Journal of
Pulmonology and
Intensive Care

Original Article

DOI: 10.51271/JOPIC-0042

Comparison of nuclear medicine techniques in surgically treated lung carcinoid tumors

Muhyettin Aslan[1], Pınar Bıçakçıoğlu[2], Koray Aydoğdu[2], Erkmen Gülhan[2], Mustafa Şevki Demiröz[3], Can Kutlay[4], Göktürk Fındık[2]

[1]*Department of Thoracic Surgery, Diyarbakır Gazi Yaşargil Training and Research Hospital, Diyarbakır, Turkiye*
[2]*Department of Thoracic Surgery, Ankara Atatürk Sanatorium Training and Research Hospital, University of Health Sciences, Ankara, Turkiye*
[3]*Department of Thoracic Surgery, Faculty of Medicine, Gazi University, Ankara, Turkiye*
[4]*Department of Thoracic Surgery, Karaman Training and Research Hospital, Karaman, Turkiye*

Cite this article: Aslan M, Bıçakçıoğlu P, Aydoğdu K et al. Comparison of nuclear medicine techniques in surgically treated lung carcinoid tumors. *J Pulmonol Intens Care.* 2024;2(4):77-81.

Corresponding Author: Muhyettin Aslan, drmuhyettinaslan@gmail.com

Received: 06/09/2024 ◆ **Accepted**: 12/11/2024 ◆ **Published**: 20/11/2024

ABSTRACT

Aims: This study aims to evaluate the efficacy of positron emission tomography (PET) computed tomography (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 patients had preoperative FDG-18 PET scans, while 17 also underwent preoperative Gallium-68 (GA-68) PET, and 11 had postoperative GA-68 PET scans. A subset of 17 patients received both PET techniques preoperatively. Compliance with normal distribution for numerical data was assessed using the Shapiro-Wilk test. For groups meeting normal distribution, the Wilcoxon signed-rank test was employed to compare continuous numerical variables. The Mann-Whitney U and Kruskal-Wallis tests were used when normal distribution assumptions were not satisfied.

Results: In patients with lung carcinoid tumors, the mean SUVmax for GA-68 PET (20) significantly exceeded that of FDG-18 PET (4.4). Specifically, for GA-68 PET, the mean SUVmax of the primary mass was 26 in typical carcinoid tumors and 5.6 in atypical carcinoid tumors. For FDG-18 PET, the mean SUVmax of the primary mass was 3.8 in typical carcinoid tumors and 5.4 in atypical carcinoid tumors.

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

Keywords: Gallium-68 DOTATE PET CT, lung carcinoid tumor, FDG-18 PET CT

INTRODUCTION

Positron emission tomography (PET) is a radiological imaging technique that provides chemical metabolism changes in tissues 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] Gallium-68 (GA-68) PET CT technique, on the other hand, is a radiological method consisting of DOTATE and GA-68 radioactive elements, which are 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]

GA PET has more specific diagnostic value in lung carcinoid tumors. Especially in typical carcinoids with pathological subtype, higher maximal standard updake (SUVmax) uptake was observed in GA PET. The success of GA PET in identifying metastatic foci also increases the preference for GA PET in advanced patients.[5,6]

METHODS

In our study, we aimed to investigate PET CT imaging techniques that may be requested preoperatively for diagnostic and staging purposes in patients with lung carcinoid tumor diagnosis. The study was approved by the ethics committee of Keçiören Hospital (Date: 25.05.2021, Decision No: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 Sanatoryum Hospital of Health Sciences University between 2009 and 2021 were retrospectively scanned. Demographic data of the patients, Gallium-68 PET and FDG-18 PET SUVmax values, type of surgical treatment applied, surgical technique used, presence of metastatic focus and pathology results were recorded.

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 test and Fisher's Exact test for comparisons. A p-value of less than 0.05 was deemed statistically significant.

RESULTS

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). Average age for typical carcinoids is 53 (26-81); the mean age of atypical carcinoids was 48 (20-71) (**Table 1**).

Table 1. Age distribution of patients by gender

Gender	N	Age (mean)
Woman	58 (%47)	26–72 (52,4)
Male	65 (%53)	20–81 (50)
Total	123	20–81 (51)

Of the patients, 72 (58.5%) were typical carcinoids and 51 (41.5%) were atypical carcinoids. While the typical carcinoid count was 39 (54%) in women and 19 (37%) atypical carcinoid count, the typical carcinoid count was 33 (46%) and atypical carcinoid count was 32 (63%) in men. No statistically significant difference was found between the incidence of typical/atypical carcinoids within the same genus (p=0.317).

Of the patients who underwent surgical treatment for carcinoid tumors, 37 patients received upper lobectomy, 45 underwent lower lobectomy, 12 had middle lobectomy, 5 had lingulectomy, 2 were treated with superior bilobectomy, 10 with inferior bilobectomy, and 8 underwent pneumonectomy.

GA-PET was performed in 28 patients and FDG-PET in 123 patients. Of the 28 patients who underwent GA-68 PET scan, 17 were preoperatively and 11 postoperatively. The application was performed in the preoperative period in all 123 patients who underwent FDG-18 PET scan (**Table 2**).

The mean SUVmax values of the main mass were 20 (0-120) in 17 patients who underwent preoperative GA-68 PET. Among these, the mean SUVmax was 26 (0-120) in 12 patients with typical carcinoids, while the mean SUVmax was 5.6 (0-9) in 5 patients with atypical carcinoids. There is a statistically significant difference between the uptake of typical and atypical carcinoids in GA-68 PET (p=0.002) (**Figure 1**).

In 123 patients who underwent preoperative FDG-18 PET, the mean SUVmax values of the main mass were 4.4 (0-32). While the mean SUVmax value was 3.8 (0-10) in 71 typical carcinoid patients in this group, the mean SUVmax value was

Table 2. Statistical values in 17 identical patients with two preoperative PETs

PET		GA-68 (n=17)	FDG-18 (n=17)	
Typical (of the mass)		n =12 ortsuvmax=27	n =12 ortsuvmax=3,4	**p=0,008**
Atypical (of the mass)		n =5 ortsuvmax=5,7	n =5 ortsuvmax=4,8	**p=0,5**
	Total	**n=17 ortsuv=19,9**	**n=17 ortsuv=3,8**	**p=0,002**
N1	Typical	n =2 ortsuvmax=0	n =2 ortsuvmax=0	
	Atypical	n =0 ortsuvmax=	n =0 ortsuvmax=	
	Total	**n= 2 ortsuv=0**	**n= 2 ortsuv=0**	**p>0,05**
N2	Typical	n =0 ortsuvmax=	n =0 ortsuvmax=	
	Atypical	n =2 ortsuvmax=5,5	n =2 ortsuvmax=2	
	Total	**n=2 ortsuv=5,5**	**n=2 ortsuv=2**	**p>0,05**
Metastatic in intrathoracic region (Thyroid, esophagus, breast, rib, thymus)	Typical	n =0 ortsuvmax=	n =2 ortsuvmax=4,7	
	Atypical	n =2 ortsuvmax=4,5	n =3 ortsuvmax=3,5	
	Total	**n=2 ortsuv=4,5**	**n=5 ortsuv=4,1**	**p>0,05**
Metastatic in extrathoracic region	Typical	n =2 ortsuvmax=7,7	n =7 ortsuvmax=6,7	
	Atypical	n =0 ortsuvmax=	n =4 ortsuvmax=3,9	
	Total	**n=2 ortsuv=7,7**	**n=11 ortsuv=5,7**	**p>0,05**
Atelectasis/consolidated area adjacent to the lesion	Typical	n =1 ortsuvmax=2,2	n =0 ortsuvmax=	
	Atypical	n =1 ortsuvmax=7,1	n =1 ortsuvmax=5	
	Total	**n=2 ortsuv=4,7**	**n=1 ortsuv=5**	**p>0,05**

PET: Positron emission tomography, GA: Gallium-68

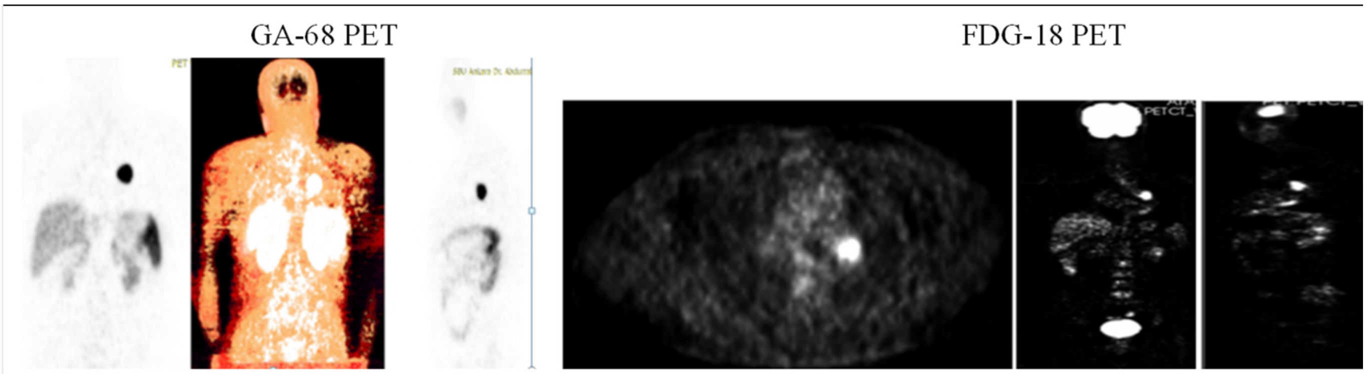

Figure 1. GA-68 PET (Left) and FDG-18 PET (Right) images of a patient with typical carcinoid diagnosis in two separate patients

5.4 (0-32) in 52 patients with atypical carcinoids. There was no statistically significant difference between the uptake of typical and atypical carcinoids in FDG-18 PET (p=0.126).

Higher SUVmax values are seen on GA-68 PET in the main mass in typical carcinoids in 17 patients scanned with both techniques. In this group, while the median SUVmax was 3.8 (0-11) in FDG-18 PET, the median SUVmax was 19.9 (0-120) in GA-68 PET. There was a statistically significant difference between the SUVmax uptake amount of the mass between FDG-18 and GA-68 PET (p=0.002) (**Figure 2**).

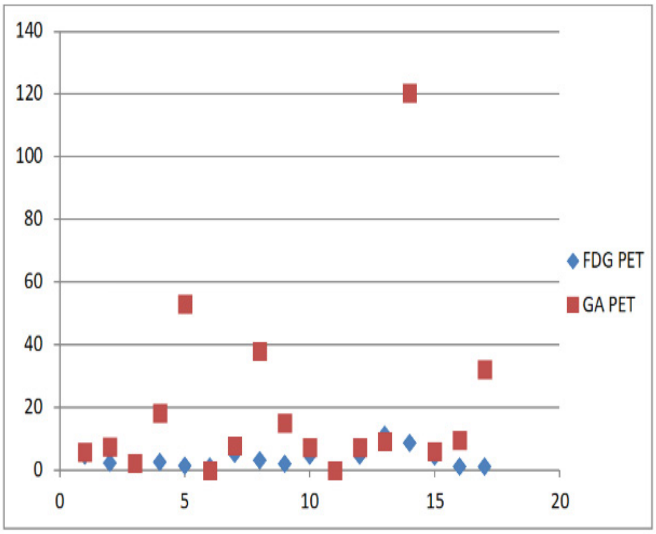

Figure 2. Distribution of SUVmax value of the mass in Preoperative GA-68 PET and FDG-18 PET in 17 patients with two PETs

In the histopathological examination, SUV uptake was observed in FDG-18 PET in 2 of 3 patients with metastatic lymph node 10, and the median SUVmax was found to be 3.21 (2.4-4). In 1 patient with lymph node metastasis no. 5, SUVmax was 11 in GA-68 PET, while SUVmax was 4 in FDG-18 PET. In 1 patient with lymph node metastasis no 4, the SUVmax was 3.99 in FDG-18 PET, while SUV uptake was not observed in GA-68 PET. While SUV uptake was not observed in FDG-18 PET in 6 patients with lymph node metastasis no. 11, only 2 of these patients had preoperative GA-68 PET and SUV involvement was not observed in them either. No SUV involvement was observed in either PET technique in 4 patients with lymph node metastases no 3, 5, 8, and 9, each separately. No statistically significant difference was found in terms of SUV involvement in both PETs of metastatic lymph nodes (p>0.05).

There were 7 patients whose preoperatively diagnosed mass had false negativity in both PET scans. SUV involvement was not observed in the mass itself in 2 patients (1 typical, 1 atypical) who underwent GA-68 PET. SUV involvement was not observed in the mass itself in 5 patients (4 typical, 1 atypical) in those with FDG-18 PET. In two PETs, there was 1 patient (typical) without SUV involvement in the mass.

DISCUSSION

Patients who did not undergo PET CT and were not diagnosed with carcinoid tumors were excluded from the study. Additionally, the study's scope was limited by the relatively small number of patients who had GA-68 PET scans.

Because of the increased mitosis in atypical lung carcinoid tumors, the sensitivity of FDG PET CT is higher than that of typical carcinoid tumors.[7,8] Due to the somatostatin receptors of lung carcinoid tumors, GA-68 PET shows high affinity for these receptors.[9] It is known that GA-68 PET scan shows high affinity for typical carcinoids in carcinoid tumors. Typical carcinoids show higher SUVmax values on GA-68 PET than atypical carcinoids.[10,11]

In a study, the specificity of GA-68 PET CT in the diagnosis of primary tumor was 91%, while its sensitivity was 93% .[10] Since the GA-68 radioisotope has a high sensitivity to somatostatin receptors, this test is preferred in NETs.[11] Some researchers have argued that Gallium-68 PET CT is more sensitive than other scintigraphic methods such as ocreotide and pentetreotide.[12,13] Gallium-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 with lung carcinoid diagnosis, the success of GA-68 PET in diagnosis was 88.4% and the median SUV max value was 15.5. The success of FDG-18 PET in diagnosis was 53.8% and the median SUVmax value was 3.2 (p=0.0025). While the success of GA-68 PET was 91.7% especially in typical carcinoid tumors, this rate remained 50% in FDG-18 PET (P= 0.076).

In our study, there were 17 patients who had both GA-68 PET and FDG-18 PET preoperatively. In these patients, the median SUVmax value of the tumor itself was 19.9 (0-120) in GA-68 PET, while the median SUVmax value in FDG-18 PET was 3.8 (0-11). 11 of these 17 patients were typical carcinoids and the median SUVmax value on GA-68 PET was 27 (0-120), while the median SUVmax value on FDG-18 PET was 3.4 (0-11). While the median SUVmax value in GA-68 PET was 5.7 (0-9) in 6 patients with atypical carcinoids, the median SUVmax value in FDG-18 PET was 4.8 (1-11). In our patient group, the difference between the success of GA-68 PET and FDG-18 PET SUVmax values in determining the main population 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 GA-68 PET was clearly superior to FDG-18 PET in determining the population, especially in typical carcinoids. But for atypical carcinoids this view is difficult to claim. Because in our study, SUV uptake of atypical carcinoids in FDG-18 PET was found to be very close to SUV values in GA-68 PET, and the difference was not statistically significant.

In a study by İrfan et al. on 18 patients, the median SUVmax value of uptake in GA-68 PET was 15, the median SUVmax value of only typical carcinoids was 33, and the median SUVmax value of atypical carcinoids was 3.5 (p=0.002). The median SUVmax value of FDG-18 PET uptake was 6, the median SUVmax value of only typical carcinoids was 4.9, while the median SUVmax value of atypical carcinoids was 16 (p=0.005). While the false positive rate was 0% in GA-68 PET, false positives were detected in 3 patients in FDG-18 PET; According to the authors, one of these areas is the hilar lymph node, while the other two are parenchymal consolidated atelectasis areas adjacent to the lesion.[17]

In our study, false positive lymph nodes were observed in 4 patients (3 typical, 1 atypical) with preoperative GA-68 PET, 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. There was no statistically significant difference between FDG-18 PET and GA-68 PET in 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 GA-PET is superior to FDG PET in detecting atelectatic areas adjacent to the lesion in lung carcinoid tumors. While the medianSUVmax values of these atelectatic tissues in GA-PET were 30.5±28.1, the medianSUVmax values in FDG PET 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) in GA-68 PET scanned with both techniques preoperatively, and the median SUVmax value was found to be 4.7 (2-7.2). On the other hand, FDG-18 PET showed uptake in 1 (atypical) patient and the SUVmax value was found to be 5. In 25 of 123 patients (11 typical, 14 atypical) with preoperative FDG-18 PET, involvement in the atelectasis and consolidated area adjacent to the lesion was detected, and the median SUVmax value was found to be 4 (1-8). 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).

Abdülrezzak et al.[18] argue that SUVmax values of GA-68 PET are higher than FDG-18 PET in liver and bone metastases of carcinoid tumors (p<0.05).

In our study, 17 patients with both preoperative PET examinations showed a median SUVmax 4.5 (4-5) uptake in 2 patients in the intrathoracic region (thyroid, esophagus, breast, rib, thymus) on GA-68 PET, while a median SUVmax was 4.5 (4-5) in FDG-18 PET. median SUVmax 4.1 (1-16) involvement was observed in the patient. Extrathoracic in 2 patients, median SUVmax 7.7 (7-8.8) was observed in 2 patients, while median SUVmax 5.7 (1-10) uptake was observed in 11 patients in FDG-18 PET. While 28 of 123 patients with preoperative FDG-18 PET had a median SUVmax of 5.2 (1-14) in the intrathoracic region, a median SUVmax of 5.8 (1-10) was observed in the extrathoracic region in 48 patients. No statistically significant difference was found between SUV involvement in the intrathoracic and extrathoracic regions in both PETs (p>0.05).

In our study, 11 patients underwent GA-68 PET CT for postoperative control and metastasis follow-up. In only 4 of these patients, mean SUVmax 12 involvement was observed in some parts of the body.

CONCLUSION

The SUVmax levels of GA-68 PET and FDG-18 PET in lung carcinoid tumors vary by tumor subtype. Typical carcinoids exhibit slower cellular metabolism compared to atypical carcinoids. GA-68 PET demonstrates higher SUV uptake in typical carcinoid tumors, establishing it as superior to FDG-18 PET for this subtype. Although GA-68 PET also 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 GA-68 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 routine use of GA-68 PET for all patients; instead, it should be requested for lesions suggestive of carcinoid tumors and for postoperative monitoring.

To draw definitive conclusions regarding the effectiveness of GA-68 PET and FDG-18 PET in diagnosing carcinoid tumors, further prospective studies are needed, involving larger patient cohorts, including those without a confirmed diagnosis of carcinoids.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was approved by the ethics committee of Keçiören Hospital (Date: 25.05.2021, Decision No: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.

REFERENCES

1. Karapolat İ. FDG PET/CT ımaging for evaluation of treatment response in lung cancer. Nukleer Tıp Seminerleri. 2018;4(1):43.
2. Kitajima K, Doi H, Kanda T, et al. Present and future roles of FDG-PET/CT imaging in the management of lung cancer. *Japan J Radiol*. 2016;34(6):387-99.
3. Krenning EP, Valkema R, Kwekkeboom DJ, et al. Molecular imaging as in vivo molecular pathology for gastroenteropancreatic neuroendocrine tumors: implications for follow-up after therapy. *J Nucl Med*. 2005;46(1 suppl):76S-82S.
4. Evangelista L, Ravelli I, Bignotto A, Cecchin D, Zucchetta P. Ga-68 DOTA-peptides and F-18 FDG PET/CT in patients with neuroendocrine tumor: a review. *Clin Imaging*. 2020;67:113-116.
5. Jiang Y, Hou G, Cheng W. The utility of 18F-FDG and 68Ga-DOTA-Peptide PET/CT in the evaluation of primary pulmonary carcinoid: a systematic review and meta-analysis. *Medicine*. 2019;98(10):e14769.
6. Lococo F, Perotti G, Cardillo G, et al. Multicenter comparison of 18F-FDG and 68Ga-DOTA-peptide PET/CT for pulmonary carcinoid. *Clin Nucl Med*. 2015;40(3):e183-e9.
7. Ramirez RA, Chauhan A, Gimenez J, Thomas KE, Kokodis I, Voros BA. Management of pulmonary neuroendocrine tumors. *Rev Endocr Metab Disord*. 2017;18(4):433-442.
8. Rosado de Christenson ML, Abbott GF, Kirejczyk WM, Galvin JR, Travis WD. From the archives of the AFIP: thoracic carcinoids: radiologic-pathologic correlation. *Radiographics*. 1999;19(3):707-736.
9. Hauso O, Gustafsson BI, Kidd M, et al. Neuroendocrine tumor epidemiology: contrasting Norway and North America. *Cancer*. 2008; 113(10):2655-2664.
10. Geijer H, Breimer LH. Somatostatin receptor PET/CT in neuroendocrine tumours: update on systematic review and meta-analysis. *Eur J Nucl Med Mol Imaging*. 2013;40(11):1770-1780.
11. Antunes P, Ginj M, Zhang H, et al. Are radiogallium-labelled DOTA-conjugated somatostatin analogues superior to those labelled with other radiometals? *Eur J Nucl Med Mol Imaging*. 2007;34(7):982-993.

12. Raphael MJ, Chan DL, Law C, Singh S. Principles of diagnosis and management of neuroendocrine tumours. *Cmaj*. 2017;189(10):E398-E404.
13. Filosso PL, Oliaro A, Ruffini E, et al. Outcome and prognostic factors in bronchial carcinoids: a single-center experience. *J Thorac Oncol*. 2013; 8(10):1282-1288.
14. Gosain R, Mukherjee S, Yendamuri SS, Iyer R. Management of typical and atypical pulmonary carcinoids based on different established guidelines. *Cancers*. 2018;10(12):510.
15. Singh S, Poon R, Wong R, Metser U. 68Ga PET imaging in patients with neuroendocrine tumors: a systematic review and meta-analysis. *J Nucl Med*. 2018;43(11):802-810.
16. Öberg K, Knigge U, Kwekkeboom D, Perren A. Neuroendocrine gastro-entero-pancreatic tumors: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. *Ann Oncol*. 2012;23(Suppl 7):vii124-vii130.
17. Kayani I, Conry BG, Groves AM, et al. A comparison of 68Ga-DOTATATE and 18F-FDG PET/CT in pulmonary neuroendocrine tumors. *J Nucl Med*. 2009;50(12):1927-1932.
18. Abdulrezzak U, Kurt YK, Kula M, Tutus A. Combined imaging with 68Ga-DOTA-TATE and 18F-FDG PET/CT on the basis of volumetric parameters in neuroendocrine tumors. *Nucl Med Commun*. 2016;37(8):874-881.