Microvascular complications: Nephropathy

Recommendations

Recommendation	Reference	Grade*
At least once a year, assess urine ACR and eGFR in all patients with type 2 diabetes, regardless of treatment	1 American Diabetes Association, 2019	B
To prevent the onset and delay the progression of CKD, people with diabetes should be treated to optimise blood glucose levels and blood pressure	2 Diabetes Canada, 2018	A, level 1A
It is recommended that adults with type 2 diabetes and CKD with either hypertension or albuminuria receive an ACE inhibitor or an ARB to delay progression of CKD	2 Diabetes Canada, 2018	A, level 1A
Combinations of ACE inhibitor, ARB or DRI should not be used in the management of diabetes and CKD	2 Diabetes Canada, 2018	A, level 1
People with diabetes on an ACE inhibitor or an ARB should have their serum creatinine and potassium levels checked at baseline and within 1–2 weeks of initiation or titration of therapy, and during times of acute illness	2 Diabetes Canada, 2018	D, consensus
For patients with type 2 diabetes and chronic kidney disease, consider use of an SGLT2 inhibitor or GLP-1 RA shown to reduce risk of CKD progression, cardiovascular events, or both	1 American Diabetes Association, 2019	C
Adults with diabetes and CKD should be given a 'sick-day' medication list that outlines which medications should be withheld during times of acute illness	2 Diabetes Canada, 2018	D, consensus
All people with diabetes and CKD should be offered a comprehensive, multifaceted program to reduce cardiovascular risk (refer to the section 'Type 2 diabetes and cardiovascular risk')	2 Diabetes Canada, 2018	A, level 1A
People with diabetes should be informed that smoking increases the risk of CKD	3 NHMRC 2009	B

ACE, angiotensin-converting enzyme; ACR, albumin-to-creatinine ratio; ARB, angiotensin receptor blocker; CKD, chronic kidney disease; CVD, cardiovascular disease; DRI, direct renin inhibitor; eGFR, estimated glomerular filtration rate; GLP-1 RA, glucagon-like peptide-1 receptor agonist; SGLT2, sodium glucose co-transporter 2

*Refer to 'Explanation and source of recommendations' for explanations of the levels and grades of evidence.

Clinical context

Diabetic nephropathy is the single leading cause of end-stage renal disease.[4]

Diabetic nephropathy occurs in one in four women and one in five men with type 2 diabetes,[5] and is more common in Aboriginal and Torres Strait Islander peoples.[6]

Some non-European groups (eg Southeast Asian, African American, Afro-Caribbean, Maori peoples) have high rates of end-stage diabetic nephropathy, possibly, but not entirely, due to later diagnosis and sub-optimal care.[7]

There is strong evidence that treatment in the early stages of chronic kidney disease (CKD) reduces progression of kidney damage, morbidity and mortality. Therefore,

people with type 2 diabetes should be screened and retested regularly to detect early indications of kidney damage and to monitor the effects of treatment.

Systolic blood pressure appears to be the best indicator of the risk of CKD in type 2 diabetes. However, the optimal and safest lower limit of systolic blood pressure has not been clearly defined. Refer to the section 'Type 2 diabetes and cardiovascular risk' and the table 'Type 2 diabetes: Goals for optimum management' for appropriate individual targets for blood pressure.

Independent of diabetes, proteinuria and reduced estimated glomerular filtration rate (eGFR) have been associated with increased risk of major cardiovascular disease; the additional presence of type 2 diabetes increases this risk to 2.4–4.6 times that of people without diabetes.[8]

In practice

Assessment

CKD is diagnosed by the persistent presence of elevated urine albumin excretion, low eGFR, or other manifestations of kidney damage.

Screening for CKD can be performed by either of the following two laboratory tests:

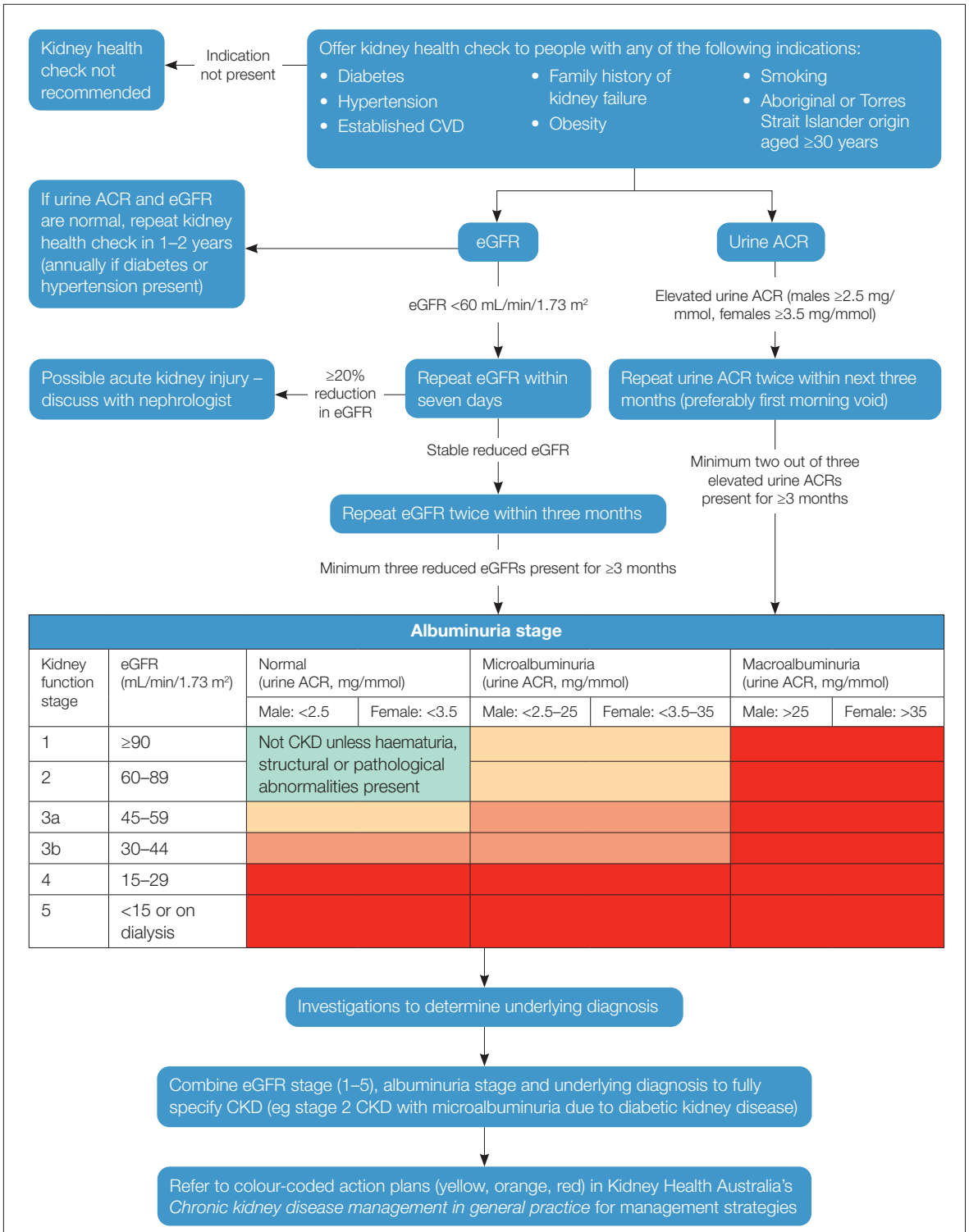
- random spot urine albumin-to-creatinine ratio (UACR; preferred method)
- serum creatinine converted into eGFR (eGFR is now automatically calculated from measurement of serum creatinine in Australia).

Any positive UACR needs to be confirmed with a repeated collection, and other possible contributors to transient albuminuria should be considered – for example:[2]

- urinary tract infection
- decompensated congestive heart failure
- menstruation
- acute severe elevation in blood glucose or blood pressure
- recent major exercise
- febrile illness.

Figure 1 provides an algorithm for the initial detection of CKD.

Figure 1. Algorithm for initial detection of chronic kidney disease[9]



ACR, albumin-to-creatinine ratio; CKD, chronic kidney disease; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate

Note: More frequent monitoring of kidney function may be required for people with glomerulonephritis, systemic lupus erythematosus or people on nephrotoxic drugs.

Source: Adapted with permission from Kidney Health Australia. Kidney Health Australia. Chronic kidney disease (CKD) management in general practice. 3rd edn. Melbourne: Kidney Health Australia, 2015.

Management of CKD

The baseline approach to managing CKD in people with type 2 diabetes is as follows:

- review medications
- exclude treatable causes of kidney disease such as renal artery stenosis, obstructive nephropathy and acute kidney injury due to dehydration
- perform CVD risk assessment – refer to the section 'Type 2 diabetes and cardiovascular risk'
- refer eligible patients to specialist renal care (Box 1), including an accredited practising dietitian or a credentialled diabetes educator for help with renal dietary recommendations.

Considerations regarding diabetes medications are as follows.

- **Metformin:** use with caution (as risks of lactic acidosis increase). Dose reduction is needed for eGFR 30–60 mL/min/1.73 m^2. Metformin should be ceased if eGFR falls below 30 mL/min/1.73 m^2.
- **Dipeptidyl peptidase-4 (DPP-4) inhibitors:**[10] no dose adjustment required for linagliptin in renal impairment due to hepatic metabolism. Reduction of dose of alogliptin, saxagliptin, sitagliptin and vildagliptin is required with eGFR <60 mL/min/1.73 m^2, due to pharmacologic accumulation without toxicity. Saxagliptin is not recommended with eGFR <15 mL/min/1.73 m^2, while others may be used with appropriate dose adjustment.[11]
- **Sulfonylureas:**[10] dose review is required, as CKD increases the risk of hypoglycaemia.
- **Sodium glucose co-transporter 2 (SGLT2) inhibitors:**[12–14] these require renal function for glycaemic effect. Dapagliflozin, empagliflozin and ertugliflozin may be used if eGFR >45 mL/min/1.73 m^2; however, non-glycaemic effects on reduction of progression of microalbuminuria and macroalbuminuria, and progression of renal disease and end-stage renal disease, have been demonstrated in recent trials down to an eGFR of 30 mL/min/1.73 m^2.[15–17]
- **Acarbose:**[10] avoid if creatinine clearance rate (CrCl) <25 mL/min.
- **Glitazones:** dose adjustment in patients with CKD is not needed.[10] Glitazones should not be used in people on dialysis, as safety in this patient group has not been established.
- **Glucagon-like peptide-1 receptor agonists (GLP-1 RAs):**[10] avoid using exenatide and liraglutide if CrCl <30 mL/min.[18,19] Initiate and escalate exenatide dose with caution if CrCl 30–50 mL/min. Dulaglutide may be used down to 15 mL/min, with no dose adjustment required.[20] GLP-1 RAs have been shown to slow microalbuminuria in recent trials.[16]
- **Insulin:** regular review of dose is indicated, as CKD increases risks of hypoglycaemia.
- Any potentially nephrotoxic medications, such as nonsteroidal anti-inflammatory drugs (NSAIDs), should be avoided.

Consider referral to a credentialled diabetes educator or accredited practising dietitian for advice on nutritional adjustments in advanced diabetic kidney disease.

Box 1. Referral criteria for specialist renal care[9]

- Estimated glomerular filtration rate (eGFR) <30 mL/min/1.73 m^2
- Stage 4 or 5 chronic kidney disease (CKD) of any cause
- Persistent significant albuminuria ≥30 mg/mmol
- Sustained decrease in eGFR of ≥25%, **or**
- Sustained decrease in eGFR of 15 mL/min/1.73 m^2 within 12 months
- CKD with hypertension despite at least three antihypertensive agents

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We acknowledge the Traditional Custodians of the lands and seas on which we work and live, and pay our respects to Elders, past, present and future.

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