Performance of ACR Lung-RADS in a Clinical CT Lung Screening Program

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Abstract

Purpose: The aim of this study was to assess the effect of applying ACR Lung-RADS in a clinical CT lung screening program on the frequency of positive and false-negative findings.

Methods: Consecutive, clinical CT lung screening examinations performed from January 2012 through May 2014 were retroactively reclassified using the new ACR Lung-RADS structured reporting system. All examinations had initially been interpreted by radiologists credentialed in structured CT lung screening reporting following the National Comprehensive Cancer Network's Clinical Practice Guidelines in Oncology: Lung Cancer Screening (version 1.2012), which incorporated positive thresholds modeled after those in the National Lung Screening Trial. The positive rate, number of false-negative findings, and positive predictive value were recalculated using the ACR Lung-RADS-specific positive solid/part-solid nodule diameter threshold of 6 mm and nonsolid (ground-glass) threshold of 2 cm. False negatives were defined as cases reclassified as benign under ACR Lung-RADS that were diagnosed with malignancies within 12 months of the baseline examination.

Results: A total of 2,180 high-risk patients underwent baseline CT lung screening during the study interval; no clinical follow-up was available in 577 patients (26%). ACR Lung-RADS reduced the overall positive rate from 27.6% to 10.6%. No false negatives were present in the 152 patients with >12-month follow-up reclassified as benign. Applying ACR Lung-RADS increased the positive predictive value for diagnosed malignancy in 1,603 patients with follow-up from 6.9% to 17.3%.

Conclusions: The application of ACR Lung-RADS increased the positive predictive value in our CT lung screening cohort by a factor of 2.5, to 17.3%, without increasing the number of examinations with false-negative results.

Key Words: Lung-RADS, CT lung screening

J Am Coll Radiol 2015;12:273-276.

INTRODUCTION

The National Lung Screening Trial (NLST) demonstrated that CT lung screening reduces lung cancer–specific mortality in high-risk patients when the minimum size of a positive pulmonary nodule is set at 4 mm [1]. Because more than half of baseline examinations in the NLST were positive for nodules 4 to 6 mm in size, 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]. Given the 0.5% positive predictive value (PPV) in the NLST of an examination positive for a nodule measuring 4 to 6 mm, increasing the threshold of positive CT lung screening results to 6 mm has the potential to increase the PPV by a factor of 1.8 (7.2% at 6 mm vs 3.8% at 4 mm) without significantly affecting the sensitivity to detect malignancy [1].

The International Early Lung Cancer Action Program reported an analogous observation: a reduction in baseline positive results to 10.2% at a 6-mm solid nodule threshold compared with 16% at a 5-mm threshold. Notably, the same number of lung cancers was detected within 12 months at both thresholds [2].

After publication of these International Early Lung Cancer Action Program findings, both the National Comprehensive Cancer Network (NCCN) and the ACR adopted 6 mm as the minimum nodule-size threshold for positive CT lung screening results [3,4]. To further decrease the frequency of false-positive CT lung screening results, ACR Lung-RADS™ version 1.0 set the size of a positive nonsolid (ground-glass) nodule to 2 cm and the duration of nodule stability required to meet criteria for benign behavior to 3 months, compared with 2 years in the NLST [4].

In this study, we retroactively applied the ACR Lung-RADS positive nodule-size thresholds to our clinical CT lung screening results. These had originally been interpreted using the NCCN Clinical Practice Guidelines in Oncology: Lung Cancer

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1546-1440/15/$36.00 ■ http://dx.doi.org/10.1016/j.jacr.2014.08.004

Table 1. Demographics

Variable	With Follow-Up	Overall
Total number	1,603	2,180
Average age (y)	63.5 ± 6.2	63.1 ± 6.2
Men	56%	53%
Active smokers	48.2%	45.8%
Average cessation (former smokers) (y)	9.8 ± 9.5	10.1 ± 8.5
Average pack-years	48.6 ± 22.7	48.6 ± 22.2
Percentage with additional lung cancer risk factor	25.3%	26.2%

Screening (version 1.2012), which set positive nodule thresholds similar to those used in the NLST (4 mm solid, 5 mm nonsolid, benign at 2-year stability). Recasting the results was performed to evaluate the resulting frequency of positive findings, PPV, and number of false negatives under the new structured reporting system.

METHODS

This was a retrospective, single-center study of our experience with clinical CT lung screening approved by the institutional review board. We reviewed consecutive, prevalence, clinical CT lung screening examinations performed at our institution from January 2012 through May 2014. To qualify for screening, individuals had to satisfy the NCCN high-risk criteria for lung cancer, be asymptomatic, have physician orders for CT lung screening, be free of lung cancer for ≥5 years, and have no known metastatic disease [3,5].

Image Acquisition and Interpretation

All CT lung screening examinations were performed on ≥64-row multidetector CT scanners (LightSpeed VCT and Discovery VCT [GE Medical Systems, Milwaukee, Wisconsin]; Somatom Definition [Siemens AG, Erlangen, Germany]; iCT [Philips Medical Systems, Andover, Massachusetts]) at 100 kV and 30 to 100 mA depending on the scanner and the availability of iterative reconstruction software. Axial images were obtained at 1.25- to 1.5-cm thickness with 50% overlap and reconstructed with both soft tissue and lung kernels. Axial maximum-intensity projections (16 × 2.5 mm) and coronal and sagittal multiplanar reformatted images were reconstructed and used for interpretation.

Original image interpretation was performed by radiologists specifically trained and credentialed in CT lung screening using a structured reporting system and the NCCN guidelines nodule follow-up algorithms [3,5]. Positive results required the identification of a solid, noncalcified nodule ≥4 mm or a nonsolid nodule ≥5 mm for which >2-year stability had not been established [5].

Application of ACR Lung-RADS

Studies positive for solid nodules <6 mm, nonsolid nodules <2 cm, and positive nodules stable for >3 months but <2 years were recategorized as benign to estimate the hypothetical ACR

Table 2. Results

	Positive Thresholds			
	NCCN Version 1.2012 (~NLST)		ACR Lung-RADS	
Overall (n = 2,180)				
Negative/benign (Lung-RADS 1 and 2)	1,579	72.4%	1,949	89.4%
Positive (Lung-RADS 3 and 4)	601	27.6%	231	10.6%
Probably benign (Lung-RADS 3)	508	23.3%	138	6.3%
Suspicious (Lung-RADS 4)	93	4.3%	93	4.3%
Clinical follow-up (n = 1,603)				
Negative/benign (Lung-RADS 1 and 2)	1,185	73.9%	1,435	89.5%
Positive (Lung-RADS 3 and 4)	418	26.1%	168	10.5%
Probably benign (Lung-RADS 3)	352	22.0%	102	6.4%
Suspicious (Lung-RADS 4)	66	4.1%	66	4.1%
Diagnosed lung cancer	29 (1.8%)		29 (1.8%)	
▪ Positive examination result				
▪ Includes 3 cases of presumed malignancy*				
Positive predictive value	6.9%		17.3%	
Biopsy-proven lung cancer	26 (1.6%)		26 (1.6%)	
▪ Positive examination result				
▪ Excludes 3 cases of presumed malignancy*				
Positive predictive value	6.2%		15.5%	

Note: NCCN = National Comprehensive Cancer Network; NLST = National Lung Screening Trial.

*Patients unable to tolerate biopsy were diagnosed with presumed lung cancer on the basis of positive results on PET, suspicious growth rate, and multidisciplinary consensus.

Table 3. Diagnosed malignancies

Patient	ACR Lung-RADS Category	Baseline Size (mm)	Time to Diagnosis (mo)	Histology
1	4	13 × 14	2	Adenocarcinoma
2	4	15 × 17	1.5	Squamous cell carcinoma
3	4	9–10	<1	Adenocarcinoma
4	4	10–11	3.5	Presumed adenocarcinoma*
5	4	70 × 90	<1	Squamous cell carcinoma
6	4	14 × 18	5.5	Adenocarcinoma
7	4	22 × 48	1	Carcinoid tumor
8	4	20 × 20	2	Squamous cell carcinoma
9	4	22 × 33	1	Adenocarcinoma
10	4	12 × 19	<1	Adenocarcinoma
11	4	13 × 17	<1	Adenocarcinoma
12	4	23 × 29	3	Adenocarcinoma
13	4	Other†	8	Adenocarcinoma
14	3	6–7	12	Squamous cell carcinoma
15	4	8 × 11	3	Adenocarcinoma
16	4	10–11	4	Squamous cell carcinoma
17	4	39 × 45	2.5	Squamous cell carcinoma
18	4	6–7	6.5	Squamous cell carcinoma
19	4	26 × 31	1.5	Adenocarcinoma
20	4	11–12	2	Adenocarcinoma
21	4	Other†	2	Adenocarcinoma
22	4	9 × 17	3	Squamous cell carcinoma
23	4	11 × 18	6.5	Presumed adenocarcinoma*
24	3	6–7	8.5	Presumed adenocarcinoma*
25	3	6–7	3	Adenocarcinoma
26	4	36 × 36	<1	Small cell lung cancer
27	3	7–8	10	Adenocarcinoma
28	4	13 × 16	1.5	Adenocarcinoma
29	4	33 × 63	2	Adenocarcinoma

*Patients unable to tolerate biopsy were diagnosed with presumed lung cancer on the basis of positive results on PET, suspicious growth rate, and multidisciplinary consensus.
†Other findings included pleural nodularity or thickening not amenable to discrete measurement.

Lung-RADS positive rate and PPV in our cohort. Cases reclassified as benign would be considered false negative if cancer was diagnosed within 12 months of the baseline examination.

For both ACR Lung-RADS and the original interpretation, solid and part-solid nodules >8 mm, growing nodules, and nonsolid nodules with growing solid components were categorized as "suspicious." All other positive nodules were categorized as "probably benign." Mediastinal and hilar lymph nodes measuring >1 cm in the short axis in the absence of pulmonary nodules and findings suspicious for infection or inflammation (most commonly areas of tree-in-bud nodularity) not currently considered positive under ACR Lung-RADS were treated as incidental findings under both schemas.

RESULTS

From January 2012 through May 2014, a total of 2,180 high-risk patients underwent clinical prevalence CT lung screening examinations (Table 1). Five hundred seventy-seven of these 2,180 (26%) were patients from outside our institution for whom clinical follow-up after the prevalence CT lung screening examination was not available during this retrospective review. Application of ACR Lung-RADS had the following impact in our specific patient cohort.

Nodule Reclassification

Three hundred seventy of 2,180 examinations (17.0%) were reclassified as benign, thus decreasing the overall positive rate from 27.6% to 10.6% (Table 2). Breaking down these reclassified cases further, 86% of these (319 of 370) were originally positive for solid or part-solid nodules between 4 and 6 mm. Notably, all 49 cases originally positive for nonsolid nodules were downgraded to benign under ACR Lung-RADS.

Lung Cancer Detection Rate

Twenty-nine lung cancers were diagnosed in patients with positive baseline screening results among the 1,603 patients with clinical follow-up (average, 480 days). All diagnosed cancers were solid or part solid at baseline screening, and all

were positive under ACR Lung-RADS (Table 3). No false negatives were found in the 152 of 250 cases (61%) reclassified as benign with 12-month follow-up.

PPV

ACR Lung-RADS increased the total PPV of the baseline CT lung screening examination by a factor of 2.5, from 6.9% (29 of 418) to 17.3% (29 of 168) (Table 2). Twenty-five of 29 cancers (86.3%) were Lung-RADS 4 "suspicious" at baseline screening, for a Lung-RADS 4 PPV of 37.9%. Excluding the 3 cases of presumed malignancy in patients unable to tolerate biopsy (and subsequently treated with stereotactic body radiotherapy) decreased the ACR Lung-RADS PPV to 15.5% (26 of 168).

Ancillary Findings

Mediastinal and/or hilar lymph nodes >1 cm in the short axis in the absence of pulmonary nodules ≥4 mm were present in 1.6% of patients and were classified as incidental findings. In the 6.1% of baseline screens (98 of 1,603) with findings suspicious for infection or inflammation, 1 cancer (small cell histology) was detected within 12 months.

DISCUSSION

No false negatives were detected in those patients of our cohort in whom positive findings were reclassified as benign when applying ACR Lung-RADS. This observation supports the notion that it is safe to follow solid nodules <6 mm and nonsolid nodules <20 mm in high-risk patients with annual CT surveillance. Our evaluation is limited by the relatively small number of patients reclassified as benign with ≥12-month follow-up (n = 152), from which we would expect to yield only 0.8 false negatives given the 0.5% PPV of these nodules in the NLST [1]. The apparent low likelihood of cancer in this group does suggest that the approach of following 4 to 6 mm solid pulmonary nodules incidentally found in lower risk patients (not meeting criteria for CT lung screening) 12 months after initial discovery is reasonable.

When we applied the ACR Lung-RADS positive thresholds to our study cohort, it reduced our positive clinical CT lung screening rate to a level similar to that reported at 6 mm by the International Early Lung Cancer Action Program [2]. Our relative increase in PPV with ACR Lung-RADS (2.5×) was greater than we calculated would have occurred in the NLST at a 6-mm threshold (1.8×), which in part results from only increasing the positive threshold for solid nodules in our NLST analysis. Also contributing are differences in the method of nodule measurement used by the NLST (maximum dimension) and the NCCN and ACR Lung-RADS (mean dimension) [3,4].

In the 1.6% of baseline screens with isolated mediastinal or hilar lymph nodes >1 cm, we observed no cases of malignancy. Should isolated mediastinal or hilar lymph nodes >1 cm be classified as "probably benign" (Lung-RADS 3) and/or "suspicious" (Lung-RADS 4) in a future revision of ACR Lung-RADS, we would expect an increase in the positive rate by 1.6% to 12.1%, which would decrease our estimated PPV to 15.5% for diagnosed malignancy and 13.8% for pathology proven cancers.

Isolated findings suspicious for infection or inflammation had a low predictive value for malignancy of 1% (1 of 98). The single case of cancer within this group was small cell carcinoma diagnosed approximately 6 months after the baseline screening. Small cell carcinoma was overrepresented in interval cancers at baseline screening in the NLST (4 of 18), likely because of its central location and rapid doubling time that does not lend itself to detection with annual CT lung screening [1]. As such, the occurrence of a case of small cell cancer is not a clear indication that this group is at sufficient risk to warrant a positive CT lung screening designation.

TAKE-HOME POINTS

- Applying ACR Lung-RADS increased the PPV of our baseline clinical CT lung screening examinations by a factor of 2.5 compared with using NLST positive thresholds, without creating additional false negatives.
- ACR Lung-RADS should increase the cost-effectiveness of CT lung screening by secondarily decreasing the number of interval scans recommended and performed.
- ACR Lung-RADS virtually eliminates CT lung screening examinations positive for nonsolid nodules.
- Given the low likelihood of cancer in high-risk patients with nodules 4 to 6 mm in size, following incidental solid pulmonary nodules of this size in lower risk patients (not meeting criteria for CT lung screening) in <12 months may be unnecessary.

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