Comparison of Neck Ultrasonography, Dual Phase ^{99m}Tc-Sestamibi with early SPECT-CT & ^{18}F-Fluorocholine PET-CT as First Line Imaging in Patients with Primary Hyperparathyroidism

Abstract

Introduction: Successful surgical treatment for primary hyperparathyroidism requires accurate localization of abnormal parathyroid tissue in terms of location and number. Imaging is important for localizing the parathyroid adenoma, and there has been significant interest in ^{18}F-fluorocholine (FCH) positron emission tomography/computed tomography (PET/CT) for this purpose. **Aim:** This study attempted to ascertain the utility of ^{18}F-FCH PET/CT as a first-line investigation in preoperative localization of abnormal parathyroid tissue in primary hyperparathyroidism, in comparison with ^{99m}Tc-sestamibi dual-phase scintigraphy with early single-photon emission computed tomography (SPECT)/CT and neck ultrasonography. **Materials and Methods:** Fifty-five patients with biochemical features of primary hyperparathyroidism were enrolled in this study. They underwent neck ultrasonography, ^{99m}Tc-sestamibi dual-phase scintigraphy with early SPECT/CT, and ^{18}F-FCH PET/CT for localization of parathyroid lesions. Thirty-three patients underwent surgical resection of the detected lesions. For two patients, clinical and biochemical follow-up was used as a gold standard. **Results:** A total of 40 lesions were resected in the 33 patients who underwent surgery. A further two lesions were localized in two patients with clinical and biochemical follow-up as the gold standard. Of these 42 lesions, 41 were detected in preoperative imaging and 1 lesion was noted intraoperatively and resected. 41/42 lesions were detected by ^{18}F-FCH PET/CT (detection rate: 97.6%), 33/42 by ^{99m}Tc-sestamibi dual-phase scintigraphy with early SPECT/CT (detection rate: 78.5%), and 30/42 by neck ultrasonography (detection rate: 71.4%). **Conclusion:** Detection rates on ^{18}F-FCH PET/CT were superior to both ^{99m}Tc-sestamibi dual-phase scintigraphy with early SPECT/CT and neck ultrasonography in preoperative localization of parathyroid lesions in patients with primary hyperparathyroidism.

Keywords: *Fluorocholine, hyperparathyroidism, primary, technetium Tc-99m sestamibi*

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Introduction

Primary hyperparathyroidism is a highly morbid condition and is diagnosed based on biochemical parameters. In these patients, only surgical resection offers a definite curative treatment.[1] However, the location of parathyroid glands and subsequently of the hyperfunctioning parathyroid glands is highly variable in the body.[2] This necessitates the preoperative localization for the number and location of lesions using imaging.

At present, neck ultrasonography and ^{99m}Tc-sestamibi scanning form the standard imaging techniques used for this purpose in most centers across the world. However, they offer only moderate sensitivity in the range of 70%–80% for the localization of hyperfunctioning glands.[3-5] Thus, a small but significant portion of patients are not localized using these imaging modalities. This forms a significant gap in imaging that needs to be addressed.

In this regard, ^{18}F-fluorocholine (FCH) positron emission tomography/computed tomography (PET/CT) has recently attracted a lot of interest as an imaging modality for preoperative localization of hyperfunctioning parathyroid lesions. It has been heavily studied in the setting of a second-line investigation in case of negative or inconclusive first-line investigations such as scintigraphy and neck ultrasonography.[6-20] These studies have produced encouraging results. In addition, various studies have also investigated

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hyperfunctioning parathyroid localization in secondary and tertiary hyperparathyroidism.[21,22]

This study was a prospective comparison of conventional first-line imaging in the form of neck ultrasonography and dual-phase ^{99m}Tc-sestamibi with early single-photon emission computed tomography (SPECT)/CT with ^{18}F-FCH PET/CT in the first-line imaging setting of primary hyperparathyroidism. The underlying aim of the study is to test if any additional benefit is provided by ^{18}F-FCH PET/CT over and above neck ultrasonography and dual-phase ^{99m}Tc-sestamibi with early SPECT/CT imaging with regard to preoperative localization of hyperfunctioning parathyroid glands. Although ^{18}F-FCH PET/CT has by now been shown to be a highly useful modality, there are a limited number of studies with this modality in the first-line setting comparing it with US and MIBI scan, and including patients with parathyroid hyperplasia and adenoma both, for primary hyperparathyroidism. In addition, some are limited due to highly selective patient groups[23] or from not concurrently studying all three investigations.[24-29] To the best of our knowledge, there is only one prospective study from India in primary hyperparathyroidism using FCH PET/CT thus far.[30]

Materials and Methods

This was a prospective study carried out over a period of 23 months. A total of 55 patients with biochemical evidence of primary hyperparathyroidism referred from the department of endocrinology were enrolled in the study. Thirty-five patients eventually were analyzed, of which 33 underwent minimally invasive parathyroidectomy and 2 had persistently elevated intact parathyroid hormone (iPTH) levels and hypercalcemia despite exclusion of all other diagnosis. Imaging findings were then compared with surgical histopathology and subsequent normalization of clinical and biochemical parameters in 33 patients or in the case of 2 patients who did not undergo surgery, with clinical and biochemical follow-up of minimum 1 year suggesting persistent true positive disease.

Inclusion criteria

1. Biochemical evidence of hyperparathyroidism, i.e., elevated serum iPTH (defined as serum iPTH >65 pg/ml), high normal to raised serum calcium, and low serum phosphorus
2. Normal renal function as measured by a serum creatinine level <1.3 mg %
3. Patients who gave given written informed consent after a detailed explanation of the procedures they will undergo, the experimental nature of the investigations being performed and the potential benefit or lack of benefit from the investigations.

Exclusion criteria

1. History of chronic renal disease
2. Clinical setting of secondary or tertiary hyperparathyroidism
3. Serum creatinine >1.3 mg %
4. Known previous history of malignancy.

Ultrasonogram neck

Each patient underwent high-resolution ultrasonography of the neck with a 7 MHz probe by a single endocrine radiologist with 10 years' experience. The ultrasonography field included a region extending from the submandibular region to the suprasternal notch. Any hypoechoic lesion with internal vascularity lying in a location suspicious for parathyroid gland was considered a parathyroid lesion.

^{99m}Tc-methoxy-isobutyl-isonitrile (MIBI) scan

A dual-phase ^{99m}Tc-sestamibi scan post 20 mCi (740 MBq) intravenous injection of the tracer with single- and double-zoom anterior planar images covering neck and mediastinum, in a 128 × 128 matrix, was taken at 15 min and 50–90 min after injection. The scanning was done on a Symbia T6 (Siemens) dual-head gamma camera with a 6-slice CT scanner. SPECT/CT was done on the same scanner after the early static planar image with acquisition in step and shoot mode with 30 steps of 6° for each head. Image reconstruction was done with iterative reconstruction using 2 iterations and 21 subsets. No intravenous or oral contrast was used.

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

^{18}F-FCH PET/CT was done 45–90 min after intravenous injection 3–5 mCi (111–185 MBq) of the radiotracer. Images of the neck and thorax were acquired on Biograph mCT (Siemens) PET/CT with LSO crystal and 64-slice CT scanner. No intravenous or oral contrast was used. PET imaging was done at 3–5 min per bed position, and images were reconstructed with iterative reconstruction using OSEM algorithm with 3 iterations and 21 subsets.

PET/CT and sestamibi scans were interpreted independently by two nuclear medicine experts who were blinded to details of other imaging investigations.

In this study, we considered focal, increased accumulation of ^{99m}Tc-sestamibi and ^{18}F-FCH at expected normal locations of parathyroid glands, not conforming to any known physiological radiotracer distribution on visual analysis associated with a structural lesion hypodense to the thyroid and not showing any necrosis or calcification, to be a parathyroid adenoma. For ectopic locations also, we used the same criteria on CT and PET. Any focus of significantly increased radiotracer uptake with corresponding lesion on CT images was considered positive. Any focus of radiotracer uptake not showing corresponding lesions on CT images or with CT findings not consistent with parathyroid lesions was considered indeterminate.

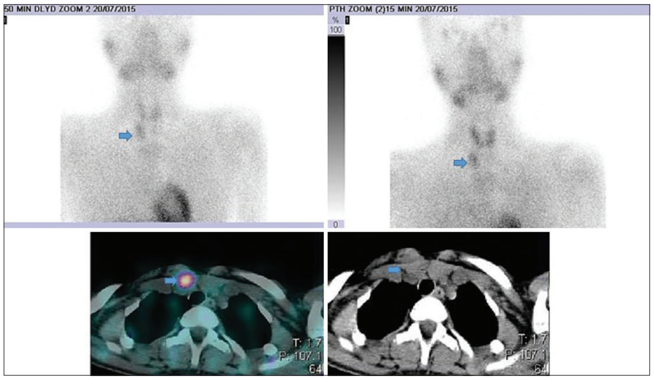

Figure 1: A 14-year-old male with right inferior parathyroid adenoma detected on sestamibi scan images (blue arrow)

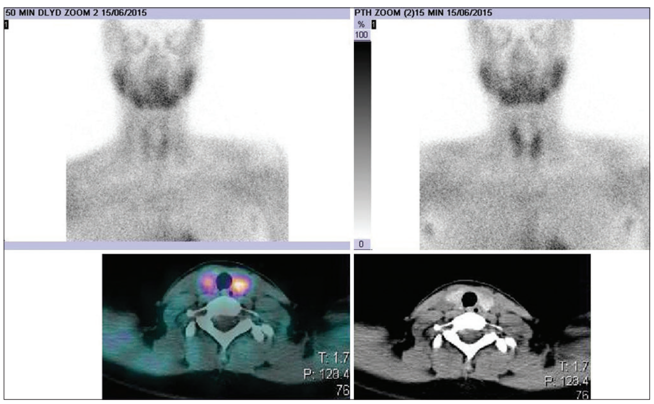

Figure 3: A 30-year-old female with features suggestive of primary hyperparathyroidism. No parathyroid lesion was localized on sestamibi scan with SPECT/CT. SPECT/CT: Single-photon emission computed tomography/computed tomography

Results

Study population

Patients who had undergone surgery and had eventual surgical histopathology for comparison or with minimum 1 year of clinical and biochemical follow-up despite not undergoing surgery were included. Hence, a study population of 35 patients was included in the eventual analysis.

Patient characteristics

The 35 patients included in the study included 20 females and 15 males [Table 2]. The mean age of the patients was 38 years (range: 11–62 years). The mean preoperative serum iPTH levels were 435.8 pg/ml (range: 66.8–1900 pg/ml). The preoperative mean serum total calcium level for the study population was 11.4 mg/dl (range: 8.6–15.2 mg/dl). The preoperative mean serum phosphate level for the study population was 2.4 mg/dl (range: 1.3–4.8 mg/dl).

Thirty-three patients underwent selective parathyroid resection based on the findings of the preoperative localization done using the investigations. Two patients were unwilling to undergo surgery and were followed up clinically. Persistently elevated iPTH levels at more than 12 months despite adequate Vitamin D levels were considered as the gold standard for diagnosis in them.

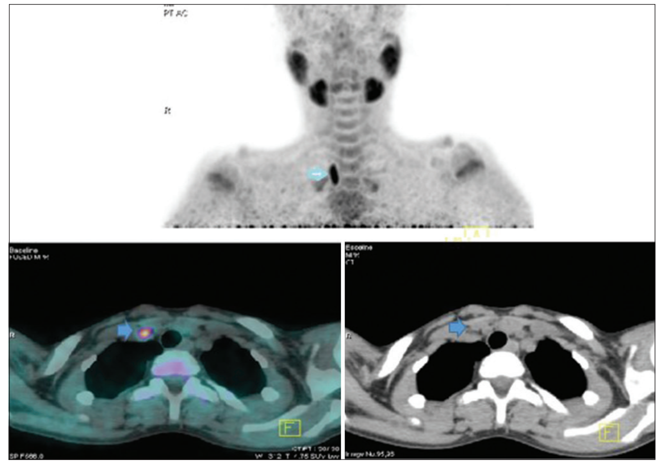

Figure 2: The same patient as in Figure 1, also showing concordant localization on ^{18}F-FCH PET/CT. PET/CT: Positron emission tomography/computed tomography, FCH: Fluorocholine

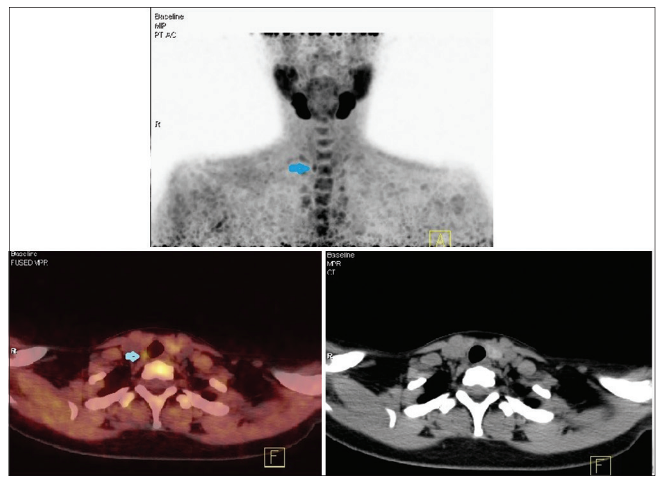

Figure 4: The above-mentioned patient [Figure 3] underwent FCH PET/CT. A small soft-tissue density lesion (6 mm × 4 mm) was localized posterior to the right lobe with increased radiotracer uptake. On surgical histopathology, the lesion was proven to be a parathyroid adenoma. PET/CT: Positron emission tomography/computed tomography. FCH: Fluorocholine

Surgical histopathology findings

Thirty-three patients underwent selective parathyroid resections and histopathology confirmation. In addition, in one patient, intraoperatively, an extra parathyroid lesion (measuring 2 mm on histopathology) was located and resected despite nonlocalization on any of the imaging modalities.

A total of 40 lesions (11 parathyroid hyperplasia in 6 patients, solitary patients with 3 parathyroid adenomas, and 26 solitary parathyroid adenomas in 26 patients) were resected.

Two lesions (one each) were concordantly localized on all in all three investigations in the two patients who did not undergo surgery. In the analysis, the lesions were treated as true positive parathyroid adenomas due to the solitary lesions and serum iPTH, calcium levels being consistently elevated.

Performance of neck ultrasonography

A total of 32 lesions were localized and classified as the culprit lesion causing hyperparathyroidism. Of these, two lesions, one adjacent to and one inside the thyroid gland, were also localized and suggested as potential sites of parathyroid lesion by neck ultrasonography. On eventual surgical resection and histopathology, one of the lesions was found to be colloid goiter and another lesion was classified as adenomatous goiter on histopathology, thus both these turned out to be false positives.

In addition, there were four lesions that were proven to be parathyroid lesions on surgical histopathology and were also visualized on ultrasonography but, due to their locations and atypical size and morphology, were reported as lymph nodes by the radiologist and were consequently not included in the set of lesions localized by neck ultrasonography. These constituted one subset of the false-negative cases in our study.

Thus compared to the available surgical histopathology/follow-up, ultrasonography was able to localize 30 out of the 42 resected (71.4% detection rate) lesions.

Of the 32 reported localizations on neck ultrasonography, 30 lesions eventually were proven to be true positives and 2 were false positives. This led to a calculated positive predictive value of 93.8%.

Performance of ^{99m}Tc-sestamibi scintigraphy

A total of 33 lesions were localized in the 35 patients. Thus, ^{99m}Tc-sestamibi scintigraphy was correctly able to localize 33 of the 42 histopathologically proven parathyroid lesions (i.e., 78.5% detection rate). There were no false positives recorded in this patient subset.

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

^{18}F-FCH PET/CT localized a total of 41 lesions in 35 patients as potential parathyroid lesions. Hence, ^{18}F-FCH PET/CT was able to localize 41 of the 42 lesions proven to be parathyroid lesions on histopathology. The calculated detection rate was 97.6%.

^{18}F-FCH concentration was noted in a case of intrathyroid colloid goiter in one of the patients. In addition to the offending adenoma, mild radiotracer concentration was also noted in an intrathyroid mass in another patient. The second lesion was found to be a case of papillary carcinoma thyroid (oncocytic variant). ^{18}F-FCH uptake can be seen in a multitude of benign and malignant conditions. The two lesions were considered low probability based on morphology; however, they were included in calculating the estimates since they were showing ^{18}F-FCH uptake at or near normal parathyroid gland location. Considering these two lesions, the positive predictive value of ^{18}F-FCH PET/CT was found to be 93.1%.

One adenoma was missed on all three modalities.

In addition, of all the resected adenomas, 5 lesions were found to be in an ectopic location, while rest of the 37 were in a eutopic location.

Further, of the 35 patients who were evaluated, 28 had single adenomas [Figures 1 and 2] and 7 had multiple parathyroid lesions (hyperplasia/adenoma).

Discussion

In our study, the estimated detection rate of neck ultrasonography was 71.4%, of dual-phase ^{99m}Tc-sestamibi scanning with early SPECT/CT was 78.6%, and of ^{18}F-FCH PET/CT was 97.6%. The estimated positive predictive

Table 1: Review of studies by various authors utilizing ^{18}F-fluorocholine positron emission tomography/computerized tomography as a first-line investigation for lesion localization in primary hyperparathyroidism

Author	Year	Sample Size	Study design	^{18}F-fluorocholine (detection rate)	Conventional scintigraphy (detection rate)	Neck ultrasonography (detection rate)
Lezaic *et al*.[24]	2014	24	Prospective comparative	92%	64%	N/A
Hocevar *et al*.[25]	2016	151	Retrospective	144/151 (95.3%)†	N/A	N/A
Thanseer *et al*.[30]	2017	54	Prospective comparative	96.30%	77.70%	62.90%
Beheshti *et al*.[26]	2018	100 (82)*	Prospective comparative	93%	61%	N/A
Bossert *et al*.[31]	2018	34 (17)*	Prospective	71%	15%	68%
Broos *et al*.[27]	2019	271 (139)*	Retrospective	96%	N/A	N/A
Khafif *et al*.[32]	2019	19	Prospective (PET/MR imaging done)	100%	84.20%	74%
Boccalatte *et al*.[28]	2020	28 (18)*	Prospective	88%	N/A	N/A
Cuderman *et al*.[29]	2020	188 (103)*	Prospective (PET/4DCT imaging done)	92%	65%	N/A

*Number included in analysis, †Calculated from study data, not reported by authors. PET: Positron emission tomography, CT: Computerized tomography, MR: Magnetic resource, N/A: Not available

Table 2: Details of patients and scans

Age	Sex	Diagnosis (if made)	USG localization	Sestamibi localization	Fluorocholine PET/CT localization	Serum calcium (preoperative)	Serum phosphate (preoperative)	iPTH (preoperative)	Postoperative iPTH	Surgical and pathological findings
38	Male	PHPT	Left inferior	Left inferior	Left inferior	12.6	2.1	831.3	58	Left superior parathyroid adenoma
58	Male	PHPT	Left sided	No localization	Left sided	12.03	2.54	292.8	3.77	Left superior parathyroid adenoma
50	Male	PHPT, ?MEN1	Left inferior	Left inferior	Right superior and left inferior	10.9	3	167.7	1.2	Right superior and left inferior parathyroid hyperplasia, in addition, mass labeled left adenoma shows a necrotizing granuloma
50	Female	PHPT	Left inferior	Left inferior	Left inferior	10.6	2.8	164.5	6	Left inferior parathyroid adenoma
22	Female	PHPT	Left superior	Left superior	Left superior	12.2	1.7	951.5	71	Left superior and left inferior parathyroid hyperplasia
35	Male	PHPT	Right sided	Right sided	Right sided	12.2	1.6	346.6	15.13	Right inferior parathyroid adenoma
43	Female	PHPT	Right inferior	Right inferior	Right inferior	11.93	1.49	324.3	23.66	Right inferior parathyroid adenoma
38	Male	PHPT, ?MEN1	No localization	Right inferior and ectopic suprasternal	Ectopic suprasternal, right inferior and left superior	10.4	1.5	173	65	Right superior parathyroid, left inferior parathyroid, and retrosternal ectopic parathyroid hyperplasia
11	Male	PHPT	Left superior	Left superior	Left superior	13.4	1.9	86.29	19.25	Left superior parathyroid adenoma
31	Female	PHPT	No definite localization	Ectopic parathyroid posterior to left SCM	Ectopic parathyroid adenoma, posterior to left SCM	10.9	2.3	358.2	24	Ectopic parathyroid adenoma, posterior to the left SCM
12	Male	PHPT	Ectopic right cervical	Ectopic right cervical	Ectopic right cervical	11.5	2.8	1021	14	Right-sided parathyroid adenoma
38	Female	PHPT	Right superior	Right sided	Right sided	11.7	1.6	677	7	Right inferior parathyroid adenoma
50	Female	PHPT	Intrathyroidal nodule, no localization	Left inferior	Left inferior parathyroid adenoma + ? intrathyroidal adenoma left lobe thyroid	10.58	2.3	255.3	N/A	Intrathyroidal mass - colloid goiter, left inferior parathyroid adenoma
14	Male	PHPT	Left inferior	Left inferior	Left inferior	15.2	2.4	1164	6.4	Left inferior parathyroid adenoma

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Table 2: Contd...

Age	Sex	Diagnosis (if made)	USG localization	Sestamibi localization	Fluorocholine PET/CT localization	Serum calcium (preoperative)	Serum phosphate (preoperative)	iPTH (preoperative)	Postoperative iPTH	Surgical and pathological findings
60	Female	PHPT	Left inferior	Left inferior	Left inferior	12.2	1.3	438.3	7.62	Left inferior parathyroid adenoma
35	Female	PHPT	Right sided	Right sided	Right sided	13	2.3	1043	1	Right superior parathyroid adenoma
23	Female	PHPT	Right superior and inferior	Right superior and inferior	Right superior and inferior	10.7	2.7	160.9	13.24	Right superior and inferior parathyroid adenoma
37	Female	PHPT	Left superior	Left superior	Left superior	11.3	2	1028	30.96	Left superior parathyroid adenoma
53	Male	PHPT	Ectopic left cervical	Ectopic left cervical	Ectopic left cervical	10.7	2.2	118	43.8	Ectopic left cervical parathyroid hyperplasia
34	Female	Recurrent PHPT	Right inferior + suspicious left sided	Right inferior	Right inferior	10.3	2.1	105	4.79	Right inferior parathyroid adenoma+left-sided thyroid nodule – adenomatous goiter
30	Female	PHPT	?Right-sided lesion	No localization	Right inferior	10.3	2.2	183	54	Right inferior parathyroid - 0.6 cm×0.4 cm×0.4 cm
48	Male	PHPT	No localization	Right inferior	Right sided and left superior	12.7	2.3	123.5	72	Right-sided parathyroid and left superior parathyroid hyperplasia
45	Female	PHPT	Right inferior	Right inferior	Right inferior	10.5	3.3	123.5	N/A	Right inferior parathyroid adenoma
46	Male	Recurrent PHPT	No localization	Ectopic posterior to right lobe thyroid	Ectopic posterior to right lobe thyroid	10.91	N/A	317	76.4	2 cm×1.5 cm×0.8 cm PT adenoma
30	Female	PHPT	Left superior	No localization	Left superior	11.1	2.5	594.2	0.01	Left superior parathyroid adenoma
35	Male	PHPT	Left inferior	Left inferior	Left inferior	8.6	4.8	66.8	N/A	Left inferior parathyroid adenoma
58	Female	PHPT	Left inferior	No localization	Left inferior	13.9	2.4	204.1	10.43	Left inferior parathyroid adenoma (0.8 cm×0.5 cm×0.4 cm,) + PCT oncocytic variant in thyroid
19	Female	PHPT	Right inferior	Right inferior	Right inferior	13.1	2.1	403.2	48.76	Right inferior parathyroid adenoma
55	Female	PHPT	No localization	Ectopic parathyroid adenoma in the left parapharyngeal space	Ectopic parathyroid adenoma in the left parapharyngeal space	12.3	2.5	326.2	37	Features are suggestive of parathyroid lesion possibly an adenoma

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Table 2: Contd...

Age	Sex	Diagnosis (if made)	USG localization	Sestamibi localization	Fluorocholine PET/CT localization	Serum calcium (preoperative)	Serum phosphate (preoperative)	iPTH (preoperative)	Postoperative iPTH	Surgical and pathological findings
62	Female	PHPT	Left-sided parathyroid adenoma	No localization	Left superior	10.6	2.71	201.7	N/A	Left superior parathyroid adenoma
29	Male	PHPT	No localization	Right inferior	Right inferior	10.5	2.3	290	8	Right inferior parathyroid adenoma
26	Male	PHPT	3 aberrant Parathyroid adenomas	1 aberrantly located adenoma localized	3 adenomas, aberrant location in neck	11.4	3.6	246	N/A	3 parathyroid adenomas
45	Female	PHPT	Left superior	Left superior	Left superior	10.6	3.6	1900	N/A	Left superior parathyroid adenoma

PET: Positron emission tomography, CT: Computerized tomography, N/A: Not available, PHPT: Primary hyperparathyroidism, iPTH: Intact parathyroid hormone, SCM: sternocleidomastoid

values for neck ultrasonography, ^{99m}Tc-sestamibi scanning, and ^{18}F-FCH PET/CT were 93.8%, 100%, and 93.1%, respectively.

In order to gain better insight with regard to the validity of our result, we reviewed the various studies undertaken in a similar setting. The results of the various studies are noted in Table 1 in brief.

The detection rates in our study for ^{18}F-FCH PET/CT are consistent with the findings of majority of the studies in Table 1.

This search of literature revealed that in the first-line setting, our study is one of the few studies to have seen patients with multiple parathyroid lesions and undergoing all three modalities. Among the studies mentioned in Table 1, Thanseer *et al*[30]., Bossert *et al*[31]., and Khafif *et al*[32]. had patients with solitary adenomas in their study. Studies done by Lezaic *et al*[24]., Broos *et al*[27]., Beheshti *et al*[26]., and Cuderman *et al*[29]. included patients with multiple parathyroid lesions in the study; however, these four did not have all three investigations that we compared.

The study by Bossert *et al*.[31] is the only study with a notably different result, predominantly with regard to the detection rate of conventional scintigraphy reported by them (78.5% in the present study vs. 15% by Bossert *et al*.). However, it must be noted that the detection rate reported by Bossert *et al*.[31] is also significantly lower than reported by various studies previously[4] and also with the other studies in Table 1.

^{18}F-FCH performed better than both ^{99m}Tc-sestamibi and neck ultrasonography in the localization of parathyroid lesions in patients with hyperparathyroidism. When compared to ^{99m}Tc-sestamibi and ultrasonography together, an incremental benefit was obtained in 8.6% of the patients (3 out of 35 patients) [Figures 3 and 4].

To the best of our knowledge, incidental detection of parathyroid adenomas on radiolabelled choline analogs was first described in case reports by Mapelli *et al*.[33] and Hodolic *et al*.[34] This led to further investigation of radiolabelled choline analogs in prospective studies using 11C-choline[35] and ^{18}F-FCH by various authors by PET/CT and more recently using PET/MRI imaging.

In addition to the improvement in detection rates and positive predictive value reported for ^{18}F-FCH PET/CT compared to neck ultrasonography and ^{99m}Tc-sestamibi scanning, there are qualitative improvements with respect to neck ultrasonography. Although not prospectively evaluated in the study, factors such as low physiological thyroid uptake compared to ^{99m}Tc-sestamibi and better coverage of potential ectopic sites of parathyroid lesions when compared to neck ultrasonography were considered significant improvements over these imaging modalities.

Absolute sensitivity and specificity could not be calculated as they would require comparison with extensive bilateral surgical neck exploration instead of focused surgery in all patients, which was not done in patients due to the morbidity associated with the procedure. This forms a limitation with regard to reporting absolute sensitivity. The ^{99m}Tc-sestamibi scans and ^{18}F-FCH PET/CT were reported by the same two nuclear medicine physicians and may have led to bias. Further, the ideal timing for ^{18}F-FCH PET/CT has been reported to be around 60 min;[36,37] however, due to the high-volume nature of our department and the infrequent production of ^{18}F-FCH at our center, patients were clubbed together for scanning, thus maintaining an ideal timing of 60 min post injection for scanning was not feasible in all patients. This forms a limitation of our study.

With regard to the timing of delayed image in ^{99m}Tc-sestamibi scintigraphy, evidence suggests that further delayed imaging at 2–3 h is helpful. Unfortunately, in our department, time constraints associated with the high volume of patients only allowed for a single delayed image at 50–90 min post injection to be taken. This forms another limitation of the study.

Despite the advantages noted above, there are certain inherent limitations with using a nonspecific radiotracer such as ^{18}F-FCH. The documented accumulation of ^{18}F-FCH in various malignancies such as prostate carcinoma,[38,39] hepatocellular carcinoma,[40] thymoma,[41] and even differentiated thyroid carcinoma[42,43] leads to a potential source of error in the investigation. Further, uptake of radiotracer in infective lymph nodes has also been noted in our study and documented in various studies, leading to another potential source of error.

Further, in this study, the authors have not compared imaging with other upcoming investigations for localization in primary hyperparathyroidism such as four-dimensional-computed tomography (4DCT)[44] and 4D-magnetic resonance imaging.[45] The high detection rate shown by these investigations and more widespread availability suggests them as good alternatives to ^{18}F-FCH PET/CT in the setting of primary hyperparathyroidism. Further, 4DCT is currently even recommended for primary hyperthyroidism by the American Head and Neck Society.[46]

Looking forward, the authors, however, are of the opinion that besides being competing modalities, the use of 4DCT and 4D-MRI in conjunction with ^{18}F-FCH PET fusion with 4DCT[15,47] and with 4D-MRI may allow for further improvement of either imaging. These combined imaging modalities may indeed be the future one-stop shop imaging for hyperparathyroidism.

Raeymaeckers *et al*. demonstrated the ability of a high-frequency multiphase 4DCT protocol consisting of 16 phases not only to detect small adenomas but also to avoid falsely identifying an enlarged lymph node as an adenoma based on a temporary rise in contrast enhancement.[48]

Kawai *et al*. studied the role of unenhanced 3T MRI along with ultrasound and MIBI scintigraphy and SPECT/CT in the presurgical workup of patients of primary hyperparathyroidism, which demonstrated a sensitivity of 92% compared to 82% and 88% for ultrasound and MIBI, respectively.[49]

Conclusion

The findings in this study suggest that ^{18}F-FCH PET/CT can detect abnormal parathyroid glands (adenomas or parathyroid hyperplasia) in the clinical setting of primary hyperparathyroidism with a high detection rate. Further, the results are encouraging with regard to the use of ^{18}F-FCH PET/CT for the localization of parathyroid lesions in primary hyperparathyroidism in comparison to the routinely used investigations such as ^{99m}Tc-sestamibi scintigraphy with early SPECT/CT and neck ultrasonography in the first-line imaging setting.

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Conflicts of interest

There are no conflicts of interest.

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