ARAŞTIRMA MAKALESİ/ORIGINAL RESEARCH

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Paratiroid Hastalıklarında Klinik ve Cerrahi Deneyimimiz; Üçüncü Basamak Tek Bir Merkezde Beş Yılın Değerlendirilmesi

Our Clinical and Surgical Experience in Parathyroid Diseases; Evaluation of Five Years at a Single Tertiary Care Center

Esra Hamurcu[1], Mehmet Tolga Kafadar[2], Mehmet Veysi Bahadır[2], Sadullah Girgin[2]

1Siverek Devlet Hastanesi Genel Cerrahi Kliniği, Şanlıurfa, Türkiye
2Dicle Üniversitesi Tıp Fakültesi Genel Cerrahi Anabilim Dalı, Diyarbakır, Türkiye

ÖZET

GİRİŞ ve AMAÇ: Bu çalışmada kliniğimize başvuran paratiroid hastalarının sosyo-epidemiyolojik verileri, preoperatif ve postoperatif laboratuvar değerleri, görüntüleme özellikleri ile kliniğimizin paratiroid hastalıklarını tedavi ederken uyguladığı yaklaşımların ve sonuçlarının retrospektif olarak incelenmesi amaçlandı.
YÖNTEM ve GEREÇLER: Bu çalışmaya 2013-2018 yılları arasında paratiroid hastalıkları nedeniyle Dicle Üniversitesi Tıp Fakültesi Genel Cerrahi Ana Bilim Dalı'nda tedavi edilen 200 hasta dahil edildi. Bu hastalara ait klinik ve laboratuvar verileri hasta dosyalarından retrospektif olarak değerlendirildi. Çalışmaya paratiroid hastalığı tanısı almış ve tedavi seçeneği olarak cerrahi planlanan olgular dahil edildi.
BULGULAR: Çalışmadaki 200 hastadan 33'ünün (%16.5) erkek, 167'sinin (%83.5) kadın olduğu gözlendi. Ortalama yaş 51.76 (18-93) idi. Ek tiroid hastalığı bulunmayan 128 (%64) hastaya unilateral cerrahi yaklaşım ve lokal eksplorasyon ile sadece paratiroid adenom eksizyonu uygulandı. Ek tiroid hastalığı olan 45 (%22.5) hastanın 41'ine bilateral total tiroidektomi, 4'üne sol tamamlayıcı tiroidektomi uygulandı. Hastaların 182 (%91)'sinde patolojik tanı paratiroid adenomu olarak raporlandı. Patolojik tanı ile preoperatif USG bulguları arasında 129 (%75.6) hastada, sintigrafi ile ise 110 (% 73.3) hastada uyum saptandı. Preoperatif yüksek olan serum PTH değerine oranla, intraoperatif, postoperatif 1. gün ve 1. ay çalışılan PTH değerinde anlamlı düşme olduğu görüldü ($p<0.001$). Preoperatif yüksek olan serum kalsiyum değerindeki postoperatif 1. gün ve 1. ay sonundaki düşmenin istatistiksel olarak anlamlı olduğu tespit edildi ($p<0.001$). Ameliyat sonrası dönemde bakılan serum fosfor değerlerindeki artışın istatistiksel olarak anlamlı olduğu gözlendi ($p<0.05$). Postoperatif dönemde 9 (% 4.5) hastada komplikasyon görüldü.
TARTIŞMA ve SONUÇ: Çalışmamızda paratiroid bozuklukları tedavisinde, cerrahinin uygun preoperatif değerlendirme ile deneyimli ellerde, dikkatli eksplorasyon yaparak, çok düşük komplikasyon oranı ile gerçekleşmesinin mümkün olacağı gösterildi. Kılavuzlara uygun olarak bu hastalıklarda öncelikle tercih edilmesi gereken tedavi yöntemi de cerrahi yaklaşım olmalıdır.
Anahtar Kelimeler: cerrahi, primer hiperparatiroidi, paratiroid adenomu

ABSTRACT

INTRODUCTION: This study aimed to retrospectively evaluate the socio-epidemiological data, preoperative and postoperative laboratory values, and imaging characteristics of patients with parathyroid disorders, as well as our clinic's approaches to treat parathyroid diseases and their outcomes.
METHODS: This study included 200 patients who were treated for parathyroid diseases at Dicle University Faculty of Medicine, Department of General Surgery between 2013 and 2018. The clinical and laboratory data of these patients were retrospectively obtained from their medical records. The study included patients who were diagnosed with parathyroid disease and intended for surgical treatment.
RESULTS: Out of 200 patients enrolled by the study, 33 (16.5%) were male and 167 (83.5%) were female. The mean patient age was 51.76 (18-93) years. Parathyroid adenoma excision with unilateral surgical approach plus local exploration alone was performed for 128 (64%) patients without accompanying thyroid disease, bilateral total thyroidectomy for 41 of 45 (22.5%) patients with accompanying thyroid disease, and left completion thyroidectomy for the remainder 4 patients with accompanying thyroid disease. The pathological diagnosis was reported as parathyroid adenoma in 182 (91%) patients. The pathological diagnosis was in agreement with preoperative USG in 129 (75.6%) patients and scintigraphy in 110 (73.3%) patients. There occurred a significant decrease in the PTH levels measured intraoperatively, on the first postoperative day, and at the first postoperative month compared with the preoperatively elevated serum PTH level ($p<0.001$). The decrease in preoperatively elevated serum calcium level on the first postoperative day and at the first postoperative month were statistically significant ($p<0.001$). The increase in serum phosphorus level at the postoperative period was statistically significant ($p<0.05$). Postoperative complications occurred in 9 (4.5%) patients.
DISCUSSION AND CONCLUSION: Our study showed that it is possible to perform surgery for parathyroid diseases with a very low complication rate, provided that an appropriate preoperative evaluation is performed and a careful exploration is carried out by experienced hands. In accordance with the current guidelines, surgical approach should become the preferred treatment method for the treatment of these disorders.

Keywords: surgery, primary hyperparathyroidism, parathyroid adenoma

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Correspondence: Doç. Dr. Mehmet Tolga Kafadar, Dicle Üniversitesi Tıp Fakültesi Genel Cerrahi Anabilim Dalı, Diyarbakır, Türkiye
E-mail:drtolgakafadar@hotmail.com

INTRODUCTION

Parathyroid glands secrete parathyroid hormone (PTH) which is very important for the regulation of calcium and phosphorus metabolism. PTH plays an important role for tooth development and bone mineralization, and it also increases bone resorption. Increased PTH secretion is termed as hyperparathyroidism (HPT), an endocrinological disorder that is classified as primary, secondary, or tertiary. Primary HPT (PHPT) is an endocrinopathological condition characterized by excessive PTH secretion, which can be caused by solitary or multiple adenomas (80%), idiopathic parathyroid hyperplasia (15%), or parathyroid carcinoma (0.5%). Secondary HPT is caused by hypocalcemia or vitamin D deficiency stimulating excessive PTH production. Chronic renal failure is the main cause of secondary HPT. The cause of tertiary HPT is the development of autonomous parathyroid hyperplasia following long-term secondary HPT, which is most commonly observed in patients with renal failure (1,2). Kidney stone formation has been reported in 10% to 25% of cases. The prevalence of bone disease is 10% to 20% in patients with PHPT. Preoperative diagnosis of parathyroid adenomas remains a diagnostic challenge despite various currently available imaging methods. Intraoperative distinction between adenoma, hyperplasia, and multiple adenomas is difficult since they can be pathologic in the absence of parathyroid gland enlargement and the parathyroid glands have a symmetrical anatomic arrangement (3). Noninvasive imaging methods used for preoperative detection and localization of parathyroid adenomas include ultrasonography, computerized tomography, magnetic resonance imaging, and radionuclide scintigraphy (4). Surgical removal of abnormal parathyroid glands remains the definitive treatment of hyperparathyroidism. The classical surgical approach is bilateral neck exploration which is associated with good success rate in expert hands. Minimal invasive parathyroidectomy has recently become an increasingly preferred technique due to lower complication rates. This technique has further highlighted the importance of preoperative localization techniques for the detection of abnormal parathyroid glands (5). The importance of the present study stems from the high prevalence of parathyroid diseases in our region and patients frequently presenting to our clinic due to its reference hospital status in the region. In this study, we retrospectively evaluated the personal, regional, laboratory, and imaging characteristics of parathyroid patients admitted to our clinic and analyzed our clinic's treatment approach to parathyroid diseases and its outcomes.

MATERIAL and METHODS

This clinical study was conducted with 200 patients who were treated for parathyroid diseases at Dicle University Faculty of Medicine Department of General Surgery between 2013 and 2018. The clinical and laboratory data of the patients were obtained retrospectively from their medical records. The study was approved by Dicle University Ethics Committee (Number: 233- 02.10.2019). It was conducted in a single center. The patients' personal data, previous clinical findings and applied treatments, preoperative diagnostic methods, applied surgical procedure, pathological diagnosis, postoperative complications, and long-term follow-up outcomes were evaluated.

Patients

This study was conducted with 200 patients aged 18 to 93 years who had parathyroid disease. It included patients who were diagnosed with parathyroid disease and planned to undergo surgery as the preferred treatment option. The patients' data obtained from their medical records (socioepidemiologocal data, treatment history, PTH, serum calcium and phosphorus levels measured before surgery, on the 1st day and 1st month after surgery, intraoperative PTH level, USG, scintigraphy, CT, and DEXA results, applied surgical technique and its complications, pathology reports, and follow-up outcomes) were recorded and analyzed.

Surgical Technique

As surgical treatment, patients underwent total parathyroidectomy, total adenoma excision, thyroid total lobectomy, bilateral total thyroidectomy, neck exploration, and parathyroid tissue seeding. A frozen section examination of some parathyroid lesions was performed during the surgical procedure. By this way, the parathyroid tissue was confirmed histopathologically and the diagnosis was made.

Statistical Analysis

The statistical analysis of the study data was performed using SPSS 16.0 software package. Categorical variables (such as gender, comorbidity, type of surgery) were expressed as frequency and percentage while continuous variables like Ca++, P, and PTH were expressed as mean (minimum-maximum where necessary). T-test was used to compare continuous variables between the study groups. Wilcoxon signed rank test was used to compare dependent variables such as preoperative and postoperative biochemical values. A p value of less than 0.05 was considered statistically significant

for all tests.

RESULTS

Preoperative findings

Out of 200 patients who participated in this study, 33 (16.5%) were male and 167 (83.5%) were female. The mean age of the patients was 51.76 (18-93) years. One hundred and eight (54%) patients were living in urban areas. Of 177 (88.5%) patients who were operated, 145 (81.9%) patients presented to the endocrinology outpatient clinic and 19 (10.7%) to nephrology outpatient clinic for various symptoms. Only 19 (9.5%) patients had received medical treatment prior to surgery. The most commonly administered medical treatment was biphosphonates in 9 (47.7%) patients. The mean time from symptom onset to hospital admission was 2.7±7.2 months; the time from symptom onset to hospital admission ranged between 1 month and 6 months in 121 (60.5%) patients. Similarly, the mean time from symptom onset to surgical intervention was 8.9±11.9 months, and it was between 1 month and 6 months in the majority of patients (112; 56%). Body mass index (BMI) was 30.6±6.2 in 17 (8.5%) patients. The demographic characteristics of the patients were summarized on Table 1. Comorbidity was present in 99 (49.5%) of the patients presented with parathyroid disease. Hypertension was diagnosed in 61 (30.5%) patients, diabetes mellitus in 22 (11%), chronic renal failure in 19 (9.5%), and nephrolithiasis in 9 (4.5%).

Preoperative laboratory levels

It was found that the patients had elevated PTH and serum calcium levels at the preoperative period. The mean PTH and serum calcium levels were 452.4 pg/ml (Normal level: 15-65 pg/ml) and 11.3±1.2 mg/dL (Normal level: 8.4- 9.7 mg/dL), respectively. On the other hand, serum phosphorus level was found to be low (2.6±0.8 mg/dL) (Normal level: 2.7-4.5 mg/dL).

Radiological and Nuclear Medicine Studies

One hundred and seventy (85%) patients underwent USG. The latter detected a pathological condition in the right lobe in 83 (51.2%) patients and an adenoma in 135 (80.4%) patients. CT was taken in 15 (7.5%) patients, which showed signs compatible with an adenoma in 3 (20%) patients and adenoma/carcinoma in 2 (13.3%) patients. A scintigraphic study was performed for 150 (75%) patients, which revealed a pathological condition in 129 (86%) patients. Scintigraphy localized the pathological condition to the right lobe in 69 (53.5%) patients. It diagnosed adenoma in 66 (51.2%) patients and adenoma and hyperplasia in 49 (38%) patients. Bone mineral density was measured with bone densitometry (DEXA) in 123 (61.5%) patients, and revealed that 44 (35.8%) patients had with osteopenia and 49 (39.8%) had osteoporosis. Preoperative Radiological and Nuclear Medicine studies were summarized on Table 2. Lesion localization by USG and scintigraphy results were presented on Table 3 and Table 4.

Table 1. The demographic characteristics and history of treatment of the patients

Characteristics	n (%)
Gender	
Female	167 (83.5)
Male	33 (16.5)
Comorbidity	
No	101 (50.5)
Yes	99 (49.5)
Place of Residence	
Country	92 (46.0)
Urban	108 (54.0)
Family History	
No	200 (100)
Yes	0 (0)
Presentation to other outpatient clinic before surgery	
No	23 (11.5)
Yes	177 (88.5)
Clinic of admission	
Endocrinology	145 (81.9)
PTR	7 (4.0)
Endocrinology+PTR	1 (0.6)
Gastroenterology	2 (1.1)
Nephrology	19 (10.7)
Ortopedics	3 (1.7)
Medical Treatment Administered	
No	181 (90.5)
Yes	19 (9.5)
Drugs used	
Biphosphonate	9 (47.7)
Zoledronic acid	7 (36.8)
Mimpara	2 (10.5)
Cinacalcet	1 (5.3)
Time from symptom onset to admission (months)	
Less than 1 month	71 (35.5)
1-6 months	121 (60.5)
More than 6 months	8 (4.0)
Time from symptom onset to surgery (months)	
Less than 1 month	18 (9.0)
1-6 months	112 (56.0)
6-12 months	31 (15.5)
More than 12 months	39 (19.5)

Table 2. Preoperative Radiological and Nuclear Medicine Studies

	Number (%)
Ultrasonography result	
No	30 (15.0)
Yes	170 (85.0)
USG- Which lobe?	
Right	83 (51.2)
Left	65 (40.1)
Bilateral	14 (8.6)
Preoperative pencil tagging	
No	143 (85.1)
Yes	25 (14.9)
USG appearance	
Normal	5 (3.0)
LAP	3 (1.8)
Nodule	14 (8.3)
Parathyroid adenoma	135 (80.4)
Parathyroid adenoma + nodule	4 (2.4)
Parathyroid hyperplasia	2 (1.2)
Parathyroid pathology	4 (2.4)
Thyroid tissue not observed	1 (0.6)
Tomography	
No	185 (92.5)
Yes	15 (7.5)
Tomographic appearance	
Normal	4 (26.7)
LAP	1 (6.7)
Thyroid nodule	5 (33.3)
Parathyroid adenoma	3 (20.0)
Adenoma/CA	2 (13.3)
Scintigraphy	
No	50 (25.0)
Yes	150 (75.0)
Pathology on scintigraphy	
No	21 (14.0)
Yes	129 (86.0)
Lobe of pathology on scintigraphy	
Right	69 (53.5)
Left	55 (42.6)
Middle	5 (3.9)
Diagnosis made by scintigraphy	66 (51.2)
P. adenoma	49 (38.0)
P. adenoma + hyperplasia	9 (7.0)
P. hyperplasia	5 (3.9)
P. pathology	
DEXA performed	
No	77 (38.5)
Yes	123 (61.5)
DEXA result	
Normal	30 (24.4)
Osteopenia	44 (35.8)
Osteoporosis	49 (39.8)

Table 3. Lesion Location (by USG result)

USG result	**Lobe n (%)**		
Region	**Right**	**Left**	**Bilateral**
Anterior	2 (2.4)	0 (0)	0 (0)
Inferior	57 (68.7)	41 (63.1)	5 (35.7)
Middle	4 (4.8)	3 (4.6)	0 (0)
Posterior	14 (16.9)	7 (10.8)	2 (14.3)
Superior	6 (7.2)	7 (10.8)	0 (0)
Lateral	0 (0)	1 (1.5)	0 (0)
More than one region	0 (0)	6 (9.2)	7 (50.0)
Total	83	65	14

Table 4. Lesion Location (by scintigraphy result)

Scintigraphy result	**Lobe n (%)**		
Region	**Right**	**Left**	**Middle**
Anterior	1 (1.4)	0 (0)	0 (0)
Inferior	59 (85.5)	45 (81.8)	4 (80.0)
Middle	4 (5.8)	1 (1.8)	1 (20.0)
Superior	5 (7.2)	9 (16.4)	0 (0)
Total	69	55	5

Operative Findings and Surgical Procedure

According to the ASA (American Society of Anesthesiologists) classification of the patients, 123 (61.5%) patients were classified as ASA class 2. The applied surgery type was shown on Table 5. One hundred and twenty-eight (64%) patients who had no accompanying thyroid disease were operated with parathyroid adenoma excision with unilateral surgical approach and local exploration alone. Of 45 (22.5%) patients with accompanying thyroid disease, 41 underwent bilateral total thyroidectomy, and 4 left total completion thyroidectomy. The pathological diagnosis was consistent with preoperative USG result in 129 (75.6%) patients and with scintigraphy result in 110 (73.3%) patients.

Postoperative Findings

Laboratory Findings

The mean preoperative PTH level was 452.4 pg/ml. The mean intraoperative PTH level was 69.2 pg/ml; and its first postoperative day and first postoperative month levels were 62.45 pg/ml and 144.48 pg/ml, respectively. Serum Ca++ level was measured 11.36 mg/dL at the preoperative period and 9.17 mg/dL at the first postoperative month. Serum P level was 2.68 mg/dL at the preoperative period and 3.40 mg/dL at the first postoperative month. The difference between the preoperative PTH level and its intraoperative, first postoperative day and first postoperative levels month was statistically significant ($p<0.001$). Serum calcium level significantly decreased on first postoperative day and at the first postoperative month compared with the preoperative level ($p<0.001$). The postoperative increase in serum P level was statistically significant ($p<0.05$). The results were presented on Table 6.

Table 5. Distribution of Patients by Surgical Data

	Number (%)
ASA	
1	14 (7.0)
2	123 (61.5)
3	59 (29.5)
4	4 (2.0)
Type of surgery	
BTT + Right P. adenoma excision	1 (0.5)
BTT + Left Lobe inf. adenoma excision	1 (0.5)
P. adenoma excision + Neck Exp.	2 (1.0)
P. adenoma excision + Right lobectomy + Neck Exp.	1 (0.5)
P. adenoma excision	128 (64.0)
Bilateral P. adenoma excision	1 (0.5)
P. adenoma excision + BTT	37 (18.5)
P. adenoma excision + Right lobectomy	7 (3.5)
P. adenoma excision + Left lobectomy	9 (4.5)
P. adenoma excision + TTT	4 (2.0)
P. adenoma excision + Right near-total lobectomy	1 (0.5)
Right upper and lower P. adenoma excision	1 (0.5)
Subtotal parathyroidectomy	5 (2.5)
Subtotal parathyroidectomy + BTT	2 (1.0)
Type of Anesthesia	
EGA	123 (61.5)
LMA	14 (7.0)
Local + Sedoanalgesia	63 (31.5)

Table 6. Mean Levels of Postoperative Blood Tests

	Preop. mean (min-max)	**Postoperativemean on the first postoperative day (min-max)**	**Postoperative mean at the first postoperative month (min-max)**	***p***
PTH (N:15-65 pg/ml)	452.40 (68-2519)	62.45 (1.86-1308)	144.48 (5.40-1959)	$P_{1-2}<0.001$ $P_{1-3}<0.001$
Ca^{++} (N:8.4-9.7 mg/dL)	11.36 (8-18)	9.07 (5.60-11.50)	9.17 (5.70-12.50)	$P_{1-2}<0.001$ $P_{1-3}<0.001$
P (N:2.7-4.5 mg/dL)	2.68 (1.20-8.20)	3.01 (1.10-9.20)	3.40 (1.50-6.60)	$P_{1-2}<0.05$ $P_{1-3}<0.001$

Pathological diagnosis and complications

The postoperative pathological diagnosis was parathyroid adenoma in 182 (91%) patients and parathyroid hyperplasia in 8 (4%) patients (Table 7). Postoperative complications occurred in 9 (4.5%) patients. No patient developed wound infection or recurrent nerve injury (Table 8).

Table 7. Postoperative Pathology Results

Pathological Diagnosis	**Number (%)**
Parathyroid adenoma	182 (91.0)
Parathyroid tissue	9 (4.5)
- Parathyroid hyperplasia	8 (4.0)
- Reactive lymph node	1 (0.5)
Total	**200 (100)**

Table 8. Postoperative Complications

Postoperative complication	n: 200 (%)
No	191 (95.5)
Yes	9 (4.5)
Postoperative complications	n: 9 (%)
Hungry bone syndrome	4 (44.4)
Hematoma	2 (22.2)
Numbness secondary to hypocalcemia	2 (22.2)
Dyspnea	1 (11.1)

Length of Hospital Stay

The mean length of hospital stay was 3.2 days in the whole study population, 3.17 days in patients without hypocalcemia on the first postoperative day, and 3.72 days in patients with hypocalcemia on the first postoperative day. It was found that the length of postoperative hospital stay ranged between 1 day and 13 days in patients who developed hypocalcemia. There was no significant difference between the groups with and without postoperative hypocalcemia regarding the length of hospital stay ($p>0.05$) (Table 9).

Table 9. Correlation between Postoperative Hypocalcemia and Length of Hospital Stay

	Patients with hypocalcemia	**Patients without hypocalcemia**	***p***
	Mean (min-max)	Mean (min-max)	
Length of hospital stay	3.72 days (1-13)	3.days (1-8)	$p>0.05$

DISCUSSION

Parathyroid gland diseases are mostly characterized by serum calcium abnormalities. Studies on parathyroid diseases have revealed that they are more than three times more common in women than men (6). In a study on PHP cases followed for a period of 6 years, Pappachan et al. (7) reported that 79% of patients were women. Karateke (8) reported that 75% of their patients were female. Our study found a female/male ratio of 4/1, which is consistent with the globally reported data.

PHPT is diagnosed either by hypercalcemia detected during routine tests or the emergence of various symptoms as the disease advances. PHPT causes significant morbidity through skeletal demineralization and fractures, hypercalciuria and kidney stone formation, cardiovascular involvement, and cognitive dysfunction (9). In our study, hypertension was detected in 30.5% of the patients and nephrolithiasis in 4.5% of them. In accordance with our study, Kirdak et al. (10) reported a prevalence of 35% for hypertension among patients operated for PHPT. In a study reported by Pappachan et al. (7), the prevalence of nephrolithiasis was 19%. History taking and physical examination has a limited role in the diagnosis of parathyroid diseases. Instead, biochemical parameters (serum Ca++, P, and PTH) and radiological imaging modalities (USG, 99mTc-sestaMiBi scintigraphy, CT imaging) are used for diagnosis. Serum Ca++ level is usually increased in PHPT (11). In our study the mean PTH level was 452 pg/ml and the mean Ca++ level was 11.36 mg/dL, which were both elevated. Kırdak et al. (10) also reported elevated levels of both parameters (220 pg/mL and 11.2 mg/dL, respectively) in patients with hyperparathyroidism. The phosphorus level (2.68 mg/dL) was higher in our study than that reported by Kirdak et al. (10) (Turkey-wide 2.4 mg/dL, Southeastern Anatolian Region 2 mg/dL). The difference between our study and that reported by Kirdak et al. (10) may have resulted from the fact that the two studies were conducted in different time windows (2004-2008 vs 2013-2018) and included patients with different socio-epidemiological characteristics. Our study showed that postoperative PTH and calcium levels significantly decreased compared with their preoperative levels. Furthermore, postoperative P level was found to be increased. In support of our study, Korukluoğlu et al. (12) found a significant difference between preoperative and postoperative PTH and calcium levels. The changes in the biochemical levels of these patients reflect treatment efficacy.

In this study, intraoperative PTH was measured

in 24 patients, and it was shown to be reduced compared with the preoperative PTH level in 95.8% of them. With the advance of definitive preoperative localization studies and the widespread use of rapid PTH tests, intraoperative PTH-guided parathyroidectomy has become the preferred surgical approach for PHPT in many centers, due largely to its success rate similar to, or even greater than, bilateral neck exploration. Surgeons use intraoperative PTH to confirm complete excision of all hyperfunctional parathyroid glands. Intraoperative PTH also warns surgeon that abnormal parathyroid tissue has been incompletely removed during surgery. Thus, it signals the need for further neck exploration (13).

Ultrasonographic evaluation is recommended as the initial diagnostic modality since it is inexpensive and fast, provides detailed anatomical information, and does not pose a radiation risk. It has a sensitivity of 65-85% for the detection of parathyroid adenoma, but that figure is lower in the presence of thyroid nodules. USG is able to locate 95% of adenomas heavier than 1000 mg. In most cases, thyroid pathology can be well visualized and differentiated from enlarged parathyroid glands. However, USG can detect less than 50% of adenomas lighter than 200 mg. In addition, the most limiting factor for the localization studies using USG is that the result is excessively dependent on user skills (14).

Radionuclide scintigraphy is characterized by a high sensitivity and specificity for the localization of parathyroid adenomas in normal and ectopic regions and in previously operated patients. Although its sensitivity for detecting parathyroid disorders reportedly ranges between 75% and 80%, the figure decreases to 60-66% in the case of multiglandular gland involvement. The nuclear imaging method that is based on altered cellular metabolic activity provides more useful information than other imaging techniques which solely determine the anatomical localization (15). In a study that investigated the effectivenesses of USG and scintigraphy in the preoperative evaluation of hyperparathyroidism, Sükan et al. (16) found a sensitivity of 70% for scintigraphy and 60% for USG for detecting PHP. In our study, the patients were imaged with USG and scintigraphy prior to parathyroid surgery. We found that USG was in agreement with the surgical result in 75% of patients while scintigraphy was agreed with the surgical result in 73.3% of our patients. In agreement with our study, Solarzano et al. (17) found that USG had an accuracy of 77% in a study where the authors compared the USG findings with the surgical results in PHPT cases. A study by Çaycı et al. (18) on patients undergoing parathyroid surgery showed that USG was 95% successful at correctly detecting adenomas while scintigraphy successfully detected 100% of adenomas.

In previously unoperated patients with hyperparathyroidism, the overall success rate of CT is 75%. Using thin sections and dynamic scans with dynamic contrast increases the chance of localizing parathyroid adenomas. CT is usually effective in detecting lower cervical adenomas, but it can detect only 50% of mediastinal adenomas. Parathyroid glands may be found at varying locations from pharynx to mediastinum as a result of their long embryological migration. However, adenomas frequently originate from the lower parathyroid gland (19). The most commonly diagnosed parathyroid disease in our study was adenoma; the most common lesion location was the inferior region according to both USG (63.6%) and scintigraphy (83.7%). Similar to our findings, Korukluoğlu et al. (12) detected PTH adenoma in 92.6% of PHPT patients but they diagnosed no parathyroid carcinoma. The clinical profile of PHPT has dramatically changed in recent years. The specific signs and symptoms of the disease formerly included the neuromuscular symptoms of hypercalcemia in addition to skeletal abnormalities (osteitis fibrosa cystica, bone cysts, and brown tumors of long bones), nephrolithiasis and nephrocalcinosis. Today, these symptoms are not clinically prominent anymore in most patients. Therefore, serum calcium level is measured as a screening test for PHPT in most countries. However, skeletal involvement and bone injury can be demonstrated by DEXA (20). DEXA was performed for approximately 60% of our patients, of which 35.8% had osteopenia and 39.8% had osteoporosis. In a study by Pappachan et al. (7) DEXA was carried out in about 80% of patients, which revealed a similar rate of osteoporosis (37%) and a lower rate of osteopenia (13%).

The aim of hyperparathyroidism treatment is to bring a patient back to the normocalcemic state, to alleviate symptoms, and to prevent disease complications or to treat the existing ones. The treatment of symptomatic PHPT and secondary hyperparathyroidism unresponsive to medical therapy is surgery. Today, all patients who are diagnosed with PHPT including the asymptomatic ones are offered surgical treatment, irrespective of age. Indeed, many studies have demonstrated the negative effects of hyperparathyroidism, such as increased risk of premature death, hypertension, myocardial hypertrophy, and bone loss, especially in elderly women. Biochemical tests return to normal

and bone density increases after parathyroidectomy in symptomatic patients (21,22). Surgical techniques to be applied are still a subject of debate. Sternotomy or thoracotomy are the first classical surgical options for some ectopic parathyroid adenomas with mediastinal location. In the past, bilateral neck exploration was necessary during surgical treatment of PHPT because there was no other way to determine whether more than one gland was abnormal/pathological without exposing and visually checking all four parathyroid glands. However, this approach was based on clinical evaluation of parathyroid glands instead of biochemical analysis and associated with worse cosmetic outcomes and a higher risk of complications such as hypocalcemia, permanent hypoparathyroidism, and recurrent laryngeal nerve injury (23).

In the presence of a parathyroid adenoma, the gold standard treatment is the surgical resection of the hyperfunctional tissue. Although the traditional definitive treatment of adenomas is bilateral neck exploration, less invasive procedures including unilateral neck exploration, such as mini-incision and localized excision, with or without radioactive material-guided or endoscopic approach, are being increasingly used by surgeons. Minimally invasive surgical technique has paved the way for outpatient parathyroid surgery with local anesthesia (24). Our study revealed that parathyroid adenoma excision was achieved by minimally invasive surgery in most patients; the generally preferred anesthesia type was general anesthesia. While advances in preoperative imaging methods have made targeted minimally invasive parathyroidectomy technique possible, the development of rapid intraoperative/intact PTH (iPTH) test has allowed surgeons to biochemically confirm the success of a procedure intraoperatively before terminating the surgical intervention (25,26). In our study iPTH was used for 24 patients, and it showed a decrease in PTH compared with preoperative PTH level.

In the light of our study, we recommend that minimally invasive parathyroidectomy be performed with the use of rapid iPTH testing by an experienced surgeon in patients with sporadic PHPT who have undergone at least one preoperative localization study. Despite the benefits of minimally invasive parathyroidectomy over conventional bilateral neck exploration, conventional treatment is still an option in multiple endocrine neoplasia, renal hyperparathyroidism, or lithium-induced hyperparathyroidism associated with more than one multiglandular PTH gland disease, or for patients having adenomas that cannot be exactly localized by imaging studies. In the literature, the rate of thyroid disorders accompanying PHPT ranges between 18% and 84% (27). In our study, simultaneous thyroidectomy was performed in 22.5% of patients operated for parathyroid disease. Kirdak et al. (10) performed simultaneous thyroidectomy due to various indications in 36% of patients operated for PHPT. Pappachan et al. (7) reported a postoperative complication rate of 9%. We found a rate of 4.5%. Our study showed that 2% of patients operated for parathyroid disease had hungry bone syndrome. This rate is considerably low compared with the literature data. Several large case series have reported that hungry bone syndrome developed in approximately 13% of patients who underwent parathyroidectomy for PHPT. Hungry bone syndrome is described as prolonged hypocalcemia followed by a normal or elevated PTH level in patients undergoing parathyroidectomy for hyperparathyroidism (28). Hypocalcemia is a common postoperative complication of hyperparathyroidism surgery. The most common signs of hypocalcemia are paresthesia, cramps and/or tetany-related clinical neuromuscular excitability. A more advanced stage of the condition is characterized by altered consciousness, seizures, and laryngospasm or bronchospasm (29). Paresthesia associated with hypocalcemia was seen in 2 (1%) of our patients. Dirican et al. (30) in a study on patients who were operated for parathyroid adenoma, detected temporary hypocalcemia in 1 (1.6%) patient and a lack of drop in postoperative Ca++ and PTH levels in 4 (11%) patients. They reported that patients stayed at hospital for a mean length of 3.4±1.6 days after parathyroid surgery. That figure was very close to the length of postoperative hospital stay found in our study (3.2±1.7 days). However, when we examined the effect of postoperative hypocalcemia on the length of hospital stay, the latter was longer in the group which developed postoperative hypocalcemia, although the difference did not reach statistical significance. This emphasizes that the surgeon needs be careful about the risk of postoperative hypocalcemia.

Conclusion

The success rate of parathyroid surgery is affected by the adequacy of a hospital's infrastructure, and the availability of a team of endocrinologists, radiologists, nuclear medicine specialists, nephrologists, pathologists and a surgeon experienced in endocrine surgery. Multidisciplinary approach is of utmost importance for the diagnosis and treatment of parathyroid diseases. Cooperation between related physicians will surely increase the rate of diagnosis and treatment. As one can

understand from our study, since surgical treatment in parathyroid disorders can be performed with a very low complication rate in experienced hands, surgical approach should be the first treatment method to be preferred in these diseases in accordance with the current guidelines.

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