

**UNIVERSITY OF MEDICINE AND PHARMACY CRAIOVA**  
**PHD STUDIES SCHOOL**

# **PhD THESIS**

**TITLE:**

**THE ROLE OF MODERN IMAGISTIC METHODS IN  
ASSESSMENT OF MEDIASTINAL LYMPH NODES**

**- ABSTRACT -**

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## **GENERAL PART**

### **PART I – THE MEDIASTINUM**

#### **1. INTRODUCTION**

The mediastinum represented a mystery for anatomists and early doctors, beginning with Galenus and Vesalius. Information added in time and complete anatomic description followed, trying overall to reveal its secrets.

At the beginning of the 20th century, surgery, guided only as a symptom-relief treatment, aided by necropsies and experimental studies, allowed the successful treatment of mediastinal diseases.

The last decades of this century brought technological break-through: the molecular biology techniques of in situ hybridisation, genetic diagnosis, immunohistochemistry. New laboratory techniques evolved side-by-side with modern surgical skills: fiberscopy, video-assistance and minimally invasive surgery.

Mediastinal pathology and bronchopulmonary cancer are frequently diagnosed by high-resolution imaging, specific laboratory identification tests, and most often, the surgical treatment is minimally invasive.

#### **2. SURGICAL ANATOMY OF THE MEDIASTINUM**

##### **2.1. OVERVIEW**

The mediastinum is the anatomic region on the middle line and in the center of the thorax. It is bordered by the sternum and anterior ribs, by the vertebral column, by mediastinal pleurae, by the diaphragmatic muscle, while superiorly communicates widely with the cervical area.

##### **2.2. SIDES OF THE MEDIASTINUM**

The mediastinum has no proper structures, as its borders are those of the thoracic skeleton and of the both pleural cavities. The mediastinum widely communicates with nearby regions, mainly with the neck area by the thoracic outlet, with the two pleural spaces through the pulmonary hilum and with the abdominal region by the diaphragm.

On the anterior, the mediastinum is bordered by the inner layer of the sternum, by the sternal articulations of the ribs, along with muscles of the thoracic wall.

On the posterior, the mediastinum is bordered by the thoracic vertebral column, situated between the two mediastinal pleuras.

The lateral sides of the mediastinum are centered on the right hilum to the right and on the left hilum by the left.

### **2.3. MEDIASTINAL STRUCTURES**

The mediastinum contains vital organs, such as the heart and the pericardium, great vessels, mediastinal trachea and the emergent main bronchi, the thoracic esophagus, fatty and lymph tissue, the possible site of primary or metastatic diseases, from near-by or distant sites.

## **PART II – BRONCHOPULMONARY CANCER**

### **3. CLINICS**

Malignant tumors of the thorax are rarely diagnosed by classic mediastinal syndrome. The clinics prove the insignificant role that mechanical compression and structural alteration by inflammation and malignancy plays in early diagnostic.

Even when symptoms of early cancer are present, they are generally not specific and patient present with widely varied signs, symptoms, and syndromes, frequently mimic more common disease.

Symptomatic manifestations of local disease include cough, hemoptysis, chest pain, dyspnea, wheezing, and pneumonia. Symptoms of locally advanced disease include hoarseness, phrenic nerve paralysis, dysphagia, stridor, superior vena cava syndrome, pleural effusion, pericardial effusion, Pancoast syndrome, evidence of lymphangitic spread, and cancer cachexia.

Manifestations of extrathoracic spread include brain metastases, bone metastases, and spread to liver, adrenal glands, and intraabdominal lymph nodes. At clinical presentation most of patients have cough, weight loss, or dyspnea. Hemoptysis, chest or bone pain, fever, and weakness occur slightly less often.

The physical examination foretells advanced disease if, among other signs, there is evidence of lymphadenopathy in the supraclavicular or cervical regions, percussion dullness suggesting a pleural effusion, or neck vein distention from superior vena cava obstruction.

However, the spectrum of lung cancer presentation remains extremely broad because it includes symptoms caused by local invasion, metastases, and paraneoplastic mechanisms.

## **4. STAGING LUNG CANCER**

### **4.1. LYMPHATIC SYSTEM**

It is important to accurately recognize and identify the lymph node stations since they are the main paths of dissemination and allow for clinical and pathological staging in accordance to the TNM staging system.

### **4.2. LYMPH NODE STATIONS**

In 1986 the International Standardized System is revised by AJCC and the International Union Against Cancer (UICC), who also decided to still use the same lymph node stations.

### **4.3. TNM STAGING**

The current TNM staging system was introduced in 2007 by Goldstraw on behalf of the International Association for the Study of Lung Cancer (IASLC) and it featured several adjustments.

All tumors larger than 7cm, which up until then were staged as T2, are now staged as T3, independently of whether or not mediastinal invasion is present. All thoracic effusions, pleural or pericardial, are now staged as M1a.

### **4.4. STAGING METHODS**

Staging of the mediastinal lymph nodes is based on non-invasive imaging techniques and minimally invasive surgical and non-surgical techniques.

The CT scan is the basis for staging and evaluating the extension of lung cancer, but it can't be used alone due its low accuracy. When non-invasive methods are not available, a surgical technique should be used for staging, the only exception being stage I or lymph nodes <1cm in its short axis. Invasive non-surgical techniques should be accompanied by minimally-invasive surgical techniques in order to establish a histological diagnostic.

## **PART III – CURRENT METHODS FOR EVALUATING MEDIASTINAL INVOLVEMENT**

### **5. MINIMALLY INVASIVE NON-SURGICAL TECHNIQUES**

Lymph nodes and tumoral masses are in close proximity to hollow organs, such as the blood vessels, lungs and heart, so in order to examine them an endoscopic ultrasound examination is needed.

Non-invasive techniques allow offer low morbidity and mortality, combined with high positive and negative predictive values, without the need of tissue dissection, and by using natural conducts and pre-existing orifices (esophagus, trachea, bronchi), needle biopsies from the masses identified on the CT scan are possible.

### **6. SURGICAL MINIMALLY INVASIVE TECHNIQUES**

Mediastinoscopy is a procedure designed for inspection of the superior mediastinum. It represents a minimally invasive surgical technique, used when lymph nodes >1cm in their short axis are identified on the CT scan, in order to determine the clinical stage and the treatment options. The method is mandatory in patients with lung cancer proposed for induction therapy.

### **7. FINAL RECOMMENDATIONS**

When enlarged lymph nodes are identified on the CT scan, minimally invasive non-surgical techniques, such as EUS and EBUS, which offer high predictive value and sensibility compared to mediastinoscopy, should be used for initial staging and assessment.

## **SPECIAL PART**

### **PART IV - THE IMPORTANCE OF IMAGING TECHNIQUES FOR THE DIAGNOSIS OF MEDIASTINAL ADENOPATHIES**

#### **8. MATERIAL AND METHOD**

The prospective study was conducted by the Craiova University of Medicine and Pharmacy - Department of Radiology and Medical Imaging and the Research Center for Gastroenterology and Hepatology between November 2009 and June 2013.

The total number of patients with enlarged lymph nodes included in the study was 388. These patients were investigated biologically and imagistically through invasive non-surgical techniques (endoscopy) and minimally invasive surgical techniques (mediastinoscopy) in order to establish the diagnosis, extension of the disease and prognosis.

## **9. CLINICAL STUDY**

The distribution of the identified mediastinal masses represented by peaked prevalence was calculated for the groups 51-60 y.o. and respectively 61-70 y.o.

Distribution of patients by sex was used in order to determine the incidence of adenopathies for each sex separately.

## **10. IMAGING STUDY**

Radiological examination of the chest was performed in all 388 cases with mediastinal masses. Shifting of the mediastinal elements and modified contours were recorded when present. Mediastinal masses located inside the mediastinal contours, as well as those hidden by normal or pathological anatomical structures, were not recorded.

CT scan was performed systematically in all investigated patients, while multiplane reconstruction, 3D VRT studies and virtual bronchoscopies were recommended in selected patients.

## **11. ULTRASOUND ENDOSCOPY STUDY**

The study enrolled patients with tumor-related mediastinal masses which were also investigated through ultrasound endoscopy, ultrasound guided fine needle aspiration (EUS-PFA) and cytology examination.

## **12. MEDIASTINOSCOPY STUDY**

A total of 147 patients benefited from mediastinoscopy in order to establish the etiology of the mediastinal masses and to confirm or infirm the existence of lung tumors without mediastinal dissemination.

Patients included in this study were divided in to two groups: patients with mediastinal masses associated with lung cancer and patients with mediastinal masses of unknown etiology.

### **13. DISCUSSIONS**

Accurate staging of patients with lung cancer is accomplished by evaluating the involvement of mediastinal lymph nodes, which is considered the best prognosis factor when distant metastasis are not present.

The study of mediastinal lymph nodes is based on imaging techniques and minimally invasive surgical and non-surgical techniques which remain the gold standard for determining whether or not mediastinal metastases are present.

### **14. PARTICULAR CASES – PERSONAL EXPERIENCE**

Re-mediastinoscopy allows for evaluation of the efficiency of oncological treatment, and can even avoid an unnecessary lung resection when tumor cells are still present in the mediastinal lymph nodes.

Re-mediastinoscopy, although more difficult than the first mediastinoscopy performed before the induction treatment, it offers the advantage of being able to acquire histological evidence for the efficiency of the oncological treatment.

Re-mediastinoscopy has similar indexes of performance when comparing it to the new minimally invasive non-surgical procedures (EUS and EBUS).

### **14. CONCLUSIONS**

The right method of treatment in patients suspected of having lung cancer and enlarged lymph nodes on the CT scan depends on confirming the diagnosis of lung cancer, as well as determining the histological type.

PET-CT scan is net superior to CT in confirming active disease in patients with enlarged mediastinal lymph nodes.

Endoscopic ultrasound guided fine needle aspiration is an efficient and safe method of evaluating patients with lung cancer, being especially useful when through bronchoscopy a large enough specimen is not obtained. EUS-FNA reduces the need for other staging procedures, thus avoiding the risks accredited to minimally invasive surgical methods.

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