Clinical question: What is the optimal management of Pancoast tumours?

Introduction

Defining operable and inoperable disease in stage III

The management of Stage III NSCLC has been divided into sections dependent on whether the disease is considered operable or inoperable at the time of diagnosis.

Stage III NSCLC encompasses a broad spectrum of disease extent from tumour involving a single nodal station identified only postoperatively despite extensive pre-operative staging to involvement of multiple contralateral mediastinal nodes and supraclavicular nodes appreciated on clinical examination. In patients with clinically equivocal involvement, pathological confirmation of nodal status should be made if it will influence management options.

The decision as to operability should be made in a multidisciplinary setting.
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Patients with Stage III NSCLC may be deemed inoperable because of patient factors (the patient’s respiratory function or co-morbidities may preclude operative intervention or the patient may choose not to proceed with surgery) or tumour factors (the extent or location of gross disease might make surgical resection technically impossible, for example left sided tumours with mediastinal nodes to the right of the aorta, N3 nodal involvement and most T4 tumours).

In the absence of other factors precluding surgery, patients with N1 disease should be considered for surgery. Patients with confirmed N2 disease should not be treated by surgery as the sole modality, but resectable cases may be considered for a multimodality approach. There is no consensus on the distinction between resectable and unresectable N2 disease. Factors influencing assessment of resectability include nodal size, number of stations involved, extracapsular extension and involvement of the recurrent laryngeal nerve.

The American College of Chest Physicians (ACCP) define a Pancoast tumour as a tumour which invades any of the structures at the apex of the chest, including the most superior ribs or periosteum, the lower nerve roots of the brachial plexus, the sympathetic chain near the apex of the chest or the subclavian vessels.[1]

The Pancoast syndrome occurs when the tumour invades the C8, T1-2 nerve roots and the sympathetic chain and consists of shoulder and arm pain, Horner’s syndrome and weakness and atrophy of the small muscles of the hand.

The presence of Pancoast syndrome is not a prerequisite for a tumour to be defined as a Pancoast tumour.[1] Pancoast tumours account for less than 5% of lung malignancies. They are considered a distinct group because of their location in the lung apex where radical treatment options are challenging due to the surrounding clinically important major blood vessels and nerves and because of their unique clinical presentation.

**Diagnostic work-up**

The aim of the diagnostic work-up is to determine whether the tumour can be resected with an acceptable complication rate and whether the patient is fit for surgical intervention.

In addition to the standard diagnostic tests of full blood count, biochemical evaluation, full respiratory function tests, computed tomography (CT scan) of chest and abdomen and positron emission tomography (PET) scan, magnetic resonance imaging (MRI) should be performed. An MRI is superior to CT in assessing structures of the thoracic inlet.[2]

Absolute and relative contra-indications to surgery based on preoperative imaging findings have been suggested.[3] Absolute contraindications include: distant metastases, N2 or N3 nodal disease, >50% vertebral body involvement, brachial plexus involvement above T1 nerve, and invasion of oesophagus/trachea. Relative contraindications to surgery include N1 or N3 nodal disease, invasion of the subclavian artery, <50% vertebral body involvement, intraforaminal extension, invasion of the common carotid or vertebral artery.

**Treatment**

No Phase III study has addressed the optimal management of Pancoast tumour.
Resectable disease

In patients deemed technically and medically fit for surgical resection, pre-operative concurrent chemoradiation followed by surgery is currently recommended as the standard treatment option for patients with Pancoast tumours.

This recommendation is based on the results of two Phase II studies conducted in a group of highly selected patients. In the North American intergroup 0160/Southwest Oncology Group (SWOG) 9416, 111 patients with T3-T4 N0-N1 tumours were treated with preoperative cisplatin and etoposide and concurrent radiation to 45Gy in 25 fractions. Following restaging at two to four weeks, patients with stable or responsive disease underwent thoracotomy. All patients were to receive an additional two cycles of chemotherapy. With this approach 75% (83 of 111) patients completed the entire treatment regimen. A complete resection (R0) was possible in 75 patients (90%) and gross total resection (R0 or R1) in 76 patients (92%). A five-year survival of 44% was reported for the entire group and for cases in which a complete response was achieved, the five-year survival was 54%. The authors reported these results were achieved with acceptable morbidity and mortality. The mortality rate was 2.7%.[4] There was no information on quality of life.

In the Japan Clinical Oncology Group (JCOG) 9806 Phase II trial, 76 patients received a regimen of two cycles of chemotherapy (mitomycin, vindesine and cisplatin) with concurrent radiation (45Gy/25f in a split-course) followed by surgical resection. Fifty-seven (76%) patients completed the regimen and a pathologic complete resection (R0) was achieved in 51 patients (68%). The five-year disease-free and overall survival rates were 45% and 56% respectively.[5] The mortality rate was 1.2% and quality of life was not addressed.

The results achieved with trimodality therapy reported in these Phase II trials appear superior to results achieved with single modality (radiation therapy alone) or bimodality therapy (radiation followed by surgery) reported in historical series. Radiotherapy alone was reported to achieve palliation of pain in 75% of patients but longterm survival remained poor with five-year survival figures of 5 -23%.[7] A review of 23 studies employing bimodality therapy of radiation followed by surgical resection demonstrated a mean five-year survival of 36.5%.[7] Local relapse was reported in 40% of patients undergoing bimodality therapy.[8] It must be remembered that many of these studies did not include highly selected patients, were conducted before CT and MRI were available and used outdated radiotherapy techniques by today’s standards.

The optimal regimen for preoperative therapy has not been established. There are concerns that the radiation dose employed in the Phase II preoperative chemoradiotherapy regimens is relatively low. This is of importance because, if an incomplete resection were performed, adjuvant radiation therapy would be offered. Thus the total radiation dose would be delivered in a split-course fashion which may allow tumour repopulation to occur resulting in suboptimal local control.[9] More intensive preoperative regimens using doses approaching 60Gy[10] or hyperfractionated accelerated radiation therapy[12] have been evaluated in single institution series and found to be feasible and tolerable. A regimen of accelerated radiotherapy (66Gy in 24 fractions, 2.75Gy/f given over 32 days, using concomitant boost) and concurrent daily cisplatin 6mg/m2 followed by surgical resection has been employed in the Netherlands.[13][14] The pathological complete response rate was 53% and the two and five-year overall survival was 74% and 33% respectively but severe late toxicity was seen in three long-term (>5 years) survivors.
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No studies have determined whether, in cancers deemed resectable at diagnosis, preoperative chemoradiation therapy is superior to surgical resection followed by postoperative chemoradiation.

The results of a single institution prospective Phase II trial of surgery followed by concurrent chemoradiation therapy for Pancoast tumours have been reported. Thirty-two patients with resectable or marginally resectable tumours treated at the MD Anderson Cancer Centre underwent segmentectomy or lobectomy with en bloc resection of the involved chest wall and complete nodal staging. Radiation therapy to a dose of 60Gy in 50 twice daily fractions of 1.2Gy if margins were negative, and 64.8Gy in 54 twice daily fractions of 1.2Gy if margins were positive, commenced 14 to 42 days post surgery and was given concurrently with two cycles of cisplatin and etoposide. The protocol completion rate was 78%. Gross total resection was achieved in all patients. The five year DFS and OS were 45% and 50% respectively. The authors concluded that surgery followed by postoperative chemoradiation is safe and effective treatment for marginally resectable superior sulcus tumours.

Unresectable disease

There are no data on how patients who are fit for radical treatment, but have unresectable disease, should be managed. Extrapolation from the data for locally advanced non-Pancoast stage III NSCLC suggests that the concurrent administration of chemotherapy and radiotherapy is the optimal treatment approach (see What is the recommended treatment approach for the definitive management of patients with good performance status and inoperable Stage III disease?).

A regimen of accelerated radiotherapy (66Gy in 24 fractions, 2.75Gy/f given over 32 days, using concomitant boost) and concurrent daily cisplatin 6mg/m2 has been employed in the Netherlands. The five-year locoregional disease-free survival was 48% and the two and five-year overall survival was 31% and 18% respectively.

For patients who are not fit for radical treatment, radiotherapy alone can offer palliation of pain.

Evidence summary and recommendations

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<th>Evidence summary</th>
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<td>For Pancoast tumours deemed to be resectable, 2 Phase II studies of trimodality</td>
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**Evidence-based recommendation**

In patients deemed technically and medically fit for surgical resection, preoperative concurrent chemoradiation followed by surgery is an acceptable treatment option for patients with Pancoast tumours.

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**Evidence-based recommendation**

For patients with unresectable Pancoast tumours and good performance status, the concurrent administration of chemotherapy and radiotherapy is recommended.

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**Evidence summary**

Radiation therapy alone can be used to palliate symptoms in patients with unresectable Pancoast tumours and poor performance status or distant metastases.

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**References**


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