

Studying Risk Factors Leading to Cardiovascular System Damage in Patients with Gout

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Abstract: The prevalence of metabolic syndrome (MS) and its individual components in patients with gout was studied. The overall cardiovascular disease (CVD) risk in this patient group was assessed. The study involved 43 patients, with the primary group consisting of 28 patients with primary chronic gout and MS, and a comparison group of 15 volunteers with MS but without gout or any other immune-inflammatory processes. All patients underwent an evaluation of their total CVD risk using the SCORE and PROCAM scales. At least one additional MS feature was identified in all examined patients. In the primary group, 7 (24.2%) patients, and in the comparison group, 1 (3.51%) patient exhibited all five additional MS features. Patients in the primary group more frequently demonstrated more than three additional MS features compared to the isolated MS group. Arterial hypertension was observed in patients with MS regardless of the presence of gout. The total CVD risk in the primary group was significantly higher compared to the isolated MS group ($p < 0.01$ for SCORE and $p < 0.05$ for PROCAM).

Keywords: SCORE, PROCAM, cardiovascular risk, uric acid, metabolic syndrome, gout, abdominal obesity.

Introduction

Cardiovascular diseases (CVD) are responsible for 38% of all male deaths under the age of 65 and are the second leading cause of death among women. Assessing and modifying correctable CVD risk factors such as hypertension, obesity, and smoking significantly reduce the risk of cardiovascular events. Metabolic syndrome (MS), also known as syndrome X or insulin resistance syndrome (IR), represents a combination of metabolic disorders, each of which is an independent risk factor for CVD. The presence of MS is associated with an increased risk of CVD and type 2 diabetes (T2D). Identifying MS combined with a 10-year CVD risk assessment can help prioritize patients who require not only lifestyle modifications but also specific medical therapy. Numerous epidemiological studies have shown that patients with chronic rheumatic diseases have a higher risk of CVD as well as increased morbidity and mortality from CVD. However, the exact pathogenic factors responsible for this remain unclear. MS in these diseases may serve as an additional link between atherosclerosis progression and active inflammation. In 1988, Reaven identified IR as a central mechanism of T2D, arterial hypertension (AH), and coronary artery disease. Subsequent studies examined the connection between IR, individual metabolic disorders, and their contribution to CVD risk. MS is considered an independent risk factor for CVD and atherogenesis due to increased levels of free fatty acids and triglycerides (TG), decreased high-density lipoprotein cholesterol (HDL-C), and apolipoprotein B, as well as the presence of abdominal obesity, IR, carbohydrate metabolism disorders, and AH. Despite extensive research and established data on the role of individual metabolic disorders in CVD pathogenesis, disagreements persist about the parameters optimally reflecting MS. Currently, there are three main MS definitions proposed by the World Health Organization (WHO), the National Cholesterol Education Program (NCEP, original and modified), and the International Diabetes Federation (IDF). Although widely used, debates continue about certain criteria, such as reducing the

abdominal obesity threshold for men's waist circumference (WC) from 102 cm to 94 cm in IDF recommendations. This reduction increased the number of MS patients in epidemiological studies, whereas CVD frequency and, more importantly, CVD mortality remained significantly higher among patients with a WC over 102 cm. In Uzbekistan, the All-Uzbek Scientific Society of Cardiologists has adopted guidelines for diagnosing and treating MS, based on IDF criteria with some modifications. Despite long-standing studies on the connections between gout, hypertension, renal failure, and cardiovascular pathology since the late 19th century, renewed interest in this problem emerged in the late 20th century within the framework of modern medicine's priorities, particularly reducing CVD morbidity and mortality. Several clinical studies have shown correlations between MS, AH, IR, T2D, and gout. In based on NHANES III data, evaluated the relationship between MS and gout. MS was identified in 62.6% of gout patients compared to only 25.5% without gout, mainly due to the high prevalence of AH, overweight, and T2D. Furthermore, the prevalence of MS in gout patients increased with age, reaching 71% among those over 40 years old. Demonstrated that the frequency of IR among gout patients is 36% higher than in non-gout patients. Apart from the obvious link between MS and IR syndrome with gout, recent studies have widely explored the association between hyperuricemia (HU) and individual MS components. AH is particularly noteworthy, with studies indicating its presence in 21–52% of gout patients, and gouty arthritis identified in 22–41% of those with AH. Recent laboratory and clinical data suggest that HU, even without gout, can increase blood pressure by stimulating the renal renin-angiotensin system, inhibiting vascular nitric oxide synthesis (a potent vasodilator), promoting vascular smooth muscle proliferation, and causing kidney damage (interstitial nephritis or tubular injury), which indirectly leads to AH. These findings highlight HU's undeniable role in AH development, requiring further large-scale studies among patients with essential AH and gout to determine whether HU correction is necessary in the absence of gouty arthritis. Metabolic disorders associated with HU and IR syndrome in gout, such as AH, lipid, and carbohydrate metabolism disorders, and obesity, are closely linked to atherosclerosis and are considered independent CVD risk factors. This necessitates treating gout as a systemic medical issue characterized by a high risk of fatal CVD events associated with atherosclerosis. In 2000, the WHO classified gout among diseases closely related to obesity, such as AH, coronary atherosclerosis, and T2D. Gout can be viewed as a metabolic disease, supported by numerous studies revealing a high prevalence of comorbid pathology, particularly CVD, among gouty arthritis patients.

Materials and Methods

The study included 43 patients, with the primary group consisting of 28 patients diagnosed with primary chronic gout and metabolic syndrome (MS) based on classification criteria. The comparison group included 15 volunteers with MS but without gout or any other immune-inflammatory processes. According to the International Diabetes Federation (IDF) recommendations, abdominal obesity was considered the main criterion for MS diagnosis. The body weight of patients in the primary group ranged from 71.0 to 170.0 kg (median: 96.0 [85.5–109.0] kg), while in the isolated MS group, it ranged from 82.0 to 106.0 kg (median: 90.0 [85.0–94.0] kg). In the primary group, body mass index (BMI) values ranged from 23.0 to 52.0 kg/m² (median: 31.0 [29.0–34.25] kg/m²), whereas in the isolated MS group, BMI values ranged from 29.05 to 40.39 kg/m² (median: 30.7 [29.39–32.78] kg/m²). The primary parameters of obesity in patients are presented in . All patients underwent individual cardiovascular disease (CVD) risk assessment using the SCORE and PROCAM scales. Key risk factors evaluated included patient age, gender, smoking status, systolic blood pressure levels, diabetes mellitus (DM) presence, family history of early CVD, and serum levels of total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglycerides (TG).

Results and Discussion

Body weight in the MS group without gout was significantly lower than in the primary group ($p < 0.05$). Obesity (BMI ≥ 30 kg/m²) was observed in 19 (67.85%) patients in the primary group, while the remaining cases were classified as overweight. The distribution of patients by obesity grade was as follows: grade I obesity in 13 (46.42%), grade II in 4 (14.28%), and grade III in 2 (7.14%) patients. In

the comparison group without gout, obesity was found in 9 (60.00%) patients: grade I obesity in 8 (50.00%), grade II in 1 (6.66%), and grade III in 1 (3.33%) patient. Abdominal obesity (waist circumference >94 cm for men and >80 cm for women) was equally common among overweight patients in both the primary group and the MS group without gout. However, grade II and III obesity were more frequently diagnosed in gout patients: 14.28% and 7.14%, respectively, compared to 6.66% and 3.33% for non-gout patients. The prevalence of additional MS features was high in both groups. Hypertension was detected in MS patients regardless of gout presence ($p < 0.001$). Hypertriglyceridemia was equally common in both groups, while reduced HDL-C levels were more characteristic of the primary group compared to the isolated MS group ($p < 0.01$). At least one additional MS feature was identified in all examined patients. In the primary group, 13 (23.21%) patients, and in the MS group without gout, 1 (3.33%) patient exhibited all five additional MS features. More than three additional MS features were identified more frequently in the primary group compared to the isolated MS group: 28 (50.00%) versus 10 (33.30%), respectively. Individual CVD risk was assessed for all 43 patients using the SCORE and PROCAM scales. The total CVD risk according to the SCORE scale was significantly higher in the primary group compared to the isolated MS group ($p < 0.01$ for SCORE and $p < 0.05$ for PROCAM). Thus, the presence of gout in MS patients increases CVD risk according to assessment scales, likely due to lipid metabolism disorders associated with hyperuricemia severity. The frequency of vascular events (e.g., coronary artery disease [CAD], stroke, chronic heart failure), as well as type 2 diabetes (T2D), was higher in gout patients with MS. For example, CAD was detected in 4 (16%) patients, 2 (5.37%) of whom had a history of myocardial infarction.

Conclusion

Patients with chronic rheumatic diseases, including those suffering from gout, are at an increased risk of cardiovascular disease (CVD) morbidity and mortality. These patients exhibit a high prevalence of traditional risk factors and metabolic syndrome (MS). These findings suggest that chronic inflammation may play a key role in the development of MS and the progression of atherosclerosis. Aggressive treatment of the underlying disease, with a focus on inflammation control, alongside the elimination of traditional risk factors, may reduce CVD morbidity and mortality. The evaluation of MS criteria, combined with a 10-year CVD risk assessment, should be utilized to identify patients who require lifestyle modifications and/or pharmacological therapy.

References

1. Tairov D.R., Berdiev D.KH. "Gout: Immunological and genetic characteristics of the disease." Volume: 3, Issue: 12, Dec-2024. journals.academiczone.net.
2. Tairov D.R., Berdiev D.KH. "Characteristics of Cardiohemodynamic Disorders in Gout Disease." SCIENTIFIC PROGRESS. Volume 2, Issue 3, 2021. ISSN: 2181-1601.
3. Tairov D.R., Berdiev D.KH. "Medication and Non-Medication Methods to Eliminate Hyperuricemia in Gout." "Science and Education" Scientific Journal. Impact Factor 3.848. May 2023, Volume 4, Issue 5.
4. Tairov D.R., Berdiev D.KH. "Characteristics of Heart Functional Disorders in Gout Disease." GALAXY INTERNATIONAL INTERDISCIPLINARY RESEARCH JOURNAL (GIIRJ). ISSN (E): 2347-6915. Vol. 10, Issue 5, May 2022.
5. Tairov D.R., Berdiev D.KH. "Cardiovascular Damage and Metabolic Syndrome Comorbidities in Patients with Gout Disease." 2nd International Congress on Multidisciplinary Studies. Indonesia. February 20th, 2021. conferencepublication.com.
6. Nasonov E.L., Karateev D.E., Satibaldiyev A.M., et al. (2015).
7. Adams P.F. "Current Estimates from the National Health Interview Survey, 1996." Vital Health Stat. Vol. 10, 1999.

8. Saag K.G., Mikuls T.R. "Recent Advances in the Epidemiology of Gout." *Curr. Rheumatol. Rep.* Vol. 7, 2005, pp. 235–241.
9. Terkeltaub R.A. "Clinical Practice. Gout." *N. Engl. J. Med.* Vol. 349, 2003, pp. 1647–1655.
10. Tairov E.S., Tairov D.R. "Metabolic Syndrome in Gout: Its Relationship with Renal Functional Disorders." *Questions of Science and Education.* No. 28 (77), 2019.
11. Wallace K.L., Riedel A.A., Joseph-Ridge N. "Increasing Prevalence of Gout and Hyperuricemia Over 10 Years Among Older Adults in a Managed Care Population." *J. Rheumatol.* Vol. 31, 2004, pp. 1582–1587.
12. Tairov D.R., Makhmudova H.D. "Cardiovascular Damage in Patients with Gout." *Scientific Progress.* Vol. 2, No. 2, 2021, pp. 242–249.
13. Yarmukhamedova S.KH., Kamolova D.ZH. "Study of Myocardial Geometry in Hypertensive Patients Using Echocardiography." *Achievements of Science and Education.* No. 12 (53), 2019.
14. Eliseev M.S., Barskova V.G., Nasonov V.A. "Clinical Significance of Metabolic Syndrome in Gout." *Clinical Gerontology.* Vol. 12, No. 2, 2006, pp. 29–33.
15. Tairov E.S., Tairov D.R., Solovyev S.K. "Gout: Diagnosis and Treatment." Tashkent, Uzbekistan, 2020.
16. Sowers M.J., Whaley-Connell A., Hayden M.R. "The Role of Obesity in Cardiorenal Syndrome." *Cardiorenal Medicine.* Vol. 1, 2011, pp. 5–12.
17. Hayden M., Tyagi S.K. "Uric Acid: A New Perspective on an Old Cardiovascular Risk Marker." *Nutr Metab (London).* Vol. 1, 2004, p. 10.
18. Jalal D.I., Chonchol M., Chen W., Targher G. "Uric Acid as a Therapeutic Target in CKD." *Am J. Dis.*, 2013, Vol. 61, pp. 134–146.
19. Johnson R.J., Segal M.S., Sautin Y., Nakagawa T., Feig D.I., Kang D.H., Gersch M.S., Benner S., Sanchez-Lozada L.G. "Potential Role of Sugar (Fructose) in the Epidemics of Hypertension, Obesity, and Metabolic Syndrome." *Am J Clin Nutr.* Vol. 86, 2007, pp. 899–906.
20. Steele T. "Human Urate Secretion: Pyrazinamide Suppression Test." *Ann Intern Med.* Vol. 79, 1973, pp. 734–737.
21. Suliman M.E., Johnson R.J., Garcia-Lopez E., et al. "J-Shaped Relationship Between Uric Acid and Mortality in CKD." *Am J. Dis.* Vol. 48, 2006, pp. 761–771.
22. Kan D.H., Nakagawa T., Feng L., Watanabe S., Han L., Mazzali M., Truong L., Harris R., Johnson R.J. "The Role of Uric Acid in Kidney Disease Progression." *J Am Soc Nephrol.* Vol. 13, 2002, pp. 2888–2897.
23. Tseng C. "Correlation of Urinary Albumin Excretion Rate with Uric Acid Levels in Type 2 Diabetes." *Kidney Int.* Vol. 68, 2005, pp. 796–801.
24. Ono I., Hosoya T., Gomi H., et al. "Serum Uric Acid and Kidney Failure Prognosis in IgA Nephropathy Patients." *Nephron.* Vol. 87, 2001, pp. 333–339.
25. Thomas G., Sehgal A.R., Kashyap S.R., Srinivas T.R., et al. "Metabolic Syndrome and Kidney Disease: A Systematic Review and Meta-Analysis." *Clin J Am Soc Nephrol.* Vol. 6, 2011, pp. 2364–2373.
26. Wright A.F., Rudan I., Hastie N.D., Campbell H. "The Complexity of Urate Transporters." *Kidney Int.* Vol. 78, 2010, pp. 446–452.
27. Gutman A.B., Yu T.F. "Urate Nephrolithiasis." *Am J Med.* Vol. 45, 1968, pp. 756–779.