

## Relationship of parathyroid adenoma volume with preoperative biochemical parameters

### Paratiroid adenom volümünün preoperatif biyokimyasal parametreler ile ilişkisi

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#### Abstract

**Aim:** Primary hyperparathyroidism (PHPT) is a clinical presentation of hypercalcemia resulting from autonomous excessive parathyroid secretion from parathyroid glands. Significant correlation between serum parathyroid hormone (iPTH), calcium (Ca), phosphorus (P) and 25-OH D3 levels and adenoma volume, have a predictive value to determine the size of parathyroid adenoma resection. In this study, we examined the relation between preoperative biochemical parameters and resected parathyroid adenoma volume.

**Methods:** Fifty-two patients with PHPT diagnosed in the endocrinology outpatient clinic of Istanbul Haydarpaşa Numune Research Hospital, between 2011 and 2014 were included in the study. Histopathological diagnosis of solitary parathyroid adenomas was made. Correlation analysis was performed between adenoma volume and preoperative serum iPTH, corrected Ca, P, 25-OH D3 and 24 hour urinary calcium levels. The study was designed a cross-sectional study.

**Results:** Fifty-two patients studied, 45 were female and 7 were male. The mean age of the patients was 53.538 ± 14.996 years. The mean preoperative iPTH level was 371.423 ± 341.8 pg / dl, corrected Ca level was 11.652 ± 0.947 mg / dl, phosphorus level was 2.285 ± 0.434 mg / dl and 25-OH D3 level was 11.442 ± 6.120 ng /dl. The calculated parathyroid adenoma volume averaged 1.612 ± 2 cm<sup>3</sup>. Correlation between parathyroid adenoma volume with parathormone levels and 24 hour urine calcium levels was positive whereas 25-OH D3 levels were negatively correlated with adenoma volume.

**Conclusion:** The adenoma size correlates with iPTH and vitamin D levels in PHPT patients. These levels may have predictive value about adenoma volume.

**Keywords:** Parathyroid adenoma volume, Biochemical parameters

#### Öz

**Amaç:** Primer hiperparatiroidizm (PHPT), paratiroid bezlerinden otonom olarak aşırı parathormon salgılanması sonucu oluşan, hiperkalsemi veya normokalseminin görüldüğü klinik bir tablodur. Serum paratiroid hormonu (iPTH), kalsiyum (Ca), fosfor (P) seviyeleri ve vitamin D düzeyleri (25-OH D3) ile adenom hacmi arasında anlamlı bir ilişki bulunması, paratiroid adenomunun rezeksiyonunun boyutunu belirlemek için prediktif değere sahip olabilir. Biz de bu çalışmamızda preoperatif biyokimyasal parametreler ile paratiroid adenom volümü arasındaki ilişkiyi inceledik.

**Yöntemler:** İstanbul Haydarpaşa Numune Eğitim ve Araştırma Hastanesi Endokrinoloji polikliniğinde 2011-2014 yılları arasında primer hiperparatiroidi tanısıyla takip edilen, operasyon sonrasında histopatolojik olarak soliter paratiroid adenomu tanısı konmuş 52 hasta çalışmaya alındı. Adenom hacmi ile preoperatif serum parathormon (iPTH), düzeltilmiş Ca, P, 25-OH D3, 24 saatlik idrarda kalsiyum düzeyi arasında korelasyon analizi yapıldı. Çalışma cross-sectional olarak dizayn edildi.

**Bulgular:** Çalışmaya alınan elli iki hastanın 45'i kadın (%86,5), 7'si erkekti (%13,5). Hastaların yaş ortalaması 53,538 ± 14,996 yıldır. Hastaların ortalama preoperatif iPTH düzeyi 371,423 ± 341,857 pg/dl, ortalama düzeltilmiş Ca düzeyi 11,652 ± 0,947 mg/dl, ortalama fosfor düzeyi 2,285 ± 0,434 mg/dl, ortalama 25-OH D3 düzeyi 11,442 ± 6,120 ng/ml, 24 saatlik idrarda kalsiyum düzeyi 337,486 ± 213,658 mg/24 saat olarak bulundu. Hastaların hesaplanan paratiroid adenom volüm ortalaması 1.612 ± 2 cm<sup>3</sup> (0,0060-11,510) idi. Paratiroid adenom volümü ile parathormon düzeyleri ve 24 saatlik idrar kalsiyum düzeyleri arasında pozitif yönde, 25-hidroksi vitamin D düzeyleri arasında negatif yönde korelasyon saptandı.

**Sonuç:** PHPT hastalarda adenom boyutu parathormon ve vitamin D düzeyi ile korelasyon göstermektedir. Bu nedenle, preoperatif iPTH ve vitamin D düzeylerinin adenom boyutu hakkında prediktif değere sahip olabileceğini düşünmekteyiz.

**Anahtar kelimeler:** Paratiroid adenom volümü, Biyokimyasal parametreler

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## Introduction

Primary hyperparathyroidism (PHPT) is a clinical presentation with hypercalcemia or normocalcemia resulting from autonomously excessive parathyroid secretion from parathyroid glands [1]. PHPT is a rare disease with a prevalence of 1-4 / 1000. It is more common in females than males [2]. The incidence has been increased with the recognition of asymptomatic patients due to routine calcium measurement. Organ complications such as specific bone diseases and nephrolithiasis are now less common due to the early detection of the disease [3,4]. The most common cause of PHPT is the solitary parathyroid adenomas. Parathyroid hyperplasia, multiple parathyroid adenomas, parathyroid carcinoma, and familial syndromes are more rare causes of hyperparathyroidism [1-5]. The primary etiology of primary hyperparathyroidism is a solitary parathyroid adenoma in approximately 85-90% of patients, and can usually be successfully treated with parathyroidectomy (approximately 95% of all) [6]. Significant correlation between serum parathyroid hormone (iPTH), calcium (Ca), phosphorus (P) levels and vitamin D levels 25-OH D3 with adenoma volume, together with imaging modalities, have been proposed to be predictive to determine the size of parathyroid adenoma resection [6,7]. However, the effect of existing parameters on the parathyroid adenoma volume is unclear [7]. We investigated the relationship, if any, between preoperative biochemical parameters and parathyroid adenoma volume in this study.

## Materials and methods

Fifty-two patients diagnosed with primary hyperparathyroidism in the endocrinology outpatient clinic of Istanbul Haydarpaşa Numune Training and Research Hospital between the years of 2011 and 2014 were included in the study. The data of the patients were evaluated retrospectively. Histopathologically confirmed solitary parathyroid adenoma was the inclusion criteria. Patients with parathyroid carcinoma, parathyroid hyperplasia, multiple parathyroid adenomas, secondary or tertiary hyperparathyroidism were excluded from the study. Demographic characteristics such as iPTH, Ca, P, albumin, creatinine, calcium excretion rate at 24 hours, 25-OH D3 level, sex and age before surgery were collected from hospital records. The parathyroid adenoma volume was calculated using the length x thickness x width x 0.52 formula [8].

### Statistical analysis

Data analysis was performed using SPSS version 22 for Windows, and the results were expressed as mean  $\pm$  SD. Correlation analysis was performed between adenoma volume and preoperative serum parathormone (iPTH), corrected Ca, P, 25-OH D3, and 24 hour urinary calcium levels. Significance was accepted if the probability values were lower than 0.05.

## Results

Out of fifty-two patients who were included in the study, 45 (86.5%) were female and 7 were male (13.5%). The mean age of the patients was  $53.538 \pm 14.996$  years. The mean preoperative iPTH level was  $371.423 \pm 341.857$  pg / dl, the mean

corrected Ca level was  $11.652 \pm 0.947$  mg / dl, the mean phosphorus level was  $2.285 \pm 0.434$  mg / dl and the mean 25-OH D3 level was  $11.442 \pm 6.120$  ng / dl. The urinary calcium level was  $337.486 \pm 213.658$  mg / 24 hours. The calculated parathyroid adenoma volume averaged  $1.612 \pm 2$  cm<sup>3</sup> (0.0060-11.510) (Table 1). Preoperative parathormone and 24-hour urinary calcium levels were positively correlated with adenoma volume whereas, 25-OH D3 levels were found to be negatively correlated (Table 2).

Table 1: Demographic characteristics of patients and laboratory parameters (preoperative)

	Values
Female (%) / Male (%)	45 (86.5) / 7(13.5)
Age (years)	$53.538 \pm 14.996$ (19 - 84)
Parathormone (pg / dl)	$371.423 \pm 341.857$ (95 - 2156)
Corrected calcium (mg / dL)	$11.652 \pm 0.947$ (10.4 - 15.4)
Phosphorus (mg/dl)	$2.285 \pm 0.434$ (1.4-3.3)
25-hydroxy vitamin D3 (ng/ml)	$11.442 \pm 6.120$ (3.46-33.63)
24 hour urine calcium (mg/24 hour)	$337.486 \pm 213.658$ (46 -1053)
Adenoma volume (cm <sup>3</sup> )	$1.612 \pm 2$ ( 0.006 -11.51)

Table 2: Correlation of parathyroid adenoma volume with laboratory parameters

	Correlation coefficient	p
Age (years)	-0.204	0.147
Corrected calcium (mg/dl)	0.147	0.299
Phosphorus (mg/dl)	-0.215	0.127
25-hydroxy vitamin D3 (ng/ml)	-0.277	0.047
Parathormone (pg / dl)	0.334	0.016
24 hour urine calcium (mg/24 hour)	0.286	0.042

## Discussion

Primary hyperparathyroidism is the most common cause of hypercalcemia in patients admitted to the outpatient clinics. Although primary hyperparathyroidism can be seen at any age, it is most common in post-50s and postmenopausal women [9]. Early recognition of primary hyperparathyroidism in recent years and increased selection of localization studies have positively affected the diagnosis and treatment of the disease. However, due to the non-rare occurrence of recurrences, difficulties in the treatment of complications and being a relatively common endocrine disease, it remains an important entity [10]. Numerous studies have been carried out on the relationship between the volume of parathyroid adenoma and biochemical parameters, as well as the etiology of the disease. While some of these studies correlate biochemical parameters with parathyroid adenoma volume [7-11], some studies have not detected any correlation [12-13]. In this study we looked for this relationship in our Turkish population.

In our study, a positive correlation was found between iPTH and adenoma volume, but unlike many studies in the literature, there was no statistically significant correlation with serum Ca and P levels [7,11,14,15]. In the literature, Rutledge and colleagues first reported a significant association between serum iPTH and calcium levels and adenoma volume [7-11]. Subsequently, Bindlish and colleagues ended up with a positive correlation between iPTH and serum Ca values and solitary parathyroid adenoma volume in a relatively small study of 63 patients. However, there was no significant correlation between adenoma volume and phosphorus level [7]. Similarly, Moretz et al. [14] found a positive correlation between preoperative iPTH levels, serum calcium levels and adenoma volume. In a recently published study, Kizilgul and colleagues [15] suggested that preoperative serum calcium and iPTH levels may be useful in predicting parathyroid adenoma weight and volume.

On the other hand, in some studies, there was no significant relationship between biochemical parameters and

adenoma size in hyperparathyroidism [12,13]. Randhawa et al. [13] reported that biochemical parameters would not accurately predict the size of parathyroid adenoma in an analysis using data from 77 patients, and as a result, postoperative calcium levels also would not correlate with parathyroid adenoma size. Although Williams and colleagues [16] found significant correlations between PTH levels and adenoma weight, this correlation disappeared after two severely heavy adenomas extracted from analysis. Resembling to this result, in our study, adenoma volumes of 5 patients with iPTH values (779-2156 pg / dl) above 750 pg / dl were found above 3 cm<sup>3</sup> (3.01-6.8 cm<sup>3</sup>) and in the case of removal of these patients from analysis, positive correlation lost its meaning.

Rao et al. [17] found an increase in adenoma volume in patients with vitamin D deficiency compared with those without vitamin D deficiency. The strong negative correlation between adenoma volume and 25-OH D3 was not impaired even in the case of extracting 5 patients with large adenomas and high iPTH values in our study. This suggests that 25-OH D3 levels play a decisive role in the growth of parathyroid adenoma. In our country, where 25-OH D3 deficiency is around 44-60% [18], in the regions of severe vitamin D deficiency, the developed parathyroid adenomas are also greater than those developed in the other parts. In support of this, the 25 -OH D3 levels of the 5 relating patients with large adenomas and high iPTH values were found to be below 8 ng / ml.

Primary limitations regarding this study are the selection bias due to the retrospective nature of the study and the small sample size.

#### Conclusion

In PHPT patients, adenoma size correlates with parathormone and vitamin D levels. For this reason, we think that preoperative iPTH and vitamin D levels may have a predictive value about adenoma size.

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