

## Rates of lymph node metastasis and survival in T1a gastric adenocarcinoma in Western populations

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**Background and Aims:** EMR and endoscopic submucosal dissection (ESD) are widely accepted in Asia for treatment of early gastric cancer (EGC). Few studies have examined lymph node (LN) metastasis of EGC in Western populations. We sought to examine EGC and LN metastasis in a heterogeneous Western population.

**Methods:** Patients with surgically resected, histologically confirmed American Joint Committee on Cancer T1a gastric adenocarcinoma were identified in the Surveillance, Epidemiology, and End Results (SEER) database from 2002 to 2012. Patients were excluded if they had stage IV disease, had multiple primary cancers, or received neoadjuvant therapy. Rates of LN metastasis were calculated, and survival analyses were performed.

**Results:** Of 923 patients in the cohort, 72 (7.8%) had at least 1 positive LN on final pathology. When stratified by race, Asian/Pacific Islanders (APIs) demonstrated the lowest rate of LN metastases ( $n = 17/327$ , 5.2%), followed by Hispanics ( $n = 12/171$ , 7.0%), whites ( $n = 27/278$ , 9.7%), and blacks ( $n = 16/147$ , 10.9%). The highest rates of stage IA disease were observed in API (93.9%) and Hispanic (92.4%) patients, followed by white (89.9%) and black (87.1%) patients ( $P = .04$ ). Survival analysis of T1a gastric cancer patients by race/ethnicity showed that 5-year overall survival was highest for API patients (API, 88%; Hispanic, 81%; black, 79%; and white, 77%;  $P < .01$ ).

**Conclusions:** The rate of LN metastasis in T1a gastric cancers in the United States is higher than the rates reported in Asia. Survival outcomes in T1a gastric cancers varied significantly by race, suggesting that definitive endoscopic treatment may not be appropriate for all patients in the United States. (Gastrointest Endosc 2016;83:1184-92.)

In 1962, the Japanese Society of Gastroenterological Endoscopy defined early gastric cancer (EGC) as adenocarcinoma confined to the mucosa and submucosa, regardless of the cancer's nodal involvement.<sup>1</sup> EMR and endoscopic submucosal dissection (ESD) have been developed in Asia for low-morbidity treatment of EGC based on the very low node-positive (N+) rates in large retrospective Asian studies of radical surgical resection in EGC cases.<sup>2,3</sup> According to the Japanese Gastric Cancer Association treatment guidelines, gastric adenocarcinomas that are (1)

clinically staged as T1a, (2)  $\leq 2$  cm, (3) well differentiated, and (4) lacking ulceration fall under the standard criteria for EMR/ESD.<sup>4</sup> Although EMR and ESD are frequently used in Asia and permit curative treatment of EGC without the morbidity of gastrectomy, the standard of care in Western countries remains formal resection.

There is growing interest in expanding the use of EMR and ESD in Western countries, including the United States. EMR and ESD were initially developed for endoscopic resection of gastric cancer, but now are also being used

*Abbreviations:* AJCC, American Joint Committee on Cancer; API, Asian/Pacific Islander; CI, confidence interval; DSS, disease-specific survival; EGC, early gastric cancer; ESD, endoscopic submucosal dissection; HR, hazard ratio; LN, lymph node; LN+, lymph node positive; OS, overall survival; SEER, Surveillance, Epidemiology, and End Results.

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for resection of T1a esophageal cancers and colon cancers. Studies including Western data report the rate of lymph node (LN) metastasis for intramucosal esophageal cancer to be 0% to 2%<sup>5,6</sup> and 1% to 3%<sup>7,8</sup> for colon cancer when the cancer is confined to the top one-third of the submucosa (sm1). However, due to the higher incidence of gastric cancer in Asia, the majority of data regarding LN metastasis rates for T1a disease are based only on Asian cohorts. Whether EMR and ESD can be applied to Western patients by using the same criteria based on LN metastasis rates in Asian T1a gastric cancer patients has not been well studied. Based on our previous work investigating disparities in gastric cancer outcomes in racial/ethnic groups in the United States, we hypothesized that LN metastasis rates may vary by racial and ethnic groups in a heterogeneous Western population.<sup>9,10</sup> Therefore, the objective of our study was to investigate the LN metastasis rate and clinical outcomes by race/ethnicity in surgically resected T1a gastric cancers by using a large national cancer registry.

## METHODS

### Patients and methods

Patient data were obtained from the Surveillance, Epidemiology, and End Results (SEER) website. The SEER catchment area covers ~28% of the United States; the dataset contains clinicopathologic information, treatment specifics, overall survival (OS), and disease-specific survival (DSS). Tumor location, grade, and histology were coded according to the International Classification of Diseases for Oncology, version 3. Tumor stage was coded according to the American Joint Committee on Cancer (AJCC) TNM staging system, 7th edition.<sup>11</sup> SEER requires registries to update disease and vital status for all cases on an annual basis.

Included in the analyses were surgically resected (codes 30-33, 40-42, 51-52, 61-63), histologically confirmed, AJCC T1a gastric adenocarcinoma patients 18 years of age or older who received a diagnosis from January 2002 to December 2012. As detailed in [Figure 1](#), patients with stage IV disease or multiple primary cancers, or patients who received neoadjuvant radiation therapy were excluded. Patients treated with endoscopic resection alone as their first course of therapy were not included. International Classification of Diseases for Oncology codes were used to identify patients with adenocarcinoma. Of the 75,921 gastric cancer patients in the SEER registry, our final sample comprised 923 patients; of these patients, 278 were white, 147 were black, 171 were Hispanic, and 327 were Asian/Pacific Islanders (APIs) ([Table 1](#)).

### Statistical analysis

Patient demographic and clinical characteristics were compared across groups by using the Pearson  $\chi^2$  test for categorical nominal data and the Jonckheere–Terpstra nonparametric test for categorical ordinal data. Univariate

and multivariate Cox proportional hazard models identified factors associated with improved DSS and OS, with results reported by using hazard ratios (HRs) and 95% confidence intervals (CIs).

Kaplan–Meier curves were used to calculate median, 3-year, and 5-year DSS and OS rates, with the log-rank test used to determine statistical differences across groups. Survival time, in months, was calculated from the date of diagnosis until the date of death. If the patient was alive, the patient was censored at the date of last contact. For the DSS analyses, patients with death due to gastric cancer (SEER cause of death recode 21020, 50060, or 50300) were identified by using the cause of death on the death certificate. Patients who died of causes unrelated to their gastric cancer diagnosis were censored at their date of death. The median follow-up time for the 763 patients alive at last contact was 46 months (interquartile range, 19-81 months; mean [SD], 52 [36] months). All analyses were performed by using SAS (SAS Institute Inc., Cary, NC), with 2-sided *P* values  $\leq .05$  considered statistically significant.

## RESULTS

### Patient demographic and tumor characteristics

The final cohort consisted of 923 patients with surgically resected T1a gastric adenocarcinoma ([Fig. 1](#)). Of those, 851 (92.2%) were node negative and 72 (7.8%) were node positive (N+). The most common histological subtypes were intestinal (189 of 923, 20.5%), diffuse (39 of 923, 4.2%), signet ring (253 of 923, 27.4%), and adenocarcinoma not otherwise specified (357 of 923, 38.7%). LN+ patients tended to have higher frequencies of tumors  $\geq 2$  cm with a higher grade compared with node negative patients ([Table 1](#)). Twenty-two of 505 tumors (4.4%)  $\leq 2$  cm were LN+, whereas 39 of 244 tumors (16.0%)  $> 2$  cm were LN+. Further details regarding patient demographic, tumor, and surgery characteristics are summarized in [Table 1](#).

### Trends in overall LN+ rates and staging by race

To investigate differences by race/ethnicity, LN+ rates for the T1a cohort were examined by race/ethnic groups. We observed lower LN+ rates in API and Hispanic patients (5.2% and 7.0%, respectively) compared with white and black patients (9.7% and 10.9%, respectively) ([Table 2](#)). API and Hispanic patients had higher rates of stage IA disease compared with white and black patients, whereas white and black patients tended to have slightly higher rates of IB and IIA disease (*P* = .04) ([Table 2](#)). API patients tended to have smaller tumors and the highest rate of  $> 15$  LNs examined ([Table 2](#)).

### Survival analyses of all T1a gastric adenocarcinoma patients

Significant differences were observed in the disease-specific survival (DSS) and overall survival (OS) of the

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