PATHOPHYSIOLOGICAL MECHANISMS AND CLINICAL IMPLICATIONS OF CHRONIC HEART FAILURE

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Abstract. *Chronic heart failure (CHF) is one of the most common and complex diseases of the cardiovascular system, characterized by the heart's inability to pump enough blood to meet the body's needs. This pathology, as a global health issue, negatively affects the quality of life and life expectancy of many patients. This article provides an in-depth analysis of the main pathophysiological mechanisms involved in the development of CHF, including hemodynamic changes, activation of neurohormonal systems (renin-angiotensin-aldosterone system and sympathetic nervous system), inflammation and oxidative stress, mitochondrial dysfunction, calcium handling disorders, and myocardial remodeling processes. These mechanisms impair the contractile function of the heart muscle and enhance cardiomyocyte necrosis, fibrosis, and apoptosis. Persistent activation of neurohormonal systems leads to morphological and functional changes in the heart muscle, contributing to the progression of heart failure. Additionally, inflammatory mediators (e.g., TNF-α, IL-1, IL-6) have been shown to cause ongoing myocardial tissue damage and remodeling.*

Keywords: *Chronic heart failure, Renin-angiotensin-aldosterone system (RAAS), Pathophysiology of heart failure, Calcium homeostasis, NYHA classification, NT-proBNP.*

ПАТОФИЗИОЛОГИЧЕСКИЕ МЕХАНИЗМЫ И КЛИНИЧЕСКИЕ ПРОЯВЛЕНИЯ ХРОНИЧЕСКОЙ СЕРДЕЧНОЙ НЕДОСТАТОЧНОСТИ

Аннотация. *Хроническая сердечная недостаточность (ХСН) является одним из наиболее распространенных и сложных заболеваний сердечно-сосудистой системы, характеризующимся неспособностью сердца перекачивать достаточное количество крови для удовлетворения потребностей организма. Эта патология, являясь глобальной проблемой здравоохранения, негативно влияет на качество и продолжительность жизни многих пациентов. В статье представлен углубленный анализ основных патофизиологических механизмов, участвующих в развитии ХСН, включая гемодинамические изменения, активацию нейрогормональных систем (ренин-ангиотензин-альдостероновой системы и симпатической нервной системы), воспаление и окислительный стресс, митохондриальную дисфункцию, нарушения обмена кальция и процессы ремоделирования миокарда.*

Эти механизмы нарушают сократительную функцию сердечной мышцы и усиливают некроз кардиомиоцитов, фиброз и апоптоз. Стойкая активация нейрогормональных систем приводит к морфологическим и функциональным изменениям в сердечной мышце, способствуя прогрессированию сердечной недостаточности. Кроме того, было показано, что воспалительные медиаторы (например, ФНО-α, ИЛ-1, ИЛ-6) вызывают продолжающееся повреждение и ремоделирование тканей миокарда.

Ключевые слова: *хроническая сердечная недостаточность, ренин-ангиотензин-альдостероновая система (РААС), патофизиология сердечной недостаточности, гомеостаз кальция, классификация NYHA, NT-proBNP.*

Introduction

Chronic heart failure (CHF) is a complex systemic disorder resulting from the heart's inability to adequately supply the body with the necessary oxygen and nutrients. It arises from various etiological factors and is characterized not only by a decline in myocardial contractile function but also by systemic imbalances affecting the entire body. According to statistics from the World Health Organization, this condition affects millions of people worldwide and ranks among the leading causes of death related to the cardiovascular system.

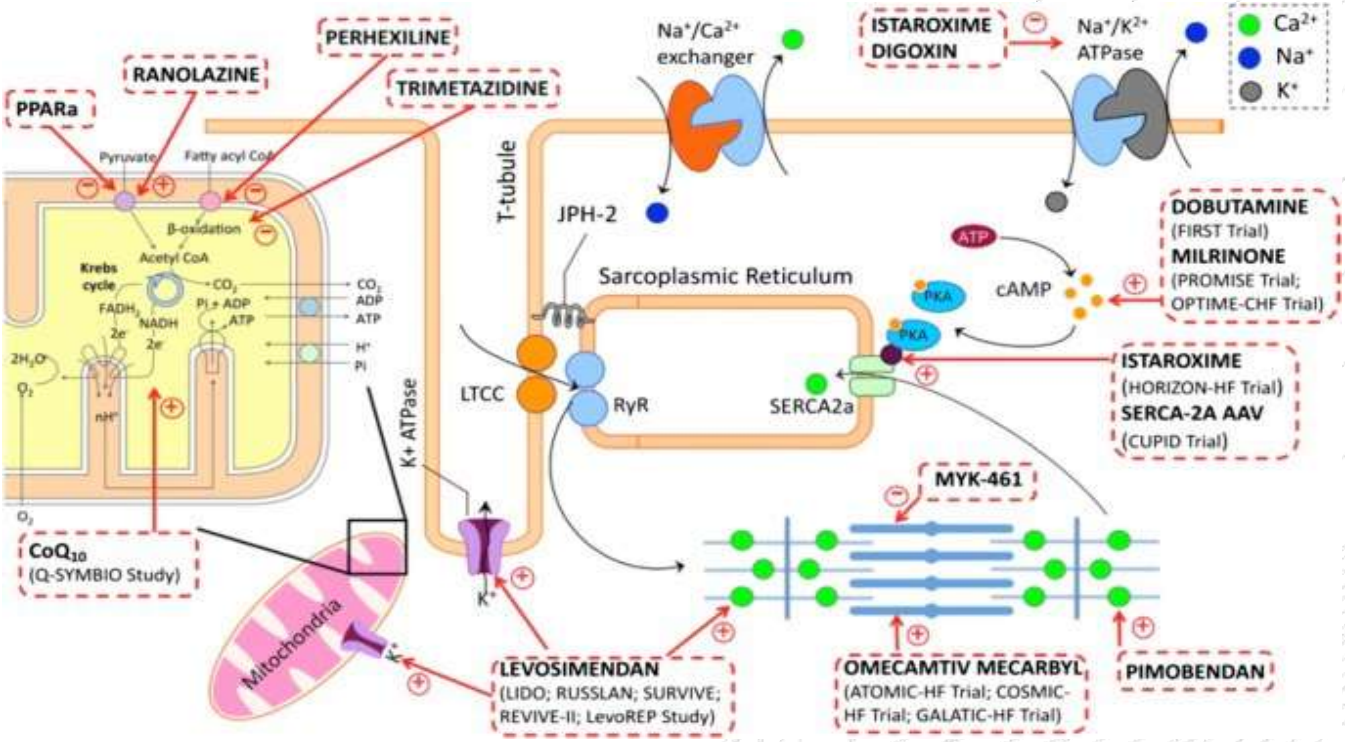
The pathophysiological changes central to CHF involve multiple interconnected and progressive processes. A reduction in cardiac output leads to insufficient blood delivery to peripheral tissues, triggering the activation of neurohormonal systems, including the renin-angiotensin-aldosterone system (RAAS) and the sympathetic nervous system (SNS). While these systems initially help maintain blood pressure, their prolonged activation contributes to morphological and functional deterioration of cardiac tissue.

Inflammatory processes also play a significant role in the pathogenesis of CHF. Elevated levels of cytokines (e.g., IL-6, TNF-α) exacerbate cellular dysfunction within cardiac tissue, resulting in oxidative stress, impaired mitochondrial function, and metabolic disturbances. These changes reduce the heart muscle's energetic capacity and promote tissue remodeling and fibrosis.

Moreover, intracellular calcium ion imbalance disrupts both diastolic relaxation and systolic contraction. Decreased activity of SERCA-2a, reduced sensitivity of the troponin complex, and dysregulation of calcium handling via calmodulin contribute to the development of diastolic dysfunction, particularly in heart failure with preserved ejection fraction (HFpEF).

As highlighted in USMLE clinical guidelines, the immune system is directly involved in CHF. The secretion of inflammatory mediators by T-lymphocytes and macrophages, along with increased activity of matrix metalloproteinases, leads to the structural degradation of cardiac muscle tissue.

The mechanism will be illustrated in the diagram below.



On the right side, the regulation of intracellular calcium is illustrated: LTCC (L-type Ca^{2+} Channels): Allows calcium to enter the cell. RyR (Ryanodine Receptor): Promotes the release of calcium into the cytosol. SERCA2a: Pumps calcium back into the sarcoplasmic reticulum. Na^{+}/Ca^{2+} exchanger & Na^{+}/K^{+} ATPase: Regulate the exchange of calcium and sodium ions. JPH-2: A junctional protein that links the cytoskeleton to the sarcoplasmic reticulum.

Methods:

During the preparation of this article, an analytical approach to literature review was employed to investigate the pathophysiological foundations of chronic heart failure and its clinical correlations. A wide range of up-to-date scientific publications were examined, and their findings were systematically synthesized.

Relevant literature was selected using key terms such as “chronic heart failure”, “cardiac remodeling”, “neurohormonal activation”, “myocardial fibrosis”, and “inflammation in heart failure”. The data were categorized thematically, allowing for an in-depth exploration of the underlying mechanisms of the condition.

Each domain-hemodynamic, neurohormonal, immunological, and metabolic-was assessed individually, with a clear emphasis on their clinical consequences. This comprehensive review ensures a structured understanding of the complex interplay between pathophysiology and clinical presentation in chronic heart failure.

Conclusion:

Chronic heart failure is a dynamic and multifactorial condition in which various pathophysiological processes—including hemodynamic imbalance, neurohormonal overactivation, inflammation, metabolic dysregulation, and impaired calcium homeostasis—interact to impair cardiac function. These mechanisms not only contribute to myocardial remodeling and reduced contractility but also play a critical role in the clinical progression of the disease. A detailed understanding of these interconnected pathways provides a foundation for better diagnostic precision and the implementation of more effective, mechanism-based therapies. Recognizing the clinical implications of each pathophysiological component supports the development of personalized treatment approaches and highlights the importance of integrated care in improving patient outcomes in chronic heart failure.

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