



Coronary Artery Disease in Patients with Diabetic Kidney Disease: Challenges and Contemporary Revascularization Strategies

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Abstract

Background: Coronary artery disease (CAD) is the leading cause of morbidity and mortality among patients with diabetic kidney disease (DKD). The coexistence of diabetes mellitus and chronic kidney dysfunction accelerates atherosclerosis through complex metabolic, inflammatory, and vascular mechanisms, resulting in more extensive coronary involvement and poorer cardiovascular outcomes than those observed in the general population.

Objective: To review the pathophysiological links between DKD and CAD, describe the distinctive coronary lesion characteristics encountered in this population, and discuss contemporary revascularization strategies aimed at improving clinical outcomes.

Methods: A narrative review of the literature was conducted using published studies, clinical trials, systematic reviews, meta-analyses, and contemporary guideline documents addressing CAD in patients with DKD. Particular attention was given to disease mechanisms, coronary anatomy, revascularization approaches, intravascular imaging, and long-term cardiovascular outcomes.

Results: Patients with DKD exhibit a high prevalence of diffuse and multivessel coronary artery disease, extensive vascular calcification, endothelial dysfunction, chronic inflammation, and accelerated plaque progression. These features contribute to increased procedural complexity and poorer outcomes following coronary revascularization. Advances in medical therapy, drug eluting stent technology, intravascular imaging, and procedural optimization have improved the safety and efficacy of percutaneous coronary intervention in this high-risk population. Coronary artery bypass grafting remains an important treatment option for selected patients with advanced multivessel disease. Contemporary revascularization strategies increasingly emphasize individualized decision making based on anatomical complexity, comorbidity burden, and expected long-term benefit.

Conclusion: Patients with DKD represent a particularly vulnerable group with a substantial burden of coronary artery disease and adverse cardiovascular outcomes. A comprehensive understanding of disease mechanisms and careful selection of revascularization strategies are essential for optimizing both procedural success and long-term prognosis. Contemporary advances in coronary intervention and imaging continue to expand therapeutic opportunities for this challenging population.

Keywords: Coronary Artery Disease, Diabetic Kidney Disease, Revascularization Strategies



Introduction

Coronary artery disease (CAD) remains the leading cause of death among patients with diabetic kidney disease (DKD), accounting for a substantial proportion of cardiovascular morbidity and mortality in this population. The coexistence of diabetes mellitus and chronic kidney dysfunction creates a particularly aggressive cardiovascular phenotype characterized by accelerated atherosclerosis, diffuse coronary involvement, and a markedly increased risk of adverse cardiovascular events compared with individuals without renal impairment. [1]

The relationship between DKD and CAD extends beyond traditional cardiovascular risk factors. Chronic inflammation, oxidative stress, endothelial dysfunction, vascular calcification, and metabolic disturbances contribute to progressive arterial injury and plaque development. These mechanisms not only promote the initiation of coronary atherosclerosis but also influence plaque composition, lesion complexity, and long-term disease progression. [2]

Patients with DKD frequently present with multivessel disease, diffuse coronary narrowing, small vessel involvement, and extensive calcification. Such anatomical characteristics increase procedural complexity and often limit the effectiveness of conventional revascularization approaches. Consequently, treatment decisions in this population require careful consideration of both cardiovascular and renal status. [3]

Although substantial advances have been achieved in medical therapy and coronary intervention, outcomes following revascularization remain less favorable in patients with DKD than in the general CAD population. The choice between percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG) continues to be challenging, particularly in individuals with advanced coronary disease and multiple comorbidities. [4]

Recent developments in intravascular imaging, drug-eluting stent technology, physiological lesion assessment, and contemporary revascularization strategies have expanded therapeutic options and improved procedural outcomes. Nevertheless, optimizing cardiovascular management in patients with DKD remains an important clinical challenge requiring an individualized and multidisciplinary approach. [5]

This review discusses the pathophysiological mechanisms linking diabetic kidney disease and coronary artery disease, highlights the distinctive coronary characteristics observed in this population, and examines current revascularization strategies aimed at improving long-term cardiovascular outcomes.

Burden of Coronary Artery Disease in Diabetic Kidney Disease

Diabetic kidney disease is one of the most important determinants of cardiovascular morbidity and mortality among patients with diabetes mellitus. As renal function declines, the incidence of coronary artery disease rises substantially, making cardiovascular complications the leading cause of death in this population. Even in the early stages of renal impairment, patients exhibit a significantly greater risk of myocardial infarction, heart failure, and cardiovascular mortality compared with individuals who have diabetes without kidney involvement. [6]

The coexistence of diabetes and chronic kidney disease creates a powerful interaction that accelerates atherosclerotic disease progression. Persistent hyperglycemia promotes endothelial injury and metabolic dysfunction, while renal impairment contributes to chronic inflammation, oxidative stress, and vascular calcification. Together, these mechanisms drive rapid progression of coronary artery disease and increase the likelihood of adverse cardiovascular events. [7]

Patients with diabetic kidney disease frequently develop more extensive coronary involvement than the general population. Coronary angiographic studies have demonstrated higher rates of multivessel disease, diffuse atherosclerosis, and severe coronary stenosis among individuals with impaired renal function. These findings contribute to greater clinical complexity and often necessitate more aggressive treatment strategies. [8]

Coronary artery calcification represents another characteristic feature of diabetic kidney disease. Disturbances in mineral metabolism, chronic inflammation, and endothelial dysfunction promote both intimal and medial arterial calcification. Progressive calcium deposition leads to increased vascular



stiffness, impaired coronary compliance, and greater procedural difficulty during coronary intervention. [9]

In addition to structural coronary abnormalities, patients with diabetic kidney disease frequently exhibit atypical clinical presentations. Silent ischemia and atypical symptoms are more common because of autonomic dysfunction and altered pain perception associated with diabetes. Consequently, coronary artery disease may remain undiagnosed until advanced stages, contributing to delayed treatment and poorer clinical outcomes. [10]

The burden of CAD continues to increase despite improvements in cardiovascular prevention and diabetes management. As the prevalence of diabetes and chronic kidney disease rises worldwide, the number of patients requiring complex coronary evaluation and revascularization is expected to grow substantially. This evolving epidemiological landscape highlights the importance of understanding the unique cardiovascular challenges associated with diabetic kidney disease and developing treatment strategies tailored to this high risk population. [11]

Pathophysiological Mechanisms Linking Diabetic Kidney Disease and Coronary Artery Disease

The association between diabetic kidney disease and coronary artery disease is driven by multiple interconnected mechanisms that promote both renal and vascular injury. Rather than functioning as separate disease processes, diabetes, chronic kidney dysfunction, and atherosclerosis interact continuously, resulting in accelerated cardiovascular damage and a substantially increased risk of adverse clinical outcomes. [12]

Endothelial dysfunction is considered one of the earliest events linking diabetic kidney disease to coronary atherosclerosis. Persistent hyperglycemia impairs endothelial nitric oxide production, increases vascular permeability, and promotes leukocyte adhesion to the vascular wall. These alterations facilitate lipid accumulation within the arterial intima and initiate atherosclerotic plaque formation. As renal function declines, endothelial injury becomes more pronounced, contributing to progressive coronary artery disease. [13]

Oxidative stress represents another major contributor to cardiovascular injury in diabetic kidney disease. Excessive production of reactive oxygen species results from chronic hyperglycemia, mitochondrial dysfunction, and activation of multiple metabolic pathways. Increased oxidative stress damages endothelial cells, promotes low-density lipoprotein oxidation, and accelerates plaque development. These effects contribute to both progression of coronary artery disease and deterioration of renal function. [14]

Inflammation plays a central role throughout the disease process. Elevated levels of inflammatory cytokines and chemokines have been consistently observed in patients with diabetic kidney disease. Persistent activation of inflammatory pathways promotes endothelial injury, vascular remodeling, plaque instability, and progressive renal fibrosis. The resulting chronic inflammatory state contributes to the high cardiovascular risk observed in this population. [15]

Abnormal activation of the renin–angiotensin–aldosterone system (RAAS) further amplifies cardiovascular and renal injury. Increased angiotensin II activity promotes vasoconstriction, oxidative stress, inflammation, and vascular smooth muscle proliferation. In addition, RAAS activation accelerates glomerular injury and contributes to progressive nephron loss. These mechanisms create a vicious cycle in which worsening kidney disease promotes cardiovascular damage and vice versa. [16]

Vascular calcification is particularly prominent among patients with diabetic kidney disease and represents an important factor contributing to adverse cardiovascular outcomes. Disturbances in calcium and phosphate metabolism, combined with chronic inflammation and oxidative stress, promote calcification of both the intimal and medial layers of the arterial wall. Coronary calcification increases vascular stiffness, impairs coronary blood flow, and complicates revascularization procedures. [17]

Metabolic abnormalities associated with diabetes also contribute significantly to accelerated atherosclerosis. Advanced glycation end products accumulate within vascular tissues and interact with specific cellular receptors, triggering inflammatory and oxidative pathways. These changes promote plaque formation, endothelial dysfunction, and progressive vascular injury throughout the coronary circulation. [18]



The cumulative effect of endothelial dysfunction, inflammation, oxidative stress, RAAS activation, vascular calcification, and metabolic dysregulation results in a particularly aggressive form of coronary artery disease. This complex pathophysiological environment explains the high prevalence of diffuse atherosclerosis, multivessel disease, and adverse cardiovascular outcomes observed in patients with diabetic kidney disease and underscores the need for comprehensive management strategies targeting both cardiovascular and renal risk factors. [19]

Coronary Anatomy and Lesion Characteristics in Patients with Diabetic Kidney Disease

Coronary artery disease in patients with diabetic kidney disease differs substantially from that observed in the general population. Beyond a higher prevalence of atherosclerosis, these patients often exhibit more advanced and anatomically complex coronary lesions. The combination of chronic hyperglycemia, systemic inflammation, endothelial dysfunction, and progressive renal impairment promotes widespread arterial injury, resulting in a distinct pattern of coronary involvement that presents significant diagnostic and therapeutic challenges. [20]

One of the most characteristic findings is diffuse coronary atherosclerosis. Rather than developing isolated focal stenoses, patients with diabetic kidney disease frequently demonstrate long segments of disease involving multiple vascular territories. Diffuse plaque accumulation may affect both proximal and distal coronary segments, reducing the availability of healthy reference vessels and complicating procedural planning during coronary intervention. This extensive disease burden contributes to higher rates of incomplete revascularization and recurrent ischemic events. [21]

Multivessel coronary artery disease is also considerably more common in this population. Coronary angiographic studies consistently demonstrate a greater prevalence of significant stenoses affecting two or more major epicardial vessels among patients with diabetic nephropathy. The coexistence of multivessel disease increases cardiovascular risk and often necessitates complex treatment decisions regarding the most appropriate revascularization strategy. [22]

Small vessel disease represents another important feature of diabetic coronary pathology. Chronic exposure to hyperglycemia promotes microvascular dysfunction and diffuse narrowing of distal coronary branches. Small vessel involvement may limit the effectiveness of both surgical and percutaneous revascularization and is frequently associated with persistent symptoms despite apparently successful treatment of major epicardial lesions. [23]

Coronary artery calcification is particularly prominent in patients with diabetic kidney disease. Disturbances in calcium-phosphate homeostasis, chronic inflammation, oxidative stress, and vascular smooth muscle cell transformation contribute to progressive calcific deposition within the arterial wall. Calcified lesions are often resistant to balloon expansion, may impair adequate stent deployment, and are associated with increased procedural complexity and higher rates of adverse cardiovascular outcomes. [24]

In addition to extensive calcification, patients with diabetic kidney disease frequently exhibit complex plaque morphology. Lesions may contain mixed fibrotic and calcific components, large plaque burden, and extensive longitudinal involvement. Conventional angiography may underestimate the true severity of disease because positive vascular remodeling can preserve luminal dimensions despite substantial plaque accumulation. Consequently, intravascular imaging techniques have become increasingly valuable for accurate lesion characterization and procedural planning. [25]

Chronic total occlusions (CTOs) are encountered more frequently among patients with long standing diabetes and renal dysfunction. Persistent inflammation and progressive plaque evolution contribute to complete vessel obstruction, often accompanied by severe calcification and extensive collateral circulation. CTO interventions in this population are technically demanding and generally require advanced procedural expertise, longer procedure times, and careful patient selection. [26]

The cumulative effect of diffuse atherosclerosis, multivessel involvement, small vessel disease, calcification, and complex lesion morphology creates a challenging anatomical environment for coronary revascularization. These features help explain the higher rates of procedural complications, restenosis, repeat revascularization, and adverse cardiovascular outcomes observed among patients with diabetic



kidney disease. Understanding these anatomical characteristics is essential for selecting appropriate treatment strategies and optimizing long term clinical outcomes. [27]

Contemporary Revascularization Strategies

The management of coronary artery disease in patients with diabetic kidney disease remains particularly challenging because of the complex interplay between extensive atherosclerotic burden, progressive renal dysfunction, and multiple cardiovascular comorbidities. Treatment decisions should consider not only the severity of coronary disease but also the patient's renal status, expected life expectancy, procedural risk, and likelihood of achieving durable revascularization. Contemporary management relies on a combination of optimal medical therapy and individualized revascularization strategies tailored to the anatomical and clinical characteristics of each patient. [28]

Optimal Medical Therapy

Optimal medical therapy remains the foundation of cardiovascular management in patients with diabetic kidney disease regardless of whether revascularization is performed. Aggressive control of cardiovascular risk factors, including hypertension, dyslipidemia, hyperglycemia, and smoking cessation, is essential for slowing disease progression and reducing cardiovascular events. Recent advances in glucose lowering therapies, particularly sodium-glucose cotransporter 2 inhibitors and glucagon-like peptide-1 receptor agonists, have demonstrated significant cardiovascular and renal benefits and have become important components of contemporary management. [29]

Lipid lowering therapy represents another critical aspect of treatment. Intensive reduction of low-density lipoprotein cholesterol with statins, with or without additional lipid lowering agents, has consistently been associated with reduced cardiovascular risk in patients with diabetes and chronic kidney disease. Antiplatelet therapy, renin-angiotensin-aldosterone system blockade, and lifestyle modification also remain essential components of comprehensive cardiovascular care. [30]

Percutaneous Coronary Intervention

Percutaneous coronary intervention has evolved considerably over the last two decades and remains the most frequently performed revascularization strategy in patients with diabetic kidney disease. Improvements in stent design, procedural techniques, and adjunctive pharmacotherapy have enhanced procedural safety and long-term outcomes. Contemporary drug eluting stents have significantly reduced rates of restenosis and repeat revascularization compared with earlier generations, making PCI an increasingly attractive option for many patients. [31]

Despite these advances, PCI in patients with diabetic kidney disease remains technically demanding. Diffuse atherosclerosis, severe calcification, long lesions, and multivessel disease often require complex interventions involving multiple stents and prolonged procedures. These anatomical challenges contribute to increased rates of procedural complications and recurrent ischemic events when compared with patients without renal dysfunction. [32]

Intravascular imaging has emerged as an important adjunct to PCI in this setting. Techniques such as intravascular ultrasound and optical coherence tomography provide detailed assessment of plaque morphology, vessel dimensions, lesion length, and stent expansion. Numerous studies have demonstrated that imaging-guided PCI improves procedural optimization and may reduce adverse cardiovascular events, particularly in patients with complex coronary anatomy. [33]

Coronary Artery Bypass Grafting

Coronary artery bypass grafting remains an important treatment option for patients with advanced multivessel disease, particularly those with extensive coronary involvement not amenable to complete percutaneous revascularization. Several studies have demonstrated superior long-term durability of surgical revascularization in selected diabetic patients, especially when complex multivessel disease is present. [34]

However, surgical revascularization is not without limitations. Patients with diabetic kidney disease often have multiple comorbid conditions that increase perioperative risk, including heart failure, anemia, peripheral vascular disease, and impaired renal function. Postoperative acute kidney injury, infection, prolonged hospitalization, and increased mortality remain important concerns, particularly among



individuals with advanced chronic kidney disease. [35]

PCI Versus CABG in Diabetic Kidney Disease

The choice between PCI and CABG remains one of the most important decisions in the management of patients with diabetic kidney disease. Current evidence suggests that no single strategy is appropriate for all patients. Coronary anatomy, lesion complexity, surgical risk, renal function, patient preference, and anticipated long-term outcomes must all be considered during treatment planning. [36]

CABG may provide superior long-term outcomes in patients with extensive multivessel disease and high anatomical complexity, whereas PCI offers a less invasive alternative associated with shorter recovery time and lower immediate procedural morbidity. Advances in PCI technology have narrowed the outcome gap between the two approaches in selected patient populations, supporting a more individualized approach to revascularization. [37]

A multidisciplinary Heart Team approach has become increasingly important when evaluating complex patients with diabetic kidney disease. Collaboration between interventional cardiologists, cardiac surgeons, nephrologists, and imaging specialists allows comprehensive assessment of both cardiovascular and renal risk and facilitates selection of the most appropriate revascularization strategy. [38]

Role of Intravascular Imaging in Contemporary Revascularization

The growing adoption of intravascular imaging has transformed coronary intervention in complex patients. IVUS and OCT provide information that cannot be obtained by angiography alone and have become valuable tools for lesion assessment, procedural planning, and stent optimization. Imaging-guided PCI is increasingly recommended in complex lesions, left main disease, long lesions, bifurcations, and heavily calcified vessels. [39]

In patients with diabetic kidney disease, intravascular imaging offers additional advantages by facilitating accurate procedural planning while minimizing contrast exposure. These benefits may contribute to improved procedural success and reduced risk of adverse cardiovascular and renal outcomes. As imaging technology continues to evolve, its role within contemporary revascularization strategies is expected to expand further. [40]

Clinical Outcomes and Prognosis

Despite substantial advances in cardiovascular care, patients with diabetic kidney disease continue to experience poorer outcomes following coronary artery disease diagnosis and treatment than the general population. The coexistence of diabetes, renal dysfunction, and extensive atherosclerotic disease contributes to a persistently elevated risk of myocardial infarction, heart failure, repeat revascularization, and cardiovascular mortality. [1]

Long term prognosis is strongly influenced by the severity of renal impairment. Progressive decline in kidney function has been consistently associated with increased rates of major adverse cardiovascular events and all-cause mortality. Even modest reductions in estimated glomerular filtration rate are associated with a significant increase in cardiovascular risk, highlighting the close relationship between renal and cardiovascular disease progression. [27]

Patients undergoing coronary revascularization frequently present with more complex coronary anatomy and a greater burden of comorbidities than individuals without diabetic kidney disease. These factors contribute to higher procedural risk and may adversely affect long term outcomes regardless of the revascularization strategy employed. Extensive calcification, diffuse disease, and multivessel involvement remain important predictors of recurrent ischemic events following treatment. [20]

The introduction of contemporary drug eluting stents, advanced procedural techniques, and intravascular imaging has improved outcomes after PCI. Imaging guided interventions have demonstrated lower rates of target lesion failure, repeat revascularization, and adverse cardiovascular events compared with angiography guided procedures, particularly in patients with complex coronary disease. [33]

Outcomes following coronary artery bypass grafting remain favorable in selected patients with extensive multivessel disease; however, perioperative complications and postoperative renal deterioration continue to represent important concerns in individuals with advanced kidney dysfunction. Therefore, careful patient selection and individualized treatment planning remain essential for optimizing long term



prognosis. [37]

Although cardiovascular outcomes have improved over recent years, patients with diabetic kidney disease continue to represent one of the highest risk groups encountered in contemporary cardiovascular practice. Continued efforts aimed at early diagnosis, aggressive risk factor modification, and optimization of revascularization strategies are required to further improve survival and quality of life. [11]

Conclusion

Coronary artery disease remains the principal cause of morbidity and mortality in patients with diabetic kidney disease and is characterized by a more aggressive clinical course than that observed in the general population. The coexistence of diabetes and chronic kidney dysfunction promotes diffuse atherosclerosis, multivessel involvement, extensive vascular calcification, and complex coronary anatomy, all of which contribute to poorer cardiovascular outcomes and greater challenges during revascularization. Contemporary management requires a comprehensive approach that combines optimal medical therapy with individualized revascularization strategies based on clinical characteristics, coronary anatomy, and renal status. Advances in percutaneous coronary intervention, drug eluting stent technology, intravascular imaging, and multidisciplinary decision making have improved the safety and effectiveness of coronary revascularization in this high risk population. Nevertheless, patients with diabetic kidney disease continue to experience substantial residual cardiovascular risk, emphasizing the need for early recognition, aggressive risk factor modification, and continued refinement of therapeutic strategies to improve long term outcomes.

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