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Diagnostic Performance of Lung-Reporting and Data System with Computed Tomography Imaging in Categorizing Pulmonary Nodules

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Abstract:

Background:Many radiologists recognize that there are common lung nodules, that majority of them are benign, and that not all benign lung nodules need the same management.The Lung Imaging Reporting and Data System (Lung-RADS) was introduced to create a framework for the analysis of screen-detected nodules and to enable nodule management further standardized. Aim of work:To assess the performance of Lung-RADS in categorization of pulmonary nodules using baseline screening CT scans. Subjects and methods:A prospective comparative study was conducted in radiodiagnosis department, Zagazig university hospitals on 30 patients referred from the chest department of Zagazig university hospitals as well as the outpatient clinics for CT lung screening during the period from August 2018 to May 2019.All patients were subjected to complete history taking, full clinical examination, MDCT imaging, PET/CT imaging in some nodules, pathological examination, clinical and imaging follow up according to the criteria of the nodules after 6 months by CT. Results:Considering only those cases classified as Lung-RADS4X for predicting malignancy, the Lung-RADS had an accuracy, sensitivity, specificity, PPV, and NPV of 76.7%, 70.6%,84.6%, 85.7%, and 68.6%, respectively. Considering Lung-RADS4A, Lung-RADS4B and Lung-RADS4X together as predictors for malignancy, the accuracy, sensitivity, specificity, PPV, and NPV were 90%, 94.1%, 84.6%, 88.9%, and 91.7%, respectively.Conclusion:The LUNG–RAD classification method is a useful conceptualising system that aids in the classification, follow-up, and improvement of the prognosis of malignant pulmonary nodules.

Keywords:Lung-RADS, Nodules, CT, Radiodiagnosis.

Introduction:

Lung cancer causes a high number of fatalities per year around the globe. The most effective solution of this disease is the definitive operation in the initial stages. Great percentage of cases, however, are diagnosed in late stages, therefore their level of illness has no solution.**[1]**

Muchresearchhas concentrated on low dose computed tomography (LDCT) scanning for cancer of lungduring the last years. In spite of the positive impact of the randomized new (CT) screening trial

for lung cancer, there are still major performance problems, involving accurate risk factors reporting and suggested screen-detected nodules workup.**[2]**

Many radiologists recognize that there are common lung nodules, that majorityof them are benign, and that not all benign lung nodules need the same management. Even so, these concepts may typically not be recognized by 1ry treatment doctors and public citizens.In fact, many patients assume that lung nodules are the same as lung cancer. The radiologist's ability to convey the nodule's malignant threat will be crucial to the success of screening CT services, as it will aid to prevent inaccurate diagnoses, repeated CTs, and procedures.**[3]**

The American College of Radiology (ACR) presented the Lung Imaging Reporting and Data System (Lung-RADS) to create a framework for the analysis of screen-detected nodules and to enable nodule management further standardized. It is divided into several groups based on the type of nodule and the diameter ranges. The treatment of nodules is tailored to the nodule's relative risk of representing or progressing to malignancy.**[4]**

The Lung-RADS comprises 6 groups that rely on the results of computed tomography, with a focus on sequential CT results. A chance of primary lung cancer and clear work-up guidelines are correlated with each group.**[3]**

Aim and objectives: To assess the performance of ACR Lung-RADS in categorization of pulmonary nodules using baseline screening CT scans.

Subjects and methods:

Technical design:This prospective comparative study was conducted in radiodiagnosis department, Zagazig university hospitals on 30 patients referred from the chest department of Zagazig university hospitals as well as the outpatient clinics for CT lung screening during the period from August 2018 to May 2019.Inclusion criteria included high risk patients with suspected PNswhile exclusion criteria involved patients with normal MDCT findings, pregnant, lactating females or lost during follow-up.

Methods:All patients were subjected to complete history taking, full clinical examination, MDCT imaging, PET/CT imaging in some nodules, pathological examination, clinical and imaging follow up according to the criteria of the nodulesafter 6 months by CT.

Administrative considerations: Written informed consent was obtained from all participantsafter clear explanation of the study and the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University (Institutional Research Board “IRB”). The work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical Analysis:

Data was collected throughout history, basic clinical examination, laboratory investigations and outcome measures coded, entered, and analyzed using Microsoft Excel software. All data were analyzed using Statistical Package for the Social Sciences (SPSS) version 20.0 (SPSS Inc., Chicago, IL, USA) and MedCalc program version 11.1(MedCalc, Mariakerke, Belgium). According to the type of data, qualitative data was represented as number and percentage while quantitative data was represented by mean ± SD. Difference and association of qualitative variables were assessed by Chi square test (X2). Differences between quantitative independent groups were assessed by t test or Mann Whitney.P value was set at <0.05 for significant results &<0.001 for high significant result.

Results:

Table (1)shows the demographics of patients and characteristics of risk-dominant nodules. We found that 46.7% of our patients were active smokers by average pack/year of 47.6±10.7 and average cessation rate of 9.8±2.5 years. There were also 26.7% of patients have additional lung cancer risk factors as exposure to some irritant substances as asbestos, radon or uranium, and exposure to radiation. There were significant differences between benign and malignant nodules as regards active smokers (P= 0.008), and average pack/year (P= 0.03). The final diagnosis of PNs and their distribution according to mean age, sex and side are demonstrated in**Table (2)**. There were 17 patients diagnosed as malignant and 13 patients as benign. We found that hamartoma was the most frequent benign tumors then TB, cryptococcosis, aspergillosis, inflammatory pseudo tumor, and perifissural nodule. The malignant cases varied from adenocarcinoma which is the most common to squamous cell carcinoma, large cell carcinoma, and small cell carcinoma.**Table (3)** demonstrates the CT imaging features of the PNs as regards final diagnosis. The analysis of the findings of CT as regard diagnostic features of PNs displayed significant differences between benign and malignant nodules as regard calcification, consistency, size, and speculation of nodules (P= 0.001, 0.001, 0.008, and 0.04, respectively). However, there were no significant differences as regard location, number, and consistency of nodules.Lung-RADS categories of the PNs identified at MDCT imaging, according to final diagnosiswere cleared in **Table (4)**. We found that of the 30 cases assessed, seven (23.3%) were classified as Lung-RADS 1, three 10%) as Lung-RADS 2, two(6.7%) as Lung-RADS 3, two (6.7%) as Lung-RADS 4A, three (10%) as Lung-RADS 4B, and 13 (43.3%) as Lung-RADS4X.Of the10 cases categorized as Lung-RADS 2 and Lung-RADS 3, none was malignant; of the two cases categorized as Lung-RADS3, one (50%) was malignant; the two cases categorized as Lung-RADS 4A were malignant (100%); of the three cases categorized as Lung-RADS 4B, two(66.7%) were malignant ;and of the 13 cases categorized as Lung-RADS4X, 12(92.3%) were malignant.**Table (5)** clears the CT imaging features of nodules as regard Lung-RADS classification. The speculation, and calcification were the most significant features that had impact on Lung-RADS (P= 0.01 and 0.02, respectively). Whereas the size of nodule and consistency did not havesignificant impact (P= 0.13 and 0.23, respectively). **Table (6)** reveals the 2×2 Table correlating Lung-RADS findings with final diagnosis.When we considered only those cases classified as Lung-RADS4X for predicting malignancy, the true positive cases were 12, the false positive cases were two, the true negative cases were 11 and the false negative cases were five. When we considered those cases classified as Lung-RADS4A, Lung-RADS4B and Lung-RADS4X for predicting malignancy, the true positive cases were 16, the false positive cases were two, the true negative cases were 11 and the false negative case was one.The diagnostic performance of Lung-RADS for diagnosis of malignant PNs was demonstrated in **Table (7)**.Considering only those cases classified as Lung-RADS4X for predicting malignancy, the Lung-RADS had an accuracy, sensitivity, specificity, PPV, and NPV of 76.7%, 70.6%,84.6%, 85.7%, and 68.6%, respectively. Considering Lung-RADS4A, Lung-RADS4B and Lung-RADS4X together as predictors for malignancy, the accuracy, sensitivity, specificity, PPV, and NPV were 90%, 94.1%, 84.6%, 88.9%,and 91.7%,respectively.

Table (1): Shows the demographics of patients and characteristics of risk-dominant nodules.

Parameter	Total	Malignant	Benign	P value
Number of patients	30	17 (56.7%)	13 (43.3%)	0.72

Age (years), Mean ±SD		57.6 ± 11.2	60.9 ± 9.7	57.8 ± 7.4	0.35
Sex	**Male**	18 (60%)	12 (70.6%)	6 (46.2%)	0.33
	Female	12 (40%)	5 (29.4%)	7 (53.8%)	
Family history of lung cancer		11 (36.7%)	7 (41.2%)	4 (30.8%)	0.84
Active smokers		14 (46.7%)	12 (70.6%)	2 (15.4%)	0.008
Average pack/year, Mean ± SD		47.6 ± 10.7	42 ± 9.3	34.6 ± 7.8	0.03
Additional lung cancer risk factors		8 (26.7%)	6 (35.3%)	2 (15.4%)	0.08

Qualitative data was represented as numbers while quantitative data was represented by mean ± SD.
P value was set at <0.05 for significant results &<0.001 for high significant result.

Table (2): Shows the final diagnosis of PNs and their distribution according to mean age, sex, and side.

Pathology		**No. of patients**	**Mean age**	**Sex**		**Side**		
				Male	**Female**	**RT**	**LT**	**Bilateral**
enign	**Hamartoma**	5	55.3	3	2	3	2	0
	TB	3	58.3	2	1	2	0	1
	Cryptococcosis	2	62.7	1	1	0	2	0
	Aspergilloma	1	70	0	1	0	1	0
	Inflammatory pseudo-tumor	1	36	0	1	1	0	0
	Perifissural nodule	1	65	0	1	1	0	0
	Total	**13**	**58.5**	**6**	**7**	**7**	**5**	**1**
Ialignant	**Adenocarcinoma**	8	62.7	6	2	5	3	0
	Squamous cell carcinoma	4	59.3	3	1	1	3	0
	Small cell carcinoma	1	67.9	1	0	1	0	0
	Large cell carcinoma	1	61	1	0	1	0	0
	Lymphoma	1	46	0	1	0	1	0
	Metastatic nodules	2	67.1	1	1	1	0	1
	Total	**17**	**61.6**	**12**	**5**	**9**	**7**	**1**

Qualitative data was represented as numberswhile quantitative data was represented by mean ± SD.

Table (3): CT imaging features of the PNs as regards final diagnosis.

Features of nodules		**All patients (n=30)**	**Malignant (n=17)**	**Benign (n=13)**	**P value**
Size (mm), Mean± SD		15.2±5.3	20.3±5.8	14.7±4.6	0.008
Location	**Left lower lobe**	5 (16.7%)	2 (11.8%)	3 (23.1%)	0.92

	Left upper lobe	7(23.3%)	5 (29.4%)	2 (15.4%)	
	Right lower lobe	6 (20%)	3 (17.6%)	3 (23.1%)	
	Right middle lobe	2 (6.7%)	1 (5.8%)	1 (7.7%)	
	Right upper lobe	8 (26.7%)	5 (29.4%)	3 (23.1%)	
	Bilateral	2 (6.7%)	1 (5.8%)	1 (7.7%)	
Number	**Solitary**	26 (13.3%)	15 (88.2%)	11 (43.3%)	0.8
	Multiple	4 (13.3%)	2 (11.8%)	2 (15.4%)	
Consistency	**Non-solid**	2 (6.7%)	0(0%)	2(15.4%)	0.001
	Part-solid	12 (40%)	3(17.6%)	9 (69.2%)	
	Solid	16 (53.3%)	14 (82.4%)	2 (15.4%)	
Speculation	**Absent**	18 (60%)	7 (41.2%)	11(84.6%)	0.04
	Present	12 (40%)	10 (58.8%)	2 (15.4%)	
Calcification	**Absent**	19 (63.3%)	17 (100%)	2 (15.4%)	0.001
	Present	11 (36.7%)	0 (0%)	11 (84.6%)	
Perifissural		1 (3.3%)	0 (0%)	1 (7.7%)	0.89

Qualitative data was represented as numbers while quantitative data was represented by mean ± SD.
P value was set at <0.05 for significant results &<0.001 for high significant result.

Table (4): Lung-RADS Categories of the PNs identified at MDCT imaging, according to final diagnosis.

Lung-RADS Category	Total No. of patients	Final Diagnosis	
		Malignant	Benign
1	7	0	7
2	3	0	3
3	2	1	1
4A	2	2	0
4B	3	2	1
4X	13	12	1
Total	30	17	13

Qualitative data was represented as numbers.

Table (5): CT imaging features of nodules as regard Lung-RADS classification.

Lung-RADS category		**Total (n= 30)**	**1 (n=7)**	**2 (n=3)**	**3 (n=2)**	**4A (n=2)**	**4B (n=3)**	**4X (n=13)**	**P value**
Size, Mean± SD		15.2± 5.5	10.2±3. 7	13.5±4. 5	13.2±3. 9	18.1±4. 3	23.4±7. 5	22.1±7. 1	0.13
Consistency (%)	**Non-solid**	2 (6.7)	1(14.3)	1 (33.3)	0	0	0	0	0.23
	Part-	12	5 (71.4)	3 (100)	1 (50)	1 (50)	0	2 (15.4)	

	solid	(40)							
	Solid	16 (53.3)	1(14.3)	1(33.3)	2 (100)	2 (100)	3 (100)	7 (53.8)	
Speculation n (%)		12 (40)	0	0	1 (50)	1 (50)	1(33.3)	7 (53.8)	0.01
Calcification, n (%)		11 (36.7)	7 (100)	3 (100)	1 (50)	0	0	0	0.02
Perifissural		1 (3.3)	1(14.3)	0	0	0	0	0	0

P value was set at <0.05 for significant results &<0.001 for high significant result.

Table (6): 2×2 Table correlating Lung-RADS findings with final diagnosis.

Final diagnosis	Lung-RADS 4X		Lung-RADS 4A+B+X	
	Positive for malignancy	Negative for malignancy	Positive for malignancy	Negative for malignancy
Malignant	12	5	16	1
Benign	2	11	2	11

Qualitative data was represented as numbers.

Table (7): The diagnostic performance of Lung-RADS for diagnosis of malignant PNs.

	Lung-RADS 4X		Lung-RADS 4 A+B+X	
	%	95% CI	%	95% CI
Accuracy	76.67	49.11 to 91.21	90	69.42 to 99.21
Sensitivity	70.59	44.04 to 89.69	94.12	71.31 to 99.85
Specificity	84.62	54.55 to 98.08	84.62	54.55 to 98.08
AUC	0.78	0.59 to 0.91	0.89	0.73 to 0.98
Positive Likelihood Ratio	4.59	1.24 to 17.03	6.12	1.70 to 22.01
Negative Likelihood Ratio	0.35	0.16 to 0.75	0.07	0.01 to 0.47
Disease prevalence	56.67	37.43 to 74.54	56.67	37.43 to 74.54
Positive Predictive Value	85.71	57.19 to 98.22	88.89	65.29 to 98.62
Negative Predictive Value	68.75	41.34 to 88.98	91.67	61.52 to 99.79

Difference and association of qualitative variables were assessed by Chi square test (X2). Differences between quantitative independent groups were assessed by t test or Mann Whitney.

Discussion:

A reliable cancer diagnosis is a crucial phase until therapy begins. In most malignant diseases, the diagnosis relies primarily on the biopsy, but the diagnosis of malignancy can be established without the need for pathological evidence with the improvements of advanced imaging modalities and precise tumor markers.**[5]**

Numerous methods for interpreting and classifying nodules found throughout a CT scan of low dose for lung cancer screening have been suggested (LCS). The American College of Radiology (ACR) concentrated on this classification system, which they call Lung-RADS, in particular to minimize the high false-positive incidence and in addition to optimize documentation of lung cancer screening when it falls into population-wide usage.**[6]**

The goal of our study was therefore to examine the diagnostic performance of Lung-RADS for predicting malignant pulmonary nodules (PNs).In our study, we found that the age range of our patients was 36-84 years, the mean age was (57.6±11.2), and the median was 63. This means that the high-risk age group to malignant changes in PNs was around 63, and the least age group exposed was 30-40 years. The mean age was higher in malignant cases (60.9 ± 9.7 years) than for benign cases (57.8 ±7.4 years). We also found that gender distribution was 56.7% males (18 cases) and 43.3% females (12 cases).

Among all the cases included in our study, 17 cases (56.7%) were diagnosed pathologically as malignant nodules, including 8 cases (26.7%) adenocarcinoma,4 cases (13.3%) squamous cell carcinoma, two cases (6.7%) metastatic nodules, one case (3.3%)large cell carcinoma, one case (3.3%) small cell, and one case (3.3%) lymphoma. The adenocarcinoma was the commonest lung malignancy and has a strong relationship with the smoking. In addition to 17 malignant nodules, we found 13 benign nodules; hamartoma was the most frequent one(five cases) (16.7%), then TB (3 cases), cryptococcosis (2 cases), aspergillosis (one case), inflammatory pseudo tumor(one case), and Perifissural nodule(one case).

Our results agree with Brandman and colleagues who found that benign nodules result primarily from infection. More than 80 percent of benign PNs are infectious granulomas, with mycobacterial infection being the most significant reason, accompanied by fungal infections, and hamartoma accounting for 10 percent of benign PNs.**[7]**

In our study, we classified the nodules according to the recommended criteria by ACR, which based on size, shape, calcification, solidity, and number of nodules (solitary or multiple).We found that the mean size of nodules was 20.3±5.8 for malignant nodules and 14.7± 4.6 for benign nodules.The solidity of the nodules was distributed as follow: two cases were non-solid, and they are both benign, 12 cases were partially solid 3 of them were malignant and 9 of them were benign, and 16 cases were solid 14 of them were malignant and 2 of them were benign.These results are matched with the study carried out by Armato and colleagues.**[8]**

In our study we found that most of pulmonary nodules presented among studied patients characterized by well-defined margin in 16 patients; 12 patients of them had benign nodule, while 4 patients had malignant nodule. Ill-defined margin in 14 patients; 1 patient of them had benign nodule, while 13 patients had malignant nodule. This was in accordance with Choromaska and Macura, who claimed that benign nodules have smooth, well-marginated margins, whereas malignant ones have ill-defined and distorted edges, although there was still a substantial overlap among these results. **[9]**

We found that nodule size had no significant impact on Lung-RADS (P= 0.13). This finding is like the study of Vanriel and colleagues. Whereas the size of nodule and consistency did not have significant impact (P= 0.13 and 0.23, respectively).**[10]**

We found also that the speculation, and calcification were the most significant features that had impact on Lung-RADS (P= 0.01 and 0.02, respectively).We found that when considering only those lesions classified as Lung-RADS 4X for predicting malignancy, the accuracy, sensitivity,specificity, PPV,and NPVof Lung-RADS classification were 76.7%, 70.6%, 84.6%, 85.7%, and 68.6%,

respectively. These results confirmed the results of the Pinsky and colleagues who reported baseline sensitivity and sensitivity after baseline of 84.9% and 78.6%, respectively. **[11]**

Using Lung-RADS classification system, our study revealed that if combined Lung-RADS 4A,Lung-RADS 4B and Lung-RADS 4X is used as a predictor for malignant PNs, the sensitivity and NPV are significantly increased (94.1% and 91.7%, respectively), whereas the specificity remained stable (84.6%). Thus, we found that the use of Lung-RADS 4A+B+X as a predictor for malignant PNs, significantly increase performance of Lung-RADS.

In our study, we had 10 patients classified as Lung-RADS 1 and 2. Those patients were followed-up after 6 months. Interestingly, no false negatives were detected in those patients. We also found that of the 30 cases assessed, seven (23.3%) were classified as Lung-RADS 1, three (10%) as Lung-RADS 2, two(6.7%) as Lung-RADS 3, two(6.7%) as Lung-RADS 4A,three (10%) as Lung-RADS 4B, and 13 (43.3%) as Lung-RADS4X.Of the10 cases categorized as Lung-RADS 2 and Lung-RADS 3, none was malignant; of the two cases categorized as Lung-RADS3, one (50%) was malignant; the two cases categorized as Lung-RADS 4A were malignant (100%); of the three cases categorized as Lung-RADS 4B, two(66.7%) were malignant;and of the 13 cases categorized as Lung-RADS4X, 12(92.3%) were malignant. These results came to be in the same line of the findings of Mckee and colleagues.**[12]**

Conclusionand recommendations:

The LUNG–RAD classification method is a useful conceptualizing system that aids in the classification, follow-up, and improvement of the prognosis of malignant pulmonary nodules by increasing the positive prognosticvalue while minimizing false negatives. By reducing the number of frequency scans indicated and conducted, ACR Lung-RADS can enhance the financial aspect of CT lung scanning.

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