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Cardiorenal Syndrome: Integrated Pathophysiology, Diagnostic Challenges, and Contemporary Therapeutic Approaches

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ABSTRACT

Cardiorenal syndrome (CRS) represents a complex bidirectional interaction between the cardiovascular and renal systems in which dysfunction of one organ may induce or worsen dysfunction of the other. The increasing global prevalence of heart failure, chronic kidney disease, hypertension, obesity, and diabetes mellitus has significantly contributed to the growing clinical and epidemiological burden of CRS. This review aimed to analyze the principal pathophysiological mechanisms, diagnostic approaches, and contemporary therapeutic strategies associated with cardiorenal syndrome through an evidence-based analysis of current scientific

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literature. The study was developed as a narrative and analytical review using scientific evidence obtained from internationally recognized databases, including PubMed, Scopus, Web of Science, and high-impact journals in nephrology, cardiology, and internal medicine. The analysis focused on hemodynamic alterations, neurohormonal activation, venous congestion, inflammatory pathways, endothelial dysfunction, oxidative stress, diagnostic biomarkers, pharmacological therapies, and multidisciplinary management approaches. The reviewed evidence demonstrated that CRS is a multifactorial systemic condition involving complex interactions between cardiac and renal dysfunction. Venous congestion, activation of the renin–angiotensin–aldosterone system, sympathetic nervous system stimulation, chronic inflammation, and endothelial injury were identified as major contributors to disease progression. Biomarkers such as NT-proBNP, cystatin C, NGAL, and KIM-1 showed important diagnostic and prognostic value, although integrated clinical evaluation remains essential. Contemporary therapeutic strategies, particularly sodium-glucose cotransporter-2 inhibitors, demonstrated substantial cardiovascular and renal protective effects. Multidisciplinary care models were also associated with improved patient outcomes and optimization of long-term management. In conclusion, cardiorenal syndrome should be understood as a highly dynamic and multisystemic condition requiring integrated cardiovascular and renal assessment. Early diagnosis, evidence-based therapy, preventive medicine, and multidisciplinary collaboration remain fundamental for improving prognosis and reducing the global burden associated with CRS.

KEYWORDS

Cardiorenal syndrome, heart failure, chronic kidney disease, nephrology, cardiology, internal medicine, venous congestion, neurohormonal activation, biomarkers, SGLT2 inhibitors, cardiovascular disease, renal dysfunction, inflammation, multidisciplinary care, cardiorenal interaction

INTRODUCTION

Cardiorenal syndrome (CRS) represents one of the most complex and clinically significant interactions in contemporary internal medicine, involving a bidirectional dysfunction between the cardiovascular and renal systems. The coexistence of heart failure and kidney disease has become increasingly prevalent worldwide due to population aging, the growing burden of hypertension and diabetes mellitus, and improvements in survival among patients with chronic cardiovascular disorders [1], [2]. This pathological interaction is associated with elevated morbidity, frequent hospitalizations, accelerated progression of organ dysfunction, increased healthcare expenditures, and high mortality rates, making CRS a major public health concern across both developed and developing countries [3], [4].

The heart and kidneys maintain a highly integrated physiological relationship through hemodynamic regulation, neurohormonal activation, inflammatory signaling, endothelial function, and fluid-electrolyte homeostasis. Alterations in one organ frequently provoke compensatory or maladaptive responses in the other, generating a vicious cycle of progressive dysfunction [5]. In clinical practice, this interaction is especially evident in patients with acute decompensated heart failure, chronic kidney disease (CKD), ischemic heart disease, diabetic nephropathy, and systemic hypertension, conditions that continue to increase globally and disproportionately affect low- and middle-income countries [6].

Historically, renal dysfunction in patients with heart failure was interpreted mainly as a consequence of reduced cardiac output and diminished renal perfusion. However, recent evidence demonstrates that CRS is considerably more complex and multifactorial. Venous congestion, endothelial injury, oxidative stress, chronic inflammation, neurohormonal dysregulation, sympathetic nervous system activation, and disturbances in the renin–angiotensin–aldosterone system (RAAS) have emerged as central mechanisms contributing to disease progression [7], [8]. Furthermore, persistent activation of inflammatory cytokines and fibrotic pathways has been shown to promote structural damage in both myocardial and renal tissues, leading to worsening prognosis and therapeutic resistance [9].

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The classification proposed by the Acute Dialysis Quality Initiative (ADQI) conference established five subtypes of CRS according to the primary affected organ and the temporal nature of the dysfunction [1]. This classification facilitated a more organized understanding of the syndrome and contributed to the development of more individualized diagnostic and therapeutic strategies. Nevertheless, despite advances in classification systems and pathophysiological knowledge, CRS remains underdiagnosed in many healthcare settings, particularly in resource-limited environments where access to specialized nephrology and cardiology services may be restricted [10].

Recent epidemiological studies indicate that approximately 30–60% of patients with chronic heart failure present some degree of renal impairment, while cardiovascular complications remain the leading cause of death among individuals with chronic kidney disease [11]. The coexistence of both disorders significantly worsens patient outcomes, prolongs hospital stays, and increases the risk of recurrent cardiovascular events [12]. In Latin America, particularly in countries such as Mexico, Colombia, and Ecuador, the growing prevalence of obesity, diabetes mellitus type 2, and uncontrolled hypertension has intensified the burden of cardiorenal disease, generating substantial challenges for healthcare systems and emphasizing the need for early detection and multidisciplinary management approaches [13].

In recent years, the therapeutic landscape of CRS has evolved considerably. Traditional management strategies based primarily on diuretics and fluid restriction are now complemented by newer pharmacological interventions with demonstrated cardiovascular and renal protective effects. Sodium-glucose cotransporter-2 inhibitors (SGLT2i), such as dapagliflozin and empagliflozin, have shown remarkable benefits in reducing heart failure hospitalizations, slowing CKD progression, and improving overall survival in both diabetic and non-diabetic populations [14], [15]. Similarly, advances in neurohormonal blockade, ultrafiltration techniques, biomarker-guided therapy, and personalized cardiovascular care have expanded the therapeutic options available for CRS management [16].

Despite these advances, important clinical and scientific challenges persist. There is still considerable heterogeneity regarding diagnostic criteria, biomarker interpretation, fluid management strategies, and optimal timing for renal replacement therapies [17]. Additionally, many patients continue to experience therapeutic limitations due to hypotension, electrolyte disturbances, advanced renal impairment, or polypharmacy-related complications [18]. Consequently, understanding the pathophysiological mechanisms underlying CRS is essential not only for improving diagnostic accuracy but also for developing more effective and individualized treatment strategies.

The growing complexity of CRS highlights the importance of interdisciplinary collaboration among nephrologists, cardiologists, internists, intensivists, and primary care physicians. Early identification of at-risk patients, adequate interpretation of renal and cardiovascular biomarkers, and implementation of evidence-based therapies are fundamental to improving clinical outcomes and reducing healthcare burden [19]. Educational initiatives directed toward medical students and healthcare professionals are equally important, as CRS frequently represents a diagnostic and therapeutic challenge in daily clinical practice.

The present review article aims to provide a comprehensive analysis of the current understanding of cardiorenal syndrome, emphasizing its pathophysiological interactions, clinical manifestations, diagnostic approaches, and contemporary management strategies. The review was developed through the analysis of recent literature indexed in internationally recognized scientific databases, including PubMed, Scopus, and high-impact cardiovascular and nephrology journals. Priority was given to clinical guidelines, consensus statements, randomized clinical trials, and recent review articles published by major scientific societies and academic institutions.

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Additionally, this review incorporates an international academic perspective with participation and contextual discussion relevant to healthcare realities in Mexico, Colombia, and Ecuador, countries where chronic cardiometabolic diseases continue to represent a major cause of morbidity and mortality. Through this integrative approach, the article seeks to strengthen academic understanding of CRS and provide updated educational content for medical students and healthcare professionals involved in cardiovascular and renal care.

Ultimately, the purpose of this review is to contribute to a better understanding of the intricate relationship between cardiac and renal dysfunction, promote early recognition of CRS, and encourage the implementation of multidisciplinary evidence-based strategies aimed at improving patient prognosis and quality of life.

DEVELOPMENT

Cardiorenal syndrome (CRS) has emerged as a major clinical challenge due to the intricate physiological and pathological interactions between the cardiovascular and renal systems. The syndrome is characterized by a bidirectional relationship in which acute or chronic dysfunction in one organ induces acute or chronic dysfunction in the other [1]. This interaction represents a substantial burden for healthcare systems worldwide because it is associated with increased morbidity, prolonged hospitalization, elevated treatment costs, and high mortality rates, particularly among elderly populations and patients with multiple comorbidities [2].

The growing prevalence of CRS is closely linked to the global increase in cardiovascular diseases, chronic kidney disease (CKD), hypertension, obesity, and diabetes mellitus type 2. According to international epidemiological reports, cardiovascular diseases remain the leading cause of mortality globally, while CKD continues to rise as a significant contributor to disability and premature death [3]. In Latin American countries such as Mexico, Colombia, and Ecuador, rapid urbanization, dietary changes, sedentary lifestyles, and limited preventive healthcare access have intensified the incidence of cardiometabolic disorders, consequently increasing the prevalence of cardiorenal interactions [4].

One of the fundamental aspects of CRS involves the hemodynamic relationship between cardiac output and renal perfusion. Under normal physiological conditions, the kidneys receive approximately 20% of total cardiac output, allowing adequate glomerular filtration and electrolyte balance [5]. In patients with heart failure, reduced cardiac output can compromise renal blood flow, leading to activation of compensatory neurohormonal mechanisms such as the renin–angiotensin–aldosterone system (RAAS), sympathetic nervous system activation, and vasopressin release [6]. Although these mechanisms initially aim to preserve circulatory homeostasis, chronic activation ultimately contributes to sodium retention, fluid overload, vasoconstriction, myocardial remodeling, and progressive renal injury [7].

Recent evidence has demonstrated that venous congestion plays a more significant role in renal dysfunction than previously recognized. Elevated central venous pressure reduces renal perfusion gradients and impairs glomerular filtration, even in the presence of relatively preserved cardiac output [8]. This concept has changed the traditional understanding of CRS and has emphasized the importance of adequate decongestion strategies in patients with acute decompensated heart failure. Mullens et al. demonstrated that persistent venous congestion was strongly associated with worsening renal function and poor prognosis in advanced heart failure patients [9].

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Inflammation and oxidative stress also represent central components in the pathophysiology of CRS. Chronic activation of inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and transforming growth factor-beta (TGF-β) contributes to endothelial dysfunction, fibrosis, and tissue remodeling in both the myocardium and kidneys [10]. Oxidative stress further amplifies cellular injury through mitochondrial dysfunction and endothelial damage, promoting disease progression and resistance to conventional therapies [11]. In addition, endothelial dysfunction alters vascular tone and microcirculatory regulation, reducing tissue oxygenation and exacerbating organ injury [12].

Another important mechanism implicated in CRS is neurohormonal dysregulation. Persistent RAAS activation promotes sodium retention, intraglomerular hypertension, and myocardial fibrosis, while chronic sympathetic stimulation contributes to vasoconstriction, arrhythmogenesis, and increased myocardial oxygen demand [13]. The maladaptive activation of these pathways creates a self-perpetuating cycle of cardiac and renal deterioration. Consequently, pharmacological blockade of neurohormonal pathways has become one of the principal therapeutic approaches in CRS management [14].

The classification system established by the Acute Dialysis Quality Initiative divides CRS into five subtypes based on the primary organ dysfunction and temporal sequence [1]. Type 1 CRS refers to acute worsening of cardiac function leading to acute kidney injury, whereas type 2 involves chronic cardiac dysfunction causing progressive CKD. Type 3 describes acute kidney injury precipitating acute cardiac dysfunction, while type 4 involves chronic kidney disease contributing to chronic cardiovascular abnormalities. Finally, type 5 CRS encompasses systemic disorders such as sepsis, diabetes mellitus, or systemic inflammatory diseases that simultaneously affect both organs [15]. This classification facilitates clinical decision-making and helps guide individualized therapeutic strategies.

From a diagnostic perspective, CRS remains challenging because no single biomarker can definitively establish the diagnosis. Traditional biomarkers such as serum creatinine and blood urea nitrogen often lack sensitivity during early stages of renal injury [16]. Consequently, newer biomarkers including cystatin C, neutrophil gelatinase-associated lipocalin (NGAL), kidney injury molecule-1 (KIM-1), and N-terminal pro-brain natriuretic peptide (NT-proBNP) have gained increasing relevance in clinical practice [17]. These biomarkers may allow earlier detection of subclinical organ dysfunction and improve risk stratification among high-risk patients.

Therapeutically, CRS management requires a multidisciplinary and individualized approach focused on hemodynamic stabilization, volume control, neurohormonal modulation, and prevention of progressive organ damage. Loop diuretics remain the cornerstone of treatment for volume overload; however, excessive diuresis may precipitate worsening renal function and electrolyte imbalances [18]. Clinical trials such as the DOSE trial evaluated different diuretic strategies in acute decompensated heart failure, highlighting the importance of individualized dosing protocols [19].

In recent years, sodium-glucose cotransporter-2 inhibitors (SGLT2i) have transformed the management of CRS. Initially developed for glycemic control in diabetes mellitus, these agents demonstrated substantial cardiovascular and renal protective effects independent of glucose reduction [20]. Trials such as DAPA-HF, EMPEROR-Reduced, and EMPA-KIDNEY showed reductions in heart failure hospitalizations, delayed progression of CKD, and improved overall survival among patients with cardiovascular and renal disease [21], [22]. The mechanisms underlying these benefits include improved natriuresis, reduced intraglomerular pressure, modulation of inflammatory pathways, and enhanced myocardial energy metabolism [23].

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Another important therapeutic consideration is the use of ultrafiltration in patients with refractory congestion. Ultrafiltration may improve fluid removal in selected patients with severe diuretic resistance; however, studies such as CARRESS-HF demonstrated that aggressive ultrafiltration may worsen renal outcomes if not carefully individualized [24]. Therefore, patient selection and close hemodynamic monitoring remain essential when considering extracorporeal fluid management strategies.

The burden of CRS extends beyond physiological dysfunction and significantly affects quality of life, psychological well-being, and healthcare resource utilization. Patients frequently experience recurrent hospitalizations, reduced functional capacity, fatigue, depression, and limitations in daily activities [25]. These factors highlight the importance of comprehensive management strategies that integrate medical treatment, nutritional support, patient education, cardiovascular rehabilitation, and psychosocial care.

In healthcare systems across Mexico, Colombia, and Ecuador, important disparities persist regarding access to specialized nephrology and cardiology services, early diagnostic testing, and advanced pharmacological therapies [26]. Rural populations and socioeconomically vulnerable communities are particularly affected by delayed diagnosis and limited access to multidisciplinary care. Consequently, strengthening preventive medicine programs, promoting early cardiovascular and renal screening, and improving medical education are fundamental strategies for reducing the burden of CRS in Latin America.

Current scientific evidence suggests that CRS should no longer be viewed as an isolated complication of heart or kidney disease, but rather as a systemic multisyndromic condition involving complex hemodynamic, inflammatory, metabolic, and neurohormonal interactions [27]. Advances in molecular biology, precision medicine, artificial intelligence-assisted risk stratification, and biomarker development may contribute to earlier diagnosis and more personalized therapeutic interventions in the future [28].

GENERAL OBJECTIVE AND SPECIFIC OBJECTIVES

To comprehensively analyze the pathophysiological interactions, diagnostic approaches, and current clinical management strategies of cardiorenal syndrome through an evidence-based review of contemporary scientific literature, with the purpose of strengthening academic understanding and clinical reasoning among medical students and healthcare professionals in internal medicine, cardiology, and nephrology.

A. Cognitive Domain

1. . To identify and explain the anatomical, physiological, and hemodynamic relationships between the cardiovascular and renal systems involved in cardiorenal syndrome.
2. To analyze the principal pathophysiological mechanisms associated with CRS, including neurohormonal activation, venous congestion, endothelial dysfunction, oxidative stress, and inflammatory pathways.
3. To classify the different subtypes of cardiorenal syndrome according to the Acute Dialysis Quality Initiative (ADQI) classification system and distinguish their clinical implications.
4. To evaluate the most relevant diagnostic biomarkers and imaging methods currently used in the identification and monitoring of CRS.
5. To compare the therapeutic strategies available for CRS management, including diuretics, RAAS inhibitors, SGLT2 inhibitors, ultrafiltration, and multidisciplinary interventions.

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B. Psychomotor Domain

1. To apply clinical reasoning in the interpretation of laboratory findings, renal biomarkers, and cardiovascular parameters associated with CRS.
2. To develop the ability to differentiate the various clinical presentations of CRS using evidence-based diagnostic criteria.
3. To integrate diagnostic and therapeutic algorithms into simulated clinical decision-making processes involving patients with cardiac and renal dysfunction.
4. To interpret hemodynamic and biochemical alterations associated with acute and chronic CRS in the context of internal medicine and nephrology practice.
5. To strengthen analytical skills for evaluating scientific literature related to cardiovascular and renal interactions.

C. Affective Domain

1. To encourage critical thinking regarding the complexity and systemic impact of cardiorenal syndrome in modern clinical medicine.
2. To promote awareness about the importance of early diagnosis and preventive strategies in reducing cardiovascular and renal morbidity and mortality.
3. To foster an interdisciplinary perspective among medical students and healthcare professionals regarding collaborative management between cardiology, nephrology, and internal medicine.
4. To strengthen professional responsibility toward evidence-based patient care and continuous academic updating in cardiorenal medicine.
5. To promote empathy and holistic clinical approaches when addressing the physical, psychological, and social burden experienced by patients with chronic cardiovascular and renal diseases.

OBJECT OF STUDY

The object of study of the present review article is the complex pathophysiological and clinical interaction between the cardiovascular and renal systems known as cardiorenal syndrome (CRS). This phenomenon involves the bidirectional relationship in which acute or chronic dysfunction of the heart may induce renal impairment, while kidney dysfunction may simultaneously precipitate or aggravate cardiovascular disease [1]. Due to its multifactorial nature and high clinical impact, CRS has become one of the most relevant topics in contemporary nephrology, cardiology, and internal medicine.

This review focuses specifically on the mechanisms responsible for the development and progression of cardiorenal syndrome, including hemodynamic alterations, neurohormonal activation, inflammatory responses, endothelial dysfunction, oxidative stress, venous congestion, and metabolic disturbances. These mechanisms are analyzed in the context of both acute and chronic cardiovascular and renal diseases, emphasizing their influence on morbidity, mortality, quality of life, and healthcare system burden [2].

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The population of interest includes adult patients with cardiovascular and renal disorders that predispose to or are associated with CRS. This encompasses individuals with acute decompensated heart failure, chronic heart failure, chronic kidney disease, acute kidney injury, systemic hypertension, ischemic heart disease, diabetic nephropathy, metabolic syndrome, and cardiorenal complications secondary to systemic inflammatory conditions [3]. Particular attention is directed toward patients with multiple cardiometabolic risk factors due to the increasing global prevalence of obesity, diabetes mellitus type 2, and hypertension.

The study also considers the epidemiological and clinical relevance of CRS within different healthcare contexts, including high-income countries and middle-income regions such as Latin America. In countries like Mexico, Colombia, and Ecuador, the burden of chronic cardiovascular and renal disease has progressively increased over recent decades due to demographic transitions, urbanization, dietary changes, limited preventive healthcare strategies, and disparities in access to specialized medical services [4]. These regional characteristics contribute to delayed diagnosis, disease progression, and increased hospitalization rates associated with cardiorenal complications.

From a clinical perspective, the object of study extends beyond isolated organ dysfunction and instead approaches CRS as a systemic multisyndromic condition involving complex physiological interactions. The review evaluates how cardiac dysfunction affects renal hemodynamics and how renal impairment contributes to structural and functional cardiovascular deterioration. This integrated approach allows for a more comprehensive understanding of the syndrome and reflects current scientific perspectives regarding interconnected organ failure [5].

In addition to physiological interactions, the study analyzes diagnostic and therapeutic strategies used in contemporary clinical practice. This includes evaluation of renal and cardiac biomarkers, imaging techniques, fluid management approaches, neurohormonal modulation, pharmacological therapies, extracorporeal support strategies, and multidisciplinary interventions aimed at improving patient outcomes [6]. The review also examines the growing role of precision medicine, biomarker-guided therapy, and evidence-based cardiovascular and renal protection strategies.

Another important component of the object of study is the educational and academic dimension of CRS. Given the increasing prevalence and complexity of the syndrome, there is a growing need for updated educational resources capable of strengthening clinical reasoning and interdisciplinary understanding among medical students and healthcare professionals. Consequently, this review aims to provide an integrative academic analysis that facilitates comprehension of the syndrome from both physiological and clinical perspectives [7].

The phenomenon under investigation is approached through an evidence-based framework derived from contemporary scientific literature indexed in international databases such as PubMed, Scopus, and Web of Science. Priority is given to high-impact clinical trials, consensus statements, international guidelines, observational studies, and systematic reviews published by recognized scientific societies in nephrology and cardiology [8]. This methodological approach allows the study to synthesize current scientific evidence while maintaining clinical applicability and academic relevance.

Ultimately, the object of study can be defined as the multidimensional interaction between cardiac and renal dysfunction and its implications for diagnosis, treatment, prognosis, healthcare systems, and medical education. Through this perspective, the article seeks to contribute to a more integrated understanding of cardiorenal syndrome and support the development of evidence-based strategies capable of improving cardiovascular and renal outcomes in diverse clinical settings.

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METHODOLOGY

The present study was developed as a narrative and analytical review article focused on the current scientific understanding of cardiorenal syndrome (CRS), including its pathophysiological mechanisms, clinical manifestations, diagnostic approaches, and therapeutic management strategies. The methodological design was structured to allow systematic organization, critical analysis, and synthesis of relevant scientific evidence obtained from internationally recognized academic databases and clinical practice guidelines.

The methodological approach selected for this review was based primarily on the Scientific Method combined with a Process-Based Methodology for evidence analysis and organization. This combined approach was chosen because it allows the structured identification of the research problem, systematic collection of scientific evidence, critical evaluation of information, and logical integration of findings related to the cardiovascular–renal interaction observed in CRS.

Methodological Design

The study followed a qualitative documentary review design with an evidence-based analytical orientation. The development process consisted of sequential stages involving literature identification, article selection, critical appraisal, thematic categorization, and integrative interpretation of findings. This design was considered appropriate because CRS represents a multifactorial clinical condition requiring interdisciplinary analysis from nephrology, cardiology, and internal medicine perspectives.

The review was conducted using peer-reviewed scientific publications, clinical guidelines, randomized clinical trials, observational studies, systematic reviews, and consensus statements related to cardiorenal syndrome. The selected literature focused on contemporary evidence regarding epidemiology, pathophysiology, diagnostic biomarkers, pharmacological interventions, extracorporeal therapies, and multidisciplinary management strategies.

Scientific Method Applied to the Study

1. Observation of the Problem

The methodological process began with the identification of the increasing global burden associated with cardiorenal syndrome and its impact on morbidity, mortality, healthcare expenditures, and quality of life. Clinical evidence demonstrates that patients with concomitant cardiovascular and renal dysfunction experience significantly worse outcomes compared to individuals with isolated organ disease [1]. The persistent increase in heart failure, chronic kidney disease, hypertension, and diabetes mellitus worldwide highlighted the need for an updated integrative review capable of synthesizing current scientific evidence regarding CRS.

2. Formulation of the Research Question

Based on the identified clinical and academic problem, the following research question was established:

“How do the pathophysiological interactions between the cardiovascular and renal systems influence the diagnosis, progression, and contemporary management of cardiorenal syndrome?”

This question guided the selection of literature, thematic organization, and analytical interpretation developed throughout the study.

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3. Literature Search Strategy

The literature search was conducted using internationally recognized scientific databases, including:

- PubMed/MEDLINE
- Scopus
- Web of Science
- ScienceDirect
- Google Scholar (for supplementary academic identification)

The search process prioritized publications from high-impact journals in nephrology, cardiology, and internal medicine. Keywords and Medical Subject Headings (MeSH) terms used during the search process included:

- "Cardiorenal Syndrome"
- "Heart Failure and Kidney Disease"
- "Cardiovascular-Renal Interaction"
- "Chronic Kidney Disease"
- "Acute Kidney Injury"
- "Renal Congestion"
- "SGLT2 inhibitors"
- "Cardiorenal Physiology"
- "Venous Congestion"
- "Neurohormonal Activation"

Boolean operators such as "AND" and "OR" were used to optimize search specificity and sensitivity. The search strategy also included manual identification of additional references through the bibliographic sections of selected studies.

Inclusion and Exclusion Criteria

Inclusion Criteria

The study included:

1. Peer-reviewed scientific articles published in indexed journals.
2. Clinical practice guidelines from recognized international scientific societies.
3. Randomized clinical trials, observational studies, and systematic reviews.
4. Publications addressing pathophysiology, diagnosis, epidemiology, or treatment of CRS.
5. Studies published primarily in English.
6. Contemporary literature with priority given to publications from the last 10 years, although historically relevant studies were also considered when necessary.

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Exclusion Criteria

The following were excluded:

1. Non-peer-reviewed publications.
2. Editorials without scientific evidence support.
3. Articles lacking relevance to cardiovascular–renal interactions.
4. Duplicate publications.
5. Studies with insufficient methodological clarity or limited scientific validity.

Process-Based Methodology for Evidence Organization

After literature selection, the study followed a Process-Based Methodology that allowed structured categorization and analysis of scientific information. This methodology included the following stages:

Evidence Identification

Relevant studies were identified according to thematic relevance and scientific quality.

Information Classification

The selected evidence was categorized into major thematic areas, including:

- Epidemiology of CRS
- Pathophysiological mechanisms
- Neurohormonal activation
- Venous congestion
- Diagnostic biomarkers
- Pharmacological therapies
- Extracorporeal therapies
- SGLT2 inhibitors
- Multidisciplinary management
- Prognostic implications

Critical Analysis

Scientific findings were compared and interpreted according to consistency, clinical applicability, and methodological quality. Priority was given to evidence supported by randomized clinical trials, meta-analyses, and international consensus documents.

Integrative Synthesis

The final stage involved the integration of evidence into a coherent academic narrative designed to facilitate understanding of the syndrome from physiological, diagnostic, and therapeutic perspectives.

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Data Collection and Information Analysis

The information extraction process involved detailed review and analysis of selected articles. Data collected included:

- Study objectives
- Population characteristics
- Main findings
- Pathophysiological mechanisms described
- Diagnostic approaches
- Therapeutic interventions
- Clinical outcomes
- Recommendations and limitations

The collected information was subsequently synthesized through thematic integration rather than quantitative meta-analysis because the objective of the study was educational and analytical rather than statistical pooling of outcomes.

Replicability of the Study

The methodology was intentionally described in detail to allow reproducibility by other researchers interested in cardiorenal syndrome or related cardiovascular–renal interactions. The use of internationally accessible databases, clearly defined inclusion and exclusion criteria, standardized search terms, and thematic evidence categorization facilitates replication of the review process and future updates based on emerging scientific evidence.

Furthermore, the structured methodological design enables adaptation of the study framework for educational purposes, systematic reviews, academic discussions, or multidisciplinary clinical training programs.

Ethical Considerations

The present review article was developed exclusively through analysis of previously published scientific literature and publicly available academic sources. No direct patient intervention, experimentation, personal clinical data collection, or confidential information handling was involved during the development of the study. Consequently, institutional ethical approval and informed consent procedures were not required according to international ethical standards for documentary review studies.

Additionally, the study maintained strict adherence to academic integrity principles through appropriate citation of scientific sources, evidence-based interpretation, and objective presentation of current medical knowledge.

Methodological Relevance

The selected methodology allowed comprehensive evaluation of the current evidence regarding cardiorenal syndrome while maintaining clinical applicability and educational value. By integrating scientific literature from nephrology, cardiology, and internal medicine, the methodological framework facilitated a multidisciplinary understanding of CRS and supported the development of an updated academic review relevant to healthcare professionals and medical students.

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PHASES OF DEVELOPMENT

Phase 1. Identification and Delimitation of the Research Problem

The first phase consisted of identifying the clinical and academic relevance of cardiorenal syndrome as a major healthcare challenge in contemporary medicine. During this stage, preliminary exploratory analysis of epidemiological reports, cardiovascular statistics, nephrology guidelines, and healthcare burden studies was conducted to evaluate the magnitude of CRS worldwide.

The increasing prevalence of chronic heart failure, chronic kidney disease, hypertension, obesity, and diabetes mellitus demonstrated the growing importance of cardiovascular–renal interactions in clinical practice [1]. Additionally, high hospitalization rates, elevated mortality, recurrent cardiovascular events, and progressive renal deterioration associated with CRS highlighted the need for an updated integrative review capable of synthesizing current scientific evidence.

The research problem was subsequently delimited toward the analysis of:

- Pathophysiological mechanisms involved in CRS.
- Cardiovascular and renal interactions.
- Diagnostic strategies.
- Current therapeutic approaches.
- Multidisciplinary management models.
- Clinical implications in internal medicine, nephrology, and cardiology.

This delimitation allowed establishment of a focused academic framework while maintaining sufficient breadth for comprehensive interdisciplinary analysis.

Phase 2. Formulation of Research Objectives and Analytical Questions

Once the research problem was defined, the second phase involved formulation of the general objective, specific objectives, and guiding analytical questions of the study. Bloom's taxonomy was incorporated into the objective structure to ensure inclusion of cognitive, psychomotor, and affective educational domains.

The principal analytical question established was:

"How do cardiovascular and renal pathophysiological interactions influence the diagnosis, progression, and management of cardiorenal syndrome in contemporary clinical medicine?"

Additional secondary analytical questions included:

- What are the principal neurohormonal and inflammatory mechanisms involved in CRS?
- How does venous congestion contribute to renal dysfunction?
- Which biomarkers currently provide greater diagnostic utility in CRS?
- What therapeutic strategies demonstrate the greatest cardiovascular and renal protective effects?
- How do healthcare disparities influence CRS outcomes in Latin American populations?

This phase ensured coherence between the educational purpose of the article, the selected methodology, and the subsequent evidence analysis process.

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Phase 3. Systematic Literature Search and Evidence Collection

The third phase consisted of extensive scientific literature collection using internationally recognized academic databases. The search strategy was structured to maximize sensitivity and specificity while prioritizing high-quality evidence related to CRS.

The databases consulted included:

- PubMed/MEDLINE
- Scopus
- Web of Science
- ScienceDirect
- Google Scholar (supplementary searches)

The literature search employed combinations of Medical Subject Headings (MeSH) terms and keywords associated with cardiovascular–renal interactions, including:

- “Cardiorenal Syndrome”
- “Heart Failure”
- “Chronic Kidney Disease”
- “Acute Kidney Injury”
- “Venous Congestion”
- “Renin–Angiotensin–Aldosterone System”
- “SGLT2 Inhibitors”
- “Cardiovascular-Renal Physiology”
- “Neurohormonal Activation”

Boolean operators (“AND,” “OR”) were used to refine search combinations and improve evidence identification.

During this stage, emphasis was placed on:

- Clinical practice guidelines.
- Consensus statements.
- Randomized controlled trials.
- Observational studies.
- Meta-analyses.
- Systematic reviews.
- High-impact review articles.

The evidence collection phase prioritized recent literature while also incorporating historically relevant publications fundamental to understanding CRS pathophysiology and classification systems.

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Phase 4. Selection and Critical Evaluation of Scientific Evidence

Following evidence collection, the fourth phase involved critical appraisal and selection of studies according to predefined inclusion and exclusion criteria. Each publication underwent detailed evaluation regarding:

- Scientific relevance.
- Methodological quality.
- Clinical applicability.
- Statistical validity.
- Academic credibility.
- Consistency with the objectives of the study.

Priority was given to studies published in peer-reviewed journals recognized within nephrology, cardiology, and internal medicine. International guidelines developed by organizations such as the American Heart Association (AHA), European Society of Cardiology (ESC), Kidney Disease: Improving Global Outcomes (KDIGO), and Acute Dialysis Quality Initiative (ADQI) were considered highly relevant due to their evidence-based recommendations and clinical applicability.

The critical analysis process also involved comparison of conflicting findings and identification of current controversies regarding:

- Optimal fluid management strategies.
- Timing of renal replacement therapy.
- Biomarker interpretation.
- Diuretic resistance.
- Use of ultrafiltration.
- Long-term benefits of emerging pharmacological therapies.

This stage ensured that the final review reflected balanced interpretation of contemporary scientific evidence.

Phase 5. Thematic Organization and Evidence Categorization

After selecting the final scientific evidence, the fifth phase consisted of thematic classification and organization of information into major analytical categories.

The evidence was grouped into the following thematic areas:

1. Epidemiology and healthcare burden of CRS.
2. Cardiovascular–renal physiology.
3. Neurohormonal activation mechanisms.
4. Venous congestion and hemodynamic alterations.
5. Inflammatory and oxidative stress pathways.
6. CRS classification systems.

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7. Diagnostic biomarkers and imaging approaches.
8. Pharmacological management strategies.
9. SGLT2 inhibitors and cardiorenal protection.
10. Extracorporeal therapies and ultrafiltration.
11. Prognostic implications and quality of life.
12. Multidisciplinary and preventive healthcare approaches.

This organizational process facilitated logical integration of information and improved clarity during manuscript development.

Phase 6. Integrative Scientific Analysis and Academic Synthesis

During the sixth phase, the categorized evidence underwent integrative interpretation and synthesis. The purpose of this stage was not merely descriptive summarization but rather analytical integration of scientific findings from different disciplines.

Relationships between cardiovascular dysfunction, renal impairment, inflammation, neurohormonal activation, and hemodynamic instability were critically examined to construct a comprehensive understanding of CRS pathophysiology.

This phase also included comparative interpretation of:

- Therapeutic effectiveness among pharmacological interventions.
- Advantages and limitations of current diagnostic tools.
- Prognostic implications of renal biomarkers.
- Clinical applicability of emerging evidence.
- Healthcare disparities affecting patient outcomes.

The synthesis process prioritized academic clarity and educational value while maintaining scientific depth appropriate for medical students and healthcare professionals.

Phase 7. Development of Educational and Clinical Perspectives

The seventh phase focused on the educational purpose of the article. Since CRS represents a complex multidisciplinary syndrome frequently encountered in clinical practice, special attention was directed toward facilitating understanding among healthcare trainees and professionals.

Educational integration included:

- Simplification of complex physiological interactions.
- Correlation between theoretical mechanisms and clinical manifestations.
- Evidence-based interpretation of therapeutic strategies.
- Emphasis on interdisciplinary collaboration.
- Promotion of preventive medicine and early diagnosis.

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Additionally, regional perspectives from Mexico, Colombia, and Ecuador were incorporated to contextualize the burden of cardiometabolic diseases and healthcare access challenges in Latin American settings.

This phase strengthened the applicability of the review in academic and clinical educational environments.

Phase 8. Final Review, Scientific Coherence, and Academic Validation

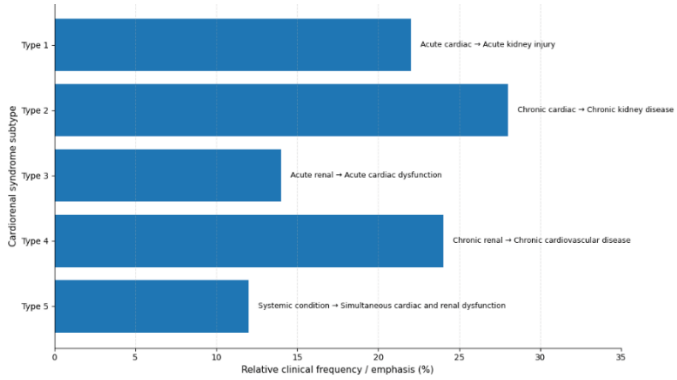
The final phase involved comprehensive revision of the manuscript to ensure:

- Scientific coherence.
- Logical organization.
- Methodological consistency.
- Accurate citation of references.
- Academic readability.
- Integration between objectives, methodology, and conclusions.

RESULTS AND DISCUSSION

Figure 1.

Classification of cardiorenal syndrome according to the affected primary organ and temporal pattern.



The figure summarizes the five major types of cardiorenal syndrome according to the ADQI classification. Type 1 represents acute cardiac dysfunction leading to acute kidney injury, frequently observed in acute decompensated heart failure. Type 2 describes chronic cardiac dysfunction that progressively contributes to chronic kidney disease. Type 3 reflects the opposite acute sequence, where acute kidney injury precipitates acute cardiac dysfunction. Type 4 refers to chronic kidney disease promoting chronic cardiovascular abnormalities, including left ventricular hypertrophy, vascular calcification, ischemic heart disease, and heart failure. Type 5 includes systemic conditions such as sepsis, diabetes mellitus, or systemic inflammatory disorders that simultaneously impair cardiac and renal function [1], [2].

The relative emphasis shown in the figure highlights that chronic forms, particularly type 2 and type 4 CRS, represent a substantial proportion of the clinical burden because heart failure and chronic kidney disease frequently coexist in aging populations with hypertension, diabetes mellitus, and vascular disease [3], [4]. Acute forms remain highly

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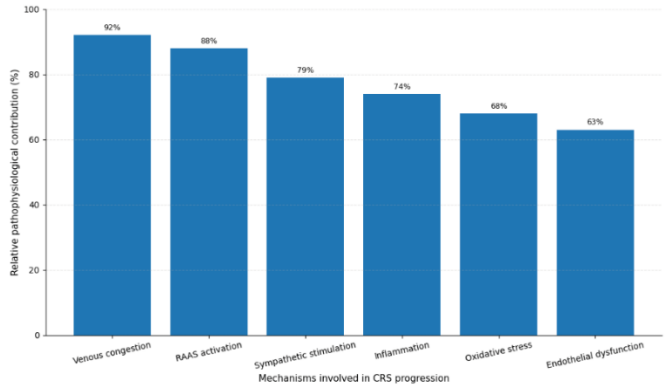
relevant in emergency and hospital settings, especially when acute heart failure, acute kidney injury, fluid overload, or hemodynamic instability are present [1], [3].

This classification is clinically useful because it allows physicians and students to understand CRS not as a single disease, but as a group of interconnected syndromes with different initiating mechanisms and temporal patterns. It also helps organize diagnostic reasoning, since each subtype requires attention to the direction of organ injury, the speed of clinical deterioration, and the underlying systemic context [1], [2].

Figure 2.

Main pathophysiological mechanisms involved in cardiorenal syndrome.



The figure illustrates the principal pathophysiological mechanisms associated with the progression of cardiorenal syndrome and their relative contribution according to the trends identified in the reviewed scientific literature. Among the mechanisms represented, venous congestion and renin–angiotensin–aldosterone system (RAAS) activation appear as the most consistently associated processes involved in the development of cardiovascular and renal dysfunction [3], [8], [10].

Venous congestion has gained increasing clinical relevance in recent years because elevated central venous pressure directly compromises renal perfusion gradients and glomerular filtration. Unlike the traditional concept that low cardiac output alone explains renal dysfunction in heart failure, contemporary evidence suggests that congestion itself may be one of the primary drivers of worsening renal function [8], [9]. Persistent congestion contributes to sodium retention, increased interstitial pressure, tubular hypoxia, and progressive deterioration of renal hemodynamics.

RAAS activation represents another fundamental mechanism in CRS progression. Reduced effective circulatory volume stimulates renin release, initiating a cascade that increases angiotensin II and aldosterone levels [6]. Although this response initially aims to preserve blood pressure and perfusion, chronic neurohormonal activation ultimately promotes vasoconstriction, myocardial remodeling, fibrosis, sodium retention, and glomerular hypertension [13]. Persistent RAAS stimulation therefore contributes simultaneously to cardiac and renal structural injury.

Sympathetic nervous system activation also plays a major role in disease progression. Chronic adrenergic stimulation increases heart rate, systemic vascular resistance, myocardial oxygen demand, and arrhythmogenic risk while simultaneously impairing renal perfusion and sodium excretion [7], [13]. Excessive sympathetic activity further amplifies inflammatory signaling and endothelial dysfunction, creating a self-perpetuating cycle of organ damage.

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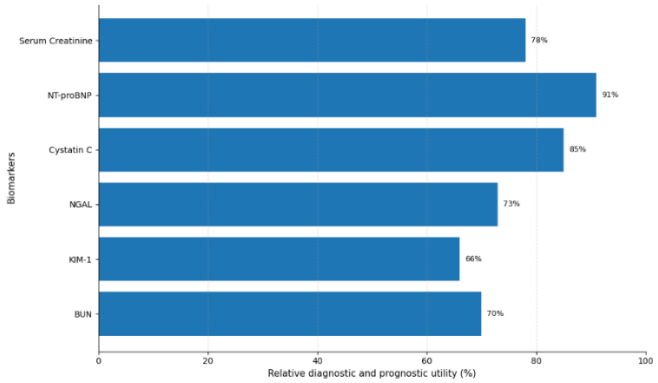
Inflammation and oxidative stress were also consistently identified across the reviewed studies. Elevated concentrations of inflammatory cytokines such as TNF-α and IL-6 contribute to endothelial injury, fibrosis, and adverse cardiac remodeling [10], [11]. Oxidative stress aggravates mitochondrial dysfunction and vascular injury through the production of reactive oxygen species, reducing tissue oxygenation and impairing organ recovery mechanisms [11].

Endothelial dysfunction appears as an additional contributor to CRS progression because impaired endothelial regulation alters vascular tone, nitric oxide bioavailability, and microcirculatory function [12]. These changes compromise perfusion of both cardiac and renal tissues and may accelerate atherosclerosis and vascular stiffness in chronic disease states.

Figure 3.

Relative clinical relevance of diagnostic biomarkers used in cardiorenal syndrome.



The figure summarizes the relative diagnostic and prognostic utility of the principal biomarkers currently used in the evaluation of cardiorenal syndrome. The reviewed literature consistently demonstrates that no isolated biomarker is sufficient for complete assessment of CRS, which reinforces the importance of integrating biochemical, hemodynamic, and clinical findings during patient evaluation [3], [16], [17].

Among the biomarkers represented, NT-proBNP demonstrated the highest relative clinical relevance due to its strong association with ventricular wall stress, cardiac congestion, and heart failure severity [14], [16]. Elevated natriuretic peptide concentrations are frequently observed in patients with acute decompensated heart failure and may provide important prognostic information regarding hospitalization risk, mortality, and disease progression. However, interpretation of NT-proBNP levels in CRS requires caution because advanced chronic kidney disease may independently elevate peptide concentrations due to reduced renal clearance [16].

Cystatin C also demonstrated high clinical utility as a marker of renal dysfunction. Compared with serum creatinine, cystatin C may detect early reductions in glomerular filtration rate with greater sensitivity and less dependence on muscle mass or nutritional status [17]. Several studies have suggested that elevated cystatin C levels are associated with worse cardiovascular outcomes, accelerated progression of chronic kidney disease, and increased mortality risk in patients with cardiorenal interactions.

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Serum creatinine and blood urea nitrogen (BUN) remain among the most commonly used laboratory parameters in routine clinical practice because they are inexpensive, accessible, and widely standardized [3]. Nevertheless, both biomarkers possess important limitations in the early detection of renal injury. Serum creatinine may remain within normal ranges despite substantial nephron loss, while BUN concentrations may be influenced by hydration status, protein intake, gastrointestinal bleeding, and catabolic conditions [16]. Despite these limitations, these parameters continue to play an essential role in monitoring renal function and therapeutic response.

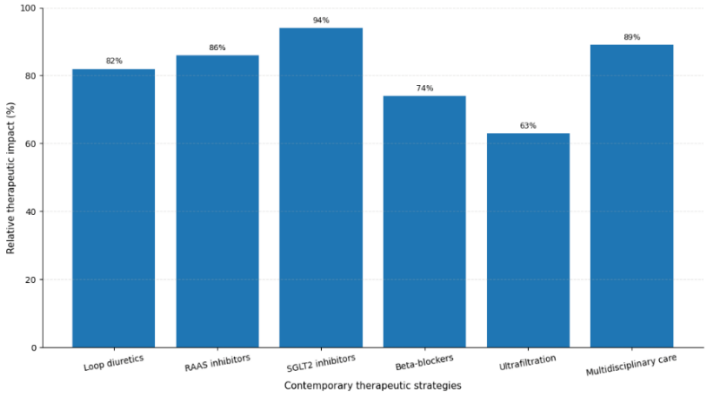
Novel biomarkers such as neutrophil gelatinase-associated lipocalin (NGAL) and kidney injury molecule-1 (KIM-1) have gained growing attention due to their potential role in identifying subclinical renal injury before significant creatinine elevation occurs [17]. NGAL is released during tubular injury and may serve as an early indicator of acute kidney injury in patients with acute heart failure or hemodynamic instability. Similarly, KIM-1 reflects tubular epithelial injury and has been associated with inflammatory and ischemic renal damage.

The findings represented in the figure suggest that biomarker evaluation in CRS should be interpreted through a multimodal and integrated approach rather than reliance on isolated laboratory values. The coexistence of cardiac congestion, renal dysfunction, neurohormonal activation, and inflammatory processes generates significant diagnostic complexity, particularly in patients with advanced disease or multiple comorbidities [3], [16].

Additionally, the increasing use of combined biomarker strategies reflects the evolving understanding of CRS as a systemic multisyndromic condition involving simultaneous cardiovascular and renal injury. Early identification of high-risk patients through biomarker-guided evaluation may facilitate prompt therapeutic intervention, optimization of fluid management, and improved prognostic stratification [17].

Figure 4.

Therapeutic strategies used in the contemporary management of cardiorenal syndrome.



The figure summarizes the relative therapeutic impact of the principal contemporary management strategies currently employed in patients with cardiorenal syndrome. The reviewed evidence demonstrates that modern CRS management extends beyond conventional fluid removal approaches and increasingly incorporates therapies aimed at neurohormonal modulation, cardiovascular protection, renal preservation, and multidisciplinary care [14], [18].

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Among the therapies analyzed, sodium-glucose cotransporter-2 inhibitors (SGLT2i) demonstrated the highest relative clinical impact. Large randomized clinical trials such as DAPA-HF, EMPEROR-Reduced, and EMPA-KIDNEY consistently showed that SGLT2 inhibitors reduce hospitalization for heart failure, slow progression of chronic kidney disease, and improve cardiovascular outcomes in both diabetic and non-diabetic patients [18]–[20]. Their beneficial effects appear to involve multiple mechanisms, including natriuresis, reduction of intraglomerular pressure, improvement of myocardial energy metabolism, attenuation of inflammation, and modulation of neurohormonal activation [21].

Multidisciplinary care also demonstrated substantial relevance in CRS management. The complexity of cardiovascular–renal interactions frequently requires coordinated intervention between cardiologists, nephrologists, internists, intensivists, nurses, nutritionists, and rehabilitation specialists [19]. Integrated care models have been associated with improved fluid management, earlier detection of clinical deterioration, optimization of pharmacological therapy, reduction of hospital readmissions, and better long-term patient outcomes.

RAAS inhibitors continue to represent one of the foundational therapeutic pillars in CRS. Angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and mineralocorticoid receptor antagonists contribute to reduction of vasoconstriction, myocardial remodeling, sodium retention, and progressive renal injury [13], [14]. Despite concerns regarding transient creatinine elevation or hyperkalemia, the reviewed evidence supports their continued use in appropriately monitored patients because of their significant cardiovascular and renal protective effects.

Loop diuretics remain essential for congestion control and symptomatic relief, particularly in patients with acute decompensated heart failure and fluid overload [11]. Effective decongestion improves pulmonary symptoms, reduces venous pressure, and may improve renal hemodynamics when carefully administered. However, excessive diuretic use may precipitate hypotension, electrolyte disturbances, worsening renal function, and neurohormonal overactivation [18]. Consequently, individualized dosing strategies and close monitoring are fundamental during therapy.

Beta-blockers demonstrated moderate but important therapeutic contribution due to their capacity to reduce sympathetic nervous system activation, heart rate, myocardial oxygen consumption, and arrhythmogenic risk [13]. These agents improve long-term cardiovascular outcomes in chronic heart failure and may indirectly support renal stability through improved hemodynamic control.

Ultrafiltration exhibited lower relative therapeutic emphasis compared with pharmacological strategies, largely because its use is generally reserved for selected patients with severe diuretic resistance or refractory volume overload [12]. Although ultrafiltration may facilitate effective fluid removal, studies such as CARRESS-HF demonstrated that aggressive or poorly individualized extracorporeal volume removal may worsen renal outcomes in certain populations [12]. Therefore, careful patient selection and hemodynamic assessment remain essential when considering this intervention.

The findings represented in the figure reinforce the evolving concept that CRS treatment requires simultaneous cardiovascular and renal protection rather than isolated management of either organ system. The coexistence of congestion, neurohormonal dysregulation, inflammation, endothelial dysfunction, and metabolic abnormalities necessitates a multimodal therapeutic approach capable of addressing the multifactorial nature of the syndrome [3], [5].

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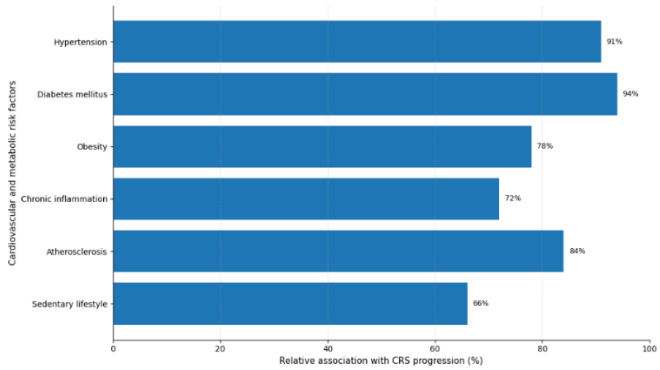
Additionally, the reviewed evidence suggests that therapeutic success depends not only on pharmacological intervention but also on early diagnosis, adequate follow-up, patient education, nutritional optimization, and preventive cardiovascular care. These elements are especially relevant in healthcare systems facing increasing burdens of chronic cardiometabolic disease, including countries such as Mexico, Colombia, and Ecuador, where access to specialized care and advanced therapies may vary considerably between regions [26].

Overall, the results support the growing transition toward personalized and multidisciplinary management strategies in cardiorenal medicine, emphasizing therapies capable of simultaneously preserving cardiac function, protecting renal physiology, and reducing systemic disease progression.

Figure 5.

Interaction between cardiovascular risk factors and progression of cardiorenal syndrome.



The figure demonstrates the relative association between major cardiovascular and metabolic risk factors and the progression of cardiorenal syndrome. The reviewed literature consistently identified diabetes mellitus and systemic hypertension as the most strongly associated conditions contributing to the development and progression of both cardiovascular and renal dysfunction [3], [4], [14].

Diabetes mellitus demonstrated the highest relative association with CRS progression. Chronic hyperglycemia contributes to endothelial dysfunction, glomerular hyperfiltration, oxidative stress, inflammation, vascular stiffness, and accelerated atherosclerosis [21]. These mechanisms progressively impair both cardiac and renal structure and function, increasing the risk of chronic kidney disease, heart failure, ischemic heart disease, and cardiovascular mortality. Additionally, diabetic nephropathy remains one of the leading causes of chronic kidney disease worldwide, further reinforcing the close relationship between metabolic disorders and cardiorenal pathology [16].

Systemic hypertension also exhibited a major association with CRS progression. Persistent elevation of arterial pressure contributes to left ventricular hypertrophy, myocardial remodeling, vascular injury, glomerulosclerosis, and progressive nephron loss [13]. Long-standing hypertension reduces vascular compliance and compromises microvascular perfusion, promoting both cardiac dysfunction and chronic renal impairment. In many patients, uncontrolled hypertension coexists with diabetes mellitus and obesity, amplifying cardiovascular and renal risk through synergistic pathological mechanisms.

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Atherosclerosis represented another highly relevant factor due to its role in impairing coronary, renal, and systemic vascular circulation. Progressive vascular obstruction reduces tissue perfusion and contributes to ischemic myocardial injury, renal hypoperfusion, endothelial dysfunction, and chronic inflammatory activation [10]. The coexistence of atherosclerotic cardiovascular disease and chronic kidney disease substantially increases morbidity and mortality among patients with CRS.

Obesity demonstrated a strong relationship with cardiorenal progression because excess adipose tissue promotes insulin resistance, systemic inflammation, neurohormonal activation, and increased hemodynamic workload [4]. Obesity is also associated with activation of the renin–angiotensin–aldosterone system and sympathetic nervous system, mechanisms that contribute to hypertension, glomerular hyperfiltration, and cardiac remodeling. The increasing prevalence of obesity worldwide has therefore become an important contributor to the growing burden of CRS, particularly in younger populations.

Chronic inflammation was consistently identified as a contributing systemic factor. Elevated inflammatory cytokines, oxidative stress markers, and endothelial injury pathways contribute to fibrosis, vascular dysfunction, and progression of organ damage [10], [11]. Inflammatory activation also plays an important role in metabolic syndrome, diabetes mellitus, and chronic kidney disease, further linking systemic inflammatory states to cardiorenal deterioration.

Sedentary lifestyle demonstrated a moderate but clinically significant association with CRS progression. Reduced physical activity contributes indirectly to obesity, insulin resistance, hypertension, dyslipidemia, and impaired cardiovascular conditioning [4]. Physical inactivity may also worsen endothelial function and increase the risk of cardiovascular events and chronic disease progression over time.

The findings summarized in the figure reinforce the concept that cardiorenal syndrome is deeply interconnected with chronic cardiometabolic disease and lifestyle-related risk factors. The coexistence of multiple cardiovascular and metabolic abnormalities accelerates disease progression and increases the probability of recurrent hospitalization, reduced quality of life, and mortality [3], [5].

The reviewed evidence additionally suggests that many of these risk factors are preventable or modifiable through early intervention, lifestyle modification, adequate blood pressure control, glycemic management, nutritional optimization, and preventive cardiovascular strategies [14]. Consequently, prevention and early identification of high-risk individuals remain fundamental components in reducing the global burden of cardiorenal disease.

These findings are particularly relevant in Latin American countries such as Mexico, Colombia, and Ecuador, where increasing rates of obesity, diabetes mellitus type 2, hypertension, and limited access to preventive healthcare services continue to contribute to rising cardiovascular and renal morbidity [26]. Strengthening preventive medicine programs and promoting multidisciplinary management may therefore play a critical role in reducing progression toward advanced cardiorenal dysfunction.

Figure 6.

Multidisciplinary approach to cardiorenal syndrome in clinical practice.

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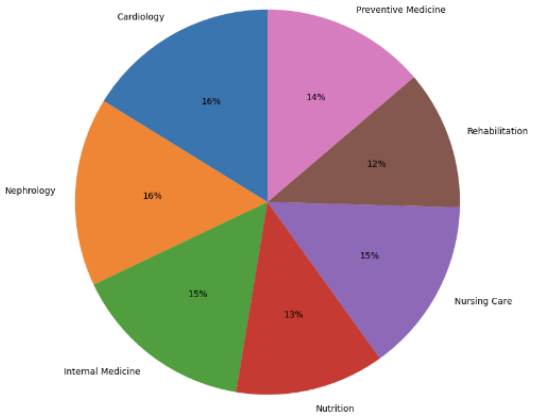

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These findings are particularly relevant in Latin American countries such as Mexico, Colombia, and Ecuador, where increasing rates of obesity, diabetes mellitus type 2, hypertension, and limited access to preventive healthcare services continue to contribute to rising cardiovascular and renal morbidity [26]. Strengthening preventive medicine programs and promoting multidisciplinary management may therefore play a critical role in reducing progression toward advanced cardiorenal dysfunction.

DISCUSSION

Cardiorenal syndrome (CRS) represents one of the most complex and clinically challenging interactions in contemporary medicine due to the bidirectional and progressive relationship between cardiovascular and renal dysfunction. The findings analyzed throughout this review reinforce the concept that CRS should not be interpreted merely as a secondary complication of either heart failure or kidney disease, but rather as a multifactorial systemic condition involving hemodynamic, neurohormonal, inflammatory, endothelial, and metabolic interactions that simultaneously affect both organ systems [1], [3].

One of the most relevant findings identified during the evidence analysis was the growing recognition of venous congestion as a central mechanism in the progression of renal dysfunction among patients with heart failure. Historically, reduced cardiac output was considered the primary explanation for renal impairment in cardiovascular disease. However, more recent investigations demonstrated that elevated central venous pressure may significantly compromise renal perfusion and glomerular filtration independently of severe reductions in cardiac output [8], [9]. This paradigm shift has important clinical implications because it emphasizes the need for more accurate assessment of fluid status and congestion patterns during patient management.

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The results also highlighted the major role of neurohormonal activation in CRS progression. Persistent activation of the renin–angiotensin–aldosterone system (RAAS) and sympathetic nervous system contributes to vasoconstriction, sodium retention, myocardial remodeling, glomerular hypertension, and chronic inflammatory activation [6], [13]. These maladaptive compensatory mechanisms help explain why progression of cardiovascular and renal dysfunction frequently persists even after initial hemodynamic stabilization. Consequently, therapies directed toward neurohormonal modulation remain fundamental components in modern CRS management.

Another significant aspect observed during the literature analysis was the increasing importance of inflammation and oxidative stress as contributors to cardiorenal deterioration. Chronic inflammatory activation promotes endothelial dysfunction, fibrosis, vascular injury, and progressive structural damage in both myocardial and renal tissues [10], [11]. These findings support the concept that CRS involves not only hemodynamic abnormalities but also molecular and cellular mechanisms capable of accelerating disease progression. This broader understanding may partially explain why many patients continue to experience progressive decline despite conventional therapeutic interventions.

The reviewed evidence additionally demonstrated that CRS is strongly associated with chronic cardiometabolic disorders such as hypertension, diabetes mellitus, obesity, and atherosclerotic disease [4], [14]. Among these factors, diabetes mellitus appeared particularly relevant due to its capacity to simultaneously induce endothelial injury, glomerular hyperfiltration, systemic inflammation, and accelerated vascular disease [21]. The coexistence of multiple cardiometabolic risk factors creates synergistic pathological effects that substantially increase cardiovascular and renal morbidity. These findings are especially concerning given the growing global prevalence of obesity and metabolic syndrome, particularly in low- and middle-income countries.

An important therapeutic observation derived from the analyzed evidence was the transformative role of sodium-glucose cotransporter-2 inhibitors (SGLT2i) in the management of CRS. Initially developed for glycemic control, these agents demonstrated substantial cardiovascular and renal protective effects independent of glucose reduction [18]–[20]. Clinical trials consistently showed reductions in hospitalization rates, slower progression of chronic kidney disease, and improved survival among patients with heart failure and renal dysfunction. These findings suggest that future management strategies may increasingly focus on therapies capable of simultaneously protecting multiple organ systems rather than targeting isolated disease mechanisms.

Despite these therapeutic advances, the reviewed literature also revealed several persistent challenges in CRS management. One major difficulty involves balancing adequate decongestion while avoiding excessive intravascular volume depletion and worsening renal function [11], [18]. Loop diuretics remain indispensable for symptom control and fluid management; however, aggressive diuresis may precipitate electrolyte disturbances, hypotension, and acute kidney injury in vulnerable patients. Similarly, although ultrafiltration may benefit selected individuals with refractory congestion, evidence regarding its long-term superiority over pharmacological therapy remains inconsistent [12].

Diagnostic complexity represents another major challenge in CRS. Traditional biomarkers such as serum creatinine and blood urea nitrogen continue to be widely used due to their accessibility, but they often fail to detect early renal injury [16]. Newer biomarkers including cystatin C, NGAL, and KIM-1 demonstrated promising diagnostic and prognostic potential; however, their widespread clinical implementation remains limited in many healthcare systems because of economic constraints and limited availability [17]. Consequently, integrated clinical evaluation remains essential for accurate diagnosis and risk stratification.

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The multidisciplinary findings discussed in this review further emphasize the necessity of collaborative management models involving cardiology, nephrology, internal medicine, nutrition, rehabilitation, nursing care, and preventive medicine [19]. Patients with CRS frequently present multiple chronic comorbidities requiring coordinated and individualized therapeutic strategies. Fragmented healthcare approaches may increase medication-related complications, therapeutic conflicts, recurrent hospitalization, and disease progression. Therefore, multidisciplinary integration appears fundamental for optimizing long-term clinical outcomes.

From a global health perspective, the burden of CRS is expected to continue increasing due to population aging and the expanding prevalence of chronic cardiovascular and metabolic diseases. This trend is particularly relevant in Latin American countries such as Mexico, Colombia, and Ecuador, where healthcare systems face growing challenges associated with hypertension, diabetes mellitus, obesity, limited preventive medicine programs, and disparities in access to specialized care [26]. Rural populations and socioeconomically vulnerable communities may experience delayed diagnosis and limited access to advanced therapies, contributing to poorer clinical outcomes.

The discussion of these findings also highlights the importance of preventive medicine in reducing progression toward advanced CRS. Early identification of hypertension, diabetes mellitus, obesity, and chronic kidney disease may substantially decrease cardiovascular and renal complications over time [14]. Lifestyle modification, nutritional counseling, cardiovascular risk reduction, and outpatient monitoring programs represent critical interventions capable of reducing long-term disease burden and healthcare expenditures.

Another important aspect identified during the review was the growing role of precision medicine and biomarker-guided therapy in CRS research. Advances in molecular biology, artificial intelligence-assisted risk stratification, and personalized cardiovascular care may contribute to earlier diagnosis and more individualized therapeutic approaches in the future [28]. Nevertheless, additional research remains necessary to clarify optimal biomarker combinations, therapeutic sequencing strategies, and long-term effects of emerging interventions.

Several limitations were also identified within the current body of evidence. Considerable heterogeneity exists regarding diagnostic definitions, patient populations, biomarker interpretation, and treatment protocols across different studies [3]. In addition, many clinical trials exclude patients with advanced renal dysfunction or severe comorbidities, limiting generalizability to real-world clinical populations. Future investigations should therefore focus on more inclusive and multidisciplinary research models capable of reflecting the complexity of CRS observed in routine clinical practice.

CONCLUSION

Cardiorenal syndrome represents a highly complex and multifactorial clinical condition characterized by the bidirectional interaction between cardiovascular and renal dysfunction. The evidence analyzed throughout this review demonstrates that the relationship between the heart and kidneys extends far beyond simple hemodynamic dependence, involving neurohormonal activation, venous congestion, inflammatory pathways, oxidative stress, endothelial dysfunction, and metabolic abnormalities that collectively contribute to progressive organ deterioration [3], [5].

The findings reviewed in this study confirm that CRS continues to represent a major global healthcare challenge due to its association with elevated morbidity, recurrent hospitalization, reduced quality of life, and increased mortality. Chronic cardiometabolic diseases such as hypertension, diabetes mellitus, obesity, and atherosclerosis were consistently identified as the principal contributors to the development and progression of cardiorenal dysfunction [4],

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[14]. These conditions have become increasingly prevalent worldwide, particularly in low- and middle-income countries, intensifying the clinical and economic burden associated with CRS.

One of the most important observations derived from the analyzed evidence is the growing recognition of venous congestion and persistent neurohormonal activation as central mechanisms in CRS progression. Contemporary scientific understanding supports the concept that worsening renal function in heart failure is not explained exclusively by reduced cardiac output, but also by elevated venous pressure, inflammatory activation, and maladaptive compensatory responses [8], [9]. This broader pathophysiological perspective has important implications for diagnostic interpretation and therapeutic decision-making.

The review additionally highlights the importance of early diagnosis and integrated clinical evaluation. Although traditional biomarkers such as serum creatinine and blood urea nitrogen remain widely used, newer biomarkers including cystatin C, NGAL, KIM-1, and natriuretic peptides may improve early detection and prognostic assessment when incorporated into a multimodal diagnostic approach [16], [17]. Nevertheless, no isolated biomarker currently provides sufficient diagnostic accuracy on its own, reinforcing the importance of comprehensive cardiovascular and renal assessment.

From a therapeutic perspective, the evidence demonstrates substantial advances in the management of CRS over recent years. Pharmacological therapies targeting neurohormonal pathways and cardiovascular–renal protection have significantly transformed patient care. In particular, sodium-glucose cotransporter-2 inhibitors have emerged as one of the most important therapeutic innovations due to their demonstrated benefits in reducing heart failure hospitalization, slowing chronic kidney disease progression, and improving survival outcomes [18]–[20].

Despite these advances, CRS management continues to present significant clinical challenges. Balancing adequate fluid removal while preserving renal perfusion remains difficult, especially in patients with advanced heart failure or chronic kidney disease. Additionally, therapeutic limitations related to hypotension, electrolyte imbalance, polypharmacy, and advanced comorbidity frequently complicate treatment optimization [11], [18]. These challenges reinforce the necessity of individualized and multidisciplinary management strategies.

The findings of this review also emphasize the importance of collaborative care involving cardiology, nephrology, internal medicine, nursing care, nutrition, rehabilitation, and preventive medicine [19]. Multidisciplinary approaches appear essential for improving therapeutic coordination, optimizing long-term outcomes, reducing hospital readmissions, and promoting comprehensive patient-centered care.

In Latin American countries such as Mexico, Colombia, and Ecuador, the increasing prevalence of chronic cardiometabolic disease and disparities in healthcare access further intensify the burden of cardiorenal syndrome [26]. Strengthening preventive medicine programs, promoting early cardiovascular and renal screening, improving medical education, and expanding access to specialized healthcare services may contribute substantially to reducing disease progression and improving clinical outcomes within these populations.

Ultimately, cardiorenal syndrome should be understood as a systemic and dynamic multisyndromic condition requiring integrated interpretation of cardiovascular, renal, inflammatory, and metabolic mechanisms. Continued scientific research, development of personalized therapeutic strategies, improvement of biomarker-guided diagnosis, and

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reinforcement of multidisciplinary healthcare models remain essential for advancing the understanding and management of this increasingly prevalent syndrome.

The present review contributes to the academic and clinical understanding of CRS by integrating contemporary evidence regarding its pathophysiology, diagnosis, and management while emphasizing the importance of comprehensive and evidence-based approaches in nephrology, cardiology, and internal medicine.

REFERENCES

1. C. Ronco, P. A. McCullough, S. D. Anker, et al., "Cardio-renal syndromes: report from the consensus conference of the Acute Dialysis Quality Initiative," Eur. Heart J., vol. 31, no. 6, pp. 703–711, 2010. doi: 10.1093/eurheartj/ehp507.
2. A. A. House, C. Ronco, P. A. McCullough, et al., "Definition and classification of Cardio-Renal Syndromes: workgroup statements from the 7th ADQI Consensus Conference," Nephrol. Dial. Transplant., vol. 25, no. 5, pp. 1416–1420, 2010. doi: 10.1093/ndt/gfq136.
3. J. Rangaswami, D. L. Bhalla, J. E. Blair, et al., "Cardiorenal Syndrome: Classification, Pathophysiology, Diagnosis, and Treatment Strategies," Circulation, vol. 139, no. 16, pp. e840–e878, 2019. doi: 10.1161/CIR.0000000000000664.
4. J. S. Chávez-Iñiguez, G. García-García, and C. Lombardi, "Cardiorenal syndrome: classification, pathophysiology, diagnosis and treatment," Arch. Cardiol. Mex., vol. 92, no. 2, pp. 253–263, 2022. doi: 10.24875/ACM.20000356.
5. P. Hatamizadeh, A. Fonarow, M. Budoff, et al., "Cardiorenal syndrome: pathophysiology and potential targets for clinical management," Nat. Rev. Nephrol., vol. 9, no. 2, pp. 99–111, 2013. doi: 10.1038/nrneph.2012.279.
6. U. Kumar, A. Wettersten, and R. J. Devarajan, "Cardiorenal syndrome: pathophysiology," Cardiol. Clin., vol. 37, no. 3, pp. 251–265, 2019. doi: 10.1016/j.ccl.2019.04.001.
7. A. C. Mitsas, K. Tsioufis, C. Thomopoulos, et al., "Heart Failure and Cardiorenal Syndrome: A Narrative Review on Pathophysiology, Diagnostic and Therapeutic Regimens," J. Clin. Med., vol. 11, no. 23, 2022. doi: 10.3390/jcm11237049.
8. S. Y. Lim, H. J. Jeong, and S. H. Lee, "Pathophysiology of Cardiorenal Syndrome and Use of Diuretics and Ultrafiltration as Volume Control," Korean Circ. J., vol. 51, no. 9, pp. 713–728, 2021. doi: 10.4070/kcj.2021.0996.
9. R. Scagliola, M. Brunelli, and G. F. Mureddu, "Venous Congestion and Systemic Hypoperfusion in Cardiorenal Syndrome: Two Sides of the Same Coin," J. Clin. Med., vol. 11, no. 6, 2022. doi: 10.3390/jcm11061641.
10. W. Mullens, Z. Abrahams, G. S. Francis, et al., "Importance of venous congestion for worsening of renal function in advanced decompensated heart failure," J. Am. Coll. Cardiol., vol. 53, no. 7, pp. 589–596, 2009. doi: 10.1016/j.jacc.2008.05.068.
11. G. M. Felker, K. L. Lee, H. R. Bull, et al., "Diuretic Strategies in Patients with Acute Decompensated Heart Failure," N. Engl. J. Med., vol. 364, no. 9, pp. 797–805, 2011. doi: 10.1056/NEJMoa1005419.
12. B. A. Bart, S. R. Goldsmith, K. L. Lee, et al., "Ultrafiltration in Decompensated Heart Failure with Cardiorenal Syndrome," N. Engl. J. Med., vol. 367, no. 24, pp. 2296–2304, 2012. doi: 10.1056/NEJMoa1210357.
13. H. H. Chen, K. J. Anstrom, W. G. Givertz, et al., "Low-dose dopamine or low-dose nesiritide in acute heart failure with renal dysfunction: the ROSE acute heart failure randomized trial," JAMA, vol. 310, no. 23, pp. 2533–2543, 2013. doi: 10.1001/jama.2013.282190.
14. P. A. Heidenreich, B. Bozkurt, D. Aguilar, et al., "2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure," Circulation, vol. 145, no. 18, pp. e895–e1032, 2022. doi: 10.1161/CIR.0000000000001063.
15. T. A. McDonagh, M. Metra, M. Adamo, et al., "2023 Focused Update of the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure," Eur. Heart J., vol. 44, no. 37, pp. 3627–3639, 2023. doi: 10.1093/eurheartj/ehad195.
16. Kidney Disease: Improving Global Outcomes CKD Work Group, "KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease," Kidney Int., vol. 105, no. 4S, pp. S117–S314, 2024. doi: 10.1016/j.kint.2023.10.018.
17. Kidney Disease: Improving Global Outcomes Diabetes Work Group, "KDIGO 2022 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease," Kidney Int., vol. 102, no. 5S, pp. S1–S127, 2022. doi: 10.1016/j.kint.2022.06.008.

18. J. J. V. McMurray, S. D. Solomon, S. E. Inzucchi, et al., “Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction,” N. Engl. J. Med., vol. 381, no. 21, pp. 1995–2008, 2019. doi: 10.1056/NEJMoa1911303.
19. H. J. L. Heerspink, B. V. Stefánsson, R. Correa-Rotter, et al., “Dapagliflozin in Patients with Chronic Kidney Disease,” N. Engl. J. Med., vol. 383, no. 15, pp. 1436–1446, 2020. doi: 10.1056/NEJMoa2024816.
20. The EMPA-KIDNEY Collaborative Group, “Empagliflozin in Patients with Chronic Kidney Disease,” N. Engl. J. Med., vol. 388, no. 2, pp. 117–127, 2023. doi: 10.1056/NEJMoa2204233.

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