

Factors Associated With Recurrence and Survival in Lymph Node–negative Gastric Adenocarcinoma

A 7-Institution Study of the US Gastric Cancer Collaborative

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Objectives: To determine pathologic features associated with recurrence and survival in patients with lymph node–negative gastric adenocarcinoma.

Study Design: Multi-institutional retrospective analysis.

Background: Lymph node status is among the most important predictors of recurrence after gastrectomy for gastric adenocarcinoma. Pathologic features predictive of recurrence in patients with node-negative disease are less well established.

Methods: Patients who underwent curative resection for gastric adenocarcinoma between 2000 and 2012 from 7 institutions of the US Gastric Cancer Collaborative were analyzed, excluding 30-day mortalities and stage IV disease. Competing risks regression and multivariate Cox regression were used to determine pathologic features associated with time to recurrence and overall survival. Differences in cumulative incidence of recurrence were assessed using the Gray method (for univariate nonparametric analyses) and the Fine and Gray method (for multivariate analyses) and shown as subhazard ratios (SHRs) and adjusted subhazard ratios (aSHRs), respectively.

Results: Of 805 patients who met inclusion criteria, 317 (39%) had node-negative disease, of which 54 (17%) recurred. By 2 and 5 years, 66% and 88% of patients, respectively, experienced recurrence. On multivariate competing risks regression, only T-stage 3 or higher was associated with shorter time to recurrence [aSHR = 2.7; 95% confidence interval (CI), 1.5–5.2]. Multivariate Cox regression showed T-stage 3 or higher [hazard ratio (HR) = 1.8; 95% CI, 1.2–2.8], lymphovascular invasion (HR = 2.2; 95% CI, 1.4–3.4), and signet ring histology (HR = 2.1; 95% CI, 1.2–3.6) to be associated with decreased overall survival.

Conclusions: Despite absence of lymph node involvement, patients with T-stage 3 or higher have a significantly shorter time to recurrence. These

patients may benefit from more aggressive adjuvant therapy and postoperative surveillance regimens.

Keywords: competing risks regression, gastric cancer, node-negative, recurrence, survival

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Despite declining global incidence, gastric adenocarcinoma (GAC) remains the fourth leading cause of worldwide cancer-related mortality.¹ The cornerstone of curative therapy for gastric cancer remains surgical resection with negative margins and an adequate lymphadenectomy,² but adjuvant chemotherapy and chemoradiation have shown survival benefits when added to resection.^{3,4} It is well established that lymph node status is among the most important prognostic factors for disease recurrence and survival in resected gastric cancer.^{5–7} Although lymph node–negative patients demonstrate substantially better outcomes than those with lymph node metastases at the time of resection, a subset of these patients experience recurrence and disease-specific death. Identifying factors associated with recurrence and decreased survival in patients with node-negative disease can improve patient selection for adjuvant therapy and surveillance.

Several reports have examined prognostic factors in node-negative GAC.^{5,8–15} However, these studies generally represent single-center experiences, the majority of which come from Eastern centers. Only 4 available studies are from Western populations.^{5,11,12,15} Here, we use data from the 7 institutions that make up the US Gastric Cancer Collaborative to identify prognostic factors for recurrence in lymph node–negative gastric cancer after curative resection in a large, modern, multicenter North American cohort.

METHODS

Study Population

The US Gastric Cancer Collaborative represents a consortium of 7 high-volume academic institutions including Emory University, Johns Hopkins Hospital, Ohio State University, Stanford University, Wake Forest University, Washington University in St Louis, and the University of Wisconsin. All patients who underwent resection for GAC via an abdominal approach between January 2000 and December 2012 at participating institutions were included. Trained research fellows collected data retrospectively from the medical record and used data validation as a measure of quality control. Furthermore, all data were compiled, cleaned, and audited by 1 primary database

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