Emergency Cancer Care

REVIEWS

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Lung cancer in the emergency department

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Abstract

Background Though decreasing in incidence and mortality in the USA, lung cancer remains the deadliest of all cancers. For a significant number of patients, the emergency department (ED) provides the first pivotal step in lung cancer prevention, diagnosis, and management. As screening recommendations and treatments advance, ED providers must stay up-to-date with the latest lung cancer recommendations. The purpose of this review is to identify the many ways that emergency providers may intersect with the disease spectrum of lung cancer and provide an updated array of knowledge regarding detection, management, complications, and interdisciplinary care.

Findings Lung cancer, encompassing 10–12% of cancer-related emergency department visits and a 66% admission rate, is the most fatal malignancy in both men and women. Most patients presenting to the ED have not seen a primary care provider or undergone screening. Ultimately, half of those with a new lung cancer diagnosis in the ED die within 1 year. Incidental findings on computed tomography are mostly benign, but emergency staff must be aware of the factors that make them high risk. Radiologic presentations range from asymptomatic nodules to diffuse metastatic lesions with predominately pulmonary symptoms, and some may present with extra-thoracic manifestations including neurologic. The short-term prognosis for ED lung cancer patients is worse than that of other malignancies. Screening offers new hope through earlier diagnosis but is underutilized which may be due to racial and socioeconomic disparities. New treatments provide optimism but lead to new complications, some long-term. Multidisciplinary care is essential, and emergency medicine is responsible for the disposition of patients to the appropriate specialists at inpatient and outpatient centers.

Conclusion ED providers are intimately involved in all aspects of lung cancer care. Risk factor modification and referral for lung cancer screening are opportunities to further enhance patient care. In addition, with the advent of newer cancer therapies, ED providers must stay vigilant and up-to-date with all aspects of lung cancer including disparities, staging, symptoms of disease, prognosis, treatment, and therapy-related complications.

Keywords Lung cancer, Emergency department, Lung cancer screening

Background

Emergency department (ED) providers encounter lung cancer patients across the continuum of their malignancy (Fig. 1). Lung cancer engenders a significant symptom burden especially affecting the respiratory system, and it is the leading cause of cancer-related deaths worldwide [1]. Tobacco use is the main risk factor for lung cancer, plus other comorbid conditions, such as cardiac disease and chronic obstructive pulmonary disease (COPD), that may bring the patient to the ED and generate an incidental lung cancer diagnosis [2–5]. Furthermore, 40 to 65% of patients with lung cancer will present to the ED at least

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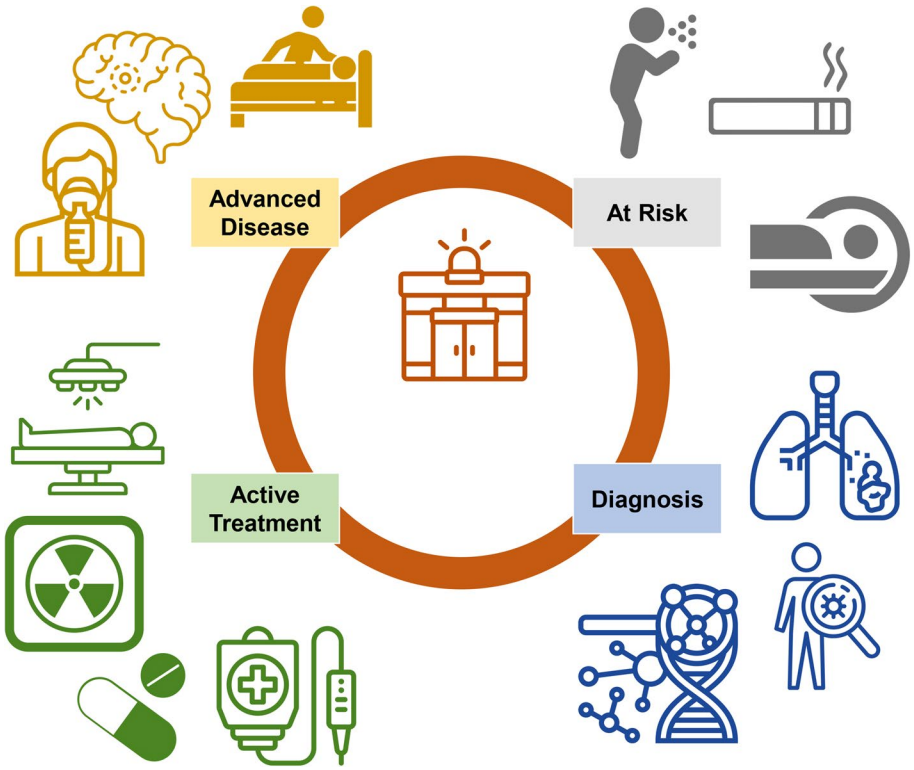

Fig. 1 Lung cancer and emergency department. ED providers may encounter lung cancer along the cancer continuum. The ED may play a role in identifying those at risk of developing lung cancer or referring for further screening those with concerning findings. Incidental lung cancer may present with or without symptoms, and appropriate staging and tissue diagnosis with molecular markers are crucial. Sequelae from active treatment may include pain, radiation-induced lung injury, or drug-related pneumonitis. In those with advanced or metastatic disease, stabilization, symptom management, and supportive care are often required

once during the course of their disease [6, 7]. Thus, it is imperative to recognize symptoms of a malignant disease as well as sequelae from various treatment modalities including chemotherapy, radiation, immunotherapy, and targeted therapies. This review highlights the epidemiology of lung cancer in the ED setting, the importance and potential role of the ED in prevention and screening, and the various clinical intersections of lung cancer and the ED.

Lung cancer: general information

Lung cancer is the most fatal cancer in both men and women with an estimated 2.2 million new cases and 1.8 million deaths per year worldwide [1]. It is a heterogeneous disease, and it can be classified as non-small cell lung cancer (NSCLC, 85%) or small cell lung cancer (SCLC, 15%). Adenocarcinoma followed by squamous cell carcinoma comprises the most common subtypes of NSCLC. One of the most important predictors of survival is cancer stage at the time of diagnosis, and although localized disease in NSCLC has a 5-year survival of 57.4%, distant metastatic disease 5-year survival is extremely poor at 5.2% [8]. Interestingly, mortality in the United States of America (USA) based on data from Surveillance, Epidemiology, and End Results Program fell sharply from 2013 to 2016, and analysis suggests both reduction in incidence and treatment advances likely explain the trend [9]. Tobacco cessation (to modify risk factor) and lung cancer screening (to detect disease early) are both opportunities where the ED could play a pivotal role. Furthermore, healthcare disparities in high-risk populations including Black individuals [10], those with human immunodeficiency virus (HIV) [11], and socially disadvantaged groups exist, and these groups are disproportionately affected by lung cancer [8]. These populations represent another avenue where the ED can optimize detection, encourage risk factor modification, and potentially facilitate further cancer care.

Lung cancer in the emergency department

Epidemiology

Common themes of ED and cancer care have been derived from the Nationwide Emergency Department Sample (NEDS) which is the largest administrative database. Cancer patients comprised 2.4 to 4.2% of the more than 100 million annual ED visits with a 60 to

65% admission rate noted in separate studies [12, 13]. Between 2006 and 2015, hospitals saw a fivefold increase in overall ED visits for oncologic treatment-related complications [14]. Risk factors for ED use include older age, non-White, male, urban-dwelling, low income, Medicaid/uninsured status, comorbidities, history of prior ED use, and end-of-life status [7, 15].

According to statewide and national healthcare utilization databases, lung cancer ranks near or at the top of reasons for cancer-related ED visits encompassing 10 to 12% of cancer-related ED visits, with 66% admission rates and 4.6% in-hospital mortality rates [7, 12, 13, 15–18]. These data reflect its high prevalence and significant morbidity and mortality [19]. Remarkably, in a 2021 single tertiary care center, in those with ED-diagnosed lung cancer, only 16% of patients had seen a primary care provider, and among the 84% eligible, only 6% had undergone screening [20]. Although small studies suggest new lung cancer workup in the ED is expedited, patients tend to have more advanced cancer stages upon presentation [20, 21]. Other sociodemographic features include low income, substance use, and disproportionately increased risk in Blacks (12.4% ED cohort vs 7.9% of the total cohort) [22]. In general, all of these features were associated with higher mortality [23].

Data representing the collective experience in the United States of America (USA) with lung cancer in the ED is limited. A 2022 review of unplanned care revealed that large national ED and hospital administrative databases do not effectively communicate with local–regional cancer registries [7]. The former is rich in International Classification of Diseases codes and demographics but short on cancer staging and treatment information while the latter fails to capture ED utilization data. Efforts to integrate data-rich electronic health records (EHR) with registries are underway but are in the early stages [24].

Literature from other countries provides valuable information about this population. Beckett and colleagues analyzed data from the UK National Lung Cancer Audit from 2006 to 2011 where 19% of patients with lung cancer were diagnosed in the ED. These patients had low socioeconomic status, advanced stage, worse performance status, and higher 1-year mortality [25]. In another study, Elliss-Brookes and associates using national United Kingdom (UK) databases from 2006 to 2008 revealed 39% of lung cancers were diagnosed in the ED and had substantially lower 1-year relative survival [26]. A French study using national databases evaluated 144,087 patients with their first hospitalization for lung cancer from 2016 to 2018; 3-month mortality was 19% and significantly higher for those older than 70, male, metastatic disease at diagnosis, and first hospitalization via the ED [27]. A 2017 systematic review of ED cancer diagnosis studies from developed countries (mostly the UK) found patients were more likely economically deprived, non-White, and non-curable and had lower survival than electively diagnosed counterparts, and lung cancer patients had the highest percentage (59%) of stage 4 presentation among all ED diagnosed cancers [28]. Similar findings regarding advanced disease and mortality in ED-diagnosed patients were seen in subsequent Australian and Canadian studies [29–31]. US studies show race and economic factors play a role in de novo ED lung cancer diagnosis and mortality [20–23]. In contrast, an analysis of 771 patients with advanced NSCLC in Japan where 13% were diagnosed in the ED showed that diagnosis following emergency admission was not an independent predictor of overall survival; however, the following were the independent predictors of overall survival: good performance status, epidermal growth factor receptor (EGFR) receptor status, stage IIIB, adenocarcinoma, and chemotherapy [32]. Interestingly, as the data for each country varies, so does the referral pattern for cancer care. For example, in Japan, patients suspected of lung cancer may directly contact their respiratory physician, whereas in the USA or UK, a referral is needed [33]. In other countries such as Belgium or France, health systems allow patients to choose their physicians directly. These studies all highlight that lung cancer patients present to the ED due to symptoms, often with advanced disease, and interestingly, results appear to vary in part related to the need for referral in different healthcare systems.

Symptoms

Patients with lung cancer can present to the ED for various reasons, and co-morbid conditions including diabetes, COPD, and vasculopathy often prompt ED visits [18, 34]. Hemoptysis, weight loss, loss of appetite, dyspnea, chest pain, fatigue, and cough were most commonly associated with lung cancer prior to diagnosis in a large population-based case–control study [35]. Neurological concerns (paralysis, seizures, headache, altered consciousness) are common extra-thoracic manifestations. Fujimoto and associates reported lung cancer patients presented in the ED with neurological complaints (23%) and respiratory issues (pleural effusions, 16%; pneumonia, 15%) [32]. In a UK cohort of 269 patients, the main reasons for ED consultation were respiratory symptoms (22.3%), fever (19.9%), and neurological issues (14.2%) [6]. Respiratory symptoms (31.5%) and neurological events (11.2%) represented the first and third most common reasons for ED visits in Japan, respectively [36].

Radiographic findings

ED patients get thoracic imaging that sometimes reveals unexpected lung lesions. In a single-center

cohort, patients who were ultimately diagnosed with lung cancer after ED imaging were more likely to have a concerning finding on computed tomography (CT) versus chest radiograph (CXR) (55.9% vs 36.8%, respectively), and CT was more likely to mention malignancy (OR 5.9, 95% CI 2.5–14.0) or metastasis (OR 30, 95% CI 7.1–12.1). In a few, findings on non-thoracic imaging ultimately led to the diagnosis [20]. Radiographic findings concerning malignancy include lung mass (greater than or equal to 30 mm), pleural effusion or thickening, mediastinal lymphadenopathy, endobronchial lesions, spiculated/lobular contours, post-obstructive pneumonia, ground glass lesions with a solid component, and growth relative to prior imaging [37]. The Fleischner Society provides guidelines for radiographic follow-up of incidental nodules based on patient risk factors, nodule size (< 6 mm low, > 8 mm high), solid or subsolid (ground glass vs part-solid), shape (rounded or irregular), location, number [38].

Prognosis

Prognosis of lung cancer patients presenting to the ED appears to be worse than other cancer patients. At a single cancer center ED, dyspnea, altered mental status, and diagnosis of lung cancer each independently predicted ICU admission and in-hospital death [39]. A retrospective study of ED intubated cancer patients evaluating 28-day mortality found the highest risk in those with lung cancer compared to non-lung cancer, with the highest being metastatic lung cancer (OR 7.17, 95% CI 2.14–24.01), followed by lung cancer patients without metastases (OR 5.89, 95% CI 1.48–23.36) [40]. A multicenter prospective cohort study of stage IV solid cancer patients in septic shock found lung cancer patients had the highest 28-day mortality at 48.1% [41]. Lastly, several large nationwide hospitalization studies have all found that among cancer patients with sepsis, lung cancer patients were the most likely to die [42–44]. These studies highlight the poor short-term prognosis of severe illness associated with lung cancer.

Additional comments

A thorough search was performed using PubMed, but the literature on the intersection of lung cancer and the ED is limited. We provide a summary of data to date, as well as highlighting the results from select studies. Cumulatively, these all provide valuable information, but variability in study design and/or selection bias can limit the results from the various studies. Further large-scale prospective and comparative trials are needed, and the assimilation of various cancer-related healthcare databases could also provide important information in the future.

Lung cancer screening

Early diagnosis and surgical resection are key to the cure and survival in lung cancer [45, 46]. In the past, CXR and sputum cytology were studied to screen cancer. Due to the overdiagnosis of more early indolent cancers that would never spread, 5-year survival artificially increased, but mortality (deaths per 100,000 per year), the true measure of intervention benefit, did not improve [47]. More recent studies centered around the use of low-dose computed tomography (LDCT). The National Lung Screening Trial (NLST) and the Nederlands-Leuvens Longkanker Screenings Onderzoek (NELSON) trials [48, 49] both provided crucial mortality reduction evidence to support the use of LDCT for lung cancer screening.

NLST

The NLST recruited 53,454 current or former smokers (who quit less than 15 years ago) with 30 pack-years, aged 55–74, randomized to either 3 annual screening CXRs or LDCTs then followed for 10 years. New nodules/masses ≥ 4 mm were referred for workup. The NLST LDCT used less than 25% of standard CT radiation dosage [50].

For the first time, mortality reduction (20%) from screening was shown. However, it was criticized for overdiagnosis of slow-growing lesions and high rates of false positives resulting in costly and invasive workups [51–54]. In 2014, the American College of Radiology created the Lung CT Screening Reporting & Data System (Lung-RADS®) that recommended increasing the "positive" nodule size threshold to 6 mm and applying evidence-based criteria to their management [55]. If these rules were applied to NLST data, there would have been a 50–75% decrease in false positives and fewer imaging and interventions [56]. Importantly, Lung-RADS® is meant for nodules found on screening, not for nodules found in practice.

NELSON trial

The Dutch-Belgian NELSON trial intentionally recruited a younger cohort with less intense smoking histories and randomized 13,195 men and 2,594 women to LDCT screening versus standard care. The screening timing was baseline, 1 year, 3 years, and 5.5 years. Unlike NLST, they designed a protocol to minimize repeat scans and invasive testing. NELSON used even lower doses of radiation [57]. Updated scanners and software allowed 3D volumetric nodule measurements. Three nodule categories (negative, indeterminate, and positive) were created based on size and other features [58]. Indeterminate nodules would be re-scanned within 3 months to determine volume doubling time. Positive and rapidly growing

indeterminate nodules would be referred for biopsy. Low-risk or slow-growing indeterminate nodules would be recorded but neither biopsied nor rescanned until the next scheduled screening [59]. The results showed a 24% mortality reduction in men and 33% in women; the small sample size made the results in women suggestive but not conclusive. False positives were only 1.2%, as opposed to 24% in NLST putting any doubts about the benefit of LDCT screening to rest [49, 60].

Additional studies

A 2013 review for the US Preventative Services Task Force (USPSTF) noted the NLST number needed to screen of 320 to prevent 1 death was better than that for breast and colon cancer screening [61]. USPSTF recommended that annual LDCT lung cancer screening be adopted, leading the Centers for Medicare and Medicaid Services (CMS) to approve LDCT screening as a preventative health benefit for all eligible Americans in 2015 [62, 63].

A 2015 National Cancer Institute study found that reducing the smoking requirement for screening to 20 pack-years would include more women and minorities [64]. Another study showed that reducing the screening age threshold to 50 would benefit Black people, who were underrepresented in the NSLT trial (4.4% of trial participants vs 12.3% US population), and were found to develop lung cancer at a younger age and decreased pack-year smoking history compared to the non-Hispanic White population [65]. Since 2012, the National Comprehensive Cancer Network (NCCN) advocated screening certain high-risk younger patients with less smoking history [66]. Due to the NELSON study, their current version 1.2023 guideline's high-risk category now includes anyone older than 50 with 20 + pack-years [67].

In 2021, the USPSTF broadened their previous 2013 recommendations for lung cancer screening with LDCT to include all current or former smokers aged 50–80 (previously 55–80) who quit less than 15 years ago and 20 pack-year (previously 30) smoking history. The broadened criteria were largely due to the NELSON trial and data from computer modeling studies by the Cancer Intervention and Surveillance Modeling Network, which found superior mortality benefits and life years gained under the new criteria. The expanded criteria would allow for a greater number of women and minority racial or ethnic groups who may develop lung cancer with lower smoking histories. CMS now covers LDCT screening for lung cancer at reduced age (50–77) and smoking (20 pack-years) criteria [68]. There have been calls to augment USPSTF recommendations even further by using risk or benefit model calculators. The American College of Chest Physicians' guidelines support the use of calculators with screening, for it may lead to greater equity across race and gender by identifying those most likely to benefit [69].

Barriers and disparities

Lung cancer screening with LDCT scanning can save lives. However, only 4% of those eligible are getting it [70]. Both patient and healthcare provider-related factors can affect screening. The adherence rates are higher in the northeast and lowest in the south [71]. Non-White race, younger age, and current smoking are predictors of non-adherence as is incomplete college education [72–74]. Interestingly, Black people with higher education and eligible for screening adhere more than their White counterparts [75]. Other potential barriers for patients include fear of positive test, radiation exposure, inconvenience, distrust of the medical system, and cost [76, 77]. Patients living in rural or remote areas may have difficulty accessing centers that provide screening and LDCT [78]. Barriers for healthcare providers may include unfamiliarity with screening guidelines, difficulty identifying eligible patients for screening, access to a specialist to address abnormal or equivocal results, skepticism about the benefits, and lack of time or personnel for follow-up [77].

Many have advocated for changes in lung cancer screening programs to promote health equity. A myriad of factors can result in disparities in screening including racial and ethnic background, access to smoking cessation interventions, use of preventive services, and geographical barriers [8]. Marketing for tobacco directed at young adults, minorities (Blacks and non-White Hispanics), and women have directly impacted trends for lung cancer incidence and mortality [1, 79, 80]. Furthermore, screening guidelines center around tobacco use, but 25% of lung cancer cases worldwide are not associated with tobacco use. Globally, lung cancer in never-smokers inherently contributes to gender disparities, as women never-smokers have a high incidence of adenocarcinoma along with unique risk factors for lung cancer [81].

Role of ED

The role of the ED in lung cancer risk factor modification and screening has garnered attention. EDs can champion smoking cessation programs, initiate referrals, and open conversations [82–84]. EDs have helped enroll patients in colon, prostate, breast, and cervical cancer screening [85–92]. It has been postulated that EDs see many patients who are eligible for lung cancer screening, but often they do not have a primary care provider. A large National Health Interview Survey sample found 25% of patients eligible for lung cancer

screening who were non-adherent had visited an ED in the prior year, thus representing an opportunity for outreach [93]. At a single safety net center, though most patients had insurance and access to primary care, no ED patient eligible for lung cancer screening had enrolled, and only 0.06% were aware of lung cancer screening [94]. Comparatively, this is much lower than for colon or breast cancer screening, and it identifies the need for education of patients and providers about lung cancer screening. One effort through California-based EDs using trained associates led to 50% of the intervention group getting screenings within 30 days, including lung cancer [95]. Similar recruitment studies also used trained research associates, implying that dedicated non-clinical staff can successfully identify and motivate patients, relieving the time burden otherwise imposed on busy EDs. Partnerships with local screening efforts will likely result in success. Finally, the ED may be able to play a role in addressing healthcare disparities in lung cancer. Additional counseling on tobacco cessation or referral to preventative services for at-risk individuals can significantly impact risk factors and disease. These grassroots efforts emphasize a valuable opportunity, and translating this into widespread ED-based recruitment is a topic ripe for future research.

Clinical workup and treatment

Lung cancer staging

Staging allows for an unanimously understood categorization system for the treatment and progression of cancer. The American Joint Committee on Cancer (AJCC) incorporates the staging system for both NSCLC and SCLC, and the 8th Edition Lung Cancer Stage Classification is the current internationally recognized system [96] (Fig. 2). Small cell lung cancer (SCLC) is categorized into limited stage and extensive stage. The limited stage incorporates local disease in one radiation field which includes ipsilateral mediastinal or supraclavicular nodal metastases while the extensive stage consists of contralateral or distant metastases and inclusion of any malignant pleural or pericardial effusion [97].

Lung cancer staging may be performed radiographically with multiple modalities (Fig. 3). Measuring tumor size with chest CT remains the first-line standard [98]. Due to its high sensitivity (77.4% CI 65.3–86.1) and specificity (90.1% CI 85.3–93.5) for mediastinal nodal metastasis detection according to the Cochrane Review of 2014, ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography (PET)/CT can be useful in differentiating the nodal stage [99]. FDG PET/CT imaging better visualizes distant extra-thoracic metastases with extremely high sensitivity and specificity [100]. PET/CT also reduces the number of

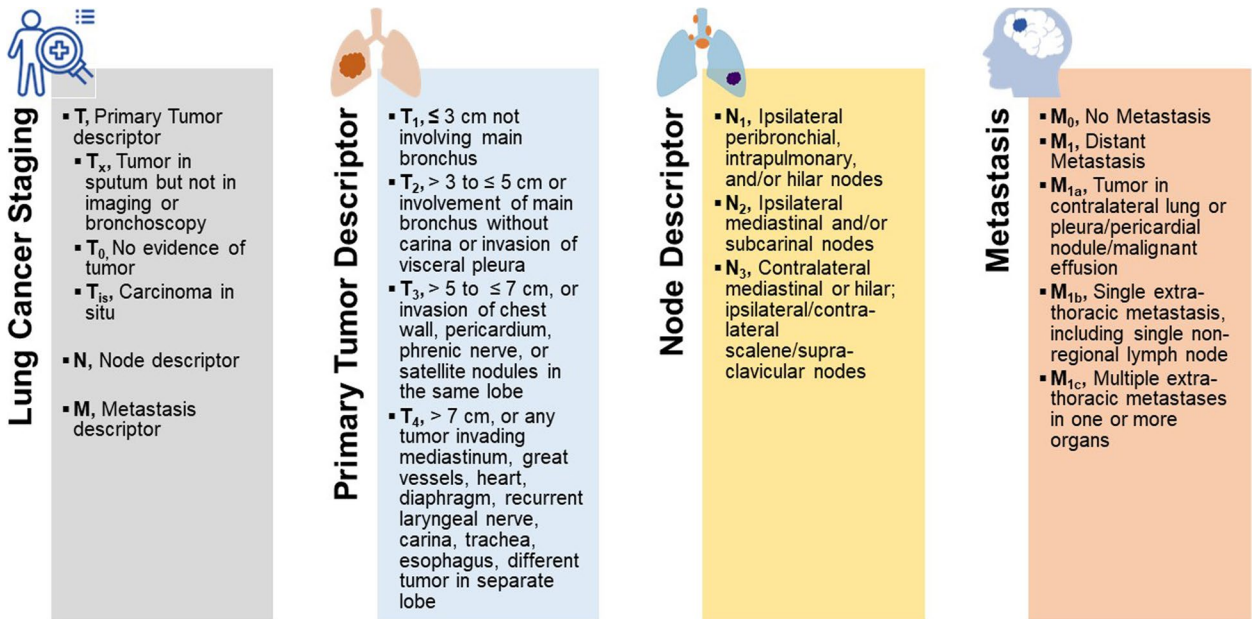

Fig. 2 Lung cancer staging. T refers to the primary tumor size and ranges from no primary tumor (T_0) to a tumor more than 7 cm in the greatest dimension (T_4). N describes regional lymph node involvement and broadly includes no regional lymph node involvement (N_0) to contralateral mediastinal, hilar, scalene, or supraclavicular or ipsilateral scalene or supraclavicular lymph node metastasis (N_3). The presence of distant metastasis is categorized as M_0 (no distant metastasis) and M_1 (distant metastasis). M_1 is further delineated into subclasses where M_{1a} consists of secondary nodules in the contralateral lung, pericardium, or pleura, with or without the presence of a malignant pleural or pericardial effusion. M_{1b} involves one extra-thoracic metastasis, and M_{1c} accounts for multiple extra-thoracic metastases. Information derived from [96]

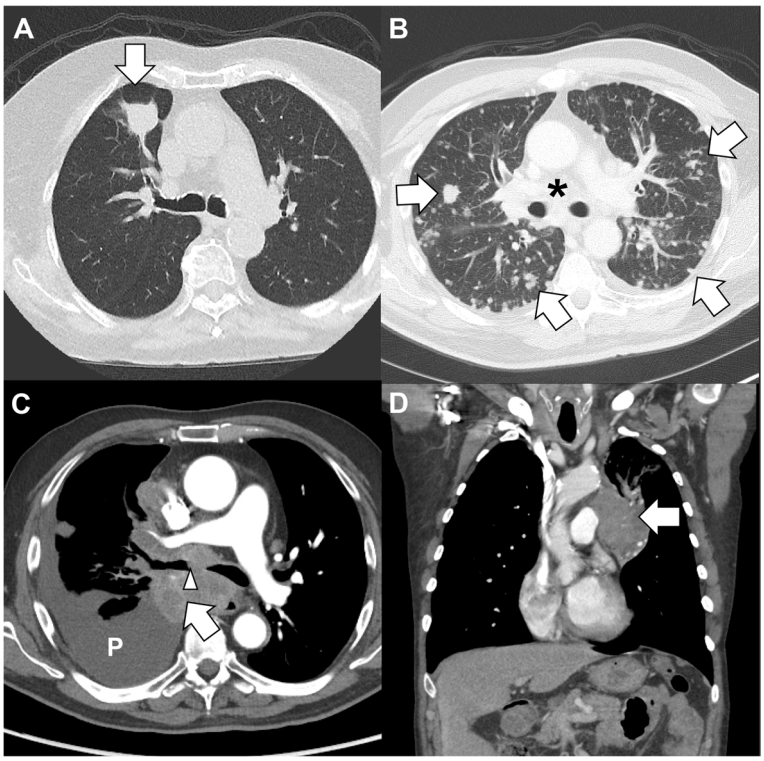

Fig. 3 ED presentations of lung cancer. **A** Elderly woman who is a never-smoker presents with cough and fatigue. Imaging revealed a 1.8-cm right upper lobe lung nodule (arrow) without hilar or mediastinal lymphadenopathy. She underwent lobectomy (stage IA, pT1c pN0 cM0). **B** Middle-aged man with metastatic adenocarcinoma of the lung was sent for anemia and fatigue. Imaging reveals innumerable pulmonary nodules (arrows) with mediastinal, bilateral hilar, and subcarinal lymphadenopathy (asterisk). **C** Middle-aged man presents with hemoptysis and dyspnea. Imaging reveals endobronchial disease in the right main bronchus at the level of the carina (arrowhead), moderate pleural effusion (P), and lung mass (arrow). **D** Middle-aged man with chronic myeloid leukemia on imatinib transferred for airway exacerbation. Imaging incidentally revealed a left upper lobe mass (arrow) contiguous with mediastinal and hilar lymphadenopathy consistent with primary lung malignancy

unnecessary thoracotomies by detecting increased mediastinal nodal metastasis detection and improves sensitivity in preoperative lung cancer staging [101].

After excluding the presence of distant metastases, clinicians must determine the extent of intrathoracic nodal metastasis. With primary peripheral pulmonary tumors < 3 cm with a negative FDG PET/CT, mediastinal sampling may not be necessary prior to surgical intervention [102]. Despite radiographic imaging, accurate invasive mediastinal staging must be obtained in order to prevent harm from understaging or overstaging of disease [103]. Depending on the availability of specialists, mediastinal lymph nodes may be sampled by interventional pulmonologists or radiologists, surgeons, or gastroenterologists. Procedures performed include endobronchial ultrasound with transbronchial needle aspiration (EBUS-TBNA), endoscopic ultrasound (EUS), CT-guided biopsy, mediastinoscopy, and mediastinotomy. Although mediastinoscopy remains the procedure with the highest negative predictive value for nodal disease, EBUS-TBNA is a minimally invasive procedure that has almost equivalent diagnostic accuracy and therefore is the standard of care when lymph nodes are accessible by this route [104].

Multi-disciplinary care

Cancer care is multi-disciplinary. Screening, staging, diagnosing, and treating lung cancer involve many different specialties including primary care, thoracic surgery, oncology, pulmonology, emergency medicine, radiology, interventional radiology, palliative care, pathology, specialty nursing, and radiation oncology [105]. Although much of cancer staging and the correlated treatment has been established in guidelines, many alternatives and adjunctive therapy can be added by multidisciplinary teams. In 2010, the incorporation of palliative care teams in patients with metastatic NSCLC improved quality of life and survival [106]. Case-by-case, a multidisciplinary team can add treatment options including management of endobronchial disease, enrollment in clinical trials, addition of radiotherapy, and management of complications related to therapy and disease progression [107].

Treatment

Treatment of lung cancer is currently limited by the clinical stage and performance status of the patient. Video-assisted thoracoscopic surgery (VATS) or thoracotomy is the standard of care for patients with stage I or II lung cancer (147). Those with stage I cancer and contraindications to surgery may benefit from stereotactic body radiotherapy (SBRT) as an alternative [108]. More advanced nodal staging shifts the focus of treatment to chemotherapy and immunotherapy. In NSCLC, first-line chemotherapy with a platinum-based doublet includes carboplatin or cisplatin in combination with taxanes, gemcitabine, vinorelbine, or pemetrexed [109]. The addition of bevacizumab, a monoclonal antibody against vascular endothelin growth factor (VEGF), is sometimes added with initial cycles of chemotherapy [110]. In those with non-squamous variants, cisplatin with pemetrexed had increased survival when compared with cisplatin and gemcitabine [111]. After 4–6 cycle induction with cisplatin/pemetrexed, maintenance pemetrexed has been shown to improve progression-free and overall survival [112]. Alternatively, SCLC treatment involves platinum therapy plus etoposide as the first-line chemotherapy [113].

Cancer immunotherapy activates the immune system to aid in the detection and destruction of tumor cells. Immune checkpoint inhibitors (ICI) are now commonplace for the treatment of lung cancer and include programmed cell death ligand 1 (PD-L1) inhibitors like atezolizumab or durvalumab and programmed cell death 1 (PD-1) inhibitors like nivolumab and pembrolizumab [114, 115]. Chemotherapy and immunotherapy combinations in SCLC have shown increased progression-free survival [116, 117].

When developing a treatment plan, tumor biomarkers are sent to aid the selection of immunotherapy. Most recently, advanced immunohistochemical and molecular profiling can assist with targeted therapy for lung cancer. Actionable mutations have been identified (KRAS, EGFR, ALK, ROS1, and others), and subsequent specific molecular inhibitors have been developed (sotorasib, osimertinib, ceritinib, crizotinib) for the treatment of these cancers [118].

Newer evidence has led to a discussion of metastases as a spectrum from limited cancer to diffusely metastatic. In the center of the spectrum is an oligometastatic disease which is characterized by less than 3–5 metastases [119]. In this rare subset, multidisciplinary surgical and radiation ablative adjunct therapies in combination with chemotherapy and immunotherapy may prolong survival.

Emergency physicians are familiar with managing airway emergencies and addressing pulmonary symptoms in critically ill patients, but symptom palliation in terminal disease requires a different perspective. Although heroic measures may not be indicated, ameliorating symptoms of breathlessness and dyspnea are paramount. The sensation of dyspnea can be multifactorial and not necessarily related to hypoxia. The American Society of Clinical Oncology guidelines recommend a hierarchical approach to dyspnea in advanced cancer including palliative care consultation, non-pharmacologic interventions (fanning directed toward the cheek, supplemental oxygen, high-flow oxygen, non-invasive positive pressure ventilation), and pharmacologic interventions (systemic opioids, short-acting benzodiazepines, systemic corticosteroids, bronchodilators) [120].

Other presentations of lung cancer

Manifestations of disease

Intrathoracic disease results from tumor involvement or spread including extrinsic compression of the tracheobronchial tree, malignant airway obstruction or endobronchial disease, vasculature (superior vena cava syndrome), diaphragmatic or vocal cord dysfunction, and pleural effusion. These may contribute to symptoms of cough, hemoptysis, chest pain, and dyspnea. Extrathoracic manifestations of disease depend on the area of involvement and if metastatic can involve the central nervous system, bone, adrenal glands, or liver (Fig. 4). Imaging reveals the lesions and helps interventionalists plan treatment.

Therapy-related sequelae

Medical, surgical, and radiation treatments of lung cancer have the risk of therapy-related injury. Postoperative surgical complications, though rare, include atelectasis, infection, pulmonary embolism, nerve injury, respiratory failure, bronchopleural fistula, hemothorax, and cardiac arrhythmias [121]. Radiation can lead to acute pneumonitis, chronic pulmonary fibrosis, dermatitis, esophagitis, radiation myelitis, and secondary malignancy [122].

ICI treatments cause autoimmune-like complications called immune-related adverse events (irAEs). irAEs can affect any organ system and may cause thyroid dysfunction, diabetes, dermatitis, myocarditis, myositis, pneumonitis (Fig. 4), colitis, hypophysitis, hepatitis, myasthenia gravis, and many others [123]. When present, irAEs frequently affect multiple organ systems. Management of irAEs may include discontinuing ICI therapy temporarily or permanently and systemic corticosteroid administration. Most cases improve or resolve with steroid treatment, but steroid-refractory cases may be treated with other immunosuppressive agents [124].

Both radiation and ICI sequelae can be long-term and affect patients long after the cancer is cured.

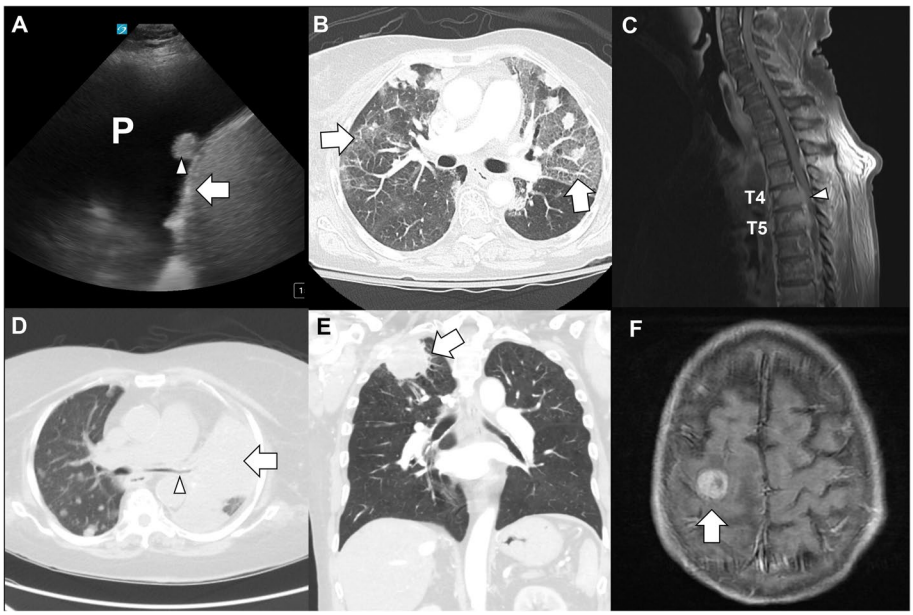

Fig. 4 Manifestations of disease. **A** Ultrasound image of suspected malignant pleural effusion (P) with nodule (arrowhead) on the diaphragm (arrow). **B** Lung cancer on immune checkpoint inhibitor with multiple nodules and ground glass infiltrates (arrows, left > right) concerning immune-mediated pneumonitis. **C** Extensive small cell lung cancer with metastatic disease to spine (T4, T5) and extension of epidural tumor (arrowhead). **D** Left lung mass (arrow) with extrinsic compression (arrowhead) of the left mainstem bronchus. **E** Elderly aged man with a right upper lobe lung mass (arrow) in the apex consistent with a Pancoast tumor (mass that originates in the superior sulcus of the lung apex which may present atypically with shoulder pain, Horner syndrome, and superior vena cava syndrome) presenting with right shoulder pain and cough. **F** Middle-aged man with metastatic poorly differentiated lung cancer presents to the emergency center after fall. Imaging reveals a 1.8-cm right posterior frontal mass (arrow) with local edema

Conclusion

ED providers must be aware of various lung cancer presentations. These include referring newly discovered or suspected cases to prompt a workup for definitive diagnosis. In addition, they must be able to discern symptoms of malignant disease from therapy-related sequelae. As the landscape of anti-neoplastic treatments evolves and includes immune-mediated and targeted therapies, patients with lung cancer may survive longer. The ED has a potentially unique role in identifying those at risk of lung cancer especially in underserved populations and referring them to cancer prevention (smoking cessation) and screening programs. Therefore, with a knowledge base regarding the newest screening guidelines, current imaging findings, updated cancer staging, medical and surgical treatment options, multidisciplinary care, and therapy-related sequelae in the community, the ED becomes a key mediator of multidisciplinary care for patients at risk for and living with lung cancer. As lung cancer detection and treatment advances, so the importance of the ED in lung cancer evolves as well.

Abbreviations

AJCC	American Joint Committee on Cancer
CMS	Centers for Medicare and Medicaid Services
CT	Computed tomography
EBUS-TBNA	Endobronchial ultrasound with transbronchial needle aspiration
EGFR	Epidermal growth factor receptor
EUS	Endoscopic ultrasound
FDG	18F-Fluorodeoxyglucose
HIV	Human immunodeficiency virus
ICI	Immune checkpoint inhibitors
irAEs	Immune-related adverse events
LDCT	Low-dose computed tomography
Lung-RADS®	Lung CT Screening Reporting & Data System
NCCN	National Comprehensive Cancer Network
NEDS	Nationwide Emergency Department Sample
NELSON	Nederlands-Leuvens Longkanker Screenings Onderzoek
NLST	National Lung Screening Trial
NSCLC	Non-small cell lung cancer
PCP	Primary care provider
PD-1	Programmed cell death 1
PD-L1	Programmed cell death ligand 1
PET/CT	Positron emission tomography/CT
SBRT	Stereotactic body radiotherapy
SCLC	Small cell lung cancer
USPSTF	US Preventative Services Task Force
VATS	Video-assisted thoracoscopic surgery
VEGF	Vascular endothelin growth factor

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Authors' contributions

JW, SF, and MS participated in the conception and design, acquisition of the data/articles for inclusion and the search strategy, drafting of the article, critical revision of intellectual content, and final approval of the version to be published. All authors analyzed the literature, interpreted the data, and

analyzed further implications. The authors drafted and revised the publication. The authors read and approved the final manuscript.

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References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021;71(3):209–49.
2. Kino A, Boiselle PM, Raptopoulos V, Hatabu H. Lung cancer detected in patients presenting to the emergency department studies for suspected pulmonary embolism on computed tomography pulmonary angiography. Eur J Radiol. 2006;58(1):119–23.
3. Hall WB, Truitt SG, Scheunemann LP, Shah SA, Rivera MP, Parker LA, et al. The prevalence of clinically relevant incidental findings on chest computed tomographic angiograms ordered to diagnose pulmonary embolism. Arch Intern Med. 2009;169(21):1961–5.
4. Lehman SJ, Abbara S, Cury RC, Nagurney JT, Hsu J, Goela A, et al. Significance of cardiac computed tomography incidental findings in acute chest pain. Am J Med. 2009;122(6):543–9.
5. Scholtz JE, Lu MT, Hedgire S, Meyersohn NM, Oliveira GR, Prabhakar AM, et al. Incidental pulmonary nodules in emergent coronary CT angiography for suspected acute coronary syndrome: impact of revised 2017 Fleischner Society Guidelines. J Cardiovasc Comput Tomogr. 2018;12(1):28–33.
6. Gorham J, Ameye L, Berghmans T, Sculier JP, Meert AP. The lung cancer patient at the emergency department: a three-year retrospective study. Lung Cancer. 2013;80(2):203–8.
7. Lash RS, Hong AS, Bell JF, Reed SC, Pettit N. Recognizing the emergency department's role in oncologic care: a review of the literature on unplanned acute care. Emerg Cancer Care. 2022;1(1):6.
8. Haddad DN, Sandler KL, Henderson LM, Rivera MP, Aldrich MC. Disparities in lung cancer screening: a review. Ann Am Thorac Soc. 2020;17(4):399–405.
9. Howlader N, Forjaz G, Mooradian MJ, Meza R, Kong CY, Cronin KA, et al. The effect of advances in lung-cancer treatment on population mortality. N Engl J Med. 2020;383(7):640–9.
10. DeSantis CE, Siegel RL, Sauer AG, Miller KD, Fedewa SA, Alcaraz KI, et al. Cancer statistics for African Americans, 2016: progress and opportunities in reducing racial disparities. CA Cancer J Clin. 2016;66(4):290–308.
11. Winstone TA, Man SFP, Hull M, Montaner JS, Sin DD. Epidemic of lung cancer in patients with HIV infection. Chest. 2013;143(2):305–14.
12. Rivera DR, Gallicchio L, Brown J, Liu B, Kyriacou DN, Shelburne N. Trends in adult cancer-related emergency department utilization: an analysis of data from the nationwide emergency department sample. JAMA Oncol. 2017;3(10): e172450.
13. Qian AS, Qiao EM, Nalawade V, Voora RS, Kotha NV, Dameff C, et al. Impact of underlying malignancy on emergency department utilization and outcomes. Cancer Med. 2021;10(24):9129–38.
14. Jairam V, Lee V, Park HS, Thomas CR Jr, Melnick ER, Gross CP, et al. Treatment-related complications of systemic therapy and radiotherapy. JAMA Oncol. 2019;5(7):1028–35.
15. Scholer AJ, Mahmoud OM, Ghosh D, Schwartzman J, Farooq M, Cabrera J, et al. Improving cancer patient emergency room utilization: a New Jersey state assessment. Cancer Epidemiol. 2017;51:15–22.
16. Mayer DK, Travers D, Wyss A, Leak A, Waller A. Why do patients with cancer visit emergency departments? Results of a 2008 population study in North Carolina. J Clin Oncol. 2011;29(19):2683–8.
17. Lash RS, Bell JF, Bold RJ, Joseph JG, Cress RD, Wun T, et al. Emergency department use by recently diagnosed cancer patients in California. J Community Support Oncol. 2017;15(2):95–102.
18. Nene RV, Brennan JJ, Castillo EM, Tran P, Hsia RY, Coyne CJ. Cancer-related emergency department visits: comparing characteristics and outcomes. West J Emerg Med. 2021;22(5):1117–23.
19. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer statistics, 2022. CA Cancer J Clin. 2022;72(1):7–33.
20. Pettit N, Cinbat M. Retrospective review of patients with lung cancer identified in the emergency department. Am J Emerg Med. 2021;50:394–8.
21. Dollar KR, Neutel BS, Hsia DW. Access to care limits lung cancer screening eligibility in an urban safety net hospital. J Prim Care Community Health. 2022;13:21501319221128700.
22. Pettit N, Sarmiento E, Kline J. Disparities in outcomes among patients diagnosed with cancer in proximity to an emergency department visit. Sci Rep. 2022;12(1):10667.
23. Su CT, Chau V, Halmos B, Shah CD, Gucalp RA, Packer SH, et al. Impact of primary care access on mortality of lung cancer patients in an underserved community. Am J Clin Oncol. 2019;42(3):298–303.
24. Thompson CA, Jin A, Luft HS, Lichtensztajn DY, Allen L, Liang SY, et al. Population-based registry linkages to improve validity of electronic health record-based cancer research. Cancer Epidemiol Biomarkers Prev. 2020;29(4):796–806.
25. Beckett P, Tata LJ, Hubbard RB. Risk factors and survival outcome for non-elective referral in non-small cell lung cancer patients–analysis based on the National Lung Cancer Audit. Lung Cancer. 2014;83(3):396–400.
26. Elliss-Brookes L, McPhail S, Ives A, Greenslade M, Shelton J, Hiom S, et al. Routes to diagnosis for cancer - determining the patient journey using multiple routine data sets. Br J Cancer. 2012;107(8):1220–6.
27. Goussault H, Gendarme S, Assie JB, Jung C, Epaud S, Algans C, et al. Risk factors for early mortality of lung cancer patients in France: a nationwide analysis. Cancer Med. 2022;11:5025.
28. Zhou Y, Abel GA, Hamilton W, Pritchard-Jones K, Gross CP, Walter FM, et al. Diagnosis of cancer as an emergency: a critical review of current evidence. Nat Rev Clin Oncol. 2017;14(1):45–56.
29. Yap S, Goldsbury D, Yap ML, Yuill S, Rankin N, Weber M, et al. Patterns of care and emergency presentations for people with non-small cell lung cancer in New South Wales, Australia: a population-based study. Lung Cancer. 2018;122:171–9.
30. Niranjan N, Sriram KB. New lung cancer diagnosis after emergency department presentation in a tertiary hospital: patient characteristics and outcomes. Hosp Pract (1995). 2022;50(5):356–60.
31. Suhail A, Crocker CE, Das B, Payne JI, Manos D. Initial presentation of lung cancer in the emergency department: a descriptive analysis. CMAJ Open. 2019;7(1):E117–23.
32. Fujimoto D, Shimizu R, Morimoto T, Kato R, Sato Y, Kogo M, et al. Analysis of advanced lung cancer patients diagnosed following emergency admission. Eur Respir J. 2015;45(4):1098–107.
33. Meert AP, Sculier JP, Berghmans T. Lung cancer diagnosis in the emergency department. Eur Respir J. 2015;45(4):867–8.
34. Caterino JM, Adler D, Durham DD, Yeung SJ, Hudson MF, Bastani A, et al. Analysis of diagnoses, symptoms, medications, and admissions among patients with cancer presenting to emergency departments. JAMA Netw Open. 2019;2(3): e190979.
35. Hamilton W, Peters TJ, Round A, Sharp D. What are the clinical features of lung cancer before the diagnosis is made? A population based case-control study Thorax. 2005;60(12):1059–65.

36. Kotajima F, Kobayashi K, Sakaguchi H, Nemoto M. Lung cancer patients frequently visit the emergency room for cancer-related and -unrelated issues. Mol Clin Oncol. 2014;2(2):322–6.
37. Herzog C, Burgener FA. Lungs. In: Burgener FA, Meyers SP, Herzog C, Zaunbauer W, editors. Differential diagnosis in computed tomography. 2nd ed. Stuttgart: Thieme; 2012. p. 592–629.
38. MacMahon H, Naidich DP, Goo JM, Lee KS, Leung ANC, Mayo JR, et al. Guidelines for management of incidental pulmonary nodules detected on ct images: from the Fleischner Society 2017. Radiology. 2017;284(1):228–43.
39. Elsayem AF, Merriman KW, Gonzalez CE, Yeung SC, Chaftari PS, Reyes-Gibby C, et al. Presenting symptoms in the emergency department as predictors of intensive care unit admissions and hospital mortality in a comprehensive cancer center. J Oncol Pract. 2016;12(5):e554–63.
40. Shin SH, Lee H, Kang HK, Park JH. Twenty-eight-day mortality in lung cancer patients with metastasis who initiated mechanical ventilation in the emergency department. Sci Rep. 2019;9(1):4941.
41. Kim YJ, Kang J, Kim MJ, Ryoo SM, Kang GH, Shin TG, et al. Development and validation of the VitaL CLASS score to predict mortality in stage IV solid cancer patients with septic shock in the emergency department: a multi-center, prospective cohort study. BMC Med. 2020;18(1):390.
42. Liu MA, Bakow BR, Hsu TC, Chen JY, Su KY, Asiedu EK, et al. Temporal trends in sepsis incidence and mortality in patients with cancer in the US population. Am J Crit Care. 2021;30(4):e71–9.
43. Sharma A, Nguyen P, Taha M, Soubani AO. Sepsis hospitalizations with versus without cancer epidemiology, outcomes, and trends in nationwide analysis from 2008 to 2017. Am J Clin Oncol-Canc. 2021;44(10):505–11.
44. Hensley MK, Donnelly JP, Carlton EF, Prescott HC. Epidemiology and outcomes of cancer-related versus non-cancer-related sepsis hospitalizations. Crit Care Med. 2019;47(10):1310–6.
45. Flehinger BJ, Kimmel M, Melamed MR. The effect of surgical treatment on survival from early lung cancer. Implications for screening. Chest. 1992;101(4):1013–8.
46. Nesbitt JC, Putnam JB Jr, Walsh GL, Roth JA, Mountain CF. Survival in early-stage non-small cell lung cancer. Ann Thorac Surg. 1995;60(2):466–72.
47. Eddy DM. Screening for lung cancer. Ann Intern Med. 1989;111(3):232–7.
48. National Lung Screening Trial Research T, Aberle DR, Adams AM, Berg CD, Black WC, Clapp JD, et al. Reduced lung-cancer mortality with low-dose computed tomographic screening. N Engl J Med. 2011;365(5):395–409.
49. de Koning HJ, van der Aalst CM, de Jong PA, Scholten ET, Nackaerts K, Heuvelmans MA, et al. Reduced lung-cancer mortality with volume CT screening in a randomized trial. N Engl J Med. 2020;382(6):503–13.
50. Larke FJ, Kruger RL, Cagnon CH, Flynn MJ, McNitt-Gray MM, Wu X, et al. Estimated radiation dose associated with low-dose chest CT of average-size participants in the National Lung Screening Trial. AJR Am J Roentgenol. 2011;197(5):1165–9.
51. Bach PB, Mirkin JN, Oliver TK, Azzoli CG, Berry DA, Brawley OW, et al. Benefits and harms of CT screening for lung cancer: a systematic review. JAMA. 2012;307(22):2418–29.
52. Silvestri GA. Screening for lung cancer: it works, but does it really work? Ann Intern Med. 2011;155(8):537–9.
53. Finigan JH, Kern JA. Lung cancer screening: past, present and future. Clin Chest Med. 2013;34(3):365–71.
54. Patz EF Jr, Goodman PC, Bepler G. Screening for lung cancer. N Engl J Med. 2000;343(22):1627–33.
55. American College of Radiology. Lung CT Screening Reporting & Data System (Lung-RADS). 2014. Available from: https://www.acr.org/Clinical-Resources/Reporting-and-Data-Systems/Lung-Rads. [Cited June 29, 2020].
56. Pinsky PF, Gierada DS, Black W, Munden R, Nath H, Aberle D, et al. Performance of Lung-RADS in the National Lung Screening Trial: a retrospective assessment. Ann Intern Med. 2015;162(7):485–91.
57. Horeweg N, van Rosmalen J, Heuvelmans MA, van der Aalst CM, Vliegenthart R, Scholten ET, et al. Lung cancer probability in patients with CT-detected pulmonary nodules: a prespecified analysis of data from the NELSON trial of low-dose CT screening. Lancet Oncol. 2014;15(12):1332–41.
58. Xu DM, Gietema H, de Koning H, Vernhout R, Nackaerts K, Prokop M, et al. Nodule management protocol of the NELSON randomised lung cancer screening trial. Lung Cancer. 2006;54(2):177–84.
59. van Iersel CA, de Koning HJ, Draisma G, Mali WP, Scholten ET, Nackaerts K, et al. Risk-based selection from the general population in a screening trial: selection criteria, recruitment and power for the Dutch-Belgian randomised lung cancer multi-slice CT screening trial (NELSON). Int J Cancer. 2007;120(4):868–74.
60. Duffy SW, Field JK. Mortality reduction with low-dose CT screening for lung cancer. N Engl J Med. 2020;382(6):572–3.
61. Humphrey LL, Deffebach M, Pappas M, Baumann C, Artis K, Mitchell JP, et al. Screening for lung cancer with low-dose computed tomography: a systematic review to update the US Preventive services task force recommendation. Ann Intern Med. 2013;159(6):411–20.
62. Centers for Medicare and Medicaid Services. Decision memo for screening for lung cancer with low dose computed tomography (LCDT) (CAG-00439N): Centers for Medicare & Medicaid Services. 2015. Available from: https://www.cms.gov/medicare-coverage-database/details/nca-decision-memo.aspx?NCAId=274. [Cited June 28, 2020].
63. Moyer VA, Force USPST. Screening for lung cancer: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med. 2014;160(5):330–8.
64. Pinsky PF, Kramer BS. Lung cancer risk and demographic characteristics of current 20–29 pack-year smokers: implications for screening. J Natl Cancer Inst. 2015;107(11):djv226.
65. Annangi S, Nutalapati S, Foreman MG, Pillai R, Flenaugh EL. Potential racial disparities using current lung cancer screening guidelines. J Racial Ethn Health Disparities. 2019;6(1):22–6.
66. Wood DE, Eapen GA, Ettinger DS, Hou L, Jackman D, Kazerooni E, et al. Lung cancer screening. J Natl Compr Canc Netw. 2012;10(2):240–65.
67. National Comprehensive Cancer Network. NCCN clinical practice guidelines in oncology: lung cancer screening (version 1.2023). 2022 [Available from: https://www.nccn.org/professionals/physician_gls/pdf/lung_screening.pdf.
68. Centers for Medicare and Medicaid Services. Screening for lung cancer with low dose computed tomography (LDCT) (CAG-00439R). Centers for Medicare & Medicaid Services; 2022 [Available from: https://www.cms.gov/medicare-coverage-database/view/ncacal-decision-memo.aspx?proposed=N&ncaid=304.
69. Mazzone PJ, Silvestri GA, Souter LH, Caverly TJ, Kanne JP, Katki HA, et al. Screening for lung cancer: CHEST guideline and expert panel report. Chest. 2021;160(5):e427–94.
70. Jemal A, Fedewa SA. Lung cancer screening with low-dose computed tomography in the United States-2010 to 2015. JAMA Oncol. 2017;3(9):1278–81.
71. Fedewa SA, Kazerooni EA, Studts JL, Smith RA, Bandi P, Sauer AG, et al. State variation in low-dose computed tomography scanning for lung cancer screening in the United States. J Natl Cancer Inst. 2021;113(8):1044–52.
72. Lam ACL, Aggarwal R, Cheung S, Stewart EL, Darling G, Lam S, et al. Predictors of participant nonadherence in lung cancer screening programs: a systematic review and meta-analysis. Lung Cancer. 2020;146:134–44.
73. Kunitomo Y, Bade B, Gunderson CG, Akgun KM, Brackett A, Cain H, et al. Racial differences in adherence to lung cancer screening follow-up: a systematic review and meta-analysis. Chest. 2022;161(1):266–75.
74. Lopez-Olivo MA, Maki KG, Choi NJ, Hoffman RM, Shih YT, Lowenstein LM, et al. Patient adherence to screening for lung cancer in the US: a systematic review and meta-analysis. JAMA Netw Open. 2020;3(11):e2025102.
75. Barta JA, Shusted CS, Ruane B, Pimpinelli M, McIntire RK, Zeigler-Johnson C, et al. Racial differences in lung cancer screening beliefs and screening adherence. Clin Lung Cancer. 2021;22(6):570–8.
76. Lei F, Lee E. Barriers to lung cancer screening with low-dose computed tomography. Oncol Nurs Forum. 2019;46(2):E60–71.
77. Wang GX, Baggett TP, Pandharipande PV, Park ER, Percac-Lima S, Shepard JO, et al. Barriers to lung cancer screening engagement from the patient and provider perspective. Radiology. 2019;290(2):278–87.
78. Eberth JM, Bozorgi P, Lebron LM, Bills SE, Hazlett LJ, Carlos RC, et al. Geographic availability of low-dose computed tomography for lung cancer screening in the United States, 2017. Prev Chronic Dis. 2018;15:E119.

79. Primack BA, Bost JE, Land SR, Fine MJ. Volume of tobacco advertising in African American markets: systematic review and meta-analysis. Public Health Rep. 2007;122(5):607–15.
80. MacRosty CR, Rivera MP. Lung cancer in women: a modern epidemic. Clin Chest Med. 2020;41(1):53–65.
81. Sun S, Schiller JH, Gazdar AF. Lung cancer in never smokers–a different disease. Nat Rev Cancer. 2007;7(10):778–90.
82. Bernstein SL, Boudreaux ED, Cydulka RK, Rhodes KV, Lettman NA, Almeida SL, et al. Tobacco control interventions in the emergency department: a joint statement of emergency medicine organizations. Ann Emerg Med. 2006;48(4):e417–26.
83. Bernstein SL, D'Onofrio G, Rosner J, O'Malley S, Makuch R, Busch S, et al. Successful tobacco dependence treatment in low-income emergency department patients: a randomized trial. Ann Emerg Med. 2015;66(2):140–7.
84. Lemhoefer C, Rabe GL, Wellmann J, Bernstein SL, Cheung KW, McCarthy WJ, et al. Emergency department-initiated tobacco control: update of a systematic review and meta-analysis of randomized controlled trials. Prev Chronic Dis. 2017;14:E89.
85. Hogness CG, Engelstad LP, Linck LM, Schorr KA. Cervical cancer screening in an urban emergency department. Ann Emerg Med. 1992;21(8):933–9.
86 Mandelblatt J, Freeman H, Winczewski D, Cagney K, Williams S, Trowers R, et al. Implementation of a breast and cervical cancer screening program in a public hospital emergency department. Cancer Control Center of Harlem. Ann Emerg Med. 1996;28(5):493–8.
87. Cummings GE, Francescutti LH, Predy G, Cummings G. Health promotion and disease prevention in the emergency department: a feasibility study. CJEM. 2006;8(2):100–5.
88. Zun LS, Downey L. Adult health screening and referral in the emergency department. South Med J. 2006;99(9):940–8.
89. Trowbridge R, King R, Byun R, Dabakis M, Talati A, Turocy J, et al. 321: facilitating colon-rectal cancer screening among emergency department patients and visitors. Ann Emerg Med. 2010;56(3):S104–5.
90. Hatcher J, Brandford A, Aroh A, Adegboyega A, Combs B, Schoenberg N. Abstract C65: promoting colorectal cancer screening in rural Appalachian emergency department. Cancer Epidemiol Biomarkers Prev. 2017;26(2_Supplement):C65.
91. Adler D, Abar B, Wood N, Bonham A. An intervention to increase uptake of cervical cancer screening among emergency department patients: results of a randomized pilot study. J Emerg Med. 2019;57(6):836–43.
92. Abar B, Dalawari P, Ogedegbe C, Santoro-Terray L, Adler D, Bradley K. Identifying cancer screening adherence in the emergency department utilizing research associates. J Emerg Med. 2020;59(6):894–9.
93. Miles RC, Flores EJ, Lopez DB, Sohn YJ, Gillis EA, Lehman CD, et al. Leveraging emergency department encounters to improve cancer screening adherence. J Am Coll Radiol. 2021;18(6):834–40.
94. Pettit N, Ceppa D, Monahan P. Low rates of lung and colorectal cancer screening uptake among a safety-net emergency department population. West J Emerg Med. 2022;23(5):739–45.
95. Coyne C, Nene R, Brennan J, Castillo E, Vilke G. 373 cancer screening education in the emergency department: an interventional study. Ann Emerg Med. 2021;78(4):S149–50.
96. Detterbeck FC, Boffa DJ, Kim AW, Tanoue LT. The eighth edition lung cancer stage classification. Chest. 2017;151(1):193–203.
97. Carter BW, Glisson BS, Truong MT, Erasmus JJ. Small cell lung carcinoma: staging, imaging, and treatment considerations. Radiographics. 2014;34(6):1707–21.
98. El-Sherief AH, Lau CT, Carter BW, Wu CC. Staging lung cancer: regional lymph node classification. Radiol Clin North Am. 2018;56(3):399–409.
99. Schmidt-Hansen M, Baldwin DR, Hasler E, Zamora J, Abraira V, Roque IFM. PET-CT for assessing mediastinal lymph node involvement in patients with suspected resectable non-small cell lung cancer. Cochrane Database Syst Rev. 2014;2014(11):CD009519.
100. Kandathil A, Kay FU, Butt YM, Wachsmann JW, Subramaniam RM. Role of FDG PET/CT in the eighth edition of TNM staging of non-small cell lung cancer. Radiographics. 2018;38(7):2134–49.
101. Fischer B, Lassen U, Mortensen J, Larsen S, Loft A, Bertelsen A, et al. Preoperative staging of lung cancer with combined PET-CT. N Engl J Med. 2009;361(1):32–9.
102. De Leyn P, Dooms C, Kuzdzal J, Lardinois D, Passlick B, Rami-Porta R, et al. Revised ESTS guidelines for preoperative mediastinal lymph node staging for non-small-cell lung cancer. Eur J Cardiothorac Surg. 2014;45(5):787–98.
103. Farjah F, Tanner NT. Mediastinal staging for lung cancer. Chest. 2021;160(4):1552–9.
104. Torre M, Reda M, Musso V, Danuzzo F, Mohamed S, Conforti S. Diagnostic accuracy of endobronchial ultrasound-transbronchial needle aspiration (EBUS-TBNA) for mediastinal lymph node staging of lung cancer. Mediastinum. 2021;5:15.
105. Berghmans T, Lievens Y, Aapro M, Baird AM, Beishon M, Calabrese F, et al. European Cancer Organisation Essential Requirements for Quality Cancer Care (ERQCC): lung cancer. Lung Cancer. 2020;150:221–39.
106. Temel JS, Greer JA, Muzikansky A, Gallagher ER, Admane S, Jackson VA, et al. Early palliative care for patients with metastatic non-small-cell lung cancer. N Engl J Med. 2010;363(8):733–42.
107. Popat S, Navani N, Kerr KM, Smit EF, Batchelor TJP, Van Schil P, et al. Navigating diagnostic and treatment decisions in non-small cell lung cancer: expert commentary on the multidisciplinary team approach. Oncologist. 2021;26(2):e306–15.
108. Thai AA, Solomon BJ, Sequist LV, Gainor JF, Heist RS. Lung cancer. Lancet. 2021;398(10299):535–54.
109. Duma N, Santana-Davila R, Molina JR. Non-small cell lung cancer: epidemiology, screening, diagnosis, and treatment. Mayo Clin Proc. 2019;94(8):1623–40.
110. Sandler A, Gray R, Perry MC, Brahmer J, Schiller JH, Dowlati A, et al. Paclitaxel-carboplatin alone or with bevacizumab for non-small-cell lung cancer. N Engl J Med. 2006;355(24):2542–50.
111. Scagliotti GV, Parikh P, von Pawel J, Biesma B, Vansteenkiste J, Manegold C, et al. Phase III study comparing cisplatin plus gemcitabine with cisplatin plus pemetrexed in chemotherapy-naive patients with advanced-stage non-small-cell lung cancer. J Clin Oncol. 2008;26(21):3543–51.
112. Paz-Ares LG, de Marinis F, Dediu M, Thomas M, Pujol JL, Bidoli P, et al. PARAMOUNT: final overall survival results of the phase III study of maintenance pemetrexed versus placebo immediately after induction treatment with pemetrexed plus cisplatin for advanced nonsquamous non-small-cell lung cancer. J Clin Oncol. 2013;31(23):2895–902.
113. Tariq S, Kim SY, de Monteiro Oliveira Novaes J, Cheng H. Update 2021: management of small cell lung cancer. Lung. 2021;199(6):579–87.
114. Brahmer JR, Govindan R, Anders RA, Antonia SJ, Sagorsky S, Davies MJ, et al. The Society for Immunotherapy of Cancer consensus statement on immunotherapy for the treatment of non-small cell lung cancer (NSCLC). J Immunother Cancer. 2018;6(1):75.
115. Gandhi L, Rodriguez-Abreu D, Gadgeel S, Esteban E, Felip E, De Angelis F, et al. Pembrolizumab plus chemotherapy in metastatic non-small-cell lung cancer. N Engl J Med. 2018;378(22):2078–92.
116. Arbour KC, Riely GJ. Systemic therapy for locally advanced and metastatic non-small cell lung cancer: a review. JAMA. 2019;322(8):764–74.
117. Horn L, Mansfield AS, Szczesna A, Havel L, Krzakowski M, Hochmair MJ, et al. First-line atezolizumab plus chemotherapy in extensive-stage small-cell lung cancer. N Engl J Med. 2018;379(23):2220–9.
118. Majeed U, Manochakian R, Zhao Y, Lou Y. Targeted therapy in advanced non-small cell lung cancer: current advances and future trends. J Hematol Oncol. 2021;14(1):108.
119 Eichhorn F, Winter H. How to handle oligometastatic disease in nonsmall cell lung cancer. Eur Respir Rev. 2021;30(159):200234.
120. Hui D, Bohlke K, Bao T, Campbell TC, Coyne PJ, Currow DC, et al. Management of dyspnea in advanced cancer: ASCO Guideline. J Clin Oncol. 2021;39(12):1389–411.
121. Agostini PJ, Lugg ST, Adams K, Smith T, Kalkat MS, Rajesh PB, et al. Risk factors and short-term outcomes of postoperative pulmonary complications after VATS lobectomy. J Cardiothorac Surg. 2018;13(1):28.
122. Spiro SG, Douse J, Read C, Janes S. Complications of lung cancer treatment. Semin Respir Crit Care Med. 2008;29(3):302–17.
123 Haanen J, Obeid M, Spain L, Carbonnel F, Wang Y, Robert C, et al. Management of toxicities from immunotherapy: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. Ann Oncol. 2022;33(12):1217-38.
124. Thompson JA, Schneider BJ, Brahmer J, Andrews S, Armand P, Bhatia S, et al. NCCN Guidelines insights: management of immunotherapy-related toxicities, version 1.2020. J Natl Compr Canc Netw. 2020;18(3):230–41.