Standard Uptake Value Predicts Survival in Non–Small Cell Lung Cancer

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Background. Integrated [^{18}F]fluorodeoxyglucose positron emission tomography–computed tomography (PET-CT) scan is a widely used modality in the evaluation of lung cancer. Our goal was to determine the ability of the standard uptake value (SUV) of the primary tumor (SUV-T) and regional lymph nodes (SUV-N) to predict survival.

Methods. From January 2005 through June 2007, 584 consecutive patients undergoing integrated PET-CT scan for suspected lung cancer were studied. Results of integrated PET-CT scans, including the maximum SUV-T and SUV-N, were recorded. A patient was defined as having a positive PET scan if the maximum SUV (T or N) was greater than 2.5. Overall survival was documented from clinical records and the Social Security Death Index. Cox regression analysis was used to evaluate the correlation between SUV and survival.

Results. Among patients with a positive PET scan (n = 329), both SUV-T and SUV-N were predictors of survival. As maximum SUV of the primary mass increased, survival decreased (hazard ratio, 1.05; $p < 0.001$). As maximum SUV of locoregional lymph nodes increased, survival also decreased (hazard ratio, 1.06; $p < 0.001$). Furthermore, among patients with no mediastinal disease identified by PET-CT scan, increased SUV-T continued to predict poor survival (hazard ratio, 1.06; $p = 0.001$).

Conclusions. Local and regional maximum SUVs defined by integrated PET-CT scanning have a strong correlation with survival in patients with non–small cell lung cancer. An elevated SUV is known preoperatively and may assist clinicians in stratifying patients at increased overall risk preoperatively.

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Lung cancer is the most lethal malignancy in this country, with up to 160,000 deaths per year [1] attributable to this disease. As such, the ability to diagnose and treat lung cancer remains a major public health concern. Positron emission tomography–computed tomography (PET-CT) scan, which is widely used in the management of lung cancer, has become an important diagnostic modality in the process of evaluating and staging patients appropriately. The PET scan, which measures the uptake and trapping of radiolabeled glucose by tissues [2], assists in determining the presence of locoregional and metastatic disease. The extent of disease detected by PET-CT scan could impact the decision to operate and guide the need for adjuvant or neoadjuvant therapy.

The results of PET-CT scan may also be able to stratify patients with lung cancer in terms of ultimate prognosis, as has been shown in previous studies [3–6]. Our goals were to determine whether the clinical stage, based on preoperative PET-CT scan, predicts overall outcome and to understand the correlation between standardized uptake value (SUV) and survival.

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Material and Methods

Patients

From January 2005 through June 2007, 584 consecutive patients undergoing integrated PET-CT scan for suspected non–small cell lung cancer were studied, regardless of whether they ultimately underwent surgery. Patients who were determined to have small cell lung cancer were excluded from the study. Approval from the institutional review board was obtained. Qualitative and quantitative results of integrated PET-CT scans, including the maximum SUV [7] of the primary mass (SUV-T) and regional lymph nodes (SUV-N), were recorded. A patient was defined as having a positive PET scan if the maximum SUV (T or N) was greater than 2.5 [8]. Overall survival was documented from clinical records and the Social Security Death Index. Cox regression analysis, Kaplan-Meier analysis, and the log-rank test were used to evaluate the correlation between SUV and survival.

Outcomes

The results of the integrated PET-CT scan, including SUV-T and SUV-N, mass size, presence of lymphadenopathy by CT criteria (>1 cm in short-axis dimension), and location of positivity were recorded. Similarly, the clinical and pathologic stages were determined, using standard TNM classifications [9], in patients who underwent surgery. Survival data was obtained through elec-

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Table 1. Demographics

Patients	584
Age (y), mean	67 ± 0.5
Male	47%
ECOG ≥2	16%
Smoking, current	20%
Pack-years	54 ± 2.6
Smoking, past	59%
Pack-years	46 ± 1.8
Smoking, never	21%

ECOG = Eastern Cooperative Oncology Group.

tronic medical records and verified using the Social Security Death Index.

Surgical procedures were performed by 3 staff surgeons at the Beth Israel Deaconess Medical Center. Each surgical procedure was performed using either video-assisted thoracoscopic surgery or an open approach, depending on patient and tumor characteristics. Preoperative staging of the mediastinum was performed using esophageal ultrasound and endobronchial ultrasound when deemed appropriate. Mediastinal lymph node sampling and dissection were performed routinely as a part of the procedure.

Positron Emission Tomography–Computed Tomography Scan

All patients fasted for greater than 4 hours before the scan. Blood glucose levels were determined before administration of 10 Ci [^{18}F]fluorodeoxyglucose (^{18}FDG). Sixty minutes after administration of ^{18}FDG, PET and CT scans were obtained from the skull base to the level of the hips. All integrated PET-CT scans were reviewed by radiologists who specialized in nuclear medicine techniques. A PET-CT scan was interpreted as positive if the maximum SUV-T or SUV-N of a study exceeded 2.5.

Images obtained from PET scan were reconstructed using standard algorithms. Abnormal ^{18}FDG uptake was defined as areas with activity greater than in surrounding tissue and unrelated to sites with normally increased uptake of tracer (myocardium) or excretion (bladder). For the calculation of SUV, circular regions of interest (≥70 pixels) were drawn on axial images adjacent to areas of increased ^{18}FDG uptake. The SUV was calculated using the following equation:

$$\text{SUV} = \frac{\text{decay} - \text{corrected activity [kBq]/tissue volume [mL]}}{\text{injected} - {}^{18}\text{FDG activity [kBq]/body weight [g]}}$$

When evaluating a mass or a lymph node, the maximum SUV within the structure was used. The highest SUV of any lymph node was used to represent SUV-N.

Statistical Analysis

Continuous variables were summarized by mean and standard error, and categorical variables were summarized by frequency and percentage. Cox proportional hazard model was used to correlate continuous independent variables with survival. The association between SUV and mortality for individual stage or grouping of stages was analyzed in combination with a Cox regression model, controlling for mass size and largest node size. The proportional hazard assumption was tested by the approach proposed by Lin and colleagues [10]. Survival functions of different populations were estimated by Kaplan-Meier estimator and compared by log-rank test. All analyses were performed by SAS 9.1 (SAS Institute Inc, Cary, NC).

Results

Demographics

The study included 584 patients. Table 1 lists the demographics of the patient population. Average age was 67 years. Tissue diagnosis was obtained in 417 patients (71%). Ultimately, 246 patients underwent mediastinoscopy or surgical resection.

Accuracy

Positron emission tomography–computed tomography scan results are listed in Table 2. A PET stage of III or higher was assigned to 36% of patients. The PET-CT scan was positive in the mediastinum in 164 patients (28%). When comparing pathologic data with PET-CT results in patients who underwent mediastinoscopy or surgical resection, the sensitivity and specificity of PET-CT scan were 87% and 43%, respectively.

Survival

Figure 1 shows survival stratified by PET stage. There was a statistically significantly correlation between PET stage and survival ($p < 0.001$), with survival decreasing as PET stage increased.

Standardized Uptake Value

The correlation between SUV and survival was examined. Patients with M1 disease identified by PET scan were excluded from analysis. All other patients were included. Table 3 shows the SUV levels for each PET

Table 2. Positron Emission Tomography–Computed Tomography Scan Results

Variable	PET Stage 0	PET Stage I	PET Stage II	PET Stage III	PET Stage IV
N	170	169	35	122	88
Mass size, mean (cm)	1.5 ± 0.1	2.3 ± 0.1	2.7 ± 0.3	3.2 ± 0.2	3.5 ± 0.2
Mass SUV, mean	. . .	7.3 ± 0.4	10.8 ± 1.4	12.1 ± 0.6	11.7 ± 0.8
Attempt at tissue procurement	36%	83%	86%	86%	91%

PET = positron emission tomography; SUV = standardized uptake value.