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Characteristics of Singapore lung cancer patients who miss out on lung cancer screening recommendations

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ABSTRACT

Introduction: The National Lung Screening Trial (NLST) identified individuals at high risk for lung cancer and showed that serial low-dose helical computer tomographic scans (CT) were able to identify lung cancer at an earlier stage and also demonstrated mortality reduction. However, there has been little evidence regarding the effectiveness of the Lung Cancer Screening Criteria in the Asian population.

Methods: To determine lung cancer patients who miss out on Lung Cancer screening criteria, we performed a retrospective audit from January to December 2018 in our hospital, and describe the characteristics of our patients diagnosed with lung cancer.

Results: We found that only 38.1% of the patients in our cohort who were diagnosed with lung cancer in 2018 fitted into NLST Criteria strictly by age and smoking criteria. However, those who fitted the inclusion criteria of lung cancer screening would derive significant benefits, as 85.4% presented at advanced stage and 54.6% did not survive one year. We explored using the United States Preventive Services Task Force criteria, which increased sensitivity to 58.7% of identifying our patients with diagnosed lung cancer. 15.5% of females with lung cancer in our cohort fitted into NLST Criteria, but their low smoking quantity is a significant contributing factor for females being excluded.

Conclusion: Majority of Singapore patients diagnosed with lung cancer would not have been picked up by NLST Criteria, especially female patients. However, those who fitted the inclusion criteria would derive significant benefit, while expanding to an older limit may yield benefits with improved sensitivity.

Keywords: Asia, early detection of cancer, lung cancer screening, lung neoplasms, Singapore

INTRODUCTION

Worldwide, lung cancer is the most common cancer diagnosed and the most common cause for cancer-related death.[1] It imposes a large disease burden in the world and often carries a grim prognosis in view of diagnosis at later stages. Among other factors, the prognosis of lung cancer is closely related to the stage of disease at diagnosis.[2] The current staging system utilised is the International Association for the Study of Lung Cancer (IASLC) 8th edition.[3]

In an effort to diagnose lung cancer at an earlier stage and reduce mortality, lung cancer screening trials such as the Nelson trial in Europe[4] and the National Lung Screening Trial (NLST) identified high risk individuals. In the NLST, they were randomly assigned to receive either annual low-dose helical computer tomographic scans (LDCT) or annual standard plain chest radiographs over a three-year period as screening for lung cancer, which demonstrated a 20% reduction in lung cancer mortality in the low-dose helical CT arm of the study.[5]

The definition of high-risk individual according to the NLST was that of "current or former heavy smokers aged 55 to 74" with "at least 30 pack-years". Since then various studies have utilised this study to determine its relevance in the local context of respective cities and countries. One particular study looking specifically at the applicability of the NLST screening criteria in Asian patients attending a major New York City Hospital in suggested that there was a similar rate of approximately 27.8% of patients meeting the NLST criteria to that estimated for the United States population as a whole.[6]

Further studies have considered the cost-effectiveness of such an approach in both insurance-based publicly-funded healthcare systems.[7-9] However, these have yet to be implemented or rolled out in large scale practice mainly due to concerns regarding cost, false positives and overdiagnosis of lung cancer.

In contrast to the NLST group, the U.S. Preventative Services Task Force (USPSTF) released a recommendation in 2014 on lung cancer screening, advising to carry out annual

screening with LDCT in adults aged 55 to 80 years who have a 30-pack year smoking history and currently smoke or have quit in the last 15 years.[10] In the July 2020 updated recommendation, the USPSTF has changed the age range and pack-year eligibility criteria, recommending annual screening with LDCT in adults aged 50 to 80 years who have a 20-pack year smoking history and who currently smoke or have quit in the past 15 years.[11]

Singapore is a multi-ethnic nation made up of Chinese (74%), Malay (13%), Indian (9%) and other ethnicities accounting for the rest.[12] Similar to other countries around the world, lung cancer remains an important cause of both mortality and morbidity as the third most commonly diagnosed cancer in Singapore.[13]

In recent years, there has been growing interest in the differences in lung cancer epidemiology between Western and Asian countries, including Singapore. In comparison to the Western countries, Singapore has significantly higher levels of lung cancers diagnosed in never-smokers – approximately 48% (according to data in 2011), compared to rates of approximately 10%–15% in other parts of the globe.[14,15] Another notable difference is the higher proportion of adenocarcinomas diagnosed in Singaporeans – approximately 78% in Singapore in 2011 as compared to 38.5% in the US.[16] This is likely in part due to adenocarcinoma being more common in never-smokers.[17,18]

For Singapore, guidelines for individual level decision for lung cancer screening had also been released since 2019 and are similar to NLST criteria.[19] Recommendations had also been suggested for an adaptive approach to lung cancer screening.[20] We seek to outline the characteristics of our patients with diagnosed lung cancer and how these screening guidelines may affect an Asian cohort in Singapore. Our hypothesis is that extrapolating NLST criteria to Singapore will miss out identifying lung cancer in a significant proportion of our patients who were diagnosed with lung cancer.

METHODS

We performed a retrospective audit from January to December 2018 in Changi General Hospital, a tertiary academic centre in Singapore with 1,000 beds, and assessed the characteristics of our patients diagnosed with lung cancer using electronic medical records. Patients had been either newly referred or on follow up at our Respiratory Medicine outpatient clinics, or seen as inpatient for a suspicion for malignancy. This can either be part of symptom evaluation or abnormal imaging. The database included patients who underwent diagnostic procedures and had histologically-proven lung cancer. Patients who underwent endobronchial ultrasound (EBUS) transbronchial needle aspiration (TBNA), computed tomography (CT) guided biopsy (TTBx), transbronchial lung biopsy (TBLB), endobronchial biopsy, thoracentesis and thoracoscopic biopsies were included for analysis. Patients with lung adenocarcionoma diagnosed had a predetermined package assessing for EGFR mutation, FISH panel and PD-L1. Patients who had non lung primaries, missing smoking status in the electronic records and those patients discharged to a different country for follow up were excluded for the purpose of this study. Our objective is to describe the characteristics of the patients diagnosed with lung cancer in 2018, and compare with NLST and USPSTF criteria. Lastly, we determined the characteristics of these groups who would not fall into lung cancer screening criteria.

We assessed characteristics like age, gender, smoking status, histology, mutation status, Eastern Cooperative Operative Group (ECOG) performance status, location of primary tumour, treatment options received, death within one year from referral, and for those who died we obtained the number of days from primary referral to death. SPSS v23.0 was used for statistical analysis. Independent sample t test was used to determine difference between 2 continuous variables. For univariate analysis, Pearson chi square was used to compare categorical groups while Fisher's Exact Test was used when the expected counts were below

5. Survival analysis was performed using Kaplan-Meier analysis. P<0.05 was used to determine statistical significance. The Singhealth Institutional Review Board granted an exemption from review.

RESULTS

126 patients diagnosed with lung cancer in 2018 were included in our analysis. 24 patients were excluded (6 lost to follow up, 16 with non lung primaries, 2 with absent smoking data). 73.8% were males. 64.3% were Chinese, 27.8% Malay, 5.6% Indian. The median age was 68 years (32-89 years old) and mean age 67.5 +/- 11.3 years old. 45.2% died in 1 year. 33.3% were non smokers. 59.5% had 30 or more pack years. The majority of our patients diagnosed with lung cancer were in stage 3 (19.8%) and 4 (54%). EBUS TBNA was performed in 33.3%, CT guided biopsy 39.7%, thoracentesis 11.9%, thoracoscopic biopsy 4.8%, transbronchial lung biopsy 7.1% and endobronchial biopsy 2.4%. The most common site of the primary lesion is in the right upper lobe (RUL) (29.4%), followed by left upper lobe (LUL) (18.3%), right lower lobe (RLL) (15.9%) and left lower lobe (LLL) (9.5%).

Most of the patients in our cohort had performance status 0 (31.9%) or 1 (46.8%) on initial review by specialist. The majority had adenocarcinoma (overall 87.3% with non small cell lung cancer (NSCLC)), 6.3% small cell, 6.3% others (lymphoepithelial like carcinoma). 27.0% (34/126) had epidermal growth factor receptor (EGFR) mutations (which represented 41% of those with adenocarcinoma), 1.6% (2.4% of adenocarcinoma) had anaplastic lymphoma kinase (ALK) rearrangements. 19.3% of our patients received surgery, 18.4% received radiation, 31.6% chemotherapy, 16.7% tyrosine kinase inhibitors, 5.3% received immunotherapy with programmed death-ligand 1 (PD-L1) inhibitors (PD-1% range 25-100%), 23.7% opted for best supportive care. The overall median survival from referral to death was 225 days while 54.8% were alive at 1 year. (Table I). For NSCLC, the median survival for stage 3 was 244 days,

compared to median survival of stage 4 at 206 days. The median survival for small cell lung cancer was 132 days.

There were significantly more males compared to females who had more than 30 pack year smoking history, and males also had significantly higher pack years compared to females. There were also significantly more females than males who had driver mutations. (Table II). 29% of our patients had driver mutations. 43/57 (75.4%) with driver mutations were alive at 1 year, compared to 46/89 (51.7%) without driver mutations who were alive at 1 year. However this was not statistically significant (p=0.28). 22/34 (64.7%) of those who had EGFR mutations were alive at 1 year.

In our cohort, most of the patients diagnosed with lung cancer less than 55 years old were females (63.6%), compared to those 55-74 years old (25%) and >74 years old (17.9%) (Table III). 63.2% of those 55-74 years old had smoked > 30 pack years compared to 9.1% aged <55 years old.

We found that only 38.1% (48/126) of our 2018 lung cancer cohort would fit into Lung Cancer Screening Criteria strictly by age and smoking criteria. If we include those patients >74 year old with >30 pack year smoking history (assuming they may have been screened earlier in life if a lung cancer screening programme had been in place), this sensitivity can potentially increase to 58.7% (74/126).

If the new USPSTF criteria was used, 58.7% (74/126) of all patients would fit into screening criteria (Table IV). The majority of patients in the group less than 50 years old were females and mostly non smokers. For the group 50-80 years old, the majority were male and most had smoked more than 20 pack years. For those more than 80 years old, most were male and slightly more than half smoked more than 20 pack years.

This sensitivity may increase to 63.5% (80/126) if those 80 years old or more with more than 20 pack years smoking history were included, assuming they were screened earlier in life

by an implemented lung cancer screening programme. 26 more patients (21%) would be picked up compared to NLST criteria in our cohort of lung cancer patients (Table V). However, 52/126 (41.3%) of the cohort will still not qualify via either screening criteria.

To study the different characteristics between these patients, we divided our patients into 5 different groups - those who fit NLST versus four other groups who would not fit into NLST criteria (Table VI). Group 1 consisted of 55-74 years old patients who had more than 30 pack year smoking history (NLST criteria). Group 2 consisted of patients younger than 55 years old. Group 3 had patients 55-74 years old and smoked less than 30 pack years. Group 4 consisted of patients older than 74 years old but smoked less than 30 pack years. Group 5 had patients more than 74 years old, and smoked more than 30 pack years.

Of all the groups, Group 1 is the largest group and these are patients who are within the inclusion criteria of NLST. Group 3 and Group 5 represent the next largest groups. The majority of those who fit NLST (Group 1) were male. Of note, 46.2% (43/93) of males fit NLST screening criteria compared to 15.5% (5/33) of females (odds ratio 3.0, CI 1.3-7.0, p=0.002). For USPSTF, 73.1% (68/93) of males fit criteria compared to 18.2% (6/33) of females (odds ratio 4.0, CI 1.9-8.4, p<0.001).

Group 1 and 5 had the least percentage of driver mutations compared to the other groups. Group 1 also presented with the highest percentage of cases (85.4%) with unresectable stage and highest mortality (54.2%) within 1 year, highlighting that this group has the most potential for benefit with lung cancer screening. In comparison, Group 2 which has the highest percentage of females, also has a high percentage of patients presenting with advanced stage, highlighting that this younger group should not be neglected in future screening.

Groups 2, 3 and 4 had a greater proportion of females and higher percentage of driver mutations compared to groups 1 and 5. Group 4 had the highest percentage of driver mutations and adenocarcinoma, while Group 5 had the largest percentage of males, lowest percentage of

driver mutations and the majority still had a good performance status. The characteristics of Group 5 resemble Group 1, and both have the lowest percentage of adenocarcinoma. The benefits of extending lung cancer screening to those more than 74 years old with more than 30 years smoking history need to be further explored.

DISCUSSION

We demonstrated how a lung cancer screening program may potentially benefit an Asian population. We also highlighted its pitfalls of using the Lung Cancer Screening Criteria in our local population and outlined the differences in characteristics between these five groups. We also explored significant characteristics of patients who will fit into lung cancer screening criteria.

Of note, only 38.1% of the patients who were diagnosed with lung cancer in 2018 would have fit into the Lung Cancer Screening Criteria strictly by age and smoking criteria. This means that the majority diagnosed with lung cancer would not have been picked up by the recommended Lung Cancer Screening Criteria. We found that the majority of those who did not fulfil lung cancer screening criteria were females.

According to an earlier local study,[21] the proportion of never smokers with lung cancer in their cohorts were 31% from 1999-2002, and 48% from 2008-2011. In our cohort, 33% were completely non smokers. In addition, 40.5% (51/126) of our cohort had smoking history less than 30 pack years. 82% of females in our cohort were non smokers/smoker or ex smoker with < 30 pack years, compared to 74% of males with significant smoking history (smoker or ex-smoker with > 30 pack years). In terms of gender proportion, 73.8% of our cohort were males, compared to 68.8% in the Toh cohort from 1999-2002, and 61.2% in the LCCS cohort from 2008-2011. As we have more male smokers in our 2018 cohort and a smaller sample size, our data may overestimate the benefits of screening with NLST criteria.

However, there are benefits for implementing a lung cancer screening program, as the majority of our patients within inclusion criteria of Lung Cancer Screening had good performance status but presented with late stage (stage 3 and 4) and more than half (54.2%) did not survive 1 year.

In 2020, Singapore's life expectancy at 65 years old is 21.3 years,[12] so extending the screening age upper limit to mirror our ageing population might also need consideration. In addition, lung cancer screening may also benefit those who are more than 74 years old as the majority have good performance status similar to their younger counterparts in other groups.

The new recommended USPSTF criteria includes patients 50-80 years old who smoked more than 20 pack years, so this will include 58.7% of our patients diagnosed with lung cancer in 2018. While the benefits of screening a larger cohort with a more expansive criteria may seem to be better in the Singapore population, this has to be balanced against screening the general population and inherently picking up more false positives. This is especially important because of the increased prevalence of tuberculosis and other granulomatous diseases in the region, that increases the risks of false positives for the younger non smoking age group.[22]

We also found that although close to half of males (46.2%) fit NLST screening criteria, only 15.5% of females would fit screening criteria. Many females are not included in the screening criteria because of their relative lack of smoking quantity compared to males. Local lung cancer screening criteria may need to be adapted to be inclusive of the female population,[20] due to their lower smoking quantity and increased prevalence of female non-smokers with adenocarcinoma in Asia.

LDCT screening is not without its risks.[23] With an annual LDCT being performed for 3 years in a row, cumulative radiation exposure can increase the risk of radiation-associated cancers especially in the younger population within the screening cohort. As aggressive cancers can develop in intervals between screening examination, patients who pass the LDCT

screening may be falsely reassured regarding their cancer risk. In addition, with an increase in the number of LDCT being performed, the incidence of false positive results will likely increase too.[24] This can in turn lead to potential harm, with an increase in biopsy rates and hence higher healthcare costs.[25] There is also increased anxiety associated with screening.[26]

While the Lung Cancer Screening Criteria may be easy and practical to implement, it can be overly simplistic. The relationship between baseline risk of developing lung cancer, treatment-related harms and competing risk of death from other causes is crucial in determining the risks and benefits of lung cancer screening. Lung cancer screening criteria may not fully consider premorbid function and life limiting comorbidities, which can preclude them from screening benefits. Lung cancer prediction models like PLCOm2012 which incorporates education level, ethnicity, personal and family history of malignancy, exist but have not been validated in our local population.[27] The role of known risk factors in never smokers including exposure to environmental tobacco smoke,[28,29] cooking fumes[30] and controversially HPV infection[31] need further assessment of their impact in our local context. Further studies are needed to determine the threshold where benefits of reducing lung cancer death outweigh the risk of dying from a competing cause and can serve to improve survival.[32]

The strengths of our paper are that we included patients who were positive for lung cancer diagnosed via all modalities. Adding to current literature, we were able to identify and describe the characteristics of these different patient groups according to lung cancer screening criteria. Most importantly, we were able to identify significant characteristics and the extent of patients who will fit into lung cancer screening criteria. Our hospital is one of several major tertiary hospitals in Singapore and the demographics of our cohort mirrors the general Singapore population with a Chinese race predominant majority.

As this is a Respiratory Medicine database (rather than Oncology), we believe that this is representative of how patients with lung cancer currently present to hospitals, as referrals for

lung cancer workup comes from similar sources – outpatient clinics, inpatient referrals (with patients coming in via the ED), with patient referral sources similar to other tertiary hospitals. In terms of lung cancer workup methods, the range of biopsy methods are standard of care similar to other institutions – with CT guided biopsies, endobronchial ultrasound needle aspiration, and thoracocentesis and thoracoscopies offered. The advantages of our lung cancer database is that it contains biopsy proven lung cancer, from a Respiratory Medicine point of view and allows us to study all-comers with lung cancer. This means that all patients were biopsy proven lung cancer were in this database, including those patients whose families later decided not for treatment. Though a tertiary hospital's referred cohort (symptoms or imaging based) may be different compared to presentations to primary care, we are unable to ascertain if patients who present to primary care would have different patient demographics or present at an earlier stage.

Limitation of the study includes its retrospective nature. Although the electronic medical records were robust and we were able to record extensive patient characteristics including smoking status and extent, cancer staging, performance status, mutation status and patient mortality at 1 year, we were unable to determine if the death was related to lung cancer or other causes. Our sample size limits our ability to make further multivariate analyses.

Our cohort represented patients who were diagnosed with lung cancer in 2018, of whom most would have presented later in their disease when they had symptoms. In contrast, a typical lung cancer screening cohort would consist of asymptomatic individuals who have risk factors. This later presentation among our study cohort likely contributed to the more advanced stages upon diagnosis, limited treatment options and therefore shorter prognosis with higher rates of death compared to a traditional screening cohort. The benefits of a lung cancer screening program would be underestimated as patients who had poor premorbid function would be

excluded as they may not have undergone biopsies and offered regular cancer treatment options.

Diagnosed non-lung primary malignancies were excluded from the analysis of this study but represented close to 10% of thoracic malignancies diagnosed in our cohort in 2018. A lung cancer screening program may allow for detection of non-lung malignancies and reduce mortality, an area which the scope of our study does not cover.

In conclusion, although NLST criteria for our local cohort may miss a large proportion of our patients with lung malignancies, the patients who were in the inclusion criteria of lung cancer screening would derive significant benefits as they presented late and had good performance status. We also found that only 15.5% of females with lung cancer fit into Lung Cancer Screening Criteria. The low smoking quantity of females in our cohort is a significant contributing factor for them to be excluded from screening criteria. Extending the upper limit of lung cancer screening age may also yield benefits for our ageing population. Further research in deriving an appropriate lung cancer screening criteria is paramount to maximise benefits and minimise risks for our local population.

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Table I. Characteristics of patients who survived versus those who died at 1 year.

Demographics	Total	Alive at 1 year (n = 69)	Deceased at 1 year (n = 57)	p-value
Age N, %				
< 55 years	11 (8.7%)	7 (10.1%)	4 (7.0%)	0.767
55-74 years	76 (60.3%)	40 (58.0%)	36 (63.2%)	
≥ 75 years	39 (31.0%)	22 (31.9%)	17 (29.8%)	
Gender N, %				
Female	33 (26.2%)	19 (27.5%)	14 (24.6%)	0.705
Male	93 (73.8%)	50 (72.5%)	43 (75.4%)	
Smoking status N, %				
Non smoker/ Smoker/Ex-smoker (< 30 pack years)	51 (40.5%)	32 (46.4%)	19 (33.3%)	0.138
Smoker/Ex-smoker (≥ 30 pack years)	75 (59.5%)	37 (53.6%)	38 (66.7%)	
Stage at diagnosis N, %				
1	22 (17.5%)	22 (31.9%)	0	< 0.001
2	11 (8.7%)	9 (13.0%)	2 (3.5%)	
3	25 (19.8%)	11 (15.9%)	14 (24.6%)	
4	68 (54.0%)	27 (39.1%)	41 (71.9%)	
ECOG status N, %				
0	40 (31.7%)	29 (42.0%)	11 (19.3%)	< 0.001
1	59 (46.8%)	35 (50.7%)	24 (42.1%)	
2	15 (11.9%)	3 (4.3%)	12 (21.1%)	
3	9 (7.1%)	0	9 (15.8%)	
4	3 (2.4%)	2 (2.9%)	1 (1.8%)	
Histology N, %				
Adenocarcinoma	83 (65.9%)	51 (73.9%)	32 (56.1%)	0.092
Squamous cell	22 (17.5%)	11 (15.9%)	11 (19.3%)	
Non-small cell (others)*	5 (4.0%)	2 (2.9%)	3 (5.3%)	
Small cell	8 (6.3%)	1 (1.4%)	7 (12.3%)	
Others†	8 (6.3%)	4 (5.8%)	4 (7.0%)	
Mutations				
ALK rearrangement	2	1	1	0.499
EGFR mutant	34	22	12	
ROS1 mutation	1	0	1	
% driver mutations	29.3%	33.3%	24.6%	

**"Non-small cell (others)" represent adenosquamous carcinoma and undifferentiated non-small cell lung cancer. †"Others" represent lymphoepithelial like carcinoma and carcinoid.*
ALK: anaplastic lymphoma kinase; ECFR: epidermal growth factor receptor; ECOG: Eastern Cooperative Operative Group; ROS1: receptor tyrosine kinase

Table II. Characteristics of patients by gender.

Demographics	Females (n = 33)	Males (n = 93)	p-value
Age (mean ± SD)	64.2 ± 13.5	68.7 ± 10.2	0.091
Number of pack years (mean ± SD)	7.3 ± 15.8	39.8 ± 26.7	< 0.001
Non smoker/Smoker/Ex-smoker (< 30 pack years)	27	24	< 0.001
Smoker/Ex-smoker (≥ 30 pack years)	6	69	
% > 30 pack years	18.2%	74.2%	< 0.001
Race			
Chinese	19	62	0.395
Malay	10	25	
Indian	2	5	
Others	2	1	
Histology			
Adenocarcinoma	25	58	0.449
Squamous cell	3	19	
Non-small cell (others)	1	4	
Small cell	1	7	
Others	3	5	
Mutations			
ALK rearrangement	2	0	
EGFR mutant	16	18	
ROS1 mutation	0	1	
% driver mutations	54.5%	20.4%	0.006

ALK: anaplastic lymphoma kinase; ECFR: epidermal growth factor receptor; ECOG: Eastern Cooperative Operative Group; ROS1: receptor tyrosine kinase; SD: standard deviation

Table III. Characteristics of patients by NLST age group.

Demographics	< 55 years (n = 11)	55-74 years (n = 76)	> 74 years (n = 39)	p-value
Gender N, %				
Female	7 (63.6%)	19 (25%)	7 (17.9%)	0.009
Smoking status N, %				
Non-smoker / < 30 pack years	10 (90.9%)	28 (36.8%)	13 (33.3%)	0.002
Smoker/Ex-smoker (≥ 30 pack years)	1 (9.1%)	48 (63.2%)	26 (66.7%)	
Race N, %				
Chinese	2 (18.2%)	48 (63.2%)	31 (79.5%)	
Malay	5 (45.5%)	24 (31.6%)	6 (15.4%)	
Indian	2 (18.2%)	3 (3.9%)	2 (5.1%)	
Others	2 (18.2%)	1 (1.3%)	0	
Stage at diagnosis N, %				
1	1 (9.1%)	10 (13.2%)	11 (28.2%)	
2	1 (9.1%)	4 (5.3%)	6 (15.4%)	
3	2 (18.2%)	20 (26.3%)	3 (7.7%)	
4	7 (63.6%)	42 (55.3%)	19 (48.7%)	
Unresectable cancer (stage 3 and 4)	9 (81.8%)	62 (81.6%)	22 (56.4%)	0.012
ECOG status N, %				
0	7 (63.6%)	28 (36.8%)	5 (12.8%)	
1	2 (18.2%)	34 (44.7%)	23 (59.0%)	
2	2 (18.2%)	6 (7.9%)	7 (17.9%)	
3	0	5 (6.6%)	4 (10.3%)	
4	0	3 (3.9%)	0	
ECOG 0-2	9 (100%)	68 (89.5%)	35 (89.7%)	0.530
Histology N, %				
Adenocarcinoma	9 (81.8%)	46 (60.5%)	28 (71.8%)	
Squamous cell	2 (18.2%)	13 (17.1%)	7 (17.9%)	
Non-small cell (others)	0	3 (3.9%)	2 (5.1%)	
Small cell	0	7 (9.2%)	1 (2.6%)	
Others	0	7 (9.2%)	1 (2.6%)	
Mutations				
ALK rearrangement	2	0	0	
EGFR mutant	3	20	11	
ROS1 mutation	0	0	1	
Driver mutations N, %	5 (45.5%)	20 (26.3%)	11 (28.2%)	0.417

ALK: anaplastic lymphoma kinase; ECFR: epidermal growth factor receptor; ECOG: Eastern Cooperative Operative Group; NLST: National Lung Screening Trial; ROS1: receptor tyrosine kinase

Table IV. Characteristics of patients by USPSTF age group.

Demographics	< 50 years (n = 8)	50-80 years (n = 107)	> 80 years (n = 11)	p-value
Gender N, %				
Female	5 (62.5%)	26 (24.3%)	2 (18.2%)	0.049
Smoking status N %				
Non-smoker / < 20 pack years	7 (87.5%)	33 (30.8%)	5 (45.5%)	0.004
Smoker/Ex-smoker (≥ 20 pack years)	1 (12.5%)	74 (69.2%)	6 (54.5%)	

USPSTF: United States Preventive Services Task Force

Table V. Patients screening using NLST versus USPSTF criteria.

		USPSTF Criteria		Total
		Excluded	Included	
NLST Criteria	Excluded	52	26	78
	Included	0	48	48
Total		52	74	126

NLST: National Lung Screening Trial; USPSTF: United States Preventive Services Task Force

Table VI. Characteristics of patients by NLST group versus groups which did not fall into NLST criteria.

	Group 1 55-74 years old; > 30 pack year (NLST criteria) (n=48)	**Group 2 < 55 years old (n = 11)**	**Group 3 55-74 years old; < 30 pack year (n = 28)**	**Group 4 > 74 years old; < 30 pack year (n = 13)**	**Group 5 > 74 years old; > 30 pack year (n = 26)**
Gender					
Female	5	7	14	7	0
Male	43	4	14	6	26
% Male	89.6%	36.4%	50%	46.2%	100%
Race					
Chinese	29	2	19	10	21
Malay	16	5	8	2	4
Indian	2	2	1	1	1
Others	1	2	0	0	0
Histology					
Adenocarcinoma	24	9	22	12	16
Squamous Cell Ca	11	2	2	1	6
NSCLC others	2	0	1	0	2
Small Cell Ca	7	0	0	0	1
Others	4	0	3	0	1
% Adenocarcinoma	50%	81.8%	78.6%	92.3%	61.5%
EGFR mutation status					
EGFR+	10	3	10	6	5
ALK+	0	2	0	0	0
ROS1+	0	0	0	1	0
% Driver mutations	20.8%	45.5%	35.7%	53.8%	19.2%
Stage					
1	5	1	5	3	8
2	2	1	2	1	5
3	17	2	3	1	2
4	24	7	18	8	11
Advanced stage malignancies (Stage 3 & 4) N, %	41 (85.4%)	9 (81.8%)	21 (75%)	9 (69.2%)	13 (50%)

Performance Status					
0	14	7	14	3	2
1	23	2	11	6	17
2	4	2	2	3	4
3	4	0	1	1	3
4	3	0	0	0	0
% ECOG 0-2	85.4%	81.8%	89.3%	92.3%	88.5%
Death within 1 year N, %	26 (54.2%)	4 (36.4%)	10 (35.7%)	6 (46.2%)	11 (42.3%)

ALK: anaplastic lymphoma kinase; Ca: carcinoma; ECFR: epidermal growth factor receptor; ECOG: Eastern Cooperative Operative Group; NLST: National Lung Screening Trial; ROS1: receptor tyrosine kinase