METABOLIC SYNDROME AND RISK CHRONIC KIDNEY DISEASE

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Abstract:
Metabolic syndrome (MS) is a combination of carbohydrate disorders metabolism, abdominal obesity, dyslipidemia and arterial hypertension. Studies show that there is a strong link between MS and chronic kidney disease (CKD).

Keyword:
Metabolic syndrome, kidney disease

Metabolic syndrome (MS) is a combination of genetic, physiological, biochemical and clinical factors these include insulin resistance, dyslipidemia, visceral obesity, arterial hypertension, hypercoagulable condition, endothelial dysfunction, hyperuricemia. Relevance of the study MS is associated with a high prevalence worldwide. About all fourth or fifth adult (depending on country and ethnic group) have metabolic syndrome. Growth is recorded with age illness The proportion of people with MS in the population over the age of 30 is 10-20%, while in the United States - 25%. Average distribution around the world among men and women - 24%. If before MS was believed to be specific to older people, followed by research The American Diabetes Association shows an increase in morbidity among young people aged 20-29 the number of patients with this syndrome is 300 million person Therefore, the World Health Organization (WHO) considers MS to be a global epidemic.Pathophysiology of metabolic syndrome and the risk of chronic kidney disease

1. Insulin resistance and the risk of CKD Insulin resistance is a condition accompanied by a decrease in the sensitivity of peripheral tissues to the action of endogenous or exogenous insulin. Insulin resistance is an important pathophysiological factor with metabolic syndrome. Insulin mechanism of action Insulin affects many types of metabolism in the body. It promotes admission glucose into muscle, adipose and other tissues, regulates fatty acid synthesis and storage glucose in the form of glycogen in the liver, prevents breakdown of fat in adipose tissue, activates lipogenesis and Na + - / K + -ATPase in many cells.

The action of insulin on target cells begins after it binds to a specific insulin receptor (IR) on the cell membrane. IRs are found in many types of cells. Their greatest amount is in liver cells and adipose tissue (up to 20,000 per cell). Insulin the receptor is a glycoprotein consisting of 2 α and 2 β subunits linked by disulfide bonds. In this case, the α-subunits IR located on the cell surface bind insulin, and β-subunits are a transmembrane protein that possesses tyrosine kinase activity. After the addition of insulin to the α-subunits, the auto phosphorylation of the β-subunits occurs,
and then intracellular proteins such as substrates of insulin receptors (IRS-1 and IRS-2). Insulin-activated phosphorylated tyrosine receptor residues initiate a signaling cascade that is carried out in two ways:
1) via phosphatidylinositol-3-kinase (PI-3K);
2) mitogen-activated protein kinase (MAPK)

As noted above, insulin resistance is due to the inability of insulin-dependent tissues to assimilate some of the glucose at normal insulin levels in the body. This may be due to the following pathological factors:
- decrease in the number of RIs and their defect;
- the production of autoantibodies to insulin receptors and insulin;
- changes in the structure of IR and insulin under the action of metabolic substances;

- mutation of genes responsible for the synthesis of IR;
- changes in the activity of lipase, glycogen synthetase;
- molecular defects in proteins that transmit insulin signals;
- a decrease in the activity of the glucose transporter GLUT-4.

One of the key features of metabolic syndrome is that normal insulin levels do not produce and the release of free fatty acids from adipose tissue cells. Adipocytes are resistant to the anti-lipolytic action of insulin, and a consistent increase in free fatty acids in plasma plays an important role in the development of insulin resistance in muscle and other target tissues. In addition, excess fatty acids block the PI-3K signaling pathway. Damage to PI-3K pathway leads to vascular endothelial dysfunction and a decrease in the synthesis of nitric oxide Studied the effect of hyperinsulinemia on renal function in a Japanese population. The study included 2,446 urban Japanese residents aged 40 to 79 years without renal impairment who have previously functional and laboratory analyzes, including glucose tolerance test. The results were interpreted using correlation analysis and serum insulin values, blood pressure, total cholesterol, low-density lipoprotein cholesterol (LDL-C), TG and body mass index (BMI), which were negatively correlated with the corresponding serum creatinine level. This study confirmed that hyperinsulinemia was significant a factor of renal dysfunction in the general population. Renal dysfunction as a result of insulin resistance and hyperglycemia is associated with activation of the renin-angiotensin system with an increase in angiotensin II and aldosterone levels. Insulin resistance and hyperinsulinemia are associated with decreased endothelial nitric oxide production and an increase in oxidative stress, which contribute to the progression of diabetic nephropathy.

Abdominal obesity and the risk of CKD Obesity, according to WHO, is abnormal or excess body fat that can harm your health. D. Villareal et al. [30] give defining obesity as unhealthy excess body fat, which increases the risk of illness and premature death. This pathology characterized by a chronization of the process and a large the likelihood of relapse. There are 3 types of obesity - android, gynoid and mixed. The android type is manifested by an uneven distribution of fat with excess deposition in the upper half of the body. This increases the amount of internal fat. Such obesity called abdominal. Abdominal obesity is an independent risk factor for irreversible deterioration of renal function. With a 10% increase in BMI, there is an increase in the likelihood a stable decrease in the glomerular filtration rate by 1.27 times.In the development of MS and its clinical consequences an important role is played by abdominal obesity. Currently, adipose tissue is considered an active endocrine organ that secretes various biologically active compounds.

The main volume of adipose tissue is occupied by adipose cells - adipocytes (from Latin adeps - fat, cytos - cell). Adipocytes, also known as lipocytes or fat cells, are cells that form adipose tissue. Their function is to store energy in the form of fat. They have a rounded shape with a diameter of 25 to 250 microns.

Adipocytes contain a large lipid droplet, surrounded by a layer of cytoplasm. The core is located on the periphery (Fig. 4). Fat is stored semi-liquid condition and consists of triglycerides and cholesterol esters. Average adul has about 30 billion fat cells 13.5 kg. With overweight, adipocytes increase in size by about 4 times with a simultaneous increase in their absolute number. Adipose tissue is characterized by pronounced cellular heterogeneity. It consists of 1/3 adipocytes and 2/3 of preadipocytes, fibroblasts mesenchymal stem cells, macrophages, T-regulatory cells, endothelial progenitor cells. Poorly differentiated fibroblasts turn into pre-adipocytes, which, after the cessation of division, are converted intoadipocytes (Fig. 5).

In recent years, it has been found that adipose tissue is no longer considered inert, which can only store fat, but is a place synthesis of a significant amount of hormones and biologically active substances. As an endocrine organ, adipose tissue is responsible for synthesis and secretion of certain hormones. These include hormones that control intake nutrients (leptin, angiotensin) responsible for insulin sensitivity.

4. Arterial hypertension and the risk of CKD AH is diagnosed in 85–95% of patients with CKD (Stages 3-5). The relationship between hypertension and CKD is cyclical. Uncontrolled high blood

pressure is a risk factor development of CKD and contributes to its more rapid progression. Hypertension counts as one of the leading causes of CKD due to pathological effects on the vasculature of the kidneys. Long uncontrolled high blood pressure leads to intraglomerular pressure, disrupting glomerular filtration. Damage glomeruli leads to increased filtration protein, which is manifested by an increased protein content in the urine (microalbuminuria or proteinuria). Microalbuminuria is the first a sign of CKD. It was found that the level of microalbumin is significantly higher in patients with hypertension with the presence of MS in comparison with patients with hypertension, not having metabolic disorders [60]. For CKD is diagnosed using an assessment GFR, which helps determine how much well the kidneys filter substances. The majority of patients with MS have an increase I hypertension and, accordingly, impaired renal function, which can be determined by changes in GFR [61] (Table 5).

Thus, the combination of the main factors involved in kidney damage in metabolic syndrome can be represented as follows (Fig. 7).

Findings:

1. There is a close relationship between MS and CKD.
2. In patients with metabolic syndrome

2.5 times more often there is a high risk of chronic kidney disease and 2 times more often - the risk of microalbuminuria.

3. With an increase in BMI, persistent decrease in GFR.
4. Renal damage in metabolic syndrome include glomerular and tubular

fibrosis, vascular renal dysfunction.

5. Risk factors for CKD in MS are: insulin resistance, obesity, dyslipidemia,

high blood pressure, active oxygen forms, inflammatory cytokines, increased activity of coagulation factors, inhibition of the fibrinolytic system.

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