International Journal of General Medicine

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

The Diagnostic Value of Serum MCP-1 Combined with OPN Detection for Early Renal Injury in Gout Patients

Haiying Chang[1], Jing Lv[1], Yinglin Zheng[2], Dongsheng Li[1], Yi Li[2]

[1]Rheumatology Department, Ganzhou People's Hospital, Ganzhou, Jiangxi, 341000, People's Republic of China; [2]Endocrinology Department, Ganzhou People's Hospital, Ganzhou, Jiangxi, 341000, People's Republic of China

Correspondence: Yi Li, Department of Endocrinology, Ganzhou People's Hospital, No. 17 hongqi Avenue, Zhanggong District, Ganzhou, Jiangxi, 341000, People's Republic of China, Tel +8618270976372, Email liaopu908378@sina.com

Objective: To explore the changes in serum Monocyte chemoattractant protein-1 (MCP-1) and Osteopontin (OPN) in gout patients and their diagnostic value for early renal injury.

Methods: In this research, 174 gout patients (January 2022–October 2024) were divided into the early renal injury group (50 cases) and non-early renal injury group (124 cases). Additionally, 169 healthy individuals were included as controls. Clinical indicators such as serum creatinine, cystatin C (CysC), and GFR were recorded. MCP-1 and OPN levels were measured using ELISA. Pearson's correlation was used to analyze relationships; Logit regression was applied to identify influencing factors, and ROC curves assessed diagnostic value, with AUC comparisons via Z-test.

Results: Serum MCP-1 and OPN levels were significantly higher in the gout group compared to controls ($P<0.05$) and further elevated in the early renal injury group ($P<0.05$). MCP-1 and OPN correlated positively with creatinine and CysC and negatively with GFR ($P<0.05$). Logit regression identified MCP-1 (OR: 2.765, 95% CI: 1.308–5.846) and OPN (OR: 3.019, 95% CI: 1.468–6.210) as independent risk factors ($P<0.05$). The AUC for diagnosing early renal injury was 0.775 (MCP-1), 0.827 (OPN), and 0.938 (combined), with the combination significantly outperforming either marker alone ($Z=3.075$, 2.273, $P<0.05$).

Conclusion: The combination of serum MCP-1 and OPN in gout patients has a higher diagnostic value for early renal injury, it is obviously higher than the individual diagnosis of each indicator, and demonstrates significant clinical implications.

Keywords: gout, early renal injury, monocyte chemoattractant protein-1, osteopontin, diagnosis

Introduction

Gout, the most common inflammatory arthritis, is becoming increasingly prevalent worldwide. It is linked to higher risks of diabetes, cardiovascular issues, and kidney disease.[1] Kidney damage in gout patients often goes unnoticed early on, complicating diagnosis. Renal function declines without obvious proteinuria, highlighting the need for more sensitive detection methods.[2] A major challenge remains the absence of diagnostic standards for early kidney injury. While some studies have identified renal changes in gout, such as tubular dilation and fibrosis, they lack specificity.[3] Thus, developing new methods to improve the screening and diagnosis of early kidney injury related to gout is crucial. Monocyte chemoattractant protein-1 (MCP-1), known as CCL2, is a member of CC chemokine family. In arthritis and bone diseases, MCP-1 serves as a major regulator for monocyte recruitment to inflammatory sites[4]. Furthermore, Zheng et al[5] found that activation of tubular Yes-associated protein and maladaptive repair may exacerbate renal inflammation by promoting MCP-1 production. This promotes the progression from acute to chronic kidney disease. Osteopontin (OPN) is a phosphorylated glycoprotein involved in immune regulation in chronic inflammatory conditions like autoimmune diseases, atherosclerosis, and cirrhosis. It is also involved in the progression of arthritis.[6] Peng et al[7] discovered that excessive activation of OPN is closely associated with the development of hypercalciuria, with elevated levels potentially causing renal damage. This work includes 174 gout patients and aims to analyze the diagnostic efficacy of combined serum MCP-1 and OPN testing for early

Received: 2 December 2024
Accepted: 2 March 2025
Published: 11 March 2025

kidney injury in gout patients, intending to improve the accuracy of clinical diagnosis for early kidney injury and provide a reference for reducing the incidence of renal injury in gout patients in the future.

Materials and Methods

General Information

From January 2022 to October 2024, 174 gout patients (62.82±11.05 years, 127 males, 47 females) were included, divided into two groups: no early kidney injury (124 cases) and early kidney injury (50 cases). A control group of 169 healthy individuals (61.54±11.68 years, 116 males, 53 females) was also included. Early renal injury groupearly renal injury group.

The criteria for gout[8] and early kidney injury[9] include: (1) Serum creatinine increase >0.3 mg/dL or >50%, or urine output <0.5 mL/kg/h for >6 hours; (2) First-time gout patients; (3) The study was approved by the ethics committee, and informed consent was obtained from patients and families.; (4) Complete case data. Exclusion criteria: (1) Kidney dysfunction caused by other reasons; (2) Patients with organ failure such as liver, heart, or lung failure; (3) Hematologic disorders; (4) Pseudo-gout or secondary gout; (5) Diabetic ketoacidosis; (6) Pregnant or breastfeeding women. The case collection flowchart is shown in Figure 1.

Methods

Collection of Serum Samples and Detection of MCP-1 and OPN Levels

On the second day (before medication) of hospitalization for the patients and on the day of the physical examination for the healthy controls. 5 mL of fasting venous blood was collected in the morning, centrifuged at −4°C, 3500 rpm for 15 minutes, and the serum was carefully extracted, aliquoted, and stored at −80°C. MCP-1 and OPN levels were measured using the ELISA method according to the manufacturer's instructions. The kits were obtained from Wuhan Baiyixin Biotechnology Co., Ltd. (Catalog number: TD711364) and Shanghai Walan Biotechnology Co., Ltd. (Catalog number: ABE10080).

Clinical Data Collection

Clinical data collected included age, gender, diabetes, hypertension, coronary heart disease, hemoglobin, albumin, serum creatinine, blood uric acid, 24-hour uric acid excretion in urine, urine pH, cystatin C (CysC), glomerular filtration rate (GFR), and homocysteine (Hcy) levels. GFR was calculated using the Cockcroft-Gault equation: 24-hour uric acid excretion in urine GFR = (140 − age) × weight / (72 × serum creatinine) × 0.85 (0.84 for males.

Statistical Analysis

IBM-SPSS 25.0 software was adopted. Categorical data and measurement data were expressed as [n (%)], and means ± standard deviations ($\bar{x} \pm s$) were used for comparison. Unpaired *t*-tests and $\chi 2$ tests were carried out. Pearson's

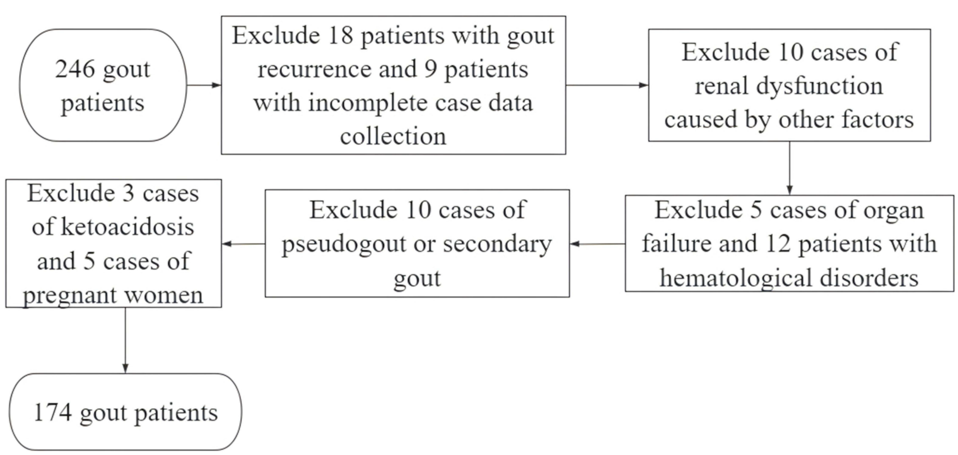

Figure 1 The case collection flowchart.

 https://doi.org/10.2147/IJGM.S508220

correlation was conducted, and Logit regression was used to analyze influencing factors. ROC curves were plotted to analyze the diagnostic value of the indicators for early kidney injury in gout patients, and Z-tests were used to compare AUCs. A p-value less than 0.05 was regarded as statistically significant.

Results

Comparison of Serum MCP-1, OPN Levels and Gender, Age Between the Control Group and Gout Group

No significant differences in gender and age were found, but serum MCP-1 and OPN levels were higher in the gout group ($P<0.05$). See Table 1.

Comparison of Serum MCP-1 and OPN Levels in Different Kidney Injury Groups

Serum MCP-1 and OPN levels were higher in the early renal injury group compared to the no early renal injury group ($P<0.05$). early renal injury groupearly renal injury group. See Table 2.

Comparison of Clinical Data in Different Kidney Injury Groups

There were no statistically significant differences between the no early renal injury group and the early renal injury group in terms of age, gender, diabetes, hypertension, coronary heart disease, hemoglobin, albumin, blood uric acid, 24-hour uric acid excretion in urine, urine pH, or Hcy ($P>0.05$). However, compared with the no early renal injury group, the early renal injury group had significantly higher levels of serum creatinine and CysC and significantly lower GFR levels ($P<0.05$). See Table 3.

Correlation Analysis of Serum MCP-1 and OPN Levels With Clinical Data

Pearson's correlation analysis showed that serum MCP-1 and OPN levels in gout patients revealed a positive relationship with serum creatinine and CysC levels, while exhibiting an inverse relationship with GFR ($P<0.05$). See Table 4.

Analysis of Influencing Factors for Early Kidney Injury

Multivariate logit regression of influencing factors for early kidney injury in gout patients was conducted. Independent variables included MCP-1, OPN, serum creatinine, CysC, and GFR, while the dependent variable was early kidney injury (assigned 1 for presence, 0 for absence). The results showed that MCP-1 (OR: 95% CI=2.765: 1.308–5.846) and OPN (OR: 95% CI=3.019: 1.468–6.210) were independent risk factors for early kidney injury in gout patients ($P<0.05$). See Table 5.

Table 1 Comparison of Serum MCP-1 and OPN Levels Between Control Group and Gout Group $(\bar{x} \pm s)$

Groups	Number	MCP-1 (ng/mL)	OPN (ng/mL)
Control group	169	94.18±28.91	12.45±3.98
Gout group	174	459.26±127.30	27.84±6.87
t	–	36.381	25.290
P	–	<0.001	<0.001

Table 2 Comparison of Serum MCP-1 and OPN Levels Between Gout Patients With Early Renal Injury Group and Those Non Early Renal Injury Group $(\bar{x} \pm s)$

Groups	Number	MCP-1 (ng/mL)	OPN (ng/mL)
Non early renal injury group	124	406.48±114.37	24.93±5.59
Early renal injury group	50	590.15±152.03	35.06±8.86
t	–	8.684	9.043
P	–	<0.001	<0.001

Table 3 Comparison of Clinical Data Between Gout Patients With Early Renal Injury Group and Those Non Early Renal Injury Group[$(\bar{x} \pm s)$/n (%)]

Indicators	Non Early Renal Injury Group (n=124)	Early Renal Injury Group (n=50)	t/χ^2	*P*
Age (years)	62.55±10.78	63.48±12.17	0.496	0.621
Gender [n (%)]			0.323	0.570
Male	89 (71.77)	38 (76.00)		
Female	35 (28.23)	12 (24.00)		
Diabetes [n (%)]	11 (8.87)	6 (12.00)	0.120	0.729
Hypertension [n (%)]	54 (43.55)	26 (52.00)	1.025	0.311
Coronary heart disease [n (%)]	9 (7.26)	5 (10.00)	0.086	0.769
Hemoglobin (g/L)	129.67±22.56	123.02±26.95	1.661	0.098
Albumin (g/L)	41.02±5.38	39.47±4.68	1.783	0.076
Serum uric acid (μmol/L)	486.96±121.05	512.78±114.65	1.292	0.198
Serum creatinine (μmol/L)	92.45±22.57	130.14±39.71	7.888	<0.001
24-hour uric acid excretion (μmol/L)	2286.34±526.09	2397.61±626.10	1.194	0.234
Urine pH value	5.82±0.78	5.79±0.64	0.241	0.810
CysC (mg/L)	0.95±0.23	1.24±0.27	7.151	<0.001
GFR (mL/min)	94.57±26.38	70.62±15.47	6.010	<0.001
Hcy (μmol/L)	5.48±1.59	5.99±1.76	1.856	0.065

Table 4 Correlation Between Serum MCP-1, OPN Levels and Clinical Data in Gout Patients

Indicators	MCP-1		OPN	
	r	*P*	*r*	*P*
Serum creatinine	0.502	<0.001	0.538	<0.001
CysC	0.513	<0.001	0.514	<0.001
GFR	−0.489	<0.001	−0.526	<0.001

Table 5 Multivariate Logistic Regression Analysis

Influence factor	*β*	*SE*	*Wald*χ^2	OR	95% CI	*P*
MCP-1	1.017	0.382	7.088	2.765	1.308~5.846	0.008
OPN	1.105	0.368	9.015	3.019	1.468~6.210	0.003
Serum creatinine	0.070	0.128	0.295	1.072	0.834~1.378	0.587
CysC	0.126	0.121	1.080	1.134	0.895~1.438	0.299
GFR	−0.094	0.105	0.807	0.910	0.741~1.118	0.369

Diagnostic Value of Serum MCP-1 and OPN Levels for Early Kidney Injury

Receiver operating characteristic analysis evaluated the diagnostic value of serum MCP-1 and OPN for early kidney injury in gout. The AUCs for MCP-1, OPN, and their combination were 0.775, 0.827, and 0.938, respectively, with the combined AUC significantly higher (Z=3.075, 2.273, P<0.05). See Figure 2 and Table 6.

Discussion

Primary gout is a metabolic disorder caused by purine metabolism dysfunction, with prevalence varying by race and region.[10] Previous studies have found that hyperuricemia and gout patients are most likely to experience kidney damage,

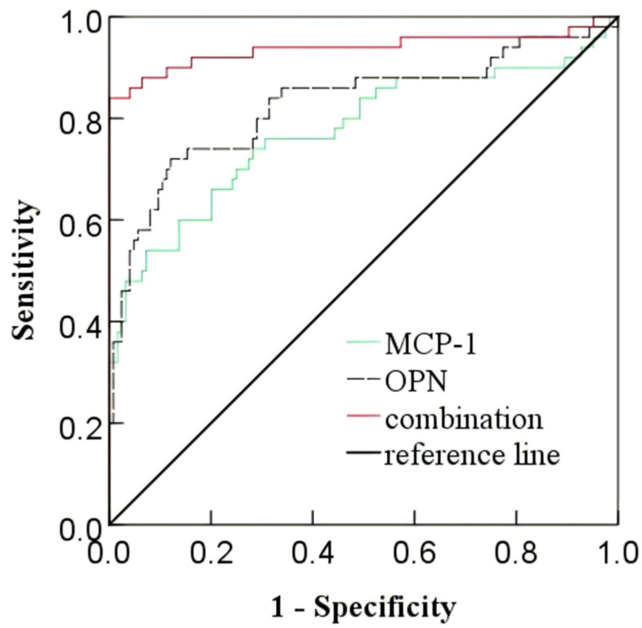

Figure 2 ROC curve of serum MCP-1 and OPN levels for diagnosing early renal injury in gout patients.

leading to uric acid kidney stone formation and decreased renal function.[11] Kidney dysfunction can further result in hyperuricemia and gout attacks, forming a causal relationship with close interdependence. Many gout patients show varying degrees of kidney damage upon autopsy, with 18% to 30% dying from end-stage renal disease.[12]

MCP-1 drives inflammation by recruiting inflammatory cells and cytokines, promoting disease progression through monocyte/macrophage migration and infiltration.[13] MCP-1 is involved in the pathogenesis of diseases like COVID-19, cancer, neuroinflammation, cardiovascular diseases, and rheumatoid arthritis.[14] Additionally, MCP-1 is involved in inflammation-dependent diseases such as hypertension, atherosclerosis, and kidney damage.[15] Hu et al[16] found that mangiferin could treat renal inflammatory damage in hypertensive rats. Liu et al[17] suggested that MCP-1 could serve as a biomarker of inflammatory kidney diseases, with increased expression directly correlating with the severity of kidney damage. Serum MCP-1 levels were higher in gout patients, especially in those with early kidney injury. These findings align with previous studies showing similar trends of MCP-1 expression in kidney-injured rats and patients. It is hypothesized that metabolic disorders and abnormal inflammatory immune states in gout patients lead to increased synthesis and secretion of MCP-1. The production of MCP-1 enhances its binding to specific receptors, promoting monocyte migration to local inflammatory sites and increasing the risk of early kidney injury.

OPN, a phosphoglycoprotein, plays a role in tissue repair, angiogenesis, bone homeostasis, wound healing, cell adhesion, and immune responses. It aids osteoclast adhesion, bone resorption, and mechanosensory stimulation of tumor, endothelial, and vascular smooth muscle cells.[18] Additionally, OPN acts as a pro-inflammatory molecule that, in certain contexts, induces dendritic cell and macrophage migration to inflammatory areas, elevating inflammation levels.[19] Xu et al[20] reported that serum OPN levels in patients experiencing acute renal transplant rejection were higher both pre- and post-operatively compared to those with stable renal function post-transplantation. Serum OPN levels were higher in early kidney injury. It is hypothesized that the biological mechanism of OPN in gout and early kidney injury may be

Table 6 ROC Curve Analysis Results

Diagnostic Indicators	Sensitivity (%)	Specificity (%)	Cutoff	AUC	95% CI	Youden Index
MCP-1	60.04	81.45	503.26 ng/mL	0.775	0.687~0.863	0.41
OPN	72.64	86.59	29.12 ng/mL	0.827	0.748~0.907	0.59
Combination	85.62	99.84	–	0.938	0.883~0.994	0.85

related to its pro-inflammatory effects. Elevated serum OPN levels promote macrophage migration and stimulate the production of other inflammatory cytokines, increasing renal inflammation levels and the risk of early kidney injury.

Untreated gout-related kidney damage may cause uric acid stones, chronic UTIs, and accelerated kidney deterioration. Multiple previous studies have shown that the persistent deposition of urate crystals in kidney tissues caused by gout is the main cause of kidney damage. Serum creatinine, cystatin C (CysC), and glomerular filtration rate (GFR) are recognized as accurate diagnostic markers for assessing kidney damage, and they have diagnostic value for gout-related kidney damage[21,22], but early-stage cases show normal lab results. By the time abnormalities appear, patients may already have developed irreversible kidney damage. Furthermore, these indicators are easily influenced by other factors, which is why further exploration of other early indicators of kidney damage related to gout is still necessary. This study found higher serum creatinine and CysC and lower GFR in gout patients with early kidney damage, aligning with previous studies.[21,22] Correlation analysis showed MCP-1 and OPN were significantly linked to kidney damage markers, suggesting their close association with kidney damage in gout Since all the patients with kidney damage included in this study were in the early stages, it indicates that serum MCP-1 and OPN levels were already abnormal at the early stage of kidney damage, with a diagnostic sensitivity higher than that of the above kidney damage markers.

The results indicated that MCP-1 and OPN are independent influencing factors for early kidney damage in gout patients. Additionally, the ROC curve results for combined diagnosis showed that MCP-1 and OPN combined can effectively predict early kidney damage. When the critical values for MCP-1 and OPN were 503.26 ng/mL and 29.12 ng/mL, respectively, the combined diagnostic sensitivity and specificity reached 85.62% and 99.84%, with an AUC of 0.938. This indicates that the combined diagnostic efficacy of MCP-1 and OPN is relatively high. This is beneficial for clinicians to promptly formulate and adjust effective targeted treatment plans. Based on the trends in MCP-1 and OPN expression, it is hypothesized that with the progression of treatment, serum MCP-1 and OPN levels may further decrease. However, this study has not yet completed follow-up for all patients, and therefore, the role of MCP-1 and OPN in treatment response could not be observed. The comorbidities included in this study, such as diabetes, hypertension, and coronary heart disease, as well as clinical indicators, may act as confounding factors that could affect the occurrence of early renal injury in gout patients. However, through univariate and multivariate analyses, the results indicate that these factors were not significant influences in this study, thus somewhat ruling out the impact of confounding factors on the study's results. This study has limitations, including a single-center design, small sample size, selection bias, and lack of follow-up, limiting generalizability and renal prognosis data. In conclusion, serum MCP-1 and OPN levels detected in gout patients are independently associated with early kidney damage, and their combined detection can effectively diagnose early kidney damage with diagnostic efficacy higher than that of either marker alone. MCP-1 and OPN may aid early kidney damage diagnosis and prognosis in gout, offering potential targets for new treatments. Larger-scale and more carefully designed clinical studies will be conducted in the future to provide more universally applicable results.

Data Sharing Statement

All original data supporting this study are included in the article.

Ethical Approval

This study was approved by the Ethics Committee of Ganzhou People's Hospital (No. PJB2025-022-01) and conducted per the 1964 helsinki Declaration. Written informed consent was obtained from all participants.

Publication Consent

All authors have consented to publication.

Funding

There is no funding to report.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Wu X, You C. The biomarkers discovery of hyperuricemia and gout: proteomics and metabolomics. *PeerJ*. 2023;11:e14554. doi:10.7717/peerj.14554
2. Dalbeth N, Gosling AL, Gaffo A, et al. Gout. *Lancet*. 2021;397(10287):1843–1855. doi:10.1016/S0140-6736(21)00569-9
3. Singh JA, Gaffo A. Gout epidemiology and comorbidities. *Semin Arthritis Rheum*. 2020;50(3S):S11–S6. doi:10.1016/j.semarthrit.2020.04.008
4. Singh S, Anshita D, Ravichandiran V. MCP-1: function, regulation, and involvement in disease. *Int Immunopharmacol*. 2021;101(Pt B):107598. doi:10.1016/j.intimp.2021.107598
5. Zheng Z, Li C, Shao G, et al. Hippo-YAP/MCP-1 mediated tubular maladaptive repair promote inflammation in renal failed recovery after ischemic AKI. *Cell Death Dis*. 2021;12(8):754. doi:10.1038/s41419-021-04041-8
6. Martín-Márquez BT, Sandoval-García F, Corona-Meraz FI, et al. Osteopontin: a bone-derived protein involved in rheumatoid arthritis and osteoarthritis immunopathology. *Biomolecules*. 2023;13(3):502. doi:10.3390/biom13030502
7. Peng Y, Peng H, Ke W. Influence mechanism of osteopontin on renal injury in patients with hereditary hypercalcemia by enzyme-linked immunosorbent assay. *Cell mol Biol*. 2023;69(5):58–62. doi:10.14715/cmb/2023.69.5.10
8. Fitzgerald JD, Dalbeth N, Mikuls T, et al. 2020 American College of Rheumatology guideline for the management of gout. *Arthritis Care Res*. 2020;72(6):744–760. doi:10.1002/acr.24180
9. Ostermann M, Bellomo R, Burdmann EA, et al. Controversies in acute kidney injury: conclusions from a Kidney Disease: improving Global Outcomes (KDIGO) conference. *Kidney Int*. 2020;98(2):294–309. doi:10.1016/j.kint.2020.04.020
10. Dehlin M, Jacobsson L, Roddy E. Global epidemiology of gout: prevalence, incidence, treatment patterns and risk factors. *Nat Rev Rheumatol*. 2020;16(7):380–390. doi:10.1038/s41584-020-0441-1
11. Li Z, He L, Jiao J, et al. Musculoskeletal ultrasound evaluates renal injury and predicts renal outcome in patients with gout. *Kidney Dis*. 2023;9 (2):94–103. doi:10.1159/000528200
12. Wang S, Zhang L, Hao D, et al. Research progress of risk factors and early diagnostic biomarkers of gout-induced renal injury. *Front Immunol*. 2022;13:908517. doi:10.3389/fimmu.2022.908517
13. Georgakis MK, Bernhagen J, Heitman LH, et al. Targeting the CCL2-CCR2 axis for atheroprotection. *Eur Heart J*. 2022;43(19):1799–1808. doi:10.1093/eurheartj/ehac094
14. Chen Y, Liu S, Wu L, et al. Epigenetic regulation of chemokine (CC-motif) ligand 2 in inflammatory diseases. *Cell Prolif*. 2023;56(7):e13428. doi:10.1111/cpr.13428
15. He S, Yao L, Li J. Role of MCP-1/CCR2 axis in renal fibrosis: mechanisms and therapeutic targeting. *Medicine*. 2023;102(42):e35613. doi:10.1097/MD.0000000000035613
16. Hu X, Zhao W, Deng J, et al. Mangiferin alleviates renal inflammatory injury in spontaneously hypertensive rats by inhibiting MCP-1/CCR2 signaling pathway. *Chin Herb Med*. 2023;15(4):556–563. doi:10.1016/j.chmed.2022.12.008
17. Liu Y, Xu K, Xiang Y, et al. Role of MCP-1 as an inflammatory biomarker in nephropathy. *Front Immunol*. 2023;14:1303076. doi:10.3389/fimmu.2023.1303076
18. Lin EY-H, Xi W, Aggarwal N, et al. Osteopontin (OPN)/SPP1: from its biochemistry to biological functions in the innate immune system and the central nervous system (CNS). *Int Immunol*. 2023;35(4):171–180. doi:10.1093/intimm/dxac060
19. Varalakshmi B, Kiranmyai VS, Aparna B, et al. Plasma osteopontin levels in patients with acute kidney injury requiring dialysis: a study in a tertiary care institute in South India. *Int Urol Nephrol*. 2020;52(5):917–921. doi:10.1007/s11255-020-02417-x
20. Xu C-X, Zhang Y-L, Huang X-Y, et al. Prediction of acute renal allograft rejection by combined HLA-G 14-bp insertion/deletion genotype analysis and detection of kidney injury molecule-1 and osteopontin in the peripheral blood. *Transpl Immunol*. 2021;65:101371. doi:10.1016/j.trim.2021.101371
21. Wu Y, Wang S, Xu X. Correlation of serum cystatin C with renal function in gout patients with renal injury. *J Interferon Cytokine Res*. 2021;41 (9):329–335. doi:10.1089/jir.2021.0034
22. Tang H, Zhao Y, Tan C, et al. Significance of serum markers and urinary microalbumin in the diagnosis of early renal damage in patients with gout. *Clin Lab*. 2021;67(5). doi:10.7754/Clin.Lab.2020.200722