The Practitioner

Early recognition of CKD can delay progression

McLaughlin M. Courtney A E. Early recognition of CKD can delay progression .
Practitioner 2013;257(1758):13-17

Dr Mary-Jo McLaughlin
MB ChB
First Year General Practice Specialty Trainee

Dr Aisling E Courtney
FRCP
Consultant Nephrologist

Regional Nephrology Unit, Belfast City Hospital, Belfast, UK

Practitioner
Medical Publishing Ltd

©Practitioner Medical Publishing Ltd.
Reprint orders to *The Practitioner*, 10 Fernthorpe Road, London SW16 6DR, United Kingdom. Telephone: +44 (0)20 8677 3508
www.thepractitioner.co.uk

Early recognition of CKD can delay progression

AUTHORS
Dr Mary-Jo McLaughlin
MB ChB
First Year General Practice Specialty Trainee

Dr Aisling E Courtney
FRCP
Consultant Nephrologist

Regional Nephrology Unit, Belfast City Hospital, Belfast, UK

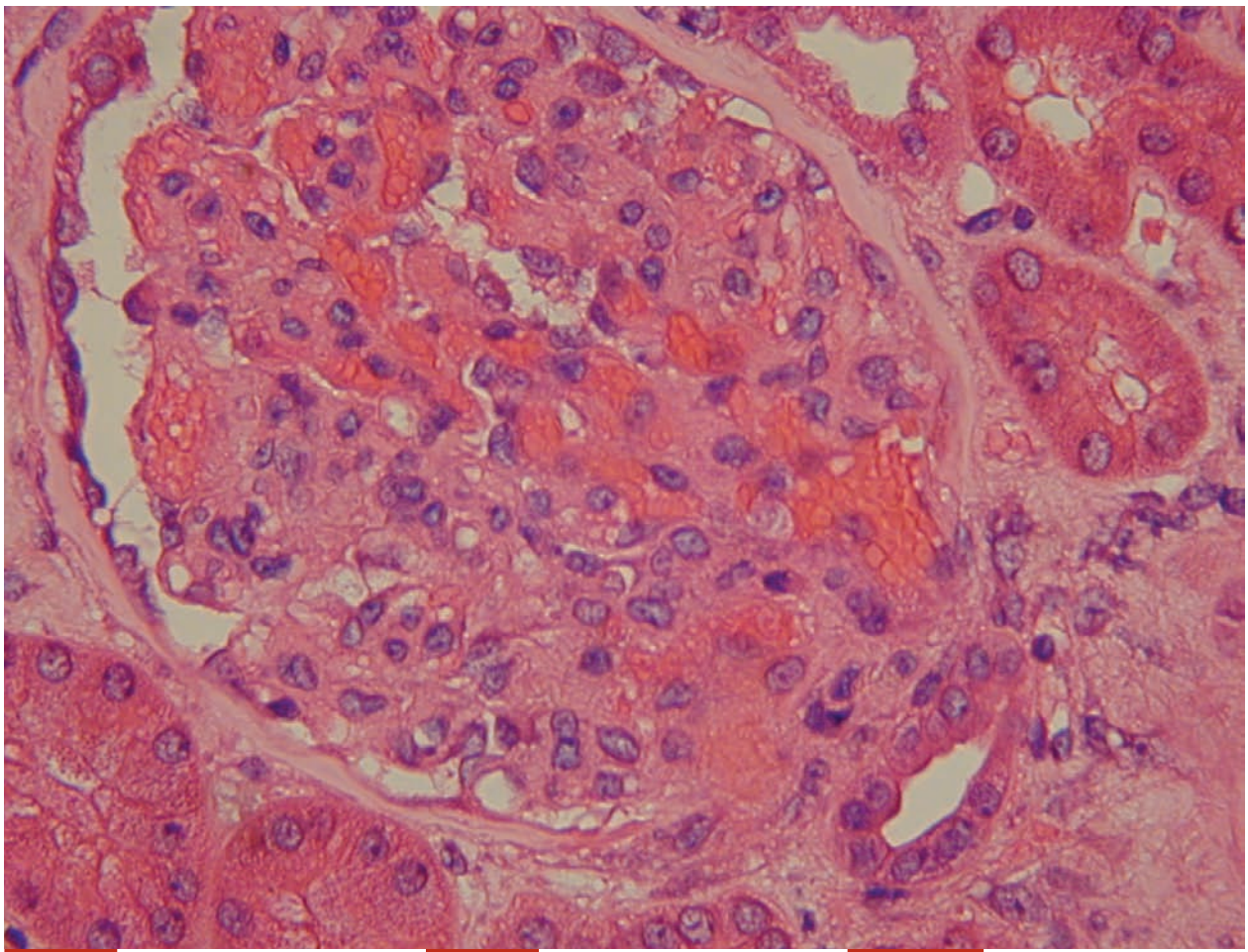


FIGURE 1
Light microscopy (haematoxylin and eosin stain) demonstrating an acutely diseased glomerulus

How should patients be investigated?

CHRONIC KIDNEY DISEASE (CKD) IS DEFINED AS A REDUCTION IN ESTIMATED GLOMERULAR FILTRATION rate (eGFR) for three consecutive months, or evidence of kidney damage alone with preserved renal function (eGFR >60 ml/min/1.73m^2). Kidney damage comprises persistent nonvisible haematuria, persistent proteinuria (albumin:creatinine ratio >30 mg/mmol) or structural abnormalities on imaging such as polycystic kidney disease.[1]

How should patients be monitored?

CKD affects 8.5% of the UK population,[2] however symptoms are often nonspecific, e.g. fatigue, or absent until the disease has reached an advanced stage. An estimated 30% of people with CKD are referred to secondary care only a short time before they need renal replacement therapy,[3] and this is associated with poorer outcomes.

Early recognition allows intervention that may delay or avoid progression to end-stage disease and modify the cardiovascular risk associated with

What are the management options?

CKD. The importance of this as a public health issue is reflected by its inclusion in the Quality and Outcomes Framework, see box 1, p14, rewarding GPs with 36 points for recognition and initial and ongoing management of CKD.[4]

CKD is classified into five stages as shown in table 1, p14.[1] The majority of individuals have stages 1-3 CKD and many of these will never progress to end-stage renal disease. It is important to provide optimal »

management to these patients in primary care, and recognise those with progressive disease and make a timely referral to specialist services.[1,3]

COMMON CAUSES OF CKD

Frequently the aetiology of reduced renal function is multifactorial. A decline in GFR with age is expected and there is debate as to whether a reduced GFR in the elderly should be considered a disease or whether it reflects the normal physiological aging process. An age-related decline in nephron mass in combination with hypertension and potentially atherosclerosis, accounts for much of the CKD burden in older individuals.

The most frequent specific renal diseases resulting in progressive CKD in the UK are:[1,3]

- diabetes mellitus
- atheromatous renal vascular disease
- glomerulonephritis (see figure 1, p13)
- chronic pyelonephritis
- inherited renal disease such as polycystic kidney disease

INVESTIGATION AND ASSESSMENT

Historically the serum creatinine concentration was used to diagnose kidney disease, however since this is dependent not only on the renal clearance of creatinine but also on its generation, those with reduced muscle mass (e.g. older patients of both sexes and women of all ages compared with men of the equivalent age) may have advanced kidney disease without a particularly high serum creatinine concentration.

Thus all laboratories in the UK now routinely provide an eGFR with a serum creatinine value in all adult patients.[5] This estimation is based on serum creatinine, age, gender, and ethnicity, and was validated in a population with CKD. Hence its accuracy in those with normal or mild CKD is not robust, and a result of >60 ml/min/1.73 m^2 is reported in this group[5]

Baseline assessment in a patient with newly diagnosed CKD should include:[1,3]

- blood pressure
- dipstick urinalysis
- urine albumin:creatinine ratio (ACR) or protein:creatinine ratio (PCR)
- glucose, lipid profile and a full blood count

An ultrasound scan should be considered in certain individuals (see box 2, below). In patients with a family history of inherited kidney disease a discussion of risks and benefits should occur before imaging, this may be more appropriately conducted by renal or genetic specialists.[1,3]

'An estimated 30% of people with CKD are referred to secondary care only a short time before they need renal replacement therapy'

Proteinuria

Proteinuria is a very important prognostic marker in CKD. The risks of overt cardiovascular disease and of progressive kidney disease are both increased in those with urinary protein leak.[6]

Commonly used urine dipsticks are cheap and an easily accessible simple screening tool, however they do not quantify the amount of protein and fail to detect very low levels of albumin. The dipstick test is a measure of

Box 1

Quality and Outcomes Framework indicators for 2012/13: Chronic kidney disease (CKD)

Records	Points
CKD1 The practice can produce a register of patients aged 18 years and over with CKD (US National Kidney Foundation: Stage 3 to 5 CKD)	6
Initial management	
CKD2 The percentage of patients on the CKD register whose notes have a record of blood pressure in the preceding 15 months	4
Ongoing management	
CKD3 The percentage of patients on the CKD register in whom the last blood pressure reading, measured in the preceding 15 months, is 140/85 mmHg or less	11
CKD5 The percentage of patients on the CKD register with hypertension and proteinuria who are treated with an angiotensin converting enzyme inhibitor (ACE inhibitor) or angiotensin receptor blocker (ARB)	9
CKD6 The percentage of patients on the CKD register whose notes have a record of a urine albumin:creatinine ratio (or protein:creatinine ratio) test in the preceding 15 months	6

Table 1

Stages of chronic kidney disease[1]

Stage	Description	eGFR (ml/min/1.73m^2)	Population prevalence (%)
1	Normal kidney function but with kidney damage	>90	3.3
2	Mild CKD with other kidney damage	60-89	3.0
3a	Mild-moderate CKD	45-59	4.3
3b	Moderate CKD	30-44	4.3
4	Severe CKD	15-29	0.2
5	Very severe or dialysis dependent CKD	<15 or on RRT*	0.2

*RRT= renal replacement therapy

Box 2

Indications for renal tract ultrasound[1,3]

- Progressive CKD
- Visible or persistent nonvisible haematuria
- Symptoms of urinary tract obstruction
- Family history of polycystic kidney disease
- Stage 4 or 5 CKD (not appropriate in all)

concentration: a normal individual may drink a minimal amount of fluid and pass 500 ml in 24 hours or drink enough to pass 2,500 ml in 24 hours, on both days the amount of protein excreted will be the same but the concentration of protein in a spot sample on the 500 ml day will be five fold greater than on the 2,500 ml day (and may have 1+ or even 2+ protein on dipstick).

Previously 24-hour collections of urine were used to assess proteinuria but these are cumbersome and inconvenient for both the patient and laboratory, and the accuracy of the collection was often uncertain. These have been largely replaced by the spot urine tests of ACR or PCR.

A urine ACR <3 mg/mmol is normal, 3-30 mg/mmol is microalbuminuria, (the earliest clinical indicator of damage in diabetic nephropathy), while >30 mg/mmol is equivalent to approximately 0.5 g of protein in 24 hours and dipstick-positive proteinuria in someone euvolaemic.[1,3] Urine PCR is less frequently used and equivalent values are shown in table 2, right. ACR is the preferred measure as it has greater sensitivity for lower levels of proteinuria and is the recommended method in those with diabetes.[1,3]

Haematuria

Haematuria is common, and although often not concerning it can occasionally be the presenting feature of significant disease. Determining which individuals need further investigation and then referring appropriately to urology or nephrology is an important skill in general practice. The initial evaluation should include:

- History – symptoms of infection/obstruction/systemic illness
- Examination – unwell/hypertension/bladder or prostate
- Urine – dipstick urinalysis/MSSU/ACR
- Blood – renal function

The Renal Association and British Society of Urological Surgeons consensus paper on haematuria is a useful guide to further management.[7] See table 3, right, for a summary of which patients should be referred, and to whom.

POTENTIAL COMPLICATIONS

The potential health problems associated with CKD can be divided into two main categories.

- Risk of progressive renal disease with the development of renal bone disease and renal anaemia
- Risk of overt cardiovascular disease.

The majority of patients, even with stage 4 CKD never progress to end-stage disease but there is an increased incidence of cardiovascular disease and premature death in this population.[8] CKD should be treated as a significant risk factor (equivalent to diabetes) when assessing cardiovascular disease risk.[1]

MONITORING AND REFERRAL

The maintenance of an accurate electronic CKD register in general practice is valuable to facilitate appropriate monitoring (as outlined in table 4, below), heighten awareness for opportunities to reduce cardiovascular risk, and potentially minimise inappropriate prescribing for those with renal impairment. Importantly it should also allow timely onward referral in the subgroup at risk of progressive disease, ensuring that the morbidity and mortality associated with late referral is reduced and that there is appropriate planning for renal replacement therapy. Patients with CKD who should be considered for renal referral are listed in box 3, p16.[1,3] »

Table 2

Approximate equivalent values of urinary albumin:creatinine ratio (ACR), protein:creatinine ratio (PCR) and urinary protein excretion

ACR (mg/mmol)	PCR (mg/mmol)	Urinary protein excretion (g/24hr)
30	50	0.5
70	100	1

Table 3

Indications for referral in patients with haematuria

Features		Urology	Nephrology
Visible	Single episode	yes	
	Associated with upper respiratory tract infection		yes
Nonvisible	Symptomatic with UTI excluded (hesitancy, frequency, urgency, etc)	yes	
	Persistent* and >40 years	yes	
	Persistent* and <40 years and hypertension		yes
Proteinuria	ACR >30 mg/mmol or equivalent		yes
CKD	Progressive decline in eGFR†		yes
	Stage 4/5 CKD		yes

*persistent: present on at least 2 out of 3 dipstick tests
† >10 ml/min at any stage within previous 5 years or a drop >5 ml/min within past year

Table 4

Monitoring patients with chronic kidney disease in general practice[1]

Stage	1	2	3	4	5
eGFR ml/min/1.73m^2	≥90 and albuminuria	60-89+ and albuminuria	30-59	15-29	<15
Tests	Annual U&E and urine ACR			As before but now 3 monthly	Check U&E 6 weekly
Treatment	Treat BP to target of <130/80 (threshold to treat 140/90) ● ACE inhibitor or ARB if urine ACR ≥30 mg/mmol in patients without diabetes ≥3 mg/mmol in patients with diabetes ● Statin if CVD risk ≥20% over 10 years ● Optimal glycaemic control in diabetes patients ● Advise lifestyle changes ● Consider aspirin 75 mg				
Referral	● Fall in eGFR by >5ml/min/1.73m^2 per year ● Rise in serum creatinine by 20% per year ± urine ACR ≥70 mg/mmol ± systolic BP ≥160 mmHg despite treatment with multiple agents			Discussion with, or referral to, renal services is usual	Usually automatic (unless not for active treatment based on comorbidity)

There are two important caveats when considering referral. First, fluctuation in renal function is common, particularly in elderly patients with CKD. A fall in eGFR can result from any intercurrent illness (e.g. chest or urinary infection), medication (commonly trimethoprim or NSAIDs), or volume depletion (caused by diarrhoea or increased diuretic therapy). Referral is this subset should ideally be made after serial eGFR measures, which show a progressive decline over time.

Second, it is important to consider the individual patient's wishes and comorbidities. The majority of elderly patients, even with severe CKD, will not have a decline in function that will lead to significant renal problems in their lifetime.[6] In such cases referral to the nephrology team may be unhelpful both for the individual themselves, who will have unnecessary anxiety and potentially investigations, and for overall service provision.

MANAGEMENT

The key issues to address are:

- Minimisation of progression of CKD — particular attention to blood pressure control and reducing proteinuria
- Management of cardiovascular risk
- Avoidance of inappropriate prescribing — i.e. nephrotoxic drugs and dose adjustment of renally excreted medication

It is important to note however that the evidence base for tight blood pressure control in elderly individuals, particularly with atherosclerotic disease, is not robust. A blood pressure of, for example, 120 mmHg systolic may actually be detrimental to renal perfusion and result in deterioration in renal function.

Box 3

Indications for referral to renal services [1,3]

- Stage 4/5 CKD with or without diabetes
- Higher levels of proteinuria (ACR ≥70 mg/mmol) unless known to be due to diabetes and appropriately treated
- Proteinuria (≥30 mg/mmol) together with haematuria
- Rapidly declining eGFR (>5 ml/min/1.73m^2 in 1 year or >10 ml/min/1.73m^2 in 5 years)
- Uncontrolled hypertension despite treatment with four antihypertensive agents
- Suspected renal artery stenosis
- Suspected rare or genetic cause of CKD

This may be most noticeable with ACE inhibitor or angiotensin receptor blocker (ARB) therapy. Withdrawal of these agents in elderly patients with progressive CKD may arrest, or even reverse, the decline in function.

Patient education

This is an integral part of improving compliance with treatment measures (e.g. antihypertensive therapy) and is of particular relevance in CKD as the condition is often asymptomatic until advanced stages. [1,3]

Lifestyle modification is also vital. Dietary advice with respect to caloric and salt restriction should be given along with support for smoking cessation.[1,3]

Pharmacotherapy

A blood pressure target < 130/80 mmHg should be aimed for in those with proteinuria (urine ACR >70 mg/mmol), and/or those with diabetes (first-line agent should be an ACE inhibitor or ARB). Otherwise the target should be <140/90 mmHg in accordance with the current NICE guidelines.[3]

ACE inhibitor/ARB therapy should be titrated to the maximum tolerated dose in those with proteinuria.

Box 4

Dose adjustment to therapy

Decline in renal function during commencement or dose increase of ACE inhibitor/ARB therapy[2]

If eGFR decrease <25% or plasma creatinine increase <30%:

- Do not modify dose
- Repeat after 1-2 weeks

If eGFR decrease ≥25% or plasma creatinine increase ≥30%:

- Investigate other causes for renal dysfunction e.g. volume depletion, NSAIDs

If no other cause found:

- Stop the ACE inhibitor/ARB therapy or reduce it to previously tolerated dose
- Commence alternative antihypertensive therapy if indicated

The eGFR and potassium should be measured before commencement of therapy and 7-10 days after initiation or a dose increase. If any changes in these values are detected guidance should be followed as shown in box 4, below.[3]

'To reduce cardiovascular disease risk, statins and antiplatelet therapy should be considered'

To reduce cardiovascular disease risk, statin therapy and antiplatelet therapy should be considered, and it is important to aim for good glycaemic control.[1]

RECENT DEVELOPMENTS

Virtual nephrology service

Some centres have developed a virtual nephrology service which may involve virtual clinics or 24-hour access to specialist advice via a telephone service. In one centre more than one-fifth of outpatient referrals were seen at a virtual clinic. Innovative approaches such as these have demonstrated a cost-effective, rapid access approach for non-complicated CKD in conjunction with the traditional outpatient clinic service.[9] There are obvious benefits for both patients and physicians, and in the present financial constraints, with an aging population, it is likely that this approach will become more widely adopted.

key points

SELECTED BY
Dr Peter Saul
GP, Wrexham and Associate GP Dean for North Wales

Chronic kidney disease (CKD) is defined as a reduction in estimated glomerular filtration rate (eGFR) for three consecutive months, or evidence of kidney damage alone with preserved renal function. CKD affects 8.5% of the UK population. Early recognition allows intervention that may delay or avoid progression to end-stage disease and modify the cardiovascular risk associated with CKD.

CKD is classified into five stages and the majority of individuals have stages 1-3, many of these will never progress to end-stage renal disease. A decline in GFR with age is expected. The most frequent specific renal diseases resulting in progressive CKD in the UK are: diabetes mellitus, atheromatous renal vascular disease, glomerulonephritis, chronic pyelonephritis and inherited renal disease.

Laboratories in the UK now routinely provide an eGFR with a serum creatinine value in all adult patients. This estimation is based on serum creatinine, age, gender, and ethnicity. Baseline assessment in a patient with newly diagnosed CKD should include: blood pressure, dipstick urinalysis, urine ACR or PCR, glucose, lipid profile and a full blood count. Fluctuation in renal function is common, particularly in elderly patients with CKD. A fall in eGFR can result from any intercurrent illness, medication, or volume depletion. Proteinuria is a very important prognostic marker in CKD, ACR is the preferred measure as it has greater sensitivity for lower levels of proteinuria and is the recommended method in those with diabetes.

The potential health problems associated with CKD can be divided into two main categories: risk of progressive renal disease with the development of renal bone disease and renal anaemia, and risk of overt cardiovascular disease.

An accurate electronic CKD register in general practice is valuable to facilitate appropriate monitoring and allow timely onward referral in the subgroup at risk of progressive disease. To minimise the risk of progression of CKD particular attention should be paid to blood pressure control, reducing proteinuria, management of cardiovascular risk and avoidance of inappropriate prescribing. ACE inhibitor/ARB therapy should be titrated to the maximum tolerated dose in those with proteinuria. The eGFR and potassium should be measured before commencement of therapy and 7-10 days after initiation or a dose increase.

Palliative care in renal disease
In certain cases of advanced CKD, dialysis would not be appropriate. This can often be gauged best by the patient's GP who has an appreciation of their overall disease burden and level of functioning. There is increasing recognition that conservative care in CKD is an important issue. Some renal services provide conservative care clinics or advice, and in the future this is likely to become more streamlined and widely available.

REFERENCES

1 Northern Ireland Guidelines for Management of Chronic Kidney Disease. Guidelines and Audit Implementation Network and the Northern Ireland Nephrology Team. February 2010. www.gainni.org/images/Uploads/ Guidelines/ Chronic%20Kidney%20Disease.pdf
2 Stevens PE, O'Donoghue DJ, de Lusignan S et al. Chronic kidney disease management in the United Kingdom: NEOERICA project results. *Kidney Int* 2007;72(1):92-9
3 National Institute for Health and Clinical Excellence. CG73. Chronic kidney disease: Early identification and management of chronic kidney disease in adults in primary and secondary care. NICE. London.2008
4 Quality and Outcomes Framework for 2012/13. March 2012 www.nhsemployers.org/Aboutus/Publications/ Documents/QOF_2012-13.pdf
5 Courtney AE, Maxwell AP, Fogarty DG. Using estimated glomerular filtration rate (eGFR) to help manage patients with chronic kidney disease. *Ulster Med J* 2007;76(3):154-6
6 Conway B, Webster A, Ramsay G et al. Predicting mortality and uptake of renal replacement therapy in patients with stage 4 chronic kidney disease. *Nephrol Dial Transplant* 2009;24(6):1930-7
7 Joint Consensus statement on the initial assessment of haematuria. Renal Association and British Association of Urological Surgeons. 2008 www.renal.org/clinical/OtherGuidelines.aspx
8 Go AS, Chertow GM, Fan D et al. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. *N Engl J Med* 2004;351(13):1296–305
9 Mark DA, Fitzmaurice GJ, Haughey KA et al. Assessment of the quality of care and financial impact of a virtual renal clinic compared with the traditional outpatient service model. *Int J Clinic Pract* 2011;65(10):1100-7

Useful information

Kidney Patient Guide
www.kidneypatientguide.org.uk/ contents.php

The Renal Association
www.renal.org

NHS Kidney Care
www.kidneycare.nhs.uk

Edinburgh Renal Unit
www.edren.org

We welcome your feedback

If you would like to comment on this article or have a question for the authors write to:
editor@thepractitioner.co.uk