REVIEW

New progress in diagnostic techniques for hyperparathyroidism in nuclear medicine

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ABSTRACT

Hyperparathyroidism (HPT) is an endocrine system disease, which is often divided into primary hyperparathyroidism (PHPT) and secondary hyperparathyroidism (SHPT). At present, HPT has gradually become a common disease of endocrine system, and the common treatment is surgical resection of related lesions. Therefore, accurate location and detection are very important for the surgical treatment and prognosis of HPT. Therefore, the author reviews the relevant imaging examination in the field of nuclear medicine to provide help for clinical diagnosis and treatment.

Key Words: Hyperparathyroidism, Radionuclide tracing imaging, Dual tracer subtraction planar imaging, Positron emission tomography, Bone mineral density, ^{99m}Tc-MIBI

1. INTRODUCTION

Generally, hyperparathyroidism (HPT) is divided into primary hyperparathyroidism (PHPT) and secondary hyperparathyroidism (SHPT), PHPT is the third most common endocrine system disease after diabetes and thyroid cancer.[1] It affects women 2 to 3 times more than men, with the highest incidence in postmenopausal women,[2] and is characterized by the release of excessive parathyroid hormone (PTH) by one or more hyperfunctional parathyroid glands, leading to a disturbance of calcium and phosphorus metabolism throughout the body. Similarly, SHPT. usually caused by chronic renal failure and small bowel absorption malnutrition syndrome etc., is a hyperplasia secondary to hypocalcaemia, hyperphosphatemia, or decreased serum vitamin D concentrations, which in turn leads to the elevated serum PYTH. Currently, the only accepted definitive treatment for PHPT is surgical removal of hyperactive parathyroid glands.[3] At the same time, studies from Lau[4] et al. have shown that patients with SHPT who do not respond to drug therapy still need parathyroidectomy. Therefore, accurate localization and detection are crucial for the treatment and prognosis of HPT surgery, that is, a non-invasive, sensitive and efficient localization and efficacy evaluation method is needed to assist surgical treatment. For HPT, it has high specificity and sensitivity in nuclear medicine-related examination items such as radionuclide imaging, positron emission computed tomography and bone densitography, in terms of molecular level and functional metabolic imaging. This article is aimed at reviewing the relevant examinations in the field of nuclear medicine in the diagnosis and treatment of HPT.

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2. RADIONUCLIDE PLANE IMAGING

Histologically, the parathyroid consists of chief cells, oxyphilic cells, hyperoxygenophile cells and clear cells. Chief cells are the most abundant cells while oxyphilic cells in parathyroid glands are thought to be derived from the main cells and contain abundant mitochondria.[5] The tracers ^{99m}Tc-MIBI and ^{99m}Tc-tetrofosmin are both lipophilic cationic complexes, which can be up-taken by cells through the negative potential of cell membranes and mitochondrial membranes,[6] showing similar biological characteristics and detection values in clinical trials,[7] due to the abundance of mitochondria in aerobic cells, a large amount of ^{99m}Tc-MIBI and ^{99m}Tc-tetrofosmin can be accumulated in hyperfunctional parathyroid glands, and the normal parathyroid tissue uptake rate is extremely low, and therefore can be used to diagnose HPT, where ^{99m}Tc-MIBI is used for single tracer and double tracer methods, and ^{99m}Tc-tetrofosmin is mainly used for dual tracer methods bound to $^{99m}TcO_{4-}$ or ^{123}I. The commonly used tracers in clinic are ^{99m}Tc-MIBI, ^{201}TI, $^{99m}TcO_{4-}$, ^{123}I and so on.

2.1 ^{99m}Tc-methoxyisobutyl isobutyl isonitrile (^{99m}Tc-MIBI) bichronous imaging

For a long time, ^{99m}Tc-MIBI bichronous imaging has been used in the field of nuclear medicine in China and is considered to be the preferred imaging technique for detecting and locating parathyroid adenomas,[8] but according to different literature reports, the sensitivity of ^{99m}Tc-MIBI c imaging varies greatly, and Kluijfhout[9] et al. have shown that nearly one-third of patients with PHT serological evidence have false-negative imaging results. In the meta-analysis made by Wong et al.,[10] the overall sensitivity for parathyroid adenomas was 86% in 1,276 patients on ^{99m}Tc-MIBI bichronous imaging. Studies conducted by Carral et al.[11] have shown that in 195 patients with PHPT, a quarter of them had negative ^{99m}Tc-MIBI scan results, which were independently correlated with the size of the adenoma and the location of the adenoma, with poor sensitivity to hyperplastic parathyroid glands.

It should be noted that the international EANM practice guidelines for parathyroid imaging state that ^{99m}Tc-MIBI can only be used for lesion localization, not for the differentiation of benign and malignant tumors.[12] However, in a recent study, it was pointed out that the retention index of ^{99m}Tc-MIBI in the parathyroid glands based on bichronous imaging can be used as an effective imaging parameter for preoperative identification of benign and malignant PHPT patients, and the differential performance is better when combined with lesion size and serum PTH.[13] In addition, the sensitivity of parathyroid imaging may also be relevant to clinical parameters, the stage of disease development at the time of imaging, and different patient populations. Obviously, for the ^{99m}Tc-MIBI of two-dimensional planar imaging, the sensitivity range is wide, there are certain limitations, if the patient's lesion is small in size and the anatomical position is deeper, its detection rate will be further reduced, and it is necessary to combine SPECT/CT with neck ultrasound to further localize.

2.2 ^{99m}Tc-MIBI SPECT/CT imaging

SPECT/CT can accurately locate and assist the diagnosis of lesions by combining the anatomical information of CT and the functional information of SPECT, and the recent meta-analysis by Treglia et al.[14] has showed that ^{99m}Tc-MIBI SPECT/CT is a very accurate method for detecting HPT, with a total detection rate of up to 88% in each patient-based and lesion-based analysis. Similarly, Shafier et al.[15] have studied the diagnostic ability of ^{99m}Tc-MIBI SPECT/CT in 48 PHPT patients, with sensitivity and specificity of 78% and 97% for parathyroid adenomas, respectively, and the results indicate that SPECT/CT is a useful tool for locating parathyroid adenomas. In the preoperative evaluation of 90 SHPT patients using ^{99m}Tc-MIBI SPECT/CT, it was found by Zhen et al.[16] that SPECT/CT had a higher sensitivity than ^{99m}Tc-MIBI bichronous imaging, and could detect more lesions of parathyroid glands and accurately depict their precise position.

Compared to the 2D planar technique of ^{99m}Tc-MIBI bichronous imaging, SPECT/CT fusion imaging can provide accurate lesion locations and precise differentiation of adjacent tissues. Therefore, collecting early and delayed ^{99m}Tc-MIBI SPECT/CT images at the same radiation dose is more conducive to improving the efficiency of lesion detection and is a commonly used first-line examination method in clinical practice.

2.3 Dual tracer planar subtraction imaging

Double tracer subtraction imaging is generally divided into ^{99m}Tc-MIBI/$^{99m}TcO_{4-}$ subtraction method and 201TI/$^{99m}TcO_{4-}$ subtraction method, the former method is more common. In general, ^{99m}Tc-MIBI has a differential metabolic rate between the thyroid gland and the parathyroid gland, so it is often used in the field of nuclear medicine as a single tracer for bichronous planar imaging of the parathyroid gland. However, in the presence of thyroid nodules, inflammatory parathyroid glands or enlarged cervical lymph nodes, ^{99m}Tc-MIBI is retained in the thyroid glands or rapidly metabolized from the parathyroid glands.[17] In this case, the use of double tracer subtraction imaging techniques is more effective. Clinically, the commonly used tracers for parathyroid subtraction imaging are $^{99m}TcO_{4-}$, ^{201}TI and ^{123}I.

Nichols et al.[18] found the sensitivity of this approach in a study of 651 HPT patients (20% with multi-gland disease and 80% with single-gland disease) who received the preoperative double tracer ^{99m}Tc-MIBI /$^{99m}TcO_{4-}$ subtraction imaging, 61% for multi-gland disease versus 97% for single-gland disease; Woods et al.[19] detected and localized parathyroid adenomas with dual tracer subtraction imaging in 224 PHPT patients with 89% specificity and 94% accuracy.

Dual tracer planar image subtraction imaging has excellent performance in detecting and locating HPT in comparison to single tracer imaging. However, compared to the single tracer method, this technique increases the additional radiation exposure of the thyroid glands, which takes more time to perform imaging and adds some cost. Notably, Giovalla et al.[20] point out in the article that when performing double tracer subtraction imaging, the usage order of the two tracers should be determined first, i.e., if thyroid imaging with $^{99m}TcO_{4-}$ is performed first, lower activity is required, about 74-111 MBq, while if thyroid scan is performed after parathyroid scan, 150 MBq is required.

3. Positron emission computed tomography

3.1 ^{18}F-fluorocholine (^{18}F-FCH) PET/CT imaging

In 2013, when Quak et al.[21] performed ^{18}F-FCH PET/CT imaging on a prostate cancer patient, they accidentally detected that ^{18}F-FCH hot spots were concentrated near the right lower pole of the thyroid gland, finally indicating parathyroid adenomas, which was the first report in the medical field to use ^{18}F-FCH PET/CT to locate parathyroid adenomas. Since then, more and more reports have discussed the sensitivity of ^{18}F-FCH PET/CT in the differentiation of parathyroid lesions. Unlike the kinetic properties of ^{99m}Tc-MIBI, ^{18}F-FCH is a phospholipid metabolic imaging agent that depends on cell type and metabolic activity.[22] Therefore, tumor cells with high value-added rates will have higher FCH uptake to meet the needs of cellular phospholipid synthesis.[23] A large amount of PTH secretion leads to increased phospholipid-dependent cholinase activity, which induces FCH uptake by parathyroid adenoma.[24]

Compared with ^{99m}Tc-MIBI SPECT/CT imaging, ^{18}F-FCH PET/CT has a higher sensitivity and spatial resolution, which is not only easier to detect smaller lesions as soon as possible, but also can accurately locate and display the internal structure of the lesion, clearly indicating the ratio of lesions to the background. Whitman et al.[25] conducted a meta-analysis of 301 patients in 10 studies and concluded that ^{18}F-FCH PET/CT was highly sensitive to parathyroid adenomas in HPT patients and increased the sensitivity from 54% for ^{99m}Tc-MIBI imaging to 96% for ^{18}F-FCH PET/CT. Similarly, Studies conducted by Lezaic et al.[26] have shown that ^{18}F-FCH PET/CT is an accurate and effective imaging method for locating hyperfunctional parathyroid tissues, especially in patients with multiple lesions or hyperplasia, with a sensitivity of 92% and specificity of 100% for parathyroid adenomas, in comparison to the sensitivity of 64% and the specificity of 100% for ^{99m}Tc-MIBI. In addition, ^{18}F-FCH is superior in locating ectopic HPT in comparison to ^{99m}Tc-MIBI and other imaging tests. In the study from Triantafyllidou et al.,[27] two patients with ectopic HPT failed to provide conclusive diagnostic results on ^{99m}Tc-MIBI planar imaging, and ^{18}F-FCH PET/CT could provide accurate localization of anterior mediastinal ectopic parathyroid adenomas, which was successfully resected by thoracoscopic methods.

In addition, ^{18}F-FCH PET/CT had a shorter acquisition time and a lower radiation dose, and Rep et al.[28] noted that the highest radiation exposure was caused by double tracer subtraction imaging at 7.4 mSv, followed by ^{99m}Tc-MIBI SPECT/CT imaging at 6.8 mSv, and ^{18}F-FCH PET/CT imaging had the lowest radiation exposure at 2.8 mSv. Therefore, many scholars believe that ^{18}F-FCH PET/CT is an effective alternative to first-line imaging methods.[29,30] Although ^{18}F-FCH PET/CT has a high sensitivity in comparison to other imaging diagnostic techniques, because ^{18}F-FCH is a broad-spectrum imaging agent and is not specific for the parathyroid glands, it is still necessary to consider its related false positive and false negative phenomena, Hocevar et al.[31] found that follicular thyroid hyperplasia, differentiated thyroid cancer, eosinophilic thyroid adenoma and inflammatory lymph nodes would ingest ^{18}F-FCH and thus produced false positives. On the contrary, some ectopic glands and in situ adenomas have non-functioning cystic structures and false-positive results.[32]

3.2 ^{11}C-methionine (^{11}C-MET) PET/CT imaging

^{11}C-MET is currently the most widely used amino acid metabolism imaging agent, which mainly reflects the level of protein anabolism in the brain. In recent years, there has been more and more researches on ^{11}C-MET PET/CT to localize parathyroid glands.

A meta-analysis by Caldarella et al.[33] have showed that ^{11}C-MET PET/CT has a sensitivity of up to 81% for parathyroid adenomas, suggesting that this imaging method may be helpful in diagnosing patients with primary hyperparathyroidism when conventional imaging techniques are negative or uncertain in locating parathyroid adenomas. In the meta-analysis by Kluijfhout et al.,[34] the sensitivity of ^{11}C-MET PET/CT in locating adenomas in HPT patients was 78%, which was significantly lower than the traditional ^{99m}Tc-MIBI SPECT/CT imaging method, but when only patients with negative or uncertain imaging results were included, the performance of ^{11}C-MET PET/CT was not decreased significantly, and the sensitivity remained 78%. Similarly, Weber et al.[35] believe that ^{11}C-MET PET/CT has a lower ability to detect hyperplastic glands in comparison to adenoma patients, with an overall sensitivity of 83% for HPT patients in comparison to only 33% for hyperplastic glands. This may be related to the fact that hypertrophic glands are usually smaller in size and lighter in weight than adenomas.[36]

In conclusion, in a large number of cases where the conventional imaging results are negative or inconsistent, ^{11}C-MET PET/CT also has an excellent detection performance and is relatively most useful. However, the main disadvantage of ^{11}C-MET is that ^{11}C has a short physical half-life and requires a field cyclotron and a complex labeling process to handle, so ^{11}C-MET PET/CT is often considered to be a second-line "alternative" imaging method when the localization of refractory HPT or initial localization is ineffective.

4. Bone densitography

At present, the effect of PTH on bones is complex, and the mechanism is not fully understood, because PTH has both catabolic and anabolic effects on bones. The most common clinical symptom is the abnormal bone metabolism of SHPT caused by long-term dialysis.[37] It has been reported that if the level of PTH is elevated for a long time, catabolic effects dominate, especially affecting cortical bone, although minor anabolic effects may also occur on cancellous bone.[38] In patients with HPT, with the continuous secretion of PTH, the markers of bone formation and bone resorption are continuously stimulated with the rate of bone turnover and bone density increased. However, it has been reported that bone density may be affected differently in different bone areas.[39] Compared with cortical bone, cancellous bone is relatively well preserved or even improved, while cortical bone porosity increases and osteoclast resorption is enhanced, resulting in the thinning of cortical bone.[40] Therefore, timely monitoring of bone density is necessary in this type of abnormal bone metabolism. Currently, bone densitography, commonly found in the field of nuclear medicine, mainly makes use of dual energy X-ray absorptiometry (DEXA).

A study showed that after surgical removal of parathyroid adenomas, bone turnover was decreased while bone density was increased and the fracture risk was decreased.[41] In other words, after surgical resection of parathyroid adenomas, continuous monitoring of bone density can effectively assess the postoperative effect and predict the fracture risk in patients. In other words, after surgical resection of parathyroid adenomas, continuous monitoring of bone density can effectively assess the postoperative effect and predict the fracture risk in patients. In the study from Guo et al.,[39] 11 untreated HPT patients who were followed up for 2 years had a significant reduction in bone density at the systemic and bilateral collum femoris, but no change in bone density in the lumbar spine. Similarly, in the study from Khosla et al.[42] of 407 untreated HPT patients who were followed up for 10 years, bone density at the distal radius was decreased earlier and most obviously in comparison to bilateral collum femoris. Therefore, timely monitoring of bone density of the distal radius and bilateral collum femoris is necessary in patients with HPT.

In conclusion, although DEXA is not the gold standard for the diagnosis of bone abnormalities, it can better reflect bone mass and the degree of change in bone mass in comparison to invasive bone biopsy pathological examination. Therefore, in the field of nuclear medicine, bone densitography can also be used as one of the monitoring methods for the diagnosis and treatment of HPT.

5. Conclusions

This article only describes the imaging examinations related to the diagnosis and treatment of HPT in the field of nuclear medicine, and does not describe other examination methods such as ultrasound. For ^{99m}Tc-MIBI bichronous imaging, although the sensitivity range is wide, the detection rate will be reduced when the anatomical position is deep and the lesion volume is small, and it is necessary to combine SPECT/CT and neck ultrasound for joint localization. Although dual tracer planar imaging has a better performance than single tracer imaging, it requires more time to develop and more radiation exposure. Therefore, ^{99m}Tc-MIBI SPECT/CT imaging is still used as the first-line preferred test; Compared with ^{99m}Tc-MIBI SPECT/CT imaging, ^{18}F-FCH PET/CT and ^{11}C-MET PET/CT are relatively expensive, but it has a higher sensitivity and spatial resolution to accurately locate smaller lesions, among which ^{11}C-MET PET/CT is often regarded as a second-line "alternative" imaging method for recalcitrant HPT localization or ineffective initial localization of HPT; bone densitography can be a good way to monitor bone mass and the degree of change in bone mass, and can also be used as one of the methods of the diagnosis and treatment of HPT.

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REFERENCES

[1] Cetani F, Marcocci C, Torregrossa L, et al. Atypical parathyroid adenomas: challenging lesions in the differential diagnosis of endocrine tumors. Endocrine-Related Cancer. 2019; 26(7): R441-R464. PMid:31085770. https://doi.org/10.1530/ERC-19-0135

[2] Fraser WD. Hyperparathyroidism. Lancet (London, England). 2009; 374: 145-58.https://doi.org/10.1016/S0140-6736(09)60507-9

[3] Singh O, Naykky M, et al. Outcomes of Parathyroidectomy in Patients with Primary Hyperparathyroidism: A Systematic Review and Meta-analysis. World Journal of Surgery. 2016; 40(10): 2359-77. PMid:27094563. https://doi.org/10.1007/s00268-016-3514-1

[4] Lau WL, Obi Y, Kalantar-Zadeh K. Parathyroidectomy in the Management of Secondary Hyperparathyroidism. Clinical journal of the American Society of Nephrology. CJASN. 2018; 13(6): 952-961. PMid:29523679. https://doi.org/10.2215/CJN.10390917

[5] Ritter CS, Haughey BH, Miller B, et al. Differential gene expression by oxyphil and chief cells of human parathyroid glands. The Journal of Clinical Endocrinology and Metabolism. 2012; 97(8): E1499-E1505. PMid:22585091. https://doi.org/10.1210/jc.2011-3366

[6] Xue J, Liu Y, Yang D, et al. Dual-phase 99mTc-MIBI imaging and the expressions of P-gp, GST-π, and MRP1 in hyperparathyroidism. Nuclear Medicine Communications. 2017; 38(10): 868-874. PMid:28806349. https://doi.org/10.1097/MNM.0000000000000721

[7] Treglia G, Sadeghi R, Schalin-Jäntti C, et al. Detection rate of (99m) Tc-MIBI single photon emission computed tomography (SPECT)/CT in preoperative planning for patients with primary hyperparathyroidism: A meta-analysis. Head & neck. 2016; 38(Suppl 1): E2159-E2172. PMid:25757222. https://doi.org/10.1002/hed.24027

[8] Rep S, Lezaic L, Kocjan T, et al. Optimal scan time for evaluation of parathyroid adenoma with [(18)F]-fluorocholine PET/CT. Radiology and oncology. 2015; 49(4): 327-333. PMid:26834518. https://doi.org/10.1515/raon-2015-0016

[9] Kluijfhout WP, Vorselaars WM, Vriens MR, et al. Enabling minimal invasive parathyroidectomy for patients with primary hyperparathyroidism using Tc-99m-sestamibi SPECT-CT, ultrasound and first results of (18)F-fluorocholine PET-CT. European journal of radiology. 2015; 84(9): 1745-1751. PMid:26047823. https://doi.org/10.1016/j.ejrad.2015.05.024

[10] Wong KK, Fig LM, Gross MD, et al. Parathyroid adenoma localization with 99mTc-sestamibi SPECT/CT: a meta-analysis. Nuclear medicine communications. 2015; 36(4): 363-375. PMid:25642803. https://doi.org/10.1097/MNM.0000000000000262

[11] Carral F, Jiménez AI, Tomé M, et al. Factors associated with negative 99mTc-MIBI scanning in patients with primary hyperparathyroidism. Revista espanola de medicina nuclear e imagen molecular. 2021; 40(4): 222-228. PMid:34218884. https://doi.org/10.1016/j.remn.2020.07.001

[12] Petranović Ovčariček, Giovanella P, Carrió Gasset L, et al. The EANM practice guidelines for parathyroid imaging. European journal of nuclear medicine and molecular imaging. 2021; 48(9): 2801-2822. PMid:33839893. https://doi.org/10.1007/s00259-021-05334-y

[13] Zhang M, et al. The value of semi-quantitative measurement of ^{99m}Tc-MIBI uptake for differentiating malignant from benign parathyroid lesions in patients with PHPT. The Journal of Nuclear Medicine. 2018; 59.

[14] Treglia G, Sadeghi R, Schalin-Jäntti C, et al. Detection rate of (99m) Tc-MIBI single photon emission computed tomography (SPECT)/CT in preoperative planning for patients with primary hyperparathyroidism: A meta-analysis. Head & neck. 2016; 38(Suppl 1): E2159-

E2172. PMid:25757222. https://doi.org/10.1002/hed.24027

[15] Shafiei B, Hoseinzadeh S, Fotouhi F, et al. Preoperative 99mTc-sestamibi scintigraphy in patients with primary hyperparathyroidism and concomitant nodular goiter: comparison of SPECT-CT, SPECT, and planar imaging. Nuclear medicine communications. 2012; 33(10): 1070-1076. PMid:22825041. https://doi.org/10.1097/MNM.0b013e32835710b6

[16] Zhen L, Li H, Liu X, et al. The application of SPECT/CT for preoperative planning in patients with secondary hyperparathyroidism. Nuclear medicine communications. 2013; 34(5): 439-444. PMid:23458854. https://doi.org/10.1097/MNM.0b013e32835f9447

[17] Kunstman JW, Kirsch JD, Mahajan A, et al. Clinical review: Parathyroid localization and implications for clinical management. The Journal of clinical endocrinology and metabolism. 2013; 98(3): 902-912. PMid:23345096. https://doi.org/10.1210/jc.2012-3168

[18] Nichols KJ, Tomas MB, Tronco GG, et al. Sestamibi parathyroid scintigraphy in multigland disease. Nuclear medicine communications. 2012; 33(1): 43-50. PMid:22001718. https://doi.org/10.1097/MNM.0b013e32834bfeb1

[19] Woods AM, Bolster AA, Han S, et al. Dual-isotope subtraction SPECT-CT in parathyroid localization. Nuclear medicine communications. 2017; 38(12): 1047-1054. PMid:28984813. https://doi.org/10.1097/MNM.0000000000000765

[20] Giovanella L, Avram AM, Iakovou I, et al. EANM practice guideline/SNMMI procedure standard for RAIU and thyroid scintigraphy. European journal of nuclear medicine and molecular imaging. 2019; 46(12): 2514-2525. PMid:31392371. https://doi.org/10.1007/s00259-019-04472-8

[21] Quak E, Lheureux S, Reznik Y, et al. F18-choline, a novel PET tracer for parathyroid adenoma?. The Journal of clinical endocrinology and metabolism. 2013; 98(8): 3111-3112. PMid:23788686. https://doi.org/10.1210/jc.2013-2084

[22] Fukumoto M. Single-photon agents for tumor imaging: 201Tl, 99mTc-MIBI, and 99mTc-tetrofosmin. Ann Nucl Med. 2004; 18: 79-95. PMid:15195755. https://doi.org/10.1007/BF02985098

[23] Vallabhajosula S. (18)F-labeled positron emission tomographic radiopharmaceuticals in oncology: an overview of radiochemistry and mechanisms of tumor localization. Semin NuclMed. 2007; 37: 400-419. PMid:17920348. https://doi.org/10.1053/j.semnuclmed.2007.08.004

[24] Ishizuka T, Kajita K, Kamikubo K, et al. Phospholipid/Ca2+ -dependent protein kinase activity in human parathyroid adenoma. Endocrinol Jpn. 1987; 34: 965-968. PMid:3450512. https://doi.org/10.1507/endocrj1954.34.965

[25] Whitman J, Allen IE, Bergsland EK, et al. Assessment and Comparison of 18F-Fluorocholine PET and 99mTc-Sestamibi Scans in Identifying Parathyroid Adenomas: A Metaanalysis. Journal of nuclear medicine: official publication, Society of Nuclear Medicine. 2021; 62(9): 1285-1291. PMid:33452040. https://doi.org/10.2967/jnumed.120.257303

[26] Lezaic L, Rep S, Sever MJ, et al. 18F-Fluorocholine PET/CT for localization of hyperfunctioning parathyroid tissue in primary hyperparathyroidism: a pilot study. European journal of nuclear medicine and molecular imaging. 2014; 41(11): 2083-2089. PMid:25063039. https://doi.org/10.1007/s00259-014-2837-0

[27] Triantafyllidou M, Strobel K, Leiser A, et al. Localisation of ectopic mediastinal parathyroid adenoma by 18F-fluorocholine PET/CT. BMJ case reports. 2018; bcr2017222089. PMid:29592976. https://doi.org/10.1136/bcr-2017-222089

[28] Rep S, Hocevar M, Vaupotic J, et al. 18F-choline PET/CT for parathyroid scintigraphy: significantly lower radiation exposure of patients in comparison to conventional nuclear medicine imaging approaches. Journal of radiological protection: official journal of the Society for Radiological Protection. 2018; 38(1): 343-356. PMid:29339573. https://doi.org/10.1088/1361-6498/aaa86f

[29] Broos W, Wondergem M, Knol R, et al. Parathyroid imaging with 18F-fluorocholine PET/CT as a first-line imaging modality in primary hyperparathyroidism: a retrospective cohort study. EJNMMI research. 2019; 9(1): 72. PMid:31367807. https://doi.org/10.1186/s13550-019-0544-3

[30] Boccalatte LA, Gómez NL, Olivera López S, et al. Hiperparatiroidismo ectópico. Detección de la localización mediastinal [Ectopic hyperparathyroidism. Detection of mediastinal localization]. Medicina. 2020; 80(1): 39-47.

[31] Hocevar M, Lezaic L, Rep S, et al. Focused parathyroidectomy without intraoperative parathormone testing is safe after pre-operative localization with 18F-Fluorocholine PET/CT. European journal of surgical oncology: the journal of the European Society of Surgical Oncology and the British Association of Surgical Oncology. 2017; 43(1): 133-137. PMid:27776943. https://doi.org/10.1016/j.ejso.2016.09.016

[32] Piccardo A, Trimboli P, Rutigliani M, et al. Additional value of integrated 18F-choline PET/4D contrast-enhanced CT in the localization of hyperfunctioning parathyroid glands and correlation with molecular profile. European journal of nuclear medicine and molecular imaging. 2019; 46(3): 766-775. PMid:30219964. https://doi.org/10.1007/s00259-018-4147-4

[33] Caldarella C, Treglia G, Isgrò MA, et al. Diagnostic performance of positron emission tomography using 11C-methionine in patients with suspected parathyroid adenoma: a meta-analysis. Endocrine. 2013; 43(1): 78-83. PMid:22801990. https://doi.org/10.1007/s12020-012-9746-4

[34] Kluijfhout WP, Pasternak JD, Drake FT, et al. Use of PET tracers for parathyroid localization: a systematic review and meta-analysis. Langenbeck's archives of surgery. 2016; 401(7): 925-935. PMid:27086309. https://doi.org/10.1007/s00423-016-1425-0

[35] Weber T, Maier-Funk C, Ohlhauser D, et al. Accurate preoperative localization of parathyroid adenomas with C-11 methionine PET/CT. Annals of surgery. 2013; 257(6): 1124-1128. PMid:23478517. https://doi.org/10.1097/SLA.0b013e318289b345

[36] Hayakawa N, Nakamoto Y, Kurihara K, et al. A comparison between 11C-methionine PET/CT and MIBI SPECT/CT for localization of parathyroid adenomas/hyperplasia. Nuclear medicine communications. 2015; 36(1): 53-59. PMid:25244350. https://doi.org/10.1097/MNM.0000000000000216

[37] Levin A, Bakris GL, Molitch M, et al. Prevalence of abnormal serum vitamin D, PTH, calcium, and phosphorus in patients with chronic kidney disease: results of the study to evaluate early kidney disease. Kidney international. 2007; 71(1): 31-38. PMid:17091124. https://doi.org/10.1038/sj.ki.5002009

[38] Rejnmark L, Ejlsmark-Svensson H. Effects of PTH and PTH Hypersecretion on Bone: a Clinical Perspective. Current osteoporosis reports. 2020; 18(3): 103-114. PMid:32222892. https://doi.org/10.1007/s11914-020-00574-7

[39] Guo CY, Thomas WE, al-Dehaimi AW, et al. Longitudinal changes in bone mineral density and bone turnover in postmenopausal women with primary hyperparathyroidism. The Journal of clinical endocrinology and metabolism. 1996; 81(10): 3487-3491. PMid:8855790. https://doi.org/10.1210/jcem.81.10.8855790

[40] Eriksen EF, Mosekilde L, Melsen F. Trabecular bone remodeling and balance in primary hyperparathyroidism. Bone. 1986; 7(3): 213-221. PMid:3768200. https://doi.org/10.1016/8756-3282(86)90020-7

[41] Rolighed L, Vestergaard P, Heickendorff L, et al. BMD improvements after operation for primary hyperparathyroidism. Langenbeck's archives of surgery. 2013; 398(1): 113-120. PMid:23132462. https://doi.org/10.1007/s00423-012-1026-5

[42] Khosla S, Melton LJ 3^{rd}, Wermers RA, et al. Primary hyperparathyroidism and the risk of fracture: a population-based study. Journal of bone and mineral research: the official journal of the American Society for Bone and Mineral Research. 1999; 14(10): 1700-1707. PMid:10491217. https://doi.org/10.1359/jbmr.1999.14.10.1700