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PARATHYROIDECTOMY IN PATIENTS WITH HYPERPARATHYROIDISM

Original scientific paper

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ABSTRACT

Aim: The aim of this study was to analyze all the factors (disease symptoms, sinthigraphic findings, biochemical parameters) that occur in patients with hyperparathyroidism, and since hyperparathyroidism itself is a common endocrine disorder. Methods: We analyzed 79 patients with primary, secondary, and tertiary hyperparathyroidism, who underwent surgery. We analyzed mean of age, male: female ratio, representation of different forms of hyperparathyroidism. In our study, we examined the indications for examination and surgery, as well as the most common symptoms and comorbidities. For localization PTG, scintigraphy was performed by a nuclear medicine specialist (at the Clinic of Radiology and Nuclear Medicine) preoperatively. Preoperative values of calcium (Ca), phosphorus (P), and parathyroid hormone (PTH) were determined in all patients, and the same values were measured postoperatively. We also analyzed correlation of dialysis length and parathyroid gland hyperplasia in patients with secondary hyperparathyroidism. Results: In our study mean of years was 51.13 ± 11.83 and most of the respondents were female. The most common operation was subtotal parathyroidectomy. The most common indication for examination of parathyroid glands (PTG) was renal failure. The most common comorbidity was arterial hypertension, which was found in 43 (53.2%) subjects, and the rarest gastrointestinal diseases and pancreatitis, in 1 (1.3%) patients. Scintigraphy showed an equal representation of enlarged lower parathyroid glands (both right and left). The mean values determined preoperatively for PTH were 796.24 pg/ml, Ca 2.58 mmol / l and P 1.35 mmol / l. The mean postoperative values for PTH were 222.33 pg/ml, Ca 2.06 mmol/l and P 1.17 mmol/l. We also showed that was a large correlation between dialysis length and hyperplasia. Conclusion: Hyperparathyroidism is a common endocrine disease, carrying potential complications of many organic systems. In most cases, regardless of the form (primary, secondary, or tertiary), it ultimately requires surgical treatment. For this reason, the clinical picture must be well known, the necessary preoperative diagnostic methods (which are complex), all with the aim of better effect of treatment of such patients.

Keywords: *hyperparathyroidism; calcium, parathyroid hormone, scintigraphy*

INTRODUCTION

Hyperparathyroidism is a very common endocrine disorder with potential complications on various systems such as skeletal, renal, neurocognitive, and cardiovascular systems (Duan, Gomez Hernandez, & Mete 2015). Hyperparathyroidism is excessive secretion of PTH and can be primary, secondary, or tertiary (Jawaid & Rajesh, 2020).

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In most cases, about 95% occur sporadically, and about 5% are associated with a hereditary syndromes: multiple endocrine neoplasia syndromes, hyperparathyroidism-jaw tumor syndrome, familial hypocalciuric hypercalcemia, familial hypercalciuric hypercalcemia, neonatal severe hyperparathyroidism, and isolated familial hyperparathyroidism. Primary hyperparathyroidism clinicopathologically includes parathyroid adenoma (80–85%), hyperplasia (10–15%), and carcinoma (<1–5%). Secondary hyperparathyroidism is mainly manifested by diffuse parathyroid hyperplasia (Duan et al., 2015). Tertiary hyperparathyroidism is a consequence of permanent stimulation of the parathyroid glands, which results in the autonomous function of PTH (Jawaid & Rajesh, 2020). Parathyroid disorders are most often present with serum calcium abnormalities. Patients with primary hyperparathyroidism are the most common cause of hypercalcemia outside the hospital, they may be asymptomatic or may have bone disease, nephrolithiasis, or neuromuscular symptoms. Patients with chronic kidney disease may develop secondary hyperparathyroidism with consequent chronic kidney disease - mineral and bone disorder (Michels & Kelly, 2013). According to Târcoveanu (2009), surgical treatment is the only curative treatment for hyperparathyroidism, and drug treatment is only preoperative preparation. Parathyroidectomy is always indicated for all symptomatic patients and should be considered for most asymptomatic patients, as it is more effective and with more benefits than patient follow-up or pharmacological treatment (Wilhelm et al., 2016). Different imaging methods can be used for the preoperative localization of enlarged parathyroid glands, which can more or less successfully determine the position and identify hyperfunctional parathyroid tissue. The most commonly used methods are ultrasound, scintigraphy, CT, and MRI. Increased values of serum calcium and PTH confirm the diagnosis (Mariani, Vaiano, Nibale, & Rubello, 2003).

MATERIAL AND METHODS

We conducted a retrospective-prospective study of 79 consecutive patients with primary, secondary, and tertiary hyperparathyroidism, who underwent surgery at our institution (total or subtotal parathyroidectomy) for a period of seven years.
Including criteria: patients with primary, secondary, or tertiary hyperparathyroidism, who underwent total or subtotal parathyroidectomy.
Excluding criteria: malignant diseases of other areas. Scintigraphy was performed by a specialist in nuclear medicine in 42 patients preoperatively. An ultrasound examination of the neck was performed on all patients. Computerized tomography (CT) scan of the neck and thorax was performed in one patient. Preoperative values of calcium (Ca), phosphorus (P), and parathyroid hormone (PTH) were determined in all patients, and the same values were measured postoperatively.
Data were collected by inspecting the protocols, medical documentation, and records of three different Clinics in our center (ENT Clinic, Clinic for Radiology and Nuclear Medicine and Polyclinic for Laboratory Diagnostics) preoperatively and postoperatively.

RESULTS

The study included 79 patients with hyperparathyroidism who underwent total or partial parathyroidectomy at our institution, in the period from January 2011 to February 2018, aged 20 to 73 years. (mean 51.13 ± 11.83). Most of the respondents were female (Figure 1).

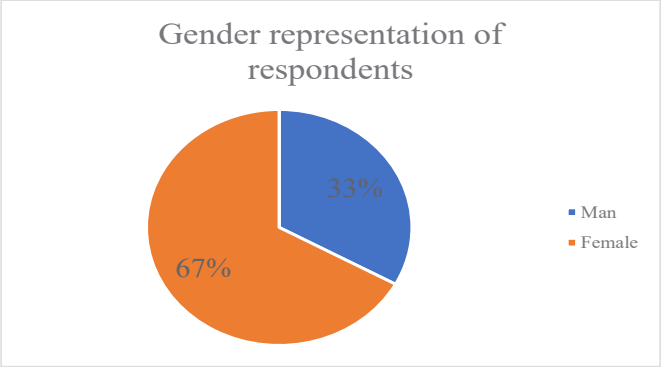

Figure 1. Gender representation of respondents

In the examined group, the most common form of hyperparathyroidism is secondary, which was found in 41 (51.9%) subjects (Figure 2).

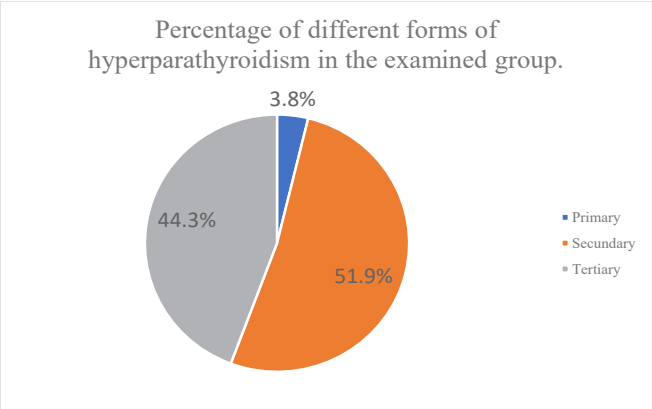

Figure 2. Percentage of different forms of hyperparathyroidism in the examined group.

Primary hyperparathyroidism was found in 35 (44.3%) and tertiary in 3 (3.8%) patients. In the study group, the indications for which patients were referred for parathyroid examination were analyzed. The most common indication for examination of parathyroid glands (PTG) was renal failure, which was found in 38 (48.1%) subjects, and the least common was elevated serum parathyroid hormone (PTH) found in 1 (1.3%) patients (Figure 3).

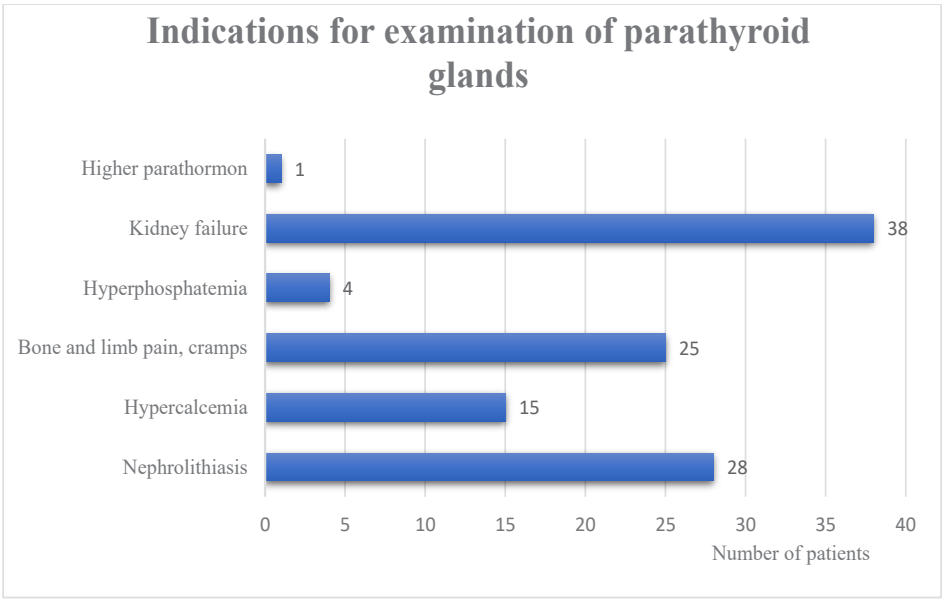

Figure 3. Indications for examination of parathyroid glands

Comorbidity analysis in subjects showed that the most common comorbidity was arterial hypertension, which was found in 43 (53.2%) subjects, and the rarest gastrointestinal diseases and pancreatitis, in 1 (1.3%) patients (Figure 4).

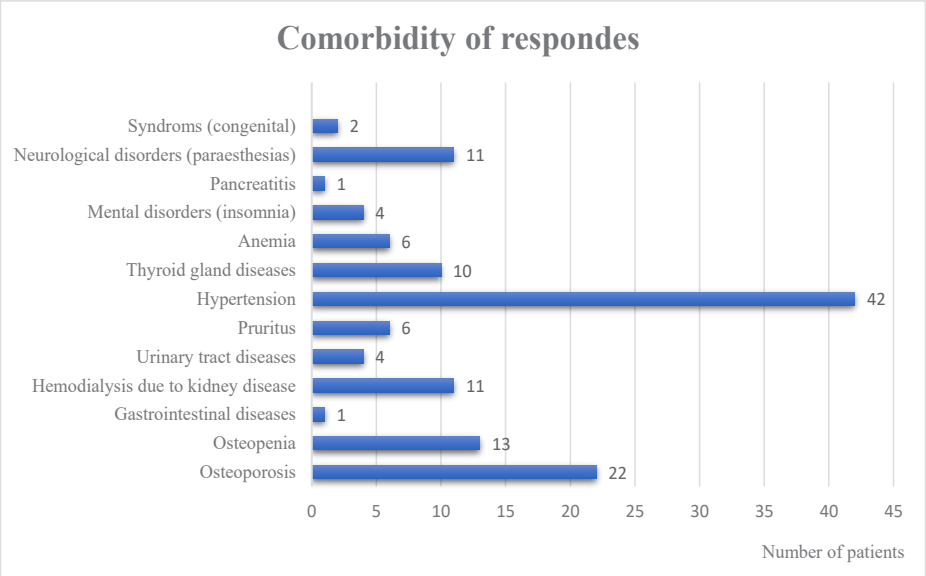

Figure 4. Comorbidity of respondents

Eight total parathyroidectomies (10%), 32 subtotal parathyroidectomies (40.5%), and 38 (48.1%) extirpations (of which 6 with two glands and 2 with two glands and lobectomy of the same side) were performed in 79 respondents of our study, and one thoracotomy (1.3%). Thoracotomy was performed in a patient with an ectopic parathyroid gland localized in the upper mediastinum. Scintigraphy was performed in 42 patients.

Table 1. Prevalence of localization of enlarged parathyroid glands according to scintigraphy

Localization	**Scintigraphy**	
	f	**%**
Right upper	3	5.4
Right lower	**20**	**36.4**
Left upper	5	9.1
Left lower	**20**	**36.4**
Ectopic localization	4	7.3
Normal results	3	5.4
Total	**55**	100.0

Scintigraphy revealed 52 enlarged and 3 normal sizes of the parathyroid gland. Scintigraphy showed an equal representation of enlarged lower parathyroid glands (both right and left), 20/55 (36.4%). The calculated sensitivity (sensitivity) of scintigraphy was 49.5% and specificity 93.3%. Table 2 shows the serum values of parathyroid hormone (PTH), calcium (Ca) and phosphorus (P), determined before and after surgery. The mean values determined preoperatively for PTH were 796.24 pg/ml, Ca 2.58 mmol/l and P 1.35 mmol/l. The mean postoperative values for PTH were 222.33 pg/ml, Ca 2.06 mmol/l and P 1.17 mmol/l.

Table 2. Comparison of preoperative and postoperative serum values of parathyroid hormone, calcium, and phosphorus

Variable	MIN	MAX	SUM	M	SD	VAR	S_k	K_u
Parathyroid hormone preoperatively	92.00	4093.00	62902.72	796.24	772.56	596847.36	1.71	3.64
Parathyroid hormone postoperatively	.00	2028.00	14896.10	222.33	349.91	122434.38	3.33	13.16
Calcium preoperatively	1.19	3.66	201.52	2.58	.41	.17	.22	1.97
Calcium postoperatively	.71	2.88	160.84	2.06	.39	.15	-.49	1.37
Phosphorus preoperatively	.48	2.71	105.45	1.35	.53	.29	.41	-.62
Phosphorus postoperatively	.51	2.38	90.03	1.17	.42	.18	.62	-.12

Since the largest number of subjects in this study had secondary hyperparathyroidism, the correlations between dialysis length and hyperplasia were analyzed by calculating the point of biserial correlation coefficient, which showed that there is a large correlation (r_{pb} = .56) of these parameters at the level of statistical significance p = .00, which is shown in Table 3.

Table 3. Coefficient of point biserial correlation of dialysis length and parathyroid gland hyperplasia

		Hyperplasia
Length of dialysis	r_{pb}	**.56**
	p	**.00**
	N	79

DISCUSSION

PHPT is most common after age 50 and has prevailed in women three to four times. In countries where routine screening exists, PHPT is identified earlier and may be asymptomatic (Khan et al., 2017). In a study involving 51 patients with PHPT, the mean age of the patients was 57.1 ± 12.1 years, of which 82.4% were women (Marchini et al., 2018). The study, which was conducted from June to August 2019, included 52 patients with secondary hyperparathyroidism who were on a dialysis program, the mean age was 51 years, male: female ratio 1: 8 (Ahmadi et al., 2016). A study by Khan (2017) supports our results regarding nephrolithiasis and cardiovascular disease. According to Khan, kidney stones are a major complication of PHPT. In Western countries, the prevalence of clinically symptomatic urolithiasis has decreased from approximately 80% of patients in the previous series to 7-20% at present. But, in patients who have been systematically examined, the diagnostic prevalence may be higher (25-55%). In the Li study (2017), 50 patients were examined and all patients with secondary hyperparathyroidism had renal failure (Li et al., 2017). Severe PHPT characterized by higher serum calcium levels (calcium ≥ 11.2 mg/dl) has been associated with an increased risk of cardiovascular mortality. PHPT thought to be associated with an increased risk of developing left ventricular hypertrophy, diastolic filling damage, and myocardial calcification. In Latin America, large epidemiological studies reported 44% of patients with kidney stones. Unlike China where the prevalence of asymptomatic PHPT is increasing, the clinical presentation of PHPT in India has not changed over the past 50 years. The main features of the presentation are still the involvement of the skeletal system followed by renal complications, as well as symptoms of hypercalcemia with less than 5% of asymptomatic presentation (Khan et al., 2017). According to Cordellat (2012), primary hyperparathyroidism is associated with hypertension. Given that parathyroid hormone receptors also exist in the vascular system, so the incidence of arterial hypertension and cardiovascular diseases has increased. Nephrolithiasis or nephrocalculosis can be seen in about 20% of patients with primary

hyperparathyroidism. About 5% of nephrolithiasis is secondary to primary. In a study by Pelizz (2001), nephrolithiasis was found in 10 patients, osteoporosis in 4, gastrointestinal problems in 1, and palpable cervical mass in 1 patient. Almost 50% of patients had more than one symptom. Gastrointestinal and neuromuscular symptoms were the most common (Von Breitenbuch et al., 2007). In our group of subjects, gastrointestinal symptoms were present in 1.3% of patients and neuromuscular in 13.9% of patients. A study by Li (2017) of patients who had serum calcium and phosphorus findings available for study 34.00% (17/50) and 76.00% (38/50) showed higher serum calcium and phosphorus levels preoperatively. In a study by Pelizz et al. (2001), all but one patient with parathyroid pathology had hypercalcemia. Von Breitenbuch et al (2007) conducted a retrospective study on 121 patients with primary hyperparathyroidism, where parathyroid hormone was monitored, all patients had elevated levels, more than 65 ng / l. In a study by Târcoveanu et al. (2009), there were 34 subjects, and in 32 patients with primary and 2 patients with secondary hyperparathyroidism performed surgical procedures were: tumor excision (73.53%), subtotal parathyroidectomy (17.6%), total parathyroidectomy (8.82%). Total thyroidectomy (26.5%) and subtotal thyroidectomy (11.8%) were performed in patients with associated thyroid disease. In another study of the 50 patients who underwent surgery, two patients had subtotal parathyroidectomy, and 48 patients had total parathyroidectomy with autotransplantation (Li et al., 2017). Of 109 patients, 80 had total parathyroidectomy with or without autotransplantation, 19 patients subtotal and 10 partial with removal of less than 4 glands (Lee, Kim, & Lee, 2015). Eight total parathyroidectomies (10%), 32 subtotal parathyroidectomies (40.5%), 38 (48.1%) extirpations (of which 6 with two glands and 2 with two glands and lobectomy of the same side) were performed in 79 respondents of our study, and one thoracotomy (1.3%). Lee et al (2015) conducted a study involving 109 patients, where they investigated the sensitivity of three methods USG, MIBI, and CT for preoperative diagnosis. USG had the highest sensitivity (91.5%) and MIBI was the lowest (56.1%) among the 3 modalities. CT sensitivity was 84.8%. The sensitivity in this study was high or higher than in other studies. Lee also researched the results of other studies, the results of which follow, including the study of Perie et al. showed that ultrasound detected 75% of hyperplastic glands, while MIBI identified 66%. A combination of both modalities identified 88% of the gland. The most pronounced glands on scintigraphy were the upper glands. Vulpio et al. reported that the sensitivity of MIBI and USG was 62% and 55%, and the sensitivity of combined techniques was 73%. A second series of 11 patients reported 91% sensitivity of MIBI in the identification of hyperplastic glands in secondary hyperparathyroidism. Another study showed a low yield of preoperative localization studies in patients with sHPT with MIBI showing only 36.6% and USG showing 35.9% of surgically confirmed enlarged glands. In a prospective study by Mohammadi et al., The sensitivity of USG and MIBI, and the combination of USG and MIBI, was 54%, 25%, and 45%, respectively. A meta-analysis that included 24 studies with 471 patients showed a 58% sensitivity of MIBI in detecting hyperplastic glands in sHPT. According to Ahmadi et al. (2016) in patients with chronic kidney disease, persistent hyperparathyroidism often leads to hyperplasia of the parathyroid glands, especially in patients on dialysis. In these patients, the severity of hyperplasia is positively correlated with the length of dialysis. The study included 52 patients with secondary hyperparathyroidism and all patients were on a hemodialysis program, and partial or total parathyroidectomy was performed. In our study, there were 41 patients with secondary hyperparathyroidism, and the correlation between the length of dialysis and hyperplasia was high, statistically significant. A prospective cohort study by Jäger et al (2017) investigated treatment options for secondary hyperparathyroidism and identified risk factors for nodular hyperplasia of the parathyroid glands. Twenty routinely collected parameters from the history of the disease, ultrasound findings of the parathyroid gland and laboratory results due to their influence on nodular hyperplasia were analyzed. Independent risk factors for nodular hyperplasia of one gland were the duration of dialysis in years, then the volume of the parathyroid gland expressed in mm^3 determined by ultrasound and the serum level of parathyroid hormone in pg/ml. From this, theoretical evaluation of the risk factor interaction showed that the duration of dialysis had the strongest influence on the value of nodular hyperplasia.

CONCLUSION

Hyperparathyroidism is a common endocrine disorder with potential complications. Most patients sooner or later require surgical treatment: partial or total parathyroidectomy.

The approach to treating these patients requires a multidisciplinary approach, a detailed history (including the presence of clinical manifestations of hyperparathyroidism, duration of dialysis in case of secondary or tertiary hyperparathyroidism), laboratory treatment, radiological methods, all in order to properly set the indication for surgery and successful operative procedure.

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