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METABOLIC SYNDROME AND RISK OF CHRONIC KIDNEY DISEASE

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Таянч сўзлар: метаболик синдром, буйракнинг сурункали касаллиги, инсулинга чидамлилик, семириш, дислипидемия, артериал гипертензия.
Ключевые слова: метаболический синдром, хроническая болезнь почек, инсулинорезистентность, ожирение, дислипидемия, артериальная гипертензия.

Metabolic syndrome (MS) is a combination of disorders of carbohydrate metabolism, abdominal obesity, dyslipidemia and arterial hypertension. Research shows that there is a strong link between MS and chronic kidney disease (CKD). The factors for the development of CKD in metabolic syndrome are an increased level of insulin and insulin resistance, reactive oxygen species, inflammatory mediators, biologically active substances, hormones, inflammatory cytokin, increased activity of coagulation factors, inhibition of the fibrinolytic system.

МЕТАБОЛИК СИНДРОМ ВА СУРУНКАЛИ БУЙРАК КАСАЛЛИГИ ХАВФИ

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Метаболик синдром (МС) - бу углевод алмашинуви бузилиши, қорин семириб кетиши, дислипидемия ва артериал гипертензия билан кечувчи ҳолат бўлиб ҳисобланади. Тадқиқотлар шуни кўрсатадики, МС ва сурункали буйрак касаллиги (СБК) ўртасида кучли боғлиқлик мавжуд. Метаболик синдромда СБК ривожланишининг омиллари инсулин ва инсулин қаршилигининг ошиши, реактив кислород турлари, биологик фаол моддалар, гормонлар, яллиғланишли цитокинлар, плазма омилларининг фаоллиги, фибринолитик тизими фаолиятининг ошиши билан боғлиқ. МС билан оғриган беморларда буйраклардаги патологик бузилишлар микроваскуляр тубулалар атрофияси, интерстициал фиброз ва глобал ёки сегментал склероз билан намоён бўлади. Микроалбуминурия - бу МС нинг дастлабки белгиси.

МЕТАБОЛИЧЕСКИЙ СИНДРОМ И РИСК ХРОНИЧЕСКОЙ БОЛЕЗНИ ПОЧЕК

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Метаболический синдром (МС) это сочетание нарушения углеводного обмена, абдоминального ожирения, дислипидемии и артериальной гипертензии. Исследования показывают, что существует тесная связь между МС и хронической болезнью почек (ХБП). Факторами развития ХБП при метаболическом синдроме являются повышенный уровень инсулина и инсулинорезистентность, активные формы кислорода, биологически активные вещества, гормоны, воспалительные цитокины, усиление активности факторов коагуляции, торможение фибринолитической системы. Патологические нарушения в почках у больных с МС проявляются микрососудистой тубулярной атрофией, интерстициальным фиброзом и глобальным или сегментарным склерозом. Микроальбуминурия является ранним маркером при МС.

Metabolic syndrome (MS), which is a combination of pathological phenomena in the form of insulin resistance, abdominal obesity, dyslipidemia and obesity, is associated with an increased risk of developing cardiovascular diseases, diabetes mellitus, non-alcoholic liver disease and has a close relationship with chronic kidney disease (CKD).

Changes in kidney function are one of the most common manifestations of various diseases. There is a clinical need for early intervention to prevent potentially detrimental changes in renal function. Unfortunately, the diagnostic process is complicated by the asymptomatic nature of kidney dysfunction for a certain time and the absence of early biomarkers of kidney damage.

Many studies link MS with CKD [10,11,12]. Each component of MS is associated with both the onset and progression of CKD. For example, obesity is one of the significant risk factors for deteriorating kidney function. An increase in BMI by 10% increases the likelihood of a decrease in the glomerular filtration rate by 1.3 times [2]. The early stages of CKD are usually diagnosed accidentally due to its asymptomatic course and lack of screening programs. A meta-analysis of eleven studies involving 30146 patients showed that MS is associated with a decrease in the estimated GFR (GFR) <60 ml / min / 1.73 m2 with an odds ratio (OR) of 1.55 [6].

It should be noted that in a number of included studies there were no patients with diabetes mellitus, which is not only a potential component of MS, but also a common cause of CKD. Thus, in the NHANES III study, in which 7800 patients with initially normal renal function were observed for 21 years, the OR for the development of CKD in patients with MS was 2.6 (95% CI: 1.68-4.03) [4]. It is not always easy to assess the pathogenetic relationship between MS and CKD, despite their widespread occurrence.

As already mentioned, unlike CKD, for MS there are no uniform diagnostic criteria; individual components of MS have rather vague meanings and are sensitive to such unmeasurable factors as lifestyle changes, drug effects, or acute diseases. The timing of both MS and CKD is often difficult to determine.

Oversimplification of the criteria for MS (for example, using only BMI without determining the circumference of the waist and hips, ignoring ethnicity) further limits the final conclusions about the links between MS and CKD.

Histological examination of the kidneys after nephrectomy in 146 patients [10] showed a high prevalence of changes characteristic of CKD, including diffuse and segmental glomerulosclerosis in patients with MS. Other features included a higher prevalence of tubular cell atrophy, interstitial fibrosis, and arterial sclerosis. Another approach is to study intrarenal hemodynamics using ultrasound diagnostics, in which parenchymal renal damage in MS can be reflected by an increase in the intrarenal resistance index.

MS as a cause of CKD. More convincing than simply combining these conditions is the hypothesis that MS acts as a cause of CKD. However, it is not yet clear whether there is one linear mechanism that leads from MS to CKD, or there are a number of separate but interdependent mechanisms leading to the development of MS and, at the same time, to kidney damage. In this context, the most acceptable explanation is the action of a combination of risk factors leading to increased expression of profibrotic factors and including insulin resistance, inflammation, impaired lipid metabolism and arterial hypertension [7].

At the same time, it is still impossible to exclude a simple association between the two common diseases. The most important pathogenetic factor of CKD among those listed is insulin resistance. Insulin is itself an anti-inflammatory hormone. Insulin resistance that occurs in type 2 diabetes leads to inflammation, then oxidative stress is activated and the combined effect of these factors contributes to kidney damage [3]. High insulin levels stimulate the release of insulin-like growth factor 1 (IGF-1), which, in turn, increases the production of connective tissue growth factor, resulting in fibrosis [6].

Moreover, obesity can lead to an increase in the secretion of pro-inflammatory adipokines by adipose tissue, such as leptin, interleukin-6, and TNF-α [11]. Leptin enhances the intrarenal production of profibrotic transforming growth factor beta (TGF-β) [9]. In addition, TNF-α increases the production of reactive oxygen species (ROS), which, in turn, contribute to renal endothelial dysfunction, mesangial proliferation, and fibrosis [12]. At the same time, the secretion of anti-inflammatory cytokines, such as, for example, adiponectin, can be reduced, which contributes to the maintenance of insulin resistance. Adiponectin deficiency is associated with intimal thickening and smooth muscle cell proliferation [3]. Hese vascular effects may be independent of insulin sensitivity and may be present in CKD. Obesity also leads to an increase in glomerular volume, podocyte hypertrophy, and proliferation of mesangial cells [6]. TG and FFA by themselves can be nephrotoxic due to the expression of proinflammatory cytokines [7]. In association with arterial hypertension, another component of MS, angiotensin II stimulates ROS synthesis, decreasing the formation of NO synthase and causing damage to renal microvessels, ischemia, andtubulointerstitial changes [3].

However, it is rather difficult to assess the contribution of each of the MS components to renal dysfunction. In this regard, the presence of MS in itself is a fundamental risk factor for the development of CKD, regardless of its individual components. There is one more hypothesis according to which hyperuricemia, which is not a “traditional” component of MS, promotes the develop-

ment of CKD due to inhibition of nitric oxide production or in connection with the formation of nephrolithiasis [3].

Studies generally support the notion of a direction of pathogenetic mechanisms from MS to CKD, although further research is still needed on this issue. The potential mechanisms of CKD in metabolic syndrome are summarized in Table 1.

Table 1.

Potential mechanisms of CKD development in MS.

Potential mechanisms of CKD development in MS
• Oxidative stress
• Increased pro-inflammatory cytokines (leptin, IL-6, TNFα)
• Increase in profibrotic factors (fibroblast growth factor, transforming growth factor β, type IV collagen)
• Increased glomerular volume and podocyte hypertrophy
• Damaging effect of triglycerides and free fatty acids
• Development of ischemia and microvascular damage (angiotensin II)
• Hyperuricemia

MS and CKD progression. Several population studies have identified an association of MS with the progression of CKD. After reaching CKD stage C3-4, the presence of MS increases the risk of developing end-stage renal failure (ESRD) over the next 2-3 years, according to a study of more than 15,000 patients [15]. In particular, impaired glucose metabolism, hypertriglyceridemia, and arterial hypertension have been associated with an increased risk of ESRD.

Similarly, a gradual increase in insulin resistance was associated with a greater rate of decline in glomerular filtration rate in a cohort of elderly CKD patients [12]. On the other hand, in the later stages of CKD, MS as a risk factor for the progression of kidney disease becomes less significant, possibly because CKD directly leads to a rapid progression in a vicious vicious circle. Another study showed [5] that even if there is a correlation between MS and albuminuria, the effect of MS on the progression of CKD does not depend on the presence of albuminuria and its severityn addition, proteinuria is a known risk factor for the progression of CKD to ESRD and is also a omponent of some definitions of MS [3]. Despite a greater than 30% risk with MS, controlling proteinuria mitigates the potential for significant reductions in GFR, ESRD, or death in the African American Kidney Disease and Hypertension study [14]. If CKD develops, it is accelerated by risk factors common to CKD and MS. First, obesity-related glomerular hyperfiltration supplements the hyperfiltration induced by CKD itself, which leads to accelerated development of glomerulosclerosis [13].

Second, the activity of inflammatory processes and oxidative stress in CKD also increases [58]. Arterial hypertension and hypertriglyceridemia are increasing. Insulin resistance can be increased by both CKD and MS [8]. Third, insulin resistance can be associated with inflammation and cause so-called "endoplasmic reticulum stress".

According to this theory [16], proteins with altered structural organization accumulate in the lumen of the endoplasmic reticulum, suppressing insulin secretion by phosphorylation of the insulin receptor (IRS-1). Finally, insulin resistance impairs renal hemodynamics by increasing retention sodium and affects the transfer of other cations and anions [3]. The activation of the sympathetic nervous system is also detrimental to renal hemodynamics and promotes the development of proteinuria. The latter promotes damage to podocytes in the nephron, and, ultimately, chronic tubulointerstitial damage, thereby worsening the course of CKD [1].

Conclusions. Thus, there is a close relationship between MS and CKD. Patients with metabolic syndrome are more likely to have a high risk of chronic kidney disease and the risk of microalbuminuria. With an increase in BMI, a persistent decrease in GFR occurs.

Renal damage in metabolic syndrome includes glomerular and tubular fibrosis, vascular renal dysfunction. Risk factors for CKD in MS are: insulin resistance, obesity, dyslipidemia, high blood pressure.

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