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Using a Dedicated Interventional Pulmonology Practice Decreases Wait Time Before Treatment Initiation for New Lung Cancer Diagnoses

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Abstract

Purpose While there is significant mortality and morbidity with lung cancer, early stage diagnoses carry a better prognosis. As lung cancer screening programs increase with more pulmonary nodules detected, expediting definitive treatment initiation for newly diagnosed patients is imperative. The objective of our analysis was to determine if the use of a dedicated interventional pulmonology practice decreases time delay from new diagnosis of lung cancer or metastatic disease to the chest to treatment initiation.

Methods Retrospective chart analysis was done of 87 consecutive patients with a new diagnosis of primary lung cancer or metastatic cancer to the chest from our interventional pulmonology procedures. Demographic information and time intervals from abnormal imaging to procedure and to treatment initiation were recorded.

Results Patients were older (mean age 69) and former or current smokers (72%). A median of 27 days (1–127 days) passed from our diagnostic biopsy to treatment initiation. A median of 53 total days (2–449 days) passed from abnormal imaging to definitive treatment. Endobronchial ultrasound-guided transbronchial needle aspiration was the most commonly used diagnostic procedure (59%), with non-small cell lung cancer the majority diagnosis (64%). For surgical patients, all biopsy-negative lymph nodes from our procedures were cancer-free at surgical excision.

Conclusions Compared to prior reports from international and United States cohorts, obtaining a tissue biopsy diagnosis through a gatekeeper interventional pulmonology practice decreases median delay from abnormal imaging to treatment initiation. This finding has the potential to positively impact patient outcomes and requires further evaluation.

Keywords Interventional pulmonology · Bronchoscopy · Lung cancer · Chest imaging · Wait time

Abbreviations

Cryo	Flexible cryoprobe biopsy and tissue extraction
EBUS-TBNA	Endobronchial ultrasound-guided biopsy transbronchial needle aspiration
ECH	El Camino Hospital
EMN	Electromagnetic navigation-guided biopsy
IP	Interventional pulmonology
NSCLC	Non-small cell lung cancer
PAMF	Palo Alto Medical Foundation
SHN	Sutter Health Network

Introduction

Lung cancer is the second-most commonly diagnosed cancer in the United States and third in the world as well as a leading cause of cancer-related deaths [1]. Five-year survival rate at diagnosis for all stages of lung cancer is

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17.7% [1], worse compared to other common cancers. However, early stage, or localized disease, carries a much better 5-year survival of 55.2% [1]. Thus, it is imperative to identify opportunities for early detection.

The National Lung Screening Trial demonstrated that screening high-risk patients with annual low-dose CT chest scans significantly reduced lung cancer mortality [2] and increased early-stage lung cancer detection with a decrease in advanced stage lung cancer incidence [3, 4]. As a result, significant efforts are underway to implement lung cancer screening protocols with low-dose CT scans [5]. While lung cancer screening remains a complex process, recent estimates place the number of Americans eligible for screening between seven to nine million [6, 7].

While historical incidence rates for pulmonary nodules in the US remained steady for many decades at 150,000 per year [8], a more recent evaluation using electronic health records and natural language processing increased the incidence tenfold to over 1.5 million nodules detected per year [9]. With so many new nodules found, healthcare providers are challenged by how to appropriately triage these results. Standardized protocols stratifying risk for cancer based on nodule characteristics exist [10], yet physician adherence to them varies substantially [11].

A significant number of these newly found nodules will ultimately undergo a diagnostic biopsy. The clinical importance of quickly obtaining a tissue diagnosis has been shown as patients with delay from imaging to diagnosis of more than four months have significantly worse survival [12] and may miss the opportunity to undergo a curative procedure [13]. Unfortunately, the time interval between initial presentation, tissue diagnosis, and treatment initiation varies quite widely, with prospective studies reporting a median time from onset of first symptoms until treatment initiation between 138 and 189 days [14, 15]. Furthermore, a recent review of wait times for cancer surgery in the US showed an increase in the median time from diagnosis to treatment [16].

Interventional pulmonologists are often the first sub-specialty physicians to evaluate patients with imaging findings concerning for lung cancer and may be able to utilize different modalities to expedite diagnosis and treatment initiation. To address this possibility, we retrospectively reviewed all patients seen in our interventional pulmonology (IP) clinic which we diagnosed with primary lung cancer or metastatic cancer to the thorax. We examined the time from our diagnostic procedure until definitive treatment initiation. We hypothesized that obtaining a tissue biopsy diagnosis through a gatekeeper IP practice would facilitate referral for definitive treatment by decreasing wait time between these two time points, with potentially positive implications for patient staging and survival.

Methods

Practice Pattern

All patients were seen at our Mountain View, California IP clinic of the Palo Alto Medical Foundation (PAMF), which is one of five medical foundations comprising the Sutter Health Network (SHN). A Northern Californian-based not-for-profit comprehensive healthcare system, SHN includes physician organizations, acute care hospitals, surgery centers, medical research facilities, and training programs. SHN partners with more than 12,000 doctors to care for more than 3 million people in its healthcare system. Approximately, 700,000 patients are seen at PAMF, which cares for patients focused in Alameda, San Mateo, Santa Clara, and Santa Cruz counties of Northern California. As the only IP clinic in SHN, our practice received referrals from physicians within SHN and from others outside this healthcare system.

All IP procedures were performed by IP fellows (BSB, MP, ES) from the joint University of California, San Francisco-PAMF fellowship under direct attending supervision (GK) at El Camino Hospital (ECH) in Mountain View, California. ECH is a non-profit hospital with 300 beds and approximately 20,000 inpatient visits and 150,000 outpatient visits in 2017. Procedures were performed in our two dedicated, fully equipped IP suites.

Study Cohort

Retrospective chart review was performed of all patients consecutively presenting to our IP clinic for evaluation of a new imaging abnormality from July 1, 2015 to December 31, 2016 who underwent a diagnostic IP procedure resulting in a new primary lung cancer or metastatic cancer to the thorax diagnosis. All patients seen and referred directly for surgery, transthoracic needle aspiration biopsy, or followed with surveillance imaging were excluded. 90 patients were identified with three patients subsequently excluded who were lost to follow-up, leaving 87 patients for further analysis.

Demographic data, including age, sex, race/ethnicity, and smoking status were obtained. Additionally, charts were reviewed for the following event dates: initial abnormal imaging study, initial evaluation in IP clinic, IP procedure, post-procedure presentation to consultative physician (thoracic surgery, medical or radiation oncology, or palliative care), and definitive treatment initiation (surgery, treatment with chemotherapy, radiation, biological, hormonal, or immunological therapy, or initiation of palliative/hospice care). The types of interventional procedure

performed were also recorded. All pathological diagnoses from interventional procedures, subsequent surgeries where applicable, and discussion with all consultative physicians were also recorded.

The study protocol was reviewed and approved by the institutional review boards of both PAMF and ECH.

Statistical Analysis

Data were analyzed with descriptive statistics to characterize the sample and median days between the stages of diagnosis and definitive treatment initiation. We used quantile regression to compare the median days between the stages of diagnosis to definitive treatment initiation by treatment type received, while controlling for patient age to control for potential differences in time to various stages. Data were analyzed with STATA, version 14.2 (College Station, TX).

Results

Demographics

From July 2015 to December 2016, 87 patients underwent an IP procedure leading to a new diagnosis of primary lung cancer or metastatic thoracic disease (Table 1). At procedure, patients were generally older (mean age 69, range 26–91) and former or current smokers (72%). The majority were female (57%) and Caucasian (77%).

Table 1 Demographic characteristics

Characteristic	Mean (range)
Age at IP procedure	69 (26–91)
	N (%)
Race/ethnicity	
White	67 (77)
Asian	13 (15)
Indian	4 (5)
Black	2 (2)
Hispanic	1 (1)
Sex	
Female	50 (57)
Male	37 (43)
Smoking status	
Current	6 (7)
Former	57 (65)
Never	24 (38)

Data are expressed as mean (range) or number (%)

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Age-Adjusted Median Wait Times

Median time from initial abnormal chest imaging to IP procedure was 17 days (1–322 days) (Table 2), with patients eventually undergoing surgery waiting longest. After our diagnostic procedure, a median of 8 days (1–68 days) elapsed before further evaluation with a consultative physician. A median of 27 days (1–127 days) elapsed from diagnostic IP procedure before definitive treatment initiation, with hospice, palliative care, or surveillance (three patients total, 2 carcinoid diagnoses, 1 metastatic renal cell carcinoma diagnosis) initiated quickest. For all patients, a median of 53 days (2–449 days) passed from abnormal imaging to definitive treatment. Our quantile regression models showed no significant differences in age-adjusted median time through the diagnostic stages by treatment type. Patients who received chemotherapy and radiation had significantly longer median times between their IP procedure and meeting with a consulting physician ($p < 0.05$).

Interventional Pulmonology Procedures

115 total IP procedures were performed on 87 patients (Table 3). Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) (59%) was used most frequently, followed by electromagnetic navigation bronchoscopy (ENB) (31%), and flexible cryoprobe biopsy and tissue extraction (Cryo) (10%) (Table 3). Multiple modalities were often used together (31% combined vs 69% single modality).

Pathology and Staging

Multiple cancers types were diagnosed by our IP procedures, with non-small cell lung cancer and pulmonary adenocarcinoma and squamous cell carcinoma comprising the majority (64%) (Table 4). Of the 21 patients undergoing surgery, a high concordance was seen between our initial pathological diagnosis and that obtained at surgery. Four diagnoses were further clarified as pulmonary adenocarcinoma [initially diagnosed as atypical cells (two), neoplastic cells (one), or non-small cell lung cancer (one)] and one diagnosis was changed from squamous cell to large cell carcinoma. Additionally, all biopsy-negative lymph nodes from our IP procedures were cancer-free after surgical excision. With this information, we compiled final staging for all patients with newly diagnosed NSCLC (Table 5).

Discussion

Lung cancer is a devastating disease with both significant morbidity and mortality. To the best of our knowledge, we present the first study looking at the impact of a dedicated IP

Table 2 Age-adjusted median wait times from initial abnormal chest imaging to interventional pulmonology procedure and to definitive treatment

Treatment	Number	Image to IP procedure	IP procedure to consultant	IP procedure to definitive treatment	Total wait time
		Median days (range)			
Surgery	21	26.6 (9–322)	11.1 (1–63)	32.1 (1–127)	72 (30–449)
Chemotherapy	23	17.5 (3–268)	9.7 (1–25)	27.2 (5–61)	50 (12–294)
Radiation	17	16.0 (1–74)	7.8 (1–47)	34.2 (1–70)	58 (2–132)
Chemotherapy and radiation	9	19.5 (6–71)	14.5 (1–29)*	42.5 (4–49)	59 (15–113)
Other therapies	11	14.2 (2–183)	5.9 (1–195)	20.3 (8–41)	31 (21–216)
Hospice/palliative care	3	10.4 (14–22)	1.9 (1–11)	4.2 (2–27)	24 (21–41)
Surveillance	3	15.4 (8–22)	8.1 (1–13)	8.5 (1–13)	27 (9–28)
Total	87	17 (1–322)	8 (1–68)	27 (1–127)	53 (2–449)

Consultant = median days to first visit with thoracic surgery, medical oncology, radiation oncology, or palliative care after IP procedure

Other therapies = biological (9), hormonal (1), and immunotherapy (1)

Surveillance = Two patients with diagnoses of carcinoid, one patient with a diagnosis of metastatic renal cell carcinoma

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*$p < 0.05$

Table 3 Interventional pulmonology procedures used to establish a new cancer diagnosis

EBUS procedures	*N* (%)	EMN procedures	*N* (%)	Cryo procedures	*N* (%)
Alone	41 (36)	Alone	15 (13)	Alone	4 (3)
With EMN	20 (17)	With EBUS	20 (17)	With EBUS	5 (4)
With Cryo	5 (4)	With Cryo	1 (1)	With EMN	1 (1)
With EMN and Cryo	1 (1)	With EBUS and Cryo	1 (1)	With EBUS and EMN	1 (1)
Total	67 (58)	Total	37 (32)	Total	11 (10)

Data are expressed as number (%)

EBUS endobronchial ultrasound-guided biopsy, *EMN* electromagnetic navigation-guided biopsy, *Cryo* flexible cryoprobe biopsy and tissue extraction

practice on wait times between tissue diagnosis and definitive treatment initiation for new lung cancer diagnoses. We found a decrease in delay from abnormal imaging date to tissue diagnosis and from tissue diagnosis to definitive treatment in our patients compared to published reports from international groups and a similar value compared to other US groups.

In our dedicated IP practice, patients waited an age-adjusted median of 17 days (1–322 days) from imaging study until biopsy diagnosis, with an additional median of 27 days (1–127 days) passing before treatment initiation (Table 2). The total delay from image abnormality to definitive treatment was a median of 53 days (2–449 days). Multiple international studies have shown a wide range of delays as patients traverse their healthcare systems. 108 NSCLC lung cancer patients undergoing curative-intent surgery in Nova Scotia, Canada waited a median of 141 and 107 days between detection and initiation of chemotherapy and surgery, respectively [17]. Similarly, 256 patients in Montreal had a median delay of 208 days from initial physician contact or symptoms onset and surgery [18]. Another study of 231 British Columbia patients reported a median delay of 65.5 days from lung cancer detection on imaging to radiation and/or chemotherapy treatment [19]. A smaller prospective study of 52 patients in Ontario reported a median delay of 138 days from symptom development to treatment [14], while a Swedish study of 134 patients reported a median time of 189 days [15] and a Finish study of 132 patients reported a delay of 112 days [20].

Reported US wait times have been generally lower, but much of the data comes from the Veterans Affairs Health Care System [21, 22], which relies on a different medical system than what is available to most Americans. A single site review of 129 patients reported a median delay from

Table 4 Pathological diagnosis from interventional pulmonology procedures and after final review with consultative services

Pathology	IP	Final
Adenocarcinoma	38 (44)	47 (54)
Squamous cell carcinoma	11 (13)	11 (13)
Non-small cell lung cancer	13 (15)	8 (9)
Metastatic cancer	6 (7)	6 (7)
Small cell cancer	5 (6)	6 (7)
Atypical cells	3 (3)	0
Neuroendocrine tumor	3 (3)	2 (2)
Carcinoid	2 (2)	3 (3)
Neoplastic cells	2 (2)	0
Other	4 (5)	4 (5)

Final = final diagnosis after review of tissue biopsies with all consultative services after surgical resection

Data are expressed as number (%)

Other includes mantle cell lymphoma (1), mesothelioma (1), PEComa (perivascular epithelioid cell tumor) (1), and Sarcoma (1)

Metastatic disease origins include colon primary (1), gynecologic primary (1), high-grade sarcoma (1), renal cell carcinoma (1), thyroid (1), and urothelial carcinoma (1)

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Table 5 Stages for newly diagnosed non-small cell lung cancers

Stage	Adenocarcinoma	Squamous cell carcinoma	NSCLC
IA	11	2	0
IB	3	1	0
IIA	2	2	0
IIB	1	0	0
IIIA	5	4	1
IIIB	4	1	1
IV	21	1	6
Total	47	11	8

Data are expressed as number

NSCLC Non-small cell lung cancer

an initial suspicion of cancer to treatment of 84 days [21]. A larger review of 2372 veterans diagnosed with lung cancer at 127 VA medical centers revealed median delays from initial radiographic suspicion to first pulmonary visit, diagnosis, and treatment of 18, 33, and 63 days, respectively [22], slightly worse than our overall data. In 2006, Medicare beneficiaries experienced a median delay of 24 days between diagnosis of lung cancer and initiation of chemotherapy [23]. A single-center review of 482 patients from the University of Texas Southwestern Medical Center revealed a median delay of 59 days from imaging to treatment, with differences between public (76 days) and private (45 days) hospitals [24]. Again, compared to these historical controls, our median time intervals are lower.

Reducing delays to lung cancer treatment initiation prevents disease progression and avoids missed opportunities for possible curative treatment. Multiple prior studies of patients undergoing planning PET-CT or interval CT scans before radiotherapy for NSCLC have shown interscan disease progression [13, 25–27]. Patients may progress to incurable disease [13], have a significant change in planned therapy from curative to palliative [25], be upstaged and/or develop distant metastases [26, 27]. Time to diagnosis alone also impacts mortality in a small study evaluating 83 patients, with those waiting more than 4 months having a statistically significant worse survival [12].

Because timely movement towards lung cancer diagnosis and treatment initiation impacts both treatment options and survival, multiple societies developed recommendations to optimize this process. A recent comparison of lung cancer guidelines in the four most populous Nordic countries, Sweden, Denmark, Finland, and Norway, recommended timing from initial referral to diagnostic workup completion be within 26–30 days with an additional 7–15 days before treatment initiation [28]. In contrast, the British Thoracic Society [29], the National Comprehensive Cancer Network [30], and the American College of Chest Physicians [31, 32] currently do not propose timelines for evaluating NSCLC. Instead, they emphasize that diagnostic and treatment strategies be decided in a multidisciplinary setting and on an individual basis with the overall goal to deliver care timely and efficiently [31].

We used EBUS-TBNA in the majority of our IP procedures for a tissue diagnosis (59%, Table 3). For mediastinal nodal staging in patients with suspected or proven NSCLC, it is recommended as the initial procedure over surgical staging [33, 34] because it has been shown to reduce time to treatment decision [35] and is ~ 90–95% accurate [36]. In our 21 surgical patients, all negative EBUS-TBNA lymph nodes were also cancer-free at surgery. While EBUS is widely used by many practitioners, debate exists over the minimum number of procedures needed for proficiency [37] as data suggests continued improvement with additional procedures [38]. Similarly, the diagnostic yield of ENB (used in ~ 30% of our procedures) also appears to increase with operator experience [39]. While controversy still exists over how best to implement quality standards for these procedures, there may be a specific role for utilizing trained IP physicians experienced in these modalities to help decrease diagnostic wait times from these important, yet elective, procedures.

While our study is limited in size, preventing our ability to detect statistically significant differences by treatment type in the examined time intervals, the overall patient population is similar to many prior published works as per the above discussion. Our retrospective analysis of a

single-center experience may not represent a diverse racial, ethnic, or socioeconomic group, and thus may not be generalizable to other populations. Since we looked at only one institution, it is also possible that our improved wait times reflect efficiencies developed within our system over time, making it challenging to directly apply or compare our improved results against historical studies. Because all patients were referred for IP clinic consultation, we were unable to capture initial symptom presentation data, necessitating using the abnormal imaging date as our initial time point. It will be of interest to determine if initial symptom presentation date can be captured in future studies to further clarify the timeline. However, we included all newly diagnosed patients, regardless of stage, in our analysis, preventing potential bias in excluding patients who may present to medical care differently and on a different timeline. We also present, for the first time, the role of a dedicated IP practice in moving patients from diagnosis to definitive treatment and describe the potential beneficial impact we have during this process.

In conclusion, this study presents, for the first time, the positive impact of a well-established, dedicated IP practice on the timely diagnosis and treatment of lung cancer. Specifically, we report shorter delays from abnormal imaging to lung cancer diagnosis and from diagnosis to definitive treatment with the use of a gatekeeper IP practice compared to historical controls. With an increased incidence of pulmonary nodules and further implementation of lung cancer screening programs likely in the future, identifying additional options for efficiently moving patients towards treatment is essential. Established IP programs offer a wide array of diagnostic tools, and based on this single-center study, may facilitate patient care from first abnormal imaging study to definitive therapy. Future multicenter studies may further substantiate the benefit of IP programs in expediting the care of patients with malignant thoracic disease.

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Compliance with Ethical Standards

Conflict of interest All authors report no disclosures and no conflicts of interest.

References

1. National Cancer Institute Surveillance, Epidemiology, and end results program. http://seer.cancer.gov/statfacts/html/lungb.html. Accessed 18 Mar 2018
2. National Lung Screening Trial Research Team, Aberle DR, Adams AM, Berg CD, Black WC, Clapp JD, Fagerstrom RM, Gareen IF, Gatsonis C, Marcus PM, Sicks JD (2011) Reduced lung-cancer mortality with low-dose computed tomographic screening. N Engl J Med 365(5):395–409
3. National Lung Screening Trial Research Team, Church TR, Black WC, Aberle DR, Berg CD, Clingan KL, Duan F, Fagerstrom RM, Gareen IF, Gierada DS, Jones GC, Mahon I, Marcus PM, Sicks JD, Jain A, Baum S (2013) Results of initial low-dose computed tomographic screening for lung cancer. N Engl J Med 368(21):1980–1991
4. Aberle DR, DeMello S, Berg CD, Black WC, Brewer B, Church TR, Clingan KL, Duan F, Fagerstrom RM, Gareen IF, Gatsonis CA, Gierada DS, Jain A, Jones GC, Mahon I, Marcus PM, Rathmell JM, Sicks J (2013) National Lung Screening Trial Research Team. Results of the two incidence screenings in the National Lung Screening Trial. N Engl J Med 369(10):920–931
5. Eberth JM (2015) Lung cancer screening with low-dose CT in the United States. J Am Coll Radiol 12(12 Pt B):1395–1402
6. Sox HC (2011) Better evidence about screening for lung cancer. N Engl J Med 365(5):455–457
7. Doria-Rose VP, White MC, Klabunde CN et al (2012) Use of lung cancer screening tests in the United States: results from the 2010 National Health Interview Survey. Cancer Epidemiol Biomarkers Prev 21(7):1049–1059
8. Tanner NT, Silvestri GA (2015) What's in a Number? When it comes to pulmonary nodules, it's all about the number. Am J Respir Crit Care Med 192(10):1149–1150
9. Gould MK, Tang T, Liu IL, Lee J, Zheng C, Danforth KN, Kosco AE, Di Fiore JL, Suh DE (2015) Recent trends in the identification of incidental pulmonary nodules. Am J Respir Crit Care Med 192(10):1208–1214
10. Gould MK, Donington J, Lynch WR, Mazzone PJ, Midthun DE, Naidich DP, Wiener RS (2013) Evaluation of individuals with pulmonary nodules: when is it lung cancer? Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest 143(5 Suppl):e93S–e120S
11. Tanner NT, Aggarwal J, Gould MK, Kearney P, Diette G, Vachani A, Fang KC, Silvestri GA (2015) Management of pulmonary nodules by community pulmonologists: a multicenter observational study. Chest 148(6):1405–1414
12. Kanashiki M, Satoh H, Ishikawa H, Yamashita YT, Ohtsuka M, Sekizawa K (2003) Time from finding abnormality on mass-screening to final diagnosis of lung cancer. Oncol Rep 10(3):649–652
13. O'Rourke N, Edwards R (2000) Lung cancer treatment waiting times and tumour growth. Clin Oncol (R Coll Radiol) 12(3):141–144
14. Ellis PM, Vandermeer R (2011) Delays in the diagnosis of lung cancer. J Thorac Dis 3(3):183–188
15. Koyi H, Hillerdal G (2002) Brandén E.Patient's and doctors' delays in the diagnosis of chest tumors. Lung Cancer 35(1):53–57
16. Bilimoria KY, Ko CY, Tomlinson JS, Stewart AK, Talamonti MS, Hynes DL, Winchester DP, Bentrem DJ (2011) Wait times for cancer surgery in the United States: trends and predictors of delays. Ann Surg 253(4):779–785
17. Saint-Jacques N, Rayson D, Al-Fayea T, Virik K, Morzycki W, Younis T (2008) Waiting times in early-stage non-small cell lung cancer (NSCLC). J Thorac Oncol 3(8):865–870
18. Liberman M, Liberman D, Sampalis JS, Mulder DS (2006) Delays to surgery in non-small-cell lung cancer. Can J Surg 49(1):31–36
19. Van de Vosse D, Chowdhury R, Boyce A, Halperin R (2015) Wait times experienced by lung cancer patients in the BC Southern interior to obtain oncologic care: exploration of the intervals from first abnormal imaging to oncologic treatment. Cureus 7(9):e330

20. Salomaa ER, Sällinen S, Hiekkanen H, Liippo K (2005) Delays in the diagnosis and treatment of lung cancer. Chest 128(4):2282–2288
21. Gould MK, Ghaus SJ, Olsson JK, Schultz EM (2008) Timeliness of care in veterans with non-small cell lung cancer. Chest 133(5):1167–1173
22. Schultz EM, Powell AA, McMillan A, Olsson JK, Enderle MA, Graham BA, Ordin DL, Gould MK (2009) Hospital characteristics associated with timeliness of care in veterans with lung cancer. Am J Respir Crit Care Med 179(7):595–600
23. Shea AM, Curtis LH, Hammill BG, DiMartino LD, Abernethy AP, Schulman KA (2008) Association between the Medicare Modernization Act of 2003 and patient wait times and travel distance for chemotherapy. JAMA 300(2):189–196
24. Yorio JT, Xie Y, Yan J, Gerber DE (2009) Lung cancer diagnostic and treatment intervals in the United States: a health care disparity? J Thorac Oncol 4(11):1322–1330
25. Everitt S, Herschtal A, Callahan J, Plumridge N, Ball D, Kron T, Schneider-Kolsky M, Binns D, Hicks RJ, MacManus M (2010) High rates of tumor growth and disease progression detected on serial pretreatment fluorodeoxyglucose-positron emission tomography/computed tomography scans in radical radiotherapy candidates with nonsmall cell lung cancer. Cancer 116(21):5030–5037
26. Mohammed N, Kestin LL, Grills IS, Battu M, Fitch DL, Wong CY, Margolis JH, Chmielewski GW, Welsh RJ (2011) Rapid disease progression with delay in treatment of non-small-cell lung cancer. Int J Radiat Oncol Biol Phys 79(2):466–472
27. Geiger GA, Kim MB, Xanthopoulos EP, Pryma DA, Grover S, Plastaras JP, Langer CJ, Simone CB 2nd, Rengan R (2014) Stage migration in planning PET/CT scans in patients due to receive radiotherapy for non-small-cell lung cancer. Clin Lung Cancer 15(1):79–85
28. Christensen NL, Jekunen A, Heinonen S, Dalton SO, Rasmussen TR (2017) Lung cancer guidelines in Sweden, Denmark, Norway and Finland: a comparison. Acta Oncol 56(7):943–948
29. Baldwin DR, White B, Schmidt-Hansen M, Champion AR, Melder AM, Guideline Development Group (2011) Diagnosis and treatment of lung cancer: summary of updated NICE guidance. BMJ 342:d2110
30. Ettinger DS, Akerley W, Borghaei H, Chang AC, Cheney RT, Chirieac LR, D'Amico TA, Demmy TL, Govindan R, Grannis FW Jr, Grant SC, Horn L, Jahan TM, Komaki R, Kong FM, Kris MG, Krug LM, Lackner RP, Lennes IT, Loo BW Jr, Martins R, Otterson GA, Patel JD, Pinder-Schenck MC, Pisters KM, Reckamp K, Riely GJ, Rohren E, Shapiro TA, Swanson SJ, Tauer K, Wood DE, Yang SC, Gregory K, Hughes M (2013) National comprehensive cancer network. Non-small cell lung cancer, version 2.2013. J Natl Compr Canc Netw 11(6):645–653. (quiz 653)
31. Ost DE, Jim Yeung SC, Tanoue LT, Gould MK (2013) Clinical and organizational factors in the initial evaluation of patients with lung cancer: diagnosis and management of lung cancer, 3rd edn: American College of Chest Physicians evidence-based clinical practice guidelines. Chest 143(5 Suppl):e121S–e141S
32. Detterbeck FC, Lewis SZ, Diekemper R, Addrizzo-Harris D, Alberts WM (2013) Executive Summary: Diagnosis and management of lung cancer, 3rd edn: American College of Chest Physicians evidence-based clinical practice guidelines. Chest 143(5 Suppl):7S–37S
33. Vilmann P, Clementsen PF, Colella S, Siemsen M, De Leyn P, Dumonceau JM, Herth FJ, Larghi A, Vazquez-Sequeiros E, Hassan C, Crombag L, Korevaar DA, Konge L, Annema JT (2015) Combined endobronchial and esophageal endosonography for the diagnosis and staging of lung cancer: European Society of Gastrointestinal Endoscopy (ESGE) Guideline, in cooperation with the European Respiratory Society (ERS) and the European Society of Thoracic Surgeons (ESTS). Endoscopy 47(6):545–559
34. Silvestri GA, Gonzalez AV, Jantz MA, Margolis ML, Gould MK, Tanoue LT, Harris LJ, Detterbeck FC (2013) Methods for staging non-small cell lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest 143(5 Suppl):e211S–e250S
35. Navani N, Nankivell M, Lawrence DR, Lock S, Makker H, Baldwin DR, Stephens RJ, Parmar MK, Spiro SG, Morris S, Janes SM (2015) Lung-BOOST trial investigators. Lung cancer diagnosis and staging with endobronchial ultrasound-guided transbronchial needle aspiration compared with conventional approaches: an open-label, pragmatic, randomised controlled trial. Lancet Respir Med 3(4):282–289
36. Yasufuku K, Nakajima T, Fujiwara T, Chiyo M, Iyoda A, Yoshida S, Suzuki M, Sekine Y, Shibuya K, Yoshino I (2008) Role of endobronchial ultrasound-guided transbronchial needle aspiration in the management of lung cancer. Gen Thorac Cardiovasc Surg 56(6):268–276
37. Folch E, Majid A (2013) Point: are> 50 supervised procedures required to develop competency in performing endobronchial ultrasound-guided transbronchial needle aspiration for mediastinal staging? Yes. Chest 143(4):888–891
38. Fernández-Villar A, Leiro-Fernández V, Botana-Rial M, Represas-Represas C, Núñez-Delgado M (2012) The endobronchial ultrasound-guided transbronchial needle biopsy learning curve for mediastinal and hilar lymph node diagnosis. Chest 141(1):278–279
39. Lamprecht B, Porsch P, Wegleitner B, Strasser G, Kaiser B, Studnicka M (2012) Electromagnetic navigation bronchoscopy (ENB): Increasing diagnostic yield. Respir Med 106(5):710–715