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ORIGINAL ARTICLE

Medicine Science International Medical Journal

Medicine Science 2023;12(3):613-7

Does the sonography-scintigraphy correlation affect the success of minimally invasive parathyroid Surgery? Results from a single center

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Received 09 March 2023; Accepted 31 May 2023
Available online 18.08.2023 with doi: 10.5455/medscience.2023.03.032

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Abstract

In patients with primary hyperparathyroidism, complete surgical resection of all hyperfunctioning parathyroid tissue is essential. The aim of this study was to evaluate the success rates of minimally invasive parathyroidectomies for primary hyperparathyroidism performed after localization studies with 99mTc-sestamibi (MIBI) scintigraphy and neck ultrasonography (USG). And also, we aimed to determine the factors affecting the success rate in surgery. Retrospective analysis of 58 consecutive patients with a diagnosis of primary hyperparathyroidism who underwent parathyroidectomy between January 2018 and December 2021 in our institution. The patients were evaluated according to Miami criteria and divided into two groups as successful or unsuccessful surgery. Demographic and clinical characteristics of the patients were obtained from hospital records. Surgical success was achieved in 50 (86.2%) of the 58 patients included in the study. In both groups, neck USG and MIBI scintigraphy showed the same localization for the lesion in a correlated manner. The clinical complaints of the patients, preoperative PTH, Ca and 24-hour urinary Ca levels were similar in both groups. In 10 (17.2%) patients, inconsistency in localization was found between USG and MIBI scintigraphy, and surgical failure was found in 4 (40%) of these patients. Surgical failure was statistically significant in patients with inconsistency in localization between USG and MIBI scintigraphy. The sono-scintigraphic scan concordance increases surgical success rates in cases where minimally invasive parathyroid surgery is planned. If there is an inconsistency between USG and MIBI, preoperative four dimentional computed tomography, intraoperative rapid PTH, gamma probe or frozen method can be used. It should be kept in mind that multiple gland pathologies may be more common in addition to solitary adenoma in lesions smaller than 1 cm in USG. In addition, in these cases, as the diagnostic value of scintigraphy is low, surgical success will also decrease.

Keywords: Primary hyperparathyroidism, minimal invasive parathyroidectomy, tc-99m methoxyisobutylisonitrile scintigraphy, neck ultrasonography

Introduction

Primary hyperparathyroidism (PHPT) is a hormonal disorder characterized by uncontrolled increased secretion of parathormone from the parathyroid glands and elevated serum calcium (Ca) levels [1]. It is more common in women and in the 55-75 age group [2]. The most common cause of PHPT is 80-85% solitary adenomas. Other causes of primary hyperparathyroidism include multiple gland hyperplasia with a frequency of 10-15%, double adenoma in 4-5%, and parathyroid cancer in less than 1% [3].

The main treatment option for primary hyperparathyroidism is surgery [4,5]. The surgical treatment of PHPT was based on surgical dissection of all parathyroid glands with bilateral neck exploration for a long time [1]. However, over time, there have been changes and developments in surgical methods. Minimally invasive parathyroidectomy (MIP) method has started to be applied more frequently in order to have solitary adenoma in approximately 85% of patients with PHPT, to provide complete cure with surgery and to reduce complications. Thus, a smaller incision and a more minimal surgical dissection resulted in a

CITATION
Ozdemir A. Kalcan S. Does the sonography-scintigraphy correlation affect the success of minimally invasive parathyroid Surgery? Results from a single center. Med Science. 2023;12(3):613-7.

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DOI: 10.5455/medscience.2023.03.032

reduction in complication rates such as hypocalcemia and vocal cord paralysis, and a reduction in postoperative pain [5].

The success of the MIP method is largely related to the localization of the diseased parathyroid gland preoperatively. Bi-phase 99mTc-sestamibi (MIBI) scintigraphy consisting of early and late phase images and neck ultrasonography (USG) are the most commonly used imaging techniques for preoperative localization. In many studies, it has been shown that the sensitivity of the localization of the parathyroid glands after the combined use of both methods is at the level of 85-95% [6,7]. USG is an effective imaging method to provide parathyroid localization and also to detect accompanying thyroid problems. However, it is insufficient in obese patients, in multiple gland pathologies, in the presence of previous neck surgery, in patients with large nodular goiter and in ectopic parathyroid pathologies [7,8]. If the parathyroid pathology could not be localized with USG and scintigraphy methods or if there is an incompatibility between these two methods or if unsuccessful surgery has developed, then 4-dimensional computed tomography (4DCT) is very valuable [9].

In our hospital, USG and biphasic 99mTc-sestamibi scintigraphy are used as imaging methods for the localization study of primary hyperparathyroidism. We aimed to determine the success rates of MIPs performed after localization study with 99mTc-sestamibi scintigraphy and USG and to determine the factors affecting unsuccessful surgery.

Material and Methods

Between January 2018 and December 2021, 66 patients who were operated on with the diagnosis of hyperparathyroidism at the Ministry of Health of the Republic of Turkey, Recep Tayyip Erdoğan University Training and Research Hospital, General Surgery Clinic were retrospectively analyzed. Of these patients, 7 were excluded because they were operated on for secondary hyperparathyroidism and 1 for tertiary hyperparathyroidism.

The demographic characteristics of the patients, clinical symptoms, preoperative PTH, Ca, vitamin D levels, neck ultrasonography, 99mTc-sestamibi scintigraphy, accompanying thyroidal diseases that required surgery, and surgical techniques, which are the data of our retrospectively designed study, were obtained from hospital records. In addition, postoperative PTH levels, Ca levels, and pathology results were added to these data.

Miami, Vienna, Halle and Rome criteria were defined to demonstrate the success of surgery performed after parathyroidectomy. The Miami criterion was defined as a PTH value of >50% reduction from the preoperative PTH value performed 5-10 minutes after excision of the lesion. Its sensitivity was 97.6%, and its specificity was 93.3% [10]. In our study, the patients were evaluated according to Miami criteria and divided into two groups as successful surgery or unsuccessful surgery. In this context, surgical success was achieved in 50 (86.2%) of 58 patients included in the study.

Ethical committee

This study was approved by the Recep Tayyip Erdogan University Faculty of Medicine, Non-Invasive Clinical Research Ethics Committee, dated 24.03.2022 and numbered 2022/82.

Statistical analysis

Data were analyzed with IBM SPSS Statistics for Windows (Armonk, NY, USA, IBM Corp.) software. Categorical data were presented with numbers and percentages, and numerical data with mean and standard deviation values. Fisher's Exact Test was used for categorical variables to determine the factors associated with surgical success. The distribution characteristics of continuous variables were determined by Shapiro Wilk and Kolmogorov Smirnov tests, and the relationship of these variables with surgical success was evaluated with the Mann Whitney U test. Statistical significance level was accepted as $p<0.05$ in all analyzes.

Results

TEight patients who were operated for reasons other than PHPT were excluded from the study. Surgical success was achieved in 50 (86.2%) of the 58 patients included in the study. The mean age of the successful surgery group was 55.7±11.1 and the mean age of the unsuccessful surgery group was 58.9±20.5 (Table 1).

39 (86%) patients who underwent successful surgery and 5 (11.4%) patients who underwent unsuccessful surgery were female patients (Table 2). No statistically significant difference was found between the two groups in terms of age and gender.

31 (53.4%) patients were symptomatic patients with clinical findings such as nephrolithiasis, osteoporosis and muscle-joint pain complaints. 27 (46.6%) cases were asymptomatic patients who were diagnosed with PHPT during the investigation of the incidentally detected hypercalcemia etiology (Table 2).

While the mean preoperative PTH levels were 303.6±208pg/ml in the successful surgery group, it was 345.9±264.5 pg/ml in the unsuccessful surgery group. While the mean preoperative serum Ca level was 11.7±0.9 mg/dl in the successful surgery group, it was 11.8±1.0 mg/dl in the unsuccessful surgery group. The mean 24-hour urinary Ca level was 416±176mg/day in the successful surgery group and 295±138mg/day in the unsuccessful surgery group. No statistically significant difference was found in terms of preoperative PTH, Ca, and 24-hour urine Ca levels in both groups (Table 1).

All patients diagnosed with hyperparathyroidism underwent preoperative localization studies with USG and MIBI scintigraphy. It was reported that parathyroid adenoma was localized by USG in 96.6% (n=56) of the patients and by MIBI scintigraphy in 84.5% (n=49) of them. In 48/58 (82.8%) patients, both USG and MIBI scintigraphy showed compatible localization and surgical success was achieved in 91.7% (n=44) of these patients (Table 2). In 17.2% (n=10) of the patients, inconsistency in USG or MIBI scintigraphy was detected and surgical failure was detected

DOI: 10.5455/medscience.2023.03.032

in 40% (n=4) of these patients. Surgical failure was statistically significant in patients with inconsistency between USG and MIBI scintigraphy. (Fishers exact test, p<0.005) (Table 2).

The dimensions of the pathological parathyroid glands were examined in preoperative USGs. In the preoperative USG reports, successful surgery was found to be 95.1% (n=39) and unsuccessful surgery was 4.9% (n=2) in PHPT patients whose size was defined as larger than 1 cm. In PHPT patients with a size less than 1 cm on USG, surgical success was found to be 64.7% (n=11), while unsuccessful surgery was found to be 35.3% (n=6). Surgical failure was found to be statistically significantly higher in patients with USG size less than 1 cm. (Fishers exact test, p<0.005) (Table 2).

While the mean weight of the removed parathyroid in the unsuccessful surgery group was 300 (±500)mg, and it was 3500 (±2400)mg in the successful surgery group. This difference was statistically significant. (Mann Whitney U test, p<0.005) (Table 1).

In the successful surgery group, adenoma was detected in 45 (77.6%) and carcinoma in 5 (8.6%) . In the unsuccessful surgery group, 6 (10.3%) of the glands could not differentiate between adenoma or hyperplasia and parathyroidal gland was not observed in 2 (3.4%) patients.

Table 1. Perioperative comparison of both surgical groups

	Succesful Surgery	Unsuccesful Surgery	p
The average age (±SD)	55.7 (±11.1)	58.9 (±20.5)	P=0.236*
Preoperative PTH (±SD) (pg/ml)	303.6 (±208)	345.9 (±264.5)	P=0.901*
Preoperative Ca (±SD) (mg/dl)	11.7 (±0.9)	11.8 (±1.0)	P=0.974*
24-hour urinary Ca (±SD) (mg/day)	416 (±176)	295 (±138)	P=0.937*
Weight of excised gland (mg) (±SD)	300 (±500)	3500 (±2400)	P<0.001*

SD: Standard deviation *: Mann Whitney U is used

Table 2. KOOS and VAS scores differentitation based on injection type

		Succesful surgery		Unsuccesful surgery		Total group		p
		n	%	n	%	N	%	
Gender	**Male**	11	78.6	3	21.4	14	24.1	P=0.341**
	Female	39	88.6	5	11.4	44	75.9	
Symptom	**Yes**	26	83.9	5	16.1	31	53.4	P=0.580**
	No	24	88.9	3	11.1	27	46.6	
Lesion size on USG	**>1cm**	39	95.1	2	4.9	39	67.2	p<0.005**
	<1cm	11	64.7	6	35.3	17	29.3	
Lesion on MIBI scintigraphy	**Yes**	44	89.8	5	10.2	49	84.5	P= 0.064**
	No	6	66.7	3	33.3	9	15.5	
USG and MIBI correlation	**Yes**	44	91.7	4	8.3	48	82.8	p<0.005**
	No	6	60.0	4	40.0	10	17.2	

MIBI: 99mTc-sestamibi scintigraphy, USG: Ultrasonography **: Fisher's Exact Test is used

Discussion

MPHPT is the most common cause of hypercalcemia detected during outpatient visits [11]. It is generally observed more frequently in patients over 50 years of age and in women [2]. In our study, the mean age of the patients was 56.1±12.6 years, and 75.9% of them were female. Demographic findings were found to be consistent with the literature [4,11].

In cases of PHPT, being symptomatic may vary regionally. While symptomatic cases are between 90% and 95% in eastern countries, this situation may decrease to 5% to 12% in western countries [11,12]. In our study, the rate of symptomatic patients was 53.4%. In terms of successful and unsuccessful surgery, no statistically significant difference was found in terms of symptomatic and asymptomatic cases (Table 2).

When the preoperative PTH, Ca, and 24-hour urinary Ca levels of the patients were compared for both groups, no statistically significant difference was found (Table 1). However, the mean value of PTH (606±250pg/ml) was found to be higher in patients with malignancy compared to patients without malignancy. In the literature, it was stated that the PTH value was higher in malignant cases and in parathyroid carcinomas than in benign diseases, but it was not considered pathognomonic in terms of preoperative diagnosis of malignancy [13].

The success of MIP in PHPT patients most often depends on

DOI: 10.5455/medscience.2023.03.032

correct preoperative localization. USG and biphasic MIBI scintigraphy are the most commonly used imaging techniques for preoperative localization. In the literature, the rate of detecting parathyroid adenomas with only USG is between 67-95% [9,14]. In our study, when the evaluation with only USG was examined, it was observed that localization was performed at a high rate of 96.6% (n=56). However, there are 17 patients reported as solitary adenoma under 1 cm according to USG, and when these patients were examined, surgical failure was found in 35.3% (n=6). Therefore, the high diagnostic value of USG in localization suggests that there may be false positivity or multi-gland hyperplasia instead of solitary adenoma.

In a meta-analysis conducted by Wei et al., it was shown that the sensitivity of 2-phase MIBI scintigraphy was between 63-84% [14,15]. In our study, parathyroid pathology was demonstrated in 84.5% (n=49) of the patients with MIBI scintigraphy. Surgical success was achieved in 89.8% of these patients. Surgical success remained at the rate of 66.7% (n=6) in patients who were not localized scintigraphically. It has been determined that the weight of the parathyroid glands has an effect on the localization determination process by scintigraphy. In many publications, scintigraphy detection rates were found to be higher for excised lesions with a weight above the cut-off value of 600mg [16,17]. In addition, the presence of solitary adenoma or multiple gland disease affects the scintigraphic diagnostic value [17,18]. Nichols et al. found that MIBI had a diagnostic value of 97% in cases with solitary adenoma, while this rate was 60% in multi-gland disease. Again, the diagnostic rate of MIBI was found to be 95% in pathological parathyroid glands greater than 600mg, while it was 84% in those with less than 600mg [16]. In our study, it was found that the scintigraphic diagnostic value was low and the rate of unsuccessful surgery was higher in pathological glands weighing less than 600 mg. (Mann Whitney U test, $p<0.005$) (Table 1).

In many studies, it has been shown that the sensitivity of the localization of the parathyroid glands after the combined use of USG and MIBI scintigraphy is at the level of 85-95% [6,7]. In our study, surgical success was achieved in 91.7% (n=44) patients in whom USG and MIBI scintigraphy determined the same localization. In 17.2% (n=10) of the patients, inconsistency was found in USG or MIBI scintigraphy, and surgical failure was found in 40% (n=4) of these patients. In this study, the high rate of surgical failure was found to be statistically significant in patients with inconsistency between USG and MIBI scintigraphy.

Adenoma was found in 77.6% (n=45) and carcinoma in 8.6% (n=5) of the successful surgical group. In 10.3% (n=6) of the unsuccessful surgery group, adenoma or hyperplasia in the glands could not be differentiated and parathyroidal gland was not observed in 2 (3.4%) patients. It has been reported in many publications that 10-15% of the causes of PHPT may be multiple gland hyperplasia and 4-5% of them may be double adenomas [3,4]. From this point of view, it comes to mind that localization may be insufficient or there may be multiple gland pathologies in cases of unsuccessful surgery. It has been reported that intraoperative rapid parathormone (rPTH) test and intraoperative gamma probe or frozen examination may be useful to increase surgical success [1,11,19]. It could not be done in our hospital because there is no rPTH test and gamma probe. In our study, frozen examination was performed in two patients and surgical success was observed in both of them.

Conclusion

Surgical success is directly related to preoperative localization. Correlation of USG and MIBI scintigraphy increases success. If there is a mismatch between USG and MIBI, preoperative 4D CT, intraoperative rPTH, gamma probe use or frozen examination can be used. It should be kept in mind that multiple gland pathologies may be more common than solitary adenoma in lesions smaller than 1 cm on USG. In these cases, because the diagnostic value of scintigraphy is low, surgical success will also decrease.

Minimally invasive surgery, depending on the surgeon's experience, is a technique that can be applied with similar surgical success as neck exploration, as well as with less complication rate. Although our study was based on data from a single center, the number of physicians who performed the operations was more than one. This suggests that physician-based learning curve may affect success.

Conflict of Interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
The authors declare that they have received no financial support for the study.

Ethical Approval
This study was approved by the Recep Tayyip Erdogan University Faculty of Medicine, Non-Invasive Clinical Research Ethics Committee, dated 24.03.2022 and numbered 2022/82.

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