Gastric cancer is the third most common cause of cancer-related deaths worldwide. Although the overall incidence of gastric adenocarcinoma has declined in some countries, there has been a general increase of cancer involving the upper third of the stomach (proximal gastric cancer) along with an increase of adenocarcinoma of the esophagogastric junction. Surgical resection remains a cornerstone of gastric cancer treatment with curative intent, but the extension of gastric resection for patients with proximal gastric cancer is debated. This issue has been addressed in the study by Khalayleh et al,1 which examined the number and site of lymph node metastases with size and location of the tumor based on clinical staging in patients undergoing upfront total gastrectomy. The analysis of 655 patients with localized adenocarcinoma of the upper third of the stomach showed that for cT1-T3N0/N1 differentiated tumors and for cT1N0/N1 poorly differentiated tumors, there were no lymph node metastases in the suprapyloric (station 5) and infrapyloric nodes (station 6) as well as in the lymph nodes along the right greater curvature or right gastroepiploic artery (station 4d). The risk of lymph node metastases increased significantly for poorly differentiated tumors and when tumor size was 4.1 cm or greater (40.0% vs 20.4%, \( P = .001 \)). According to these results, Khalayleh and colleagues1 suggest that proximal gastrectomy can be safely performed when a differentiated cT1-T3N0/N1 or poorly differentiated cT1N0/N1 gastric cancer less than 4.1 cm is diagnosed preoperatively.

Proximal gastrectomy is the surgical procedure that involves the removal of the proximal half of the stomach with the cardia and distal esophagus, while the distal half of the stomach with the pylorus are preserved. Total gastrectomy has been historically considered the optimal treatment for cancers of the proximal stomach. However, this procedure is associated with different sequelae including malnutrition, anemia, and dumping syndrome. As it became evident that nodal metastases around the distal stomach are rare, at least in early gastric cancer of the proximal stomach, proximal gastrectomy was proposed as an alternative to total gastrectomy. The preservation of the distal stomach can provide several theoretical advantages, including improved nutritional status and quality of life, less postoperative morbidity and less anemia compared with total gastrectomy. Two recent meta-analyses compared postoperative and long-term outcomes of these 2 procedures. Of note, the analyzed studies do include in most cases patients with early gastric cancer and are almost exclusively retrospective, lacking randomized prospective trials in this setting. Although proximal and total gastrectomy had similar rates of overall morbidity, in-hospital mortality, anastomotic leakage, and comparable survival rates, proximal gastrectomy was associated with reduced hemoglobin loss, less weight loss, and reduced vitamin B\(_{12}\) supplementation compared with total gastrectomy.2,3 On the other hand, the risk of postoperative reflux was significantly higher after proximal gastrectomy,3 suggesting that optimization of reconstructive techniques to decrease reflux will be an important topic.

Other 2 issues should be considered if a more conservative surgery would be desirable. The first one is the accuracy of preoperative staging with a specific focus on T and N parameters. After initial diagnosis by endoscopy with multiple biopsies followed by histological evaluation, diagnostic work-up can include computed tomography of chest-abdomen-pelvis, endoscopic ultrasound and 18F-fluorodeoxyglucose positron emission tomography. Multidetector computed tomography is helpful in differentiating tumors limited to submucosa (T1) or muscularis propria (T2) from T3-T4 cancers. Endoscopic ultrasound, an operator-dependent technique, provides sensitivity and specificity of 86% and 90% in discriminating T1-T2 from T3-T4 tumors, and it has similar sensitivity.

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and specificity rates in distinguishing between T1 and T2 lesions. The preoperative evaluation of N parameter is more problematic. Two meta-analyses showed good sensitivity but low specificity in detecting lymph node metastases for both endoscopic ultrasound and computed tomography (sensitivity of more than 80% but specificity of less than 70%), with a sensitivity of only 34% for computed tomography when evaluating early gastric cancer. One can suggest that the evaluation of N status is clinically less relevant because lymphadenectomy is performed during proximal gastrectomy, and Khalayleh and colleagues provided evidence that cN1 tumors can be safely treated with this procedure. However, it should be emphasized that the difference between cN1 and cN2 tumors depends on the number of positive lymph nodes, but this could be a difficult goal for current preoperative investigations. A planned proximal gastrectomy with D1/D1+ lymphadenectomy may become a total gastrectomy with D2 lymphadenectomy based on intraoperative findings, unless the patient is not considered fit for major surgical procedure.

Khalayleh and colleagues identified proximal gastrectomy as the surgical procedure for what is a heterogeneous group of tumors, including differentiated cT1-T3N0/N1 or poorly differentiated cT1NO/N1 gastric cancer less than 4.1 cm. Endoscopic mucosal resection and endoscopic submucosal dissection should be considered for early gastric cancers with specific features (ie, differentiated tumor less than or equal to 20 mm limited to the mucosa with no ulceration, no lymph node metastases, and no lymphovascular invasion) with similar survival and much less complications compared with gastric resection. On the other hand, there is increasing evidence that neoadjuvant or perioperative chemotherapy is associated with increased survival in patients with T2 or higher gastric cancer and/or any N+ status. Neoadjuvant treatment has become the standard of care for patients with locally advanced gastric cancer in Western countries, and the role for conservative gastric resection following neoadjuvant therapy should be specifically evaluated. Therefore, the contemporary indication for upfront proximal gastrectomy may be limited to early gastric cancers not amenable to endoscopic treatment and possibly to cT2NO differentiated tumors. Finally, a note of caution should be placed on the exact anatomic location of what is called “proximal gastric cancer.” In this setting we should consider tumors arising from the proximal stomach and at most cancers arising 2 to 5 cm below the esophagogastric junction—the so-called Siewert III tumor—thus excluding tumors arising above or within the esophago-gastric junction as they are classified as esophageal cancers.

The findings by Khalayleh et al should be tested and validated in adequately powered, controlled, prospective randomized trials. However, the development and spread of endoscopic techniques to treat early gastric cancer and the increasingly frequent use of neoadjuvant chemotherapy for advanced gastric cancer complicate the design of such trials.


