Chirurgia (2023) 118: 146-152
No. 2, March - April
Copyright© Celsius
http://dx.doi.org/10.21614/chirurgia.2821

Uric Acid in Primary Hyperparathyroidism: Assessment of Surgical versus Conservative Approach

Theodor Eugen Oprea[1], Carmen Gabriela Barbu[1,2]*, Sorina Carmen Martin[1,2], Anca Elena Sarbu[1,2], Ruxandra Ioana Calapod[2], Irina Manuela Nistor[1], Simona Vasilica Fica[1,2]

[1]Carol Davila University of Medicine and Pharmacy, Bucharest, Romania
[2]Department of Endocrinology, Elias Emergency and University Hospital, Bucharest, Romania

*Corresponding author:
Carmen Gabriela Barbu, M.D.
Department of Endocrinology
Elias University and Emergency Hospital
Marasti Boulevard, no 17, Bucharest
Romania
E-mail: carmen_gabriela_barbu@yahoo.co.uk

Abbreviations:
PHPT: primary hyperparathyroidism;
PTH: parathyroid hormone;
SUA: serum uric acid;
ABCG2: ATP-binding cassette G2;
MEN: multiple endocrine neoplasia;
BMI: body mass index;
ESR: erythrocytes sedimentation rate;
Mg: magnesium;
HDL-chol: high density lipid cholesterol;
trig: triglycerides;
GGT: gamma-glutamyl transferase;
SD: standard deviation.

Received: 30.01.2023
Accepted: 27.03.2023

Rezumat

Acidul uric în hiperparatiroidismul primar: evaluarea abordării medicale vs chirurgicale

Introducere: Sugerată din lucrări timpurii, asocierea dintre hiperparatiroidismul primar (PHPT) şi hiperuricemie este încă controversată; asemenea este şi potențialul beneficiu pentru metabolismul acidului uric (SUA) al paratiroidectomiei comparativ cu tratamentul conservator.

Material şi Metode: Studiul nostru retrospectiv este format din 125 de pacienți caucazieni, diagnosticați cu PHPT cu indicație operatorie şi evaluați clinic între anii 2017 şi 2021 în cadrul secției de Endocrinologie a Spitalului Universitar de Urgență "Elias", Bucureşti. Ne-am propus să descriem caracteristicile metabolismului uric la pacienții cu PHPT şi să evaluăm diferențele nivelurilor de SUA între cei 38 de pacienți vindecați chirurgical şi cei 41 de pacienți tratați conservator.

Rezultate: Cei 34 de pacienți cu PHPT şi hiperuricemie au prezentat niveluri semnificativ mai crescute ale calcemiei totale (11.55[11.05;12.42] vs. 11.2[10.8;11.96], p=.039) comparativ cu cei 91 de subiecți normouricemici. La prima evaluare, nivelurile SUA s-au corelat cu vârsta, nivelurile calciului (p=.004, r=.328), creatininei, trigliceridelor si magneziului. Un model de regresie lineară a identificat calcemia ca o covariată cu contribuție unică pentru variabilitatea nivelurilor SUA. Cei 38 de pacienți vindecați chirurgical au prezentat postoperator niveluri mai scăzute ale SUA (4.95[3.52;6.3] vs. 5.65[4.49;7.45], p=.011) comparativ cu prima evaluare.

Concluzii: Pacienții cu PHPT şi hiperuricemie au niveluri semnificativ mai crescute ale calcemiei totale, aceasta fiind, de asemenea,

un determinant independent al variabilității SUA. Pacienții care beneficiază de paratiroidectomie curativă au demonstrat o scădere semnificativă a nivelului SUA în timpul unui an de urmărire.

Cuvinte cheie: hiperparatiroidism primar, acid uric seric, hiperuricemie, hipercalcemie, paratiroidectomie

Abstract

Introduction: Although suggested in early papers, the association between primary hyperparathyroidism (PHPT) and hyperuricemia is still debated, as is the potential benefit of parathyroidectomy compared to conservative treatment in serum uric acid (SUA) metabolism.
Material and Methods: Our retrospective study of 125 Caucasian PHPT patients with surgical criteria evaluated between 2017 and 2021 at Elias Emergency and University Hospital, Bucharest, Romania aims to describe the characteristics of hyperuricemia in PHPT patients and to assess the differences in SUA levels between 38 surgically cured and 41 conservatively managed patients.
Results: Our hyperuricemic PHPT patients (N=34) had significantly higher levels of calcium (11.55[11.05;12.42] vs. 11.2[10.8;11.96], p=.039) than the normouricemic subjects (N=91). At baseline, SUA correlated with age, serum total calcium (p=.004, r=.328), creatinine, triglycerides, and magnesium levels. A linear regression model identified calcium as a covariate with unique contribution for SUA variability. After successful parathyroidectomy, the 38 cured patients showed significantly lower serum calcium (9.3[8.7;9.75] vs. 11.55[11;12.12], p<.001) and SUA (4.95[3.52;6.3] vs. 5.65[4.49;7.45], p=.011) levels compared to baseline.
Conclusions: Hyperuricemic PHPT patients have significantly higher levels of serum calcium, which is also an independent determinant of SUA variability. Patients who undergo successful parathyroidectomies show a significant decrease in SUA during 1 year of follow-up.

Key words: primary hyperparathyroidism, serum uric acid, hyperuricemia, hypercalcemia, parathyroidectomy

Introduction

The clinical presentation of primary hyperparathyroidism (PHPT) varies from the classic, symptomatic form to a less severe, modern form of the disease with a heterogeneous presentation, depending on the progress of medical technology. The association between parathyroid hormone (PTH) and hyperuricemia was suspected in early papers that revealed a 25% prevalence of hyperuricemia in PHPT patients (1). Yan Duh et al. showed in 1986 a correlation between SUA levels and decreased renal clearance and a significant decrease in SUA after parathyroidectomy (1). Quality evidence on this topic was recently provided by a systematic review and meta-analysis that included a total of nine cohort studies and 1372 patients with PHPT who were compared to controls, and showed that significantly higher levels of SUA can be found in patients diagnosed with PHPT (2).

The pathophysiology behind this relationship is intricate, and recent studies presume that PTH decreases urate filtration by inhibiting the ATP-binding cassette G2 transporter (ABCG2) (3). In addition to PTH, elevated serum calcium may contribute to hyperuricemia by regulating extracellular volume depletion due to osmotic diuresis (4).

Uric acid is no longer deemed an inert end-product of purine metabolism and is responsible only for articular manifestations (5). The

perspective of hyperuricemia as a cardiovascular risk factor has also shifted in recent decades, and many authors have suggested that lowering SUA levels may positively influence arterial stiffness (6), ventricular mass (7) and even lower the blood pressure and the risk of myocardial infarction (6), (8). Additionally, hyperuricemia was associated with valvular calcifications and nephrolitiasis in patients with primary hyperparathyroidism (9), (10), and has been suggested to play a causal role in the development of type 2 diabetes mellitus (11)

Literature to date fails to show any significant role of uric acid in the management of PHPT, as current guidelines for diagnosis and management do not clearly recommend uric acid measurement due to inconclusive evidence (12).

The objectives of our study were to describe the prevalence of hyperuricemia in PHPT patients and to assess the differences in SUA levels between PHPT patients who were cured by parathyroidectomy and those who were conservatively managed.

Materials and Methods

Our retrospective study included 158 consecutive presentations referred for PHPT between 2017 and 2021 in the Endocrinology Department of Elias Emergency and University Hospital, Bucharest, Romania. Inclusion criteria consisted of a PHPT-positive diagnosis based on concomitantly elevated iPTH and serum calcium. Exclusion criteria were as follows: various multiple endocrine neoplasia (MEN) syndromes (8 patients), a single postsurgical evaluation (8 patients), and "asymptomatic PHPT" with no surgical criteria (17 patients). The baseline presentation was considered when the PHPT diagnosis was established. For follow-up, the last presentation available in the authors' database was registered. Of the remaining 125 Caucasian patients, 46 patients were lost to follow-up after diagnosis, 38 patients were surgically cured, and 41 patients received surgical treatment without PHPT curation (N = 3) or medical treatment (N = 38). As all patients included had surgical criteria, the reasons for medical treatment were lack of autonomous parathyroid localization, contraindication for surgery or patients' choice.

All patients signed an informed consent form that allowed the use of their medical records for scientific research and data reports. All the planning, collecting, and reporting of human data were in accordance with the Helsinki Declaration of 2013 and approved by the Ethics Board of Elias Emergency and University Hospital, decision no. 9299/02.10.2017.

We clinically assessed demographic data such as age, height, and weight to compute the body mass index (BMI), personal and family medical history of different comorbidities, and Allopurinolum usage. Erythrocyte sedimentation rate (ESR), SUA, creatinine, glucose, total serum calcium, magnesium (Mg), total high-density lipid (HDL), triglycerides (trig), gamma-glutamyl transferase (GGT), and iPTH levels were measured using an automated hematology analyzer (Sediplus), chemistry analyzer (Beckman Coulter) and electrochemiluminescence (Cobas). Hyperuricemia diagnosis was based on SUA levels higher than 5.7 mg/dl in females and 7 mg/dl in males. Surgery criteria were based on the 4th International Workshop Guidelines for the Management of Asymptomatic Primary Hyperparathyroidism 2014 (13).

Statistical Analysis

Statistical analysis was performed using IBM software SPSS version 26. The normal distribution of variables was assessed using the Shapiro-Wilk test. We expressed categorical variables as numbers (percentages) and compared them using the chi-square test. While continuous variables were described as the mean or mean ± standard deviation (SD) or median [interquartile range 25; 75], comparisons between groups were conducted using Student's t test or Mann–Whitney test, depending on their distribution. We calculated their association using Spearman's correlation

coefficients, and the Wilcoxon signed-rank test was used to conduct a paired difference test between repeated measures of nonparametric continuous variables. A linear regression model was used to predict the variability of SUA as a continuous variable. The statistical significance was set at $p < .05$.

Demographics and Results

Our 125 patients with PHPT had a median age of 62.59 years [53.07; 69.38] and a mean BMI of 29.28±6.02 kg/m^2. Nine patients (7.2%) had normocalcemic PHPT. Hyperuricemia was encountered in 34 patients (27.2%), of whom 5 were undergoing treatment with Allopurinolum. These 34 hyperuricemic PHPT patients were significantly older (64.74±13.72 vs. 57.92±10.92, p = .012) and had higher values of total serum calcium (11.55 [11.05; 12.42] vs. 11.2 [10.8; 11.96], p = .039) and creatinine (0.82 [0.76; 0.99] vs. 0.73 [0.68; 0.81], p = .001) with similar BMI (29.15 ± 5.98 vs. 28.62 ± 6.28, p = .729) and PTH levels (170 [117.1; 311.45] vs. 122.85 [82.48; 202.5], p = .151), compared to the 91 normocalcemic PHPT patients.

SUA correlated with: age (p = .006. r =.295), BMI (p = .071. r = .222), total calcium (p = .004, r = .328), iPTH (p = .076, r = .197), creatinine (p < .001, r = .609), glucose (p = .042, r = .221), HDL-chol (p = .004, r = .491), trig (p < .001, r = .491), ESR (p = .008, r = .294), Mg (p < .001, r = -.478) and GGT (p = .003, r = .338).

A linear regression model that accounts for 51.5% of SUA level variability using age, serum calcium levels, creatinine, magnesium, ESR, and triglycerides as covariates identified age (p =.003), creatinine (p <.001), calcium (p =.019) and triglycerides (p =.005) as covariates with unique contributions.

Table 1 presents the demographic and biochemical data of cured patients in comparison with conservatively treated patients. At baseline, the only significantly different parameters between the two subgroups were serum calcium levels (11.55 [11; 12.12] vs. 11 [10.42; 11.47], p =.007) and SUA levels (5.65 [4.49; 7.45] vs. 5 [4.56; 6.55], p =.026), and no statistically significant difference in regard to age and BMI was noted among surgically and medically treated patients. After successful parathyroidectomy, the 38 cured patients showed statistically lower serum calcium, SUA, and Mg levels compared to their baseline, while the 41 medically treated patients showed no statistically significant difference in the analyzed parameters.

Discussions

Our study aimed to evaluate the distinctive parameters and comorbidities of patients diagnosed with a comparable type of PHPT. Therefore, we excluded individuals with asymptomatic PHPT, and the results of this study are based on a cohort with at least one

Table 1. Demographic and biochemical data of surgically cured vs. conservatively managed patients

	Successful PTX (N = 38)			Medical approach (N = 41)		
Age at baseline (yo)	58.93±11.38			62.97±11.04		
Follow-up (years)	1 [0.3; 2.72]			2.5 [1.1; 3.2]		
BMI (kg/m^2)	27.96±4.3			30.47±6.88		
	Baseline	**Last presentation**		**Baseline**	**Last presentation**	
Serum total calcium (mg/dl)	11.55 [11; 12.12]	9.3 [8.7; 9.75]	p < .001	11 [10.42; 11.47]	10.75 [10.5; 11.2]	NS
SUA (mg/dl)	5.65 [4.49; 7.45]	4.95 [3.52; 6.3]	p = .011	5 [4.56; 6.55]	5.6 [4.95; 6]	NS
Creatinine (mg/dl)	0.76 [0.67; 0.92]	0.76 [0.7; 0.96]	NS	0.73 [0.66; 0.88]	0.8 [0.69; 0.92]	NS
Triglycerides (mg/dl)	117 [93.5; 191]	106 [82; 143]	NS	106 [81; 140]	100 [78; 137]	NS
HDL-chol (mg/dl)	49 [39.5; 59.5]	52 [45; 60.5]	NS	59 [46.5; 73]	56 [48; 68.5]	NS
ESR (mm/h)	12.5 [6.5; 22]	15.5 [7; 28.25]	NS	13.5 [9; 22]	13 [8; 19.5]	NS
Mg (mg/dl)	2.08 [1.9; 2.26]	1.92 [1.8; 2]	p = .002	2 [1.86; 2.14]	2.01 [1.77; 2.13]	NS

surgical criterion.

Hyperuricemia was found in 27.2% of our PHPT patients, while Bergenfelz et al. showed that 9.9% of the 323 patients operated on for sporadic PHPT had increased levels of serum uric acid. This lower prevalence of hyperuricemia might be due to the different cutoffs used for hyperuricemia diagnosis in the Bergenflez study: over 7.06 mg/dl for women and over 8.07 mg/dl for men (14).

The association between PTH and SUA was demonstrated not only in PHPT patients but also in the general population, as a study with 8316 American participants over 18 yo highlighted that PTH levels are independently associated with SUA levels and with hyperuricemia (15). The underlying mechanism, first thought to be associated with the decrease in uric acid renal clearance since PHPT is associated with renal damage (1), (16), cannot explain this association in the general population with normal levels of serum PTH and normal renal function. Therefore, as it is known that PTH can affect certain transporters in the proximal tubule of the kidney (17), it has been suggested that, through a similar mechanism, it can also affect the secretory and absorptive transporters at the basolateral and apical membranes that are involved in the kidney transportation of uric acid by the ATP-binding cassette transporter G2 (2,3,18).

Our 34 PHPT patients with hyperuricemia had a significantly higher mean age and significantly higher median values of both serum creatinine and calcium levels than those with normal levels of SUA. In our opinion, this may suggest that a slow progressive form of PHPT leads to hyperuricemia, as higher calcium levels were seen in older patients.

In our study group, SUA levels had a weak positive correlation with serum calcium levels and only a very weak positive correlation with iPTH levels. In the Miller study, which consisted of 736 osteoporotic patients treated with teriparatide, subjects with moderate renal impairment displayed an increase in SUA levels > 9 mg/dl, along with an increase in the levels of serum calcium > 10.6 mg/dl 4-6 h postdose. The study indicates an increase in SUA levels after exogenous PTH administration, which may look like a straightforward PTH-SUA fallout, but we find it noteworthy that this increase was found in the same cohort that also showed a calcium increase; therefore, a calcium moderated mechanism cannot be easily excluded from the connection between PTH and SUA (19).

When we ran a linear regression model with SUA variability as the output variable, we identified calcium as a covariate with a unique contribution, advocating that calcium is a key contributor to SUA variability. These results are endorsed by a Mendelian randomization analysis published by Yuan S. in 2022, which revealed that the risk of hyperuricemia is significantly higher in patients with hypercalcemia (20).

Similar to other studies (1,14,21,22,23,24), our results reveal a statistically significantly lower SUA level at the 1-year median follow-up postparathyroidectomy. The mechanism behind this reduction is still unknown, as the creatinine level remained similar to the preoperative level. With similar results, Bergenfelz suggests a hypothesis that introduces the syndrome of insulin resistance alongside the production of uric acid induced by the PHPT state (14). Castrillo's study, however, revealed that, after more than 5 years of follow-up, parathyroidectomized patients showed a significant SUA increase, up to levels higher than before the surgery (25). As this long follow-up period may be a confounder, the SUA increase should not be considered a rebound; it should more likely be associated with the deterioration of renal function observed in older patients. For a more reliable depiction, a control PHPT group with no curative surgical treatment, followed up for a similar period of time, could be useful.

Our PHPT patients who were medically treated or received unsuccessful parathyroidectomy displayed a nonsignificant, although higher level of SUA in their 2.5-year follow-up period. Their slightly older age, the increase in their creatinine level during the

follow-up period, or their constant hyperparathyroidism state despite the usage of calcium-lowering medication may explain the different SUA levels compared to the surgically cured PHPT patients.

It has been observed that PHPT, even in its modern presentation, is a risk factor for cardiovascular events (26,27) as is hyperuricemia (28). Bergenfelz et al. suggested that patients who had SUA normalization as a consequence of parathyroidectomy had a lower 10-year mortality risk and advocated for at least considering assessing SUA levels in patients with PHPT (14). Since some papers, including ours, indicate a significant lowering effect of curative parathyroidectomy on SUA levels, we also suggest measuring serum uric acid in patients with PHPT, as more quality evidence is needed for the integration of uric acid in the therapeutic course of action of primary hyperparathyroidism.

The strengths of our study are that this is the first Romanian study that we know of that evaluates the prevalence of hyperuricemia in PHPT and the relationship between SUA levels and calcium metabolism, which is important considering the shortfall of demographic data in Eastern European populations on this topic; the present data highlight a distinct trajectory of SUA levels depending on therapeutic choice, emphasizing the benefits of curative parathyroidectomy.

This study has some limitations, including a relatively low number of patients, especially with normocalcemic PHPT compared to those with hypercalcemic PHPT. A larger sample size could offer a better insight into the implication of calcium metabolism in hyperuricemia. In addition, the study was conducted in an endocrinology tertiary care center, which could imply a recruitment bias, explaining the low number of normocalcemic patients. There was a lack of quantitative data regarding Allopurinolum usage, diuretic agents, and antiresorptive drugs, which could interfere directly or indirectly with the metabolism of uric acid in both surgically and medically treated subgroups. Finally, we were unable to integrate vitamin D measurements and supplementation, overlooking its possible implications in uric metabolism.

Future prospects are as follows: large double-arm prospective trials in both symptomatic and asymptomatic PHPT, integration of 25(OH) vitamin D in the PTH-SUA feedback loop, and integration of SUA level measurements in therapeutic decisions.

Conclusions

Patients with PHPT and hyperuricemia have significantly higher serum calcium levels. Serum calcium levels positively correlate with SUA levels in PHPT patients and are independent predictor of uric acid values.

Patients who underwent curative parathyroidectomy showed a significant decrease in SUA levels during 1 year of follow-up.

Conflict of Interest and Source of Funding

The authors declare none.

Authors' Contribution

TO conceived the study's conceptualization and methodology, performed the statistical analysis, interpreted the results, and drafted the manuscript. CB participated in the development of the design and in the analysis and interpretation of the data, as well as in the review and editing of the study. IN and RC participated in data curation and formal analysis. CB, SM, AS, and SF referred to the patients and supervised data collection and interpretation. All authors critically revised the manuscript, approved the final version, and agree to be accountable for all the aspects of the work.

References

1. Duh QY, Morris RC, Arnaud CD, Clark OH. Decrease in serum uric acid level following parathyroidectomy in patients with primary hyperparathyroidism. World J Surg. 1986;10(4):729-736.
2. Ponvilawan B, Charoenngam N, Ungprasert P. Primary hyperparathyroidism is associated with a higher level of serum uric acid: A systematic review and meta-analysis. Int J Rheum Dis. 2020;23(2):174-180.
3. Sugimoto R, Watanabe H, Ikegami K, Enoki Y, Imafuku T, Sakaguchi Y, et al. Down-regulation of ABCG2, a urate exporter, by parathyroid hormone

enhances urate accumulation in secondary hyperparathyroidism. Kidney Int. 2017;91(3):658-670.
4. Weinman EJ, Eknoyan G, Suki WN. The influence of the extracellular fluid volume on the tubular reabsorption of uric acid. J Clin Invest. 1975; 55(2):283-291.
5. Kanbay M, Jensen T, Solak Y, Le M, Roncal-Jimenez C, Rivard C, et al. Uric acid in metabolic syndrome: From an innocent bystander to a central player. Eur J Intern Med. 2016;29:3-8.
6. Grimaldi-Bensouda L, Alpérovitch A, Aubrun E, Danchin N, Rossignol M, Abenhaim L, et al. Impact of allopurinol on risk of myocardial infarction. Ann Rheum Dis. 2015;74(5):836-42.
7. Kao MP, Ang DS, Gandy SJ, Nadir MA, Houston JG, Lang CC, et al. Allopurinol benefits left ventricular mass and endothelial dysfunction in chronic kidney disease. J Am Soc Nephrol. 2011;22(7):1382-9.
8. Baldwin W, McRae S, Marek G, Wymer D, Pannu V, Baylis C, et al. Hyperuricemia as a mediator of the proinflammatory endocrine imbalance in the adipose tissue in a murine model of the metabolic syndrome. Diabetes. 2011;60(4):1258-69.
9. Purra S, Lone AA, Bhat MH, Misgar RA, Wani AI, Bashir MI, et al. Cardiac structural and functional abnormalities in primary hyperparathyroidism. J Endocrinol Invest. 2022;45(2):327-335.
10. Zhou Y, Chu X, Jiang D, Wu X, Xu J, Qi H, et al. Development and validation of a nomogram for risk prediction of nephrolithiasis recurrence in patients with primary hyperparathyroidism. Front Endocrinol (Lausanne). 2022;13:947497.
11. Johnson RJ, Nakagawa T, Sanchez-Lozada LG, Shafiu M, Sundaram S, Le M, et al. Sugar, uric acid, and the etiology of diabetes and obesity. Diabetes. 2013;62(10):3307-15.
12. Bilezikian JP, Khan AA, Silverberg SJ, El-Hajj Fuleihan G, Marcocci C, Minisola S, 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.
13. Bilezikian JP, Brandi ML, Eastell R, Silverberg SJ, Udelsman R, Marcocci C, et al. Guidelines for the management of asymptomatic primary hyperparathyroidism: summary statement from the Fourth International Workshop. J Clin Endocrinol Metab. 2014;99(10):3561-9.
14. Bergenfelz A, Bladström A, Their M, Nordenström E, Valdemarsson S, Westerdahl J. Serum levels of uric acid and diabetes mellitus influence survival after surgery for primary hyperparathyroidism: a prospective cohort study. World J Surg. 2007;31(7):1393-1402.
15. Hui JY, Choi JW, Mount DB, Zhu Y, Zhang Y, Choi HK. The independent association between parathyroid hormone levels and hyperuricemia: a national population study. Arthritis Res Ther. 2012;14(2):R56.
16. Klinenberg JR, Gonick HC, Dornfeld L. Renal function abnormalities in patients with asymptomatic hyperuricemia. Arthritis Rheum. 1975;18(6 Suppl):725-730.
17. Girardi AC, Titan SM, Malnic G, Rebouças NA. Chronic effect of parathyroid hormone on NHE3 expression in rat renal proximal tubules. Kidney Int. 2000;58(4):1623-1631.
18. Lipkowitz MS. Regulation of uric acid excretion by the kidney. Curr Rheumatol Rep. 2012;14(2):179-188.
19. Miller PD, Schwartz EN, Chen P, Misurski DA, Krege JH. Teriparatide in postmenopausal women with osteoporosis and mild or moderate renal impairment. Osteoporos Int. 2007;18(1):59-68.
20. Yuan S, Yu L, Gou W, Wang L, Sun J, Li D, et al. Health effects of high serum calcium levels: Updated phenome-wide Mendelian randomisation investigation and review of Mendelian randomisation studies. EBioMedicine. 2022;76:103865.
21. Ljunghall S, Akerström G. Urate metabolism in primary hyperparathyroidism. Urol Int. 1982;37(2):73-78.
22. Pepersack T, Jabbour N, Fuss M, Karmali R, Van Geertruyden J, Corvilain J. Hyperuricemia and renal handling of urate in primary hyperparathyroidism. Nephron. 1989;53(4):349-352.
23. Broulik PD, Stěpán JJ, Pacovský V. Primary hyperparathyroidism and hyperuricaemia are associated but not correlated with indicators of bone turnover. Clin Chim Acta. 1987;170(2-3):195-200.
24. Bibik EE, Dobreva EA, Elfimova AR, Miliutina AP, Eremkina AK, Gorbacheva AM , et al. Primary hyperparathyroidism in young patients is associated with metabolic disorders: a prospective comparative study. BMC Endocr Disord. 2023;23(1):57.
25. Castrillo JM, Díaz-Curiel M, Rapado A. Hyperuricemia in primary hyperparathyroidism: incidence and evolution after surgery. Adv Exp Med Biol. 1984;165 Pt A:151-157.
26. Ybarra J, Doñate T, Jurado J, Pou JM. Primary hyperparathyroidism, insulin resistance, and cardiovascular disease: a review. Nurs Clin North Am. 2007;42(1):79-vii.
27. Nilsson IL, Yin L, Lundgren E, Rastad J, Ekbom A. Clinical presentation of primary hyperparathyroidism in Europe--nationwide cohort analysis on mortality from nonmalignant causes. J Bone Miner Res. 2002;17 Suppl 2:N68-N74.
28. Høieggen A, Alderman MH, Kjeldsen SE, Julius S, Devereux RB, Ulf De Faire, et al. The impact of serum uric acid on cardiovascular outcomes in the LIFE study. Kidney Int. 2004;65(3):1041-9.