Use of Endoscopic Ultrasound in the Preoperative Staging of Gastric Cancer: A Multi-Institutional Study of the US Gastric Cancer Collaborative

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BACKGROUND: Endoscopic ultrasound (EUS) can be used to guide the therapeutic plan for patients with gastric adenocarcinoma (GAC), but data on its use and accuracy remain poorly defined. We sought to define the use of EUS, as well as characterize the diagnostic accuracy of EUS among patients with GAC.

STUDY DESIGN: We identified 960 patients who underwent resection of GAC between 2000 and 2012 from 7 major academic institutions participating in the US Gastric Cancer Collaborative. Clinicopathologic and EUS data were collected and analyzed using chi and kappa statistics.

RESULTS: Of 960 patients, 223 (23.2%) underwent evaluation with preoperative EUS. Among patients who underwent EUS, 74 (33.2%) received neoadjuvant chemotherapy; 149 (66.8%) proceeded directly to resection. Among patients who did not receive neoadjuvant therapy and received curative intent gastric resection, the EUS T classifications were T1 (33.3%), T2 (35.6%), T3 (18.9%), T4 (12.1%) and the N classifications were N0 (68.1%) and N $\geq$ 1 (31.9%). In contrast, when tumor stage was based on the final surgical specimen, there was a higher proportion of cases with more advanced T stage (T1, 36.4%; T2, 14.4%; T3, 23.5%; T4, 25.7%) and N stage (N0, 51.3%; N $\geq$ 1, 48.7%). The agreement of preoperative EUS compared with surgical staging for T (kappa = 0.28, $p < 0.001$) and N (kappa = 0.33, $p < 0.001$) classification was only fair.

CONCLUSIONS: Less than one-quarter of patients with GAC underwent preoperative EUS staging. In patients who did not receive preoperative chemotherapy, tumor stage on EUS often did not correlate with T stage and N stage on final pathologic analysis. Endoscopic ultrasound should be combined with other staging modalities to optimize staging of patients with GAC. (J Am Coll Surg 2015;220:48–56. © 2015 by the American College of Surgeons)

Gastric adenocarcinoma is the fourth most common cancer worldwide and the second most common cause of cancer-related deaths.[1,2] The incidence of gastric adenocarcinoma has significant geographic variation. In fact, the incidence of gastric cancer is higher in Asia, Eastern Europe, and South America compared with the

CME questions for this article available at http://jacscme.facs.org

Disclosure Information: Authors have nothing to disclose. Timothy J Eberlein, Editor-in-Chief, has nothing to disclose.

Support: Dr Ejaz was supported in part by the Eleanor B Pillsbury Foundation for surgical research.

Received April 20, 2014; Revised June 19, 2014; Accepted June 30, 2014.

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http://dx.doi.org/10.1016/j.jamcollsurg.2014.06.023
ISSN 1072-7515/14

Abbreviations and Acronyms
EUS = endoscopic ultrasound
GAC = gastric adenocarcinoma
IQR = interquartile range
OR = odds ratio
pT = final pathologic T staging
uT = preoperative endoscopic ultrasound T staging

United States (US) and Western Europe. This variability is likely related to differences in the prevalence of various risk factors such as diet, ethanol intake, tobacco smoking, and rates of *Helicobacter pylori* infection. Despite the lower incidence of gastric cancer in the US, the impact is still substantial, with an estimated 21,600 new cases and 11,000 deaths in 2010.[3]

For patients with localized disease, surgical resection of the primary tumor along with an associated lymphadenectomy provides the best option for long-term survival.[4,5] Prognosis after curative intent resection is dependent on various tumor-specific factors including extent of local invasion and lymph node involvement, among others.[6] Depending on the extent of disease at presentation, 5-year overall survival is estimated anywhere between 5% and 90%.[7-13] As such, neoadjuvant therapies are often used in an effort to improve survival after surgical resection. However, the indication for and effectiveness of neoadjuvant chemotherapy are still not well defined.[14,15] In general, neoadjuvant therapy is often offered to patients with advanced T (T2−3 and higher) and/or node-positive disease based on preoperative imaging studies.

In contrast to other malignancies such as rectal cancer,[16] the accuracy of T-staging for gastric cancer has been shown to be comparatively low. Imaging modalities such as MRI, CT, and PET have been reported to have an accuracy of only approximately 60% in defining the T stage of gastric cancer.[17,18] As such, EUS has been used in the preoperative evaluation of gastric cancer, due to its potential ability to assess both depth of local tumor infiltration and regional lymph node involvement with greater accuracy.[19-23] The indication and accuracy of EUS, however, are still controversial. Although some studies have shown accurate results in the staging of advanced gastric tumors, other studies have shown poor results for overall EUS accuracy.[17,24-26] Many of these previous studies were small, single institution studies. The objective of this study was to define the overall use of EUS in a large multi-institutional cohort of patients undergoing curative intent resection for gastric adenocarcinoma. Furthermore, we aimed to determine the accuracy of EUS compared with the final pathologic specimen with regard to tumor depth and nodal status.

METHODS

Patient selection

All patients who underwent curative intent surgery for gastric adenocarcinoma in 1 of the 7 major academic institutions participating in the US Gastric Cancer Collaborative (Johns Hopkins Hospital, Baltimore, MD; Emory University, Atlanta GA; Stanford University, Palo Alto, CA; Washington University, St Louis, MO; Wake Forest University, Winston-Salem, NC; University of Wisconsin, Madison, WI; The Ohio State University, Columbus, OH) between 2000 and 2012, were identified. Standard data on demographic, clinicopathologic, preoperative clinical assessment and stage, tumor, and therapy-related variables were collected. Specifically, patient demographic and clinicopathologic characteristics, including age, sex, American Society of Anesthesiologists (ASA) score, body mass index, preoperative bleeding, significant preoperative weight loss (>10 lb), and comorbidities were collected. Tumor characteristics that were collected included tumor size, tumor location, number of lesions, histologic type and grade, depth of invasion, number of metastatic lymph nodes, and American Joint Committee on Cancer (AJCC) stage.[27] Treatment data were also collected, including extent of lymphadenectomy (D1 vs D2), operative time, estimated blood loss, and the need for perioperative blood transfusions. Margin status was classified as microscopically negative (R0), microscopically positive (R1), or macroscopically positive (R2). Information on the type and duration of chemotherapy and radiotherapy, if applicable, were also noted.

Data on postoperative outcome metrics such as length of hospital stay, type of complication, and Clavien-Dindo stage, if applicable, were collected.[28] Date of last follow-up, vital status (as recorded from the Social Security death index), and recurrence-free survival were also collected. Recurrence was defined as the presence of a biopsy-proven tumor showing adenocarcinoma cells or the presence of imaging highly suspicious of tumor recurrence.

Statistical analysis

Demographic and clinical characteristics of the study population were categorized according to whether or not the patient underwent preoperative EUS. The data were correspondingly reported as numbers (percentage) or medians with interquartile ranges (IQR). Univariate comparisons were assessed using the Mann-Whitney test for continuous variables and the chi-square test or Fisher's exact test for dichotomous and categorical variables. Univariate and multivariate logistic regression models were constructed to explore the association of preoperative covariates with the receipt of EUS. To