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 computed tomography could identify lung cancer at an earlier stage, leading to mortality reduction. However, there is little evidence regarding the effectiveness of the NLST criteria for the Asian population.

Methods: We performed a retrospective audit in our hospital from January 2018 to December 2018, with the aim to describe the characteristics of patients diagnosed with lung cancer and to identify patients who would miss out on lung cancer screening when the NLST criteria was applied.

Results: We found that only 38.1% of our cohort who were diagnosed with lung cancer met the NLST criteria strictly by age and smoking status. Patients who met the screening criteria would have derived significant benefits from it, as 85.4% of our patients had presented at an advanced stage and 54.6% died within 1 year. When the United States Preventive Services Task Force criteria was applied, it increased the sensitivity of lung cancer diagnosis to 58.7%. Only 15.5% of the female patients with lung cancer met the NLST criteria; their low smoking quantity was a significant contributing factor for exclusion.

Conclusion: The majority of Singapore patients diagnosed with lung cancer, especially females, would not have been identified with the NLST criteria. However, those who met the inclusion criteria would have benefited greatly from screening. Extending the screening age upper limit may yield benefits and improved sensitivity in the Singapore context.

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 of cancer-related death.[1] It imposes a large disease burden and often carries a grim prognosis, especially when diagnosed at later stages 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 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), were conducted to identify high-risk individuals. In NLST, subjects were randomly assigned to receive either annual low-dose helical computed tomography (LDCT) or annual standard plain chest radiography over a 3-year period as screening for lung cancer; the LDCT arm of the study demonstrated a 20% reduction in lung cancer mortality.[5]

The definition of high-risk individual according to NLST was "current or former heavy smokers aged 55 to 74 years" with "at least 30 pack-years". Since the NLST results in 2011, various studies have utilised this study to determine its relevance

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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 suggested that approximately 27.8% of Asian patients met the NLST criteria, which is similar to that estimated for the US population as a whole.[6] Further studies have considered the cost-effectiveness of such an approach in both insurance-based and publicly funded healthcare systems.[7-9] However, this has 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 United States Preventive Services Task Force (USPSTF) released a recommendation in 2014 on lung cancer screening, with the advice to carry out annual screening with LDCT in adults aged 55–80 years who have a 30 pack-year smoking history and who currently smoke or have quit in the last 15 years.[10] In the July 2020 updated recommendation, USPSTF changed the age range and pack-year eligibility criteria, recommending annual screening with LDCT in adults aged 50–80 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%), Indians (9%), and other ethnicities (4%).[12] Lung cancer is the third most commonly diagnosed cancer in Singapore and remains an important cause of mortality and morbidity, similar to countries around the world.[13] In recent years, there has been growing interest in the differences in lung cancer epidemiology between Western and Asian countries, including Singapore. Compared to the west, Singapore has significantly a higher proportion of lung cancer diagnosed in never smokers (approximately 48% according to data in 2011), compared to rates of approximately 10%–15% reported in other parts of the world.[14,15] Another notable difference is the higher proportion of adenocarcinomas diagnosed in the Singapore population — approximately 78% in 2011 as compared to 38.5% in the USA.[16] This is likely in part due to adenocarcinoma being more common in never smokers.[17,18]

The Singapore guidelines for individual-level decision for lung cancer screening were released in 2019 and are similar to the NLST criteria.[19] Recommendations for an adaptive approach to lung cancer screening have also been formulated.[20] In this study, we aimed to outline the characteristics of patients with diagnosed lung cancer and how these screening guidelines may affect an Asian cohort in Singapore. Our hypothesis is that extrapolating the NLST criteria to Singapore will result in a significant proportion of the local patients missing out on lung cancer screening.

METHODS

We performed a retrospective audit from January 2018 to December 2018 in Changi General Hospital, a tertiary academic centre in Singapore with 1000 beds, and assessed the characteristics of patients diagnosed with lung cancer using electronic medical records. Patients were newly referred or on follow-up at our Respiratory Medicine outpatient clinics, or seen as inpatients for a suspicion for malignancy — this could 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, computed tomography (CT)-guided biopsy, transbronchial lung biopsy (TBLB), endobronchial biopsy, thoracentesis and thoracoscopic biopsies were included for analysis. Patients diagnosed with lung adenocarcinoma had a predetermined package assessing for epidermal growth factor receptor (EGFR) mutation, fluorescence in situ hybridisation panel and programmed death-ligand 1 (PD-L1). Patients who had non-lung primaries, patients with missing smoking status in the electronic records and patients discharged to a different country for follow-up were excluded for the purpose of this study. Our objective was to describe the characteristics of patients diagnosed with lung cancer in 2018 and compare them against the NLST and USPSTF criteria. Lastly, we determined the characteristics of patients that would not fall into lung cancer screening criteria.

We assessed characteristics like age, gender, smoking status, histology, mutation status, Eastern Cooperative Operative Group performance status, location of primary tumour, treatment received, death within 1 year from referral and the number of days from primary referral to death. Statistical analysis was done using IBM SPSS Statistics version 23.0 (IBM Corp, Armonk, NY, USA). Independent sample *t*-test was used to determine differences between two continuous variables. For univariate analysis, Pearson's chi-square test was used to compare categorical groups, while Fisher's exact test was used when the expected counts were <5. Survival analysis was performed using Kaplan–Meier analysis. A P value < 0.05 was considered as statistically significant. An exemption from review was granted by the SingHealth Institutional Review Board.

RESULTS

We accessed the electronic medical records of 150 patients diagnosed with lung cancer in 2018. Twenty-four patients were excluded from the study (six lost to follow-up, 16 with non-lung primaries, two with absence of smoking data). A total of 126 patients were included in our analysis. Of these, 73.8% were males, and 64.3% were Chinese, 27.8% Malay and 5.6% Indians. The median and mean ages of the patients were 68 (range 32–89) years and 67.5 ± 11.3 years, respectively. Of the 126 patients, 45.2% died within 1 year, 33.3% were non-smokers and 59.5% had ≥ 30 pack-years. The majority of our patients diagnosed with lung cancer were in stage 3 (19.8%) and stage 4 (54.0%). Endobronchial ultrasound transbronchial

needle aspiration was performed in 33.3%, CT-guided biopsy in 39.7%, thoracentesis in 11.9%, thoracoscopic biopsy in 4.8%, TBLB in 7.1% and endobronchial biopsy in 2.4% of patients. The most common site of the primary lesion was the right upper lobe (29.4%), followed by the left upper lobe (18.3%), right lower lobe (15.9%) and left lower lobe (9.5%).

Most of the patients in our cohort had performance status 0 (31.9%) or 1 (46.8%) on initial review by a specialist. The majority had adenocarcinoma (overall 87.3% with non-small cell lung cancer [NSCLC]), 6.3% had small cell lung cancer and 6.3% had others (lymphoepithelioma-like carcinoma). Moreover, 27.0% (34/126) had EGFR mutations (which represented 41% of those with adenocarcinoma) and 1.6% (2.4% of adenocarcinoma) had anaplastic lymphoma kinase rearrangements. In terms of treatment, 19.3% of the patients received surgery, 18.4% radiation, 31.6% chemotherapy, 16.7% tyrosine kinase inhibitors, 5.3% immunotherapy with PD-L1 inhibitors (PD-L1 range 25%–100%), and 23.7% opted for best supportive care. The overall median survival from referral to death was 225 days, and 54.8% were alive at 1 year [Table 1]. For NSCLC, the median survival for stage 3 was 244 days vs. 206 days for stage 4. The median survival for small cell lung cancer was 132 days.

A significantly higher number of males had more than 30 pack-year smoking history, and males also had significantly higher pack-years compared to females. There were significantly more females than males who had driver mutations [Table 2]. Twenty-nine percent of the patients had driver mutations; 43/57 (75.4%) patients with driver mutations were alive at 1 year, as compared to 46/89 (51.7%) without

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

Variable	*n* (%)			*P*
	Total (*n*=126)	Alive (*n*=69)	Deceased (*n*=57)	
Age (yr)				
<55	11 (8.7)	7 (10.1)	4 (7.0)	0.767
55–74	76 (60.3)	40 (58.0)	36 (63.2)	
≥75	39 (31.0)	22 (31.9)	17 (29.8)	
Gender				
Female	33 (26.2)	19 (27.5)	14 (24.6)	0.705
Male	93 (73.8)	50 (72.5)	43 (75.4)	
Smoking status				
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				
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				
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				
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)[a]	5 (4.0)	2 (2.9)	3 (5.3)	
Small cell	8 (6.3)	1 (1.4)	7 (12.3)	
Others[b]	8 (6.3)	4 (5.8)	4 (7.0)	
Mutations				
ALK rearrangement	2 (1.6)	1 (1.4)	1 (1.8)	0.499
EGFR mutant	34 (27.0)	22 (31.9)	12 (21.1)	
ROS1 mutation	1 (0.8)	0	1 (1.8)	
Driver mutations (%)	29.3	33.3	24.6	

[a]Represents adenosquamous carcinoma and undifferentiated non-small cell lung cancer. [b]Represents lymphoepithelial-like carcinoma and carcinoid. ALK: anaplastic lymphoma kinase, ECOG: Eastern Cooperative Operative Group, EGFR: epidermal growth factor receptor, ROS1: receptor tyrosine kinase

driver mutations who were alive at 1 year. However, this was not statistically significant (P = 0.28). We found that 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 who were aged <55 years were females (63.6%), as compared to those aged 55–74 years (25%) and >74 years (17.9%) [Table 3]. In addition, 63.2% of those aged 55–74 years had smoked >30 pack-years compared to 9.1% aged <55 years.

We found that only 38.1% (48/126) of our lung cancer cohort would fit into the lung cancer screening criteria strictly by age and smoking criteria. If we include those patients aged >74 years 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).

Based on the new USPSTF criteria, 58.7% (74/126) of patients were found to meet the screening criteria [Table 4]. The majority of patients in the group aged <50 years were females and mostly non-smokers. In the group aged 50–80 years, the majority were males and most had smoked >20 pack-years. Among those aged >80 years, most were males and slightly more than half smoked >20 pack-years. This sensitivity may increase to 63.5% (80/126) if patients aged >80 years with >20 pack-years smoking history were included, assuming they were screened earlier in life by an implemented lung cancer screening programme. Twenty-six more patients (21%) would be picked up as compared to the NLST criteria in our cohort of lung cancer patients [Table 5]. However, 52/126 (41.3%) of the cohort would still not qualify on using either of the screening criteria.

To study the different characteristics between these patients, we divided our patients into five groups: one group that met the NLST criteria versus four groups that did not meet the NLST criteria [Table 6]. Group 1 (met NLST criteria) consisted of patients aged 55–74 years who smoked >30 pack-years. The other groups comprised the following: Group 2: patients aged <55 years; Group 3 patients aged 55–74 years who smoked <30 pack-years; Group 4: patients aged >74 years who smoked <30 pack-years; and Group 5: patients aged >74 years who smoked >30 pack-years.

Of all the groups, Group 1 was the largest and consisted of patients who were within the inclusion criteria of NLST. Group 3 and Group 5 represented the next largest groups. The majority of those who met the NLST criteria (Group 1) were males. Of note, 46.2% (43/93) of males met the NLST screening criteria compared to 15.5% (5/33) of females (odds ratio 3.0, 95% CI 1.3–7.0, P = 0.002). Regarding USPSTF, 73.1% (68/93) of males met the criteria compared to 18.2% (6/33) of females (odds ratio 4.0, 95% CI 1.9–8.4, P < 0.001).

Table 2. Characteristics of patients by gender.

Variable	Mean±SD/n(%)		*P*
	Female (*n*=33)	Males (*n*=93)	
Age (yr)	64.2±13.5	68.7±10.2	0.091
No. of pack years	7.3±15.8	39.8±26.7	< 0.001
Smoking status			
Non-smoker/ smoker/ex-smoker (<30 pack-years)	27 (81.8)	24 (25.8)	<0.001
Smoker/ ex-smoker (≥30 pack-years)	6 (18.2)	69 (74.2)	
Race			
Chinese	19 (57.6)	62 (66.7)	0.395
Malay	10 (30.3)	25 (26.9)	
Indian	2 (6.1)	5 (5.4)	
Others	2 (6.1)	1 (1.1)	
Histology			
Adenocarcinoma	25 (75.8)	58 (62.4)	0.449
Squamous cell	3 (9.1)	19 (20.4)	
Non-small cell (others)	1 (3.0)	4 (4.3)	
Small cell	1 (3.0)	7 (7.5)	
Others	3 (9.1)	5 (5.4)	
Mutations			
ALK rearrangement	2 (6.1)	0	
EGFR mutant	16 (48.5)	18 (19.4)	
ROS1 mutation	0	1 (1.1)	
Driver mutations (%)	54.5	20.4	0.006

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

Groups 1 and 5 had the lowest 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 would benefit the most from lung cancer screening. In comparison, Group 2, which had the highest percentage of females, also had 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 higher 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 and lowest percentage of driver mutations, with the majority still having a good performance status. The characteristics of Group 5 resembled those of Group 1, and both had the lowest percentage of adenocarcinoma. The benefits of extending lung cancer screening to those above 74 years old with more than 30 pack-years of smoking history need to be further explored.

Table 3. Characteristics of patients by NLST age group.

Variable	*n* (%)			*P*
	<55 years (*n*=11)	55–74 years (*n*=76)	>74 years (*n*=39)	
Gender				
Female	7 (63.6)	19 (25)	7 (17.9)	0.009
Smoking status				
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				
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				
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 (stages 3 and 4)	9 (81.8)	62 (81.6)	22 (56.4)	0.012
ECOG status				
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	
0–2	9 (100)	68 (89.5)	35 (89.7)	0.530
Histology				
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 (18.2)	0	0	
EGFR mutant	3 (27.3)	20 (26.3)	11 (28.2)	
ROS1 mutation	0	0	1 (2.6)	
Driver mutations	5 (45.5)	20 (26.3)	12 (30.8)	0.417

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

Table 4. Characteristics of patients by USPSTF age group.

Variable	*n* (%)			*P*
	<50 years (*n*=8)	50–80 years (*n*=107)	>80 years (*n*=11)	
Gender				
Female	5 (62.5)	26 (24.3)	2 (18.2)	0.049
Smoking status				
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

DISCUSSION

In this study, we demonstrated that a lung cancer screening programme may potentially benefit an Asian population. We also highlighted the pitfalls of using the recommended lung cancer screening criteria in our local population and outlined the differences in characteristics among five groups of patients. We also explored significant characteristics of patients who would meet the lung cancer screening criteria.

Table 5. Patients screening using the NLST versus USPSTF criteria.

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

Data presented as *n*. NLST: National Lung Screening Trial, USPSTF: United States Preventive Services Task Force

Of note, only 38.1% of the patients who were diagnosed with lung cancer in 2018 would meet 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 based on the recommended lung cancer screening criteria. We found that the majority of patients who did not meet the lung cancer screening criteria were females.

According to an earlier local study,[21] the proportion of never smokers with lung cancer in its cohorts was 31% from 1999

Table 6. Characteristics of patients who met the NLST criteria (Group 1) versus patients who did not meet the NLST criteria (Groups 2–5).

Variable	*n* (%)				
	Group 1 (*n*=48)	Group 2 (*n*=11)	Group 3 (*n*=28)	Group 4 (*n*=13)	Group 5 (*n*=26)
Gender					
Female	5 (10.4)	7 (63.6)	14 (50)	7 (53.8)	0
Male	43 (89.6)	4 (36.4)	14 (50)	6 (46.2)	26 (100)
Race					
Chinese	29 (60.4)	2 (18.2)	19 (67.9)	10 (76.9)	21 (80.8)
Malay	16 (33.3)	5 (45.5)	8 (28.6)	2 (15.4)	4 (15.4)
Indian	2 (4.2)	2 (18.2)	1 (3.6)	1 (7.7)	1 (3.8)
Others	1 (2.1)	2 (18.2)	0	0	0
Histology					
Adenocarcinoma	24 (50)	9 (81.8)	22 (78.6)	12 (92.3)	16 (61.5)
Squamous cell carcinoma	11 (22.9)	2 (18.2)	2 (7.1)	1 (7.7)	6 (23.1)
NSCLC others	2 (4.2)	0	1 (3.6)	0	2 (7.7)
Small cell carcinoma	7 (14.6)	0	0	0	1 (3.8)
Others	4 (8.3)	0	3 (10.7)	0	1 (3.8)
Adenocarcinoma (%)	50	81.8	78.6	92.3	61.5
EGFR mutation status					
EGFR+	10 (20.8)	3 (27.3)	10 (35.7)	6 (46.2)	5 (19.2)
ALK+	0	2 (18.2)	0	0	0
ROS1+	0	0	0	1 (7.7)	0
Driver mutations (%)	20.8	45.5	35.7	53.8	19.2
Stage					
1	5 (10.4)	1 (9.1)	5 (17.9)	3 (23.1)	8 (30.8)
2	2 (4.2)	1 (9.1)	2 (7.1)	1 (7.7)	5 (19.2)
3	17 (35.4)	2 (18.2)	3 (10.7)	1 (7.7)	2 (7.7)
4	24 (50.0)	7 (63.6)	18 (64.3)	8 (61.5)	11 (42.3)
Advanced stage malignancies (Stage 3 & 4)	41 (85.4)	9 (81.8)	21 (75)	9 (69.2)	13 (50)
Performance status					
0	14 (29.2)	7 (63.6)	14 (50.0)	3 (23.1)	2 (7.7)
1	23 (47.9)	2 (18.2)	11 (39.3)	6 (46.2)	17 (65.4)
2	4 (8.3)	2 (18.2)	2 (7.1)	3 (23.1)	4 (15.4)
3	4 (8.3)	0	1 (3.6)	1 (7.7)	3 (11.5)
4	3 (6.3)	0	0	0	0
ECOG 0–2 (%)	85.4	81.8	89.3	92.3	88.5
Death within 1 year	26 (54.2)	4 (36.4)	10 (35.7)	6 (46.2)	11 (42.3)

Group 1: aged 55–74 years, >30 pack-years (NLST criteria); Group 2: aged <55 years; Group 3: aged 55–74 years, <30 pack-years; Group 4: aged >74 years, <30 pack-years; Group 5: aged >74 years, >30 pack-years. ALK: anaplastic lymphoma kinase, ECFR: epidermal growth factor receptor, ECOG: Eastern Cooperative Operative Group, NLST: National Lung Screening Trial, NSCLC: non-small cell lung cancer, ROS1: receptor tyrosine kinase

to 2002 and 48% from 2008 to 2011. In our cohort, 33% were never smokers. In addition, 40.5% (51/126) of our cohort had smoking history of less than 30 pack-years. Eighty-two percent of females in our cohort were non-smokers/smokers or ex-smokers with <30 pack-years, compared to 74% of males with a significant smoking history (smoker or ex-smoker with >30 pack-years). In terms of gender proportion, 73.8% of our cohort were males, as compared to 68.8% in the Toh *et al*'s[22] cohort from 1999 to 2002 and 61.2% in the Lung Cancer Consortium Singapore cohort[21] from 2008 to 2011. As we had more male smokers in our 2018 cohort and a smaller sample size, our data may overestimate the benefits of screening with the NLST criteria.

However, there are benefits of implementing a lung cancer screening programme, as the majority of our patients who met the inclusion criteria for lung cancer screening had good performance status but presented with late-stage disease (stages 3 and 4), and more than half (54.2%) did not survive for 1 year. In 2020, Singapore's life expectancy at age 65 years was 21.3 years;[12] in view of this increasing longevity, we may need to consider extending the screening age upper limit to mirror Singapore's ageing population. In addition, lung cancer screening may also benefit those older than 74 years of age, as our study showed that the majority in this age group have a good performance status, similar to their younger counterparts in other groups.

The newly updated USPSTF criteria include patients aged 50–80 years who smoked more than 20 pack-years; this would include 58.7% of our patients diagnosed with lung cancer in 2018. While the benefits of screening a larger cohort with 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, which increases the risks of false positives in the younger, non-smoking age group.[23]

We also found that although close to half of the males (46.2%) met the NLST screening criteria, only 15.5% of females met them. Many females were 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 the increased prevalence of female non-smokers with adenocarcinoma in Asia.

Screening with LDCT is not without its risks.[24] With an annual LDCT being performed consecutive for 3 years, 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 the intervals between screening examination, patients who pass LDCT screening may be falsely reassured regarding their cancer risk. In addition, with the increase in the number of LDCT being performed, the incidence of false-positive results will also likely increase.[25] This can, in turn, lead to potential harm, with an increase in biopsy rates and thus higher healthcare costs.[26] There is also increased anxiety associated with screening.[27]

While the lung cancer screening criteria may be easy and practical to implement, they can be overly simplistic. The relationship among 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. There are other lung cancer prediction models like Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial Model 2012, which incorporates education level, ethnicity, personal and family history of malignancy, but they have not been validated in our local population.[28] The roles of known risk factors in never smokers, including exposure to environmental tobacco smoke,[29,30] cooking fumes[31] and, controversially, human papillomavirus infection,[32] need further assessment to study their impact in our local context. Further studies are needed to determine the threshold where the benefits of reducing lung cancer death outweigh the risk of dying from a competing cause, and this can serve to improve survival.[33]

The strength of our paper is is the inclusion of patients who were positive for lung cancer diagnosed by all modalities. Adding to the current literature, we were able to identify and describe the characteristics of these different patient groups according to the lung cancer screening criteria. Most importantly, we were able to identify significant characteristics and the extent of patients who would meet the lung cancer screening criteria. In addition, 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.

In our study, the patient data were obtained from a respiratory medicine database (rather than oncology). This could be representative of how patients with lung cancer currently present to hospitals, as referrals for lung cancer workup come from sources similar to those of other tertiary hospitals — outpatient clinics and inpatient referrals (with patients referred from the emergency department). In terms of lung cancer workup methods, the range of biopsy methods was the standard of care similar to that offered by other institutions, and these included CT-guided biopsies, EBUS needle aspiration, thoracocentesis and thoracoscopies. The advantage of our lung cancer database is that it contains biopsy-proven lung cancer data from a respiratory medicine

point of view, and allows us to study all comers with lung cancer. This means that all patients with biopsy-proven lung cancer were in this database, including those whose families later decided not to seek treatment. Though a tertiary hospital's referred cohort (symptoms or imaging based) may be different from patients who present 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.

One limitation of the study is 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 whether deaths were related to lung cancer or other causes. Furthermore, our sample size also limits our ability to conduct further multivariate analyses.

Our cohort represented patients who were diagnosed with lung cancer in 2018, most of whom would have presented later in their disease when symptoms arose. 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 programme would be underestimated, as patients who had poor premorbid function would be excluded as they may not have undergone biopsies and may not have been 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 programme may allow for detection of non-lung malignancies and reduce mortality, an area which the scope of our study did not cover.

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

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Conflicts of interest

There are no conflicts of interest.

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