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MIBI SPECT Scan and Ultrasonography in Preoperative Imaging of Primary Hyperparathyroidism

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Abstract

Objectives: In patients who have parathyroid adenoma, combination of ultrasonography and technetium Tc 99m sestamethoxyisobutylisonitrile scan (also called sestamibi or MIBI scan), which allows anatomic and functional information about parathyroid adenomas, is used commonly to maximize operative cure. The sensitivity of MIBI scan may be increased by adding single photon emission computed tomography (SPECT) and computed tomography (CT) as a combined MIBI-SPECT CT scan. We assessed the accuracy of ultrasonography and parathyroid MIBI-SPECT scan in detecting parathyroid adenoma and evaluated the potential benefit of the combined protocol of ultrasonography and MIBI-SPECT parathyroid scan.

Methods: In 58 patients who had biochemical evidence of primary hyperparathyroidism, we retrospectively reviewed the preoperative ultrasonography and MIBI-SPECT scans. The results of these studies were correlated with surgical findings.

Results: In the 58 patients, surgery showed that 43 patients (74%) had solitary parathyroid adenoma. The sensitivity, specificity and accuracy of MIBI-SPECT for parathyroid adenoma was (72%,80%,74%) and for ultrasonography (53%,60%,55%) respectively. The highest sensitivity is noted with the combination of MIBI-SPECT and ultrasonography (79%), . 9 adenomas (21%) were missed by both modalities. In the 20 adenomas that were missed by ultrasound 11 were detected by MIBI SPECT.

Conclusion: The MIBI-SPECT had better performance than ultrasonography for parathyroid adenoma localization. The combined MIBI SPECT and ultrasonography has the highest sensitivity for parathyroid adenoma detection (79%). An alternative strategy may be to use MIBI-SPECT initially, and to proceed to ultrasonography only in patients with negative MIBI- SPECT. This may avoid many ultrasonography procedures.

Keywords: Primary hyperparathyroidism; Sestamibi scan; MIBI SPECT scan; Diagnosis

Introduction

Surgical resection of the abnormal parathyroid gland is the standard treatment for primary parathyroid adenoma, and the goal of treatment is durable biochemical cure. The standard treatment of bilateral neck exploration and excision of all grossly abnormal glands has changed to a minimally invasive and selective technique for parathyroid exploration with decreased operative time and lower operative morbidity [1]. The more selective surgical approach is aided by accurate preoperative imaging and a rapid intraoperative parathyroid hormone (PTH) assay [2].

A combination of ultrasonography and technetium Tc 99m sestamethoxyisobutylisonitrile scan (also called sestamibi or MIBI scan), which allows anatomic and functional information about parathyroid adenomas, is used commonly to maximize operative cure. Magnetic resonance imaging and computed tomography scans usually are used as second-line tests for persistent or recurrent hyperparathyroidism. Ultrasonography is a simple noninvasive technique commonly used with acceptable sensitivity of 72% to 89% [3-5]. Pitfalls of ultrasonography include operator dependence; in addition, a multinodular goiter may obscure a parathyroid adenoma that is located posterior to the thyroid gland, and ectopic parathyroid adenoma may be missed [5,6].

The MIBI scan may show radionuclide uptake and retention in abnormal parathyroid adenoma and rapid washout from the normal thyroid gland. Since the introduction of dual phase MIBI scan in 1989, multiple techniques have been used to improve the sensitivity of the parathyroid scan [7]. The reported sensitivity of dual-phase MIBI scan for planar images is >70% and is increased to >90% by adding single photon emission computed tomography (SPECT). The combination of Tc 99m SPECT-CT is markedly better than dual-phase planar or SPECT scan alone [8]. The use of hybrid image SPECT-CT changed the operative approach in 19% patients and provided additional data in 39% patients, particularly with ectopic parathyroid adenoma, compared with planar parathyroid MIBI scan [9,10].

In the setting of re-operative parathyroid surgery pin hole collimator and a combination of Tc 99 MIBI / Iodine 123 subtraction method followed by SPECT/CT might offer optimal detection and localization of parathyroid adenoma [11,12]. The use of intraoperative gamma probe, which is more sensitive than gamma camera, permit easier surgical approach and shorter operation time particularly in patients going for bilateral neck exploration with negative pre-

operative scintigraphy [13]. Some surgeons favor use of combined MIBI-SPECT and ultrasonography as a routine practice for all patients with primary hyperparathyroidism. Other surgeons use ultrasonography and reserve MIBI-SPECT for patients who have negative ultrasonography, or use MIBI-SPECT and reserve ultrasonography for patients who have negative MIBI-SPECT [14].

The purpose of this study was to assess the accuracy of ultrasonography and MIBI-SPECT parathyroid scan in detecting parathyroid adenoma at our hospital and to evaluate the potential benefit of the combined protocol of ultrasonography and MIBI-SPECT parathyroid scan in detecting parathyroid adenoma.

Materials and Methods

Patients

In this retrospective study, we enrolled 58 consecutive patients who had biochemical evidence of primary hyperparathyroidism and histopathologic correlation and who underwent preoperative ultrasonography and MIBI-SPECT within 6 weeks of each other for parathyroid localization between 2008 and 2012 at our university hospital. 23 patients under went MIBI SPECT-CT for exact localization of the MIBI uptake. This study carried out with the approval from our center research ethics board.

Imaging

Parathyroid ultrasonography: High resolution ultrasonography examination of the neck was performed in real time with a linear array transducer (7.5-15 MHz) (Philips iU22 XMATRIX, Philips Healthcare, Best, The Netherlands) (Siemens Sonoline Antares, Siemens Healthcare, Erlangen, Germany) that had good resolution for superficial soft tissue such as thyroid and parathyroid.

The MIBI-SPECT scan: After intravenous injection of 925 MBq (25 mCi) of Tc 99m MIBI, planar images were obtained in the supine position with a low energy, high resolution collimator. Dual-phase planar images for 5 minutes were obtained using a 256 × 256 matrix immediately and 120 minutes after MIBI injection. The SPECT and/or SPECT-CT were obtained 120 minutes after MIBI injection , where SPECT of the neck and upper thorax was acquired with a dual-head gamma camera for SPECT acquisition and 128 × 128 matrix and low-power dual-head CT scanner (Siemens Symbia T6, Siemens Healthcare).

Interpretation of the scintigraphic scans

All scans were interpreted by experienced nuclear medicine physicians. All scans showing persistent MIBI uptake in comparison with the thyroid gland in planar or SPECT images were reported as positive for parathyroid adenoma. The exact locations of the parathyroid adenomas determined by MIBI-SPECT were compared with surgical results.

At the time of surgery if parathyroid adenoma was not identified or no drop of intraoperative parathyroid hormone (PTH) >50%, bilateral neck exploration was carried out. Follow up calcium and PTH was performed to ensure surgical cure.

Statistical analysis

Data analysis was performed with statistical software (IBM SPSS Statistics 22 IBM Corp, Armonk, NY). We calculated sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of ultrasonography and MIBI-SPECT, and the results of these studies were correlated with surgical findings. Average values were reported as mean ± SD, and numeric data were reported as number (%). Comparisons were made with chi-square test and kappa statistic. Statistical significance was defined by $P \leq .05$.

Result

There were 42 females (72%) and 16 males (28%). The result of clinical, Calcium level, parathyroid hormone level (PTH), thyroid function test, vitamin D level was available for all patients (Table 1). Mean calcium levels 2.49 +/-0.3 mmol/L (range 1.89-3.14) mean PTH 41.3 +/-35 Pmol/L (range 6.65-194.2). The parathyroid adenomas varied in size from 10 mm to 26 mm in diameter.

Variable	Median	Mean ± SD	(Min-Max)
Age (y)	48.0	48 ± 17	(18-82)
Parathyroid hormone (Pmol/L)	31.99	41 ± 35	(6.65-194.2)
Calcium (mmol/L)	2.490	2.5 ± 0.3	(1.89-3.14)
Vitamin D(nmo l/L)	35.15	40 ± 20	(7.5-88.4)
Thyroxine (T4)(Pmol/L)	13.80	14 ± 2	(9.75-17.55)
Thyroid stimulating hormone (TSH) (uIU/L)	2.095	2.2 ± 0.8	(0.88-4.23)
*N=58 patients who had biochemical evidence of primary hyperparathyroidism.			

Table 1: Clinical and Laboratory Results of Patients with Hyperparathyroidism*

In the 58 patients, surgery showed that 43 patients (74%) had solitary parathyroid adenoma, 7 patients (12%) had parathyroid hyperplasia, 3 patients (5%) had multiple adenomas, and 5 patients (9%) had no parathyroid pathology identified.

In the 43 patients who had solitary parathyroid adenomas, 31 adenomas were accurately localized in MIBI-SPECT, 23 adenomas were detected by ultrasonography, and 34 adenomas were detected with the combination of both tests (MIBI-SPECT and ultrasonography) (Table 2). The sensitivity was highest with the combination of MIBI-SPECT and ultrasonography (79%), specificity was highest with MIBI-SPECT alone (80%), and accuracy was highest with MIBI-SPECT alone (74.1%) (Table 2). There were 9 adenomas identified at surgery that had been missed by both MIBI-SPECT and ultrasonography (21%) (Table 2). Ultrasonography failed to detect 20 adenomas and had low sensitivity (53.5%) and 11 of these adenomas were detected by MIBI-SPECT. Only 3 adenomas were detected by ultrasonography and missed by MIBI-SPECT.

Parathyroid hyperplasia was observed in 7 patients (surgical pathology), but MIBI-SPECT was negative in 6 of these 7 patients, ultrasonography was negative in 5 patients, and 2 patients had false positive ultrasonography for misinterpretation as parathyroid adenoma. In 3 patients, bilateral adenomas were detected at surgery; in

2 of these patients, MIBI-SPECT and ultrasonography were negative, and in 1 patient, MIBI-SPECT detected the bilateral adenoma but ultrasonography detected only 1 adenoma. 5 patients (8%) have chronic renal insufficiency. In the follow up period, postoperative normocalcemia was achieved in 94.8%.

Statistical analysis showed poor agreement between MIBI-SPECT and ultrasonography in the localization of parathyroid adenoma in relation to the pathology results, Kappa test 0.3 (Table 3).Further analysis of the reliability of the tests for exact lateralization of the parathyroid adenoma (right vs. left) showed that accuracy of MIBI-SPECT was 100% and ultrasonography was 83% in lateralization of parathyroid adenoma (Table 2).

Test		Pathology		Sensitivity	Specificity	Accuracy	P ≤ †
		Right	Left				
MIBI-SPECT	Right	15	0	100%	100%	100%	0.0001
	Left	0	16				
Ultrasonography	Right	7	3	83%	83%	83%	0.006
	Left	1	12				

*N = 31 parathyroid adenomas detected by MIBI-SPECT and 23 parathyroid adenomas detected by ultrasonography. Abbreviations: MIBI-SPECT, technetium Tc 99m sestamethoxyisobutylisonitrile scan (sestamibi) scan combined with single photon emission computed tomography. †Chi-square test.

Table 2: Sensitivity, Specificity, and Accuracy of Imaging Tests For Lateralization of Parathyroid Adenoma*

Discussion

In the present study, MIBI-SPECT showed moderate sensitivity (72%), specificity (80%), and accuracy (74.1%) for parathyroid adenoma (Table 3). Ultrasonography had lower performance than MIBI SPECT for parathyroid adenoma localization (Table 3). The combination of MIBI-SPECT and ultrasonography was aimed to increase the likelihood of successful localization for parathyroid adenoma , the sensitivity, specificity, and accuracy of the combined MIBI-SPECT and ultrasonography were (79%, 47%, 70.7%)) (Table 3).

Test	Test Result	Surgical Pathology		Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Accuracy
		Positive	Negative					
MIBI-SPECT	Positive	31	3	72%	80%	91%	50%	74.1%
	Negative	12	12					
Ultrasonography	Positive	23	6	53.5%	60%	79%	69%	55.2%
	Negative	20	9					
MIBI-SPECT and ultrasonography	Positive	34	8	79%	47%	81%	44%	70.7%
	Negative	9	7					

*N = 58 patients who had biochemical evidence of primary hyperparathyroidism. **Abbreviation:** MIBI-SPECT, technetium Tc 99m sestamethoxyisobutylisonitrile scan (sestamibi) scan combined with single photon emission computed tomography.

Table 3: Sensitivity, Specificity, and Accuracy of Imaging For Parathyroid Adenoma In Relation to Surgical Results*

21% adenomas were missed by both modalities, and only 3 adenomas were missed by MIBI-SPECT and detected by ultrasonography. In the 20 adenomas that were missed by ultrasonography, 11 adenomas were detected by MIBI. However, there was poor agreement between the 2 studies in the localization of parathyroid adenoma (Table 4).

Test		Ultrasonography		Kappa	P ≤ †
		Positive	Negative		

MIBI-SPECT	Positive	20	11	0.328	NS
	Negative	3	9		

*N = 43 patients who had parathyroid adenoma. Abbreviation: MIBI-SPECT, technetium Tc 99m sestamethoxyisobutylisonitrile scan (sestamibi) scan combined with single photon emission computed tomography. †Kappa test. NS, not significant (P > .05).

Table 4: Agreement between Imaging Tests in the Diagnosis of Parathyroid Adenoma*

Varied sensitivity of Tc 99m MIBI for parathyroid adenoma has been reported in previous studies, including 56% in 1 study [15] 45% in another [16] and 39% to 90% in a large meta-analysis of 52 studies [16]. Another study reported 90% sensitivity and 91% accuracy [17]. The MIBI SPECT and MIBI SPECT-CT were introduced to provide greater contrast resolution, decreased physiologic thyroid uptake, localization of ectopic parathyroid adenoma, and increased sensitivity by 20% in comparison to planer MIBI images [10,17,18]. Several factors can affect sensitivity of MIBI such as small adenomas, multinodular goiter, hyperplasic glands, preoperative calcium level, parathyroid hormone level, and use of calcium channel blockers [12,19,20].

In previous studies, the reported sensitivity of ultrasonography for parathyroid adenoma was 72% to 89% [3,4,21]. Varied sensitivity is likely related to deep seated adenoma, multinodular goiter, small adenoma size, and operator technique. The combined single day scintigraphy and ultrasound protocol change the therapeutic strategy in more than one third of patients with parathyroid disease, where scintigraphy was superior to ultrasound in ectopic and deep seated adenomas and ultrasound was useful in cases with low intensity MIBI retention suspected for parathyroid enlargement [22].

The present data suggest that the combination of MIBI-SPECT and ultrasonography has the highest sensitivity (79%) for parathyroid adenoma detection in comparison to MIBI SPECT or ultrasound alone. MIBI-SPECT sensitivity (72%) and accuracy (74.1%) are moderate for precise preoperative localization of parathyroid adenomas and ultrasonography had the lowest sensitivity and accuracy (53.5%, 55%). Based on our data, the routine use of ultrasonography for all patients with primary hyperparathyroidism for preoperative localization is not justified. An alternative strategy may be to use MIBI-SPECT initially because this test has higher sensitivity than ultrasonography, and to proceed to ultrasonography only in patients with negative MIBI-SPECT. This may avoid many ultrasonography procedures. When inconclusive results of MIBI-SPECT and ultrasonography are noted, a 4-dimensional CT scan may be used. A prospective study is needed to determine whether ultrasonography can be safely added after negative MIBI-SPECT in the imaging algorithm for parathyroid adenoma. Limitations of our study included the small number of patients and retrospective design which could affect statistical power.

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