



## Technetium-99m-Sestamibi Scintigraphy with SPECT / CT in the Diagnosis of Primary Hyperparathyroidism: Single Center Experience

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### Abstract

**Objective:** In about two-thirds of patients with primary hyperparathyroidism, Tc-99m sestamibi scintigraphy allows the determination of parathyroid adenoma and the surgeon to plan appropriate surgery. In our study, in the patients with the diagnosis of primary hyperparathyroidism; we aimed to investigate the relationship between serum calcium (Ca), phosphorus (P) and parathyroid hormone (PTH) levels and Tc-99m sestamibi parathyroid scintigraphy.

**Material and Methods:** The study was conducted between January 2015 and January 2018 in the Department of Endocrinology and Metabolism Diseases of Göztepe Training and Research Hospital, Istanbul Medeniyet University. A retrospective analysis of the files of the patients diagnosed as primary hyperparathyroidism with clinical, biochemical and ultrasonographic findings was performed. A total of 79 patients (68 females, 11 males) who underwent parathyroid scintigraphy were included in the study. Age distribution of the patients was similar in both gender (women 22-83, men 19-79 years). Scintigraphic evaluation was indicated as positive or negative. Serum Ca, P and PTH levels were compared to scintigraphy results.

**Results:** In 38 patients (female: 32, male: 6), parathyroid scintigraphy was reported as suspicious for adenoma. Adenoma was not detected in 33 patients (female: 29, male: 4). In 8 patients (female: 7, male: 1), differentiation between parathyroid adenoma and thyroid nodule could not be made. Mann Whitney Test was used to determine the relationship between the presence of adenoma and independent variables. According to this test, the presence of adenoma was significantly associated with PTH and Ca levels, while it was not associated with P levels. The average PTH levels were found to be 371 pg / mL in the adenoma group and 125 pg / mL in the group without parathyroid adenoma. In regression analysis, there was a correlation between the presence of adenoma and PTH levels, but no correlation was found between the variables such as Ca and P. When cut-off PTH level was taken as 103.2 pg / mL; the sensitivity and specificity of PTH were 81.1% and 52%, respectively, for the presence of adenoma in scintigraphy.

**Conclusion:** In our study, parathyroid scintigraphy was found to be positive in approximately half of the patients diagnosed with primary hyperparathyroidism according to clinical, biochemical and ultrasonographic findings. The probability of obtaining a positive scintigraphy was only related to PTH levels. The higher the PTH levels, the higher the sensitivity of scintigraphy to indicate the presence of adenoma.

**Keywords:** Primary hyperparathyroidism, Parathyroid scintigraphy, Parathormone

## **INTRODUCTION**

Primary hyperparathyroidism is characterized by high parathyroid hormone (PTH) levels and clinical symptoms and signs of hypercalcemia. It is one of the most common causes of hypercalcemia. Parathyroid adenoma, parathyroid hyperplasia and parathyroid carcinoma may play role in the etiology (1-3). In our study, we aimed to investigate the relationship between serum calcium (Ca), phosphorus (P) and parathyroid hormone (PTH) levels and Tc-99m sestamibi parathyroid scintigraphy findings in the patients with the diagnosis of primary hyperparathyroidism.

## **MATERIALS AND METHODS**

In this study, medical records of the patients diagnosed with primary hyperparathyroidism between January 2015 and January 2018 in the Department of Endocrinology and Metabolism Diseases of Göztepe Education and Research Hospital, Istanbul Medeniyet University were retrospectively evaluated. The diagnosis of the subjects had been made according to clinical, biochemical and ultrasonographic findings. Inclusion criteria were patient age > 18 years, diagnosis of primary hyperparathyroidism and complete file data. Subjects with missing file data were excluded. Patients who underwent 99m tc sestamibi scintigraphy with spect / bt for the diagnosis of primary hyperparathyroidism were evaluated. Scintigraphic evaluation was indicated as positive or negative. Patients' age, gender, demographic data, serum calcium (Ca), phosphorus (P), PTH levels and neck ultrasonography findings were recorded. Patients' demographic data, clinical features, Tc-99m sestamibi and post-operative findings, laboratory values and histopathologic results of all patients are expressed as mean  $\pm$  SD. Preoperative and postoperative laboratory values, neck ultrasonography and parathyroid scintigraphy findings of the patients with primary hyperparathyroidism were compared by means of paired Student t test. IBM SPSS 22 was used as a statistical analysis program. P <0.05 was considered statistically significant.

## **RESULTS**

Medical records of 68 patients were evaluated retrospectively. 58 (85.3%) of the patients were female and 10 (14.7%) were male. The mean age of the patients was  $54.7 \pm 12.6$  years (min: 19-max: 83) (table 1). According to parathyroid scintigraphy findings, 37 patients had parathyroid adenoma and 25 patients had no adenoma, while parathyroid adenoma and thyroid nodule differentiation could not be made in 6 patients (table 2). Mann Whitney Test was used for statistical analysis to determine the relationship between the presence of adenoma and independent variables. According to this test, the presence of adenoma was significantly associated with PTH and Ca levels, while it was not associated with P levels. The mean serum PTH levels in the group with parathyroid adenoma was 371 pg / mL and 125 pg / mL in the group without parathyroid adenoma. In regression analysis, there was a correlation between the presence of adenoma and PTH levels, but no correlation was found with age, serum Ca and P variables. In Roc curve analysis, when PTH cut off value was taken as 103.2 pg / mL, the sensitivity of PTH was 81.1% and the specificity was 52% for the presence of adenoma in scintigraphy (figure 1).

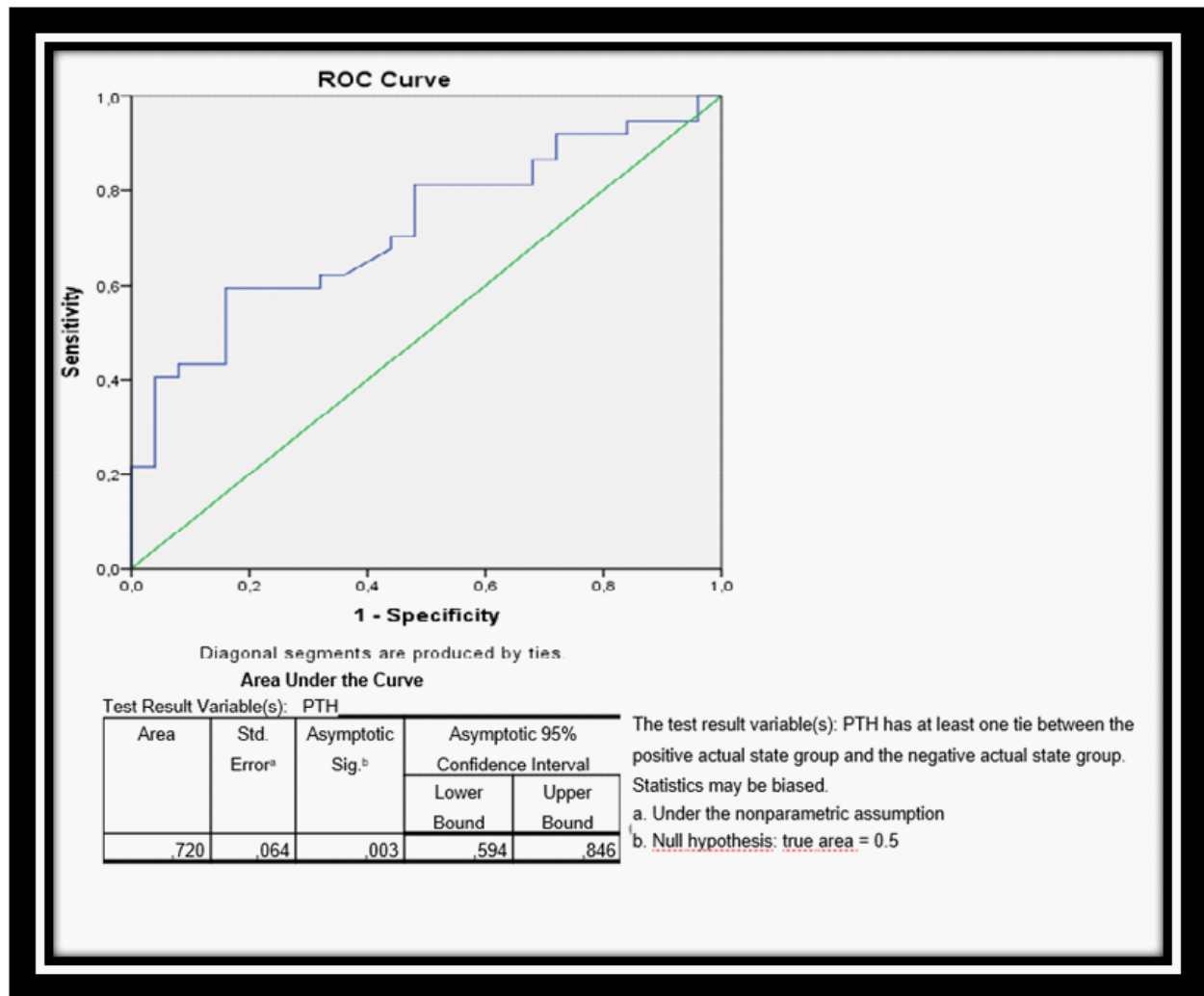
**Table1.** *Clinical and demographic data in patients with primary hyperparathyroidism*

		The reference range
Age	57.7 $\pm$ 12.6 years	
Gender (F / M)	58/10	
PTH	275.5 (min:28, max: 2909)	12–65 ng/L
Alkaline phosphatase (ALP)	124.1 $\pm$ 92.7	30–120 U/L
Albumin	4.2 $\pm$ 0.3	3.5–5.5 g/dl.
Adjusted Calcium level	10.6 $\pm$ 1.8	8.8–10.6 mg/dL
Phosphorus (P)	3 $\pm$ 0.9	2.5–4.5 mg/dL
25-OH-vitamin D	21.8 $\pm$ 20.3	30-50 ng/mL

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**Table2.** Parathyroid scintigraphy results and postoperative histopathological findings

Parathyroid scintigraphy findings (n: 68)	Postoperative histopathological findings (n: 31)
<ul style="list-style-type: none"> <li>Parathyroid adenoma (n: 37)</li> <li>Parathyroid focus undetectable (n: 25)</li> <li>Parathyroid adenoma-thyroid nodule can not be differentiated (n: 6)</li> </ul>	<ul style="list-style-type: none"> <li>Parathyroid adenoma (n: 27)</li> <li>Parathyroid hyperplasia (n: 1)</li> <li>Parathyroid carcinoma (n: 1)</li> <li>Normal parathyroid tissue (n: 1)</li> <li>Parathyroid tissue not detected (n: 1)</li> </ul>



**Figure1.** Roc curve analysis for PTH in patients with primary hyperparathyroidism with a focus on parathyroid scintigraphy

**DISCUSSION**

Following biochemical diagnosis of primary hyperparathyroidism, localization should be performed by imaging. Neck ultrasonography is very effective in detecting parathyroid diseases, but is inadequate for mediastinum.

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If mediastinum is considered as localization, magnetic resonance imaging or computed tomography should be used. Tc99m-sestamibi imaging is the most important preoperative localization detection method before minimally invasive parathyroidectomy. In some cases, intraoperative PTH can be measured (2,4). In their study, Hughes DT et al. (5) suggested that the higher the parathormone level, the more accurate the localization accuracy of USG and Tc99m-sestamibi scintigraphy. There was a significant correlation between Tc99m-sestamibi localization and serum PTH level ( $p < 0.05$ ). In the study by Mshelia DS et al. (6), serum Ca and PTH levels and parathyroid (99m) Tc-MIBI scintigraphy findings were compared in 111 patients. They found that 99m Tc-MIBI parathyroid scintigraphy was highly likely to detect and localize the parathyroid adenoma when both serum PTH and calcium levels were elevated, while the localization by (99m) Tc-MIBI parathyroid scintigraphy was lower when Ca level was  $< 2, 51 \text{ mmol / L}$  ( $< 10.04 \text{ mg / dL}$ ). In our study, in the roc curve analysis performed in cases with localizing parathyroid scintigraphy, the PTH value cut off was found to be  $103.2 \text{ pg / mL}$ , while the sensitivity of this value was 81.1% and specificity was 52%. In the study by Ciappuccini R et al. (7), two-phase 99m-Tc sestamibi scintigraphy with SPECT / CT used and approximately 2/3 of patients with primary hyperparathyroidism was diagnosed with parathyroid adenoma, while the ability of scintigraphy to localize adenoma was positively affected by serum Ca or PTH levels. In the study by Qiu ZL et al. (8), the relationship between 99m-Tc-MIBI, bone scintigraphy and preoperative PTH levels, tumor diameter, clinical or pathological variables were investigated in patients with newly diagnosed primary hyperparathyroidism. In this study, the optimal thresholds for tumor diameter and PTH in the ROC analysis were 1.03 cm and  $127.60 \text{ ng / L}$ . As a result, 99m-Tc-MIBI scintigraphy was reported to detect  $> 70\%$  of adenomas in primary hyperparathyroidism. In their study, Parikshak M et al. (9) retrospectively evaluated 102 patients with primary hyperparathyroidism and mild hypercalcemia who underwent preoperative scintigraphy. They reported that in patients with serum  $\text{Ca} > 11.3 \text{ mg / dL}$  and serum PTH level  $> 160 \text{ pg / mL}$ , the probability of detecting the focus of parathyroid disease with scintigraphy was higher. In the study conducted by Ozcelik et al. (10), 52 patients with primary hyperparathyroidism were evaluated. Ozcelik et al. reported that the size of parathyroid adenoma was correlated with serum PTH level and parathyroid scintigraphy detected larger adenomas more easily. Technical aspects of Tc 99m sestamibi such as determining the optimal spatial resolution, such as matrix size, number of angles, and time per view may be different, which might be the main limitation of our study.

### **CONCLUSION**

In our study, parathyroid scintigraphy was found to be positive in approximately half of the patients diagnosed as primary hyperparathyroidism according to clinical, biochemical and ultrasonographic findings. The probability of obtaining positive scintigraphy results was only related to serum PTH levels. The higher the PTH levels, the higher the sensitivity of scintigraphy to detect the presence of adenoma.

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