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Coronary Microvascular Dysfunction as a Preclinical Marker of Uraemic Cardiomyopathy in Early Chronic Kidney Disease

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Abstract: Chronic kidney disease is associated with a markedly increased risk of cardiovascular morbidity and mortality, even in the absence of obstructive coronary artery disease. Traditional cardiovascular risk factors do not fully explain the high burden of cardiac complications observed in patients with renal dysfunction, suggesting the involvement of additional pathophysiological mechanisms. Coronary microvascular dysfunction has emerged as a potential contributor to myocardial injury in chronic kidney disease. It refers to abnormalities in the coronary microcirculation that impair myocardial perfusion despite normal epicardial coronary arteries. Growing clinical and imaging evidence indicates that impaired coronary microvascular function may occur early in the course of chronic kidney disease. This review examines the relationship between coronary microvascular dysfunction and chronic kidney disease and explores the possibility that microvascular dysfunction may represent a preclinical stage in the development of uraemic cardiomyopathy. The paper discusses current clinical evidence, underlying mechanisms including endothelial dysfunction, inflammation, oxidative stress, uremic toxin accumulation, and neurohormonal activation, as well as available diagnostic approaches. Understanding the role of coronary microvascular dysfunction in chronic kidney disease may improve early cardiovascular risk assessment and support strategies aimed at preventing progression to structural myocardial remodeling.

Keywords: *Coronary Microvascular Dysfunction; Chronic Kidney Disease; Uraemic Cardiomyopathy; Cardiorenal Syndrome; Endothelial Dysfunction; Myocardial Remodeling.*

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I. INTRODUCTION

Chronic kidney disease represents a major global public health challenge and is associated with substantial morbidity and mortality. A large proportion of this burden is attributable to cardiovascular disease rather than progression to end-stage renal failure alone. Patients with chronic kidney disease experience a significantly increased risk of cardiovascular events, hospitalization, and premature death when compared with individuals with preserved renal function [1], [16]. Cardiovascular disease therefore remains the leading cause of death among patients with chronic kidney disease.

The increased cardiovascular risk observed in chronic kidney disease cannot be explained solely by traditional atherosclerotic risk factors such as hypertension, diabetes mellitus, dyslipidemia, and aging. Instead, several non-traditional mechanisms related to renal dysfunction contribute to cardiovascular injury, including chronic inflammation, oxidative stress, endothelial dysfunction, neurohormonal activation, and abnormalities in mineral metabolism [12], [16]. These interrelated processes promote vascular dysfunction, myocardial remodeling, and progressive impairment of cardiac performance.

One of the most characteristic cardiac manifestations associated with renal dysfunction is uraemic cardiomyopathy. This condition is characterized by structural and functional myocardial abnormalities including left ventricular hypertrophy, diffuse myocardial fibrosis, and impaired diastolic function [2], [10]. These changes contribute significantly to heart failure, arrhythmias, and sudden cardiac death in patients with chronic kidney disease. Structural cardiac remodeling associated with uraemic cardiomyopathy is increasingly recognized as a major determinant of cardiovascular morbidity in this population.

In recent years, growing attention has been directed toward coronary microvascular dysfunction as a possible contributor to myocardial injury in chronic kidney disease.

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Coronary microvascular dysfunction refers to abnormalities in the structure or function of the coronary microcirculation that impair myocardial perfusion despite the absence of obstructive epicardial coronary artery disease [8]. The coronary microvasculature plays a critical role in regulating myocardial blood flow according to metabolic demand, and dysfunction at this level may lead to myocardial ischemia even when large coronary arteries appear angiographically normal.

Emerging evidence suggests that patients with chronic kidney disease frequently exhibit impaired coronary microvascular function. Studies using advanced imaging techniques have demonstrated reduced coronary flow reserve and abnormal myocardial perfusion in individuals with chronic kidney disease, including those in earlier stages of renal dysfunction [4], [9]. These findings suggest that coronary microvascular abnormalities may develop early and may represent an important mechanism linking chronic kidney disease with myocardial injury.

Persistent impairment of myocardial perfusion at the microvascular level may promote chronic subclinical ischemia, which can contribute to cardiomyocyte injury, interstitial fibrosis, and ventricular remodeling over time. Consequently, coronary microvascular dysfunction has been proposed as a potential preclinical stage in the development of uraemic cardiomyopathy. Understanding this relationship may provide important insights into the pathogenesis of cardiovascular complications in chronic kidney disease and may improve strategies for early detection and prevention of cardiac disease.

The aim of this review is to examine the relationship between coronary microvascular dysfunction and chronic kidney disease and to explore the hypothesis that coronary microvascular dysfunction may represent an early functional marker of myocardial injury preceding the structural changes characteristic of uraemic cardiomyopathy.

II. OBJECTIVES

The primary objective of this review is to examine the relationship between coronary microvascular dysfunction and chronic kidney disease and to explore the hypothesis that coronary microvascular dysfunction may represent an early functional stage in the development of uraemic cardiomyopathy.

This review aims to summarize current evidence regarding cardiovascular complications associated with chronic kidney disease, describe the structural and functional characteristics of uraemic cardiomyopathy, and review the physiological basis of coronary microvascular dysfunction. In addition, the review evaluates clinical and imaging studies linking renal dysfunction with impaired coronary microvascular function and discusses potential pathophysiological mechanisms connecting renal disease, microvascular abnormalities, and myocardial remodeling. By integrating current findings from cardiology and nephrology research, this study seeks to highlight the potential role of coronary microvascular dysfunction as an early marker of cardiac injury in patients with chronic kidney disease.

III. METHODOLOGY

This narrative review was conducted to evaluate the relationship between coronary microvascular dysfunction and chronic kidney disease, with particular focus on its potential role in the development of uraemic cardiomyopathy. Relevant literature was identified through searches of major biomedical databases including PubMed, Scopus, and Google Scholar. Keywords used included chronic kidney disease, coronary microvascular dysfunction, coronary flow reserve, uraemic cardiomyopathy, and cardiorenal syndrome. Priority was given to clinical studies, imaging-based investigations, mechanistic research, and review articles addressing cardiovascular complications in CKD and coronary microvascular abnormalities. Reference lists of selected articles were also screened to identify additional relevant studies [7], [8].

IV. CHRONIC KIDNEY DISEASE AND CARDIOVASCULAR RISK

Chronic kidney disease is widely recognized as an independent risk factor for cardiovascular morbidity and mortality. Epidemiological studies have consistently demonstrated that individuals with impaired renal function exhibit a significantly higher incidence of cardiovascular events including myocardial infarction, heart failure, stroke, and sudden cardiac death compared with individuals with normal renal function [1], [16]. Importantly, many patients with chronic kidney disease experience cardiovascular complications even before progression to end-stage renal disease.

The risk of cardiovascular disease increases progressively with declining renal function. Even mild reductions in estimated glomerular filtration rate have been associated with increased cardiovascular mortality and hospitalization [1], [20]. In addition to reduced glomerular filtration rate, markers of renal injury such as albuminuria have also been shown to correlate with increased cardiovascular risk.

Traditional cardiovascular risk factors such as hypertension, diabetes mellitus, dyslipidemia, and advanced age are highly prevalent among individuals with chronic kidney disease and contribute significantly to the development of cardiovascular disease. However, these conventional risk factors alone do not fully explain the markedly elevated cardiovascular risk observed in CKD populations.

Several non-traditional mechanisms associated with renal dysfunction contribute to cardiovascular pathology. These include chronic inflammation, oxidative stress, endothelial dysfunction, disturbances in mineral metabolism, and activation of neurohormonal pathways [12], [16]. These processes promote vascular injury and myocardial

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remodeling, thereby increasing the risk of heart failure and other cardiovascular complications.

The interaction between the heart and kidneys is commonly described as the cardiorenal axis, which reflects the bidirectional relationship between cardiac and renal dysfunction. Renal impairment can lead to fluid retention, activation of the renin–angiotensin–aldosterone system, and increased sympathetic nervous system activity. These changes contribute to hypertension, vascular stiffness, and myocardial remodeling [19].

Patients with chronic kidney disease frequently exhibit vascular abnormalities including arterial stiffness, vascular calcification, and endothelial dysfunction**,** all of which impair coronary perfusion and increase cardiac workload. Over time, these alterations contribute to the development of structural cardiac changes characteristic of uraemic cardiomyopathy.

Major cardiovascular complications associated with chronic kidney disease are summarized in Table 1.

Table 1 Major Cardiovascular Complications Associated with Chronic Kidney Disease

Cardiovascular complication	Underlying mechanism	Clinical consequence
Left ventricular hypertrophy	Pressure overload, RAAS activation	Heart failure
Vascular calcification	Disturbances in mineral metabolism	Arterial stiffness
Endothelial dysfunction	Oxidative stress and inflammation	Impaired vascular regulation
Coronary microvascular dysfunction	Microvascular endothelial injury	Myocardial ischemia
Myocardial fibrosis	Chronic inflammation and remodeling	Diastolic dysfunction
Arrhythmias	Structural myocardial changes	Sudden cardiac death

V. URAEMIC CARDIOMYOPATHY

Uraemic cardiomyopathy is a distinct form of cardiac remodeling that occurs in patients with chronic kidney disease and is characterized by structural and functional myocardial abnormalities independent of significant obstructive coronary artery disease. The condition has been increasingly recognized as a major contributor to cardiovascular morbidity and mortality among CKD patients. Structural cardiac changes associated with uraemic cardiomyopathy include left ventricular hypertrophy, diffuse myocardial fibrosis, and impaired diastolic function, which together predispose patients to heart failure, arrhythmias, and sudden cardiac death [2], [10].

One of the most prominent features of uraemic cardiomyopathy is left ventricular hypertrophy (LVH). LVH develops frequently in patients with CKD due to chronic pressure overload resulting from hypertension, arterial stiffness, and volume expansion. Neurohormonal activation—particularly stimulation of the renin–angiotensin–aldosterone system and increased sympathetic nervous system activity—also contributes significantly to myocardial hypertrophy [2], [3]. These mechanisms promote cardiomyocyte growth and structural remodeling of the myocardium.

Another hallmark of uraemic cardiomyopathy is diffuse myocardial fibrosis, which involves excessive deposition of extracellular matrix components within the myocardial interstitium. Chronic inflammation, oxidative stress, and metabolic abnormalities associated with renal dysfunction stimulate fibroblast activation and collagen deposition within cardiac tissue [3], [10]. Fibrotic remodeling reduces myocardial compliance and contributes to impaired ventricular relaxation and diastolic dysfunction.

In addition to structural changes, uraemic cardiomyopathy is associated with functional abnormalities in myocardial relaxation and ventricular filling. Diastolic dysfunction is commonly observed in CKD patients and may occur even before the development of overt systolic dysfunction. Reduced ventricular compliance resulting from myocardial hypertrophy and fibrosis leads to elevated ventricular filling pressures and impaired diastolic relaxation. These alterations contribute to the development of heart failure with preserved ejection fraction, which is frequently observed in individuals with chronic kidney disease [11].

Recent evidence has also highlighted the potential role of microvascular abnormalities in the pathogenesis of uraemic cardiomyopathy. Structural alterations in the coronary microcirculation, including capillary rarefaction and endothelial dysfunction, may impair myocardial perfusion and promote ischemia at the tissue level. Unlike obstructive coronary artery disease, which affects epicardial vessels, these abnormalities involve the small intramyocardial vessels responsible for regulating coronary blood flow.

Persistent impairment of microvascular perfusion may lead to chronic subclinical myocardial ischemia**,** which can promote cardiomyocyte injury and progressive myocardial fibrosis. Over time, this process contributes to ventricular remodeling and the structural cardiac abnormalities characteristic of uraemic cardiomyopathy. The key structural and functional features of uraemic cardiomyopathy are summarized in Table 2.

Table 2 Structural and Functional Characteristics of Uraemic Cardiomyopathy

Cardiac feature	Pathophysiological mechanism	Clinical consequence
Left ventricular hypertrophy	Pressure overload and neurohormonal activation	Increased cardiac workload
Myocardial fibrosis	Chronic inflammation and collagen deposition	Reduced myocardial compliance

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Capillary rarefaction	Microvascular injury	Impaired myocardial perfusion
Diastolic dysfunction	Fibrosis and ventricular stiffness	Heart failure with preserved ejection fraction
Electrical instability	Structural myocardial remodeling	Arrhythmias and sudden cardiac death

VI. CORONARY MICROVASCULAR DYSFUNCTION

Coronary microvascular dysfunction (CMD) refers to abnormalities in the structure or function of the coronary microcirculation that impair myocardial perfusion despite the absence of significant obstructive epicardial coronary artery disease. The coronary microcirculation consists of a network of small arteries, arterioles, and capillaries that regulate myocardial blood flow according to metabolic demand. Proper functioning of this microvascular system is essential for maintaining adequate oxygen delivery to myocardial tissue during both resting conditions and periods of increased cardiac workload [8].

Under normal physiological circumstances, coronary blood flow increases significantly during periods of increased myocardial oxygen demand through vasodilation of coronary arterioles and recruitment of additional capillary networks. This adaptive capacity is commonly evaluated using coronary flow reserve (CFR)**,** defined as the ratio of maximal coronary blood flow during stress to resting myocardial blood flow. Impairment of coronary flow reserve is considered a hallmark feature of coronary microvascular dysfunction and reflects an inability of the coronary microvasculature to appropriately respond to metabolic demands [7], [17].

Both structural and functional abnormalities can contribute to the development of CMD. Structural alterations include microvascular remodeling and capillary rarefaction, which reduce the density of perfused microvessels within myocardial tissue. Functional abnormalities may include endothelial dysfunction, impaired nitric oxide signaling, abnormal vascular smooth muscle reactivity, and increased microvascular resistance. These abnormalities disrupt normal regulation of coronary blood flow and may result in inadequate myocardial perfusion during physiological stress [8].

Endothelial dysfunction plays a central role in the pathogenesis of CMD. The vascular endothelium regulates vascular tone through the release of vasoactive mediators such as nitric oxide. In pathological conditions including hypertension, diabetes mellitus, and chronic kidney disease, endothelial injury reduces nitric oxide bioavailability and impairs vasodilatory responses of the coronary microvasculature. Reduced endothelial function contributes to increased microvascular resistance and diminished coronary flow reserve [14].

Clinically, coronary microvascular dysfunction has gained increasing recognition as an important cause of myocardial ischemia in patients who do not exhibit significant obstructive coronary artery disease. Advances in cardiovascular imaging techniques have enabled non-invasive assessment of coronary microvascular function. Modalities such as positron emission tomography, cardiac magnetic resonance imaging, and transthoracic Doppler echocardiography allow measurement of myocardial blood flow and coronary flow reserve, thereby providing valuable insights into coronary microvascular physiology and pathology [17].

Persistent impairment of microvascular perfusion may lead to chronic subclinical myocardial ischemia, which can initiate cardiomyocyte injury and interstitial fibrosis. Over time, these changes may contribute to myocardial remodeling and ventricular dysfunction. Understanding the physiology of the coronary microcirculation is therefore essential for recognizing the role of CMD in systemic diseases such as chronic kidney disease.

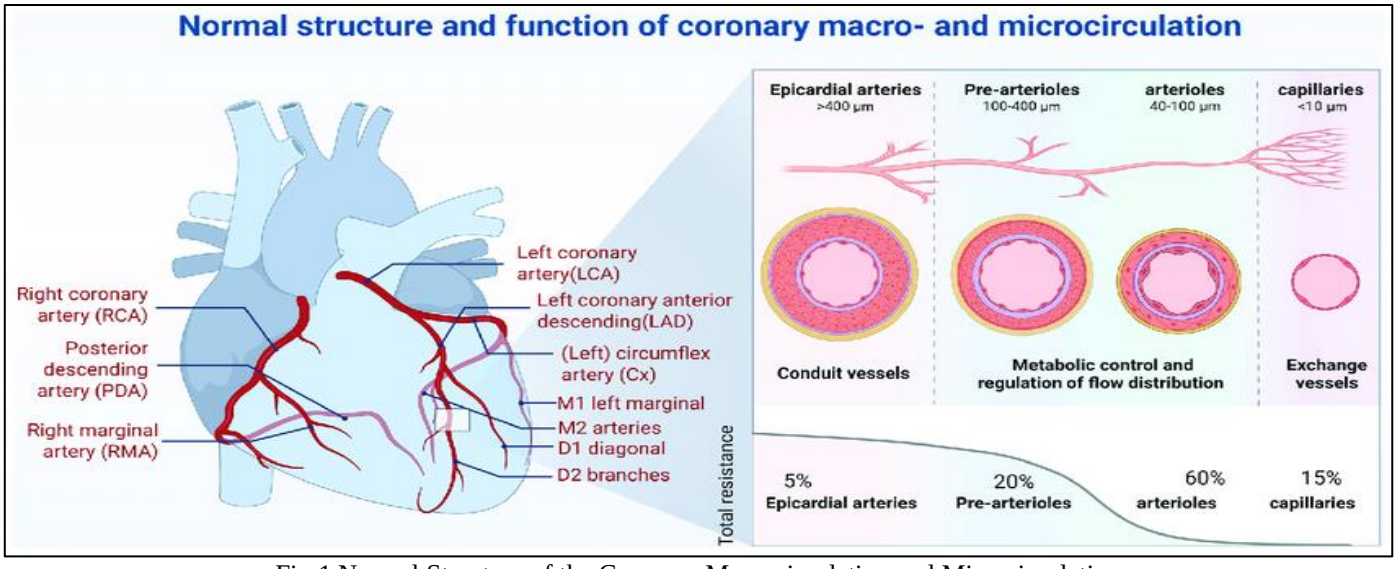

Fig 1 Normal Structure of the Coronary Macrocirculation and Microcirculation

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The coronary circulation consists of epicardial arteries that act as conductance vessels and a network of small intramyocardial vessels responsible for regulating myocardial blood flow. The organization of the coronary macrocirculation and microcirculation is illustrated in Fig. 1. Adapted from Camici and Crea [8].

VII. LINK BETWEEN CHRONIC KIDNEY DISEASE AND CORONARY MICROVASCULAR DYSFUNCTION

Accumulating evidence suggests a significant association between chronic kidney disease and coronary microvascular dysfunction. Patients with CKD frequently demonstrate abnormalities in coronary microvascular regulation even in the absence of obstructive epicardial coronary artery disease. These findings indicate that renal dysfunction may contribute to impaired coronary perfusion at the microvascular level, thereby promoting myocardial ischemia and structural cardiac remodeling [4], [9].

Several clinical studies have demonstrated that patients with reduced renal function exhibit impaired coronary flow reserve, reflecting a diminished capacity of coronary microvessels to dilate in response to increased myocardial oxygen demand. Reduced coronary flow reserve has been reported in patients with early stages of chronic kidney disease, suggesting that microvascular abnormalities may occur before the development of overt cardiovascular disease [4].

Advanced cardiovascular imaging techniques have provided further insight into this relationship. Positron emission tomography studies have demonstrated reduced myocardial flow reserve in CKD patients, even in individuals without significant epicardial coronary artery stenosis. These observations support the hypothesis that microvascular dysfunction represents an important mechanism of myocardial injury in renal disease [4], [5].

Markers of renal dysfunction have also been associated with impaired coronary microvascular function. Reduced estimated glomerular filtration rate and the presence of albuminuria have both been linked with abnormalities in coronary flow reserve and myocardial perfusion. Albuminuria is considered an indicator of systemic endothelial dysfunction and may reflect widespread microvascular injury affecting both renal and coronary vascular beds [6].

Several pathophysiological mechanisms may explain the association between CKD and coronary microvascular dysfunction. Chronic inflammation, oxidative stress, endothelial injury, and accumulation of uremic toxins contribute to impaired vascular regulation and increased microvascular resistance [15]. In addition, activation of the renin–angiotensin–aldosterone system and increased sympathetic nervous system activity may further exacerbate microvascular dysfunction by promoting vasoconstriction and vascular remodeling.

Persistent impairment of coronary microvascular perfusion may result in chronic subclinical myocardial ischemia, which can promote cardiomyocyte injury, interstitial fibrosis, and progressive ventricular remodeling. Over time, these structural changes may contribute to the development of uraemic cardiomyopathy. Therefore, coronary microvascular dysfunction may represent an early functional stage linking renal dysfunction with myocardial structural abnormalities**.**

Key clinical studies investigating the relationship between chronic kidney disease and coronary microvascular dysfunction are summarized in Table 3.

Table 3 Selected Clinical Studies Linking Chronic Kidney Disease with Coronary Microvascular Dysfunction

Study	Study population	Key finding
Charytan et al. [4]	Early CKD patients	Reduced coronary flow reserve compared with controls
Koivuviita et al. [5]	CKD patients without CAD	Increased myocardial perfusion heterogeneity
Chade et al. [9]	Mild renal insufficiency	Impaired coronary flow reserve
Kubo et al. [6]	CKD with albuminuria	Association between albuminuria and CMD

VIII. PATHOPHYSIOLOGICAL MECHANISMS LINKING CHRONIC KIDNEY DISEASE AND CORONARY MICROVASCULAR DYSFUNCTION

The development of coronary microvascular dysfunction in patients with chronic kidney disease is mediated by several interrelated pathophysiological mechanisms. These mechanisms include endothelial dysfunction, chronic inflammation, oxidative stress, accumulation of uremic toxins, and neurohormonal activation. Together, these processes impair microvascular regulation and contribute to myocardial ischemia and structural cardiac remodeling.

- *Endothelial Dysfunction*

Endothelial dysfunction plays a central role in the development of coronary microvascular abnormalities in chronic kidney disease. The vascular endothelium regulates vascular tone through the release of vasoactive substances such as nitric oxide. In CKD, endothelial injury leads to reduced nitric oxide bioavailability and impaired vasodilatory responses of coronary microvessels. This results in increased microvascular resistance and diminished coronary flow reserve [14]. Endothelial dysfunction also promotes vascular inflammation and contributes to structural remodeling of the coronary microcirculation.

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➢ *Chronic Inflammation*

Chronic kidney disease is associated with persistent low-grade systemic inflammation. Elevated levels of inflammatory mediators such as cytokines and acute-phase proteins contribute to vascular injury and endothelial dysfunction. Chronic inflammation promotes fibrosis, vascular remodeling, and myocardial injury, thereby contributing to the development of microvascular dysfunction and cardiac structural abnormalities [16].

➢ *Oxidative Stress*

Oxidative stress is another important contributor to microvascular dysfunction in CKD. Increased production of reactive oxygen species can damage endothelial cells, impair nitric oxide signaling, and promote vascular dysfunction. Oxidative stress also stimulates inflammatory pathways and accelerates vascular remodeling, further impairing coronary microvascular function.

➢ *Uremic Toxins*

Accumulation of uremic toxins is a characteristic feature of renal dysfunction and has been implicated in vascular injury and cardiovascular disease. Compounds such as indoxyl sulfate and p-cresyl sulfate have been shown to induce endothelial damage, promote oxidative stress, and impair vascular function. These toxins contribute to microvascular injury and may play an important role in the development of coronary microvascular dysfunction in CKD patients [15].

➢ *Neurohormonal Activation*

Activation of neurohormonal systems, particularly the renin–angiotensin–aldosterone system and sympathetic nervous system, is frequently observed in patients with chronic kidney disease. These pathways promote vasoconstriction, vascular remodeling, and myocardial hypertrophy. Persistent neurohormonal activation therefore contributes to both microvascular dysfunction and structural cardiac changes characteristic of uraemic cardiomyopathy [12], [19].

Collectively, these mechanisms impair coronary microvascular regulation and reduce myocardial perfusion. Persistent microvascular ischemia may initiate cardiomyocyte injury and interstitial fibrosis, eventually leading to ventricular remodeling and the development of uraemic cardiomyopathy.

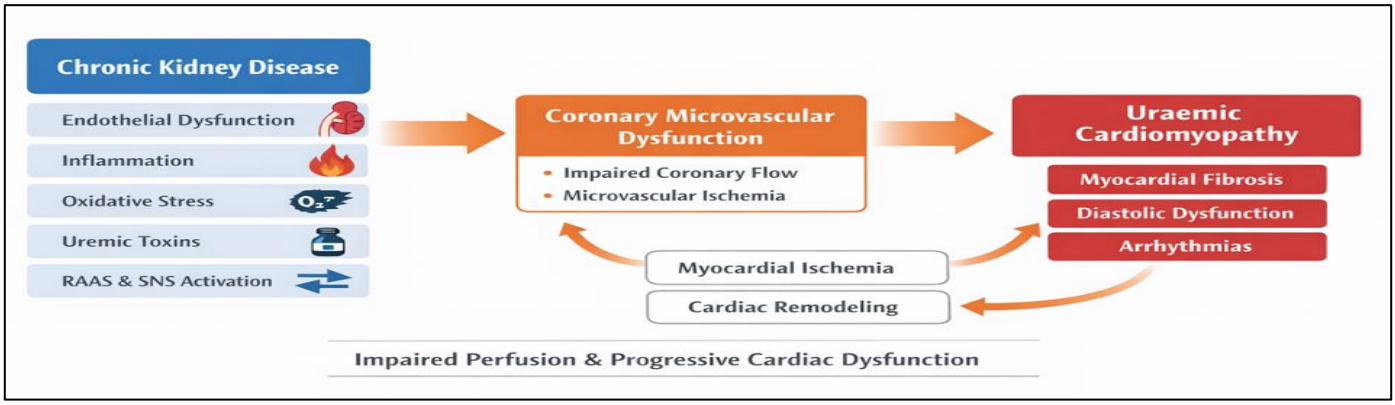

Fig 2 Pathophysiological Mechanisms Linking Chronic Kidney Disease, Coronary Microvascular Dysfunction, and Uraemic Cardiomyopathy.

Chronic kidney disease leads to endothelial dysfunction, inflammation, oxidative stress, uremic toxin accumulation, and neurohormonal activation, resulting in coronary microvascular dysfunction, impaired myocardial perfusion, and progressive cardiac remodeling.

IX. DIAGNOSTIC APPROACHES FOR CORONARY MICROVASCULAR DYSFUNCTION

Accurate assessment of coronary microvascular function is essential for identifying myocardial perfusion abnormalities in patients with chronic kidney disease. Because coronary microvascular dysfunction occurs in the absence of significant epicardial coronary artery stenosis, conventional coronary angiography may appear normal despite the presence of microvascular abnormalities.

Several non-invasive imaging techniques have been developed to evaluate coronary microvascular function. Positron emission tomography (PET) is considered one of the most reliable methods for measuring myocardial blood flow and coronary flow reserve. PET imaging allows quantitative assessment of myocardial perfusion and can detect impaired coronary flow reserve associated with microvascular dysfunction [17].

Cardiac magnetic resonance imaging (CMR) is another valuable modality for evaluating myocardial perfusion and detecting microvascular abnormalities. Stress perfusion CMR can identify areas of reduced myocardial blood flow and has been increasingly used for assessing coronary microvascular dysfunction.

Transthoracic Doppler echocardiography can also be used to measure coronary flow reserve in the left anterior descending artery. Although operator dependent, this technique offers a non-invasive and relatively accessible method for evaluating coronary microvascular function.

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In addition to non-invasive techniques, invasive coronary physiological testing may be performed during coronary angiography. Measurements such as coronary flow reserve and the index of microvascular resistance provide direct evaluation of microvascular function and can help identify microvascular abnormalities in patients with unexplained ischemic symptoms.

These diagnostic approaches provide important insights into coronary microvascular physiology and may help identify early myocardial perfusion abnormalities in patients with chronic kidney disease. Early detection of coronary microvascular dysfunction may improve cardiovascular risk stratification and guide preventive strategies.

X. CLINICAL IMPLICATIONS

Recognition of coronary microvascular dysfunction in patients with chronic kidney disease has important clinical implications. Because microvascular abnormalities may occur before the development of overt structural cardiac disease, identifying coronary microvascular dysfunction may allow earlier detection of cardiovascular risk in CKD patients. Early recognition of impaired coronary microvascular function may therefore provide an opportunity for timely intervention aimed at preventing progression to myocardial remodeling and heart failure.

Assessment of coronary microvascular function may also improve cardiovascular risk stratification in individuals with chronic kidney disease. Traditional cardiovascular risk models often underestimate cardiovascular risk in CKD populations. Evaluation of microvascular function through advanced imaging techniques may help identify patients at higher risk of developing cardiac complications.

In addition, understanding the role of coronary microvascular dysfunction in CKD may support the development of targeted therapeutic strategies. Interventions aimed at improving endothelial function, reducing inflammation and oxidative stress, and controlling neurohormonal activation may potentially improve microvascular function and reduce cardiovascular complications. Optimal management of blood pressure, glycemic control, and treatment with agents that modulate the renin–angiotensin–aldosterone system may also play an important role in protecting microvascular integrity.

Recognizing coronary microvascular dysfunction as an early manifestation of cardiovascular injury in chronic kidney disease may therefore improve prevention strategies and reduce the burden of cardiovascular disease in this high-risk population.

XI. FUTURE RESEARCH DIRECTIONS

Despite growing evidence linking chronic kidney disease with coronary microvascular dysfunction, several important questions remain unresolved. Future research should focus on longitudinal studies evaluating whether coronary microvascular dysfunction precedes the structural cardiac changes characteristic of uraemic cardiomyopathy. Establishing this temporal relationship would help clarify whether CMD can serve as a reliable early biomarker of myocardial injury in CKD.

Further investigations are also needed to better understand the molecular and cellular mechanisms underlying microvascular injury in renal disease. In particular, the roles of endothelial dysfunction, oxidative stress, inflammatory pathways, and uremic toxins in promoting coronary microvascular abnormalities require additional exploration.

Advances in non-invasive imaging techniques may also improve early detection of coronary microvascular dysfunction in CKD patients. Future studies should evaluate the clinical utility of imaging modalities such as PET and cardiac magnetic resonance imaging for routine cardiovascular risk assessment in this population.

Finally, clinical trials are needed to determine whether therapeutic interventions targeting microvascular dysfunction can prevent or delay the progression of myocardial remodeling and uraemic cardiomyopathy. Identifying effective strategies to preserve coronary microvascular function may ultimately improve cardiovascular outcomes in patients with chronic kidney disease.

XII. CONCLUSION

Chronic kidney disease is associated with a substantially increased risk of cardiovascular morbidity and mortality, and cardiovascular disease remains the leading cause of death among CKD patients. While traditional cardiovascular risk factors contribute to this burden, they do not fully explain the high prevalence of cardiac complications observed in individuals with renal dysfunction.

Coronary microvascular dysfunction has emerged as an important mechanism that may link chronic kidney disease with myocardial injury and structural cardiac remodeling. Evidence from clinical and imaging studies suggests that impairment of coronary microvascular function may occur early in the course of renal disease, even before the development of overt cardiovascular pathology.

Persistent microvascular dysfunction can lead to impaired myocardial perfusion, chronic subclinical ischemia, and progressive myocardial fibrosis. These processes may contribute to the development of uraemic cardiomyopathy. Recognizing coronary microvascular dysfunction as a potential preclinical marker of cardiac injury in CKD may improve early cardiovascular risk assessment and support the development of preventive and therapeutic strategies aimed at reducing cardiovascular complications in patients with chronic kidney disease.

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