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The impact of age on nodal metastases and survival in gastric cancer

A. Ahmad, MD,^{a,b} H. Khan, MD,^{a,b} G. Cholankeril, MD,^{a,b} S.C. Katz, MD,^{a,b} and P. Somasundar, MD, MPH^{a,b,*}

^a Department of Surgery, Roger Williams Medical Center, Providence, Rhode Island

^b Boston University School of Medicine, Boston, Massachusetts

ARTICLE INFO

Article history:

Received 2 January 2016

Received in revised form

3 February 2016

Accepted 26 February 2016

Available online 16 March 2016

Keywords:

Gastric cancer

Elderly

Lymph node metastases

Survival

ABSTRACT

Background: In gastric adenocarcinoma, the disparity in lymph node involvement between different age groups has not been thoroughly investigated. The objective of our study was to compare age-associated differences in adequate lymph node harvest and nodal involvement in gastric adenocarcinoma patients.

Methods: We analyzed data extracted from the Surveillance, Epidemiology and End Results database on 13,165 patients diagnosed with stage I-III gastric adenocarcinoma between 2004 and 2011. All patients underwent surgical resection. Statistical comparisons between various age groups were done using the chi-square test and Cox regression.

Results: Among 13,165 gastrectomy patients, proportion of patients that had >15 lymph nodes examined decreases significantly with increasing age ($P < 0.0001$). When adequately staged, older patients had a significantly lower proportion of node-positive tumors ($P < 0.0001$). Adequate nodal staging was also associated with improved 5-y disease-specific survival across all age groups.

Conclusions: In gastric adenocarcinoma, older patients are less likely to be adequately staged. However, when adequately staged, they are less likely to have node-positive tumors. Adherence to national guidelines, regardless of age, is associated with improved survival outcomes and may alter multimodality management of gastric cancer in the elderly.

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Introduction

In the United States, the incidence of gastric cancer is declining but the mortality rate remains high.¹ Overall 5-y survival rate for all stages combined is around 28%.¹ Metastatic involvement of regional lymph nodes is one of the most important prognostic determinants of survival after resection of gastric cancer.²⁻⁵ National guidelines recommend pathologic assessment of at least 15 lymph nodes from a gastrectomy specimen for accurate staging.⁶ Improvement in

survival outcomes has been associated with adequate lymphadenectomy specifically in patients with node-positive disease.⁷⁻⁹ In gastric cancer, the sensitivity of diagnostic modalities used for preoperative assessment of nodal involvement is limited. Therefore, adequate surgical staging remains the cornerstone of management.^{8,9}

Gastric cancer is a disease of the elderly with a median age of 69 y at diagnosis. In older patients, comorbidities and limited ability to tolerate systemic treatment may complicate decisions regarding adequate surgical resection. In the Dutch

* Corresponding author. Division of Surgical Oncology, Roger Williams Medical Center, 825 Chalkstone Avenue, Providence, RI 02908. Tel.: +1 347 553 3511; fax: +1 401 456 6708.

E-mail address: psomasun@chartercare.org (P. Somasundar).
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<http://dx.doi.org/10.1016/j.jss.2016.02.043>

Gastric Cancer Group Trial, age >70 years was independently associated with worse overall survival.³ However, optimal management should be tailored to individual physiological characteristics and properly selected elderly patients may benefit from aggressive treatment. As such, accurate identification of elderly patients at high risk for recurrence is of paramount importance.

The objective of our study was to assess the frequency of adequate lymph node retrieval in resectable gastric cancer in the elderly and its impact on staging and survival when compared to younger patients.

Materials and methods

Data for our study were extracted from November 2013 submission of the Surveillance Epidemiology and End Results (SEER) database on adult patients diagnosed with gastric adenocarcinoma between 2004 and 2011. The SEER database combines records of 18 cancer registries across the United States representing approximately 28% of the population. Cases were selected based on gastric anatomic site (International Classification of Disease-Oncology, third edition), adenocarcinoma histology (World Health Organization classification), and stage (AJCC seventh edition TNM classification). Patients with gastroesophageal junction tumors or those under the age of 20 years were excluded from the study. Similarly, patients with distant metastases (M1), those who underwent palliative intent gastrectomy or those with positive surgical margins (R1/R2) were excluded. Of the 20,425 patients diagnosed with stage I-III gastric adenocarcinoma, 13,165 underwent curative intent gastrectomy with negative margins (R0) and fulfilled the criteria for our study (Fig. 1).

The study population was then subcategorized into the following age groups: 20-49 y, 50-64 y, 65-74 y, 75-84 y, and ≥85 y. Variables pertaining to the grade of tumor, number of lymph nodes examined (LNE) and the number with metastases were extracted from pathology reports. Neoadjuvant chemotherapy data were derived from a SEER flag for “yp” staging. In an attempt to maintain uniformity in data, nodal stage was re-defined according to the AJCC seventh edition TNM staging system (N1 = 1-2 positive nodes; N2 = 3-6 positive nodes; N3 ≥7 positive nodes). Odds ratio (OR) was calculated for quantitative assessment of association between age, histopathology, LNE, and lymphatic metastases. Statistical comparison was tabulated using the Pearson chi-square test.

The Kaplan–Meier method was used to estimate survival in various groups. Overall survival (OS) was calculated by SEER using time from initial diagnosis till last contact, date of death or date of cutoff for database. For disease-specific survival (DSS), the event used was death from disease with all other events deemed censored. Univariate comparison between groups was performed using the log-rank test. Multivariate analysis was conducted to calculate hazard ratios using the Cox regression analysis. All statistical analyses report 95% confidence intervals and were performed using SPSS for windows (SPSS Inc, Chicago, IL). Significance of difference was assumed at $P < 0.05$.

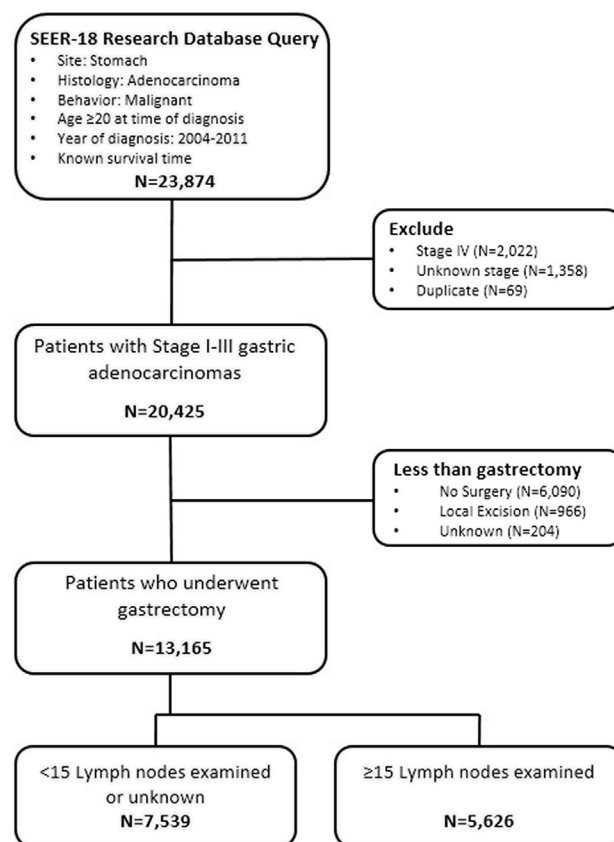


Fig. 1 – Selection criteria flowchart.

Results

Demographic and tumor characteristics of all patients are shown in Table 1. The male-to-female ratio was approximately 1.75:1 and remained constant throughout various age groups. Seventy percent of patients were >65 y of age. Tumor location was anatomically distributed among proximal (32%), body (8%), distal (31%), and whole stomach (28%). Most patients had T1/T2 tumors (72%).

Sixty eight percent of patients aged 20-49 y had high grade tumors (grade III/IV), and this proportion decreased with increasing age. When compared to patients aged <65 y, older patients had a lower proportion of high grade tumors (OR = 0.84, 95% confidence interval [CI] = 0.78-0.91, $P < 0.001$).

In the entire study group, 12% of patients received neoadjuvant therapy. This proportion was the highest in patients aged 20-49 y (18%) and decreased with increasing age to 17% in 50-64 y, 12% in 65-74 y, 5% in 75-84 y, and 1% in patients aged >85 y.

Nodal status

Among all patients, only 43% of patients who underwent gastrectomy had appropriate nodal staging defined as ≥15 LNE on histopathologic analysis. Median number of lymph nodes examined for patients aged 20-49 y was 14; however, it declined with increasing age to a median of 8 in patients aged

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