



Original Research Article

INCIDENCE OF CARDIOVASCULAR DISEASE IN PATIENTS WITH CHRONIC KIDNEY DISEASE

Article History:

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Abstract: Chronic kidney disease (CKD) is characterized by the presence of kidney damage or an estimated glomerular filtration rate (eGFR) of less than 60 mL/min/1.73 m², persisting for 3 months or more, irrespective of the cause. CKD has become a significant health issue globally, impacting a considerable segment of the population. It is strongly associated with cardiovascular disease (CVD), as people with CKD are at a heightened risk of cardiovascular incidents, making cardiovascular-related mortality a major concern in advanced stages of CKD. Chronic kidney disease is segmented into five stages, with kidney failure being the most severe. Cardiovascular issues are the predominant causes of mortality among individuals with kidney failure. These patients are at an increased cardiovascular risk, which can present as coronary artery disease, heart failure, arrhythmias, and unexpected cardiac death. This relationship is likely due to several underlying mechanisms, involving shared risk factors (like diabetes and hypertension) as well as additional elements such as inflammation, anaemia, and volume overload. Traditional risk factors associated with cardiovascular disease are relevant in the early phases of CKD. In the intermediate and later stages, non-traditional risk contributors, including iso-osmotic and non-osmotic sodium retention, volume overload, anaemia, inflammation, malnutrition, over activity of the sympathetic nervous system, disorders of mineral bone metabolism, the build-up of so-called 'uremic toxins', and a range of hormonal abnormalities are pivotal in hastening the development of cardiovascular disease in these patients. CKD induces a systemic, chronic inflammatory condition that promotes vascular and myocardial remodelling, leading to atherosclerotic changes, vascular aging, myocardial fibrosis, and calcification of heart valves. In this context, CKD resembles an accelerated aging process of the cardiovascular system. Reducing the risk of CVD in CKD patients requires a collaborative strategy involving cardiologists, nephrologists, and various other healthcare professionals. This article encapsulates the current insights regarding cardiovascular disease in individuals with chronic kidney disease.

Keywords: Chronic kidney disease, cardiovascular disease, glomerular filtration rate, sudden cardiac death, kidney damage.

INTRODUCTION

Chronic Kidney Disease (CKD) has increasingly emerged as a significant global health issue. Various terms such as "chronic renal failure," "pre-dialysis," "chronic renal insufficiency," and "pre-end-stage renal ailment" have been utilized to describe chronic kidney disease (CKD)[1]. Chronic kidney disease (CKD) impacts 15–20% of adults worldwide and heightens the chances of different cardiovascular disease (CVD) complications, such as coronary artery disease, stroke, peripheral artery disease, arrhythmias, and heart failure. Cardiovascular disease (CVD) is considered a primary cause of early death and illness in individuals suffering from chronic kidney disease (CKD) [2]. Richard Bright, a physician from Britain, was the first to report the link between chronic kidney disease (CKD) and cardiovascular disease (CVD) [3]. The widespread influence of chronic kidney disease (CKD) on the cardiovascular system is due to various pathophysiological processes that connect CKD with cardiovascular disease (CVD). In the initial phases of CKD, traditional CVD risk factors have a significant impact. However, as CKD progresses to intermediate and advanced stages, non-traditional risk factors start to take precedence. These factors include iso-osmotic and non-osmotic sodium retention, increased fluid volume, anaemia, inflammation, nutritional deficiencies, over activity of the sympathetic nervous system, disorders of mineral and bone metabolism, accumulation of uremic toxins, and hormonal imbalances, all of which facilitate the rapid advancement of CVD in these individuals [4]. Patients with chronic kidney disease (CKD) experience changes in the myocardium and blood vessels that result in various cardiovascular issues, including cardiomyopathy, atherosclerosis, increased arterial stiffness, calcification, and ultimately ischemic heart disease, heart failure, cerebrovascular and cardiovascular mortality, as well as the worsening of renal function leading to end-stage renal disease (ESRD)[5]. Several novel treatments, including sodium-glucose co-transporter 2 inhibitors, can reduce the risk of cardiovascular disease in individuals with chronic kidney disease. However,

RISK FACTORS FOR CVD IN CKD PATIENTS

In individuals with chronic kidney disease (CKD), both traditional (like hypertension and diabetes) and non-traditional risk factors (such as albuminuria or inflammation) results in remodelling of myocardium and blood vessels.

effectively addressing cardiovascular disease risk in CKD patients necessitates a collaborative approach that includes nephrologists, cardiologists, and various other healthcare providers [6].

METHODOLOGY

1. Objective

Our objective was to be scientifically analyze, synthesize and critically appraise in detail the research from the last 10 years (2015–2025) especially focus on recent literature too on the relation between cardiovascular disease and chronic kidney disease.

2. Study Type

Systematic narrative Review without meta-analysis,

3. Literature Search Strategy

Databases: PubMed, Embase, Web of Science, Scopus

Keywords/MeSH Terms: "Cardiovascular Events", "cardiovascular disease", "Genome-renal complications", "chronic kidney disease", "cardiomyopathies".

Time Frame: January 2015 – July 2025

Language: Limit to articles in English

4. Inclusion Criteria

- Original studies and systematic reviews focusing on relation between cardiovascular disease and chronic kidney disease
- GWAS, large cohort studies, multi-omics investigations, studies reporting risk scoring
- Human studies, clinical trials

5. Exclusion Criteria

- Non-human studies, case reports, editorials, conference abstracts
- Studies not specifically addressing relation between cardiovascular disease and chronic kidney disease

8. Data Synthesis

- Qualitative synthesis of identified risk scores, and mechanisms

Summarize emerging trends, technological advances, and relation between cardiovascular disease and chronic kidney disease.

This change can lead to the onset and advancement of cardiomyopathy, atherosclerosis, arterial stiffness, and calcification. If left untreated, these

changes can advance to ischemic heart disease, heart failure, cerebrovascular disease, worsening

renal function, and ultimately, cardiovascular death. [7]

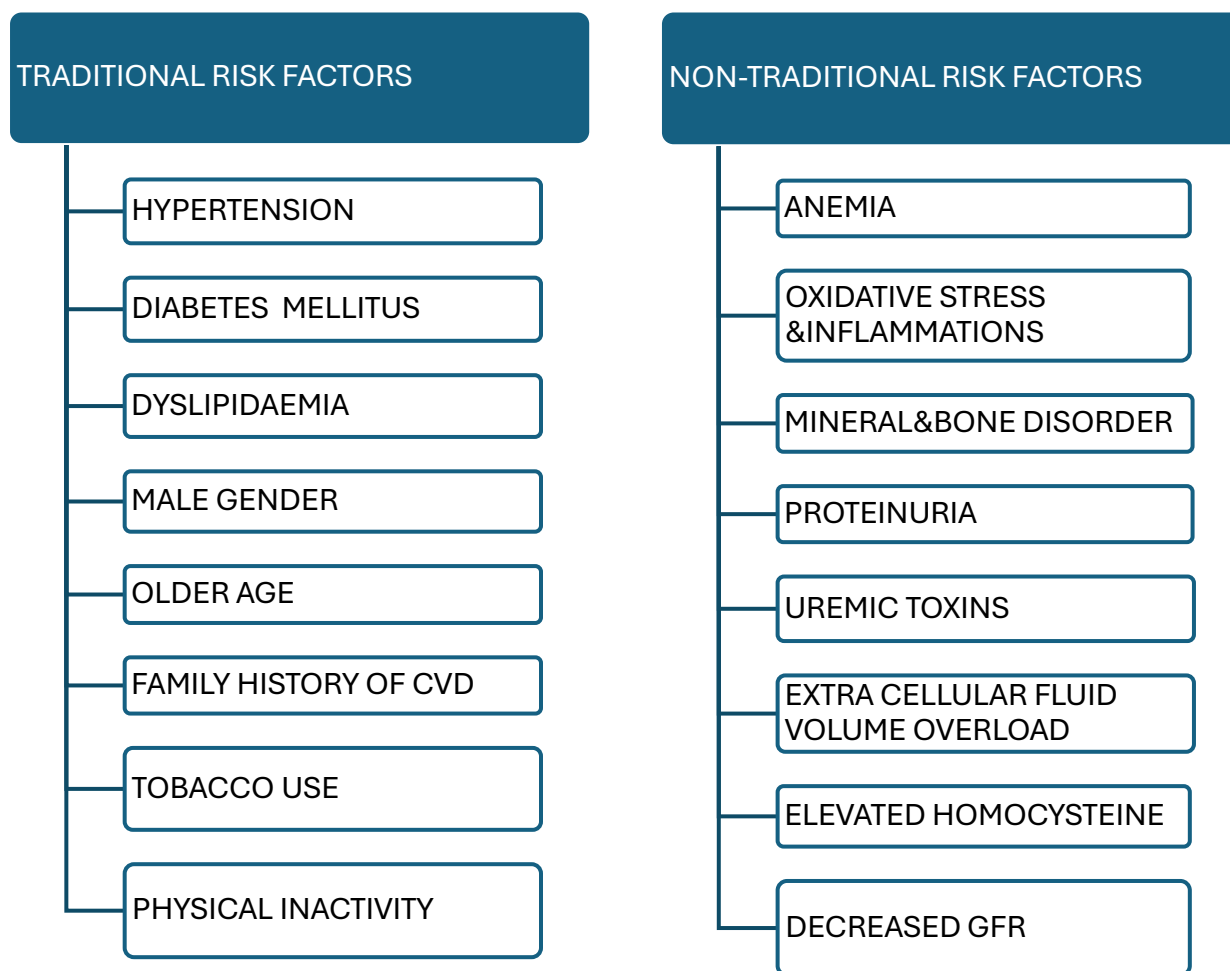


Figure1:traditional &non-traditional risk factors for cvd in ckd .

Race and ethnicity

Young Black adults diagnosed with chronic kidney disease (CKD) presented greater cardiovascular risk factors—such as systolic blood pressure, body mass index, albumin levels in urine, and LDL cholesterol levels—than their white adults. Additionally, these populations demonstrated notably higher incidences of heart failure, overall mortality, and progression of CKD. [8]

Hypertension

Hypertension is a common and significant complication of chronic kidney disease (CKD), influenced by various kidney-related factors.

Increased activity of the renin-angiotensin-aldosterone system (RAAS) leads to higher levels of angiotensin II, a direct vasoconstrictor that elevates blood pressure by narrowing blood vessels, increases vascular resistance, arterial pressure and also enhances, sodium reabsorption in the proximal tubule. [9] Furthermore, the non-osmotic sodium accumulation triggers inflammatory and immune responses, leading to additional rises in blood pressure. A decreased glomerular filtration rate (GFR) results in greater volume and an increase in cardio tonic steroids such as ouabain, which contribute to raise BP by impairing vasodilatory mechanisms. [10]

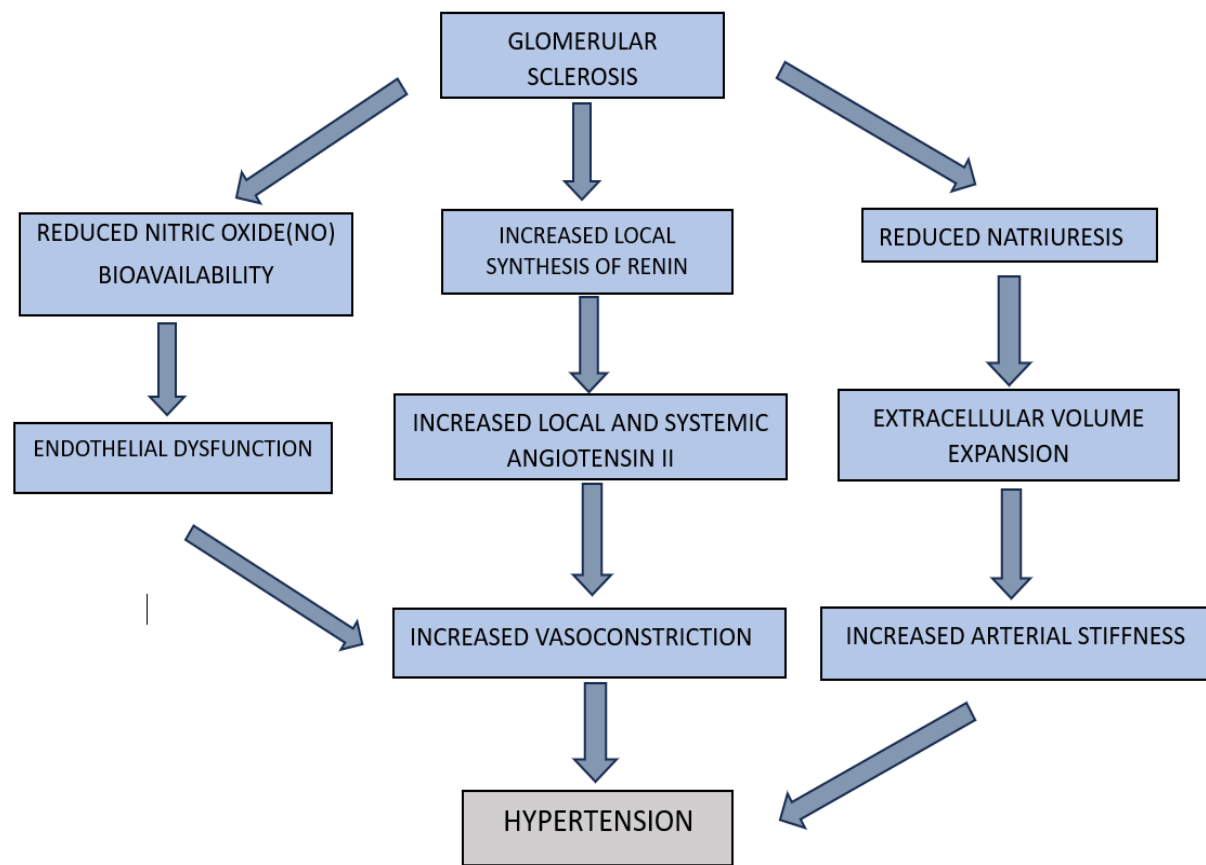


Figure 2: pathophysiological alterations leading to hypertension in CKD .

Obesity & diabetes

Obesity and type 2 diabetes are significant factors contributing to chronic kidney disease (CKD) and elevate the risk of cardiovascular disease (CVD), primarily through inflammatory mechanisms. Persistent high blood sugar levels harm both small and large blood vessels by raising oxidative stress, enhancing glycosylation, and leading to the build-up of glycosylated proteins—these processes stimulate inflammation driven by epigenetic changes. In individuals with CKD, an imbalance between pro-inflammatory (like leptin, resistin, TNF- α , IL-1 β , and IL-6) and anti-inflammatory (such as adiponectin and IL-10) adipokines contributes to both heart and kidney damage [11]. Clinical trials using monoclonal antibodies that target IL-1 β and IL-6 have shown these cytokines play a key role in atherosclerosis and related conditions. Furthermore, inflammation driven by gut microbiota contributes to this risk in cases of obesity and diabetes. These interconnected

processes closely associate diabetes, CKD, and systemic inflammation with an increased risk of cardiovascular events, particularly in patients with diabetic kidney disease[12].

Dyslipidaemia

Changes in lipoprotein metabolism occur in chronic kidney disease (CKD). The liver produces very low-density lipoprotein (VLDL), which is rich in triglycerides. Triglycerides are broken down by lipoprotein lipase (LPL), leading to the transformation of VLDL particles into intermediate-density lipoprotein (IDL) particles, and eventually low-density lipoprotein (LDL) cholesterol particles. LDL particles transport cholesterol to both the liver and various tissues in the body. The process of reverse cholesterol transport, which is facilitated by HDL cholesterol, is dysfunctional in this condition. In CKD patients, both HDL and LDL undergo modifications that increase their potential to promote atherosclerosis [13].

Extracellular volume expansion

The expansion of extracellular volume can lead to volume overload, which results in significant negative consequences such as left ventricular hypertrophy (LVH), hypertension, and heart failure (HF), becoming more prevalent from stage 3 to stage 5 CKD. In individuals undergoing dialysis, volume overload increases the risk of death by twofold, regardless of hypertension and other contributing factors. In patients with chronic kidney disease (CKD), a high intake of sodium and resultant volume expansion are directly and independently associated with a higher risk of cardiovascular disease and mortality[14].

Sympathetic over activity

In CKD, persistent sympathetic over activity driven by signals from diseased kidneys and comorbidities like sleep apnoea, heart failure, and obesity causes increased heart stress. This heightened sympathetic tone leads to left ventricular hypertrophy (LVH), structural heart changes, and arrhythmias, all of which significantly increase the risk of cardiovascular disease and death, especially in dialysis patients [15].

Anaemia

Macrocytic anaemia may act as an individual cardiovascular risk factor for patients with chronic kidney disease (CKD) and can lead to cardiovascular events [14]. Anaemia increases the heart's workload to compensate for lower oxygen availability, resulting in left ventricular hypertrophy (LVH), changes in arterial structure, and the thickening of the intima-media layer, along with arteriosclerosis [16]. In chronic kidney disease (CKD), reduced erythropoietin (EPO) production causes anaemia, which decreases oxygen supply to various tissues, including the heart. Although intravenous iron dextran is utilized to address anaemia, it may generate oxygen-derived free radicals that can harm coronary arteries and worsen atherosclerosis [17].

Metabolic acidosis

In CKD, impaired kidney function leads to reduced ammonia production, poor proton secretion, and decreased bicarbonate reabsorption, resulting in

metabolic acidosis (low plasma bicarbonate). As CKD progresses, the prevalence of acidosis increases significantly. Metabolic acidosis contributes to cardiovascular disease by promoting myocardial injury and inflammation, left ventricular dysfunction, increased risk of heart failure, stroke, myocardial infarction, and cardiovascular death. Thus, metabolic acidosis in CKD patients is a key contributor to increased cardiovascular morbidity and mortality [18].

Mineral bone disorder

In CKD, impaired phosphate excretion triggers hormonal changes, including elevated FGF23 and PTH levels. These changes lead to reduced vitamin D activation, causing low calcium absorption and hypocalcaemia, increased PTH secretion (secondary hyperparathyroidism), disturbances in calcium, phosphate, PTH, and FGF23 level. These abnormalities contribute to vascular calcification, left ventricular hypertrophy, and arterial stiffness, significantly increasing the risk of cardiovascular events and death in CKD and dialysis patients[19].

Sedentary lifestyle, scarce physical exercise

In CKD and dialysis patients, limited physical activity is common due to high comorbidity. A sedentary lifestyle independently increases the risk of cardiovascular disease (CVD) and death, regardless of other risk factors. Physical inactivity contributes to poor cardiovascular fitness, worsening metabolic health, increased inflammation and arterial stiffness. This leads to a higher incidence of CV events and mortality in the CKD population[20].

Uremic toxins and endocrine alterations

In CKD, impaired kidney function leads to the accumulation of uremic toxins (e.g., ADMA, beta-2 macroglobulin, indoxyl sulphate, para-cresyl sulphate) and disruptions in endocrine balance. These changes result in endothelial dysfunction, vascular damage, systemic inflammation and oxidative stress. These harmful effects promote atherosclerosis, vascular stiffness, and cardiac remodelling, significantly increasing the risk of cardiovascular disease and mortality in CKD patients [21].

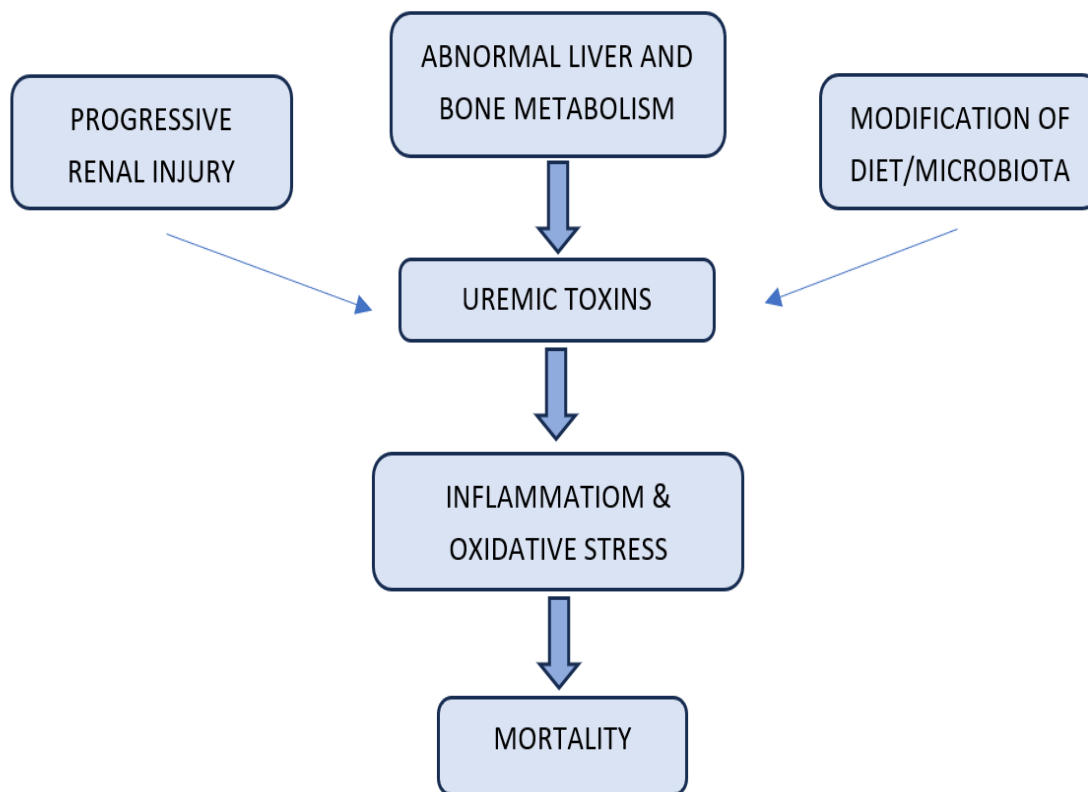


Figure 3:relationship between uremic toxins, inflammation& oxidative stress impinging upon cardiovascular risk in CKD.

Inflammation and malnutrition

Chronic low-grade inflammation is common in CKD and in dialysis patients. Markers of inflammation, including C-reactive protein (CRP), IL-6, and TNF- α , are found to be elevated in CKD and are closely associated with microalbuminuria, which indicates vascular damage and as an active participant in atherosclerosis by contributing to the initiation, development, and rupture of plaques [22]. Inflammation interferes with regular lipid metabolism, encourages vascular calcification, and increases oxidative stress all of which accelerate arterial damage. These combined mechanisms create a pro-atherogenic scenario that greatly elevates the risk of cardiovascular incidents and mortality among patients with chronic

kidney disease (CKD) [23]. This inflammatory milieu fosters endothelial dysfunction, increases oxidative stress, and leads to insulin resistance, all of which hasten the process of atherogenesis [24].

Acute kidney injury

Acute Kidney Injury (AKI) significantly increases cardiovascular risk, even independently of chronic kidney disease (CKD). AKI is associated with 86% increased risk of cardiovascular (CV) death and 38% increased risk of major CV events. In CKD patients, episodes of AKI worsen kidney function, promote inflammation, endothelial dysfunction, and fluid imbalance, all of which contribute to a higher likelihood of heart failure, myocardial infarction, and CV mortality [25].

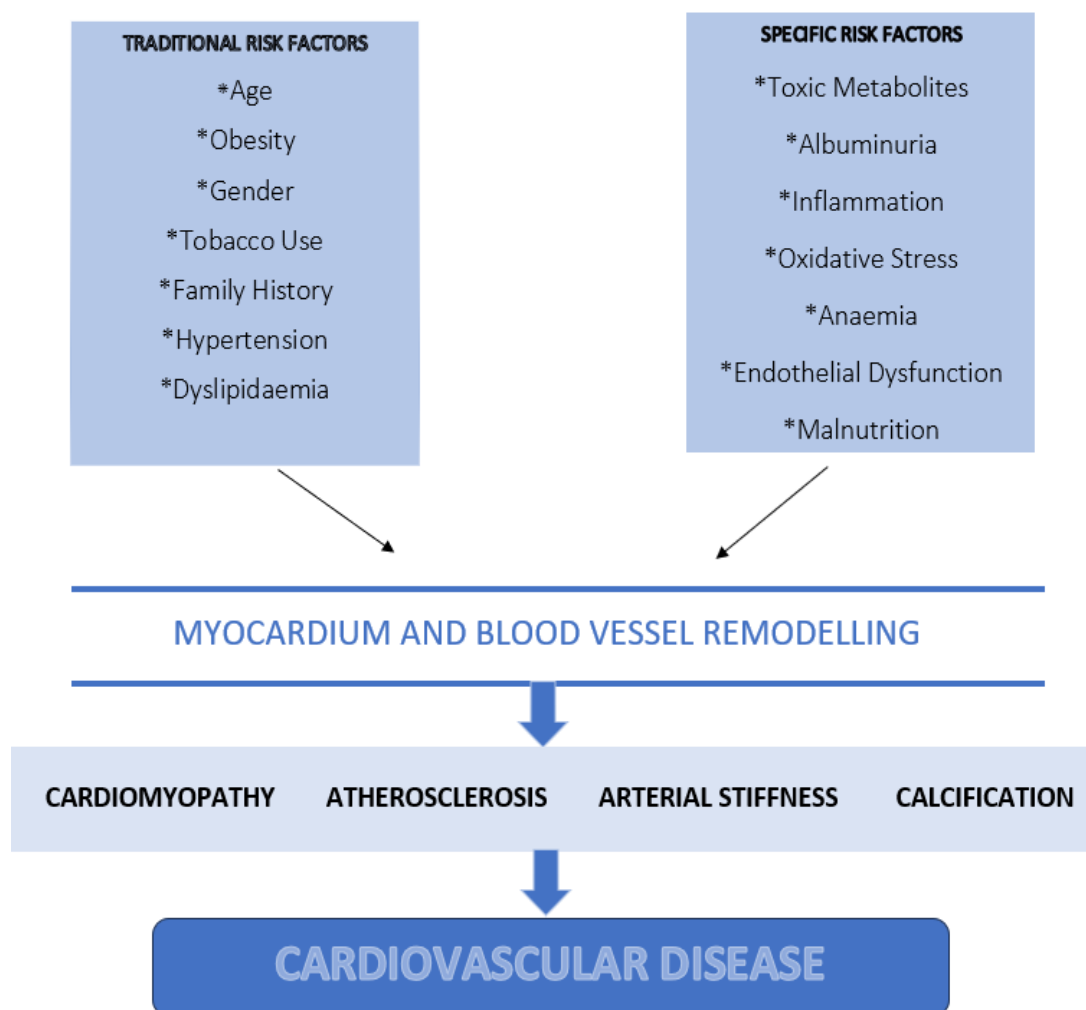


Figure 4: Risk factors for cardiovascular morbidity and mortality in patients with chronic kidney disease (CKD)

PATHOPHYSIOLOGY OF CVD IN CKD

Generally, alongside traditional risk factors, two primary mechanisms are believed to play a role in the onset of cardiovascular disease (CVD) in chronic kidney disease (CKD). Firstly, the kidneys

can produce hormones, enzymes, and cytokines in response to kidney damage or function loss, resulting in specific changes within the blood vessels. Secondly, mediators linked to CKD, along with alterations in hemodynamic, contribute to cardiac injury [26].

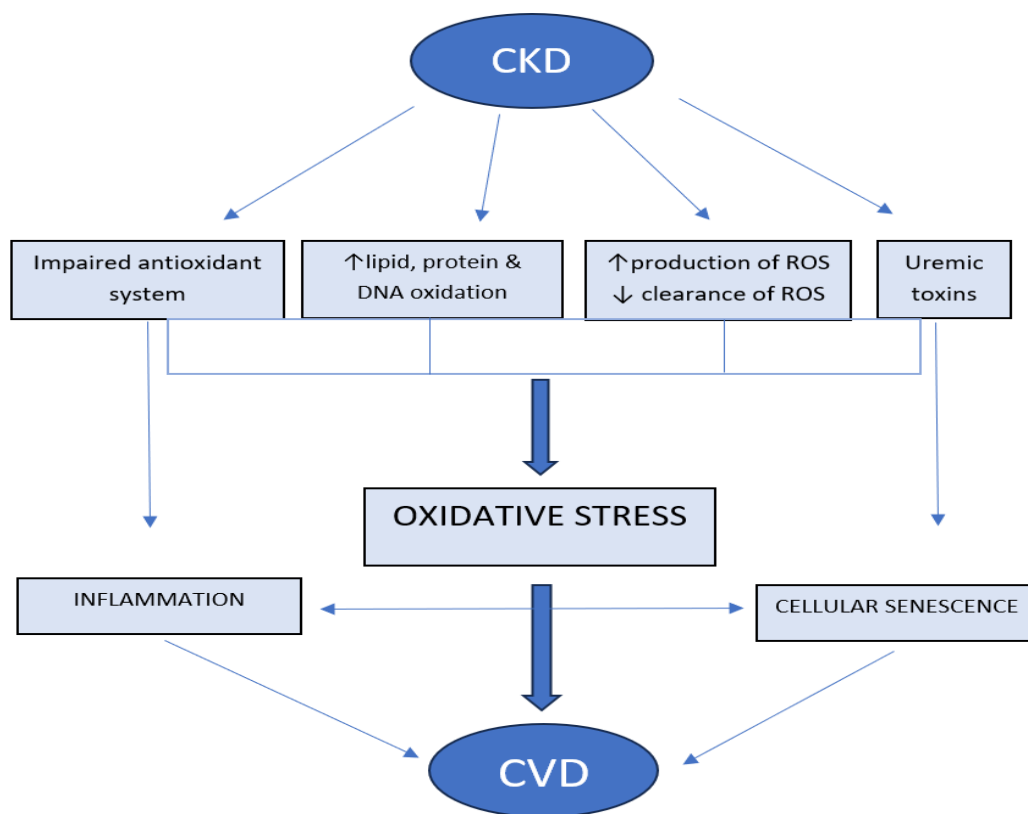


Figure 5: Relationship between oxidative stress and CKD-associated cardiovascular disease

CKD leads to increased damage of biomolecules (such as lipids, proteins, and DNA), impairment of the antioxidant system, increased levels of reactive oxygen species (ROS), decreased ROS clearance, and high concentration of uremic toxins in circulation. This process increases the levels of oxidative stress. CKD is also associated with systemic inflammation, mitochondrial dysfunction, loss of proteostasis, altered intercellular communication, and cellular senescence. Combined, these factors contribute to increased levels of oxidative stress in this patient population. However, cellular senescence and inflammation also participate in the development and progression of CVD [27].

DIAGNOSIS OF CVD IN CKD

CKD is classified according to glomerular filtration rate (GFR) and the degree of albuminuria. Even in cases where eGFR is normal (≥ 60 mL/min/1.73 m²), the existence of albuminuria or other kidney issues may signify CKD. Albuminuria serves not only as an initial sign of nephropathy but also represents a significant and independent risk factor for cardiovascular disease (CVD) and overall mortality. The assessment of the urinary albumin-to-creatinine ratio (UACR) is useful for pinpointing individuals at higher cardiovascular risk, independent of their kidney function [28].

OXIDATIVE STRESS BIOMARKERS	•Malondialdehyde •Asymmetric dimethylargine •Glycolysis end products
CARDIOSPECIFIC BIOMARKERS	•Tropinin •H-FABP
BIOMARKERS OF MINERAL METABOLISM DISORDERS	•Osteoprotegerin •Fetuin-A •Fibroblast growth factor-23 •Vitamin D/parathyroid hormone
NEUROHORMONES	•Natriuretic peptides •Endothelin •Arginine vasopressin
BIOMARKERS OF ACUTE KIDNEY INJURY	•KIM-I(kidney injury molecule-1) •NGAL(neutrophil gelatinase – associated lipocalin)
INFLAMMATION BIOMARKERS	•C-reactive protein •IL-6,IL-8,IL-18 •Pentraxin-3
METABOLIC HORMONES	•Adiponectin •Leptin •Cortisol
BIOMARKERS ASSOCIATED WITH THE MATRIX	•Galectin 3 •Matrix metalloproteinase •ST 2

Figure 6:Biomarkers of cardiovascular disease in chronic kidney disease.[8]

Cardiac biomarkers that are typically utilized in the general population tend to be less accurate for individuals with chronic kidney disease (CKD). Increased levels of markers such as troponins can happen in the absence of myocardial tissue damage, likely due to silent micro infarctions and myocardial apoptosis rather than impaired clearance [29].

CKD and related variables such as eGFR and albuminuria are rarely included in CVD risk prediction tools, limiting their use for stratification, investigation and management of these patients.

Cardiac biomarkers such as troponins and N-terminal pro B-type natriuretic peptide are frequently raised in CKD, limiting their specificity for cardiac abnormality [30].

Electrocardiography (ECG)

Widely available but low specificity used to detect Left ventricular hypertrophy (LVH), Arrhythmias, Ischemic changes, Bundle branch blocks

Echocardiography

Low cost and accessible.2D Transthoracic echocardiogram (TTE) measures LV mass index, wall motion, valve disease.

Exercise testing

Low utility due to limited exercise tolerance.

Cardiac MRI

Excellent for evaluating myocardial fibrosis and myocardial scars.stress MRI is highly sensitive(100%)and specific(90%) for 70%stenosis. Use with caution in patients with eGFR <30 ml/min/1.73m².

Coronary CT Angiography

High accuracy in general population. Limited in advanced CKD due to contrast use and heavy coronary calcification.not always compared with gold standards.

Single photon emission CT(SPECT)

Reduced sensitivity in CKD due to baseline vasodilation and anti-anginas.High negative predictive value.

Dobutamine stress echo (DSE)

Useful for prognosis. Reduced sensitivity and PPV due to LVH and submaximal HR.

Stress thallium scintigraphy

More sensitive(62%), but less specific than DSE(76%)

Myocardial perfusion scintigraphy

Better in CKD patients with hypertension or arrhythmias. Useful in identifying ischemia and risk stratifications [31].

Pharmacological stress echocardiography and nuclear myocardial perfusion scans are more widely available and are not subject to the same risk profiles, however they provide a lower sensitivity and specificity when compared to the gold standard tools, and when used in non-CKDpatients [32].

MANAGEMENT OF CVD IN CKD PATIENTS

The management of chronic kidney disease (CKD) and its associated cardiovascular issues relies heavily on lifestyle changes such as a balanced diet, regular physical activity, maintaining a healthy weight, quitting smoking, and moderating alcohol consumption to enhance overall well-being and slow the progression of the disease. Prompt intervention, particularly when albuminuria is present, is crucial as it indicates an increased risk for both cardiovascular and renal issues. Nutritional approaches, including lower protein consumption, minimized acid load, and salt reduction, are advantageous for the health of both the kidneys and the heart [33]. Cardiovascular management involves strict control of blood pressure, utilization of renin-angiotensin-aldosterone system (RAAS) inhibitors, and a cautious approach to invasive tests. The treatment of heart failure generally includes ACE inhibitors and β -blockers, although evidence in patients with advanced CKD is limited. Even with a significantly higher cardiovascular risk, patients with CKD frequently receive inadequate treatment, which contributes to a rise in mortality rates [34].

Pharmacological Interventions for Cardiovascular Disease (CVD) in chronic kidney disease (CKD)

SL NO	CATEGORY	AGENTS	DOSE	KEY NOTES
1	DIABETES MELLITUS& HYPERTENSION MANAGEMENT	ACE INHIBITORS: Captopril Ramipril	25-50mg 2-3 times daily 5-10 mg once daily	Cardioprotective effects, ↓proteinuria,BP
		ARB BLOCKERS: Losartan Valsartan	100 mg once daily 160-320 mg once daily	↓proteinuria, BP, CV events
		β -BLOCKER Carvedilol	25-50 mg twice daily	↑left ventricular function
2	LIPID MANAGEMENT	STATINS: Atorvastatin Pravastatin	10-80 mg once daily 10-40 mg once daily	↓LDL, stabilize atherosclerotic plaques.
3	ANTIPLATELET AGENTS	Aspirin clopidogrel	75-100mg once daily 75 mg once daily	1 st line for CVprevention P2Y12 inhibitor

4	PHOSPHATE BINDER	CaCO ₃ Al(OH) ₃	500-1500mgwith meals tid 300-600mg with meals	↓LVH&arterial stiffness
5	CALCIMIMETICS	Cinacalcet Etelcalcetide	30 mg once daily 5mg 3 times/week	Supress PTH, ↓PO ₄ ²⁻ &Ca ²⁺
6	VITAMIN-D &ANALOGUES	Calcitriol paricalcitol	0.25-0.5mcg/day 1-2mcg/day	Improves cardiac remodeling
7	VITAMIN K	Phylloquinone(vit-k1) Menaquinon7 (vit-k2)	0.5-1 mg daily 90-360 mcg daily	Inhibit vascular calcification
8	MAGNESIUM	MgO MgCO ₃	250-400 mg/day 100-360 mg/day	Reduce arterial stiffness
9	RENAL REPLACEMENT THERAPY	Haemodialysis	3times/week	Remove fluid overload
		Kidney transplantation	One time surgery+ lifelong medicines (tacrolimus, prednisone)	Restore endocrine fluid&BP balance

NOVEL PHARMACOLOGICAL THERAPEUTIC APPROACHES IN CKD AND CVD

The novel treatments, particularly SGLT2 inhibitors, finerenone, SIRT1, and SNF472, signify significant advancements in the treatment of cardiovascular disease (CVD) in chronic kidney disease (CKD). They provide protective benefits that extend beyond just managing glucose levels or fluid volume, addressing various underlying pathophysiological processes.[35]

SGLT2 Inhibitors (Sodium-Glucose Cotransporter-2 Inhibitors)

Originally developed for managing Type 2 diabetes mellitus (T2DM), it is now recognized for its cardiovascular and renal protective effects, even in non-diabetic chronic kidney disease (CKD). The advantages of SGLT2 inhibitors include decreasing glomerular hyperfiltration by reducing intraglomerular pressure. They also help regulate sodium reabsorption in the kidneys, which results in Lowered blood pressure, decreased albuminuria, and reduced interstitial volume (without significantly impacting intravascular volume, unlike traditional diuretics). This approach limits the neurohumoral activation typically associated with diuretics. Furthermore, it enhances myocardial metabolism while decreasing oxidative stress and inflammation[36].

Finerenone – A Selective Nonsteroidal MRA

Mechanism of Action: Inhibits mineralocorticoid receptors (MRs), primarily those stimulated by

aldosterone. In contrast to older medications (spironolactone, eplerenone), finerenone penetrate evenly in both heart and kidney tissues, alters various amino acids at the MR ligand binding site, and results in distinct gene expression that reducing cardiac fibrosis and inflammation [37].

The silent information regulator sirtuin 1 (SIRT1)

SIRT1, a NAD⁺-dependent deacetylase, may serve a protective function in chronic kidney disease (CKD) and its effects on the cardiovascular system by regulating fibrosis, apoptosis, senescence, oxidative stress, inflammation, vascular calcification (VC), and the aging process. It could be considered a promising target for managing cardiovascular disease (CVD) in CKD, as it inhibits the osteoblastic trans differentiation of vascular smooth muscle cells (VSMCs) stimulated by hyperphosphatemia[38].

SNF472: myo-inositol hexaphosphate

SNF472, a hexasodium derivative of the active substance myo-inositol hexaphosphate (IP6) or phytate, has demonstrated promising advantages in experimental studies. By binding to the growth sites of hydroxyapatite crystals, SNF472 inhibits the initiation and progression of calcification. This mechanism seems to operate independently of the primary cause of calcification and may provide an opportunity to interrupt the final common pathway of vascular calcification (VC)[39].

NON-PHARMACOLOGICAL TREATMENTS FOR CVD IN CKD PATIENTS

Non-pharmacological management encompasses treatments that exclude the use of medicines, focusing on addressing intricate health needs and enhancing overall wellness. These approaches

consist of Nutritional adjustments, Exercise and physical activity, Changes in lifestyle habits, Cognitive Behavioural Therapy (CBT) – advantageous for mental health[40].



Figure 7: non-pharmacological interventions of CVD in CKD[12]

Embracing healthy lifestyle habits greatly diminishes cardiovascular risk for individuals with chronic kidney disease (CKD). Essential suggestions include quitting smoking, engaging in regular exercise, and achieving a healthy weight—much like the general population[41]. Following a low-protein diet aids in decreasing proteinuria and slows the progression of CKD, while limiting sodium intake helps manage fluid overload and high blood pressure, enhancing cardiovascular health. In advanced CKD cases, where there is a risk of hyperkalaemia, potassium restriction is recommended. Otherwise, a diet abundant in fruits

and vegetables is encouraged. Stress reduction and mental health support can improve adherence and reduce CVD risk. Achieving and maintaining healthy weight helps control blood pressure, diabetes, and lipid abnormalities, reducing CVD risk. Dietary sodium restriction combined with fluid management helps reduce volume overload, which stresses the heart. Smoking Cessation IS Essential to reduce CVD risk, as smoking accelerates vascular damage and CKD progression. Dietary Modifications such as Sodium restriction helps to control hypertension, reducing cardiovascular risk. Moderate protein restriction

may slow CKD progression and reduce cardiovascular burden. Regular moderate aerobic exercise improves cardiovascular fitness, reduces blood pressure, and improves endothelial function[42]

NOVEL NON-PHARMACOLOGICAL THERAPEUTIC APPROACHES IN CKD AND CVD

Various innovative non-drug therapies demonstrate potential for enhancing the quality of life for individuals with chronic kidney disease (CKD), particularly those receiving dialysis:

- Using cooler dialysate can help alleviate issues like intradialytic hypotension, fatigue, ischemic damage, cardiovascular mortality, and restless leg syndrome, while also improving sleep quality and everyday functioning.
- Neuromuscular electrical stimulation (NMES) has the ability to boost muscle strength, functional capacity, and overall quality of life, making it particularly beneficial during acute flare-ups when exercise isn't feasible.
- Nature-based interventions (NBIs) could have positive effects on both psychological and physical health for individuals with long-term conditions (LTCs), although evidence concerning CKD remains sparse.
- Art therapy has been found to positively impact mental health, motivation, self-esteem, and the overall dialysis experience. The Renal Arts Group in the United Kingdom has developed guidelines for incorporating artistic activities into dialysis sessions.[43]

CONCLUSION

The association between CKD and CVD has been extensively documented in the literature. It is well recognized that patients with CKD are a group at high risk for developing CVD and cardiovascular events. Both CKD and CVD share common traditional risk factors, such as smoking, obesity, hypertension, diabetes mellitus, and dyslipidaemia. However, cardiovascular disease remains often underdiagnosed and undertreated in patients with CKD. Chronic kidney disease even in its early stages can cause hypertension and potentiate the risk for cardiovascular disease. Various studies have demonstrated that low eGFR and increased albuminuria are associated with a higher incidence of CVD. Other factors associated with CKD can increase the risk for CVD. The renin-angiotensin

and the sympathetic nervous systems are over stimulated and result in the increased production of superoxide, interleukin 6, and other pro-inflammatory cytokines. Also, the activity of renalase, an enzyme produced by the kidneys that inactivates catecholamines, is decreased in patients with CKD. Assessment for proteinuria is determined by the urinary albumin-to-creatinine ratio. Based on these measurements CKD is categorized in 5 levels of GFR and three stages of proteinuria. Levels of apolipoprotein A1 are decreased and levels of homocysteine, lipoprotein(a), fibrinogen, and C-reactive protein are increased among patients with chronic kidney disease. The cardiovascular mortality in patients with stage 3 CKD was twofold higher and threefold higher in patients with stage 4 CKD. The risk of developing congestive heart failure (CHF), atrial fibrillation, stroke, coronary heart disease (CAD), and peripheral artery disease (PAD) is increased two-fold in patients with eGFR<60 mL/min/1.73m².

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