



Less Than Ten: Defining the Role of Splenic Hilar Lymph Node Dissection in Gastric Cancer

Jonathan B. Greer, MD

Department of Surgery, Johns Hopkins University School of Medicine, Baltimore, MD

We do not often think of precision medicine in the context of surgical therapy but there have been substantial efforts underway in Asia for years trying to determine the extent of lymphadenectomy in gastric cancer. International conformity to standards regarding lymphadenectomy has been slow, with European and American centers taking longer to accept the D2 lymphadenectomy, particularly with concerning early findings from a large Dutch multi-center randomized trial.¹ Long-term follow-up data from the Dutch trial suggesting a benefit to D2 lymphadenectomy² have led to the adoption of D2 lymphadenectomy as standard of care in the National Comprehensive Cancer Network (NCCN) guidelines.³

The splenic hilar lymph nodes, also known as the number 10 (No. 10) nodes, have historically been part of the D2 lymphadenectomy but their inclusion in routine gastrectomy for advanced proximal gastric cancers has been questioned. This was, in part, because a splenectomy was thought to be necessary for complete removal of this basin. While a bulky greater curvature tumor invading the spleen, or close to it, will often necessitate a splenectomy, it has been unclear what to do in other tumors that may be at risk, so called ‘proximal tumors without greater curvature involvement’. This subset of tumors was studied in a randomized controlled trial in Japan (JCOG0110), which found no survival benefit to splenectomy in this population with increased morbidity and mortality.⁴ Subsequently, No. 10 nodes were removed from the definition of D2

lymphadenectomy in the most recent Japanese guidelines.⁵ However, as the surgical techniques for gastrectomy and lymph node dissection (LND) have improved, including with minimally invasive techniques, further attempts have been made to assess both the necessity and benefit of a spleen-preserving No. 10 LND.^{6,7} These nodes are positive in a wide range of cases, anywhere from 9.8 to 27.9%.^{8,9}

Several groups in Asia have published series on the laparoscopic total gastrectomy with spleen-preserving No. 10 LND. The CLASS-04 study was a prospective, multi-center cohort study that found this procedure to be safe in expert hands.⁶ A second series, a single-institutional series, used propensity matching to try and determine which patients precisely benefited from this surgical approach.¹⁰ As reported in *JAMA Surgery* in November, Lin et al. have published the first prospective, randomized controlled trial to address the benefit of laparoscopic total gastrectomy with spleen-preserving No.10 LND in patients with advanced proximal gastric cancers without greater curvature invasion.¹¹

This was a single-center study enrolling 536 patients, of whom 526 completed the trial. The inclusion criteria were notable for clinical stage T2-4, N0-3/M0 patients with tumors that did not involve the greater curvature of the stomach. The stomach was divided into quadrants based on imaging, endoscopy, or laparoscopic findings, and patients were enrolled if the tumor was not involving the greater curvature. The trial was open from January 2015 to October 2018, with a 3-year minimum follow-up required. The primary outcome was 3-year disease-free survival (DFS), with secondary outcomes of 3-year overall survival (OS) and 30-day perioperative morbidity and mortality. All patients underwent a laparoscopic total gastrectomy, with half undergoing a spleen-preserving No. 10 LND plus a standard D2 lymphadenectomy, and the other half undergoing a D2 lymphadenectomy alone.

The groups were evenly matched, with 74.5% of males and a mean age of 60.6 years. There was no difference in 3-year DFS between the groups (70.3% in No. 10 LND and 64.3% in D2; $p = 0.11$). While there was a difference in 3-year OS (75.7% vs. 66.5%; $p = 0.02$), this effect washed out on multivariate analysis. The overall morbidity rates in this paper were strikingly low, 16.9% overall, and were even between groups. Only one patient in the No. 10 LND group required a splenectomy, and none in the D2 group. The No. 10 LND added a median of 13 min to the operative time. The groups were even in their receipt of adjuvant systemic chemotherapy. Intriguingly, stratification by tumor location found that *posterior* tumors had substantially better DFS and OS when undergoing a No. 10 LND versus a D2 alone, an effect that was also present after multivariate analysis and was particularly pronounced in >T2 tumors (DFS 92.9% vs. 39.3%, OS 92.9% vs. 42.9%; both $p < 0.001$). However, it should be noted that this subgroup analysis was comprised of only 66 patients. As expected, the number of lymph nodes dissected was higher in the No. 10 LND group compared with the D2-alone group (44 vs. 38), the difference of which was accounted for by the No. 10 nodes. Overall, 13.3% of the No. 10 nodes were positive and varied by T stage (4.9% T1 → 22.9% T4a). In the subgroup analysis, in the posterior group, the percentage of positive No. 10 nodes was 17.6% versus 12.7% in the non-posterior group.

There are valid criticisms of this trial, although first and foremost the authors should be saluted for performing a well-designed surgical randomized trial—it is a testament to what is possible in this disease at high-volume centers with experienced surgeons. That said, it should be clear that this is a negative study that did not find a survival benefit to spleen-preserving No. 10 LND and D2 lymphadenectomy, over D2 lymphadenectomy alone, in patients undergoing laparoscopic total gastrectomy for advanced proximal gastric cancer not involving the greater curvature. Furthermore, the application of these data to Western populations is limited, given the exclusion of patients who received neoadjuvant chemotherapy. By clinical T stage alone, all of these patients would have been given neoadjuvant chemotherapy according to NCCN guidelines. While the omission of these patients is in line with Asian standards and affords some intellectual purity to this study, applying these findings to a patient treated with neoadjuvant chemotherapy would be a mistake. These authors previously examined this population in their propensity-matched study, but this group was only 23 patients and a survival difference for No. 10 LND in neoadjuvant patients was not observed.¹⁰ This study was not powered to find a difference in *posterior* patients ($n = 66$), and thus positing that there is a real benefit to No. 10 LND in these posterior tumors would be premature

as well. Lastly, I doubt that this technique can be rapidly translated throughout the United States and Europe, given the relative paucity of high-volume minimally invasive surgeons performing this operation compared with Asia.

We are inching closer to precision surgery in gastric cancer, and papers such as that by Lin et al. are getting us there. If we are still operating for gastric cancer years from now, it is not far-fetched to assume that the spleen-preserving No. 10 LND will be part of the armamentarium, as the West has gradually adopted the standards set by high-volume, trailblazing surgeons in Asia. However, knowing which patients will benefit and when to perform this in the setting of neoadjuvant chemotherapy remain critical questions. In the meantime, the authors should be saluted for this true technical advance.

DISCLOSURES Jonathan B. Greer has no disclosures to declare.

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