Correspondence

Survival in lymph node-negative gastric cancer: the Western experience

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Lymph node status is the strongest prognostic indicator for survival after gastrectomy for gastric adenocarcinoma (GAC) (1). However, for patients who undergo resection and are deemed to be 'node-negative' based on pathologic exam, the relevant prognostic indicators and guidelines for adjuvant therapy remain unclear. Our group has recently published the long-term survival results of a large, multi-institutional database of North American patients undergoing gastrectomy for GAC, of which 317 patients were lymph node-negative (2). To date, it is the largest published series of a Western experience with node-negative GAC. The median follow-up time was significant at 68 months, and the overall recurrence rate was 17%. We evaluated endpoints of time to recurrence and overall survival (OS). Our data showed that greater depth of tumor invasion (indicated by T-stage) was independently significant in predicting shorter time to recurrence in a competing risks regression model whereas OS was negatively impacted by higher tumor stage, lymphovascular invasion, signet ring histology, and having less than 15 nodes examined.

In commentary by Hsu *et al.*, the authors contrast the differences between our cohort and two previously published studies of survival in node-negative GAC (3,4). As there are few large Western series in this patient population, the Eastern experience serves as both an educational example as well as a study of contrasts. In a study published in 2013 by Chou *et al.*, recurrence rates for T2–T4 tumors were 8.6%, 12.5%, and 26.5%, respectively (3). In comparison, recurrence rates in our cohort were 9.1%, 29.7% and 35%, respectively (2). In another study published by the same group, the authors found that extensive lymphadenectomy with >25 lymph nodes examined resulted in better long-term survival than the examination of <15 or 16–25 nodes did, and that greater extent of lymphadenectomy did not increase surgical complication or hospital mortality rates (4). While our data also indicated that having >15 nodes examined did prolong OS, the mean number of nodes examined in our cohort was 16, with interquartile range of 9–22 (2). Both of these differences help to highlight the disparate experiences with GAC in Asia and the West. While the higher recurrence rates seen in our cohort by T stage may very well be related to understaging with fewer total lymph nodes examined, it should also be noted that our overall population was older, had greater comorbidity burden (63% in our cohort *vs.* 27% in Chou *et al.*), and had a much higher perioperative complication rate (40% in our cohort *vs.* 11% in Hsu *et al.*), a risk factor that we have shown to be independently significant for recurrence and survival in gastric cancer (5). Additionally, the cohort presented by Chou *et al.* did not include any patients who received neoadjuvant chemotherapy, whereas 23% of patients in our cohort received neoadjuvant therapy. Despite the known survival advantage of perioperative chemotherapy for GAC, our data showed that while controlling for other clinicopathologic features, patients who received neoadjuvant therapy did worse in terms of recurrence and survival, correlating with a preoperative assessment of more locally advanced and aggressive disease. Furthermore, several factors may be driving the difference in number of lymph nodes retrieved and examined between the Eastern and Western experience, including the greater technical challenge in Western patients with higher BMIs and greater comorbidities as well

as differences in pathology practice, as a recent publication from Memorial Sloan Kettering Cancer Center showed that more extensive *ex-vivo* lymphadenectomy increased the median yield from 21 to 30 lymph-nodes (6). Despite these differences, these data do highlight an opportunity for improvement in the number of lymph nodes both retrieved and examined in North American GAC patients.

While the differences that these studies highlight are an interesting comparison of surgical practice and outcomes, this is not the primary purpose of our analysis. Our aim was to explore what factors can guide clinicians who are choosing adjuvant treatment strategies for patients deemed node-negative after curative resection for GAC. Certainly, the high percentage of patients who were technically understaged in our cohort is concerning and the possibility for stage migration is not trivial. However, as reoperation for adequate staging is unrealistic, data is needed to guide clinicians treating this cohort of node-negative patients. While under-staging in some other solid tumor types is in and of itself an indication for adjuvant therapy, as yet there are no firm guidelines for understaged patients with GAC (7). Our data indicates that patients with higher T stage have significantly increased risk of both recurrence and death, and should strongly be considered for adjuvant chemotherapy and/or radiotherapy, even if they are deemed lymph node-negative.

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Footnote

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