Combined Tc-99m sesta MIBI scintigraphy and Ultrasonography in preoperative detection and localization of parathyroid adenoma

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Abstract Purpose: To evaluate the role of combined high resolution ultrasonography and technetium Tc-99m methoxyisobutylisonitrile (MIBI) parathyroid scintigraphy in preoperative detection and localization of parathyroid adenoma, for better operative outcome.

Patients and methods: 40 patients were included in this study, 25 of them were females and 15 were males, with age ranging between 31 and 75 (mean 46 ± 15). All patients presented with some of symptoms of hyperparathyroidism with venous blood sampling showed elevated parathyroid hormone (PTH). Parathyroid imaging was evaluated by ultrasonography, double phase Tc-99m MIBI parathyroid scintigraphy with surgical findings and results of clinical follow-up as a reference standard.

Results: Among the 40 patients, Ultrasonography correctly identified 35 adenomas (87.5%) and MIBI scintigraphy identified 34 adenomas (85%), but when both modalities were applied together, 37 adenomas were correctly detected (92.5%).

Minimally invasive parathyroidectomy under local anesthesia with unilateral incision was successfully performed in 34 (85%) patients.

Conclusions: Accurate localization of adenomas should be obtained prior to surgery for minimal invasive surgical procedure. In this study, combined ultrasonography and Tc-99m MIBI improved localization of parathyroid adenomas.

1. Introduction

Hyperparathyroidism is a term used to describe the consequences of excessive secretion of parathyroid hormone (PTH), either due to primary disease of the parathyroid gland or secondary to renal disease.

Primary hyperparathyroidism is usually caused by a single parathyroid adenoma. Occasionally there may be multiple adenomas. Malignant transformation can also occur (1).

Primary hyperparathyroidism, whether caused by an adenoma or hyperplasia, can be cured surgically with a high rate of success. When performed by experienced surgeons,
traditional surgical therapy bilateral four gland exploration is successful in more than 95% of cases. The development of unilateral and focused surgical approaches over the past decade, however, has made it even more imperative for imaging to accurately locate abnormal parathyroid glands before surgery. With optimized preoperative mapping, the success rate of these less invasive techniques equals that of the traditional bilateral approach (2).

A variety of imaging techniques have been used in the past to provide pre-surgical localization for parathyroid surgery. Currently favored approaches use Ultrasound and technetium 99m sestamibi (3).

The two techniques are complementary. The nuclear scan offers functional information, whereas ultrasound shows more detailed anatomic information (4).

The purpose of this study, which was performed in Ain Shams University Specialized hospital, Egypt, is to assess the accuracy of complementary Ultrasonography and Sestamibi parathyroid scintigraphy for better localization of parathyroid adenomas.

2. Patients and methods

2.1. Patient selection

40 patients were selected, between February 2013 and March 2014, after exclusion of 6 patients because of nonaccessibility of follow-up of their operative results. All patients were selected as having primary hyperparathyroidism and presented with some of the symptoms of hypercalcemia, as bone pains, fractures or brown tumors of bones, and renal calculi.

Venous blood samplings were done for serum parathyroid hormone (PTH), calcium (Ca), and phosphorous (P) measurement. And Hyperparathyroidism was confirmed by documenting elevated Ca and PTH levels.

All patients were subjected to Ultrasonography and double-phase Tc-99m MIBI parathyroid scintigraphy.

2.2. Imaging protocols

Patients were examined with US and Tc-99m MIBI parathyroid scintigraphy to detect parathyroid adenoma.

(a) US technique:
The patient was scanned in supine position with a pillow beneath the shoulders to slightly hyperextend the neck. Gray-scale imaging was done to the thyroid and parathyroid gland by an expert radiologist using GE LOGIC 500 PRO series and a multifrequency 6–14 MHz high-frequency linear transducer. The parathyroid adenoma was imaged regarding the size and volume which were also recorded. Gray-scale imaging was supplemented by color and power Doppler to study lesion vascularity.

(b) Tc-99m Sestamibi scan technique:
All patients underwent parathyroid sestamibi scan after intravenous administration of 15 mCi of Tc-99m MIBI. Anterior planar images of the neck were obtained at 15 min (early) and 2 h (delayed) after the injection using a large field of view gamma camera with pinhole collimator.

An anterior planar image of the neck and anterior chest to the level of the diaphragm was also obtained using high-resolution parallel-hole collimator attached to the same gamma camera. Oblique images were obtained for the optimal visualization of posterior parathyroid glands.

2.3. Image interpretation

All data were interpreted by two experienced radiologists.

As regards Ultrasnonography, the adenoma was described regarding its site, size, echo-texture and vascularity.

Regarding Tc-99m MIBI, early and delayed MIBI images were evaluated. Foci of activity were considered positive if they were increased relative to thyroid tissue.

The abnormal parathyroid glands were localized to one of four quadrants in relation to the thyroid gland.

3. Results

40 patients were subjected to this study, 25 of which were females (62.5%) and 15 were males (37.5%), with age range between 31 and 75 years (mean age 46 ± 15).

The sizes of adenomas varied dimensionally from 0.7 × 0.8 × 0.8 cm to 3.5 × 2.7 × 2.5 cm, whereas the volume ranged from 0.448 g to 23.6 g (mean 1.7 ± 2.8 g). All adenomas were localized to one of the four quadrants of the thyroid gland. No ectopic adenoma was detected in our study.

Among the 40 patients, 40 adenomas were identified (as two patients had hyperplasia with no definite adenoma and two had two adenomas). Ultrasonography correctly identified 35 adenomas (87.5%) and MIBI scintigraphy identified 34 adenomas (85%), but when both modalities were applied together, 37 adenomas were correctly detected (92.5%).

Ultrasonography missed detection of parathyroid adenoma in four cases (10%), one of them was found to have thyroid disease (multinodular goiter), another one proved to be multidrug resistant syndrome, and the other two cases were found to have hyperplasia with no definite adenoma. Ultrasonography also misdiagnosed one case (2.5%) of multinodular goiter with posterior nodule as parathyroid nodule (false positive).

MIBI scintigraphy missed detection of 4 cases (10%), one of them was found to be of small size (less than 5 times the normal gland size) to be correctly detected by MIBI scintigraphy, another one proved to be multidrug resistant syndrome, and the other two were found to be in early hyperplasia stage with no definite adenoma.

P-glycoprotein or multidrug-resistance-associated protein expression may play an important role in false-negative parathyroid scintigraphy results. Parathyroid adenomas that express either P-glycoprotein or the multidrug-resistance-related protein are less likely to accumulate Tc-99m sestamibi (5).

When both modalities were combined, three cases (7.5%) were missed, two of them were found to be hyperplasia with no definite adenomas, and the other third one was proved to be of multidrug resistant syndrome.

The results are summarized in Table 1.
Ultrasonography correctly identified 35 adenomas (87.5%) and MIBI scintigraphy identified 34 adenomas (85%), but when both modalities were applied together, 37 adenomas were correctly detected (92.5%). Ultrasonography was found to have higher sensitivity and specificity values than MIBI scintigraphy; yet, their combination had better results in sensitivity and specificity.

Ectopic parathyroid tissue was not observed in our patients.

Minimally invasive parathyroidectomy under local anesthesia with unilateral incision was successfully performed in 34 patients that had adenoma and postoperative histopathologic examination confirmed intrathyroidal parathyroid adenoma.

4. Illustrated cases

See Figs. 1–3.

5. Discussion

Without imaging, bilateral cervical exploration is curative in 92–95% of patients who undergo surgery for PHPT, as shown by older studies done before modern imaging was available. Indeed, an experienced surgeon can identify most pathologic glands (3).

In agreement with recommendations, we think that preoperative imaging should always be performed. Good imaging should be effective, provide morphologic and functional information, noninvasive, and not to be too expensive. These conditions can be fulfilled by combining cervical ultrasound and scintigraphy.

In our study, it was shown that the most successful technique is US to detect the parathyroid adenoma. US has 94.6% sensitivity, while the combined use of US and scintigraphy has 97.3% sensitivity. Once the parathyroid adenoma was detected, the other side of parathyroid gland must be evaluated carefully for the presence of second adenoma or hyperplasia.

Minimally invasive surgery with unilateral parathyroidectomy was performed to 34 parathyroid adenoma patients, limiting the dissection to the abnormal parathyroid gland, and therefore, the operative time is significantly reduced.

The common treatment of primary hyperparathyroidism is conventional neck exploration. With this procedure, the neck is explored to identify all parathyroid glands and to remove the enlarged ones. Conventional neck exploration is a time-consuming and surgically demanding procedure because of the many vulnerable structures of the neck that need to be explored to allow identification of the parathyroid glands.

Recently, minimally invasive surgery has been successfully established. During minimally invasive surgery, the surgeon, guided by means of an imaging-based road map, carefully approaches the lesion through a small incision in the skin and removes the lesion with minimal damage to the vulnerable structures of the neck. Advantages of minimally invasive surgery compared with conventional neck exploration include reduction in surgical time and hospital stay, with subsequent reduction in costs.

### Table 1 Positive and negative results by US and MIBI.

<table>
<thead>
<tr>
<th></th>
<th>True positive</th>
<th>True negative</th>
<th>False positive</th>
<th>False negative</th>
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decreased costs, improved cosmetic results, and restriction of postoperative fibrosis to the immediate area of the removed gland, which facilitates repeat surgery in cases of disease recurrence (6).

So in order to confirm the parathyroid adenoma localization and to discriminate other parathyroid gland pathologies (second parathyroid gland adenoma and ectopic parathyroid tissue), we performed both imaging modalities.

Histopathological examination of the excised nodules was done and confirmed parathyroid adenoma.

In clinical follow-up after surgery, the biochemical parameters of patients were improved except for one patient in whom adenoma was bilateral.

In our study, we found that US had 97.2% sensitivity and scintigraphy had 92% sensitivity alone, but their combination had a sensitivity of 100%. This was found to be higher results than other studies as we conceited only on primary hyperparathyroid nodule, and exclude all secondary causes or ectopic parathyroid glands. In addition, small percentage of hyperplasia cases were included in our study.

A study done by Cakal et al. (7) proved that US has 89.7% sensitivity, scintigraphy had 71.8% alone, and their combined use had a sensitivity of 92.3%.

Tublin et al. (8) have found that the sensitivity and positive predictive value of sonography for identifying abnormal parathyroid glands were 74% and 90%, respectively.

Sukan et al. (9) have compared the efficacy of scintigraphy and US imaging in hyperparathyroidism. They evaluated 69 patients with primary and secondary hyperparathyroidism. The overall specificity of MIBI and US was found to be 87% and 91% respectively.

The study done by Marie et al. (10) on 49 patients revealed that ultrasonography had 67% sensitivity and 94% specificity, while MIBI scintigraphy had 71% sensitivity and 89% specificity.
specificity, but their combination resulted in 96% sensitivity and 83% specificity. They explained their lower results percentage by high percentage of hyperplastic nodules (approximately 80%) that often were not detected due to their small dimensions and to morphologic characteristics that were similar to those of normal parathyroid glands and thyroid tissue.

In our study, US missed parathyroid adenoma in 7.5 % of cases due to concomitant multinodular goiter.

In the study by Cakal et al. (7), US significantly missed parathyroid adenoma in 25% patients with thyroid disorder. Tresoldi et al. (11) evaluated 64 patients with primary hyperparathyroidism. Seventy-four enlarged glands in 64 patients were identified at US. Per-patient sensitivity and positive predictive values, respectively, were 84% (64/76) and 99% (64/65) for US, 68% (44/65) and 100% (44/44) for scintigraphy, and 91% (59/65) and 98% (59/60) for both techniques combined.

Concomitant thyroid disease also contributes to imaging pitfalls. Enlarged multinodular thyroid glands can limit the sonographic evaluation of parathyroid adenomas (12).

Minimally invasive surgery for parathyroid adenomas has been developed and has equal success with traditional surgery; however, there is a need for accurate localization of adenomas.

In this study, preoperative approach that combines both the anatomic information of sonography and the physiologic information of scintigraphy has been shown to predict the presence and precise location of adenomas more accurately than either technique alone.

6. Conclusion

Accurate localization of adenomas should be obtained prior to surgery for minimal invasive surgical procedure. In this study, combined ultrasonography and Tc-99m MIBI improved localization of parathyroid adenomas.

US remains the most sensitive approach for the detection of parathyroid adenomas, especially those of smaller size.

Conflict of interest

We have no conflict of interest to declare.

References