

RADIOLOGICAL STAGING IN THORACIC ONCOLOGY

Dr. J. Reynolds – Birmingham Heartlands Hospital.

Lung cancer is the second most common cancer in the UK: 14% of the total cancer incidence, in 1999. A male predominance is present with a 7:4, male:female ratio. The incidence in men has been steadily decreasing, reflecting smoking rates. Similarly, mirroring rates of cigarette consumption among women, female lung cancer rates increased through the 70s and 80s until the early 90s, since when they have essentially reached a plateau. Breast cancer has a higher incidence, but there are more deaths from lung cancer [1]. Imaging plays a pivotal role in both the detection and staging of lung cancer.

Detection

Patients commonly present in one of three ways:

- i. Symptoms resulting from local disease
- ii. Symptoms relating to distant metastases
- iii. Non-specific constitutional symptoms.

The first process in diagnosis involves the detection of a suspicious lesion, usually on a chest radiograph. Sometimes the pick up is on CT, performed for other reasons, or following a normal CXR when there is a high suspicion of lung cancer. The second part of the process is to positively identify the lesion, with a histological or cytological diagnosis being required in the majority of cases [1].

The initial imaging technique used in suspected lung cancer is the chest radiograph but this is a relatively insensitive test and cancers of less than 1 cm diameter are rarely detected this way. Eighty five per cent of missed cancers are small peripheral nodules of less than 2 cm diameter and are common in the upper zones where there are numerous overlying structures [2].

On computed tomography, features suggestive of lung cancer include size greater than 3 cm, lobulation, spiculation and pleural retraction.

Staging

Having established an imaging diagnosis of likely lung cancer, accurate staging is the next step. This provides prognostic information and determines optimum management and most importantly, whether a lesion is potentially resectable. CT scanning is the primary cross-sectional technique for lung cancer staging and protocols are described in the Royal College of Radiologists guidelines on oncology imaging [3]. For non-small cell lung cancer the TNM International System is used [4].

CT is very good at determining that a lesion is unresectable but less good at indicating resectability. Patients with equivocal imaging findings should be given the benefit of the doubt and not denied potentially curative surgery.

For small cell lung cancer the staging is simpler with two groups:

- Limited stage – tumour confined to one hemithorax, including ipsilateral or contralateral and supraclavicular nodes.
- Extensive disease – beyond these bounds.

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Positron emission tomography (PET) provides metabolic information not available with CT and potentially provides more accurate assessment of mediastinal nodal involvement with tumour and more reliable detection of extra-thoracic metastatic disease. Toloza et al [5] published a meta-analysis assessing mediastinal staging with PET and also the clinical evaluation of metastatic disease. The sensitivity and specificity of PET for nodal disease were 84% and 89% with the corresponding figures for CT being 57% and 82%.

In our local practice we have adopted the NICE guidelines [6] and PET is performed as a final step prior to surgery in all NSCLC cases except those with staging of T1N0M0.

Screening for Lung Cancer

The low resection and cure rates for lung cancer have led to many attempts to devise a satisfactory screening programme for asymptomatic patients with early stage lung cancer. In one influential study from New York, 1000 high risk cases were screened and 233 lesions were found that required further assessment. 28 patients subsequently underwent biopsy and of these, 27 were malignant [7]. The subject is, however, controversial. Sceptics point out that screening tends to find peripheral, slow growing cancers that patients may have died with and not from. There are various in-built biases in evaluating screened patients. The resources required for such a programme would be huge.

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NOTES

SURGICAL STAGING IN THORACIC ONCOLOGY

Mr. K. Papagiannopoulos – St James' Hospital, Leeds.

Introduction

Staging for lung cancer has matured dramatically with the advent of newer technologies in imaging and endoscopic surveillance.

Surgical staging

The procedures employed for surgical staging focuses mainly in the **mediastinum** since N status determines prognosis.

2 distinct group of patients for whom mediastinal staging is important:

1. those where N2 or N3 disease needed be excluded preoperatively
2. those potential surgical candidates following neoadjuvant treatment in whom confirmation of 'sterilisation of the mediastinum is important.

There might be a third group where mediastinal staging could prove important in patients with extrathoracic malignancies, metastasizing to the lung in whom metastatectomies could provide a survival benefit.

- **Mediastinoscopy**

Used over 50 years.

Indications: evaluation of mediastinal lymph nodes, evaluation of mediastinum, evaluation of proximal main bronchi, evaluation of medially based right sided tumours in the upper lobe abutting the parietal pleura.

Results: Sensitivity >0.8 depending on the study, specificity 1

Complications: Morbidity 1%-2,3% Mortality 0%-0.3%.

- **Mediastinotomy (Chamberlain incision)**

Used alone or in combination with Mediastinoscopy.

Indications: Evaluation of nodes in position 5 and 6 according to Naruke map, evaluation of central tumours close to A-P window, inspection of pericardium and intrapericardial inspection for appropriate T staging

Results: Sensitivity 0.8, Specificity 1

Complications: as for mediastinoscopy.

Both procedures have been recently enhanced with the use of Digital Video technology providing better accuracy

- **Video Assisted Thoracic Surgery**

Indications: Mainly used to assess N2 nodes not accessible by Mediastinoscopy, assess pleural disease/involvement and T status in large tumours where CT is not accurate.

- **Thoracotomy**

Indications: it is the final procedure with or without formal resection when all other attempts for surgical staging have been exhausted.

Although there seems to be a greater movement towards the use of non-invasive tools for lung cancer staging, clinicians must still rely on histological confirmation for accuracy of staging.

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NOTES

STAGE SPECIFIC SURGICAL INTERVENTION FOR NON-SMALL CELL

LUNG CANCER

Mr. D. Waller – Glenfield, Leicester.

This lecture will cover the multidisciplinary management of non-small cell lung cancer. Each stage of the disease will be addressed separately and the following issues will be discussed :

Stage I (T1-2 N0)

In the management of the solitary pulmonary nodule VATS excision biopsy (with intraoperative frozen section) is preferable to preoperative percutaneous biopsy.

Matsugama H et al. Risk of pleural recurrence after needle biopsy with resected early stage lung cancer. Ann Thorac Surg 2005;80:2026-31

Routine PET is not justified for solitary pulmonary nodules

Detterbeck FC et al. Seeking a home for PET. Chest 2004;125:2294-9

Routine mediastinoscopy is not indicated.

Canadian Lung Oncology Group. (1995). Investigation for mediastinal disease in patients with apparently operable lung cancer. Canadian Lung Oncology Group. Ann Thorac Surg, 60, 1382-9

In selected stage I tumours Lobectomy may NOT be the gold standard

Ginsberg, R.J. & Rubinstein, L.V. (1995). Randomized trial of lobectomy versus limited resection for T1 N0 non-small cell lung cancer. Lung Cancer Study Group. Annals of Thoracic Surgery, 60, 615-22; discussion 622-3.

In selected stage I tumours VATS lobectomy is the treatment of choice

McKenna, R.J., Jr., Wolf, R.K., Brenner, M., Fischel, R.J. & Wurnig, P. (1998). Is lobectomy by video-assisted thoracic surgery an adequate cancer operation? Annals of Thoracic Surgery, 66, 1903-8

Adjuvant chemotherapy may not be beneficial.

Stage II (T1-2 N1, T3N0)

Primary surgical treatment is advocated for isolated chest wall invasion

En-bloc chest wall resection/reconstruction is mandatory in T3 (chest wall) tumours

Lobe specific systematic lymph node dissection is the recommended method of Intraoperative lymph node management

Graham, A.N., Chan, K.J., Pastorino, U. & Goldstraw, P. (1999). Systematic nodal dissection in the intrathoracic staging of patients with non-small cell lung cancer. Journal of Thoracic & Cardiovascular Surgery, 117, 246-51.

Adjuvant chemotherapy confers a modest survival benefit.

Sedrakyan A, Van derMeulen J, O'Byrne KJ, Prendiville J, Hill J, Treasure T. Postoperative chemotherapy for non-small cell lung cancer : systematic review and meta-analysis. J Thorac Cardiovasc Surg 2004;128:414-9

Stage IIIa (T1-3 N2, T3N1)

Clinical IIIa should be further investigated by PET and mediastinoscopy

Mediastinoscopy positive patients should receive induction chemotherapy / chemoradiotherapy
Van Meerbeek JP et al. EORTC 08941 trial. Abstract No. 7015, proc ASCO 2005

“Downstaging” should be confirmed pathologically

Only pathologically “downstaged” patients should go on to further resection.

De Waele M et al. Nodal status at repeat mediastinoscopy determines survival in NSCLC with mediastinal nodal involvement treated by induction therapy. Eur J Cardiothorac Surg;29:240-3.

Pancoast tumours should receive induction chemoradiotherapy

Anonymous. (1997). Clinical practice guidelines for the treatment of unresectable non-small-cell lung cancer. Adopted on May 16, 1997 by the American Society of Clinical Oncology. Journal of Clinical Oncology, 15, 2996-3018.

Stage IIIb (T4 or N3)

T4 satellite lesions should undergo resection.

Mountain, C.F. (1997). Revisions in the International System for Staging Lung Cancer. Chest, 111,1710-7.

T4N0 locally invasive tumours may not benefit from surgery.

Stage IV (M1)

Truly Oligometastatic disease may be treated by resection of the primary and isolated metastasectomy
ACCP Lung Cancer Guidelines Panel (2003). Diagnosis and Management of Lung Cancer. Chest 123(suppl 1) 1S-338S

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STAGE SPECIFIC TREATMENT OF LUNG CANCER: NON-SURGICAL

ONCOLOGY

Dr. D. Farrugia – 3 Counties Cancer Network

Surgery remains the treatment of choice in early lung cancer. However, relapse rates remain substantial and therefore it was vital that trials of adjuvant chemotherapy were undertaken. The 1995 metanalysis suggested an absolute benefit of platinum-based chemotherapy of 5% at 5 years but with wide confidence intervals (1% detriment to 10% benefit) (1). More recently, several large trials in this setting have been reported. While a few found no benefit, the majority demonstrated a survival benefit, which was also confirmed by a recent metanalysis (2). Magnitude of benefit is smaller in T1 node negative disease probably making chemotherapy not worthwhile in this group but the benefit is correspondingly greater in node positive disease. Earlier small trials of pre-operative chemotherapy suggested a survival benefit, but further results are awaited from larger randomised trials such as LU-22.

Radiotherapy still has no established role in the post operative setting in completely resected patients (3). In patients with locally advanced disease radiotherapy using CHART or combined chemoradiotherapy with standard fractionation are suitable alternatives. Both techniques are superior to conventionally fractionated radiotherapy used alone. Several randomised trials backed by a Cochrane metanalysis (4) showed that concurrent chemo-radiotherapy is superior to sequential chemo-radiotherapy but that the former is associated with greater toxicity, leading many UK centres to adopt sequential therapy as standard of care.

In advanced disease (IIIB and IV), the 1995 metanalysis established a role for platinum based chemotherapy combinations in the palliative treatment of non small cell lung cancer (1). The Big lung Trial (5) confirmed this benefit with a 9% improvement in median survival. Cisplatin or carboplatin were initially combined with agents such as Etoposide or vinca alkaloids. More recent agents such as taxanes, gemcitabine and Vinorelbine have replaced older agents and these new agents appear to have similar efficacy (6). Single agent chemotherapy remains the treatment of choice for older patients giving the same benefit but with less toxicity. Second line chemotherapy is also available for patients with good performance status in the form of taxotere or pemetrexed.

We are now entering the era of biological therapies. Gefitinib (Iressa) and erlotinib (Tarceva) are two examples of small-molecule tyrosine kinase inhibitors being developed in this role. Despite promising results from single agent studies of second line gefitinib in relapsed disease (7), combination of gefitinib with chemotherapy in the first line setting failed to improve outcome (8). Unlike Gefitinib, erlotinib as second line therapy was also associated with a survival benefit (9), but this benefit was limited to a subgroup of never-smokers when erlotinib was studied in the first line setting combined with chemotherapy (10). Other biological therapies in clinical testing include antibodies towards EGFR such as cetuximab and anti-angiogenesis agents such as the monoclonal antibody bevacizumab.

References

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NOTES

SURGERY FOR BENIGN OESOPHAGEAL DISEASE

Mr. J. Duffy – Nottingham City Hospital.

Involvement of cardiothoracic surgeons has declined over the last 20 years. The reasons for this are multifactorial but include the specialisation of general surgeons in upper GI surgery, the advent of laparoscopic techniques and the shortage of thoracic surgeons in the UK.

Nevertheless there is still a need for the cardiothoracic surgeon to have an understanding of benign oesophageal disease. Those surgeons practicing oesophageal surgery will clearly have an interest in oesophageal disease. They will need to embrace laparoscopic techniques whilst maintaining their skills in transthoracic surgery which upper GI surgeons will have little experience in. They will be involved in the management of complex cases and elective reoperative surgery. The cardiothoracic surgeon needs an understanding of the basic principles of management of reflux disease and motility disorders since although he may not be undertaking the primary surgery he may be asked to help deal with complicated cases. He will also need to be able to deal with those situations which might present to a cardiothoracic surgeon as an emergency.

It is not possible to cover all of benign oesophageal disease in a short lecture so the following topics will form the core of the lecture:

Surgery for gastroesophageal reflux

- pathophysiology
- principles of treatment and surgical options
- new techniques
- Barrett's oesophagus its significance and management

Paraoesophageal hernia

- pathophysiology
- complications
- treatment – open and laparoscopic techniques

Oesophageal perforation

- pathophysiology
- treatment options

Motility disorders of the oesophagus

- pathophysiology
- diagnostic features
- management

Further information

Surgery of the oesophagus in Surgical Clinics of North America 77(5) October 1997 Eds Hunter JG and Pellegrini CA

Laparoscopic oesophageal surgery Surgical Clinics of North America 80(4) 1213-42 2000

Watson DI, Jamieson GG
Antireflux surgery in the laparoscopic era
BJS 85(9) 1173-84 1998

Arts J, Tack J, Galmiche JP
Recent advances in clinical practice: endoscopic antireflux procedures
Gut 2004; 53:1207 – 1214

Shaheen N, Ransohoff DF
Gastrooesophageal reflux, Barrett esophagus, and esophageal cancer. Scientific review
JAMA 2002; 287, 15:1972- 1981

Brinster CJ, Singhal S, Lee L et al
Evolving options in the management of esophageal perforation
Annals Thoracic Surgery 77(4): 1475-83 2004

Whyte RI, Iannettoni MD, Orringer MB
Intrathoracic perforation. The merit of primary repair.
JCTS 109(1): 140-4. 1995

CTS net website – Experts Techniques section: laparoscopic treatment of achalasia, reflux and paraoesophageal hernia

Complete (cPR) versus partial (pPR) responders

Only logical to avoid surgery in those with a complete pathological response (cPR), but this is difficult to ascertain without surgery!

Until Chemo+DXT can achieve consistently high rates of locoregional control, surgery should remain an integral part of the multi-modality treatment of oesophageal cancer.

References

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Preoperative (neoadjuvant) chemoradiotherapy in oesophageal cancer
Br J Surg 2001,88:338-356
2. Medical Research Council Oesophageal Cancer Working Party
Surgical resection with and without preoperative chemotherapy in oesophageal cancer: a randomised controlled trial
Lancet 2002,359:1727-1733
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Chemotherapy followed by surgery compared with surgery alone for localized esophageal cancer
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Chemoradiation with and without surgery in patients with locally advanced squamous carcinoma of the esophagus
J Clin Oncol 2005,23:2310-2317

NOTES

MINIMALLY INVASIVE OESOPHAGECTOMY

Mr. R. Berrisford – Royal Devon and Exeter Hospital.

Many different hybrid operations, in which one part of the procedure is performed by a minimally invasive approach, have been reported in the literature as “minimally invasive oesophagectomy”. Examples of these procedures include thoracoscopic mobilisation of the oesophagus with laparotomy, laparoscopic gastric tube formation with thoracotomy, laparoscopically assisted transhiatal oesophagectomy, or even gastric tube formation with hand port or fashioning of the gastric tube through a minilaparotomy. Most of these series are small.

The classic MIE (minimally invasive oesophagectomy), however, is a thoracoscopic, laparoscopic subtotal oesophagectomy with laparoscopic creation of gastric tube and a cervical anastomosis. This has been pioneered by James Luketich (University of Pittsburgh Medical Centre, UPMC) where almost 700 of these procedures have been performed to date. The Pittsburgh group have published their initial series of 77 cases with no mortality and low morbidity (1) and subsequently a series of 222 cases with mortality of only 1.4% (3/222) (2). Hospital stay was shorter than most open series (7 days) but morbidity was not significantly different from good open series of oesophagectomies. Survival in this series was no different from many open series, and actually there is a surprisingly poor survival of Stage II patients compared with Stage III patients. This may relate to stage migration due to inadequate nodal analysis/harvest as the mean lymph node harvest was only n=17.

It is remarkable that no other significant series have been published since 2002, despite many surgeons' interest in the concept of MIE. Why is this and why are there no significant series in the literature other than that from UPMC?

MIE (or, in the UK, MIO) is technically a very demanding procedure, requiring advanced laparoscopic and thoracoscopic skills with extensive experience in open oesophagectomy. There are few surgeons who acquire enough experience in VATS as well as advanced laparoscopy, and few units where a true multidisciplinary surgical team-approach is adopted. Add to this a steep learning curve, with very long initial operating times, and the potential for serious technical errors early in a series; it is perhaps not surprising that MIO has not caught on fast.

There is a paucity of literature, not only on the outcome of the procedure in centres other than UPMC, but on the effect of the procedure on quality of life. The Pittsburgh series reported good quality of life outcome and shorter hospital stay, but the Brisbane group (n=25) reported quality of life no different to open oesophagectomy (3). There are recent series of open oesophagectomy with excellent preservation of quality of life also (4)

In the UK, the procedure has been adopted by very few centres, among which Exeter has the largest series. To date, 65 patients have undergone MIO with one death (30 day and in-hospital). Length of stay is no different from open oesophagectomy and morbidity is similar. We have, however, seen significant benefits in terms of increased radicality of resection, increased lymph node harvest and faster return of quality of life (prospective evaluation currently 2 years).

We have overcome significant difficulties with gastric tube formation (initially found to be shorter than at open surgery) and with long operating times (now routinely below 5 hours). However, we are still concerned at a higher anastomotic leak rate (approx 10%) and a small but significant incidence of gastric tube tip necrosis (4/65) and gastric conduit necrosis (2/65). This has been a significant issue of concern expressed by the few other UK centres performing MIO.

There is some evidence from animal studies that interruption of the left gastric artery 14 days preoperatively improves the vascularity of the gastric tube, reduces leak rate and strengthens the anastomosis. We are currently performing laparoscopic ligation of the left gastric artery 2 weeks prior to resection, and combining this in some patients with radical upper abdominal lymphadenectomy. Early results are encouraging.

So the jury remains out on MIO. The handful of units worldwide which have adopted this procedure with good outcomes are finding benefits in terms of early return of quality of life, although this has yet to be substantiated in the literature. It is unlikely that a randomised controlled trial will be possible. There are several anecdotal reports of serious technical errors from units which have decided to “have a go” at an MIO. MIO has been evaluated by the National Institute for Clinical Excellence (NICE) whose guidelines can be downloaded (5). The advice for surgeons considering MIO is that “surgeons undertaking this surgery should have special expertise and specific training in laparoscopic and thoracoscopic surgical techniques and should perform their initial procedures with an experienced mentor.” They also insist that procedures be submitted to the MIGOCS or AUGIS database.

1. Luketich JD, Schauer PR, Christie NA, Weigel TL, Raja S, Fernando HC, Keenan RJ, Nguyen NT. Minimally invasive esophagectomy. *Ann Thorac Surg.* 2000 Sep;70(3):906-11; discussion 911-2
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5. http://www.nice.org.uk/page.aspx?o=ip_326

NOTES

CURRENT STATUS OF LUNG TRANSPLANTATION

Professor W. Klepetko – Vienna Medical University.

Lung transplantation, performed in humans for the first time as early as 1964, became a clinical reality only in the beginning of the early 1980ies. Today, worldwide around 1500 transplantations are reported annually by the ISHLT registry and the procedure is well established in numerous departments of the world.

According to data of the ISHLT registry more than 50% of all single lung transplantations are performed for emphysema/COPD, with the recipients being predominantly 50 – 64 years old. The most common indication for bilateral lung transplantation is cystic fibrosis followed by emphysema/COPD. For vascular lung diseases, combined heart-lung transplantation is increasingly replaced by isolated lung transplantation except for complex congenital defects. The decision for transplantation will not only be made based on functional criteria, but also takes the prognosis and course of the specific disease and especially the subjective impression of quality of life into account.

Internationally, an increasing scarcity of donor organs can be observed throughout the last years. This is due to increasing demands as well as to existing limitations in donation. Organ donation rates vary through the different countries from as low as 12 /million population in Germany to as high as 32/million population in Spain. These huge differences are based on different legislative backgrounds as well as on effectiveness of different organisational systems.

Donor organ shortage has led to the extension of stringent donor organ criteria and stimulated research in non heart-beating lung donation.

For bilateral lung transplantation the sequential technique has completely replaced the en-bloc technique due to its simplicity and its superior results. The standard approach for bilateral lung transplantation currently is a transversal transsternal thoracotomy, the so called Clamshell incision, however in several institutions two anterolateral thoracotomies are performed. Several advanced operative techniques have been developed within the recent years mainly intending to improve organ availability.

The use of oversized organs has become possible by different methods of downsizing. Another approach to overcome the current shortage of donor organs is living related and unrelated lobar lung donation, especially for paediatric and young adult patients. Mainly used in cystic fibrosis patients, where a bilateral transplantation is performed with the use of lower lobes from two different donors, this method achieves results comparable to cadaveric transplantation.

Changes in immunosuppression and development of new drugs have substantially improved the results of lung transplantation. Maintenance immunosuppression after lung transplantation generally remains a triple therapy based on calcineurin inhibitors. To achieve sufficient plasma levels early after transplantation, intravenous therapy usually starts intraoperatively or immediately after transplantation. Besides corticosteroids and the calcineurin-inhibitors cyclosporine and tacrolimus, either azathioprine, mycophenolat mofetil, sirolimus and everolimus are used for immunosuppression in lung transplantation. The use of induction therapy for lung transplantation remains controversial.

Long term survival after lung transplantation is still mainly limited by the development of obliterative bronchiolitis. Since the histological proof of obliterative bronchiolitis is not always achieved, a functional definition of a so called bronchiolitis obliterans syndrome (BOS) has been established. Potentially causative factors for BOS include number of acute and recurrent rejection episodes, lymphocytic bronchitis or bronchiolitis, cytomegalovirus and other viral based infections as well as higher degrees of HLA mismatches and inadequate immunosuppression.

Survival statistics provided by the International Society for Heart and Lung Transplantation (ISHLT) report about 1 year, 3 year and 5 year survival rates of 74%, 56% and 44% respectively. Results of functional outcome after lung transplantation are satisfying. Most patients experience a major improvement in functional capacity and have no restriction in activity at the end of the first year.

Refinements in organ procurement, lung preservation and immunosuppression will hopefully contribute to increased long term survival rates.

NOTES

PET STAGING OF LUNG CANCER

Dr. P. Guest – University Hospital Birmingham Foundation Trust.

Some of the best evidence for the use of PET scanning is in thoracic oncology.

Draft guidance from NICE, the DOH and the Royal Colleges suggest that:

1. An FDG PET scan should be performed to investigate solitary pulmonary nodule where a biopsy is not possible or has failed.
2. Patients who are staged as candidates for surgery on CT should have an FDG-PET scan to look for involved intrathoracic nodes and distant metastases.
3. Patients who are candidates for radical radiotherapy on CT should have an FDG PET scan

In addition PET is very helpful in differentiating recurrence from post surgical or radiotherapy change. There may be a role in radiotherapy planning, and staging of small cell lung cancer.

I would advise PET scanning in patients being considered for metastectomy of apparently isolated lesions.

There is good evidence of its routine use in the routine pre-operative staging of oesophageal cancer.

This presentation will review the evidence for some of the above recommendations and illustrate the physics and physiological principles for PET scanning, with illustrative examples of normal, benign and malignant findings.

The additional benefit of PET-CT fusion scanners/images will also be illustrated.

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3. Draft NICE lung cancer guidelines
4. Rohren E: Clinical Applications of PET in oncology Radiology 2004; 231:305-332

SURGICAL MANAGEMENT OF N2 NON-SMALL CELL LUNG CANCER

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Lung cancer that has lymphatic involvement adversely affects prognosis, especially when metastases are present in mediastinal lymph nodes. Many physicians believe operation is not indicated when N2 disease is found before thoracotomy because the risk of surgical resection may outweigh the benefits. Rarely do patients with obvious bulky mediastinal disease benefit from surgical resection; however, long-term survival has been reported in certain subgroups of patients with N2 disease. PET scan and CT scan can alert the clinician to the possibility of metastatic disease in N2 nodes and mediastinoscopy can be useful to further evaluate those nodes. The 5-year survival in selected patients who have positive mediastinoscopy and undergo complete resection is only 9.0%. However, some patients who have negative mediastinoscopy or who do not undergo prethoracotomy mediastinoscopy are found to have N2 disease at thoracotomy. These patients with clinically negative mediastinal findings who are found to have N2 disease at the time of thoracotomy should undergo as complete resection as possible to render the patient tumor free. Because metastases can involve any lymph node in the mediastinum, extensive and complete mediastinal lymph node dissection should be performed, irrespective of the location of the primary tumor. The 5-year survival of patients who underwent complete resection was 23.7%. Patients who undergo gross resection and who are at either high or intermediate risk for local recurrence and death are likely to benefit from adjuvant postoperative irradiation. In our experience, the survival of patients with N2 disease was affected by age, the extent of curative resection, the number and level of lymph nodes metastases, and whether adjuvant radiation therapy was administered. Postoperative radiation therapy was also associated with a decrease incidence of local recurrence.

Several trials evaluating neoadjuvant therapy in N2 disease have demonstrated the feasibility, tolerability and benefits in selected patients. At least two randomized trials have reported improved survival in patients with stage III NSCLC treated with preoperative chemotherapy followed by surgical resection compared to surgery alone. Up to now, most regimens have been platinum based and resulted in a radiographic response between 35% to 60%. However, pathological complete response (CR) have been much less, around 10%. While the added benefit of adding radiation therapy to preoperative chemotherapy are not fully clear at this point, there is indication that thoracic radiation may add substantially to preoperative cytoreduction, increase resection rate and CR rate in bulky N2 disease. This might be accomplished at the expense of greater toxicity and higher incidence of postoperative complications. The survival benefits of surgical resection preceded by chemo/radiation in the neoadjuvant setting has been tempered by the increase in postoperative mortality, in particular when a right pneumonectomy became necessary. The best approach remains to be determined.

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