Original Article

Early thoracic surgery consultation and location of therapy impact time to esophagectomy

Ashley L. Deeb[1], Aaron R. Dezube[1], Antonio Lozano[2], Anupama Singh[1], Luis E. De Leon[1], Suden Kucukak[1], Michael T. Jaklitsch[1], Jon O. Wee[1]

[1]Division of Thoracic Surgery, Brigham and Women's Hospital, Boston, MA, USA; [2]Boston University School of Medicine, Boston, MA, USA

Contributions: (I) Conception and design: AL Deeb, AR Dezube, LE De Leon, S Kucukak, MT Jaklitsch, JO Wee; (II) Administrative support: MT Jaklitsch, JO Wee; (III) Provision of study materials or patients: AL Deeb, A Singh, LE De Leon, S Kucukak; (IV) Collection and assembly of data: A Lozano, A Singh; (V) Data analysis and interpretation: All authors; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Anupama Singh, MD. Division of Thoracic Surgery, Brigham and Women's Hospital, 15 Francis St, Boston, MA 02115, USA. Email: anupamasingh0312@gmail.com.

Background: Neoadjuvant chemoradiation therapy (nCRT) followed by esophagectomy is the standard treatment for resectable, locally advanced esophageal cancer. The ideal timing between neoadjuvant therapy and esophagectomy is unclear. Delayed esophagectomy is associated with worse outcomes. We investigated which factors impacted time to esophagectomy in our patients.

Methods: We conducted a retrospective analysis of prospectively collected data of patients with pT0-3N0-2 esophageal cancers who underwent CROSS trimodality therapy from May 2016 to January 2020. Sociodemographic factors, comorbidities, and neoadjuvant factors (location of CRT, treatment toxicity, discontinuation of treatment) were compared between patients who underwent surgery within 60 days and those after 60 days.

Results: In total, 197 patients were analyzed of whom 137 underwent esophagectomy within 60 days (early surgery, ES) and 60 were outside that window (delayed surgery, DS). More DS patients had a history of myocardial infarction (MI) or stroke (both 11.67% *vs.* 3.65%, P=0.05) and required CRT dose reduction (16.67% *vs.* 6.57%, P=0.04). Fewer DS patients received CRT at Dana-Farber Cancer Institute (DFCI) or a DFCI satellite site (33.33% *vs.* 58.4%, P=0.01) and saw our surgeons before CRT completion (68.33% *vs.* 89.78%, P=0.001). CRT at DFCI [odds ratio (OR) 2.63, P=0.01] or a satellite site (OR 3.07, P=0.01) and evaluation by a thoracic surgeon (OR 4.07, P=0.001) shortened time to esophagectomy. History of MI (OR 0.29, P=0.04), stroke (OR 0.29, P=0.04), and CRT dose reduction (OR 0.35, P=0.03) delayed time to esophagectomy.

Conclusions: Improving access to multispecialty cancer centers and increasing satellite sites may improve time to esophagectomy.

Keywords: CROSS trimodality therapy; delayed esophagectomy; esophageal cancer

Submitted Feb 27, 2024. Accepted for publication Jun 14, 2024. Published online Sep 21, 2024.
doi: 10.21037/jtd-24-316
View this article at: https://dx.doi.org/10.21037/jtd-24-316

Introduction

A diagnosis of esophageal cancer has traditionally been associated with poor survival rates (1). However, the landmark CROSS trial demonstrated improved survival with neoadjuvant chemoradiation therapy (nCRT) followed by esophagectomy compared to esophagectomy alone (2,3). Since the publication of the CROSS trial long-term outcomes, nCRT followed by esophagectomy has become the standard treatment for locally advanced esophageal cancer.

The ideal timing from completion of nCRT to esophagectomy has been debated. Traditionally, prolonged time between nCRT completion and surgery was believed to lead to disease progression and poor outcomes. A 2016 study found that prolonged interval between nCRT and surgery resulted in significantly increased morbidity and mortality. Patients were divided into three interval groups (7-, 8-, and 9-week post-nCRT surgery) and were evaluated at day 30 and day 90. A longer time interval between nCRT and esophagectomy was associated with decreased overall survival (4). Another study found lower rates of cervical anastomotic leaks in patients who had surgery less than 35 days post-nCRT. Additionally, delayed esophagectomies were found to be more challenging given adhesion formation and increased rates of anastomotic complications (5).

Conversely, other studies have concluded that delaying esophagectomy after nCRT resulted in complete pathologic response and improved patient outcomes (6). Some data also suggest that there is no relationship between timing of esophagectomy after nCRT and patient outcomes (7).

Regardless of the optimal timing between nCRT and esophagectomy, prompt and coordinated treatment is crucial for these patients. Few studies have examined factors which are barriers to timely esophagectomy. One study utilizing the National Cancer Database found that lower socioeconomic status (SES) was associated with prolonged time to esophagectomy and worse outcomes (8). However, other factors which may delay surgery after nCRT are currently unknown. We aimed to examine our cohort of esophageal cancer patients to identify additional modifiable factors that may contribute to delayed esophagectomy. We hypothesized that patients with lower SES, living outside the greater Boston area, and those requiring dose reduction would experience more delays in esophagectomy after nCRT. We present this article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-316/rc).

Highlight box

Key findings

- Early thoracic surgery consultation and availability of satellite sites are associated with shorter times to esophagectomy after neoadjuvant chemoradiation therapy (nCRT). nCRT dose reduction is associated with delayed time to esophagectomy (>60 days).

What is known and what is new?

- nCRT followed by esophagectomy is currently the standard treatment for locally advanced esophageal cancer, and esophageal cancer is associated with poor survival rates.
- Delayed esophagectomy is associated with worse outcomes; however, limited studies have examined the factors associated with timely esophagectomy.

What is the implication, and what should change now?

- Esophageal cancer remains prevalent. Therefore, it is important for providers to be aware of both patient-specific and external variables that can influence time to esophagectomy and subsequently survival. This will allow physicians to provide holistic care and intervene accordingly.

Methods

This study was approved by the Institutional Review Board (IRB) at Brigham and Women's Hospital (BWH) (protocol #2014P002478). Informed consent for this retrospective study was waived. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). A retrospective analysis of prospectively collected clinical data was performed. Patients were obtained through an esophageal cancer database maintained within the Division of Thoracic and Cardiac Surgery, and additional variables were collected through retrospective chart review. All patients who underwent CROSS trimodality therapy between May 2016 and January 2020 for adenocarcinoma and squamous cell carcinoma of the esophagus were included (cT1-3N0-1).

Variables and outcomes

We compared sociodemographic factors [race, gender, place of residence (instate *vs.* out-of-state and inside or outside the greater Boston area), median county income], comorbidities (Charlson Comorbidity Index), and treatment factors (location of neoadjuvant therapy, consultation with the operating surgeon before completion of nCRT, completion of therapy, dose reduction, treatment toxicity) between those with early esophagectomy and those with delayed esophagectomy. We defined a delayed esophagectomy as one that occurred greater than 60 days after completion of nCRT. Additional variables were gathered including adverse events (based on Clavien-Dindo classification), hospital length of stay, return to the operating room (RTOR) within 30 days of the index operation, and 30- and 90-day mortality rates.

Statistical analysis

All statistical analyses were performed using Stata 16.

Categorical variables were analyzed with Chi-squared or Fisher's exact test when appropriate and Wilcoxon rank sum was utilized for continuous variables. We then created a univariable logistic regression model to examine the impact of different variables [age, gender, race, instate, out-of-state, within the greater Boston area, median income, evaluation by our thoracic surgeons, location of nCRT, body mass index (BMI), comorbidities, nCRT factors] on the odds of receiving early esophagectomy. Statistical significance was considered with a P value ≤0.05.

Results

197 patients were included in the analyses (137 patients underwent surgery within 60 days and 60 patients underwent surgery more than 60 days after completion of neoadjuvant therapy). The median age for the cohort was 66 years [interquartile range (IQR) 11.04 years], and the median Charlson Score was 5 (IQR 2). The overall cohort was predominantly White (182, 92.39%), male (163, 82.74%), and resided in state (126, 63.96%), but was outside the greater Boston area (111, 56.35%). With regards to treatment, most patients had a consultation with the operating thoracic surgeon before completion of nCRT (164, 83.25%). Most patients received nCRT at an outside facility compared to our cancer center (Dana-Farber Cancer Institute, DFCI) or a DFCI satellite site (49.24% *vs.* 28.93% and 21.83%, respectively). Finally, 81.73% (161) of patients completed nCRT, 9.64% (nineteen) required a dose reduction, and 8.12% (sixteen) had their therapy discontinued.

With regards to sociodemographic factors and comorbidities, those who received surgery within 60 days (early surgery, ES) and those who received surgery after 60 days (delayed surgery, DS) were largely similar (*Table 1*). DS patients were older (68.45 years, IQR 10.08 *vs.* 65.82 years, IQR 13.00, P=0.01) and more were current smokers (86.67% *vs.* 66.42%, P=0.003). Additionally, more DS patients had a history of myocardial infarction (MI) or stroke (both 11.67% *vs.* 3.65%, P=0.05). These events occurred prior to their diagnosis of esophageal cancer. There was no significant difference in clinical stage between groups [(75.91% of ES patients had T3 tumors *vs.* 63.33% of DS patients, P=0.11), (55.47% of ES patients had N0 status *vs.* 45% of DS patients, P=0.22)].

When examining treatment factors, a smaller portion of DS patients received CRT at DFCI or a DFCI satellite site (20.00% DFCI and 13.33% satellite *vs.* 32.85% DFCI and 25.55% satellite, P=0.01) (*Table 2*). Additionally, fewer DS patients saw the operating surgeon before CRT completion (68.33% *vs.* 89.78%, P=0.001). Finally, more patients requiring neoadjuvant dose reduction experienced delayed timing of surgery (16.67% *vs.* 6.57%, P=0.04).

In univariable logistic regression, sociodemographic factors were not associated with having an early esophagectomy. Factors that were associated with early surgery included CRT at DFCI [odds ratio (OR) 2.63, 95% CI: 1.24–5.59, P=0.01] or a DFCI satellite (OR 3.07, 95% CI: 1.29–7.31, P=0.01) and evaluation by the operating surgeon before CRT completion (OR 4.07, 95% CI: 1.87–8.84, P=0.001). History of MI (OR 0.29, 95% CI: 0.09–0.94, P=0.04), cerebrovascular disease (OR 0.29, 95% CI: 0.09–0.94, P=0.04), smoking (OR 0.3, 95% CI: 0.13–0.69, P=0.005), and requiring a CRT dose reduction (OR 0.35, 95% CI: 0.13–0.92, P=0.03) were associated with increased odds of delayed surgery (*Table 3*).

When examining outcomes, 41 patients experienced complete pathologic response (pT0-N0-M0), sixteen (39%) of whom were in the DS group. One hundred and three patients experienced some adverse event, 35 (34%) of whom had delayed surgery. In the DS group, 21 patients experienced grade III adverse events, and six patients experienced grade IV adverse events (*Table 4*). One patient had a grade V event and died from sepsis due to an anastomotic leak. This was the only 30-day mortality in the entire cohort. Comparison of outcomes between the early surgery and delayed surgery group are summarized in Table S1.

Discussion

This retrospective study identified several factors that impact timing of esophagectomy after neoadjuvant therapy. Variables that increased the odds of early surgery included nCRT at DFCI or at a DFCI satellite and evaluation by the operating thoracic surgeon before nCRT completion. Although there were differences in sociodemographic factors between those who had DS, defined as more than 60 days in our study, and those who did not, these factors did not impact timing of surgery. Rather, the variables that were associated with DS included a history of MI, stroke, smoking, and nCRT dose reduction.

Advancements in thoracic surgery over the years have resulted in improved survival after esophagectomy.

Table 1 Sociodemographic factors of patients with early and delayed esophagectomy

Characteristics	≤60 days from nCRT to esophagectomy, N=137	>60 days from nCRT to esophagectomy, N=60	Overall, N=197	P value
Age (years), median (IQR)	65.82 (13)	68.45 (10.08)	66.35 (11.04)	0.01*
Gender (male), n (%)	115 (83.94)	48 (80.00)	163 (82.74)	0.50
Charlson Comorbidity Index, median (range)	5 (2.0)	5 (2.5)	5 (2.0)	0.04*
BMI (kg/m^2), median (IQR)	28.06 (7.11)	26.35 (6.54)	27.29 (6.87)	0.15
Smoking (current or <30 days before surgery), n (%)	91 (66.42)	52 (86.67)	143 (72.59)	0.003*
Race, n (%)				>0.99
White	125 (91.24)	57 (95.00)	182 (92.39)	
Asian	4 (2.92)	1 (1.67)	5 (2.54)	
African American	2 (1.46)	1 (1.67)	3 (1.52)	
American Indian	1 (0.73)	0 (0.00)	1 (0.51)	
Declined	3 (2.19)	1 (1.67)	4 (2.03)	
Other	2 (1.46)	0 (0.00)	2 (1.02)	
Greater Boston area, n (%)				0.88
Inside	59 (43.07)	27 (45.00)	86 (43.65)	
Outside	78 (56.93)	33 (55.00)	111 (56.35)	
State, n (%)				0.88
In state	87 (63.50)	39 (65.00)	126 (63.96)	
Out-of-state	50 (36.50)	21 (35.00)	71 (36.04)	
Median county income (dollars) (range)	71,895 (21,072)	72,186.5 (24,532)	71,895 (21,072)	0.44

*, P values are statistically significant (P<0.05). nCRT, neoadjuvant chemoradiation; IQR, interquartile range; BMI, body mass index.

Table 2 Treatment variables between early and delayed esophagectomy

Characteristics	≤60 days from nCRT to esophagectomy, N=137	>60 days from nCRT to esophagectomy, N=60	Overall, N=197	P value
Thoracic surgery evaluation prior to nCRT completion, n (%)				0.001*
Yes	123 (89.78)	41 (68.33)	164 (83.25)	
No	14 (10.22)	19 (31.67)	33 (16.75)	
nCRT location, n (%)				0.01*
BWH/DFCI	45 (32.85)	12 (20.00)	57 (28.93)	
DFCI satellite	35 (25.55)	8 (13.33)	43 (21.83)	
Outside	57 (41.61)	40 (66.67)	97 (49.24)	
nCRT course, n (%)				
Complete	116 (84.67)	45 (75.00)	161 (81.73)	0.11
Discontinued	11 (8.03)	5 (8.33)	16 (8.12)	>0.99
Dose reduction	9 (6.57)	10 (16.67)	19 (9.64)	0.04*
Toxicity	96 (70.07)	42 (70.00)	138 (70.05)	0.99

*, P values are statistically significant (P<0.05). nCRT, neoadjuvant chemoradiation therapy; BWH, Brigham and Women's Hospital; DFCI, Dana Farber Cancer Institute.

Table 3 Univariable logistic regression analyzing odds of receiving a timely esophagectomy (within 60 days)

Variables	Odds ratio	95% CI	P value
Age (≥70), years (ref. <70)	0.6	0.32–1.13	0.11
Gender (ref. female)	1.31	0.60–2.85	0.50
Race (ref. White)	1.2	0.78–1.83	0.40
Greater Boston area	0.92	0.50–1.70	0.80
In state	0.94	0.50–1.77	0.84
County median income	1	0.99–1.00	0.36
Seen by thoracic surgery prior to treatment completion	4.07	1.87–8.84	0.001*
Location of CROSS	1.9	1.24–2.92	0.003*
BMI	1.03	0.98–1.10	0.20
Charlson Comorbidity Index	0.84	0.71–0.99	0.04*
ECOG score	0.74	0.46–1.18	0.21
History of myocardial infarction	0.29	0.09–0.94	0.04*
Congestive heart failure	1.1	0.21–5.83	0.11
Peripheral vascular disease	0.61	0.27–1.35	0.22
Cerebrovascular disease	0.29	0.09–0.94	0.04*
COPD	0.53	0.19–1.50	0.23
Peptic ulcer disease	0.72	0.17–3.11	0.66
Mild LVD	N/A		
Moderate/severe LVD	0.43	0.03–7.05	0.56
Diabetes mellitus	1.34	0.61–2.97	0.47
Moderate/severe chronic kidney disease†	1.77	0.19–16.22	0.61
Atrial fibrillation	0.93	0.36–2.42	0.88
Coronary artery disease	0.53	0.25–1.14	0.10
Hypertension	0.85	0.46–1.56	0.59
Chronic anticoagulation	0.51	0.22–1.19	0.12
Deep venous thrombosis	1.02	0.26–4.10	0.97
Immunocompromised	3.04	0.66–13.91	0.15
Smoking (current or <30 days before surgery)	0.3	0.13–0.69	0.005*
Neoadjuvant treatment complete	1.84	0.87–3.88	0.11
Neoadjuvant treatment discontinued	0.96	0.32–2.90	0.94
Dose reduction	0.35	0.13–0.92	0.03*
Toxicity (yes)	1	0.52–1.95	0.99

*, P values are statistically significant (P<0.05); †, as defined by the Charlson Comorbidity Index. CI, confidence interval; CROSS, Chemoradiotherapy for Oesophageal Cancer Followed by Surgery Study; BMI, body mass index; ECOG, Eastern Cooperative Oncology Group; COPD, chronic obstructive pulmonary disease; LVD, left ventricular dysfunction.

Table 4 Breakdown of grade III and IV adverse events (based on Clavien-Dindo classification) for the delayed esophagectomy group (>60 days)

Grade	Adverse events	N
Grade III (n=21)	Pneumothorax requiring chest tube	1
	Anastomotic leaks	4
	Chylothorax requiring ligation of the thoracic duct	3
	Copious secretions requiring clearance via bronchoscopy	2
	Intraoperative splenic laceration	1
	Bilateral recurrent laryngeal nerve injury	1
	Left vocal cord paralysis	1
	J-tube dislodgement	1
	Gastric outlet obstruction	1
	Delayed gastric emptying	1
	Intraoperative enterotomy	1
	Pneumatosis	1
	Wound infection	1
	Abdominal wall abscess	1
	anastomotic stricture	1
Grade IV (n=6)	Respiratory failure	3
	Sepsis	1
	ARDS	1
	Anastomotic leak	1

ARDS, acute respiratory distress syndrome.

Currently, five-year survival after Ivor Lewis esophagectomy is 50–60% (9). Delayed esophagectomy has been associated with decreased survival. Bajaj *et al.* demonstrated that patients with stage II/III esophageal cancer who underwent early esophagectomy (nine – seventeen weeks) had improved 5-year survival (42%) compared to those who underwent a delayed esophagectomy (21–29 weeks, 23%). This difference was not seen when analyzing stage I patients (10). The challenge lies in defining 'delayed esophagectomy,' for there is no one agreed upon definition. A meta-analysis of thirteen studies encompassing over 15,000 patients demonstrated that undergoing surgery beyond seven-eight weeks after nCRT was associated with higher 30-day mortality and a lower two-year and five-year overall survival. Given this, we chose to use 60 days as a cutoff for what constituted as delayed esophagectomy in our cohort (11). Furthermore, there is a paucity of data on factors that impact timing of esophagectomy, with the only known association being lower SES and DS. Our study identified additional factors.

Over the years, there has been a growing presence of satellite centers in rural communities, especially those offering specialized oncologic treatment. These centers are often affiliated with large tertiary or quaternary care hospitals. Patients can receive high-quality services close to home without worrying about the burden of transportation (12). This is especially important because lack of transport or prolonged travel time to health care centers has been associated with delayed access to health care (i.e., missed or rescheduled appointments, delayed medication pick-up), resulting in poorer outcomes (13,14). The availability of DFCI satellite sites might explain why we did not see a difference in timing of surgery between patients residing within or outside of the Greater Boston area. Patients were likely able to receive timely care and the same caliber of care that they would have received at the main DFCI site.

Our results also demonstrated that evaluation by the operating thoracic surgeon during the neoadjuvant period was associated with early esophagectomy. This highlights the importance of a multidisciplinary team (MDT) and coordinated care, especially for complex cancer diagnoses. Cancer remains the leading cause of morbidity and mortality worldwide, and as the incidence of cancer continues to rise, the need for a multidisciplinary approach in healthcare becomes more prevalent. MDT evaluation can offer an individualized, holistic, patient-centered approach and can also improve communication amongst all involved team members (15,16). Complex cancer diagnoses, such as esophageal cancer, often involve a multi-stage treatment approach, which can be overwhelming for patients. MDT involvement can help establish clearer perioperative pathways, resulting in increased patient compliance and timely treatment (17).

In our analysis, a history of MI, stroke, or smoking resulted in delayed esophagectomy. The impact of these factors on peri-operative risks is well-established (18-21). If possible, delayed operative intervention is recommended for these patients (at least two months for MI, six-nine months for stroke, and one-two months for smoking) (18,21,22). A greater percentage of patients who had DS were either currently smoking or had only quit within the last 30 days. We don't know the timing of the MI or stroke for the patients in our cohort given that we were limited to patient recall and chart documentation. However, even if the patients were safely outside the recommended waiting period for surgery after their initial stroke or MI, the physiologic insults can be long-lasting and may contribute to prolonged recovery. This might necessitate delaying surgery if possible. Additionally, there is some evidence to suggest that risks for adverse events may remain elevated for many years after the inciting event. For instance, patients have a 20% risk of experiencing cardiovascular events (e.g., non-fatal stroke or another MI) 36 months after the initial MI (23). Given the elevated risks and sustained physiologic insults, patients in our cohort with a history of MI or smoking perhaps underwent a more extensive pre-operative workup (e.g., cardiac clearance), which could have contributed to DS.

Patients who required an nCRT dose reduction were also more likely to have delayed esophagectomy. It's possible that after the dose adjustment, these patients needed to be monitored longer to assess for effectiveness of the drug and for development of adverse events because early side effects of radiation may only manifest a few weeks after beginning therapy (24). It's probable that the initial dose administered took a heavy physiologic toll on the patients, and they needed a longer time to recover. This would also explain the delayed timing of surgery.

There are several limitations of our study. First, this is a single-center, retrospective study at a large, specialized center. Although we found several significant factors associated with DS, causality cannot be established especially given the smaller sample size. Second, some of our findings may not be applicable to other centers. For instance, distance from the hospital may be significantly associated with DS at other institutions where satellite centers may not be as prevalent. Additionally, tertiary care centers like DFCI and BWH are rich in resources and can cater to many patients in a timely manner, provide highly specialized care, and augment coordinated care. For example, BWH has more than 20 thoracic surgeons. Although we did not specifically assess the impact of availability of surgeons on timing of surgery, this might be a significant factor in more resource-limited areas. The variables we identified are by no means a comprehensive list, and further studies are necessary to identify additional factors that were not accounted for in our study.

Conclusions

Advancements in esophageal cancer have resulted in improved outcomes, but further work needs to be done to identify factors that influence survival. Several studies have analyzed the detrimental effects of delayed esophagectomy on patient outcomes; however, data was lacking regarding factors that contributed to delayed surgery. Our study identified several such factors including history of MI, stroke or smoking and requiring nCRT dose reduction. Esophageal cancer remains prevalent in the United States population, and it's essential for providers to be aware of both patient-specific and external variables that can affect survival to then provide holistic care and intervene accordingly.

Acknowledgments

Funding: This study is supported by the John D. Mitchell Thoracic Oncology Fellowship (to A.S. and A.L.D).

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-316/rc

Data Sharing Statement: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-316/dss

Peer Review File: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-316/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-316/coif). A.L.D. and A.S. were supported by the John D. Mitchell Thoracic Oncology Fellowship. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was approved by the Institutional Review Board (IRB) at Brigham and Women's Hospital (BWH) (protocol #2014P002478). Informed consent for this retrospective study was waived. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

References

1. He H, Chen N, Hou Y, et al. Trends in the incidence and survival of patients with esophageal cancer: A SEER database analysis. Thorac Cancer 2020;11:1121-8.
2. 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.
3. Eyck BM, van Lanschot JJB, Hulshof MCCM, et al. Ten-Year Outcome of Neoadjuvant Chemoradiotherapy Plus Surgery for Esophageal Cancer: The Randomized Controlled CROSS Trial. J Clin Oncol 2021;39:1995-2004.
4. Franko J, Voynov G, Goldman CD. Esophagectomy Timing After Neoadjuvant Therapy for Distal Esophageal Adenocarcinoma. Ann Thorac Surg 2016;101:1123-30.
5. Roh S, Iannettoni MD, Keech J, et al. Timing of Esophagectomy after Neoadjuvant Chemoradiation Therapy Affects the Incidence of Anastomotic Leaks. Korean J Thorac Cardiovasc Surg 2019;52:1-8.
6. Haisley KR, Laird AE, Nabavizadeh N, et al. Association of Intervals Between Neoadjuvant Chemoradiation and Surgical Resection With Pathologic Complete Response and Survival in Patients With Esophageal Cancer. JAMA Surg 2016;151:e162743.
7. Kim JY, Correa AM, Vaporciyan AA, et al. Does the timing of esophagectomy after chemoradiation affect outcome? Ann Thorac Surg 2012;93:207-12; discussion 212-3.
8. Chen KA, Strassle PD, Meyers MO. Socioeconomic factors in timing of esophagectomy and association with outcomes. J Surg Oncol 2021;124:1014-21.
9. Pather K, Mobley EM, Guerrier C, et al. Long-term survival outcomes of esophageal cancer after minimally invasive Ivor Lewis esophagectomy. World J Surg Oncol 2022;20:50.
10. Bajaj SS, Shah KM, Potter AL, et al. Early vs Delayed Surgery for Esophageal Cancer During the COVID-19 Pandemic. J Am Coll Surg 2022;235:174-84.
11. Qin Q, Xu H, Liu J, et al. Does timing of esophagectomy following neoadjuvant chemoradiation affect outcomes? A meta-analysis. Int J Surg 2018;59:11-8.
12. Curtis ML, Eschiti VS. Geographic Health Disparities: Satellite Clinics for Cancer Care in Rural Communities. Clin J Oncol Nurs 2018;22:500-6.
13. Syed ST, Gerber BS, Sharp LK. Traveling towards disease: transportation barriers to health care access. J Community Health 2013;38:976-93.
14. Varela C, Young S, Mkandawire N, et al. Transportation Barriers to Access Heath Care for Surgical Conditions in Malawi: A cross sectional nationwide household survey. BMC Public Health 2019;19:264.
15. Ziabari Y, Wigmore T, Kasivisvanathan R. The Multidisciplinary Team Approach for High-Risk and Major Cancer Surgery. BJA Education 2017;17:255-61.
16. Selby P, Popescu R, Lawler M, et al. The Value and Future Developments of Multidisciplinary Team Cancer Care. Am Soc Clin Oncol Educ Book 2019;39:332-40.
17. Lamb BW, Taylor C, Lamb JN, et al. Facilitators and barriers to teamworking and patient centeredness in multidisciplinary cancer teams: findings of a national study. Ann Surg Oncol 2013;20:1408-16.
18. Livhits M, Ko CY, Leonardi MJ, et al. Risk of surgery following recent myocardial infarction. Ann Surg 2011;253:857-64.
19. Musallam KM, Rosendaal FR, Zaatari G, et al. Smoking and the risk of mortality and vascular and respiratory events in patients undergoing major surgery. JAMA Surg 2013;148:755-62.
20. Gallucci G, Tartarone A, Lerose R, et al. Cardiovascular risk of smoking and benefits of smoking cessation. J Thorac Dis 2020;12:3866-76.
21. Mehdi Z, Birns J, Partridge J, et al. Perioperative management of adult patients with a history of stroke or transient ischaemic attack undergoing elective non-cardiac surgery. Clin Med (Lond) 2016;16:535-40.
22. Myers K, Hajek P, Hinds C, et al. Stopping smoking shortly before surgery and postoperative complications: a systematic review and meta-analysis. Arch Intern Med 2011;171:983-9.
23. Jernberg T, Hasvold P, Henriksson M, et al. Cardiovascular

risk in post-myocardial infarction patients: nationwide real world data demonstrate the importance of a long-term perspective. Eur Heart J 2015;36:1163-70.

24. Majeed H, Gupta V. Adverse Effects Of Radiation Therapy. 2022 Sep 14. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan.

Cite this article as: Deeb AL, Dezube AR, Lozano A, Singh A, De Leon LE, Kucukak S, Jaklitsch MT, Wee JO. Early thoracic surgery consultation and location of therapy impact time to esophagectomy. J Thorac Dis 2024;16(9):5615-5623. doi: 10.21037/jtd-24-316