

The Significance of Multifocal Atherosclerosis in the Development of Renal Dysfunction in Patients with Ischemic Heart Disease

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Abstract Although the term atherosclerosis is widely used in practice, the resulting damage occurs at different levels and in the order of the vessels in different areas, depending on the age, gender and comorbidities of the patients. In most cases, the atherosclerotic process develops in the aorta, heart, brain, kidneys, internal and external carotid arteries, hip and knee arteries. In addition, the pathogenic mechanisms and risk factors (RF) of atherosclerotic vascular injury in different basins are the same, although the presence and importance of each risk factor in this situation differ. Accordingly, high serum cholesterol levels are important for coronary atherosclerosis, stroke is associated with arterial hypertension (AH) and kidney damage, and vascular damage in the legs is associated with diabetes and smoking. An organic relationship was found between renal artery stenosis and diabetes mellitus (DM). Often the co-occurrence of these diseases is due to the fact that they have many common risk factors. In this case, there is a high risk of rapid and irreversible deterioration of renal function and difficulty in treatment.

Keywords Ischemic heart disease, Atherosclerosis, Renal artery stenosis, Diabetes, Kidney dysfunction, Risk factors

1. Introduction

Atherosclerosis is a systemic disease characterized by damage to vessels in several basins at the same time. In the literature, stenosing lesions of vessels in two or more basins are referred to as "multifocal atherosclerosis" (MFA). Its presence worsens the course and outcome of chronic and acute diseases, reduces the effectiveness of treatment [9]. But ischemic and cerebral complications can also be observed in vascular damage that does not have hemodynamic significance. Especially in patients with severe MFA, the probability of developing life-threatening conditions is very high. The presence of comorbid diseases in MFA negatively affects the exacerbation of the disease in a stable state and its outcome. Atherosclerosis, one of the most common manifestations of atherosclerosis in the world, including in Uzbekistan, is the main cause of ischemic heart disease (IHD) and related atherothrombosis and thromboembolism are considered one of the most important problems of modern medicine. According to the definition, atherosclerosis is a systemic damage of large and medium-sized arteries, a disease that causes local and general hemodynamic disturbances due to the accumulation of lipids, the growth of fibrotic tissue, and endothelial dysfunction in the vessel wall. According to the report of the

World Health Organization (WHO), 16.6 million people die from its complications every year. a person dies [1,2]. In recent years, although the number of age-related deaths has decreased, in 2016, 18 million deaths were observed in the world due to cardiovascular system diseases (CVD), mainly atherosclerosis of the heart and cerebrovascular vessels, which accounted for more than 30% of all deaths [15,17].

Although the word atherosclerosis is widely used in practice, the damage caused by it occurs in different degrees and order in the vessels of different branches depending on the age, gender and comorbid conditions of the patients. Atherosclerosis damages vessels of medium and large caliber, elastic (large arteries, aorta) and muscle elastic (mixed-carotid, brain and heart vessels). In most cases, the atherosclerotic process develops in the aorta, heart, brain, kidney, internal and external carotid arteries, femoral and knee veins. Damage to coronary vessels and cerebral vessels is most often fatal [1,2,15].

Although the pathogenetic mechanisms of atherosclerotic damage of blood vessels in different basins and the leading risk factors (XO) are the same, the participation and importance of each risk factor in this situation is different. Based on this, the high level of cholesterol in the blood serum is important for atherosclerosis of coronary vessels, for stroke - arterial hypertension (AG) and kidney damage, and for damage of leg vessels - diabetes and smoking. Cigarette smoking is considered an important modifiable factor leading to atherosclerotic damage of vessels in all

basins [8,17].

Atherosclerotic changes are located mainly in the bifurcation of the aorta and in the arteries that come out of it. This disease mostly occurs in men aged 45-50 years (3-4 times more than women), but in recent years it has also been observed among young people. Death due to the complications of atherosclerosis accounted for 50% of all deaths, and 1/3 of the 3565-year-olds [1,8].

2. The Main Findings and Results

Detection of signs of atherosclerotic changes in the aorta indicates that the process will soon spread to the vascular system in other areas. Atherosclerosis of the aortic arch and the vessels arising from it (including the branch of the coronary vessels and intercostal arteries), bifurcation of the aorta, and iliac arteries is severe. Among the coronary vessels, the main branch that supplies the myocardium with blood is more seriously damaged, and the atherosclerotic plaque is located in the area near the root of the arteries in most cases. Atherosclerosis of the coronary vessels has a characteristic of diffuse distribution. Their narrowing can be of different degrees, but atherosclerotic damage occupies the entire inner layer of the vessel [4,11,20]. Therefore, atherosclerosis is considered the main disease that simultaneously causes myocardial infarction, various other forms of stroke, cerebral stroke, blood circulation disorders in the legs, abdominal aorta, mesenteric and renal arteries [8,17].

Narrowing of the vascular gap by 70% or more has hemodynamic significance, and in this case, it is noted that the risk of developing ischemic complications is very high. If the atherosclerotic plaque has a large size, the risk of vessel wall damage and thrombosis is high [1,18].

According to the methodological analysis of four population studies with atherosclerotic coronary artery disease, which included 23,706 patients, the incidence of $\geq 50\%$ carotid artery damage was 0.2 to 7.5% in men aged 50 and 80, and 0.1 in women, respectively. % and 5.0%. Carotid artery narrowing $\geq 70\%$ is 0.1% in men younger than 50 years and increases to 6.1% in men ≥ 80 years and older. The incidence of carotid stenosis is slightly lower in women, at 0.1%, and increases with age to 3.9% [17,20].

According to data obtained by Paraskevas and other co-authors during the analysis of 388 cases, ischemic and embolic stroke occurred in 62% of patients after aortic-coronary bypass (ACS), and hypoperfusion was observed in 9% of patients, and hemorrhagic stroke was observed in 1% of patients. When the time to stroke development was analyzed, 45% of embolic and 56% of hypoperfusion acute cerebrovascular events occurred on the first day after surgery [14,21].

In recent years, the risk of atherosclerosis, resulting in disability, disability and death, has surpassed that of injuries, infectious and oncological diseases [16,20].

According to Aboyans V. and other authors, during the examination of patients preparing for US practice, the

narrowing of carotid arteries along with coronary vessels by $\geq 50\%$ was 10.3% 22.3%, and narrowing by $\geq 80\%$ was 4.0% – 10 was in the range of .0%. Analyzing the indicators of patients suffering from CKD with risk factors such as smoking, hypercholesterolemia, and older age, carotid artery narrowing of more than 60% was found in 35% [4,16,19].

According to the international REACH list, approximately 20% of patients with CHD, cerebral ischemic disease, and atherosclerotic atherosclerosis of the leg vessels have symptoms of atherothrombosis in more than one vessel at the same time, and in 2% in 3 vessel basins. If the research is carried out using additional methods, taking into account the asymptomatic course of the disease, the percentage of multifocal lesions will increase by several tens of percent. Atherosclerosis of the coronary vessels, brain and legs, depending on the level of damage, clinical symptoms of the disease appear [5,10].

According to the results of research carried out in recent years, damage to the coronary vessels, carotid artery and peripheral vessels was observed in 30-65% of cases. At the same time, atherosclerosis of vessels of one basin serves as XO in the damage of vessels in another area [1].

Sumin A.N. and according to the results of scientific research conducted by co-authors, multifocal atherosclerosis was detected in 27.3% of 1018 patients under control, and although there was no reliable difference in terms of gender, most women had coronary vessels and carotid arteries at the same time (16.6%), in men and damage to the coronary vessels and arteries in the legs (12.6%) was determined [8].

Risk factors for the development of atherosclerotic stenosis of the kidney and coronary arteries are mostly the same. Their atherosclerotic stenosing damage is observed more often in patients with previously disseminated atherosclerosis, changes in the coronary vessels, carotid, cerebral and peripheral arteries. In most cases of this group, there is hyperlipidemia, clinically evident UIK, history of MI or acute coronary syndrome (ACS), acute disorders of cerebral blood circulation (stroke, transient ischemic attack), transient lameness [5,9,15].

Atherosclerotic stenosis of renal arteries should be considered as an important risk factor for cardiovascular disease. Its presence indicates the aggressiveness of the course of atherosclerosis, serious disorders of lipoprotein metabolism and the presence of other problems. [10,11].

Among patients with severe atherosclerosis of the coronary vessels, the prevalence of hemodynamically significant damage to the renal arteries ranges from 18.7 to 75.5%, and the mortality rate from complications caused by the combination of these diseases is 25-50%. The combined damage of the kidney and heart arteries has a negative effect on the heart muscle and kidney function, worsening the outcome of the disease. Atherosclerosis of renal arteries is the main cause of vasorenal hypertension in 90% of cases [11,18]. It is somewhat difficult to determine the prevalence of renal artery stenosis in the general population, since the disease is asymptomatic in its early stages. It also depends on gender and is observed in 9.1% of elderly men and 5.5%

of women. When it was studied in relation to age, it was found that the disease is more common in men aged 55 and older and in women older than 60. The pathological process in the kidney can be accompanied by blood circulation disorders in the coronary vessels and the brain. Addition of thrombosis and embolism to the process worsens the outcome of the disease [11,20].

Stenosis of the renal vessels is observed much more often in patients with previously diagnosed heart vessel damage compared to the general population. Atherosclerosis of the renal artery in patients with CKD is detected incidentally during angiographic examination. According to a number of data, severe narrowing ($\geq 50\%$ of the arterial diameter) was detected in 10-15% of patients who underwent coronary angiography on suspicion of this disease, while less severe stenosis was observed in the same number of cases [13,15].

An association between renal artery stenosis and diabetes mellitus (DM) has been observed. Often, the coexistence of these diseases is due to the fact that they have many common risk factors. In this situation, there is a high risk of rapid and irreversible deterioration of kidney function and difficulty in treatment [6,14].

Atherosclerotic stenosis of the renal artery is most often located in the proximal third of one or both renal arteries. Due to aortic wall damage, atherosclerotic plaque is observed in the basin of the renal artery in 30-70% of cases, and in 75% of patients, renal artery atherosclerosis is observed in the area of the vessel's progression. According to a number of authors, 41% of patients had an exacerbation of renal artery damage and its complete closure within two years. During the 5-7 years after the diagnosis of renal artery stenosis, 7-16% of patients had segmental or vessel-wide occlusion. According to Oskin T. C. and co-authors, occlusion of one renal artery was observed in 95 (23.1%) of 397 patients with atherosclerotic damage to the renal artery, and atherosclerotic damage to the second kidney was observed in 66% of patients. According to them, in 35% of patients with a slight stenosis of the renal artery, atherosclerotic damage in the second renal artery has progressed to the level of hemodynamic significance. Due to a sharp decrease in blood circulation in both kidneys, their function slows down and an uncontrollable level of AG develops, which seriously affects the kidneys. According to the data provided by Caps M. and co-authors, renal atrophy develops on the affected side in 20.8% of patients with renal artery stenosis $\geq 60\%$ within 33 months [14,12,20].

Clinically, renal artery stenosis can be asymptomatic, or with poor-quality AG and symptoms of renal failure. The outcome of the disease depends not only on the level of blood pressure, but also on the condition of the kidney as a target organ. In 60-70% of this group of patients, the increase in blood pressure is associated with renal ischemia due to atherosclerotic plaques located in the renal arteries. The results of multidisciplinary pathomorphological examinations showed the presence of ICU in 18.7 - 75% of patients with renovascular hypertension. In addition, stenosis of the renal artery (regardless of its etiology) worsens the activity of the

cardiovascular system, leads to the exacerbation and complications of adjacent cardiovascular diseases, and has a negative effect on the outcome of the disease. It depends on the relationship between kidney function and systemic hemodynamics. The renin-angiotensin -aldosterone system (RAAS) imbalance and fluid separation from the body, the active influence of a large amount of protein loss through the urine and many other factors - all this affects the circulating blood volume, vascular tone, blood circulation in internal organs, and the pharmacokinetics of drugs. [5,8,21].

The 5-year survival rate was 65% for patients with 50% renal artery stenosis, compared with 86% for those without renal artery stenosis. The survival rate depends on the degree of renal artery stenosis and the number of affected vessels. In bilateral stenosis of the renal artery, chronic kidney disease (CKD), exacerbation of left ventricular hypertrophy, and a sharp decrease in left ventricular contractility are observed during decompensation. Clinical signs are evident in patients with LVEF or myocardial infarction (MI) [5,13].

As a result of a series of epidemiological investigations, it has been confirmed that the very early subclinical period of kidney damage is an important independent risk factor for the development and complications of CKD diseases and the occurrence of death from them. Among patients with chronic kidney disease, death due to chronic kidney disease is 1020 times more common [8,20].

A number of scientific studies have proven the existence of a link between kidney dysfunction and the severity of coronary atherosclerosis, disease progression and complications (development of MI or stroke) or sudden death in patients with coronary artery disease [4,13,16].

The problem of multifocal atherosclerosis is urgent and multifaceted, and its solution has not yet been resolved. Atherosclerotic damage of arteries in different vascular basins, common pathogenetic mechanisms of development have a number of features that determine the difference in treatment and prevention approaches, making it difficult to develop the principles of treatment of multifocal injuries [4,17,19].

3. Conclusions

The above data showed that atherosclerosis is a systemic disease, that this disease affects blood vessels in several basins at the same time in different degrees, and this process takes place for a long time without any clinical symptoms. Atherosclerosis is primarily caused by damage to the aorta and the vessels that come out of it, causing diseases of the heart, kidneys and brain. Atherosclerosis of vessels in one area is a risk factor for damage of vessels in another area. CHD, a type of coronary atherosclerosis, is considered one of the main causes of disability and death among the population all over the world, including in Uzbekistan. Deterioration of kidney function due to atherosclerosis in patients with CKD causes exacerbation, complications and death of this disease. In most patients, kidney damage occurs without any clinical symptoms in the early stages of the

disease, and there is no change in the usual laboratory and instrumental examination methods carried out in the primary and secondary links of the health care system. The appearance of symptoms of chronic kidney disease in this group of patients leads to a 1020-fold increase in death due to chronic kidney disease. In atherosclerosis, especially in patients with CKD, assessment of renal function, early diagnosis, and prevention of the development of chronic kidney disease have not been sufficiently studied, and the literature devoted to solving this problem is limited.

Early detection and timely treatment of kidney dysfunction in patients with CKD, as well as creation of preventive measures, lead to prevention of exacerbation and complications of the main disease. At the same time, it makes it possible to reduce the number of re-admissions of patients to the hospital and the amount of expenses for their treatment, as well as to improve the quality of life and prolong life.

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