SMGroup

Reserach Article

Journal of Surgical Oncology and Clinical Research

Percentage of Surgical Lung Cancers Missed by National Screening Criteria

Hannah A Lee[1]*, Asa Dewan MS[2], Kelly Rubino BSN[3], Mila Lachica BA[1,2], Arthur A Topilow[4] and Thomas L Bauer[3]

[1]*Axelrod Research Group, Jersey Shore University Medical Center, USA*
[2]*Office of Research Administration, Jersey Shore University Medical Center, USA*
[3]*Department of Surgery, Jersey Shore University Medical Center, USA*
[4]*Meridian Cancer Care/Research, Jersey Shore University Medical Center, USA*

Article Information

Received date: Aug 15, 2017
Accepted date: Sep 12, 2017
Published date: Sep 22, 2017

***Corresponding author**

Hannah A. Lee, Axelrod Research Group, Jersey Shore University Medical Center, Neptune, NJ, USA,
Tel: (732) 865-5967;
Email: hannlee@sas.upenn.edu

Keywords Lung cancer; Screening; Criteria

Abbreviations USPSTF (United States Protective Services Task Force); LDCT (Low-Dose Computerized Tomography); HMH (Hackensack Meridian Health)

Abstract

Background: The US Preventive Services Task Force (USPSTF) recommends screening for smokers based on age, pack-years of smoking, and years since past smokers quit (quit-time). Previous studies determined low-dose computerized tomography (LDCT) to be the best method, but have not identified the population at highest risk. This study sought the percentage of lung cancer patients that would have been excluded by USPSTF criteria.

Method: A retrospective chart review identified 170past and present smokers who had undergone lung cancer resection at Hackensack Meridian Health (HMH) hospitals between September 15, 2014 and 2016. Data was collected from the Society of Thoracic Surgeons database. Descriptive statistics and Wilcoxon Rank-Sum tests were used to analyze differences between included and excluded patients.

Results: The percentage of patients that would have been excluded by screening criteria was 46.5% (95% CI: 38.8-54.3%). The difference between ages of included and excluded patients was not quite significant (p=0.051), with only17.1% (95% CI: 11.7-23.6%) of all patients excluded by age. Pack-years of included patients were significantly higher than of the excluded (p<0.001), and 25.3% (95% CI: 18.9-32.6%) had insufficient pack-years. Quit-time was also a significant variable (p<0.001) and excluded 37.9% (95% CI: 29.1-49.4%) of past smokers. The percentage included by USPSTF criteria increased from 53.5% to 59.4% when quit-time was set to 25 years, and61.2% when extended to 30 years.

Conclusion: USPSTF criteria would have excluded almost half of the ever-smokers with surgically resectable lung cancers. Age would not have excluded a significant percentage, but inclusion criteria should account for smokers with less than 30 pack-years or who quit over 15 years ago. Future reviews should examine screening efficacy in larger databases. Prospective studies should investigate correlation between age and smoking history, and look to include secondhand smoking and occupational exposure as risk factors for screening.

Introduction

Lung cancer causes more deaths than any other cancer in the United States. Eighty percent of these deaths can be attributed to smoking, and over half of all lung cancers are diagnosed after 70 years of age [1]. When diagnosed at an early stage, primary cancers can be resected, resulting in a higher chance of survival.

In order to detect lung cancer, past screening utilized Chest X-rays (CXR) and sputum cytology [2]. In 1992, the International Early Lung Cancer Action Program (I-ELCAP) was founded to compare the detection rates of chest radiography and Low-Dose CT (LDCT) [3]. The New York ELCAP screened 1,000 males and females over 60 years old who smoked for at least10 pack-years the number of cigarette packs per day times the number of years smoked and found LDCT to be more effective than CXR because it detected more malignant tumors (2.7% vs 0.7%) and non-metastatic cancers (96.3% *vs* 57.1%) [4]. Follow-up cohorts at the Mayo Clinic and European Institute of Oncology screened individuals of 50 years or older and with at least 20 pack-years of smoking history [5,6]. Other sites screened smokers starting from 45, 50, and 55 years old with at least 10 pack-years, since I-ELCAP allowed sites to determine enrollment eligibility [7-9].

In 2011, the National Lung Screening Trial (NLST) randomly assigned subjects to be screened by either CXR or LDCT, and found that lung cancer mortality decreased by 20.0% when using LDCT instead of CXR [10]. The study enrolled male and female smokers between 55 and 74 years of age who smoked at least 30 pack-years of smoking [10]. Subjects must have been current smokers, or ceased within the past 15 years.

All past trials determined LDCT to be the most effective screening technique, but the population at highest risk has not yet been determined. Based on NLST findings, the US Preventive Services Task Force (USPSTF) currently recommends LDCT screening of adults between 55 and 80 years of age, with at least a 30 pack-year smoking history, and who are current smokers or had quit within the past 15 years [11].

Since lung cancer victims encompass a range of ages and smoking history, USPSTF guidelines may fail to include many cancers that can be surgically removed. In a 2015 cohort study, Yang et al. followed the proportion of lung cancer patients that met USPSTF criteria from 1984 to 2011 [12]. The trends showed a steady decrease in patients who would have met screening guidelines, but separate variables (age, pack-years, and quit-years) were not closely examined [12]. In a follow-up study, Yang et al. suggested that USPSTF criteria include past smokers who had stopped smoking for 15-30 years [13]. However, the results may be inaccurate since nonsmokers were included even though they would have been ineligible for screening, and current smokers were included in the quit-time analysis, despite not quitting [12,13]. The purpose of this study was to determine the percentage of surgical lung cancer patients who have smoked, but would have been excluded by USPSTF guidelines. If this percentage is significant, we would make suggestions so that more surgically resectable cases could be detected by lung cancer screening scans.

Materials and Methods

This was an Institutional Review Board approved, retrospective chart review of surgical lung cancer cases at the Jersey Shore University Medical Center, Riverview Medical Center, Ocean Medical Center, and Bayshore Community Hospital of Hackensack Meridian Health (HMH).Data for lung cancer resections on past and present smokers between September 15, 2014 and September 15, 2016 were collected from the Society of Thoracic Surgeons (STS) database. Patients with insufficient smoking information or who had never smoked were omitted, since they could not be categorized by USPSTF guidelines. Variables analyzed were age, gender, race, tumor stage, cancer type, and smoking history in pack-years and time since smoking ceased (quit-time) of 170 patients. Many variables affect one's risk for lung cancer but only age (55-80 years), pack-years (≥30), and quit-time (≤15 years)were used to determine inclusion or exclusion by USPSTF guidelines.

Summary statistics were calculated for all study measures including frequency and percentage for categorical variables in addition to range, mean, standard deviation, median, and interquartile range for continuous variables. Exact two-sided 95% confidence intervals were calculated for percentages. Categorical variables were compared between group susing Chi-squaredor Fisher's exact tests, dependent on expected cell counts. Continuous measures were checked for normality using the Shapiro-Wilk test and then compared between groups using two-sided independent t-tests or Wilcoxon rank-sum tests depending on the result. Ordinal variables were compared between groups using the Wilcoxon rank-sum test. All tests were performed at the 0.05 level of significance.

Inclusion criteria for age, pack-years, and quit-time were individually studied to determine how many cases would have been excluded by each variable alone. Significant percentages of cases that would have been excluded by USPSTF recommendation would prompt further analysis to determine criteria that better includes those at high risk for lung cancer.

Results

Of the 170 cases reviewed, 46.5% (95% CI: 38.8-54.3%) would have been excluded by USPSTF-recommended inclusion criteria for lung screening. In both included and excluded groups, most patients were female and almost all were Caucasian. Overall clinical and pathological staging categorized about 70% of tumors in Stage I. Histologically, cases excluded by USPSTF guidelines were mostly adenocarcinomas and neuroendocrine tumors, while there were more squamous cell carcinomas among the included patients (*p<0.001*).

The ages of surgery in the chart review ranged from 43 to 87 years old, but only those between 55 and 80 inclusive, would have been screened by USPSTF criteria. Overall, the difference between the age distributions was not statistically significant (Table 1). Criteria for smoking history were specified in pack-years and quit-time, or years since past smokers quit. Excluded patients smoked between 0.8 and 120 pack-years, while the included group's range was 30 to 160 pack-years. The USPSTF guideline for quit-time only applies to past smokers. The Meridian STS database had 117 past smokers who quit between one month and 62 years before surgery, but they were only eligible for screening if they quit15 or fewer years before. The distributions of both pack-years and quit-time differed significantly between the included and excluded patients (Table 2).

Many excluded patients were up to 5 years younger or older than the required age range, but even more met the USPSTF age criteria and were excluded by pack-years or quit-time (Figure 1). Less than 20% fell outside the required range (Figure 2), so the high percentage of excluded patients must be more related to smoking history.

Of all patients, approximately 25% smoked less than 30 pack-years – a larger exclusion percentage than age (Figure 2). Over half of the excluded patients smoked for less than 30 pack-years: 34.6% between 15 and 29 pack-years and 20.5% for less than 15 pack-years (Figure 3).

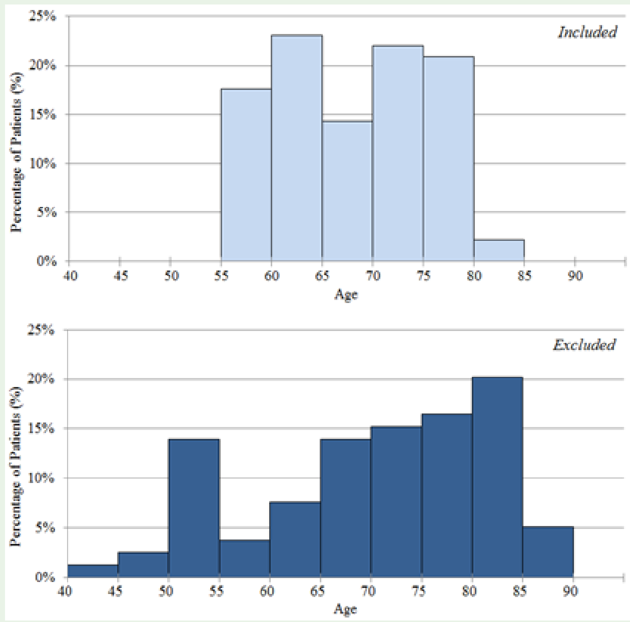

Figure 1: Age Distributions of Patients Included (n=91) and Excluded (n=75) by USPSTF Criteria.
Bars display percentage of patients who fall within each five-year interval. Of included patients, $\bar{x}$ = 67.63 and s=7.33; of excluded patients, $\bar{x}$ = 69.66 and s=11.52. The included patients between 80 and 85 years were both 80 years of age.

Table 1: Descriptive Statistics of Meridian STS Patients Excluded (n=79) and Included (n=91) by USPSTF Criteria.

		Excluded, n (%)		Included, n (%)	
Gender	Male	34	(43.0%)	38	(41.8%)
	Female	45	(57.0%)	53	(58.2%)
Age	<50	3	(3.8%)	0	(0.0%)
	50-54	11	(13.9%)	0	(0.0%)
	55-59	3	(3.8%)	16	(17.6%)
	60-64	6	(7.6%)	21	(23.1%)
	65-69	11	(13.9%)	13	(14.3%)
	70-74	12	(15.2%)	20	(22.0%)
	75-80	18	(22.8%)	21	(23.1%)
	>80	15	(19.0%)	0	(0.0%)
Race	Asian	1	(1.3%)	0	(0.0%)
	Black	1	(1.3%)	1	(1.1%)
	Caucasian	77	(97.5%)	89	(97.8%)
	Other	0	(0.0%)	1	(1.1%)
Smoking History					
Smoking Status	Past Smoker	16	(20.3%)	37	(40.7%)
	Present Smoker	63	(79.7%)	54	(59.3%)
Pack-years	0-29	42	(53.2%)	0	(0.0%)
	30-59	28	(35.4%)	61	(67.0%)
	60-89	4	(5.1%)	16	(17.6%)
	90-119	0	(0.0%)	10	(11.0%)
	≥120	1	(1.3%)	4	(4.4%)
	n/a	4	(5.1%)	0	(0.0%)
Quit-time	0-9	30	(38.0%)	77	(84.6%)
	10-19	7	(8.9%)	14	(15.4%)
	20-29	20	(25.3%)	0	(0.0%)
	30-39	10	(12.7%)	0	(0.0%)
	40-49	7	(8.9%)	0	(0.0%)
	≥50	4	(5.1%)	0	(0.0%)
	n/a	1	(1.3%)	0	(0.0%)
Lung Cancer Information					
Clinical Stage	IA	40	(50.6%)	54	(59.3%)
	IB	9	(11.4%)	8	(8.8%)
	IIA	6	(7.6%)	6	(6.6%)
	IIB	5	(6.3%)	4	(4.4%)
	IIIA	13	(16.5%)	14	(15.4%)
	IIIB	2	(2.5%)	2	(2.2%)
	IV	4	(5.1%)	3	(3.3%)
Pathology Stage	IA	38	(48.1%)	48	(52.7%)
	IB	13	(16.5%)	18	(19.8%)
	IIA	10	(12.7%)	15	(16.5%)
	IIB	7	(8.9%)	3	(3.3%)
	III	10	(12.7%)	6	(6.6%)
	IV	1	(1.3%)	1	(1.1%)
Histology	Adenocarcinoma	61	(77.2%)	52	(57.1%)
	Squamous Cell	8	(10.1%)	32	(35.2%)
	Large Cell	1	(1.3%)	2	(2.2%)
	Small Cell	2	(2.5%)	0	(0.0%)
	Neuroendocrine	6	(7.6%)	1	(1.1%)
	Mixed	1	(1.3%)	4	(4.4%)

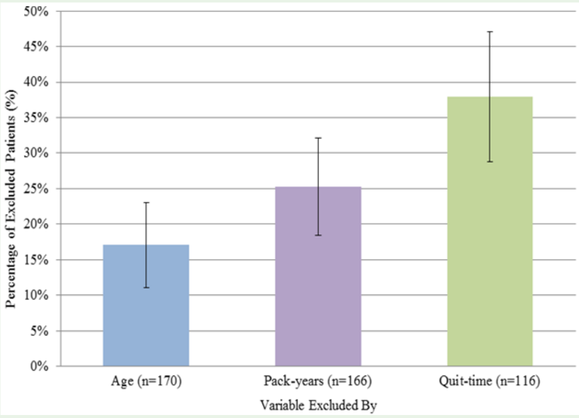

Figure 2: Percentage of All Patients Excluded by USPSTF Age, Pack-year, and Quit-time Criteria.
Age and pack-year criteria apply to all patients (n=170), but there was insufficient pack-year data for 4 patients. Quit-time only applies to past-smokers (n=116). Bars also display 95% confidence intervals for the percentage of excluded patients by each variable.

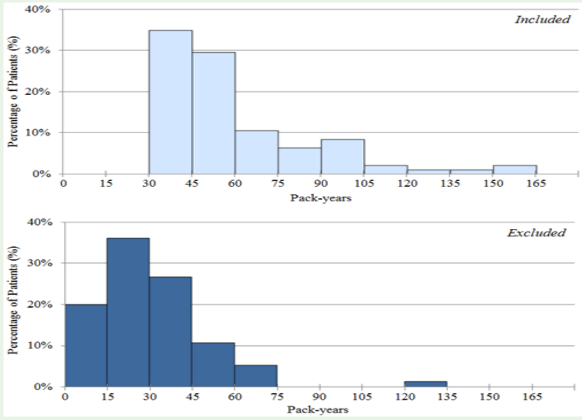

Figure 3: Pack-year Distributions of Patients Included (n=91) and Excluded (n=79) by USPSTF Criteria.
Bars display percentage of patients who fall within each fifteen pack-year interval. Of included patients, $\bar{x}$ = 57.68 and s=27.89; of excluded patients, $\bar{x}$ = 28.07 and s=19.22. Four excluded patients had unavailable pack-year data and were excluded by age or quit-time.

Of past smokers excluded by USPSTF criteria, almost 75% had quit over 15 years prior to surgery (Figure 4). The remaining patients who did quit smoking within the past 15 years were disqualified by age, pack-years, or both. There were 116 past smokers in this study, and 37.9% (95% CI: 29.1-47.4%) had quit smoking more than 15 years before. A large percentage of excluded patients can be attributed to quit-time.

Table 2: Medians and Significance of Age, Pack-years, and Quit-time of Excluded and Included Patient Distributions.

Criteria	Excluded Median (IRQ, n)	Included Median (IRQ, n)	Significance
Age	72 (62-80, n=79)	67 (61-74, n=91)	p=0.051
Pack-years	25 (15-36, n=75)	50 (40-64, n=91)	p<0.001
Quit-time (years)	22 (12-32, n=54)	2.5 (0.33-10, n=62)	p<0.001

Note: Age and pack-year criteria were for all patients (n=170), but quit-time only applied to past smokers (n=117). There were unavailable pack-year data for 4 patients and unavailable quit-time data for 1 patient.

Table 3: Percent of HMH Patients (n=170) Who Would Have Been Excluded by Past Criteria at Different ELCAP Sites.

ELCAP Program	Criteria	Excluded (%)
NY-ELCAP, NY [4]	≥60 years old ≥10 pack-years	26.47%
Mayo Clinic, Minnesota [5]	≥50 years old ≥20 pack-years	17.65%
European Institute of Oncology, Milan [6]	≥50 years old ≥20 pack-years	17.65%
Physimed Medical Center, Quebec [7]	≥45 years old ≥10 pack-years	7.65%
Sylvester Comprehensive Cancer Center, Florida [8]	≥50 years old ≥10 pack-years	8.82%
University Health Network, Toronto [9]	≥55 years old ≥10 pack-years	14.71%
International-ELCAP [14]	≥40 years old >0 pack-years*	0.00%

Quit-time was unspecified for all sites. These past guidelines would have excluded fewer resectable lung cancer cases than current USPSTF guidelines.
* I-ELCAP participants could also have been nonsmokers at risk due to secondhand or occupational exposure.

There were 104 patients who met USPSTF criteria for pack-years (≥30) and quit-time (≤15 years), but 13 (12.5%, 95% CI: 6.8-20.4%) were excluded from screening due to age (Figure 5). There were also 13 patients (12.5%, 95% CI: 6.8-20.4%) included by age and quit-time criteria, but excluded by pack-years -- few were excluded solely by pack-years. Of past smokers between 55 and 80 years old who smoked over 30 pack-years, 23.9% (95% CI: 14.6-35.5%) were excluded by the quit-time criteria (Figure 5). This variable would have excluded more surgical lung cancer cases from screening than age and pack-years would have.

If each criterion was modified individually, an extension of quit-time by 15 years would optimize the percentage of included patients. Patients in the study were within approximately 10 years of the USPSTF age range, but only about 5% more would have been included

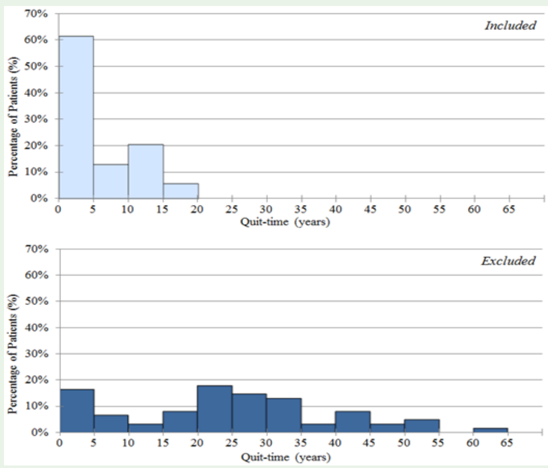

Figure 4: Quit-timed Distributions of Past Smokers Included (n=54) and Excluded (n=62) by USPSTF Criteria.
Bars display percentage of patients within each 5-year quit-time interval. Of included patients, $\bar{x}$ = 4.71 and s=4.98; of excluded patients, $\bar{x}$ = 23.07 and s=15.09. Current smokers (n=53) were omitted since they never quit. Quit-time for 1 patient was unavailable.

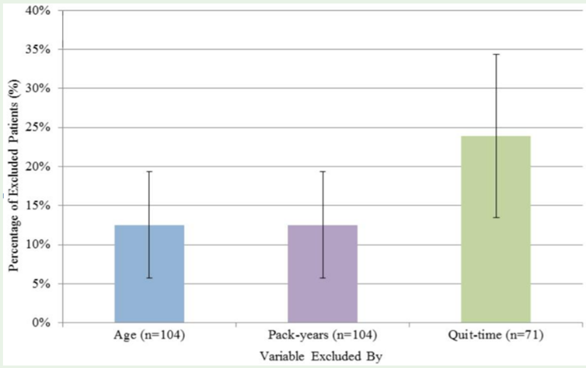

Figure 5: Percentage of Patients Excluded by Each USPSTF Criteria Variable Given Others Were Met.
One hundred and four patients met pack-year (≥30 pack-years) and quit-time (≤15 years) criteria. There were 108 patients within the age range (55-80 years) and quit-time limit, but there was insufficient pack-year data for 4 of these patients. Quit-time only applies to the 116 past-smokers, of which 71 met age and pack-year criteria. Bars also display 95% confidence intervals for the percentage of excluded patients by each variable.

if the range was extended that many years (Figure 6). Reducing the pack-year criteria to 20 pack-years (10 pack-year reductions) would have included almost 60% of all patients, while disregarding the pack-year criteria altogether would have included up to 61.2% (Figure 6). Since removing the pack-year criteria would expose light smokers to unnecessary radiation, smaller alterations in quit-time would be more reasonable. The percentage of Meridian patients included by USPSTF criteria increased to 59.4% when quit-time was set to 25 years (10 year extension) and 61.2% when extended to 30 years (Figure 6).

However, since many patients would have been excluded by more than one variable, it is important to consider alterations in multiple variables. Pack-years and quit-time had significantly different distributions, as well as large exclusion percentages (Figure 7).

Although USPSTF criteria would have excluded almost half of Meridian cases, it fared better than NLST which would have excluded 58.8% (95% CI: 51.0-66.3%) of the same 170 cases. On the other hand, the NY-ELCAP would have only excluded 26.5% (95% CI: 20.0-34.8%), while the Mayo Clinic and European Institute of Oncology

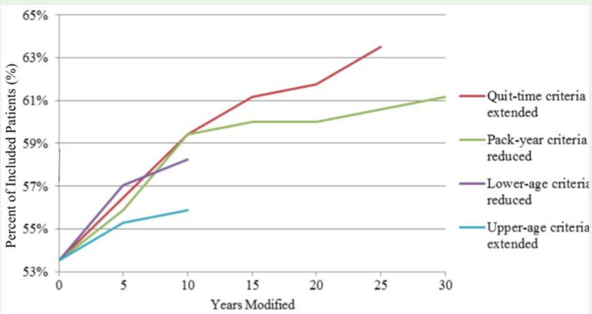

Figure 6: Percentage of All Patients (n=170) Included by USPSTF Criteria When Quit-time, Pack-year, and Age Criteria Were Extended.
Current guidelines include 53.5% of patients at 0 years of criteria extension. Each variable was extended by 5 years or pack-years until no more patients would have been included by that variable. The age range was extended below 55 years of age and then above 80 years of age.

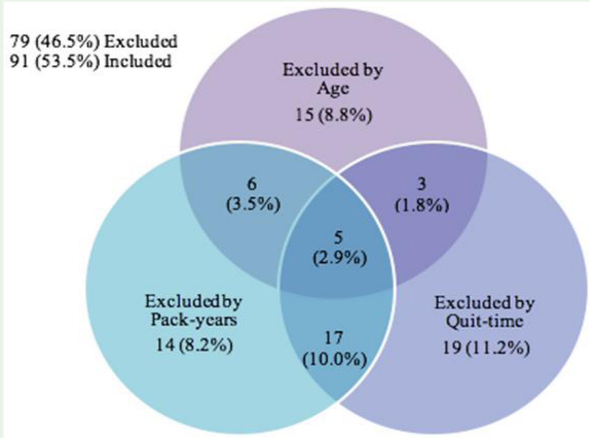

Figure 7: Patients (n, % of total) Excluded by Combinations of USPSTF Screening Criteria Variables. Totals of 29 excluded by age, 42 by pack-years, and 44 by quit-time.

ELCAP sites would have only excluded 17.7% (95% CI: 12.2-24.2%) of the cases (Table 3). These sites had wider age ranges, lower pack-year requirements, and no limit on quit-time.

Discussion

Since most lung cancers are caused by heavy smoking, it is possible to detect them earlier by screening smokers at high risk. Past trials showed that low-dosage CT scans are most effective, but few studies have been conducted to determine the optimal population [4,10]. Current guidelines advise lung screening to past and present smokers who meet certain age and smoking history criteria. Almost half of the surgical lung cancer cases at Meridian Health would have been excluded by these guidelines.

National inclusion criteria specify age and pack-years of smoking, as well as quit-time for past smokers. According to our analysis, the criteria for age and pack-years would not have excluded as many HMH patients as quit-time. The data supports Yang et al.'s suggestion that the upper limit for quit-time be extended [14]. In fact, earlier studies did not have quit-time criteria, and would have excluded fewer patients. Based on our results, if a quit-time guideline must be set, we suggest extending it from 15 to 25 years.

Since some patients would have been excluded by more than one variable, there may be correlation between age, pack-years, and quit-time. Alterations in one variable can affect another; for example, older age entails more time to have smoked or longer periods of cessation. As suggested by exclusion rates by ELCAP criteria, small adjustments in all variables can significantly change the percentage of excluded patients.

Cost effectiveness, accessibility, and insurance coverage must be considered to ensure that the benefits outweigh the costs and risks. Safety is also a priority since low-dose CT scans impose radiation danger on scanned subjects [15]. ELCAP sites would have detected a significantly higher percentage of patients than USPSTF recommendations, but also would have increased health risk to potential patients and financial cost to national programs. Further studies should investigate the financial costs and health risks of wider screening criteria.

Besides age and smoking history, other factors increase lung cancer risk. Prospective studies should inquire information on secondhand smoking, occupational risks, and prolonged exposure to air pollution [1]. Currently, nonsmokers are ineligible for screening, as well as those with history of cancer or prior CT scans, recent unexplained weight loss, or hemoptysis [10]. In the future, symptoms and medical history should be considered in data collection. Additionally, the data collected was at time of surgery, so past smokers who reported quitting less than a year before may have been current smokers at time of diagnosis. The Meridian sample is not a perfect reflection of all lung carcinomas, so a larger sample may yield more accurate results. Yet, if it is true, the national screening guideline is failing to detect lung cancer in high risk populations.

In conclusion, the study revealed that current USPSTF recommendations for lung screening fail to account for many lung cancer patients that can potentially be saved. We believe that the national criteria can be adjusted to detect cancer in high risk populations without unnecessary radiation exposure. From this analysis, we noted that past smokers who quit more than 15 years ago are still likely to develop lung cancer. Further studies should examine secondhand smoking and occupational exposure as risk factors, taking national cost and radiation danger into consideration.

Acknowledgements

Special thanks to Dr. Herbert Axelrod (1927-2017) for funding the Hackensack Meridian Health Scholars Research program at Jersey Shore University Medical Center. Dr. Axelrod generously donated funds to sponsor undergraduate research and mentorship during summers at Jersey Shore University Medical Center.

References

1. Sharma D, Newman TG, Aronow WS. Lung cancer screening: History, current perspectives, and future directions. Archives of Medical Science. 2015; 11: 1033.

2. Midthun DE. Early detection of lung cancer. F1000 Res. 2016.

3. International Early Lung Cancer Action Program. About I-ELCAP. Accessed July 24, 2017.

4. Henschke CI, Mc Cauley DI, Yankelevitz DF, Naidich DP, McGuinness G, Miettinen OS, et al. Early lung cancer action project: A summary of the findings on baseline screening. Oncologist. 2001; 6: 147-152.

5. Swensen SJ, Jett JR, Hartman TE. CT screening for lung cancer: Five-year prospective experience. Radiology. 2005; 235: 259-265.

6. Pastorino U, Bellomi M, Landoni C. Early lung-cancer detection with spiral CT and positron emission tomography in heavy smokers: 2-year results. The Lancet. 2003; 362: 593-597.

7. Physimed Cancer Screening Center. Lung Cancer Screening. Accessed July 24, 2017.

8. Project focuses on early detection. Quest Magazine of the University of Miami Sylvester Comprehensive Cancer Center. 2006; 48.

9. University Health Network. Early Lung Cancer Screening. Accessed July 24, 2017.

10. Aberle DR, Adams AM, Berg CD, Black WC, Clapp JD, Fagerstrom RM, et al. Reduced lung-cancer mortality with low-dose computed tomographic screening. The New England Journal of Medicine. 2011; 365: 395-409.

11. USPSTF A and B recommendations. US Preventive Services Task Force Website.

12. Wang Y, Midthun DE, Wampfler JA, Deng B, Stoddard SM, Zhang S, et al. Trends in the proportion of lung cancer patients meeting screening criteria. JAMA. 2015; 313: 853-855.

13. Yang P, Wang Y, Wampfler JA, Xie D, Stoddard SM, She J, et al. Trends of high-risk subpopulations for lung cancer. Journal of thoracic oncology: official publication of the International Association for the Study of Lung Cancer. 2016; 11: 194-202.

14. The International Early Lung Cancer Action Program Investigators. Survival of patients with stage I lung cancer detected on CT screening. The New England Journal of Medicine. 2006; 355: 1763-1771.

15. De Koning H, Meza R, Plevritis SK. Benefits and harms of CT lung cancer screening strategies. A comparative modeling study for the U.S. preventive services task force. Ann Intern Med. 2014; 160: 311-320.