

Positron emission tomography/computed tomography (PET/CT) and CT for N staging of non-small cell lung cancer

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ABSTRACT

Aim The aim of this study is to investigate the possibilities of non-invasive diagnostic imaging methods, positron emission tomography/computed tomography (PET/CT) and CT, in clinical N staging of non-small cell lung cancer (NSCLC).

Methods Retrospective clinical study included 50 patients with diagnosed NSCLC who have undergone PET/CT for the purpose of disease staging. The International association for the study of lung cancer (IASLC) nodal mapping system was used for analysis of nodal disease. Data regarding CT N-staging and PET/CT N-staging were recorded. Two methods were compared using χ^2 test and Spearman rank correlation coefficient.

Results Statistical analysis showed that although there were some differences in determining the N stage between CT and PET/CT, these methods were in significant correlation. CT and PET/CT findings established the same N stage in 74% of the patients. In five patients based on PET/CT findings the staging was changed from operable to inoperable, while in four patients staging was changed from inoperable to operable.

Conclusion PET/CT and CT are noninvasive methods that can be reliably used for N staging of NSCLC.

Key words: pulmonary cancer, multimodal imaging, lymph nodes

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INTRODUCTION

Lung cancer is a malignant disease with the highest mortality rate despite advances in diagnosis, staging and treatment (1). Of the total number of diagnosed lung cancers, 75-85% are classified as non-small cell lung cancer (NSCLC) (2).

Best results in the treatment and long-term survival are achieved when surgical resection of the cancer is possible. Accurate staging of NSCLC is obligatory (3) in order to properly select the patients who will have the benefits of surgical treatment and to mitigate unnecessary surgical procedures in the advanced stages of the disease (4). The NSCLC staging is based on the TNM system, using the tumour (T), node (N) and metastasis (M) evaluations provided by non-invasive and invasive procedures (5). Traditionally, computed tomography (CT) of thorax and upper abdomen is used for the staging of NSCLC, while recently there is a tendency to use positron emission tomography/computed tomography (PET/CT). This method combines anatomic information of CT and metabolic information of the PET (6).

Accurate N staging is an important prognostic factor and is critical in deciding the best treatment option. Stage N1 and N2 of the disease may be resectable, while N3 is considered to be inoperable and could be treated with concurrent chemo-radiation therapy (7).

Mediastinal nodal disease is evaluated using CT scan and more recently PET/CT has been used for the evaluation of metastatic spread in the mediastinal lymph nodes (8). Size of the lymph node is the criterion used on CT scan to distinguish benign from malignant nodes: a node with short axis diameter of more than 1 cm is generally considered to be malignant (9-11).

The use of size cut-off can be problematic because inflammatory lymph nodes larger than 1 cm can be considered as malignant and metastatic lymph nodes smaller than 1 cm can be considered as benign (12). On the other hand, hybrid imaging method PET/CT enables obtaining anatomical data regarding the presence and size of lymph nodes as well as functional information regarding eventual pathological metabolic activity in these lymph nodes (7,13).

The aim of this study was to investigate the possibilities of CT and PET/CT non-invasive diag-

nostic imaging methods in clinical N staging of NSCLC. Results of this study should provide additional information that should be considered when deciding on a diagnostic method to be used for staging of NSCLC, e. g. whether to give the preference to traditional method - CT or insist on the newer method - PET /CT.

PATIENTS AND METHODS

Patients and study design

The retrospective clinical study conducted at the Radiology Clinic of the University Clinical Centre of Sarajevo, Bosnia and Herzegovina, during the period June 2015 – October 2016 included 50 patients with diagnosed NSCLC who have undergone PET/CT for the purpose of disease staging. Before the realisation of PET/CT examination for the purpose of staging, diagnosis of NSCLC was confirmed based on histopathological analysis of tumour tissue samples obtained during bronchoscopy or by biopsy under CT control for all patients included in the study.

Methods

The PET/CT was performed using a scanner GE Discovery (GE Healthcare, General Electric, Milwaukee, Wisconsin, USA). Multislice CT and PET emission data were acquired from the skull to the mid-thigh in all the patients. Image acquisition started 60 min after intravenous injection of 370–550 MBq of ¹⁸F-FDG. CT (120 kV; auto mA: 15-200 mAs; slice thickness for CTAC – 3.75 mm and for interpretation – 1.25 mm; pitch – 1.75; rotation time, 0.8 s) was performed. CT scan was acquired in a middle respiratory position. Directly after CT, the PET acquisition was started. The acquisition time was 1.45 min per bed position (5–8 bed positions per patient). During imaging of the chest, patients were instructed to breathe shallowly. Each position had 35 scanning planes with a 14.6-cm longitudinal field of view and a 1-slice overlap between scanning positions. PET images were reconstructed using CT attenuation correction and an ordered-subset expectation maximization algorithm. Scans were evaluated separately for CT alone and combined PET/CT using standard criteria for the evaluation of CT and PET/CT.

The International Association for the Study of

Lung Cancer (IASLC) nodal mapping system was used for an analysis of nodal disease (14).

CT findings were analysed and the study was interpreted as positive based on shape and size of mediastinal lymph nodes. Lymph nodes were measured on the short-axis diameter and lymph nodes were considered abnormal if they were 1 cm or greater in short axis diameter on CT (15,16).

PET images were analysed qualitatively for regions of focally increased glucose metabolism as well as quantitatively by determining standardized uptake values. An increase in the glucose uptake to a level greater than that in the surrounding tissue at qualitative analysis and a standard glucose uptake value of more than 2.5 were considered to characterize malignancy. For fused PET/CT data sets the same criteria used to determine malignancy among the individual CT and PET data sets were applied. However, lymph nodes with increased glucose uptake were deemed positive for metastatic spread even when they were smaller than 1 cm in short-axis diameter. PET-negative lymph nodes were characterized as benign even when they were larger than 1 cm in short-axis diameter (17).

Data regarding CT N-staging, PET/CT N-staging and sex were also recorded.

Statistical analysis

The test results were analysed using descriptive statistics, which included determining the absolute values (N) and percentage (%). Two methods were compared using χ^2 test and Spearman rank correlation coefficient. Accepted statistical significance was $p < 0.05$.

RESULTS

Of the total of 50 patients, 25 (50%) were males and 25 (50%) were females.

Statistical analysis showed that although some differences in determining the N stage between CT and PET/CT were found there was significant correlation between these two methods ($\rho = 0.723$; $p = 0.0001$). According to both methods the majority of the cases were staged as N2 both according to CT (21; 42.0%) and PET/CT (17; 34.0%) while the least number of cases were staged as N3 both according to CT (5; 10.0%) and PET/CT (10; 20.0%) (Table 1).

Table 1. N staging of patients with diagnosed non-small cell lung cancer (NSCLC) based on positron emission tomography/computed tomography (PET/CT) and CT imaging

N stage	No (%) of patients	
	CT	PET-CT
N0	8 (16.0)	11 (22.0)
N1	16 (32.0)	12 (24.0)
N2	21 (42.0)	17 (34.0)
N3	5 (10.0)	10 (20.0)
Total	50 (100.0)	50 (100.0)

CT and PET/CT findings established the same N stage in 37 (74%), while the staging was not analogous in 13 (26%) patients.

In four (6%) patients PET/CT determined lower N stage of NSCLC comparing to CT, while in nine (18%) patients –PET/CT determined higher N stage comparing to CT (Table 2).

Table 2. Changes of CT based N staging compared to positron emission tomography/computed tomography (PET/CT) findings

N stage CT	No (%) of patients	
	PET-CT change	
Up-staged		
N0	0	
N1	4 (8.0)	in N2
N1	1 (2.0)	in N3
N2	4 (8.0)	in N3
N3	0	
Total	9 (18.0)	
Down staged		
N0	0	
N1	0	
N2	3 (6.0)	in N0
N2	1 (2.0)	in N1
N3	0	
Total	4 (8.0)	

Changes of N stage based on PET/CT findings were presented in 13 patients. In five patients based on PET/CT findings the N stage changed from operable to inoperable (N1 to N2 in four and to N3 in one case), while in four patients staging changed from inoperable to operable (N2 to N0 in three cases and to N1 in one case) (Table 2). Due to small counts it was impossible to conduct valid statistical analysis ($\chi^2 = 58.182$; $p = 0.0000000001$).

DISCUSSION

Considering the increasing number of diagnosed cases of NSCLC and all advances in the therapy of this disease, the correct staging is essential in order to avoid unnecessary surgery (3).

The gold standard for the evaluation of metastatic involvement of hilar and mediastinal lymph nodes is mediastinoscopy. Since the mediastinos-

copy is an invasive method, the tendency is to replace it with non-invasive methods such as PET/CT and CT (6). Numerous studies have demonstrated higher sensitivity and specificity of PET/CT compared to CT in N staging of NSCLC. The conclusion of those studies is that when it comes to N staging NSCLC the preference should be given to PET/CT as a non-invasive method of choice (17,18).

In our study we did not observe a significant difference in N staging based on PET/CT and CT examinations. Such result can be explained by the fact that the CT scans were analysed by a radiologist with extensive experience in thoracic radiology who deals with NSCLC staging on a daily basis. Also, the limited number of patients should be taken into account and the fact that patients did not undergo mediastinoscopy, which is the gold standard for determining the N staging.

However, in our study out of the total number of discrepant findings regarding N staging, based on PET/CT N staging five patients were reclassified from operable stage of the disease to inoperable

stage which assumes chemo-radiotherapy and the postponing of surgical procedures, while four patients were under-staged from inoperable to operable stage of the disease. An additional advantage of PET/CT certainly is that this method allows analysis of larger regions with the consequent possibility of detecting distant metastases which influence the staging of disease, all conducted simultaneously without requiring the patient to be exposed to multiple and different examinations (18). On the other hand CT is, especially in the South East European countries, far more accessible and more widespread method.

In conclusion, both PET/CT and CT are noninvasive methods that can be reliably used for N staging of NSCLC.

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Pozitronska emisiona tomografija/kompjuterizirana tomografija (PET/CT) i CT u N-stagingu nemikrocelularnog karcinoma pluća

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SAŽETAK

Cilj Istražiti mogućnosti neinvazivnih dijagnostičkih slikovnih metoda, pozitronske emisiona tomografije/kompjuterizirane tomografije (PET/CT) i CT-a, u kliničkom N-stagingu nemikrocelularnog karcinoma pluća.

Metode Retrospektivna klinička studija obuhvatila je 50 pacijenata s dijagnosticiranim nemikrocelularnim karcinomom pluća, kojima je urađeno PET/CT u svrhu *staginga* bolesti. Za analizu zahvaćenosti limfnih čvorova bolešću korišten je sistem za mapiranje predložen od strane Međunarodnog udruženja za proučavanje karcinoma pluća. Zabilježeni su podaci koji se odnose na CT N-staging i PET/CT N-staging. Ove dvije metode su komparirane korištenjem χ^2 -testa i Spearmanovog koeficijenta korelacije ranga.

Rezultati Statistička analiza je pokazala, iako su ustanovljene određene razlike u određivanju N-stadija korištenjem CT-a i PET/CT-a, da ove metode pokazuju signifikantnu korelaciju. Nalaz CT-a i PET/CT-a ukazao je na isti N-stadij kod 74% pacijenata. Kod pet pacijenata, na osnovu nalaza PET/CT-a, stadij bolesti je promijenjen iz operabilnog u inoperabilni, dok je kod četiri pacijenta stadij promijenjen iz inoperabilnog u operabilni.

Zaključak PET/CT i CT su neinvazivne metode koje se mogu pouzdano koristiti za N-staging nemikrocelularnog karcinoma pluća.

Ključne riječi: karcinom pluća, multimodalni *imaging*, limfni čvorovi