Comparison Of Sestamibi Scintigraphy And Ultrasonography In Preoperative Localization Of Primary Hyperparathyroidism

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Abstract

Aims

To determine the utility of ultrasonography for the preoperative localization of enlarged parathyroid glands in primary hyperparathyroidism, and to compare this method with 99m technetium sestamibi scintigraphy.

Patients and Methods

The results of ultrasonography for localization of enlarged parathyroid glands were determined in 80 consecutive patients with primary hyperparathyroidism and compared with findings at surgery and with the results of 99m technetium sestamibi scintigraphy.

Results

Ultrasonography predicted surgical findings in 61 of 80 patients (76.1%), including 59 of 76 patients with solitary parathyroid adenomas (77.6%) with a sensitivity of 83.5 % and a positive predictive value (PPV) of 89.7%. Sestamibi scintigraphy findings were correlated with surgical findings in 63 (78.8%) patients including 62 of 76 patients with solitary eutopic parathyroid adenomas (81.5%), with a sensitivity of 85 % and a PPV of 91.3%.

Conclusion

Sensitivity and positive predictive values of ultrasonography are not significantly different from values of sestamibi scintigraphy in localization of pathologic parathyroid glands in primary hyperparathyroidism.

INTRODUCTION

The incidence of primary hyperparathyroidism (PHPT) is increasing, with an incidence of 42/100000 per year, while in women over 60 years of age, the average annual incidence rate approaches 190/100000 per year [1]. A certain number of these patients require surgical treatment. For many years, preoperative localization studies in primary neck explorations for PHPT have been regarded as unnecessary by many experienced endocrine surgeons, because, in their hands, bilateral neck exploration results in success rates exceeding 95% with only minimal morbidity [2,3]. However, others have advocated the use of routine preoperative localization, arguing that not all surgeons have the full experience for accurate surgical exploration, it can result in a shorter operation time, avoid the need for bilateral neck exploration and identify rare patients with ectopic parathyroid adenomas [4].

The aim of this study was to evaluate sensitivity, positive predictive value (PPV) and usefulness of high resolution neck ultrasonography (US) and ^{99m}Tc-sestamibi scintigraphy (SS) as preoperative noninvasive localization procedures in patients with PHPT undergoing parathyroidectomy.

PATIENTS AND METHODS

All patients undergoing neck exploration with a diagnosis of hyperparathyroidism between September 2005 and September 2007 were included in this study. Patients undergoing re-exploration for recurrent or persistent PHPT were excluded. We recorded each patient's age, preoperative serum calcium level, preoperative intact parathyroid hormone (PTH) level, preoperative localization findings in US and SS, surgical findings, localization and parathyroid adenoma weight. We also recorded 24-hours postoperative serum calcium levels. In cases with multiple laboratory

serum determinations, the most recent values were used for analysis. All patients were studied with a single experienced radiologist and operated on by a single experienced surgeon with exploration of all parathyroid glands.

PARATHYROID SCINTIGRAPHY

Dual phase SS was performed with a small-field-of-view gamma camera (209 apex ELSCINT; general electric; Milwaukee, WI) with a pinhole collimator. Ten planar anteroposterior images (dynamic acquisition, Matrix 128*128) were obtained immediately after intravenous injection of 555 μBq ^{99m} Tc-methoxyisobutylisonitrile and sestamibi (early phase) and 2 hours later (late phase). A static image was taken of the thorax and mediastinum (300 seconds, Matrix 128*128, parallel collimator) to search for ectopic glands.

ULTRASONOGRAPHY

Sonographies were performed by a single experienced radiologist with a EUB-525 scanner (Hitachi-Japan) with a 7.5 MHz linear-array transducer. Images were obtained from the angle of the mandible to the sternal notch. An enlarged parathyroid gland on grey-scale imaging appeared as a hypoechoic or isoechoic (in few cases) nodule posterior or lateral to the thyroid lobe, but separated from it and not adherent to surrounding tissues, or within the thyroid parenchyma.

ANALYSIS

Results of imaging studies as determined from the official radiology report were compared with operative findings. Correct localization or a true positive (TP) result was the identification of an abnormal parathyroid gland during surgery on the same location as reported by the imaging study.

Abnormal parathyroid glands that were not identified by imaging technique were considered false negative (FN). Abnormalities reported by imaging that did not correspond to an abnormal parathyroid gland were considered false positive (FP). Sensitivity was calculated as TP/(TP+FN) and positive predictive value was calculated as TP/(TP+FP).

We also determined the sensitivity for combined results considering ultrasound and sestamibi as a single test. In this analysis, the results considered as “TP” if either of the studies correctly localized the abnormal gland. Abnormal parathyroid glands not imaged by either technique were recorded as FN, and all imaged abnormalities that did not correspond to abnormal parathyroid glands for both tests were recorded as FP. The TNs were not recorded in this analysis because of ambiguity of the definition.

All reported data are expressed as mean ± SD and comparisons between different groups were performed using Student's t-test, Fisher's exact test and chi-square test where appropriate. A p-value of less than 0.05 was considered statistically significant.

RESULTS

There were 80 patients with primary hyperparathyroidism who underwent US and SS examination for enlarged and overactive parathyroid glands, including 66 women and 14 men. Mean age ±SD was 47 ± 1.6.

Mean values (±SD) for recent biochemical tests prior to surgery were: serum calcium 11.3±1.4 mg/dl (range 10-17) and serum intact PTH 451.6±378.8 ng/L (range 70-2028).

Histopathologic findings included 76 (95%) eutopic solitary adenoma, one (1.3%) ectopic adenoma (mediastinal), one (1.3%) double adenoma. Moreover, 2 (2.5%) patients had diffuse parathyroid hyperplasia. The mean size of removed parathyroid glands was 14.8±0.88 mm (range 4-41 mm). The mean weight of removed glands was 2.6±2.2 g (range 0.4-15 g).The diagnostic accuracy values of SS, US and SS plus US are shown in Table 1.

Figure 1

Table 1: Comparison between US and SS in 80 patients with primary hyperparathyroidism.

Method	Number(%) of positive results	TP	FP	FN	PPV	Sensitivity
US	68(85%)	61(76.3%)	7(8.75%)	12(15%)	89.7%	83.5%
SS	69(86.25%)	63(78.8%)	6(7.5%)	11(13.75%)	91.3%	85%
Combination of US and SS	78(97.5%)	73(91.3%)	5(6.25%)	2(2.5%)	93.5%	97.3%

TP: True Positive; FP: False Positive; FN: False Negative; PPV: Positive Predictive Value; SS: Scintigraphy Scan; US: Ultrasonography

SS was positive in 86.25% of patients and accurately localized the pathology in 78.8% according to surgery, including 62 of 76 patients with solitary eutopic parathyroid adenomas (81.5%), the patient with ectopic (mediastinal) adenoma and none of the patients with hyperplasia and double adenoma. SS had a false positive rate of 7.5%, false negative rate of 13.75%, sensitivity of 85 % and PPV of 91.3%.

US was positive in 85% of patients which localized the

pathology in 76.1% preoperatively according to surgery, including 59 of 76 patients with solitary eutopic parathyroid adenomas (77.6%), one of two patients with hyperplasia, the only patient with double adenoma and not the patient with ectopic (mediastinal) adenoma. US had a false positive rate of 8.75%, false negative rate of 15%, sensitivity of 83.5% and PPV of 89.7%.

If we use US and SS only to specify the side (left or right) of the pathology, their sensitivity and positive predictive values will be 84.6% and 97% vs. 87% and 97.1%, respectively.

Combination of the two techniques yielded a sensitivity of 97.3% and PPV of 93.5%. There was a statistically significant difference between the diagnostic accuracies of US, SS and US plus SS as shown via comparison between two proportions version 8. The combination of SS and US enhanced sensitivity compared with either technique alone.

In order to determine which factors may interfere in accuracy of US and SS, we compared preoperative serum calcium level, serum intact PTH level and parathyroid adenoma weight between correctly localized vs. undetected patients by US and SS examinations. According to US results, no significant differences could be found in the above factors between the two groups with negative and positive sonogram (table 2), whereas there was a significant difference in the mean intact preoperative PTH level of correctly localized vs. undetected patients by SS (506.6 ± 382.8 vs. 247.6 ± 290.5, p-value = 0.01). Differences in other parameters between the two groups with negative and positive scintigraphy were not statistically significant (table 3).

At last, in all of the patients, cure from the hyperparathyroidism state has been achieved and they remained normocalcemic in postoperative follow-up.

Figure 2

Table 2: Serum calcium, serum parathyroid hormone, and weight of parathyroid adenomas in patients with primary hyperparathyroidism according to results of ultrasonographic localization

Parameter	Sonogram negative	Sonogram positive	*P*
Serum calcium (mg/dl)	11.6±2	11.1±1.1	N/S
Serum PTH (ng/L)	363.9 ±276.4	480.8±405	N/S
Weight of adenomas (g)	1.9 ±1.3	2.8 ±2.4	N/S

Data shown are means ± SD. N/S: P >0.05 by Student's t-test

Figure 3

Table 3: Serum calcium, serum parathyroid hormone, and weight of parathyroid adenomas in patients with primary hyperparathyroidism according to results of scintigraphic localization

Parameter	Scintigram negative	Scintigram positive	*P*
Serum calcium (mg/dl)	11.6±2	11.1±1.1	N/S
Serum PTH (ng/L)	247.6 ±290.5	506.6±382.8	0.01
Weight of adenomas (g)	2.4 ±2.2	2.7 ±2.2	N/S

Data shown are means ± SD. N/S: P >0·05 by Student's t-test

DISCUSSION

This large study of 80 unselected patients, confirms the validity of US for the preoperative localization of parathyroid adenomas in patients with PHPT. Ultrasonography provided positive imaging results in 85% of these patients and the reliability of positive ultrasonographic imaging was high with an 89.7% positive predictive value based on correlation with surgical findings. Overall, US correctly predicted the surgical findings in 76.3% of patients with enlarged parathyroid glands found at surgery. The sensitivity of US was 83.5% in this study. The ability of ultrasonography to correctly localize enlarged parathyroid glands in primary hyperparathyroidism ranges from 44-87% [5,6,7] in the literature, with the most recent series reporting a sensitivity of 67-87% in patients without prior parathyroid surgery [5,6,8] . Previously reported positive predictive values of 89-97% [5,6,8] are also similar to the present results. It is likely that the reported accuracy of US for preoperative localization of enlarged parathyroid glands is highly dependent on the skill and experience of the examiner [5] .

In order to determine whether patients with more severe hypercalcemia, higher PTH levels and larger abnormal parathyroid glands might be more likely to have positive tests, we compared the parameters in patients localized and not localized with US and SS examinations.

Only the mean intact preoperative PTH level was significantly different in correctly localized vs. undetected patients (by SS), other factors were not statistically significant between these two groups.

Different techniques were used in performing parathyroid scintigraphy with ^{99m}Tc-Sestamibi alone [9,10] and ^{99m}Tc-Sestamibi in conjunction with ^{123}I or Pertechnetate, with similar results [11,12] . In this study, we compared dual phase parathyroid scintigraphy with ultrasonography. The present

study confirms the utility of SS; that was positive in 86.25% and correctly predicted the surgical findings in 78.8% of patients with PHPT, which was not significantly higher than the corresponding value for US, that was positive in 85% of patients and predicted the surgical findings in 76.3%.

The sensitivity and positive predictive value for the two methods were similar for US and SS based on correlation with surgical findings (83.5% and 89.7% vs. 85% and 91.3%).

Among previous reports that have directly compared US and SS in patients undergoing initial parathyroid surgery, Mazzeo et al. (1996) [13] and De feo et al. (2000) [6] reported that the two methods were similar in their ability to correctly predict the surgical findings, while Casas et al. (1993) [14] and Lumachi et al. (2000) [1] found that SS imaging was superior. In a large study including US in 449 patients and SS in 700 patients, Cha Puis et al. (1996) [15] found that US provided better results.

Taken together with the present series, it would appear that there is little overall difference in the ability of US and SS to correctly localize abnormal glands in patients without prior surgery for PHPT.

CONCLUSION

Our data shows that sensitivity and positive predictive values of ultrasonography are not significantly different from sensitivity and positive predictive values of sestamibi scintigraphy in localization of pathologic parathyroid glands in patients with primary hyperparathyroidism.

This study shows that combination of SS and US enhances sensitivity and positive predictive value compared with either technique used alone. This is consistent with previous reports that combined testing with two methods provides superior sensitivity to one of the methods alone [1,6,16].

These two methods can be complementary because SS provides functional information about nodules whereas US yields anatomic details [17]. Unlike US, SS can visualize adenomas inferior to the thyroid in sonographically silent regions [18].

Because surgical removal of adenomas is the only safe and final treatment of PHPT, both techniques give directions to the surgeon and may reduce operating stress and duration.

We suggest using US first and reserve SS for negative US findings. If the surgeon wants to do unilateral neck exploration or minimally invasive surgery, both US and SS are recommended.

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