Lung cancer: diagnosis, staging and treatment

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Abstract

Lung cancer is common and has a high mortality. Radical (curative intent) surgical resection is recommended for most early-stage lung non-small cell lung cancers and is also increasingly considered for higher stage tumours. Patients may have co-morbidities that restrict their suitability for surgery. All patients in the UK should be managed via a specialist lung cancer multidisciplinary team, including a thoracic surgeon, to ensure appropriate patient selection for surgery. Chemotherapy and radiotherapy may be used as sole treatment, with surgery or as part of a palliative management pathway.

Keywords Curative resection; lung cancer; operability; palliation; resectability; staging; TNM classification

Introduction

Lung cancer is the second commonest cancer in the UK and has the highest mortality rate of common cancers. About 80—90% of lung cancers can be attributed to smoking.[1] The incidence of lung cancer in men has declined over the last 10 years as smoking rates have reduced in this population. Conversely, the incidence in women has increased and in part relates to their increased smoking rates. With newer treatments, including increasing rates of surgical resection, there have been significant reductions in mortality from lung cancer. In 2011, the 1-year survival rate for men was 29% and for women 33%; this had significantly increased from a 17% 1-year survival rate in 1990.[1] However, it is still below many other advanced countries.

This article focuses on the surgical management of primary lung malignancies and considers several aspects of the diagnosis and treatment planning processes that each patient will undergo. Although the diagnosis and referral pathway may vary considerably in different countries and different healthcare systems; this chapter is an overview, focused largely on the UK system and the senior author's experience.

Histological subtypes of lung cancers

Broadly speaking, primary lung malignancies may be divided into non-small cell lung cancers (NSCLC) and small cell lung cancers (SCLC) This division is useful for considering treatment options and likely prognosis.

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The majority of lung cancer resections are for NSCLC. Only a small proportion of early-stage SCLC may be considered for surgical resection.[2] Further sub-division of NSCLC is detailed in Box 1.

Secondary malignancies in the lung may also be considered for resection. Generally, this involves a non-anatomical wedge resection of an isolated lung metastasis from a colorectal or other primary.

Presentation

Unfortunately, most lung cancers present late. Common localizing symptoms include persistent cough and progressive dyspnoea. Other patients may present with symptoms of metastatic spread, for example headache, ascites and pathological fractures. Paraneoplastic syndromes do occur, but they are rare (2% of patients).[3] In most cases, these symptoms will be initially investigated by the patient's general practitioner who will often request baseline investigations such as a chest X-ray and blood tests.

Once there is sufficient clinical suspicion/evidence of a lung malignancy, the case will be referred to the local lung cancer multidisciplinary team (MDT) to plan further investigations and ultimate management. This referral may be made by the patient's general practitioner or hospital doctor.

Options for managing lung cancer

Several treatment modalities exist for lung cancer management, including surgery, radiotherapy and chemotherapy. Depending on the circumstances, each of these treatments may be undertaken with either 'radical' or 'palliative' intent. Radical treatment is that which aims to substantially improve survival and may potentially cure the patient. Palliative treatment is any which is given to improve quality of life; accepting that any prolongation of life which may occur is a secondary benefit.[4,5]

When planning radical surgical intervention, there are several factors to consider in order to determine whether this is a suitable treatment pathway for the patient. These factors are detailed in Table 1.

Summary of division into NSCLC and SCLC[3]

Non-small cell lung cancer (NSCLC) — 75% of primary lung cancers

- Adenocarcinoma (35%)
- Squamous cell carcinoma (30%)
- Large cell carcinoma (10%)
- Bronchoalveolar carcinoma (<5%) ('adenocarcinoma in situ' — occurs in non-smokers — localized or diffuse ground glass opacities on imaging)
- Mucoepidermoid
- Adenocystic
- adenosquamous
- Carcinoid (1%) (not associated with smoking)

Small cell lung cancer (SCLC) — 25% of primary lung cancers

Box 1

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Key factors to consider when planning radical surgery

Tumour-related factors	Size Anatomical location Histological subtype Evidence of metastases	'Resectability' and stage of tumour
Patient-related factors	Co-morbidities Baseline lung function Baseline performance status Patient wishes	'Fitness for surgery'/ 'operability'

Table 1

The role of the MDT

MDT meetings are undertaken to plan further investigation and management of suspected/proven lung cancers. The MDT aims to ensure all patients are adequately assessed and appropriate management is planned in a prompt fashion. This may include extensive investigations to confirm diagnosis prior to consideration of surgery; however, this process may also involve avoidance of unnecessary procedures which would not alter the planned intervention, as well as identifying patients for whom surgery is not possible or appropriate. Within this team, the surgeon is able to offer expert advice, individualized to each patient, including making a judgement on the resectability of a mass and the most appropriate approach (Box 2). This can also guide further investigation and discussions with the patient.[6]

Preoperative diagnostic/staging investigations

There are a range of preoperative diagnostic and staging investigations that may be performed and these are detailed below (Table 2). Several of these may be completed prior to any MDT discussion; however, most will be undertaken as part of the MDT-driven diagnostic procedure.

Occasionally, patients may undergo lung resection without prior histological confirmation of a malignancy. This is often the case in patients where the clinical suspicion of malignancy is high and there is concern that a biopsy may result in tumour seeding along the biopsy track; or that the wait for biopsy results may delay progression to definitive surgery in patients where there is concern about rapid disease progression (e.g. in small tumours, suspected of being SCLC). A 'straight to resection' approach may also be taken in patients with an isolated small mass for whom the surgical procedure would not be altered by confirming the histological diagnosis. In these patients, a frozen section diagnosis is often performed intraoperatively to ensure sufficient resection margins are taken.

Alongside these investigations, which aim to confirm the diagnosis of malignancy and assess the tumour stage, there are several investigations performed to assess the general health of the patient and their suitability to undergo surgery. These are discussed later in this article.

Staging

The current tumour/node/metastasis (TNM) classification for lung malignancies is the seventh edition from the American Joint Committee on Cancer (AJCC),[8] shown in Table 3. See also Figure 1 for the lymph node map and Table 4 for the calculation of a tumour's stage from its TNM scores.

The new, eighth edition of the AJCC guidelines is expected to make several changes including altering the tumour size criteria for the T element,[9] reclassifying M1b to include only a single distant metastasis and introducing M1c for multiple distant metastases.[10] The new guidelines are also proposing new staging categories, for example stage 3C, which will include all T3 and T4 tumours that are N3 but M0.[10] All changes are based on analysis of the new International Association for the Study of Lung Cancer (IASLC) database of over 90,000 cases of lung cancer.[9]

Traditionally, stage 1—3 tumours were considered resectable by 'standard' techniques and T4 tumours were irresectable given their involvement in vital structures. With altered, 'non-standard' surgical techniques, resection of these T4 tumours may be possible with acceptable results (Box 4). Figure 2 shows example images for tumours of different stages which have all undergone surgical resection, including a stage 3A (T4N1M0) tumour.

It is not uncommon for there to be uncertainty over the precise tumour stage, especially when considering the exact criteria for a 'positive node'. Often, the MDT will agree on a lower stage to allow more aggressive radical therapy to be offered to patients to improve survival, bearing in mind the individual patient's fitness and personal wishes.

Resectability and operability

This is a judgement on the possibility of complete surgical resection of a cancer.[4] It is dependent on the cell type, anatomical position, extent of local invasion and distant spread. The surgeon will assess whether a resection is possible with adequate margins but without damage to other important structures.

R	Definition
R0	Complete microscopic and macroscopic resection
R1	Residual microscopic disease
R2	Residual macroscopic disease

The aim of surgery with curative intent is to leave no residual disease (R0). Incomplete resections are associated with poorer outcomes, i.e. higher rates of local recurrence and reduced survival.[7] Occasionally this may still be considered the best option for a patient, particularly in the context of multi-modality treatment. In cases of unexpected incomplete resection the multidisciplinary team will discuss the merits of further surgery or intervention, local radiotherapy or chemotherapy.

Fitness for surgery/operability

Operability is related to the extent of the proposed surgery and the overall capacity of the patient to withstand the requirements of surgery, general anaesthesia and a return to a level of function that is acceptable to them. There are several guidelines for assessing fitness for surgery and these are discussed below.

Box 2

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