RESEARCH ARTICLE

Staging with PET-CT in Patients with Locally Advanced Non Small Cell Lung Cancer is Superior to Conventional Staging Methods in Terms of Survival

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Abstract

Background: Of patients with non small cell lung cancer (NSCLC), around one third are locally advanced at the time of diagnosis. Because only a proprotion of stage III patients can be cured by surgery, in order to improve the outcomes , sequential or concurrent chemoradiation, or concurrent chemoradiation with induction or consolidation is offered to the patients with locally advanced NSCLC. Today, PET combined with computerized tomography (PET-CT) is accepted as the most sensitive technique for detecting mediastinal lymph node and extracranial metastases from NSCLC. We aimed to compare PET-CT and conventional staging procedures for decisions regarding curative treatment of locally advanced NSCLC. Materials and Methods: A total of 168 consecutive patients were included from Acibadem Kayseri Hospital, Acibadem Adana Hospital and Kayseri Research and Training Hospital in this study. Results: While the median PFS was 13.0±1.9 months in the PET-CT group, it was only 6.0±0.9 in the others (p<0.001). The median OS values were 20.5±15.6 and 11.5±1.5 months, respectively (p<0.001). Discussion: As a result, we found that staging with PET CT has better results in terms of survival staging. This superiority leads to survival advantage in patients with locally advanced NSCLC.

Keywords: Lung cancer - locally advanced - PET CT - survival

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Introduction

It is widely known that lung cancer is the leading cause of cancer releated deaths in worlwide (Parkin et al., 2005; Demirci et al., 2013). Approximetely 80% of newly diagnosed lung cancers are non small cell lung cancer (NSCLC). At the time of diagnosis approximately 43% of patients who are suffering from NSCLC are locally advanced (Tachfouti et al., 2012). According to the 7th edition of Tumor, Node, Metastasis (TNM) in lung cancer, locally advanced NSCLC consists of stage III A (T1a,b T2 a,b N2M0/T3N1,2M0/T4N0,1M0) and IIIB (T4N2M0/T any N3M0) disease (Marshall et al., 2012). Currently, surgical resection remains the primary strategy for the treatment of patients with NSCLC at stage I, II, and IIIA (Wang et al., 2012). But only 20% of patients with stage III are cured by surgery. Therefore there is a disagreement among the oncologists in terms of whether surgery is necessary for treatment of locally advanced NSCLC or not. In order to improve the outcomes of the locally advanced NSCLC, sequential chemoradiation (Le Chevalier et al., 1992; Sause et al., 1995; Dillman et al., 1996; Brown et al., 2013), concurrent chemoradiation (Furuse et al., 1999; Zatloukal et al., 2004; Curran et al., 2011), concurrent chemoradiation with induction or consolidation (Albain et al., 2002; Gandara et al., 2003; Belani et al., 2005; Vokes et al., 2007; Driesen et al., 2013) have been investigated.

Positron emission tomography (PET) with the glucose analogue, 2-[18F]-fluoro-2-deoxy-d-glucose (FDG) has been successfully used in the care of patients with NSCLC such as the staging procedures, radiotherapy planning and the evaluation of response to the treatment (Paesmans et al., 2010). Compared to computerized tomography (CT), PET has been demonstrated to have superior sensitivity and specificity in the detection of mediastinal lymph nodes metastases (Gupta et al., 1999; Birim et al., 2005). Today, PET combined with computerized tomography (PET-CT) is accepted as the most sensitive technique for detecting extracranial metastases from NSCLC (Antoch et al., 2003; Gámez et al., 2006; Li et al., 2013; Silvestri et al., 2013).

In presented study, we aimed to compare the superiority of PET-CT and conventional staging procedure to the decision of curative treatment in locally advanced NSCLC.

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Table 1. Characteristics of Groups

Treatment Schedule		PET CT (n:82) n %	Conventional Methods (n:86) n %	P value
Age (mean) (year)		62.3±9.3	63.3±9.9	0.57
Gender	Male	82 (100)	81 (94)	0.028
	Female	0 (0)	5 (6)	
Histology	Epidermoid	38 (46)	51 (59)	0.356
	Adenocarcinom	19 (23)	17 (20)	
	Not Other Specified	22 (27)	15 (17)	
	Other	3 (4)	3 (4)	
T Stage	T1	2 (2)	2 (2)	0.162
	T2	3 (4)	9 (11)	
	T3	41 (50)	29 (34)	
	T4	31 (38)	36 (42)	
	Unknown	5 (6)	10 (12)	
N Stage	N0	29 (35)	16 (19)	0.224
	N1	5 (6)	2 (2)	
	N2	31 (38)	35 (41)	
	N3	10 (12)	6 (7)	
	Unknown	7 (8)	27 (31)	
Stage	IIIa	39 (48)	45 (52)	0.481
	IIIb	43 (52)	41 (48)	
Comorbidity	Yes	32 (39)	25 (29)	0.173
	No	50 (61)	61 (71)	
Smoking	Yes	52 (63)	57 (66)	0.184
	No	30 (37)	29 (34)	

Table 2. Treatment Protocols

Treatment Protocols	PET CT (n:82) n %	Conventional Methods (n:86) n %	P value
Neoadjuvan CT→CRT	31 (38)	13 (15)	0.001
CRT→Consolidation CT	28 (34)	27 (31)	

Materials and Methods

The patients diagnosed with locally advanced NSCLC from Acıbadem Kayseri Hospital, Acıbadem Adana Hospital and Kayseri Research and Training Hospital were included in this study. Between the years 2006-2011, total of 168 consequitive patients who were diagnosed with locally advanced NSCLC were analysed retrospectively, with the age of using hospital records. The patients were divided into two groups according to staging procedure for baseline staging: PET-CT or conventional methods which include CT and/or brain MR, bone scintigraphy. Staging was made according to the 6th or 7th version of TNM lung cancer staging system. PET-CT and conventional groups consisted of 82 and 86 patients, respectively. The patients received one of chemoradiotherapy, induction chemotherapy followed chemoradiotherapy or surgery and chemoradiotherapy followed consolidation chemotherapy for curative treatment regimen.

Age, gender, histological subtypes of cancer, tumor (T) stage, nodal (N) stage, stage, comorbidity and smoking status (current or former smoker) were recorded to Statistical Package for the Social Sciences 16.0 (SPSS16.0) statistical software for analysis.

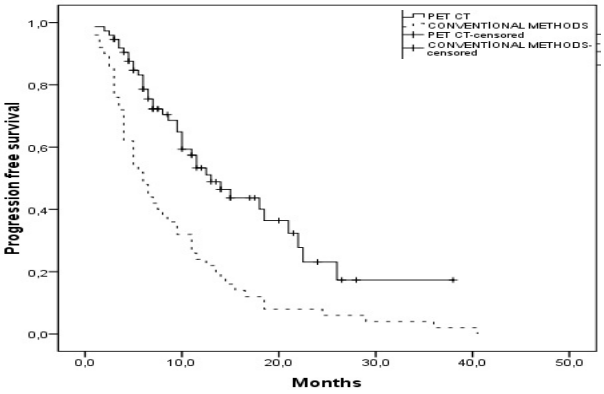

Figure 1. Progression Free Survival Curves

PET-CT Protocol

The patients were injected about 10 mCi (370 MBq) of FDG in travenously. After one-hour-relaxing in a silent room, the patient was imaged by using an integrated PET/CT camera. PET/CT scan was performed by using PET-CT (Siemens Biography 6, LSO, 3D). The CT portion of the study was done without intravenous contrast medium, and used for defining anatomical signs and marks, also for attenuation correction of the PET reconstruction.

Descriptive tests, chi square, independent-samples tests and survival analyses were performed for analysis. Survival time was estimated by the Kaplan–Meier method and the survival difference between groups was assessed by the log-rank test. $P<0.05$ was considered as a significant statistic.

Results

The characteristics of patients were given in Table 1. Mean age of patients were 62.3±9.3 in PET CT groups and other groups were 63.3±9.9 (p=0.570). The male and female ratio had a significant difference between these groups (p=0.028). However, there was no significant difference regarding histology of cancer (p=0.356), T stage (p=0.162), N stage (p=0.224), stage (p=0.481), comorbidity (p=0.173) and smoking status (p=0.184).

Considering treatment protocols, while Neoadjuvan Chemotherapy→ Chemoradiotherapy was mostly offered to the patients in PET-CT groups (38%), Chemoradiotherapy was offered mostly in the other group (54%). Treatment protocols in the groups were given in Table 2 and chemotherapy regimens that were offered as neoadjuvant or concurrent with radiotherapy or consolidation were given in Table 3.

When we evaluated the groups in terms of survival, both of progression free survival (PFS) and overall survival (OS) significantly differed between the groups.

Table 3. Chemotherapy Regimens

	Cisplatin or Carboplatin	Carboplatin+Paclitaxel	Cisplatin or Carboplatin+ Gemcitabine	Cisplatin or Carboplatin+ Vinorelbine	Cisplatin or Carboplatin+ Docetaxel
Neoadjuvant	0 (0%)	10 (22.7%)	20 (45.5%)	1 (2.3%)	13 (29.5%)
Consolidation	0 (0%)	25 (45.5%)	11 (20%)	2 (3.6%)	17 (30.9%)
Concurrent	43 (62.3%)	21 (30.4%)	2 (2.9%)	2 (2.9%)	1 (1.5%)

Table 4. Progression Free Survival and Overall Survival

	PET CT	Conventional Methods	P value
PFS (median)	13±1.9	6.0±0.9	<0.001
OS (median)	20.5±15.6	11.5±1.5	<0.001

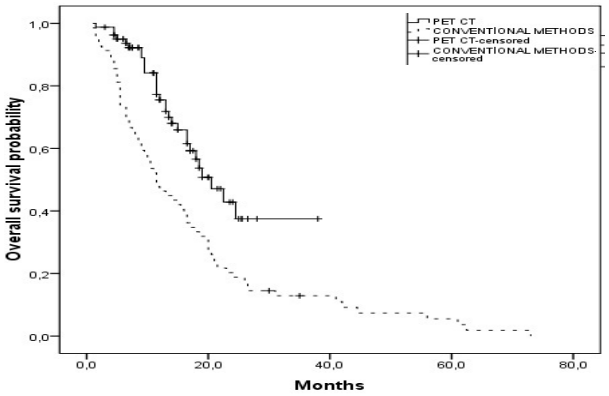

Figure 2. Overall Survival Curves

While the median PFS were 13.0±1.9 (95%CI 9.16-16.8) in PET-CT groups, it was respectively 6.0±0.9 (95%CI 4.07-7.92) in other groups (p<0.001). The median OS was 20.5±15.6 (95% CI 15.59-25.40) in PET-CT groups and 11.5±1.5 (95% CI 8.45-14.55) in the conventional methods group (p<0.001). PFS and OS of groups were depicted in Table 4. In addition to that PFS was shown in Figure 1 and OS was shown in Figure 2.

Discussion

Currently, PET-CT is accepted as the most sensitive technique for detecting the extracranial metastases and it has superior sensitivity and specificity in the detection of mediastinal lymph nodes metastases for baseline staging at the time of diagnosis in NSCLC. In locally advanced NSCLC (potentially curable disease especially stage IIIA), PET-CT is considered as the first line imaging test (Christian, 2010).

In presented study, we did not aim that whether PET-CT is superior to conventional staging procedure or not in terms of staging of patients with locally advanced NSCLC. We evaluated that whether the superiority of PET-CT in terms of staging was leading to the survival advantage in patients who were accepted as locally advanced NSCLC according to baseline staging. And we found that both of PFS and OS were significantly different. The patients who were staged with PET-CT at the time of diagnosis had better PFS and OS.

It has been reported that PET-CT reveals the occult distant metastases in additional 5-29% of patients as CT alone (Schrevens et al., 2004). Our findings maybe related to this result that was mentioned above. Due to occult metastases which were not detected by conventional staging methods, the patients who had distant metastases could be accepted as locally advanced NSCLC; and curative treatment modalities were offered by them. In addition to that it has been reported that the staging with PET-CT had additional value for radiotherapy planning (Grégoire et al., 2007; Ding et al., 2013). This result may save the patients from toxic deaths.

As a result, we found that the staging with PET-CT has better results in terms of survival like staging. The superiority of PET-CT in staging is leading to survival advantage in patients with locally advanced NSCLC.

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