Introduction

Lung cancer is the most common cancer in the adult population in Hong Kong. According to the Hong Kong cancer registry statistics in 2012, there was a total of 4610 new cases registered. This accounts for 20.6% of all cancers in male patients and 12.3% in female patients in our locality. Lung cancer has a great impact on mortality and accounts for 29.2% of all cancer-related deaths in Hong Kong.

Availability of prompt and suitable management strategy for lung cancer patients, particularly those suffering from early-stage non–small-cell lung cancer (NSCLC), can effectively reduce the overall mortality rate. In pursuance of this aim, it is heavily dependent on accurate TNM staging. Compared to contrast computed tomography (CT) thorax, positron emission tomography–computed tomography (PET/CT) has great clinical impact, with significant reduction of futile curative surgery.

Abstract

The aim of this retrospective study is to evaluate the clinical impact and efficacy of fluorodeoxyglucose (FDG) positron emission tomography–computed tomography (PET/CT) on management decisions for patients suffering from clinically operable non–small-cell lung cancer (NSCLC). A retrospective review of 186 potentially operable NSCLC patients who underwent whole-body PET/CT examination in 2012 was performed. The patients were further analyzed via the electronic patient record (ePR) system for relevant findings. Overall change in management was assigned if a patient avoided unnecessary surgery due to disease upstaging or if a patient underwent further neoadjuvant treatment or investigation before the curative surgery. Of all 186 subjects, 65 (34.9%) became inoperable after PET/CT due to disease upstaging. The remaining 121 (65.1%) of patients remained operable after PET/CT examination. Nineteen out of 121 potentially operable patients did not receive curative surgery eventually, as 11 patients had poor clinical condition and 8 patients refused surgery. One hundred two out of 186 (54.8%) patients received curative operation following PET/CT. Among these 102 individuals, 97 patients (95%) proceeded to surgery without further neoadjuvant treatment or other investigatory procedures. Of the remaining 5 patients, 4 (3.9%) received neoadjuvant treatment and 1 (1.0%) had further investigation after PET/CT. Seventy of the 186 (37.6%) patients underwent changes in management plans after PET/CT study. Out of the 186 individuals, a subgroup of 141 (75.8%) patients underwent dedicated CT thorax before PET/CT examination. Forty-seven (33.3%) patients had avoided futile surgery due to disease upstaging. Fifty-one of the 141 (36.2%) patients underwent changes in management plans after PET/CT. PET/CT had great clinical impact, with significant reduction of futile curative surgery.

Keywords: Clinical impact, curative surgery, fluorodeoxyglucose positron emission tomography–computed tomography, potentially operable non–small-cell lung cancer
computed tomography (PET/CT) demonstrated better ability in determining the regional nodal status and staging distant metastatic disease. With the Hospital Authority Standard Service protocol, introduced since April 2012, potentially operable NSCLC patients would be exempted from the charges for PET/CT for the purpose of preoperative staging. The objective of this study is to evaluate the clinical impact and efficacy of fluorodeoxyglucose (FDG) PET/CT at our center on management decisions for patients suffering from potentially operable NSCLC.

**Materials and Methods**

A retrospective review of 186 potentially operable NSCLC patients who underwent whole-body PET/CT examination (from vertex to upper thigh) at the Clinical Positron Tomography Centre, Queen Elizabeth Hospital, Hong Kong was performed. All patients were exempted from the standard charges for PET/CT under the Hospital Authority (HA) PET Standard Service. The study period ranged from June 1, 2012 to November 30, 2012. All the included patients underwent PET/CT for preoperative staging. The referral criteria for the PET Standard Service included patients with clinically operable NSCLC, as judged by the referring cardiothoracic surgeons or other physicians. Patients were then further analyzed via the electronic patient record (ePR) system for relevant histological, radiological, and surgical findings. Histological correlation was obtained in patients who underwent surgical resection. Overall change in management was assigned if a patient was to avoid unnecessary surgery due to disease upstaging or downstaging, or if a patient underwent further neoadjuvant treatment or investigation (radiological or histological) before the curative surgery. The clinical impact of PET/CT on the subsequent management of patients was evaluated. Statistical analysis was performed using the SPSS software package (Version 15.0, SPSS, Inc., Chicago, IL, USA).

Concerning our PET/CT protocol, all patients were fasted at least 6 h before intravenous FDG injection. Scanning was initiated 60 min after administration. Images were taken from the head to the proximal thigh with PET/CT scanner (Discovery LS, GE Healthcare) in our department with a spatial resolution of 6.6 mm in the center of the field of view. Then, 370 MBq of FDG was injected intravenously. Seven bed positions were performed with 3 min per bed position. In the delayed image, 5 min per bed position was performed in order to partially compensate for the count decay. Four-slice CT was performed for attenuation correction, lesion localization, and characterization. The CT scanner had a rotating anode oil-cooled x-ray tube installed that operated at 140 kV. It was operated from 120 mA to 200 mA according to the patient size. Rotate-fixed ring geometry was used. Images were acquired in the helical mode with slice thickness of 5 mm (beam coverage of 2 cm in each gantry rotation). Cross-sectional reconstruction images with the matrix size of 512 × 512 were produced. The obtained images were reconstructed using ordered subsets expectation maximization (OSEM) iterative reconstruction algorithm. Regions of interest were drawn for FDG uptake quantification on visible lesions with increased uptake, and the maximum standardized uptake value (SUVmax) was semiquantitatively analyzed with the equation $\text{SUV} = \frac{A}{(\text{ID}/\text{BW})}$, where $A$ represents the decay- and attenuation-corrected activity in tissue (in MBq per milliliter), $\text{ID}$ represents the injected dose of FDG (in MBq), and $\text{BW}$ represents the patient’s body weight (in g). Delayed 3.5-h thoracic PET/CT series was acquired after FDG injection in an equivocal case.

**Results**

Of all 186 patients, 164 (88.2%) patients had histologically proven NSCLC before PET/CT. Twenty-two (11.8%) patients were clinically diagnosed as suffering from NSCLC by the referring cardiothoracic surgeon. Of the histologically proven NSCLC patients, 105 patients had adenocarcinoma, 40 patients had squamous cell carcinoma, 3 patients had lymphoepithelioma-like carcinoma of the lung, 2 patients had adenosquamous carcinoma, and 1 patient had primary synovial sarcoma. The remaining 13 patients suffered from NSCLC without further histological characterization.

Of all the 186 potentially operable subjects, 65 (34.9%) patients became inoperable after PET/CT due to disease upstaging in either T, N, or M status [Figures 1–4]. The remaining 121 (65.1%) patients were potentially operable after PET/CT exam. A total of 19 out of 121 potentially operable patients did not receive curative surgery, as 11 patients had poor general condition and 8 patients refused surgery. Eventually, 102 out of 186 (54.8%) patients received curative operation following PET/CT. Among the 102 patients who received curable surgery after PET/CT, 97 patients (95%) proceeded to surgery without further neoadjuvant treatment or investigatory procedure. Of the remaining patients, 4 (3.9%) patients received neoadjuvant treatment after PET/CT (including chemotherapy or irradiation therapy) and 1 (1.0%) patient had further investigation (mediastinoscopy) after PET/CT. Within our studied sample, 70 of 186 (37.6%) patients underwent changes in management plans after PET/CT study. Details of TNM upstaging among these 70 patients are summarized in Table 1 with references to the seventh edition of the American Joint Committee on Cancer Cancer Staging Manual (Seventh AJCC).
Of all 186 patients, 141 (75.8%) patients received dedicated CT thorax before PET/CT examination. Among these 141 patients, 47 (33.3%) patients avoided futile surgery due to disease upstaging. All 4 patients who received neoadjuvant treatment had prior CT thorax before PET/CT examination. Fifty-one of 141 (36.2%) patients underwent changes in management plans after PET/CT study among patients with prior CT thorax.

**Discussion**

FDG PET/CT has played a crucial role in the diagnosis and clinical management of lung cancer in the past decade. According to the National Institute for Clinical Excellence (NICE) guidelines, PET/CT has been advocated for patients with potentially treatable NSCLC, or in cases where conventional CT staging is indeterminate. Other studies suggested that FDG PET/CT
The point prevalence of detecting unknown brain metastases in oncology patients is not uncommon. We have shown that FDG PET/CT can demonstrate interval increase in FDG metabolism in delayed imaging. We therefore proposed that FDG PET/CT cannot reliably differentiate malignant SPNs from pulmonary tuberculomas, even with the assistance of dual-phase FDG PET/CT technique. Further interventions or investigations remained crucial in that subgroup of patients.

In our FDG PET/CT oncology protocol, we always incorporate the brain within the range of scanning. We strive to detect the previously unknown large-sized metastatic brain lesions that can lead to significant morbidity and mortality; despite all that, we recognize that FDG PET is insensitive in picking up small brain lesions due to the limited spatial resolution and intense FDG uptake in normal brain tissue. We performed a retrospective review of 1876 patients in 2009 to investigate the prevalence and clinical impact of detecting unknown brain metastases in oncology patients. The point prevalence of detecting unknown cerebral metastases by PET/CT was 2.1%. Of the patients with newly diagnosed brain metastases confirmed with either magnetic resonance imaging (MRI) or CT, 94.1% received immediate treatment for cerebral metastasis. Interestingly, among the patients with newly diagnosed cerebral metastases in our study, 62.5% suffered from primary bronchogenic carcinoma, while this disease entity accounted for only 17.4% of our total referrals during the study period. Our results further consolidate the generally accepted fact that the most common primary site of metastatic brain lesion is the lung.

We believed that inclusion of the brain in FDG PET/CT scanning protocol in lung cancer patients may be useful for the evaluation of sizable cerebral metastases, such that timely treatment can be offered to reduce morbidity and mortality.

PET/CT guided the referring cardiothoracic surgeons or physicians to abandon unnecessary curative surgical intervention in 65 (34.9%) out of the 186 patients initially assigned to undergo curative thoracotomies. Our findings may carry economic impact along with prevention of unnecessary curative surgery, which is worth further relevant investigations.

This study had several limitations. First, the patients included belonged to a highly selected group of early-stage NSCLC patients who were potentially operable. Second, PET/CT scans in most of our recruited individuals were performed using routine oncology protocols without dedicated three-dimensional (3D) brain imaging, which were suboptimal for the detection of cerebral metastases. Third, in our PET/CT protocol, intravenous contrast material was not given in most of our patients. With the low-dose CT used in our oncology PET/CT protocol, it should be noted that the diagnostic accuracy of CT in this study can be lower than that of conventional diagnostic CT.

To conclude, FDG PET/CT changed clinical management decisions in 37.6% patients with potentially operable NSCLC in our study. Availability of PET/CT had led to a significant reduction of futile curative surgery.

| Total no. of patients with change in clinical management plan after PET/CT | No. of patients upstaged to stage IIIA* (either T1N3M0/T2N3MO/T3N3MO/T4N2MO/T4N3MO) and become inoperable after PET/CT | No. of patients upstaged to stage IV* (any T/any N with M1a or M1b) and become inoperable after PET/CT | No. of patients upstaged to stage IIIB* (either T1N3M0/T2N3MO/T3N3MO/T4N2MO/T4N3MO) and become inoperable after PET/CT |
|---|---|---|---|
| 70 | 18 | 47 | 5 |

*TNM staging according to the latest (seventh) AJCC cancer staging edition. PET/CT: Positron emission tomography-computed tomography
34.9% of patients. The inclusion of FDG PET/CT for the evaluation of lung cancer can have significant clinical impact. With significant improvement in disease staging, unnecessary curative surgery can be spared, with a reduction in the number of futile interventions.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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