

Diagnostic Accuracy of Contrast Enhanced Computed Tomography in Detecting Bronchogenic Carcinoma-Experience At Liaquat National Hospital

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ABSTRACT

Background: Lung cancer is one of the most common malignancies worldwide. Cigarette smoking is considered as the major risk factor for bronchogenic carcinoma. The four common types namely – squamous cell; small cell; adeno and large cell carcinomas account for more than 90% cases of Bronchogenic carcinoma. Initially it is detected by plain chest radiography but it is considered as an insensitive. Computed Tomography can detect early stage disease 6-10 times more frequently than X-rays.

Objective: To determine diagnostic accuracy of Contrast Enhanced Computed Tomography in detecting Bronchogenic Carcinoma taking histopathology as Gold Standard.

Methods: Total 157 patients presented with pulmonary nodule or suspicious lesion on X-Ray and had history of haemoptysis, weight loss, cough and chest pain for more than two months were included. CT was performed with I/V contrast. Axial images were taken with patients lying supine. Images were analyzed. The same radiologist assessed the patient included in the study. All patients then underwent biopsy and samples were sent for histopathology. Sensitivity, specificity, and accuracy of computed tomography were calculated using histopathology as gold standard.

Results: There were 101 male and 56 female patients. The mean age was 59.77 ± 7.97 years. On CT Scan 89 patients were diagnosed with bronchogenic carcinoma. On histopathology, 90 patients were diagnosed with bronchogenic carcinoma. The sensitivity of CT Scan was 90.0%, specificity was 88.0% and diagnostic accuracy was 89.1%.

Conclusion: CT scan is a sensitive imaging modality in diagnosing malignancy in pulmonary lesions

Key words: Diagnostic Accuracy, bronchogenic carcinoma, CT Scan, Histopathology

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INTRODUCTION

Lung cancer accounts for more deaths per year than breast, prostate, colon and ovarian cancers combined.^{1,2}

In western world, it is a leading cause of cancer related deaths accounting to 32% in males and 25% in females and the age group affected is between 40-70 years. In

developing countries like Pakistan, death rate due to lung cancer is continuously increasing but the true incidence is not known in Pakistan due to lack of available data.^{3,4}

The four common types namely – squamous cell; small cell; adeno and large cell carcinomas account for more than 90% cases of Bronchogenic carcinoma. However, the manifestations are different in all 4 types.⁵ Cigarette smoking is considered as the major risk factor for bronchogenic carcinoma and is implicated in more than 85% of cases.² Other risk factors include exposure to asbestos, radioactivity and some industrial chemicals like uranium, hematite, pitch blende, chromate, and nickel and arsenic.⁴ The prognosis of Bronchogenic carcinoma is definitely

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poor malignancy is the leading cause of cancer-related death in the United States⁶ Majority of the cases are initially detected by plain chest radiograph but it is considered as an insensitive measure to detect early stage disease and especially mediastinal involvement.⁷ Sensitivity of chest x-rays for lung cancer is found to be 78.3%.⁸ Computed Tomography (CT) Scan can detect early stage disease 6-10 times more frequently than plain chest x-rays.⁹ Magnetic Resonance Imaging (MRI) and Positron Emission Tomography (PET) are modalities which are used in situations where CT is equivocal because of their limitations.^{10,11} CT is considered as the modality of choice because of its better spatial resolution and provides precise characterization of size, contour, extent and tissue composition of suspicious lesion.¹² Sensitivity of Contrast Enhanced (CE) CT for lung cancer is 88.9% with specificity of 92.6% thus making it superior to plain films in respect of sensitivity.⁸ It can also indicate the presence or absence of fluid, contour of pleural spaces and whether or not nodules or masses are present on pleural surface.⁷

The current role of diagnostic imaging is to try to determine in the most precise matter whether a discovered Solitary Pulmonary Lesion (SPL) is benign or malignant in order to plan further management. CT scan is a safe, non-invasive and easily accessible modality which can help the clinician in diagnosing as well as staging Bronchogenic Carcinoma. Early detection will definitely improve the mortality rate, 5 year survival of patients and will also reduce the financial burden on health care system. It also reduces the need of biopsy which decreases patient's compliance and increases the morbidity of the disease. Hundreds of international studies were performed on this topic and suggested similar results. However, local data from Pakistan is almost nonexistent on this topic. To our knowledge on one similar study was performed in 2011 in Pakistan including 53 patients which is quite small number as compared to our study. To date this study includes largest number of patients population from Pakistan and performed in a largest tertiary care hospital of biggest city of Pakistan. According to the World Health Organization, in 2004 Pakistan pulmonary tuberculosis had a projected incidence of 181 per 100,000 population per year and a mortality rate of 41 per 100,000 population per year.⁹ The particularly variable presentations of pulmonary tuberculosis and its far greater prevalence in Pakistan can thus present serious pitfalls and errors in radiological evaluation of other diseases such as Carcinoma of lung.^{15,16} This highlights the need for determination of the diagnostic accuracy of CT based diagnosis of malignancy in pulmonary lesions in our local setting.

MATERIAL & METHODS

Total 157 patients of both genders, age 45 to 70 years presented with history of haemoptysis, weight loss, cough and chest pain for more than two months and had pulmonary nodule or suspicious lesion on X-Ray were included in this cross sectional study to determine the diagnostic accuracy of Contrast Enhanced Computed Tomography in detecting Bronchogenic Carcinoma taking histopathology as Gold Standard. Patients with already diagnosed malignancy, and allergic to contrast material were excluded in from the study. The sample subjects were selected through Radiology department, Liaquat National Postgraduate Medical Centre, Karachi, from May 2010 to November 2010. The approval of institutional research & ethical committee and informed consent was taken prior to commencement of the study. The sample size was calculated by using sensitivity and specificity of CT scan for diagnosis of Bronchogenic Carcinoma. The sample was collected through non-probability consecutive sampling technique.

CT diagnosis of nature of lesion, either benign or malignant, was made using the following criteria. Scoring is done as follows:

- Not suspicious for malignancy: homogenous, round, well-defined-margins, <3cm.
- Low suspicion: Non homogenous, round, well-defined margins, <3cm.
- Intermediate suspicion: non homogenous attenuation, well-defined margins, >3 cm.
- Moderately high suspicion: Irregular margins, > 3cm, non homogenous attenuation.
- High suspicion: non homogenous attenuation, lobulated, spiculated margins, >3 cm.

Solitary Pulmonary lesions (SPLs) in category a, b, c were considered benign and category d and e were considered malignant.¹³

CT was performed on Toshiba Asteion Multi Slice Scanner with I/V contrast. Axial images were taken with patients lying supine. The scanning values were 5 mm section thickness; 17.2 sec average scan time, 7mm reconstruction interval, 200 mAs and 120 KVP. Images were analyzed by a senior radiologist on console. The same radiologist assessed the patient included in the study. Patient's bio-data, duration of presenting complains and CT findings were recorded on the proforma. All patients then underwent biopsy and samples were sent for histopathology. The results were recorded on proforma and compared with the CT diagnosis by the principal researcher.

Diagnostic accuracy of CT was measured by calculating sensitivity, specificity, positive predictive value, negative predictive value taking histopathological findings as gold standard. Result was considered true positive when the nodule is malignant on CT and histopathology both. Homogenous attenuation/enhancement favored benignity and attenuation of greater than 20 HU/heterogeneous enhancement favored malignancy. If the nodule was malignant on CT and benign on histopathology then it was false positive. False negative was benign on CT and malignant on histopathology. True negative was considered when nodule was benign on CT & histopathology both.

Data compilation and analysis was done on SPSS version 21. Descriptive statistics were calculated. Quantitative variables i.e. age and duration of symptoms were expressed as Mean±SD and qualitative variables i.e. gender, CT findings (size of lesion, margins of nodules, internal attenuation, cavity, mass, intranodular fat as important indicator of benignity, intranodular calcification), CT diagnosis and histopathology diagnosis were presented in terms of frequency and percentages. Sensitivity, specificity, positive predictive value, negative predictive values, and diagnostic accuracy of CT scan for detecting bronchogenic carcinoma were calculated but taken histopathology as a gold standard. Stratification was done with regards to age and gender to see the effect on outcome.

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. Informed consent was obtained from all patients for being included in the study.

RESULTS

In this study out of total study subjects, 101(80.8%) patients were male and 56(19.1%) patients were female. The mean age was 59.77±7.97 years. Age of 27(17.0%) patients was 45-50 years, 55(35.0%) patients belonged to age 51-60 years, and rests of the 75(47.7%) patients were aged 61-70 years.

On computed tomography examination, it was observed that among all study subjects, 89(56.7%) patients were found with bronchogenic carcinoma and 68(43.3%) patients were diagnosed as benign lesion (Figure 1). On subsequent histopathology 90(57.3%) lesions came out to be bronchogenic carcinoma and 67(42.7%) patients had benign pathology

Figure 1: Percentage of CT scan findings



Figure 2: Percentage of histopathological findings

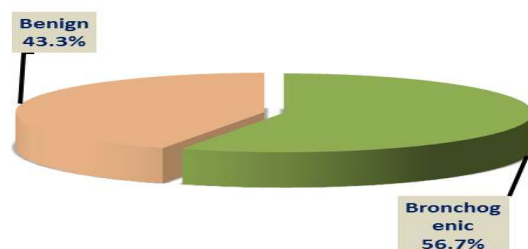


Table-1: Frequency distribution for diagnosis of bronchogenic carcinoma

(n=192)		Frequency	%
CT Scan Findings	Bronchogenic Carcinoma	89	56.7%
	Benign	68	43.3%
Histopathology Findings	Bronchogenic Carcinoma	90	57.3%
	Benign	67	42.7%

On CT examination it was also found that 89(56.7%) patients had poorly defined mass and 68(43.3%) patients had well defined masses. 98(62.4%) patients had heterogeneous internal attenuation while 59(37.5%) patients had homogenous internal attenuation. 61 patients (38.8) had nodule > 3 cm in size while 51 patients (32.4%) had nodule < 3 cm in size. 57 patients (36.3%) had spiculated/lobulated margins and 55 Patients (35.03%) had regular margins of nodule. 32 patients (20.3%) had thick walled cavity and 13 patients (8.2%) had thin walled cavity lesion.

On histopathological findings among 90 malignant lesions, 30(33.3%) were squamous cells carcinoma, 27(30.1%) were adenocarcinoma, 22(24.4%) were small cell carcinoma while 11(12.2%) were large cell carcinoma. In benign lesions, 48(71.6%) were tuberculous lesions, 10(14.9%) lesions with chronic inflammation, 5(7.5%) showed fibrous tissue, 2(3.0%) were hamartoma, 1(1.5%) granular cell tumor, and 1(1.5%) myxoid neoplasm.

In both procedures CT and histopathology, Bronchogenic Carcinoma was diagnosed among 81 patients (true positive, correctly diagnosed) and it was not diagnosed in 59 patients (true negative, correctly diagnosed). The overall sensitivity of computed tomography was found to be 90.0%, specificity was 88.0% and diagnostic accuracy was 89.1%, positive predictive value was 91.0%, negative predictive value was 86.7% and diagnostic accuracy was 89.1% (Table-2).

Table-2: Diagnostic accuracy of CT in diagnosing bronchogenic carcinoma

(n=157)		Histopathological Findings		Total
		Bronchogenic Carcinoma	Benign	
CT Findings	Bronchogenic Carcinoma	81 (90.0%)*	8	89
	Benign	9	59 (88.0%)**	68
Total		90	67	157

*Sensitivity PPV= 91.0%
 **Specificity NPV= 86.7%
 Diagnostic accuracy=89.1%

DISCUSSION

According to the literature, cancer is the second leading cause of deaths and the most common cause of cancer related death is lung cancer.^{14,15} According to one study, lung cancer has been the leading cause of cancer in men for years and since 1988 it has also become number one cause of cancer related deaths in women. The impact of lung cancer related deaths far out stretches breast, prostate and colon cancers combined¹⁷. According to a study, estimated cases of breast cancer are nearly 2.5 fold higher than lung cancer but the estimated death rate for lung cancer is nearly two fold higher.¹⁸

The efficacy of lung cancer screening using chest x-ray is insufficient. Therefore, more effective approach is required to decrease lung cancer deaths. CT provides the most detailed imaging information hence it is generally used as a routine imaging procedure in TNM staging of patients with lung cancer.¹⁷

In Pakistan, CT is the most commonly used non invasive modality for evaluating pulmonary lesions. Therefore, it is important to evaluate and verify the diagnostic accuracy of CT. According to our study, the sensitivity and specificity of CT in diagnosing bronchogenic carcinoma is 90.0% and 88.0% respectively. The diagnostic accuracy is found to be 89.1%. These results

closely matches the study of Toyoda et al in which sensitivity and specificity was found to be 88.9% and 92.6% respectively.⁸ Another study done by Choi et al concluded that sensitivity and specificity of 92.0% and 89.0% respectively.¹⁸

In Pakistan, according to a recent study lung cancer does not rank among first ten cancers in women.¹⁹ In our study, there were 68 males and 22 females having bronchogenic carcinoma. The reason, being high prevalence of smoking in men in our population and not in women. This is in contrast with the western data, where the lung cancer is the leading cause of cancer related deaths in women.²⁰ According to a survey, lung cancer is rarely diagnosed in people younger than 40 years and most cases occur in people over age of 60 years.^{20,21} In our study, bronchogenic carcinoma is more common at the age group of 61-70 years and there were 75 patients of this age group and mean age came out to be 59.7 years.

In our study, lesions were assessed according to a set criterion in which size of nodule, its margins and internal attenuation were given special attention. Other criteria like wall thickness of cavitating lesions, well definition or poor definition of mass, intranodular calcification and fat were also considered. These features are discussed separately in detail.

The size criteria to reliably distinguish benign from malignant lesions has been researched a lot. In general, small nodules are more likely to be benign and larger lesions particularly those exceeding 3 cm (masses) are more likely to be malignant.²³ 80% of benign nodules are less than 2cm in diameter. However, small size alone does not exclude lung cancer because 15% of malignant nodules are less than 1cm in diameter and 42% are less than 2cm in diameter.²⁴ In our study, there were 57 nodules more than 3 cm in size and 51 were malignant and 6 were benign while 55 nodules less 3 cm and only 6 were malignant and rest were benign.

Nodule margins and contours can be classified as smooth, lobulated or spiculated. Although most nodules with smooth and well defined margins are benign, these features are not always diagnostic for a benign cause and 21% of malignant nodules have well defined margins.²⁵ Nodule with an irregular or spiculated margin with distortion of adjacent vessels (often described as having sunburst or corona radiata appearance) is likely to be malignant.²⁶ Corona radiata sign is very fine linear strand extending 4-5 mm outwards from a nodule. In our study, 57 nodules had

spiculated or lobulated margins and among which 51 were malignant and rest were benign. 55 nodules had smooth / regular margins and in them 49 were benign and 6 were malignant.

Homogenous attenuation is seen at thin section CT in both benign (55%) and malignant (20%) nodule.²⁴ In our study, there are 98 lesions with heterogeneous internal attenuation among which 90 were malignant and 8 were benign. 59 lesions had homogenous internal attenuation and all were benign. American College of Radiology Imaging Network assessed the nodule as being soft tissue, ground glass, mixed ground glass and soft tissue, fluid water, fat or calcified.

Although cavitation can occur in malignant pulmonary nodules, particularly squamous cell carcinoma, inflammatory lesions such as abscess, infectious granulomatous lesions, Wegener's granulomatosis, and pulmonary infarcts can also cavitate. Most nodules with wall thickness >16mm are malignant and those with wall thickness <4mm are benign.⁶⁴ Unfortunately, there is significant overlap and wall thickness alone cannot be used alone to confidently differentiate malignant from benign cavitary nodules. In current study, there were forty five cavitary nodules. Thirty two had wall thickness >16 mm among which 30 were malignant and 2 were benign. Thirteen had <4mm wall thickness among which 10 were benign and 3 were malignant.

Presence and patterns of calcification in a solitary pulmonary nodule can also help differentiate benign from malignant nodules. There are four benign patterns of calcification. "Central, diffuse solid, laminated and pop-corn". The first three patterns are typically seen with prior infections particularly tuberculosis or histoplasmosis. Pop-corn calcification is characteristic of chondroid calcification in hamartoma. When present, these patterns are reliable indicator of benign cause. Unfortunately, 38-63% of benign nodules are not calcified and reported prevalence of calcification in hamartoma at CT varies from 5-50%.²⁴ Calcification in lung cancer is rarely observed at chest x-ray but seen in CT in upto 6% of cases and is typically diffused and amorphous. Punctate calcification can also occur in lung cancer due to engulfment of pre-existing calcified granulomatous lesion and metastasis. Fat is seen at CT in upto 50% of hamartoma and is best visualized at thin section CT.²⁴ Growth rate of a nodule can be estimated if previous images are available to allow accurate measurement of changes in its size. The volume doubling time for malignant lung tumors is

rarely less than a month or more than two years.^{26,27} But in our study, this criteria is not considered as our study time was limited.

CONCLUSION

CT scan is a quick, easy, noninvasive, sensitive yet not very specific imaging modality in diagnosing malignancy in pulmonary lesions. It is a good localizing tool however for definitive diagnosis, biopsy is required.

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