ORIGINAL PAPER

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Correlation Between the Parathyroid Glands Size and Parathormones Value in Patients with Hyperparathyroidism

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ABSTRACT

Introduction: Hyperparathyroidism is a common endocrine disorder with potential complications of bone, renal, neurocognitive and cardiovascular system. **Aim**: To determine the correlation between the size of parathyroid glands and parathormone values in the patients with hyperparathyroidism. **Methods**: We analyzed a retrospective-prospective database of 79 consecutive patients who underwent parathyroidectomy for hyperparathyroidism at our institution between January 2011 and February 2018. The values of parathormone, calcium and phosphorus were determined in all patients before and after surgery. Ultrasonography were performed before surgery. Imaging results were confirmed by pathology. We analyzed the correlation between the sizes parathyroid glands obtained trough ultrasonography and pathology with parathormone values. **Results**: The median age of the patients were 51 age (range 20-73) and 67,1% of the patients were female. Our study demonstrated that between actual glands sizes (volumes), expresses in millimeters, measured on pathohistological analysis and ultrasound examination and size value of parathormone its increased value does not affect the size of the gland. We investigate the correlation between the size of glands measured according to the pathohistological finding and the value of parathormone we obtained the correlation results close to the statistical features. The correlation value of parathormone and glands sizes according to the pathohistological finding measured trough the determined assessment scale we determined the statistically important of medium value. **Conclusion**: One of the important factors for parathyroidectomy is the value of parathormone. Serum parathormone level might be predictable by a total size of parathyroid glands and could be an effective the predictor of gland localisation.

Keywords: hyperparathyroidism, parathormone, size of the parathyroid gland.

1. INTRODUCTION

Hyperparathyroidism is a common endocrine disorder with potential complications of bone, renal, neuro-cognitive and cardiovascular system. Clinicopathological primary hyperparathyroidism includes the parathyroid gland adenoma (80-85%), parathyroid gland hyperplasia (10-15%) and cancer (<1-5%). Secondary hyperparathyroidism is generally manifested in parathyroid hyperplasia, while tertiary hyperparathyroidism reflects the occurrence of autonomous parathormone production (PTH) neoplasm (and) from secondary parathyroid hyperplasia (1).

According to Boutshan (2) normal parathyroid glands measures are 3x5x7 mm. The total weight of all parathyroid glands is 90 to 130 mg. Parathyroid glands secrete parathormone (PTH). Their role is in the regulation of calcium concentration in serum and bone metabolism (3).

Parathyroid glands react to the low calcium level in serum by releasing parathormone. The increased level of parathormone is maintained by hypocalcemia and leads to cell replication and increased gland mass (4). When the level of parathormone remains higher than 800 pg/ml, for more than 6 months, besides the exhaustive medical interventions, Lau (5) claims that there is a monoclonal proliferation with consequent nodular hyperplasia. Some authors tried to create an index for the prediction of enlarged parathyroid glands on the basis of parathormone value and the size/weight of parathyroid gland, one of those is the Wisconsin Index (6).

2. AIM

The purpose of this study was to determine the correlation between the size of parathyroid glands and parathormone values in the same pa-

tients. We measured the size of the gland preoperatively with ultrasound method and postoperatively with patho-histological analysis, and then we measured the para-thormone values preoperatively and postoperatively. We measured the patients' values of calcium and phosphorus before the surgery.

3. METHODS

The study is of a retrospective-prospective character, and it included 79 consecutive patients that underwent partial or total parathyroidectomy (with or without auto transplantation) at the ENT Clinic of the University Clinical Centre Tuzla, in the period between January 2011 and February 2018. The values of calcium (Ca), phosphorus (P) and parathormone (PTH) were determined in all patients preoperatively and postoperatively. The values of serum Ca and P were measured on Siemens machine, Dimension RXL Max, and the measuring of the serum PTH concentration was performed on Wallac Wizard 1470 automatic gamma counter.

Ultrasound check was performed on ultrasound "real time" machine Toshiba SSA-220A, with the use of 7.5 MHz linear probe. The size, echo structure and localisation was measured for each parathyroid gland.

Standard HE (haematoxylin eosin) coloring was used for pathohistological diagnosis. Additional immunohistochemical analysis was used in the cases of doubt on benign and malignant tumors.

The data collected by research were processed by program package SPSS (version 20). The descriptive analysis was applied for all data processing. In the statistic data processing, the following were applied: Wilcoxon rank test, Kolmogorov-Smirnov test, Spearman rank correlation coefficient. The level of check importance was set on 5% (p <0,05).

4. RESULTS

79 patients with hyperparathyroidism were included in our research, and they underwent parathyroidectomy, aging 20 to 73 (average 51,13±11,83), and 67,1% (53/79) were women. According to the type of hyperparathyroidism, the most common was the secondary one. Of the 79 patients, 51,9% (41/79) had secondary, 4,3% (35/79) had primary and 3,8% (3/79) had tertiary hyperparathyroidism. Through the investigation of the results of preoperative and postoperative parathormone values (PTH), calcium (Ca) and phosphorus (P), it was noticed that there were significant divergences in the results of preoperative and postoperative values in these variables.

Wilcoxon rank test revealed some statistically significant differences between these values, for parathormone (Z =−6,765) and calcium (Z =−7,217) at the significance level p < 0,001, and phosphorus (Z =−3,105) p = 0.002. Wilcoxon rank test revealed some statistically significant differences between these values at the level of statistical significance p < 0,05. Parathormone median went down from Md =637,00 pg/ml to Md = 93,25 pg/ml, calcium from Md = 2,56 mmol/l to Md = 2,08 mmol/l, and phosphorus from Md = 1,33 mmol/l to Md = 1,12 mmol/l.

Correlation rank		Parathormone
The sum of glands values (volumes) - US	p	-0,04
	p	0,74
	N	79
The sum of glands values (volumes) - PHN	p	0,21
	p	0,06
	N	79
The sum of glands values according to the scale - PHN	p	0,46
	p	0,00
	N	79

Table 1. The assessment of correlation between the size of parathyroid glands and parathormone serum values (Spearman coefficient), US- the ultrasound examination, PHN- parathormone

We assessed the size of parathyroid glands through the ultrasound findings and pathohistological examination. Thereby, a number of enlarged glands was found during the surgery, not with the ultrasound pathological analysis, and they were sent on pathohistological analysis. By ultrasound examination, the largest number of increased parathyroid glands (56 or 54,5%) was in the range of 1 to 1.5 cm. In the pathohistological finding, the highest number of parathyroid glands was greater than 1.5 cm.

After that, we isolated the glands that match in localisation operatively and through ultrasound, in other words found during the surgery and measured at pathohistological and found and measured by ultrasound examination. The highest number of parathyroid glands 57 (54,8%) in ultrasonography was 1 to 1.5 cm in size, while in the pathohistological findings the highest number of parathyroid glands was 56 (53,8%), which was greater than 1.5 cm.

We investigated the correlation between the sizes (volume) obtained through ultrasound examination and pathohistological finding with parathormone (PTH) values. Between the actual glands sizes (volumes), expressed in millimeters, measured on pathohistological analysis and ultrasound examination and the value of parathormone, we determined that its increased value does not affect the size of the gland (calculating the Spearman coefficient). However, when we investigated the correlation between the size of the gland measured according to the pathohistological finding and the value of parathormone we obtained the correlation results (p = 0,21; p = 0,06), which was close to the statistical features, and through the investigation of correlation value of parathormone and gland size according to the pathohistological finding measured through the determined assessment scale (i.e. when we divided the glands in three groups: smaller than 1 cm, 1 to 1.5 centimeter and larger than 1.5 cm), (p = 0.46; p = 0.00), which is less precise compared to real measures in millimeters, and where the statistically important difference of medium value, they indicate that the correlation between the actual size values and PTH could be important if the research is repeated on larger

number of patients. With this we partially confirmed our hypothesis (Table 1).

Besides that, we were determining the correlation between the total number of localizations of enlarged parathyroid glands and PTH in our research, and we determined that they show a statistically significant, small correlation between the total number of localizations obtained through the ultrasound examination and PTH (p = 0.29), and moderate correlation between the total number of localizations obtained by surgery and PTH (p = 0.47), with the level of importance p < 0,01. These results can be used as the basis for other research, on larger pattern, in order to determine whether the PTH value can be a predictor for the total number of localizations, and in that way it could be assumed in advance how many parathyroid glands should be searched for at all.

5. DISCUSSION

In Marchini's study (7) hypercalcemia was present in 84.3% patients before parathyroidectomy. Eight out of 51 patients with normal calcium levels had increased PTH levels. Only two patients did not have PTH above the normal volume, although both of them had increased calcium levels. After parathyroidectomy, the number of patients with hypercalcemia was significantly reduced (n = 4; 7,8%), increased PTH (n = 17; 33,3%) and hypophosphatemia (n = 3; 5,9%) (P <0,001).

In Cheah's study all patients had increased PTH level (from 43 to 4 times higher values than the reference ones). The size of parathyroid gland correlated with the PTH values. Parathyroidectomy and lobectomy of thyroid gland was performed in all patients (8). The diameter of lesions determined by pathohistological analysis did not show a significant linear correlation with PTH levels (9).

Stawicki (10) noticed that higher diagnostic PTH levels (> 150 pg / mL) were correlated with the removed glands with larger mass (p <0.05) and larger volume (p <0.05). The interesting thing is that the patients with problems with thyroid gland had a significantly higher PTH level compared to the patients who had problems with several glands (155 compared to 109 pg / mL, p <0,05). According to Fang's et al. (11), the positive correlation was found between the size and weight of parathyroid gland and PTH, in patients with secondary hyperparathyroidism, after surgery. A significant reduction of PTH values after surgery was proved. Larger parathyroid glands secreted more PTH.

Ahmadi et al. (12) investigated the relation between the weight and volume and blood load of parathyroid glands and PTH secretion. There was no significant correlation between the total gland mass and serum concentration of PTH. There were no significant correlations noticed between total central and peripheral blood flow of parathyroid glands and PTH level in serum. The same author investigated other results, and so Matsuka and associates show that the correlation between the gland volume and PTH was weak. The research by Ahmadi show that PTH secretion neither depends on total weight nor on blood flow through parathyroid glands. In fact, these two indices may not be the indications for the determination of types of treatments in these patients. In a similar study by McCarron and associates the total size of parathyroid gland is not predictive by basal C-terminal PTH levels.

If we review the literature, the correlations between the size of parathyroid gland and the value of parathormone we can see that the results are contrary. By determining the connection between the total number of localizations of enlarged parathyroid glands in our patients with hyperparathyroidism, obtained by surgery, and PTH we showed a moderate correlation (p = 0.47), at the level of significance p < 0,01.

6. CONCLUSION

For a successful parathyroidectomy, a surgeon needs a precise localisation and the number of parathyroid glands that have to be removed. Therefore, an adequate preoperative diagnostic patient processing. One of the important factors for the indication of surgery is, among others, the value of parathormone. Our research proved the correlation between the size of parathyroid gland and parathormone value, but for the decision whether the parathormone value can be for sure the predictor of gland localisation, the research has to be done on larger number of patients.

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