vascular invasion, the numbers of the cases with LNM were 7 (63.6%) and 31 (12.8%), respectively [Figure 2e]. The numbers of cases with LNM in flat (n = 16), elevated (n = 65), or depressed gastric cancer (n = 172) were 1 (6.3%), 2 (3%) and 35 (20.3%), respectively [Figure 2f].

**Comparison of the numbers of lymph nodes harvested in laparoscopic gastrectomy and open gastrectomy**

Among 253 patients with EGC, 32 cases underwent laparoscopic gastrectomy, including proximal gastrectomy (n = 2) and distal gastrectomy (n = 30). And 221 cases underwent open gastrectomy, including proximal gastrectomy (n = 18), distal gastrectomy (n = 185) and total gastrectomy (n = 18). According to our results, there was no significant difference between the numbers of LNs harvested in open gastrectomy and laparoscopic gastrectomy [P > 0.05, Table 3].

**DISCUSSION**

Gastric cancer is one of the most common malignant tumours in the digestive duct. [12] Although researches have explored the issue of predicting risk factors for LNM in EGC, as yet there are no definitive criteria. Multi-detector computerised tomography (CT) is the most popular technology to detect LNM; however, the sensitivity (50%) and specificity (75%) for LNM diagnosis are not satisfied. [13] Ultrasound endoscope has been applied to detect metastatic lymphadenopathy, and the sensitivity of ultrasound for LNM diagnosis has been reported to range between 59.5% and 97.2%, whereas its specificity ranges between 40.0% and 100%. [14,15] Besides, the experience of the operators could also influence the examine results. Thus,
Jiao, et al.: Laparoscopic gastrectomy and risk factors of LNM in EGC

According to our findings, tumour location, tumour size, depth of invasion, gross type, vascular invasion and histological type were associated with LNM. Poorly undifferentiated carcinoma, submucosal cancer, blood vessel invasion and tumour size ≥2 cm were the independent risk factors for LNM in EGC patients.

Recently, endoscopic mucosal resection and ESD have been used for treating patients with early mucosal gastric cancer. According to the Japanese Classification of Gastric Carcinoma established by the Japanese Research Society for Gastric Cancer, endoscopic resection has become one of the standard procedures, the indications of which are included mucosal tumours, tumours <2 cm in size and those without LNM. However, LN dissection could not be performed by endoscope ESD. Thus, pre-operative

Table 3: Comparison of lymph node dissection between open gastrectomy and laparoscopic surgery

| Group                  | Cases | Numbers of lymph node dissection | P   |
|------------------------|-------|----------------------------------|-----|
| Laparoscopy group      | 32    | 17.34±8.43                       | 0.739|
| Open gastrectomy group | 221   | 18.02±10.54                      |     |

Figure 2: Rates of lymph node metastasis in early gastric cancer rates of lymph node metastasis in regards to tumour site (a), depth of invasion (b), tumour size (c), histologic type (d), lymphatic invasion (e), and gross type of lesion (f)
evaluation of LNM is of great importance when deciding a treatment strategy for EGC. Our results indicated that determination of the risk factors is important for predicting LNM. EGC patients with LNM should undergo gastrectomy with LN dissection to reduce the probability of recurrence and to prolong the survival time.

Compared with open gastrectomy, laparoscopic surgery has the advantages of small trauma, quick recovery and short hospitalisation time. With the advancement of endoscopic technology, some minimally invasive techniques such as ESD have been introduced and gradually recognised as a safe and effective choice for EGC treatment.

Laparoscopic gastrectomy is superior to traditional operation in reducing operating trauma. Compared to open surgery, laparoscopic surgery has the advantages of quick recovery and short hospitalisation time. Meanwhile, there were no significant difference between the two groups in the number of LNs acquired and the safety of surgical margin. In addition, several studies have shown that laparoscopic gastrectomy is a safe and feasible method in the treatment of EGC.

LNM mostly remains within N1 and N2 LNs in EGC patients. Several studies have shown that the rate of LNM was 12.7% in N1 LNM while it is 7.2% in N2 LNM. We demonstrate that the risk factors of LNM in EGC and propose that EGC patients should be accepted gastrectomy and LN dissection.

**CONCLUSION**

LNM is correlated with several factors and its one of the critical factors that should be taken into consideration when deciding on the optimal therapeutic strategy. EGC patients with high-risk factors of LNM should be accepted surgical gastrectomy with LN dissection and especially accepted minimal invasive operation which fit for the indications of the laparoscopic surgery.

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**Conflicts of interest**

There are no conflicts of interest.

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