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Measurement of primary tumor volume by PET–CT to evaluate risk of mediastinal nodal involvement in NSCLC patients with clinically negative N2 lymph nodes

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ABSTRACT

Aim: The study aimed to determine a prognostic value of primary tumor volume measured on the basis of integrated positron emission tomography–computerized tomography (PET–CT) in terms of mediastinal nodal metastases (N2) prediction in non-small-cell lung cancer (NSCLC) patients with PET–CT N2 negative lymph nodes.

Methods: The records of 70 potentially operable NSCLC patients treated with surgical resection were analyzed. All patients underwent diagnostic, preoperative PET–CT, which was the basis for tumor volume calculations as well as the evaluation of N2 nodes status. The logistic regression analysis was employed to determine correlation between mediastinal nodal involvement and volume of primary tumor (izoSUV2.5 volume), that is the volume of primary tumor inside SUV 2.5 line, tumor histology, location (peripheral vs. central), hilar node status.

Results: A statistically significant correlation between mediastinal node involvement and izoSUV2.5 volume, tumor histology, locations peripheral vs. central and hilar node status was found. The risk of mediastinal lymph node metastasis is 24% for tumor volume of 100 cm^3 and increases up to 40% for tumor volume of 360 cm^3. An increase of tumor volume by 1 cm^3 increases the risk of lymph node disease by 0.3%. Tumor histology adenocarcinoma vs. squamous cell carcinoma increases the risk of mediastinal lymph node involvement by 195%, location central vs. peripheral by 68% and hilar node involvement by 166%.

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Conclusions: The study demonstrates that izoSUV2.5 volume of primary tumor may be considered as a prognostic factor in NSCLC patients, since it strongly correlates with mediastinal lymph node pathological status. This correlation is modified by primary tumor location, histology and hilar node involvement.

1. Background

The most absorbing issue in modern oncology of non-small-cell lung cancer (NSCLC) is the implementation of integrated positron emission tomography–computerized tomography (PET–CT) to the diagnostic process. PET–CT offers superior sensitivity and specificity compared to CT or PET alone and may improve staging accuracy. Mediastinal lymph nodes status in NSCLC patients has important therapeutic and prognostic implications. The current consensus is that a positive mediastinal nodal uptake on PET–CT should be verified histologically by mediastinoscopy or transbronchial needle aspiration while negative uptake in the mediastinum should proceed to resection. A significant proportion of PET–CT mediastinum negative cases will turn out to be positive following resection. There is a high probability that tumor volume has great value in predicting lymph node involvement, a feature, which decreases 5-year survival by 30–40%.

1.1. Aim

The study aimed to determine a prognostic value of primary tumor volume measured on the basis of PET–CT (izoSUV2.5 volume) in terms of mediastinal nodal metastases prediction in NSCLC patients.

2. Material and methods

2.1. Selection of patients

Between September 2008 and December 2009, a total number of 70 consecutive potentially operable NSCLC patients were treated with a curative intent. From the total number of 425 evaluated by PET–CT newly diagnosed NSCLC patients, 355 (83%) presented a more advanced disease. Diagnostic PET–CT performed in all 70 did not depict mediastinal lymph node involvement (PET–CT N2 negative patients). All these patients were treated radically, 62 of them underwent anatomical resections and 8 of them wedge resections. As regards anatomical resections, 8 pneumonectomies – all left-sided, 6 inferior bilobectomies and 48 lobectomies (22 right-sided and 26 left-sided) were performed. All patients underwent a systematic lymph node dissection and were then examined pathologically. The patients were given antibiotics and antithrombotic prophylaxis perioperatively.

The mean age of patients was 63 years, ranging from 22 to 78; 44 of them were male (62.9%) and 26 female (37.1%). The clinical staging was based on the following criteria: general clinical examination, biopsy, routine blood cell counts, blood chemistry profile, chest X-ray and chest CT, abdominal ultrasonography, bronchoscopy and pulmonary function test. The pathological diagnosis of most patients was squamous cell carcinoma in 35 patients (50%), adenocarcinoma in 26 (37%), large cell carcinoma in 8 (12%) and mucoepidermoid carcinoma in 1 (2%) case. The grading was: G_1 in 1, G_2 in 28, G_3 in 17 and unknown in 24 cases. Primary tumor stage was T1 in 23, T2 in 35, T3 in 12 patients. There were 33 PET N1 positive cases and 37 negative ones. Peripheral location was determined in 55 patients while central in 15.

2.2. Image analysis

All patients underwent PET–CT examination as a routine procedure before the decision of surgery. The whole body scan (Biograph 6 and Biograph 16, Siemens, Erlangen, Germany) was performed for the evaluation of primary tumor, lymph node involvement, distant metastases and tumor volume computations. All patients were fasted for at least 6 h before the examination. Blood glucose levels were determined before injection of 5–7 MBq/kg [^{18}F]fluorodeoxyglucose (FDG). FDG was produced in our own laboratory. Sixty minutes after administration of FDG, PET–CT scans were obtained from the skull base to the ¼ upper level of the hips. Diagnostic CT was done in 6–7 beds, 2 min each, of PET imagining performed according to the height of the patient. Images were reconstructed using 3D iterative reconstruction.[1,2]

Whole body images in DICOM formats were sent online via PACS system (Siemens, Erlangen, Germany) to the external beam radiotherapy treatment planning system. Tumor area was identified and delineated on each PET–CT scan by the oncologist with the assistance of a nuclear medicine specialist, who was unaware of clinical and pathological findings. IzoSUV2.5 volumes, that is the volume of primary tumor inside SUV 2.5 line, were calculated automatically using the True D radiotherapy treatment planning system (Siemens, Erlangen, Germany; Fig. 1).

Lymph nodes greater than 10 mm in the short axis and SUV > 2.5 were interpreted as metastatic.

2.3. Statistical analysis

Pathologically confirmed mediastinal lymph node involvement was the endpoint of the study. The correlation between mediastinal nodal metastasis occurrence (pathologically confirmed) and such parameters as: izoSUV2.5 volume, SUV max, tumor pathological type and grade, primary tumor stage, diameter and location (peripheral vs. central), hilar node status (PET N1) as well as patient's age and sex were determined using the univariate logistic regression. Correlation between statistically significant variables and lymph node involvement were assessed using the multivariate logistic regression