Cardiorenal syndrome: updated diagnostic and therapeutic approach

Síndrome cardiorrenal: abordagem diagnóstica e terapêutica atualizada

Síndrome cardiorenal: enfoque diagnóstico y terapéutico actualizado

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RESUMO

Objetivo: A Síndrome Cardiorrenal (SCR) representa um desafio clínico complexo, caracterizado pela interconexão patofisiológica entre o coração e os rins. Este artigo apresenta uma revisão integrativa da literatura, com foco na abordagem diagnóstica e terapêutica atualizada da SCR. A pesquisa foi realizada na base de dados PubMed, abrangendo o período de 2020 a 2025, resultando na seleção de 10 artigos científicos relevantes. Os achados destacam a importância de biomarcadores emergentes (NGAL, cistatina C, KIM-1), a utilidade da ultrassonografia Doppler (VExUS) para avaliação da congestão venosa, e o papel transformador de novas classes terapêuticas, como os inibidores do cotransportador sódio-glicose 2 (SGLT2i), agonistas do receptor do peptídeo semelhante ao glucagon 1 (GLP-1 RA) e inibidores do receptor da angiotensina/neprilisina (ARNI). A personalização do tratamento e a abordagem multidisciplinar são cruciais para otimizar os desfechos cardiorrenais. Este trabalho visa fornecer uma síntese abrangente das evidências mais recentes, contribuindo para uma compreensão aprofundada e um manejo mais eficaz da SCR.

Palavras-chave: Síndrome Cardiorrenal 1; Insuficiência Cardíaca 2; Doença Renal Crônica 3; Biomarcadores 4.

ABSTRACT

Objective: Cardiorenal Syndrome (CRS) represents a complex clinical challenge characterized by the pathophysiological interconnection between the heart and kidneys. This article presents an integrative literature review, focusing on the updated diagnostic and therapeutic approach to CRS. The research was conducted in the PubMed database, covering the period from 2020 to 2025, resulting in the selection of 10 relevant scientific articles. The findings highlight the importance of emerging biomarkers (NGAL, cystatin C, KIM-1), the utility of Doppler ultrasonography (VExUS) for assessing venous congestion, and the transformative role of new therapeutic classes, such as sodium-glucose cotransporter 2 inhibitors (SGLT2i), glucagon-like peptide 1 receptor agonists (GLP-1 RA), and angiotensin receptor/neprilysin inhibitors (ARNI). Personalized treatment and a multidisciplinary approach are crucial for optimizing cardiorenal outcomes. This work aims to provide a comprehensive synthesis of the latest evidence, contributing to a deeper understanding and more effective management of CRS.

Keywords: Cardiorenal Syndrome 1; Heart Failure 2; Chronic Kidney Disease 3; Biomarkers 4.

RESUMEN

Objetivo: El Síndrome Cardiorrenal (SCR) representa un desafío clínico complejo caracterizado por la interconexión fisiopatológica entre el corazón y los riñones. Este artículo presenta una revisión integradora de la literatura, centrándose en el enfoque diagnóstico y terapéutico actualizado del SCR. La investigación se realizó en la base de datos PubMed, abarcando el período de 2020 a 2025, lo que resultó en la selección de 10 artículos científicos relevantes. Los hallazgos destacan la importancia de los biomarcadores emergentes (NGAL, cistatina C, KIM-1), la utilidad de la ecografía Doppler (VExUS) para evaluar la congestión venosa y el papel transformador de nuevas clases terapéuticas, como los inhibidores del cotransportador de sodio-glucosa 2 (SGLT2i), los agonistas del receptor del péptido similar al glucagón 1 (GLP-1 RA) y los inhibidores del receptor de angiotensina/neprilisina (ARNI). El tratamiento personalizado y un enfoque multidisciplinario son cruciales para optimizar los resultados cardiorrenales. Este trabajo tiene como objetivo proporcionar una síntesis completa de la evidencia más reciente, contribuyendo a una comprensión más profunda y un manejo más eficaz del SCR.

Descriptores: Síndrome Cardiorrenal 1; Insuficiencia Cardíaca 2; Enfermedad Renal Crónica 3; Biomarcadores 4.

REVISÃO

Introduction

Cardiorenal Syndrome (CRS) encompasses complex dysfunctions involving the cardiac and renal systems, triggering a cascade of feedback processes that culminate in various impairments to both systems. Identifying the causal nexus of this syndrome can be challenging, given that risk factors such as arterial hypertension, diabetes, atherosclerosis, and dyslipidemia exert an intrinsic influence on both systems.[1].

Regarding the diagnostic approach, biomarkers are important diagnostic and prognostic assessment tools, as they reflect hemodynamic alterations that reveal cardiac and renal damage. Among the main cardiac biomarkers, cardiac troponins and natriuretic peptides stand out, and when elevated, indicate cardiovascular (CV) risk and, in parallel, worsening of Chronic Kidney Disease[2] (CKD) status.

Concerning renal biomarkers, serum creatinine and the glomerular filtration rate (GFR) remain widely used, although influenced by non-renal factors, which reinforces the value of new biomarkers such as cystatin C and NGAL.[2]

The treatment of CRS becomes a challenge due to its complexity. Biomarkers influence the therapeutic approach; therefore, medications that slow the decline of renal function while improving cardiovascular indices are prioritized, being relevant to the prognosis.

Objective

This article aims to discuss the updated diagnostic and therapeutic approach to CRS, based on an integrative literature review.

Methodology

This study consists of an integrative literature review on the updated diagnostic and therapeutic approach to CRS. The search was conducted in the PubMed/MEDLINE database using a strategy built from a combination of MeSH terms and keywords, employing the descriptors “Cardiorenal Syndrome,” “Diagnosis,” “Biomarkers,” and “Therapeutics,” combined with the AND/OR operators. The search covered the last five years (2020–2025), resulting in 34 initial publications after applying filters for free full text and studies in humans.

Strict selection criteria were applied, including: articles published in English, Portuguese, or Spanish, complete texts focused on the clinical and therapeutic aspects of CRS, especially those aligned with the most recent updates such as the KDIGO 2024 guidelines.

The analysis involved screening titles and abstracts, followed by a critical reading of the study designs and results of the preselected articles. Among the identified publications, priority was given to those presenting robust evidence on

emerging biomarkers (NGAL, cystatin C, KIM-1), imaging methods (VExUS), and the transformative role of new therapeutic classes (SGLT2i, ARNI, GLP-1 RA).

The final selection included the most relevant studies addressing aspects from pathophysiology to therapeutic interventions, providing a comprehensive view of the topic. This approach identified 10 key studies that met all inclusion criteria, forming the final review sample. The selection process followed the standard steps for systematic reviews: identification, screening, eligibility, and inclusion.

Results

The analysis of the selected articles reveals significant progress in understanding CRS, emphasizing early identification, risk stratification, and personalized management strategies.

The classification of CRS into five types is fundamental for guiding differential diagnosis and therapeutic choices. A remarkable advancement in early diagnosis lies in the use of biomarkers. Studies explore the potential of biomarkers such as NGAL, KIM-1, and cystatin C to identify acute kidney injury at early stages, which can improve risk stratification and allow more timely interventions.[3]

The coexistence of heart failure (HF) and CKD demands an integrated and multidisciplinary diagnostic approach, highlighting the need to consider patient symptoms alongside other factors. Venous congestion emerges as a key diagnostic factor in congestive nephropathy, requiring an assessment of fluid overload and its systemic effects. In this context, Doppler ultrasonography, particularly the Venous Excess Ultrasound Score (VExUS), has proven to be a promising tool, as it assesses venous congestion and predicts acute kidney injury, offering a noninvasive evaluation of renal and venous hemodynamics.

Furthermore, studies reinforce the utility of VExUS as a diagnostic tool to assess vascular congestion in type 1 CRS, which is central to the pathophysiology of heart failure (HF) [4, 6, 9, 10].

In patients with heart failure with preserved ejection fraction (HFpEF), diagnostic complexity and the need for specific criteria are evident, given the increasing prevalence and management challenges.

The treatment of CRS aims to optimize both cardiac and renal functions. Effective decongestion remains a cornerstone, with loop diuretics as standard therapy. However, the heterogeneity of CRS and variable response to diuretics underline the need for more refined strategies[7,2].

Recent therapeutic advances have transformed CRS management. Sodium-glucose cotransporter-2 inhibitors (SGLT2i), glucagon-like peptide-1 receptor agonists (GLP-1 RA), and angiotensin receptor–neprilysin inhibitors (ARNI) have demonstrated the ability to improve cardiorenal outcomes, offering protection to both the heart and kidneys. Moreover, SGLT2i have proven effective in reducing congestion and improving renal outcomes. Personalized treatment is facilitated by the use of biomarkers, which can guide both pharmacological and non-pharmacological therapies.[5, 6, 3].

A multidisciplinary approach integrating HF and CKD management provides a more comprehensive and effective care strategy. The importance of organized care is evidenced by the creation of specialized cardiorenal units, designed to optimize diagnosis and management of complex patients, ensuring implementation of therapies that reduce cardiovascular mortality and hospitalizations.

Finally, decongestion guided by VExUS represents a promising therapeutic strategy. By enabling a more precise and individualized management of diuretic therapy, VExUS optimizes treatment response and contributes to renal function recovery, especially in type 1 CRS.[4, 8, 9, 10].

Discussion

CRS represents a growing clinical and pathophysiological challenge, requiring a diagnostic and therapeutic approach that transcends the compartmentalized view of heart and kidneys. This integrative review, by synthesizing the latest evidence, supports the need for an integrated and multidisciplinary understanding of CRS, as advocated by several authors.[2,6]

One of the most significant advances in CRS management lies in the ability to identify renal injury at earlier stages when addressing improved biomarker and imaging-based diagnostics. The historical reliance on serum creatinine and GFR presents well-documented limitations, such as non-renal influences and delayed injury detection.[2] In this context, emerging biomarkers such as NGAL, KIM-1, and cystatin C offer an opportunity for earlier risk stratification and intervention.[3] These biomarkers reflect tubular damage and glomerular dysfunction more sensitively than traditional markers, allowing more accurate assessment of the cardiorenal prognosis.

In parallel, assessment of venous congestion has emerged as a key diagnostic pillar, especially in type 1 CRS (acute). Congestion, not just low cardiac output, is a major factor in congestive nephropathy.[6] Doppler ultrasonography, particularly the VExUS score, represents a noninvasive and promising tool for quantifying fluid overload and predicting acute kidney injury.[9] Although some studies indicate that VExUS-guided decongestion did not significantly improve renal recovery in type 1 CRS, it did enhance the likelihood of achieving effective decongestion.[10] This suggests that VExUS is an excellent guide for diuretic therapy, optimizing fluid removal, which is crucial for HF management and indirectly beneficial for renal protection.

The past decade has witnessed a true revolution in the pharmacological management of CRS, driven by new drug classes offering dual protection for the heart and kidneys. SGLT2 inhibitors, such as dapagliflozin and empagliflozin, stand out for their ability to reduce congestion and improve renal outcomes regardless of diabetic status, as they alter renal hemodynamics and promote metabolic and anti-inflammatory effects beneficial to the cardiorenal axis[5].

In addition to SGLT2 inhibitors, ARNIs and GLP-1 RAs have also demonstrated a transformative role. ARNIs, by inhibiting neprilysin, increase natriuretic peptide levels, promoting vasodilation and natriuresis, which is beneficial for both heart failure and renal function [4]. The inclusion of these therapies, along with finerenone (a non-steroidal mineralocorticoid receptor antagonist), reflects a paradigm

shift, where treatment targets not only the symptom but also the modification of the disease in both organs[5].

The complexity of CRS, especially in patients with heart failure with preserved ejection fraction, where renal dysfunction and HFpEF are "two sides of the same coin", demands a personalized approach. Risk stratification guided by biomarkers and congestion monitoring through VExUS allows more targeted therapies, overcoming the variability in loop diuretic response[7].

The need for an integrated approach culminates in the proposal for organized care. The establishment of specialized Cardiorenal Units (CRUs), as discussed by León-Román et al.,[8] is essential to optimize diagnosis and management of complex patients. CRUs ensure the implementation of evidence-based therapies proven to reduce cardiovascular mortality and hospitalizations, fostering closer collaboration between cardiologists and nephrologists.

In summary, the evolution of CRS management is marked by a shift from reactive to proactive and predictive care. The combination of more sensitive diagnostics (biomarkers and VExUS), disease-modifying therapies (SGLT2i, ARNI, GLP-1 RA), and structured care in CRUs signals a new era in CRS treatment, one aimed at optimizing cardiorenal outcomes and improving patient quality of life.

Final Considerations

CRS is a complex condition that requires an integrated and multidisciplinary diagnostic and therapeutic approach. Recent advances in the identification of emerging biomarkers, the use of imaging tools such as VExUS for assessing venous congestion, and the introduction of new therapeutic classes — including SGLT2i, GLP-1 RAs, and finerenone — have significantly transformed CRS management. Personalized treatment, guided by a deep understanding of the pathophysiology and interrelated mechanisms between the heart and kidneys, is essential to optimize clinical outcomes and enhance patient quality of life.

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