Section 6: Kidney Care

<table>
<thead>
<tr>
<th>Concern</th>
<th>Care/Test</th>
<th>Frequency</th>
</tr>
</thead>
</table>
| Kidney Care | ▪ Check albumin/creatinine ratio for microalbuminuria using a random urine sample; Goal < 30 mg/g  
▪ Check serum creatinine and estimate GFR  
▪ Perform routine urinalysis          | **Type 1**: At puberty or after 5 years duration, then annually  
**Type 2**: At diagnosis, then annually  
At diagnosis, then annually  
At diagnosis, then as indicated |

MAIN TOPICS INCLUDED IN THIS SECTION:
- Screening for Kidney Disease and Interpreting the Results
- Serum Creatinine and Estimated Glomerular Filtration Rate (eGFR)
- Management of Kidney Disease
- Blood Pressure Control
- Hypoglycemia
- Ongoing Evaluation and Monitoring of Therapy
- Referral to a Nephrologist and Coordination of Care
- Additional Resources
- References
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High blood glucose associated with poorly controlled diabetes is the leading cause of chronic kidney disease in the United States. Diabetic nephropathy occurs in 20-40% of people with diabetes. Without treatment, individuals with diabetic kidney disease often progress to kidney failure. Progression of diabetic kidney disease is influenced primarily by glycemic control and use of agents that block the rennin-angiotensin-aldosterone system (angiotensin converting enzyme inhibitors or angiotensin receptor blockers) to control blood pressure. These agents should not be used in women planning a pregnancy or are pregnant. Interventions after early detection of kidney damage, such as careful blood glucose control and angiotensin II blockad reduce the risk of the development and progression of diabetic nephropathy. Furthermore, cardiovascular risk increases as albuminuria increases and the estimated glomerular filtration rate (eGFR) decreases. Screening for and treating diabetic kidney disease adds years to life and is cost effective.

People with diabetes should be informed of the link between diabetes and kidney disease and should understand how they can decrease their risk. Special educational, cultural, and literacy needs must be taken into consideration while respecting the individual’s willingness to change behavior. Key educational points include:

- The role of blood glucose control in preventing or slowing the progression of kidney disease
- The importance of blood pressure control for cardiovascular health
- The use of specific agents for kidney-protection
- The importance of an annual kidney function test and appropriate follow-up. People in the early stages of chronic kidney disease are typically asymptomatic
- The importance of lifestyle modifications (e.g., weight loss, physical activity, tobacco cessation, and dietary changes) as needed for preventing or slowing the progression of kidney disease and any individual sodium and protein restrictions
- The benefits of early referral to a nephrologist for declining eGFR and what to expect from the visit

Ongoing support and continued reinforcement are essential for self-management and for learning to cope with chronic complications of declining kidney function.

Screening for Kidney Disease and Interpreting the Results

Kidney disease in people with diabetes generally progresses from microalbuminuria (loss of small amounts of albumin in the urine) to macroalbuminuria (loss of large amounts of albumin in the urine), and eventually leads to loss of kidney function. However, people with type 2 diabetes do not necessarily follow this progressive and detectable sequence and often present with more advanced kidney disease.

People with type 2 diabetes should be screened for microalbuminuria using an albumin/creatinine ratio test (using a random urine sample) and have a serum creatinine test to estimate glomerular filtration rate (GFR) at the time of diagnosis and annually thereafter.

People with type 1 diabetes should be screened for microalbuminuria using an albumin/creatinine ratio test (using a random urine sample) after five years of disease duration or at the onset of puberty (whichever occurs first) and annually thereafter. They should also have a serum creatinine test to estimate glomerular filtration rate (GFR) at the time of diagnosis and annually thereafter. If the initial screening test is positive (> 30 mg/dL), the albumin/creatinine ratio test should be repeated in 3-6 months to confirm the diagnosis. See the Tool: Screening and Initial Recommendations for Diabetic Kidney Disease Pathway located in the Tools Section.
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Screening should also be considered for certain groups, such as those with a family history of kidney disease and/or hypertension, those with a history of chronically poor glycemic control, and those of African American, Hispanic/Latino, or American Indian race/ethnicity. Interpretation of albumin/creatinine ratio results are presented in Table 6-1.

Table 6-1: Albumin/Creatinine Ratio Results

<table>
<thead>
<tr>
<th>Condition</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt; 30 mg/g</td>
</tr>
<tr>
<td>Microalbuminuria</td>
<td>30-300 mg/g</td>
</tr>
<tr>
<td>Macroalbuminuria</td>
<td>&gt; 300 mg/g</td>
</tr>
</tbody>
</table>

It is appropriate to obtain a routine urinalysis when a person is diagnosed with diabetes and then to check as indicated to assess for infection, ketones, or any other abnormalities. A routine urinalysis is not sensitive enough to detect microalbuminuria and is therefore not an appropriate test for early detection of diabetic kidney disease.

The albumin/creatinine ratio (sometimes called a microalbumin/creatinine ratio) from a random urine sample is the most accurate and easiest test available to assess microalbuminuria. It can be used to both screen for and track the progression of proteinuria and the response to treatment. Check with your lab to find out how to order the albumin/creatinine ratio, as a lab may request that you order both a urine microalbumin and a urine creatinine together, as shown in the example in the box below. Some labs provide the calculated ratio while others require that you calculate the ratio yourself.

Example: Calculating the albumin/creatinine ratio in mg/g

If the urine microalbumin is 10 mg/L and the urine creatinine is 100 mg/dL, then the albumin/creatinine ratio is 10 mg/g. In this example, you first need to multiply the urine creatinine value by 10 in order to convert mg/dL to mg/L (i.e., 100 mg/dL x 10 dL/L = 1000 mg/L). Then simply divide the urine albumin value (10 mg/L) by the urine creatinine value (1000 mg/L) to arrive at the ratio (10 mg/L /1000 mg/L = 0.01). Then multiply by 1000 to express the value as (mg albumin/g creatinine). If the two values are already in the same units, simply divide the albumin value by the creatinine value and then multiply by 1000.

There are several other ways to measure microalbuminuria; these tend to be less accurate or in the case of timed collections (e.g., overnight or 24-hour urine collections), more cumbersome. Albumin excretion can vary from day to day and can be affected by uncontrolled blood pressure, high blood glucose, fever, urinary tract infection, hematuria, and strenuous physical activity.

Once a person has an albumin/creatinine ratio of > 300 mg/g (macroalbuminuria), a protein/creatinine ratio is an appropriate method to track changes in proteinuria. The protein/creatinine ratio can be measured from a random urine sample and can be used to follow progression of kidney disease and response to therapy. A mid-morning collection is considered most accurate.
Serum Creatinine and Estimated Glomerular Filtration Rate (eGFR)

An estimated glomerular filtration rate (eGFR), derived from serum creatinine, is also recommended at diagnosis and then annually in all adults with diabetes regardless of the degree of urine albumin excretion. Estimated GFR is considered the best marker of kidney function in people with chronic kidney disease. A serum creatinine alone (without eGFR) is inadequate to estimate kidney damage or function.

Multiple calculators are available to estimate GFR based on a serum creatinine and other individual characteristics. The Cockcroft Gault equation requires a person’s weight. The Modification of Diet in Renal Disease (MDRD) Study equation requires serum creatinine, age, gender, and race. Two web-based calculators are provided below:


The MDRD Study equation is most accurate for individuals with eGFRs < 60 ml/min/1.73 m² (stage 3 chronic kidney disease and higher). Based on the level of eGFR, individuals with diabetic kidney disease can be placed into one of five stages, as shown in Table 6-2. This is helpful in designing a clinical action plan.

<table>
<thead>
<tr>
<th>Chronic Kidney Disease Stage</th>
<th>GFR (ml/min/1.73 m²)</th>
<th>Action (including action from preceding stages)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1: Kidney damage with normal or ↑ GFR²</td>
<td>≥ 90</td>
<td>Diagnosis, treatment, treatment of comorbid conditions, slowing progression, cardiovascular disease risk reduction</td>
</tr>
<tr>
<td>Stage 2: Kidney damage with mild ↓ GFR</td>
<td>60-89</td>
<td>Estimate progression</td>
</tr>
<tr>
<td>Stage 3: Moderate ↓ GFR</td>
<td>30-59</td>
<td>Evaluate and treat complications; refer to a nephrologist</td>
</tr>
<tr>
<td>Stage 4: Severe ↓ GFR</td>
<td>15-29</td>
<td>Preparation for kidney replacement therapy; referral to a nephrologist (if not already done); possible referral for transplantation</td>
</tr>
<tr>
<td>Stage 5: Kidney failure &lt; 15 (or dialysis)</td>
<td>Kidney replacement therapy (if uremia present)</td>
<td></td>
</tr>
</tbody>
</table>

² most commonly microalbuminuria

Estimated GFR is most valid for values less than 60 mL/min/1.73 m², which includes the clinically significant chronic kidney disease categories. While many labs in Wisconsin now automatically report eGFR when a serum creatinine is ordered, some labs provide the absolute number when the value is < 60 mL/min/1.73 m² and report “> 60 mL/min/1.73 m²” when the value is above 60 mL/min/1.73 m² to account for the uncertainty of the calculation at that value.
Management of Kidney Disease

Angiotensin-converting Enzyme (ACE) inhibitors or Angiotensin Receptor Blockers (ARBs) are effective treatments for microalbuminuria or macroalbuminuria. They slow the progression of diabetic kidney disease independent of their effect on lowering blood pressure. No adequate head-to-head comparisons have been made between ACE inhibitors and ARBs; therefore, clinical judgment should be used to guide treatment decisions, taking an individual’s characteristics into account. The use of ARBs has been studied more thoroughly in people with type 2 diabetes than in people with type 1 diabetes. An ACE inhibitor is a reasonable first line option for cost and efficacy in controlling progression of microalbuminuria. If there is persistent proteinuria and/or ACE inhibitor intolerance, changing to an ARB is reasonable.

The effect of ACE inhibitors/ARB therapy on albuminuria is dose dependent. Medium to high ACE inhibitor/ARB doses were used in clinical trials. Adverse effects from the use of ACE inhibitors and ARBs are more common in people with chronic kidney disease. The most common side effects (e.g., early decrease in eGFR, hypotension, and hyperkalemia) can usually be managed without discontinuing the agent. With careful monitoring of therapy, ACE inhibitors or ARBs can treat most people, even those with low eGFRs.

Blood Pressure Control

In addition to ACE inhibitor/ARB therapy, aggressive blood pressure control is a priority in people with diabetic kidney disease. According to recent studies, most people require more than one antihypertensive agent to meet the blood pressure target of < 130/80 mmHg. If blood pressure remains high on ACE inhibitors/ARBs alone, adding medication from a second class of antihypertensive can help achieve blood pressure control. Diuretics are particularly effective when added to ACE inhibitors or ARBs. For additional information, see the Kidney Disease Outcomes Quality Initiative Guidelines on Hypertension and Antihypertensive Agents in Chronic Kidney Disease: http://www.kidney.org/professionals/kdoqi/guidelines.cfm.

Caution: Do not prescribe ACE inhibitor/ARB therapy to women of childbearing age who are not using contraception or to pregnant women because of the potential risk for fetal abnormalities.

Hypoglycemia

Hypoglycemia is a major concern for people with CKD and diabetes. Insulin and some oral medications may have a prolonged half-life when kidney function is impaired. It is imperative for people on insulin therapy or oral agents that can lead to hypoglycemia (e.g., sulfonylureas) to monitor their glucose levels closely and reduce doses of oral medications and insulin as needed to avoid hypoglycemia.
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Ongoing Evaluation and Monitoring of Therapy

Evaluate individuals with diabetes annually for kidney disease. This includes checking for microalbuminuria, hypertension, and decreased eGFR (serum creatinine to estimate the GFR). For people with documented chronic kidney disease, base ongoing follow-up on clinical circumstances (e.g., blood pressure, kidney function, potassium level, and medication dose changes). Repeat the albumin/creatinine ratio or the protein/creatinine ratio every three to six months to monitor progression of kidney disease and response to therapy.

People with diabetes and CKD have increased risk of cardiovascular disease and commonly have dyslipidemia. Treat these people according to current lipid guidelines for high-risk groups.

Referral to a Nephrologist and Coordination of Care

Referral to a nephrologist is recommended in all of the following circumstances:
- The eGFR is less than 60 mL/min/1.73 m²
- Loss of kidney function is rapid (i.e., greater than 10-15 mL/min/1.73 m² loss per year)
- The blood pressure target cannot be achieved
- Anytime the primary care provider feels he or she needs assistance in carrying out the recommended action plan (see Table 6-2)

Caring for people with kidney disease is challenging and requires expertise from a variety of specialists (e.g., dietitians, mental health care providers, nurses, pharmacists, social workers), all of whom must carefully integrate diabetes and kidney disease care. Early intervention and timely referrals for consultation with kidney experts and other specialty services can lead to optimal management of diabetes and kidney disease.

Epidemiologic data have shown that early referral to nephrologists for subjects with chronic kidney disease are associated with better long-term outcomes.

Additional Resources

2. Educational DVD Titled: The Links to Chronic Kidney Disease: Diabetes High Blood Pressure, and Family History, Most of Us Don’t Know the Half of it! Website located at: http://wlf.info/index.php?option=com_content&view=article&id=37&Itemid=40&28e5bbf660cb545fc854f5c048c7be7c=b55b09b55cbea4590b9e105f86de8b0f.
References


