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Comparison of 18F-FDG and 68Ga-DOTATATE PET/CT in surgically treated lung carcinoid tumors

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ABSTRACT

Aims: This study aims to compare the efficacy of FDG-18 PET/CT and 68Ga-DOTATATE PET/CT imaging techniques in patients with lung carcinoid tumors, identifying the most appropriate preoperative nuclear medicine technique for diagnosis and staging.

Methods: We retrospectively analyzed data from 123 patients who underwent surgery for lung carcinoid tumors at our center between 2009 and 2021. All of the patients were scanned with FDG-18 PET/CT before surgery. In addition to FDG-18 PET/CT, 68Ga-DOTATATE PET/CT scanning was performed in 28 patients: 17 in the preoperative and 11 in the postoperative period. Demographic data, mean higher maximal standard uptake (SUVmax) values of primary mass, lymph nodes and extrathoracic foci, pathologic subtype, and type of surgery were recorded. Compliance with normal distribution for numerical data was assessed using the Shapiro-Wilk test. The Wilcoxon signed-rank test was employed for groups meeting normal distribution to compare continuous numerical variables. The Mann-Whitney U and Kruskal-Wallis tests were used when normal distribution assumptions were unsatisfied.

Results: The mean SUVmax value in 68Ga-DOTATATE PET/CT was significantly higher than FDG-18 PET/CT in patients with a lung carcinoid tumor (20 vs 4.4). For 68Ga-DOTATATE PET/CT scan, typical carcinoids had higher mean SUVmax value than atypical carcinoids (26 and 5.6 respectively), and the difference was statistically significant (p=0.002). For that FDG-18 PET/CT, on the contrary, the mean SUVmax value was higher in atypical carcinoids than typical carcinoids (5.4 and 3.8, respectively), and the difference was not significant (p=0.126)

Conclusion: The SUVmax values from 68Ga-DOTATATE PET/CT and FDG-18 PET/CT in lung carcinoid tumors vary by tumor subtype. 68Ga-DOTATATE PET/CT demonstrates higher SUVmax values in typical carcinoid tumors, indicating its superiority over FDG-18 PET/CT for this subtype. Although 68Ga-DOTATATE PET/CT also shows elevated SUVmax in atypical carcinoid tumors, the difference compared to FDG-18 PET/CT does not reach statistical significance.

Keywords: FDG-18 PET/CT, 68Ga-DOTATATE PET/CT, lung carcinoid tumor, surgery

INTRODUCTION

Positron emission tomography (PET) is a radiological imaging technique that provides tissue chemical metabolism changes as molecular radiological images. In fluorodeoxyglucose (FDG) PET/CT integrated with computed tomography (CT), an image is obtained by quantifying the increased glucose metabolism of FDG labeled with the F-18 isotope.[1,2] On the other hand, the Gallium-68 (Ga-68) PET/CT technique is a radiological method consisting of DOTATE and Ga-68 radioactive elements, a synthetic form of natural somatostatin hormone. Neuroendocrine (NET) cells have an excess of somatostatin receptors. In this way, Ga-68 adheres to the somatostatin receptors of cancerous cells, making the lesion visible on PET/CT.[3,4]

68Ga-DOTATATE PET/CT has a more specific diagnostic value in lung carcinoid tumors. Especially in typical carcinoids with pathological subtypes, higher maximal standard uptake (SUVmax) was observed in 68Ga-DOTATATE PET/CT. The success of 68Ga-DOTATATE PET CT in identifying metastatic foci also increases its usage in advanced patients.[5,6]

METHODS

Our study aimed to compare two PET/CT imaging techniques used perioperatively for diagnostic and staging purposes in patients with lung carcinoids. The study was approved by the ethics committee of Keçiören Training and Research Hospital (Date: 25.05.2021, Decision No:2012-KAEK-15/2303). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. The data of 123 patients who were operated on with the diagnosis of lung carcinoid in Ankara Atatürk Sanatorium Hospital of Health Sciences University between 2009 and 2021 were retrospectively scanned. Demographic data, mean SUVmax values of primary mass, lymph nodes and extrathoracic foci, pathologic subtype, and type of surgery were recorded.

Statistical Analysis

All analyses were conducted using IBM SPSS Statistics version 25.0. Continuous numerical variables are presented as mean±standard deviation or median (minimum-maximum) values, while categorical variables are expressed as counts (percentages). The distribution of categorical variables between groups was assessed using the Pearson chi-square and Fisher's Exact tests for comparisons. A p-value of less than 0.05 was deemed statistically significant.

RESULTS

Patients, Type of Resection, and Subtype

Patients who did not undergo PET/CT and were not diagnosed with carcinoid tumors were excluded from the study. Of 123 patients, 58 (47%) were female and 65 (53%) were male. The mean age of women was 52.4 (26-72), while the mean age of men was 50 (20-81). For surgical treatment, lobectomy was performed in 106 patients, segment resection in 9, and pneumonectomy in 8 patients. Histopathological examination revealed typical carcinoid tumors in 72 (58.5%) patients and atypical carcinoid tumors in 54 (41.5%) patients (**Table 1**).

Table 1. Age, gender, type of resection, and histopathologic subtype of the patients

	n (%)
Age (mean)	
Female	52.4 (26-72)
Male	50 (20-81)
Gender	
Female	58 (47)
Male	65 (53)
Type of resection	
Wedge/segmentectomy	9 (7.3)
Lobectomy/bilobectomy	106 (86.2)
Pneumonectomy	8 (6.5)
Histopathologic subtype	
Typical carcinoid	72 (58.5)
Atypical carcinoid	51 (41.5)

The mean ages for typical and atypical carcinoids were 53 (26-81) and 48 (20-71), respectively. Typical carcinoid tumors concluded 54% (39) of women and 46% (33) of men, while atypical carcinoid tumors concluded 37% (19) of women and 63% (32) of men. No statistically significant difference was found between the incidence of typical/atypical carcinoids within the same genus (p=0.317).

FDG-18 PET/CT and 68Ga-DOTATATE PET/CT

Primary Mass: For 123 patients evaluated with FDG-18 PET/CT preoperatively, the mean SUVmax values of the primary mass were 4.4 (0-32). The mean SUVmax value was 3.8 (0-10) in typical carcinoid tumors and 5.4 (0-32) in atypical carcinoids. There was no statistically significant difference between the SUVmax value of typical and atypical carcinoids in FDG-18 PET/CT (p=0.126).

A total of 28 patients were evaluated with a 68Ga-DOTATATE PET/CT scan. While 17 patients had a preoperative scan, 11 patients were scanned postoperatively for detection of other foci. The mean SUVmax values of the primary mass were 20 (0-120) in 17 patients who underwent preoperative 68Ga-DOTATATE PET/CT. The mean SUVmax value was 26 (0-120) in typical carcinoid tumors (n=12) and 5.6 (0-9) (n=5) in atypical carcinoids. There was a statistically significant difference between the SUVmax value of typical and atypical carcinoids in 68Ga-DOTATATE PET/CT (p=0.002).

Further analysis of 17 patients who scanned with both techniques in the perioperative period showed that the SUVmax value of the primary mass was significantly higher for 68Ga-DOTATATE PET/CT than FDG-18 PET/CT. The mean SUVmax value was 3.8 (0-11) in FDG-18 PET/CT and 20 (0-120) in 68GA-DOTATATE PET/CT, and the difference was statistically significant. On the other hand, there were false negative results for the primary mass itself in both techniques. For 68Ga-DOTATATE PET/CT, two patients (1 typical, 1 atypical) and for FDG-18 PET/CT, five patients (4 typical, 1 atypical) did not present any pathologic uptake (SUVmax=0) (**Figure, Table 2**).

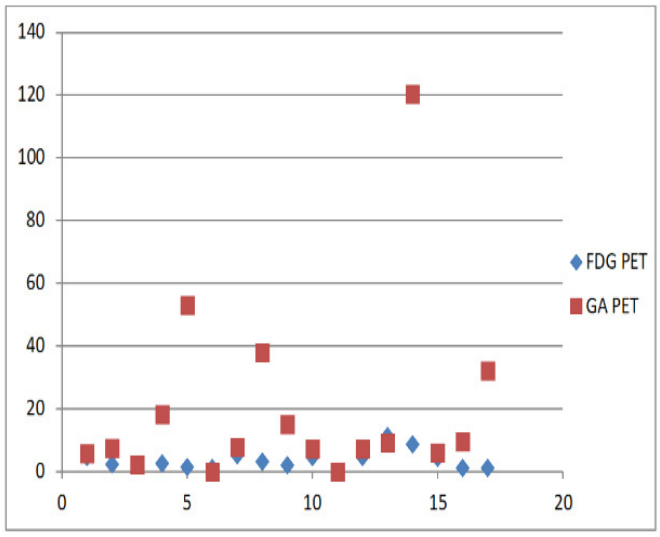

Figure. Distribution of SUVmax value of the mass in preoperative GA-68 PET and FDG-18 PET in 17 patients with two PETs

Metastatic Lymph Nodes and Other Foci: The analysis of mediastinal lymph nodes revealed that neither technique is sufficient to identify metastatic lymph nodes. Thirteen patients (10.5%) had pathologically confirmed lymph node metastasis, and four patients had multiple lymph metastatic lymph nodes. The most common metastatic lymph nodes were N1, no. 10 (hilar) and 11 (inter-lober). For patients with a metastatic no. 11 lymph node, only three of them were evaluated with both techniques, and there was no pathologic uptake on both FDG-18 PET/CT and 68Ga-DOTATATE PET/CT (SUVmax=0). For patients with metastatic no. 10 lymph nodes, none of them evaluated by preoperative 68Ga-DOTATATE PET/CT, the median SUVmax value in FDG-18 PET/CT was 3.2 (2.4-4).). In 1 patient with lymph node metastasis no. 5, SUVmax was 11 in 68Ga-DOTATATE PET/CT, while SUVmax was 4 in FDG-18 PET/CT. Number 3,4,7,8,9 nodes were metastatic for one

Table 2. The mean SUVmax values of 17 patients evaluated with both preoperative 68GA-DOTATATE PET/CT and FDG-18 PET/CT

	68GA-DOTATATE SUVmax, mean	FDG-18 SUVmax, mean	p-value
Histopathologic subtype			
All (n=17)	20	3.8	**p=0,002***
Typical carcinoid (n=12)	27	3.4	**p=0,008***
Atypical carcinoid (n=5)	5.7	4.8	p=0,5
Lymph nodes			
N1 (n=3)	0	0	p>0,05
N2 (n=1)	5	4	p>0,05
Other foci in the thoracic region (thyroid, esophagus, breast, rib, thymus) (n=9[a])	4.6	4.1	p>0,05
Other foci in the extrathoracic region (n=13[b])	7.7	5.7	p>0,05
Atelectasis/consolidated area adjacent to the primary mass (n=3[c])	4.7	5	p>0,05

*: p-value <0.05, statistically significant. [a]: 5 patients had pathologic uptake on 18-FDG and four on GA-DOTATE. [b]: 11 patients had pathologic uptake on 18-FDG and two on GA-DOTATE. [c]: 1 patient had pathologic uptake on 18-FDG and two on GA-DOTATE

patient each. No significant uptake was also present with both techniques. As a result, no statistically significant difference was found for metastatic lymph nodes in terms of SUVmax values in either technique (p>0.05) (**Table 2**).

For 17 patients who were evaluated with both techniques preoperatively, in the thoracic region, four patients had a median SUVmax of 4.5 (2.2-7.1) (thyroid, esophagus, breast, rib, thymus) on 68GA-DOTATATE PET/CT, while five patients had a median SUVmax of 3,8 (2.5-6.3) on FDG-18 PET/CT. In the extrathoracic regions (gastrointestinal, genitourinary) 2 patients had a median SUVmax of 7.7 (6.9-8.6) on 68GA-DOTATATE PET/CT, while ten patients had a median SUVmax of 5.4 (3-9.3) on FDG-18 PET/CT. No statistically significant difference was found between SUV involvement in the intrathoracic and extrathoracic regions in both PETs (p>0.05) (**Table 2**).

DISCUSSION

Because of the increased mitosis in atypical lung carcinoid tumors, the sensitivity of FDG-18 PET/CT is higher than that of typical carcinoid tumors.[7,8] Due to the somatostatin receptors of lung carcinoid tumors, 68GA-DOTATATE PET/CT shows a high affinity for these receptors.[9] On the other hand, it is known that 68GA-DOTATATE PET/CT scans show a high affinity for typical carcinoids. Typical carcinoids show higher SUVmax values on 68GA-DOTATATE PET/CT than atypical carcinoids.[10,11] Our results are also compatible with the literature.

In a study by Antunes et al., the specificity of 68GA-DOTATATE PET/CT CT in the diagnosis of the primary tumor was 91%; in comparison, its sensitivity was 93%.[10] Since the GA-68 radioisotope has a high sensitivity to somatostatin receptors, it is preferred in NETs.[11] Some researchers have argued that Ga-68 PET/CT is more sensitive than other scintigraphic methods, such as octreotide and pentetreotide.[12,13] Ga-68 PET/CT is used in preoperative staging, body scanning, metastasis, and postoperative treatment follow-up due to its high sensitivity and specificity rates in carcinoid tumors.[14-16]

In a study conducted by Lococo et al.[6] in 62 patients focusing on diagnosing carcinoid tumors, the success of 68GA-DOTATATE PET/CT in diagnosis was 88.4%, and the median SUVmax value was found to be 15.5. The success of FDG-18 PET/CT in diagnosis was 53.8%, and the median SUVmax value was 3.2 (p=0.0025). While the success of 68GA-DOTATATE PET/CT was 91.7%, especially in typical carcinoid tumors, this rate remained at 50% in FDG-18 PET/CT (p=0.076) .

In our study, 17 patients had 68GA-DOTATATE PET/CT and FDG-18 PET/CT preoperatively. In these patients, the mean SUVmax value of the tumor itself was 20 (0-120) in 68GA-DOTATATE PET/CT, while the median SUVmax value in FDG-18 PET/CT was 3.8 (0-11). 11 of these 17 patients were typical carcinoids, and the median SUVmax value on 68GA-DOTATATE PET/CT was 27 (0-120), while the median SUVmax value on FDG-18 PET/CT was 3.4 (0-11). While the median SUVmax value in 68GA-DOTATATE PET/CT was 5.7 (0-9) in 6 patients with atypical carcinoids, the median SUVmax value in FDG-18 PET/CT was 4.8 (1-11). In our study group, the difference between the success of 68GA-DOTATATE PET/CT and FDG-18 PET/CT in detecting the primary mass was statistically significant for patients with a diagnosis of typical carcinoids (p=0.008) but not for patients with a diagnosis of atypical carcinoids (p=0.5).

Our data showed that 68GA-DOTATATE PET/CT was superior to FDG-18 PET/CT in determining the primary mass, especially in typical carcinoids. However, reaching a definitive conclusion for atypical carcinoids is difficult. In our study, SUV uptake of atypical carcinoids in FDG-18 PET/CT was very close to SUV values in 68GA-DOTATATE PET/CT, and the difference was not statistically significant.

In a study by Kayani et al.[17] on 18 patients, the median SUVmax uptake value in 68GA-DOTATATE PET/CT was 15; it was 33 for typical carcinoids and 3.5 for atypical subtype (p=0.002). On the other hand, the median SUVmax value of FDG-18 PET/CT was 6; it was 4.9 for typical carcinoids and 16 for atypical subtype (p=0.005). The same study reported a 0% false positive rate for 68GA-DOTATATE PET/CT and 16.7% (3 patients) for FDG-18 PET/CT. According to the authors, one of these areas is the hilar lymph node. At the same time, the other two are parenchymal consolidated atelectasis areas adjacent to the lesion.[17] In our study, the false positivity rate of the primary mass was 0% for both techniques. However, in our study, false positive lymph nodes were observed in 4 patients (3 typical, 1 atypical) with preoperative 68GA-DOTATATE PET/CT, and the median SUVmax in the lymph nodes was 3.7 (3-5). False positivity was detected in the lymph nodes of 51 patients who underwent FDG-18 PET/CT. There was no statistically significant difference between FDG-18 PET/CT and 68GA-DOTATATE PET/CT in detecting false-positive lymph nodes (p>0.05). Our patients were evaluated based on the cut-off value of 2.5 for false lymph node positivity, and lymph nodes with an SUVmax above 2.5 were interpreted as false positive.

Jiang et al.[5] argued that 68GA-DOTATATE PET/CT is superior to FDG-18 PET/CT in detecting atelectatic areas adjacent to

the lesion in lung carcinoid tumors. While the median SUVmax values of these atelectatic tissues in 68GA-DOTATATE PET/CT were 30.5±28.1, the median SUVmax values in FDG-18 PET/CT were found to be 2.1±2.3 (p<001). In our study, uptake was observed in atelectasis and consolidated areas adjacent to the lesion in 2 patients (1 typical, 1 atypical) with a mean SUVmax value of 4.7 (2-7.2) in 68GA-DOTATATE PET/CT scan. On the other hand, FDG-18 PET/CT showed uptake in 1 (atypical) patient, and the SUVmax value was 5. There was no statistically significant difference in SUVmax values between the two PET techniques of atelectasis and consolidated areas adjacent to the lesion (p>0.05).

Limitations

The study's scope was limited by the relatively small number of patients evaluated by FDG-18 PET/CT and 68Ga-DOTATATE PET/CT. To draw definitive conclusions regarding the effectiveness of FDG-18 PET/CT, 68Ga-DOTATATE PET/CT in diagnosing carcinoid tumors, further prospective studies are needed involving larger patient cohorts, including those without a confirmed diagnosis of carcinoids.

CONCLUSION

The SUVmax levels of 68GA-DOTATATE PET/CT and FDG-18 PET/CT in lung carcinoid tumors vary by tumor subtype. Typical carcinoids exhibit slower cellular metabolism compared to atypical carcinoids. 68GA-DOTATATE PET/CT demonstrates higher SUV uptake in typical carcinoid tumors, making it superior to FDG-18 PET/CT for this subtype. Although 68GA-DOTATATE PET/CT shows increased SUV uptake in atypical carcinoid tumors, this difference does not achieve statistical significance, likely due to the limited sample size.

We recommend using 68GA-DOTATATE PET/CT for both preoperative evaluation and postoperative follow-up in patients with suspected lung carcinoid tumors scheduled for surgery. However, we do not endorse the routine use of 68GA-DOTATATE PET/CT for all patients; instead, it should be requested for lesions suggestive of carcinoid tumors.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was approved by the ethics committee of Keçiören Training and Research Hospital (Date: 25.05.2021, Decision No: 2012-KAEK-15/2303).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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