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EVALUATION OF SURGICAL TREATMENT OUTCOMES FOR PRIMARY HYPERPARATHYROIDISM: A SINGLE CENTER EXPERIENCE

PRİMER HİPERPARATİROİDİZM İÇİN CERRAHİ TEDAVİ SONUÇLARININ DEĞERLENDİRİLMESİ: TEK MERKEZ DENEYİMİ

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ABSTRACT

AIM: Primary hyperparathyroidism (PHPT) is a disease characterized by excess parathyroid hormone (PTH) secretion from one or more of the four parathyroid glands. Surgical removal of abnormal parathyroid glands is the most effective treatment method for the disease. This study aims to present our clinical and surgical experience of patients operated on for PHPT.

MATERIAL AND METHOD: The data of patients who were operated with a diagnosis of PHPT in the breast and endocrine surgery department of our hospital between January 2014 and March 2019 were retrospectively analyzed.

RESULTS: A total of 334 patients (range 16 to 86) with a median age of 54 were included in this study. Of these, 285 (85.3%) were female and 49 (14.7%) were male. In preoperative localization studies, the highest accurate detection rate was obtained sestamibi with single-photon emission computed tomography and ultrasonography, which defined 85.7% of abnormal parathyroid glands. Minimally invasive method was preferred in 22.16% of the patients, and bilateral neck exploration was preferred in 76.94% of the patients. Sternotomy was required in 3 patients. Ectopic localization of pathological glands was present in 26 (7.78%) patients. Concomitant thyroidectomy was performed in 124 (37.12%) patients. Incidental thyroid malignancies were diagnosed in 14 (11.29%) patients. The prevalence of persistent and recurrent disease was determined as 6.88% and 4.19%, respectively.

CONCLUSION: PHPT requires a multidisciplinary approach. Surgical treatment can provide over 95% improvement with low complication rates. We believe that careful localization studies for abnormal glands and detailed examinations for accompanying thyroid pathologies will further incress the the surgery success.

Keywords: *primary hyperparathyroidism, parathyroid localization, parathyroidectomy, surgery.*

ÖZET

AMAÇ: Primer hiperparatiroidizm (PHPT), dört paratiroid bezinin bir veya daha fazlasından aşırı paratiroid hormonu (PTH) salgılanmasıyla karakterize bir hastalıktır. Anormal paratiroid bezlerinin cerrahi olarak çıkarılması, hastalığın en etkili tedavi yötemidir. Bu çalışma, PHPT nedeniyle ameliyat edilen hastaların klinik ve cerrahi deneyimlerimizi sunmayı amaçlamaktadır.

GEREÇ VE YÖNTEM: Ocak 2014 - Mart 2019 tarihleri arasında hastanemiz meme ve endokrin cerrahisi bölümünde PHPT tanısı ile ameliyat edilen hastaların verileri geriye dönük olarak incelendi.

BULGULAR: Bu çalışmaya medyan yaşı 54 olan toplam 334 hasta (dağılım 16-86) dahil edildi. Bunlardan 285'i (% 85,3) kadın, 49'u (% 14,7) erkekti. Preoperatif lokalizasyon çalışmalarında, en yüksek doğru tespit oranı, anormal paratiroid bezlerinin % 85.7'sini tanımlayan sestamibili tek foton emisyonlu bilgisayarlı tomografi ve ultrasonografi ile elde edildi. Hastaların % 22.16'sında minimal invaziv yöntem, %76,94'ünde bilateral boyun eksplorasyonu tercih edildi. 3 hastada sternotomi gerekti. Patolojik bezlerin ektopik lokalizasyonu 26 (% 7.78) hastada mevcuttu. Eş zamanlı tiroidektomi 124 (% 37.12) hastaya uygulandı. 14 (% 11.29) hastada rastlantısal tiroid maligniteleri teşhis edildi. Persitent ve rekürren hastalık görülme sıklıkları sırasıyla 6.88% ve 4.19% olarak tespit edildi.

SONUÇ: PHPT, multidisipliner bir yaklaşım gerektirir. Cerrahi tedavi, düşük komplikasyon oranları ile% 95'in üzerinde iyileşme sağlayabilir. Anormal bezler için dikkatli lokalizasyon çalışmaları ve eşlik eden tiroid patolojileri için ayrıntılı incelemelerin ameliyat başarısını daha da artıracağına inanıyoruz.

Anahtar Kelimeler: *Pimer hiperparatiroidizm, paratiroid lokalizasyonu, paratiroidektomi, cerrahi.*

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Local ethics board approval was obtained for this study, through registration number E-1-21-1469 (date: January 20, 2020).

INTRODUCTION

Primary hyperparathyroidism (PHPT) is a disease caused by excessive parathyroid hormone (PTH) secretion from one or more of the four parathyroid glands and often accompanied by hypercalcemia. It differs from the secondary and tertiary forms of hyperparathyroidism (HPT) by the absence of renal dysfunction. The estimated prevalence for PHPT, which is the most common cause of ambulatory hypercalcemia, is 0.86%. It is 3-4 times more common in women, and it peaks at the age of 55-75, especially in the postmenopausal period (1,2). The diagnosis of PHPT is biochemical. Although the presence of elevated PTH levels that are not suppressed usually accompanied by increased serum calcium levels is typical, some patients may also present with normal calcium levels (3). In the last four decades, with the introduction of biochemical screening tests into routine use, the clinical presentation of patients diagnosed with PHPT has changed from classical symptomatic (osteoporosis, fractures, nephrolithiasis, easy fatigability and weakness, etc.) to an asymptomatic disease. The most common cause of PHPT is single adenomas (approximately 80-85% of patients). In 5% of patients, adenomas might be double. Multigland disease (four glands parathyroid hyperplasia) accounts for 5-15% of patients. The rarest cause of PHPT is parathyroid cancer that occurs less than 1% (2,3). Parathyroidectomy is the most effective treatment for patients with PHPT and provides cure when performed by experienced parathyroid surgeons, with the rates exceeding 95% surgical success (4). While surgical treatment is recommended for all symptomatic patients with PHPT, surgical indications for asymptomatic patients are as follows; <50 years, >1 mg/dl above upper limit of normal serum calcium (consistently), kidney stones & nephrocalcinosis, hypercalciuria (>400 mg/day), fractures and <-2,5 at lumbar spine, hip or distal one-third radius (5). After preoperative imaging methods and a meticulous localization study, the surgical success achieved does not only provide a biochemical cure. There are many publications in the literature showing that bone and kidney manifestations improved, and neuromuscular and even cognitive functions improved following parathyroidectomy (6,7). However, 5-10% of patients may need to be operated again due to persistent or recurrent disease after parathyroidectomy (8).

The aim of this study is to evaluate the demographic, indications, validity of preoperative localization studies and operative details with surgical treatment outcomes in patients underwent parathyroidectomy for PHPT.

MATERIAL AND METHOD

We retrospectively evaluated the data of 334 patients diagnosed with PHPT at the breast and endocrine surgery department of a single tertiary level referral center between January 2014 and March 2019. Local ethics board approval was obtained for this study, through registration number E-1-21-1469 (date: January 20, 2020). This study was conducted in accordance with the Declaration of Helsinki. Written informed consent form was obtained from patients at the time of the registry.

Serum total calcium (Ca+2), ionized Ca+2, phosphorus (P), albumin, creatinine, PTH, 25-hydroxyvitamin D3 (25-OH D), and 24-hour urine Ca+2, P and creatinine values and lumbar, femur and radius bone mineral density was measured. Normal laboratory values in patients were determined as follows; Ca+2: 8.8-10 mg/dl, P: 2.3-4.7 mg / dl, albumin: 32-48 gt/L, creatinine: 07-1,3 mg/dL, PTH: 18-68 pg/ml, 25-OH D: 30-100 ng/mL and 24-hour urine Ca+2 level: 100-400 mg/dl. Results outside of these reference values were evaluated by the Department of Endocrine and Metabolic Diseases. Patients diagnosed with pHPT were evaluated for multiple endocrine neoplasia (MEN) and other hereditary diseases, and patients with an indication for surgery were consulted to our clinic. Urinary system ultrasonography (US) was performed to all patients to detect kidney stones or nephrocalcinosis. Technetium 99mTc-sestamibi using single-photon emission computed tomography (SPECT) and neck US were applied in the preoperative localizing the aberrant parathyroid tissues. Magnetic resonance imaging (MRI) and computed tomography(CT) were used to identify suspected ectopic disease in the mediastinum in case of persistent HPT. The accuracy rates of the radiological localization were calculated based on the surgically confirmed pathological parathyroid gland localization. A minimally invasive approach was preferred in cases where imaging studies were compatible and pointed to a common point for pathological parathyroid tissue. Minimally invasive parathyroidectomy was performed under general anesthesia, with an elliptical or midline 2-4 cm lateralized transverse incision in a skin fold on the side indicated by preoperative radiological localization studies. Intraoperative success and failure were assessed by measuring intact PTH levels. Success was defined as a "drop of 50% or more in the PTH level" relative to the measured levels just before surgery 10 minutes after removal of the abnormal gland(s). In case of failure, the incision was lengthened, and all four glands were evaluated with bilateral neck exploration.

Surgical methods, histopathological results, serum Ca+2 and PTH results in the early postoperative period and after the 6th month were also evaluated. Recurrence of hypercalcemia and occurrence of high PTH values within 6 months postoperatively was considered as persistent hyperparathyroidism, whereas occurrence of this condition after 6 months was accepted as recurrent hyperparathyroidism. In addition, the frequency of concomitant thyroidectomy performed during parathyroid surgery and thyroid pathologies accompanying PHPT were analyzed.

Statistical Analysis:

All statistical tests were performed using SPSS, version 18.0, software (SPSS Inc., Chicago, IL). The Shapiro-

Wilk test was used to assess the normality of data distribution. Continuous data were presented as the mean value ± standard deviation (SD) or median and interquartile range (IQR) according to data distribution. Categorical variables were demonstrated with frequency and percentage values.

RESULTS

A total of 334 patients (ranging from 16 to 86) with a median age of 54 years were included in this study. Of these, 285 (85.3%) were female and 49 (14.7%) were male. The most common symptom was related to the musculoskeletal system. According to the clinical administration of PHPT, 241 (72.15%) of the patients were classified as symptomatic, and 93 (27.85%) were asymptomatic. Baseline characteristics of PHPT patients were shown in **Table 1.**

Table 1. Baseline characteristics of PHPT patients (n=334)

Characteristics	n (%)
Age (year)	53.56±12.32
Gender (Female/Male)	285/49 (85.3/14.7)
Total calcium (mg/dL)	11.05±0.90
Ionized calcium (mg/dL)	5.7±0.5
Phosphorus (mg/dL)	2.54±0.53
Creatinine (mg/dL)	0,83±0,18
Alkaline phosphatase (IU/L)	113.72±88.39
Parathyroid hormone (pg/mL)	219.54±206.61
25-OH D (ng/mL)	17.54±21.46
24-hour urinary calcium (mg/day)	358.2±274.6
Kidney stone & nephrocalcinosis	59 (17.7)
Osteoporosis	153 (45.8)
Osteopenia	112 (33.53)
Symptomatic PHPT	241 (72.15)
Asymptomatic PHPT	93 (27.85)

Data are presented as mean±SD for age, preoperative total and ionized calcium, phosphorus, creatinine, alkaline phosphatase, parathyroid hormone, 25-OH D and 24-hour urinary calcium.

Preoperatively, Technetium 99m Tc-sestamibi using SPECT was performed in 323 patients, USG in 283, MRI in 37, and CT in 8 patients. MEN syndrome was detected in 5 (1.49%) patients. Data on the diagnostic accuracy of preoperative imaging studies in the localization of the pathological parathyroid gland (s) are shown in **Figure 1.** Medical treatment for hypercalcemia was applied to 69 (20.65%) patients before surgery. All patients operated under general anesthesia, and 74 (22.16%) of the patients were operated with the minimally invasive method, 257 (76.94%) of them with conventional neck exploration. Sternotomy was required in 3 patients to remove pathological parathyroid tissue located intrathoracically.

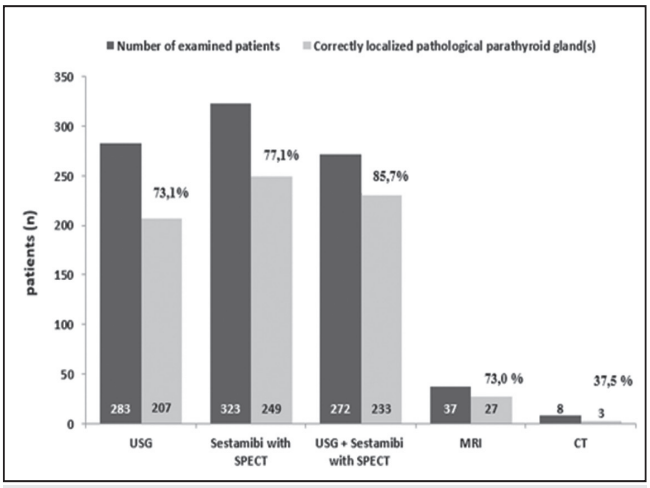

Figure 1. Diagnostic accuracy rates of preoperative imaging studies in the localization of pathological parathyroid gland(s)

Concomitant thyroidectomy was performed in 124 (37.12%) patients. Total thyroidectomy was performed in 91 patients and lobectomy in 33 patients. When postoperative complications were evaluated, transient and permanent hypocalcemia were observed in 17 (5.08%) and 9 (2.69%) patients, respectively. Unilateral recurrent laryngeal nerve injury was observed in 3 patients; while the injury was temporary in 2 patients, it became permanent in 1. Postoperative hemorrhage and hematoma were observed in 8 (2.39%) patients, but none required surgical intervention, all reabsorbed spontaneously. Ectopic localization of pathological glands was present in 26 (7.78%) patients. Of these, 11 were in thyrotymic tissue and thymus, 5 were in the thyroid, 4 were in the carotid sheath, 3 were in the anterior mediastinum, and 3 in tracheoesophageal groove. As a result of the pathology, single adenomas were the most defined pathology with 281 (84.13%) patients. Surgical details and histopathological results are presented in Table 2. Recurrent PHPT was observed in 14 (4.19%) patients (6 patients received medical follow-up, 2 patients were out of follow-up, 5 patients were reoperated with clinical improvement), 23 (6.88%) patients had persistent (11 patients were reoperated, 7 patients selected medical follow-up and 4 patients were not followed). When thyroid pathologies of concomitant thyroidectomies are examined, co-incidental thyroid malignancies were diagnosed in 14 (11.29%) patients, and all were papillary micro-carcinomas (≤1 cm). Other pathologies were as follows; multinodular goiter in 79 (63.70%), nodular goiter in 5 (4.03%), and thyroiditis in 26 (20.96%). The mean follow-up time after surgery was 17.24±3.55 months (10.84-26.55 months)

DISCUSSION

The incidence of PHPT has increased significantly over the past four decades, and the disease has become diagnosed at an asymptomatic stage due to the routine of biochemical screening and advances in imaging techniques (6,9). Surgery is the only curative treatment for symptomatic

patients and patients with asymptomatic PHPT who meet the criteria determined by the guidelines (1,5). On the other hand, close follow-up (annual assessment of serum calcium, bone mineral density, creatinine clearance, radiologic imaging for renal manifestations) is recommended for patients whose surgical indication has not yet occurred because the disease may progress over the years (5). A 15-year observational study by Rubin et al. revealed that; Although many patients initially not candidates for parathyroid surgery remained stable throughout the study period, a significant number of patients tended to worsen hypercalcemia, particularly between the 8th and 15th years, and developed criteria for parathyroid surgery with low hip and distal radial bone density (10).

In this study, in which we presented our series of 334 patients who were operated on for PHPT, the median age of the patients was 54 (16-86), consistent with the literature, and there was a significant female predominance (F/M: 5.81/1) (1-3). Symptoms that occur in PHPT are usually associated with increased PTH levels (bone disease and nephrolithiasis) and thus hypercalcemia (anorexia, constipation, polyuria, polydipsia and nausea). On the other hand, in a group of patients, we defined as asymptomatic, nonspecific complaints such as fatigue, weakness, decreased appetite, mild depression, and decreased cognitive functions may be the reason for referral to the physician (3). In our study, the most common reason for admission in symptomatic patients was musculoskeletal complaints, while the most common surgical indications in asymptomatic patients were decreased bone mineral density and urinary system stones. Although the surgical indications, symptoms, and laboratory findings of our patients were consistent with the literature, the number of symptomatic patients (%72.15) was higher than expected, contrary to the western literature (1,11,12). However, we are of the opinion that this rate cannot be generalized for our country. Because our hospital is a reference hospital and an institution that provides tertiary healthcare services. Some of our patients were diagnosed in town hospitals and were initially asymptomatic and followed for many years. Moreover, patients referred from centers with limited facilities where preoperative localization studies cannot be performed and patients who are preferred follow-up protocols due to comorbid diseases may increase the presentation with "symptomatic disease", too. As mentioned in the literature and confirmed by our study, single adenomas are the most common cause of PHPT. Less commonly, double adenomas, multiglandular disease, and rarely parathyroid carcinomas can be included in the etiology. The excision of the abnormally functioning parathyroid gland is the main goal of surgical treatment. In order to achieve this goal, it is necessary to correctly localize the abnormal gland before surgery in patients who have been biochemically diagnosed with PHPT. For this purpose, neck US and Sestamibi with SPECT are the most commonly used imaging methods in our clinic. Although US is cheap and non-invasive, does not require ionizing radiation, and allows evaluation of thyroid pathologies, the evaluation may not be optimal in cases with ectopic localization (mediastinum, retroesophageal region, etc.). Although the sensitivity rates reported for US to identify parathyroid glands vary between 72% and 89% in the literature, this rate is 73% in our study (3). This wide range can possibly be explained by the fact that US is operator dependent. On the other hand, sestamibi with SPECT is more useful in detecting posterior and small adenomas owing to its improved contrast resolution and providing 3-dimensional information. However, its sensitivity in the identification of a single adenoma varies between 80% and 90%, but this rate decreases in the case of double adenomas and multigland hyperplasia (13-14). In our study, while the rate of correct detection of sestamibi with SPECT was 77.1%, concordant sestamibi with SPECT and US identified 85.7% of abnormal parathyroid glands. Concordant findings obtained with different methods in preoperative localization studies may encourage surgeons to perform MIP. We performed MIP in only 22.16% (n = 74) of our patients. Of course, better cosmetic results, less postoperative pain, shorter operation time and same day discharge, together with low complication rates (1-3%) and high cure rates (98%) make this surgery very advantageous. Still, MIP may not be suitable for every patient (4). Bilateral neck exploration may be essential in cases with multiglandular hyperplasia, double adenomas, or ectopic localization. In our series, 14 (4.19%) of the patients had double adenomas and 37 (11.07%) had multiglandular hyperplasia. Although these rates are compatible with those in the literature, 124 of our patients underwent simultaneous thyroidectomy mostly due to existing pathologies and sometimes for better exploration. Intraoperative PTH monitoring is a routine practice in patients undergoing parathyroid surgery in our clinic. As in our series, the causes of failure seen in 16 (6.64%) patients were mostly double adenomas and cases with multiglandular hyperplasia.

Concomitant thyroid pathologies in patients with PHPT have been reported in 17-84% of patients (15). We performed simultaneous thyroidectomy in 124 (37.12%) of our patients. Although the accompanying pathologies in PHPT patients are mostly benign, co-incidental micropapillary thyroid cancer was diagnosed in 14 (11.29%) of our patients. Ryan et al. reported that they performed simultaneous thyroidectomy in 25% of PHPT patients and detected thyroid malignancy in 18% of their patients (8 of 45 patients) (15). Considering the postoperative complication rates in our study **(Table 2)**, our experience has shown that in the presence of concurrent hyperparathyroidism and nodular thyroid disease, it can be safely performed with one surgery in the same session.

Although surgical success is high in PHPT, it is reported that 1-10% recurrence, 2-22% persistent disease may develop (16-17). Lou et al. reported a recurrence rate of 14.8% of their patients after ten years of follow-up (18).
Inadequate preoperative localization studies and especially the presence of multiglandular hyperplasia and multiple adenomas are often reported as related factors.

Table 2. Features of surgery, complications and histopathological results.

Characteristics		n (%)
Surgical Procedure (n=334)	Minimally invasive parathyroidectomy	74 (22.16%)
	Conventional bilateral neck exploration	257 (76.94%)
	Sternotomy	3 (0.9%)
Intraoperative PTH monitoring (n=241)	Success	225 (93.36%)
	Failure	16 (6.64%)
Post-operative hypocalcemia	Temporary	17 (5.08%)
	Permanent	9 (2,69%)
RLN injury	Temporary	3 (0,89%)
	Permanent	1 (0.29%)
Postoperative hemorrhage		8 (2.39%)
Wound infection		3 (0.89%)
Removed parathyroid size (mm)		16 (5-62)*
Histopathological results	Single adenoma	281 (84.13%)
	Double adenomas	14 (4.19%)
	Multiglandular hyperplasia	37 (11.07%)
	Parathyroid carcinoma	2 (0.59%)
Persistent disease		23 (6.88%)
Recurrent disease		14 (4.19%)
Postoperative follow-up (month)		16.85 (10.84-26.55)

Data are presented as median (min-max) for removed parathyroid size and postoperative follow-up time.

The rate of persistent disease in our patients was 6.88%, and recurrent disease was 4.19%. A second adenoma with an ectopic location was detected in 5 of 11 patients who were persistent and operated again. In 2 patients, the existing single adenoma, which could not be found at the first operation due to inadequate imaging study, could only be removed in the second operation. Multiglandular hyperplasia was detected in the remaining 4 patients.

The most important limitation of this study is its retrospective nature and that the only center of the study limits the generalizability of statistics. Another limitation is the lack of data regarding the improvement in clinical signs of patients after parathyroidectomy. However, the strengths of our study are that the number of patients is sufficient for a single-center, all operations were performed by experienced endocrine surgeons, and the postoperative follow-up period of the patients was sufficient.

In conclusion, PHPT is a disease in which a multidisciplinary approach is inevitable. Surgical treatment can provide over 95% cure with low complication rates (19). However, as we reported in the series we present, there are some points to keep in mind. A preoperative comprehensive localization study is absolutely necessary for patients diagnosed with PHPT and scheduled for surgery. MIP may be the first choice in patients with compatible imaging methods in terms of localization, and intraoperative PTH monitoring may contribute to operative success. On the other hand, thyroid pathologies accompanying PHPT prove the necessity of careful examination of the thyroid gland before the operation. It should be kept in mind that although the accompanying pathologies are often benign, this may make it difficult to localize the preoperative abnormal parathyroid gland correctly. Despite the possibility of persistent and recurrent disease, postoperative follow-up should be continued for sufficient time.

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Statement of Ethics: Local ethics board approval was obtained for this study, through registration number E-1-21-1469 (date: January 20, 2020). This study was conducted in accordance with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Written informed consent form was obtained from patients at the time of the registry.

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REFERENCES

1.)Bilezikian JP, Bandeira L, Khan A, et al. Hyperparathyroidism.

Lancet. 2018; 13; 391: 168-78. doi: 10.1016/S0140-6736(17)31430-7.
2.)Bilezikian JP. Primary Hyperparathyroidism. J Clin Endocrinol Metab. 2018;103: 3993-4004. doi: 10.1210/jc.2018-01225.
3.)Machado NN, Wilhelm SM. Diagnosis and Evaluation of Primary Hyperparathyroidism. Surg Clin North Am. 2019; 99(4): 649-666. doi: 10.1016/j.suc.2019.04.006.
4.)Augustine MM, Bravo PE, Zeiger MA. Surgical treatment of primary hyperparathyroidism. Endocr Pract. 2011 ;17: 75-82. doi: 10.4158/EP10359.RA.
5.)Wilhelm SM, Wang TS, Ruan DT, et al. The American Association of Endocrine Surgeons Guidelines for Definitive Management of Primary Hyperparathyroidism. JAMA Surg. 2016; 151: 959-968. doi: 10.1001/jamasurg.2016.2310.
6.)Bilezikian JP, Cusano NE, Khan AA, et al. Primary hyperparathyroidism. Nat Rev Dis Primers. 2016; 2: 16033. doi: 10.1038/nrdp.2016.33.
7.)Udelsman R, Lin Z, Donovan P. The superiority of minimally invasive parathyroidectomy based on 1650 consecutive patients with primary hyperparathyroidism. Ann Surg. 2011; 253: 585-91. doi: 10.1097/SLA.0b013e318208fed9.
8.)Mazotas IG, Yen TWF, Doffek K, et al. Persistent/Recurrent Primary Hyperparathyroidism: Does the Number of Abnormal Glands Play a Role? J Surg Res. 2020; 246: 335-341. doi: 10.1016/j.jss.2019.08.007.
9.)Pallan S, Rahman MO, Khan AA. Diagnosis and management of primary hyperparathyroidism. BMJ. 2012; 344:e1013. doi: 10.1136/bmj.e1013.
10.)Rubin MR, Bilezikian JP, McMahon DJ, et al. The natural history of primary hyperparathyroidism with or without parathyroid surgery after 15 years. J Clin Endocrinol Metab. 2008; 93: 3462-70. doi: 10.1210/jc.2007-1215.
11.)Yadav SK, Johri G, Bichoo RA, et al. Primary hyperparathyroidism in developing world: a systematic review on the changing clinical profile of the disease. Arch Endocrinol Metab. 2020; 64: 105-110. doi: 10.20945/2359-3997000000211.
12.)Oberger Marques JV, Moreira CA. Primary hyperparathyroidism. Best Pract Res Clin Rheumatol. 2020; 34: 101514. doi: 10.1016/j.berh.2020.101514.
13.)Lavely WC, Goetze S, Friedman KP, et al. Comparison of SPECT/CT, SPECT, and planar imaging with single- and dual-phase (99m)Tc-sestamibi parathyroid scintigraphy. J Nucl Med. 2007 ;48: 1084-9. doi: 10.2967/jnumed.107.040428.
14.)Berri RN, Lloyd LR. Detection of parathyroid adenoma in patients with primary hyperparathyroidism: the use of office-based ultrasound in preoperative localization. Am J Surg. 2006;191: 311-4. doi: 10.1016/j.amjsurg.2005.10.027.
15.)Ryan S, Courtney D, Moriariu J, et al. Surgical management of primary hyperparathyroidism. Eur Arch Otorhinolaryngol. 2017;274: 4225-32. doi: 10.1007/s00405-017-4776-4.
16.)Kartal A, Çitgez B, Öden S, et al. Risk factors in the occurance of persistent primary hyperparathyroidism. Sisli Etfal Hastan Tip Bul. 2014; 48: 213-26.
17.)Bagul A, Patel HP, Chadwick D, et al. Primary hyperparathyroidism: an analysis of failure of parathyroidectomy. World J Surg. 2014; 38: 534-41. doi: 10.1007/s00268-013-2434-6.
18.)Lou I, Balentine C, Clarkson S, et al. How long should we follow patients after apparently curative parathyroidectomy? Surgery. 2017; 161: 54-61. doi: 10.1016/j.surg.2016.05.049.
19)Zhu CY, Sturgeon C, Yeh MW. Diagnosis and Management of Primary Hyperparathyroidism. JAMA. 2020; 323(12): 1186-87. doi: 10.1001/jama.2020.0538.

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Local ethics board approval was obtained for this study, through registration number E-1-21-1469 (date: January 20, 2020).