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THU0405

SERUM METABOLIC PROFILING ANALYSIS OF GOUT PATIENTS BASED ON UHPLC-Q-TOF/MS

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Background: Gout is a common kind of inflammatory arthritis with metabolic disorders. The detailed pathogenesis of gout remains largely unknown. Metabolomics has become an important tool in detecting the new pathogenesis and biomarkers. However, few studies have focused on the serum metabolic profiling of gout.

Objectives: The study aims to investigate the metabolic profiling of gout patients with ultra-performance liquid chromatograph quadrupole time-of-flight mass spectrometry (UPLC-Q-TOF-MS), and explore the potential pathological mechanisms and biomarkers.

Methods: Serum samples from 31 gout patients and 31 healthy controls were analyzed by UPLC-Q-TOF-MS. Principal components analysis (PCA), orthogonal partial least squares-discriminant analysis (OPLS-DA) and Hierarchical clustering analysis were performed to detect different compounds between the two groups. Receiver operating characteristic (ROC) curve analysis and pathway analysis of the different metabolites were conducted.

Results: A total of 9192 compounds were detected, of which 138 significantly different compounds were selected, according to the criteria of (Variable importance in projection (VIP)>3, $P<0.05$). Eventually, 96 reliable metabolites matched the HMDB database were confirmed. ROC curve results showed that the area under the curve (AUC) value of 4-hydroxytriazolam for gout was 0.933 (CI95%: 0.875-0.992), yielding a highest AUC value, with the sensitivity of 83.9% and specificity of 93.5%. The pathway analysis results indicated that the significantly different metabolites were mainly involved in "primary bile acid biosynthesis", "purine metabolism" and "glycerophospholipid metabolism".

Conclusion: The serum metabolic profiling in gout patients were significantly different from healthy subjects. 4-hydroxytriazolam was the potential biomarkers. Primary bile acid biosynthesis may be a novel metabolic pathway of gout.

Figure 1 A: Hierarchical clustering analysis of the significantly different compounds. B: Pathway analysis of the significantly different metabolites.

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THU0406

IDENTIFICATION OF INTRACELLULAR VACUOLES IN SYNOVIAL FLUID WITH CALCIUM PYROPHOSPHATE AND MONOSODIUM URATE CRYSTALS

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Background: Synovial fluid analysis using polarized microscopy is the gold standard for the diagnosis of crystal-related arthritis. In our experience, we have

noted that, when calcium pyrophosphate (CPP) crystals are observed, they sometimes appear within intracellular vacuoles. However, this phenomenon is not seen in those samples containing monosodium urate (MSU) crystals. This finding has been scantily reported in the literature, but may be useful in clinical practice to ensure accurate crystal identification.

Objectives: Our study aims to assess whether the presence of vacuoles contributes to identifying the type of crystal, and also to gauge the frequency of their presentation.

Methods: We conducted an observational study in a rheumatology unit between February and June of 2019. Synovial fluids containing CPP or MSU crystals, obtained in daily clinical practice, were consecutively included for analysis. Two observers simultaneously analyzed the presence of vacuoles by ordinary light and phase contrast microscopy in less than 24 hours after their extraction, using a microscope equipped with two viewing stations. The primary study variable was to determine whether CPP and MSU crystals are seen inside intracellular vacuoles, and to calculate the frequency of this finding for each type of crystal, estimating their 95% confidence interval (95% CI) and comparing rates using Fisher's exact test.

Results: Twenty-one samples were obtained. Data is given in the Table. MSU crystals were present in 7 (33.3%) and CPP crystals in 14 (66.6%). Interestingly, none of the MSU samples showed crystal-containing vacuoles (95% CI 0-35.4%). On the contrary, cytoplasmic vacuoles containing crystals were present in all of the CPP samples (95% CI 78.5-100%). The findings were confirmed by phase-contrast microscopy. Differences were statistically significant ($p<0.001$).

Table.

SAMPLES ACCORDING TO TYPE OF MICROCRYSTAL (n=21)	SAMPLES WITH VACUOLS (UNDER ORDINARY LIGHT)	SAMPLES WITH VACUOLS (UNDER PHASE CONTRAST)
CPP (14; 66.6%)	14 (100%) (95%CI 78.5-100%)	14 (100%) (95%CI 78.5-100%)
MSU (7; 33.3%)	0 (0%) (95%CI 0-35.4%)	0 (0%) (95%CI 0-35.4%)

Conclusion: The presence of vacuoles may be a useful and easy way to differentiate MSU and CPP crystals when performing synovial fluid microscopy in clinical practice, since it appears to be a distinctive feature in CPP crystal fluids.

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Image 1. Microscopy with ordinary light. Cells with cytoplasmic vacuoles are observed, as well as abundant intra and extracellular CPP crystals.

Image 2. Microscopy with phase contrast technique. Cells with intracellular vacuoles are observed inside which have microcrystals with parallelepiped morphology, compatible with CPP.

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THU0407

THE VALUE OF SONOGRAPHY IN THE INTERCRITICAL PHASE OF GOUT

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Background: Disease remission is the goal of therapy for many chronic rheumatic diseases. In 2016, provisional gout remission criteria were proposed (1). To the best of our knowledge, no studies have compared ultrasound (US) findings in gouty patients with and without remission.

Objectives: To determine the prevalence of US pathologic findings in patients with gout fulfilling and not fulfilling the provisional remission criteria and to investigate the value of the US findings as predictors of a gouty flare within 6 months.

Methods: Patients with a diagnosis of gout according to the 2015 classification criteria (2) were recruited in this prospective, monocentric study. The following clinical information was recorded at baseline and after 6 months: number of gouty flares in the preceding 6 months, number of subcutaneous tophi, current serum urate level, and patient reported outcomes (pain visual analogue scale and patient global assessment visual analogue scale). Bilateral US assessment of the following anatomical areas was performed (3): elbow, wrist, II metacarpophalangeal joint, knee, ankle and I metatarsophalangeal joint. US evidence of tophi, aggregates, double contour sign and synovitis were recorded according to the correspondent OMERACT definitions.

Results: Forty-nine patients with gout were consecutively enrolled. The remission criteria were satisfied in 9 (18.4%) patients. Monosodium urate (MSU) deposits and findings of synovitis were observed by US less frequently in patients in remission (55.6% and 22.2%), compared with those not fulfilling the criteria (100.0% and 72.5%) (p values < 0.01). The US MSU total score was 1.0; 0.0–2.0 (median and inter-quartile range) for patients in remission, compared with 6.0; 5.0–7.0 for those not fulfilling the criteria (p < 0.01). US synovitis total score was significantly correlated with patient global assessment (R = 0.55, p < 0.01), patient pain (R = 0.51, p < 0.01) and number of gouty attacks in the previous 6 months (R = 0.36, p = 0.03), whereas MSU total score was associated with the number of gouty attacks in the previous 6 months (R = 0.49, p < 0.01), the number of subcutaneous tophi (R = 0.45, p < 0.01), patient pain (R = 0.41, p = 0.01), patient global assessment (R = 0.41, p < 0.01). At logistic regression analysis, the presence of

subcutaneous tophi (OR = 2.8, p = 0.02), CRP level (OR = 6.5, p = 0.04) and US synovitis score (OR = 2.0, p = 0.04) and were predictors of subsequent development of gouty flare within 6 months.

Conclusion: This study provides new insights into the inter-critical phase of gout, highlighting the clinical relevance of US synovitis as a predictor of subsequent development of gouty flare and joint pain. Despite MSU deposits are still detectable in patients satisfying the 2016 provisional remission criteria for gout, the remission is associated with less US detected MSU deposits.

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THU0408

EFFECT OF NEW-ONSET GOUT ON KIDNEY TRANSPLANT OUTCOMES: A RETROSPECTIVE COHORT ANALYSIS OF THE UNITED STATES RENAL DATA SYSTEM

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Background: Gout is a frequent comorbidity in kidney transplant (KT) recipients. However, assessing the independent effect of gout on KT outcomes is difficult because of multiple confounders (e.g., temporal changes in estimated glomerular filtration rate [eGFR], cyclosporine or tacrolimus dose, urate-lowering medication use) that obscure a clear picture of gout's potential impact.

Objectives: This investigation assessed if the development of new-onset gout after KT was an independent risk factor for loss of graft function, as assessed by the need for maintenance hemodialysis following KT.

Methods: This retrospective cohort study analyzed data on patients in the United States Renal Data System (USRDS) who received a primary KT between 1/1/2008 and 12/31/2015. The date of transplantation was the 'index' date. Eligible patients were required to have ≥24 months of Medicare coverage and no prior history of gout, defined as ≥1 claim with a gout diagnosis code in the 24 months prior to the index date. All patients were also required to have ≥12 months of coverage post index. Patients who died, experienced graft failure, or returned to dialysis <12 months post index were excluded. Because the first year following transplant is associated with the highest frequency of rejections, we evaluated subjects beginning 1 year after transplant. The exposure of interest was new-onset gout, defined as the presence of ≥2 claims for gout post index, and the primary endpoint was return to dialysis >12 months post index. Baseline time-invariant confounders included recipient and donor demographics and clinical characteristics at index. Time-varying confounders included body mass index (BMI) adjusted tacrolimus and cyclosporine dose, eGFR, and urate-lowering medication use post index. Patients who died or lost Medicare coverage >12 months post index were censored; all patients remaining at the end of the study period (12/31/2016) were also censored. A marginal structural model (MSM) was fitted to determine the relative risk of new-onset gout on return to dialysis, while controlling for both time-invariant and time-varying confounders.

Results: 18,525 of 466,589 KT recipients in the USRDS met study eligibility. Within the observation period, 1,399 (7.6%) developed new-onset gout and 1,420 (7.7%) returned to dialysis >12 months post index. Median time from index to new-onset gout and from index to return to dialysis was 16.2 months (IQR: 33.4) and 32.8 months (IQR: 28.4), respectively. Adjusting for baseline time-invariant and time-varying confounders via the MSM showed new-onset gout was associated with a 51% increased risk of return to dialysis >12 months post index (RR: 1.51, 95% CI: 1.03, 2.20).