NSCLC/SCLC – Diagnosis and staging of thoracic tumours

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AIMS

To provide knowledge about epidemiology, mortality, risk factors and prognostic factors.
To describe the staging procedure.
To outline the diagnostic strategies

SUMMARY

Thoracic tumours and especially lung cancer have a high incidence. Lung cancer has a poor prognosis with overall only little progress regarding survival. But some subgroups have now a better prognosis. In order to detect lung cancer at an early stage radiological changes in the lungs should get a definitive diagnosis whenever possible. Regarding screening at the moment no firm recommendation can be made, although the National Lung Screening Trial from the USA suggests a survival advantage of 20% in the lung cancer specific mortality in risk patients and in the US screening is now widely recommended.

The prognosis is determined by the extent of the disease, the histology and biology of the tumour and the patient conditions.

Extent of the disease

The extent of the disease is evaluated according to the 7th edition of TNM-staging [1]. From 2017 on the 8th edition of TNM will be in place [2]. In patients with suspected or known lung cancer a careful clinical evaluation including history and physical examination is necessary. Usually the anatomic evaluation begins with a CT scan of the chest with contrast including the upper abdomen (liver and adrenal glands). If no pleural or systemic metastases are found the local intrathoracic spread has to be evaluated. For local mediastinal infiltration or infiltration of the chest wall additional methods such as thoracic ultrasound or MRI or VATS may be necessary. In case of mediastinal lymph node enlargement (> 1 cm in short axis) in CT scan and in the absence of evidence for metastasis, the evaluation of mediastinal lymph node status is necessary before treatment decisions regarding the primary tumour are made. Here PET/CT scans can be performed for mediastinal and in addition extrathoracic staging. In case of a mediastinal lymph node change or enlargement and in the absence of evidence of metastasis (M0-status), a definitive evaluation of the lymph node status is strongly recommended before the intended curative treatment. Depending on the experience of the investigator, endobronchial ultrasound with needle biopsy/aspiration (EBUSTBNA), oesophageal ultrasound with needle biopsy/aspiration (EUS-FNA), bronchoscopic needle aspiration (TBA), transthoracic needle biopsy/aspiration (TTNA) and surgical procedures such as mediastinoscopy or VATS are suitable approaches. Transbronchial / transthoracic and endosonographic needle aspiration procedures primarily confirm, but do not exclude mediastinal lymph node metastasis. In case of a suspicious mediastinal lymph node change or enlargement and a negative pathologic finding of a needle technique (EBUS, EUS, TBNA, TTNA), a mediastinoscopy, VATS other suitable surgical techniques are usually performed [3].
**Histology**

Histology is including subtyping of adenocarcinoma and testing of specific genetic alterations. At the moment an activating EGFR mutation and EML4-ALK or ROS-1 overexpression is now of prognostic and predictive relevance. Histological classification should be performed according to the recommendations of the ATS/IASCL/ATS task force [4]. The amount of “not otherwise specifyable” NSCLC (NOS) should be then very small. Molecular testing outside of research settings is focusing on mutations of the receptor of the epidermal growth factor (EGFR) and the expression of the EML4-ALK-fusion protein as well as ROS-1. In patients with adenocarcinoma and in never smokers we perform a mutation analysis of EGFR of exons 18 to 21. If this is negative we add a break-apart FISH regarding EML4-ALK and ROS-1. For EML4-ALK an immunohistological pretesting can be done. Further molecular testing is useful, if one can treat the patient with specific drugs.

**Diagnostic algorithm**

In patients suspected of having lung cancer who are eligible for treatment a CT scan of the chest including the application of contrast material should be performed as next step. In case of enlarged mediastinal lymph nodes and the differential indication of radiochemotherapy or surgery a FDG-PET-CT can differentiate between metabolically active and inactive changes. Imaging should be performed before invasive procedures are done, as knowledge of the anatomical changes increases the diagnostic yield of the investigation. Bronchoscopy represents the most important method for confirming the diagnosis. In peripheral lesions < 2 cm in size TTNA or bronchoscopy using modern navigation methods such as radial probe ultrasound or electromagnetic techniques are performed.

The treatment strategies depend on the extent of the disease, histology and biology and the patient characteristics. The relevance of patient characteristics is also true for systemic treatments. But most limitations are given for surgery and radiotherapy. Especially performance status and patient comorbidities including geriatric assessments in the elderly are relevant. Most are based primarily on clinical judgement, but for limitations of lung function (FEV1, DLCO, spiroergometry) and the cardiac situation the European recommendations about “Fitness for radical therapy” are of great help [5].

**REFERENCES**

   *The actual staging system for lung cancer*

   *Proposal for the revised TNM staging system, valid from 2017*

   *Guideline including all aspects of the management of lung cancer*

   *Guide for histological classification, also including remarks regarding biology and diagnosis in small tumour samples*

*Guidelines retrieving the evidence for radiotherapy and surgery and giving recommendations primarily for surgery*