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Diagnostic Performance of ^{18}F-fluorocholine PET/CT Compared to ^{99m}Tc-Sestamibi Scintigraphy in Diagnosis of Parathyroid Adenoma

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Abstract

Background: In most hyperparathyroidism cases, the disease is related to parathyroid adenoma (PTA). Owing to the inconsistencies of currently approved imaging methods, novel methods for detecting PTA are being evaluated. This study aimed to compare ^{18}F-fluorocholine PET/CT with ^{99m}Tc-sestamibi SPECT/CT in identifying PTA in Saudi patients.

Methods and Results: The study included 40 adult patients with PTA diagnosed by histopathological findings. ^{99m}Tc-sestamibi SPECT/CT and ^{18}F-fluorocholine PET/CT examinations were performed for each patient, and parathyroid hormone (PTH) levels and histologic findings were recorded. The diagnostic ability of ^{18}F-fluorocholine PET/CT (AUC=0.720; P=0.029) was superior to ^{99m}Tc-sestamibi SPECT/CT (AUC=0.623; P=0.214) in identifying PTA. The sensitivity and accuracy of ^{18}F-fluorocholine PET/CT (81.5% and 75.0%, respectively) were significantly (P<0.05) higher than that of ^{99m}Tc-sestamibi SPECT/CT (63.0% and 62.5%, respectively). ^{18}F-fluorocholine PET/CT findings were correlated significantly (P=0.023) with PTH results.

Conclusion: ^{18}F-fluorocholine PET/CT is a diagnostic imaging method superior to conventional modality ^{99m}Tc-sestamibi SPECT/CT in the detection of PTA and, thus, allows for accurate preoperative localization.**(International Journal of Biomedicine. 2024;14(1):83-87.)**

Keywords: ^{18}F-fluorocholine PET/CT • parathyroid adenoma • hyperparathyroidism

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Abbreviations

4DCT, four-dimensional computed tomography; **FCH**, fluorocholine; **HPT**, hyperparathyroidism; **PTA**, parathyroid adenoma; **PET/CT**, positron emission tomography/computed tomography; **SPECT**, single photon emission computed tomography; **PTH**, parathyroid hormone.

Introduction

Worldwide, around 1% of the general population is affected by hyperparathyroidism (HPT), characterized by excess parathyroid hormone (PTH) release and hypercalcemia.(1) In up to 85% of cases, this disorder results from parathyroid adenoma (PTA). Parathyroid carcinoma and hyperplasia are less common causes.(2) In most patients, HPT is asymptomatic and is detected incidentally during routine blood tests. In patients with symptomatic disorders, cardiovascular, neural, gastrointestinal, urinary, and musculoskeletal systems are affected.(3)

In both asymptomatic and symptomatic cases, surgical treatment (parathyroidectomy) of the hyperfunctioning

gland remains the only curative method.[4] For a minimally invasive parathyroidectomy, preoperative localization of the hyperfunctioning gland is needed, and this, in turn, is related to a decreased risk of disability and complications after surgery.[4] Preoperative adenoma localization is complex, and imaging methods and recommendations vary significantly. ^{99m}Tc-sestamibi SPECT/CT and neck ultrasonography are the most frequently used methods. Other imaging modalities are available to facilitate localization, including MRI and four-dimensional computed tomography (4DCT).[5] These methods can be used alone or in combination; both methods have disadvantages and advantages. Moreover, their diagnostic accuracy significantly varies depending on the skill of individual sonographers, the adenoma size, and the location of the affected glands.[4,5]

Grimaldi et al.,[6] in their study, emphasize that ^{18}F-FCH PET/CT is a promising modality in challenging presurgical localization of hyperfunctioning parathyroid glands, such as inconclusive standard imaging, recurrence after surgery, or suspected multiple gland disease. In several small studies, ^{18}F-FCH PET/CT has demonstrated promising results, possibly leading to an expanded role for this tracer.[7,8] In clinical practice, it has become clear that ^{18}F-FCH PET/CT may have diagnostic ability superior to other modalities and may become the gold standard diagnostic method for HPT.

In this study, we aimed to compare the diagnostic performance of ^{18}F-FCH PET/CT with ^{99m}Tc-sestamibi SPECT/CT for preoperative identification of PTA. Patients were identified with the gold standard histologic examination.

Materials and Methods

Study Design

This retrospective study, which included 40 patients, was performed from January 2017 to December 2021 at the endocrinology and nuclear medicine unit of 3 hospitals in Riyadh (Saudi Arabia): King Abdulaziz Medical City Hospital (KAMC), Prince Sultan Military Medical City (PSMMC), and King Abdullah bin Abdulaziz University Hospital (KAAUH). The ethical approval of the study protocol was obtained from the Institutional Review Board (IRB) at King Abdulaziz Medical City Hospital (KAMC), Prince Sultan Military Medical City (PSMMC), and Princess Norah University. All data was obtained from the patient's medical records, and thus, the need to obtain informed consent was waived.

The study included adult patients with PTA diagnosed by histopathological findings, a gold standard, during the period between January 2017 and December 2021. All patients had at least one image to identify a hyperfunctional parathyroid gland with PTA using ^{99m}Tc-Sestamibi SPECT/CT and ^{18}F-FCH PET/CT scan. Lab tests, age and gender of the patient were also involved. A total of 40 patients fulfilled the inclusion criteria. Patients who had previously undergone thyroid surgery and patients who had other pathologic conditions that could modify phosphocalcic metabolism, such as progressive neoplasia, multiple endocrine neoplasia, sarcoidosis, hyper- or hypovitaminosis D, or chronic renal failure, were excluded. Also, patients with renal stones, hypothyroidism, and osteoporosis were excluded.

^{99m}Tc-sestamibi SPECT/CT

An early parathyroid scan was obtained 15 minutes after ^{99m}Tc-sestamibi (555 MBq15mCi) injection. After 2 hours and 30 minutes after the injection, another delayed parathyroid scan was obtained. Compared to the background, the parathyroid scan positive result was elevated ^{99m}Tc-sestamibi uptake on the delayed image. Immediately after the delayed ^{99m}Tc-sestamibi scan, a delayed ^{99m}Tc-sestamibi SPECT/CT scan was performed using a Hawkeye 4 apparatus(GE Healthcare, USA).For 10 and 20 minutes, CT and SPECT images were taken. CT images were obtained using a standard filter with 512×512 matrices, 2.5mA, 140kV, and 5.0mm slice thickness. SPECT images were acquired with 128×128 matrices, 1.59 zoom, with step-and-shoot scan mode. Automatically by intrinsic software, the CT and SPECT images were fused. A positive result for ^{99m}Tc-sestamibi SPECT/CT was a focal elevated uptake lesion rather than the surrounding thyroid gland. ^{99m}Tc-sestamibi SPECT/CT images were assessed in the blinded condition by physicians' agreement.

^{18}F-FCH PET/CT

^{18}F-FCH PET/CT was taken one hour after intravenous injection of ^{18}F-FCH (150-185 MBq) using a Discovery PET/CT 710 Elite imager (GE Healthcare, USA). The strategy was in the following order: CT tomogram, low-dose attenuation-correction CT scan, PET acquisition, and additional IV contrast-enhanced diagnostic CT scan. Instead of the attenuation-correction CT scan, a diagnostic CT scan was obtained if the contrast medium was contraindicated. The acquisition protocol included a 12 0kV tension, display field-of-view of 70 cm, 1.25 mm interval, 2.5 mm thickness, and automatic mA regulation. The acquisition was centered on the cervicothoracic region. With the Q-Clear algorithm (GE Healthcare), PET image iterative reconstruction was performed to improve the signal-to-noise ratio using a β of 600. Contrast-enhanced CT permits more precise anatomic localization; thus, iodinated contrast medium was injected 80 seconds before the CT acquisition for fused-image analysis and to optimize the CT. Mediastinal or neck hyper uptake matching a scanner image of hyperplasia or adenoma was detected. SUVmax adjusted for lean body mass was determined to quantify the uptake intensity.

Statistical analysis was performed using statistical software package SPSS version 20.0 (Armonk, NY: IBM Corp.) and GraphPad Prism (version 8.0; GraphPad Prism Software Inc., San Diego, CA, USA). Baseline characteristics were summarized as frequencies and percentages for categorical variables. For the descriptive analysis, results are presented as mean (M) ± standard deviation (SD). Group comparisons with respect to categorical variables are performed using chi-square tests or, alternatively, Fisher's exact test when expected cell counts were less than 5. For data with normal distribution, inter-group comparisons were performed using Student's t-test. Receiver operating characteristic (ROC) curve analyses were performed. We calculated the sensitivity, specificity, positive predictive value, and negative predictive value to determine the diagnostic value of signs. A probability value of $P<0.05$ was considered statistically significant.

Results

Forty patients (7 males and 33 females) underwent histopathological examination and all imaging studies; 27 had histopathologically confirmed PTA, and 13 were without PTA. There was no significant difference between patients with and without PTA, except for PTH (143 [40-185] vs. 44 [29-121] ng/L, *P*=0.000) (Table 1).

Table 1.

Characteristics of patients.

Variable	Patients		*P*-value
	With PTA	Without PTA	
Number	27	13	
Male/Female	4/23	3/10	0.235
Age, years	48.4±16.3	47.9±15.3	0.314
Weight, kg	74.1±20.6	75.1±22.3	0.216
Height, m	155.7±11.7	160.1±16.1	0.344
Calcium, mmol/L	2.57±0.34	2.31±0.6	0.092
PTH, ng/L	143 (40-185)	44 (29-121)	0.000

^{99m}Tc-sestamibi SPECT/CT (Figure 1) and ^{18}F-FCH PET/CT (Figure 2) examinations were performed for each patient, and PTH levels and histologic findings were recorded. The diagnostic ability of ^{18}F-FCH PET/CT (Figure 3A; AUC=0.720; P=0.029) was superior to ^{99m}Tc-sestamibi SPECT/CT (Figure 3B; AUC=0.623; P=0.214) in identifying PTA. The sensitivity of ^{18}F-FCH PET/CT was significantly (*P*<0.05) higher than that of ^{99m}Tc-sestamibi SPECT/CT (conventional imaging method), with specificity similar to that of ^{99m}Tc-sestamibi SPECT/CT. Diagnostic performances of both methods are given in Table 2. In contrast to ^{99m}Tc-sestamibi SPECT/CT (*P*=0.252), ^{18}F-FCH PET/CT findings were correlated significantly (*P*=0.023) with PTH results (Table 3).

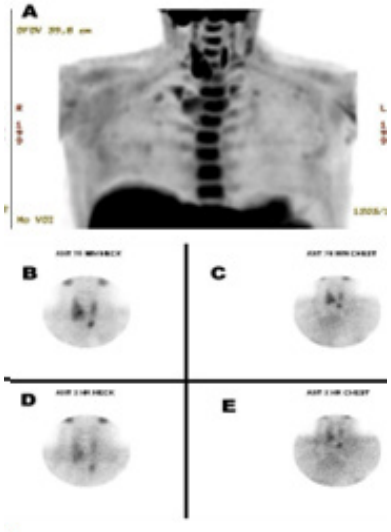

Fig. 1. *^{99m}Tc-sestamibi SPECT/CT.*

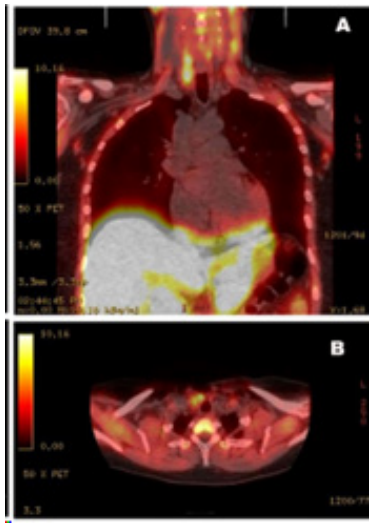

Fig 2. *^{18}F-FCH PET/CT.*

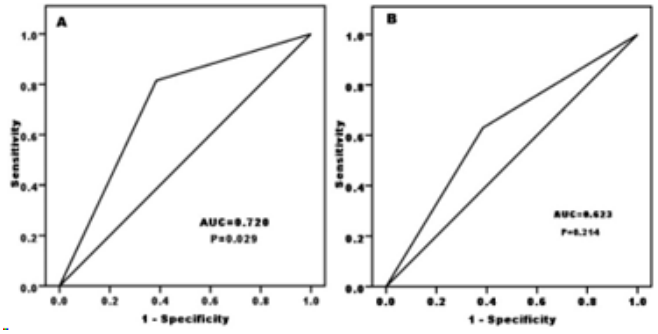

Fig. 3. *(A):^{18}F-FCH PET/CT (AUC=0.720, P=0.029); (B): ^{99m}Tc-sestamibi (SPECT/CT AUC=0.623, P=0.214)*

Table 2.

Diagnostic values (%) for different imaging modalities.

Imaging method	TP	TN	FP	FN	SN	SP	PPV	NPV	Acc
^{99m}Tc-sestamibi SPECT/CT	17	8	5	10	63.0	61.5	77.3	44.4	62.5
^{18}F-FCH PET/CT	22	8	5	5	81.5	61.5	81.5	61.5	75.0

Acc, accuracy; TP, true positive; TN, true negative; FP, false positive; FN, false negative; SN, sensitivity; SP, specificity; PPV, positive predictive value; NPV, negative predictive value.

Table 3.

^{99m}Tc-MIBI SPECT/CT and ^{18}F-FCH PET/CT results × PTH ng/L cross tabulation

		PTH, ng/L		*P*-value
		Positive	Negative	
		n=27	n=13	
^{99m}Tc-MIBI SPECT/CT	Positive	17	5	0.252
	Negative	10	8	
^{18}F-FCH PET/CT	Positive	22	5	0.023
	Negative	5	8	

Discussion

Many literature studies support and encourage ^{18}F-FCH PET/CT utility.[9] However, data on ^{18}F-FCH PET/CT utility in detecting and localizing PTA and HPT remain relatively sparse, and comparison of ^{18}F-FCH PET/CT to traditional imaging modalities is limited.[4]

Our ROC analysis revealed that ^{18}F-FCH PET/CT had a superior diagnostic ability (AUC=0.720; *P*=0.029) to ^{99m}Tc-sestamibi SPECT/CT (AUC=0.623; *P*=0.214) in identifying PTA. The sensitivity and accuracy of ^{18}F-FCH PET/CT (81.5% and 75.0%, respectively) were significantly (*P*<0.05) higher than that of ^{99m}Tc-sestamibi SPECT/CT (63.0% and 62.5%, respectively). In contrast to ^{99m}Tc-sestamibi SPECT/CT (*P*=0.252), ^{18}F-FCH PET/CT findings were correlated significantly (*P*=0.023) with PTH results.

Our results agree with Thanseer et al.,[10] who reported that ^{18}F-FCH PET/CT detected 52 of 54 patients with histopathologically confirmed PTA (sensitivity of 96.3%). This was superior to ^{99m}Tc-sestamibi SPECT/CT (sensitivity of 80.7%). Bossert et al. found that abnormal parathyroid gland detection rates were 71% for ^{18}F-FCH PET/CT compared to 15% and 68% for ^{99m}Tc-sestamibi scintigraphy and neck US, respectively.[11] Amadou et al.[12] evaluated ^{18}F-FCH PET/CT to guide surgery compared to other imaging modalities, including ^{99m}Tc-sestamibi SPECT/CT in patients with primary HPT and prior neck surgery. They found that ^{18}F-FCH PET/CT is a promising method in the challenging population of reoperative primary HPT patients.

More recently, Boudousq et al.,[13] in a total of 149 pathologic parathyroids, found that ^{18}F-FCH PET/CT detected 148 of 149 pathologic parathyroids with only one false-negative and 4 false-positives. The sensitivity and accuracy of ^{18}F-FCH PET/CT (99.3% and 98%) were superior to ^{99m}Tc-sestamibi SPECT/CT (65.1% and 81%), neck ultrasonography (75.2% and 84%), and their combination (89.9% and 91%). Also, Dudoignon et al.[14] compared ^{18}F-FCH PET/CT with conventional imaging in primary HPT. On a patient basis, sensitivity and accuracy for detecting abnormal parathyroid glands were 76%/76% for ^{18}F-FCH PET/CT, 33%/33% for neck ultrasonography, and 71%/71% for ^{99m}Tc-MIBI scintigraphy.

In 103 patients with primary HPT, Cuderman et al.[8] compared ^{18}F-FCH PET/CT with conventional scintigraphic methods, consisting of ^{99m}Tc-sestamibi dual-phase imaging, ^{99m}Tc-sestamibi/pertechnetate subtraction imaging and ^{99m}Tc-sestamibi SPECT/CT. The diagnostic performance of ^{18}F-FCH PET/CT surpassed these combined or separate conventional scintigraphy. Its sensitivity was 92% compared to 39%-56% for conventional imaging methods. Also, in differentiating multiple from single hyperfunctioning glands, they found that ^{18}F-FCH PET/CT was the most valuable method (sensitivity of 88%).

In addition to diagnostic values that are better than those of ^{99m}Tc-MIBI scintigraphy, ^{18}F-FCH PET/CT has other advantages that justify its systematic use in patients with clinically suspected HPT for the initial evaluation. Compared to ^{99m}Tc-MIBI scintigraphy, ^{18}F-FCH PET/CT generated a lower radiation dose and is more efficient.[13] Due to a higher spatial resolution, ^{18}F-FCH PET/CT generates better image quality and increased sensitivity and allows the detection of smaller lesions.[13,15] Also, it requires shorter acquisition times, one hour after injecting the tracer, compared to >2 hours for ^{99m}Tc-MIBI scintigraphy, and thus, the patient experiences less discomfort and spends less time under the camera.[13]

In conclusion, our results, for the first time in Saudi Arabia, clearly demonstrated that ^{18}F-FCH PET/CT is a diagnostic imaging method superior to conventional modality ^{99m}Tc-sestamibi SPECT/CT in the detection of PTA and, thus, allows for accurate preoperative localization. These findings suggested using ^{18}F-FCH PET/CT as a first-line evaluation in preference to other conventional modalities, including ^{99m}Tc-sestamibi SPECT/CT and neck ultrasonography.

Competing Interests

The authors declare that they have no competing interests.

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