Lung cancer: A focus on the new lines of management

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Received April 26, 2016; Accepted April 27, 2016; Published May 16, 2016

Abstract

Lung cancer, also known as lung carcinoma is a malignant lung tumor characterized by uncontrolled cell growth in tissues of the lung. There are two main types of lung cancer; small cell lung cancer and non-small cell lung cancer and the most common symptom is coughing up blood. Treatment for lung cancer depends on the cancer’s specific cell type, spread, and the person’s status. Common treatments include palliative care, surgery, chemotherapy, and radiation therapy. Targeted therapy of lung cancer is growing in importance for advanced lung cancer.

Key words: Lung; Cancer; Focus; Management

1 Introduction

Cancer is a group of diseases characterized by unregulated cell growth and differentiation [1]. Lung cancer is a malignant tumor of the lung characterized by uncontrolled cell growth in tissues of the lung [2]. If left untreated, this growth can spread beyond the lung by the process of metastasis into nearby tissue or other parts of the body [3]. Most cancers that start in the lung, known as primary lung cancers, are carcinomas [4]. The two main types are small-cell lung carcinoma (SCLC) and non-small-cell lung carcinoma (NSCLC) [5]. The most common symptoms are coughing up blood, weight loss, shortness of breath, and chest pains [6].

The majority of cases of lung cancer are due to long-term tobacco smoking. About 10–15% of cases occur in people who have never smoked [7]. These cases are often caused by a combination of genetic factors and exposure to radon gas, asbestos, second-hand smoke, or other forms of air pollution [8,9]. Lung cancer may be seen on chest radiographs and computed tomography (CT) scans. The diagnosis is confirmed by biopsy which is usually performed by bronchoscopy or CT-guidance [10]. Prevention is by avoiding risk factors including smoking and air pollution [11]. Worldwide in 2012, lung cancer occurred in 1.8 million people and resulted in 1.6 million deaths. This makes it the most common cause of cancer-related death in men and second most common in women after breast cancer [12]. The most common age at diagnosis is 70 year. Overall, 17.4% of people in the United States diagnosed with lung cancer survive five years after the diagnosis, while outcomes on average are worse in the developing world [13].

Treatment for lung cancer depends on the cancer’s specific cell type, how far it has spread, and the person’s performance status. Common treatments include palliative care, surgery, chemotherapy, and radiation therapy. Targeted therapy of lung cancer is growing in importance for advanced lung cancer [14].

2. Lung cancer surgery

It is indicated in non-small cell lung cancer, stages IA, IB, IIA, and IIB are suitable for surgical resection [15]. In performing surgery to treat lung cancer, the doctor may utilize one of two approaches (Thoracotomy and VATS). In reviewing these options, it is important to note that both accomplish the very same purpose. The only difference between them is the method of accessing the problem site. In simpler terms, for both surgical approaches, the “what” [gets done inside your body] is the same;
it's only the “how” it gets done that change.

2.1. Traditional Open Surgery (Thoracotomy)

The first approach that surgeons may use to treat lung cancer is called thoracotomy. This procedure would be described as the more traditional open surgery, serving as the only surgical option to treat lung cancer until more advanced medical techniques and equipment were popularized in the 1990s. Utilizing this approach, a surgeon removes all or part of a lung through a large incision on one side of the chest (thorax). To reach the lung, instruments called retractors are applied to open the chest cavity at the site of the incision and spread the ribs (surrounding the lungs) wider apart to allow optimal access to the problem site. When a patient has had previous surgeries or if the tumor is very centrally located, an open approach may be undertaken [16].

2.2. Minimally Invasive Surgery VATS

Involves insertion of a long, thin tube (Thoracoscope) through a small incision, or port. The thoracoscope’s miniature camera allows the surgeon to view and examine the chest cavity. Additional specially designed instruments inserted through one or two more ports enable the surgeon to remove tissue. For more extensive operations, such as lung resection for cancer, an extra incision measuring about 5 centimeters is made for the removal of the lung tissue [17].

2.3. Benefits of VATS over Traditional Open Approach

VATS has faster recovery and return to normal activities, shorter hospital stay, less pain, little scarring, minimal blood loss, no cutting of the ribs or breastbone (sternum) and possible improved cure rates for cancer than the traditional open approach [18]. All surgical procedures may carry a risk and complications may occur. Possible complications include the risks associated with the medications and methods used during surgery, the risks associated with any surgical procedure, and the risks associated with the patient’s medical condition and history. Risks specific to VATS include the possibility of conversion to an open procedure and the risks specific to an open procedure [19].

3. Radiotherapy

Radiotherapy uses high energy rays to kill cancer cells. Cancer specialists use radiotherapy to treat all types of lung cancer. For early stage lung cancer, the radiotherapy may aim to get rid of the cancer completely. For non-small cell lung cancer you may have radiotherapy on its own. Or you may have it with another treatment, such as chemotherapy or surgery [20].

A refinement of this technique is continuous hyper fractionated accelerated radiotherapy (CHART), in which a high dose of radiotherapy is given in a short time period [21]. Postoperative thoracic radiotherapy generally should not be used after curative intent surgery for NSCLC [22]. Some people with mediastinal N2 lymph node involvement might benefit from post-operative radiotherapy [23]. For potentially curable SCLC cases, chest radiotherapy is often recommended in addition to chemotherapy [10].

If cancer growth blocks a short section of bronchus, brachytherapy (localized radiotherapy) may be given directly inside the airway to open the passage. Compared to external beam radiotherapy, brachytherapy allows a reduction in treatment time and reduced radiation exposure to healthcare staff [24]. Evidence for brachytherapy, however, is less than that for external beam radiotherapy [25]. Prophylactic cranial irradiation (PCI) is a type of radiotherapy to the brain, used to reduce the risk of metastasis. PCI is most useful in SCLC. In limited-stage disease, PCI increases three-year survival from 15% to 20%; in extensive disease, one-year survival increases from 13% to 27% [26].

Recent improvements in targeting and imaging have led to the development of stereotactic radiation in the treatment of early-stage lung cancer. In this form of radiotherapy, high doses are delivered over a number of sessions using stereotactic targeting techniques. Its use is primarily in patients who are not surgical candidates due to medical comorbidities [27]. For both NSCLC and SCLC patients, smaller doses of radiation to the chest may be used for symptom control (palliative radiotherapy) [28].

4. Chemotherapy

The chemotherapy regimen of choice depends on the tumor type. Small-cell lung carcinoma (SCLC), even relatively early stage disease, is treated primarily with chemotherapy and radiation. Chemotherapy improves survival and is used as first-line treatment, provided the person is well enough for the treatment [29]. Typically, two drugs are used adjuvant chemotherapy refers to the use of chemotherapy after apparently curative surgery to improve the outcome. In NSCLC, samples are taken of nearby lymph nodes during surgery to assist staging. If stage II or III disease is confirmed, adjuvant chemotherapy improves survival by 5% at five years [30]. Adjuvant chemotherapy for people with stage IB cancer is controversial, as clinical trials have not clearly demonstrated a survival benefit [31]. Chemotherapy before surgery in NSCLC that can be removed surgically also appears to improve outcomes [32]. The NSCLC Meta-Analyses Collaborative Group recommends if the recipient wants and can tolerate treatment, then chemotherapy should be considered in advanced NSCLC [33].

4.1. Treatment of small cell lung cancer

Treatment protocols for small cell lung cancer (SCLC) are provided below, including first-line therapy, therapy for limited-stage disease, and therapy for extensive-stage disease.

4.1.1. Treatment recommendations for limited-stage SCLC

Limited-stage disease is typically treated with a combination of chemotherapy and radiation. Sequential therapy can also be given for limited-stage disease for patients unable to tolerate concurrent chemoradiation; chemotherapy is given first, followed by radiation therapy because of the high rate of responsiveness to chemotherapy for SCLC. T3-4 tumors due to multiple ipsilateral lung nodules are treated as extensive-stage disease. Radiotherapy for limited-stage disease should start with cycle 1 or 2 of chemotherapy [34].

4.1.2. Second-line chemotherapy for relapsed or refractory disease

Second-line chemotherapy is until disease progression as tolerated in some cases. Patients who have relapsed disease more than 6 months after completing first-line chemotherapy can be
treated with that original first-line regimen (typically a platinum-based doublet) [34]. Carboplatin AUC 5 plus irinotecan 50 mg/m2 [35] or Topotecan 2.3 mg/m2 [36] or Cisplatin 30 mg/m2 plus irinotecan 60 mg/m2 plus irinotecan 60 mg/m2 [37] or Paclitaxel 80 mg/m2 are usually used [38].

4.1.3. Third-line chemotherapy for relapsed or refractory disease

Etoposide 50 mg/m2 or topotecan 2.3 mg/m2 [38] or carboplatin AUC 5 plus irinotecan 50 mg/m2 or Cisplatin 60 mg/m2 plus irinotecan 60 mg/m2 are typically used [37]. Patients with mixed SCLC/non-SCLC histology should be given the same treatment as patients with SCLC. Prophylactic cranial irradiation is recommended for SCLC patients with a complete or partial remission (total of 25 Gy in 10 fractions or 30 Gy in 10-15 fractions). Dose dense or dose escalation chemotherapy regimens are not recommended outside of a randomized clinical trial. Patients with brain metastases can receive chemotherapy prior to brain radiation due to high response rates with chemotherapy [34]. Advancement in treatment has come with the emergence of immune checkpoint inhibitors. Studies are now investigating the administration of single-agent pembrolizumab in patients with non-SCLC [39]. A study evaluating treatment of patients with stereotactic body radiation therapy concluded that it is a promising alternative to surgery for patients with stage I non-SCLC [40].

4.2. Treatment of non-small cell lung cancer

Surgery is recommended for patients with stage I or II non–small cell lung cancer (NSCLC) and may provide the best possibility for a cure. Surgery (radiation if the patient is not a surgical candidate), with or without adjuvant chemotherapy based on risk factors, for stages IB and II is generally appropriate. Adjuvant chemotherapy after surgical resection provides an absolute increase in 5-y survival. No benefit has been shown for adjuvant chemotherapy after surgery for stage I disease; the benefit of adding adjuvant chemotherapy increases as disease stage increases. Stereotactic body radiotherapy (SBRT) may be used in early-stage NSCLC tumors that are smaller than 5 cm without lymph node involvement. This has become a viable and effective option for patients with early-stage NSCLC who are not surgical candidates and in those with significant comorbidities [41].

4.2.1. Adjuvant chemotherapy regimens for stage I or II NSCLC

With chemotherapy for stage I or II NSCLC, the goal is to complete four cycles. Acceptable adjuvant chemotherapy regimens include cisplatin 50mg/m2 plus vinorelbine 25 mg/m2 or Cisplatin100mg/m2 plus etoposide 100 mg/m2 [41]. Patients with comorbidities or patients not able to tolerate cisplatin may alternatively use carboplatin AUC 6 plus paclitaxel 200 mg/m2 [42].

4.2.2. Chemotherapy for Stage IIIa or IIIb disease

Treatment recommendations include the use of concurrent chemotherapy and radiation, or chemotherapy and radiation can be given sequentially if necessary. Selected patients (predominantly those with stage IIIa) may be surgical candidates; these patients may receive chemotherapy alone or chemotherapy with radiation before surgical resection. Stage IIIa and IIIb disease are typically treated with a combination of chemotherapy and radiation if the patient is not a surgical candidate [41].

Chemotherapy and radiation therapy are preferably given concurrently, but in patients with poor performance status, these therapies may be given sequentially; the decision to treat the patient with concurrent chemoradiation rather than surgery, radiation, or chemotherapy individually should be made by a multidisciplinary tumor board (including a medical oncologist, radiation therapist, and thoracic surgeon) [43]. The chemotherapy/radiation therapy includes cisplatin 50 mg/m2 plus etoposide 50 mg/m2 [44] or cisplatin 100 mg/m2 plus vinblastine 5 mg/m2 [45] or Carboplatin AUC 2 plus paclitaxel 50 mg/m2 [46] or Carboplatin AUC 5 plus pemetrexed 500 mg/m2 [47] or Cisplatin 75 mg/m2 plus pemetrexed 500 mg/m2 [48]. The sequential chemotherapy/radiation therapy includes cisplatin 100 mg/m2 plus vinblastine 5 mg/m2 followed by radiation therapy [49].

4.2.3. Chemotherapy for stage IV or recurrent disease

Patients with metastatic disease (stage IV) or recurrent disease after primary therapy should be considered for chemotherapy in order to improve quality of life, palliate symptoms, and improve overall survival [50]. The goal is to treat for four to six cycles unless otherwise specified. Chemotherapy regimens, including platinum-based doublets such as cisplatin 75 mg/m2 plus paclitaxel 175 mg/m2 or Cisplatin 100 mg/m2 plus gemcitabine 1000 mg/m2 or Cisplatin 75 mg/m2 plus docetaxel 75 mg/m2 or carboplatin AUC 6 IV plus paclitaxel 175-225 mg/m2 or carboplatin AUC 5 plus gemcitabine 1250 mg/m2 [51]. Patients with contraindications to carboplatin or cisplatin are treated with gemcitabine 1100 mg/m2 plus docetaxel 100 mg/m2 [52]. Denosumab is a monoclonal antibody directed against receptor activator of nuclear factor kappa-B ligand. It may be useful in the treatment of bone metastases [55].

5. Targeted therapy

Several drugs that target molecular pathways in lung cancer are available, especially for the treatment of advanced disease. Erlotinib, gefitinib and afatinib inhibit tyrosine kinase at the epidermal growth factor receptor. Denosumab is a monoclonal antibody directed against receptor activator of nuclear factor kappa-B ligand. It may be useful in the treatment of bone metastases [55].

6. Bronchoscopy

Several treatments can be administered via bronchoscopy for the management of airway obstruction or bleeding. If an airway becomes obstructed by cancer growth, options include rigid bronchoscopy, balloon bronchoplasty, stenting, and microdebridement [56]. Laser photosection involves the delivery of laser light inside the airway via a bronchoscope to remove the obstructing tumor [57].

7. Palliative care

Palliative care when added to usual cancer care benefits people even when they are still receiving chemotherapy. These approaches allow additional discussion of treatment options and
provide opportunities to arrive at well-considered decisions. Palliative care may avoid unhelpful but expensive care not only at the end of life, but also throughout the course of the illness. For individuals who have more advanced disease, hospice care may also be appropriate [57].

8. Conclusion

Most lung cancers that start in the lung, known as primary lung cancers, are carcinomas, there are two main types 1)(SCLC) and the most common symptoms are coughing. Lung cancer is treated by many approaches like surgery, radiotherapy, chemotherapy and other lines of treatment. The treatment of lung cancer depends on its type, whether SCLC or NSCLC. The most effective preventive method for lung cancer is to avoid the risk factors such as smoking and air pollution

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