Timeliness of surgery for early-stage lung cancer: Patient factors and predictors

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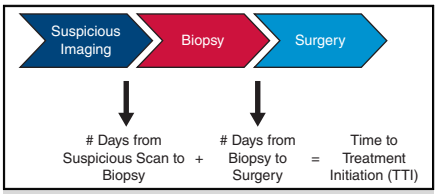
ABSTRACT

Objectives: Time-to-treatment initiation is an important consideration for patients undergoing thoracic surgery for early-stage lung cancer because delays have the potential to adversely affect outcomes. This study seeks to quantify time-to-treatment initiation for patients with clinical stage I lung cancer, explore patient factors and predictors that lead to an increased time-to-treatment initiation, and compare surgeon perception of appropriate time-to-treatment initiation to the results.

Methods: Time-to-treatment initiation was determined for patients enrolled in the Mount Sinai Initiative for Early Lung Cancer Research on Treatment study who underwent surgical resection for clinical stage I lung cancer between March 2016 and December 2021. The following dates were determined: (1) date of first suspicious radiologic imaging, (2) date of first biopsy, and (3) date of surgery. A total of 15 thoracic surgeons who participated in the Mount Sinai Initiative for Early Lung Cancer Research on Treatment were assessed on their perception on time-to-treatment initiation.

Results: For 638 patients, median time from first suspicious imaging findings to biopsy was 40 days, biopsy to surgery was 37 days, and suspicious imaging to surgery was 84 days. Significant factors that resulted in longer time-to-treatment initiation in the multivariate analysis were African American or Black race ($P = .005$), vascular disease ($P = .01$), and median household income less than $75,000 ($P = .04$). Although the surgeon's perception was that the average time from biopsy to surgery was 28 days, it was longer for 63.5% of participants; surgeon perception of maximum time between diagnosis and surgery was 84 days and longer for 28.7% of participants.

Conclusions: Patient factors such as race, income, and comorbidities were found to have differences in time-to-treatment initiation. Delays to surgery exceeded the expectations of thoracic surgeons. (JTCVS Open 2024;19:325-37)



Patient factors affected time to treatment and exceeded the expectations of surgeons.

CENTRAL MESSAGE

Patient factors such as Black or African-American race, income, and vascular disease were associated with increased time to treatment. Delays to surgery exceeded the expectations of thoracic surgeons.

PERSPECTIVE

It is important to understand the time to treatment for patients with early-stage lung cancer because extra delay decreases overall survival. The results may be correlated with volume doubling times or other measures regarding the aggressiveness of lung cancers. Surgeons should be made aware of these delays for lung cancer resection and prioritize these surgeries over those considered more elective.

Supplemental material is available online.

Lung cancer is the leading cause of death in the United States, with an estimated 236,000 new cases diagnosed in 2022 and resulting in more than 130,000 deaths. Surgical resection remains the gold standard for treatment and is

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Abbreviations and Acronyms

CT = computed tomography
IELCART = Initiative for Early Lung Cancer on Treatment
PET = positron emission tomography
TTI = time-to-treatment initiation
TTI-b-s = time from first tissue sampling until treatment
TTI-r-b = time from suspicious imaging until first tissue sampling

highly curable when treated as stage I.[1] Therefore, delays in time-to-treatment initiation (TTI) should be minimized to avoid the possibility of lung cancer transitioning from an early stage to a more advanced stage. Unfortunately, due to the COVID-19 pandemic and its shock to the healthcare system, delays in TTI were unavoidable.[2-4]

Extensive research on the association between TTI and survival for lung cancer has recently been summarized in a meta-analysis that found the analysis was limited due to heterogeneity of the data.[5-8] However, when looking at the individual studies, the analysis of the National Cancer Database predicts that each additional week of delay will reduce the overall survival of patients with stage I non–small cell lung cancer by 3.2%.[9] Another study found a greater impact of delays on survival for larger cancers (T2) than smaller cancers (T1a-T1c).[10] This result aligns with a recent study modeling the impact of the inherent time delays resulting from diagnostic workups of indeterminate nodules, which concluded that for any given time delay, the extent of decrease in prognosis increased with increasing nodule size.[11]

Health disparities have been found to adversely impact TTI, particularly for patients of African American or Black race, of Hispanic ethnicity, and with Medicaid insurance, lower educational attainment, and lower income status.[6,12,13] Additionally, reasons for delays in TTI have been due to the healthcare facility, mainly due to preoperative workup before treatment.[7,10,14-19] Before undergoing surgery for early-stage lung cancer, patients typically require additional testing to determine the extent of disease, which may include positron emission tomography (PET), tissue sampling (biopsy, bronchoscopy), brain magnetic resonance imaging, cardiac clearance, stress tests, pulmonary function tests, and COVID-19 testing.

Although the sources for TTI delays due to provider and treatment requirements have been explored, there is a paucity of research on delays from the patients. Our study seeks to establish a foundation in this understudied topic by (1) quantifying TTI for patients who underwent surgical resection with intent to cure for clinical stage I lung cancer, (2) exploring patient factors and predictors that lead to an increased TTI, and (3) comparing surgeon perception of appropriate TTI with the actual results.

MATERIALS AND METHODS

We reviewed all participants enrolled in the prospective cohort study Initiative for Early Lung Cancer Research on Treatment (IELCART) in the Mount Sinai Health System since its start in 2016 through 2021. Once diagnosed with lung cancer, participants were approached before treatment, after treatment, and each time they came for treatment follow-up. All signed consent for publication of study data was approved by the Icahn School of Medicine at Mount Sinai Institutional Review Board (Study-15-01021, January 26, 2016), which was compliant with the Health Insurance Portability and Accountability Act. For this study, we included all patients who underwent surgical resection for clinical stage I (T1a-c, T2a) lung cancer (TNM 8th edition classification). We included patients with previously diagnosed lung cancer who had pathologic stage I (T1a-c, T2a) lung cancer and were treated at least 3 years before entry into IELCART and had no evidence of recurrence or mediastinal, hilar, or parenchymal metastases before enrollment.

Date of first suspicious radiologic findings was defined as the date of imaging that ultimately led to ordering tissue sampling of the suspicious nodule, typically computed tomography (CT) or PET (Figure 1). Date of first biopsy was defined as the first tissue sampling of the suspicious nodule. Examples include needle biopsies (fine-needle aspiration, core biopsy), endobronchial biopsies, and transbronchial biopsies, whether the procedure resulted in a definitive diagnosis or not. Date of surgery was defined as the date of surgical resection with intent to cure the suspicious nodule. All participants underwent surgery at the Mount Sinai Hospital. Resection type included sublobar (wedge, segmentectomy), lobectomy, bilobectomy, or pneumonectomy. Date of surgery refers to the index surgery to which the participant was recruited for IELCART.

TTI is typically defined as the number of days from diagnosis to the time of treatment. Because delays from the time of suspicious findings to the diagnosis will have an additive impact, we also quantified this using the term "TTI-r-b," which defines the time from suspicious imaging until first tissue sampling, the term "TTI-b-s," which defines the time from first tissue sampling (diagnosis) to treatment, and the term "TTI" to represent

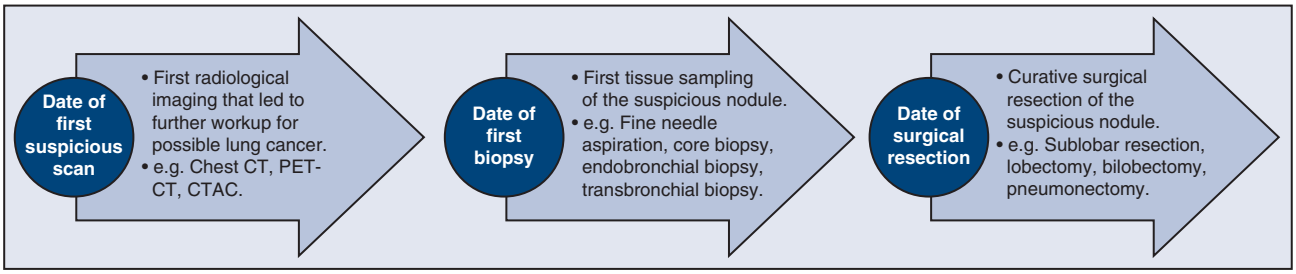

FIGURE 1. The pathway to diagnosis from date of first suspicious scan result to date of first biopsy to date of surgical resection. *CT*, Computed tomography; *PET*, positron emission tomography; *CTAC*, computed tomography angiography chest.

TTI-r-b + TT-b-s. Although common for indeterminate nodules to be followed for long intervals before tissue sampling, for the purposes of this study we are counting the CT or PET that led to biopsy as the starting point. Patients who received surgical biopsy would have a TTI-b-s value of zero.

Additionally, we wanted to measure the effect that the COVID-19 pandemic had on TTI for our patient population, given the additional time required for COVID testing, and various hospital policies applied to procedures. Patients who had suspicious CT results before March 16, 2020, were defined as "pre-COVID," and patients who had suspicious CT results after March 16, 2020 were defined as occurring during COVID. For comparisons of TTI-r-b, the cutoff date of COVID was defined by the date of suspicious imaging results. For comparisons of TTI-b-s, the cutoff date of COVID was defined by the date of biopsy. To visualize the effect that the COVID-19 pandemic had on TTI, nonparametric locally weighted smoothing curves were used to fit the time points and to show the trend of days for TTI-r-b and TTI-b-s before and during the COVID pandemic. To identify patient predictors and factors that may result in increased TTI, we correlated IELCART study data collected with TTI. Nodule consistency and surgical extent were analyzed with the TTI data, as well as ZIP code–level median household income, which was obtained through the US Census Bureau.[20] The measures of TTI were presented as medians and interquartile ranges, and Mann–Whitney *U* tests were used to compare the TTI measures between categorical variables mentioned above. Univariate and multiple linear regression models were used to explore the relationship between the TTI measures and the parameters. TTI was log-transformed to improve model fit by reducing skewness and heteroscedasticity. The log transformation has been widely used in biomedical research to address skewed data, providing both theoretical and practical justifications for its application in such contexts.[21] Stepwise selection based on Akaike Information Criterion was used for variable selection in the parsimonious multivariable model. All *P* values were 2-sided.

To explore the thoracic surgeon's perceptions regarding appropriate TTI, 15 IELCART-participating thoracic surgeons completed a survey questionnaire in person or through an emailed REDCap link (Table E1). To assess their perception about TTI, we asked what they consider to be a reasonable average time from diagnosis to surgery for clinical stage I lung cancer and the maximum time a patient can safely wait for surgery. We asked if they thought that every week that surgery was delayed would increase the risk of death for the patient and if certain nodule or patient characteristics would change their view. Finally, we asked what factors they thought caused the longest delay from diagnosis to surgery for clinical stage I lung cancer.

RESULTS

A total of 638 participants were included in this analysis (382 [60%] women, 256 [40%] men) (Table 1). The median age of participants was 70 years (interquartile range, 63-76). Of these participants, 175 (27%) do not smoke, 398 (62%) had a smoking history, and 65 (10%) currently smoke. A total of 384 (60%) participants identified as White; 105 (16%) identified as African American or Black; 77 (12%) identified as Asian; 89 (14%) identified as Hispanic or Latino ethnicity; and 72 (11%) identified as other. A total of 365 participants (57%) had an education level of college or above, and 248 participants (39%) had an education level of below college level.

TABLE 1. Summary of demographic characteristics of 638 patients

Category	Total
Age, y (median, IQR)	70 (63-76)
Sex	
Female	382 (60%)
Male	256 (40%)
Smoking status	
Person who smokes	65 (10%)
Person with smoking history	398 (62%)
Person who does not smoke	175 (27%)
Race	
White	384 (60%)
African American/Black	105 (16%)
Asian	77 (12%)
Others	72 (11%)
Ethnicity	
Non-Hispanic	543 (85%)
Hispanic	89 (14%)
Unknown	6 (0.9%)
BMI	
Normal	240 (38%)
Preobesity	194 (30%)
Obesity	158 (25%)
Unknown	46 (7.2%)
Education	
College and above	365 (57%)
No college	248 (39%)
Unknown	25 (3.9%)
ZIP code–level income ($)	
<75,000	211 (33%)
75,000-150,000	312 (49%)
>150,000	110 (17%)
Unknown	5 (1%)
Nodule consistency	
None-solid	35 (5.5%)
Part-solid	110 (17.2%)
Solid	493 (77.3%)
Nodule size category	
≤10 mm	134 (21%)
10-20 mm	298 (47%)
20-30 mm	206 (32%)
Surgery extent	
Sublobar	354 (55%)
Lobectomy	269 (42%)
Bilobectomy	9 (0.4%)
Pneumonectomy	2 (0.3%)
Other/unknown	4 (0.6%)
COVID, surgery before vs during COVID	
Pre-COVID	480 (75%)
COVID era	158 (25%)

(Continued)

TABLE 1. Continued

Category	Total
COVID, suspicious imaging before vs during COVID	
Pre-COVID	505 (79.2%)
COVID-era	133 (20.8%)
COVID, biopsy before vs during COVID	
Pre-COVID	495 (77.6%)
COVID-era	143 (22.4%)

IQR, Interquartile range; *BMI*, body mass index.

Univariate and Multivariable Analyses

The median TTI (interquartile range) measures were TTI-r-b of 40 (24-65) days. TTI-b-s was 37 (21-62) days. TTI was 84 (56-133) days (Table 2). TTI was significantly longer for African American or Black patients compared with White patients (109 vs 77 days; $P < .001$) (Figure 2, *A*) (Table 3). TTI was longer for those with an educational attainment below college compared with those with educational attainment college or above (91.5 vs 80 days; $P = .05$) (Figure 2,

TABLE 2. Median days between computed tomography and surgery, computed tomography and biopsy, biopsy and surgery

Parameter	N (638)	TTI, median (IQR)	*P* value	TTI-r-b, median (IQR)	*P* value	TTI-b-s, median (IQR)	*P* value
Sex			.69		.45		.52
Female	382	84 (55.2-131)		39.5 (22.2-65)		39 (22-61)	
Male	256	84 (56-136)		41 (25-64.2)		36 (21-62.2)	
Smoking status			.73		.43		.81
Person who smokes	65	91 (64-122)		45 (27-80)		36 (22-64)	
Person with smoking history	398	83 (55-133)		40.5 (23-65)		36 (21-60)	
Person who does not smoke	175	86 (55.5-140)		38 (23.5-63)		40 (21-66.5)	
Race			**<.001**		.07		**<.001**
White	384	77 (54-122)		38.5 (22-60)		35 (21-56)	
African American/Black	105	109 (83-152)		48 (25-86)		50 (32-89)	
Asian	77	81 (53-121)		41 (28-68)		35 (16-49)	
Others	72	95.5 (62-146)		40 (22.8-68.5)		40.5 (20.8-74.5)	
Ethnicity			.51		.36		.76
Non-Hispanic	543	84 (55-130)		40 (23-63)		36 (22-61)	
Hispanic	89	91 (62-144)		45 (27-77)		40 (20-63)	
Unknown	6	67 (49.5-126)		18 (9.5-35.5)		49.5 (20.5-71)	
BMI			.67		.24		.42
Normal	240	83.5 (53-135)		40 (24-67)		36 (19-63)	
Pre-obesity	194	84 (58.2-120)		38.5 (23-57.8)		37 (22-58)	
Obesity	158	87.5 (60-138)		41.5 (24.5-74.8)		39 (23-67.8)	
Unknown	46	89 (57.5-129)		43.5 (25.2-76.8)		36 (19.5,54.8)	
Education			**.01**		**.01**		.29
College and above	365	80 (53-122)		38 (22-60)		36 (21-58)	
No college	248	91.5 (63-139)		45.5 (26-74.5)		39 (22-69.2)	
Unknown	25	89 (56-142)		40 (25-68)		41 (28-66)	
ZIP Code–level Income ($)			**<.001**		**.01**		**.004**
<75,000	211	94 (62-148)		40 (24-70)		41 (25-77)	
75,000-150,000	312	84 (59-131)		42 (25-64)		37 (21-59)	
>150,000	110	65 (46-99)		32 (19-48)		32 (20-46)	
Unknown	5						
Nodule consistency			.85		**.009**		**.04**
None-solid	35	95 (61.5-126)		63 (39-94.5)		35 (0-45.5)	
Part-solid	110	85 (59.2-124)		40 (24-60.2)		41 (22.2-59)	
Solid	493	84 (55-136)		39 (23-64)		36 (21-64)	
Nodule size category			.77		.08		.21
≤10 mm	134	90 (53.2-137)		42 (25-70.5)		39.5 (21-58)	
10- 20 mm	298	84 (56.2-132)		41 (25-67.8)		36 (21.2-57)	
20-30 mm	206	84 (56-128)		37.5 (21-56)		41 (22-69)	

(Continued)

TABLE 2. Continued

Parameter	N (638)	TTI, median (IQR)	*P* value	TTI-r-b, median (IQR)	*P* value	TTI-b-s, median (IQR)	*P* value
Surgery extent			.27		.11		**<.001**
Sublobar	354	83 (56-129)		41 (25.2-68)		35 (19.2-55)	
Lobectomy	269	89 (56-140)		38 (20-63)		43 (25-72)	
Bilobectomy	9	97 (84-150)		30 (25-63)		69 (44-144)	
Pneumonectomy	2	82 (82-82)		30.5 (17.8-43.2)		51.5 (38.8-37)	
Other/unknown	4	54 (37.5-76.5)		23 (10.2-43.5)		26.5 (18.8-37)	
COVID*			.83		**.04**		.24
Pre-COVID	505	84 (56-133)		40 (22-63)		38 (21-64)	
COVID era	133	91 (56-132)		44 (27-74)		36 (22-55)	
Comorbidities							
Cardiac							
Yes	84	80.5 (60-153)	.63	40 (21.8-66.5)	.83	35.5 (21.8-62.5)	.87
No	554	84.5 (55.2-130)		40 (24-65)		37 (21-61.8)	
Vascular							
Yes	353	90 (61-146)	**.002**	42 (25-71)	**.009**	37 (23-64)	.17
No	285	78 (53-120)		38 (21-61)		37 (20-59)	
COPD							
Yes	129	84 (57-140)	.80	41 (26-64)	.59	36 (21-62)	.92
No	509	84 (55-130)		40 (24-65)		37 (22-62)	
Asthma							
Yes	77	104 (62-152)	**.02**	44 (25-68)	.06	44 (29-83)	.22
No	561	84 (55-129)		36 (21-60)		40 (23-63)	
Diabetes							
Yes	124	93.5 (57-147)	.31	41 (26.8-67.2)	.42	37 (21-67.2)	.72
No	514	84 (55-128)		40 (23-64)		37 (21-59.8)	
Other cancers							
Yes	195	84 (53.5-138)	.64	39 (22-64)	.41	35 (22-59.5)	.81
No	443	84 (56.5-130)		41 (24-67)		38 (21-63)	
Liver or kidney disease							
Yes	330	92 (60-144)	**.01**	44 (25-71)	**.01**	38 (23-66.5)	.13
No	308	78.5 (54-123)		38 (22-62)		36 (21-57.2)	

$P \leq .05$ indicates statistical significance indicated in bold. *TTI*, Time-to-treatment initiation; *IQR*, interquartile range; *TTI-r-b*, time from suspicious imaging until first tissue sampling; *TTI-b-s*, time from first tissue sampling until treatment; *BMI*, body mass index; *COPD*, chronic obstructive pulmonary disease. *For the comparison of TTI/TTI-r-b between pre-COVID and COVID-era patients, patients who had CT before 3/16/2020 were defined as pre-COVID patients and patients who had CT on or after 3/16/2020 were defined as COVID-era patients. For the comparison of TTI-b-s between pre-COVID and COVID-era patients, patients who had biopsy before 3/16/2020 were defined as pre-COVID patients and patients who had biopsy on or after 3/16/2020 were defined as COVID-era patients.

B). It was also longer for patients with different comorbidities—vascular disease (90 vs 78 days; $P = .003$) (Figure 2, *C*), asthma (104 vs 84 days; $P = .05$) (Figure 2, *D*), and liver or kidney disease (92 vs 78.5 days; $P = .047$) (Figure 2, *E*)—than those without these comorbidities. Additionally, TTI was higher for those in the lowest income group (<$75,000) compared with those in the highest income group (>$150,000) (94 vs 65 days; $P < .001$) (Figure 2, *F*). The significant patient factors for the TTI-r-b and TTI-b-s measures are shown in Table 2.

Multivariable analysis indicated that race, income, and vascular disease were independent factors associated with the log-transformed days between CT and surgery. African American or Black patients ($P = .005$), vascular disease ($P = .01$), and household income <$75,000 ($P = .04$) were associated with longer TTI (Table 4).

Table 5 displays the average marginal effects of race, income, and vascular disease on TTI. The findings suggest that Black or African American race is associated with a statistically significant increase in TTI days (27% on average) compared with White race. Having a household income of more than $150,000 is associated with a statistically significant decrease in TTI days (18% on average) compared with a household income less than $75,000. Having vascular disease is associated with a 16% average increase in TTI days, which is also statistically significant. These effects are controlled for other factors in the model, reflecting the average impact of each factor on TTI.

Effect of the COVID-19 Pandemic

TTI-b-s showed no significant difference since the pandemic ($P = .24$); however, the TTI-r-b has increased

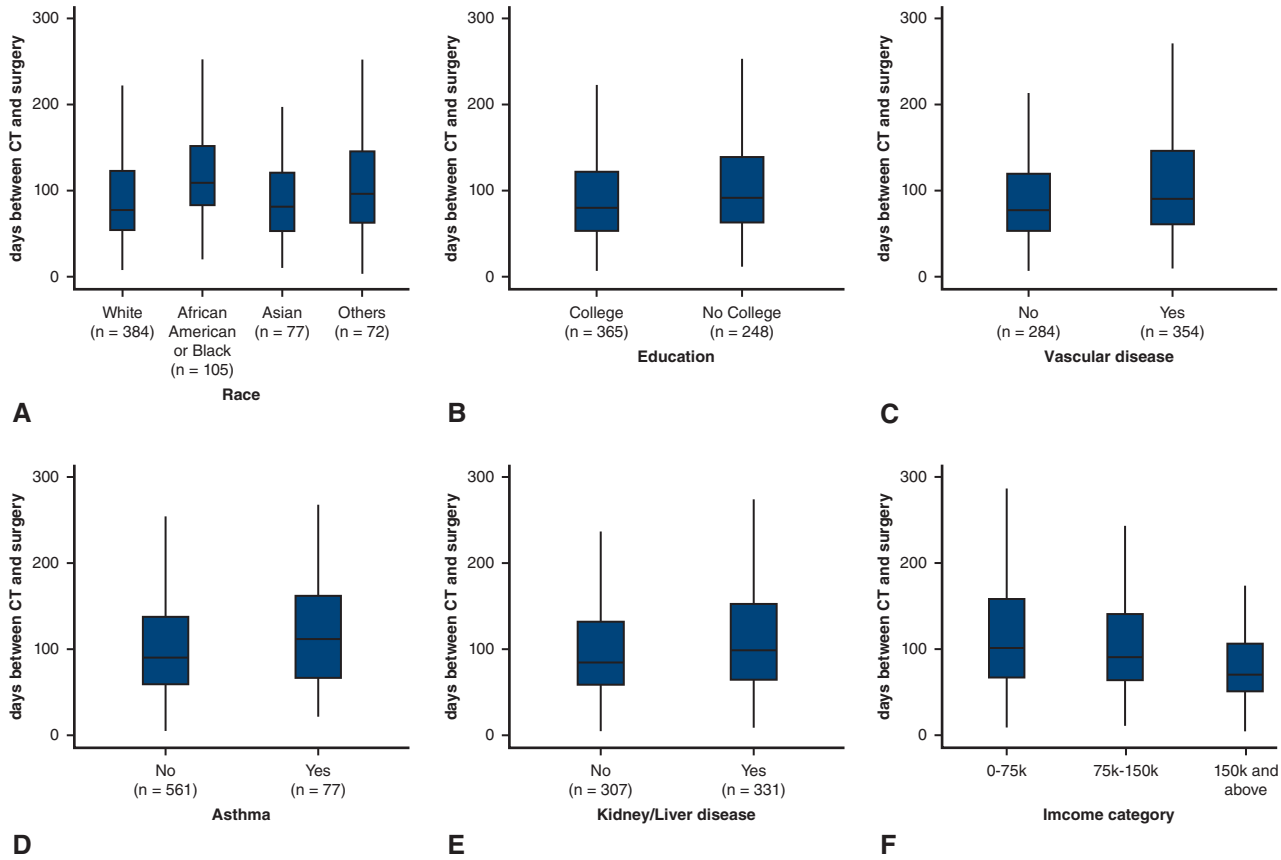

FIGURE 2. A, Differences in TTI by racial groups among 638 participants. B, Differences in TTI by educational attainment of college or above versus below college among 613 participants. C, Differences in TTI by not having vascular disease versus having vascular disease among 638 participants. D, Differences in TTI by not having asthma versus having asthma among 638 participants. E, Differences in TTI by not having liver/kidney disease versus having liver/kidney disease among 638 participants. F, Differences in TTI by ZIP Code–level median household income among 633 participants. *CT*, Computed tomography.

greatly from the pre-COVID group compared with the COVID group. This shows that since the pandemic, TTI-r-b increased over time (median 40 vs 44 days; $P = .04$) and has been responsible for increasing treatment delay (Table 2 and Figure 3, *A* and *B*).

Surgeons' Perception of Time-to-Treatment Initiation

The median response of what surgeons believed was the average TTI-b-s was 28 days, with responses ranging from 14 to 70 days (Table E1). A total of 12 of 15 surgeons (80%) believed their stated average time from diagnosis to surgery was an appropriate amount of time to surgery. The actual median time was 37 days, with 405 (63.5%) participants having TTI-b-s exceeding 28 days.

When asked for the maximum TTI-b-s, the median surgeon response was 56 days, with responses ranging from 21 to 84 days (Figure 4). The actual median TTI-b-s was 37 days, with 183 patients (28.7%) having times that exceeded 56 days. A total of 97 patients (15.2%) had times that exceeded 84 days, the highest recorded response (Figure 5).

When considering factors that contribute most to surgical delays, 10 of 15 surgeons believed that patient comorbidities and the surgeon's schedule and operating room availability were the biggest contributors. Five of 15 of the participating surgeons mentioned patient apprehension and patient life events as the most important factors for delay. Some participating surgeons added additional staging tests, PET, and pulmonary function testing as important factors for delay.

DISCUSSION

This exploration of TTI for patients with clinical stage I lung cancer undergoing curative surgical resection has revealed several factors associated with increased delays. Patients who identified as African American or Black had significantly longer TTI. Similar findings were reported in a recent study exploring TTI in more than 162,000 stage I lung cancer cases from 2010 to 2018; it showed an increase

TABLE 3. Median days between computed tomography and surgery, and parameter estimates of the regression analysis for demographic and clinical factors associated with the Log of days between computed tomography and surgery

Parameter	N (638)	TTI, median (IQR)	Estimate	SE	*P* value
Sex					
Female	382	84 (55.2-131)	ref		
Male	256	84 (56-136)	0.017	0.059	.77
Age			0.0046	0.0029	.12
Pack-y			0.0014	0.001	.19
Smoking status					
Person who smokes	65	91 (64-122)	ref		
Person with smoking history	398	83 (55-133)	−0.03	0.11	.80
Person who does not smoke	175	86 (55.5-140)	−0.07	0.07	.30
Race					
White	384	77 (54-122)	ref		
African American/Black	105	109 (83-152)	0.30	0.081	**<.001**
Asian	77	81 (53-121)	0.01	0.091	.91
Others	72	95.5 (62-146)	0.075	0.094	.42
Ethnicity					
Non-Hispanic	543	84 (55-130)	ref		
Hispanic	89	91 (62-144)	0.080	0.084	.34
Unknown	6	67 (49.5-126)	−0.4	0.30	.18
BMI					
Normal	240	83.5 (53-135)	ref		
Preobesity	194	84 (58.2-120)	−0.02	0.071	.77
Obesity	158	87.5 (60-138)	0.078	0.075	.30
Unknown	46	89 (57.5-129)	−0.03	0.12	.82
Education					
College and above	365	80 (53-122)	ref		
No college	248	91.5 (63-139)	0.12	0.06	**.05**
Unknown	25	89 (56-142)	−0.007	0.15	.96
ZIP code–level income ($)					
<75,000	211	94 (62-148)	ref		
75,000-150,000	312	84 (59-131)	−0.09	0.06	.15
>150,000	110	65 (46-99)	−0.29	0.09	**<.001**
Unknown	5				
Nodule consistency					
None-solid	35	95 (61.5-126)	ref		
Part-solid	110	85 (59.2-124)	−0.019	0.14	.90
Solid	493	84 (55-136)	−0.062	0.13	.63
Surgical extent					
Sublobar	354	83 (56-129)	ref		
Lobectomy	269	89 (56-140)	0.092	0.059	.12
Bilobectomy	9	97 (84-150)	0.39	0.25	.12
Pneumonectomy	2	82 (82,82)	−0.041	0.52	.94
Other/unknown	4	54 (37.5-76.5)	−0.45	0.37	.22
COVID					
Pre-COVID	505	84 (56-133)	ref		
COVID era	133	91 (56-132)	−0.004	0.07	.96
Comorbidities					
Cardiac					
Yes	84	80.5 (60-153)	0.023	0.086	.78
No	554	84.5 (55.2-130)	ref		

(Continued)

TABLE 3. Continued

Parameter	N (638)	TTI, median (IQR)	Estimate	SE	*P* value
Vascular					
Yes	353	90 (61-146)	0.18	0.06	**.003**
No	285	78 (53-120)	ref		
COPD					
Yes	129	84 (57-140)	−0.024	0.073	.74
No	509	84 (55-130)	ref		
Asthma					
Yes	77	104 (62-152)	0.17	0.089	**.05**
No	561	84 (55-129)	ref		
Diabetes					
Yes	124	93.5 (57-147)	0.045	0.074	.55
No	514	84 (55-128)	ref		
Other cancers					
Yes	195	84 (53.5-138)	−0.0009	0.063	.99
No	443	84 (56.5-130)	ref		
Liver or kidney disease					
Yes	330	92 (60-144)	0.11	0.058	**.047**
No	308	78.5 (54-123)	ref		

$P \leq .05$ indicates statistical significance indicated in bold. *TTI*, Time-to-treatment initiation; *IQR*, interquartile range; *SE*, standard error; *BMI*, body mass index; *COPD*, chronic obstructive pulmonary disease.

of 22% in TTI for African American or Black patients compared with White patients.[17]

Lower educational attainment and household income were associated with longer TTI, findings consistent with other research.[14] The significant difference in TTI of 29 days from the lowest income group to the highest shows that socioeconomic factors heavily influence timely treatment of lung cancer.

Medical comorbidities were associated with higher TTI. Measures of comorbidities, for example, Charlson-Deyo Index, have been found to increase TTI for lung cancer.[9] None of these comorbidities were significant for TTI-b-s, so it is possible delays from medical comorbidities were cleared by the time of the biopsy. Vascular disease was independently associated with higher TTI, whereas vascular disease, liver or kidney disease, and asthma were associated with higher TTI in the univariate analysis. Increased delay from vascular disease may be due to an institutional policy to hold renin angiotensin inhibitors, angiotensin-converting enzyme inhibitors, and diuretics before surgery. Additionally, anticoagulants are stopped 5 to 10 days before surgery, which contributes to more delay.

Nodule consistency was shown to be a significant factor, because increased TTI was found with patients having non-solid and part-solid nodules compared with solid nodules. Subsolid nodules are widely accepted to be more indolent, which may account for lesser urgency to treat and more likely subject to repeat CT over biopsy.

The comparison of TTI from patients who underwent surgery before and after the COVID-19 pandemic revealed that

TABLE 4. Multivariable regression results for the factors associated with the Log of days between computed tomography and surgery

Parameter	Estimate	SE	*P* value
Race			
White	ref		
African American/Black	0.24	0.09	**.005**
Asian	0.004	0.10	.96
Others	−0.02	0.10	.97
Vascular			
No	ref		
Yes	0.15	0.06	**.01**
ZIP code–level income ($)			
<75,000	Ref		
75,000-150,000	−0.03	0.07	.62
>150,000	−0.20	0.10	**.04**
Unknown			

$P \leq .05$ indicates statistical significance indicated in bold. *SE*, Standard error.

TABLE 5. Average marginal effects of demographic and clinical factors on time to treatment initiation

Parameter	Average marginal effect (95% CI)	SE	*P* value
African American/Black race	1.27 (1.08-1.51)	0.09	**.004**
Asian race	1.01 (0.83-1.20)	0.09	.99
Other race	0.98 (0.80-1.21)	0.10	.87
Vascular disease	1.16 (1.04-1.30)	0.06	**.01**
Income >$150,000	0.82 (0.68-0.99)	0.10	**.04**
Income $75,000-$150,000	0.97 (0.84-1.11)	0.07	.10

$P \leq .05$ indicates statistical significance indicated in bold. *CI*, Confidence interval; *SE*, standard error.

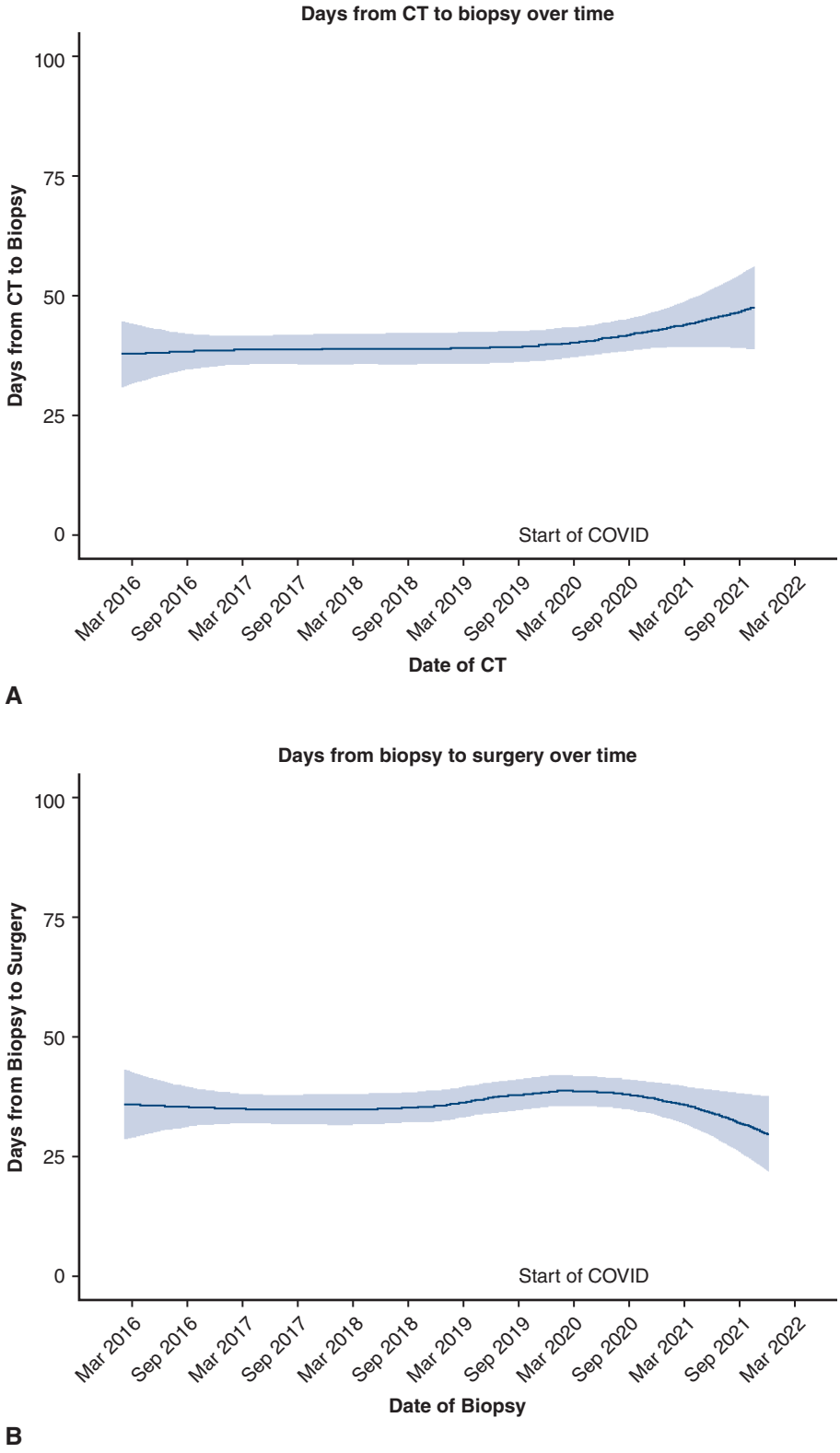

FIGURE 3. Nonparametric locally weighted smoothing curves of days (A) from CT to biopsy against time of CT and (B) from biopsy to surgery against time of biopsy showing the trends of TTI before and after COVID. *CT*, Computed tomography.

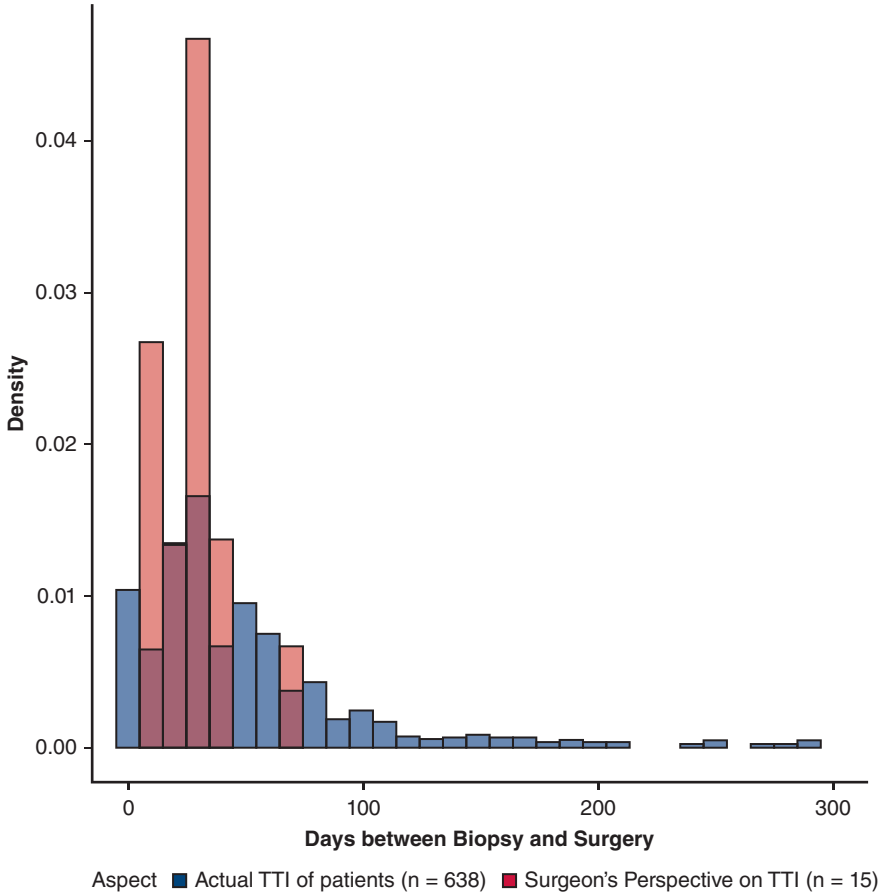

FIGURE 4. Density plot of TTI-b-s among 638 participants and perspective of maximum TTI-b-s among 15 IELCART–participating surgeons. *TTI*, Time-to-treatment initiation.

TTI has increased over time. The findings show a significant increase in TTI-r-b for the pre-COVID group compared with the COVID group, with an increase in 4 days. This could be explained by COVID protocols being put in place in healthcare facilities, which reduced the number of allowed procedures each day, causing a backlog of patients. TTI remains inflated and has not returned to pre-COVID levels. At the outset of the pandemic, multiple organizations recommended deferring lung cancer screening and extending the management of suspicious nodules to triage resources.[19] Interestingly, these delays have manifested in the TTI-r-b, rather than TTI-b-s. TTI-b-s has decreased after the pandemic, possibly due to a lower patient load to surgery and less competition for slots in the operating room schedule.

Surgeons' perception of TTI is less than the actual TTI, because only 36.5% of participants have met the perceived average TTI-b-s of 28 days. Notably, 28.7% of the study participants have a TTI-b-s that exceeded the perceived maximum TTI of 56 days, whereas 15.2% of participants exceeded the highest response of 84 days. Through medical record review of the patients who had TTI-b-s 84 days or more, the leading causes of delay included first biopsies that were nondiagnostic, atypical, or unsuccessful (38%), surgical clearance or extended treatment discussion (29%), and continued surveillance imaging after biopsy (20%).

One possible explanation for the surgeon-perceived TTI to be shorter is that he/she did not account for the time before the consultation. Some patients come to the surgical consultation with a diagnosis. The surgeon may be considering the actual TTI as the time from their consultation with the patient to surgery. This does not factor into the possible time delay from when the nodule was first detected to the time that it required further workup.

Study Limitations

First, the TTI measured could be inflated by the biopsy, because there could be nondiagnostic findings, unpleasant side effects, and repeat biopsies. A total of 574 patients (90%) in the dataset attempted a biopsy before surgery, and approximately 20% of biopsies yielded nondiagnostic or atypical results, which could be followed up with a CT, rather than immediate surgery. To prevent the overinflation of TTI, we used the date of the scan that led to biopsy, rather

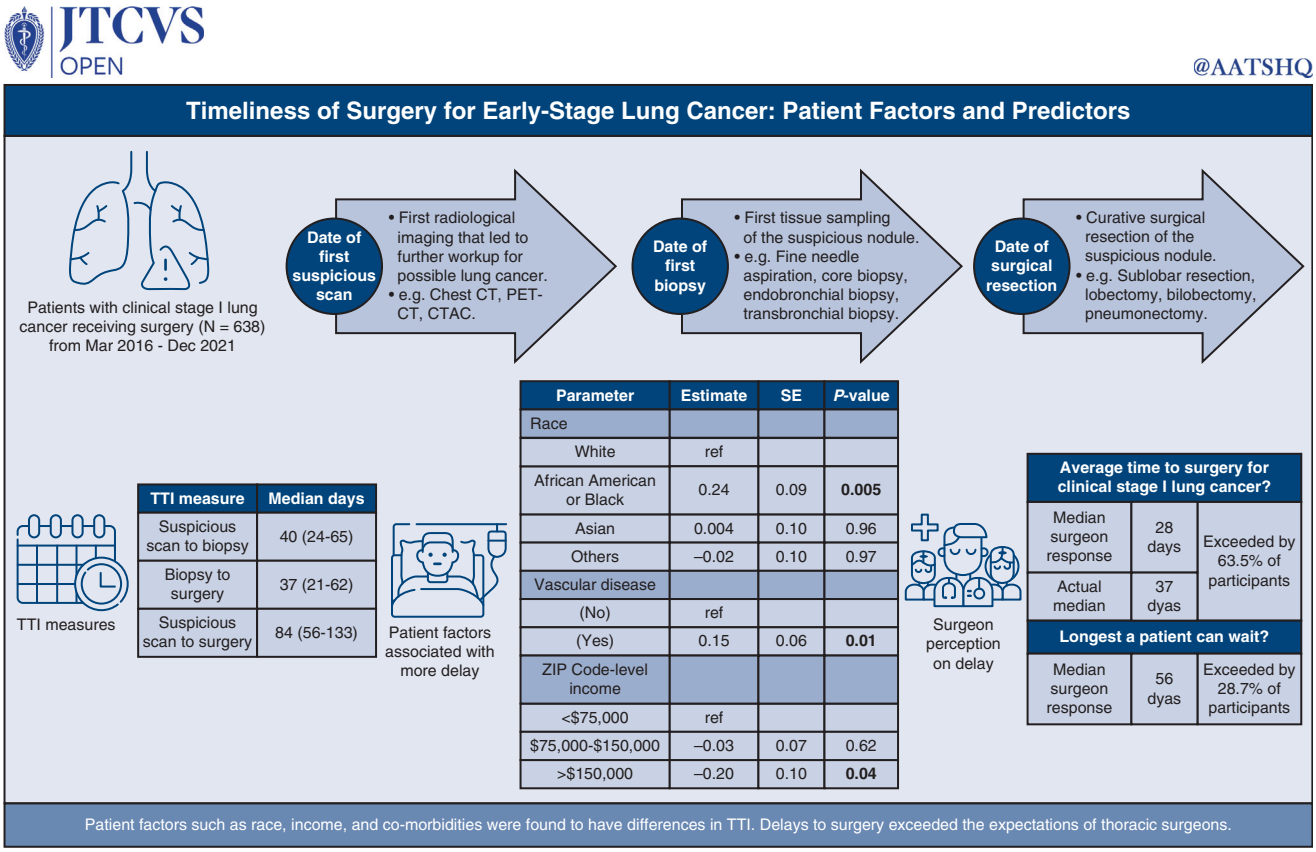

FIGURE 5. Several patient factors were indepently associated with increased delay and delays to surgery exceeded surgeon perception. *CT*, Computed tomography; *PET*, positron emission tomography; *CTAC*, computed tomography angiography chest; *TTI*, time-to-treatment initiation; *SE*, standard error.

than prior scans with "suspicious" findings. Additionally, we used median values of TTI rather than the average, because large outliers would skew the data.

Second, the exploration of potential delay predictors was limited to patient characteristics and conditions. The complex pathway to diagnosis could involve the initial scan that found the nodule, repeated annual CT, PET, various methods of tissue sampling, and other preclearance workup. For this study, this was all distilled into the date of the first suspicious scan result, first biopsy, and surgical resection. The details of potential delays from each step of the pathway to diagnosis are not fully captured through this analysis. Also, as a single-center study, there may be sources of delay that are consistent with this healthcare system that are not reported. To explore treatment delays from a patient perspective and figure out if other factors came into play, we have conducted 104 qualitative interviews from a subset of this reported study population to elicit patient experiences with delay. These findings were reported in a past academic conference.[22]

An important limitation regarding the surgeon's questionnaire is that the questions only addressed TTI-b-s. Some surgeons mentioned the delay from CT scans and biopsies, which may attribute to much of the delay. It may be important to assess surgeon perception of the entire pathway, including the time from when the nodule was first detected on imaging. We will consider exploring the surgeon perception of time delays in future research.

CONCLUSIONS

This research demonstrates the extent of TTI for patients with early-stage lung cancer undergoing surgery exceeded surgeons' expectations. Through the quantification of 2 component intervals for these TTIs, from suspicious scan result to biopsy and from biopsy to surgery, we were able to tease out different patient characteristics that may have contributed to extensive delay. Reasons primarily included racial and socioeconomic disparities, and medical comorbidities. This study also found that surgeons may not be aware of the extent of surgical delay that their patients undergo. As information regarding harms related to delays in treatment delays is incorporated into overall treatment considerations, this should lead to more efficient protocols to guide recommendations on surgical timeliness.

Conflict of Interest Statement

D.F.Y. is a named inventor on a number of patents and patent applications related to the evaluation of chest dis-

eases including measurements of chest nodules; has received financial compensation for the licensing of these patents; is a consultant and co-owner of Accumetra, a private company developing tools to improve the quality of CT imaging; is on the advisory board and owns equity in HeartLung, a company that develops software related to CT scans of the chest; is on the medical advisory board of Median Technology that is developing technology related to analyzing pulmonary nodules; and is on the medical advisory board of Carestream, a company that develops radiography equipment and has consulted for Genentech, AstraZeneca, and Pfizer. C.I.H. is an inventor of the patents and pending patents owned by Cornell Research Foundation (as of April 2009, she has divested herself of all royalties and other interests arising from these) and is on the medical advisory board for LungLife AI. All other authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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Key Words: delays, early-stage lung cancer, lung cancer, surgical delays, time to treatment, time to treatment initiation

TABLE E1. Surgeons questionnaire

Surgeon	How many weeks, on average do you think it takes from the diagnosis of a clinical stage 1 lung cancer (of any size <4 cm) in a patient until they receive surgery?	Do you believe this is the appropriate amount of time?	What do you believe is the maximum amount of time from diagnosis of a nodule until surgery that a patient can safely wait?	Do you believe that every week that passes before surgery creates an increased risk of death for the patient?	Does the size of the nodule matter in this characterization?	If yes, is immediate treatment more important if the nodule is small or large?	Does the location of the nodule matter in this characterization?	If yes, is immediate treatment more important if the nodule is central or peripheral?	Does the histology of the nodule matter in this characterization?	Does a patient's smoking history impact this characterization?	If yes, is immediate treatment most important if the patient is a former, current, or never smoker?	Does a patient's family history of cancer impact this characterization?	If yes, is immediate treatment more important if the patient does or does not have a family history of cancer?	Other	What factors, if any, do you believe most contribute to a time lapse between diagnosis and surgery?-Patient apprehension	What factors, if any, do you believe most contribute to a time lapse between diagnosis and surgery?-Patient life events (ie, vacation)	What factors, if any, do you believe most contribute to a time lapse between diagnosis and surgery?-Comorbidities	What factors, if any, do you believe most contribute to a time lapse between diagnosis and surgery?- Insurance coverage	What factors, if any, do you believe most contribute to a time lapse between diagnosis and surgery?-Need for second opinion	What factors, if any, do you believe most contribute to a time lapse between diagnosis and surgery?-Case complexity	What factors, if any, do you believe most contribute to a time lapse between diagnosis and surgery?-Surgeon's schedule/OR availability	What factors, if any, do you believe most contribute to a time lapse between diagnosis and surgery?- Other/Explain	Explanation	Other comments
Surgeon 1	2	Yes	6	Neutral	Yes	Large	Yes	Central	Yes	Yes	Never Smoker	No	n/a		1	0	1	0	0	0	1	0		
Surgeon 2	2	Yes	4	Neutral	Yes	Large	No	n/a	Yes	No	n/a	No	n/a	Asbestos	0	1	1	0	1	0	1	0		
Surgeon 3	3	Yes	8	Neutral	Yes	Large	Yes	Central	Yes	No	n/a	No	n/a		0	0	1	1	0	0	1	0		
Surgeon 4	4	Yes	4	Neutral	Yes	Large	Yes	Central	Yes	No	n/a	No	n/a	PET	1	1	0	0	0	0	0	0		
Surgeon 5	4	Yes	8	Completely Disagree	Yes	Large	Yes	Central	Yes	Yes	Current Smoker	No	n/a		1	1	1	1	0	1	0	0		
Surgeon 6	10	No	3	Somewhat Agree	Yes	Large	Yes	Central	Yes	No	n/a	No	n/a		1	0	1	0	0	1	0	0		
Surgeon 7	4	Yes	12	Completely Disagree	Yes	Large	No	n/a	Yes	No	n/a	No	n/a		0	1	1	0	0	0	1	0		
Surgeon 8	3	Yes	12	Somewhat Agree	Yes	Large	Yes	Central	Yes	Yes	Current Smoker	No	n/a		0	0	1	0	0	0	1	0		
Surgeon 9	2	Yes	5	Somewhat Disagree	Yes	Large	No	n/a	Yes	No	n/a	No	n/a	comorbidities	0	0	0	0	0	0	1	0		Waiting time for biopsy, PET, operation
Surgeon 10	2	Yes	4	Somewhat Agree	Yes	Large	Yes	Central	No	Yes	Current Smoker	No	n/a	comorbidities	0	0	1	0	0	0	1	0		
Surgeon 11	4	Yes	8	Neutral	Yes	Large	No	n/a	Yes	No	n/a	Yes	Does		1	1	1	0	0	1	0	0		
Surgeon 12	4	No	6	Somewhat Agree	Yes	Large	Yes	Central	Yes	No	n/a	No	n/a		0	0	1	0	0	0	1	1	Time from nodule identification to biopsy and for staging/physiologic testing	
Surgeon 13	4	Yes	8	Neutral	Yes	Large	Yes	Central	Yes	No	n/a	No	n/a		0	0	0	0	0	0	1	1	Need for additional staging studies and/or interrogations after diagnosis (PET, EBUS)	
Surgeon 14	6	No	8	Somewhat Agree	Yes	Large	Yes	Central	No	No	n/a	No	n/a	nodule consistency	0	0	0	0	0	0	1	1	Obtaining CT PET scans, PFTs	
Surgeon 15	4	Yes	8	Somewhat Disagree	Yes	Large	Yes	Central	Yes	No	n/a	Yes	Does	PET	0	0	0	0	0	0	0	1	How do you define diagnosis of stage I LC (CT finding vs pathological confirmation). Time to treatment from pathologic confirmation to surgery is quick. However, all the steps in workup from CT finding to pathological confirmation can sometimes take a long time.	Most valid measurement would be date of initial finding on CT scan to date of surgery or radiation.

CT, Computed tomography; *EBUS*, endobronchial ultrasound; *n/a*, not available; *PET*, positron emission tomography.