limit (BQL) and gave higher overall trough concentrations (C_{min}) compared to pegloticase monotherapy in the phase 3 studies.

Pegloticase 8 mg IV every 2 weeks co-treatment with MTX 15 mg weekly was associated with an improved response rate for pegloticase in association with improved drug levels in these patients with uncontrolled gout compared to pegloticase monotherapy in the phase 3 studies.

REFERENCES:

- [1] Botson J., et al. *J Rheumatol*. 2020; doi: 10.3899/jrheum.200460
- [2] Goss S. L., et al. *Clin Ther*;2018, 40 (2).
- [3] Lipsky P. E., et al. *Arthritis Res Ther*;2014, 16 (2).
- [4] Sundry J. S., et al. *JAMA*;2011, 306 (7).
- [5] Yue C. S., et al. *ASCP*, Atlanta, 2010.

*Data that are BQL (Below quantitation limit of 0.6 µg/mL) were imputed as 0.3 µg/mL (LLOQ/2).
Closed circles: Responders (11/14 in MIRROR OL; 36/85 in C0405 and C0406);
Open triangles: Non-responders (3/14 in MIRROR OL; 49/85 in C0405 and C0406).
Lower, middle and upper lines represent Q1, median and Q3 of data range.
Median pegloticase C_{min} and C_{max} were calculated based on observed values across visits.

Figure 1. Comparison of pegloticase exposures (C_{max} and C_{min}) in methotrexate co-treatment (MIRROR OL) and monotherapy trials (C0405 and C0406)

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POS1137 IDENTIFYING ADULT HYPOPHOSPHATASIA IN THE RHEUMATOLOGY UNIT

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Background: The most frequent manifestation in adult Hypophosphatasia (HPP) is musculoskeletal pain.^{1,2} The unspecific nature of its clinical presentation may prevent correct diagnosis.³

Objectives: Identifying adult hypophosphatasia in the rheumatology unit.

Methods: Over a period of 10 years 9,522 patients were screened in a rheumatological outpatient unit. Serum ALP levels ≤ 40 U/l were found in 524 patients. After screening for secondary causes, 73 patients were invited for clinical evaluation. Genetic testing was performed in 23 patients with suspected HPP. Logistic regression models were used to estimate the association of each clinical factor with HPP.

Results: Mutations in the *ALPL* gene were observed in 57% of genetically screened patients. Arthralgia, fractures and pain were the leading symptoms in HPP patients. Chondrocalcinosis (OR 29.12; 95% CI 2.02-1593.52) and dental disease (OR 8.33; 95% CI 0.93-143.40) were associated with HPP independent of BMI. Onset of symptoms in HPP was at 35.1 (14.3) years, with a mean duration from symptoms to diagnosis of 14.4 (8.1) years. Bone mineral density (BMD) and trabecular bone score (TBS) as well as bone turnover markers were not indicative for HPP.

Conclusion: HPP can mimic joint diseases.⁴ Thus, in patients with uncertain rheumatologic complaints and low ALP, HPP should be considered as potential diagnosis.

REFERENCES:

- [1] Durrrough C, Colazo JM, Simmons J, et al. Characterization of physical, functional, and cognitive performance in 15 adults with hypophosphatasia. *Bone* 2021;142:115695.
- [2] Seefried L, Kishnani PS, Moseley S, et al. Pharmacodynamics of asfotase alfa in adults with pediatric-onset hypophosphatasia. *Bone* 2021;142:115664.
- [3] Högl W, Langman C, Gomes da Silva H, et al. Diagnostic delay is common among patients with hypophosphatasia: initial findings from a longitudinal, prospective, global registry. *BMC musculoskeletal disorders* 2019;20(1):80.
- [4] Seefried L, Dahir K, Petryk A, et al. Burden of Illness in Adults With Hypophosphatasia: Data From the Global Hypophosphatasia Patient Registry. *Journal of bone and mineral research: the official journal of the American Society for Bone and Mineral Research* 2020;35(11):2171-78.

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POS1138 SERUM URIC ACID-TO-CREATININE RATIO: A POTENTIAL MARKER FOR GOUT

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Background: Serum uric acid-to-creatinine ratio (SUA/Cr) is a useful index of renal function-normalized serum uric acid (SUA), which reflects endogenous SUA levels more precisely than SUA. SUA/Cr relates to disease activity and prognosis of several metabolic disorders, like metabolic syndrome, non-alcoholic fatty liver disease, and diabetes mellitus [1]. Besides, the urine uric acid-to-creatinine ratio is valuable for the assessment of gout [2]. However, no study focuses on the relationship between SUA/Cr and gout.

Objectives: We aimed to investigate the relationship between SUA/Cr and the features of demography, manifestations, laboratory tests, and urate-lowering therapies (ULTs) in gout patients.

Methods: This cross-sectional study was performed from December 2015 to February 2020. Medical records of gout patients who were regularly undergone follow-up were evaluated. Characteristics of gout patients, included age, gender, the duration of gout, body mass index (BMI), tophus, complications, the number of flares, C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR), were recorded. Complications were defined as hypertension, coronary artery diseases, diabetes, strokes, and/or metabolic diseases. Information about ULT was obtained as well. The Spearman correlation analysis was used to assess the relationship between continuous variables. The Mann-Whitney U test or Kruskal-Wallis test was employed to compare the differences of SUA/Cr between genders, ULTs, and whether patients had tophus or complications. A $P < 0.05$ was considered as statistically significant.

Results: (1) Of 627 gout patients who were involved, 608 (96.97%) were male. Their median (range) of age and the duration of gout were 30.00 (51.00) years and 5.00 (30.00) years, respectively. (2) SUA/Cr negatively correlated with age ($r = -0.71$, $P < 0.05$). SUA/Cr was similar between genders. (3) SUA/Cr positively correlated with BMI ($r = 0.14$, $P < 0.05$), while the coefficient correlation for the duration of gout and the number of flares did not reach statistically significant ($P > 0.05$). SUA/Cr was significantly higher in patients with complications than the others [5.56 (9.26) vs. 4.16 (8.34), $P < 0.05$], but whether patients with tophus or not shared similar SUA/Cr. (4) CRP and ESR did not associate with SUA/Cr ($P > 0.05$). (5) Patients with combination therapy with xanthine oxidase inhibitor and uricosuric agent had a lower SUA/Cr compared with those who used ULTs monotherapy [3.44 (7.10) vs. 4.53 (7.91), $P < 0.05$].

Conclusion: SUA/Cr relates to some features of gout, so it may be a potential marker for its assessment.

REFERENCES:

- [1] *Medicine (Baltimore)* 2020;99(17):e19959.
- [2] *J Korean Med Sci* 2020;35(13):e95.

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POS1139

COMPARISON OF THE FREQUENCY OF DETECTION OF EARLY SIGNS OF ATHEROSCLEROSIS IN PATIENTS WITH CALCIUM PYROPHOSPHATE CRYSTAL DEPOSITION DISEASE AND OSTEOARTHRITIS

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Background: Crystal-induced inflammation can significantly increase cardiovascular risk (CVR) and cause early development of atherosclerosis [1]. However, no studies have been performed in patients with calcium pyrophosphate crystal deposition disease (CPPD).

Objectives: To compare the presence of atherosclerosis early signs (increased thickness of the intima-media complex (CMT)) in patients with CPPD and osteoarthritis (OA).

Methods: A cross-sectional study included 48 patients, aged 18 to 65 years, 26 patients with crystal-verified diagnosis of CPPD (McCarty criteria) (6 (23%) men and 20 (77%) women) and 22 patients with OA (7 (32%) men and 15 (68%) women). Exclusion criteria are the presence of other rheumatic diseases with symptoms of arthritis, diabetes mellitus, coronary heart disease (CHD), prior myocardial infarction, stroke or myocardial revascularization surgery, estimated glomerular filtration rate (eGFR) <60 ml/min/1.73 m², high and very high CVR on the SCORE scale. The examination of the patients included the history taking, assessment of anthropometric parameters and the following laboratory tests: determination of serum creatinine level (eGFR according to the MDRD formula), total cholesterol (TC), high density lipoprotein cholesterol (HDL cholesterol) and low density lipoprotein cholesterol (LDL cholesterol), C-reactive protein (CRP). Doppler ultrasound of the carotid arteries with an assessment of the thickness of the intima media complex (CMT) was made for all patients - CMT up to 0.9 mm was taken as the norm, CMT > 0.9 mm and <1.3 mm as increased, and CMT >1.3 mm was regarded as an atherosclerotic plaque. Statistica 12.0 package was used for statistical data processing.

Results: The groups were completely comparable by gender, age and all laboratory parameters (see Table 1), an increase in CRP >5 mg/l was more often detected in patients with CPPD - 31% vs 14% patients with OA (p=0.16).

Table 1. Clinical characteristics of patients included in the study.

Parameters	CPPD (n=26)	OA (n=22)	p value (reliable at p<0,05)
Age, years M±SD	55.9±5.9	52.4±8.3	0.14
Gender, men/women, n (%)	6 (23)/20 (77)	7 (32)/15 (68)	0.50
Smoking, n (%)	5 (19)	6 (27)	0.50
Systolic blood pressure, mmHg, M±SD	134±20	127±15	0.19
Arterial hypertension, n (%)	13 (50)	10 (45)	0.75
Family history of CVD, n %	6 (23)	7 (32)	0.50
TC, mmol/L, M±SD	5.4±1.3	5.3±1.3	0.95
TC >5.0 mmol/L, n (%)	17 (65)	10 (45)	0.17
HDL, mmol/L M±SD	1.7±0.5	1.4±0.5	0.10
LDL, mmol/L, M±SD	2.9±1.3	3.4±1.4	0.33
Creatinine, µmol/L, M±SD	73.2±13.8	78.9±11.5	0.16
CRP, mg/l, Me [25-75th percentiles]	1.1 [0.6; 6.4]	1.2 [0.3; 2.8]	0.60
CRP ≥5 mg/l, n (%)	8 (31)	3 (14)	0.16

Mean CMT values on the right (0.76±0.22 mm vs 0.70±0.18 mm) and on the left (0.75±0.18 mm vs 0.70±0.17 mm) did not significantly differ in CPPD and OA (p=0.34 and 0.32, respectively), the maximum CMT values on the right (0.67±0.16 mm vs 0.67±0.16 mm) and on the left (0.67±0.14 mm vs 0.66±0.16 mm) with CPPD and OA were also comparable (p=0.95 and 0.77, respectively). However, an increase in CMT > 0.9 mm was found in 13 (50%) patients with CPPD and only 5 (23%) with OA (p=0.02). No increase in CMT >1.3 mm was found in patients of both groups.

Conclusion: Early signs of atherosclerosis are detected in 50% of patients with CPPD without clinical signs of atherosclerosis and with low or moderate CVR

according to SCORE, significantly more often than in patients with OA (23%), which can be reflection of chronic crystal-induced inflammation.

REFERENCES:

- [1] Hoseini Z, Sepahvand F, Rashidi B, Sahebkar A, Masoudifar A, Mirzaei H. NLRP3 inflammasome: Its regulation and involvement in atherosclerosis. *J Cell Physiol.* 2018 Mar;233(3):2116-2132. doi: 10.1002/jcp.25930. Epub 2017 May 23. PMID: 28345767.

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POS1140

RISK FACTORS FOR THE DEVELOPMENT OF DIABETES MELLITUS IN PATIENTS WITH GOUT ACCORDING TO A 6-YEAR PROSPECTIVE FOLLOW-UP STUDY

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Background: Gout is often associated with diabetes mellitus (DM), but the role of serum uric acid (sUA) and urate-lowering drugs in its development in patients with gout remains controversial [1].

Objectives: To study risk factors for DM in patients with gout based on the results of long-term prospective follow-up study.

Methods: The prospective study included 444 patients with a crystal-verified diagnosis of gout, aged ≥18 years, 49 (11%) women, 395 (89%) men. Patients were followed up at the V.A. Nasonova Research Institute of Rheumatology from 2010 to January 2021, the median follow-up was 6.1 [2.8; 7.8] years. The exclusion criteria were the presence of other rheumatic diseases with symptoms of arthritis, DM. DM was diagnosed on the 1998 WHO criteria. The following parameters were considered as risk factors: gender, family history for diabetes mellitus, body mass index (BMI) >25 kg/m² and > 30 kg/m², waist volume ≥88 cm for women and ≥102 cm for men, alcohol consumption > 20 units per week, chronic kidney disease (CKD), intake of diuretics and glucocorticoids, and serum total cholesterol >5 mmol/l, triglycerides >2.25 mmol/l, serum C-reactive protein (CRP) level > 5 mg/l, as well as clinical manifestations of gout: subcutaneous tophi, polyarthritis (simultaneous involvement of ≥5 joints), intake of urate-lowering drugs, sUA (> 480 µmol/L, > 420 µmol/L, > 360 µmol/L, > 300 µmol/L). Statistica 12.0 package was used for statistical data processing.

Results: A total of 444 patients were included, the mean age was 51.0±12.9 years, the median follow-up was 6.1 [2.8; 7.8] years. In dynamics: 35 (8%) patients died, 6 (1%) patients were not available, 403 patients were examined (44 (11%) - women and 359 (89%) - men). 290 (72%) patients received urate-lowering therapy (263 (65%) patients used allopurinol, 27 (7%) - febuxostat). The target sUA <360 µmol/L was reached by 165 (41%) patients and <300 µmol/L - by 92 (23%) patients. All patients with sUA <300 µmol/L received urate-lowering therapy, 62 (67%) patients used allopurinol, 17 (18%) - febuxostat, 13 (14%) - uricosuric drugs. Diabetes mellitus was developed in 106 (26%) patients. The factors influencing the risk of developing diabetes were - the presence of diabetes in family history (odds ratio (OR) 2.27, 95% confidence interval (CI) 1.37; 3.76; BMI > 30 kg / m² (OR 1.79, 95% CI 1.14; 2.80), diuretics (OR 2.32, 95% CI 1.36; 3.96) and sUA > 300 µmol / l (OR 2.89, 95% CI 1.50, 5.56).

Conclusion: The risk of developing DM in patients with gout is associated with sUA > 300 µmol/l, which may be one of the probable reasons for choosing this as a target level. Large prospective studies are needed to confirm the antidiabetic effect of urate-lowering drugs.

REFERENCES:

- [1] Chang HW, Lin YW, Lin MH, Lan YC, Wang RY. Associations between urate-lowering therapy and the risk of type 2 diabetes mellitus. *PLoS One.* 2019 Jan 7;14(1):e0210085. doi: 10.1371/journal.pone.0210085.

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