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Original Article

Effective factors on the sensitivity of preoperative sestamibi scanning for primary hyperparathyroidism

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Abstract: Introduction: Preoperative accurate localization of enlarged adenoma (s) in primary hyperparathyroidism (PHPT) is a vital necessity. Technetium 99m sestamibi scanning is commonly used with reported acceptable sensitivities; however, false negative scan studies remain a problem. Determining effective factors on the sensitivity of the scan might improve the diagnostic value of the study by selecting the correct candidates. Material and Methods: Patients with PHPT indicated for parathyroidectomy from June 2008 to June 2013 who had positive ultrasonographic findings for single adenoma were included in the study. All patients underwent 99m-Tc MIBI scintigraphy before the surgery. Postoperative histopathology results were used as gold standard. The effect of patients' age, gender, preoperative serum PTH level, volume of the gland and having cystic components in the adenoma on the results of the scan were investigated. Results: A total of 70 patients (mean age: 47.76 ± 11.80; 87.1% (n = 61), female) were included. Mean PTH level was 508.01 ± 360.47 pg/mL and mean volume of the parathyroid gland was 1.94 ± 1.52 cc. 27.1% (n = 19) of the adenomas had a cystic component in the ultrasonography. Sensitivity of MIBI scan was 70%. Mean PTH level was 588.86 ± 372.95 pg/mL in positive MIBI scans compared with 319.38 ± 247.19 pg/mL in negative scans. Sensitivity of the scan increased significantly with higher levels of serum PTH level. Age and gender of the patients as well as volume of the gland were not related with scan results. Adenomas with cystic component had significantly higher volume and lower serum PTH levels; and although false negative studies were more common than solid adenomas, the difference was not statistically significant. Conclusion: Sensitivity of the MIBI scan reduces significantly in lower levels of preoperative serum PTH. This should be particularly considered in adenomas with cystic components. Concomitant use of Ultrasonography can increase the accuracy of preoperative localization in such cases.

Keywords: Sensitivity, sestamibi scan, primary hyperparathyroidism

Introduction

Primary hyperparathyroidism (PHPT) is one of the most common endocrine diseases with a frequency of 1% in adults that rises to 2% and even more in people older than 55 years old. With the increasing biochemical screening in recent decades most patients are asymptomatic and characterized by overproduction of parathyroid hormone (PTH) and hypercalcemia. More than 85% of PHPT cases are due to single adenomas. Given the fact that the treatment of the condition is mainly surgical resection of the abnormal gland (s), accurate detection of the enlarged gland (s) before the surgery can lead to performance of a minimally invasive parathyroidectomy as opposed to the traditional neck exploration of the four glands [1-3].

Several non-invasive imaging studies have been introduced for preoperational localization of the abnormal parathyroid gland (s) with ultrasonography and sestamibi scan being the most commonly employed modalities. Although both ultrasonography (US) and sestamibi scan have comparable high sensitivities in detecting the parathyroid adenomas, their results highly depend on the experience and skill of the operator and the facility performing the imaging study [5-7].

Technetium 99 m sestamibi scan and technetium 99 m sestamibi SPECT is nowadays a widely accepted imaging study for preoperative localization of parathyroid adenoma with reported sensitivities ranging from 54% to 100%; however the occurrence of false nega-

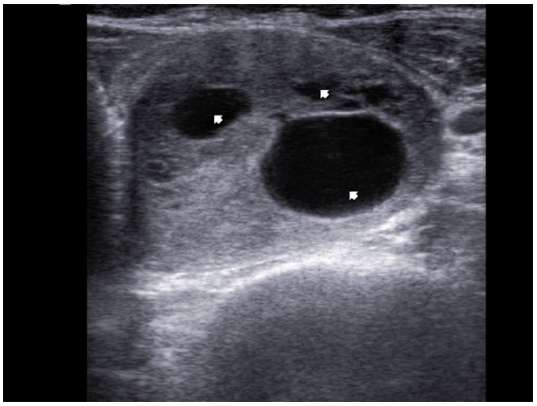

Figure 1. Ultrasonogram shows a large cystic hypoechoic parathyroid adenoma.

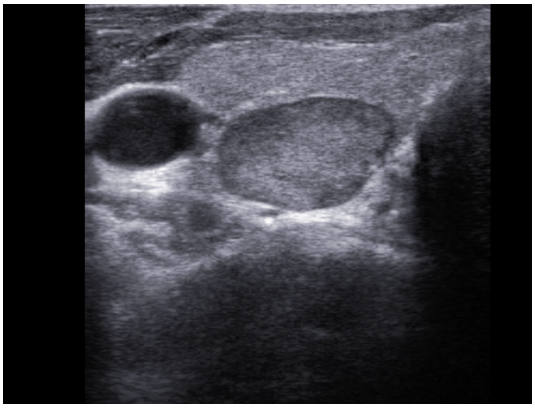

Figure 2. Ultrasonogram shows a hypoechoic solid parathyroid adenoma.

tive studies remains a problem. Investigating the effective factors on the results of the MIBI scan and predictors of a false negative study might contribute to improvement of the sensitivity of test as well as better interpretation of the inconclusive results [8, 9].

The aim of the present study was to find the diagnostic capacity of the MIBI scan in PHPT patients with solitary adenoma, determine the sensitivity of the modality and compare the characteristics of the patients with true positive and false negative scan results.

Material and method

This cross sectional study was carried out from June 2008 to June 2013. Consecutive patients already diagnosed with primary hyperparathyroidism (PHPT) who had positive ultrasonographic findings for PHPT due to single adenomas were included in the study. Patients underwent 99m-Tc MIBI scans prior to parathyroidectomy with traditional unilateral neck dissection. We prospectively evaluated the imaging data of these patients and compared them to postoperative histopathology results as the gold-standard method for determining the diagnostic accuracy of these imaging modalities in the diagnosis of parathyroid adenoma. The patients' sex, age, and serum intact parathyroid hormone (iPTH) were collected from their records. The university review board approved the study.

A single radiologist with six years' experience performed all of the US examinations with an ultrasound device (Toshiba Nemio 30; Toshiba CO. Ltd., Tokyo, Japan), using a high-frequency (11 MHz) linear array transducer. The patients' hyperextended necks were examined in a supine position from the level of the mandibular angle to the sternal notch. All of the US examinations were performed before the results of the 99m-Tc MIBI scan.

In grayscale sonography, enlarged parathyroid glands appear as round or oval-shaped homogenous hypo-echoic nodules in the posterior part of the thyroid lobes, and are clearly separated from the thyroid lobes by an echogenic ring composed of capsules of adenoma and surrounding fatty tissue. The nodules with this sonographic appearance were considered to be parathyroid adenomas. Parathyroid adenomas were divided to two groups of parathyroid adenoma with cystic component (**Figure 1**) and solid parathyroid adenoma (**Figure 2**) based on sonographic results. The parathyroid gland volume was measured. Images were obtained in both transverse and sagittal views.

In 99m-Tc MIBI scintigraphy, the thyroid images were acquired from an antero-posterior view of the neck and upper part of the thorax over five minutes, using a gamma camera 20 minutes after the intravenous administration of 99m-Tc pertechnetate (20 mCi). The images were obtained with patients in a supine position. The parathyroid scan was acquired 15 minutes (thyroid phase) and 120 minutes (parathyroid phase) after intravenous administration of 15-20 mCi of 99m-TcMIBI. The images were obtained with a single-head gamma camera (ADAK, Epic, Netherlands) over 10 minutes, using a pinhole collimator. The MIBI scan was considered to be positive for parathyroid lesions when an increase in uptake was detected in the thyroid phase.

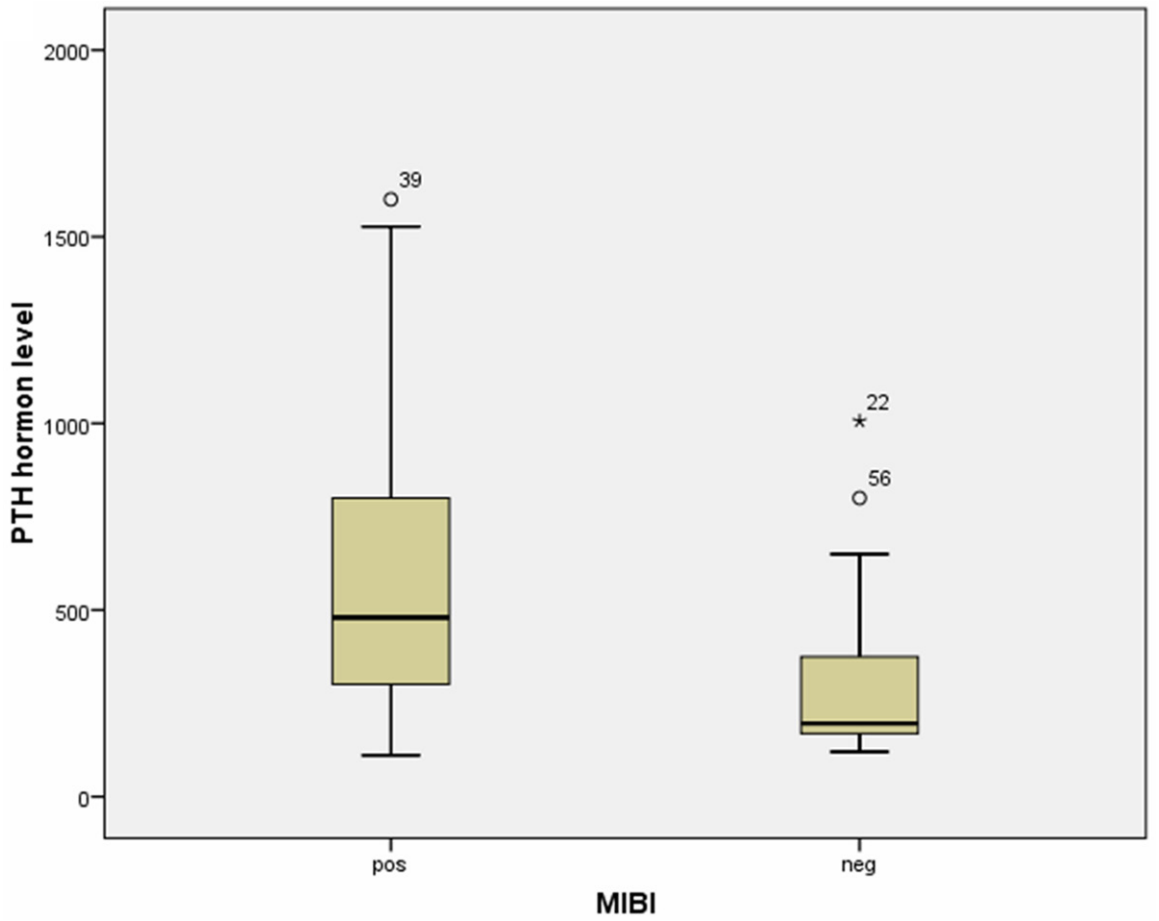

Figure 3. Higher levels of serum PTH level are significantly related with positive MIBI scan.

The 99m-Tc MIBI single-photon emission computed tomography (SPECT) was performed 20-30 minutes after IV injection, and reconstructed to produce three-dimensional projections. The SPECT was performed in a full anterior (180-degree) view as 32 frames, at 30 seconds per frame. Focal increased uptake in the parathyroid site was considered positive. Our nuclear physician specialist was blinded to the results of ultrasound examination.

Statistical analysis was performed using SPSS software version 20. Data are presented as percentages and mean ± standard deviation. Effect of variables on the results of MIBI scan was studied using chi square and independent t test. A p value <0.05 is considered statistically significant.

Results

A total of 70 cases of primary hyperparathyroidism with single adenoma in ultrasonography were studied. Mean age was 47.76 ± 11.80 (range: 21-72) and 87.1% (n = 61) were female. Of the 70 adenomas, 27.1% (n = 19) had a cystic component in the ultrasonography. Mean PTH level was 508.01 ± 360.47 pg/mL (range: 111-1600). Mean volume of the parathyroid gland according to sonography was 1.94 ± 1.52 cc (range: 0.20-7.50).

MIBI scan was truly positive in 70% (n = 49) of the cases and falsely negative in 30% (n = 21). Sensitivity of MIBI scan was 70%. Scan positive patients had mean age of 47.51 ± 11.43 years (43 women, 6 men) while in scan negative patients mean age was 48.33 ± 12.89 years (18 women, 3 men). The differences in age and gender were not statistically significant.

Mean PTH level was 588.86 ± 372.95 pg/mL in positive MIBI scans compared with 319.38 ± 247.19 pg/mL in negative scans. Independent t test showed that serum level of PTH was significantly related with MIBI scan results (P = 0.001;

Figure 3). A serum PTH level greater than 510 pg/mL correlated with positive scans in 85.8 percent as opposed to 59.5% in those with lower levels. Mean serum PTH level in solid adenomas was significantly higher than cystic adenomas (555.35 ± 393.91 pg/mL vs. 380.95 ± 209.05 pg/mL).

Mean volume of the gland in scan positive and negative patients was not different significantly (2.08 ± 1.58 cc vs. 1.61 ± 1.33 cc, respectively). Sensitivity of the MIBI scan did not differ significantly in adenomas with and without cystic components. Solid adenomas were significantly more common among patients with older age (independent t test, P = 0.004). Mean volume of adenomas with cystic component was significantly higher than solid adenomas (2.65 ± 1.03 cc vs. 1.68 ± 1.59 cc; P = 0.004).

Discussion

We studied the diagnostic value of MIBI scan in a total of 70 PHPT patients with single adenoma indicated for parathyroidectomy surgery and investigated the predictors of a true positive scan. In our study MIBI scan had a sensitivity of 70% which is comparable to the sensitivities reported in previous studies. In all the 21 patients with falsely negative MIBI scans, ultrasound was positive. This finding is in consistent with a previous study by Untch et al. that concluded ultrasound by an expert performer can be superior to MIBI scan [10] and also support the previous studies that in cases with inconclusive radionucleotide studies, adding a second modality (mainly sono) can be of value and increase the sensitivity and positive predictive value of the preoperative localization imaging [4, 11-13].

It has been mentioned that while US and sestamibi scanning have comparable sensitivities in detecting abnormal parathyroid adenomas, adding ultrasonography is of particular value in patients with thyroid abnormalities, secondary hyperparathyroidism and the adenomas in which parathyroid scintigraphy is negative because of their prevalent cystic components (n = 19 cases in our study) [5, 8, 14]. Although the difference was not statistically significant, of the total 70 adenomas in our study, MIBI scan was positive in 38 of the 51 solid adenomas compared with 11 of the 19 cystic adenomas. It must be considered that mean PTH level in solid adenomas was significantly higher than adenomas with cystic components (P = 0.020).

According to our results, higher levels of PTH were significantly related with a true positive scan (P = 0.001). Mean PTH level in patients with true positive scan was 588.86 ± 372.95 pg/mL and 319.38 ± 247.19 pg/mL with false negative scans. Thus there was a correlation between the sensitivity of the MIBI scan and the level of preoperative PTH level. Meanwhile, none of the other studied factors such as volume of the gland, age and gender of the patients and having cystic component in the adenoma were related with MIBI scan results. Literature review demonstrated controversial results on the impact of patient and gland related factors such as age, gender, serum PTH, Ca and P levels, weight and volume of the gland on the sensitivity of preoperative MIBI scan in PHPT.

Consistent with our findings, Parikshak et al. [15] concluded that lower preoperative PTH and calcium levels correlated with decreased sensitivity of the MIBI scan. In their study, mean PTH level was found 158 pg/mL among the 74 patients as opposed to mean PTH level of 508.01 ± 360.47 among our 70 patients. Similarly, Siegel et al. [16] reported a correlation between the sensitivity of parathyroid scintigraphy and presurgical PTH. In their retrospective review of 83 scans, the mean PTH in patients with true-positive scans was 367 pg/mL (range, 46-3231 pg/mL) and with false-positive and false-negative scans was 148 pg/mL (range, 46-390 pg/mL). In our 70 patients, mean PTH level was found 588.86 ± 372.95 pg/mL and 319.38 ± 247.19 pg/mL in patients with true positive and false negative scans, respectively.

Moreover, Westerdahl and Bergenfelz [17] showed that high glandular weight and high level of serum PTH were important factors for detectability of the single adenoma in the MIBI scan. Goldstein et al. [18] reported that in general gland weight and serum PTH were the two factors related to the probability of a positive MIBI scan. They found that the relation between higher PTH level and a positive MIBI scan is significantly stronger among female patients than male patients. In our study gender was not effective neither on serum PTH level nor MIBI scan results.

In contrast, Vassy et al. [9] reviewed charts of 37 PHPT patients and found that neither calcium nor PTH correlated significantly with sestamibi scan score. They also concluded that only true positive scan can predict the ability of completing a minimally invasive parathyroidectomy while preoperative PTH or calcium doesn't have an effective relation. Similarly, Cermik et al. [19] found no significant correlation between MIBI uptake ratios and increased preoperative i-PTH and serum Ca levels as well as gland volume. We also found no significant relation between volume of the gland with MIBI scan results, although adenomas with cystic component in our study had significantly higher volumes in comparison to solid adenomas ($P = 0.004$).

With the increasing number of patients with primary Hyperparathyroidism indicated for minimally invasive surgery, accurate preoperative localization with non-invasive imaging techniques such as US and MIBI scan becomes a more important issue. Selecting the correct population of the patients for each imaging protocol and understanding the limitations and effective factors in each modality contribute to optimized preoperative localization of the adenomas and thus higher success rates of minimally invasive surgery. Although our results might be limited due to small study population and the retrospective nature of the study, they still emphasize the importance of preoperative serum PTH level in predicting the results of the MIBI scan and the value of combining US in patients with negative scan particularly in adenomas with cystic components. Further large cohorts are needed for a definite consensus on the effective factors on the MIBI scan results.

Disclosure of conflict of interest

The authors report no conflicts of interest.

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