



# Contrast Enhanced [99mTc] MIBI SPECT/CT In Primary Hyperparathyroidism



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## Contrast Enhanced [99mTc] MIBI SPECT/CT In Primary Hyperparathyroidism

**OBJECTIVE:** The aim of the present study was to compare the surgical results with contrast-enhanced [99mTc] MIBI SPECT/CT results by adding the simultaneous single phase contrast to the [99mTc] MIBI SPECT/CT examination.

**METHOD:** Between November 2016 and January 2018, 24 (21 female, 3 male) patients who underwent an operation after preoperative contrast-enhanced [99mTc]MIBI SPECT/CT, and 49 asymptomatic patients (42 female, 7 male), who did not undergo surgery, were included in the study.

**RESULTS:** Sensitivity and specificity rates of contrast enhanced [99mTc] MIBI SPECT / CT were 100% and 100% when evaluated together with surgical results. The rate of detection in asymptomatic patients was found to be 93.8%.

**CONCLUSIONS:** With the contrast-enhanced [99mTc] MIBI SPECT/CT imaging, both high sensitivity and specificity values were achieved in the preoperative localization of parathyroid adenomas and high detection rates were obtained in the asymptomatic group. The use of contrast IV during the [99mTc] MIBI SPECT/CT in patients without contraindications increased both preoperative localization rates of adenomas and detection rates of asymptomatic hyperparathyroidism cases.

**KEY WORDS:** Parathyroid adenoma, Primer Hyperparathyroidism, [99mTc]MIBI, SPECT/CT

## Introduction

Primary hyperparathyroidism is the third most common endocrine disorder following diabetes mellitus and hypothyroidism, affecting about 0.3% of the general population<sup>1,2</sup>. Developments in the preoperative localization of the adenoma in patients with primary hyper-

parathyroidism has enabled a transition from the conventional bilateral neck exploration to the selective excision of the preoperatively localized adenoma. In order for minimally invasive parathyroidectomy techniques to be successful, the preoperative localization must be definite<sup>3</sup>. Cervical ultrasonography and [99mTc] MIBI planar scintigraphy are the techniques used for the routine preoperative imaging and localization of parathyroid adenoma. These two methods have been used as complementary techniques for many years. [99mTc] MIBI planar scintigraphy provides functional information, while ultrasonography gives more detailed anatomical information. The use of technetium-99m (Tc-99m) methoxyisobutylisonitrile (MIBI) for parathyroid imaging was first reported in 1989<sup>4</sup>. An important limitation of

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parathyroid imaging with ultrasonography (USG) or Tc-99m MIBI parathyroid scintigraphy is that thyroid nodules imitating parathyroid lesions or other metabolically active tissues such as lymph node and thyroid cancer may cause a false positive result in the [99mTc] MIBI scanning<sup>5</sup>. Some centers routinely use [99mTc] MIBI SPECT/CT as the only test that can present both functional and anatomic information. A study by Lavelly et al.<sup>6</sup> showed that early stage [99mTc] MIBI SPECT/CT for adenoma localization increased accuracy and improved inter-observer agreement. [99mTc] MIBI SPECT/CT is a non-invasive, mildly radiating and easily accessible method that provides a significant contribution to the detection of parathyroid adenomas<sup>7</sup>. Including [99mTc]MIBI SPECT/CT, the sensitivity reported in parathyroid scintigraphy ranges from 53% to 92%, in primarily retrospective studies<sup>7-9</sup>. Unlike ultrasonography, scintigraphy can detect deeply located or ectopic parathyroid adenomas (PTA). In an article published in 2009, Randall GJ et al.<sup>10</sup> described the imaging features of parathyroid adenomas in single-phase contrast-enhanced CT and the CT findings were shown to be correlated with the surgical findings.

Contrast-enhanced CT, termed 4D CT because it is derived from multiple contrast phases, is based on the generally high and early accumulation of contrast material in parathyroid adenomas. This single application method has provided promising results for the preoperative localization of parathyroid adenomas<sup>11,12</sup>.

Dynamic contrast-enhanced computed tomography (CT) has emerged as the second favorite imaging method in symptomatic or asymptomatic cases. Recent developments in magnetic resonance imaging (MRI) and recent studies for the development of several new positron emission tomography (PET) radiotracers have been promising and have shown that the roles of these modalities can expand.

In this study, the preoperative single-phase contrast-enhanced [99mTc] MIBI SPECT/CT results were compared with the surgery results in patients with primary hyperparathyroidism and the rate of parathyroid adenoma detection in asymptomatic patients was evaluated.

## Material-Method

The present study included 141 patients, who were referred to Gazi Yasargil Training and Research Hospital Nuclear Medicine Clinic due to hyperparathyroidism between November 2016 and January 2018, and whose clinical histories, laboratory data, imaging data, and surgical and pathological results could be obtained. Of these patients, 67 were excluded from the study due to secondary and tertiary hyperparathyroidism. One patient was excluded from the study due to Multiple Endocrine Neoplasia (MEN). Approval for the study was granted by the Local Ethics Committee. (permit no : 056/2018)

## LABORATORY DATA

Serum parathormone (PTH), serum calcium (Ca), phosphorus (P), 25 hydroxy vitamin D, eGFR (estimated glomerular filtration rate), T scores obtained from bone mineral densitometry (from the lumbar vertebrae or the femur neck or the total hip), and urine calcium values of all the patients were recorded.

## IMAGING PROTOCOL

Imaging of all the patients was applied with a dual-headed SPECT/CT gamma camera (Discovery 670™, GE Healthcare, Milwaukee, USA) and a low-energy high-resolution collimator in a manner to include the neck upper mediastinum in the image area 45 minutes after the injection of 740 MBq mCi [99mTc] MIBI IV. The SPECT imaging parameters were 10\*-minute images taken at 18s/frame. Automatic body contouring was used. IV contrast was applied at 2-4 ml/sec after the SPECT image from 1.5 ml/kg. CT imaging was applied after 50 to 70 seconds (120 kVp, 50-110mAs, helical rotation 1s, pitch of 1.375: 1, 512x512 matrix, 50 cm FOV, cross-sectional thickness 3.75 mm). The data obtained was evaluated after being processed on the Xeleris™ 3 (GE Healthcare, Milwaukee, USA) workstation.

## EVALUATION OF THE IMAGES

The images were evaluated by 2 experienced nuclear medicine specialists independently of laboratory, pathology and surgical findings. The lesions detected anatomically and functionally on SPECT/CT were accepted as positive.

## STATISTICAL ANALYSIS

The sensitivity, specificity, positive and negative predictive values and accuracy were calculated from the [99mTc] MIBI single-phase IV contrast-enhanced SPECT/CT images. In addition, the lesion detection rates were calculated in asymptomatic patients.

## Results

The present study initially enrolled 141 patients who were referred to our clinic for hyperparathyroidism. Of these patients, 67 were excluded from the study due to secondary hyperparathyroidism and 1 because of Multiple Endocrine Neoplasia (MEN). Thus evaluation was made of 73 primary hyperparathyroidism patients (64 females, 9 males) with a mean age of 51.9 ± 13.59 years (range, 20-82 years). The patients were divided into two groups as symptomatic and asymptomatic. Of the symptomatic

TABLE I - Laboratory findings of the patients who underwent an operation.

	Median	Range	Normal
PTH	235.3 ± 171.6	77-767	15-65 pg/ml
Ca	11.67 ± 0.93	9.26-13.2	8,8-10.6 mg/dl
P	2.57 ± 0.81	1.11-4.9	2,5-4,5 mg/dl
Vit D	17.5 ± 7.97	4.2-41	>30 ng/dl
eGFR ml/min	85.8 ± 10.3	61-90	
BMD T	-1.33 ± 1.36	-3.6+1.4	
24 h urine ca	428 ± 185.81	187-784	

TABLE II - Laboratory findings of the patients with asymptomatic primary hyperparathyroidism.

	Median	Range	Normal
PTH	161.73±113,31	70-625	15-65 pg/ml
Ca	10.48±0.70	8.9-11.4	8,8-10.6 mg/dl
P	2.95±0.85	1.8-6.7	2.5-4.5 mg/dl
Vit D	18.64±11.45	3-57.6	>30 ng/dl
eGFR ml/min	88.12±4.61	70-90	
BMD T	-0.49±1.40	-4+1.5	
24 h urine ca	150.83±83.06	23.4-325	

patients, 24 (21 females, 3 males, mean age 49.9 ± 14.4 years) underwent an operation. One of these patients had previously undergone total thyroidectomy due to multinodular goiter. The mean PTH value of the patients was 235.3±171.6 pg/ml (77-767 Pg/ml, normal value 15-65 pg/ml).

The mean Ca value was 11.67±0.9mg/dl (9.26-13.2 mg/dl, normal value 8.5-10.5 mg/dl). The laboratory findings of the patients are shown in Table I. Coexisting thyroid nodules were detected on USG in 18 patients (18/24, 75%).

In 49 patients evaluated as asymptomatic (42 females, 7 males, mean age 52.61±13.44 years, age range, 22-87 years), the mean PTH value was 161.73±113.31 pg/ml (70-625 Pg/ml, normal value 15-65 Pg/ml). The mean Ca value was 10.48±0.70mg/dl (8.9-11.4 mg/dl, normal value 8.5-10.5 mg/dl). The laboratory findings of the patients are shown in Table II. Of the 49 patients, 21 had coexisting thyroid nodules on USG.

No thyroid scintigraphy was needed to separate hyperactive nodule/PTA for any patient. None of the patients had (99mTc) MIBI and IV contrast allergies.

#### SURGICAL DATA

All 24 patients underwent parathyroidectomy. Of these patients, 5 also underwent thyroidectomy. Papillary microcarcinoma was found in 2 patients and minimally invasive follicular carcinoma in 1 patient who underwent thyroidectomy. A total of 25 adenomas were removed from 24 patients. Right paratracheal ectopic parathyroid adenoma was removed from 1 patient. Multiglandular adenoma was removed from 1 patient. Parathyroid adenoma was removed from 4 patients by applying the ROLL (Radioguided Occult Lesion Localization) technique. Of the glands removed, 8 were from the right lower, 1 was from the right upper, 13 were from the left lower and 2 were from the left upper pole and 1 from the right upper paratracheal area. There was no parathyroid carcinoma in any patient. The sizes of parathyroid adenomas varied from 4 to 21 mm.

#### IMAGING DATA

When the contrast-enhanced [99mTc] MIBI SPECT/CT images were evaluated, all 25 lesions in 24 patients showed both IV contrast involvement and increased [99mTc] MIBI involvement. The contrast involvements were evaluated through comparison with the thyroid gland. The smallest of the surgically removed adenomas was measured to be 4 mm in size. The localizations of the parathyroid adenomas obtained with contrast-enhanced [99mTc] MIBI SPECT/CT were consistent with surgical localizations. The sensitivity, specificity PPV, and NPV values of IV contrast-enhanced [99mTc] MIBI SPECT/CT were 100%, 100%, 100% and 100%, respectively. Of the 49 asymptomatic patients, 46 were determined to have parathyroid pathology with the use of contrast-enhanced [99mTc] MIBI SPECT/CT. The detection rate in patients with asymptomatic primary hyperparathyroidism was 93.8%. Of the 49 asymptomatic patients, 11 had findings related to parathyroid pathology on USG. Example patients Fig. 1.

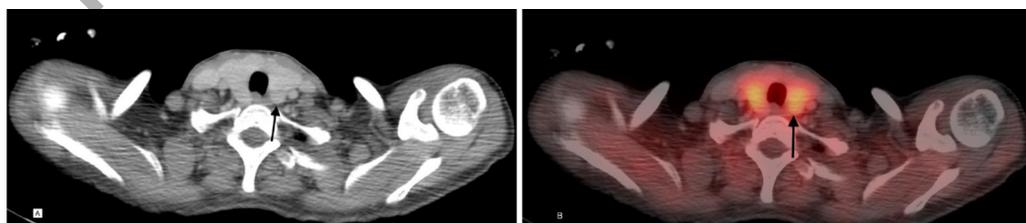


Fig. 1: 58-year old female patient PTH:767 Ca:13,2 localization of adenoma on contrast-enhanced MIBI SPECT/CT **A**) Parathyroid adenoma 11mm in size in the thyroid gland left lobe lower pole on CT (marked with black arrow, **B**) parathyroid adenoma in the left lobe lower pole (marked with black arrow) on fusion images.

## Discussion

The only treatment of primary hyperparathyroidism is the surgical extraction of PTAs<sup>1</sup>. In patients with numerous adenomas, some problems may arise in parathyroid surgery due to the inadequate localization of adenomas<sup>13</sup>. Two common surgical approaches are minimally invasive parathyroidectomy (MIP) and conventional four-gland neck exploration. The preoperative localization of PTAs reduces postoperative complications such as recurrent laryngeal nerve injury and postoperative hypocalcemia and improves the success rate of MIP with a smaller surgical incision and a shorter hospital stay<sup>14-17</sup>. There are several imaging techniques for the preoperative localization of PTA, including USG, CT, MRI, and [99mTc] MIBI scans<sup>18,19</sup>. There are studies in literature performed with each of these methods separately and comparatively. In the present study, the IV contrast application was added to the [99mTc] MIBI SPECT/CT study to obtain both anatomic and functional images, and both the imaging of lesions and differentiation from the surrounding tissues were ensured more easily with the use of contrast.

In a study of 77 patients with single-phase contrast-enhanced MDCT, 55 (69.6%) of 79 adenomas were detected. While 92.7% of these adenomas showed intense contrast involvement, 7.3% showed contrast involvement at an equal level. In the same study, 10 small adenomas, 7 < 1 cm which could not be detected in the [99mTc] MIBI planar scintigraphy, were detected on contrast-enhanced MDCT<sup>10</sup>.

The sensitivity of pre-operative [99mTc] MIBI SPECT/CT was found to be 80% in the study conducted by Keidar Z et al., where [99mTc] MIBI SPECT/CT and surgical findings were evaluated together in patients with hyperparathyroidism (HPA), and the compatibility of [99mTc] MIBI SPECT/CT with surgery was shown<sup>20</sup>. Sensitivity was 98.3% and accuracy was 98.8% in the [99mTc] MIBI SPECT/CT study by Ozkan ZG et al., which was conducted retrospectively on 103 patients<sup>21</sup>. In a cohort study of 200 patients, 83% of the [99mTc] MIBI SPECT/CT adenomas were correctly detected. The specificity and PPV values of the [99mTc] MIBI SPECT/CT were found to be 96% and 88%, respectively. In the same study, the detection rates of adenomas weighing at least 210 mg with [99mTc] MIBI SPECT/CT ranged from 68.4% to 88.3%, and the rate of detection increased with the increasing weight of the adenoma<sup>22</sup>.

Mandal R et al. found the localization accuracy, sensitivity, specificity, PPV and NPV in the early phase to be 76% , 84.4%, 89.4%, 90.5% and 84.0%, respectively, in a contrast-enhanced [99mTc]MIBI SPECT/CT of 75 patients, where early and late phases were evaluated together together, and the values found were higher than those of the late phase<sup>23</sup>. The amount of radiation dosage received by the patients was increased as CT was applied twice to each patient.

In the present study, all patients evaluated in surgery had complete consistency of imaging with surgical and pathology results, and the sensitivity, specificity, PPV, and NPV values were 100%, 100%, 100% and 100%, respectively. This study yielded higher results than previous MDCT studies and [99mTc] MIBI SPECT/CT studies. Qiu ZL et al. reported that the optimal threshold for the localization of parathyroid lesions on [99mTc] MIBI scintigraphy was 1.03 cm in ROC analysis<sup>24</sup>. In the present study, adenomas <1 cm were localized with contrast-enhanced [99mTc] MIBI SPECT/CT. In a meta-analysis of 43 studies investigating the preoperative localization techniques in primary HPA, the sensitivity and PPV values were reported to be 89.4% and 93.5%, respectively, with the use of 4D CT<sup>11</sup>. However, Lubitz CC et al. found a lower sensitivity value (60%) for 4D CT<sup>12</sup>.

In a study by Suh YJ et al., which included 38 patients and where 4D CT, ultrasound, and [99mTc]MIBI SPECT/CT methods were compared, the sensitivity, specificity, specificity, PPV, NPV and accuracy values of the 4D CT method were found to be 92.1%, 95.6%, 87.5%, 97.3%, and 94.7%, respectively. These values were 84.2%, 90.4%, 74.4%, 94.5%, and 88.8% for [99mTc] MIBI SPECT/CT, and 84.2%, 86.8%, 68.1%, 94.3%, and 86.2% for USG. In the same study, the images were taken at the 30<sup>th</sup>, 60<sup>th</sup>, and 90<sup>th</sup> seconds before the contrast, and the most intense contrast occurred at the 60<sup>th</sup> second, and washout occurred at the 90<sup>th</sup> second<sup>25</sup>.

Single-phase contrast was used in this study and images were taken at 50 and 70 seconds after contrast. This was the time when the highest involvement occurred as was noted in the above-mentioned study and had a lower HU value than vascular structures and the thyroid gland. It was therefore easier to distinguish the adenoma from the surrounding tissues.

In the present study, the proportion of coexisting thyroid nodules in the selected group was 75%, while it was 49% in the asymptomatic group. This complies with the rates of nodular thyroid disease (20%-75%) seen in endemic regions such as Turkey<sup>26</sup>. IV contrast-enhanced [99mTc] MIBI SPECT/CT is very useful in distinguishing parathyroid pathologies from thyroid nodules. The sensitivity and specificity rates of [99mTc] MIBI SPECT/CT in a series of 48 patients with coexisting thyroid nodules were 77.5% and 96.77%, respectively<sup>27</sup>. Despite the high proportion of the thyroid nodules in the present study, the sensitivity and specificity rates were also quite high.

In a study by Cheng Z. et al. of 94 patients with asymptomatic parathyroid adenoma, positive results were found on [99mTc] MIBI SPECT/CT in 48 patients. However, 34 of 59 patients (57.6%) with surgical criteria were found to have a positive result. In the same study, after a 15-year of follow-up, the probability of patients with asymptomatic hyperparathyroidism and positive sestamibi

parathyroid scans, who did not initially meet the surgical criteria to undergo operation was found to be much higher than the negative sestamibi study<sup>28</sup>. In the present study, positive results were obtained on contrast-enhanced [99mTc] MIBI SPECT/CT in 46 of 49 asymptomatic patients.

In this study, 9.6% of the cases had multiglandular disease and this is similar to the results obtained in previous studies<sup>1</sup>. High sensitivity and specificity rates have been shown in recent studies that included 11C-methionine or 18F-choline and were performed with PET/CT<sup>29,30</sup> and studies on this subject continue.

Limitations of the study were the low number of patients undergoing surgery and the poor follow-up of asymptomatic patients with SPECT/CT positive.

In conclusion, with contrast-enhanced [99mTc] MIBI SPECT/CT imaging, both high sensitivity and specificity values were obtained in the preoperative localization of parathyroid adenomas and high detection rates were achieved in the asymptomatic group. The use of IV contrast during the [99mTc] MIBI SPECT/CT in all patients without contraindications increased both preoperative localization of adenomas and detection rates in asymptomatic hyperparathyroidism.

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#### Riassunto

Scopo di questo studio è quello di confrontare i risultati in camera operatoria con quelli di localizzazione preoperatoria ottenuti con l'impiego della MIBI SPECT / CT con miglioramento del contrasto [99mTc], aggiungendo il contrasto simultaneo a fase singola all'esame MIBI SPECT/CT [99mTc].

Lo studio è stato condotto tra novembre 2016 e gennaio 2018 su 24 pazienti (21 femmine, 3 maschi) sottoposti a intervento chirurgico dopo localizzazione preoperatoria con MIBI SPECT/CT potenziato con 99mTc, e 49 pazienti asintomatici (42 donne, 7 maschi), non sottoposti a intervento chirurgico.

Come risultato le percentuali di sensibilità e specificità del potenziamento con [99mTc] della MIBI SPECT/CT sono state del 100% e ancora del 100% quando valutate insieme ai risultati chirurgici. Il tasso di rilevazione in pazienti asintomatici è risultato pari al 93,8%.

Si conclude che con l'imaging MIBI SPECT/CT con contrasto aumentato mediante [99mTc], sono stati raggiunti valori di alta sensibilità e specificità nella localizzazione preoperatoria degli adenomi paratiroideali e sono stati ottenuti elevati tassi di rilevamento nel gruppo asintomatico. L'uso del contrasto IV durante il [99mTc] MIBI SPECT/CT in pazienti senza controindicazioni ha aumentato sia i tassi di localizzazione preoperatoria degli adenomi che i tassi di rilevamento dei casi di iperparatiroidismo asintomatico.

#### References

1. Fraser WD: *Hyperparathyroidism*. Lancet, 2009; 374:145-58.
2. Adami S, Marcocci C, Gatti D: *Epidemiology of primary hyperparathyroidism*.
3. Rodgers SE, Hunter GJ, Hamberg LM, et al: *Improved preoperative planning for directed parathyroidectomy with 4-dimensional computed tomography*. Surgery, 2006; 140:932-40.
4. Coakley AJ, Kettle AG, Wells CP, et al: *99Tcm sestamibi: A new agent for parathyroid imaging*. Nucl Med Commun, 1989; 10: 791-94.
5. Taillefer R, Boucher Y, Potvin C, et al: *Detection and localization of parathyroid adenomas in patients with hyperparathyroidism using a single radionuclide imaging procedure with technetium-99m-sestamibi (double-phase study)*. J Nucl Med, 1992; 33:1801-807.
6. Lavelly WC, Goetze S, Friedman KP, et al: *Comparison of SPECT/CT, SPECT, and planar imaging with single- and dual-phase (99m)Tc-sestamibi parathyroid scintigraphy*. J Nucl Med, 2007; 48: 1084-089.
7. Ciappuccini R, Morera J, Pascal P, et al: *Dual-phase 99mTc sestamibi scintigraphy with neck and thorax SPECT/CT in primary hyperparathyroidism: A single-institution experience*. Clin Nucl Med, 2012; 37:223-28.
8. Cheung K, Wang TS, Farrokhyar F, et al: *Metaanalysis of preoperative localization techniques for patients with primary hyperparathyroidism*. Ann Surg Oncol, 2012; 19:577-83.
9. Neumann DR, Obuchowski NA, Difilippo FP: *Preoperative 123I/99mTc-sestamibi subtraction SPECT and SPECT/CT in primary hyperparathyroidism*. J Nucl Med, 2008; 49:2012-017.
10. Randall GJ, Zald PB, Cohen JI, et al: *Contrast-enhanced MDCT characteristics of parathyroid adenomas*. AJR, 2009; 193:538 [web]: W139-W143.
11. Cheung K, Wang TS, Farrokhyar F, et al.: *A meta-analysis of preoperative localization techniques for patients with primary hyperparathyroidism*. Ann Surg Oncol, 2012; 19:577-83.
12. Lubitz CC, Hunter GJ, Hamberg LM, et al: *Accuracy of 4-dimensional computed tomography in poorly localized patients with primary hyperparathyroidism*. Surgery, 2010; 148:1129-137.

13. Hindie E, Zanotti-Fregonara P, Tabarin A, et al: *The role of radionuclide imaging in the surgical management of primary hyperparathyroidism*. J Nucl Med, 2015; 56:737-44.
14. Ebner Y, Garti-Gross Y, Margulis A, et al: *Parathyroid surgery: Correlation between pre-operative localization studies and surgical outcomes*. Clin Endocrinol, 2015; 83(5):733-38.
15. Grant CS, Thompson G, Farley D, et al: *Primary hyperparathyroidism surgical management since the introduction of minimally invasive parathyroidectomy: Mayo Clinic experience*. Arch Surg, 2005; 140:472-78.
16. Westerdahl J, Bergenfelz A: *Unilateral versus bilateral neck exploration for primary hyperparathyroidism: Five-year follow-up of a randomized controlled trial*. Ann Surg, 2007; 246:976-80.
17. Kunstman JW, Udelsman R: *Superiority of minimally invasive parathyroidectomy*. Adv Surg, 2012; 46:171-89.
18. Patel CN, Salahudeen HM, Lansdown M, et al: *Clinical utility of ultrasound and 99mTc sestamibi SPECT/CT for preoperative localization of parathyroid adenoma in patients with primary hyperparathyroidism*. Clin Radiol, 2010; 65:278-87.
19. Hinson AM, Lee DR, Hobbs BA, et: *Preoperative 4D CT localization of nonlocalizing parathyroid adenomas by ultrasound and SPECT-CT*. Otolaryngol Head Neck, 2015; 153:775-78.
20. Keidar Z, Solomonov E, Karry R, et al: *Preoperative [99mTc]MIBI SPECT/CT interpretation criteria for localization of parathyroid adenomas-correlation with surgical findings*. Mol Imaging Biol, 2017; 19:265-70.
21. Ozkan ZG, Unal SN, Kuyumcu S, et al: *Clinical utility of Tc-99m MIBI SPECT/CT for preoperative localization of parathyroid lesions*. The Indian Journal of Surgery, 2017; 79(4):312-18.
22. Sandqvist P, Nilsson IL, Gryback P, et al: *SPECT/CT's advantage for preoperative localization of small parathyroid adenomas in primary hyperparathyroidism*. Clin Nucl Med, 2017; 42:109-114.
23. Mandal R, Muthukrishnan A, Ferris RL, et al: *Accuracy of early-phase versus dual-phase single-photon emission computed tomography/computed tomography in the localization of parathyroid disease*. Laryngoscope, 2015; 125:1496-501.
24. Qiu ZL, Wu B, Shen CT, et al: *Dual-phase (99m)Tc-MIBI scintigraphy with delayed neck and thorax SPECT/CT and bone scintigraphy in patients with primary hyperparathyroidism: correlation with clinical or pathological variables*. Ann Nucl Med, 2014; 28:725-35.
25. Suh YJ, Choi JY, Kim SJ, et al: *Comparison of 4D CT, ultrasonography, and 99mTc sestamibi SPECT/CT in localizing single-gland primary hyperparathyroidism*. Otolaryngol Head Neck Surg, 2015; 152(3):438-43.
26. Hurley DL, Gharib H: *Evaluation and management of multinodular goiter*. Otolaryngol Clin N Am, 1996; 29:527-40.
27. Shafiei B, Hoseinzadeh S, Fotouhi F, et al: *Preoperative Tc-99m-sestamibi scintigraphy in patients with primary hyperparathyroidism and concomitant nodular goiter: comparison of SPECT-CT, SPECT, and planar imaging*. Nucl Med Commun, 2012; 33:1070-076.
28. Cheng Z, Zou S, Peng D, et al: *Prognostic value of 99mTc-sestamibi parathyroid scintigraphy in predicting future surgical eligibility in patients with asymptomatic primary hyperparathyroidism*. Clin Nucl Med, 2018; 143:151-54.
29. Caldarella C, Treglia G, Isgro MA, et al: *Diagnostic performance of positron emission tomography using <sup>11</sup>C-methionine in patients with suspected parathyroid adenoma: A meta-analysis*. Endocrine, 2013; 43: 78-83.
30. Kluijfhout WP, Pasternak JD, Drake FT, et al: *Use of PET tracers for parathyroid localization: A systematic review and meta-analysis*. Langenbecks Arch Surg, 2016; 401(7):925-35.