OTJHS
Online Turkish Journal of Health Sciences

e-ISSN: 2459-1467

OTSBD
Online Türk Sağlık Bilimleri Dergisi

Online Turkish Journal of Health Sciences 2023;8(2):228-232 *Online Türk Sağlık Bilimleri Dergisi 2023;8(2):228-232*

The Relationship of Solitary Parathyroid Adenoma Volume with Pre- and Post-operative Parathormone and Calcium Levels

Soliter Paratiroid Adenom Hacminin Ameliyat Öncesi ve Sonrası Parathormon ve Kalsiyum Seviyeleri ile İlişkisi

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ABSTRACT

Objective: Parathyroid size, weight, position and histopathological characteristics have been investigated as possible candidates of predictive value. We aimed to investigate the relationship between the volume of the parathyroid gland as calculated by sonographic measurements and the amount of postoperative decrease in serum calcium and parathyroid hormone (PTH) levels.

Materials and Methods: Preoperative and postoperative plasma levels of corrected calcium and intact PTH were noted. The size of each adenomatous parathyroid gland was calculated as an ellipsoid based on the preoperative sonographic measurements using the formula "V=π/6 x diameters".

Results: A total of 61 (76.3%) females and 19 (23.8%) males were included in the study. The median age of the patients was 58 years. The average volume of the adenomatous parathyroid gland was calculated to be 13.4 cm3. Plasma levels of both calcium and PTH significantly decreased following surgery (p: 0.000, p: 0.000, respectively). There was significant correlation between the adenoma volume and the change in calcium value (r: -0.500, p: 0.000) but not for the PTH value (r: 0.036, p: 0.750).

Conclusion: Our significant results may suggest a relationship between the volume of adenoma and plasma calcium levels, but more extended studies with larger patient groups are needed for more consistent results.

Keywords: Adenoma, calcium, parathyroid, volume

ÖZ

Amaç: Paratiroid boyutu, ağırlığı, pozisyonu ve histopatolojik özellikleri olası prediktif değer adayları olarak araştırılmıştır. Bu çalışmamızda bizde sonografik ölçümlerle hesaplanan paratiroid bezi hacmi ile postoperatif serum kalsiyum ve parathormon (PTH) düzeylerindeki azalma miktarı arasındaki ilişkiyi araştırmayı amaçladık.

Materyal ve Metot: Ameliyat öncesi ve sonrası düzeltilmiş kalsiyum ve intakt PTH plazma seviyeleri kaydedildi. Her bir adenomatöz paratiroid bezinin boyutu, "V=π/6 x çaplar" formülü kullanılarak, ameliyat öncesi sonografik ölçümlere dayalı olarak bir elips şeklinde hesaplandı.

Bulgular: Çalışmaya toplam 61 (%76,3) kadın ve 19 (% 23,8) erkek dahil edildi. Hastaların medyan yaşı 58 idi. Adenomatöz paratiroid bezinin ortalama hacmi 13,4 cm3 olarak hesaplandı. Ameliyattan sonra hem kalsiyum hem de PTH'nin plazma seviyeleri önemli ölçüde azaldı (sırasıyla p<0,001, p<0,001). Adenom hacmi ile kalsiyum değerindeki değişiklik arasında anlamlı bir korelasyon varken (r: -0.500, p<0,001), PTH değeri için anlamlı bir ilişki yoktu (r: 0,036, p: 0,750).

Sonuç: Sonuçlarımız adenom hacmi ile plazma kalsiyum seviyeleri arasında bir ilişki olduğunu düşündürebilir ancak daha tutarlı sonuçlar için daha geniş hasta grupları ile daha kapsamlı çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Adenom, hacim, kalsiyum, paratiroid

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Yayın Bilgisi / Article Info:
Gönderi Tarihi/ Received: 29/12/2022
Kabul Tarihi/ Accepted: 14/03/2023
Online Yayın Tarihi/ Published: 06/06/2023

Atıf / Cited: Naycı AE and et al. The Relationship of Solitary Parathyroid Adenoma Volume with Pre- and Post-operative Parathormone and Calcium Levels. *Online Türk Sağlık Bilimleri Dergisi* 2023;8(2):228-232. doi: 10.26453/otjhs.1226045

INTRODUCTION

Primary hyperparathyroidism (PHTP), with an estimated annual incidence of 34 to 120 cases per 100,000 people, is a relatively common endocrine disorder caused by parathyroid adenomas in 80-85% of the cases.[1]

Due to the increasing availability of routine laboratory testing, many parathyroid adenomas are discovered incidentally during diagnostic workups for other pathologies, increasing the overall incidence. Many parathyroid adenomas are diagnosed while still asymptomatic.[2] Depending on the etiology of hyperparathyroidism, plasma calcium and vitamin D levels might be normal or low, while plasma PTH might be "inappropriately normal", i.e., unsuppressed despite hypercalcemia.[3]

The preferred mode of treatment of primary hyperparathyroidism for all symptomatic cases and asymptomatic cases fulfilling any of the following criteria is surgery. Surgery in asymptomatic patients offers the promise of a definitive cure and should be recommended to those who meet any one of the following criteria: hypercalcemia level consistently >1 mg/dL above average; fracture; renal stones, hypercalciuria and other stone risk factors; T-score <−2.5 at any site; and age <50 years.[4] While surgery aims to achieve a significant decrease in serum parathyroid hormone (PTH), which results in the correction of previously elevated serum calcium levels, hypocalcemia is a common and potentially severe complication.[4,5] Therefore, it is of paramount importance for endocrine surgeons to predict the extent of the decrease in calcium levels after surgery to be able to take the necessary precautions before the onset of symptoms.

Numerous studies attempted to estimate the effect of parathyroidectomy on postoperative calcium and PTH levels. Parathyroid size, weight, position, and histopathological characteristics have been investigated as possible candidates for predictive value.[6] Unfortunately, a correlation between any of these parameters and postoperative change in either calcium or PTH levels is yet to be established by multiple studies and widely accepted by the endocrine community.[5] Since preoperative imaging studies are routinely performed in most endocrine surgery centers, data derived from such studies can be made readily available at no extra cost.

Thus, we aimed to investigate the relationship between the volume of the parathyroid gland as calculated by sonographic measurements and the change in postoperative values compared to preoperative calcium and PTH values.

MATERIALS AND METHODS

Ethics Committee Approval: For this study, it was obtained from the Istanbul Training and Research Hospital Clinical Research Ethics Committee (Date: 08/11/2019, decision no: 2047). Informed consent was obtained from all patients, and the study was performed according to international declarations.

Patient Feature: Data from 80 consecutive patients with PHPT operated in a single center with experience in endocrine surgery was retrospectively analyzed. Patients with multiple adenomatous parathyroid glands or a history of prior neck surgery were excluded. The age and gender of the patients, as well as the localization of the adenomatous glands, were recorded.

Analysis: Both preoperative (before any medical treatment) and postoperative (one day after surgery) plasma levels of corrected calcium and intact PTH were analyzed. The size of each adenomatous parathyroid gland was calculated as an ellipsoid based on the preoperative sonographic measurements, using the formula $V=\pi/6 \times ABC$ (A, B and C being the dimensions in cm).

Statistical Analysis: Statistical analysis was performed using the IBM® SPSS® Statistics 26.0 software (IBM, Armonk, New York, USA). Mean, standard deviation, median, minimum, and maximum values, frequency, and percentage were used for descriptive statistics. The distribution of variables was tested using the Kolmogorov-Smirnov test. Wilcoxon signed-rank test was used for the analysis of repeated measurements. The correlation was determined using Spearman's rank correlation coefficient. The p-value less than 0.05 were considered statistically significant.

RESULTS

Of the 80 patients included, 61 (76.3%) were female, and 19 (23.8%) were male. The ages of the patients ranged from 22 years to 82 years, with a mean age of 57.4±13.3 years. The adenomatous gland was most commonly the lower left parathyroid, with 35 cases (43.8%), followed by 26 (32.5%) in the lower right, 11 (13.8%) in the upper left, and 8 (10.0%) in the upper right. The average volume of the adenomatous parathyroid gland was calculated to be 13.4 cm^3 and the minimum and maximum sizes were 9 and 21 cm^3 respectively (Table 1).

Plasma levels of both calcium and PTH significantly decreased following surgery ($p<0.05$). The calcium and PTH measurements are summarized in Table 2.

Spearman's rank correlation test demonstrated a significant correlation between the adenoma volume with preoperative and postoperative plasma calcium levels and the change in calcium. However, no such correlation of statistical significance was present between the adenoma volume and plasma PTH levels. Table 3 lists the correlation coefficients for the different variables.

Table 1. The demographic data of the patients and the location of the adenomas.

		Patients (n:80)
Age of patients (years), mean ±SD		57.4±13.3
Adenoma volume (cm^3), mean ±SD		13.4±19.9
Gender, n (%)	Female	61 (76.3)
	Male	19 (23.8)
Localization of the adenoma, n (%)	Lower left	35 (43.8)
	Lower right	26 (32.5)
	Upper left	11 (13.8)
	Upper right	8 (10.0)

Table 2. The preoperative and postoperative analysis of the calcium and parathyroid hormone.

	Preoperative	Postoperative	p-value
Ca, mean ±SD	11.6±1.1	9.0±0.9	0.001
PTH, mean ±SD	316.5±261.7	49.4±39.7	0.001

Ca: corrected plasma calcium (mg/dL); PTH: intact parathyroid hormone (pg/mL).

Table 3. Correlation analysis of the volume of parathyroid adenoma with serum calcium (pre- and post-operative) and serum PTH levels.

	Ca			PTH		
	Preoperative	**Postoperative**	**% change**	**Preoperative**	**Postoperative**	**% change**
r	0.384	-0.300	-0.500	0.154	0.179	0.036
p-value	0,001	0.007	0,001	0.174	0.113	0.750

Ca: corrected plasma calcium (mg/dL); PTH: intact parathyroid hormone (pg/mL); r: Spearman's correlation coefficient.

DISCUSSION AND CONCLUSION

For a successful parathyroidectomy, a surgeon needs a precise localization and the number of parathyroid glands that must be removed. Therefore, an adequate preoperative diagnostic patient processing is needed . One of the important factors for the indication of surgery is, among others, the value of parathormone.

Predicting the presence of a large parathyroid adenoma and measuring surgical specimen dimensions after excision may have some clinical importance. In fact, as the parathyroid adenoma expands, the proportion of solitary components increases more and the likelihood of it being benign decreases. However, a giant parathyroid adenoma may sometimes mask the presence of a second, smaller adenoma.[7]

The concordance of an accurate preoperative localization and high preoperative PTH values with the excision of a large adenoma and a rapid decrease of PTH makes the presence of a solitary adenoma very likely.[8]

In our study, the female-to-male ratio was approximately 3:1, and among a group ranging from 22 to 82 years of age, the mean age was 57.4 years (±13.3), with the median also at 58. Median adenoma volume is 13,4 cm^3. Lower left localization is the most common position (%43,8) of the adenoma . Sekond most common position is lower right (%32,5).

These findings are similar the literature based on both historical and recent data from different populations.[9] Despite significant differences among ethnic groups and a drastic increase in the incidence of the disease, mainly attributed to the incidental diagnosis of asymptomatic or mildly symptomatic cases, the male-to-female ratio is consistent. However, contrary to epidemiological studies, which demonstrate that the age-adjusted incidence of PHPT increases with age, the ages of our study population had clustered in the late 50 years.[10] This is due to the design of our study, which includes only patients operated for PHPT rather than being a population survey. Patient age being one of the indications for surgery and early postmenopausal women being more likely to undergo bone mineral density scanning than the elderly, resulting in increased diagnoses of asymptomatic osteoporosis, are possible reasons for the age distribution of our study population. Other studies based on operative findings have also reported similar results, which supports our interpretation.[11]

Adenomatous parathyroid glands were most frequently the inferior parathyroids, with a tendency for left-sided adenomas. Matsushita et al. demonstrated in 1984 that the functional level of the inferior parathyroid glands was higher than the superior ones. As such, they tend to have a greater capacity for hyperplasia and a decrease in size in states of suppressed PTH secretion.[12] The larger parenchymal area and higher potential for hyperplasia might be why ade-

nomas develop more frequently in the inferior glands.

Numerous studies have investigated the relationship between adenoma size and biochemical parameters such as PTH, vitamin D, calcium, and phosphorus. As a measure of the size of the adenoma, different studies used either weight or volume.

A review in the literature is the most extensive series correlating preoperative calcium and PTH values with operative findings of gland size and several diseased glands. Although a lower calcium value predicts somewhat more multi-gland disease, the poor correlation should make the parathyroid surgeon aware that preoperative laboratory testing cannot predict gland size and multi-gland disease.[13]

Randhawa et al. have measured both weight and volume of the adenomas and found a strong correlation, making it possible to compare results from studies measuring either the weight or the volume of the adenomatous parathyroid gland.[11]

Since it can be calculated preoperatively by data obtained from ultrasonography alone, volume is more useful in predicting biochemical variables well in advance of the operation.

The results from the current study suggest a statistically significant relationship between adenoma volume and plasma calcium levels but not PTH. Results from other studies in the literature could be more consistent.

Gatu et al. from Romania concluded that the volume of a parathyroid adenoma was related to preoperative PTH but not calcium levels.[14] Other studies have observed a correlation between parathyroid size and both calcium and PTH levels.[15] Jubran reported that the size of the parathyroid gland not correlated with the preoperative PTH values in 35 cases.[16]

In conclusion, primary hyperparathyroidism is among common endocrine disorders, usually caused by adenomas which may lead to morbidity and mortality. Former studies have focused on the preoperative estimation of parathyroidectomy on postoperative serum calcium and PTH levels. In our study, we aimed to evaluate the possible role of the volume of solitary parathyroid adenoma in predicting postoperative serum levels of PTH and calcium. Our significant results may suggest a relationship between the volume of the adenoma and plasma calcium levels, but extended studies with larger patient groups are needed for more consistent results.

Ethics Committee Approval: Our study was approved by the Saglik Bilimleri University, Istanbul Training and Research Hospital Ethics Committee (Date: 08/11/2019, decision no: 2047). The study was carried out following the international declaration, guidelines, etc.

Conflict of Interest: No conflict of interest was declared by the authors.

Author Contributions: Concept – AEN, SD; Supervision – OS, AF; Materials – SD, OS; Data Collection and/or Processing – AEN, SD, OS, AF; Analysis and/or Interpretation – – AEN, SD, OS, AF; Writing — AEN, SD, OS, AF.

Peer-review: Externally peer-reviewed.

REFERENCES

1. Duan K, Hernandez KG, Mete O. Clinicopathological correlates of hyperparathyroidism. J Clin Pathol. 2015;68(10):771-787. doi:10.1136/jclinpath-2015-203186
2. Hamidi S, Aslani A, Nakhjavani M, et al. Are biochemical values predictive of adenoma's weight in primary hyperparathyroidism? ANZ J Surg. 2006;76(10):882–885. doi:10.1111/j.1445-2197.2006.03896.x.
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. Bilezikian JP. Primary Hyperparathyroidism. J Clin Endocrinol Metab. 2018;103(11):3993-4004. doi: 10.1210/jc.2018-01225
5. Insogna KL. Primary hyperparathyroidism. N Engl J Med. 2018;379(11):1050-1059. doi:10.1056/NEJMcp1714213
6. Yeh MW, Ituarte PHG, Zhou HC, et al. Incidence and prevalence of primary hyperparathyroidism in a racially mixed population. J Clin Endocrinol Metab. 2013;98(3):1122-1129. doi:10.1210/jc.2012-4022
7. Keidar Z, Solomonov E, Karry R, Frenkel A, Israel O, Mekel M. Preoperative [(99m)Tc]MIBI SPECT/CT Interpretation Criteria for Localization of Parathyroid Adenomas-Correlation with Surgical Findings. Mol Imaging Biol. 2017;19(2):265–270.
8. Al-Hraishawi H, Dellatore PJ, Cai X, Wang X. Intact parathyroid hormone levels and primary hyperparathyroidism. Endocr Res. 2017;42(3):241–245.
9. Stern S, Mizrachi A, Strenov Y, et al. Parathyroid adenoma: a comprehensive biochemical and histological correlative study. Clin Otolaryngol. 2017;42(2):381-386. doi:10.1111/coa.12761
10. Darbà J, Marsà A. Epidemiology and management of parathyroid gland disorders in Spain over 15 years: A retrospective multicentre analysis. PLoS One. 2020;15(3):e0230130. doi: 10.1371/journal.pone.0230130
11. Randhawa PS, Mace AD, Nouraei SAR, Stearns MP. Primary hyperparathyroidism: Do perioperative biochemical variables correlate with parathyroid adenoma weight or volume? Clin Otolaryngol. 2007;32(3):179-184. doi:10.1111/j.1365-

2273.2007.01447.x
12. Matsushita H, Hara M, Shishiba Y, Nakazawa H. An evaluation of the size of the parathyroid glands. Endocrinol Jpn. 1984;31(2):127-31. doi:10.1507/endocrj1954.31.127
13. Naples R, Thomas JD, Monteiro R, et al. Preoperative Calcium and Parathyroid Hormone Values Are Poor Predictors of Gland Volume and Multigland Disease in Primary Hyperparathyroidism: A Review of 2000 Consecutive Patients. Endocr Pract. 2022;28(1):77-82. doi:10.1016/j.eprac.2021.08.003
14. Gatu A, Velicescu C, Grigorovici A, et al. The volume of solitary parathyroid adenoma is related to preoperative PTH and 25OH-D3, but not to Calcium levels. Acta Endocrinol (Copenh). 2017;13(4):441-446. doi:10.4183/aeb.2017.441
15. Lin X, Fan Y, Zhang Z, Yue H. Clinical Characteristics of Primary Hyperparathyroidism: 15-Year Experience of 457 Patients in a Single Center in China. Front Endocrinol (Lausanne). 2021;12:602221. doi:10.3389/fendo.2021.602221
16. Jubran AF. Correlations between parathyroid hormone level, adenoma size, and serum calcium level in patients with primary hyperparathyroidism. Saudi Surgical Journal. 2018;6(4):122-12.