# The Value of F18-FDG PET/CT in Medullary Thyroid Cancer Patients with Persistent Elevated Calcitonin Levels

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## ABSTRACT

## Purpose of the Study

In this retrospective study, we reported our experience with FDG-PET/CT in evaluation of medullary thyroid cancer (MTC) patients with persistent elevated calcitonin levels.

## Materials and Methods

A total of 33 F-18 FDG PET/CT scans and 9 somatostatin receptor imaging (SRI) (6 In-111 octreotide and 3 Ga-68 DOTATATE PET/CT) of 25 MTC patients with persistently elevated calcitonin levels, performed for staging and restaging, were analyzed retrospectively. The scans were compared lesion by lesion with histopathological data and other imaging methods. Because all patients had abnormally high calcitonin levels defined as persistent disease, negative F-18 FDG PET/CT scans accepted as false negative. Because there was no true-negative study, only sensitivity and positive predictive value (PPV) were calculated. Calcitonin levels and SUVmax values were assessed by Mann-Whitney U test and the ROC curve analysis.

### Results

There were 11 true-positive, 11 false-positive and 11 false-negative F-18 FDG PET/CT scans. Sensitivity and PPV were 50% and 50% respectively. Difference of mean calcitonin level between true-positive cases and the others was nonsignificant. SUVmax of true-positive lesions were significantly higher than of the others. All 9 SRIs were negative.

## Conclusions

FDG PET/CT scan appeared to be less sensitive. However, it should be considered that F-18 FDG PET/CT was performed to the patients with only no lesion had been detected by the other imaging modalities in this group. Because F-18 FDG PET/CT was not performed when a residual or recurrent lesion had clearly been detected before, sensitivity of 50% was considered to be acceptable.

Key words: Medullary thyroid carcinoma; FDG; PET/CT; Calcitonin; Thyroid cancer.

## INTRODUCTION

Medullary thyroid carcinoma (MTC) is a rare neuroendocrine tumor that originates from parafollicular C cells of the thyroid gland and occurs both in hereditary (25%) and sporadic (75%) forms. In recent studies, MTC accounts for approximately 2-3% of all thyroid cancers, much lower incidence than previously reported (5%), because of the marked increase in the relative

incidence of papillary thyroid carcinoma (PTC) over the past several decades. Parafollicular C cells produce several hormones or biogenic amines such as calcitonin, carcinoembryonic antigen (CEA), adrenocorticotropic hormone (ACTH) and somatostatin. Among all of them, calcitonin and CEA are most valuable tumor markers for MTC [1, 2].

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The only curative treatment option of MTC is surgical resection (total thyroidectomy and lymph node dissection) in patients without distant metastasis. The most frequent metastasis sites of MTC are cervical and mediastinal lymph nodes, lungs, liver and bone. The patients with distant metastasis would not be candidates for extensive loco-regional surgery with curative intent and show poor response to chemotherapy and radiation therapy. Therefore, the most important prognostic factor in patients with MTC is early diagnosis that facilitates early surgical intervention before metastatic spread [2, 3].

Measurements of the serum calcitonin level are important in the follow-up of patient with MTC. Two or three months after surgery is the optimal time to determine the lowest level of serum calcitonin. Persistently or increasingly elevated calcitonin level is indicative for residual or recurrent disease in MTC patients [2]. These patients are evaluated with conventional imaging methods such as ultrasonography (US), computed tomography (CT), magnetic resonance imaging (MRI) and nuclear medicine imaging methods with several types of radiopharmaceuticals such as indium-111 octreotide (In-111 octreotide), technetium-99m pentavalent dimercaptosuccinic acid (Tc-99m (V) DMSA), gallium-68 (Ga-68) labelled somatostatin analogues, fluorine-18 fluorodeoxyglucose (F-18 FDG), fluorine-18 dihydroxyphenylalanine (F-18 DOPA) [4-7]. But no consensus has yet been reported on their selective use. In this study, we reported our experience with F-18 FDG positron emission tomography/computed tomography (PET/CT) in the evaluation of this specific group.

## MATERIALS and METHODS

#### Patients

We examined the patients who diagnosed with MTC and were performed F-18 PET/CT scans at Ege University Medicine Faculty, Department of Nuclear Medicine retrospectively. Between October 2011 and June 2018, 44 F-18 FDG PET/CT scans were performed on 25 patients (8 men, 17 women; mean age: 50.3±13.7 years old; min: 23, max: 73 years) with MTC and persistently elevated calcitonin levels. Eleven PET/CT scans performed for treatment response were excluded from the study. All F-18 PET/CT scans (33 scans of 25 patients) included in the study were performed for localization of residual or recurrent disease and restaging. Before F-18 FDG PET/CT scans, all patients had undergone bilateral total thyroidectomy and had elevated serum calcitonin level (mean: 615±667 pg/ml; min: 40, max: 2000 pg/ml) at the follow-up examinations. In 9 patients, somatostatin receptor imaging (SRI) (6 In-111 octreotide and 3 Ga-68 DOTATATE PET/CT scans) was also performed.

## Imaging Protocol of F-18 FDG PET/CT

F-18 FDG PET/CT scans were performed after minimum of 6 hours fasting. Data acquisition started about 60 minutes after injection of 5-7 MBq/kg of F-18 FDG intravenously. The blood glucose levels of all patients were checked before radiopharmaceutical administration. All patients were scanned from the base of the skull to the mid thighs. The PET emission images were acquired for 2 min acquisition period at each bed position. CT images (90 kV and 120 mA, slice thickness of 5 mm)

were used for attenuation correction and for anatomic localization. PET, CT, and PET/CT fused images were automatically generated by dedicated software and shown on a workstation.

#### **Image Interpretation**

F-18 FDG PET/CT images were evaluated visually and semiquantitatively. F18 FDG uptake was considered abnormal, if it had higher F-18 FDG uptake intensity then the background blood-pool or adjacent normal tissue. For semi-quantitatively analysis, the maximum standardized uptake value (SUVmax) of the lesions was measured in the region of interest by standard method [8].

#### Data analysis

The results of F-18 FDG PET/CT scans were compared lesion by lesion with histopathological data and clinical official reports of other imaging methods including neck and abdominal US, thorax CT and abdominal MRI.

Positive F-18 FDG PET scans were considered as true positive for local recurrence or metastasis if confirmed by one of the following criteria: (a) a positive histopathology result from fine needle aspiration biopsy or resection, (b) a detectable lesion was present at the corresponding site on follow-up conventional imaging studies when the histopathology results were not available, (c) a lesion size and/or metabolism increased on follow-up scans. Positive F-18 FDG PET scans were classified as false positive if imaging findings were not confirmed by either these 3 criteria. Because all calcitonin levels were abnormally high defined as persistent disease, F-18 FDG PET scans were accepted as false negative if any abnormal finding was not detected by F-18 FDG PET scan. When viewed from this aspect, because there was no true-negative study, only sensitivity and positive predictive value (PPV) were calculated.

#### Statistical analysis

Serum calcitonin levels and SUVmax values were assessed by Mann-Whitney U test. A P value less than 0.05 was considered as indicating a significant difference. The receiver operating characteristic (ROC) curve was performed for calculation the best cut-off point. Accuracy of the tests was measured by area under the curve (AUC).

#### RESULTS

A total of 33 F-18 PET/CT scans included in the study were performed on 25 patients for localization of residual or recurrent disease and restaging. All patients had undergone bilateral total thyroidectomy and have elevated serum calcitonin level (mean serum calcitonin level: 615±667 pg/ml; min: 40, max: 2000 pg/ml) at the follow-up examinations. The mean clinical follow-up time was 50.3±13.7 months (min: 2, max: 84 months) after F-18 FDG PET/CT scans.

Patients' characteristics, F-18 FDG PET/CT scan results and further details have been presented in Table 1. There were 11 true-positive, 11 false-positive and 11 false-negative F-18 FDG

PET/CT scans. Because there was no true-negative results, specificity and negative predictive value were not calculated. Sensitivity and PPV were 50% and 50% respectively. The serum calcitonin mean level was 809±775 pg/ml in true-positive cases, and 518±602 pg/ml in other cases. Difference of mean serum

 Table 1: Patient Characteristics

calcitonin level between true-positive cases and the others was nonsignificant (p=0.29). Somatostatin receptor imaging (6 In-111 octreotide and 3 Ga-68 DOTATATE PET/CT scans) of 9 patients with negative F-18 FDG PET/CT scans were also negative.

Patient no	Sex	Scan no	Age	Calcitonin (pg/mL)	Metastatic regions (max SUVmax)	F/U time after PET (months)	Confirmation	FDG PET Result	FDG PET classification
1	М	1	55	113	-	22.4		PET normal	FN
		2	56	173	-	2.7		PET normal	FN
2	W	1	29	100	LN (4.8)	58.2	US, F/U	LN reactive	FP
3	W	1	50	43	-	78.1	-	PET normal	FN
4	W	1	39	51	LN (3.8)	63.4	US, F/U	LN reactive	FP
5	W	1	48	42	LN (5.4)	84	Exc	LN met.	ТР
6	W	1	60	57	-	77.9	-	PET normal	FN
7	W	1	56	501	LN (6.7)	39.6	Bx	LN met.	TP
		2	58	553	LN (5.2)	10.6	Exc	LN met.	ТР
8	М	1	40	957	LN (4.3)	61.4	US, F/U	LN reactive	FP
		2	43	1382	LN (4.9)	24.6	US, F/U	LN reactive	FP
9	М	1	54	57	-	16.2	-	PET normal	FN
10	W	1	59	1162	LN (3.6)	39.6	US, F/U	LN reactive	FP
11	М	1	60	2000	-	39.4	-	PET normal	FN
12	W	1	63	1713	LN (9)	51.9	Exc	LN met.	ТР
		2	65	890	LN (2.6)	22.8	US, F/U	LN reactive	FP
13	М	1	38	906	LN (2.1), lung (0.6)	4.1	Exc, CT	LN/lung met.	FN
14	W	1	46	1308	LN (4.9)	62.5	Bx	LN reactive	FP
15	W	1	71	90	LN (8.3)	45.5	US, F/U	LN met.	TP
		2	72	603	LN (8.5), bone (5.1)	25.9	US, F/U	LN/bone met.	TP
16	М	1	23	2000	LN (5.6), lung (1.8), bone (5.2), liver (4.0)	62.7	CT, MRI, F/U	LN/lung/ bone/liver met.	ТР

		2	26	2000	LN (6.8), lung (1.3), bone (12.4), liver (4.1)	17.5	CT, MRI, F/U	LN/lung/ bone/liver met.	ТР
17	W	1	47	59	LN (3.9)	79	US, F/U	LN reactive	FP
18	W	1	70	108	LN (2.7)	75	US, F/U	LN reactive	FP
19	М	1	49	1143	LN (9.1), lung (1.1), bone (9.6), liver (5.9)	4.9	US, bx, CT, MRI, F/U	LN/lung/ bone/liver met.	TP
20	W	1	48	54	LN (4.1)	41.6	US, F/U	LN reactive	FP
21	W	1	36	153	LN (4.4)	26.7	Exc	LN met.	ТР
		2	37	376	-	12.8	-	PET normal	FN
		3	38	1325	-	7.5	-	PET normal	FN
22	W	1	44	105	-	61.5	-	PET normal	FN
23	W	1	70	123	Lung (1.5), liver (3.7)	59.4	CT, MRI, F/U	Nonmetabolio met.	e FN
24	W	1	34	40	LN (3.2)	63.1	US, F/U	LN reactive	FP
25	М	1	73	97	LN (10.5), lung (0.7), bone (5.5)	1.9	US, CT, F/U	LN/lung/ bone met.	TP

M: man, W: woman, LN: lymph node, Bx: biopsy, Exc: excision, SUV: standardized uptake value, met: metastasis, US: ultrasound, CT: computed tomography, MRI: magnetic resonance imaging, F/U: follow-up, TP: true positive, FP: false positive, FN: false negative

In 23 F-18 FDG PET/CT scans performed on 18 patients, 5 metastatic lymph nodes which had normal F-18 FDG uptake, 53 metastatic lymph nodes which had increased F-18 FDG uptake (SUVmax mean of metastatic lymph nodes:  $6.1\pm2.2$ ) and 20 non-metastatic lymph nodes which had increased F-18 FDG uptake (SUVmax >2.5, SUVmax mean:  $3.7\pm0.8$ ) were detected. The mean SUVmax of metastatic lymph nodes was significantly higher than of non-metastatic lymph nodes (p<0.05). When we used the SUVmax cut-off value of 2.5, the sensitivity and specificity of F-18 FDG PET/CT for identification of lymph nodes were 91.4% and 10.0% respectively. Using the SUVmax cut-off value of 5.05 the sensitivity and specificity were found 72.4% and 100% respectively according to the ROC curve analysis. AUC of SUVmax was 0.83.

Multiple millimetric non-metabolic lung metastases were seen in 6 F-18 FDG PET/CT scans performed on 5 patients. Nineteen hypermetabolic metastatic bone lesions (SUVmax mean: 6.7±2.9; min: 2.7, max: 12.4) were detected in 5 F-18 FDG PET/CT scans performed on 4 patients. Furthermore, the SUVmax level of at least one of metastatic bone lesion was higher than 5, in each F-18 FDG PET/CT scans detected

metastatic bone lesion. Seven metastatic liver lesions (SUVmax mean: 4.5±0.9; min: 3.6, max: 5.9) were detected in 5 F-18 FDG PET/CT scans performed on 4 patients. All metastatic liver lesions had F-18 FDG uptake equal to physiological liver uptake, except one lesion (SUVmax: 5.9).

## DISCUSSION

The calcitonin is the most useful biochemical marker in the follow-up of medullary thyroid carcinoma. Persistently or increasingly elevated calcitonin level is biochemical evidence for residual or recurrent disease in underwent MTC patients [9]. According to the American Thyroid Association, after surgery the patients with serum calcitonin level above 150 pg/ml should be evaluated by imaging procedures, including neck ultrasound, chest CT, contrast-enhanced MRI or three-phase contrast-enhanced CT of the liver, and bone scintigraphy, and MRI of the pelvis and axial skeleton [10]. When there was a suspicious lesion or no lesion in these conventional methods, F-18 FDG, F-18 DOPA or somatostatin receptor PET/CT should be considered in patients with suspected residual or recurrent MTC [2].

In some studies, negative F-18 FDG PET/CT results in patients with elevated calcitonin levels were considered false-negative as in our study. The sensitivity of F-18 FDG PET/CT to detect recurrent or residual disease on a per patient basis analysis was reported to be from 41% to 62% in these studies [11-14]. Our study showed that a sensitivity of F-18 FDG PET/CT was %50, within the range of reported data. Conversely, other studies considered the same patients as true negative in the literature. The sensitivity of F-18 FDG PET/CT to detect recurrent or residual disease on a per patient basis analysis was reported to be from % 65.7 to 93% in these studies (15-20). In a meta-analysis published by Treglia et al, a detection rate of F-18 FDG PET/CT was defined due to these different considerations in the literature. The detection rate of F-18 FDG PET/CT in patients with recurrent or residual was reported 59 % on a per patientbased analysis in the meta-analysis [21].

According to the literature, the diagnostic performance of F-18 FDG-PET/CT increases in MTC patients with higher serum calcitonin level [14, 21]. However, we didn't find a significant difference in serum calcitonin level between the true positive cases and the others. This observation may be related to the small number of cases in each group of our study.

In our study, the SUVmax mean of metastatic lymph nodes was found 6.1±2.2 which is generally low compared with other cancer type and may reflect the slow growth rate and low proliferation index of MTC lesions and it agrees with literature data [12, 20, 22]. However, we found that the mean SUVmax of metastatic lymph nodes was significantly higher than of nonmetastatic lymph nodes. When we calculated the SUVmax cutoff value of 2.5, the specificity of F-18 FDG PET/CT for identification of lymph nodes was 10.0% which is below acceptable value. Nevertheless, using the SUVmax cut-off value of 5.05 the sensitivity and specificity were found 72.4% and 100% respectively.

As shown in the literature, F-18 FDG PET is low sensitive for lung and liver metastasis [10, 23, 24]. In our study, all patients with multiple millimetric lung metastases had non-metabolic lung lesions. We observed only one slightly hypermetabolic metastatic liver lesion, other metastatic liver lesions were non-metabolic.

Somatostatin receptor PET/CT is a valuable imaging method for patients with neuroendocrine tumors and has a significantly higher diagnostic accuracy compared to somatostatin receptor scintigraphy [4, 25]. The recent studies have shown that there was no significant difference between the sensitivity of F-18 FDG PET/CT and somatostatin receptor PET/CT. However, somatostatin receptor PET/CT is a useful complementary imaging method for patients with MTC and could be beneficial to identify the patients for somatostatin receptor-targeted radionuclide therapy [5, 7, 26]. In our study, somatostatin receptor imaging (6 In-111 octreotide scintigraphy and 3 Ga-68 DOTATATE PET/CT scans) of 9 patients with negative F-18 FDG PET/CT scans were also negative.

Our study has several limitations. This is a retrospective study with a relatively small number of patients included as the disease is rare. According to the literature, the sensitivity of F-18 FDG PET/CT improves in patients with shorter the doubling time of serum calcitonin level [21, 27]. Unfortunately, we couldn't calculate the doubling time of serum calcitonin level due to this information was not available for all patients. Additionally, we obtained no histopathological confirmation of some lesions. When histopathological data was not available, we have evaluated the patients with other imaging modalities during follow-up.

## CONCLUSIONS

F-18 FDG PET/CT scan appeared to be less sensitive (50%) to find a residual or recurrent lesion in medullary thyroid carcinoma patients with persistently elevated calcitonin levels. However, it should be considered that F-18 FDG PET/CT was performed to the patients with only no lesion or a suspicious lesion had been detected by the other imaging modalities in this group. Because F-18 FDG PET/CT was not performed when a residual or recurrent lesion had clearly been detected before, the sensitivity of 50% was considered to be acceptable.

## REFERENCES

- Raue F, Frank-Raue K. Epidemiology and clinical presentation of medullary thyroid carcinoma. InMedullary Thyroid Carcinoma, Springer, Cham. 2015;61-90.
- 2. Wells Jr SA, Asa SL, Dralle H, Elisei R, Evans DB, Gagel RF, et al. Revised American Thyroid Association guidelines for the management of medullary thyroid carcinoma: the American Thyroid Association Guidelines Task Force on medullary thyroid carcinoma. Thyroid. 2015;25(6):567-610.
- Maxwell JE, Sherman SK, O'Dorisio TM, Howe JR. Medical management of metastatic medullary thyroid cancer. Cancer. 2014;120(21):3287-301.
- 4. Yamaga L, Cunha M, Campos Neto G, Garcia M, Yang J, Camacho C, et al. Ga-DOTATATE PET/CT in recurrent medullary thyroid carcinoma: a lesion-by-lesion comparison with In-octreotide SPECT/CT and conventional imaging. European Journal of Nuclear Medicine & Molecular Imaging. 2017;44(10).
- Treglia G, Castaldi P, Villani MF, Perotti G, De Waure C, Filice A, ET AL. Comparison of 18 F-DOPA, 18 F-FDG and 68 Gasomatostatin analogue PET/CT in patients with recurrent medullary thyroid carcinoma. European journal of nuclear medicine and molecular imaging. 2012;39(4):569-80.
- 6. Bozkurt MF, Ugur O, Banti E, Grassetto G, Rubello D. Functional nuclear medicine imaging of medullary thyroid cancer. Nuclear medicine communications. 2008;29(11):934-42.
- Ozkan ZG, Kuyumcu S, Uzum AK, Gecer MF, Ozel S, Aral F, et al. Comparison of 68Ga-DOTATATE PET-CT, 18F-FDG PET-CT and 99mTc-(V) DMSA scintigraphy in the detection of recurrent or metastatic medullary thyroid carcinoma. Nuclear medicine communications. 2015;36(3):242-50.
- 8. Boellaard R, Delgado-Bolton R, Oyen WJ, Giammarile F, Tatsch K, Eschner W, et al. FDG PET/CT: EANM procedure guidelines for tumour imaging: version 2.0. European journal of nuclear medicine and molecular imaging. 2015;42(2):328-54.
- 9. Groot JW, Kema IP, Breukelman H, Veer EV, Wiggers T, Plukker JT, et al. Biochemical markers in the follow-up of medullary thyroid cancer. Thyroid. 2006;16(11):1163-70.

- Kloos RT, Eng C, Evans DB, Francis GL, Gagel RF, Gharib H, et al. Medullary thyroid cancer: management guidelines of the American Thyroid Association. Thyroid. 2009;19(6):565-612.
- De Groot JW, Links TP, Jager PL, Kahraman T, Plukker JT. Impact of 18 F-fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET) in patients with biochemical evidence of recurrent or residual medullary thyroid cancer. Annals of Surgical Oncology. 2004;11(8):786-94.
- 12. Ong SC, Schöder H, Patel SG, Tabangay-Lim IM, Doddamane I, Gönen M, et al. Diagnostic accuracy of 18F-FDG PET in restaging patients with medullary thyroid carcinoma and elevated calcitonin levels. Journal of Nuclear Medicine. 2007;48(4):501-7.
- 13. Skoura E, Rondogianni P, Alevizaki M, Tzanela M, Tsagarakis S, Piaditis G, et al. Role of [18F] FDG-PET/CT in the detection of occult recurrent medullary thyroid cancer. Nuclear medicine communications. 2010;31(6):567-75.
- 14. Skoura E, Datseris IE, Rondogianni P, Tsagarakis S, Tzanela M, Skilakaki M, et al. Correlation between calcitonin levels and [18F] FDG-PET/CT in the detection of recurrence in patients with sporadic and hereditary medullary thyroid cancer. ISRN endocrinology. 2012.
- 15. Diehl M, Risse JH, Brandt-Mainz K, Dietlein M, Bohuslavizki KH, Matheja P, et al. Fluorine-18 fluorodeoxyglucose positron emission tomography in medullary thyroid cancer: results of a multicentre study. European journal of nuclear medicine. 2001;28(11):1671-6.
- Iagaru A, Masamed R, Singer PA, Conti PS. Detection of occult medullary thyroid cancer recurrence with 2-deoxy-2-[F-18] fluoro-D-glucose-PET and PET/CT. Molecular Imaging and Biology. 2007;9(2):72-7.
- 17. Gómez-Camarero P, Ortiz-de Tena A, Borrego-Dorado I, Vázquez-Albertino RJ, Navarro-González E, Ruiz-Franco-Baux JV, et al. Evaluation of efficacy and clinical impact of 18F-FDG-PET in the diagnosis of recurrent medullary thyroid cancer with increased calcitonin and negative imaging test. Revista Española de Medicina Nuclear e Imagen Molecular (English Edition). 2012;31(5):261-6.
- Ozkan E, Soydal C, Kucuk ON, Ibis E, Erbay G. Impact of 18F-FDG PET/CT for detecting recurrence of medullary thyroid

carcinoma. Nuclear medicine communications. 2011;32(12): 1162-8.

- Jiang J, Yang Z, Zhang Y, Xu X, Wang M, Hu S, et al. Clinical value of [18F] FDG-PET/CT in the detection of metastatic medullary thyroid cancer. Clinical imaging. 2014;38(6):797-801.
- Rodríguez-Bel L, Sabaté-Llobera A, Rossi-Seoane S, Reynés-Llompart G, Conejero JL, Cos-Domingo M, et al. Diagnostic Accuracy of 18F-FDG PET/CT in Patients With Biochemical Evidence of Recurrent, Residual, or Metastatic Medullary Thyroid Carcinoma. Clinical nuclear medicine. 2019;44(3):194-200.
- 21. Treglia G, Villani MF, Giordano A, Rufini V. Detection rate of recurrent medullary thyroid carcinoma using fluorine-18 fluorodeoxyglucose positron emission tomography: a meta-analysis, Endocrine. 2012;42: 535-545.
- 22. Giraudet AL, Vanel D, Leboulleux S, Aupérin A, Dromain C, Chami L, et al. Imaging medullary thyroid carcinoma with persistent elevated calcitonin levels. The Journal of Clinical Endocrinology & Metabolism. 2007;92(11):4185-90.
- Giraudet AL, Al Ghulzan A, Aupérin A, Leboulleux S, Chehboun A, Troalen F, et al. Progression of medullary thyroid carcinoma: assessment with calcitonin and carcinoembryonic antigen doubling times. European Journal of Endocrinology. 2008;158(2): 239-46.
- Szakáll S, Ésik O, Bajzik G, Repa I, Dabasi G, Sinkovics I, et al. 18F-FDG PET detection of lymph node metastases in medullary thyroid carcinoma. Journal of Nuclear Medicine. 2002;43(1):66-71.
- Geijer H, Breimer LH. Somatostatin receptor PET/CT in neuroendocrine tumours: update on systematic review and metaanalysis. European journal of nuclear medicine and molecular imaging. 2013;40(11):1770-80.
- 26. Treglia G, Rufini V, Salvatori M, Giordano A, Giovanella L. PET imaging in recurrent medullary thyroid carcinoma. International journal of molecular imaging 2012.
- 27. Yang JH, Camacho CP, Lindsey SC, Valente FO, Andreoni DM, Yamaga LY, et al. The combined use of calcitonin doubling time and ^ sup 18^ f-fdg pet/ct improves prognostic values in medullary thyroid carcinoma: the clinical utility of ^ sup 18^ f-fdg pet/ct. Endocrine Practice. 2017;23(8):942.