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RESEARCH

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Impact of intraoperative intact PTH monitoring on reoperation rates and surgical success in primary hyperparathyroidism

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Abstract

Background Primary hyperparathyroidism (PHPT) is caused by excessive parathormone secretion from one or more parathyroid glands. The primary treatment for PHPT is surgery. Due to anatomical variations in the parathyroid glands, preoperative localization, surgical approaches, and success rates can vary. With the development of advanced imaging techniques and the introduction of intraoperative intact PTH (i-PTH) measurement, traditional extended surgical approaches have increasingly been replaced by focused surgeries.

Objective Intraoperative i-PTH measurement has been applied by different surgeons using various criteria. This study aims to evaluate the effectiveness of intraoperative i-PTH measurement in improving surgical success, particularly in cases with inconclusive preoperative imaging results.

Methods Between January 2010 and September 2020, 203 adult patients who underwent surgery for PHPT in our clinic were included in the study. Patients were categorized into two groups: Group A (with intraoperative i-PTH measurement) and Group B (without i-PTH measurement). Persistent hyperparathyroidism was defined as elevated calcium levels occurring shortly after surgery, whereas recurrence was defined as calcium elevation after the 6th postoperative month. The absence of recurrence or persistent hypercalcemia was considered an indicator of surgical success.

Results The mean age of the patients was 54.6 ± 12.7 years. Of the 203 patients, 40 (19.7%) were male and 163 (80.3%) were female. No correlation was found between recurrence or persistence and patient age. The overall success rate was 93.6%. Surgical success was achieved in 97.8% of patients in Group A and 90% in Group B, indicating a statistically significant difference between the groups ($p = 0.023$).

Conclusion Intraoperative i-PTH measurement significantly increases the success rate of PHPT surgery, reducing the incidence of recurrent or persistent cases and the need for secondary operations. Consequently, it helps prevent complications associated with reoperations. These findings highlight the pivotal role of intraoperative i-PTH monitoring in optimizing surgical outcomes, especially in complex PHPT cases.

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Keywords Primary hyperparathyroidism (PHPT), Intraoperative parathyroid hormone (i-PTH), Parathyroidectomy, Persistent, Recurrence

Introduction

In primary hyperparathyroidism (PHPT), excessive secretion of parathormone (PTH) occurs due to the development of one or more adenomas in the parathyroid glands [1, 2]. The primary treatment for PHPT is surgery. If there is no contraindication or significant comorbidity, surgical treatment is recommended even in asymptomatic patients [3].

Typically, there are four parathyroid glands: two located posterior to the upper thyroid lobes and two located posterior to the lower lobes. Due to their embryological development, these glands may sometimes be located ectopically, making localization challenging [4, 5].

Targeted parathyroidectomy using minimally invasive techniques can generally be performed in patients whose diseased glands are localized through preoperative imaging. In cases with uncertain localization or discordant imaging findings, bilateral neck exploration—meaning four-gland exploration—may be required instead of a focused approach. After the introduction of intraoperative intact PTH (i-PTH) measurement, many surgeons began using this method to assess surgical success in real-time. In this approach, i-PTH is measured 10 min after removal of a parathyroid gland that is either enlarged or suspected to be pathologic based on preoperative imaging or intraoperative evaluation. If the measured value decreases by more than 50% compared to the baseline level at the beginning of surgery, the operation is terminated—this is known as the Miami criterion. This strategy helps reduce the risk of complications from extended exploration, shortens the duration of surgery, limits anesthesia exposure, and reduces overall costs [6]. In our clinic, intraoperative i-PTH monitoring was adopted into routine practice in accordance with the Miami criteria [7].

In our study, patients with persistently elevated postoperative calcium (Ca) were considered to have persistent hyperparathyroidism, while calcium elevation occurring after the 6th postoperative month was classified as recurrence. The absence of recurrence or persistent hypercalcemia was accepted as an indicator of surgical success.

We aimed to evaluate whether intraoperative i-PTH monitoring is effective in improving the success rate of surgery. While intraoperative i-PTH monitoring is already well-established in parathyroid surgery, this study uniquely assesses its impact on reoperation rates in a cohort with variable preoperative imaging results. Additionally, our study highlights the potential benefits of i-PTH monitoring in reducing recurrence and persistence rates, particularly in challenging cases with ectopic or poorly localized glands.

Material and method

Between January 2010 and September 2020, adult patients who underwent surgery for primary hyperparathyroidism (PHPT) at the General Surgery Clinic of Gazi University were evaluated. The prospectively recorded data of these patients were retrospectively reviewed and analyzed. Demographic characteristics, as well as preoperative, intraoperative, and postoperative biochemical parameters, radiological, scintigraphic, and histopathological findings of 203 patients who met the study criteria were included in the analysis.

Patients with known multiglandular disease, such as those with Multiple Endocrine Neoplasia (MEN), were excluded to focus solely on sporadic cases of PHPT. In cases where the intraoperative i-PTH decrease was insufficient, bilateral exploration was performed and all parathyroid glands were evaluated to prevent incomplete resections. Patients with impaired renal function, particularly those undergoing dialysis, were excluded to avoid potential confounding effects on PTH metabolism. Patients were divided into two main groups: Group A and Group B. Intraoperative frozen section analysis was performed in all cases.

Patients in Group A were evaluated for preoperative serum i-PTH levels. Based on radiological and nuclear medicine imaging, a targeted incision was made, and the tissue suspected to be a parathyroid adenoma was sent for frozen section analysis. In Group A, intraoperative i-PTH was first measured immediately after induction of anesthesia to establish a baseline. A second sample was obtained exactly 10 min after removal of the suspected parathyroid gland. If the PTH decrease was less than 50%, a third sample was taken at the 20th minute. No further intraoperative i-PTH measurements were performed beyond this point. Surgical decisions were guided by both i-PTH dynamics and frozen section results.

The operation was concluded when the i-PTH level decreased by more than 50% and frozen section confirmed the excised tissue as parathyroid. If the expected decrease in i-PTH did not occur and frozen section was inconclusive, further exploration was performed to identify the adenoma. In cases where either the i-PTH dropped adequately but frozen section did not confirm parathyroid tissue, or vice versa, surgical exploration was continued to minimize the risk of incomplete resection.

In Group B, intraoperative i-PTH levels were not measured. Surgery was guided solely by preoperative imaging results. The excised tissue was sent for frozen section analysis. If parathyroid tissue was confirmed, the operation was concluded. If the frozen section did not confirm parathyroid tissue, surgical exploration continued until a parathyroid adenoma was identified.

Patients were assigned to Group A or Group B based on the availability of intraoperative i-PTH monitoring equipment at the time of surgery. Baseline characteristics between the groups—including age, gender, and preoperative imaging results—were compared, and no significant differences were found, minimizing potential selection bias.

Patients with elevated serum PTH levels and normocalcemia were evaluated separately to distinguish primary hyperparathyroidism from other potential causes of hyperparathyroidism. These patients were considered for additional diagnostic workup to exclude secondary causes.

Serum PTH, calcium, phosphorus, and vitamin D levels were analyzed preoperatively and re-evaluated at 24 h and 6 months postoperatively. The first follow-up visit was scheduled for postoperative day 1, and long-term follow-up was conducted at 6 months. Definitive histopathological reports were typically available within 5–7 working days after surgery.

Intraoperative i-PTH measurements and frozen section analyses were performed during surgery. Preoperative localization of parathyroid glands was determined by ultrasonography (USG), technetium-99 m sestamibi (Tc-99 m), or single-photon emission computed tomography (SPECT), with standardized imaging protocols applied to all patients. Discrepancies in imaging findings were compared with intraoperative findings.

Normal reference ranges for laboratory parameters in adults were: 12–88 pg/mL for intact PTH, 8.5–10.5 mg/dL for serum calcium, 2.5–4.5 mg/dL for serum phosphorus, and 30–100 ng/mL for vitamin D. Serum calcium levels were corrected for albumin using a standardized formula provided by the clinical laboratory. Bone mineral density (BMD) of the lumbar vertebrae was assessed using T scores. T scores of -1.0 and above were classified as normal, between −1.0 and −2.5 as osteopenia, and −2.5 or below as osteoporosis. Histopathological findings were classified into four categories: normal parathyroid tissue, parathyroid adenoma, parathyroid carcinoma, and parathyroid hyperplasia. Because parathyroid adenomas are typically bean-shaped, their volume was calculated using the ellipsoid formula [8].

In our laboratory, CLIA (chemiluminescence immunoassay) is used for routine serum i-PTH measurement, while ECLIA (electrochemiluminescence immunoassay) is used intraoperatively for rapid i-PTH analysis. As the two methods differ in measurement principles and reference ranges, results were only compared when measured by the same method. For intraoperative rapid i-PTH assessment, an adequate blood sample was collected in EDTA tubes as per standard protocol.

Only conventional (open) parathyroidectomy was performed in our clinic. Two main surgical approaches were used: targeted parathyroidectomy was generally preferred when preoperative imaging provided accurate localization and there was no need for concurrent thyroid surgery. If no lesion was found at the location indicated by imaging, or if frozen section findings were inconsistent with parathyroid tissue, or if laboratory results (i.e., intraoperative i-PTH decrease less than 50%) did not confirm complete excision, extended exploration was performed. Extended procedures were defined as unilateral when continued on the same side, and bilateral when extended to the opposite side of the neck.

PTH and serum calcium levels were measured at 24 h postoperatively in both groups. A serum calcium level below 10.5 mg/dL and a PTH level within the normal range on the first postoperative day were considered indicators of initial surgical success. Both parameters were evaluated together to assess early biochemical response. Serum PTH, calcium, phosphorus, and vitamin D levels were reassessed at the 6-month follow-up visit. Relationships among these variables were also examined.

Patients with elevated postoperative calcium levels were considered to have persistent hyperparathyroidism. Those with elevated calcium levels appearing after the 6th postoperative month were classified as recurrent cases. In this study, surgical success was defined as the absence of both recurrence and persistence.

All procedures in this study were conducted in accordance with the ethical standards of the institutional research committee and the principles of the 1964 Declaration of Helsinki and its subsequent amendments. This retrospective study was approved by the Gazi University Faculty of Medicine Institutional Review Board (Approval No: 757 – 09.11.2020). The need for individual informed consent was waived by the ethics committee due to the retrospective nature of the study.

Statistical analysis

Descriptive statistics were used to evaluate gender and age distributions, frequencies of preoperative imaging and intraoperative findings, number of imaging studies, and pathology results according to surgical method. The Chi-square test was employed to analyze categorical variables such as the presence of recurrence or persistence, type of surgery, laterality, additional surgical procedures, and multifocality, as well as the occurrence of recurrence or persistence according to age groups and PTH level categories in patients with and without intraoperative i-PTH monitoring (Groups A and B).

Table 1 Gender and age distribution of patients

	Male		Female	
	A group	B group	A group	B group
n	13	27	80	83
Age. Mean ± SD	53 ± 13.6	57.6 ± 13.7	55.1 ± 11.5	53.5 ± 13.4
Age. minimum	20	20	23	21
Age. maximum	70	78	77	86
Total. n (%)	40 (19.7%)		163 (80.3%)	

SD: standard deviation. n: number

For continuous variables such as excised gland weight, volume, PTH decline rate, and comparisons of weight and volume based on the surgical technique, the Mann-Whitney U test was applied as a nonparametric alternative, since the data did not follow a normal distribution. Spearman's correlation test was used to evaluate the relationships between the PTH decline rate and preoperative PTH levels, gland weight and volume, calcium/phosphorus ratio, and vitamin D levels due to the presence of outliers.

All statistical analyses were performed using SPSS version 26.0 (License No.: 9869264, SPSS Inc., Chicago, IL, USA) and R Studio software. A p-value of < 0.05 was considered statistically significant.

Results

Of the 203 patients included in the study, 163 (80.3%) were female. The mean age of the patients was 54.6 ± 12.7 years. Patients were divided into two groups: Group A ($n = 93$) underwent intraoperative PTH measurement, whereas Group B ($n = 110$) did not **(**Table 1**)**.

The localizations of the parathyroid glands that were considered pathological during intraoperative evaluation and excised as single glands were analyzed. The most common localization was the left inferior ($n = 77$, 37.9%), followed by the right inferior ($n = 71$, 35%), left superior ($n = 14$, 6.9%), and right superior ($n = 6$, 3%). In addition, 22 patients (10.8%) had ectopic parathyroid glands, located in the retrosternal area ($n = 8$), thyrothymic ligament ($n = 6$), carotid sheath ($n = 3$), intrathyroidal region ($n = 3$), and anterior mediastinum ($n = 2$).

More than one gland was excised in 13 patients; in all of them, no more than two glands were removed. In 5 (2.5%) of these cases, the excised glands were unilateral, while in 8 (3.9%) they were bilateral. Preoperative imaging findings (USG, SPECT, and Tc-99 m sestamibi) and intraoperative localization results were recorded and analyzed. Multifocality was initially suspected intraoperatively based on the removal of more than one parathyroid lesion, but final classification was confirmed by histopathological examination. Cases in which more than one lesion was removed were considered multifocal **(**Table 2**)**.

In this study, the absence of recurrence or persistent disease was considered an indicator of surgical success. A total of 190 patients (93.6%) achieved surgical success. When evaluated separately, 91 patients (97.8%) in Group A and 99 patients (90%) in Group B achieved surgical success. This difference between groups was statistically significant ($p = 0.023$).

Multifocality status was also analyzed separately for the two groups. In Group A, multifocality was found in 7 patients (7.5%), and none of these patients developed recurrent or persistent PHPT. In Group B, multifocality was observed in 6 patients (5.5%), and recurrent or persistent PHPT developed in 3 of them. Statistical analysis revealed no significant difference between the groups regarding multifocality ($p = 0.548$). Overall, multifocal disease was observed in 13 patients (6.4%): 7 patients (7.5%) in Group A and 6 patients (5.5%) in Group B. Among these, 3 patients in Group B developed recurrent or persistent PHPT, while none of the multifocal patients in Group A experienced recurrence or persistence **(**Table 3**)**.

Not all patients underwent the same number of preoperative imaging studies. While some underwent only

Table 2 Localizations according to preoperative imaging and intraoperative findings

Localization	Intraoperative		USG		SPECT		TC-99 m sestamibi	
	n	%	*n*	%	*n*	%	*n*	%
Right superior	6	3.0	4	2.0	0	0	2	1.0
Right inferior	71	35.0	61	30.0	24	11.8	41	20.0
Left superior	14	6.9	11	5.4	4	2.0	6	3.0
Left inferior	77	37.9	67	33.0	27	13.3	43	21.2
Two localizations on the same sides	5	2.5	4	2.0	1	0.5	4	2.0
Two localizations on different sides	8	3.9	1	0.5	0	0	3	1.5
Ectopic	22	10.8	12	5.9	15	7.4	14	6.9
No examination	-	-	23	11.3	116	57.1	73	36.0
Normal	0	0	20	9.9	16	7.9	17	8.4
Total	203	100	203	100	203	100	203	100

n. number, USG: ultrasonography, SPECT: single photon emission computed tomography, TC-99: technetium 99

Table 3 Multifocality. Type of surgery. Laterality. Additional surgery. Recurrent or persistent PHPT rates

	A group (*n* = 93)		B group (*n* = 110)		*p*
	n	%	*n*	%	
Recurrent or persistent PHPT					
Positive	2	2.2	11	10	0.023
Negative	91	97.8	99	90	
Surgery type					
Focused	64	68.8	65	59.1	0.151
Extended	29	31.2	45	40.9	
Laterality					
Unilateral	15	16.1	17	15.4	0.237
Bilateral	14	15.1	28	25.5	
Additional surgery					
Total Thyroidectomy	1	1.1	4	3.6	0.750
Lobectomy	3	3.2	7	6.4	
Thymectomy	2	2.2	2	1.6	
Multifocality					
Positive	7	7.5	6	5.5	0.548
Negative	86	92.5	104	94.5	

n: number, p: value, PHPT: Primary Hyperparathyroidism

p value < 0.05 is considered a statistically significant difference

Table 4 Comparison of parathyroid gland weight and volume in patients with and without recurrent or persistent disease, intraoperative PTH decrease rate and recurrent-persistent disease

	Relapse or persistent (+) (min-max)	Relapse or persistent (-) (min-max)	*p*
Weight, (g)	0.50 (0.11–2.1)	0.8 (0.1–14)	0.066
Volume, (mm^3)	314 (4.19–3140)	688 (14.1-19792)	0.024
i-PTH decline rate, n			
<50%, 7	1 (50%)	6 (6.6%)	
50–70%, 17	1(50%)	16 (17.6%)	
>70%, 69	0 (0%)	69 (75.8%)	
Total, 93	2 (100%)	91 (100%)	

g: gram, mm^3: cubic millimeter, min: minimum, max: maximum, p: value, n: number, PTH: parathormone, i-PTH: intact parathormone

one imaging modality (e.g., USG or SPECT), others had two or even three different imaging procedures. In Group A (i-PTH), two patients with recurrence had three preoperative imaging studies. In Group B (non-i-PTH), five patients with recurrence also underwent three imaging studies. Neck ultrasonography (USG) could not be performed in some cases due to technical limitations or scheduling issues. In several cases of recurrence or persistence, preoperative imaging failed to localize an enlarged parathyroid gland, potentially contributing to incomplete resection. These findings underscore the added value of intraoperative i-PTH monitoring in such challenging cases.

When the final pathology results of the patients were analyzed ($n = 203$), 183 (90.1%) had parathyroid adenoma, 13 (6.4%) had parathyroid hyperplasia, 1 (0.5%) had parathyroid carcinoma, and the remaining 6 patients (3%) had histologically normal parathyroid tissue without pathological findings.

A total of 13 patients developed either recurrence or persistence. Of these, 2 were from Group A and 11 were from Group B. In Group A, both patients had adenomas confirmed by preoperative imaging and pathology. One of them underwent reoperation and achieved biochemical cure, while the other was managed conservatively due to comorbidities. In Group B, 4 patients had persistent disease, and 7 developed recurrence. Among them, 3 underwent reoperation: 2 achieved cure, and 1 continued to have biochemical abnormalities due to failure to localize ectopic parathyroid tissue. The pathological diagnoses in these patients included 6 adenomas, 3 histologically normal parathyroid tissues, and 2 hyperplasias.

Postoperative calcium, PTH, and phosphorus levels varied depending on recurrence status, but were generally elevated in active disease cases. Based on pathology reports, the weights and volumes of the excised glands were calculated. Gland diameters in all three axes were recorded, and since parathyroid glands are typically bean-shaped, the volume was estimated using the "rotator ellipse" formula.

When patients with recurrence or persistence were compared with those without, the median gland weight in the non-recurrent group was approximately twice as high. However, this difference did not reach statistical significance ($p = 0.066$). On the other hand, the volume of excised glands was significantly lower in patients with recurrence or persistence and this difference was statistically significant ($p = 0.024$) (Table 4**).**

One of the causes of recurrence or persistence is undetected multiglandular disease. In our study, when recurrence or persistence rates were analyzed according to age, 6 of 127 patients under 60 years of age and 7 of 76 patients over 60 years of age were affected. This difference was not statistically significant ($p = 0.166$) (Fig. 1**).**

PTH decline rates were calculated for the 93 patients in whom intraoperative PTH was measured (Fig. 2**).** Upon analysis, it was strikingly noted that none of the patients with a PTH decline rate greater than 70% developed recurrence or persistence. In contrast, one patient with a decline between 50 and 70% and one patient with a decline below 50% experienced recurrent or persistent disease. Among those without recurrence or persistence, 75.8% had an intraoperative PTH decline above 70%, 17.6% between 50 and 70%, and 6.6% below 50%. The median PTH decline was 80.6 (18.09–98.45) in patients without recurrence or persistence, and 16.8 (-28.7–62.5) in those with recurrence or persistence ($p = 0.042$) (Fig. 3; Table 4**).**

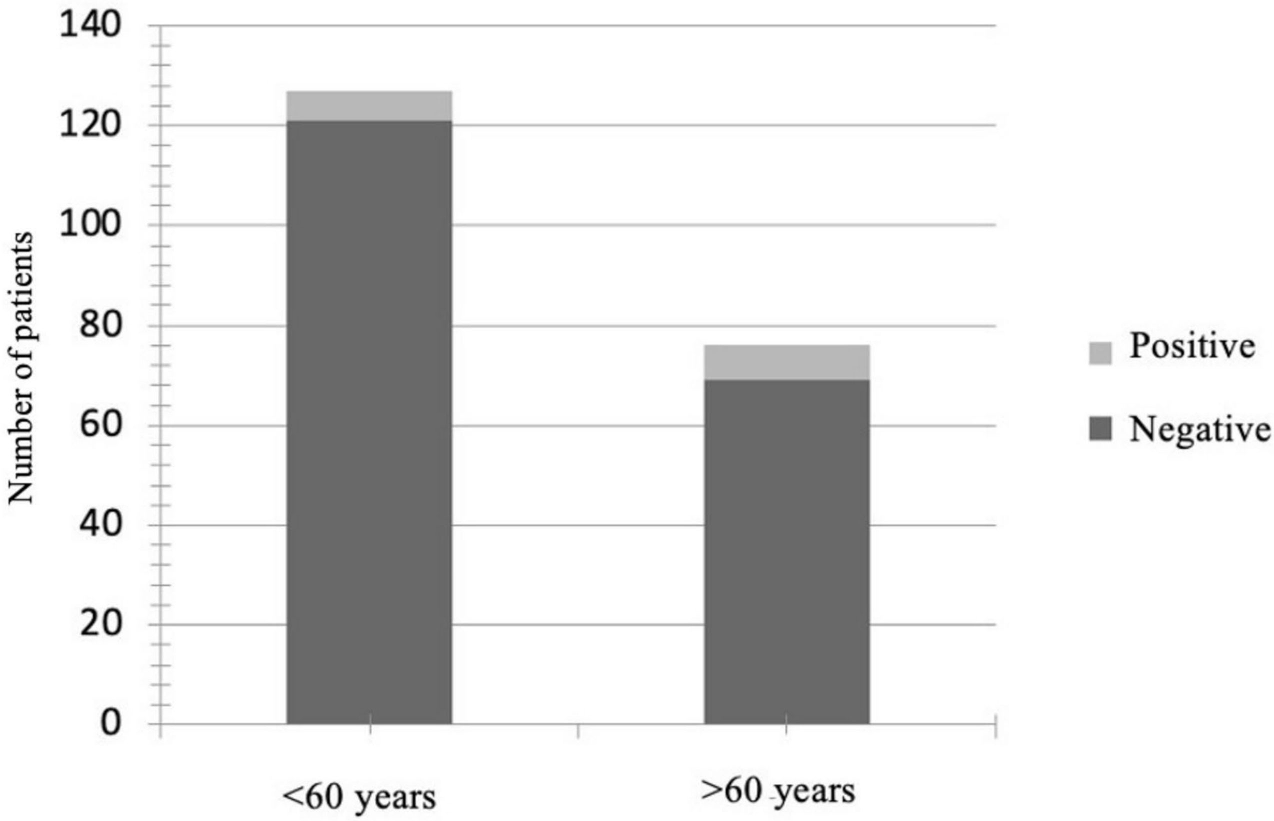

Fig. 1 Relapse or Persistence rate by age

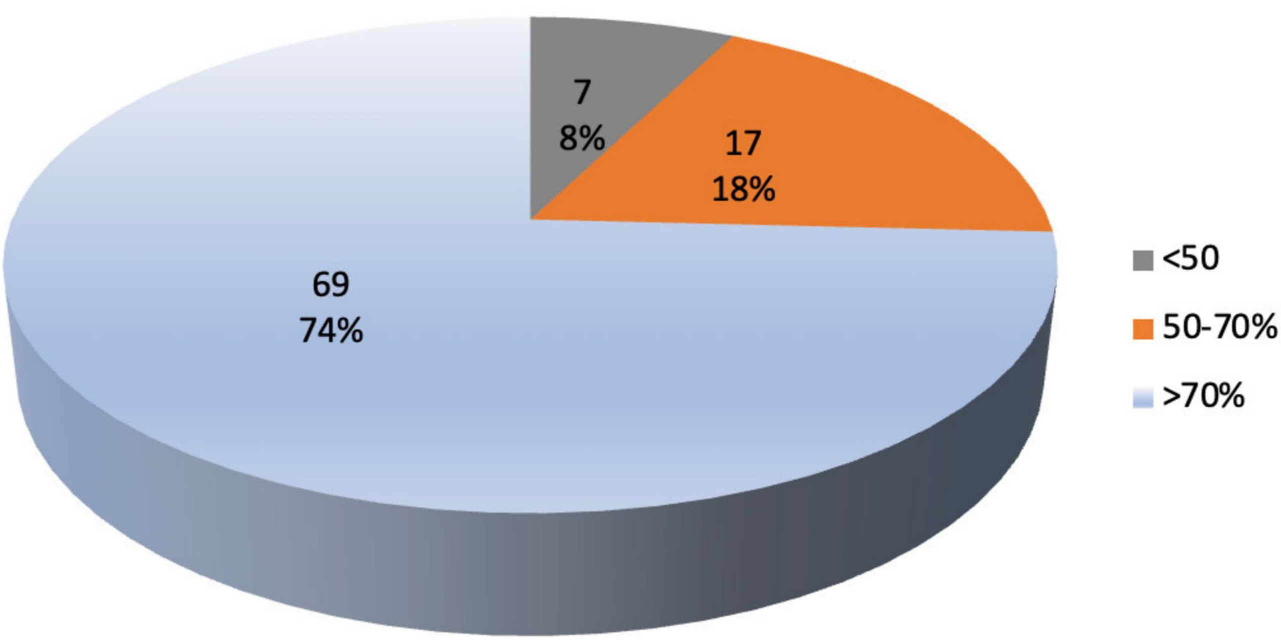

Fig. 2 Intraoperative PTH decline ratio distribution

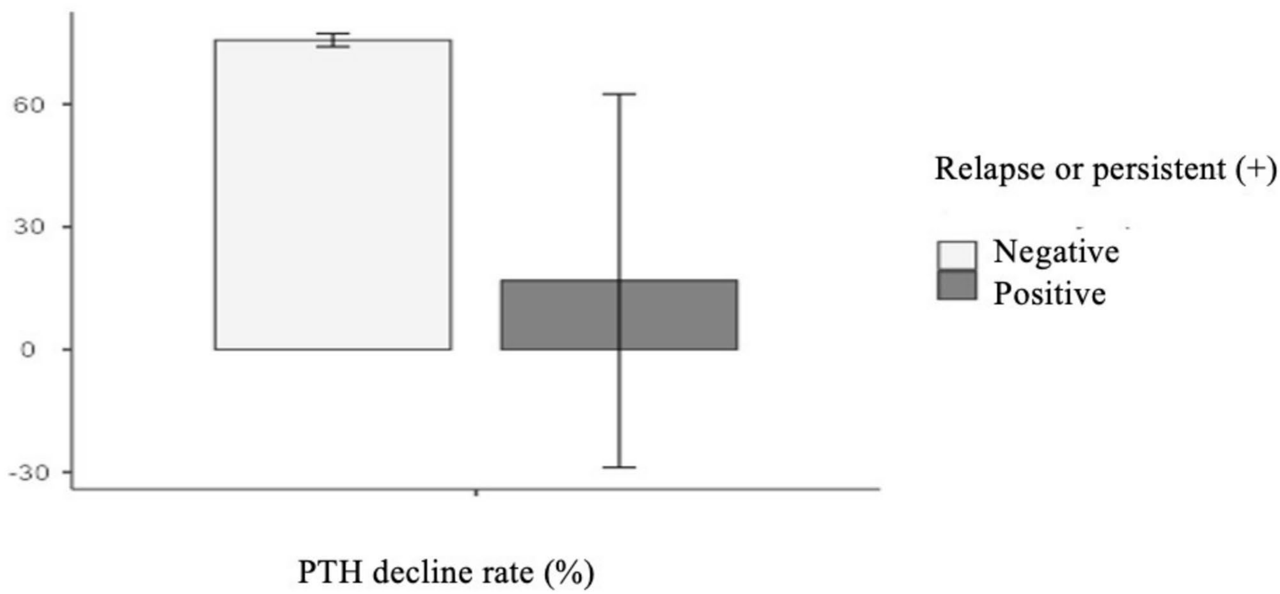

Fig. 3 Relapse or persistence and PTH decline rate

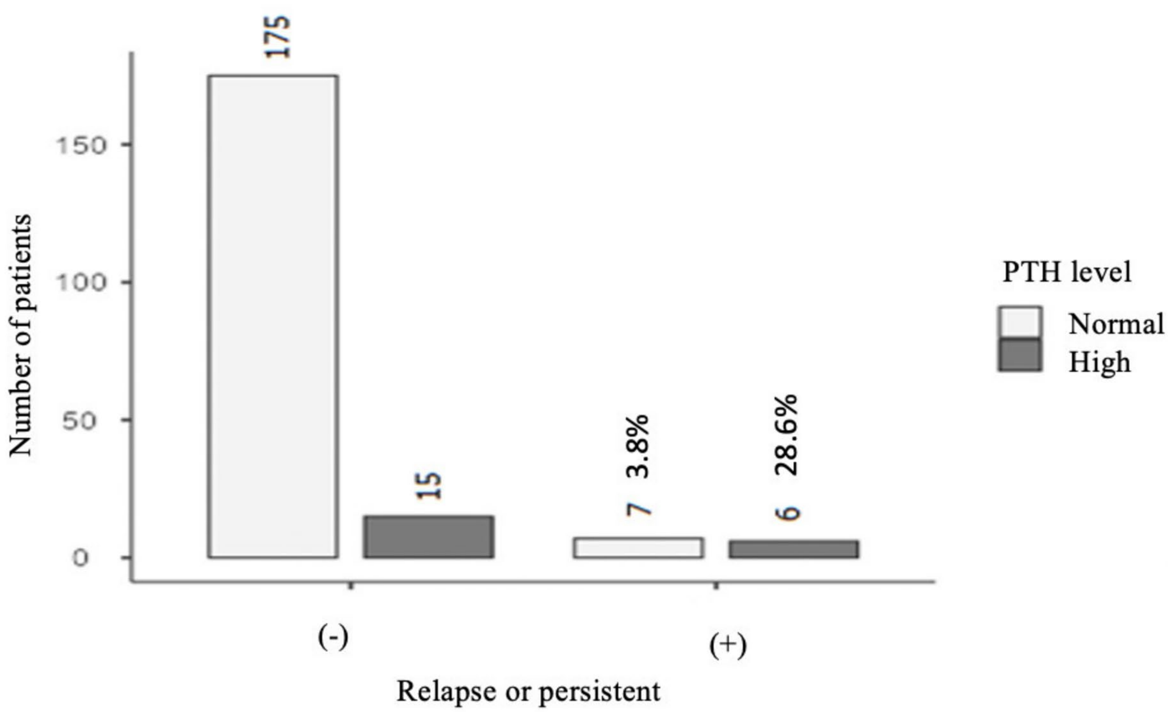

Fig. 4 Recurrence or persistence rate with postoperative PTH

Postoperative PTH values on the first day were within the normal range (≤ 88 pg/mL) in 182 patients (89.6%) and elevated (> 88 pg/mL) in 21 patients (10.4%). Among those with normal postoperative PTH, recurrence or persistence occurred in 2 patients from Group A and 5 from Group B. Among those with elevated postoperative PTH, no recurrence or persistence occurred in Group A, while 6 patients in Group B experienced recurrent or persistent disease. This difference was statistically significant ($p < 0.001$) (Fig. 4).

At the sixth postoperative month, PTH levels were normal (≤ 88 pg/mL) in 163 patients (80.2%) and elevated (> 88 pg/mL) in 40 patients (19.8%). Recurrence or persistence was observed in 3 of the 163 patients (1.8%)

Table 5 Preoperative and postoperative laboratory results of the patients

Test	Preoperative	Postoperative	Postoperative 6th month
PTH (pg/ml), mean ± SD	233.21 ± 300.8	55.75 ± 164.9	79.36 ± 138
Phosphorus (mg/dL), mean ± SD	2.74 ± 0.59	-	3.30 ± 0.67
Calcium (mg/dL), mean ± SD	11.12 ± 0.73	9.50 ± 0.76	9.48 ± 0.74
Vitamin D (ng/mL), mean ± SD	18.97 ± 9.56	-	24.68 ± 14.10
Ca/P ratio, mean ± SD	4.25 ± 1.01	-	3.03 ± 0.974

PTH: parathormone, Ca: calcium, P: phosphorus, SD: standard deviation

with normal PTH and in 10 of the 40 patients (25%) with elevated PTH levels. Among the 30 patients who had elevated PTH levels at the sixth month but did not develop recurrence or persistence, 25 had vitamin D deficiency, while 5 did not. The effect of vitamin D deficiency on postoperative PTH elevation was not statistically significant ($p = 0.818$).

When comparing preoperative and postoperative laboratory values, there was a significant reduction in serum intact PTH and serum calcium levels. Additionally, the mean serum phosphorus level increased from 2.74 ± 0.59 mg/dL preoperatively to 3.30 ± 0.73 mg/dL postoperatively (Table 5).

Of the 116 patients who underwent lumbar vertebral bone mineral density (BMD) evaluation, 42 (36%) had osteopenia, 16 (13.7%) had osteoporosis, and 58 (50%) had normal BMD values. A positive correlation was found between preoperative PTH and the calcium/phosphorus (Ca/P) ratio ($p < 0.001$, $r = 0.278$) (Fig. 5). The correlation between PTH decline rate and Ca/P ratio was not statistically significant ($p = 0.909$). A negative correlation was observed between vitamin D levels and preoperative Ca/P ratio ($p = 0.018$, $r = -0.166$) (Fig. 6).

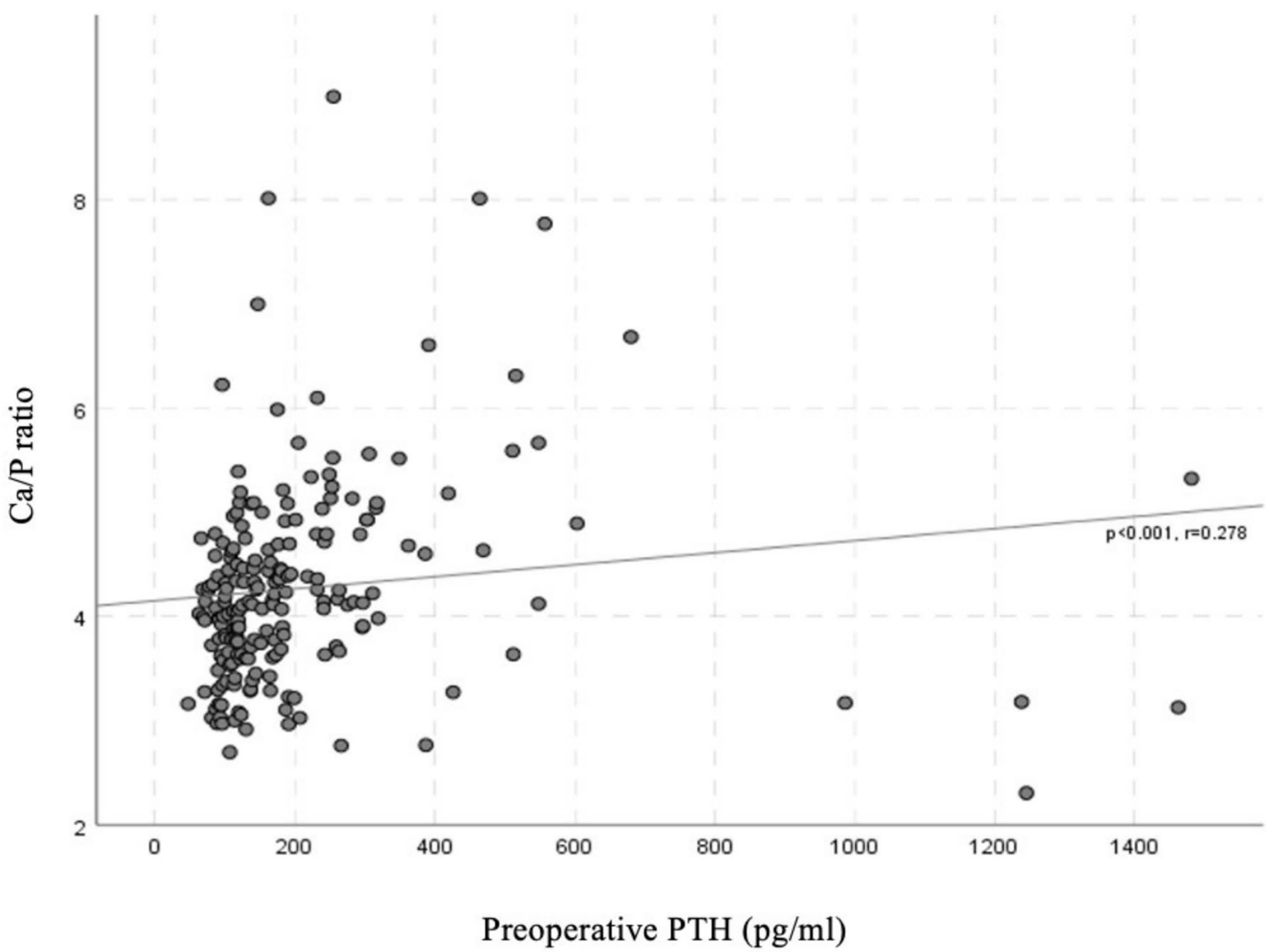

Fig. 5 Correlation between preoperative PTH and calcium/phosphorus (Ca/P)

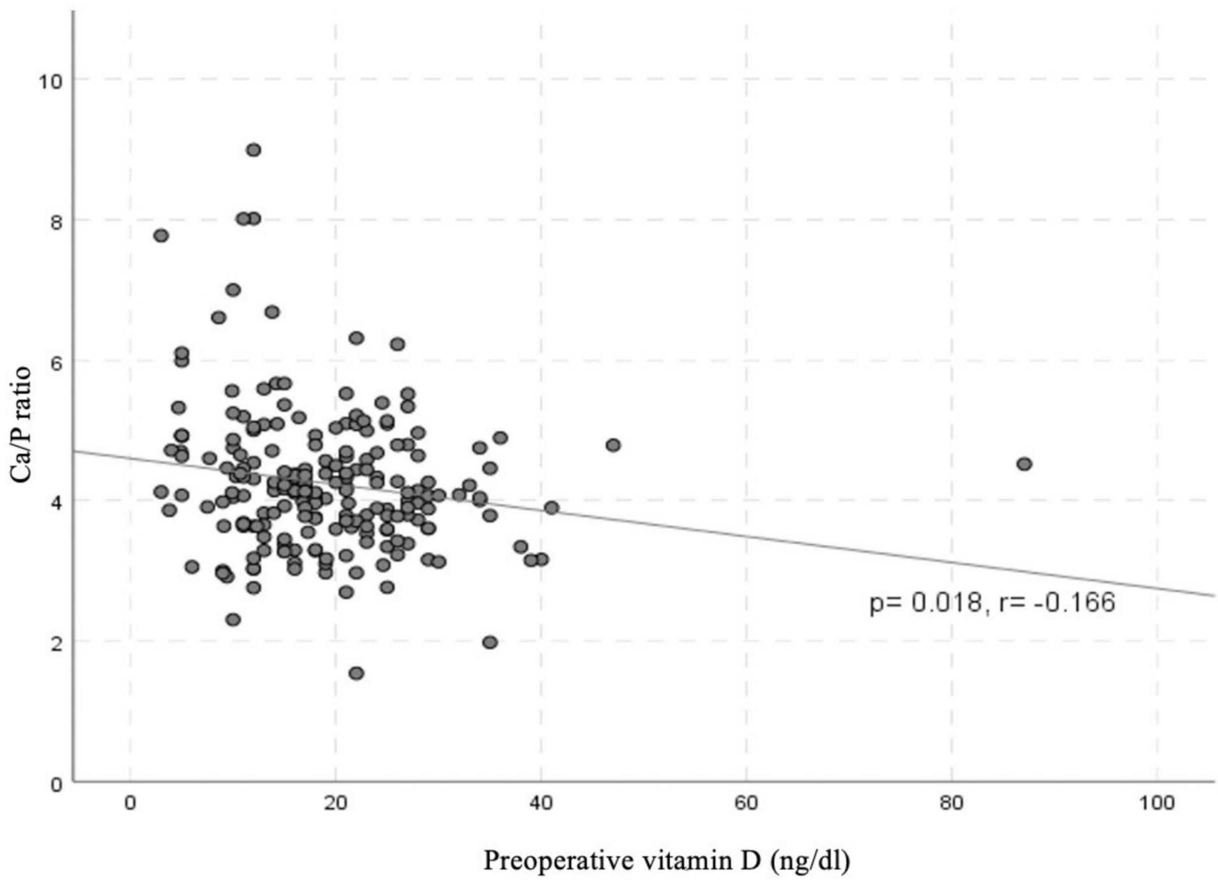

Fig. 6 Correlation between preoperative Ca/P ratio and vitamin D

Discussion

Primary hyperparathyroidism (PHPT) is an endocrine disorder characterized by excessive parathormone (PTH) secretion, leading to hypercalcemia due to adenoma, hyperplasia, or, rarely, carcinoma of the parathyroid glands. This hypercalcemic state results in a spectrum of symptoms, particularly affecting the renal and skeletal systems. PHPT most commonly occurs in individuals aged 50 to 60, with a reported female-to-male ratio of approximately 4:1 [9–12]. In our retrospective study, the mean patient age was 54 years, and the female-to-male ratio was consistent with the literature.

The primary aim of this study was to evaluate the effectiveness of intraoperative intact PTH monitoring in improving surgical success and reducing the need for reoperation in PHPT. While neck ultrasonography (USG), single-photon emission computed tomography (SPECT), and Tc-99 m sestamibi imaging are well-established in preoperative localization, intraoperative i-PTH measurement adds a dynamic biochemical parameter to support intraoperative decision-making. Our findings suggest that i-PTH monitoring can provide significant benefits, particularly in cases with inconclusive or discordant imaging findings, as well as in cases of ectopic or poorly localized glands.

The primary treatment for PHPT is surgery, with common approaches including unilateral exploration, bilateral exploration, and focused (targeted) exploration. Focused surgery is less invasive and associated with fewer complications and shorter recovery periods [13–17]. In our study, we compared preoperative localization with intraoperative findings. The success rates of preoperative imaging modalities were 74.4% for USG, 65.3% for Tc-99 m sestamibi, and 46.4% for SPECT. These results are comparable with those reported in the literature [4, 18], although deviations may occur due to differences in interpretation, multiple gland disease, or concurrent thyroid pathologies.

The localization of parathyroid lesions based on imaging (left/right inferior/superior) was largely consistent with intraoperative findings. Ectopic localization was observed in 10% of patients, and multiglandular disease was present in 6%. Histopathological analysis revealed adenoma in 93%, hyperplasia in 6.4%, and carcinoma in 0.5% of patients, aligning with literature data [5, 19].

A decline in i-PTH levels by more than 50% after removal of the suspected pathological gland is commonly interpreted as indicative of surgical success, a concept forming one of the pillars of this study. i-PTH monitoring was applied in 93 patients (Group A), while the remaining 110 (Group B) did not undergo this procedure. A significant difference was observed in surgical success between the two groups ($p = 0.02$), supporting the value of i-PTH measurement in improving outcomes.

Although not all comparisons reached statistical significance, we observed trends suggesting that i-PTH monitoring contributed to more targeted surgeries and reduced the need for extended exploration. Notably, none of the patients with multifocal disease in Group A experienced recurrence or persistence, while 3 patients in Group B did. This suggests that intraoperative i-PTH monitoring may improve detection of multiglandular disease. Literature reports support this observation, particularly when imaging fails to localize all pathological glands [20]. Our data partially support this as well: among the 13 patients with multifocal disease, none in Group A experienced recurrence or persistence, whereas 3 out of 6 in Group B did. Thus, i-PTH monitoring appears to facilitate more accurate intraoperative assessment of disease extent.

Many studies have emphasized the importance of intraoperative PTH monitoring, especially in older patients, who are at increased risk of multiglandular disease. The reported surgical success rate with intraoperative PTH monitoring can reach up to 98% [6, 13, 21–23]. In our study, the success rate in the i-PTH group was 97.8%, closely matching those figures.

Improved success rates directly translate to fewer secondary surgeries, reduced recurrence, and a decrease in associated complications and costs [24]. Consequently, intraoperative i-PTH monitoring has become a routine part of surgical practice in our clinic.

Although intraoperative PTH testing adds approximately 50 min to the procedure (including sampling, transport, analysis, and reporting), the frozen section process—which takes 30–40 min—was performed in both groups, resulting in comparable intraoperative waiting times. The additional delay was around 30 min, which we consider clinically acceptable, especially when weighed against the benefits of avoiding unnecessary exploration.

We acknowledge that routine frozen section analysis for all patients is not common practice in high-volume endocrine centers due to cost, time, and resource considerations. However, in our institution, it was implemented as a standard part of the conservative surgical protocol. While frozen section aids intraoperative confirmation of parathyroid tissue, it does not preclude the presence of additional pathological glands and should not be solely relied upon to terminate exploration.

In some patients, postoperative PTH levels remained elevated despite a significant intraoperative i-PTH decline. A high proportion of these patients had vitamin D deficiency, a potential confounding factor. Considering these and similar factors, the normalization thresholds suggested by the Rotterdam and Ann Arbor frameworks may need to be reconsidered. Multicenter, high-volume studies are necessary to clarify and standardize these criteria.

In focused surgical interventions, preoperative imaging guides the surgeon, while a > 50% intraoperative PTH drop provides real-time confirmation of adequate gland removal. These combined strategies enable safe, limited dissection without compromising surgical success.

Our study has several limitations. These include limited access to patient records, single-center design, a relatively small patient cohort, variability in operating surgeons, and differences in radiological reporting. Moreover, complications such as hypoparathyroidism or vocal cord paralysis, and the technical difficulty of reoperations in persistent/recurrent cases, underline the necessity for experienced surgeons in high-volume centers.

Finally, optimal management of PHPT requires collaboration between skilled endocrine surgeons, experienced radiologists, and advanced laboratories capable of performing rapid and accurate biochemical testing at all stages of care.

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Author contributions
Y.F.A., F.N., E.G., R.K., Ç.B., Ö.Ş. and Ö.G. wrote the main manuscript text.Y.F.A., K.D., M.A. prepared tables and figures. All authors reviewed the manuscript.

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Data availability
The database of this study is open to sharing. It can be obtained from the authors upon request.

Declarations

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Conflict of interest
The authors declare that they have no conflict of interest.

Ethics approval and consent to participate
This retrospective study was approved by the Gazi University Faculty of Medicine Institutional Review Board (Approval No: 757 – 09.11.2020) and conducted in accordance with the ethical standards of the 1964 Helsinki Declaration and its later amendments. The need for individual informed consent was waived by the ethics committee due to the retrospective nature of the study. As a university hospital, all patients provide general approval for the use of anonymized clinical data in scientific research upon admission.

Scientific responsibility statement
The authors declare that they are responsible for the scientific content of the article, including study design, data collection, analysis and interpretation, writing, part or all of the outline, preparation and scientific review of the content, and approval of the final version of the article.

Clinical trial number
Not applicable.

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References
1. Rutledge S, Harrison M, O'Connell M, O'Dwyer T, Byrne MM. Acute presentation of a giant intrathyroidal parathyroid adenoma: a case report. J Med Case Rep. 2016;10(1):286. https://doi.org/10.1186/s13256-016-1078-1.
2. Miller AB, Frank E, Simental AA Jr, Feng M. Surgery for nonlocalizing hyperparathyroidism in high volume center. Head Neck. 2024;46(7):1788–94. https://doi.org/10.1002/hed.27686.
3. Del Rio P, Boniardi M, De Pasquale L, et al. Management of surgical diseases of primary hyperparathyroidism: indications of the united Italian society of endocrine surgery (SIUEC). Updates Surg. 2024;76(3):743–55. https://doi.org/10.1007/s13304-024-01796-5.
4. Gawrychowski J, Buła G, Niedzielski Z, Gawrychowska A, Bednarczyk A, Kowalski G. Primary hyperparathyroidism due to mediastinal parathyroid lesions. Kardiochir Torakochirurgia Pol. 2021;18(1):55–9. https://doi.org/10.5114/kitp.2021.105189.
5. Makey IA, Geldmaker LE, Casler JD, El-Sayed Ahmed MM, Jacob S, Thomas M. Localization and surgical approach to mediastinal parathyroid glands. J Cardiothorac Surg. 2022;17(1):299. https://doi.org/10.1186/s13019-022-02052-w.
6. Pereira C. Role of intraoperative parathyroid hormone in guiding parathyroidectomy. Acta Biomed. 2023;94(2):e2023040. https://doi.org/10.23750/abm.v94i2.13998.
7. Govind K, Paruk IM, Motala AA. Characteristics, management and outcomes of primary hyperparathyroidism from 2009 to 2021: a single centre report from South Africa. BMC Endocr Disord. 2024;24(1):53. https://doi.org/10.1186/s12902-024-01583-8.
8. Ha EJ, Baek JH, Baek SM. Minimally invasive treatment for benign parathyroid lesions: treatment efficacy and safety based on nodule characteristics. Korean J Radiol. 2020;21(12):1383–92. https://doi.org/10.3348/kjr.2020.0037.
9. Gopal RA, Acharya SV, Bandgar T, Menon PS, Dalvi AN, Shah NS. Clinical profile of primary hyperparathyroidism from Western India: a single center experience. J Postgrad Med. 2010;56(2):79–84. https://doi.org/10.4103/0022-3859.65279.
10. Köroğlu EY, Tam AA, Fakı S, et al. The clinical significance of calcium/magnesium ratio in primary hyperparathyroidism: unveiling a clinical association. Hormones (Athens). Published Online Febr. 2024;9. https://doi.org/10.1007/s42000-024-00530-5.
11. Thanveer AS, Kamalanathan S, Badhe BA, Palui R, Rashmi KG, Nadeem NF. Clinicopathological profile of primary hyperparathyroidism with special reference to Ki-67 labelling index. Indian J Endocrinol Metab. 2023;27(1):73–9. https://doi.org/10.4103/ijem.ijem_208_22.
12. Martlı HF, Saylam B, Er S, Yücel Ç, Tez M. Evaluation of preoperative Procollagen type 1 N-terminal peptide and collagen type 1 C-telopeptide levels in the prediction of postoperative hypocalcemia in patients undergoing parathyroidectomy due to primary hyperparathyroidism. Langenbecks Arch Surg. 2023;408(1):71. https://doi.org/10.1007/s00423-023-02813-8.
13. Ahmad S, Kuraganti G, Steenkamp D. Hypercalcemic crisis: a clinical review. Am J Med. 2015;128(3):239–45. https://doi.org/10.1016/j.amjmed.2014.09.030.
14. Bilezikian JP, Silverberg SJ, Bandeira F, et al. Management of primary hyperparathyroidism. J Bone Min Res. 2022;37(11):2391–403. https://doi.org/10.1002/jbmr.4682.
15. Choudhry KS, Malik MZ, Buggs-Saxton C. Hypercalcemic crisis due to primary hyperparathyroidism in systemic lupus erythematosus (SLE). Lupus. 2013;22(8):847–50. https://doi.org/10.1177/0961203313491847.
16. Cannon J, Lew JI, Solórzano CC. Parathyroidectomy for hypercalcemic crisis: 40 years' experience and long-term outcomes. Surgery. 2010;148(4):807–13. https://doi.org/10.1016/j.surg.2010.07.041.
17. Okuyama H, Sato R, Enomoto K, Asakura J, Hatakeyama T. Hypercalcemic crisis due to parathyroid adenoma improved by continuous Hemodialysis with a common calcium concentration dialysate: discussion of therapeutic management. Intern Med. 2024;63(8):1139–47. https://doi.org/10.2169/internalmedicine.1764-23.
18. Abdulsalam MS, Devanayagam S, Santosham R, Ganapathy V, Menon M, Simon S. Mediastinal parathyroid adenoma removal by video-assisted thoracoscopic surgery. Ann Afr Med. 2021;20(2):150–3. https://doi.org/10.4103/aam.aam_5_20.
19. Bilezikian JP, Khan AA, Silverberg SJ et al. Evaluation and Management of Primary Hyperparathyroidism: Summary Statement and Guidelines from the Fifth International Workshop. J Bone Miner Res. 2022;37(11):2293–2314. https://doi.org/10.1002/jbmr.4677
20. Schneider DF, Ojomo KA, Mazeh H, Oltmann SC, Sippel RS, Chen H. Significance of rebounding parathyroid hormone levels during parathyroidectomy. J Surg Res. 2013;184(1):265–8. https://doi.org/10.1016/j.jss.2013.04.024.
21. Lorenz FJ, Beauchamp-Perez F, Manni A, Chung T, Goldenberg D, Goyal N. Analysis of time to diagnosis and outcomes among adults with primary hyperparathyroidism. JAMA Netw Open. 2022;5(12):e2248332. https://doi.org/10.1001/jamanetworkopen.2022.48332.
22. Kafetzis ID, Diamantopoulos A, Christakis I, Leoutsakos B. The history of the parathyroid glands. Horm (Athens). 2011;10(1):80–4. https://doi.org/10.14310/horm.2002.1297.
23. Liang G, Kaur MN, Wade CG, et al. Patient-reported outcome measures for primary hyperparathyroidism: a systematic review of measurement properties. Health Qual Life Outcomes. 2024;22(1):31. https://doi.org/10.1186/s12955-024-02248-9.
24. Ward BK, Magno AL, Walsh JP, Ratajczak T. The role of the calcium-sensing receptor in human disease. Clin Biochem. 2012;45(12):943–53. https://doi.org/10.1016/j.clinbiochem.2012.03.034.

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