Surgery ■■ (2017) ■■–■■

Contents lists available at ScienceDirect

Surgery

journal homepage: www.elsevier.com/locate/ymsy

Society of University Surgeons

Preoperative enteral access is not necessary prior to multimodality treatment of esophageal cancer

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ARTICLE INFO

Article history:
Accepted 27 September 2017

ABSTRACT

Background. Surgical enteral access prior to multimodality treatment for esophageal cancer is controversial as dysphagia is often used for feeding tube referral. We hypothesized that enteral access before neoadjuvant chemoradiation for esophageal cancer provides no benefit compared to that placed during definitive esophagectomy.

Methods. Patients undergoing esophagectomy for esophageal malignancy from 2007 – 2014 were retrospectively identified. Clinicopathologic factors were recorded including preoperative enteral access, weight change, nutritional laboratory works, and perioperative complications.

Results. Of 156 identified patients, 99 (63.5%) received neoadjuvant chemoradiation and comprised the study cohort. Fifty (50.5%) underwent enteral access (gastrostomy [14], jejunostomy [32], other [4]; "Access Group") prior to chemoradiation followed by esophagectomy and were compared to 49 "No-Access" patients who underwent enteral access during esophagectomy. Clinicopathologic variables were similar between cohorts. The Access and No-Access cohorts had similar reported dysphagia (86% vs 75.5%, respectively; $P = .2$) and mean preesophagectomy serum albumin (3.9 vs 4 gm/dL, respectively; $P = .2$). Weight loss ± 6-month periesophagectomy was similar between access versus No-Access cohorts (–11.2% vs –15.4%, respectively; $P = .1$). Weight loss during this period was likewise similar for patients with dysphagia in the Access (–11%) versus No-Access group (–15.2%, $P = .1$). No difference in complication rates was noted between Access (64%) and No-Access groups (51%, $P = .2$).

Conclusion. Despite healthcare provider bias, there seems to be no nutritional or perioperative benefit for enteral access before neoadjuvant chemoradiation for esophageal malignancy. Patients with esophageal malignancy should therefore proceed to appropriate neoadjuvant and surgical therapy with enteral access performed during definitive resection or reserved for those with frank obstruction on endoscopy. (Surgery 2017;160:XXX-XXX.)

The incidence of esophageal cancer has been increasing in the United States with an estimated 17,000 new cases in 2017 and an annual death rate of nearly 16,000 cases, demonstrating the deadly nature of this disease.[1] Although evidence exists for potential cure with chemoradiation alone in patients with squamous cell carcinoma of the esophagus, surgical resection remains the only durable cure, coupled with multimodality treatment to include chemoradiation.[2,3] These patients present with variable degrees of dysphagia, malnutrition, and cachexia, which can make it difficult for the clinician to decide if supplemental enteral nutrition is needed and how best to deliver it. As such, many patients are referred for surgically placed feeding tubes in an effort to prevent weight loss or for fear that they will develop esophageal obstruction during chemoradiation.

This surgical enteral access is not without potential complications,[4–6] reported as high as 44%, although their placement prior to neoadjuvant chemoradiation has been proven safe.[7,8] However, studies have shown that symptoms of dysphagia often abate by the end of the first cycle of chemoradiation, allowing the patient to continue oral nutrition without the need for a surgically placed feeding tube in many cases.[9,10] Nevertheless, the need for optimizing perioperative nutrition is clear, as patients with

Presented at the 12th Annual Academic Surgical Congress in Las Vegas, NV, February 7 – 9, 2017.

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https://doi.org/10.1016/j.surg.2017.09.046

malnutrition and cachexia have increased perioperative morbidity, mortality, and cancer recurrence.[11-15]

As such, we hypothesized that placement of enteral access in patients with esophageal cancer prior to neoadjuvant chemoradiation, especially in patients with a presenting symptom of dysphagia, is not necessary and provides no nutritional or oncologic benefit in this patient population.

Methods

The Institutional Review Board at the University of Florida approved all details of this study, and Health Insurance Portability and Accountability Act compliance for all protected patient information/identifiers was used. Informed consent was waived under the University of Florida Institutional Review Board for this retrospective study. A retrospective database was created of patients undergoing esophagectomy for malignancy at the University of Florida from 2007 – 2014. Patients were identified by CPT code via the departmental billing office. Routine demographic, clinicopathologic, operative, and perioperative complication variables were collected from the electronic medical record. Patients underwent preoperative staging and treatment in accordance with National Comprehensive Cancer Network guidelines.[16] Those patients who received neoadjuvant chemoradiation comprised the study cohort, as these patients are at most risk for perioperative malnutrition[13] and to limit cohort heterogeneity.

Patients were subsequently stratified based on undergoing a procedure to potentially improve nutrition via enteral access prior to esophagectomy. Those patients who underwent endoscopic esophageal stent placement, gastrostomy (either endoscopic or surgical) or jejunostomy tube placement (either percutaneous or surgical) comprised the "Access Group." Patients who did not undergo such procedures prior to definitive esophagectomy comprised the "No-Access Group."

Statistical analyses were performed utilizing Stata 13 software (StataCorp; College Station, TX). Identified patients were divided into 2 cohorts based on the receipt of preesophagectomy enteral access and summary statistics performed comparing the Access Group with the No-Access Group. Student t test and χ^2 test was used to compare continuous and categorical variables, respectively. Recurrence free survival (RFS) was defined as the period of time from esophagectomy to radiographic or endoscopic detection of malignancy, death secondary to esophageal malignancy, or last follow-up, at which point the data were censored. Overall survival (OS) was defined as the period of time from esophagectomy to all-cause death. The Kaplan-Meier log-rank method was used to estimate RFS and OS based on preesophagectomy enteral access. A 2-sided P value of .05 and a 95% confidence interval (CI) were used for all analyses.

Results

Cohorts and demographic information

A total of 156 patients were identified between 2007 – 2014 who underwent esophagectomy for malignancy. Because patients who undergo neoadjuvant chemoradiation have been shown to be at increased risk for malnutrition,[13] we specifically chose to investigate this population of patients ($n = 99$) as they theoretically stand to benefit the most from placement of enteral access prior to esophagectomy and also to control for patients with early stage cancer who are typically asymptomatic and diagnosed incidentally, which may lead to selection bias. Their clinical and demographic variables are presented in Table 1.

Esophageal adenocarcinoma was the most common histology in the entire cohort (78.8%), followed by squamous cell carcinoma (19.2%), and other histology (2%). Of the identified patients, 99 (63.5%) received neoadjuvant chemoradiation with curative intent. Patients received 45 – 50.4 Gy external beam radiation per National Comprehensive Cancer Network recommendations,[16] with one patient receiving a boost to the primary tumor for a total radiation dose of 55 Gy. Concurrent chemotherapy administration consisted of carboplatin/paclitaxel (28.8%), cisplatin/5-fluoruracil (47.9%), or other (23.3%) and make up the entire study cohort. All patients completed planned preoperative chemoradiation and underwent surgical resection. Patients were divided into 2 cohorts based on the receipt of ancillary enteral access at the discretion of the treating physician. This included 32 jejunostomy tube placements (32.3%), 14 gastrostomy tubes (14.1%), 1 endoscopic esophageal stent placement (1%), 1 nasoenteric tube (1%), and 1 combination of the above (1%). There were no patients in the No-Access Group who subsequently converted to needing enteral access at a later time prior to esophagectomy. The demographics of the entire cohort and the Access versus No-Access Group are presented in Table 1, which demonstrated no statistically significant difference between the No-Access and Access cohorts. The majority of patients were male in both groups (70% vs 77.6%, respectively; $P = .39$) with a median age of 66.6 years vs 64.2 years, respectively ($P = .37$).

Perioperative comparison

The preoperative cancer staging for both cohorts was similar, with the majority of patients having a T3 primary tumor or positive nodal disease (N1; Table 1) as staged by endoscopic ultrasound or positron emission tomography computed tomography (PET-CT). Additionally, tumor location did not have an impact on the receipt of preoperative enteral access, as the primary tumor location (proximal, mid, or distal esophagus) was similar between groups (Table 1, $P = .7$). All patients completed their neoadjuvant treatment and went on to receive definitive esophagectomy, with the vast majority undergoing esophagectomy <90 days from completion of treatment in the No-Access and Access cohorts (95.6% vs 97.4%, respectively; $P = .66$). Despite the additional planning time required for placement of enteral access, the mean duration of time from diagnosis to definitive esophagectomy in the No-Access group (128 days) was similar to the Access Group (136 days, $P = .3$), suggesting that establishing pretreatment enteral access does not significantly delay the receipt of neoadjuvant chemoradiation or surgery. Perioperative parameters including operative time, operative blood loss, and hospital duration of stay were similar between the 2 cohorts (Table 2). Of note, the overall complication rate for the entire cohort was 57.6% with a similar rate between the No-Access and Access Groups (51% vs 64%, respectively; $P = .19$). In particular, there was no difference in pulmonary complications between the No-Access versus Access cohorts (20.4% vs 12%, respectively; $P = .26$), which included: pneumonia, reintubation, and intubation >48 hours postoperatively. Additionally, while the anastomotic leak rate, as demonstrated on imaging (upper gastrointestinal swallow study and/or CT esophagram) with/without clinical symptoms, was lower in the No-Access Group (8.2%) versus the Access Group (22%), this was not statistically significant ($P = .06$). Given that other factors may play a role in anastomotic leak rates, there was no difference noted in anastomotic leak rates based on cervical versus thoracic anastomosis location (13.7% vs 19.2%, respectively; $P = .5$) or on operative approach (open 17.9% vs minimally invasive 12.3% vs hybrid/converted 33.3%; $P = .35$). Furthermore, despite the theoretical risk of conduit ischemia and the potential for increased anastomotic leak rates with the presence of a gastrostomy tube, there was no difference in anastomotic leak rates in patients with preoperative gastrostomy tube (21.4%) versus other modalities of preoperative enteral access (22.2%, $P = .95$). Finally, the rates of

Please cite this article in press as: Thomas K. Jenkins, Alexandra N. Lopez, George A. Sarosi, Kfir Ben-David, and Ryan M. Thomas, Preoperative enteral access is not necessary prior to multimodality treatment of esophageal cancer, Surgery (2017), doi: 10.1016/j.surg.2017.09.046