Can J Diabetes 42 (2018) S201–S209

Contents lists available at ScienceDirect

Canadian Journal of Diabetes

journal homepage: www.canadianjournalofdiabetes.com

2018 Clinical Practice Guidelines

Chronic Kidney Disease in Diabetes

Diabetes Canada Clinical Practice Guidelines Expert Committee

Philip McFarlane MD, PhD, FRCPC, David Cherney MD, PhD, FRCPC, Richard E. Gilbert MBBS, PhD, FACP, FRACP, FRCPC, Peter Senior MBBS, PhD, FRCP

KEY MESSAGES

- Identification of chronic kidney disease in people with diabetes requires screening for proteinuria, as well as an assessment of serum creatinine converted into an estimated glomerular function rate (eGFR).
- All individuals with chronic kidney disease should be considered at high risk for cardiovascular events and should be treated to reduce these risks.
- The development and progression of renal damage in diabetes can be reduced and slowed through intensive glycemic control and optimization of blood pressure. Progression of chronic kidney disease in diabetes can also be slowed through the use of medications that disrupt the renin angiotensin aldosterone system.

KEY MESSAGES FOR PEOPLE WITH DIABETES

- The earlier that the signs and symptoms of chronic kidney disease in diabetes are detected, the better, as it will reduce the chance of progression to advanced kidney disease and the need for dialysis or transplant.
- You should have your blood and urine tested annually for early signs of chronic kidney disease in diabetes.
- If you are found to have signs of chronic kidney disease, your health-care provider may recommend lifestyle or medication changes to help delay more damage to your kidneys.

PRACTICAL TIPS

Management of Potassium and Creatinine During the Use of Angiotensin Converting Enzyme (ACE) inhibitor or Angiotensin II Receptor Blocker (ARB) or Direct Renin Inhibitor (DRI) Therapy

- Check serum potassium and creatinine at baseline and within 1 to 2 weeks of initiation or titration of therapy AND during times of acute illness.
- If potassium becomes elevated or creatinine increases by more than 30% from baseline, therapy should be reviewed and serum creatinine and potassium levels should be rechecked.
- Mild-to-moderate stable hyperkalemia:
  - Counsel on a low-potassium diet.
  - If persistent, non-potassium-sparing diuretics and/or oral sodium bicarbonate (in those with a metabolic acidosis) should be considered.
  - Consider temporarily reducing or holding RAAS blockade (i.e. ACE inhibitor, ARB or DRI).
- Severe hyperkalemia:
  - In addition to emergency management strategies, RAAS blockade should be held or discontinued.

Introduction

Diseases of the kidney are a common finding in people with diabetes, with up to one-half demonstrating signs of renal damage in their lifetime (1–3). Diabetes is the leading cause of kidney disease in Canada (4). Kidney disease can be a devastating complication, as it is associated with significant reductions in both length and quality of life (5,6). A variety of forms of chronic kidney disease (CKD) in diabetes can be seen, including diabetic nephropathy, ischemic nephropathy related to vascular disease, hypertensive nephrosclerosis, as well as other renal diseases that are unrelated to diabetes (7,8) (Figure 1). This chapter discusses how to screen for and diagnose CKD in people with diabetes, how to slow its progression, and the impact of CKD on other aspects of diabetes management.

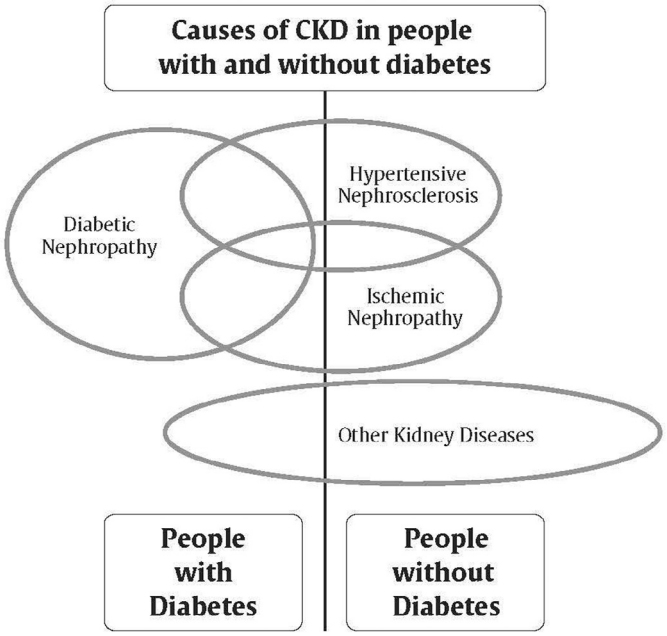

Figure 1. Causes of CKD in people with and without diabetes. *CKD*, chronic kidney disease.

Conflict of interest statements can be found on page S207.

https://doi.org/10.1016/j.jcjd.2017.11.004

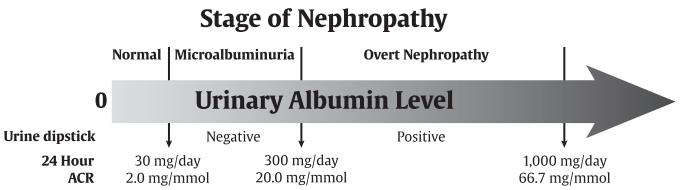

Figure 2. Level of urinary albumin by various test methods and stage of CKD in diabetes.
ACR, albumin to creatinine ratio; *CKD*, chronic kidney disease.

Diabetic Nephropathy

The classical description of diabetic nephropathy is a slow and progressive increase in albuminuria, followed later in the disease by a decrease in estimated glomerular filtration rate (eGFR) below 60 mL/min/1.73 m^2, which can, eventually, lead to end stage renal disease (ESRD) (1,9,10) (Figure 2). Key risk factors include long duration of diabetes; non-optimal glycemic, blood pressure and plasma lipid control; obesity (11); and cigarette smoking(12). Many of these risk factors are modifiable.

The earliest stage of diabetic nephropathy is hyperfiltration, where the glomerular filtration rate (GFR) is significantly higher than normal. Identification of hyperfiltration is not clinically useful, as it is difficult to determine from routine testing and is not present in all people with early diabetic nephropathy. Persistent albuminuria is considered the earliest clinical sign of diabetic nephropathy. Initially, small amounts of albumin are leaked, below the detection threshold of a urine dipstick. This stage is referred to as "microalbuminuria". Over time, albuminuria can worsen so that the urinary albumin excretion is sufficiently high to be detectable by a urine dipstick, a stage known as "overt nephropathy" (Table 1). The rate of progression from normoalbuminuria to microalbuminuria, then to overt kidney disease, is usually slow, typically taking five years or longer to progress through each stage (13,14). During the early stages of diabetic nephropathy, the rate of loss of renal function is relatively slow (a decrease in eGFR of 1 to 2 mL/min/1.73 m^2/year), and not impressively higher than what is seen in the general population (0.5 to 1.0 mL/min/1.73 m^2/year) (15). However, late in the overt kidney disease phase, the rate of decline of renal function can accelerate (5 to 10 mL/min/1.73 m^2/year). Thus, significant renal dysfunction is not usually seen until late in the course of diabetic nephropathy (16).

It is important to note that the rate of progression can vary between individuals, and that the clinical markers of the disease (i.e. eGFR, urinary albumin levels) do not always correlate well with the severity of renal disease seen on biopsy (17). Additionally, intensive glycemic control, optimization of blood pressure (BP), and the use of renal protective drugs, can slow or stop progression of diabetic nephropathy.

Other Kidney Diseases in People with Diabetes

Diabetic nephropathy is a major cause of CKD in diabetes; however, people with diabetes can also get CKD from other causes, including hypertensive nephrosclerosis or ischemic nephropathy from atherosclerotic changes to small or large renal arteries. In addition, there can be significant overlap (Figure 1). Ischemic nephropathy is characterized by a reduced GFR, usually with minimal or no increase in albuminuria. Kidney biopsy series in people with type 2 diabetes have found that non-diabetic glomerular disease, particularly ischemic kidney disease, is as common as CKD in diabetes in people with diabetes (7). Clinical studies have suggested that one-quarter to one-half of people with diabetes and significant kidney function impairment do not have albuminuria (18–20). These studies suggest that testing for albuminuria may be insufficient in identifying all people with diabetes who have renal disease. In addition to measurements of urinary albumin excretion, estimations of the level of kidney function and urinalyses are required to identify people with kidney disease other than diabetic nephropathy.

In most cases, the risk of ESRD in diabetes does not appear to matter whether the renal diagnosis is one of diabetic nephropathy or an alternative diagnosis, and the management is the same (21). However, Table 2 lists some concerning clinical and laboratory features that would lead to suspicion of a kidney disease unrelated to diabetes and require additional testing or referral, and possible renal biopsy (22–25).

Screening for Chronic Kidney Disease in People with Diabetes

Screening for CKD in people with diabetes involves an assessment of urinary albumin excretion and a measurement of the overall level of kidney function through an eGFR. Persistent abnormalities (lasting >3 months) of either urinary albumin excretion or eGFR, or significant urinalysis abnormalities lead to the diagnosis of CKD in people with diabetes. People with type 1 diabetes are not expected to have kidney disease at the time of onset of diabetes, so screening can be delayed until the duration of diabetes exceeds 5 years. Significant renal disease can be present at the time of diagnosis of type 2 diabetes (26,27), so screening should be initiated immediately at the time of diagnosis in this group.

Screening for Albuminuria

When screening for albuminuria, the test of choice is the random urine albumin to creatinine ratio (urine ACR). The 24-hour urine collection for protein/albumin remains the gold standard; however, it is cumbersome to implement on a large scale, inconvenient for people, and is often performed incorrectly (28–32). The random urine for albumin is insufficient, as the urinary albumin concentration can

Table 1
Stages of diabetic nephropathy by level of urinary albumin level

Stages of Diabetic Nephropathy by Level of Urinary Albumin Level			
Stage of nephropathy	**Urine dipstick for protein**	**Urine ACR (mg/mmol)**	**24-hour urine collection for albumin**
Normal	Negative	<2	<30 mg/day
Microalbuminuria	Negative	2-20	30-300 mg/day
Overt nephropathy	Positive	>20 >67	>300 mg/day >1,000 mg/day
Values are for urinary albumin, not total urinary protein, which will be higher than urinary albumin levels. ACR results may be elevated with conditions other than diabetic nephropathy (see text and Table 4).			

ACR, albumin to creatinine ratio.