Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.JournalofSurgicalResearch.com

Predictive factors for lymph node metastasis in early gastric cancer with signet ring cell histology and their impact on the surgical strategy: analysis of single institutional experience

*Zheng Wang, MD, Xingmao Zhang, MD, Junjie Hu, MD, Weigen Zeng, MD, Jianwei Liang, MD, Haitao Zhou, MD, and Zhixiang Zhou, MD**

Department of Abdominal Surgical Oncology, Cancer Hospital of the Chinese Academy of Medical Sciences, Peking Union Medical College, Beijing, P.R.China

ARTICLE INFO

Article history:
Received 18 December 2013
Received in revised form
19 March 2014
Accepted 21 March 2014
Available online 27 March 2014

Keywords:
Early gastric cancer
Signet ring cell carcinoma
Lymph node metastasis
Endoscopic treatment

ABSTRACT

Background: The prognosis of early gastric cancer (EGC) with signet ring cell histology is more favorable than other undifferentiated gastric adenocarcinomas. An accurate assessment of potential lymph node metastasis is important for the appropriate treatment of EGC with signet ring cell histology. Therefore, this study analyzed the predictive factors associated with lymph node metastasis in patients with this type of EGC.

Methods: A total of 136 EGC with signet ring cell histology patients who underwent D2 radical gastrectomy were reviewed in this study. The clinicopathologic features were analyzed to identify predictive factors for lymph node metastasis.

Results: The overall rate of lymph node metastasis in EGC with signet ring cell histology was 10.3%. Using a univariate analysis, the risk factors for lymph node metastasis were identified as the tumor size, depth of tumor invasion, and lymphovascular invasion. The multivariate analysis revealed that tumor size >2 cm, submucosal invasion, and lymphovascular invasion were independent risk factors of lymph node metastasis ($P < 0.05$).

Conclusions: The risk of lymph node metastasis of EGC with signet ring cell histology was high in those with tumor sizes ≥2 cm, submucosal tumors, and lymphovascular invasion. A minimally invasive treatment, such as endoscopic resection, might be possible in highly selective cases of EGC with signet ring cell histology with intramucosal invasion, tumor size <2 cm, and no lymphovascular invasion.

1. Introduction

In 1962, the Japanese Society of Gastroenterological Endoscopy defined early gastric cancer (EGC) as a lesion confined to the mucosa and/or submucosa, regardless of lymph node metastatic status [1]. EGCs have a low incidence of lymph node metastasis and a favorable outcome after surgery [2]. Although radical gastrectomy including lymph node dissection has been recognized as the standard surgical operation for EGC, unnecessary surgery could be avoided and endoscopic treatment might be a consideration in patients with EGC with negligible risk of lymph node metastasis.

* *Corresponding author*. Department of Abdominal Surgical Oncology, Cancer Hospital of the Chinese Academy of Medical Sciences, Peking Union Medical College, Nanli 17, Panjiayuan Road, Chaoyang District, Beijing 100021, P.R.China. Tel./fax: +86 010 8778 7110.
E-mail address: zhouzx2014@gmail.com (Z. Zhou).

0022-4804/$ – see front matter © 2014 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.jss.2014.03.065

Many investigations have shown that patients with EGC with signet ring cell histology have a more favorable prognosis than patients with other undifferentiated gastric adenocarcinomas, because EGC with signet ring cell histology has a lower probability of lymph node metastasis [3]. Consequently, it might be considered as an indication of endoscopic surgery. However, the feasibility of endoscopic treatment for this type of EGC is still in debate.

The present retrospective study was designed to evaluate the factors that can be predicted the presence of lymph node metastasis with signet ring cell histology of EGC. Using these predictive factors, we established suitable criteria to elucidate which subgroup of EGC with signet ring cell histology patients could be treated with endoscopic treatment instead of radical surgery.

2. Patients and methods

This study enrolled 136 EGC with signet ring cell histology patients, those were pathologically proven after curative gastrectomy with lymph node dissection from January 1994 to December 2012 at the Department of Abdominal Surgical Oncology, Cancer Hospital of the Chinese Academy of Medical Sciences, Peking Union Medical College.

All the patients routinely underwent an upper alimentary tract barium meal and electronic gastroscope examination before surgery to identify the diseased region and the pathologic type to confirm the diagnosis of malignant neoplasm of the stomach after pathologic examination. The preoperative routine chest x-ray, abdominal ultrasound, and upper abdominal computed tomography (CT) examination showed no pulmonary, hepatic, or other distant metastases, and no tumor directly invading the pancreas, spleen, liver, or colon. Endoscopic ultrasound examination was not performed routinely. All patients underwent radical subtotal or total gastrectomies, depending on the tumor location and intraoperative verification of tumor-free resection margins and D2 lymphadenectomies. No patient has received neoadjuvant therapy before surgery. The methods of reconstruction after distal gastrectomy include Billroth I, II, or Roux-en-Y. Roux-en-Y reconstruction and jejunal interposition are the most common methods used after a total gastrectomy. All specimens were examined after resection. World Health Organization criteria for histologic typing of gastric tumours were used, where signet ring cell carcinoma is defined as an adenocarcinoma in which a predominant component (more than 50% of the tumour) is made up of isolated or small groups of malignant cells containing intracytoplasmic mucin [4]. A single pathologist retrieved all lymph nodes by palpation under gross inspection. No size limitation was imposed for lymph node harvesting. The lymph nodes were cut into two pieces along the long axis, embedded in paraffin blocks, and stained with haematoxylin and eosin. The status of the lymph nodes was not evaluated by immunohistochemistry.

The patients' clinical characteristics and histopathologic parameters were analyzed. Clinicopathologic factors, such as gender, age, tumor size, tumor location, macroscopic appearance, depth of tumor invasion, ulceration, lymphovascular invasion and lymph node status, were defined according to the General Rules of the Japanese Classification of Gastric Carcinoma (second English edition) [5]. The maximum diameter of tumor was recorded as tumor size. Macroscopic type included elevated (I, protruded and IIa, superficial elevated), flat (IIb, superficial flat), depressed (IIc, superficial depressed and III, excavated). The depth of tumor invasion was classified as mucosa and submucosa carcinoma. Lesions with ulceration or scarring from previous ulceration (converging folds or deformity of the muscularis propria, or fibrosis in the submucosal or deeper layer) within them were regarded as ulcerated lesions [6]. Lymphovascular invasion was defined as the presence of tumor emboli either in the lymphatic duct or the vascular lumen.

2.1. *Statistical analysis*

Univariate and multivariate analyses of risk factors associated with lymph node metastasis were performed using the χ^2 test and logistic regression models, respectively. $P < 0.05$ was considered statistically significant. Statistical analyses were performed with SPSS software, version 15.0 for Windows (SPSS Inc, Chicago, IL).

3. Results

The study involved 91 men and 45 women, with a male-to-female ratio of 2.02:1. The median age of the enrolled patients was 58 y (24–82 y). A total of 96 patients had tumors located in the lower third of the stomach, 34 patients had tumors in the middle third of the stomach, whereas six patients had tumors in the upper third of the stomach. Sixty nine cases had tumors ≥2.0 cm in diameters, whereas 67 cases were <2.0 cm. Tumor invasion was limited to the mucosal layer in 79 patients, whereras in 57 patients, the tumors had invaded the submucosal layer. Elevated-type tumors were macroscopically observed in 10 patients, flat-type tumors were observed in 18 patients, and depressed-type tumors were observed in the remaining 108 patients. Twenty four patients had ulcer finding. There were 18 cases of lymphovascular invasion.

The univariate analysis of factors predicting lymph node metastasis is presented in Table 1. Tumor size, depth of tumor invasion, and lymphovascular invasion were significantly correlated with lymph node metastasis. There was no significant difference in gender, age, tumor location, macroscopic type, and ulceration. The multivariate analysis revealed that tumor size ≥2.0 cm, submucosal invasion, and lymphovascular invasion were independent risk factors associated with lymph node metastasis (Table 2). To identify the subgroup of patients who could be amenable to endoscopic treatment, the lymph node metastasis in EGC with signet ring cell histology cases were evaluated according to the depth of invasion, tumor size, and the presence of lymphovascular invasion (Table 3). The numbers in parentheses represent the number and percentage of cases with lymph node metastasis. None of the 59 patients with a mucosa-confined tumor <20 mm in diameter and no lymphovascular invasion showed lymph node metastasis. No lymph node metastasis was observed in five patients with submucosal tumors <2.0 cm in diameter