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PRELIMINARY FINDING OF THE ROLE OF LOW DOSE COMPUTED TOMOGRAPHY OF THE CHEST IN EARLY DETECTION OF LUNG CANCER AND OTHER RESPIRATORY DISEASES AMONG GROUP OF IRAQI MALE SMOKERS

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ABSTRACT

The aim of the Study:-To see the role of the low dose CT scan of the chest in early detection of lung cancer and other lung disease. **Patients and Method**:-This cross sectional study was conducted in Oncology teaching hospital and Baghdad Teaching Hospital- medical city complex from December 2018 to December 2019. Screening by low dose CT scan of the chest was performed using (64 -slice –Siemens CT) on a total of 200 male smokers, their age (50-73) years with at least 25pack years of smoking. **Results:**-Positive CT findings detected in 45 participants (22.5%) of the total study. lung cancer stage 4x detected in one participant. **Conclusion: -** Lung cancer screening with LDCT of the chest is important in early detection of lung cancer and other respiratory disease such as interstitial lung disease and emphysema.

KEYWORDS: Low-Dose Computed Tomography, Screening, Early Detection, Lung Cancer, Baghdad.

INTRODUCTION

Lung cancer is the most frequently diagnosed cancers worldwide and the leading cause of cancer (CA) death in both males and females.[1] In Iraq malignant neoplasm's represented the second leading cause of death (9.05%) of the top 10 leading cause of death in 2016. The lung cancer was the second most common cancer (8.31%) the first was breast cancer (19.55%).[2] Smoking is thought to be directly responsible for at least 90% of lung carcinomas, Exposure to naturally occurring radon and atmospheric pollution (including tobacco smoke) or industrial products (e.g. asbestos, beryllium, cadmium and chromium) are associated with lung cancer.[3] patients are usually diagnosed at an advanced stage which cause the poor prognosis thus Early detection may improve lung cancer survival.[4] National Lung Cancer Screening Trial (NLST) reported a 20% reduction of lung cancer mortality after regular screening low dose computed tomography (LDCT).[5] As most patients with lung cancer are smokers and likely to have chronic obstructive pulmonary disease (COPD),symptoms such as cough (which is the commonest symptom of lung cancer) and worsening breathlessness may be overlooked by the patient and the doctor so healthcare professionals should be alert to the possibility of lung cancer.[6] LDCT has shown high sensitivity and acceptable specificity for the detection of lung cancer in high-risk persons.[7] The American Cancer Society recommends annual lung cancer screening with a LDCT for certain people at higher risk for lung cancer who meet the screening criteria.[8] The American college of radiology (ACR) developed the "Lung-RADS" classification system to standardize follow-up and management decisions in LDCT screening studies. Five potential numerical Lung-RADS categories (0-4) may be assigned when reporting nodules on screening LDCT and their follow up.[9,10] Lung-RADS criteria, been shown to significantly reduce the "false positive" rate.[11] by increasing the threshold for a positive screen to a nodule ≥6 mm reduces the false positive rate while still capturing nearly 100% of lung cancers. This change in criteria is only valid in the context of a screening program in which nodules smaller than this would routinely be followed with an annual scan anyway. For individuals with incidental nodules discovered outside of the screening context, the proper follow up guidelines would be the updated Fleischer criteria.[12]

PATIENT AND METHODS

Study Design

This cross sectional study was conducted in the Oncology teaching hospital and Baghdad Teaching Hospital- medical city complex during the period from December 2018 to December 2019. on a total of 200out of 300 male participants who belong to Iraqi ministry of oil and Iraqi ministry of transport who have a health insurance, their age (50-80) years with history of at least 25 pack year of smoking and Not previously diagnosed with lung cancer or any chronic respiratory illness. Screening by LDCT scan of the chest was performed using (64 –slice –Siemens CT). Nodules or other suspicious findings were classified as positive results. A thoracic radiologist interprets screening scans and produces a structured report on the basis of (Lung-RADS).

Ethical considerations

The ethical approval was taken from hospital authorities.

A written informed consent was taken from all the study participants.

No conflict of interest

SPSS® Software (version 23.0 for Linux®) was used to perform the statistical analysis for this study. Qualitative data are represented as numbers and percentages, while continuous numerical data are represented as mean ± standard deviation. Quantification of smoking intensity was calculated using pack-year, which was calculated as follows

Pack-year = packs/day ×years as a smoker. P-value of less than 0.05 was considered statistically significant. And the result presented as tables and/or graphs. Statistical analysis of the study was done by statistician who is Specialist in Community Medicine

RESULTS

This cross sectional study included a total of (200) male smokers who were aged between (50 -73) years, with a mean age of (56.02 ± 4.36) years and a median age of (56) years.

Figure (3.1) illustrates the age group distribution among study participants.

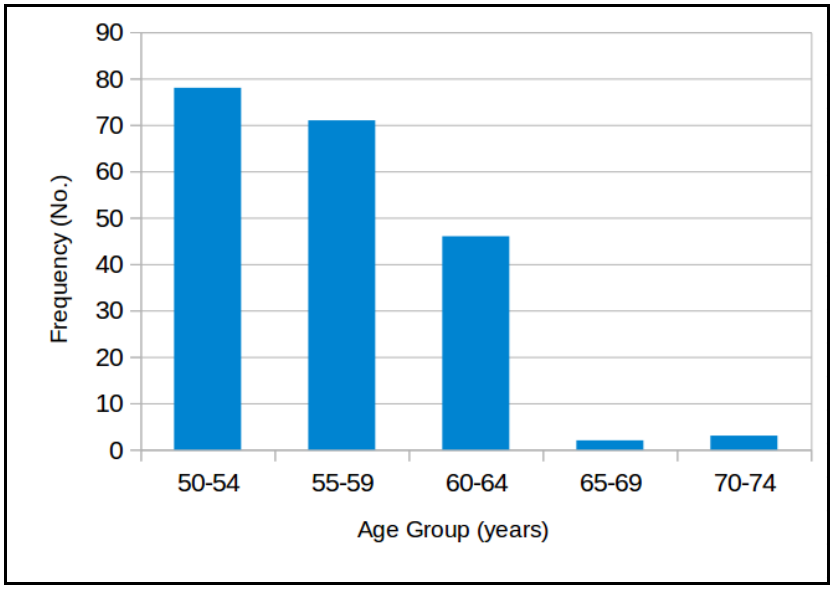

Figure (3.1): Age group Distribution of Study Participants by Study group.

Majority of participants were employees (97.0%), and all of them were smoking tobacco. However, ten individuals (5.0%) were also smoking water pipe. Quantification of smoking intensity was calculated using pack-year. The mean pack-year among study participants was (44.21 ± 21.59), ranging from (25–160) pack-year (Table 3.1).

Table (3.1): Intensity of Smoking among Study Participants.

Smoking Intensity (pack-year)	Frequency	Percentage
25 - 34	86	43.0%
35 - 44	52	26.0%
45 - 54	13	6.5%
55 - 64	20	10.0%
65 - 74	7	3.5%
> 74	22	11.0%

Certain exposures and risk factors, including passive smoking, occupational exposure (to smoke particles coming from Oil refineries, gas pipe lines), incense exposure, and alcohol, were summarized in Table (3.2).

Table (3.2): Exposure to Certain Risk Factors.

Factors	Exposure No. (%)	
	Present	Not present
Passive Smoking	157 (78.5%)	43 (21.5%)
Occupational Exposure	126 (63.0%)	74 (37.0%)
Incense	1 (0.50%)	199 (99.50%)
Alcohol	4 (2.0%)	196 (98.0%)

Various symptoms were reported by study participants, with the highest being cough in (44%) of participants, followed by shortness of breath in (27.0%) of them Table (3.3) provides the details of symptoms reported by the study participants.

Table (3.3): Symptoms Reported by Study Participants.

Symptoms	Frequency	Percentage
Cough	88	44%
Shortness of Breath	54	27%
Snoring	42	21%
Sputum	36	18%
Fatigue	5	2.5%
Chest Pain	3	1.5%
Wheeze	2	1.00%
Loss of Appetite	2	1.00%
Shoulder Pain	1	0.50%
Recurrent Infection	1	0.50%
Choking	1	0.50%
Hoarseness	1	0.50%
Dysphagia	1	0.50%
Weight Loss	1	0.50%
Stridor	1	0.50%
Mouth Breath	1	0.50%

Regarding lung RADS, category 1 (RAD1) was described in (90.0%) of participants, followed by (RAD2) in (6.5%) participants. Category3 (RAD3) was described in (3.0%) of participants, while category 4 (RAD4 X) was described in one participants (Table 3.4).

Table (3.4): Lung RADS among Study Participants.

Lung RADS	Frequency	Percentage
RAD 1 No nodules or definitely benign nodules	180	90.0%
RAD 2 Benign appearance or behavior of nodules	13	6.5%
RAD 3 Likely benign nodules	6	3.0%
RAD 4X Suspicious nodules	1	0.50%

Among those with RAD1 classification; normal CT scan was found in 155 participants (86.11%), while positive findings were found in the remainder 25 participants (Table 3. 5), seven of which had a clinically or potentially significant non-lung cancer finding (RAD1 S).Those patients with RAD1 had emphysematous changes in 11 participants; Hemangioma was found in 4 participants. Other less frequent findings were calcified nodules, calcified lymph nodes, and bronchiectasis changes.

Table (3.5): CT scan Findings among RAD1 Individuals.

CT Findings (RAD1 patients)	Frequency	Percentage
Normal CT Scan	155	86.11%
Positive CT Findings	25	13.89%

Among participants with RAD2 classification, majority had nodules in various lobes of the lungs, with ground glass components in 2 participants. RAD3 patients had nodules in 4 participants, while 2 participants had emphysematous bullae with bilateral ground-glass appearance.RAD4X was found in one participant, who had a soft tissue mass at the right Para esophageal region that measures (18x17) mm, associated with collapse consolidation of medial segment of right lower lobe, and irregular pleural thickening. The participants also had multiple bilateral soft tissue nodules, suggesting metastasis. Enlarged lymph node in the carina was observed, that measures (21x12) mm, with lytic lesion in D11 vertebra that was seen on abdominal CT scan too. On native and contrast CT scan of the chest, the findings were suggestive of bronchogenic carcinoma. Histopathological study confirmed that this participant had squamous cell carcinoma of the lung of stage IV, and he was managed on chemotherapy by the oncologist.

Positive CT findings detected in 45 participants (22.5%) of the total study with higher Proportion among those smokers who exposed to passive smoking compared to those not exposed to it, however, this difference was not significant statistically, with P-value of (0.054) (Table 3.6).

Table (3.6): Positive CT Findings by Passive Smoking Exposure.

Passive Smoking	CT Findings No. (%)		Total	P-value
	Normal CT	Positive Findings		
Yes	117 (74.52%)	40 (25.48%)	157 (100%)	0.054
No	38 (88.37%)	5 (11.63%)	43 (100%)	
Total	155 (77.50%)	45 (22.50%)	200 (100%)	
Chi-square = 3.71 , d.f. = 1 , P-value = 0.054				

Similarly, no significant difference was observed between those with occupational exposure and those without it regarding positive CT findings, with P-value of 0.127 (Table 3.7).

Table (3.7): Positive CT Findings by occupational Exposure.

Occupational Exposure	CT Findings No. (%)		Total	P-value
	Normal CT	Positive Findings		
Yes	102 (80.95%)	24 (19.05%)	126 (100%)	0.127
No	53 (71.62%)	21 (28.38%)	74 (100%)	
Total	155 (77.50%)	45 (22.50%)	200 (100%)	
Chi-square = 2.33 , d.f. = 1 , P-value = 0.127				

Nodules were present in 19 participants of various RAD classifications, forming (9.5%) of total study participants. 12 participants (63.16%) had single nodule while the remaining 7 participants (36.84%) had two or more nodules. Details of nodules characteristics are provided in (Table 3.8).

Table (3.8): Nodules Characteristics among Study Participants.

Nodule Characteristics		Frequency	Percentage
Presence of Nodules	Present	19	9.5%
	Not Present	181	90.5%
Site of Nodules	Both Lungs	4	2.0%
	Left Lung	6	3.0%
	Right Lung	9	4.5%
Lobe of Nodules	Upper	4	2.0%
	Middle	4	2.0%
	Lower	11	5.5%

Type of Nodules	Soft Tissue	2	1.0%
	Calcified (granuloma)	4	2.0%
	Solid	3	1.5%
	Fat & Bone (hamartoma)	1	0.5%
	Ground Glass	1	0.5%
	Sub-solid	1	0.5%
	Solid & Soft tissue	1	0.5%
	Solid & Ground Glass	1	0.5%
	Others	5	2.5%
Number of Nodules	1	12	6.0%
	2	5	2.5%
	3 or more	2	1.0%
Nodule Size	Mean ± SD (mm)	7.85 ± 5.77	
	Range (mm)	4 - 19	

Presence of nodules among participants was compared with smoking intensity represented by pack-year in Table (3.9).There was no statistically significant correlation between pack-year and presence of nodules, P-value = 0.704.

Table (3.9): Presence of Nodules by Smoking Intensity.

Pack-year	Presence of Nodules		Total	P-value
	Present	Not present		
< 30	3 (11.54%)	23 (88.46%)	26 (100%)	0.704
≥ 30	16 (9.20%)	158 (90.80%)	174 (100%)	
Total	19 (9.50%)	181 (90.50%)	200 (100%)	
Chi-square = 0.14, d.f. = 1, P-value = 0.704.				

Other incidental findings were found in 26 participants (57%) of those with positive study and include left adrenal small adenoma which was 2 cm in diameter, as well as suspicion of small polyp in the inner surface of the right vocal cord, renal PUJ obstruction, hiatus hernia, and hepatic aerobilia. Details of the incidental findings are summarized in (Table 3.10).

Table (3.10): Incidental findings among participants.

Incidental Findings	Frequency	Percentage
Emphysematous changes	14	7.0%
Mediastinal lymph node lesion	5	2.5%
Hemangioma	4	2.0%
Bronchiectasis changes	3	1.5%
Vertebral lesion	3	1.5%
Interstitial lung disease	2	1.0%
Adrenal adenoma	1	0.5%
Hepatic aerobilia	1	0.5%
Hiatus hernia	1	0.5%
Renal PUJ obstruction	1	0.5%
Thyroid CA	1	0.5%
Vocal cord polyp	1	0.5%

DISCUSSION

In this study positive finding was detected in 45 participants (22.5%) of the total study which is approximate to the result of other study in china with much higher participant's number, in which the positive result was detected in (22.9%).[13] And higher than other French study in which positive finding was detected only in (5.7%).[14] Passive smoking present in 78.5% of the study group and when we compared between CT findings of those smokers participants who had history of passive smoking exposure and those who are not we found that positive CT scan finding was higher among those smoker who also exposed to passive smoking compared to those who were not exposed to it, however, this difference was not statistically significant, with P-value of (0.054).Consideration of exposure to occupational and environmental lung carcinogens is especially important because they can synergize with smoking history to increase risk in a greater-than-additive fashion.[15] This study also consider occupational exposure to oil refineries and gas pipe

smoke particles , and it was found in 126(63%) of the study participants, However, when we compared Between those with history of exposure and those without it regarding positive CT finding, no significant difference was observed between two, with P value of (0.127) which is statistically not significant, and this is not the expected because occupational exposure to carcinogens is one of the risk factors for lung cancer, And these results disagree with the results of other studies such as the meta-analysis of six studies with a total of (466,066) residents living near petrochemical industry complex in six countries that had a 19% higher risk of lung cancer compared to those who lived farther away.[16] This disagreement because the study design and data collection are different, In that study observation of the residents for at least seven years provided sufficient latency period to estimate the risk and this may explain why in our study we could not find the expected increase in the risk or positive CT scan findings because our study is a prospective study and just an initial finding were reported and also we don't know the number of years that our participant spend with exposure to these carcinogens, and disagree with other study in US which concluded that CT scan screening for lung cancer among high-risk workers leads to a favorable yield of early-stage lung cancers and that there is a correlation between two.[17] All recommendations for lung cancer screening specify that individual should be asymptomatic at the time of screening, but there was some discussion about the definition of asymptomatic for individuals at high risk of developing lung cancer. Joanna Stoms, cancer plan manager at the Pennsylvania Department of Health, noted that a patient with a 30 pack-year history of smoking often presents with some symptoms of COPD which could also mimic signs of lung cancer.[18] In this study 47.5% of the participants were asymptomatic while symptoms were reported by the remaining study participants, with the highest being cough in (44%) of participants, followed by shortness of breath in (27.0%) of them, and other symptoms with less frequency, This finding reflect the importance of symptoms assessment in the screening program s as most of the smokers complain from it, so either over or underestimation of it may cause missing important causes such as COPD or lung cancer. In this study nodules were detected in 19 person of various RAD classifications, forming (9.5%) of total study participants. with size range (4-19 mm). The detected nodules were mainly single in (12 cases 6.0%), in the upper lobe (4cases 2%) and in the middle lobe (4cases 2%) and mainly on the right side (9 cases 4.5%) which similar to the results of other Chinese study.[19] when we compared between the presence of nodules among the participants and the smoking intensity represented by pack-year there was no statistically significant correlation (P-value = 0.704).In this study incidental findings were detected in 26 cases (57%) of those with positive study which is higher than other studies like in Western Australia and Cleveland in which incidental findings were detected in(9.6% , 15 %) respectively that required further investigation.[20,21] Since emphysema is associated with an increased risk of lung cancer, finding evidence of emphysema on Chest CT in asymptomatic person may compel providers to recommend serial (LDCT) lung cancer screening.[22] In this study Emphysematous changes were observed in 14 person, forming (7%) of the total study sample which is lower than other study in which emphysema was identified in 28.5% (20.6%, and 1.6% of current, former, and never smokers, respectively on baseline LDCT[23] and lower than other study in which emphysema was identified in 8.29%.[24] Regarding lung cancer detection in this study, RAD4X was found in one person (0.5%), who had mass at right side, diagnosed as stage 4lung cancer that was beyond surgery, it was not possible to detect his cancer at early stage because he didn't seek medical service before as he was asymptomatic apart from the usual cough and SOB that he attributed it to his smoking and no previous supported screening program for lung cancer in Iraq so that he can participate in it, this reflect the importance of availability of screening program for early detection of lung cancer. He presented with this stage of cancer after only 25 pack year of smoking and this means that even smokers with less than 30 pack years could present with cancer and should be included in the screening programs and this is why in this study we used 25 pack years of smoking as a lower limit. He has also a positive history of exposure to oil refineries smoke and gases so further studies with larger samples and follow up of other workers in the same place especially those with lung nodules in this study is important and this may give us clear ideas about whether there is a relation between these factors and lung cancer at its different stages. In other study RAD 4B or 4X present in 3% of the study and lung cancer has been diagnosed in two of them (0.7%)[25] Which is approximate to the result of this study? Screened people also carry the risk of developing other smoking related diseases, and advice for smoking cessation at any point is beneficial and broadens the impact of any screening program well beyond the endpoints of cancer diagnosis. (26).lung cancer screening with LDCT has a high false-positive rate.[27] In this study the size of nodules was between (4-19mm) so all considered as positive and since this study is a prospective study and this is only the preliminary finding so continuation of the screening study and further imaging of the participants is important to detect false positive and false negative test and this is difficult because the study is not supported financially.

CONCLUSIONS

Lung cancer screening with LDCT of the chest is important in early detection of lung cancer and other respiratory disease such as interstitial lung disease and emphysema.

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