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# CT Scan Characteristics in Patients Referred with Pleural Effusion: Discriminating between Tuberculosis and Malignancy in a Middle East Country

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## Abstract

**Background:** The current study decided to assess CT scan findings in patients with any kind of pleural effusion to obtain any diagnostic value of this modality of imaging to discriminate malignant conditions from benign ones, especially pleural or pulmonary tuberculosis.

**Methods:** Through a cross-sectional design, patients with pleural effusion enrolled in this study when their diagnosis was known as malignancy or tuberculosis. The findings of chest CT-scan were compared between the two conditions and the frequency and statistically different variables were reported as discriminating factors between malignancy and tuberculosis.

**Results:** Among our findings, male sex was prone to tuberculosis, but pleural thickening >10 *mm*, lung collapse and lung mass in CT-scan, were the most prevalent findings in malignancy and absent in tuberculosis cases. No significant differences were observed in the free or loculated effusion, air-fluid level and gas, Hounsfield score and loculation involvement between groups.

**Conclusion:** CT scan, despite its unconfirmed diagnostic values, could be considered as a very useful part of diagnosing malignancies against benign or infective causes of pleural effusion, especially in terms of pleural thickening more than 10 *mm*, lung collapse and lung mass disregarding transudative or exudative as well as uni- or bilateral, free or loculated, mild or severe, or other kinds. CT scan scoring system may be the next topic to work on by authors.

**Keywords:** CT-scan, Diagnosis, Discrimination, Malignancy, Pleural effusion, Tuberculosis

## Introduction

Pleural effusion is a common problem involving not only pulmonologists but also general physicians over the world which is caused by a long list of medical conditions simply from heart diseases to metastatic cancers (1,2). Chest CT scan is now an integral part of the process to assess undiagnosed pleural effusion (3). In 2020, a research team showed that CT scan and fluid cytology had separately equal values of sensitivity, specificity and accuracy but their combination could improve both sensitivity and accuracy even up to 20%. They reported more than 90% specificity for each alone in non-small-cell lung cancer or pulmonary metastases (4,5). In addition, CT scan scoring system has been raised for years as a reliable way to confirm malignant pleural effusion diagnosis through some works such as Burnazovic-Ristic's (6). On the contrary, some do not rely on CT scan due to suboptimal sensitivity and other diagnostic characteristics like negative predictive value in thoracic malignancy (7).

The purpose of current study was to assess CT scan findings in patients with any kind of pleural effusion to obtain any diagnostic value of this modality of imaging to discriminate malignant conditions from benign ones, especially pleural or pulmonary tuberculosis.

## Materials and Methods

Through a cross-sectional design, the current study tried to find out the diagnostic value of CT scan for pleural effusion focused on malignancy besides disclosing the frequency and some other characteristics by participating records of referrals in an 8-year period of time between 2009 and 2017 which had been studied with CT scan.

Individuals who had pleural effusion with CT scan report disregarding the type of effusion or age and gender and had been admitted, enrolled in the study *via* their hospitalization records. Charts with imperfect data and information were excluded. All the comorbidities as well as any condition the participants had, were accepted to enroll in the study. Basic demographics, type of effusion, past medical history, familial history, individual manners, laboratory acid fast test and sputum culture as well as pathologic assessment were checked for all the participants to confirm their diagnosis including malignancy and Tuberculosis (TB). Progress notes, follow-up outcome, examinations and even medications were mined in order to disclose any disease or condition to be the main cause of pleural effusion. Transudative and exudative pleural effusion were defined regarding the "Light's criteria".

Using a recording system named "HIS (Hospital Information System)", we found patients with pleural effusion referring to our tertiary hospital and prominent referral center for respiratory diseases. Then, all the relevant charts were gathered and studied for all the previously named information. Patients who had clear diagnosis in their charts attended the study directly and the charts which had no clear diagnosis were checked for progress notes and later tests results to disclose their confirmed disease among which biopsy results were the golden clue for malignancy while three cultures of sputum were the standard test for TB. Then other causes of pleural effusion excess TB and malignancy were excluded.

Due to the wide range of malignancies including rare and common ones, we preferred to gather all the of the fields under the general label of "malignancy". TB exclusive participants were clear. Malignant cases were confirmed through biopsy and pathology. CT scan had been done for all the participants and we compared CT findings among them.

### *Statistics*

Data entered SPSS 18 (IBM Corp., Armonk, New York, USA) for windows after being completely gathered and confirmed before being analyzed by quantitative and qualitative tests comprising Chi-square and independent t-test. Confidence interval of 95% and type one error ($\alpha$=0.05) beside significance of 0.05 were defined to get 0.8 study power. At first, frequency of each diagnosis was obtained regarding every positive test including cytology, BAL, biopsy and clinical opinions.

### *Ethics*

The current study was approved by the ethics committee of our center under the unique code "SBMU1.REC. 1394.88". Patients' charts were the source of information. Hence, nobody suffered extra charge or ineffectual tests and even no new visits.

All the information was safely kept by the principal investigators. The patients had been perfectly informed regarding their diseases and probable outcome.

## Results

Participants were 130 totally, including 69 (53.1%) males and 61 (46.9%) females with the mean±SD age of 58.63±18.34 years. The youngest was 15 years old and the oldest 94. The type of effusion was exudative in 124 (95.4%) of the cases, but transudative effusion was observed in 6 (4.6%). Tuberculosis was diagnosed in 22 (16.9%) cases and malignancy was indicated in 108 (83.1%).

### *Tuberculosis CT-scan findings*

Tuberculosis cases aged 19-85 years with the mean±SD of 52.55±22.02 years containing 16 (72.7%) males and 6 (27.3%) females from which only one had transudative and the rest reported exudative pleural effusion. TB showed bilateral effusion in only 5 cases but unilateral effusion was more frequent. Moderate effusion was the most frequent severity as can be seen in table 1. Interestingly, 20 (90.9%) of the TB cases presented free fluid while one case demonstrated loculated and one multiloculated effusion. The Hounsfield score was 25.82±18.40 in average which ranged 7-91. Air-fluid level and effusion gas were observed in 1 (4.5%) and 5 (22.7%) of the TB patients, respectively; and pleural thickening occurred in 100% of the TB cases which all were <10 *mm*. The nodularity of pleura rated 9.1% showed by 2 patients and the majority indicated smooth pleura in CT-scan (72.7%). Circumferential and mediastinal pleural involvement occurred equally in 5 (22.7%) while extent fissures were seen in 2 (9.1%) of the TB patients. There was no pleural mass or mass-like lesion or consolidation in TB. Four TB cases reported parenchymal consolidation but collapse consolidation was indicated in 7 (31.8%) and collapsed lung in 6 (27.3%). The majority of parenchymal pattern was nodular although only occurred in 4 (18.2%) cases of TB. Like fibrodestructive lesions, no cavitary lesions were seen in TB through CT-scan study. Ground-glass opacity was observed only in 2 (9.1%) cases of tuberculosis. Bronchiectasis was found in 2 (9.1%) of the TB cases.

### *Malignancy CT-scan findings*

Participants with malignancy were 108 with the mean age±SD of 59.87±17.35 ranged 15-94 including 53(49.1%) males and 55 (50.9%) females having exudative effusion in 103 (95.4%). The distribution of effusion was similar in malignancy cases but right-sided effusion was a bit more frequent (40.7%). Severe pleural effusion occurred in 47 (43.52%) followed by moderate and mild. Majority of the malignant cases had free-fluid effusion (78.7%) but loculation was observed in 19 (17.6%) of them. The Hounsfield score was similar to TB with the mean±SD of 27.22±15.60 ranged 2-80. Air-fluid level and pleural gas were more frequent in malignancy as seen in table1. Like TB, malignant cases indicated more pleural thickening<10 *mm* (77.1%) but 27 (22.9%) presented >10 *mm* thickening which was not seen in TB. The rate of pleural nodularity was 16.7% in malignancy. However, 76 (70.4%) of the malignant cases showed smooth pleura. Mediastinal involvement occurred in 23 (21.3%) while fissures were affected in 10 (9.3%) of the malignant cases and circumferential involvement was showed by 14 (13%). Pleura presented 5 (4.6%) cases with mass-like lesions. Parenchyma indicated 10 (9.3%) consolidation, 11 (10.2%) collapsed lung, 46 (42.6%) collapsed consolidation, 23 (21.3%) mass, and 8 (7.4%) mass-like consolidation. Malignancy also demonstrated 11 (10.2%) ground-glass opacity. With a long distance, nodular parenchyma was the most frequent pattern in malignancy (17.6%) compared with reticular and reticulonodular ones. Like bronchiectasis and fibrodestructive, cavitary lesions were rare in malignancy (Table 1).

### *Comparison of CT-scan findings*

The participants in TB and malignancy groups differed in terms of sex (p-value=0.035) but their age was similar statistically. Type, distribution and severity of pleural effusion were statistically the same. There was difference between the two situations regarding neither free or loculated effusion, nor air-fluid level and gas in addition to the Hounsfield score. Interestingly, pleural thickening was statistically different (p-value=0.006) between TB and malignancy. Similarly, other CT-scan findings but lung collapse (p-value=0.041) and lung mass (p -value=0.009) failed to discriminate malignancy from

**Table 1.** Characteristics of the participants and CT findings in both groups

| Characteristics | | Tuberculosis | Malignancy | Sig |
|---|---|---|---|---|
| Mean Age (Mean±SD) | | 52.55±22 | 59.87±17.35 | 0.055 |
| Sex | Male (%) | 16 (72.7) | 53 (49.1) | 0.035 |
| | Female (%) | 6 (27.3) | 55 (50.9) | |
| Pleural Effusion | Transudate (%) | 1 (4.5) | 5 (4.6) | 0.732 |
| | Exudate (%) | 21 (95.5) | 103 (95.4) | |
| Distribution | Right-sided (%) | 9 (40.9) | 44 (40.7) | 0.584 |
| | Left-sided (%) | 8 (36.4) | 32 (29.6) | 0.349 |
| | Bilateral (%) | 5 (22.7) | 32 (29.6) | 0.355 |
| Severity | Mild (%) | 4 (18.2) | 27 (24.98) | |
| | Moderate (%) | 12 (54.5) | 34 (31.5) | 0.068 |
| | Severe (%) | 6 (27.3) | 47 (43.52) | |
| Loculation | Free (%) | 20 (90.9) | 85 (78.7) | 0.151 |
| | Loculated (%) | 1 (4.5) | 9 (8.3) | 0.468 |
| | Multiloculated (%) | 1 (4.5) | 10 (9.3) | 0.412 |
| Pleural Involvement | Thickening <10*mm* (%) | 22 (100) | 81 (77.1) | 0.006 |
| | Thickening >10*mm* (%) | 0 (0) | 27 (22.9) | |
| | Nodularity (%) | 2 (9.1) | 18 (16.7) | 0.296 |
| | Smooth pleura (%) | 16 (72.7) | 76 (70.4) | 0.524 |
| | Circumferential (%) | 5 (22.7) | 14 (13) | 0.193 |
| | Extent fissure (%) | 2 (9.1) | 10 (9.3) | 0.670 |
| | Mediastinal (%) | 5 (22.7) | 23 (21.3) | 0.539 |
| Parenchymal Involvement | Consolidation (%) | 4 (18.2) | 10 (9.3) | 0.191 |
| | GGO (%) | 2 (9.1) | 11 (10.2) | 0.618 |
| | Collapse consolidation (%) | 7 (31.8) | 46 (42.6) | 0.244 |
| | Nodularity (%) | 4 (18.2) | 19 (17.6) | 0.578 |
| | Bronchiectasis (%) | 2 (9.1) | 1 (0.9) | 0.074 |
| | Mass (%) | 0 (0) | 23 (21.3) | 0.009 |

tuberculosis. Thus, three major discriminating factors to distinguish malignancy from TB were finally pleural thickening, especially more than 10 *cm*, lung mass and collapse which all had tendency to diagnose malignancy (Table 1).

## Discussion

The current study attempted to find noninvasive way to discriminate TB and malignancy among patients who referred with pleural effusion. Through this way, we used CT-scan findings after comprehensive evaluation for cytology in our previous research which found weak results. We succeeded to name major factors to discriminate the two medical conditions in some cases including pleural thickening, lung mass and lung collapse. However, more debates and conclusions would need much more works on the topic. Porcel *et al* described a CT scan-based scoring system to differ malignant cases of pleural effusion from benign ones in 2015 studying 228 participants to finally obtain 88% sensitivity and 94% specificity in this regard (3). On the contrary, Yang *et al* in 2018 concluded that imaging data including X-ray, CT scan and even PET scan are only supportive and it is needed to rely only pathology and Immunohistochemistry (IHC) to confirm any diagnosis in this field 8.

This study showed similar pleural effusion distribution for both named medical conditions, but moderate effusion was more diagnostic for TB whilst severe effusion was for malignancy but only the latter was significantly confirmed. Meanwhile, malignancy although not significant, correlated with loculated effusion meaning that malignant individuals reported higher rate of this sign being on the way with some authors who believe that loculated effusion may raise pleural infarction and adhesion due to malignancy or metastases (9,10). Bakhshayesh Karam *et al* in 2016 reported just lower than 60% loculated pleural effusion in 17 primary Malignant Pulmonary Mesothelioma (MPM) cases while more than 70% of 39 metastatic cases presented free effusion (11). However, free or loculated effusions did not correlate with tuberculosis in the current work. Air-fluid level, pleural gas and pleural enhancement were the findings which selected completely separate ways from TB and malignancy and showed no value to discriminate them. Bronchiectasis and Ground-Glass Opacity (GGO) did likely too. However, Yogi *et al* found ground-glass attenuation in 36% of their acute T-cell lymphoma/leukemia cases in 2019 which may have no significant diagnostic value (12).

In special conditions like malignancy and tuberculosis that are expected to determine any sign of cellular overgrowth, pleural thickness, masses and nodularity are at the focal point in addition to lung parenchymal invasion and fissure extensions. Hence, despite pleural thickening less than 10 *mm* which was significantly diagnostic particularly in TB, it was pronouncedly diagnostic in both TB and malignancy when higher than 10 *mm* with a tendency to malignancy diagnosis successfully. Bakhshayesh Karam *et al* reported 88% pleural thickening in MPM in 2016 (11). Contrarily, nodularity was not able to separate tuberculosis from malignancy while malignancy non-significantly doubled TB in this regard. Extension to mediastinal pleura could not distinguish TB and malignancy due to existence in both. Circumferential involvement of the pleura was another finding looking for in the current study but no value was found in this regard to separate malignancy from TB, although Fortin *et al* in 2020 reported significant ability of the named sign for diagnosing malignant pleural mesothelioma from benign cases (13).

As expected, parenchymal consolidation and mass were more seen in malignancy which significantly could discriminate it from TB. Unlikely, pleural mass-like consolidation could not raise TB, unexpectedly. Yao *et al* showed in 2018 that CT scan, in spite of untypical findings, could help diagnosing Primary Pulmonary Llymphoma (PPL) through fuzzy shadow at the edge of lung mass with air bronchogram; long lasting lung mass shadow; and pneumonia-like changing without clear infection manifestation (14). Finally, CT-scan fibrodestructive changes could not help discriminate between TB and malignancy.

Having a glance at the Leung's criteria in 1990 may disclose the value of CT scan in differentiating benign and malignant pleural conditions (15). Leung *et al* explained four characteristics in CT scan which helped them discriminate 28 of 39 malignant cases from benign patients with 72% sensitivity and 83% specificity using only CT scan as follows:

Circumferential pleural thickening

Nodular pleural thickening

Parietal pleural thickening greater than 1 *cm* Mediastinal pleural involvement

## Conclusion

To sum up, CT scan, despite its unconfirmed diagnostic values, could be considered as a very useful part of diagnosing malignancies against benign or infective causes of pleural effusion, especially in terms of pleural thickening more than 10 *mm*, lung collapse and lung mass disregarding transudative or exudative as well as uni- or bilateral, free or loculated, mild or severe, or other kinds. CT scan scoring system may be the next topic to work on by authors.

## Conflict of Interest

The authors declare no competing interests.

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