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Performance of community-based lung cancer screening program in a Histoplasma endemic region

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ABSTRACT

Objectives: Lung cancer screening with low dose computed-tomography (LDCT) is currently recommended for high-risk populations based on mortality benefit shown in the National Lung Screening Trial (NLST). This study evaluated performance of a community-based lung cancer screening program in a *Histoplasma* endemic region.
Materials and Methods: Demographic and clinical information was collected through retrospective review of patients in the Lung Cancer Screening program of a Kentucky (*Histoplasma* endemic region) health system from 2016 and 2017. A positive LDCT screen is defined as Lung-RADS version 1.0 assessment categories 3 or 4. Patients characteristics, initial screening results and follow up were analyzed and compared to NLST results.
Results: A total of 4500 LDCT screens were performed in 2016 (39%) and 2017 (61%) with 43% adherence rate to repeat annual screen in 2017. Mean age of patients was 64 years, with majority being females (54%) and current smokers (69%) with average 52-pack year smoking history. The rate of positive LDCT was 13.3% (600) varying based on baseline (14.6%) and annual (9.5%) screen. A total of 70 lung cancers were diagnosed among all positive LDCT screens (11.7%) with a false positive rate of 12%.
Conclusions: Baseline positive screens in our study are similar to NLST data with Lung-RADS criteria implementation (14.6% vs 13.6%, p = 0.15) despite being a *Histoplasma* endemic region. Our study shows a successful performance of a community-based lung cancer screening program in a *Histoplasma* endemic region.

1. Introduction

Lung cancer is aggressive and remains the leading cause of cancer-related mortality in the United States. The National Lung Cancer Screening Trial (NLST) [1], a large prospective randomized control trial, reported in 2011 a 20% relative reduction in mortality from lung cancer among heavy smokers receiving screening with annual chest low-dose computed tomography (LDCT) as compared to annual chest x-ray. Based on this study, lung cancer screening with annual LDCT became a guideline recommendation for high-risk populations [2].

High false positive rate from the NLST is a big concern due to need for additional testing with a risk of more radiation exposure, invasive procedures, and additional cost. Using the published data from the several LDCT screening studies, the American College of Radiology (ACR) derived the Lung Imaging Reporting and Data System (Lung-RADS) criteria to standardize lung cancer screening CT reporting with a variable size threshold that is dependent on nodule morphology. The size threshold for a positive baseline screen for solid nodule was increased from 4 mm in NLST to 6 mm with Lung-RADS [3]. A retrospective assessment of the NLST with application of Lung-RADS criteria showed a substantial decrease in false positive rate [4].

Histoplasma, a dimorphic fungi endemic to the Ohio River Valley, causes granulomatous disease and can contribute to higher positive baseline LDCT screens as shown by re-analysis of NLST data [5]. Patients enrolled in sites in *Histoplasma* endemic region were 30% more likely to have a positive baseline LDCT screen (OR = 1.30, 95% CI = 1.21–1.40).

This study evaluated the performance of a community-based lung cancer screening program in a *Histoplasma* endemic region.

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2. Methods

2.1. Study setting and participants

Centered in the Ohio River Valley, Kentucky is a *Histoplasma* endemic region [6]. This study was conducted in a Kentucky Health system Lung cancer screening program comprising of 21 centers. All these centers are accredited by the American College of Radiology (ACR) and participate in the Lung Cancer Screening Registry. This lung cancer screening program was started in 2015 after the United States Preventative Services Task Force Grade B recommendation of LDCT lung cancer screening in high risk populations. This study was a part of the Kentucky Lung Cancer Education Awareness Detection Survival (LEADS) Collaborative and approved by the University of Louisville Institution Review Board and other participating centers.

All patients who received LDCT screening for lung cancer in 2016 and 2017 were identified using the lung cancer screening CPT code G0297. Demographic and clinical information were retrospectively collected through medical chart review. Patient characteristics included age, sex, insurance status, smoking status and year of screen. Patients with missing information on demographics or LDCT screen were excluded.

2.2. Lung cancer screening LDCT

Every LDCT screen was reviewed and respective Lung-RADS score were collected. LDCT screens were divided in two groups: baseline screen and annual screen. Baseline screen is the first or initial LDCT screen, while annual screen is the follow up screen after 1 year of the baseline screen. A positive LDCT screen is defined as Lung-RADS version 1.0 assessment categories 3 or 4. Patients diagnosed with cancer on subsequent follow up were identified.

2.3. Statistical analysis

Patients characteristics, initial screening results, follow up and cancer diagnosis were analyzed and compared to NLST results. For comparison, NLST [1] and re-analysis of the NLST using Lung-RADS criteria were both utilized [4]. Analyses were performed in SAS v9.4 (SAS Institute, Cary, NC, USA).

3. Results

3.1. Demographics

A total of 4500 LDCT screens were performed in 2016 (39%) and 2017 (61%). Table 1 summarizes the demographic data. Median age of patients was 62 years (IQR 11), majority being females (54%) and current smokers (69%) with average 52-pack year smoking history.

3.2. Lung cancer screening results

Among the total of 4500 LDCT screens, 3428 (76.3%) were baseline screens and 1067 (23.7%) were annual screens. The results of LDCT screens by Lung-RADS category are shown in Table 1. The rate of positive LDCT was 13.3% (600/4500) varying based on baseline (14.6%) and annual (9.5%) screen. A total of 70 lung cancers were diagnosed among all positive LDCT screens (11.7% of all positive screens and 1.55% of all screened patients) with a false positive rate of 12%. In 2016, out of the total 1762 LDCT screens, 1546 (87.7%) had Lung-RADS category 1 and 2 scores and were recommended to continue with annual LDCT. But only 772 people had a follow up annual screen in 2017 with an annual adherence rate of 49.9%.

About 53% of LDCT screens had other incidental findings, 33% screens had only one, and 20% had 2 or more incidental findings. Most common incidental findings were emphysema or chronic obstructive pulmonary disease (32%), coronary artery disease (15.9%), and abnormal lymph nodes (4.2%). Among incidental findings, 11 other cancers were diagnosed: seven renal cell carcinoma, one papillary thyroid cancer, one breast cancer, one pancreatic cancer, and one Hodgkin's lymphoma.

Table 1
Demographics and clinical findings of Lung Cancer Screening patients, 2016–2017.

	All Screens (N = 4500)	2016 (N = 1762)	2017 (N = 2738)	
Median Age, years (IQR)	62 (11)			
	n (%)	n (%)	n (%)	p-Value
Sex				
Male	2066 (45.9)	840 (47.7)	1226 (44.8)	0.06
Female	2434 (54.1)	922 (52.3)	1512 (55.2)	
Insurance				0.03
Medicare	1736 (38.6)	666 (37.8)	1070 (39.1)	
Medicare Replacement	499 (11.1)	182 (10.3)	317 (11.6)	
Commercial	1511 (33.6)	583 (33.1)	928 (33.9)	
Medicaid	754 (16.8)	331 (18.8)	423 (15.4)	
Smoking Status				0.67
Current	3107 (69.0)	1223 (69.4)	1884 (68.8)	
Former	1393 (31.0)	539 (30.6)	854 (31.2)	
Indication				< 0.001
Baseline scan	3433 (76.3)	1467 (83.2)	1966 (71.8)	
Annual scan	1067 (23.7)	295 (16.8)	772 (28.2)	
Lung-RADS				
1	2561 (56.9)	1007 (57)	1554 (56.7)	
2	1339 (29.8)	539 (30.6)	800 (29.2)	
3	294 (6.5)	108 (6.1)	186 (6.8)	
4A	187 (4.1)	67 (3.8)	120 (4.4)	
4B	98 (2.2)	38 (2.2)	60 (2.2)	
4X	21 (0.5)	3 (0.2)	18 (0.7)	
Cancer diagnosed				
NSCLC	55 (1.2)	29 (1.65)	26 (0.95)	
SCLC	15 (0.33)	6 (0.34)	9 (0.33)	
Other[a]	11 (0.24)	9 (0.51)	2 (0.07)	

[a] Refers to other type of cancer diagnosed – Renal cell cancer (7), Hodgkin's Lymphoma (1), Papillary Thyroid cancer (1), Pancreatic cancer (1), Breast cancer (1).

4. Discussion

Potential generalizability of the NLST results to the community setting is an important concern as one of the criticisms is that patients in NLST were from large academic centers. Our study is one of the largest reported community-based lung cancer screening programs. In a community setting, our study demonstrated a lung cancer detection rate of 1.55%, slightly higher than the NLST (1%) [1] but comparable to other previously published studies in community settings [7–9]. Unlike NLST, our study has a low adherence rate of 49.9%. High adherence to LDCT (95%) is one of the factor that contributed to the success of NLST [1]. While improving adherence to screening is important and linked to the success of a screening program, the reasons for low adherence are unclear. Some speculated causes include transportation problem, people might believe that a single negative scan means further scans are not needed or low priority, and lower motivation outside of a clinical trial [7].

Another important aspect of our study is that it is based in a histoplasma endemic region. Lung-RADS criteria has a variable size threshold that is dependent on nodule morphology and has shown to reduce the false positive rate of lung cancer screening with LDCT [4]. Compared with this re-analysis of the NLST using Lung-RADS criteria, our data has similar positive baseline screens (14.6% vs 13.6%, $p = 0.15$) despite being in a *Histoplasma* endemic region. As mentioned before, one analysis of NLST did show a higher positive baseline screens

in histoplasma endemic region [5] while another analysis of NLST showed no difference [10]. As a result of our statewide analysis, we recommend that healthcare providers should not be deterred from ordering LDCTs out of concern for greater false positivity in high risk lung cancer patients living in endemic regions.

This study has certain limitations including those of a retrospective study. Some patients received additional scans and treatment outside our health system, thus leading to missing data. Some patients after cancer diagnosis moved to a different hospital system for treatment, therefore cancer staging is not a part of the study as it was not uniformly available. Our screening program is also relatively new and therefore lacks long term follow up.

5. Conclusion

Our study has similar rate of baseline positive screens as compared to NLST. These findings show a successful performance of a community-based lung cancer screening program in a *Histoplasma* endemic region with comparable results to NLST.

Disclosures

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Declaration of Competing Interest

Shruti Bhandari, Prashant Tripathi and Danh Pham have nothing to disclose.

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