



Role of CT and modified Response Evaluation Criteria in Solid Tumors (RECIST criteria) in response evaluation of malignant pleural mesothelioma

Thesis

*Submitted for partial fulfillment of Master degree in
Diagnostic Radiology*

Presented by

Basma Abdelbaset Mohamed Mohamed
M.B, B.Ch.

Supervised by

Prof. Dr. Khalid Esmat Allam
*Professor in Diagnostic Radiology
Faculty of Medicine, Ain Shams University*

Dr. Hend Galal El-Deen Mohamed
*Lecturer of Diagnostic Radiology
Faculty of Medicine, Ain Shams University*

Faculty of Medicine
Ain Shames University

2020

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قَالَ

سُبْحَانَكَ لَا عِلْمَ لَنَا
إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ
الْعَلِيمُ الْعَظِيمُ

صدق الله العظيم

سورة البقرة الآية: ٣٢

Acknowledgment

*First and foremost, I feel always indebted to **ALLAH**,
the Most Kind and Most Merciful.*

*I'd like to express my respectful thanks and
profound gratitude to **Prof. Dr. Khalid Esmat
Allam**, Professor in Diagnostic Radiology, Faculty of
Medicine, Ain Shams University for his keen guidance,
kind supervision, valuable advice and continuous
encouragement, which made possible the completion of
this work.*

*I am also delighted to express my deepest
gratitude and thanks to **Dr. Hend Galal El-Deen
Mohamed**, Lecturer of Diagnostic Radiology, Faculty
of Medicine, Ain Shams University, for her kind care,
continuous supervision, valuable instructions, constant
help and great assistance throughout this work.*

*I would like to express my hearty thanks to all my
family for their support till this work was completed.*

*Last but not least my sincere thanks and
appreciation to all patients participated in this study.*

Basma Abdelbaset

List of Contents

Title	Page No.
List of Tables	i
List of Figures	ii
List of Abbreviations.....	iv
Introduction.....	1
Aim of the Work.....	4
Review of Literature	
☞ Anatomy of the Pleura	5
☞ Malignant Pleural Mesothelioma	17
☞ Role of imaging in diagnosis, Staging and Evaluation of Malignant Pleural Mesothelioma	29
☞ Follow up by CT and Modified RECIST Criteria.....	43
Patients and Methods.....	48
Results	52
Case Presentations	59
Discussion.....	79
Summary, Conclusion and Recommendations	85
References	87
Arabic Summary	١

List of Tables

Table No.	Title	Page No.
Table (1):	Morphological Subtypes of Malignant Pleural Mesothelioma.....	23
Table (2):	The American Joint Committee on Cancer (AJCC) and the Union Internationale Contre le Cancer (UICC) Staging System	26
Table (3):	TNM Staging.....	28
Table (4):	CECT technique in El Demerdash Hospital.....	50
Table (5):	The age groups of the studied patients:	52
Table (6):	Geographic distribution among the studied patients:	53
Table (7):	Laterality among the studied patients:	54
Table (8):	Improvement of tumor size among the studied patients	54
Table (9):	Relation between findings by CT and clinical examination:.....	55
Table (10):		55
Table (11):	Relation between findings by CT and clinical examination.....	56
Table (12):	Diagnostic accuracy of CT as a predictor for outcome of the studied patients according to clinical examination	56
Table (13):	Comparison between tumor size at 2 nd follow up and Nadir by CT.....	57
Table (14):	Comparison between tumor size at 2 nd follow up and baseline by CT	57
Table (15):	Comparison between tumor size at baseline and at 2 nd follow up by CT.....	58
Table (16):	Diagnostic accuracy of CT as a predictor for responders of the studied patients according to clinical examination.....	58

List of Figures

Fig. No.	Title	Page No.
Figure (1):	The parietal and viscera pleura, and the pleural cavity	5
Figure (2):	Anatomy of the pleura cavity.....	6
Figure (3):	The parts of parietal pleura	6
Figure (4):	Pleural recess	10
Figure (5):	Nerves supplying the pleural layers	13
Figure (6):	The five pleural layers can be seen in this EVG-stained image	14
Figure (7):	Epidemic of mesothelioma in Egypt	19
Figure (8):	Photograph of the gross pathologic specimen (cut sagittally)	22
Figure (9):	Malignant pleural mesothelioma. Standard posteroanterior chest X-ray.....	31
Figure (10):	Malignant pleural mesothelioma. Axial contrast-enhanced CT images in arterial.....	34
Figure (11):	Malignant pleural mesothelioma. Axial contrastenhanced CT image	35
Figure (12):	Malignant pleural mesothelioma. Axial T1-weighted MR images showing a iso/hypointense	38
Figure (13):	Malignant pleural mesothelioma. Axial fused wellcollimated PET/CT image	41
Figure (14):	Malignant pleural mesothelioma. Axial US scan.....	42
Figure (15):	Axial CT image demonstrating 2 measurements taken at the same level	45
Figure (16):	Gender distribution among the studied patients	53
Figure (17):	Improvement of tumor size among the studied patients	54
Figure (18):	Case (1): Contrast enhanced axial CT scan of the chest.....	59
Figure (19):	Contrast enhanced axial CT scan of the chest.....	60
Figure (20):	Contrast enhanced axial CT scan of the chest.....	61

List of Figures (Cont...)

Fig. No.	Title	Page No.
Figure (21): Case (2):	Contrast enhanced axial CT scan of the chest.....	63
Figure (22):	Contrast enhanced axial CT scan of the chest.....	64
Figure (23):	Contrast enhanced axial CT scan of the chest.....	65
Figure (24): Case (3):	Contrast enhanced axial CT scan of the chest.....	67
Figure (25):	Contrast enhanced axial CT scan of the chest.....	68
Figure (26):	Contrast enhanced axial CT scan of the chest.....	69
Figure (27): Case (4):	Contrast enhanced axial CT scan of the chest.....	71
Figure (28):	Contrast enhanced axial CT scan of the chest.....	72
Figure (29):	Contrast enhanced axial CT scan of the chest.....	73
Figure (30): Case (5):	Contrast enhanced axial CT scan of the chest.....	75
Figure (31):	Contrast enhanced axial CT scan of the chest.....	76
Figure (32):	Contrast enhanced axial CT scan of the chest.....	77

List of Abbreviations

Abb.	Full term
<i>ADC</i>	<i>Apparent diffusion coefficient</i>
<i>AJCC</i>	<i>American Joint Committee on Cancer</i>
<i>CECT</i>	<i>Contrast-enhanced computed tomography</i>
<i>CR</i>	<i>Complete response</i>
<i>CT</i>	<i>Computed tomography</i>
<i>DMM</i>	<i>Diffuse malignant mesothelioma</i>
<i>FOV</i>	<i>Field of view</i>
<i>IMIG</i>	<i>International Mesothelioma Interest Group</i>
<i>IV</i>	<i>Intravenous</i>
<i>IVC</i>	<i>Inferior vena cava</i>
<i>Kv</i>	<i>Kilovolt</i>
<i>LMMs</i>	<i>Localized malignant mesotheliomas</i>
<i>M</i>	<i>Distant metastases</i>
<i>mA</i>	<i>milliampere</i>
<i>MDCT</i>	<i>Multidetector computed tomography</i>
<i>MM</i>	<i>Malignant mesothelioma</i>
<i>MPM</i>	<i>Malignant pleural mesothelioma</i>
<i>mRECIST</i>	<i>Modified Response Evaluation Criteria in Solid Tumors</i>
<i>MRI</i>	<i>Magnetic resonance imaging</i>
<i>N</i>	<i>Regional lymph nodes</i>
<i>PA</i>	<i>Posteroanterior</i>
<i>PD</i>	<i>Progressive disease</i>

List of Abbreviations (cont...)

Abb.	Full term
<i>PET</i>	<i>Positron emission tomography</i>
<i>PR</i>	<i>Partial response</i>
<i>RECIST</i>	<i>Response Evaluation Criteria in Solid Tumors</i>
<i>SD</i>	<i>Stable disease</i>
<i>SUV</i>	<i>Standardized uptake value</i>
<i>SV40</i>	<i>Simian vacuolating virus 40</i>
<i>T</i>	<i>Primary tumor</i>
<i>UICC</i>	<i>Union Internationale Contre le Cancer</i>
<i>US</i>	<i>Ultrasonography</i>
<i>WDPMs</i>	<i>Well differentiated papillary mesotheliomas</i>
<i>WHO</i>	<i>World Health Organization</i>

INTRODUCTION

Malignant pleural mesothelioma is an infrequent neoplasm. However, MPM is the most common primary malignancy of the pleura (*Dogan et al., 2012*).

It is locally aggressive neoplasm that originate in the serosal membrane that line the thoracic cavity with invasion of the chest wall, mediastinum and diaphragm (*Truong et al., 2013*).

The disease has become an important health issue over recent years since the incidence of malignant pleural mesothelioma has risen for some decades and is expected to peak between 2010 and 2020 due to the patterns of occupational exposure (*Moore et al., 2008*).

There is strong association between malignant mesothelioma and asbestos exposure is observed however, reports suggest that radiotherapy may also cause mesothelioma and genetic factors may also play a role in malignant pleural mesothelioma (*Testa et al., 2013*).

So those employed in manufacture and industrial use of asbestos and those remotely connected with asbestos or living near asbestos plants are at risk of developing mesothelioma.

The prognosis is poor, with a median survival time of 12 months after diagnosis. Several factors have been shown to correlate with reduced survival time which are intrathoracic lymph node metastases, distant metastatic disease, and extensive pleural involvement (*Nickell et al., 2014*).

Malignant pleural mesothelioma is not a simple disease to diagnose and most frequently achieved with careful review of clinical and radiological finding in addition to confirming tissue biopsy (*Husain et al., 2009*).

Radiological imaging plays an important role in diagnosis, staging, treatment planning, response assessment, and follow up of Malignant pleural mesothelioma patients. Several modalities are available including computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET), and PET/CT. CT scan is the primary imaging technique that used because of its ability to provide anatomic details of both normal and abnormal structures, its wide availability, and relatively low cost (*Armato III et al., 2008*).

Key CT findings that suggest malignant pleural mesothelioma include unilateral pleural effusion, nodular pleural thickening and interlobar fissure thickening. Growth typically leads to tumoral encasement of the lung with a rind like appearance (*Nickell et al., 2014*).

Most patients with malignant pleural mesothelioma are candidates for chemotherapy during the course of their disease. Assessment of the response with conventional criteria depend on computed tomography (CT) measurements is challenging, due to the circumferential and axial pattern of growth of MPM. Such difficulties discourage an accurate evaluation of clinical study results and make the clinical management of patients

critical. Several radiological response systems have been proposed, but neither WHO criteria nor the recent RECIST unidimensional criteria nor hybrid uni- and bidimensional criteria seem to apply to tumor measurement in this disease. Recently, modified RECIST criteria for malignant pleural mesothelioma have been published (**Robinson & Lake 2005**).

The current clinical method for tumor response assessment in mesothelioma is the modified Response Evaluation Criteria in Solid Tumors (RECIST) guidelines, which calls for two linear measurements of tumor thickness to be summed from each of three axial sections, primarily in computed tomography (CT) scans. To classify patients into response categories, progressive disease (PD) is a summed measurement increase between scans larger than 20%, partial response (PR) is a summed measurement decrease of 30% or more, and stable disease (SD) is any measurement change between -30% and $+20\%$ (**Labby et al., 2012**).

AIM OF THE WORK

To assess the value of CT and modified RECIST criteria in follow up evaluation patients of malignant pleural mesothelioma during treatment with chemotherapy.

ANATOMY OF THE PLEURA

1) Gross anatomy

Pleura is a serous membrane which folds back on itself to form a two-layered membranous pleural sac. It consisting of two layers: The outer layer is called parietal pleura and attaches to the chest wall, The inner layer is called visceral pleura and covers the lungs, blood vessels, nerves, and bronchi (*Adeyinka and Pierre, 2018*). Between them There's a potential thin space known as the pleural cavity that contains a small amount of pleural fluid (*Charalampidis et al., 2015*) (Fig.1)

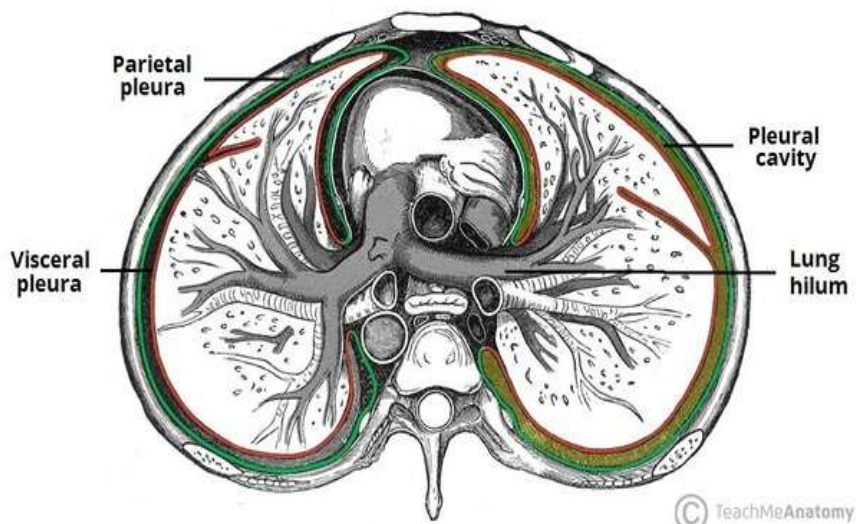


Figure (1): The parietal and viscera pleura, and the pleural cavity
(*TeachMeAnatomy, 2020*)

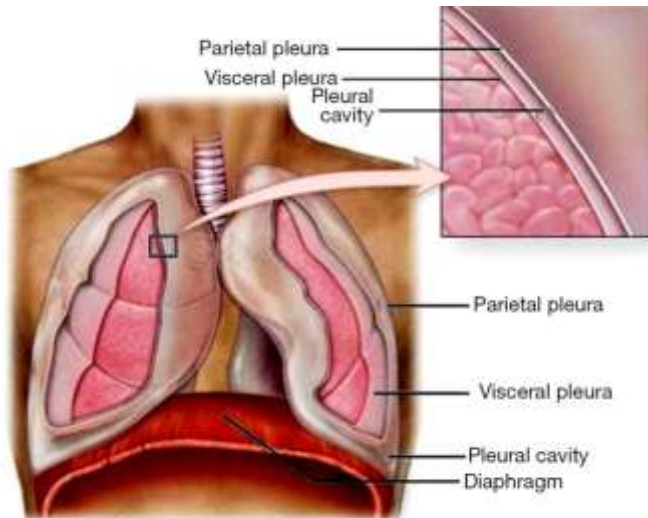


Figure (2): Anatomy of the pleura cavity (*Charalampidis et al., 2015*)

Parietal Pleura

Different portions of the parietal pleura have received special names which indicate their position thus (*Gray, 2012*) (Fig. 3)

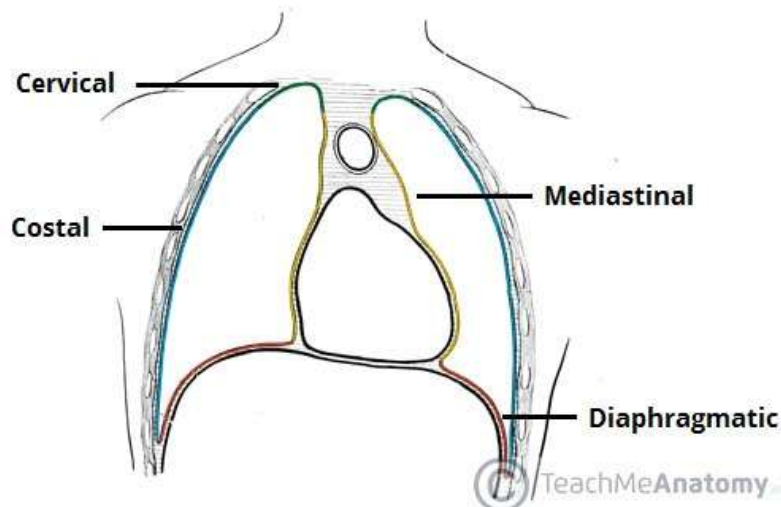


Figure (3): The parts of parietal pleura (*TeachMeAnatomy, 2020*)