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Oncologic Quality Indicators in Thoracic Surgery

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Synopsis

This article outlines a structure for assessing thoracic surgical quality and provides an overview of evidence-based quality metrics for surgical care in both lung cancer and esophageal cancer, with a focus on process and outcome measures in the pre-, intra-, and post-operative setting.

Keywords

Quality; Lung cancer; Esophageal cancer; Staging; R0 Resection; Lymphadenectomy;
Multidisciplinary treatment

1. Introduction

Quality in surgical care is notoriously difficult to define, but a thorough discussion of quality indicators rests on an understanding of this concept as well an organized structure in which to consider multiple aspects of the care provided. Oncologic quality is essentially an assessment of the value of the various aspects of medical care provided to a patient from their first contact with a physician through completion of their care, with a goal of treatment or cure of disease, prolongation of survival, palliation of suffering, improvement in quality of life, or achievement of other aims important to the patient or society.

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Donabedian¹ outlined a central framework in which the quality of medical care could be analyzed, focusing specifically on the patient-provider interaction. This model divides the assessment of quality into three categories: structure, process, and outcome measures (Figure 1). These classifications of quality indicators build on each other and can be fragmented further to allow for a detailed analysis of the entire course of patient care.

Structure measures are defined as the characteristics of the environment and the medical providers that account for the overall setting in which care is provided. These metrics focus on the most physical aspects of care: hospitals, operating suites, instruments, and technology, as well as the experience-related aspects of care: training of surgeons and staff, availability of multiple medical specialties, volume, and centralization of care. The philosophy behind assessing these measures is that optimization of the setting will facilitate the provision of ideal medical care. Certain structure measures will be discussed later within this series, so an in-depth discussion will be deferred here.

Process measures are defined as evaluations of how care is provided to the patient in the setting described above. These measures look at diagnostics, patient selection for appropriate care, and the treatments or interventions provided. Assessing these measures allows one to determine if high-quality care has been provided to the patient. This is based on the idea that patients receiving complete application of evidence-based medicine will have better outcomes. Process measures are of particular interest because these identify specific points in the patient's treatment where practice could potentially be changed to enhance the patient's eventual outcome.

Outcomes measures are defined as metrics tracking the results of the entire medical process that the patient experiences. Outcomes are classically the most easily comprehensible of the three types of measures, since they often track the discrete events that are easily identifiable and able to be precisely quantified. This category includes measures such as survival, cancer recurrence, and treatment-related complications. These outcome measures are susceptible to effects of factors other than simply the care provided. In the Donabedian framework, variables are often closely linked. As example, the completeness of an oncologic operation contributing to disease-free survival. Examples of these measures can be seen in Figure 2. A subset of outcomes measures is now of national interest and tracked by multiple entities. Organizations such as the American College of Chest Physicians (ACCP), the British Thoracic Society (BTS), the European Society of Thoracic Surgeons (ESTS), the American College of Surgeons (ACS), the National Comprehensive Cancer Network (NCCN), and the Society of Thoracic Surgeons (STS) have proposed, and intermittently updated treatment guidelines aimed at improving the quality, effectiveness, and efficiency of cancer care worldwide. These guidelines often represent a combination of best available evidence and expert opinion.

With a special focus on process and outcome measures, this framework will be used to evaluate quality indicators currently relevant in thoracic surgical oncology in the preoperative, intraoperative, and postoperative phases. We explore current quality measures for lung and esophageal cancer, and discuss the relevant evidence and guidelines supporting use of these quality measures.

2. Oncologic Quality Indicators in Surgically Resectable Non-Small Cell Lung Cancer

Innumerable quality process indicators for non-small cell lung cancer (NSCLC) have been reported in the literature. Recently, a multidisciplinary expert panel used a modified Delphi process and concluded that while mortality, morbidity, survival, and length of stay were the most important outcomes indicators, they were insufficient metrics of quality oncologic care delivery. Instead, they recommended 12 evidence-based and 5 consensus-based process and outcomes measures related to preoperative assessment, pathologic staging and evaluation, surgical resection, and adjuvant therapy². Subsequently, Numan et al used the Donabedian framework for two systematic reviews to identify supported indicators for quality pre- and post-operative care for stage I–IIIA NSCLC^{3, 4}. Both strategies identified factors such as hospital size or teaching status, surgeon specialty, and access to multi-disciplinary care teams as significant contributors to favorable oncologic outcomes. Surgeon or hospital procedural volume was not clearly related to postoperative mortality, as discussed elsewhere in this issue³. However, as this chapter focuses on measures that lend themselves to easier targeted intervention, these structural measures will not be addressed further. Instead, the actionable process measures which are strongly linked to patient outcomes have been coalesced into 9 divisions, addressing each evidence-based element in turn as well touching on important issues of clinical equipoise. The discussion about improving survival in lung cancer will be further framed by the pre-, intra-, and post-operative points of intervention (Figure 3).

A. Preoperative Quality Measures in Clinical Stage I–IIIA NSCLC

Preoperative quality measures are intended to ensure accurate diagnoses, adequate staging, and efficient care delivery. Table 1 summarizes the current evidence-based preoperative process quality measures. This discussion will focus on three specific measures: preoperative mediastinal staging, tissue diagnosis, and early surgical resection.

In patients with suspected NSCLC, adequate patient management is contingent upon accurate oncologic staging. However, data suggest that it is poorly done^{5–7}. When disease is localized to the chest, accurate preoperative mediastinal staging is critical^{6–8}. Several observational studies have shown improved staging accuracy with the utilization of complementary techniques^{9, 10}. Farjah et al¹¹ retrospectively assessed the benefit of multimodality mediastinal staging for stage I–III NSCLC and found that those who underwent bimodality staging tests (CT plus PET or CT plus invasive tissue sampling) or trimodality staging tests (CT, PET, and invasive staging) had significantly lower risk of death, even when adjusted for stage [hazard ratio 0.58 (0.56–0.60) for bimodality and hazard ratio 0.49 (0.45–0.54) for trimodality]. However, two under-powered randomized control trials showed no benefit of CT plus PET on diagnostic accuracy, cost savings, or survival^{12, 13}. In the absence of higher level evidence, quality mediastinal staging entails bimodal preoperative imaging. One should note that the influence of PET on treatment delays remains under debate.

Patients with peripheral, clinical stage I NSCLC without concerning PET findings can be considered adequately staged. With extensive mediastinal infiltration, definitive invasive mediastinal staging is indicated⁸. Generally speaking, rigid bronchoscopy with washings, brushes, and forceps biopsies (FB) are insufficiently sensitive (43–57%), though can be improved when combined with fluoroscopy for peripheral lesions. The diagnostic yield of FB is 50.5–81.5%, which is further improved with cytopathologic examination⁴. In both visible and non-visible tumors, transbronchial or ultrasound-guided fine needle aspirations increase the diagnostic yield ~20% over bronchoscopy with FB^{4, 6}. The sensitivities and specificities of most image-guided techniques are similar, but the false negative rate is higher for needle aspirations than for mediastinoscopy (Table 2). High negative predictive values often necessitate confirmatory testing^{4, 6, 8}. Emerging data support the complementary roles of EUS-NA, EBUS-NA, and mediastinoscopy to avoid futile surgery^{4, 8, 14}. In conclusion, there is high level evidence to support PET-CT, endosonography, and the combination of histological and cytological pathology for quality oncologic staging of the mediastinum^{4, 6}.

Diagnosis at an earlier stage and screening of high risk individuals are known to improve patient survival¹⁵. However, the median time from diagnosis to treatment for NSCLC has increased over the last decade¹⁶. While patient-specific factors influence treatment delays, even when adjusted for higher risk characteristics, surgical resection greater than 8 weeks from diagnosis is independently associated with pathologic upstaging and decreased median survival yet nearly 20% of patients experience significant care delay¹⁷. This is particularly alarming for socioeconomically disadvantaged patients who already suffer from disparities in treatment and outcome for NSCLC^{18, 19}. Ensuring quality care via timely surgical resection requires acknowledgement of disease-specific, systemic, and cultural barriers to meeting this metric.

B. Intraoperative Quality Measures in Clinical Stage I–IIIA NSCLC

Intraoperative quality measures are designed to balance maximizing oncologic benefit while minimizing the risk of serious surgical complications. Tables 3 and 4 summarize the current evidence-based intraoperative process quality measures, specific to clinical stage. This discussion will focus on four specific measures: anatomic resection, complete (R0) resection, minimally invasive operations, and adequate lymph node (LN) sampling (Figure 3).

While some nuances remain, complete (R0) anatomic resection, when feasible, is considered the standard of care^{2, 3, 20–22}. Similarly, minimally invasive approaches should be undertaken when feasible as they correlate with shorter length of stay, improved pain control, though variable LN assessment despite similar overall survival^{4, 20, 22, 23}. Yet, the definition of adequate LN staging has been more nebulous. Pathologic examination of higher number of LN is associated with increased disease-free and overall survival²⁴. The Commission on Cancer recommends pathologic examination of at least 10 LN while the NCCN encourages sampling from 3 mediastinal nodal stations (Table 3)²⁵. When compared to systematic sampling, lymphadenectomy/lymph node dissection for stage I–IIIA NSCLC identified more N2 disease but was not associated with improved survival. Therefore, systematic sampling is likely sufficient^{3, 26}.

Samson et al explored adherence to quality measures in stage I NSCLC resection using the National Cancer Database, with special attention to anatomic resection, R0 resection, sampling of 10 lymph nodes, and surgery within 8 weeks of diagnosis. They reported that adherence to an increased number of quality metrics was associated with statistically significant higher rates of pathologic upstaging but also improved overall survival. As it pertains to lymph node sampling, a slight temporal trend was noted, yet only 34% of patients in 2013 had greater than 10 lymph nodes sampled. Thus, real-world compliance remains suboptimal²⁷.

C. Postoperative Quality Measures in Clinical Stage I–IIIA NSCLC

Postoperative quality measures are designed to optimize adjuvant therapy and disease surveillance while minimizing unnecessary risks and costs. Therefore, metrics vary based on pathologic stage. Tables 5 and 6 summarize the current evidence-based postoperative process quality measures for stage I–II and stage IIIA NSCLC, respectively.

The nuances of adjuvant therapy are beyond the scope of this discussion, but are stratified in Table 6 by the current recommendations based on pathologic stage and adequacy of surgical resection. Pathologic microscopic invasion of the bronchial stump (R1) has a significantly worse prognosis, with 1- and 5-year survival rates between 20–50% and 0–20%, respectively^{28, 29}. Since peribronchial residual disease is associated with metastatic lymph node involvement and functional limitations, subsequent treatment, including re-resection, remains controversial (Table 6)^{4, 8, 20, 30}

There is high-level evidence to support multidisciplinary oncology care teams. Within a multidisciplinary care model for NSCLC, Numan et al elucidated the novel process quality measure of clinical care⁴. The elements of such standardized care pathways can be seen in Table 5 and correlate with decreased length of stay, fewer pulmonary complications, and improved pain control. Specifically, several randomized control trials demonstrated improved pain control with preemptive epidural analgesia or nerve block and decreased air leaks with chest tubes managed on water seal³. Implementation of a clinical care pathway for NSCLC can lead to widespread improved performance on quality metrics³¹.

3. Oncologic Quality Indicators in Surgically Resectable Esophageal Cancer

As in lung cancer, there are several important recommended process and outcome quality metrics for esophageal cancer.

A. Evidence that Quality Matters for Patient Survival

A recent review by Courrech Staal et al.³² explored the published evidence behind a very wide range of quality metrics that have been suggested in esophageal cancer operations using the Donabedian framework of structure, process, and outcome measures. With regards to structural measures that affected postoperative mortality, the authors found there was strong or considerable evidence for high volume hospitals and surgeons, as well as surgeons with thoracic specialty training. Within the process measures, they found that patient

selection (which was captured in their review as age and functional status), staging, and neoadjuvant chemoradiation affected patient survival. Of the outcome measures assessed, they noted substantial evidence supporting improved survival in R0 resections, patients with higher nodal counts, and those who escaped postoperative complications. This review nicely outlines the overall level of support behind various quality metrics.

Several studies have examined discretely the effect that adherence to sets of quality measures can have on patient survival in esophageal cancer. Recently, Samson et al³³ evaluated the survival implications in NCDB patients of achieving an R0 resection, performing a lymphadenectomy of 15 or more nodes, and utilizing induction treatment for locally advanced cancer. This study found a temporal trend towards increasing attainment of more quality metrics, and demonstrated a reduction in mortality corresponding to the number of measures achieved. Additionally, meeting all selected quality measures decreased the mortality hazard ratio to 0.21 (0.14–0.32) for early stage cancer and to 0.54 (0.40–0.73) for locally advanced cancer. A summary of the observed improvement in median survival for both early and locally advanced esophageal cancer based on quality measures can be found in Table 1.

The effect of a quality score in a single institutional cohort of locally advanced esophageal cancer patients was examined by Molena et al. In this study, a score was generated by examining seven quality indicators based on NCCN guidelines: histologic classification, tumor location, tumor grade, surgery, induction chemoradiation, staging with PET-CT and EUS, and two restaging scans. Patient outcomes were compared between two groups, those above (high quality care) and those below (low quality care) the median score, and the authors again found an improvement in survival of an additional 6 months for those patients receiving higher quality care, with a hazard ratio of 0.58 (0.37–0.90)³⁴.

B. Selected Quality Measures

These studies demonstrate an improvement in patient survival with adherence to quality guidelines, but also demonstrate the variation in definition of quality metrics. In the sections below, we will discuss the evidence behind 4 of the most widely used process and outcome quality measures in esophageal cancer: staging with PET- CT and EUS, achieving an R0 resection, performing an adequate lymphadenectomy, and administering induction chemoradiation for locally advanced esophageal cancer (See Figure 4).

C. Staging with PET-CT and EUS

Following diagnosis with endoscopy and biopsy, staging in esophageal cancer should include PET and CT to assess for regional and distant spread, and, if no metastatic disease is noted, EUS should be used to assess the extent of local and regional disease. PET and CT should be performed to evaluate for regional and distant spread, and repeated following induction therapy to reassess resectability. A summary of studies supporting the use of these staging modalities can be reviewed in Table 9.

EUS use is recommended for routine staging when there is no evidence of distant metastases because of its utility in locoregional staging. This is supported by a large meta-analysis³⁵ that pooled 49 studies to include over 2500 patients which found that EUS is sensitive and

specific for both tumor and node staging, with the following sensitivities and specificities by stage: T1: 82%, 99%; T2: 81%, 96%; T3: 91%, 94%; T4: 92%, 97%, and N: 85%, 85%. EUS performs better than PET or CT for local and regional staging because of the ability to distinguish layers of the esophageal wall for tumor staging and examine periesophageal stations of mediastinal lymph nodes for nodal staging. One meta-analysis³⁶ compared all three staging modalities and confirmed that EUS is the most sensitive for detection of nodal metastasis (80% vs 50–57%) but less specific than PET or CT (70% vs 83–85%). Another systematic review³⁷ on PET scanning in esophageal cancer found the imaging to be most helpful for detecting distant metastases (sensitivity 67% and specificity 97%).

STS Guidelines on Staging³⁸ and NCCN Guidelines³⁹ recommend that for both early and locally advanced esophageal cancer, staging should include a CT scan of the chest and abdomen, PET scan, with the addition of EUS for patients with apparent locoregional disease.

D. R0 Resection

The importance of an R0 resection has been demonstrated time and again in numerous malignancies, and multiple studies have specifically demonstrated a survival benefit of an R0 resection in esophageal cancer. A summary of selected studies supporting the importance of negative margins can be seen in Table 10.

A large propensity score matched study by Markar et al.⁴⁰ demonstrated that a microscopically positive margin was an independent predictor of poor prognosis for patients undergoing esophagectomy. They retrospectively analyzed survival from a group of over 2800 patients and found that an R1 resection increased the hazard ratio of both mortality and recurrence. Survival was decreased substantially for both patients with node positive disease (66.0 vs 24.4 months) and node negative disease (23.0 vs 16.6 months). Another smaller single center study by Wang et al.⁴¹ examined the impact of a positive proximal resection margin on survival again through propensity score matching and also demonstrated a similar survival benefit of R0 resection (68.0 vs 25.0 months). These authors also found improved survival with adjuvant therapy in patients with R1 resection, although this remains controversial.

Siewert et al.⁴² conducted a large cohort study of over 1000 patients which also demonstrated that R0 resection was a dominant factor in multivariate analysis that significantly predicted overall survival for esophageal cancer patients both at 5 years (38.7% vs 13.7%) and at 10 years (28.3% vs 11.6%). Another 10-year single center series of over 200 patients by Mulligan et al.⁴³ demonstrated decreased tumor recurrence and a significant increase in survival with an R0 resection.

E. Adequate Lymphadenectomy

Numerous studies have shown a survival benefit in esophageal cancer with increasing extent of lymphadenectomy. A summary of relevant primary studies with recommended lymph node counts can be seen in Table 11.

A study⁴⁶ based on Worldwide Oesophageal Cancer Collaboration (WECC) database of over 4500 patients explored the number of lymph nodes that should be examined by stage of disease in patients undergoing upfront surgery. They found that for any pathologically node-negative cancers that were moderately or poorly differentiated, as well as for all cancers with positive nodes, a more extensive lymphadenectomy was associated with improved 5-year survival. Additionally, they suggested the following minimum lymph node counts were optimal based on pathologic tumor status: 10 nodes for pT1, 20 nodes for pT2, and 30 nodes for pT3 or greater. Stiles et al.⁴⁷ aimed to apply these guidelines to 135 patients who had received neoadjuvant treatment and found that having a guideline-supported lymphadenectomy was predictive of survival, but this was also highly correlated with post-induction pathologic tumor staging.

Peyre et al.⁴⁸ conducted a multicenter database study of over 2000 patients to identify a threshold for benefit of lymph node removal, and found that 23 nodes was optimal. Similar to what was observed in the WECC study, they noted the benefit of this more extensive lymphadenectomy was greater for higher stage disease.

A pair of studies examined the impact of the extent of lymphadenectomy using Surveillance, Epidemiology, and End Results (SEER) data. Schwarz et al.⁴⁹ examined over 2500 patients and quantified the relative increase in overall survival per 10 additional lymph nodes resected and found it increased 4–5%. They found that both negative lymph node counts greater than 15, and total lymph node counts greater than 30 were associated with improved overall survival. These findings were consistent with additional single institution studies.^{50, 51} Greenstein et al.⁵² using the SEER data confirmed that increasing lymph node count was associated with improved survival, but settled on 18 as the optimal number, consistent with the number Rizk et al.⁵³ had identified as needed for accurate staging through recursive partitioning analysis of an institutional database of over 300 patients.

The data overall are clear that a more extensive lymphadenectomy improves the accuracy of staging and observed overall survival, though it remains debatable how much of the observed survival benefit is due to stage migration. NCCN Guidelines³⁹ recommend that at least 15 lymph nodes are removed and pathologically examined across all stages of esophageal cancer, though evidence from the primary literature is clearly mixed with regards to the optimal count, especially following induction chemoradiation.

F. Induction Chemoradiation

Randomized controlled trials have shown a survival benefit of induction chemoradiation for stage IIB or higher esophageal cancer. A summary of these studies can be seen in Table 12.

The primary trial supporting induction therapy for locally advanced esophageal cancer was the CROSS trial.^{54, 55} This randomized controlled trial included over 350 esophageal cancer patients, 75% of which had adenocarcinoma, who were clinically staged as T1N1, T2–3N0–1. This trial randomized patients to induction chemoradiation versus surgery and found no difference in perioperative mortality or morbidity with a substantial increase in overall median survival for the induction therapy group (49.4 vs 24.0 months), as well as a decrease in ultimate esophageal cancer specific mortality (85% vs 94%), with very low rates of

chemoradiation mortality (0.6%) and failure to proceed to surgery (6.0%). When these patients did undergo resection, they also were much more likely to get an R0 resection (92% vs 69%). A five year follow up study of the CROSS patients⁵⁶ revealed that the initially observed survival benefits persisted, and provided data on the median survival benefit difference between squamous cell and adenocarcinoma.

This landmark trial was preceded by two other older randomized trials that showed a benefit of induction chemoradiation. The CALGB 9781 trial⁵⁷ enrolled over 50 patients and again randomized patients to preoperative chemoradiation or surgery alone and demonstrated a survival benefit (4.48 vs 1.79 years), no difference in complications (24 reported complications in each group), and no difference in mortality (one infection-related mortality in the induction group and one perioperative death in the surgery group). Similarly, Walsh et al.⁵⁸ enrolled over 100 patients who were randomized to induction therapy versus surgery alone. Again, there was a demonstrated benefit for trimodality therapy.

STS Practice Guidelines⁵⁹ are supported by this evidence and include that patients with locally advanced disease should undergo preoperative chemoradiation, should be restaged following induction therapy, and should undergo surgical resection even in the setting of complete pathologic response. The NCCN Guidelines³⁹ also support preoperative chemoradiation followed by an assessment of response.

4. Summary

In conclusion, there is substantial evidence that quality metrics within process and outcome measures can be identified for lung and esophageal cancer, and that adhering to evidence-based quality recommendations have implications for survival in thoracic malignancies. Furthermore, prior studies show that adherence to these metrics remains suboptimal. We must continue to strive towards further refining these measures and achieving greater adherence to established ones.

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Key Points

1. Quality of care can be evaluated through structure, process, and outcome measures.
2. Adherence to evidence-based quality metrics improves patient survival outcomes.
3. Strongly supported quality measures for lung cancer include: preoperative mediastinal staging, timely anatomic resection via a minimally invasive approach, R0 resections, adequate lymph node sampling, multidisciplinary care team, and clinical care pathways.
4. Strongly supported quality measures for esophageal cancer include: staging with PET-CT and EUS, achieving an R0 resection, performing an adequate lymphadenectomy, and administering induction chemoradiation for locally advanced disease.

Figure 1.

A model for understanding quality of care in medicine as proposed by Donabedian. The three categories outlined provide a framework for discussion. (*Adapted from Donabedian A. Evaluating the quality of medical care. Milbank Meml Fund Q. 1966;33(4):691–729. doi: 10.2307/3348969; with permission*)

Figure 2.

Examples of Quality Measures for Thoracic Cancers (Data from Courrech Staal EFW, Wouters MWJM, Boot H, et al. Quality-of-care indicators for oesophageal cancer surgery: A review. *Eur J Surg Oncol.* 2010;36(11):1035–1043. doi:10.1016/j.ejso.2010.08.131)

Figure 3.
Quality Indicators in Lung Cancer

Figure 4.
Quality Indicators in Esophageal Cancer

Table 1**Preoperative Quality Measures in Clinical Stage I–IIIA NSCLC**

Preoperative Measures			
Category	Quality Metric	Recommended By	Evidence grade
Bronchoscopy	Unless obstructing lesion, preferably performed during planned resection	BTS NCCN	2A
Clinical staging	Clarified and recorded prior to surgery	BTS STS	--
Diagnostics	Pulmonary function testing and electrocardiogram. Further physiologic testing as clinically indicated	ACCP BTS NCCN Darling	2A
Imaging	Contrast CT of chest and upper abdomen including adrenals. FDG-PET skull base to knees or whole body. If stage IIB-III, contrast brain MRI	BTS NCCN Darling Numan	2A
Neoadjuvant therapy, <i>N0-N1 disease</i>	Not recommended	ACCP NCCN Numan et al.	1A-1C
Neoadjuvant therapy, <i>discrete N2 disease</i>	Surgery is not the first course of treatment with discrete N2 disease. Give either definitive chemoradiation or induction therapy followed by surgery	ACCP NCCN Numan et al.	1A-1C
Prophylactic cranial irradiation	Not recommended outside of a clinical trial if complete response after concurrent chemoradiotherapy	ACCP	2C
Radiotherapy	Consider in stage III to increase mediastinal downstaging.	Numan et al.	2B
Radiotherapy, definitive	Do not give only radiotherapy if good performance status. Preferable to no therapy if unable to tolerate sub-anatomic resection. In stage III, may increase mediastinal downstaging.	ACCP BTS Numan et al.	1A-1C
Restaging	Repeat CT/PET after induction therapy to exclude disease progression	NCCN Numan et al.	2A
Timing of surgery	Surgery within 8 weeks of diagnosis. Caveat: If neoadjuvant therapies are indicated, they should be within 4 months preoperatively	ACCP Reifel et al. Samson et al.	
Tissue diagnosis	Should obtain prior to anatomic resection. Select least invasive biopsy with highest yield. If strong clinical suspicion, specimen not needed pre-operatively	ACCP BTS NCCN	1C-2A

Preoperative Measures			
Category	Quality Metric	Recommended By	Evidence grade
		Numan et al.	
Treatment planning	Surgical resection unless contraindicated	ACCP BTS Darling et al. Numan et al.	1B

American College of Chest Physicians (ACCP), British Thoracic Society (BTS), computed tomography (CT), magnetic resonance imaging (MRI), National Comprehensive Cancer Network (NCCN), positron emission tomography (PET), Society of Thoracic Surgeons (STS).

Data from Refs^{2–4, 6, 17, 20, 21, 30, 60–62}

Table 2

Techniques for mediastinal staging, in order of increased invasiveness of technique, with available associated performance metrics.

Diagnostic modality	Sensitivity, mean (range)	Specificity, mean (range)	False negatives, mean (range)	False positives, mean (range)
EUS-NA	84% (45–100%)	99.5% (88–100%)	19% (0–32%)	0.4% (0–7%)
TBNA	78% (14–100%)	100% (96–100%)	28% (0–66%)	0% (0–11%)
EBUS-NA	90% (79–95%)	100%	24% (1–37%)	0%
TTNA	90% (72–100%)	100%	0%	0%
VATS staging	--- (37–100%)	100%	15% (0–58%)	0%
Mediastinoscopy	80% (40–97%)	100%	10% (3–20%)	0%

Adapted from Detterbeck FC, Lewis SZ, Diekemper R, et al. Executive Summary: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest*. 2013;143(5):7S–37S. doi:10.1378/chest.12-2377; with permission.

Table 3**Intraoperative Quality Measures in Clinical Stage I–IIIA NSCLC**

Intraoperative Measures			
Category	Quality Metric	Recommended By	Evidence grade
Anatomic Resection	Lobectomy, if feasible, otherwise: anatomic sublobar resection, margins > maximal tumor diameter or 2cm for larger tumors	ACCP BTS NCCN Darling et al. Numan et al.	1B, 1C
Anatomic Resection	R0 sleeve or bronchoplastic resection preferable to pneumonectomy	ACCP NCCN Darling et al. Numan et al.	2C
Anatomic Resection	Sublobar resection with negative margins in predominantly ground glass opacity lesions <2cm	ACCP	2C
Complete Resection	R0 resection.	ACCP NCCN Darling et al. Numan et al.	1A
Mediastinal Assessment	At least 10 nodes are removed and examined	ACS Commission on Cancer Darling et al.	2A
Mediastinal Assessment	Minimum sampling of 3 mediastinal nodal stations (R: 2R, 4R, 7, 8, 9 L: 4L, 5, 6, 7, 8, 9)	ESTS NCCN Darling et al.	2A
Mediastinal Assessment	Systematic mediastinal lymph node sampling or dissection at time of resection	ACCP ESTS NCCN Darling et al.	1B
Minimally Invasive Operation	Video-Assisted Thoracoscopic Surgery approach when feasible	ACCP NCCN Numan et al.	2C
Tissue diagnosis	If not definitive preoperative, must obtain intra-operatively prior to anatomic resection	ESTS NCCN	2A

American College of Chest Physicians (ACCP), American College of Surgeons (ACS), British Thoracic Society (BTS), computed tomography (CT), endobronchial ultrasound fine-needle aspiration (EBUS-FNA), European Society of Thoracic Surgeons (ESTS), endoscopic ultrasound with fine needle aspiration (EUS-FNA), National Comprehensive Cancer Network (NCCN)

Data from Refs^{2–4, 20, 21, 25, 30, 63}

Table 4Intraoperative Quality Measures Specific to Clinical Stage IIIA (N2-N3, M0) NSCLC ^{20, 61}

Intraoperative Measures			
Category	Quality Metric	Recommended By	Evidence grade
Anatomic Resection	Pneumonectomy is ill-advised after neoadjuvant therapy	NCCN	2A
Mediastinal Assessment <i>if confirm suspected N2 disease</i>	Abort operation	ACCP	2C
Mediastinal Assessment <i>if find occult N2 disease</i>	If complete resection of primary tumor is feasible, perform mediastinal lymph node dissection or systematic sampling	ACCP	2C

American College of Chest Physicians (ACCP), National Comprehensive Cancer Network (NCCN)

Data from NCCN Clinical Practice Guidelines in Oncology: Non-Small Cell Lung Cancer (National Comprehensive Cancer Network). 2017. https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed March 29, 2017; and Ramnath N, Dilling TJ, Harris LJ, et al. Treatment of Stage III Non-small Cell Lung Cancer. *Chest*. 2013;143(5):e314S–e340S. doi:10.1378/chest.12-2360.

Table 5

Postoperative Quality Measures in Clinical Stage I–IIIA NSCLC

Postoperative Measures			
Category	Quality Metric	Recommended By	Evidence Grade
Fast track/care pathway	Introduce a clinical care pathway emphasizing management of (1) pain, (2) chest tube, (3) mobilization, (4) nutrition, (5) intravenous infusion, (5) oxygen support, (7) wound care, (8) patient education, (9) discharge, and (10) aspiration prevention	Numan et al.	2A-2B
Surveillance after definitive therapy	Serial chest CT. No routine PET or brain MRI	NCCN	2A
Timely adjuvant chemotherapy	Systemic chemotherapy is given within 6 months postoperatively	ACCP	2B
Timely hospital discharge	Prolonged postoperative hospital course after elective lobectomy for lung cancer is defined as >14 days (risk adjusted by STS)	STS Darling et al. Numan et al.	---

American College of Chest Physicians (ACCP), National Comprehensive Cancer Network (NCCN), Society of Thoracic Surgeons (STS), computed tomography (CT), positron emission tomography (PET), magnetic resonance imaging (MRI).

Data from Refs^{2, 3, 20, 30, 61, 64}

Table 6

Postoperative Quality Measures Specific to Clinical Stage I–II NSCLC

Postoperative Measures				
Category	Subcategory	Quality Metric	Recommended By	Evidence Grade
Adjuvant chemotherapy	R0 in Stage IA	Not currently recommended	ACCP BTS Numan et al.	1B
Adjuvant chemotherapy	R0 in Stage IB	Controversial	ACCP BTS Numan et al.	2C
Adjuvant chemotherapy	R0 in Stage IIA or IIB	Platinum-based chemotherapy	ACCP BTS Numan et al.	1A
Radiotherapy	R0 in Stage II	Not currently recommended	ACCP Burdett et al. Numan et al.	2A
Radiotherapy	R1 resection in Stage I or II	Controversial	ACCP Numan et al.	2C
Positive margins (R1 and R2)	Pathologic stage IA	Re-resection (preferred) or radiotherapy	NCCN	2A
Positive margins (R1 and R2)	Pathologic stage IB–IIB	Re-resection (preferred) with or without adjuvant therapy	NCCN	2A

American College of Chest Physicians (ACCP), British Thoracic Society (BTS), National Comprehensive Cancer Network (NCCN).

Data from Refs^{4, 20, 21, 30, 65}

Table 7

Postoperative Quality Measures Specific to Clinical Stage IIIA (N2-N3, M0) NSCLC

Postoperative Measures			
Category	Quality Metric	Recommended By	Evidence grade
Adjuvant chemo-radiotherapy	Concurrent combination platinum-based chemotherapy and radiotherapy, tailored to performance, nodal status, and completeness of resection	ACCP BTS NCCN	1A-2C
Positive margins (R1 and R2)	No re-resection. Give planned adjuvant chemoradiotherapy	NCCN	2A

American College of Chest Physicians (ACCP), British Thoracic Society (BTS), National Comprehensive Cancer Network (NCCN).

Data from Refs^{20, 21, 61}

Table 8

Survival Based on Number of Quality Measures Met: Including R0 Resection, Lymphadenectomy of at least 15 Nodes, and Induction Therapy for Locally Advanced Disease

Number of Quality Measures Met	Early Stage		Locally Advanced	
	Median Survival (months)	Percentage of Patients	Median Survival (months)	Percentage of Patients
0	23.7 +/- 3.6	70.1%	14.4 +/- 2.4	1.5%
1	104 +/- 4.9		19.5 +/- 0.9	10.5%
2	123 +/- 12.6	29.9%	31.1 +/- 0.8	55.9%
3	Not Applicable: No Induction Treatment		36.1 +/- 1.8	32.1%

Adapted from Samson P, Puri V, Broderick S, et al. Adhering to Quality Measures in Esophagectomy Is Associated With Improved Survival in All Stages of Esophageal Cancer. *Ann Thorac Surg*. January 2017. doi:10.1016/j.athoracsur.2016.09.032; with permission.

Table 9

A Summary of Studies Supporting Staging with PET, CT, and Endoscopic Ultrasound for Esophageal Cancer.

Study	Design Year of Study	Number of Patients	Conclusions
PET			
Systematic review of the staging performance of 18F-fluorodeoxyglucose positron emission tomography in esophageal cancer³⁷	Systematic Review (2004)	12 studies n=421 for nodal analysis n=452 for metastatic analysis	PET is helpful for detecting regional and distant metastases <ul style="list-style-type: none"> Sensitivity and specificity were as follows: <ul style="list-style-type: none"> Nodal: 51%, 84% Distant: 67%, 97%
EUS			
Staging accuracy of esophageal cancer by endoscopic ultrasound³⁵	Meta-analysis and Systematic Review (2008)	49 studies n=2558	EUS is sensitive and specific for tumor and node staging <ul style="list-style-type: none"> EUS is more accurate in higher than lower stage disease EUS performs better than PET and CT in identifying mediastinal disease Sensitivity and specificity by stage were as follows: <ul style="list-style-type: none"> T1: 82%, 99% T2: 81%, 96% T3: 91%, 94% T4: 92%, 97% N: 85%, 85%
Comparison of EUS, PET, and CT			
Staging investigations for oesophageal cancer³⁶	Meta-analysis		EUS is the most sensitive for detecting lymph node metastases, but CT and PET are more specific <p>Sensitivity and specificity by modality were as follows:</p> <ul style="list-style-type: none"> EUS <ul style="list-style-type: none"> N: 80%, 70% CT <ul style="list-style-type: none"> N: 50%, 83% M: 52%, 91% PET <ul style="list-style-type: none"> N: 57%, 85% M: 71%, 93%

Data from Refs 35–37.

Table 10

A Summary of Studies Supporting the Importance of an R0 Resection for Esophageal Cancer.

Study	Design Year of Study	Number of Patients	Conclusions
Significance of Microscopically Incomplete Resection Margin After Esophagectomy for Esophageal Cancer ⁴⁰	Multicenter retrospective study: propensity score matched 1:3 (2016)	2815	R1 resection margin was an independent predictor of poor prognosis <ul style="list-style-type: none"> Increased mortality with a hazard ratio of 1.57 Increased recurrence with a hazard ratio of 1.56 Survival with N0 disease was 66.0 months with R0 resection vs 24.4 months with R1 resection Survival with N1 disease was 23.0 months with R0 resection vs 16.6 months with R1 resection
Positive esophageal proximal resection margin: an important prognostic factor for esophageal cancer that warrants adjuvant therapy ⁴¹	Single center retrospective study: propensity score matched 1:2 (2016)	111	R1 proximal resection margin conveyed worse prognosis <ul style="list-style-type: none"> Survival was 68.0 months with R0 resection vs 35.0 months with R1 resection
Margin involvement and outcome in oesophageal carcinoma: a 10-year experience in a specialist unit ⁴³	Single center cohort (2004)	212	Negative margins were associated with decreased cancer recurrence and improved survival (RR 2.16) on multivariate analysis
Extent of oesophageal resection for adenocarcinoma of the oesophagogastric junction ⁴⁴	Retrospective cohort (2003)	94	Positive margins impacted survival <ul style="list-style-type: none"> Survival was 36.3 months with R0 resection vs 11.1 months with R1 resection
Surgical therapy for adenocarcinoma of the cardia: modalities of recurrence and extension of resection ⁴⁵	Retrospective cohort (2001)	116	Survival was correlated with microscopically positive margins <ul style="list-style-type: none"> Survival was 31.0 months with R0 resection vs 18.0 months with R1 resection
Adenocarcinoma of the esophagogastric junction: Results of surgical therapy based on anatomical/topographic classifications in 1,002 consecutive patients ⁴²	Single center cohort (2000)	1002	R0 resection was one of the most important prognostic factors on multivariate analysis <ul style="list-style-type: none"> 5-year survival was 38.7% with R0 resection vs 13.7% with R1/R2 resection 10-year survival was 28.3% with R0 resection vs 11.6% with R1/R2 resection

Data from Refs 40–45

Table 11

A Summary of Studies Supporting Increased Extent of Lymphadenectomy

Study	Design Year of Study	Number of Patients	Recommendations
WECC Guidelines for lymphadenectomy predict survival following neoadjuvant therapy ⁴⁷	Prospective cohort (2012)	135	>10 for T1 or less >20 for T2 >30 for T3/4
Optimum lymphadenectomy for esophageal cancer ⁴⁶	Retrospective review from WECC database (2010)	4627	For N0 cancers: <ul style="list-style-type: none"> • 10–12 for pT1 • 15–22 for pT2 • 31–42 for pT3/4 For N1-2 cancers: <ul style="list-style-type: none"> • 10 for pT1 • 15 for pT2 • 29–50 for pT3/4
Total number of lymph nodes predicts survival in esophageal cancer ⁵⁰	Retrospective review of single institution database (2008)	264	Overall survival improved with increasing lymphadenectomy
The Number of Lymph Nodes Removed Predicts Survival in Esophageal Cancer: An International Study on the Impact of Extent of Surgical Resection ⁴⁸	Retrospective database review, data compiled from 9 international centers (2008)	2303	> 23 lymph nodes
Effects of the Number of Lymph Nodes Sampled on Postoperative Survival of Lymph Node-Negative Esophageal Cancer ⁵²	Retrospective database review based on SEER (2008)	972	>18 lymph nodes
Clinical Impact of Lymphadenectomy Extent in Resectable Esophageal Cancer ⁴⁹	Retrospective database review based on SEER (2007)	2597	>30 lymph nodes >15 negative lymph nodes
The prognostic importance of the number of involved lymph nodes in esophageal cancer: implications for revision of the AJCC staging system ⁵³	Retrospective review, single institution (2006)	336	>18 lymph nodes for diagnostic accuracy
Staging of Esophageal Carcinoma: Length of Tumor and Number of Involved Regional Lymph Nodes. Are These Independent Prognostic ⁵¹	Single institution study (2006)	213	>15 negative lymph nodes

Data from Refs 46–53

Table 12

A Summary of Studies Supporting Induction Chemoradiation for Locally Advanced Esophageal Cancer.

Study	Design, Year of Study	Number of Patients	Conclusions
Preoperative Chemoradiotherapy for Esophageal or Junctional Cancer (CROSS) ^{54, 55}	Randomized controlled trial (2012)	366	Favored induction chemoradiation <ul style="list-style-type: none"> • T1N1, T2-3N0-1 patients • No difference in perioperative mortality or complication rates • Survival was 49.4 months with CRT vs 24.0 months with surgery alone
Neoadjuvant chemoradiotherapy plus surgery versus surgery alone for oesophageal or junctional cancer (CROSS): long-term results of a randomized controlled trial ⁵⁶	Randomized controlled trial – long-term follow up for initial CROSS trial (2015)	366	Favored induction chemoradiation <ul style="list-style-type: none"> • T1N1, T2-3N0-1 patients • Confirmed findings from the initial CROSS trial remained true long-term • Adenocarcinoma survival: 43.2 months with CRT vs 27.1 months with surgery alone • Squamous cell carcinoma survival: 81.6 months with CRT vs 21.1 months with surgery alone
Phase III trial of trimodality therapy with cisplatin, fluorouracil, radiotherapy, and surgery compared with surgery alone for esophageal cancer: CALGB 9781 ⁵⁷	Randomized controlled trial (2008)	56	Favored induction chemoradiation <ul style="list-style-type: none"> • T2-3N0-1, T4N0 patients • No difference in treatment mortality or postoperative complication rates • Survival was 4.48 years with CRT vs 1.79 years with surgery alone
A comparison of multimodal therapy and surgery for esophageal adenocarcinoma ⁵⁸	Randomized controlled trial (1996)	102	Favored induction chemoradiation <ul style="list-style-type: none"> • Survival was 16 months with CRT vs 11 months with surgery alone based on intention to treat • Survival was 32 months with CRT vs 11 months with surgery alone based on treatment received

Data from Refs 54–58