



شبكة المعلومات الجامعية
التوثيق الإلكتروني والميكروفيلم

بسم الله الرحمن الرحيم



MONA MAGHRABY



شبكة المعلومات الجامعية
التوثيق الإلكتروني والميكروفيلم



شبكة المعلومات الجامعية التوثيق الإلكتروني والميكروفيلم



MONA MAGHRABY



شبكة المعلومات الجامعية
التوثيق الإلكتروني والميكروفيلم

جامعة عين شمس التوثيق الإلكتروني والميكروفيلم

قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها
علي هذه الأقراص المدمجة قد أعدت دون أية تغييرات



يجب أن

تحفظ هذه الأقراص المدمجة بعيدا عن الغبار



MONA MAGHRABY

**Patterns of Care and Treatment Pathways
for Non-Surgically Managed Early and
Locally Advanced Non-Small Cell Lung
Cancer Patients at Ain Shams University
Clinical Oncology Department:
a Retrospective and Descriptive Analysis**

Thesis

*Submitted for Partial Fulfilment of Master's Degree
in Clinical Oncology & Nuclear Medicine*

By

Christina Gamil Garas

M.B.B.Ch, Faculty of Medicine, Ain Shams University

Under Supervision of

Dr/ Khaled Abdel Karim

*Professor of Clinical Oncology and Nuclear Medicine
Faculty of Medicine, Ain shams University*

Dr/ Khaled Nagib

*Assistant Professor of Clinical Oncology and Nuclear Medicine
Faculty of Medicine, Ain shams University*

Dr/ Ahmed Hassan Abd El Aziz

*Lecturer of Clinical Oncology and Nuclear Medicine
Faculty of Medicine, Ain shams University*

Faculty of Medicine, Ain shams University

2020

Acknowledgments

*First and foremost, I feel always indebted to **Allah** the Most Beneficent and Merciful.*

*I wish to express my deepest thanks, gratitude and appreciation to **Dr/ Khaled Abdel Karim**, Professor of Clinical Oncology and Nuclear Medicine, Faculty of Medicine, Ain Shams University, for his meticulous supervision, kind guidance, valuable instructions and generous help.*

*Special thanks are due to **Dr/ Khaled Magib**, Assistant Professor of Clinical Oncology and Nuclear Medicine, Faculty of Medicine, Ain shams University, for his sincere efforts, fruitful encouragement.*

*I am deeply thankful to **Dr/ Ahmed Hassan Abd El Aziz**, Lecturer of Clinical Oncology and Nuclear Medicine, Faculty of Medicine, Ain shams University, for his great help, outstanding support, active participation and guidance.*

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

Christina Gamil Garas

List of Contents

Title	Page No.
List of Tables.....	4
List of Figures.....	6
List of Abbreviations.....	7
Introduction.....	- 1 -
Aim of the Work.....	12
Review of Literature	
Epidemiology.....	13
Risk Factor and Screening.....	17
Diagnosis and Staging.....	19
Pathology and Molecular Signaling Cascads.....	27
Stage-Based Management.....	32
Acute and Late Toxicities of Combined Chemoradiotherapy for Locally Advanced Non-Small Cell Lung Cancer.....	57
Patients and Methods.....	69
Results.....	77
Discussion.....	104
Summary.....	127
Recommendations.....	130
References.....	131
Arabic Summary	

List of Tables

Table No.	Title	Page No.
Table 1:	2015 WHO classification of malignant epithelial tumors of lung	28
Table 2:	Demographic & clinical characteristics of the study population	78
Table 3:	Disease characteristics for study population	80
Table 4:	Baseline characteristics of radically treated group.....	82
Table 5:	Disease characteristics for radically treated group.....	83
Table 6:	Baseline characteristics of palliatively treated group.....	84
Table 7:	Disease characteristics for palliatively treated group.....	85
Table 8:	Chemotherapy.....	86
Table 9:	Definitive Radiotherapy	88
Table 10:	Palliative Radiotherapy to the primary tumor.....	88
Table 11:	Treatment time	89
Table 12:	Toxicity	90
Table 13:	Cases summary for all study population	92
Table 14:	Mean and median progression free survival for all study population	92
Table 15:	Cases survival according to the aim of treatment modality (palliative, Radical, and Supportive).....	93
Table 16:	Mean and median progression free survival according to the aim of treatment modality (palliative, Radical, and Supportive)	93
Table 17:	Cases summary for radically treated group	94
Table 18:	Mean and median progression free survival for radically treated group.....	95
Table 19:	Cases summary for palliatively treated group	96
Table 20:	Mean and median progression free survival for palliatively treated group	96

List of Tables cont...

Table No.	Title	Page No.
Table 21:	Cases summary for all study population	98
Table 22:	Mean and median overall survival for all study population	98
Table 23:	Cases summary according to the aim of treatment modality	99
Table 24:	Mean and median overall survival according to the aim of treatment modality	99
Table 25:	Cases summary for radically treated group	100
Table 26:	Mean and median overall survival for radically treated patients	101
Table 27:	Cases summary for palliatively treated group	102
Table 28:	Mean and median overall survival for palliatively treated group	102

List of Figures

Fig. No.	Title	Page No.
Figure 1:	Estimated number of new cases in 2018, EGYPT, both sexes, all ages.....	14
Figure 2:	Estimated number of new cases in 2018, EGYPT, males, all ages.....	15
Figure 3:	Estimated number of new cases in 2018, EGYPT, females, all ages.....	15
Figure 4:	Algorism of NSCLC staging system.....	26
Figure 5:	CT showing acute radiation pneumonitis	61
Figure 6:	Mechanisms of radiation-induced cardiovascular injury.....	65
Figure 7:	Median progression free survival for all study population	92
Figure 8:	Median progression free survival according to the aim of treatment modality	94
Figure 9:	Median Progression free survival for radically treated group	95
Figure 10:	Median progression free survival for palliatively treated group.....	97
Figure 11:	Median overall survival of all study population	98
Figure 12:	Median overall survival according to the aim of treatment modality.....	100
Figure 13:	Median overall survival for radically treated group.....	101
Figure 14:	Median overall survival for palliatively treated group.....	103

List of Abbreviations

Abb.	Full term
ASUCOD	<i>Ain Shams University Clinical Oncology Department</i>
ALARA	<i>As low as reasonable achieved</i>
ALK	<i>Anaplastic lymphoma kinase</i>
ASCO	<i>American Society of Clinical Oncology</i>
AUC	<i>Area under the curve</i>
BSC	<i>Best supportive care</i>
CALGB	<i>Cancer and Leukemia Group B</i>
cCRT	<i>Concurrent Chemoradiotherapy</i>
CRT	<i>Chemoradiotherapy</i>
CKD	<i>Chronic kidney disease</i>
CINV	<i>Chemotherapy induced nausea and vomiting</i>
COPD	<i>Chronic obstructive pulmonary disease</i>
CHART	<i>Continuous hyperfractionated accelerated radiotherapy</i>
CHF	<i>Congestive heart failure</i>
CM	<i>Conventional mediastinoscopy</i>
CPS	<i>Combined Positive Score</i>
CR	<i>Complete response</i>
CT	<i>Computed tomography</i>
CVA	<i>Cerebrovascular accident</i>
DNA	<i>Deoxyribonucleic acid</i>
DM	<i>Diabetes Mellites</i>
EBUS	<i>Endobronchial ultrasound</i>
ECOG	<i>Eastern Cooperative Oncology Group</i>
EGFR	<i>Epidermal growth factor receptor</i>
EORTC	<i>European Organization for Research and Treatment</i>
EUS-NA	<i>Endoscopic Ultrasound Needle Aspiration</i>
EML4	<i>Echinoderm microtubule-associated protein like4</i>
FDA	<i>Food and Drug Administration</i>

List of Abbreviations cont...

Abb.	Full term
<i>FDG-PET</i>	<i>Flurodeoxyglucose Positron emission tomography</i>
<i>IHC</i>	<i>Immunohistochemistry</i>
<i>IHD</i>	<i>Ischemic heart disease</i>
<i>IGRT</i>	<i>Image guided radiotherapy</i>
<i>IMRT</i>	<i>Intensity modulated radiotherapy</i>
<i>KRAS</i>	<i>Kirsten Rat Sarcoma</i>
<i>LDCT</i>	<i>Low dose computed tomography</i>
<i>LC</i>	<i>Lung cancer</i>
<i>MET</i>	<i>Mesenchymal-to-epithelial transition</i>
<i>MIDs</i>	<i>Molecular Immune Density Score</i>
<i>MRI</i>	<i>Magnitic Resonance Imaging</i>
<i>NLST</i>	<i>National lung screening trial</i>
<i>NCCN</i>	<i>National Comperhinsive Cancer Network</i>
<i>NOS</i>	<i>Not otherwise specified</i>
<i>NSCLC</i>	<i>Non-small cell lung cancer</i>
<i>NPV</i>	<i>Negative Predictive Value</i>
<i>OS</i>	<i>Overall survival</i>
<i>PCI</i>	<i>Prophylactic cranial irradiation</i>
<i>PD</i>	<i>Progressive disease</i>
<i>PD-1</i>	<i>Programmed death-1</i>
<i>PD-L1</i>	<i>Programmed death ligand 1</i>
<i>PFS</i>	<i>Progression free survival</i>
<i>PR</i>	<i>Partial response</i>
<i>PS</i>	<i>Performance status</i>
<i>RECIST</i>	<i>Response evaluation criteria in solid tumor</i>
<i>RP</i>	<i>Radiation Pneumonitis</i>
<i>SBRT</i>	<i>Stereotactic body radiation therapy</i>
<i>SCC</i>	<i>Squamous cell carcinoma</i>
<i>sCRT</i>	<i>Sequential Chemoradiotherapy</i>
<i>SEER</i>	<i>Surveillance, Epidemiology, and End Results</i>
<i>SD</i>	<i>Stable disease</i>

List of Abbreviations cont...

Abb.	Full term
<i>SPN</i>	<i>Solitary pulmonary nodules</i>
<i>SUV</i>	<i>Standardized uptake value</i>
<i>SVCO</i>	<i>Superior vena cava obstruction</i>
<i>TKIs</i>	<i>Tyrosine kinase inhibitors</i>
<i>TPS</i>	<i>Tumor Propotion Score</i>
<i>TTF-1</i>	<i>Thyroid transcription factor</i>
<i>USPSTF</i>	<i>The United States Preventive Services Task Force</i>
<i>VAM</i>	<i>Video-assisted mediastinoscopy</i>
<i>VATS</i>	<i>Video-assisted thoracoscopic surgery</i>
<i>VMAT</i>	<i>Volumetric modulated arc therapy</i>
<i>WHO</i>	<i>World health organization</i>

INTRODUCTION

Lung cancer continues to be the leading cause of cancer-related deaths worldwide. Unfortunately, 50% to 60% of cases has been diagnosed with metastatic or advanced stage in different countries (*Costa et al., 2016*).

Despite improvements in survival for many other types of cancer in recent years, 5-year survival for lung cancer has remained relatively poor, mainly because by the time a diagnosis is made, lung cancer is often well advanced and treatment options are limited (*Costa et al., 2016*).

Additionally, Stage III non-small cell lung cancer (NSCLC) includes a highly heterogeneous group of patients with differences in the extent and localization of disease. Many aspects of the treatment of stage III disease are controversial. Unfortunately, the data supporting treatment approaches in specific patient subsets are often subject to a number of limitations; for example, that the trials involved heterogeneous patient populations; the definition of stage III disease has changed over time; and early studies were frequently inadequately powered to detect small differences in therapeutic outcome, were not randomized, or had limited duration of follow-up. Major improvements in therapy, including the use of more active chemotherapy agents and refinements in radiation and surgical techniques, also limit the interpretation of earlier clinical trials. Finally, improvements in pre-treatment staging have led to

reclassification of patients with relatively minimal metastatic disease as stage IV rather than stage III, leading to a prolonging in the apparent overall survival of both stage III and IV patients. Unavoidably, locally advanced NSCLC management guidelines from various groups do have some differences reflecting the opinions and treatment philosophy of the physicians involved in their generation (*Walraven et al., 2017*).

Despite multimodality treatment, the prognosis for unresectable stage III NSCLC remains poor, with five-year overall survival (OS) rates of approximately 15 percent. Therefore, newer treatment paradigms have evolved, for example, incorporation of immunotherapy (*Aupérin et al., 2010*).

AIM OF THE WORK

This retrospective observational study aims to describe the pattern of care and treatment pathways for non-metastatic unresected NSCLC in Ain Shams University Clinical Oncology Department (ASUCOD) from January 2015 till December 2018.