UKMi North West

NICE Bites

September 2014: No 67

A summary of prescribing recommendations from NICE guidance

Chronic kidney disease

NICE CG182; 2014

This guideline covers the identification and management of CKD in adults in primary and secondary care.

Definition of terms

CKD	chronic kidney disease
CVD	cardiovascular disease
HF	heart failure
ACR	albumin:creatinine ratio
PCR	protein:creatinine ratio
GFR	glomerular filtration rate (measured OR estimated)
eGFR	estimated GFR
BP	blood pressure
Hb	haemoglobin
NSAID	non-steroidal anti-inflammatory drug
ACEI	angiotensin-converting enzyme inhibitor
ARB	angiotensin-receptor blocker

Chronic kidney disease

CKD is defined as abnormalities of kidney function or structure present for >3 months. This includes people with markers of kidney damage and those with a GFR<60ml/min/1.73m^2 on at least 2 occasions separated by a period of at least 90 days (with or without markers of kidney damage).

Classification of CKD

CKD is classified according to eGFR and ACR using 'G' to denote GFR category and 'A' to denote ACR category – **see Table 1**(final page).

Measuring kidney function

GFR can be estimated in different ways:

Creatinine-based estimate of GFR (eGFRcreatinine)

- Clinical laboratories should report eGFRcreatinine using a prediction equation as well as reporting serum creatinine.
- Advise people not to eat any meat in the 12 hours before a blood test for eGFRcreatinine. Ensure that blood samples are received and processed within 12 hours of venepuncture.
- In people with extremes of muscle mass e.g. bodybuilders, people with an amputation or with muscle wasting disorders – interpret eGFRcreatinine with caution. (Reduced muscle mass will lead to overestimation and increased muscle mass to underestimation of the GFR).
- In people of African-Caribbean or African family origin apply a correction factor to GFR values estimated using the CKD-EPI creatinine equation (multiply eGFR by 1.159).

Cystatin C-based estimate of GFR (eGFRcystatinC)

- Consider using eGFRcystatinC when an improved assessment of risk is needed and at initial diagnosis to confirm/exclude CKD in people with:
  - an eGFRcreatinine of 45 to 59ml/min/1.73m^2 sustained for at least 90 days, **AND**
  - no proteinuria (ACR <3mg/mmol) or other marker of kidney disease.
- Clinical laboratories should report eGFRcystatinC using a prediction equation as well as reporting serum cystatinC.
- Interpret eGFRcystatinC with caution in people with uncontrolled thyroid disease because values may be falsely elevated in people with hypothyroidism and reduced in people with hyperthyroidism.
- **Do NOT** diagnose CKD in people with:
  - an eGFRcreatinine of 45 to 59ml/min/1.73m^2 **AND**
  - an eGFRcystatinC >60ml/min/1.73m^2, **AND**
  - no other marker of kidney disease.

Other

- Consider a reference standard measure (inulin, Cr-EDTA, I-iothalamate or iohexol) when a highly accurate measure of GFR is required e.g. during chemotherapy monitoring and evaluation of renal function in potential living donors.

Reporting and interpreting eGFR values

- Confirm an eGFR result of <60ml/min/1.73m^2 in a person not previously tested by repeating the test within 2 weeks. Allow for biological and analytical variability of serum creatinine (±5%) when interpreting changes in eGFR.
- If GFR is >90ml/min/1.73m^2, use an increase in serum creatinine concentration of >20% to infer significant reduction in kidney function.
- Interpret eGFR values of ≥60ml/min/1.73m^2 with caution, as estimates of GFR become less accurate as true GFR increases.

Proteinuria

- **Do NOT** use reagent strips to identify proteinuria unless they are capable of specifically measuring albumin at low concentrations and expressing the result as an ACR.
- Use urine ACR in preference to PCR, because it has greater sensitivity for low levels of proteinuria.
- For quantification and monitoring of high levels of proteinuria (ACR ≥70mg/mmol), PCR can be used as an alternative.
- ACR is the recommended method for people with diabetes.
- For initial detection of proteinuria, if ACR is:
  - between 3 and 70mg/mmol, confirm by a subsequent early morning sample,
  - ≥70mg/mmol a repeat sample is not needed.
- Regard a confirmed ACR of ≥3mg/mmol as clinically important proteinuria.
- Quantify urinary albumin or urinary protein loss for people:
  - with diabetes,
  - without diabetes with a GFR of <60ml/min/1.73m^2,
  - with a GFR of ≥60ml/min/1.73m^2 if there is a strong suspicion of CKD.

Haematuria – see NICE pathway

See **NICE pathway: Chronic kidney disease**

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Assessment of kidney function

- Monitor GFR at least annually in people prescribed nephrotoxic drugs e.g. calcineurin inhibitors (cyclosporin or tacrolimus), lithium and NSAIDs.
- Offer testing for CKD using eGFRcreatinine and ACR to people with any of the following risk factors:
  - diabetes,
  - hypertension,
  - acute kidney injury,
  - CVD,
  - structural renal tract disease, recurrent renal calculi or prostatic hypertrophy,
  - multisystem diseases with potential kidney involvement e.g. systemic lupus erythematosus,
  - family history of end-stage kidney disease or hereditary kidney disease,
  - opportunistic detection of haematuria.
- **Do NOT** use age, gender or ethnicity as risk markers to test people for CKD. In the absence of metabolic syndrome, diabetes or hypertension, do not use obesity alone as a risk marker to test people for CKD.

Establishing the cause of CKD

- Agree a plan to establish the cause of CKD during an informed discussion with the person with CKD, particularly if the cause may be treatable.
- Use the person's GFR and ACR categories to indicate their risk of adverse outcomes and discuss this with them.

Indications for renal ultrasound – see NICE pathway

Frequency of monitoring

- Agree the frequency of monitoring (eGFRcreatinine and ACR) with the person with, or at risk of CKD. Bear in mind that CKD is not progressive in many people.
- Use **Table 1** to guide the frequency of monitoring but tailor to the person according to:
  - underlying cause of CKD,
  - past patterns of eGFR and ACR (be aware that CKD progression is often non-linear),
  - comordities, especially HF,
  - changes to their treatment e.g. renin-angiotensin-aldosterone system antagonists, NSAIDs, diuretics,
  - intercurrent illness,
  - whether they have chosen conservative management of CKD.

Risk factors for CKD progression

- Work with people who have any of the following risk factors for CKD progression to optimise their health:
  - CVD,
  - proteinuria,
  - acute kidney injury,
  - hypertension,
  - diabetes,
  - smoking,
  - African, African-Caribbean or Asian family origin,
  - chronic use of NSAIDs,
  - untreated urinary outflow tract obstruction.
- In people with CKD the chronic use of NSAIDs may be associated with progression, and acute use is associated with a reversible decrease in GFR. Exercise caution when treating people with CKD with NSAIDs over prolonged periods of time. Monitor the effects on GFR, particularly in people with a low baseline GFR and/or in the presence of other risks for progression.

Acute kidney injury and CKD

- Monitor people for the development or progression of CKD for at least 2 to 3 years after acute kidney injury, even if serum creatinine has returned to baseline.
- Advise people who have had acute kidney injury that they are at increased risk of CKD developing or progressing.

See NICE pathway: Acute kidney injury.

Identifying progression

- Define accelerated progression of CKD as:
  - a sustained decrease in GFR of ≥25% and a change in GFR category within 12 months, **OR**
  - a sustained decrease in GFR of 15ml/min/1.73m^2 per year.
- Take the following steps to identify the rate of progression of CKD:
  - obtain a minimum of 3 GFR estimations over a period of not less than 90 days,
  - in people with a new finding of reduced GFR, repeat the GFR within 2 weeks to exclude causes of acute deterioration of GFR e.g. acute kidney injury or starting renin–angiotensin system antagonist therapy.
- Be aware that people with CKD are at increased risk of progression to end-stage kidney disease if they have either:
  - a sustained decrease in GFR of ≥25% over 12 months, **OR**
  - a sustained decrease in GFR of ≥15ml/min/1.73m^2 over 12 months.
- When assessing CKD progression, extrapolate the current rate of decline of GFR and take into account when planning intervention strategies, particularly if it suggests that the person might need renal replacement therapy in their lifetime.

Referral criteria

- Take into account the individual's wishes and comorbidities when considering referral.
- People in the following groups should normally be referred for **specialist assessment:**
  - GFR <30ml/min/1.73m^2 (G4 or G5), with or without diabetes,
  - ACR ≥70mg/mmol, unless known to be caused by diabetes and already appropriately treated,
  - ACR ≥30mg/mmol (A3), together with haematuria,
  - sustained decrease in GFR of ≥25%, and a change in GFR category or sustained decrease in GFR of ≥15ml/min/1.73m^2 within 12 months,
  - hypertension that remains poorly controlled despite the use of at least 4 antihypertensive drugs at therapeutic doses (see NICE pathway: Hypertension)
  - known or suspected rare or genetic causes of CKD,
  - suspected renal artery stenosis.
- People with CKD and renal outflow obstruction should normally be referred to urological services, unless urgent medical intervention is required e.g. for the treatment of hyperkalaemia, severe uraemia, acidosis or fluid overload.
- Consider discussing management issues with a specialist by letter, email or telephone in cases where it may not be necessary for the person to be seen by the specialist.
- Once a referral has been made and a plan jointly agreed (between the person with CKD/their carer and the healthcare professional), routine follow-up may take place at the GP surgery rather than a specialist clinic. Criteria for future referral or re-referral should be specified.

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Lifestyle advice

- Encourage people with CKD to exercise, achieve a healthy weight and stop smoking.

Dietary interventions

- Offer dietary advice about potassium, phosphate, calorie and salt intake appropriate to the severity of CKD.
- **Do NOT** offer low-protein diets (dietary protein intake <0.6 to 0.8g/kg/day).

Self-management – see NICE pathway

Pharmacological treatment

Blood pressure control

- Aim to keep the systolic BP <140mmHg (target range 120 to 139mmHg) and the diastolic BP <90mmHg.
- In people with CKD and diabetes, and people with ACR of ≥70mg/mmol, aim to keep the systolic BP <130mmHg (target range 120 to129mmHg) and diastolic BP <80mmHg.

Renin-angiotensin system antagonists

- Offer a low-cost renin-angiotensin system antagonist e.g. ACEI/ARB to people with CKD and:
  - diabetes and ACR of ≥3mg/mmol (A2 or A3),
  - hypertension and an ACR of ≥30mg/mmol (A3),
  - an ACR of ≥70mg/mmol (irrespective of hypertension or CVD).
- **Do NOT** offer a combination of renin-angiotensin system antagonists.
- For people with CKD, hypertension and an ACR of <30mg/mmol (A1, A2), follow NICE pathway: Hypertension if they do not have diabetes.
- To improve concordance, inform people about the importance of:
  - achieving the optimal tolerated dose, **AND**
  - monitoring eGFR and serum potassium to achieve this safely.

Monitoring

- Measure serum potassium and eGFR before starting treatment. Repeat between 1 and 2 weeks after starting treatment and after each dose increase.
- **Do NOT** routinely offer a renin-angiotensin system antagonist if pre-treatment serum potassium is >5.0mmol/litre. Investigate and treat other factors known to promote hyperkalaemia and recheck serum potassium.
- Concurrent use of drugs known to promote hyperkalaemia is not a contraindication to the use of renin-angiotensin system antagonists, but more frequent monitoring of serum potassium may be required.
- Stop renin-angiotensin system antagonists if serum potassium increases to ≥6.0mmol/litre and other drugs known to promote hyperkalaemia have been discontinued.
- If there is a decrease in eGFR or an increase in serum creatinine after starting treatment/dose increase but it is <25% (eGFR) or <30% (serum creatinine) repeat test in 1 to 2 weeks. Do not modify the dose if either the change in eGFR is <25% or change in serum creatinine is <30%. from baseline.
- If the eGFR change is ≥25%, or the change in serum creatinine is ≥30%:
  - investigate other causes of a deterioration in renal function, such as volume depletion or concurrent medication e.g. NSAIDs,
  - if no other cause is found, stop the drug or reduce the dose to a previously tolerated lower dose, and add an alternative antihypertensive if required.

Statins - see NICE pathway: Lipid modification

Antiplatelets and anticoagulants

- Offer antiplatelet drugs for the secondary prevention of CVD, but be aware of the increased risk of bleeding.
- Consider apixaban in preference to warfarin in people with a confirmed eGFR of 30 to 50ml/min/1.73m^2 and non-valvular atrial fibrillation who have one or more of the following risk factors:
  - prior stroke or transient ischaemic attack,
  - age ≥75 years,
  - hypertension,
  - diabetes mellitus,
  - symptomatic HF.

Possible complications

Anaemia

- Check the Hb level in people with a GFR of <45ml/min/1.73m^2 (G3b, G4 or G5) to identify anaemia (Hb <110g/litre [11.0g/dl]), See NICE pathway: Anaemia management in people with CKD.
- Determine the subsequent frequency of testing by the measured value and the clinical circumstances.

Bone conditions

- Measure serum calcium, phosphate and parathyroid hormone (PTH) concentrations in people with a GFR of <30ml/min/1.73m^2 (G4 or G5). Determine subsequent frequency of testing by the measured values and clinical circumstances. Where doubt exists, seek specialist opinion.
- **Do NOT** routinely measure calcium, phosphate, PTH and vitamin D levels in people with GFR of ≥30ml/min/1.73m^2 (G1, G2 or G3).

Bisphosphonates

- Offer bisphosphonates if indicated for the prevention and treatment of osteoporosis in people with GFR of ≥30ml/min/1.73m^2 (G1, G2 or G3). See NICE pathway: Osteoporosis.

Vitamin D

- **Do NOT** routinely offer vitamin D supplementation to manage or prevent CKD–mineral and bone disorders.
- Offer colecalciferol or ergocalciferol to treat vitamin D deficiency in people with CKD.
- If vitamin D deficiency has been corrected and symptoms of CKD–mineral and bone disorders persist, offer alfacalcidol (1-alpha-hydroxycholecalciferol) or calcitriol (1-25-dihydroxycholecalciferol) to people with a GFR <30ml/min/1.73m^2 (G4 or G5).
- Monitor serum calcium and phosphate concentrations in people receiving alfacalcidol or calcitriol supplements.

Oral bicarbonate supplements

- For detailed advice on management of metabolic acidosis – seek advice from local renal service.
- Consider oral sodium bicarbonate supplementation for people with a GFR <30ml/min/1.73m^2 **AND** serum bicarbonate <20mmol/litre.

See **NICE pathway: Chronic kidney disease**

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Table 1: Classification of CKD using GFR and ACR categories and frequency of monitoring (number of times per year, by GFR and ACR category)

GFR and ACR categories and risk of adverse outcomes, and Frequency of monitoring (no of times per year: ≤1 to ≥4)			ACR categories (mg/mmol), description and range		
			<3 Normal to mildly increased	3–30 Moderately increased	>30 Severely increased
			A1	A2	A3
GFR categories (ml/min/1.73m^2), description and range	≥90 Normal and high	G1	No CKD in the absence of markers of kidney damage ≤1	1	≥1
	60–89 Mild reduction related to normal range for a young adult	G2		1	≥1
	45–59 Mild–moderate reduction	G3a[1]	1	1	2
	30–44 Moderate–severe reduction	G3b	≤2	2	≥2
	15–29 Severe reduction	G4	2	2	3
	<15 Kidney failure	G5	4	≥4	≥4

Increasing risk (↓)

Increasing risk (→)

[1] Consider using eGFRcystatinC for people with CKD G3aA1

Abbreviations: ACR, albumin:creatinine ratio; CKD, chronic kidney disease; GFR, glomerular filtration rate

Adapted with permission from Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group (2013) KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney International (Suppl. 3): 1–150

Notes

- Using the table above a person with an: eGFR of 25ml/min/1.73m^2 and an ACR of 15mg/mmol has CKD G4A2
- Be aware that:
  - increased ACR is associated with increased risk of adverse outcomes,
  - decreased GFR is associated with increased risk of adverse outcomes,
  - increased ACR and decreased GFR in combination multiply the risk of adverse outcomes.
- ACR is an important indicator of cardiovascular risk and progression.