HHS Public Access
Author manuscript
J Community Health. Author manuscript; available in PMC 2020 December 09.

Published in final edited form as:
J Community Health. 2020 October ; 45(5): 1038–1042. doi:10.1007/s10900-020-00826-8.

Examining Gender Differences in Lung Cancer Screening

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Abstract

It is unknown if gender influences outcome of lung cancer screening with Low Dose CT (LDCT), especially with frequent and continued underrepresentation of women in clinical trials. We examined a balanced cohort of men and women with the hypothesis that there would be no difference in participation or results between men and women undergoing lung cancer screening. In an urban, academic medical center, we prospectively collected data on patients referred for lung cancer screening from October 2015 to August 2018. We studied gender, age, ethnicity, level of education and smoking history. We measured results of LDCT using Lung-RADS reporting system. 546 patients underwent LDCT between October 2015 and August 2018. 279 (51%) were female and 267 (49%) were males. Age, education status or smoking patterns did not significantly differ between females and males There was a significant difference between males and females in the distribution of LDCT results ($p = 0.05$). 81 females and 105 males were diagnosed with Lung-RADS 1; 99 females and 92 males with Lung-RADS 2; 15 females and 8 males with Lung-RADS 3; 19 females and 11 males with Lung-RADS 4. Overall, 10 females (3.5%) and 3 males (1.1%) were diagnosed with lung cancer (risk difference 2.4, 95% CI—0.0006–0.05, $p = 0.09$). Women are often underrepresented in clinical trials. Preliminary results from our lung cancer screening program demonstrate equal participation and equal benefit from the screening program. Long term data is needed to study survival benefit.

Keywords

Lung cancer screening; Low dose CT scan; Smoking cessation

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Presented at the IASLC 19th World Conference on Lung Cancer, Toronto, Canada September 23–26, 2018.

Conflict of interest All authors declare that they have no conflict of interest.

Background

Over the last 41 years, lung cancer incidence has dropped by 35 percent for men while it has risen by 87 percent for women. [1] Lung cancer mortality in women has increased over 600% since 1950 [2] and it remains the number one cancer killer in females. In 2011, the National Lung Screening Trial (NLST) demonstrated a 20% reduction of lung cancer deaths with the use of low dose CT scan (LDCT) for screening in high risk populations [3].However, 59% of NLST participants were male, raising questions about the generalizability of screening results to women. Multiple studies of lung cancer in women have indicated that there are differences in risk factors, histology, pathophysiology, treatment outcomes and prognosis as compared to men [4–6]. Results of a recent Korean study (28% women) indicate that for the female population, nationwide chest radiography surveillance with intervals of less than 3 years was associated with earlier stage lung cancer and increased surgical resectability, and was an independent predictor of improved survival [7]. Additionally, findings from the Dutch-Belgian Lung Cancer Screening trial (NELSON) showed screening reduced lung cancer mortality by 61% in women and 26% in men [8]. A major criticism of the NELSON trial is the low participation of women (16%). Similarly, the largest implementation study to date was conducted in the Veterans Health Administration which only had 3.4% women participating in lung cancer screening [9].

Lung cancer may be significantly different in men and women to justify a gender-specific approach to screening, including targeted recruitment, different screening criteria and differences in expected outcomes. However, without datasets with equivalent representation of men and women, comparison of gender in lung cancer screening is challenging. For these reasons, we sought to compare results of lung cancer screening in a balanced cohort of men and women. We developed a lung cancer screening program including gender-neutral recruitment strategies and screening protocols. We hypothesized that there would be no difference in participation or results between men and women undergoing lung cancer screening.

Methods

Recruitment of Patients

We developed a comprehensive, multidisciplinary lung cancer screening program in our urban, academic health care center. Prior to implementation, we sought the advice of individuals within our community and their healthcare providers. We conducted focus groups within community centers and explored the interest in lung cancer screening, familiarity with the screening paradigm and barriers to obtaining screening. From this discussion, we formulated a survey of community members addressing interest in lung cancer screening. We also formulated a survey to health care providers within the community addressing their perceptions about screening [10]. The results of these studies demonstrated sufficient interest to implement a comprehensive lung cancer screening program. These early studies also informed a recruitment strategy for individuals as well as their health care providers. To recruit individuals to lung cancer screening, we participated in multiple community events, including health fairs, community education seminars and collaboration with “Block Captains” who educate a specified geographic area in the surrounding community. We also developed printed and web-based information with in English, Spanish and Chinese at the 4th grade reading level. To recruit health care providers to refer eligible patients, we developed educational programs for providers including CME courses, provider office visits, a resident curriculum for lung cancer screening and ground rounds talks. We also created printed and web-based information to support the education of health care providers.

Lung Cancer Screening

Eligible patients were referred to lung cancer screening and to our study by community physicians. Patient eligibility was decided based on NLST criteria (ages 55–74, greater than 30 pack-year smoking history, active or quit less than 15 years). Our lung cancer screening team confirmed lung cancer screening eligibility with patients by telephone prior to the multi-disciplinary lung cancer screening visit[11, 12]. During the screening visit, a physician from specializing in lung cancer screening engaged patients in a shared decision-making (SDM) discussion and a consent process for patients opting for LDCT. Results were reported to the patient using lung-RADS (Lung Imaging Reporting and Data System) scoring system developed by the American College of Radiology. The lung cancer screening team then arranged for follow-up studies and consultations. Former smokers were educated on the importance of staying smoke-free, and active smokers received counseling consisting of the five major steps to intervention (5 A's: Ask, Advise, Assess, Assist, and Arrange) [13, 14].

Lung Cancer Screening Assessment

The results of the low dose CT (LDCT) scans were collected prospectively between October 2015 and August 2018. We examined the gender, age, ethnicity, level of education, and smoking pattern history of our lung cancer screening population. Any patient with suspicious findings, i.e., Lung-RADS 3 and Lung-RADS 4, were discussed with our multi-disciplinary team, and any decision for an intervention was approved after consensus between chest radiology, pulmonary medicine, medical oncology and thoracic surgery. Finally, we analyzed the treatment and reported any complications at a short term follow up of a minimum of 3 months and maximum follow up of 3 years. Temple University's Human Research Protection Program (HRPP) Institutional Review Board (IRB) approved the study protocol and consent forms. All participants were informed of the purpose of the study and that participation would have no bearing on their clinical care. At any time, patients could withdraw consent and contribution of their data.

Statistical Analysis

Data are reported as a mean with standard deviation, range, or percentage as appropriate. Chi-square tests and t tests were used to assess gender differences in categorical and continuous descriptive characteristics, respectively. For all statistical analysis, the level of significance was set at $p \leq 0.05$. All statistical analyses were performed in Microsoft Excel and STATA version 15 (STATA Corp., TX, USA).

Results

Five hundred and forty-six patients were referred to the comprehensive lung cancer screening program between October 2015 and August 2018. Of the 546 participants in the study, 279 (51%) were female and 267 (49%) were males (Table 1). Age did not significantly differ between females (mean 60.6 years, standard deviation 5.7) and males (mean 60.97 years, standard deviation 5.65; p = 0.423). There was no statistically significant difference between males and females in participants education status (p = 0.35). Smoking patterns were also similar, with 166 (59.5%) females and 155 (58%) males being active smokers (p = 0.658).

Of the 546 patients, there was a significant difference between males and females in the distribution of LDCT results (p = 0.05). Eighty-one (29%) females and 105 (39%) males were diagnosed with Lung-RADS 1. Ninety-nine (35.5%) females and ninety-two (34.5%) males were diagnosed with Lung-RADS 2. Fifteen (5.4%) females and eight (3%) males were diagnosed with Lung-RADS 3. Nineteen (6.8%) females and eleven (4.1%) males were diagnosed with Lung-RADS 4. Overall, ten females (3.5%) and three males (1.1%) were diagnosed with lung cancer (risk difference 2.4, 95% CI—0.0006–0.05, p = 0.09). Seven females and 2 males underwent surgery, and one female underwent chemotherapy for stage 4 disease. One male underwent chemotherapy, radiation therapy and surgery for stage III disease. One female underwent radiation therapy and one female refused treatment. There were no complications or deaths from diagnostic procedures or treatment.

Discussion

The number of female deaths attributed to lung cancer currently far exceeds that from breast, colon and cervical cancers combined [1]. While women are increasingly participants of breast and cervical cancer screening, utilization of lung cancer screening by women has been strikingly low, from 2.5% in 2010 to 4% in 2015.[15, 16] Furthermore, women are underrepresented in lung cancer screening trials including the NLST, NELSON and implementation studies. Low uptake in lung cancer screening rates in women may arise from the lack of awareness; few women realize that lung cancer is the most commonly diagnosed cancer in women [17]. Together, these studies suggest that women are missing out on potentially lifesaving technology.

Our study had an equal participation of men and women. We attribute these results to our recruitment strategy focused on education of community members and health care providers. We emphasized that anyone meeting eligibility criteria would likely benefit from lung cancer screening. In our population, we do not recommend gender-specific recruitment strategies to individuals or health care providers. Recruitment resources should focus on all eligible people. Our results are based on the cumulative collaboration of individuals, health care providers to screen based on eligibility criteria, regardless of gender. It is unknown if there are gender differences at the patient level, health care provider level or screening program level. Further study into the multi-level factors of lung cancer screening participation should be done to answer these questions.

Of those participating in lung cancer screening, there were no differences between men and women in terms of age, smoking history or education. These results suggest that components of screening including educational materials, shared decision making, decision making aids and smoking cessation counseling do not necessarily require a gender-specific approach. The implementation of the multiple components of lung cancer screening is already a challenge without complicating the process with a separate protocol for men and women. Additional studies with balanced cohorts will be needed before justifying gender-specific lung cancer screening protocols.

Our study also showed a significant difference in women having positive screening results and slight trend towards more females being diagnosed than males with lung cancer. Our early results are consistent with the NELSON trial. However, longer-term follow will be needed to determine if women have significantly different outcomes from screening compared to men.

Our study has limitations. This is a single institution sampling of lung cancer screening that may not be general-izable to all populations. Our study is an overall comparison of men and women and their participation and results of lung cancer screening. We did not study potential gender differences at the individual, health care provider or health systems level. Another limitation was our short term follow up. Longer term follow up will be needed to demonstrate a difference in mortality outcomes between men and women.

In conclusion, if men and women are given equal opportunity to participate in lung cancer screening, both groups are likely to benefit from lung cancer screening equally.

Acknowledgements

This study was partially supported by TUFCCC/HC Regional Comprehensive Cancer Health Disparity Partnership, Award Number U54 CA221704(5) (Contact PIs: Grace X. Ma, PhD and Olorunseun O. Ogunwobi, MD, PhD) from the National Cancer Institute of National Institutes of Health (NCI/NIH). The content is solely the responsibility of the authors and does not necessarily represent the official views of the NCI/NIH.

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Table 1

Patient demographics and results

	Female number (percent)	Male number (percent)	p value
Total number of patients (n = 546)	279 (51)	267 (49)	
Age	60.58 (SD 5.7)	60.97 (SD 5.65)	0.263
Race			0.018
African American	169 (60.6)	130 (48.7)	
Caucasian	71 (25.4)	95 (35.6)	
Hispanic	34 (12.2)	32 (12)	
Asian	5 (1.8)	10 (3.7)	
Education			0.305
8th grade	19 (6.8)	19 (7.1)	
9–11th grade	69 (24.7)	64 (24)	
High school	93 (33.3)	94 (35.2)	
Some college	9 (3.2)	17 (6.4)	
Associate degree	51 (18.2)	31 (11.6)	
Bachelor degree	13 (4.6)	14 (5.2)	
Graduate	14 (5)	12 (4.5)	
Smoking history			0.658
Active smokers	166 (59.5)	155 (58.1)	
Ex smokers	108 (38.7)	109 (40.8)	
Pack years	49.34 (SD 24.9)	51.87 (SD 26.7)	0.263
Lung-RADs			0.05
0	4 (1.4)	1 (0.4)	
1	81 (29)	105 (39.3)	
2	99 (35.5)	92 (34.5)	
3	15 (5.4)	8 (3)	
4	19 (6.8)	11 (4.1)	