# MEDÜLLER TİROİD KARSİNOMALI HASTALARIN TAKİBİNDE FDG PET

## FDG PET in the Follow-up of Medullary Thyroid Carcinoma Patients

Ebuzer KALENDER[1], Hasan Deniz DEMİR[1], Umut ELBOĞA[1], Hüseyin KARAOĞLAN[1], Ertan ŞAHİN[2], Y. Zeki ÇELEN[1]

[1]Gaziantep Üniversitesi, Nükleer Tıp Anabilim Dalı, Gaziantep

[2]Namık Kemal Üniversitesi, Nükleer Tıp Anabilim Dalı, Tekirdağ

Ebuzer KALENDER, Yrd. Doç. Dr.
Hasan Deniz DEMİR, Uzm. Dr.
Umut ELBOĞA, Yrd. Doç. Dr.
Hüseyin KARAOĞLAN, Uzm. Dr.
Ertan ŞAHİN, Yrd. Doç. Dr.
Y. Zeki ÇELEN, Prof. Dr.

**İletişim:**
Yrd. Doç. Dr. Umut ELBOĞA
Gaziantep Universitesi Tıp Fakültesi Şahinbey Hastanesi, Nükleer Tıp Anabilim Dalı
Gaziantep
**Tel:** 0342 360 60 60
**e-mail:**
umutelboga@hotmail.com

Geliş tarihi/Received: 12.05.2014
Kabul tarihi/Accepted: 09.08.2014

Bozok Tıp Derg 2014;4(3):14-8
Bozok Med J 2014;4(3):14-8

## ÖZET

**Amaç:** Çalışmanın amacı cerrahi sonrası yüksek kalsitonin seviyelerine sahip medüller tiroid karsinomlu (MTK) hastaların takibinde florodeoksiglikoz pozitron emisyon tomografisinin (FDG PET) etkinliğini değerlendirmektedir.
**Gereç ve Yöntemler:** Çalışmaya yüksek kalsitonin seviyeleri nedeniyle kliniğimize FDG PET görüntüleme için yönlendirilen MTK tanılı 6 hasta dahil edildi. Bütün hastalar erkekti. Yaş ortalaması 52±8 idi.
**Bulgular:** Kalsitonin seviyeleri sırasıyla75 pg/ml, 90pg/ml, 94 pg/ml ve 127 pg/ml olan 4 hastada FDG PET görüntülemede MTK'nın rekürrens ya da metastazını düşündürecek bulgu izlenmedi. Kalsitonin seviyeleri 1300 pg/ml ve 2110 pg/ml olan 2 hastada ise FDG PET bulguları pozitifti. Bu hastalarda lenf nodu ve kemik metastazları saptandı.
**Tartışma:** Öyle görünüyor ki MTK'nın rutin görüntülemesinde FDG PET'e yer yoktur. Ancak burada kalsitonin seviyeleri önem arz etmektedir. Kalsitonin seviyeleri 1000 pg/ml'den yüksek hastalarda FDG PET oldukça faydalı olabilmekte ve birçok lezyon odağını tespit edebilmektedir. Ayrıca tüm vücut görüntülemeye olanak sağlaması da önemli bir avantajıdır.
**Anahtar kelimeler:** *Medüller tiroid karsinomu, FDG PET, Kalsitonin.*

## ABSTRACT

**Objective:** The aim of study is to evaluate the impact of fluorodeoxyglucose positron emission tomography (FDG PET) in the follow-up of medullary thyroid carcionma (MTC) patients who had elevated calcitonin levels after surgery.
**Materials and Methods:** Six patients diagnosed with MTC who referred to our clinic for FDG PET imaging because of the elevated calcitonin levels were included. All were male. Mean age was 52±8 years.
**Results:** In 4 patients whose calcitonin levels were 75 pg/ml, 90pg/ml, 94 pg/ml and 127 pg/ml respectively, there was no evidence for recurrence or metastasis of MTC on FDG PET. FDG PET findings were positive in 2 patients whose calcitonin levels were 1300 pg/ml and 2110 pg/ml respectively. In these patients lymph node metastases and bone metastases were detected.
**Conclusion:** It seems that there is no place to FDG PET for routine imaging of MTC. But here calcitonin levels are important. In patients who have calcitonin levels higher than 1000 pg/ml FDG PET can be very useful and detect a lot of lesion foci. Also allowing to whole body imaging is a significant advantage of it.
**Key words:** *Medullary thyroid carcinoma, FDG PET, Calcitonin.*

## INTRODUCTION

Medullary thyroid carcionma (MTC) is a rare neuroendocrine tumor which originates from thyroid parafollicular C-cells. C cells produce calcitonin hormone, for this reason calcitonin uses as a tumor marker for the follow-up of MTC patients after surgery (1). Elevated calcitonin levels indicate residual, recurrent, or metastatic disease (2-4). Finding the source of increased calcitonin is important, because surgery is the main and effective treatment method of MTC (1). A lot of imaging techniques are used for the eveluation of MTC patients. One of them is fluorodeoxyglucose positron emission tomography (FDG PET). The benefit of FDG PET on the follow up of MTC patients is still controversial. The aim of this study is to evaluate the impact of FDG PET in the follow-up of MTC patients who had elevated calcitonin levels after surgery.

## MATERIAL AND METHODS

Six patients who had histologically proven MTC after surgical treatment (total thyroidectomy and neck dissection) referred to Gaziantep University Nuclear Medicine Depertmant for FDG PET imaging because of the elevated calcitonin levels. All patients were male. Mean age was 52±8 years. All patients had elevated calcitonin level after surgery. This stuation was thought that there was recurrence or metastasis. But there was no evidence for recurrence or metastasis in morphologicial imaging methods, ultrasonography (USG) and computed tomography (CT) for 2 patients. Two patients who had calcitonin level higher than 1000 pg/ml were referred to FDG PET firstly. In one patient there was a mass in the left lung on thorax CT and, in other patient there was a hypodense nodular lesion in left adrenal gland on abdominal CT. Based on high calcitonin levels, patients were referred to FDG PET imaging for restaging. Calcitonin was determined using an enzyme-linked immunosorbent assay (Biomerica) with a reference value of 0.3–12 pg/ml. FDG PET was performed by Siemens Biograph 2 device. After 6-h fasting, blood glucose was measured by glucometer from the finger. Patients who had blood glucose level under 150 mg/dL were injected 0.15–0.20 mCi/kg FDG intravenously. After radiopharmaceutical injection, patients were seated in a quiet and relaxed atmosphere in a 60 min for ensure ideal tumor involvement. End of the waiting period, patients were placed on FDG PET scanner bed in the supine position. PET images were obtained after CT images which used for attenuation correction and anatomical localization. On the evaluation, the maximum standardized uptake value (SUVmax) was determined in lesions.

## RESULTS

In two patients whose calcitonin levels were 90pg/ml ve 94 pg/ml respectively, FDG-PET findings were negative. Neck USG, thorax and abdominal CTs of these patients were also negative. In a patient whose calcitonin level was 75 pg/ml, there was a hypodense nodular lesion in left adrenal gland on abdominal CT. On FDG PET, there was a minimal FDG uptake in this lesion area (SUVmax:3). This lesion was considered as benign adrenal adenoma. In a patient whose calcitonin was 127 pg/ml, there was a lung mass in the left on thorax CT. On FDG PET, there was a hypermetabolic lung mass with irregular margins in the left and SUVmax was 9,2. Biopsy was taken from the lung mass, histopathological examination reported as nonsmall cell lung carcinoma (secondary malignancy). FDG PET findings were positive in two patients whose calcitonin levels were 1300 pg/ml and 2110 pg/ml respectively. In a patient whose calcitonin level was 2110 pg/ml, there were hypermetabolic inferior cervical, mediastinal and supraclavicular lymph nodes and vertebral lesions (Figure 1). In other patient whose calcitonin level was 1300 pg/ml there were hypermetabolic mediastinal lymph nodes and sternal lesion (Figure 2).

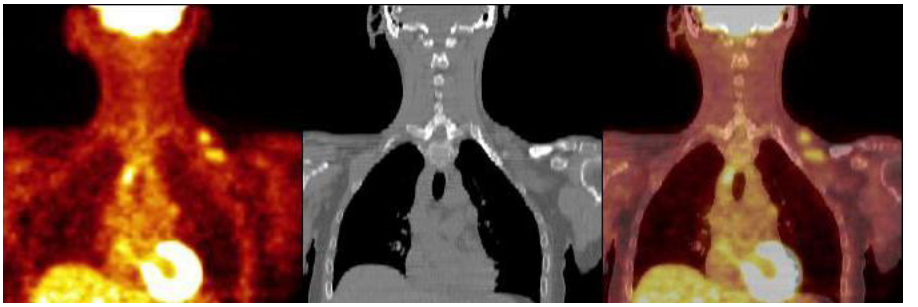

**Figure 1:** Left supraclavicular and right paratracheal lymph node metastases in a patient whose calcitonin level was 2110 pg\ml.

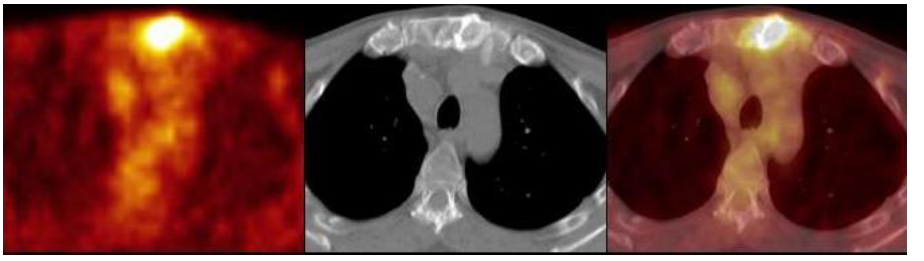

**Figure 2:** Sternal bone metastasis in a patient whose calcitonin level was 1300 pg\ml.

## DISCUSSION

MTC is a rare neuroendocrine tumor accounting for about 3%–10% of all thyroid malignancies (5). It has sporadic (75%) and familial (25%) forms. The familial forms include isolated familial MTC and multiple endocrine neoplasia types 2A and 2B (2). Metastasis are not rare, most frequent sites of metastatic disease are cervical and mediastinal lymph nodes, lungs, liver, and bone. Cervical and mediastinal lymph nodes metastases are seen up to 35% of patients at the initial diagnose (6). Distant metastases are seen approximately in 20% of MTC patients (7). The main treatment for MTC is surgical resection. In metastatic patients therapeutic options are limited because this tumor does not concentrate radioiodine and shows poor response to chemotherapy and radiation therapy (8). Postsurgically, serum calcitonin is the main marker that used for the follow-up. Another frequently used marker is carcinoembryonic antigen (CEA) but it is less spesific (9). Calcitonin levels are usually below 10 pg/ml in postoperative 8-10th weeks after a successful surgery in nonmetastaic patients. Elevated calcitonin levels after surgery indicate residual, recurrent, or metastatic disease (2-4). It is important to find the source of the elevated calcitonin and distinguish between local disease and systemic disease. Because local recurrence may be curable with surgery, but the treatment of systemic disease is palliative. Multiple morphological and functional imaging methods are used for detection of elevated calcitonin source in MTC patients. It can not be easy to determine recurrences and metastases of MTC patients and there is not fully effective diagnostic method viewing these foci. In about half of the patients, persistent MTC cannot be detected with any morphologic or functional imaging modalities (10, 11). FDG PET is an important imaging modality using for evaluation of many tumors, but its effectiveness in MTC patients is controversial. Neuroendocrine tumors usually show low FDG uptake (12), but in dedifferentiation of the tumor FDG uptake may increase. The sensitivity of FDG PET for MTC patients who had elevated calcitonin levels was reported as 41% to 78% in many studies (10, 13-16). Diehl et al. was reported the sensitivity of FDG PET as 78% in a multicenter study of 55 patients(14). On the other hand de Groot et al. reported a sensitivity of only 41% for 26 patients (15).

Another important subject is to which calcitonin level is significant for detection of recurrence and metastasis. The sensitivity of FDG PET is increased in patients who have higher calcitonin level. Ong et al. reported the sensitivity for lesion detection of FDG PET as 62% in MTC patients (10). However, the sensitivity was 78% when the calcitonin level was greater than 1,000 pg/mL (10). On the other hand sensitivity was only 20% when calcitonin level was below 500 pg/ml (10). Similarly, de Groot et al. was reported that the FDG PET sensitivity was increased from 41% to about 73% when the calcitonin level was greater than 1,000 pg/mL (15). In our study, FDG PET positive two patients had calcitonin levels greater than 1000 pg/ml. Also 18F-FDG PET might be more sensitive in patients with a short calcitonin doubling time (17). The most important reason of negative imaging findings in MTC patients with elevated calcitonin level is liver metastasis. In these patients it is not unusual to detect subcapsular liver metastasis on laparoscopy (18). Liver metastases were detected better with CT or MRI than with 18F-FDG PET (19).

New functional nuclear medicine procedures were developed for metabolic imaging of MTC. 18F-Dihydroxyphenylanaline (18F-DOPA) PET one of them and it is based on the increased activity of large amino acid transporter (LAT) systems in neuroendocrine tumors. It was reported that 18F-DOPA PET detects more tumor-positive regions and lesions than FDG PET and morphologic imaging methods (CT or MRI) (20, 21). Another promising new functional nuclear medicine procedur is gastrin receptor scintigraphy. This method is based on the high expression of the cholecystokinin 2 receptor in MTC patients (22). 99mTc(V) dimercaptosuccinic acid scintigraphy (DMSA-V) and 111In-octreotide scintigraphy other functional imaging methods usinf for evaluation of MTC.

Most important limitation of this study is small number of patients. But it can be suggestive about the use of FDG PET for follow-up of MTC patients.
In conclusion; it seems that there is no place to FDG PET for routine imaging of MTC. At this point calcitonin levels are very important. Calcitonin levels are very important for the use of FDG PET on the follow up of MTC patients. In patients who have calcitonin levels higher than 1000 pg/ml FDG PET can be very useful and detect a lot of lesion foci. Also allowing to whole body imaging is a significant advantage of it.

## REFERENCES

**1.** Vitale G, Caraglia M, Ciccarelli A, Lupoli G, Abbruzzese A, Tagliaferri P, et al. Current approaches and perspectives in the therapy of medullary thyroid carcinoma. Cancer. 2001;91(9):1797–808.
**2.** Leboulleux S, Baudin E, Travagli JP, Schlumberger M. Medullary thyroid carcinoma. Clin Endocrinol (Oxf). 2004;61(3):299–310.
**3.** Busnardo B, Girelli ME, Simioni N, Nacamulli D, Busetto E. Non parallel patterns of calcitonin and carcinoembryonic antigen levels in the follow-up of medullary thyroid carcinoma. Cancer. 1984;53(2):278–85.
**4.** Quayle FJ, Moley JF. Medullary thyroid carcinoma: including MEN 2A and MEN 2B syndromes. J Surg Oncol. 2005;89(3):122–9.
**5.** Hundahl SA, Fleming ID, Fremgen AM, Menck HR. A National Cancer Data Base report on 53,856 cases of thyroid carcinoma treated in the U.S, 1985-1995. Cancer. 1998;83(12):2638–48.
**6.** Lairmore TC, Wells SA Jr. Medullary carcinoma of the thyroid: current diagnosis and management. Semin Surg Oncol. 1991;7(2):92–9.
**7.** Bergholm U, Adami HO, Bergström R, Johansson H, Lundell G, Telenius-Berg M, et al. Clinical characteristics in sporadic and familial medullary thyroid carcinoma: a nationwide study of 249 patients in Sweden from 1959 through 1981. Cancer. 1989;63(6):1196–204.
**8.** Pitt SC, Moley JF. Medullary, anaplastic, and metastatic cancers of the thyroid. Semin Oncol. 2010;37(6):567-79.
**9.** Kebebew E, Ituarte PH, Siperstein AE, Duh QY, Clark OH. Medullary thyroid carcinoma: clinical characteristics, treatment, prognostic factors, and a comparison of staging systems. Cancer. 2000;88(5):1139–48.
**10.** 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. J Nucl Med. 2007;48(4):501–7.

**11.** Khan N, Oriuchi N, Higuchi T, Endo K. Review of fluorine-18-2-fluoro-2-deoxy- D-glucose positron emission tomography (FDG-PET) in the follow-up of medullary and anaplastic thyroid carcinomas. Cancer Control. 2005;12(4):254–60.
**12.** Rufini V, Treglia G, Perotti G, Leccisotti L, Calcagni ML, Rubello D. Role of PET in medullary thyroid carcinoma. Minerva Endocrinol. 2008;33(2):67–73.
**13.** Brandt-Mainz K, Muller SP, Gorges R, Saller B, Bockisch A. The value of fluorine-18 fluorodeoxyglucose PET in patients with medullary thyroid cancer. Eur J Nucl Med. 2000;27(5):490–6.
**14.** 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. Eur J Nucl Med. 2001;28(11):1671–6.
**15.** De Groot JW, Links TP, Jager PL, Kahraman T, Plukker JT. Impact of 18F-fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET) in patients with biochemical evidence of recurrent or residual medullary thyroid cancer. Ann Surg Oncol. 2004;11(8):786–94.
**16.** Hoegerle S, Altehoefer C, Ghanem N, Brink I, Moser E, Nitzsche E. 18F-DOPA positron emission tomography for tumour detection in patients with medullary thyroid carcinoma and elevated calcitonin levels. Eur J Nucl Med. 2001;28(1):64–71.
**17.** Beheshti M, Pöcher S, Vali R, Waldenberger P, Broinger G, Nader M,et al. The value of 18F-DOPA PET-CT in patients with medullary thyroid carcinoma: comparison with 18F-FDG PET-CT. Eur Radiol. 2009;19(6):1425–34.
**18.** Aide N, Bardet S. Would patient selection based on both calcitonin blood level and doubling time improve 18F-FDG PET sensitivity in restaging of medullary thyroid cancer? J Nucl Med. 2007;48(9):1574-5.
**19.** Szakáll S Jr, Esik O, Bajzik G, Repa I, Dabasi G, Sinkovics I, et al. 18F-FDG PET detection of lymph node metastases in medullary thyroid carcinoma. J Nucl Med. 2002;43(1):66–71.
**20.** Koopmans KP, De Groot JW, Plukker JT, De Vries EG, Kema IP, Sluiter WJ, et al. Links TP. 18F Dihydroxyphenylalanine PET in patients with biochemical evidence of medullary thyroid cancer: relation to tumor differentiation. J Nucl Med. 2008; 49(4):524–31.
**21.** Treglia G, Rufini V, Salvatori M, Giordano A, Giovanella L. PET Imaging in Recurrent Medullary Thyroid Carcinoma. Int J Mol Imaging. 2012 Jul 18;2012:324686. doi: 10.1155/2012/324686.
**22.** Gotthardt M, Béhé MP, Beuter D, Battmann A, Bauhofer A, Schurrat T, et al. Improved tumour detection by gastrin receptor scintigraphy in patients with metastasised medullary thyroid carcinoma. Eur J Nucl Med Mol Imaging. 2006;33(11):1273–9.