



## Tumor differentiation is not a risk factor for lymph node metastasis in elderly patients with early gastric cancer

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### Abstract

**Background:** The aim of this study was to identify risk factors for lymph node metastasis in elderly patients (70 years or more) with early gastric cancer.

**Methods:** We reviewed the prospectively collected database of 6893 patients with early gastric cancer who had undergone curative gastrectomy in 3 tertiary cancer centers between January 2003 and December 2009 in Korea. Patients were sorted into 4 groups according to age: less than 50, fifties, sixties, and 70 years or more. Risk factors for lymph node metastasis in early gastric cancer were analyzed.

**Results:** One thousand and thirty five patients (15.0%) were 70 years or more. As age increased, the frequency of large differentiated tumor, lymphatic and submucosa invasion increased. Old age was associated with a lower risk for lymph node metastasis in patients with early gastric cancer (Odds ratio [OR], OR, 0.622; 95% CI, 0.5466–0.830,  $P = 0.010$ ). Ulceration or differentiation of tumor was not associated with lymph node metastasis in elderly patients with early gastric cancer.

**Conclusions:** Elderly patients with undifferentiated type histology early gastric cancer without other risk factors for lymph node metastasis may be candidates for endoscopic resection.

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**Keywords:** Gastric cancer; Elderly; Endoscopic procedure

### Introduction

Gastric cancer is a common cancer worldwide.<sup>1</sup> Gastric cancer surgery in the elderly is increasing because of the rise in the numbers of elderly people in the population and the increased incidence of cancer with age.<sup>2</sup>

Although surgical and postoperative care techniques have improved, age is still an important risk factor for

morbidity and mortality after surgery.<sup>3,4</sup> As age increases, the frequency of comorbid diseases increases, functional status decreases, mental status is frequently altered, and tolerance for surgical treatment decreases.<sup>5</sup>

Endoscopic resection (ER), including endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD), is an alternative treatment option for a subset of patients with early gastric cancer.<sup>6</sup> Currently, ER is considered as a standard treatment for early gastric cancer (EGC) that meets the criteria for absolute indication: an intramucosal differentiated-type adenocarcinoma  $\leq 2$  cm in size and without ulcerative findings or lymphatic-vascular involvement. Recent studies have shown that long-term results after ER are comparable to those after surgery.<sup>7,8</sup>

Characteristics of elderly patients with gastric cancer include frequent combination with comorbid diseases,

**Abbreviations:** LADG, laparoscopy assisted distal gastrectomy; ODG, open distal gastrectomy; HR, hazard ratio; CI, confidence interval; ER, endoscopic resection; EMR, endoscopic mucosal resection; ESD, endoscopic submucosa dissection; EGC, early gastric cancer.

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differentiated tumor, and higher frequency of female patients.<sup>9,10</sup> However, risk factors for lymph node metastasis of elderly patients with early gastric cancer have rarely been reported.

The aim of this study was to investigate risk factors for lymph node metastasis in elderly patients with early gastric cancer.

## Patients and methods

### *Study cohort and data sources*

The study cohort was composed of 7111 patients with early gastric cancer who were treated by open or laparoscopy-assisted gastric cancer surgery between January 2003 and December 2009 at one of three institutions in Korea: Chonnam National University Hwasoon Hospital, National Cancer Center, and Samsung Medical Center. Patients who (i) had a histologically confirmed gastric adenocarcinoma, (ii) had a tumor with a depth confined to the mucosa or submucosa, and (iii) had newly diagnosed cancer without previous treatment were included in the analysis. Two hundreds and eighteen patients with less than 15 lymph nodes retrieved for proper nodal staging or remnant gastric cancers due to that their lymphatic flow was changed after the primary surgery were excluded to avoid incorrect staging.<sup>11</sup> Finally, 6893 patients with early gastric cancer were analyzed in this study. All information was obtained with appropriate Institutional Review Board waivers and data were collected without revealing any personal information.

### *Personal characteristics and clinical data*

All patient characteristics were obtained from databases of prospectively collected data. Demographic characteristics included age and sex. Clinicopathological characteristics included tumor location, tumor size, differentiation, gross type, depth of invasion, lymphatic invasion, and lymph node metastasis. We classified the histological types of tumor according to the WHO classification. The histological types were grouped into two subgroups; 1) the differentiated type, consisting entirely of well- or moderately differentiated tubular components or papillary components or a mixture of these components, 2) the undifferentiated type consisting of the other histological types or a mixture of them. When the tumor was a mixture of differentiated and undifferentiated types, the tumor was classified according to the major component of the tumor (50% or more). All pathological data was assessed on surgical specimens.

In patients with multiple synchronous gastric cancers, the lesion with the deepest infiltration of the gastric wall was regarded as the main lesion and any others were regarded as accessory lesions. The clinicopathological characteristics of the main lesion were used for the analysis.

### *Operative procedures*

The surgical procedures and reconstruction methods were as follows. Gastrectomy was performed for a tumor-free margin of 2 cm. Extent of lymph node dissection was determined using the recommendations of the Japanese Research Society for Gastric Carcinoma.<sup>12</sup> After open or laparoscopic laparotomy, surgeons examined the intra-abdominal cavity and inspected the peritoneum, diaphragm, liver capsule, and pelvic cavity. All patients enrolled in the present study underwent gastrectomy with D1 +  $\beta$  or more lymph node dissection.<sup>12</sup> Tumors were staged in accordance with the 6th UICC tumor node metastasis (TNM) classification.<sup>11</sup>

### *Statistical methods and analyses*

Patients were grouped according to their ages: less than 50, fifties, sixties, and 70 or more. Continuous variables were expressed as medians with ranges. Statistical significance was estimated by using the appropriate statistical methods for matched data. Continuous variables were compared by using the Student's *t* test, and categorical variables were compared by using the Chi-square test or Fisher's exact test. Categorical variables were compared by conditional logistic regression.

## Results

### *Patient characteristics*

Clinical and pathological characteristics are shown in [Table 1](#). The median age of the 6893 patients was 58 years (range: 21–88 years). One thousand and thirty five patients (15.0%) were 70 years old or older. With increasing age, the frequency of large differentiated tumor, lymphatic invasion, and submucosa invasion was significantly increased whereas the frequency of ulceration was decreased.

### *Lymph node metastasis and risk factors for lymph node metastasis in all patients*

The overall rate of lymph node metastasis was 10.3%. The median number of invaded nodes was 0 (range; 0–64). There was no significant difference in the rate of lymph node metastasis among different age groups ([Table 1](#)). Univariate and multivariate analyses showed that ulceration (OR, 1.191; 95% CI, 1.003–1.416,  $P = 0.047$ ), tumor differentiation (OR, 1.840; 95% CI, 1.535–2.206,  $P < 0.001$ ), lymphatic invasion (OR, 5.478; 95% CI, 4.536–6.615,  $P < 0.001$ ), tumor size (OR, 2.207; 95% CI 1.723–2.826,  $P < 0.001$ ), and tumor depth (OR, 3.664; 95% CI, 2.947–4.556,  $P < 0.001$ ) were significantly associated with lymph node metastasis ([Table 2](#)).

When elderly patients were compared with other patients, multivariate analysis showed that old age

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