CHEST

The American College of Radiology Lung Imaging Reporting and Data System

Potential Drawbacks and Need for Revision

Hiren J. Mehta, MD; Tan-Lucien Mohammed, MD; and Michael A. Jantz, MD

Lung cancer screening using low-dose CT scanning reduces lung-cancer-specific and overall mortality in high-risk patients. A significant limitation of lung cancer screening is the false-positive rate. The American College of Radiology Lung Imaging Reporting and Data System (Lung-RADS) was designed to standardize reporting of low-dose lung cancer screening results and to decrease the false-positive rate without significantly compromising sensitivity. Implementing Lung-RADS can also improve cost-effectiveness. However, Lung-RADS has never been studied in a prospective fashion. It also does not have a specific reporting category for patients with isolated hilar and mediastinal adenopathy or pleural effusion in the absence of lung nodules. We report four such cases from our lung cancer screening program. We believe that this is a significant limitation of Lung-RADS and should be revised in its new version.

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The National Lung Screening Trial (NLST) demonstrated that CT lung screening reduces lung-cancer-specific mortality in high-risk patients.[1] Based on the results of the NLST, the US Preventive Services Task Force recommended (grade B) lung cancer screening with low-dose CT (LDCT) for high-risk current and former smokers.[2] Several professional organizations have promulgated lung cancer screening guidelines, many of which define a positive screening result and include nodule management.[3-5]

One of the major concerns with the NLST has been the high false-positive rate of screening with LDCT (27.3%). More than one-half of baseline examinations in the NLST were positive for nodules that were 4 to 6 mm. Raising the threshold for a positive result to 6 mm would decrease the baseline NLST positive rate from 27.3% to approximately 13.4%.[1] Another concern with widespread implementation of lung cancer screening was that there was also no standard way of reporting lung cancer screening CT scanning results. Because of these concerns, the American College of Radiology (ACR) began efforts to standardize the reporting of LDCT screening results in a manner analogous to the use

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ABBREVIATIONS: ACR = American College of Radiology; LDCT = low-dose CT; Lung RADS = Lung Imaging Reporting and Data System; NLST = National Lung Screening Trial

AFFILIATIONS: From the Division of Pulmonary, Critical Care, and Sleep Medicine (Drs Mehta and Jantz) and Department of Radiology (Dr Mohammed), University of Florida, College of Medicine, Gainesville, FL.

CORRESPONDENCE TO: Hiren J. Mehta, MD, Division of Pulmonary, Critical Care, and Sleep Medicine, University of Florida, 1600 SW Archer Rd, Room M452, Gainesville, FL 32610-0225; e-mail: hiren.mehta@medicine.ufl.edu

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TABLE 1] Summary of Lung-RADS Classification

Lung-RADS Category	Baseline Screening	Subsequent Screening
1	No nodules; nodules with calcification	No nodules; nodules with calcification
2	Solid/partially solid < 6 mm	Solid/partially solid < 6 mm
	GGN: < 20 mm	GGN: < 20 mm or unchanged/slowly growing
		Category 3 or 4 nodules unchanged at ≥ 3 mo
3	Solid: ≥ 6 to < 8 mm	Solid: New ≥ 4 to < 6mm
	Partially solid: ≥ 6 mm with solid component < 6mm	Partially solid: new < 6 mm
	GGN: ≥ 20 mm	GGN: new ≥ 20 mm
4A	Solid: ≥ 8 to < 15 mm	Solid: growing < 8 mm or new ≥ 6 and < 8 mm
	Partially solid: 8 mm with solid component ≥ 6 and < 8 mm	Partially solid: ≥ 6 mm with new or growing solid component < 4 mm
4B	Solid: ≥ 15 mm	Solid: new or growing ≥ 8 mm
	Partially solid: solid component ≥ 8 mm	Partially solid: ≥ 6 mm with new or growing solid component ≥ 4 mm
4X	Category 3 or 4 nodules with additional features; imaging findings that increase the suspicion of cancer	Category 3 or 4 nodules with additional features; imaging findings that increase the suspicion of cancer

GGN = ground-glass nodule; Lung-RADS = Lung Imaging Reporting and Data System.

of the Breast Imaging Reporting and Data System for mammography, based on the best available data.[6] This effort included defining a positive result on lung cancer screening CT scan in the most effective manner, attempting to reduce the substantial false-positive result rate while having the least possible effect on test sensitivity, and suggesting management recommendations depending on lung cancer risk. Based on consensus and review of various studies, the ACR developed a reporting system called Lung CT Screening Reporting and Data System (Lung-RADS).[7] Table 1 describes the primary criteria for defining Lung-RADS categories. Compared with the NLST criteria, Lung-RADS increased the size threshold for a positive baseline screening result from a 4-mm greatest transverse diameter to a 6-mm transverse bidimensional average (and 20 mm for nonsolid nodules) and required growth of preexisting nodules for them to be reported as positive.

In a study by Pinsky et al,[8] which applied Lung-RADS to the NLST group at baseline, the false-positive rate decreased from 26.6% to 12.8%; after baseline, it decreased from 21.8% to 5.3%. Baseline sensitivity was 84.9% (95% CI, 80.8%-89.0%) for Lung-RADS vs 93.5% (95% CI, 90.7%-96.3%) for the NLST, and sensitivity after baseline was 78.6% (95% CI, 74.6%-82.6%) for Lung-RADS vs 93.8% (95% CI, 91.4%-96.1%) for the NLST.[8] Lung-RADS, version 1.0, is the only system currently accepted by the Centers for Medicare & Medicaid Services as an approved registry and therefore is likely the most used. The performance of Lung-RADS,

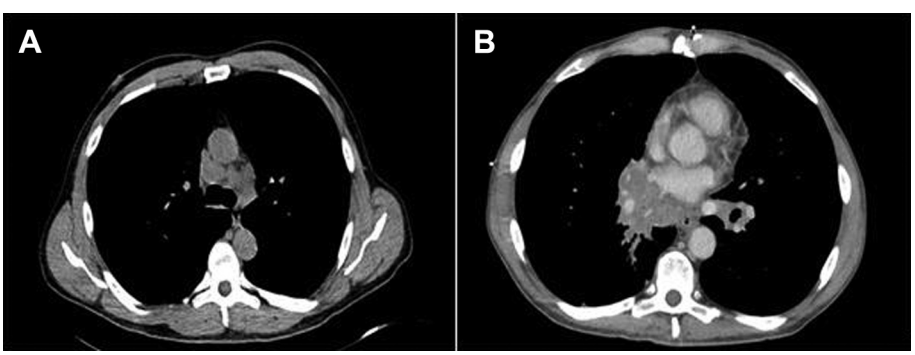

Figure 1 – *A, Lung cancer screening CT scan showing enlarged paratracheal lymph nodes. No lung nodules are present. B, Chest CT scan when patient presented 6 months later with pneumonia. Large right hilar mass is evident. Biopsy results confirmed large-cell lung cancer.*

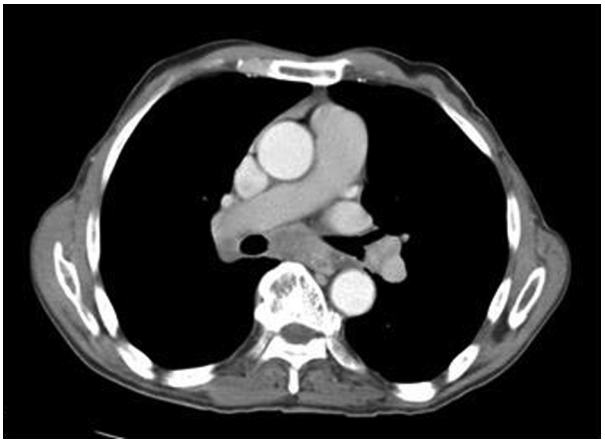

Figure 2 – *Chest CT scan shows subcarinal adenopathy; no lung nodules were seen. This was picked up by the patient's pulmonologist and biopsy showed primary lung adenocarcinoma.*

however, has never been evaluated in a prospective real-world setting.

At the University of Florida, we have implemented a lung cancer screening program with LDCT and have used Lung-RADS, version 1.0, for reporting of the same. In the current manuscript, we report four cases of patients undergoing lung cancer screening CT scans and having isolated hilar and mediastinal adenopathy or isolated pleural effusion without lung nodules, for which Lung-RADS reporting could potentially miss a malignancy.

Case 1

A 56-year-old man with COPD and depression was referred by his primary care provider (PCP) for CT lung cancer screening. The patient underwent LDCT in October 2015; the results showed no lung nodules but revealed hilar and mediastinal adenopathy, the largest node measuring 2.5 cm in the short axis. This was reported; however, the overall scan was read as Lung-RADS category 1 (benign), and continuing yearly LDCT for lung cancer screening was recommended. The patient presented 9 months later with pneumonia and was found to have a large right hilar mass. Bronchoscopy and biopsy were performed and the patient was diagnosed with large-cell lung cancer. Figure 1 shows images of his screening chest CT scan from October 2015 and the chest CT scan when he presented with pneumonia-like symptoms in June 2016.

Case 2

A 76-year-old man with emphysema who was an active smoker underwent CT lung cancer screening ordered by his pulmonologist. He was found to have multiple enlarged right paratracheal and solitary enlarged subcarinal lymph nodes. No lung nodules were identified. The interpretation of the CT scan noted the adenopathy, but the final report was Lung-RADS category 1, and annual follow-up was recommended. However, after review of the scan with the radiologist and pulmonologist, a decision was made to perform a biopsy. The patient underwent endobronchial ultrasonography (EBUS)-guided fine-needle aspiration of the subcarinal lymph node and was diagnosed with primary adenocarcinoma of the lung. Figure 2 shows the CT image.

Case 3

A 67-year-old man with a 35-pack-year smoking history and who had quit smoking 7 years previously was referred for LDCT for lung cancer screening by his PCP. The chest CT scan did not show any lung nodules and was reported as Lung-RADS 1. However, the patient had bulky hilar and mediastinal adenopathy. He was referred for a pulmonary biopsy. The patient underwent EBUS-guided fine-needle aspiration, which showed suspicious cells. The patient was then sent for mediastinoscopy, and

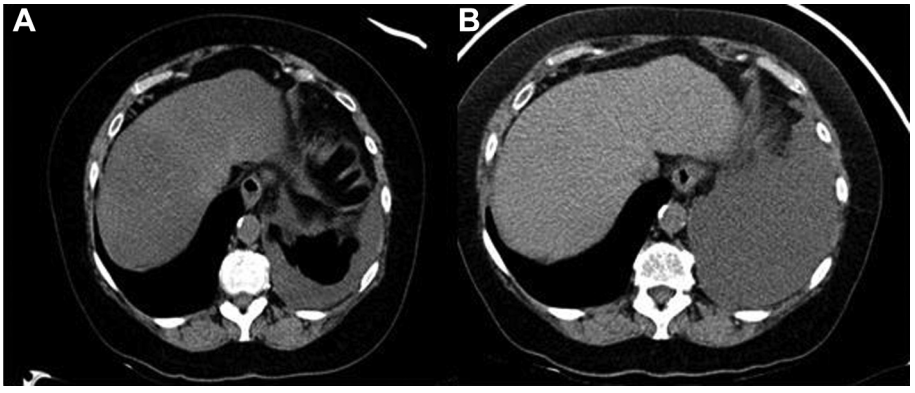

Figure 3 – *A, Small left pleural effusion noted on initial screening scan. No nodules were seen. B, Lung cancer screening a year later showed moderate left effusion, which on thoracentesis revealed primary adenocarcinoma of the lung.*

a right paratracheal node was resected. The final diagnosis was Hodgkin lymphoma.

Case 4

A 75-year-old woman with a 70-pack-year smoking history had quit smoking 3 years previously. She underwent a lung cancer screening scan recommended by her PCP. The CT scan showed a small left-sided effusion and no lung nodules. Findings were reported as Lung-RADS 1. A subsequent chest CT scan a year later showed that the left pleural effusion was now of moderate size. No lung nodules were detected. This time the patient was referred to the pulmonary medicine department and a thoracentesis was performed, which showed lung adenocarcinoma. Figure 3 shows her representative original CT images as well as those from a year later. Table 2 shows details of the individual cases.

Discussion

The NLST showed that screening with LDCT could reduce lung-cancer-specific mortality by 15% to 20%; however, the downside of the NLST is a very high false-positive rate of about 25%.[1] This means that one-quarter of the patients, nearly all of whom did not have cancer, would have to undergo additional imaging or biopsy in selected cases to confirm the finding. In part to reduce the high false-positive rate and in part to standardize reporting for lung cancer screening as it comes into population-wide use, the ACR embarked on a classification scheme they call Lung-RADS.[7] Applying Lung-RADS increases the positive predictive value of baseline CT lung screening examinations by a factor of 2.5 compared with using NLST positive thresholds, without creating additional false-negative results.[8] It also increases the cost-effectiveness of CT lung screening by secondarily decreasing the number of interval scans recommended and virtually eliminates CT lung screening examinations that are positive for nonsolid nodules.[7]

There are, however, several limitations of using Lung-RADS over the NLST protocol. It has never been prospectively studied in the real-world setting. It is unknown how the decrease in the sensitivity of Lung-RADS, compared with the NLST protocol, would affect the mortality benefit of LDCT screening. The effect of delaying diagnosis in cases of cancer missed by Lung-RADS is unknown, and it cannot be assumed that most are indolent and would not affect lung cancer mortality rates. The sensitivity of Lung-RADS will be an important quality indicator of LDCT screening in

TABLE 2] Summary of Patients With Lung Cancer Screening Scans That Were Reported Normal by Lung-RADS

Age	Sex	Total Pack-Years	Current Smoking Status	LDCT Ordering Provider	Initial LDCT Findings	Lung-RADS Category	Follow-up	Final Diagnosis	Delayed Diagnosis (mo)
56	Male	40	Active	PCP	Mediastinal adenopathy	1	Chest CT scan 6 mo later	Large-cell lung cancer	9
76	Male	55	Active	Pulmonologist	Hilar and mediastinal adenopathy	1	EBUS-guided FNA	Lung adenocarcinoma	None
67	Male	35	Quit 7 y previously	PCP	Massive mediastinal adenopathy	1	Mediastinoscopy	Hodgkin lymphoma	None
75	Female	70	Quit 3 y previously	PCP	Left pleural effusion	1	Screening CT scan 1 yr later	Lung adenocarcinoma	12

FNA = fine-needle aspiration; LDCT = low-dose CT; PCP = primary care physician. See Table 1 legend for expansion of other abbreviations.

clinical practice, and moving forward it will be critical to monitor it using population screening registries. Lung-RADS does not have a specific category of reporting for patients with isolated hilar and mediastinal adenopathy or pleural effusion (or both) without any lung nodules and classifies these patients in the Lung-RADS 1 (probably benign) category (in the presence of lung nodules, these findings can be reported as Lung-RADS category 4X). This can further reduce the sensitivity of the Lung-RADS reporting system in patients undergoing LDCT for lung cancer screening. It is unclear how many patients had isolated hilar and mediastinal adenopathy or pleural effusion, or both, in the absence of lung nodules in the NLST. We have reported four cases in our lung cancer screening program with LDCT who had isolated adenopathy/pleural effusion and were reported to have Lung-RADS 1, who on further testing were found to have malignant disease. Two of our four cases were picked up by the referring provider on the initial chest CT scan by reviewing the detailed report and the images with the radiologist; however, the other two cases (cases 1 and 4) were missed and later presented with advanced malignancy and poor performance status.

Based on our experience, we believe that particular caution should be exercised in reporting Lung-RADS 1 category for patients with adenopathy/pleural effusion with no lung nodules, as a majority of the lung cancer screening scans will be ordered by PCPs who may not necessarily have expertise in interpreting CT scans of the chest and may not have time to look at scans in their busy practices and may rely on the radiologist's final interpretation of the scans, which, as in our cases, will be rightfully reported as Lung-RADS 1 (benign). Lung-RADS has the potential to significantly decrease the false-positive results in patients undergoing LDCT for lung cancer screening. In the long run, it may be more cost-effective than the NLST protocol. However, as with any new system, an ongoing evaluation of the performance of Lung-RADS should be conducted so that the sensitivity and mortality benefit seen in the NLST trial is not compromised. As prospective performance characteristics of Lung-RADS become available, it is expected that it will be revised, similar to the process the ACR has used to revise the Breast Imaging Reporting and Data System classification scheme for breast cancer screening, which is now in its fifth edition.[9] We strongly believe, based on our experience with these four cases, that the new version of Lung-RADS, version 2.0, should incorporate these shortcomings and have a separate category for findings that are highly suspicious for malignancy but do not have an accompanying lung nodule.

Conclusions

Lung cancer screening using LDCT scanning reduces lung-cancer-specific and overall mortality in high-risk patients. A significant limitation of lung cancer screening is the false-positive rate. Lung-RADS was designed to standardize reporting of low-dose lung cancer screening scans and to decrease the false-positive rate without significantly compromising sensitivity. Implementing Lung-RADS can also improve cost-effectiveness. However, Lung-RADS has never been studied in a prospective fashion. In addition, it does not have a specific reporting category for patients with isolated hilar and mediastinal adenopathy or pleural effusion in the absence of lung nodules. We report four such cases from our lung cancer screening program. We believe that this is a significant limitation of Lung-RADS and should be revised in its new version.

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