

UK Consensus Conference on Early Chronic Kidney Disease

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Detection of adults with early chronic kidney disease (CKD) is important because some will progress to end stage kidney disease and most are at higher risk of premature cardiovascular disease. Early identification provides the greatest opportunity to modify the course of disease and the associated cardiovascular risk.

WHAT IS EARLY CKD?

An international classification of CKD has identified 5 stages. Early CKD is described as stages 1-3. Stages 1 and 2 are characterised by structural abnormalities, presence of persistent proteinuria or albuminuria or haematuria. Stage 3 is characterised by impaired kidney function as defined by estimated glomerular filtration rate (eGFR) of between 30-59 ml/min/1.73m² on at least 2 occasions at a minimal interval of 3 months.

Using this definition it is estimated that as many as 10% of the UK adult population have early CKD, of whom half will have stage 3. This increases with age to approximately 20% over 65 yrs and more than 30% over 80 yrs.

IMPROVING DETECTION OF EARLY CKD

There is a lack of evidence to support the cost effectiveness of general population screening. The majority of cases will be detected from blood sampling and chronic disease management clinics in primary care using eGFR.

Estimating GFR: Measurement of GFR is the best indicator of kidney function but it is impractical to apply to large populations. An estimate can be provided by the laboratory (eGFR) from serum creatinine, gender, age and race (MDRD4v equation). The eGFR has important limitations and demonstrates increasing uncertainty at values greater than 60 ml/min/1.73m². Moreover, the creatinine measurements used in the equation are subject to both analytical and biological variability. To enable a uniform classification of patients into CKD stages across health care communities, it is recommended that all laboratories should:

- use zero biased creatinine methods and consider funding enzymatic assays to improve assay specificity and precision or apply recognised slope and intercept modifiers to the MDRD equation to allow more uniform application of the evidence base across communities;
- not routinely report specific values when an eGFR is greater than 60 ml/min/1.73m²;
- indicate that an eGFR greater than 60 does not exclude CKD stages 1 and 2 which, when suspected, requires urinalysis and further investigations where appropriate;
- provide indicators of the significance of change between serial results (e.g. reference change value);
- provide specific recommendations on standardised collection procedures to minimise biological and other sources of variation (e.g. avoidance of recent meat meal or vigorous exercise prior to sampling and advice on sample storage and transport).

For patients with an eGFR greater than 60, where CKD 1 and 2 is suspected, urinalysis and further investigations may be required. A rise in serum creatinine may indicate progressive kidney disease in these patients.

IMPROVING CLASSIFICATION OF EARLY CKD

Using the existing classification at least 4% of the adult population have stage 3 CKD, many of whom are elderly. They are at increased risk of cardiovascular disease but most will not progress to end stage kidney disease. The priority should therefore be to identify those at risk of kidney disease progression: persistent proteinuria (protein:creatinine ratio (PCR) greater than 100 mg/mmol) is the best indicator of this risk. In diabetic patients urinary albumin estimations will continue to be used.

We recommend that all patients with suspected early CKD should have a urine dipstick for proteinuria and, if positive, quantification of the PCR. This should be included in the next revision of the Quality and Outcomes Framework for general practice. Urine albumin:creatinine ratio (ACR) should be used in line with national guidelines in people with diabetes.

We recommend sub-classifying CKD stage 3 into 2 groups, 3A and 3B:

- 3A defines a lower risk group with eGFR of 45-59.
- 3B defines a higher risk group with eGFR of 30-44.

We recommend a further stratification by applying the suffix p to all stages to reflect the risk of progressive kidney disease in patients who have had proteinuria (PCR greater than 100) e.g. CKD stages 2p, 3Bp.

IMPROVING ORGANISATION OF CARE

Improvements in patient care and outcomes require effective multidisciplinary working between primary and secondary care in partnership with patients. This requires explicit local referral guidance and shared care, effective IT systems and education programmes. Establishment of these services will require funding which recognises the associated work load. The use of eGFR reporting has the potential to “medicalise” large sections of the population and it is important to focus resources on those with progressive disease who will benefit most from intervention.

In patients classified as stages 1, 2 and 3A, cardiovascular risk factors should be managed in accordance with national guidelines. Patients require an annual review which includes re-estimation of their GFR, urinalysis and blood pressure measurement.

Patients classified as stage 3B should be managed as above but with 6 monthly review.

In patients with significant proteinuria (suffix p) important objectives of therapy to delay the progression of CKD are optimise blood pressure control and reduce proteinuria.

Referral for specialist opinion should be considered in:

- younger patients (less than 55 yrs);
- those with evidence of progressive kidney disease (Δ GFR greater than 4 mls/min/year), after confirmation with a second blood test;
- those with proteinuria (PCR greater than 100).

CLINICAL RECOMMENDATIONS

Lifestyle: Successful lifestyle modification is an important objective of treatment and can reduce both cardiovascular risk and CKD progression. Effective interventions include smoking cessation, weight reduction, regular exercise and dietary salt restriction.

Blood pressure: There is strong evidence that blood pressure lowering reduces cardiovascular disease risk and the progression of CKD. Treatment should be offered to those with blood pressure equal to or greater than 140/90 mmHg but the optimal treatment target remains poorly defined. For most patients in stages 1, 2, 3A and 3B, the primary objective is to reduce the risk of stroke and heart disease and choice of therapy should follow national guidelines (initial therapy less than 55 yrs; ACE inhibitor, greater than 55 yrs; calcium channel blockers or diuretic). In the absence of proteinuria, it is acceptable for general practitioners to “exemption code” patients from the requirement for ACEi/ARB prescription if blood pressure control is satisfactory.

For patients with early CKD and proteinuria (suffix p), blood pressure control is more important and, based on limited evidence, a target of less than 130/80 has been recommended. An ACE inhibitor or ARB should be part of the treatment strategy for this patient group.

Cardiovascular risk management: Many of the patients with early CKD will already have evidence of vascular disease and/or diabetes and will be receiving lipid lowering therapy and low dose aspirin according to national guidelines. There is uncertainty about the benefits of these treatments in patients with isolated reduction of eGFR and no established vascular disease, diabetes or hypertension.

Bone mineral disorders: Clinically significant bone mineral disorders due to kidney impairment are uncommon in people with early CKD. Though biochemical abnormalities can develop, routine requests for PTH assays are not recommended in primary care.

Anaemia: Anaemia due to kidney disease is uncommon in early CKD except in those with diabetes or an eGFR of less than 45. All patients with anaemia should be investigated for alternative causes before ascribing it to CKD. The use of erythropoiesis stimulating agents is unlikely to be required in early CKD.

Medicines management: All patients with early CKD should have their medications reviewed to avoid potential nephrotoxic agents (in particular NSAIDs) or other metabolic complications e.g. hyperkalaemia or metabolic acidosis.

Research: This conference has identified a shortfall in the research evidence base to underpin robust recommendations in many areas of disease management for patients with early CKD.