Original Article

Role of ^{18}Fluorocholine Positron Emission Tomography/Computed Tomography in the Localization of Culprit Lesions in Patients of Persistent/Recurrent Primary Hyperparathyroidism: A Prospective Study in COVID Times

Ritwik Wakankar, Yamini Dharmashaktu, A. Nishikant Damle, Praveen Kumar, Chandrasekhar Bal, Rakesh Kumar, Madhavi Tripathi, Shipra Agarwal[1], Rajesh Khadgawat[2], Sunil Chumber[3], Chitresh Kumar[4]

Departments of Nuclear Medicine, [1]Pathology, [2]Endocrinology, [3]Surgery and [4]Surgical Oncology, All India Institute of Medical Sciences, New Delhi, India

Abstract

Introduction: Recurrent/persistent primary hyperparathyroidism in patients who have undergone previous parathyroidectomy is a challenging condition. Imaging is important for localizing the parathyroid adenoma for re-exploration and ^{18}F-Fluorocholine (^{18}F-FCH) positron emission tomography/computed tomography (PET/CT) seems ideal for this purpose. **Aim:** This prospective study attempted to ascertain the utility of ^{18}F-FCH PET/CT as an investigation in preoperative localization of abnormal parathyroid tissue in recurrent/persistent primary hyperparathyroidism while comparing it with ^{99m}Tc-Sestamibi dual-phase scintigraphy with early single-photon emission CT (SPECT)/CT and neck ultrasonography (USG). **Methods:** Twenty patients with biochemical features of recurrent/persistent primary hyperparathyroidism were enrolled into this study. They underwent neck USG, ^{99m}Tc-Sestamibi dual-phase scintigraphy with early SPECT/CT and ^{18}F-FCH PET/CT for localization of parathyroid lesions. Six patients underwent surgical resection of the detected lesions, 3 were awaiting surgery, and 11 were managed conservatively. One patient died due to COVID. **Results:** The calculated positive predictive values on a per-lesion basis of neck USG, ^{99m}Tc-sestamibi scintigraphy and early SPECT/CT and ^{18}F-FCH PET/CT in the cohort of the 5 operated patients were 75% (3/4), 71.4% (5/7), and 71.4% (5/7), respectively. On a per-patient basis, the lesion detection rate was 100% for ^{99m}Tc-sestamibi scan and FCH PET (5/5) and 80% on neck USG (4/5). **Conclusion:** ^{18}F-FCH PET/CT is a highly accurate imaging modality for the detection of parathyroid lesions in patients with recurrent/persistent primary hyperparathyroidism.

Keywords: *^{18}F-Fluorocholine, ^{99m}Tc-sestamibi, neck ultrasonography, persistent, primary hyperparathyroidism, recurrent*

Introduction

Recurrent and persistent primary hyperparathyroidism is defined by the presence of elevated intact parathyroid hormone (iPTH) after 6 months and within 6 months of parathyroidectomy. The causes include a quiescent parathyroid adenoma, missed parathyroid hyperplasia, incomplete removal of adenoma, parathyromatosis, and parathyroid carcinoma. Most of the times, patients are diagnosed with recurrent/persistent primary hyperparathyroidism only on abnormal biochemistry on postoperative follow-up and are mostly asymptomatic. A repeat parathyroidectomy is the only definitive treatment in these cases but only after a precise localization of the hyperfunctioning parathyroid tissue due to altered tissue planes of the neck that makes it difficult for the surgeon to navigate the surgical field; therefore, the best surgery is one that focuses on a specific lesion.[1,2] The conventional first-line imaging techniques are ^{99m}Tc-sestamibi scintigraphy with early single-photon emission computed tomography (SPECT)/CT and neck ultrasonography (USG). However, these modalities have many limitations in the setting of patients requiring repeat surgery, like the lesser utility of USG in obese patients due to lack of adequate acoustic window, poor detection rates for small parathyroid adenomas, or the user-dependent nature of neck USG; ^{99m}Tc-sestamibi scintigraphy has low sensitivity in patients with multiglandular disease, poor spatial

How to cite this article: Wakankar R, Dharmashaktu Y, Damle AN, Kumar P, Bal C, Kumar R, *et al.* Role of ^{18}Fluorocholine positron emission tomography/computed tomography in the localization of culprit lesions in patients of persistent/recurrent primary hyperparathyroidism: A prospective study in COVID times. Indian J Nucl Med 2023;38:218-23.

Address for correspondence:
Dr. A. Nishikant Damle, Department of Nuclear Medicine, All India Institute of Medical Sciences, New Delhi, India.
E-mail: nishikantavinash@gmail.com

Received: 07-02-2022
Revised: 20-01-2023
Accepted: 25-01-2023
Published: 10-10-2023

Access this article online

Website: www.ijnm.in

DOI: 10.4103/ijnm.ijnm_31_22

Quick Response Code:

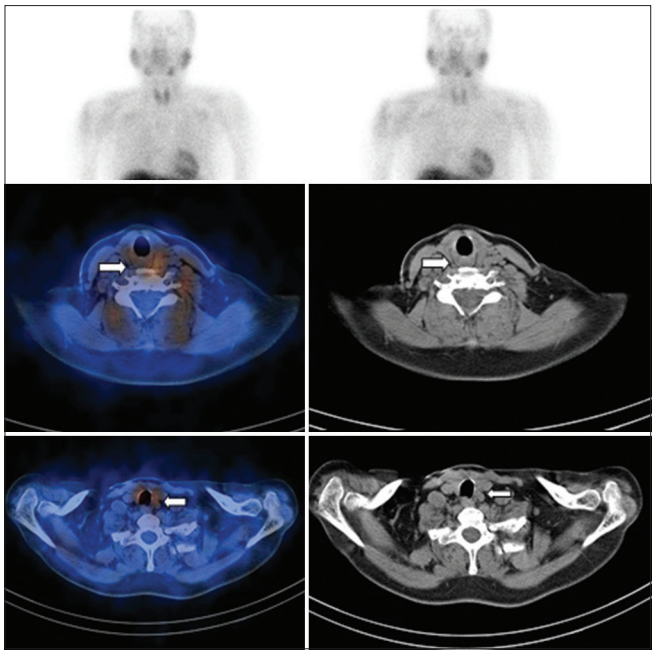

Figure 1: ^{99m}Tc-sestamibi scintigraphy of a 51-year-old female with persistent primary hyperparathyroidism with no obvious parathyroid lesion visible. Axial SPECT/CT images demonstrating two non-MIBI avid right superior (white arrow middle row) and left inferior lesions (white arrow bottom row). SPECT/CT: Single photon emission computed tomography/computed tomography

resolution, uses ionizing radiation, and requires multiple images to be acquired at various time points, making the procedure quite long. ^{18}F-Fluorocholine (^{18}F-FCH) positron emission tomography/CT (PET/CT) has gained interest for parathyroid imaging due to higher spatial resolution, shorter scan duration, and less radiation dose to the patient.[1] In this study, the use of ^{18}FCH PET/CT as an imaging modality was evaluated and compared with neck USG and ^{99m}Tc-sestamibi scintigraphy with early SPECT/CT.

Methods

Patient selection

A prospective cohort of 20 patients diagnosed with recurrent/persistent primary hyperparathyroidism between June 2019 and September 2021 was selected for this study. Any patient younger than 18 years, with deranged renal function at the time of referral to our department, who refused to give informed consent for the procedure, or who had a history of head and neck malignancy were excluded from the study. All patient data, including baseline patient characteristics and scan findings, were entered into a database and analyzed.

Informed consent

Written informed consent was taken from all participants for the use of their data for scientific purposes. Apart from the standard imaging protocol and clinical management, no additional treatments or imaging were performed. The study was approved by the Institutional Ethics Committee in June 2019 (Reference No. IECPG-444/June 27, 2019).

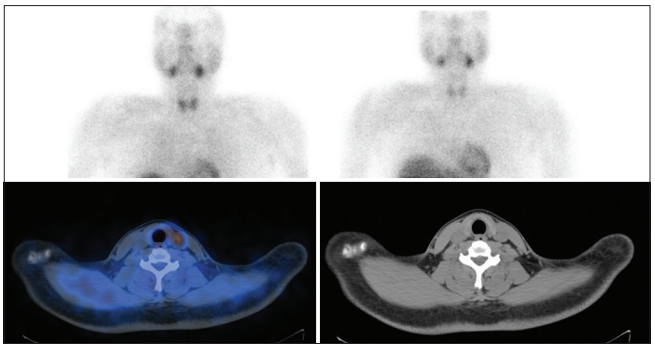

Figure 2: ^{99m}Tc-sestamibi scintigraphy images of a 34-year-old male patient with recurrent primary hyperparathyroidism with no obvious parathyroid lesion visible. SPECT/CT images demonstrating nonlocalization of culprit lesion (bottom row). SPECT/CT: Single-photon emission computed tomography/computed tomography

Scan acquisition

^{18}F-FCH PET/CT was done between 45 and 60 min of intravenous (IV) injection of 3–5 mCi (111–185MBq) of the radiotracer. The PET/CT scan was done from the orbit to the diaphragm on a Siemens Biograph mCT PET/CT with LSO crystal and 64 slice CT scanner. No IV or oral contrast was used. CT was done at 100–150 mAs. PET imaging was done at 3 min/bed position and images were reconstructed with an ordered subset expectation maximization algorithm with 3 iterations and 21 subsets. No special patient preparation was required.

Image interpretation

^{18}F-FCH PET/CT scan findings were reviewed by two experienced nuclear medicine physicians along with biochemical and clinical patient details and results were recorded. Each finding on ^{18}F-FCH PET/CT was scored as negative, suspicious, or positive for hyperfunctioning parathyroid tissue. Any lesion detected in the typical anatomical location of parathyroid tissue, hypodense to the thyroid with increased uptake of FCH was considered to be positive, lesions with increased FCH uptake but atypical locations without alternative explanation were considered suspicious, and lesions with increased FCH uptake in atypical locations and an alternative explanation rather than hyperfunctioning parathyroid tissue or no FCH uptake were considered to be negative.

Statistical analysis

Histopathology/biochemical follow-up/four-dimensional (4D)-CT neck findings were taken as reference standards. Detection rates were calculated on a per-patient basis for all 20 patients whereas per-lesion-based analysis was done for only operated patients who had histopathology reports available at the time of analysis. Continuous data were expressed as mean ± standard deviation and

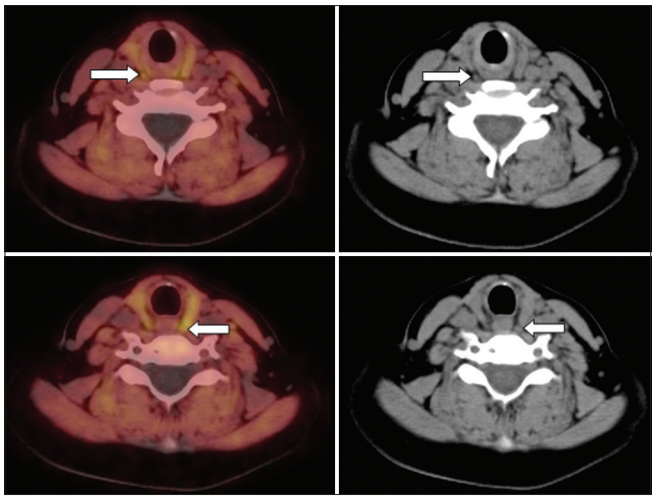

Figure 3: Axial ^{18}F-FCH PET/CT images of the same patient demonstrating double adenomas, one in the right superior location (white arrow upper row) and the other in the left inferior location with significant ^{18}F-Fluorocholine uptake (white arrow bottom row). PET/CT: Positron emission tomography/computed tomography

95% confidence interval (CI). Noncontinuous data were expressed as numbers with percentages.

Results

Study population

For the purpose of this study, a total of 20 patients with clinically diagnosed recurrent/persistent primary hyperparathyroidism were recruited out of which 11 patients (55%) had recurrent and 9 patients (45%) had persistent primary hyperparathyroidism. Despite localization of the culprit lesion on one or more of the imaging modalities being tested (i.e., neck USG, ^{99m}Tc-Sestamibi Scintigraphy and early SPECT/CT, ^{18}F-FCH PET/CT) 5 patients were managed conservatively. Of the remaining 15 patients, no culprit lesion(s) could be localized on any of the above-mentioned imaging modalities in 6 patients, these were also managed conservatively. Three patients were still awaiting corrective surgery at the time of analysis.

Therefore, only six patients underwent surgery and had eventual surgical histopathology for comparison. For the remaining 14 patients, follow-up with serial serum iPTH and serum calcium levels and/or concordance between ^{18}F-FCH PET/CT and 4D-CT neck were used as reference standards for deciding the diagnostic accuracy of the imaging findings.

Of the 20 patients included in the final analysis, there were 12 females (60%) and 8 males (40%). The mean age of these patients was 44.95 ± 6.11 years (95% CI: 38.8–51.1 years).

The mean prescan serum iPTH levels were 212.41 ± 66.5 pg/ml (95% CI: 146–279 pg/ml). The prescan mean serum calcium levels for the study population was 10.45 ± 0.51 mg/dl (95% CI: 9.9–11 mg/dl). The prescan mean serum phosphate level for the study population was 3.12 ± 0.63 mg/dl (95% CI: 2.5–3.8 mg/dl).

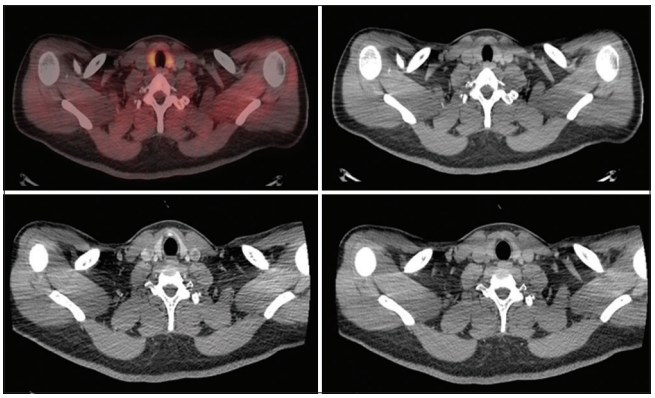

Figure 4: Axial ^{18}F-FCH PET/CT images of the same patient as mentioned above demonstrating nonlocalization of culprit lesion (upper row) and corresponding axial 4D-CT neck arterial and venous phase images also demonstrate nonlocalization (lower row). PET/CT: Positron emission tomography/computed tomography, 4D-CT: Four-dimensional-computed tomography

As mentioned above, 6/20 (30%) patients underwent parathyroidectomy based on the preoperative localization carried out using the above-mentioned imaging modalities (i.e., Neck USG, ^{99m}Tc-Sestamibi Scintigraphy and early SPECT/CT, ^{18}F-FCH PET/CT), 11/20 (55%) patients were put on conservative therapy and 3/20 (15%) patients were awaiting surgery at the time of analysis.

Group of patients who underwent surgery with histopathology findings

Six patients underwent parathyroidectomy of the culprit lesion.

A total of 8 lesions (1 hyperplastic gland in 1 patient, 2 normal parathyroid glands and 1 adenoma in another patient, 3 adenomas in 3 patients, and 1 lymph node in 1 patient) were resected. Thus, the positive predictive values (PPV) on a per-patient basis were 83% and on a per-lesion basis was 62.5%.

In one patient who had imaging findings consistent with an ectopic parathyroid adenoma in the submandibular region and underwent surgical excision of the culprit lesion. On histopathologic evaluation, the excised specimen turned out to be a reactive lymph node with follicular hyperplasia. Therefore, in view of serially elevated iPTH levels and the negative histopathology, the culprit lesion localized on ^{18}F-FCH PET/CT was a false positive.

In another patient, a total of 3 culprit lesions were detected out of which 2 turned out to be normal parathyroid tissue and 1 was confirmed histopathologically to be a parathyroid adenoma.

Group of patients with scan localization of culprit lesion but being managed conservatively

5/14 (35.7%) of the patients with scan localization of the culprit lesion(s) were managed conservatively by their physicians.

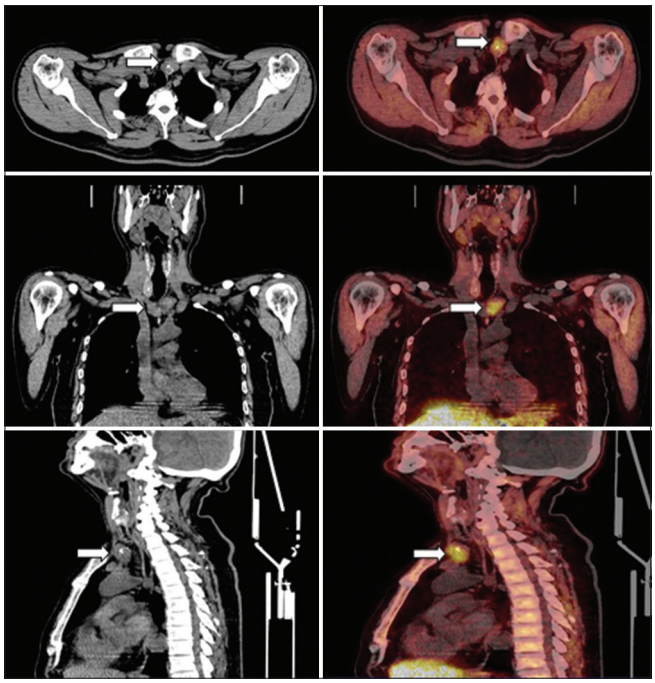

Figure 5: ^{18}F-FCH PET/CT of a 65-year-old male with recurrent primary hyperparathyroidism demonstrating intensely FCH avid lesion (white arrow) with internal calcification in the inferior pole of the erstwhile left thyroid lobe seen in axial, coronal, and sagittal sections. PET/CT: Positron emission tomography/computed tomography

Biochemical follow-up was available for all five patients, and additionally, one patient also underwent a 4D-CT neck.

In this patient, the culprit lesion was also localized to the same location as was seen on ^{18}F-FCH PET/CT.

Although these patients did not undergo surgery, based on the serially elevated serum iPTH levels and concordant findings on 4D-CT neck as mentioned above, it can be said that the localized culprit lesions on ^{18}F-FCH PET/CT were likely to be true positives. However, since surgical corroboration is not available, we have not taken this group for analysis.

Group of patients with no scan localization of culprit lesion and being managed conservatively

6/20 (30%) of the patients recruited in this study had no scan localization of the culprit lesion on ^{18}F-FCH PET/CT.

Out of these six patients, 3 (50%) had undergone additional 4D-CT neck along with ^{18}F-FCH PET/CT while the remaining 3 (50%) patients had not.

Biochemical follow-up was available for 5/6 (83.3%) of the patients with nonlocalizing ^{18}F-FCH PET/CT as one 63-year-old patient expired from COVID-19-related complications and follow-up could not be done.

Based on the concordance between ^{18}F-FCH PET/CT and 4D-CT neck in this subgroup of patients, these nonlocalizing scans are likely to be true negatives. Whereas, in the subgroup of patients with nonlocalizing ^{18}F-FCH PET/CT and no corroborating 4D-CT, we based our judgment on the available biochemical follow-up iPTH values. These were elevated in 1 scan negative patient and within normal limits in one patient.

Group of patients with scan localization of culprit lesion and awaiting surgery

3/14 (21.4%) of the patients with scan localization of culprit lesion(s) had their surgeries postponed as elective surgeries were stopped due to the COVID-19 pandemic at our institution.

Out of these three patients, 1 (33.3%) had also undergone an additional 4D-CT neck along with ^{18}F-FCH PET/CT while the remaining 2 (66.7%) patients had not.

Biochemical follow-up was available for 2/3 (66.7%) of the patients as one patient, a resident of a remote area was unable to get regular biochemical follow-up done after the ^{18}F-FCH PET/CT due to the situation of COVID-19 in her state.

Based on the concordance between ^{18}F-FCH PET/CT and 4D-CT neck in this 1 patient, it is likely to be a true positive. Whereas, in the subgroup of patients with localizing ^{18}F-FCH PET/CT and no corroborating 4D-CT, we based our judgment on the available biochemical follow-up iPTH value. This was elevated in 1 patient. However, since surgical corroboration is not available, we have not taken this group for analysis.

The analysis was performed in two ways: one comprising of only the 6 patients that were operated, and the other comprising of 18 patients whose ^{18}F-FCH PET/CT findings were corroborated on surgical histopathology/biochemical follow-up/4D-CT neck. Two patients were excluded from the analysis as no surgical histopathology/biochemical follow-up/4D-CT neck was available for them.

Neck ultrasonography

Of the total 18 patients that were included in the analysis recurrent (10 patients)/persistent (8 patients), neck USG was able to detect the culprit lesion in 8/18 (44.4%) of the patients. Within this cohort of patients neck USG lateralized the culprit lesion to the left side of the midline in four patients and to the right side in four patients.

^{99m}Tc-sestamibi scintigraphy and single-photon emission computed tomography/computed tomography

^{99m}Tc-Sestamibi Scintigraphy and SPECT/CT were able to detect the culprit lesion in 8/18 (44.4%) of the patients with recurrent/persistent primary hyperparathyroidism [Figures 1 and 2].

^{18}F-fluorocholine positron emission tomography/computed tomography

^{18}F-FCH PET/CT was able to detect a culprit lesion in 13/18 (72.2%) of the patients with recurrent/persistent primary hyperparathyroidism [Figures 3-5].

A total of 20 ^{18}F-FCH PET/CT scans were done in the 20 recruited patients out of which 6 (30%) scans did not localize any culprit lesions and were reported as negative. In the remaining 14 (70%) scans, a total of 21, either singular or multiple lesions were detected.

Twelve out of 20 patients (60%) were normocalcemic (S. Calcium ≤10.5 mg/dL) while the remaining 8 out of 20 patients (40%) were hypercalcemic (S. Calcium >10.5 mg/dL).

Of the 11 patients that were managed conservatively, 9 (81.8%) were normocalcemic while 2 (18.2%) were hypercalcemic. Similarly, out of the six patients that underwent surgical resection of parathyroid lesions 5 (83.3%) were hypercalcemic and 1 (16.7%) patient was normocalcemic.

Nineteen out of 20 patients recruited in this study had an overall biochemical follow-up period of 6 ± 2.1 months (95% CI: 3.9–8.1 months). One patient contracted the SARS-CoV-2 virus and died of COVID-19 complications soon after undergoing ^{18}FCH PET/CT therefore no biochemical follow-up was available for her. Another patient, a resident of a remote area was not able to get regular biochemical follow-up done after the ^{18}F-FCH PET/CT.

Only 5 out of the six patients that underwent surgical resection for their recurrent/persistent primary hyperparathyroidism were considered for analysis because the culprit lesion detected on ^{18}F-FCH PET/CT was not operated on during repeat surgery in one patient and was not seen on other investigations.

Therefore, the calculated PPV on a per lesion basis of neck USG, ^{99m} Tc-sestamibi scintigraphy, and early SPECT/CT and ^{18}F-FCH PET/CT in the cohort of these 5 operated patients was 75% (3/4), 71.4%(5/7), and 71.4% (5/7), respectively. On a per-patient basis, the lesion detection rate was 100% for MIBI scan and FCH PET (5/5) and 80% for USG (4/5).

The postoperative biochemical follow-up period for these 5 patients was 6.45 ± 4.29 months (95% CI: 2.2–10.7 months).

The postoperative biochemical parameters such as iPTH, serum calcium, and serum phosphate for these 5 operated patients were 38 ± 12.2 pg/ml (95% CI: 25.8–50.2), 9.7 ± 0.3 mg/dl (95% CI: 9.4–10), and 2.9 ± 0.3 mg/dl (95% CI: 2.6–3.2), respectively.

Discussion

The utility of ^{18}FCH PET/CT as an imaging modality in patients with persistent/recurrent primary hyperparathyroidism was evaluated. Many studies that have been published on ^{18}F-FCH PET/CT have used it as a second-line modality in patients with primary hyperparathyroidism when conventional imaging had failed.[3-6] Besides ^{18}F-FCH PET/CT, another promising modality is 4D-CT neck, but it uses iodinated contrast which makes it unsuitable for patients with deranged renal function. A pilot study demonstrated that ^{18}F-FCH PET/CT is comparable in performance to 4D-CT neck,[7] another study showed that the combination of ^{18}F-FCH PET with 4D-CT had additional value,[5] and a third study concluded that 4D-CT appears as a confirmatory imaging modality.[6] An interesting development is the use of ^{18}F-FCH PET/magnetic resonance imaging, which reduces radiation dose and increases soft-tissue resolution.[8] A noteworthy portion of the patients did not undergo surgery and was managed conservatively or are awaiting surgery, this is attributable to the COVID-19 pandemic in the country. Most asymptomatic/mildly symptomatic patients had to defer their elective hospital visits due to logistical issues.

Furthermore, due to drastic changes in logistics, the supply of ^{18}F-FCH PET/CT radiotracer was adversely affected. This made it difficult to perform the ^{18}F-FCH PET/CT in some potential candidates.

Our study demonstrates that ^{18}F-FCH PET/CT is superior to conventional first-line imaging modalities such as neck USG and ^{99m}Tc-sestamibi scintigraphy and early SPECT/CT at detecting lesions in recurrent/persistent primary hyperparathyroidism patients. This is likely due to its superior spatial resolution, larger scanning field compared to neck USG and the fact that it is not affected by the P-glycoprotein expression in parathyroid adenoma cells, factors which plague the conventional first-line imaging modalities. Another important aspect to be looked at in the comparison between ^{18}F-FCH PET/CT and other imaging modalities utilizing ionizing radiation is the radiation exposure to the patient. Mahajan *et al*., Parikh *et al*., and Rep *et al*. in their studies have demonstrated that ^{18}F-FCH PET/CT had the lowest effective dose among all the available imaging modalities for parathyroid lesions that use ionizing radiation.[9-11]

However, the small sample size of 20 patients and the even fewer number of patients being operated on during this study is a major limitation, however, the fact that this was largely a consequence of the onset of the COVID-19 pandemic is equally noteworthy.

Furthermore, uptake of the radiotracer in reactive lymph nodes was also noted in our study leading to yet another potential source of error. This becomes even more significant in the Indian clinical scenario with its high rates of tuberculosis and other infectious diseases. Prabhu *et al*. demonstrated the value of early dynamic ^{18}F-FCH PET/CT in detecting parathyroid adenoma(s) and differentiating between them and cervical lymph nodes using time activity curves for the thyroid, lymph nodes, and parathyroid adenoma(s). They showed that it was possible to differentiate between parathyroid adenoma(s)

and cervical lymph nodes in early dynamic images based on the differences in the time to peak (t-peak) of their respective standardized uptake values.[12]

Conclusion

This study suggests that ^{18}F-FCH PET/CT can detect more lesions (parathyroid adenomas or parathyroid hyperplasia) in the clinical setting of persistent/recurrent primary hyperparathyroidism compared to other routine modalities as mentioned previously. However, this study was restricted by COVID-related logistic issues and there is a need for larger studies with longer follow-up periods to ascertain the true utility of this modality. Finally, logistical issues regarding the availability of ^{18}F-Fluorcholine have to be addressed before we can think of widespread use of ^{18}F-FCH PET/CT.

Ethical approval

All procedures performed in the study were in accordance with the ethical standards of the institutional ethics committee and with the principles of the Declaration of Helsinki and its later amendments.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Broos WA, Wondergem M, Knol RJ, van der Zant FM. Parathyroid imaging with 18F-fluorocholine PET/CT as a first-line imaging modality in primary hyperparathyroidism: A retrospective cohort study. EJNMMI Res 2019;9:72.
2. UCLA Endocrine Center; Re-do Parathyroid Surgery. [Place Unknown: Publisher Unknown]. Available from: https://www.uclahealth.org/endocrine-center/re-do-parathyroid-surgery. [Last accessed on 2021 Dec 11].
3. Michaud L, Balogova S, Burgess A, Ohnona J, Huchet V, Kerrou K, *et al*. A pilot comparison of 18F-fluorocholine PET/CT, ultrasonography and 123I/99mTc-sestaMIBI dual-phase dual-isotope scintigraphy in the preoperative localization of hyperfunctioning parathyroid glands in primary or secondary hyperparathyroidism: Influence of thyroid anomalies. Medicine (Baltimore) 2015;94:e1701.
4. Quak E, Blanchard D, Houdu B, Le Roux Y, Ciappuccini R, Lireux B, *et al.* F18-choline PET/CT guided surgery in primary hyperparathyroidism when ultrasound and MIBI SPECT/CT are negative or inconclusive: The apach1 study. Eur J Nucl Med Mol Imaging 2018;45:658-66.
5. Piccardo A, Trimboli P, Rutigliani M, Puntoni M, Foppiani L, Bacigalupo L, *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. Eur J Nucl Med Mol Imaging 2019;46:766-75.
6. Amadou C, Bera G, Ezziane M, Chami L, Delbot T, Rouxel A, *et al.* 18F-fluorocholine PET/CT and parathyroid 4D computed tomography for primary hyperparathyroidism: The challenge of reoperative patients. World J Surg 2019;43:1232-42.
7. Taywade SK, Damle NA, Behera A, Devasenathipathy K, Bal C, Tripathi M, *et al.* Comparison of 18F-fluorocholine positron emission tomography/computed tomography and four-dimensional computed tomography in the preoperative localization of parathyroid adenomas-initial results. Indian J Endocrinol Metab 2017;21:399-403.
8. Khafif A, Masalha M, Landsberg R, Domachevsky L, Bernstine H, Groshar D, *et al.* The role of F18-fluorocholine positron emission tomography/magnetic resonance imaging in localizing parathyroid adenomas. Eur Arch Otorhinolaryngol 2019;276:1509-16.
9. Parikh AM, Grogan RH, Morón FE. Localization of parathyroid disease in reoperative patients with primary hyperparathyroidism. Int J Endocrinol 2020;2020: ID no. 9649564. page: 1-15 doi: 10.1155/2020/9649564.
10. Mahajan A, Starker LF, Ghita M, Udelsman R, Brink JA, Carling T. Parathyroid four-dimensional computed tomography: Evaluation of radiation dose exposure during preoperative localization of parathyroid tumors in primary hyperparathyroidism. World J Surg 2012;36:1335-9.
11. Rep S, Hocevar M, Vaupotic J, Zdesar U, Zaletel K, Lezaic L. 18F-choline PET/CT for parathyroid scintigraphy: Significantly lower radiation exposure of patients in comparison to conventional nuclear medicine imaging approaches. J Radiol Prot 2018;38:343-56.
12. Prabhu M, Kumari G, Damle NA, Arora G, Kumar P, Kumar R, *et al.* Assessment of the role of early dynamic PET/CT with 18F-fluorocholine in detection of parathyroid lesions in patients with primary hyperparathyroidism. Nucl Med Commun 2018;39:1190-6.