SAR Journal of Anatomy and Physiology

Abbreviated Key Title: *SAR J Anat Physiol*
Home page: https://sarpublication.com/journal/sarjap/home
DOI: https://doi.org/10.36346/sarjap.2025.v06i01.003

OPEN ACCESS

ISSN 2707-7713 (P)
ISSN 2709-6874 (O)

Review Article

The Relationship between Cardiac Syndrome and Kidney Function: Review Article

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Article History: | Received: 27.12.2024 | Accepted: 01.02.2025 | Published: 07.02.2025 |

Abstract: Cardiac syndrome is a varied condition, both clinically and pathophysiologically, including several pathogenic pathways. The management of this illness poses a significant challenge to the treating physician. Patients frequently want medical attention due to persistent and debilitating chest discomfort, sometimes necessitating recurrent and expensive invasive and non-invasive evaluations. Thoroughly examining the patient to find underlying pathophysiological mechanisms and ruling out other possible causes of chest pain, along with taking into account psychosocial factors, can help reduce the stress and distress these people are feeling. This article examines the existing research on the pathophysiology and ongoing debates over the therapy of this challenging disease.

Keywords: Cardiac syndrome, varied condition, pathophysiologically, kidney function.

INTRODUCTION

The heart and kidney would be regarded as organ that play a very significant role in CV homeostasis. Like cardiac action that pumps blood and oxygen round the body, the kidney takes part in fluid, electrolyte and acid–base balance; form's hemoglobin and also other metabolites. Still more to learn on how heart and kidney work hand in hand to control the hemodynamics stability. Neural and hormone systems including Renin – Angiotensin – Aldosterone controls these kidney functions [1].

In 1803, Richard Bright was able to differentiate scientifically, for the first time, that there is an implication of cardiac and kidney diseases, which he did a hundred years later. Modern tendencies in patient management with health care systems focus on the facts that CVD frequently coexist or develop together with renal dysfunction and vice versa, Because heart and kidneys are paired organs, heart failure and renal failure occur at a more rapid rate if one organ is affected. Due to the high prevalence of the CV and kidney diseases, concepts of CRS categorize heart and kidney as being in acute or chronic failure if an organ undergoes acute or chronic dysfunction the other organ is also involved. Indeed, in a formally clinically appropriate manner it provides an encompassing summary clinically oriented account that has not been addressed clinically or in clinical research [2].

For this reason, while it is clear that renal dysfunctions in CVD are predominantly hemodynamic in origin due to activation of neurohormonal system, clinical aspects of cardiorenal syndromes are much more complex for many reasons. However, their interaction to produce both CV and renal dysfunctions may be attributed to intuitive CV risk factors such as hypertension, DM, obesity, dyslipidemia and smoking as well as non-intuitive CV risk factors such as BMD, inflammation, anemia and malnutrition as reported by Hatamizadeh *et al*., [3].

The relationship between cardiac syndrome and kidney function is recognized as Cardiorenal syndrome the initials CVS and CRF appeared together to form the term CRS because it was known that the CV and renal systems are related for quite some time now. In 1913 Rowntree *et al*., first reported how blood congestion in a dog's kidney affects kidney function [4]. Winton confirmed this finding when he researched the urine

outflow blockage in the tubules during increased intrarenal pressure in 1937 [5]. In 1949, Blake and coworkers3 identified the impact of raising the renal venous pressure on the renal circulation In the year 2004, Working Group of the National Heart, Lung, and Blood Institute attempted to define CRS as follows: Body fluids spread between the heart and kidneys more easily and escalate both heart failure progression and kidney disease severity. In 2008 ADQI made a model structured around primary blood flow changes to define five distinct forms of CRS [6]. Renal failure EMAIL as expected affect Establishing the relationship between the affected heart and kidneys usable clinically regardless of the type of the condition; acute or chronic. In the present analysis of the literature on the current topic, we present a detailed explication of the acute and chronic courses of CRS and how its pathophysiology informs its treatment, holding that the pathophysiological approach is fundamentally crucial to the determination of the optimal therapeutic strategy for the disease.

Definition, Classification, and Epidemiology

ESRD related complications including CVD are significant reasons for mortality contributing to 43.6% of CKD related deaths. Today, approximately one in three adults in the United States have been documented to have CV disease which includes hypertension, ischemic heart disease, or heart failure [7]. Medical tests revealed coronary ischemic disease and left ventricular hypertrophy in 40% and 75% of this ESRD group. New research shows the US adult population now has an estimated 13% CKD rate or 29 million patients. Research shows CVD causes half of CRS patient deaths and affects patients with CRS up to 20 times more than people without CRS in their age group. These conditions were part of the initial definitions we created which highlighted how heart damage increases the risk of renal failure progression. New research helps medical experts understand that when people have CKD their kidneys or hearts start showing harm first. Either organ can fail first in patients experiencing this syndrome because their heart and kidneys fail together regardless of when it happens [7].

CRS in the acute setting

CRS-1 is therefore described by a dramatic decrease on the ability of heart to deliver blood, translating into AKI. Heart failure patients starting treatment need to face acute kidney injury during 23% of their illness. The research found CRS-1 occurred in 25.4% of patients. Percent and renal outcome were categorized by AKI; Thirty-three percent of heart failure patients suffered from chronic kidney problems and his latest ten patients had serum creatinine values above 2.0mg/dl [8]. Reduced cardiac output produces kidney hypoperfusion which WRF studies prove. Research shows this impact works best when treating serious cases of ADHF but does not help most people. ADHF leads to volume overload plus an elevated CVP. High CVP and attendant venous hypertension impair the flow gradient created by glomerular capillary system, and lead to ‘sluggish’ intravascular glomerular kidney function, and reduced urine output. CVP rises have also been proved to be proportional to the renal function improvement [8]. Treatment goals to block RAAS action began because this system influences how renal damage worsens in heart failure patients. Your body activates neurohormonal pathways to boost blood flow in patients who have HF. The kidneys sustain multiple harmful effects under systemic stress but when renin levels rise they create more angiotensin II (Ang II) [8].

Ang II leads to more blood entering the glomerulus and tightens renal efferent arterioles which creates lower hydrostatic pressure during salt transportation while boosting salt absorption in the proximal tubule and boosting the liquid's osmotic strength around the tube. Ang II stimulates the synthesis of endothelin-1 and activates aldosterone production to shift sodium-potassium exchange in distal renal tubular cells. The vasoactive peptide endothelin-1 is recognized for its role in producing damage to kidneys that leads to inflammation and fibrosis .

The body uses various mechanisms including expanded volume plus nerve and blood pressure systems to increase oxidative stress at its start. Serum levels of the biomarkers of oxidative stress were measured in patients with ADHF and AKI; patients with CRS had higher levels of the oxidative stress biomarkers [9]. During HF hospitalization WRF suddenly develops in patients who either start taking RAAS blockers or increase their doses of these drugs while their physician also intensifies their urine removal methods. At the time of admission of ADHF patients, other renal toxic drugs also lead to WRF such as iodinated contrast, NSAIDs and certain antibiotics [9].

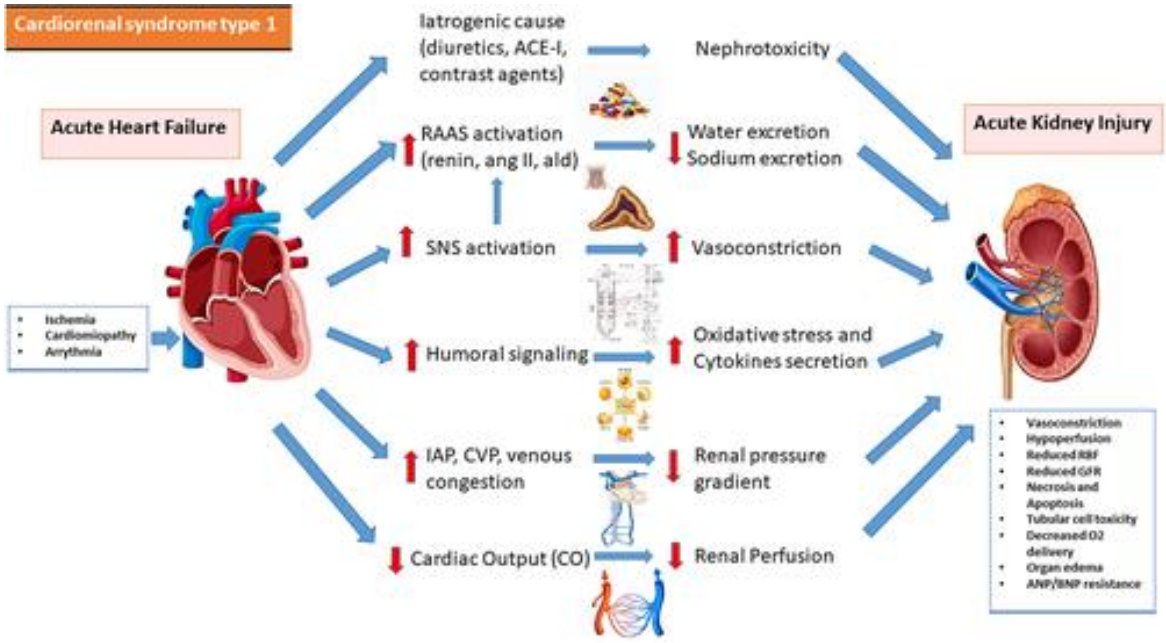

Figure 1: Also provides the summary of the pathophysiology of CRS-1

CRS in the chronic setting

CRS-2 progresses in patients with chronic heart failure to gradually form CKD. Inflammatory diseases CKD and HF generate harmful substances that damage both systems. Organ damage in both processes creates fibrosis and kills cells. Data shows that chronic heart failure patients develop CKD at rates between 20% and 57% throughout the condition [10]. The main health conditions driving CRS-2 are heart diseases such as ischemic heart disease, heart birth defects, atrial fibrillation and both types of heart failure with normal and reduced cardiac efficiency. According to CRS-2 you need to develop chronic kidney disease (CKD) as a result of continuous heart failure issues. An unwanted focus is placed on how long-term inflammation boosts cellular damage beyond its normal capacity. When TNF-alpha and IL-6 boost monocyte chemotactic factor levels they attract more inflammatory cells to the kidney interstitium. The protein TNF-alpha harms glomerulus structures by making mesangial cells destroy themselves through cell death. Medical research links the acute phase protein C-reactive protein to different pathways of atherosclerosis [11]. Erythropoietin deficiency shows up regularly in patients with CKD [12]. Erythropoiesis-stimulating drugs in HF patients with CKD and anemia reduce left ventricular size and volume to enhance the heart. The RED-HF study however uncovered minimal impact on hospitalization or death rates from treatment among HF patients who receive standard medications. Researchers showed darbepoetin alfa treatment raised patients' risk of blood clots [13]. Our research leaves out patients who have severe anaemia levels below 9.0 gram per deciliter. Increasing hemoglobin levels in severe anaemia cases will make the argument stronger. CRS-3 develops rapidly because kidney failure from AKI, ischaemia, or glomerulonephritis damages heart performance. Research shows that AKI raises heart failure risk by 58% (RR 1.58; 95% CI 1.46-1.72) and SCA risk by 40% (RR 1.40; 95 percent CI 1.23-1.59). Additionally, absolute cerebrovascular disease risk rises by 15% [10]. Fluid accumulation brought on by AKI may lead to pulmonary oedema and increased mortality. User: 4 SNS activation may also cause constriction of blood vessels. AKI causes electrolyte homeostasis to become disrupted, especially hyperkalaemia, which increases the risk of arrhythmias. ADHF results from a combination of factors that cause arrhythmia and ischemia impacted by oxidative stress, including an increase in preload and after load, a decrease in contractility, a direct increase in pulmonary vasoconstriction, and an indirect effect.

Therefore, the occurrence of CKD resulting from cardiac dysfunction can be characterised as CRS-4. One of the more recent independent risk factors for CV disease is chronic renal impairment. Approximately 40% of ESRD patients experience ischaemic coronary disease and chronic heart failure equally [8]. CRS-4, which has been linked to renal damage, endothelial cell proliferation inhibition, and worse wound healing that speeds up the course of CKD, was facilitated by RAAS activation and SNS [14]. Cardiorenal fibrosis resulted from PBUTs' worsening of the kidneys' and heart's oxidative stress. A strong risk factor for CV death in individuals with CKD and ESRD, FGF23 is a hormone that plays a role in the kidney's catabolism of phosphorus and vitamin D. In individuals with severe chronic kidney disease, privileged FGF23 levels are associated with longitudinal hypertrophy and mortality [14].

Systemic CRS

Early within 3–7 days of diagnosis, early sub-acute within 7–30 days, fatal beyond 30 days, and immediate within 0–72 hours of diagnosis. Ease simultaneously. Hyperacute, 0–72 hours; acute, 3–7

days; subacute, 7–30 days; and chronic, anything longer than 30 days, are among them. In terms of the disease's progression and severity, CRS-5 can be categorized into four stages: after diagnosis the disease state progresses in four distinct stages: acute (3 to 7 days), subacute (7 to 30 days), chronic (7 to 30 days) while hyperacute develops within the first 72 hours. Conditions linked to the development of CRS-5 include cirrhosis, amyloidosis, sarcoidosis, sepsis, and systemic lupus erythematosus. Research shows septic AKI results from reactive oxygen species and inflammatory proteins active at specific times. The body's inflammatory response including complement factors and cytokines leads to both kidney damage and heart problems and these targets determine which types of CRS will be effective. Abdominal tissues receive reduced blood flow through their blood vessels which may trigger sepsis-related damage and start a damaging cascade of oxidative stress and IL-6 activity [15]. The main causes of AKI in sepsis patients include ischemia and inflammatory mediators: In septic shock patients both endothelial regulation breaks down and the body produces more prostate growth factors like prostacyclin and thromboxane plus IL-1 and tumour necrosis factor.

Biomarkers and Diagnosis

Biomarkers of glomerular function

Based on clinical guidelines creatinine and urea measurements in plasma remain the leading markers for testing eGFR and tracking renal health in patients with heart failure. Doctors use serum urea tests everywhere because they show both the kidney's filtering system and its ability to reabsorb material which depends on hormone and nervous system activities. Organically produced serum creatinine stands as the preferred measurement tool compared to other tests. Potassium movement through the tubule during filtration makes this substance imperfect as a standard filter damage monitor. Doctors use cystatin C testing alongside creatinine measurement because cystatin C only goes through the glomerulus without adding to the urine directly [16]. The toxin detects the glomerulus then passes to the renal tubular epithelial cells for breakdown. The team of Murty examined how early AKI is detected by using blood cystatin-C levels to support their findings. Cystatin-C analysis showed higher blood levels in all patients with AKI compared to controls but serum creatinine increased in half the AKI patients. Cystatin-C shows better results in finding early kidney problems than creatinine testing for patients with Acute Kidney Injury. Studies now show that increased cystatin-C in blood makes CAD patients more likely to experience stroke and nonfatal heart attacks [17]. Numerous formulas are available for determining GFR using creatinine, cystatin C, or both. Serum creatinine levels alone are likely to be sufficient for evaluating several clinical situations. Including cystatin C in certain clinical situations provides additional information about the mortality-CKD risk relationship that cannot be obtained only from creatinine levels. The degree of improved risk discrimination capacity for those reclassified with cystatin C as opposed to creatinine might be measured using net reclassification improvement (NRI), a metric frequently used to assess how well developing biomarkers can perform in prognostication [17].

Biomarkers of tubular function

Scientists have studied multiple different ways to test how well the tubes of the kidney work but doctors disagree on which method to select. Damage to the proximal part of the kidney's filtering unit increases KIM-1 levels both in the blood and urine during ischemic and toxic kidney harm. Akcimic Kidney Injury shows higher KIM-1 plasma levels in patients than people with normal renal health and those without AKI at the end of heart surgery. Similar results were noted in 193 people. In a large CKD 2–4 investigation, the high diagnostic accuracy of NGAL in renal failure was also investigated in HF patients in order to assess the association between high-urine NGAL [18], and the risk of advancing CKD and the advancement of ESRD. Patients with CRS and those without CRS HF were compared. Urinary NGAL's potential as a diagnostic indicator for renal impairment in HF patients is assessed in this study. Compared to HF patients without renal derangement, CRS patients had significantly higher levels of urine NGAL, suggesting that elevated urine NGAL and KIM-1 can predict the onset of WRF in ADHF patients. Realizing that NGAL was an independent predictor of CV events including SCA, aortic dissection, and CV mortality in 252 CKD patients without a history of previous CV events. Tubular function has also been shown by a metric called liver fatty acid binding protein (L-FABP). According to research by Lai *et al*., on ADHF patients with AKI, patients with AKI had greater urine L-FABP concentrations than those without AKI. An analytical biomarker for anticipating the increasing worsening of ERSD and the early indications of CV injury in CKD could be a high urine L-FABP level, according to Matsui *et al*., 2016 [19].

Urinary biomarkers

Tests on urine tubular impairment markers, such as urine sediment and electrolyte, demonstrate tubular function and damage, whereas creatinine clearance, urine creatinine, and albuminuria are effective indicators of glomerular function and podocyte damage. Urinary electrolyte concentration and, more crucially, volume can be used as a functional assessment of tubular function among the measured electrolytes, and this may be quite relevant to heart failure. One of the difficulties with HF is the issue of partial collections; in non-steady state status, plasma creatinine fluctuates slowly and may contain mistakes linked to GFR calculation. HF also deteriorates the natriuretic response early and advances with congestion. Therefore, albuminuria is a reasonable technique for assessing the severity of glomerular involvement. While determining the development of AKI, other tests measuring the almost normal glomerular filtration and its injured tubular function are using

urinary tubular indicators. In addition, the elevation of urinary tubular damage markers does not select those with a poor prognosis HF or patients with poor diuretic effects [20]. As such, the use of these urinary tubular damage biomarkers in patients with HF is somewhat restricted.

Cardiac biomarkers

It was again clearly seen that the TnT levels were significantly elevated in AKI patients after heart surgery (n=100) than the non-AKI patients (n=259). In general, the concentrations of NP can rise because of renal failure, however, they have proved to be natriuretic peptide with confirmed diagnostic and predictive values regarding HF. Natriuretic peptides (NPs) hold significant diagnostic and prognostic value across various types of cardiorenal syndromes (CRS). As noted by Aslam,2020 [21]. NP levels are elevated not only in CRS types 1 and 2 but also in CRS-4. B-type natriuretic peptide (BNP) serves as a key marker for acute heart failure (HF) in patients with chronic kidney disease (CKD). The study aimed to assess whether cardiovascular (CV) events could be predicted using these biomarkers. Elevated plasma concentrations of MR-proANP (midregional pro-atrial natriuretic peptide) and MR-proADM (midregional proadrenomedullin) were associated with a higher incidence of CV events—including sudden cardiac arrest (SCA), aortocoronary bypass surgery, cerebrovascular accidents, and all-cause mortality—in a cohort of 908 patients with acute decompensated heart failure (ADHF) [22]. Additionally, BNP levels were correlated with an increased risk of renal dysfunction, underscoring their role in both cardiovascular and renal prognostication. Consequently, while higher sST2 has been associated with increased cardial mortality, the researchers are still debating the significance of h-galactosidase-binding lectin in CRS. In the study, copeptin percentiles contributed to the higher risks of stroke, sudden death, and all-cause mortality in the hemodialysis individuals [23].

Management Approach

CRS in the acute setting

CRS-1. According to the Cardio-Renal Dysfunction Study Group patients need to have their kidney functions checked frequently during Heart Failure through the CRS-1 system. By examining WRF cases doctors can study what causes WRF as it relates to diuretic therapy and physical state. Full decongestion remains the top sign of hospital readmission so we need to keep working to successfully eliminate fluids from patients who benefit from diuretics [24]. Urine volume measurement, the best dosage, early evaluation of the diuretic response by sodium excretion, and, if necessary, diuretic dose up-titration are all crucial. Additionally, if the diuretic response is inadequate or if functional status in WRF begins to deteriorate in any of the HF participants with decreased EF, (re)evaluation and alternative explanations should be provided. First, conditions like genitourinary obstruction or ascites, which result in elevated intra-abdominal pressure, may be reversible. The 2021 ESC Heart Failure guidelines tell doctors to give vasodilators to patients with self-optimized heart failure who have normal heart rhythms when their SBP stays above 90 mmHg. These guideline standards outline the beginning of heart failure along with its sources and show how diuretic response relates to heart functioning. Patients with diuretic sensitivities need total congestion resolution before discharge because residual bleeding after discharge leads to highest risk of returning to the hospital. Using test results about sodium elimination and urine output helps doctors at first determine the ideal diuretic amount before adjusting it when necessary. All HF patients with reduced ejection fraction must have their RAAS inhibitors reassessed and their settings optimized to get better results. When the diuretic therapy does not work or kidney function degrades physicians need to find different treatment methods. Carefully look for any factors that could be causing these symptoms reversibly such as urinary blockage or increases in abdominal fluid. According to 2021 ESC HF guidelines vasodilators become a preferred treatment option for patients with ADHF and stable blood pressure above 90 mmHg [24]. It is crucial to use the right dosage, assess the diuretic response early using urine volume estimation and sodium excretion, and, if required, increase the dosage of the medication as soon as possible. Additionally, wherever possible, RAAS blocker (re)initiation and up-titration should be investigated in all HF participants with decreased EF. When diuretics do not help patients reach their treatment goals or their condition worsens we need to search for alternative medical reasons. Our test starts by finding out if problems with genitourinary or ascites can reverse the symptoms. Vasodilators work best for patients with acute decompensated heart failure who maintain stable blood pressure above 90 mmHg according to heart failure guidelines published by the European Society of Cardiology in 2021. Patients needing better control of their worsening fluid burden and kidney injury have one clear resolution which is dialysis. When patients with ADHF show decreased diuretic response alongside low blood pressure and decreased circulation they need vasopressor and inotropic treatments plus possible temporary cardiac support. Patients who need CRS-2 therapy receive medication from both ACE inhibitors and ARNIs groups plus MRAs and SGLT2 inhibitors [20]. Initial testing shows SGLT2 inhibitors affect eGFR yet ACE inhibitors and ARBs lead to direct kidney function reduction. SGLT2 transporters enhance sodium reabsorption by interacting with NHE3 which lowers sodium movement through the kidney and occasions reductions in filtrate flow and glomerular filtration rate together with lowered glomerular pressure. Depending on the cause and degree of acute kidney damage (AKI), which can be treated with immunotherapy, resuscitation, or surgery, the treatment is called CRS-3. Loop diuretics and volume overload conditions are required for non-oliguric AKI, and RRT may be required if there is no reversible aetiology of AKI. According to McCallum *et*

al., 2020 [25], loop diuretics increase blood flow to the kidneys by lowering kidney vascular resistance through its action on the sodium-potassium-chloride co-transporter system. Evidence suggests that changes in kidney hydrodynamic conditions may actually cause GFR to decline reversibly. Chronic oxidative stress and chronic inflammation can both be brought on by CKD and CRS-4. Beta-blockers, ACE-I, and ARBs may improve the cardiovascular survival of individuals with impaired renal function. The prospective ability of ARNI therapy to control oxidative stress, apoptosis, fibrosis, and mitochondrial damage makes it cardiorenal protective. In all CKD populations, SGLT2 inhibitors reduce GLP and the consequences of renal and heart failure. "Cardioprotective dialysis," as opposed to conventional haemodialysis, improves haemodynamic stability, decreases inflammation and stress, and lowers tiny and medium-sized toxins. This study demonstrates the efficacy of both high-flux and low-flux hemofiltration in improving blood pressure regulation, reducing the incidence of intradialytic hypotension, and lowering hospitalisation rates.

Systemic CRS

CRS-5. Therapeutic treatments in CRS-5 focus on the management of the basic ailment, renal and cardiac renal impairment, and its consequences. It is advised to treat septic CRS-5 with antibiotics, additional supportive therapies, and the elimination of the infection's source. Doctors must use intravenous fluids in addition to vasopressor or inotropic drugs to treat cardiac muscle depression and wide blood vessel dilation during early intervention [26]. Higher venous return and improved heart function lead to enhanced CO, which may improve renal blood perfusion and urine production. If renal damage persists after haemodynamic and fluid optimisation, RRT is advised.

REFERENCES

1. Deferrari, G., Cipriani, A., & La Porta, E. (2021). Renal dysfunction in cardiovascular diseases and its consequences. *Journal of nephrology*, *34*(1), 137-153.
2. Zoccali, C., Vanholder, R., Massy, Z. A., Ortiz, A., Sarafidis, P., Dekker, F. W., Fliser, D., Fouque, D., Heine, G. H., Jager, K. J., & Kanbay, M. (2017). The systemic nature of CKD. *Nature Reviews Nephrology*, *13*(6), 344-358.
3. Hatamizadeh, P., Fonarow, G. C., Budoff, M. J., Darabian, S., Kovesdy, C. P., & Kalantar-Zadeh, K. (2013). Cardiorenal syndrome: pathophysiology and potential targets for clinical management. *Nature Reviews Nephrology*, *9*(2), 99-111.
4. Makhmusayev, E. J., Sh, N. A., & Ibragimova, N. U. (2024). The Relationship between Chronic Heart Failure and Renal Dysfunction. *European Journal of Modern Medicine and Practice*, *4*(5), 588-595.
5. Tamayo-Gutierrez, A., & Ibrahim, H. N. (2022). The kidney in heart failure: the role of venous congestion. *Methodist DeBakey Cardiovascular Journal*, *18*(4), 4.
6. Rangaswami, J., & Mathew, R. O. (2018). Pathophysiological mechanisms in cardiorenal syndrome. *Advances in chronic kidney disease*, *25*(5), 400-407.
7. Bello, A. K., Okpechi, I. G., Levin, A., Ye, F., Damster, S., Arruebo, S., ... & Zaidi, D. (2024). An update on the global disparities in kidney disease burden and care across world countries and regions. *The Lancet Global Health*, *12*(3), e382-e395.
8. Gallo, G., Lanza, O., & Savoia, C. (2023). New insight in cardiorenal syndrome: from biomarkers to therapy. *International Journal of Molecular Sciences*, *24*(6), 5089.
9. Tasić, D., & Dimitrijević, Z. (2024). The Role of Oxidative Stress as a Mechanism in the Pathogenesis of Acute Heart Failure in Acute Kidney Injury. *Diagnostics*, *14*(18), 2094.
10. Uduman, J. (2018). Epidemiology of cardiorenal syndrome. *Advances in chronic kidney disease*, *25*(5), 391-399.
11. Lee, H., & Jose, P. A. (2021). Coordinated contribution of NADPH oxidase-and mitochondria-derived reactive oxygen species in metabolic syndrome and its implication in renal dysfunction. *Frontiers in Pharmacology*, 12, 670076.
12. Palazzuoli, A., Gallotta, M., Quatrini, I., & Nuti, R. (2010). Natriuretic peptides (BNP and NT-proBNP): measurement and relevance in heart failure. *Vascular health and risk management*, 411-418.
13. Anand, I., & Gupta, P. (2020). How I treat anemia in heart failure. Blood, The Journal of the *American Society of Hematology*, *136*(7), 790-800.
14. Chinnappa, S., Tu, Y. K., Yeh, Y. C., Glorieux, G., Vanholder, R., & Mooney, A. (2018). Association between protein-bound uremic toxins and asymptomatic cardiac dysfunction in patients with chronic kidney disease. *Toxins*, *10*(12), 520.
15. Di Lullo, L., Bellasi, A., Barbera, V., Russo, D., Russo, L., Di Iorio, B., ... & Ronco, C. (2017). Pathophysiology of the cardio-renal syndromes types 1–5: An uptodate. *Indian heart journal*, *69*(2), 255-265.
16. West, M., Kirby, A., Stewart, R. A., Blankenberg, S., Sullivan, D., White, H. D., ... & Tonkin, A. M. (2022). Circulating cystatin C is an independent risk marker for cardiovascular outcomes, development of renal impairment, and long-term mortality in patients with stable coronary heart disease: the LIPID study. *Journal of the American Heart Association*, *11*(5), e020745.
17. Chen, D. C., Shlipak, M. G., Scherzer, R., Bansal, N., Potok, O. A., Rifkin, D. E., ... & Estrella, M. M. (2022). Association of intra-individual differences in estimated GFR by creatinine versus cystatin C with incident heart failure. *American Journal of Kidney Diseases*, *80*(6), 762-772.

18. Yeh, H. M., Lin, T. T., Yeh, C. F., Huang, H. S., Chang, S. N., Lin, J. W., ... & Chu, C. L. (2017). Biomarkers and echocardiography for evaluating the improvement of the ventricular diastolic function after surgical relief of hydronephrosis. *Plos one*, *12*(11), e0188597.
19. Matsui, K., Kamijo-Ikemori, A., Imai, N., Sugaya, T., Yasuda, T., Tatsunami, S., ... & Kimura, K. (2016). Clinical significance of urinary liver-type fatty acid-binding protein as a predictor of ESRD and CVD in patients with CKD. *Clinical and experimental nephrology*, 20, 195-203.
20. Mullens, W., Damman, K., Testani, J. M., Martens, P., Mueller, C., Lassus, J., ... & Coats, A. (2020). Evaluation of kidney function throughout the heart failure trajectory–a position statement from the Heart Failure Association of the European Society of Cardiology. *European journal of heart failure*, *22*(4), 584-603.
21. Aslam, O. (2020). Cardiorenal Syndrome: The Review of Current Understanding. Actual Problems of Nephrology, (26-27), 32-41.
22. Aringazina, A. M., Narmanova, O. Z., Nuskabaeva, G. O., Tagaeva, Z. A., & Mendybaev, E. S. (2020). Chronic kidney disease: Prevalence and risk factors (literature review). *Health risk analysis*, (2), 164-174.
23. Mueller, T., Gegenhuber, A., Leitner, I., Poelz, W., Haltmayer, M., & Dieplinger, B. (2016). Diagnostic and prognostic accuracy of galectin-3 and soluble ST2 for acute heart failure. *Clinica Chimica Acta*, 463, 158-164.
24. Metra, M., Cotter, G., Senger, S., Edwards, C., Cleland, J. G., Ponikowski, P., ... & Davison, B. A. (2018). Prognostic significance of creatinine increases during an acute heart failure admission in patients with and without residual congestion: a post hoc analysis of the PROTECT data. *Circulation: Heart Failure*, *11*(5), e004644.
25. McCallum, W., Tighiouart, H., Testani, J. M., Griffin, M., Konstam, M. A., Udelson, J. E., & Sarnak, M. J. (2020). Acute kidney function declines in the context of decongestion in acute decompensated heart failure. *Heart Failure*, *8*(7), 537-547.
26. Ferrari, C. L. (2022). The Impact Of Early Goal Directed Sepsis Bundle Sets In The Emergency Department And The Impact Of Sep-1 Compliance Rates.