ХРОНИЧЕСКАЯ БОЛЕЗНЬ ПОЧЕК И СОСТОЯНИЕ СЕРДЕЧНО-СОСУДИСТОЙ СИСТЕМЫ

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Аннотация. Хроническая болезнь почек (ХБП) значительно увеличивает риск сердечно-сосудистых осложнений и смерти. У больных ХБП часто наблюдается эндотелиальная дисфункция, которая играет важную роль в развитии сердечно-сосудистых осложнений. В данной статье обсуждаются развитие сердечно-сосудистого риска, последствия эндотелиальной дисфункции, а также важность ранней диагностики и стратегии лечения.

Ключевые слова: хроническая болезнь почек, сердечно-сосудистый риск, эндотелиальная дисфункция, артериальная гипертензия, атеросклероз.

CHRONIC KIDNEY DISEASE AND CONDITION CARDIOVASCULAR SYSTEM

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Abstract: Chronic Kidney Disease (CKD) presents significant cardiovascular morbidity and mortality risks. Patients with CKD frequently exhibit endothelial dysfunction, which plays a pivotal role in cardiovascular complications. This article discusses the mechanisms underlying cardiovascular risks in CKD, the implications of endothelial dysfunction, and the importance of early diagnosis and treatment strategies.

Keywords: Chronic Kidney Disease, cardiovascular risk, endothelial dysfunction, hypertension, atherosclerosis.

INTRODUCTION

Chronic Kidney Disease is a progressive condition characterized by a gradual loss of kidney function over time. It is associated with various complications, primarily cardiovascular diseases. Patients with CKD are at a markedly increased risk for cardiovascular events compared to the general population. This increased risk is closely linked with endothelial dysfunction, a condition characterized by an imbalance in the production and regulation of endothelial-derived factors.

Chronic Kidney Disease (CKD) is a progressive condition characterized by a gradual and irreversible decline in kidney function over time. It encompasses a range of kidney disorders that prolong for at least three months, resulting in the kidneys' inability to filter waste products from the blood effectively. This impairment leads to a variety of systemic complications, severely impacting patient quality of life and increasing the risk of cardiovascular diseases. CKD is commonly classified based on the estimated glomerular filtration rate (eGFR), a key indicator of kidney function that can be calculated using serum creatinine levels. CKD is divided into five stages according to the eGFR: Stage 1: eGFR ≥ 90 mL/min/1.73 m² with other kidney damage markers. Stage 2: eGFR 60-89 mL/min/1.73 m² with kidney damage. Stage 3: eGFR 30-59 mL/min/1.73 m², further divided into 3a (eGFR 45-59) and 3b (eGFR 30-44). Stage 4: eGFR 15-29 mL/min/1.73 m²; severe reduction in kidney function.Stage 5: eGFR < 15 m L/min/1.73 m², indicating kidney failure, often requiring dialysis or kidney transplantation.

MAIN PART

The progression of CKD is often insidious and asymptomatic in its early stages, thus requiring regular monitoring, particularly for high-risk populations. CKD is a prevalent public health issue, affecting approximately 10-15% of the global population [5]. The burden is particularly high among older adults, with age being a notable risk factor. Patients with CKD are at high risk for cardiovascular events such as myocardial infarction and stroke. Factors contributing to this increased risk include traditional risk factors (hypertension, dyslipidemia) and non-traditional factors such as inflammation, mineral metabolism disorders, and anemia [6].

Epidemiology of Cardiovascular Disease in CKD. Individuals with CKD have a substantially higher cardiovascular mortality rate compared to the general population. The risk of cardiovascular events increases progressively with the decline in renal function, particularly evident in patients with an eGFR of less than 60 mL/min. Studies have shown that cardiovascular disease accounts for approximately 50% of deaths in patients with CKD, especially in the advanced stages of the disease [6].

Several pathophysiological mechanisms explain the heightened cardiovascular risk in CKD patients:

- CKD is frequently associated with traditional risk factors for cardiovascular disease, including hypertension, diabetes, and dyslipidemia. These conditions are often prevalent in CKD patients due to shared risk factors like obesity and an unhealthy lifestyle. Chronic hypertension, for example, not only contributes to kidney damage but also exacerbates cardiovascular complications.
- As mentioned in the first key point, endothelial dysfunction is a hallmark of CKD. The impairment of endothelial cell function leads to reduced bioavailability of nitric oxide, essential for vascular dilation, and increased oxidative stress. This dysfunction contributes to increased vascular resistance, promoting hypertension and atherosclerosis [2, 9].
- CKD is characterized by a state of chronic systemic inflammation. Elevated levels of inflammatory markers, such as C-reactive protein (CRP) and interleukin-6 (IL-6), have been observed in CKD patients. This chronic inflammation contributes to atherogenesis and plaque instability, promoting cardiovascular events [7, 8].
- Dysregulation of calcium and phosphate metabolism in CKD results in secondary hyperparathyroidism and vascular calcification. These abnormalities can lead to arterial stiffness and increased cardiovascular risk. Elevated serum phosphate levels have been correlated with increased mortality in CKD patients [3].
- The accumulation of uremic toxins, such as asymmetric dimethylarginine (ADMA), in CKD contributes to endothelial dysfunction and cardiovascular risk. These toxins disrupt nitric oxide synthesis and promote oxidative stress and inflammation [1].

The Role and Mechanisms of Endothelial Dysfunction in CKD

Endothelial dysfunction is a key player in the pathophysiology of cardiovascular diseases in CKD. Impaired endothelial function leads to increased vascular stiffness, reduced nitric oxide availability, and enhanced thrombogenicity, further promoting atherosclerosis [2].

The endothelium, a monolayer of cells lining blood vessels, plays a crucial role in maintaining vascular homeostasis. It regulates vascular tone, blood flow, and hemostasis by producing a variety of factors, including nitric oxide (NO), which is essential for vasodilation. Endothelial dysfunction refers to the impaired ability of the endothelium to produce these factors, leading to increased risks for both microvascular and macrovascular complications. In the context

of CKD, endothelial dysfunction is a significant contributor to the increased cardiovascular morbidity and mortality observed in these patients. It manifests as:

-Reduced Nitric Oxide Availability: In CKD, there is an impairment in the synthesis of nitric oxide due to factors such as oxidative stress and the accumulation of uremic toxins. The resulting decrease in NO availability leads to vasoconstriction, increased arterial stiffness, and hypertension.

- Increased Vascular Inflammation: Patients with CKD often exhibit elevated levels of pro-inflammatory cytokines and adhesion molecules, promoting leukocyte adhesion and migration to the vessel wall. This inflammatory response is critical in the development of atherosclerotic plaques and vascular calcification.

-Thrombogenic State: Endothelial dysfunction shifts the balance towards coagulation, increasing the risk of thrombus formation. This is particularly important in CKD patients, as they often exhibit altered platelet function and increased levels of coagulation factors.

Several intertwined mechanisms contribute to the development of endothelial dysfunction in CKD:

Oxidative Stress: Elevated levels of reactive oxygen species (ROS) are commonly observed in CKD due to the accumulation of uremic toxins and metabolic dysregulation. Increased oxidative stress leads to endothelial injury, reduced NO bioavailability, and enhanced vascular inflammation [1].

Inflammation: CKD induces a chronic inflammatory state characterized by elevated levels of inflammatory markers, such as C-reactive protein (CRP) and interleukin-6 (IL-6). This inflammation promotes endothelial cell activation, stimulating the expression of adhesion molecules, which fosters the recruitment of leukocytes to the endothelium [7].

Dysregulation of the Renin-Angiotensin System: In CKD, there is often dysregulation of the renin-angiotensin-aldosterone system (RAAS). Increased activity of angiotensin II results in vasoconstriction and further endothelial dysfunction. Angiotensin II promotes inflammation and oxidative stress by enhancing the production of ROS and pro-inflammatory cytokines from the endothelium and surrounding tissues [6].

Hyperphosphatemia and Mineral Disorders: CKD causes dysregulation of phosphate metabolism, leading to hyperphosphatemia, which has been linked to vascular calcification and endothelial dysfunction. Elevated phosphate levels can stimulate vascular smooth muscle proliferation and inhibit endothelial cell function, contributing to arterial stiffness and cardiovascular risk [3].

Asymmetric Dimethylarginine (ADMA): ADMA is an endogenous inhibitor of nitric oxide synthase that accumulates in CKD. Increased ADMA levels impair NO production, further contributing to endothelial dysfunction. The accumulation of ADMA correlates with the severity of CKD and is associated with increased cardiovascular risk.

Clinical Implications. The intricate relationship between Chronic Kidney Disease (CKD), cardiovascular risk, and endothelial dysfunction necessitates a comprehensive and proactive approach to patient care. Understanding the clinical implications can facilitate timely interventions and improve patient outcomes. Patients with CKD should be subject to regular cardiovascular risk assessments. This includes:

- Hypertension is prevalent in CKD and must be assessed frequently to adjust treatment plans accordingly.

- CKD patients have altered lipid metabolism, increasing their risk of atherosclerosis. Regular monitoring helps manage dyslipidemia effectively.

- Anemia is common in CKD and contributes to decreased exercise tolerance and quality of life. Regular assessments of hemoglobin levels can facilitate timely treatment interventions, such as iron supplementation or erythropoiesis-stimulating agents (ESAs).

- Although direct measurements of endothelial function are not routinely performed in clinical practice, awareness through evaluating risk factors and clinical symptoms is essential for patient management.

CONCLUSION

The interplay between Chronic Kidney Disease, cardiovascular risk, and endothelial dysfunction presents significant challenges for patient care. Endothelial dysfunction is a crucial mediator of cardiovascular complications in CKD, driven by multiple mechanisms such as oxidative stress, inflammation, dysregulation of the renin-angiotensin system, and the accumulation of uremic toxins. Understanding these complexities allows healthcare providers to implement proactive measures to monitor and manage cardiovascular risks in CKD patients effectively. A comprehensive approach that emphasizes regular monitoring, the control of traditional and non-traditional cardiovascular risk factors, and a collaborative healthcare model will significantly enhance patient outcomes and reduce the burden of cardiovascular disease.

The integration of targeted interventions aimed at improving endothelial function and minimizing cardiovascular risk factors can set the foundation for a multidisciplinary strategy that not only improve kidney health but also enhances overall patient quality of life. Continued research and clinical vigilance are essential for optimizing care pathways for CKD patients, ultimately paving the way to better cardiovascular outcomes and improved longevity.

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