COMPARATIVE DESCRIPTION OF CLINICAL, IMMUNOLOGICAL AND GENETIC FEATURES OF THE DEVELOPMENT OF CHRONIC KIDNEY DISEASE IN PATIENTS WITH HEART FAILURE

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Abstract: *Chronic kidney disease (CKD) frequently develops in patients with heart failure (HF), forming a complex pathophysiological entity commonly referred to as the cardiorenal syndrome. The progression of CKD in this population is driven by intertwined clinical, immunological, and genetic mechanisms. This review provides a comparative analysis of these determinants, emphasizing differences in their contribution to renal dysfunction across heart failure phenotypes. Clinical hemodynamic impairment, systemic inflammation, and genetic susceptibility collectively shape disease trajectory. A multidimensional model integrating these factors is proposed to improve risk stratification and personalized therapeutic strategies.*

Keywords: *chronic kidney disease, heart failure, cardiorenal syndrome, inflammation, cytokines, genetic polymorphism, renal fibrosis, neurohormonal activation.*

Main Text

Introduction

Heart failure and Chronic kidney disease frequently coexist, significantly worsening morbidity and mortality. The interaction between cardiac dysfunction and renal impairment is bidirectional and multifactorial. While hemodynamic compromise has traditionally been considered the primary driver of renal injury in HF, emerging evidence highlights the importance of immune activation and genetic predisposition.

This review comparatively analyzes clinical, immunological, and genetic features contributing to CKD development in patients with HF.

1. Comparative Clinical Features

Hemodynamic Mechanisms

In heart failure with reduced ejection fraction (HFrEF), diminished cardiac output leads to renal hypoperfusion and activation of compensatory neurohormonal pathways. In contrast, heart failure with preserved ejection fraction (HFpEF) is more strongly associated with venous congestion and elevated central venous pressure, resulting in impaired renal venous outflow and increased intrarenal pressure.

Key clinical contributors include:

- Reduced cardiac output
- Elevated central venous pressure
- Activation of the renin–angiotensin–aldosterone system (RAAS)
- Sympathetic nervous system overactivity
- Use of nephrotoxic agents

Comparatively, congestion appears to play a more dominant role in HFpEF-related CKD, whereas hypoperfusion predominates in HFrEF.

2. Immunological Characteristics

Chronic systemic inflammation is a hallmark of both HF and CKD. Comparative immunological findings include:

- Elevated pro-inflammatory cytokines (TNF-α, IL-6, IL-1β)
- Increased C-reactive protein (CRP)
- Activation of monocytes/macrophages
- Enhanced oxidative stress
- Endothelial dysfunction

In HFrEF, inflammatory activation is often secondary to myocardial injury and remodeling. In HFpEF, inflammation is frequently linked to metabolic comorbidities such as obesity and diabetes, contributing to microvascular dysfunction.

Renal consequences of immune activation include:

- Podocyte apoptosis
- Tubulointerstitial inflammation
- Fibroblast activation and collagen deposition
- Progressive renal fibrosis

Thus, immune-mediated injury represents a common but phenotypically variable pathway in CKD progression among HF patients.

3. Genetic Determinants

Genetic predisposition influences susceptibility to both cardiac and renal dysfunction.

Frequently studied polymorphisms include:

- ACE gene insertion/deletion (I/D) polymorphism
- AGT (angiotensinogen) gene variants
- NOS3 gene polymorphisms affecting endothelial nitric oxide synthesis
- NPPA and NPPB gene variants (natriuretic peptides)

Patients carrying high-activity RAAS genotypes may exhibit accelerated renal decline due to enhanced vasoconstriction and profibrotic signaling.

Emerging research also emphasizes:

- Titin (TTN) mutations in dilated cardiomyopathy
- Epigenetic modifications (microRNAs regulating fibrosis and inflammation)
- Genetic regulators of oxidative stress pathways

Comparatively, genetic factors appear to modulate disease severity rather than initiate CKD directly, interacting with hemodynamic and inflammatory stressors.

4. Integrative Comparative Model

A comparative framework suggests that CKD development in HF results from interaction among:

1. **Hemodynamic stress** (hypoperfusion vs. congestion dominance).

2. **Neurohormonal activation** (RAAS and sympathetic overdrive).
3. **Chronic inflammation and immune dysregulation**.
4. **Genetic and epigenetic susceptibility**.

The relative contribution of each component differs by HF phenotype, comorbidity burden, and individual genetic background.

This model supports a precision-medicine approach integrating clinical phenotype, inflammatory biomarkers, and genetic profiling.

Conclusion

Chronic kidney disease in patients with heart failure arises from complex and interrelated clinical, immunological, and genetic mechanisms.

- Clinical factors determine the hemodynamic foundation of renal injury.
- Immunological processes accelerate inflammatory and fibrotic damage.
- Genetic determinants modulate individual vulnerability and progression rate.

A comparative understanding of these mechanisms enables improved risk stratification and targeted therapeutic interventions aimed at interrupting the cardiorenal continuum.

REFERENCES

1. McDonagh T.A. et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure.
2. KDIGO 2022 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease.
3. Ronco C., Haapio M., House A.A. Cardiorenal syndrome. *Journal of the American College of Cardiology*, 2008.
4. Mann D.L., Felker G.M. Inflammatory pathways in heart failure. *Circulation Research*, 2020.
5. Zannad F., Rossignol P. Cardiorenal interactions and neurohormonal activation. *European Heart Journal*, 2018.