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Tc-99m Sestamibi Accuracy in Detecting Parathyroid Tissue Is Increased When Combined With Preoperative Laboratory Values: A Retrospective Study in 453 Greek Patients With Chronic Renal Failure Who Underwent Parathyroidectomy

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ABSTRACT

Purpose. Technetium^{99m} sestamibi (MIBI) has poor sensitivity and specificity when applied to patients with secondary hyperparathyroidism. We investigated whether the combination of MIBI with preoperative parameters increased its accuracy.

Patients and Methods. This prospective study of 453 consecutive patients with secondary hyperparathyroidism who underwent parathyroidectomy (bilateral neck exploration) included preoperative MIBI scintigraphy compared with intraoperative and histopathology findings. Four patient groups were comprised according to the results: true positivity (TP), true negativity (TN), false positivity (FP), and false negativity (FN).

Results. MIBI scintigraphy sensitivity, specificity, positive predictive value, and negative predictive value were 66.4%, 50%, 76.3%, and 37.9%, respectively. For the TP group, mean age and mean parathormone (PTH) value were 56 years and 754, respectively. The binary logistic regression for the prediction (1) or not (2) of TP was as follows: 0.138 + (−.011) * age + 0.001 * PTH (P = .012). For the TN group, the mean age and mean phosphate value were 49 years and 5.24, respectively. The binary logistic regression for the prediction (1) versus not (2) of the TN was as follows: −1.463 + age * (−.029) + phosphate * 0.233 (P = .012).

Conclusion. MIBI accuracy in patients with secondary hyperparathyroidism was increased when combined with other preoperative parameters. The sensitivity was increased as patients were older and the PTH levels were lower. The specificity was increased as patients were younger and the phosphate levels were lower.

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THE ABILITY to preoperatively localize enlarged hyperfunctioning parathyroid glands by Technetium^{99m} sestamibi (MIBI) has been well established in renal disease patients.[1] However, the reported sensitivity of this method is low, ranging from 34% to 66%.[2,3] Therefore, most authors agree that MIBI scintigraphy has limited value in secondary hyperparathyroidism and that bilateral neck exploration remains the gold standard.[4]

Attempts have been made to increase the sensitivity of MIBI scintigraphy by combining it with another imaging modality (mainly neck ultrasound), increasing it to >80%.[3,5] In addition, it is well established that weight and inferior localization of the hyperplastic parathyroid glands are associated with a higher detection rate using scintigraphy.[4]

This report sought to establish an association between simple preoperative parameters and the MIBI scintigraphy readings. This association could become a guide to whether to "trust" the reported preoperative localization of hyperfunctioning glands for patients with secondary hyperparathyroidism.

PATIENTS AND METHODS

The disease leading to 587 parathyroidectomies for secondary hyperparathyroidism was diagnosed clinically using the serum concentrations of calcium, alkaline phosphatase, and parathormone, using skeletal X-ray imaging, and occasionally using bone biopsy. Parathyroid gland preoperative localization imaging included ultrasound, computed tomography (CT) scan, and MIBI most of the time. All patients underwent bilateral cervical exploration with attempted identification of all 4 parathyroid glands, regardless of the results of the imaging studies.

MIBI scintigraphy was performed in 453 patients: 20 mCi, iv, images at 15 and 180 minutes postinjection. MIBI readings were compared with intraoperative and histopathologic findings. A gland was arbitrarily considered hyperplastic if it weighed >75 mg.[6] The scintigraphy readings were called: (1) true positive (TP), if MIBI accurately detected all hyperplastic glands; (2) true negative (TN) if a negative image corresponded to 4 nonhyperplastic glands; (3) false positive (FP) if MIBI detected potential hyperplastic glands opposite from the side that they were actually identified during the cervical exploration; and (4) false negative (FN) if despite a negative image, 1 or more hyperplastic glands were surgically identified.

Four patient groups were comprised according to the scintigraphy results: (1) TP group for true positivity; (2) TN group for true negativity; (3) FP group for false positivity; and (4) FN group for false negativity. We recorded patient age and preoperative parathormone (PTH), calcium, phosphate, and alkaline phosphatase (ALP) values.

Statistical analysis was performed retrospectively, using the SPSS statistical package (version 11.0 for Mac OS X). Quantitative results were expressed as mean values ± SD, unless otherwise stated. Analysis of variance was used for continuous data comparisons; χ^2 test was used for categorical data comparisons. Multivariate binary logistic regression analysis was used for the accurate (value = 1) versus not (value = 2) prediction of TP and TN of the MIBI scintigraphy.

Table 1. Mean Values of Demographic Data and Preoperative Parameters Stratified by MIBI Scintigraphy TP or Not (Upper Half of the Table) and TN or Not (Lower Half of the Table)

Parameter	Group	Mean Value	*P*
TP			
Age	TP	56 ± 14	.005*
	TN + FP + FN	52 ± 14	
Preoperative PTH	TP	754 ± 751	.005*
	TN + FP + FN	1098 ± 696	
Preoperative calcium	TP	9.42 ± 1.43	.478
	TN + FP + FN	9.55 ± 1.57	
Preoperative phosphate	TP	6.19 ± 2.01	.284
	TN + FP + FN	5.84 ± 2.01	
Preoperative ALP	TP	188 ± 102	.057
	TN + FP + FN	245 ± 200	
TN			
Age	TN	49 ± 13	.002*
	TP + FP + FN	55 ± 14	
Preoperative PTH	TN	694 ± 614	.138
	TP + FP + FN	970 ± 752	
Preoperative calcium	TN	9.45 ± 1.27	.848
	TP + FP + FN	9.50 ± 1.55	
Preoperative phosphate	TN	5.24 ± 2.23	.020*
	TP + FP + FN	6.19 ± 1.92	
Preoperative ALP	TN	179 ± 110	.198
	TP + FP + FN	227 ± 171	

*Statistically significant.

RESULTS

The median age for the 453 patients was 55 years (range, 18–85). Two hundred thirty-four subjects (51.7%) were females. Mean PTH, calcium, phosphate, and ALP values were 936 ± 740 IU/mL, 9.49 ± 1.5 mg/dL, 6.01 ± 2.01 mg/dL, and 217 ± 161 IU/mL, respectively.

Based on MIBI readings, 213 (47%), 66 (14.6%), 66 (14.6%), and 108 (23.8%) patients were allocated to TP, TN, FP, and FN groups, respectively. Based on these values, the scintigraphy sensitivity, specificity, positive, and negative predictive value were 66.4%, 50%, 76.3%, and 37.9%, respectively.

For the TP group, the mean age, PTH, calcium, phosphate, and ALP values were 56 ± 14 years, 754 ± 751 IU/mL, 9.42 ± 1.43 mg/dL, 6.19 ± 2.01 mg/dL, and 188 ± 102 IU/mL, respectively. For the other 3 groups combined (ie, TN + FP + FN), the mean age, PTH, calcium, phosphate, and ALP values were 52 ± 14 years, 1098 ± 696 IU/mL, 9.55 ± 1.57 mg/dL, 5.84 ± 2.01 mg/dL, and 245 ± 200 IU/mL, respectively. Statistical significance of differences between these 2 cohorts (ie, TP vs TN + FP + FN) was observed only for age ($P = .005$) and PTH ($P = .005$) values (Table 1). Based on these results, a multivariate binary logistic regression analysis was constructed for the accurate (value = 1) or not (value = 2) prediction of TP of the MIBI scintigraphy ($P = .012$). The equation is as follows:

$$\text{Predictive binary value of TP} = 0.138 + (-0.011) * \text{age} + 0.001 * \text{PTH}$$

For the TN group, the mean age, PTH, calcium, phosphate, and ALP values were 49 ± 13 years, 694 ± 614 IU/mL, 9.45 ± 1.27 mg/dL, 5.24 ± 2.23 mg/dL, and 179 ± 110 IU/mL, respectively. For the other 3 groups combined (ie, TP + FP + FN), the mean age, PTH, calcium, phosphate, and ALP values were 55 ± 14 years, 970 ± 752 IU/mL, 9.50 ± 1.55 mg/dL, 6.19 ± 1.92 mg/dL, and 227 ± 171 IU/mL, respectively. Between these 2 cohorts (ie, TN vs TP + FP + FN), statistical significance was observed only for age ($P = .002$) and phosphate ($P = .02$) values (Table 1). Based on these results, a multivariate binary logistic regression analysis was constructed for the accurate (value = 1) or not (value = 2) prediction of TN of the MIBI scintigraphy ($P = .012$). The equation is as follows:

$$\text{Predictive binary value of TN} = -1.463 + (0.029) * \text{age} + 0.233 * \text{phosphate}$$

DISCUSSION

The sensitivity and specificity of MIBI scintigraphy for secondary hyperparathyroidism reported in this series of patients is within the range already reported by other authors.[1,3]

This study showed that the older the patient and the lower the PTH level the more likely is a positive MIBI reading to be true, ie, sensitivity is increased. This is counterintuitive because one would think that bigger hyperplastic parathyroid glands, which produce more PTH, would be easier to be detected using scintigraphy. In this series, although subjects with high PTH values showed a positive MIBI reading, this was not the case for all hyperplastic glands in a given patient, leading to a higher false-negative rate (data not shown). It is tempting to assume that patients with long-standing secondary hyperparathyroidism and high PTH values have glands that do not take up the radioactive tracer in a similar way, leading to a higher false-negative rate.

In addition, this study showed that the younger the patient and the lower the phosphate level the more likely is a negative MIBI reading to be true, ie, specificity is increased. This is an expected finding because the younger a patient is and the lower the phosphate level is the more likely is the disease to have been present for fewer years and, therefore, less likely to have hyperplastic parathyroid glands. The high rate of true-negatives reported in this study (14.6%) comes from the fact that the threshold for calling a gland hyperplastic was arbitrarily set at 75 mg. Indeed, if the threshold was set at 50 mg the rate of true-negatives would decrease to 2.9% (data not shown).

In conclusion, preoperative scintigraphy for localization of enlarged glands is of questionable value in patients with secondary hyperparathyroidism because a full neck exploration is required to remove all 4 (or more) of them. However, if the MIBI findings do not correlate with the intraoperative ones and the preoperative parameters described in this study suggest that the scintigraphy results should be trusted, the surgeon should repeat a more thorough exploration before wound closure.

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