Managing Coronary Atherosclerotic Disease in Diabetic Nephropathy: From Risk Assessment to Revascularization

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Abstract

Background: Diabetic kidney disease (DKD) is associated with a markedly increased risk of coronary artery disease (CAD) and cardiovascular death. The combined effects of chronic hyperglycemia and impaired renal function promote endothelial injury, inflammation, oxidative stress, vascular calcification, and accelerated atherosclerosis. Consequently, patients with DKD frequently develop more complex and widespread coronary disease and experience less favorable cardiovascular outcomes than individuals without renal involvement.

Objective: This review summarizes the mechanisms underlying the association between DKD and CAD, outlines the characteristic pattern of coronary involvement in affected patients, and evaluates current approaches to coronary revascularization in this high-risk population.

Methods: Relevant evidence was reviewed from clinical studies, randomized and observational trials, systematic reviews, meta-analyses, and recent professional guidelines concerning coronary disease in patients with DKD. The review focused on pathophysiological mechanisms, coronary lesion complexity, percutaneous and surgical revascularization, the role of intracoronary imaging, procedural considerations, and long-term clinical outcomes.

Results: Coronary disease in patients with DKD is commonly characterized by diffuse atherosclerosis, multivessel involvement, severe calcification, endothelial dysfunction, and rapid progression of plaque burden. These abnormalities increase technical difficulty during coronary intervention and are associated with higher rates of ischemic and procedural complications. Nevertheless, improvements in guideline-directed medical therapy, contemporary drug-eluting stents, intravascular imaging, and lesion preparation techniques have enhanced the feasibility and outcomes of percutaneous coronary intervention. Coronary artery bypass grafting continues to provide an important revascularization option, particularly in patients with extensive or anatomically complex multivessel CAD. Selection of the optimal strategy should therefore incorporate coronary anatomy, kidney function, diabetes-related comorbidities, procedural risk, and anticipated long-term clinical benefit.

Conclusion: The coexistence of DKD and CAD defines a population with particularly high cardiovascular risk and complex coronary anatomy. Successful management requires integration of optimal medical therapy with carefully selected revascularization strategies tailored to individual clinical and anatomical characteristics. Continued advances in coronary devices, intravascular imaging, and procedural techniques may further improve outcomes in these challenging patients.

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

Introduction

Cardiovascular disease is a major determinant of prognosis in patients with diabetic kidney disease. When diabetes and chronic renal dysfunction occur together, their vascular consequences are not simply additive. Instead, they interact to create a particularly aggressive form of atherosclerotic disease characterized by faster progression, broader coronary involvement, and a greater probability of adverse cardiovascular events. Thus, deterioration of kidney function in a patient with diabetes should be viewed not only as progression of renal disease but also as an important marker of increasing cardiovascular vulnerability. **[1]**

The coronary disease encountered in this setting also differs clinically and anatomically from uncomplicated atherosclerotic CAD. Patients frequently have diffuse disease extending over long coronary segments, multivessel involvement, extensive vascular calcification, and distal or small-vessel disease. These abnormalities can reduce the likelihood of complete revascularization and increase the technical demands of both percutaneous and surgical procedures. **[2]**

Therapeutic decisions are further complicated by competing risks. Revascularization may relieve ischemia and improve prognosis in appropriately selected patients, but renal dysfunction simultaneously increases susceptibility to procedural complications, acute kidney injury, bleeding, and adverse long-term outcomes. Accordingly, coronary management in DKD requires simultaneous consideration of ischemic burden, anatomical complexity, renal reserve, procedural risk, and expected durability of treatment. **[3]**

Cardiovascular Burden Across the Diabetes–Kidney Disease Continuum

Renal involvement substantially modifies cardiovascular risk in diabetes. Even relatively early impairment of kidney function is associated with increased rates of myocardial infarction, heart failure, and cardiovascular death. With progressive renal dysfunction, the contribution of both traditional cardiovascular risk factors and kidney-specific abnormalities becomes increasingly important, producing a progressively higher-risk clinical phenotype. **[4]**

Atherosclerotic progression in DKD reflects sustained exposure to multiple damaging influences. Hyperglycemia promotes glycation, endothelial injury, and metabolic disturbance, whereas chronic kidney dysfunction adds oxidative stress, inflammation, abnormalities of mineral metabolism, and vascular calcification. These processes develop concurrently and help explain why coronary disease may become more extensive than expected from conventional risk factors alone. **[5]**

Clinical recognition can also be difficult. Autonomic dysfunction related to diabetes may attenuate typical ischemic symptoms, allowing important coronary disease to present with atypical discomfort, dyspnea, reduced exercise tolerance, or even silent ischemia. Consequently, significant CAD may already be anatomically advanced when it becomes clinically apparent. **[6]**

Biological Basis of Accelerated Coronary Injury

Endothelial dysfunction represents an important connection between metabolic disease, kidney impairment, and atherosclerosis. Chronic hyperglycemia disrupts nitric oxide availability, alters endothelial permeability, and facilitates inflammatory-cell adhesion. These changes favor lipid entry into the arterial wall and promote the early stages of plaque formation. Declining renal function can intensify this endothelial disturbance, supporting continued progression of coronary atherosclerosis. **[7]**

Oxidative stress acts in parallel with endothelial dysfunction. Increased formation of reactive oxygen species, mitochondrial abnormalities, and metabolic pathway activation promote oxidative modification of lipoproteins and further injure the vascular endothelium. Oxidative damage therefore contributes simultaneously to coronary plaque progression and deterioration of the renal microvascular environment. **[8]**

Persistent inflammation further amplifies this process. Patients with DKD frequently demonstrate sustained activation of inflammatory pathways capable of promoting endothelial dysfunction, vascular remodeling, and plaque instability. At the renal level, similar pathways contribute to progressive fibrosis and nephron loss. Cardiovascular and kidney damage therefore share several biological mechanisms rather than developing as independent complications of diabetes. **[9]**

Activation of the renin–angiotensin–aldosterone system provides another pathway linking the two organs.

Angiotensin II promotes vasoconstriction, inflammatory signaling, oxidative injury, and vascular smooth-muscle proliferation while simultaneously contributing to intraglomerular injury and progressive renal dysfunction. Continued activation may therefore reinforce a cycle in which worsening renal disease increases cardiovascular injury and progressive cardiovascular disease further compromises renal function. **[10]**

Vascular calcification becomes particularly relevant as kidney dysfunction advances. Abnormal calcium-phosphate metabolism, inflammation, oxidative stress, and phenotypic transformation of vascular smooth-muscle cells encourage calcium deposition within arterial walls. In the coronary circulation, this may produce rigid vessels and heavily calcified plaques that are difficult to dilate and prepare adequately for stent implantation. **[11]**

These mechanisms collectively generate what may be considered the diabetic cardiorenal coronary phenotype: extensive plaque burden, diffuse atherosclerosis, calcification, multivessel involvement, and persistent vascular dysfunction. Recognition of this phenotype is clinically important because anatomical complexity directly influences the feasibility, completeness, and durability of coronary revascularization. **[12]**

How Diabetic Kidney Disease Alters Coronary Anatomy

Diffuse rather than isolated coronary narrowing is common in DKD. Long diseased segments may involve both proximal and distal portions of the coronary circulation, leaving fewer normal reference segments for procedural planning. This pattern also increases the probability that apparently successful focal treatment will leave substantial residual atherosclerotic burden elsewhere in the coronary tree. **[13]**

Multivessel disease represents another major feature. Significant stenoses frequently involve two or more major epicardial coronary arteries, thereby increasing the complexity of choosing between PCI and surgery. The clinical question is therefore often not whether a single lesion can technically be treated, but whether the selected strategy can provide sufficiently complete and durable revascularization. **[14]**

Small-vessel involvement can further limit treatment. Diabetes promotes microvascular disease and narrowing of distal vessels, while diffuse atherosclerosis may reduce the quality of potential distal targets. Persistent angina or ischemic symptoms may consequently remain even when major epicardial lesions have been successfully revascularized. **[15]**

Calcification adds another dimension of difficulty. Heavily calcified plaques may resist balloon expansion, interfere with adequate lesion preparation, and increase the likelihood of suboptimal stent expansion. These factors can affect both immediate procedural success and subsequent clinical outcomes, making careful characterization and preparation of calcified lesions particularly important in DKD. **[16]**

Angiography alone may not always reveal the entire structural burden. Positive remodeling can partly preserve the angiographic lumen despite substantial plaque accumulation, while calcium distribution and vessel dimensions may be difficult to appreciate accurately using two-dimensional angiography. These limitations explain the increasing role of intravascular imaging when complex lesions are treated. **[17]**

Medical Treatment as the Foundation of Revascularization

Revascularization should not be considered a substitute for intensive cardiovascular risk reduction. Blood-pressure control, lipid lowering, glycemic management, smoking cessation, antiplatelet treatment when indicated, and therapies targeting the renin–angiotensin system remain important components of long-term management. Effective medical therapy is particularly important because the diffuse nature of DKD-associated atherosclerosis means that untreated coronary segments remain at continued risk even after technically successful revascularization. **[18]**

The therapeutic landscape of diabetes has also changed considerably. Sodium-glucose cotransporter-2 inhibitors and glucagon-like peptide-1 receptor agonists have become important components of contemporary care because of demonstrated cardiorenal benefits in appropriate patient populations. Their incorporation into overall management emphasizes that successful treatment of CAD in DKD requires attention to the underlying systemic disease rather than focusing exclusively on coronary stenoses. **[18]**

Percutaneous Coronary Intervention in the Modern Era

PCI has changed substantially with improvements in stent technology and procedural technique.

Contemporary drug-eluting stents have markedly reduced restenosis and repeat revascularization compared with older devices and have enabled percutaneous treatment of increasingly complex coronary anatomy. For many patients with DKD, PCI therefore provides an effective and less invasive means of achieving coronary revascularization. **[19]**

Nevertheless, technical success may be more difficult to achieve than in patients without renal disease. Long stenoses, multiple diseased vessels, severe calcification, and diffuse coronary involvement may require multiple devices, extensive lesion preparation, and longer procedures. The challenge is not merely crossing or dilating a stenosis but obtaining adequate lesion preparation and optimal final stent expansion across anatomically unfavorable coronary segments. **[20]**

Another important issue is renal protection. Patients with already impaired kidney function have limited renal reserve and may be vulnerable to further renal deterioration surrounding coronary procedures. Procedural planning should therefore aim to avoid unnecessary contrast exposure and reduce other preventable causes of peri-procedural kidney injury while maintaining adequate coronary treatment. **[3]**

Intravascular Imaging and Procedural Optimization

Intravascular ultrasound and optical coherence tomography have expanded the ability to assess complex coronary lesions. These techniques permit detailed evaluation of vessel dimensions, plaque distribution, calcium, lesion length, and the final result after stent implantation. This information can identify inadequate stent expansion or other technical problems that may not be obvious on angiography alone. **[21]**

Imaging may be particularly valuable in the diabetic cardiorenal population because of the high prevalence of diffuse disease and calcification. Accurate measurement of the vessel and identification of calcium distribution can guide lesion preparation, stent sizing, and optimization. In appropriately selected procedures, image-guided strategies may also support efforts to reduce reliance on repeated contrast injections. **[21]**

The increasing emphasis on procedural optimization reflects an important shift in PCI strategy. Rather than considering successful angiographic stent placement to be the final objective, contemporary intervention aims for adequate lesion preparation, appropriate device sizing, full stent expansion, and avoidance of major edge or apposition problems. Such principles are especially relevant when baseline coronary anatomy already predicts a high risk of recurrent events. **[21]**

Surgical Revascularization

CABG remains an important option in diabetic patients with extensive multivessel coronary disease. Surgical bypass can provide revascularization beyond multiple proximal stenoses and may offer greater durability when disease is widespread or when percutaneous treatment would require numerous long stents. This potential advantage is particularly relevant when achieving satisfactory anatomical completeness with PCI is unlikely. **[22]**

The benefits of surgery must, however, be considered together with its early hazards. Patients with DKD commonly have associated anemia, heart failure, peripheral vascular disease, metabolic abnormalities, and reduced kidney reserve. These conditions may increase operative morbidity, while postoperative acute kidney injury, infection, and prolonged hospitalization remain important clinical concerns in patients with advanced renal dysfunction. **[22]**

Thus, the presence of diabetes and multivessel disease does not automatically establish CABG as the preferred strategy for every patient. The expected durability of bypass surgery must be balanced against perioperative risk, renal status, coronary targets, life expectancy, functional condition, and patient preference. **[23]**

PCI or CABG: Moving Beyond a Single-Strategy Approach

Comparison between PCI and CABG is one of the most difficult areas in the treatment of DKD-associated coronary disease. Surgical revascularization may offer an important long-term advantage when multivessel disease is extensive and anatomical complexity is high. Conversely, PCI avoids major surgery, generally permits faster recovery, and may be more suitable in patients whose comorbidity burden makes operative treatment unattractive. **[23]**

Contemporary decision-making therefore increasingly depends on individual anatomy rather than diagnostic labels alone. The number and location of significant stenoses, left main involvement, lesion length, degree of calcification, distal vessel quality, likelihood of complete revascularization, ventricular function, renal impairment, operative risk, and overall clinical condition should all influence the strategy chosen. **[24]**

A multidisciplinary approach is particularly valuable in borderline cases. Integrating the perspectives of interventional cardiology, cardiac surgery, nephrology, and cardiovascular imaging can provide a more balanced estimate of immediate procedural risk and long-term benefit. This is especially important when both PCI and CABG are technically possible but neither option is clearly superior for a particular patient. **[24]**

Outcomes and Residual Cardiovascular Risk

Despite improvements in coronary treatment, patients with DKD continue to experience worse cardiovascular outcomes than lower-risk CAD populations. Renal dysfunction is itself strongly associated with cardiovascular events and mortality, while diffuse coronary disease, calcification, and multiple comorbidities contribute additional risk following revascularization. **[25]**

The severity of renal impairment is particularly relevant to prognosis. Progressive loss of kidney function is accompanied by increasing rates of major cardiovascular events and all-cause mortality. Consequently, assessment of coronary prognosis should not be separated from evaluation of renal disease trajectory. **[25]**

Modern PCI has nevertheless improved outcomes through better drug-eluting stents, enhanced lesion preparation, and greater use of intracoronary imaging. Similarly, CABG continues to provide durable treatment in properly selected patients with extensive disease. The remaining challenge is identifying which patients derive sufficient long-term benefit from an invasive approach to justify its immediate cardiovascular and renal risks. **[21,23]**

Residual risk after either procedure also highlights the systemic nature of the disease. Revascularization treats clinically important coronary lesions but does not eliminate the metabolic, inflammatory, endothelial, and calcific processes responsible for continuing atherosclerosis. Long-term management must therefore combine technically successful coronary treatment with persistent control of cardiovascular and renal risk factors. **[18,25]**

Future Perspective

Further improvement in outcomes will likely depend less on simply expanding the number of available interventions and more on selecting and performing them appropriately. Better identification of patients most likely to benefit from revascularization, increased use of anatomical and intracoronary assessment, improved management of calcified lesions, and strategies that reduce kidney injury may allow treatment to become increasingly individualized.

The concept of cardiorenal management is particularly relevant to DKD because the heart and kidneys cannot be managed independently in advanced disease. Coronary interventions should be planned with preservation of renal function in mind, while renal therapies should form part of broader cardiovascular prevention. Such integration may be more important to long-term prognosis than any single procedural innovation.

Conclusion

Coronary artery disease in diabetic kidney disease represents a distinct and particularly complex form of atherosclerotic cardiovascular disease. Diffuse plaque involvement, multivessel disease, severe calcification, distal vessel abnormalities, and reduced renal reserve make both the disease itself and its treatment more challenging.

Contemporary PCI, modern drug-eluting stents, improved lesion preparation, and intravascular imaging have broadened percutaneous treatment possibilities, whereas CABG retains an important role when extensive multivessel anatomy favors durable surgical revascularization. Neither approach should be applied routinely on the basis of diabetes or kidney disease alone.

Optimal management requires integration of coronary anatomy, renal function, procedural risk, comorbid disease, likelihood of complete revascularization, and expected long-term benefit. Combining

individualized revascularization with intensive cardiorenal medical therapy remains the most appropriate strategy for improving outcomes in this vulnerable population.

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