Diabetic Kidney Disease

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Recommendations for screening

- At least once a year, assess urinary microalbumin (e.g., spot urinary albumin–to–creatinine ratio) and estimated glomerular filtration rate in patients with type 1 diabetes with duration of >5 years, in all patients with type 2 diabetes, and in all patients with comorbid hypertension. B

Recommendations for Treatment

- Optimize glucose control to reduce the risk or slow the progression of diabetic kidney disease. A
- Optimize blood pressure control to reduce the risk or slow the progression of diabetic kidney disease. A
- For people with non dialysis-dependent diabetic kidney disease, dietary protein intake should be approximately 0.8 g/kg body weight per day (the recommended daily allowance). For patients on dialysis, higher levels of dietary protein intake should be considered. B
- In nonpregnant patients with diabetes and hypertension, either an ACE inhibitor or an angiotensin receptor blocker is recommended for those with modestly elevated urinary albumin–to–creatinine ratio (30–299 mg/g creatinine) B and is strongly recommended for those with urinary albumin–to– creatinine ratio >300 mg/g creatinine and/or estimated glomerular filtration rate < 60 mL/min/1.73 m2. A

Recommendations for Treatment

- Periodically monitor serum creatinine and potassium levels for the development of increased creatinine or changes in potassium when ACE inhibitors, angiotensin receptor blockers, or diuretics are used. B
- Continued monitoring of urinary albumin–to–creatinine ratio in patients with albuminuria treated with an ACE inhibitor or an angiotensin receptor blocker is reasonable to assess the response to treatment and progression of diabetic kidney disease. E
- An ACE inhibitor or an angiotensin receptor blocker is not recommended for the primary prevention of diabetic kidney disease in patients with diabetes who have normal blood pressure, normal urinary albumin–to–creatinine ratio (<30 mg/g creatinine), and normal estimated glomerular filtration rate. B

Recommendations for Treatment

- When estimated glomerular filtration rate is <60 mL/min/1.73 m2, evaluate and manage potential complications of chronic kidney disease. E
- Patients should be referred for evaluation for renal replacement treatment if they have an estimated glomerular filtration rate <30 mL/min/1.73 m2. A
- Promptly refer to a physician experienced in the care of kidney disease for uncertainty about the etiology of kidney disease, difficult management issues, and rapidly progressing kidney disease. B

Selected complications of CKD

Complications	Medical and laboratory evaluation
Elevated blood pressure	Blood pressure and weight
Metabolic acidosis	Serum electrolytes
Anemia Volume overload	Hemoglobin, iron testing if indicated History, physical exam and weight
Electrolyte abnormalities	Serum electrolytes
Metabolic bone disease	Serum calcium, phosphate, PTH, vitamin D 25 OH

Complications of CKD generally become prevalent when eGFR falls below 60 mL/min/1.73 m_2 (stage 3 CKD or greater) and become more common and severe as CKD progresses. Evaluation of elevated blood pressure and volume overload should occur at every possible clinical contact; laboratory evaluations are generally indicated every 6–12 months for stage 3 CKD, every 3–5 months for stage 4 CKD, and every 1–3 months for stage 5 CKD, or as indicated to evaluate symptoms or changes in therapy. PTH, parathyroid hormone; 25(OH)D, 25-hydroxyvitamin D

Treatment of Diabetes with CKD
Glycemia

- Intensive glycemic control with the goal of achieving near-normoglycemia has been shown in large prospective randomized studies to delay the onset and progression of albuminuria and reduced eGFR in patients with type 1 diabetes and type 2 diabetes.
- The presence of diabetic kidney disease affects the risks and benefits of intensive glycemic control and a number of specific glucose-lowering medications.

Specific Glucose Lowering Medicines

- Some glucose-lowering medications also have effects on the kidney that are direct, i.e., not mediated through glycemia. For example, SGLT2 inhibitors reduce renal tubular glucose reabsorption, weight, systemic blood pressure, intraglomerular pressure, and albuminuria and slow GFR loss through mechanisms that appear independent of glycemia. Glucagon-like peptide 1 receptor agonists and dipeptidyl peptidase 4 inhibitors also have direct effects on the kidney and have been reported to improve renal outcomes compared with placebo.

Specific Glucose Lowering Medicines

- Patients with diabetic kidney disease are at high risk of cardiovascular events, and some SGLT2 inhibitors and glucagon- like peptide 1 receptor agonists have demonstrated cardiovascular benefits. Namely, in EMPA-REG OUTCOME, CANVAS, and LEADER, empagliflozin, canagliflozin, and liraglutide, respectively, each reduced cardiovascular events, evaluated as primary outcomes, compared with placebo.
- However, the cardiovascular benefits of empagliflozin, canagliflozin, and liraglutide were similar among participants with and without kidney disease at baseline.

Specific Glucose Lowering Medicines

- With reduced eGFR, drug dosing may require modification. The U.S. Food and Drug Administration (FDA) revised guidance for the use metformin in diabetic kidney disease in 2016, recommending use of eGFR instead of serum Cr to guide treatment and expanding the pool of patients with kidney disease for whom metformin treatment should be considered. Revised FDA guidance states that metformin is contraindicated in patients with an eGFR <30 mL/min/ 1.73 m2, eGFR should be monitored while taking metformin, the benefits and risks of continuing treatment should be reassessed when eGFR falls <45 mL/min/1.73 m2, metformin should not be initiated for patients with an eGFR <45 mL/min/1.73 m2, and metformin should be temporarily discontinued at the time of or before iodinated contrast imaging procedures in patients with eGFR 30–60 mL/min/ 1.73 m2

Treatment of Diabetics with CKD

- ACE inhibitors or ARBs are the preferred first-line agent for blood pressure treatment among patients with diabetes, hypertension, eGFR <60 mL/min/1.73 m2, and UACR >300 mg/g Cr because of their proven benefits for prevention of CKD progression. In general, ACE inhibitors and ARBs are considered to have similar benefits and risks. In the setting of lower levels of albuminuria (30–299 mg/g Cr), ACE inhibitor or ARB therapy has been demonstrated to reduce progression to more advanced albuminuria (>300 mg/g Cr) and cardiovascular events but not progression to ESRD

Treatment of Diabetics with CKD

- Absent kidney disease, ACE inhibitors or ARBs are useful to control blood pressure but may not be superior to alternative proven classes of antihypertensive therapy, including thiazide-like diuretics and dihydropyridine calcium channel blockers
- In a trial of people with type 2 diabetes and normal urine albumin excretion, an ARB reduced or suppressed the development of albuminuria but increased the rate of cardiovascular events. In a trial of people with type 1 diabetes exhibiting neither albuminuria nor hypertension, ACE inhibitors or ARBs did not prevent the development of diabetic glomerulopathy assessed by kidney biopsy.
- ACE inhibitors or ARBs are not recommended for patients without hypertension to prevent the development of diabetic kidney disease.

Treatment of Diabetics with CKD

- Two clinical trials studied the combinations of ACE inhibitors and ARBs and found no benefits on CVD or diabetic kidney disease, and the drug combination had higher adverse event rates (hyperkalemia and/or AKI)
- Mineralocorticoid receptor antagonists (spironolactone, eplerenone) in combination with ACE inhibitors or ARBs remain an area of great interest. Mineralocorticoid receptor antagonists are effective for management of resistant hypertension, have been shown to reduce albuminuria in short-term studies of diabetic kidney disease, and may have additional cardiovascular benefits. There has been, however, an increase in hyperkalemic episodes in those on dual therapy, and larger, longer trials with clinical outcomes are needed before recommending such therapy.

Referral to Nephrologist

- Consider referral to a physician experienced in the care of kidney disease when there is uncertainty about the etiology of kidney disease, difficult management issues (anemia, secondary hyperparathyroidism, metabolic bone disease, resistant hypertension, or electrolyte disturbances), or advanced kidney disease (eGFR < 30 mL/min/1.73 m2) requiring discussion of renal replacement therapy for ESRD.

Thank you