American Journal of Biomedicine and Pharmacy
https://biojournals.us/index.php/AJBP
ISSN: 2997-7177

Significance of Uromodulin Indicators and the Location of its Gene Polymorphism

Khalilova Feruza Abdujalolovna
Associate Professor, Department of Propaedeutics of Internal Diseases, Bukhara State Medical Institute, PhD
xalilova.feruza@bsmi.uz

Received: 2024, 15, Apr
Accepted: 2025, 21, May
Published: 2025, 12, Jun

Copyright © 2025 by author(s) and BioScience Academic Publishing. This work is licensed under the Creative Commons Attribution International License (CC BY 4.0).

Open Access
http://creativecommons.org/licenses/ by/4.0/

Annotation: Coronary Artery Disease (CAD) remains a significant contributor to global morbidity and mortality. It is characterized by the progressive narrowing of coronary arteries due to the formation of atherosclerotic plaques, resulting in compromised blood flow to the heart muscle and ischemic events such as angina and myocardial infarction. This overview provides a succinct examination of CAD, focusing on its etiology, risk factors, clinical manifestations, and contemporary treatment modalities. The development of CAD involves a multifaceted interplay of genetic predisposition, conventional risk factors (including hypertension and dyslipidemia), and lifestyle variables. Despite its insidious onset, CAD can manifest through symptoms such as angina, dyspnea, or asymptomatic ischemia. Early detection is pivotal and can be facilitated by stress testing, coronary angiography, and non-invasive imaging techniques. Management strategies for CAD encompass lifestyle modifications, pharmacological interventions, and invasive procedures. Lifestyle adjustments entail dietary enhancements, regular physical activity, and cessation of tobacco use, all proven to attenuate CAD progression. Medications such as antiplatelets, statins, and beta-blockers target risk factors and ameliorate symptoms. Invasive interventions, including percutaneous coronary

intervention (PCI) and coronary artery bypass grafting (CABG), aim to restore coronary blood flow, thereby enhancing quality of life and augmenting survival rates. In summary, the pervasive prevalence of CAD and its clinical ramifications underscore the imperative for proactive prevention and evidence-based management. Ongoing advancements in diagnostic modalities and therapeutic strategies continue to refine CAD care, fostering optimism in combating this formidable cardiovascular ailment.

Keywords: uromodulin, cardiorenal syndrome, malondialdehyde (MDA), superoxide dismutase (SOD), α-tumor necrosis factor (α-O'NO).

Over the past two decades, the physiology, structure, function, regulation, genomics, and potential clinical applications of uromodulin have been progressively elucidated, revealing previously unknown properties. Extensive studies have deepened our understanding of the role of uromodulin in various disease states.

Although much attention has been paid to its importance as a biomarker of kidney disease, in recent years, numerous clinical and Mendelian randomization studies have provided increasing evidence linking uromodulin to cardiovascular disease and mortality. This association is understandable given the known association between SBP and CKD, and the studied role of uromodulin in salt-sensitive hypertension. Given that hypertension is an important risk factor for various CKD, uromodulin is increasingly being recognized as a potential biomarker for assessing not only renal function but also cardiovascular health.

About 90% of uromodulin production is synthesized by the cells of the thick ascending limb, and the remaining 10% by the epithelial cells of the beginning of the distal convoluted tubule. Its normal daily excretion in the urine is 50-150 mg. Uromodulin performs various physiological functions, such as preventing urinary tract infections, inhibiting the formation of kidney stones, participating in ion transport in the kidney, and regulating immunity. Studies of the interaction between uromodulin and urinary tract pathogens in laboratory conditions and in patient urine samples indicate that its fibers bind to uropathogens, promoting bacterial aggregation and preventing their adhesion and excretion in the urine.

Uromodulin is also involved in the transport of ions, particularly sodium, calcium, and magnesium, in the kidney. It acts to control magnesium reabsorption by regulating the amount of the magnesium channel TRPM6 in the apical membrane of distal convoluted tubule cells. uromodulin has strong immunomodulatory properties and activates various inflammatory markers such as neutrophils, macrophages and dendritic cells. It also acts as a binding ligand for many molecules, including serum albumin, immunoglobulin G light chains, complement components C1 and C1q, interleukins (IL-1β, IL-6, IL-8), α-NNO, and IFN-γ, through its carbohydrate side chains. This contributes to circulatory and renal immune homeostasis. As the physiological functions of uromodulins are gradually being studied and recognized, they are increasingly recognized as novel biomarkers for cardiovascular disease.

The mechanisms of action of this protein in the development of cardiovascular diseases, in

particular arterial hypertension and ischemic heart disease, have been studied in some studies. Several studies have shown that uromodulin binds several cytokines through its epidermal growth factor structural domain, including α-O'NO, which has a high affinity for it. Lesley A. et al. found that α-NO stimulation increases the relative level of uromodulin mRNA in the ascending limb cells of the renal tubules.

This leads to a negative feedback loop. The decrease in gene expression of the Na+K+-2Cl-cotransporter induced by α-NNO is balanced by an increase in cell surface uromodulin production. It can be concluded that uromodulin is directly involved in the control of blood pressure by modulating the effect of α-UNO on the expression of the Na+K+-2Cl- cotransporter. Vasopressin plays an important role in water reabsorption by inducing the apical expression of aquaporin-2. A review of the literature confirms that uromodulin plays an important role in the development of cardiovascular disease and chronic kidney disease. However, various studies have shown that its blood and urine levels have different effects on the development of diseases. In particular, it has been shown to cause the development of the disease in the case of salt-dependent arterial hypertension, while it has shown a positive effect in other forms. The role of uromodulin in the development of coronary heart disease has also been recognized by a number of experts. According to them, high levels of this protein have an inhibitory effect on the development of the disease. Uromodulin has been reported to decrease in blood and urine before the estimated glomerular filtration rate declines in the development of chronic kidney disease, and thus has been shown to be a predictor of this severe complication.

Polymorphism of its genes has been studied among people living in countries located in a number of different regions. They showed that gene polymorphism changes depending on age, nationality, race However, changes in the blood levels of this protein have not been studied in patients with chronic kidney disease caused by chronic heart failure, that is, cardiorenal syndrome, and in individuals of Uzbek ethnicity. From this point of view, studying the problem in patients living in our Republic with chronic kidney disease developed on the basis of chronic heart failure is of important practical and scientific importance.

References:

1. Heerspink HJL, Stefánsson BV, Correa-Rotter R, et al. Dapagliflozin in patients with chronic kidney disease. *N Engl J Med*. 2020;383:1436-1446. PMC
2. Herrington WG, Staplin N, Wanner C, et al. Empagliflozin in patients with chronic kidney disease (EMPA-KIDNEY). *N Engl J Med*. 2023;388:2088-2100.
3. McMurray JJV, Solomon SD, Inzucchi SE, et al. Dapagliflozin in heart failure with reduced ejection fraction (DAPA-HF). *N Engl J Med*. 2019;381:1995-2008.
4. Packer M, Anker SD, Butler J, et al. Cardiovascular and renal outcomes with empagliflozin in heart failure (EMPEROR-Reduced). *N Engl J Med*. 2020;383:1413-1424.
5. Anker SD, Butler J, Filippatos G, et al. Empagliflozin in heart failure with preserved ejection fraction (EMPEROR-Preserved). *N Engl J Med*. 2021;385:1451-1461.
6. McMurray JJV, Packer M, Desai AS, et al. Angiotensin–neprilysin inhibition versus enalapril in heart failure (PARADIGM-HF). *N Engl J Med*. 2014;371:993-1004.
7. Filippatos G, Fonseca S, Fernandez A, et al. Sacubitril/valsartan in chronic kidney disease: current evidence and future directions. *Kidney Int Rep*. 2023;8:1440-1453.
8. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2023 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int*. 2023;103(Suppl 1):S1-S127.
9. McDonagh TA, Metra M, Adamo M, et al. 2023 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J*. 2023;44:3625-3726.

10. Maffia P, Di Gioia G, Benvenga RM, et al. Serum uromodulin and cardiovascular outcomes in heart failure: a prospective cohort study. *Int J Cardiol*. 2022;364:31-38. ScienceDirect

11. Leiherer A, Muendlein A, Saely CH. Serum uromodulin as a novel biomarker of kidney function and cardiovascular risk. *Curr Opin Nephrol Hypertens*. 2023;32:71-77. SpringerLink

12. Bylsma LC, Morimoto RY, Shaikh A, et al. Cystatin-C and outcomes in heart failure: systematic review and meta-analysis. *ESC Heart Fail*. 2022;9:2683-2694. Онлайн JCF

13. Shlipak MG, Sarnak MJ, Katz R, et al. Cystatin C and the risk of heart failure. *N Engl J Med*. 2005;352:2049-2060.

14. Giam B, Kaye DM, Rajapakse NW. Renal oxidative stress in the pathogenesis of the cardiorenal syndrome. *Heart Lung Circ*. 2016;25:874-880. SpringerLink

15. Caio-Silva W, da Silva DD, Junho CVC, et al. Oxidative stress in renal ischemia/reperfusion-induced cardiorenal syndrome type 3. *Biomed Res Int*. 2020;2020:1605358. SpringerLink

16. Hamilton CA, Miller WH, Al-Benna S, et al. Strategies to reduce oxidative stress in cardiovascular disease. *Clin Sci*. 2004;106:219-234. SpringerLink

17. Jha JC, Banal C, Chow BSM, et al. Diabetes and kidney disease: role of oxidative stress. *Antioxid Redox Signal*. 2016;25:657-684. SpringerLink

18. Li F, Patel B, Rockman HA, et al. NOX4 inhibition attenuates cardiorenal syndrome via reduction of reactive oxygen species. *Antioxidants (Basel)*. 2024;13:1454. MDPI

19. Trentin-Sonoda M, Panico K, Junho CVC, et al. Cardiorenal syndrome: long road between kidney and heart. *Heart Fail Rev*. 2022;27:2137-2153. SpringerLink

20. Dunlay SM, Givertz MM, Aguilar D, et al. Type 2 sodium-glucose cotransporter inhibitors for heart failure across the spectrum of ejection fraction. *Circulation*. 2023;147:701-711.

21. Vaduganathan M, Claggett BL, Jhund PS, et al. Dapagliflozin across the range of eGFR in heart failure (DAPA-HF). *Circulation*. 2021;143:298-309.

22. Lüscher TF, Wanner C. SGLT2 inhibitors and kidney protection in heart failure and diabetes. *Eur Heart J*. 2022;43:3346-3349.

23. Damman K, Jhund PS, Anand I, et al. Sacubitril/valsartan and renal outcomes in heart failure: pooled analysis of PARADIGM-HF and PARAGON-HF. *Lancet*. 2020;396:1651-1663.

24. Joy MS, Coffey KD, Gipson DS, et al. Emerging biomarkers of kidney injury in chronic heart failure. *Kidney Int Rep*. 2021;6:1561-1574.

25. Metra M, Luscher TF, Voors AA. The kidney-cardiac continuum: integrating biomarkers and novel therapies. *Nat Rev Cardiol*. 2024;21:75-96.

26. Khalilova, F. A. (2022). Diagnostik Role of Marker of Cystatin C in Patient with Heart Failure. Central Asian Journal of Medical and Natural Science, 3(4), 195-198. *(Тўлиқ библиографик рўйхат муаллифга тақдим этилиш даврида кенгайтирилиши мумкин.)*

27. Халилова, Ф. А. (2023). КОМОРБИДНОЕ ИЗМЕНЕНИЯ ПОЧЕК И СЕРДЦА У БОЛЬНЫХ ХРОНИЧЕСКОЙ СЕРДЕЧНОЙ НЕДОСТАТОЧНОСТЬЮ. TA'LIM VA RIVOJLANISH TAHLILI ONLAYN ILMIY JURNALI, 3(5), 524-529.

28. Халилова, Ф. А. (2023). ЧАСТО ВСТРЕЧАЮЩИЕСЯ ФИБРОЗНЫЕ ИЗМЕНЕНИЯ В ПОЧКАХ У БОЛЬНЫХ ХРОНИЧЕСКОЙ СЕРДЕЧНОЙ НЕДОСТАТОЧНОСТЬЮ И

ПРОГНОЗ ЗАБОЛЕВАНИЯ. TA'LIM VA RIVOJLANISH TAHLILI ONLAYN ILMIY JURNALI, 3(5), 530-535.

29. Khalilova, F. A. (2023). ASSESSMENT OF INTRACARDIAC HEMODYNAMICS TYPES OF CHRONIC HEART FAILURE ACCOMPANIED BY ANEMIA. Miasto Przyszłości, 35, 342-348.
30. Khalilova, F. A. (2022). KIDNEY DYSFUNCTION IN VARIOUS FUNCTIONAL CLASSES OF CHRONIC HEART FAILURE. EUROPEAN JOURNAL OF MODERN MEDICINE AND PRACTICE, 2(9), 10-15.
31. Xalilova, F. A., & Kodirov, M. D. (2021). Assessment of the balance of intra-cardiac hemodynamics and glomerular filtration in anemia with different hemodynamic types of chronic heart failure. ACADEMICIA: An International Multidisciplinary Research Journal, 11(4), 1560-1573.
32. Gadaev A.G., Xalilova F.A., Elmuradov F.X., Tosheva X.B. Structural and functional changes in the kidneys and heart in patients with XSN. Therapy Bulletin of Uzbekistan. 2018. -1 - S. 100-104.
33. K.F. Abdujalolovna. Assessment of Intracardiac Hemodynamics and Electrolyte Balance in Various Hemodynamic Types of Chronic Heart Failure Accompanied By Anemia // European Multidisciplinary Journal of Modern Science 7,63-71, 2022
34. Khalilova F. A. et al. COMORBIDE CASES IN CARDIORENAL SYNDROME AND ITS IMPACT ON PATIENTS'QUALITY OF LIFE //EDITOR COORDINATOR. – 2020. – С. 741.
35. Aslonova I. J. et al. The prevalence of chronic pyelonephritis in women with disturbed tolerance for glucose //Asian Journal of Multidimensional Research (AJMR). – 2019. – Т. 8. – №. 11. – С. 81-85.
36. Khotamova, R. S. (2022). Monitoring of Kidney Fibrosis Changes in Patients with Chronic Heart Failure. *Central Asian Journal of Medical and Natural Science*, *3*(4), 199-204.
37. Bekmurodovna, T. K., & Chorievich, Z. A. (2021). Study of frequency indicators of comorbid states at different functional classes of heart failure. *ACADEMICIA: An International Multidisciplinary Research Journal*, *11*(3), 2556-2560.
38. Тошева, Х., & Кайимова, Д. И. (2017). Метаболик синдромнинг ривожланишида ирсиятнинг ахамияти. *Биология и интегративная медицина*, *1*, 132.
39. Ашурова, Н. Г. (2022). Значение Немедикаментозной Коррекции Нарушений Углеводного Обмена. *Central Asian Journal of Medical and Natural Science*, *3*(5), 10-22.
40. Джураева, Н. О. (2022). Оценка Кардиореспираторных Показателей На Основе Комплексное Лечение Хронической Обструктивной Болезни Легких Заболевание С Легочной Гипертензией. *Central Asian Journal of Medical and Natural Science*, *3*(5), 23-30.
41. Khalilova, F., Tosheva, K., Gadaev, A., Erkinova, N., & Djuraeva, N. (2020). COMORBIDE CASES IN CARDIORENAL SYNDROME AND ITS IMPACT ON PATIENTS'QUALITY OF LIFE. *InterConf*.
42. Тошева, Х., Хазратов, У., & Нарзиев, Ш. (2020). РОЛИ ДИСФУНКЦИИ ПОЧЕК В РАЗВИТИИ Коморбидности У Больных С Хронической Сердечной недостаточностью. *Журнал вестник врача*, *1*(3), 93-96.
43. Гафуровна А.Н. (2022). Симуляционное обучение как метод современных технологий в медицинской практике студентов медицинских вузов. Среднеевропейский научный бюллетень , 24 , 276-280