World Bulletin of Public Health (WBPH)
Available Online at: https://www.scholarexpress.net
Volume-40, November 2024
ISSN: 2749-3644

EARLY DIAGNOSIS OF RENAL DYSFUNCTION IN HIGH-RISK PATIENTS WITH ISCHEMIC HEART DISEASE

Rakhimova M.E., Norbo'toyev O.M.
Tashkent Medical Academy №2 Department of Internal Medicine in Family Medicine. Tashkent, Uzbekistan.
Mirzayev O.V.
Samarkand State Medical University, Republic of Uzbekistan, Samarkand.
Abdullayeva O.Y.
Central Clinical Hospital No. 2 of the Main Medical Department under the Administration of the President of the Republic of Uzbekistan. Tashkent. Uzbekistan.

Article history:
Received: August 20th 2024
Accepted: September 14th 2024

Abstract:
Early diagnosis of changes in kidney function in patients with coronary heart disease (CHD), taking into account existing risk factors (RF) and comorbid conditions, has not been sufficiently studied and is currently considered one of the urgent problems of medicine. This article represents the results of investigation dedicated to the renal dysfunction in patients with stable angina. The results obtained and their analysis confirmed that the calculation of GFR based on serum cystatin C, the determination of fetuin A in the blood, proteinuria and podocyturia allows early diagnosis of renal dysfunction (RD) in CKD.

Keywords: atherosclerosis, coronary heart disease, risk factor, impaired renal function, glomerular filtration rate, creatinine, cystatin S, fetuin, podocyturia.

In atherosclerosis, including stable forms of CAD, renal dysfunction (RD) begins in the early stages of the disease, but its first clinical signs are detected in the late stages of the underlying disease or when they become complicated [1, 2, 16, 17]. Heart and kidney diseases have common "traditional" risk factors (arterial hypertension, diabetes mellitus, obesity, dyslipidemia, etc.), and when they occur together, "non-traditional" renal factors (hyperhydration, anemia, impaired phosphorus-calcium metabolism, systemic inflammation, and hypercoagulation) are also added, which affect the development of cardiovascular diseases (CVD). The results of scientific research conducted in recent years have shown that even the earliest subclinical impairment of renal function affects the progression of CVD and its complications, as well as mortality rates, as an independent risk factor. Several studies have shown that patients with BD have a pronounced development of microvascular dysfunction, leading to coronary artery atherosclerosis and myocardial ischemia [1, 4, 5, 6, 10, 12, 17].

According to clinical guidelines, pathological processes in the kidneys are detected based on the level of serum creatinine, glomerular filtration rate (GFR), micro- and macroalbuminuria (MAU) [2, 3, 8, 10]. However, in patients with reduced muscle mass and on a vegetarian diet, as well as in the presence of various comorbid diseases, differences in constitutional body composition (lean or muscular), age, gender, and representatives of different races, GFR determined on the basis of creatinine does not fully reflect the distinguishing features of the kidneys [6, 7, 13, 15, 16]. In recent years, cystatin-C has been used as an early indicator of impaired excretory function to assess the functional state of the kidneys. [3, 4, 8, 10, 15, 18].

Ectopic calcification, which is observed in atherosclerosis and many degenerative diseases, is inhibited in 50% of cases by fetuin A (FA). Its decrease or disappearance in serum leads to massive calcification of ectopic tissues and blood vessels [1, 5, 9, 11, 14]. FA may be an independent and currently under-appreciated factor affecting the development of CVDs, and changes in its level are considered a factor associated with cardiac remodeling, renal fibrosis, vascular calcification, and accelerated atherosclerosis [3, 5, 11, 12, 14, 17].

Recent studies have shown that proteinuria does not always fully reflect the degree of glomerular damage, and podocyturia, on the contrary, is a factor that allows for a more accurate assessment of this process [3, 6, 7, 9, 12, 16].

Scientific research aimed at early detection of BD in patients with IBD is one of the most relevant areas of medicine today, and we set ourselves the goal of studying it.

OBJECTIVE: Early diagnosis of BD in patients with IBD, a high comorbidity index, and multiple comorbidities.

MATERIALS AND METHODS: This research study included 167 patients with stable angina pectoris,

World Bulletin of Public Health (WBPH)
Available Online at: https://www.scholarexpress.net
Volume-40, November 2024
ISSN: 2749-3644

with an average age of 61.47±8.42 years, treated in the cardiology and cardiorehabilitation departments of the Multidisciplinary Clinic of the Tashkent Medical Academy in 2020-2022. Of the patients in the main group, 112 (67.1%) were men (average age 61.29±8.3 years) and 55 (32.9%) were women (average age 61.85±8.7 years). The diagnosis was based on the classification criteria adopted by the European Society of Cardiology (ESC Guidelines for the diagnosis and management of chronic coronary syndromes). For comparison, 36 volunteers (mean age 61.6±6.3 years, 22 men and 14 women) matched for age and sex without CHD were selected.

In addition to biochemical analysis, all patients underwent electrocardiography (ECG), Holter monitoring, echocardiography (EchoCG), and Doppler studies of the kidneys and jugular veins. In order to assess kidney function, creatinine, cystatin C, and PA were determined in the blood, and protein and podocytes were determined in the urine. In addition, KFT was calculated based on serum creatinine and cystatin C.

Study results: KFT in the control patients was calculated based on CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration, 2021) and based on the results obtained, they were divided into 2 groups. The first group consisted of 111 (66.5%) patients with a creatinine clearance ≥ 90 ml/min/1.73 m2, and the second group consisted of 56 (33.5%) patients with a creatinine clearance ≤ 89 ml/min/1.73 m2. Although signs of renal dysfunction were not observed in patients with ICU during general examination and laboratory tests, 33.5% of them had a creatinine clearance ≤ 89 ml/min/1.73 m2, and 83.9% had proteinuria, as calculated based on serum creatinine. The correlation of creatinine clearance with other indicators is presented .

Table 1.
Cross-sectional analysis of available data on coronary heart disease.

Кўрсатгичлар	Indications All patients n=167 p		p
	GF ≥ 90 mL/min/1.73 m2 (n=111)	GF≤ 89 ml/min/1.73 m2 (n=56)	
Men, n(%)	91 (81,9%)	21 (37,5%)	X^2=33.34 P<0.001
Women, n(%)	20 (18.1%)	35 (62,5%)	X^2=33.34 P<0.001
Average age	58,6±0,71	67,16±0,97	P<0.05
Diabetes, n (%)	17 (15.3%)	20 (35,7%)	X^2=8.98 P<0.001
Smokers, n (%)	22 (19.8%)	8 (14,3%)	X^2=0.774 P>0.05
Had a history of myocardial infarction, n (%)	13 (11,7%)	6 (10,%)	X^2=0.037 P>0.05
Arterial hypertension in the anamnesis n (%)	91 (82%)	50 (89,3%)	X^2=33.34 P<0.001
Proteinuria, n (%)	54 (48,6%)	47 (83,9%)	P<0.05

According to the data presented in Table 1 above, men accounted for 81.9% of the first group and 37.5% of the second (X2=33.34 P<0.001). Women were more numerous in the second group than in the first, accounting for 18.1% and 62.5%, respectively (X2=33.34 P<0.001). In the second group, older patients (p<0.005), patients with a history of hypertension (p<0.01) and CVD (X2=8.98 P<0.001), anemia (p<0.001) and patients with harmful habits were significantly more likely to be in the first group. The comorbidity index (CI) was 7.3 in the first group and 8.7 in the second (p<0.001).

When calculating the GF based on creatinine and cystatin C, the results obtained in both groups of patients were significantly different, and the

World Bulletin of Public Health (WBPH)
Available Online at: https://www.scholarexpress.net
Volume-40, November 2024
ISSN: 2749-3644

proportion of patients with BD was found to be significantly higher ($p < 0.001$).

Table 2.
Comparative analysis of renal function indicators and biochemical analysis results across groups (n = 167).

Indicators	GF ≥ 90 mL/min/1.73 m2 (n=111)	GF≤ 89 ml/min/1.73 m2 (n=56)	P
Creatinine, (mmol/l)	65,8±6,9	91,4±7,7	P<0,05
Cystatin S (mg/l)	1,2±0,01	1,3±0,02	P<0,05
GF based on creatinine, based on ml/min/1.73m2.	99,9±1,6	79,9±1,4	P<0.001
KFT based on cystatin C, based on ml/min/1.73m2	91,8±1,6	72,4±1,3	P<0.001
Proteinuria (g/l)	0,005±0,018	0,017±0,048	P>0,05
Fetuina-A, mg/l	237,2±16,06	216,3±15,5	P>0,05
Podocyturia, ng/ml	5,2±0,06	6,4±0,08	P<0.001

In the first group of patients, serum creatinine was 65.8±6.9 mmol/l, cystatin C was 1.2±0.01 mg/l, and in the second group, these indicators were 91.4±7.7 mmol/l and 1.3±0.02 mg/l, respectively ($p<0.05$). When calculated based on serum creatinine, the average GF was 99.9±1.6 in the first group and 79.9±1.4 ml/min/1.73m2 in the second group ($P<0.001$). In all patients, GF was 91.8±1.6 and 72.4±1.3 ml/min/1.73m2, respectively, which was lower than that calculated based on creatinine ($p<0.05$). Among the control patients, 59.3% had a GF ≥ 90 ml/min/1.73 m2, and 40.7% had a GF ≤ 89 ml/min/1.73 m2 ($r<0.05$). According to this result, when GF was calculated based on cystatin C, compared to those determined based on creatinine, BD was 7.2% more common ($r<0.05$). The number of patients diagnosed with proteinuria was 29.4% more in the second group than in the first group ($p<0.05$). The level of FA in the blood was 237.2±16.06 ng/ml in the first group and 216.3±15.5 ng/ml in the second. This indicator was significantly lower in both groups compared to the control group (324.7±18.5) mg/l ($p<0.001$). At the same time, when analyzing the patients by group, it was observed that the level of FA in the blood was significantly higher in the first group than in the second group ($P<0.05$).According to the results, an increase in total cholesterol (TC), low-density lipoprotein (LDL) and very-low-density lipoprotein (VLDL) in the blood was accompanied by a decrease in the amount of PA. At the same time, it was found that the amount of PA in the blood had a positive correlation with total serum protein, high-density lipoprotein (HDL) and CPT, and a negative correlation with creatinine and cystatin-C ($r = 0.316$, $P <0.0001$). The correlation between proteinuria and CPT was slightly lower than that with PA ($r = 0.285$, $P <0.0001$).

In order to assess the renal function of patients with IBD under control, we determined podocyteuria in their urine and studied the relationship of this indicator with BD factors.

Podocyteuria (6.5-11.2 ng/ml) was observed in 73 (43.7%) patients in the main group. Podocytes were not detected in the urine analysis of the comparison group. When examining the cross-section of the groups, podocyteuria was noted in 17 (15.3%) patients with EGR ≥ 90 ml/min/1.73 m2, and in all (56 -100%) patients with EGR ≤ 89 ml/min/1.73 m2. At the same time, podocyteuria was 5.2±0.06 ng/ml in the first group and 6.4±0.08 ng/ml in the second group ($P<0.001$). According to this result, podocyturia was significantly higher in patients with low GF ($P<0.001$).

The level of podocyturia was positively correlated with serum creatinine and cystatin C ($r=-0.36$; $p<0.05$), fetuin A ($r= 0.52$; $p<0.001$), and inversely correlated with GF ($r=-0.46$; $p<0.05$), diastolic BP ($r=-0.36$; $p<0.05$). The highest positive correlation was observed between podocyturia and serum creatinine ($r=0.7$; $p<0.001$) and cystatin C

World Bulletin of Public Health (WBPH)
Available Online at: https://www.scholarexpress.net
Volume-40, November 2024
ISSN: 2749-3644

(r=0.9; p<0.001), while an inverse correlation was found with GF.

Based on the above data, it can be concluded that in patients with stable angina pectoris, despite the absence of clinical signs of kidney damage, 47% of them had microalbuminuria and 33.5% of them had BD when calculating the KF based on serum creatinine. The increase in cystatin C in the blood and the decrease in KF determined based on it actually confirmed that the proportion of BD in this group of patients was even higher. These results, unlike cystatin C creatinine, allow for the early detection of BD in patients with IHD, independent of factors such as the patient's gender, age, and body weight. It was confirmed that the detection of fetuin A and podacituria in serum in this group of patients is more reliable than the level of microalbuminuria in the early diagnosis of BD. It allows for early detection of BD in patients with IHD, as well as assessment of the severity and degree of complications of the underlying disease, prevention of life-threatening complications, selection of the right treatment strategy, and evaluation of its effectiveness.

CONCLUSION:

1. In patients with atherosclerosis-induced CAD and stable angina pectoris, even in the absence of complaints and clinical signs of kidney damage, the determination of serum cystatin C-based CFT allows for the early diagnosis of BD compared to creatinine and proteinuria.

2. For the early diagnosis of BD in patients with CAD, it is necessary to determine PA in the blood and podocytes in the urine, along with generally accepted tests.

USED LITERATURE

1. Барбараш О.Л., Кашталап В.В. Управление риском развития ишемических событий у пациентов с мультифокальным атеросклерозом и сахарным диабетом 2-го типа. Атеротромбоз. 2020;(1):34–44. doi: 10.21518/2307-1109-2020-1-34-44;
2. Белялов Ф.И. Ишемическая болезнь сердца и нарушение функции почек // Рациональная фармакотерапия в кардиологии. – 2017. - №13(3). – С. 409 – 415.
3. Гадаев А.Г., Рахимова М.Э., Тургунова М.У. Роль цистатина с при оценке функционального состояния почек у больных с ИБС. O‘zbekiston terapiya axborotnomasi. Ilmiy- amaliy jurnal 2022. № 4 С 104-110. ISSN 2181–5887;
4. Кирпатовский В.И, Орлова Е.В., Харламова Л.А., Голованов С.А., Дрожжева В.В., Фролова Е.В. Значимость динамического определения концентрации Цистатина С в крови как маркера риска перехода острого повреждения почек в хроническую почечную недостаточность и эффективности нефропротективной терапии. Экспериментальная и клиническая урология 2021;14(4):20-29; https://doi.org/10.29188/2222-8543-2021-14-4-20-29
5. Махиева А.Т., Мамбетова А.М.Роль фетуина А в предотвращении развития сердечно-сосудистой кальцификации при хронической болезни почек С5Д. Трудный пациент №6–7, ТОМ 18, 2020. 15-18 с.;
6. Устинова М.А., Батюшин М.М. Анализ влияния маркеров почечного повреждения при нарушении углеводного обмена на риск появления неселективной протеинурии. - // Клиническая нефрология. – 2017. -№ 4. - С. 51-55.;
7. Bonse J., Wennmann D.O., Kremerskothen J., Weide T., Michgehl U., Pavenstadt H., Vollenbroker B.2018. Nuclear YAP localization as a key regulator of podocyte function. *Cell Death Dis*. **9** (9), 850.https://doi.org/10.1038/s41419-018-0878-1
8. Canney M., Sexton D.J., O’Connell M.D.L., Kenny R.A., Little M.A., O’Seaghdha C.M. Kidney function estimated from cystatin C, but not creatinine, is related to objective tests of physical performance in community-dwelling older adults // J Gerontol A Biol Sci Med Sci. – 2017. – Vol. 72. – P. 1554 - 60.;
9. Carracedo, M., & Bäck, M. (2018). Fetuin-A in aortic stenosis and valve calcification: Not crystal clear. *International Journal of Cardiology*, *265*, 77-78. doi: 10.1016/j.ijcard.2018.04.115;
10. Cheuiche A.V., Queiroz M., Azeredo-da-Silva A.L. et al. Performance of cystatin C - based equations for estimation of glomerular filtration rate in diabetes patients: a prisma - compliant systematic review and meta-analysis // Sci Rep. - 2019. - Vol. 9 (1). - P. 14 - 18. DOI: 10.1038/s41598-018-38286-9.
11. Herrmann, M., Babler, A., Moshkova, I., Gremse, F., Kiessling, F., Kusebauch, U., Nelea, V., Kramann, R., Moritz, R. L., McKee, M. D., et al. (2020). Lumenal calcification and microvasculopathy in fetuin-A-deficient mice lead to multiple organ morbidity. *PloS one,*

World Bulletin of Public Health (WBPH)
Available Online at: https://www.scholarexpress.net
Volume-40, November 2024
ISSN: 2749-3644

15(2), e0228503. doi: 10.1371/journal.pone.0228503

12. Jirak, P.; Stechemesser, L.; Moré, E.; Franzen, M.; Topf, A.; Mirna, M.; Paar, V.; Pistulli, R.; Kretzschmar, D.; Wernly, B.; et al. Clinical implications of fetuin-A. Adv. Clin. Chem. 2019, 89, 79–130.,
13. Kim S., Hwang S., Jang H. R. et al. Creatinine- and cystatin C-based estimated glomerular filtration rate slopes for the prediction of kidney outcome: a comparative retrospective study // BMC Nephrol.— 2019.—Vol. 20 (1)—P. 214.
14. Nascimbeni F, Romagnoli D, Ballestri S et al. Do nonalcoholic fatty liver disease and fetuin-A play different roles in symptomatic coronary artery disease and peripheral arterial disease? Diseases 2018; 6: 17
15. Osaki T., Satoh M., Tanaka F. et al. The Value of a Cystatin C-based Estimated Glomerular Filtration Rate for Cardiovascular Assessment in a General Japanese Population: Results from the Iwate Tohoku Medical Megabank Project // J. Epidemiol. — 2019. — May 25. doi: 10.2188/jea.JE20180274
16. Oweis A.O., Alawneh K.M., Alshelleh S.A. et al. Renal dysfunction among rheumatoid arthritis patients: a retrospective cohort study // Ann Med Surg (Lond). - 2020. - Vol. 60. - P. 280 - 284. DOI: 10.1016/j.amsu.2020.11.011.;
17. Summerhill V.I.et al. Th e Atherogenic Role of Circulating Modifi ed Lipids in Atherosclerosis. I. J. Mol. Sci. 2019; 20 (14): 3561.
18. Van der Laan S., Fall T., Soumaré A., et al. Cystatin C and Cardiovascular Disease: A Mendelian Randomization Study // J Am Coll Cardiol, 2016. Vol. 68(9). P. 934–945. doi:10.1016/j.jacc.2016.05.092.