Enteral Access is not Required for Esophageal Cancer Patients Undergoing Neoadjuvant Therapy

Mary E. Huerter, MD, MA, Eric J. Charles, MD, Emily A. Downs, MD, Yinin Hu, MD, Christine L. Lau, MD, MBA, James M. Isbell, MD, MSCI, Timothy L. McMurry, PhD, and Benjamin D. Kozower, MD, MPH

Department of Surgery, University of Illinois at Chicago, Chicago, Illinois; and Department of Surgery, University of Virginia, Charlottesville, Virginia

Background. **The nutritional status of esophageal cancer patients during neoadjuvant therapy remains a challenging problem. The objective of this study was to determine whether routine enteral feeding tube placement improved nutritional status and perioperative outcomes for patients undergoing neoadjuvant therapy for esophageal cancer.**

Methods. **The Society of Thoracic Surgeons database was used to identify patients who underwent neoadjuvant therapy and esophagectomy at our institution between 2010 and 2014. Nutritional status before and after neoadjuvant therapy was determined through standardized nutrition consultations. Predictors of change in nutrition and adverse events were evaluated with multivariable and univariate logistic regressions.**

Results. **Two hundred thirty-four esophagectomy patients were identified, and 127 (54%) received neoadjuvant therapy. Of those receiving neoadjuvant therapy, 80% (102/127) presented with dysphagia, and 48% (61/127) received enteral feeding access (EA). Multivariable regression revealed that high initial albumin level, high initial body mass index, and presence of EA were associated with nutritional stability during neoadjuvant therapy. However, 27.9% (17/61) of patients who received EA did not use their access at all or did not use it consistently during the course of preoperative treatment. The preoperative grades of malnutrition and esophagectomy outcomes were similar between groups (EA vs no EA).**

Conclusions. **EA is associated with improved nutritional status for patients undergoing neoadjuvant therapy for esophageal cancer. However, adverse events and suboptimal use are common. Esophagectomy outcomes were similar for patients with and without EA. These results support judicious patient selection for EA, expedited neoadjuvant therapy, and close collaboration with nutritionists.**

(Ann Thorac Surg 2016;102:948–54)

Maintaining or improving the nutritional status of esophageal cancer patients during neoadjuvant therapy is challenging. These patients endure a malignancy-induced catabolic state along with dysphagia and early satiety [1]. Esophageal cancer patients frequently have locally advanced disease at the time of diagnosis and experience one of the highest median percentages of weight loss for cancer [2]. Malnutrition develops in nearly 80% of these patients, and it has significant implications for their overall survival and ability to tolerate oncologic treatment [3]. Nutritional status is well recognized as a major factor in the development of infectious adverse events and poor outcomes after major surgical procedures [4].

Neoadjuvant chemotherapy and chemoradiotherapy are critical components in the curative treatment of locally or regionally advanced esophageal cancer. Management of dysphagia and preservation of adequate nutrition during treatment are important clinical considerations. Degree of dysphagia has been found to be an independent predictor of protein-calorie malnutrition [5]. Several strategies for nutritional support have been explored, including endoscopic stent placement and percutaneous or surgical gastrostomy or jejunostomy tube placement. Each of these interventions has its own associated adverse event [6–11]. Although esophageal cancer patients are at risk for the development of malnutrition, particularly those undergoing neoadjuvant treatments, not all patients require support with enteral feeding access (EA) [10–14]. Neoadjuvant therapy has the potential to reduce dysphagia symptoms and may obviate the need for surgical EA for selected patients [13–15]. Recent literature reports suggest that patients can experience significant relief from dysphagia when they complete the first cycle of a platinum-based chemotherapy [14]. The objective of this

Accepted for publication March 7, 2016.

Presented at the Sixty-Second Annual Meeting of the Southern Thoracic Surgical Association, Orlando, FL, Nov 4–7, 2015.

Address correspondence to Dr Kozower, University of Virginia, General Thoracic Surgery, Box 800679, Charlottesville, VA 22908-0679; email: bdk8g@virginia.edu.

0003-4975/$36.00
http://dx.doi.org/10.1016/j.athoracsur.2016.03.041

study was to determine whether routine enteral feeding tube placement improved nutritional status and perioperative outcomes for patients undergoing neoadjuvant therapy for esophageal cancer.

Patients and Methods

The Society of Thoracic Surgeons (STS) database at our institution was used to identify all patients who underwent neoadjuvant therapy and esophagectomy between 2010 and 2014. Data collected from medical chart review included age, gender, history of smoking, presence of dysphagia at initial evaluation, type of feeding access, American Society of Anesthesiologists (ASA) class, feeding access adverse event, and esophagectomy adverse event. We also collected the albumin, weight, and body mass index (BMI) at the time of initial evaluation and just before operation.

Nutritional status before and after neoadjuvant therapy was determined through standardized nutrition consultations at our institution. Nutritional status grade (none, mild, moderate, severe) was documented at the time of initial evaluation and preoperatively based percentage of weight loss over time, amount of intake, muscle depletion, fluid accumulation, and functional capacity [16, 17]. For example, a weight loss greater than 10% over 6 months or more than 5% over 1 month was classified as severe malnutrition [16, 17]. For statistical comparisons, patients' BMI was stratified by less than 18.5 (underweight), 18.5 to 35 (normal to moderately obese), and greater than 35 (severely obese) [18]. Patients assessed before neoadjuvant therapy were given EA based on the attending surgeon's evaluation. Several patients referred from outside institutions presented after the completion of neoadjuvant therapy or with EA already in place. All patients received jejunostomy tubes at the time of esophageal resection if one was not placed for induction therapy. Tube feeds are standardly initiated on postoperative day 2, and patients are discharged with cycled tube feedings, giving them 12 to 16 hours of feeding per day. We initiate oral intake 2 weeks after operation, typically with the patient at home (the median length of stay is 10 days). Tube feedings are then weaned as oral intake increases, and the tube is removed. Adverse events after feeding access placement and esophagectomy were also documented according to the STS database's definitions. Major morbidity was defined according to the STS definitions and included reoperation for bleeding, anastomotic leak, pneumonia, reintubation, ventilation beyond 48 hours, and death [19].

We compared differences in continuous variables between the EA and no EA groups using *t* tests, and discrete variables using either the χ^2 test or Fisher's exact test. Predictors of change in nutritional status were evaluated by multivariable logistic regression. We evaluated predictors of adverse events using univariate logistic regression because the number of adverse events was too small to allow for multivariable modeling. All analyses were performed with R statistical software, version 3.2.1.

Results

From 2010 to 2014, a total of 234 esophagectomy patients were identified, 127 (54%) of whom received neoadjuvant therapy and were included in our study. The mean age was 61.5 years, and 84% (107/127) were male. The demographics of the study group are shown in Table 1 and are separated by EA and no EA. At the time of initial evaluation, 80% (102/127) of patients receiving neoadjuvant therapy presented with dysphagia, and 48% (61/127) of all patients receiving neoadjuvant therapy had EA placed. None of our patients, EA or no EA, received enteral stenting at any point during their neoadjuvant treatment.

Enteral Access

On initial visit 30% (38/127) of patients were graded as severely malnourished, and the majority (68%) received EA (Table 2). Of those who received EA at our institution or at a referring institution, 80.7% (49/61) underwent open or laparoscopic jejunostomy placement of feeding tubes, and the remainder received percutaneous gastric tubes (PEG). The median albumin levels at initial visit were similar between the EA and no EA groups (3.9 g/dL vs 4.0 g/dL). The rate of adverse events for EA placement in these patients was 36% (22/61). The adverse events included bleeding, infection, dislodgement, and tube site problems such as leaking or excoriation. One patient experienced postoperative hypoxia requiring reintubation, and 2 patients experienced small bowel obstruction requiring exploratory laparotomy.

Table 1. Patient Demographics

Characteristic	No EA	EA	*p* Value
Patients (n) undergoing neoadjuvant therapy	66	61	
Age, mean (SD)	62.0 (10.5)	61.0 (9.0)	0.60
Sex (male)	57 (86.4%)	50 (82.0%)	0.66
Dysphagia	42 (63.6%)	59 (96.7%)	<0.01
BMI, kg/m^2			0.18
<18.5 1	(1.6%)	4 (6.9%)	
18.5–35	54 (84.4%)	50 (86.2%)	
>35	9 (14.1%)	4 (6.9%)	
Albumin, g/dL, mean (SD) (initial visit)	3.9 (0.4)	4.0 (0.4)	0.04
Grade of malnutrition at initial evaluation			0.02
None	37 (56.9%)	15 (25.0%)	
Mild	9 (13.8%)	10 (16.7%)	
Moderate	7 (10.8%)	9 (15.0%)	
Severe	12 (18.5%)	26 (43.3%)	

Demographics of patients (N=127) meeting inclusion criteria, completing neoadjuvant therapy and esophagectomy. Results with the presence of dysphagia, BMI, albumin, and grade of malnutrition at documented initial evaluation.

BMI = body mass index; EA = enteral access; SD = standard deviation.

Table 2. Risk Factors for Major Adverse Events After Esophagectomy

Factor	n	Odds Ratio	95% CI	*p* Value
Access (EA)	61	1.60	0.69–3.80	0.28
Malnutrition (severe)	47	0.76	0.30–1.81	0.55
Smoking	99	4.45	1.21–28.87	0.05
ASA of 3	87	0.96	0.40–2.45	0.93
BMI, kg/m^2 (<18.5 or >35)	15	0.87	0.19–3.00	0.84

Univariate logistic regression performed for major adverse event risk factors after esophagectomy. Major adverse events after esophagectomy were not associated with presence of EA.

ASA = American Society of Anesthesiologists class; BMI = body mass index; CI = confidence interval; EA = enteral access.

Table 4. Predictors of Stable or Improved Nutrition During Neoadjuvant Therapy

Factor	Odds Ratio	95% CI	*p* Value
(Intercept)	0.71	0.19–2.60	0.61
Enteral access	1.30	1.07–1.57	0.01
Age, years	0.99	0.99–1.00	0.55
Initial albumin, g/dL	1.39	1.09–1.77	0.01
Initial BMI, kg/m^2	0.99	0.97–1.00	0.05

Multiple logistic regression performed for predictors of stable or improved nutrition during neoadjuvant therapy. Nutritional stability was found to be associated with EA, initial albumin, and initial BMI.

BMI = body mass index; CI = confidence interval; EA = enteral access.

Nutritional Stability

Overall, 71 patients (56.8%) had stable or improved nutrition, and 54 patients (43.2%) showed worsened nutrition (initial malnutrition assessment was not available for 2 patients) over the course of neoadjuvant treatment (Table 3). We had 80% power to detect an improvement in stable or improved nutrition from 45% for patients not receiving EA to 69% for patients receiving EA. Patients with worse malnutrition at their initial visit were more likely to receive EA. In those with worsening nutrition, there was wide variability in the degree of decline (mild to severe, mild to moderate, moderate to severe). Importantly, in univariate analysis, patients with high initial albumin levels were more likely to show stable or improved nutrition during neoadjuvant therapy. This result continued to hold in multivariable analysis after adjustment for EA, age, and initial BMI (Table 4). In univariate analysis, BMI at initial visit was also associated with stable or improved nutrition. However, after adjustment for EA, age, and albumin, BMI was not statistically significant (Table 4). These results indicate that patients presenting in a significantly malnourished state tended to continue to do poorly despite EA placement, although it appeared easier to preserve nutrition for those presenting in a less severe state. Obese patients appeared less likely to show stable or improved nutrition than were their counterparts. There were no significant differences by ASA class and no obvious pattern of stable/improved nutrition with age in univariate analysis.

Overall, EA was associated with improved nutrition among patients who initially presented in a malnourished state (odds ratio 1.3; 95% confidence interval 1.07 to 1.57). However, 27.9% (17/61) of patients who received feeding access did not use it at all or did not use it consistently during the course of preoperative treatment. The preoperative grades of malnutrition were similar between groups (EA vs no EA). Unfortunately, 37% (47/127) of patients, with or without access, were severely malnourished at the time of esophagectomy compared with 29.9% (38/125) at initial evaluation.

Table 3. Perioperative Nutritional Status

Status	No EA, n (%)	EA, n (%)	*p* Value
Preoperative malnutrition			
None	16 (24.2)	14 (23.0)	0.3679
Mild	12 (18.2)	17 (27.9)	
Moderate	14 (21.2)	7 (11.5)	
Severe	24 (36.4)	23 (37.7)	
Nutritional status at time of esophagectomy			
Stable	21 (32.3)	18 (30.0)	
Improved	8 (12.3)	24 (40.0)	0.0009
Worsened	36 (55.4)	18 (30.0)	

Grade of malnutrition before operation evaluated as related to presence or absence of EA. Patients who received EA had improved nutrition; however, those with severe malnutrition were less likely to improve.

EA = enteral access.

Adverse Events

There were two in-hospital or 30-day postoperative deaths after esophagectomy (1.6%). Seventy patients had adverse events after esophagectomy (55%), with 28 patients (22%) having a major adverse event. Major adverse events after esophagectomy were not associated with EA (Table 2). The adverse events observed included pneumonia, respiratory failure, atrial fibrillation, sepsis, anastomotic leak, pneumothorax, conduit necrosis, fistula, stricture, chylothorax, wound infection or dehiscence, abscess, and vocal cord paresis.

Comment

The objective of this study was to determine the impact of EA on nutritional status and perioperative outcomes for esophagectomy patients treated with neoadjuvant therapy. Esophageal cancer patients frequently present with dysphagia and signs of malnutrition, as we observed in our cohort [6, 20, 21]. Neoadjuvant treatment can be very demanding for patients, with studies reporting a dropout rate (not proceeding to esophagectomy) of 10% to 15% [22, 23]. Side effects are common, with up to 28% of patients experiencing radiation-induced esophagitis [20, 24]. Given the tenuous nutritional status of these patients, some authors propose routine placement of EA in all patients receiving neoadjuvant therapy [25, 26]. However,

the rates of adverse events for EA placement have been reported to be as high as 25% [10, 15, 25–28]. Our series demonstrated an even higher total adverse event rate of 36% and a major adverse event rate of 22%. However, all patients receiving EA at our institution with the plan for neoadjuvant therapy followed by esophagectomy were able to proceed to operation, with a 0% dropout rate. In addition, major adverse events after esophagectomy were not associated with EA.

Several authors have explored stent placement as an alternative to relieve dysphagia and improve oral intake [6, 7, 29]. Metal stents have the potential to induce inflammation and make subsequent surgical procedures more difficult [29, 30]. As a result, metal stents are no longer routinely used for patients undergoing neoadjuvant therapy. Newer-generation self-expanding silicon stents may be repositioned or removed, and they may avoid some of the adverse events associated with metal stents such as perforation and negative impact on oncologic outcomes [6, 29]. Silicone stents have been used to treat esophageal anastomotic leaks, strictures, and dysphagia from esophageal malignancy [6, 9, 31]. Although silicone stenting may be an attractive option, some patients may have a nondilatable stricture or other considerations precluding placement. The primary limitation with silicone stents is migration, with varying rates reported to be as high as 46% to 53% [9, 20, 32]. Stenting and EA allow nutritional support but are not without their own risks. Sepsis, perforation, and intestinal ischemia, among other serious adverse events, may jeopardize the patient's ability to complete curative treatment.

Reports of clinically significant improvement in dysphagia with neoadjuvant treatment identified the feasibility of preserving nutrition without EA [13, 14, 33]. Sunde and colleagues [14] demonstrated that significant relief could be observed with the first treatment of a platinum-based therapy in combination with 5-fluorouracil and radiotherapy. Similar results were achieved by Cools-Lartigue and colleagues [13] in Toronto, with taxotere, cisplatin, and 5-fluorouracil (TCF), epirubicin, cisplatin, and 5-fluorouracil (ECF), or docetaxel, oxaliplatin, leucovorin, and 5-fluorouracil (FLOT) demonstrating improvement of dysphagia after the first cycle. With timely initiation of therapy, the majority of patients in these series were able to maintain their nutrition without requiring EA or stenting.

Our results showed that EA was associated with improved nutritional status for selected patients undergoing neoadjuvant therapy for esophageal cancer. However, adverse events and suboptimal use were common. Our results indicate a substantial need for improvement in preoperative nutrition optimization, given that 36% of our patients, with or without access, were severely malnourished at the time of esophagectomy. We identified a variety of reasons why patients suboptimally used their EA, such as discomfort with use, lack of interest, skin excoriation, or tube leaking. Currently, all patients with esophageal cancer undergoing neoadjuvant therapy (with or without EA) at our institution now receive a nutrition consultation to help address this critical problem and to improve nutritional management throughout the receipt of neoadjuvant therapy. Our nutritionists reinforce teaching points to our patients and explore alternative nutrition strategies early if something is not working well for a patient.

The most efficacious strategy for preserving or improving nutritional status in patients undergoing neoadjuvant therapy is not known. Our current indications for EA placement are severe malnutrition or dysphagia precluding adequate oral intake, including full liquids, at initial evaluation. The ability to preserve oral intake and nutrition with timely neoadjuvant therapy suggests that selective placement of EA is appropriate. Personalized assessment and management with designated teams of nurses and nutritionists recognizes patients' varying needs as they progress through treatment [34]. Early intervention with formal support by a dietician has been shown to decrease the rates of weight loss and to reduce hospital admissions [12]. Dieticians can provide guidance in various strategies such as frequent small meals and commercially available oral supplements [34]. Alternative feeding programs given in close consultation with nutritionists may additionally improve patient satisfaction or quality of life while preserving their nutritional status.

The overall esophagectomy outcomes were similar between groups (EA vs no EA). These results suggest that those receiving EA were not superior to those without. However, because of the retrospective nature of this study, it is not known whether the EA group of patients would have been able to tolerate neoadjuvant therapy and be candidates for esophagectomy if they had not received EA. Comprehensive nutritional support is essential for esophageal cancer patients. The potential risk and associated costs of EA placement should be carefully considered in their nutritional management. Our results demonstrate that malnutrition can be improved with EA. However, patients with low initial albumin levels and severe malnutrition remain at risk despite EA and require more aggressive and ongoing nutritional support throughout the course of neoadjuvant therapy. Presentation with a chief complaint of dysphagia does not necessarily require EA, and many patients can be appropriately treated with modification and supplementation of their oral intake.

Our study has several limitations. As a retrospective study it is subject to selection bias. These results do not facilitate a thorough understanding of what happens to all patients who undergo neoadjuvant therapy for esophageal cancer. Many of the patients referred to our institution receive their neoadjuvant therapy at outside hospitals and as a result are not captured in our database if they do not undergo esophagectomy. Thus, we are not able to accurately acquire information from referring hospitals regarding patients who died during neoadjuvant treatment, were unable to tolerate or complete neoadjuvant treatment, or were not referred for operation after neoadjuvant therapy. In addition, some patients are

referred to us only after they have completed neoadjuvant therapy. Therefore, this study cannot fully address whether EA increases a patient's chance of completing neoadjuvant therapy and the patient's ability to proceed to esophagectomy. However, we do know that all patients treated with EA and a plan for neoadjuvant therapy at our institution were able to receive their esophagectomy. In addition, although we are able to demonstrate improvement or stability in nutrition with EA, our sample size is underpowered to determine whether EA improves perioperative outcomes.

In conclusion, our data support the selective use of EA for patients undergoing neoadjuvant therapy for esophageal cancer. EA was associated with improved nutritional status during neoadjuvant therapy. However, we have learned that simply placing EA and referring a patient for nutritional assessment is not adequate because many of these patients do not receive the optimal benefit from their EA. On the basis of these data and our experience, we now place EA for patients unable to tolerate full liquids or those with severe malnutrition identified at their initial office visit. Our preference is to place a feeding jejunostomy, but we have not had any major esophagectomy adverse events related to PEG placement performed at outside institutions before patient referral. Our data also indicates that it is critically important to have careful and ongoing follow-up with a nutritionist for all patients throughout neoadjuvant therapy in an effort to optimize their nutritional status.

References

1. Tisdale MJ. Mechanisms of cancer cachexia. Physiol Rev 2009;89:381–410.
2. Aoyagi T, Terracina KP, Raza A, Matsubara H, Takabe K. Cancer cachexia, mechanism and treatment. World J Gastrointest Oncol 2015;7:17–29.
3. Rouvelas I, Zeng W, Lindblad M, et al. Survival after surgery for oesophageal cancer: a population-based study. Lancet Oncol 2005;6:864–70.
4. Bozzetti F, Group SW. Screening the nutritional status in oncology: a preliminary report on 1,000 outpatients. Support Care Cancer 2009;17:279–84.
5. Christein JD, Hollinger EF, Millikan KW. Prognostic factors associated with resectable carcinoma of the esophagus. Am Surg 2002;68:253–8.
6. Siddiqui AA, Glynn C, Loren D, Kowalski T. Self-expanding plastic esophageal stents versus jejunostomy tubes for the maintenance of nutrition during neoadjuvant chemoradiation therapy in patients with esophageal cancer: a retrospective study. Dis Esophagus 2009;22:216–22.
7. Siddiqui AA, Sarkar A, Beltz S, et al. Placement of fully covered self-expandable metal stents in patients with locally advanced esophageal cancer before neoadjuvant therapy. Gastrointest Endosc 2012;76:44–51.
8. Llaguna OH, Kim HJ, Deal AM, et al. Utilization and morbidity associated with placement of a feeding jejunostomy at the time of gastroesophageal resection. J Gastrointest Surg 2011;15:1663–9.
9. Adler DG, Fang J, Wong R, Wills J, Hilden K. Placement of Polyflex stents in patients with locally advanced esophageal cancer is safe and improves dysphagia during neoadjuvant therapy. Gastrointest Endosc 2009;70:614–9.
10. Schrag SP, Sharma R, Jaik NP, et al. Complications related to percutaneous endoscopic gastrostomy (PEG) tubes. A comprehensive clinical review. J Gastrointestin Liver Dis 2007;16:407–18.
11. Maple JT, Petersen BT, Baron TH, et al. Direct percutaneous endoscopic jejunostomy: outcomes in 307 consecutive attempts. Am J Gastroenterol 2005;100:2681–8.
12. Odelli C, Burgess D, Bateman L, et al. Nutrition support improves patient outcomes, treatment tolerance and admission characteristics in oesophageal cancer. Clin Oncol (R Coll Radiol) 2005;17:639–45.
13. Cools-Lartigue J, Jones D, Spicer J, et al. Management of dysphagia in esophageal adenocarcinoma patients undergoing neoadjuvant chemotherapy: can invasive tube feeding be avoided? Ann Surg Oncol 2015;22:1858–65.
14. Sunde B, Ericson J, Kumagai K, et al. Relief of dysphagia during neoadjuvant treatment for cancer of the esophagus or gastroesophageal junction. Dis Esophagus 2015 Mar 23; [Epub ahead of print].
15. Starr B, Davis S, Ayala-Peacock D, Blackstock WA, Levine EA. Reassessment of the role of enteral tube feedings for patients with esophageal cancer. Am Surg 2014;80:752–8.
16. Nitenberg G, Raynard B. Nutritional support of the cancer patient: issues and dilemmas. Crit Rev Oncol Hematol 2000;34:137–68.
17. White JV, Guenter P, Jensen G, et al. Consensus statement: Academy of Nutrition and Dietetics and American Society for Parenteral and Enteral Nutrition: characteristics recommended for the identification and documentation of adult malnutrition (undernutrition). JPEN J Parenter Enter Nutr 2012;36:275–83.
18. Flegal KM, Kit BK, Orpana H, Graubard BI. Association of all-cause mortality with overweight and obesity using standard body mass index categories: a systematic review and meta-analysis. JAMA 2013;309:71–82.
19. Wright CD, Kucharczuk JC, O'Brien SM, et al. Predictors of major morbidity and mortality after esophagectomy for esophageal cancer: a Society of Thoracic Surgeons General Thoracic Surgery Database risk adjustment model. J Thorac Cardiovasc Surg 2009;137:587–95; discussion 596.
20. Nagaraja V, Cox MR, Eslick GD. Safety and efficacy of esophageal stents preceding or during neoadjuvant chemotherapy for esophageal cancer: a systematic review and meta-analysis. J Gastrointest Oncol 2014;5:119–26.
21. Di Fiore F, Lecleire S, Pop D, et al. Baseline nutritional status is predictive of response to treatment and survival in patients treated by definitive chemoradiotherapy for a locally advanced esophageal cancer. Am J Gastroenterol 2007;102:2557–63.
22. Mariette C, Dahan L, Mornex F, et al. Surgery alone versus chemoradiotherapy followed by surgery for stage I and II esophageal cancer: final analysis of randomized controlled phase III trial FFCD 9901. J Clin Oncol 2014;32:2416–22.
23. Fiorica F, Di Bona D, Schepis F, et al. Preoperative chemoradiotherapy for oesophageal cancer: a systematic review and meta-analysis. Gut 2004;53:925–30.
24. Van Hagen P, Hulshof MC, van Lanschot JJ, et al. Preoperative chemoradiotherapy for esophageal or junctional cancer. N Engl J Med 2012;366:2074–84.
25. Ben-David K, Kim T, Caban AM, et al. Pre-therapy laparoscopic feeding jejunostomy is safe and effective in patients undergoing minimally invasive esophagectomy for cancer. J Gastrointest Surg 2013;17:1352–8.
26. Date RS, Clements WD, Gilliland R. Feeding jejunostomy: is there enough evidence to justify its routine use? Dig Surg 2004;21:142–5.
27. Han-Geurts IJ, Verhoef C, Tilanus HW. Relaparotomy following complications of feeding jejunostomy in esophageal surgery. Dig Surg 2004;21:192–6.
28. Tapia J, Murguia R, Garcia G, de los Monteros PE, Onate E. Jejunostomy: techniques, indications, and complications. World J Surg 1999;23:596–602.
29. Mariette C, Gronnier C, Duhamel A, et al. Self-expanding covered metallic stent as a bridge to surgery in esophageal

cancer: impact on oncologic outcomes. J Am Coll Surg 2015;220:287–96.
30. Tan CJ, Dasari BV, Gardiner K. Systematic review and meta-analysis of randomized clinical trials of self-expanding metallic stents as a bridge to surgery versus emergency surgery for malignant left-sided large bowel obstruction. Br J Surg 2012;99:469–76.
31. Radecke K, Gerken G, Treichel U. Impact of a self-expanding, plastic esophageal stent on various esophageal stenoses, fistulas, and leakages: a single-center experience in 39 patients. Gastrointest Endosc 2005;61:812–8.
32. Dan DT, Gannavarapu B, Lee JG, Chang K, Muthusamy VR. Removable esophageal stents have poor efficacy for the treatment of refractory benign esophageal strictures (RBES). Dis Esophagus 2014;27:511–7.
33. Ribi K, Koeberle D, Schuller JC, et al. Is a change in patient-reported dysphagia after induction chemotherapy in locally advanced esophageal cancer a predictive factor for pathological response to neoadjuvant chemoradiation? Support Care Cancer 2009;17:1109–16.
34. Riccardi D, Allen K. Nutritional management of patients with esophageal and esophagogastric junction cancer. Cancer Control 1999;6:64–72.

DISCUSSION

DR JONATHAN SPICER (Montreal, QC, Canada): I thought that was a great paper. We published on this maybe 3 or 4 years ago looking at induction chemotherapy, and it took about 2 weeks after starting a fast-track preoperative chemotherapy program for patients' dysphagia to improve. I didn't quite catch what the induction regimen was and what was the time line to improvement in their dysphagia scores?

DR HUERTER: Thank you for that question. Unfortunately, we weren't able to tease out some of those additional details that would have been helpful in terms of types of regimens that patients received. Several of our patients receive their treatment at outside hospitals and presented only for esophagectomy. The time course of the improvement of dysphagia varied, and we were limited by documentation that we were retrospectively looking at. It would be ideal to prospectively to go through and really tease out what the time course of relieving dysphagia is and if there is any variation with regard to the type of regimen that they received.

DR BRIAN E. LOUIE (Seattle, WA): That was a very nice talk, I guess partly because it supports what I do in practice, which is the selective use of EA before esophagectomy. I am really curious to know about what you do with those really difficult patients that you have to place a tube and you are having all sorts of trouble running the feeds. These are the clinical conundrums that people run into. For example, I have 1 patient where we have tried six formulas; we can't get them tolerated. Also, what type of J tubes do you use?

DR HUERTER: The type of J tube was attending specific, and we didn't follow specifically the type of J tube or the feeding formulation. Certainly, moving forward, those would be interesting details to keep a closer eye on. What we learned and what we were suspicious of is that even though we were placing access, patients were frequently deciding on their own not to use it or they didn't like it. They had a variety of barriers with regard to using it to the best of their ability. So I think the learning point was getting our nutritionist colleagues involved so that they could closely follow these patients up, and if something is not working to invest in alternative strategies earlier on.

DR LOUIE: I think the addition of a nutritionist to our cancer institute has been a huge benefit to these particular patients with much more closer follow-up, a lot of troubleshooting, and I commend you on that. Thank you.

DR HUERTER: Thank you.

DR JOSEPH B. ZWISCHENBERGER (Lexington, KY): Dr Huerter, like all retrospective analyses of large databases, it almost becomes a study in physician bias. So, you uncovered three sources of bias that intrigue me. The first is the fact many of the surgeons didn't even recognize malnutrition in the first place; second, that it was once recognized, many of them did not think it was necessary to replenish the malnourishment that they dutifully recognized; and third, given that there is no real demonstrable improvement in outcomes, why bother in the first place?

DR HUERTER: Your points are well taken, and thank you.

DR SHANDA BLACKMON (Rochester, MN): On that note, if you had a patient and they had completed neoadjuvant chemoradiotherapy and they are a month out and you are seeing them to get them ready for esophagectomy and they had a prealbumin level that was far less than 17, what would you do?

DR HUERTER: Certainly you are under somewhat of a time clock trying to get these patients to the operating room in a timely fashion.

DR BLACKMON: Are you really?

DR HUERTER: You would want to not delay them indefinitely, of course. I would be more hopeful to be aggressive earlier with their nutrition to keep them on track. I think what our results showed is that the opportunity was missed in a lot of these patients.

DR BLACKMON: So they got their treatment in the community, they got their neoadjuvant therapy, nobody wanted to put a feeding tube in, and they are landing on your doorstep ready for operation. Would you put the feeding tube in at that point and delay, or would you just go ahead and operate?

DR HUERTER: I would be hesitant to go ahead and operate on those types of patients.

DR BLACKMON: So you would put a feeding tube in, and you get their nutrition better and maybe delay it a few weeks or a month and then operate?

DR HUERTER: Yes, I would get them nutritional support.

DR BLACKMON: I think that's the take-home message—right, Dr Kozower?

DR BENJAMIN D. KOZOWER (Charlottesville, VA): Mary has done an outstanding job presenting our study and answering questions. She is a third-year general surgery resident and she is

back home now at her home institution. It was enlightening for us to see these data. None of us like to think, as Dr Zwischenberger pointed out, that we are as inept as we actually were. We have changed our clinical practice to improve how we manage these patients. I am not in love with the idea of putting a J tube in a malnourished patient and then going back to operate 3 weeks later. I would prefer to place a Dobhoff tube or try a supervised period of full liquids with nutritional supplements. If that doesn't work, then I would place a J tube or even a PEG and postpone the esophagectomy until the patient's nutritional status has improved.

DR DANIEL L. MILLER (Marietta, GA): Just to follow up on that point, I agree we would go with a Dobhoff in that situation if we had not planned for a J tube. What we usually did for a planned esophagectomy after neoadjuvant therapy was to operate within 4 to 6 weeks after completion of all treatment. We have taken that out longer now, to allow the patient to recover more and to get the full effect of neoadjuvant chemoradiation. We place a feeding tube (14 French) in all neoadjuvant-treated patients and patients with a history of more than 8% weight loss; this accounts for about 70% of our patients. An insurance issue in Georgia is that we cannot send someone home on tube feeds at any rate unless they are completely barred from receiving anything by mouth. I used to give patients 50% of their requirement for 12 hours overnight and eat what they could during the day. I know more and more institutions are sending patients home with 100% tube feed support and nothing by mouth, but we have not gone that route yet; our patients like to eat too much. In the patients for whom I do not place a feeding tube at the time of their resection, I tack the jejunum to the posterior abdominal wall in the normal position for a J tube and mark it with clips so the interventional radiologist can place the J tube if necessary because of an adverse event or failure to thrive in the postoperative period. This proactive procedure will avert the need for the patient to undergo an open procedure.

DR HUERTER: Thank you for that.

DR DANIEL RAYMOND (Cleveland, OH): I enjoyed your talk and congratulations. It is not easy standing up there as a resident. I was wondering if you could characterize the rate of adverse events a little more. How severe were those adverse events (36% is kind of surprisingly high), and what percentage of those actually led to harm as far as delaying therapies, delaying operations? The other side of that is whether there were benefits of having had a J tube in, such as decreasing the length of the operation that was performed, a faster return of gastrointestinal function after the esophagectomy, and detection of occult peritoneal metastatic disease that prevented you from going on and sticking a scope in after having done partial therapy on someone. And finally, how do you do your J tubes: open, or laparoscopic? If you are doing laparotomies versus doing laparoscopic, would that make a difference?

DR HUERTER: Thank you for your questions. I will answer them in reverse order, if I may. The J tube technique varied whether it was laparoscopic versus open. It was entirely the surgeon's preference, but the majority were laparoscopically placed. In terms of benefits of the J tube placement, such as faster return of bowel function and so forth, we didn't look in specific detail with regard to those finer points, and certainly that would be a perfect idea moving forward to look at the potential benefits of placement. And then with regard to the adverse events that we saw with our J tube placement, we had 2 patients who had particularly severe adverse events that required a repeated laparotomy and return to the operating room. The majority of adverse events were problems with the tube such as leaking, excoriation of the skin, bleeding, and infection, all of which usually were not severe. We were very honest with regard to our collection of those types of adverse events, and we wanted to get a very good handle on what sorts of things patients were dealing with any time we placed a J tube because sometimes it factored into their use of the tube.

DR PIERRE DE DELVA (Jackson, MS): Nicely done. Just one comment. You might want to include in the report whether there were any stents in the non-EA group, because that may change how they did nutritionally versus the other group.

DR HUERTER: Thank you.