CHRONIC KIDNEY DISEASE – DIAGNOSIS

Endorsed by CWHHE Diabetes Strategy Group

WHO SHOULD BE TESTED FOR CKD

Offer testing for CKD using eGFR, creatinine and ACR to people with any of the following risk factors:

- diabetes
- hypertension
- previous history of acute kidney injury
- cardiovascular disease (ischaemic heart disease, chronic heart failure, peripheral vascular disease or cerebral vascular disease)
- structural renal tract disease, recurrent renal calculi or prostatic hypertrophy
- multisystem disease eg. Systemic lupus erythematosus
- family history of end-stage kidney disease (GFR category G5) or hereditary kidney disease
- Haematuria

INTERPRETING eGFR VALUES

- Interpret eGFR values of > 60 ml/min/1.73 m2 with caution - estimates of GFR become less accurate as the true GFR increases
- eGFR is unreliable at extremes of body weight:
  - eGFR underestimates in patients with high BMI (>30)
  - eGFR overestimates in patients with low BMI (<20)
- Confirm an eGFR result of <60 ml/min/1.73 m^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)

CLASSIFICATION OF CKD USING eGFR AND ACR CATEGORIES

GFR and ACR categories and risk of adverse outcomes			ACR categories (mg/mmol) description and range		
			<3 Normal to mildly increased	3-30 Moderately increased	>30 Severely increased
			A1	A2	A3
GFR categories, description and range	≥ 90 Normal and high	G1	No CKD in the absence of markers of kidney damage*		
	60-89 Mild reduction related to normal range for a young adult	G2			
	45-59 Mild-moderate reduction	G3a			
	30-44 Moderate-severe reduction	G3b			
	15-29 Severe reduction	G4			
	≤15 Kidney failure	G5			

Increasing risk

Increasing risk

HAEMATURIA

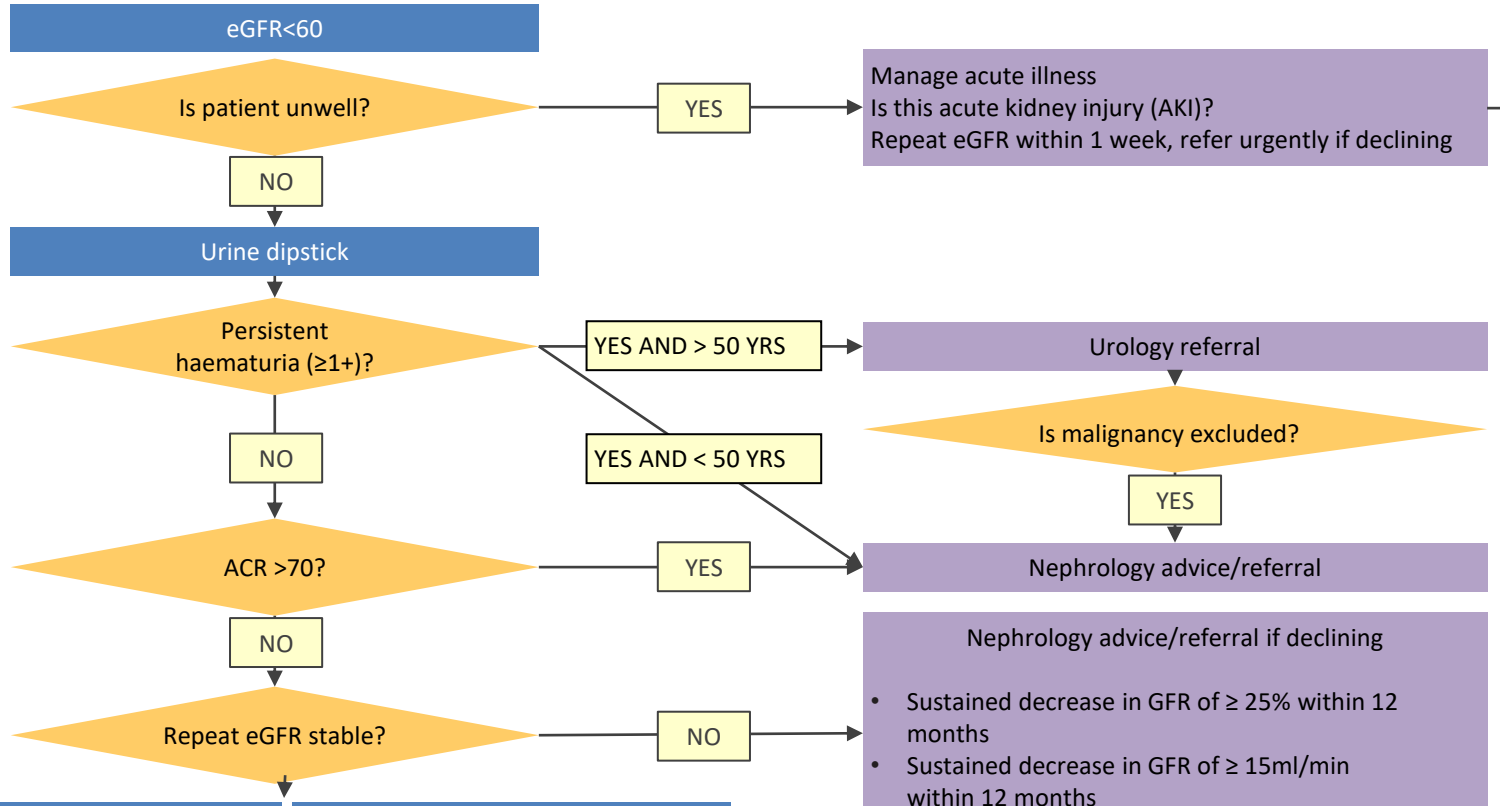
- Use dipstick reagent strips rather than urine microscopy
- Evaluate further if there is a result of 1+ or more (rpt in 2 weeks)
- Dipstick haematuria not diagnostically useful with concurrent mense, infection or in catheter samples

PROTEINURIA

- Proteinuria is a useful marker of kidney damage and complication risk
- ACR is the recommended method for assessing proteinuria
- If initial ACR = 3-70 confirm with a subsequent early morning sample
- If initial ACR > 70 mg/mmol, a repeat sample need not be tested
- Confirmed ACR ≥ 3 signifies clinically important proteinuria.

CHRONIC KIDNEY DISEASE – REFERRAL ALGORITHM

Endorsed by CWHHE Diabetes Strategy Group



URGENT REFERRAL

- Suspected multisystem disease with evidence of renal involvement
- Acute kidney injury (without an obvious cause manageable in primary care)
- Newly diagnosed eGFR < 15
- Nephrotic syndrome
- Accelerated hypertension
- Severe hyperkalaemia (>6.5mmol/L)

Minimum information for referral

- Dates and results of previous creatinine/eGFR measurement
- Medical history
- Drug history
- Current BP
- Urine dipstick and ACR if dipstick positive

Renal Ultrasound if:

- accelerated progression of CKD
- visible or persistent invisible haematuria
- symptoms of urinary tract obstruction
- family history of polycystic kidney disease and are aged over 20 years
- eGFR of <30 ml/min/1.73 m2 (GFR category G4 or G5)

Email advice for North West London primary care:
ICHC-tr.ckdadvice@nhs.net
(nephrology consultant response within 24 hours weekdays)

CHRONIC KIDNEY DISEASE – ONGOING MANAGEMENT

Endorsed by CWHHE Diabetes Strategy Group

MANAGEMENT OF STABLE CKD

Agree management plan with patient

Lifestyle advice (Exercise/Weight/Meditation)
Smoking cessation advice

BP:
- Encourage home BP monitoring
- Target BP: < 140/90 if ACR ≤ 70
  < 130/80 if ACR > 70
- Caution of BP targets in frailty (See page 7)
- Prioritise ACEi/ARB with associated sick day guidance

Cardiovascular risk:
- Aspirin – if CV risk at 10yrs >20%
- Statins – treat according to national guidelines

Avoid NSAIDs

Vaccinate for influenza and pneumococcus

RENAL ANAEMIA

Renal Anaemia can present when the eGFR<45 and nephrology advice may be needed if other causes for the anaemia have been eliminated.

This may require treatment with erythropoietin.

FREQUENCY OF MONITORING eGFR (NUMBER OF TIMES PER YEAR)

GFR and ACR categories and risk of adverse outcomes			ACR categories (mg/mmol) description and range		
			<3 Normal to mildly increased	3-30 Moderately increased	>30 Severely increased
			A1	A2	A3
GFR categories, description and range	≥ 90 Normal and high	G1	**≤1**	**1**	**≥1**
	60-89 Mild reduction related to normal range for a young adult	G2	**≤1**	**1**	**≥1**
	45-59 Mild-moderate reduction	G3a	**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

RENIN-ANGIOTENSIN SYSTEM INHIBITORS IN CKD (ACEI and ARB)

- ACEi and ARB prevent scarring in CKD and should be used preferentially in patients with proteinuria
- Assess kidney function and electrolytes. 1-2 weeks after initiating therapy, watch out for hyperkalemia
- Assess kidney function after any subsequent increase in dose
- A small rise in creatinine or a mild fall in eGFR values is expected with therapy – repeat the assessment of kidney function if the rise in creatinine is greater than 15%
- STOP therapy - If serum creatinine rises by >30% or eGFR falls by >25% fall seek specialist advice (to exclude possible renovascular disease)
- If K>6.0 stop ACEi/ARB and start low potassium diet – if the patient has proteinuria and would benefit from an ACEi/ARB seek Nephrological advice as introduction of frusemide or bicarbonate can facilitate reintroduction of these agents
- Cautious use of ACEi/ARB with spironolactone and other potassium sparing diuretics, very close monitoring of potassium required.

CHRONIC KIDNEY DISEASE – COMMON DRUGS

Proton-pump inhibitors (PPIs)

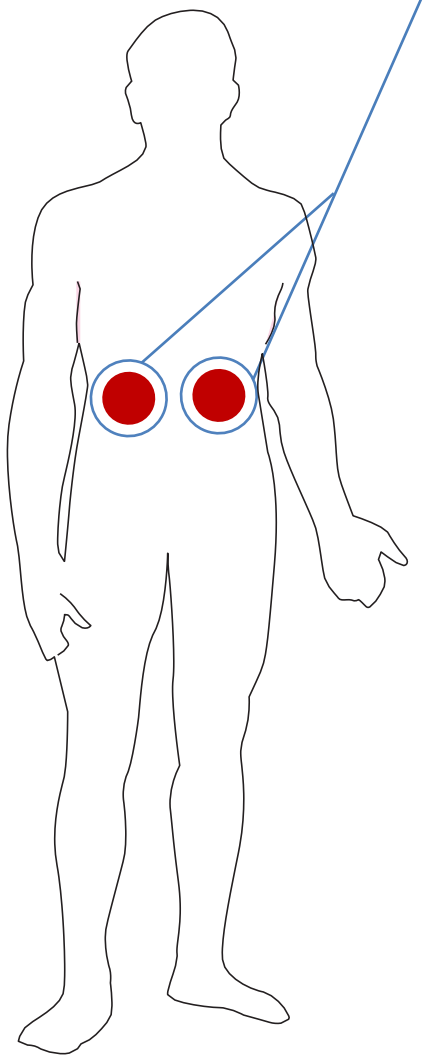
- Should be considered if there is a higher risk of gastric irritation with aspirin or when the patient has more advanced CKD (eGFR <20)
- Observational data suggest PPIs may cause insidious inflammatory kidney injury – therefore switch to ranitidine if eGFR falling whilst on PPIs

ANTIBIOTIC	Issue in reduced kidney function	Recommendation for use
Trimethoprim	Raises serum potassium and creatinine ~20% (affects tubular function but not nephrotoxic per se)	Safe for use if eGFR>30 but may transiently elevate K and creatinine – repeat bloods 1-2 weeks later to ensure resolution
Nitrofurantoin	Requires filtration and tubular secretion. Reduced excretion in CKD and high levels cause peripheral neuritis	Do not use if eGFR<45. May cause toxicity and not reach high enough urinary concentrations to be effective
Penicillin	Risk of crystalluria	Generally safe but avoid maximum doses if eGFR<15
Macrolides (eg. Clarithromycin)	Renally excreted, can cause neurotoxicity	Reduce dose by 50% when eGFR<30
Quinolones (eg. Ciprofloxacin)	Renally excreted, risk of tendonopathy and potentially nephrotoxic	Reduce dose by 50% when eGFR <15
Tetracyclines	Partly renally cleared; doxycycline safer	Reduce dose when eGFR<45

HYPOGLYCAEMIC AGENT	eGFR = 45-59 (CKD stage 3a)	eGFR = 30-44 (CKD stage 3b)	eGFR <30 (CKD stage 4-5)
Metformin	Safe to use	Reduce dose	Stop
Gliclazide	Safe to use	Safe to use	Use with caution; reduce dose
DPP-4 inhibitors (eg. Linagliptin, Sitagliptin)	Safe to use	Adjust dose according to licence (only Linagliptin unchanged = 5mg OD)	Adjust dose according to licence (only Linagliptin unchanged = 5mg OD)
SGLT-2 inhibitors (eg. Canagliflozin, Empagliflozin)	Reduce dose (Cana- and Empa-gliflozin) Stop Dapagliflozin	Stop	Stop
GLP-1 inhibitors (eg. Liraglutide, Exanatide)	Adjust dose according to licence	Adjust dose according to licence	Liraglutide, Dulaglutide licenced to eGFR 15 Stop if eGFR<15
Pioglitazone	Safe to use	Safe to use	Safe to use

TYPE 2 DIABETES – PREVENTING RENAL COMPLICATIONS

Endorsed by CWHHE Diabetes Strategy Group



All patients with Diabetes should be on a register and minimum data should include annual measures for microvascular disease. Please see Cardiovascular Risk for additional requirements.

DIABETIC NEPHROPATHY

Diabetic Nephropathy is characterised by the excretion of abnormal amounts of albumin in the urine, arterial hypertension or progressive decline in kidney function

ALBUMINURIA

Albuminuria is the earliest sign of kidney involvement in Type 2 Diabetes and is best assessed by laboratory measurement of the albumin creatinine ratio (ACR).

Secondary care services sometimes use protein creatinine ratio (PCR) and broadly ACR is usually 70% of measured PCR.

Albuminuria is an independent CV risk factor. It is also associated with a higher risk of progression to end-stage kidney disease.

All patients with albuminuria should be on maximal ACEi or ARB therapy and have BP controlled to target (See page 3)

SEEK RENAL ADVICE IF

Unexplained sudden increases in albuminuria
Unexplained eGFR decline in absence of albuminuria

MANAGEMENT OF INDIVIDUAL WITH DIABETIC NEPHROPATHY

Patient education is an integral part of overall management

Lifestyle changes, weight loss and smoking cessation should be advised

Target HbA1c:
- 48 - 53 mmol/mol (6.5% - 7%) in CKD G3a
- 53 – 68 mmol/mol in CKD G3b/G4 (individualisation of patient target)

Maintain blood pressure below 140/90 (130/80 if ACR > 70)
- **Maximal** doses of ACE inhibitors or Angiotensin II receptor blockers (ARBs) are recommended first line drugs (unless contraindicated)
- Calcium channel blocker (non-dihydropyridine class) drugs and low dose thiazide diuretics are useful second line agents
- Loop diuretics are useful in the presence of volume overload (e.g. leg oedema not caused by the side effects of calcium channel blockers)
- Additional antihypertensive therapy may be required.

Monitor
Treat dyslipidaemia (serum cholesterol, LDL cholesterol and serum triglycerides to targets)

Aspirin therapy if eGFR <60 and ACR>70

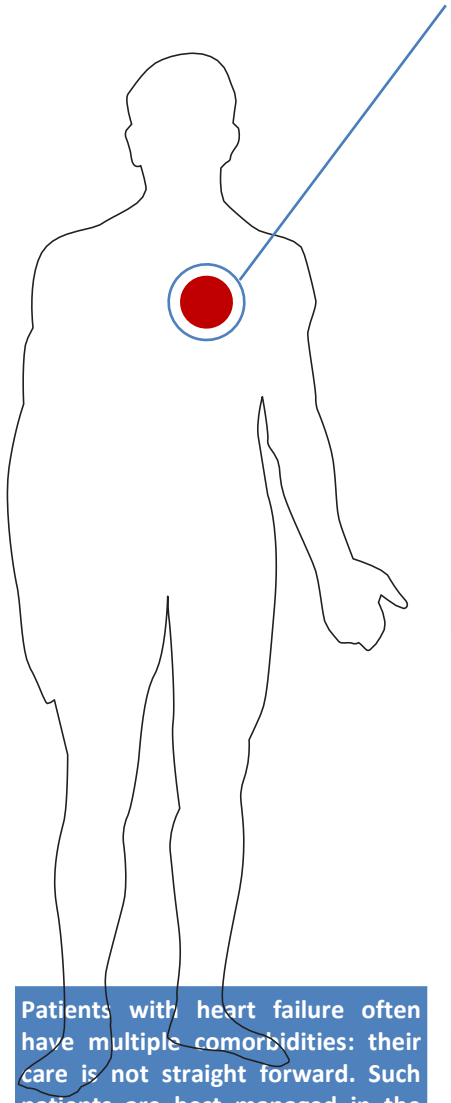
Ensure patient understands sick day guidance for relevant drugs eg ACE/ARBs/ Metformin

PROTEINURIA MEASUREMENTS AND BLOOD PRESSURE TARGETS

ACR	PCR	BP target
≤ 70	≤ 100	140/90
> 70	> 100	130/80

CHRONIC KIDNEY DISEASE AND HEART FAILURE

Developed in conjunction with Dr. C. Plymen, Cardiology Consultant, Imperial College NHS



Patients with heart failure often have multiple comorbidities: their care is not straight forward. Such patients are best managed in the context of a multidisciplinary team.

BACKGROUND POINTS

Signs and symptoms of heart failure are often non- specific and can overlap with symptoms of CKD (e.g.dyspnoea, peripheral and pulmonary oedema). Heart failure is not a benign disease: there is a 10% inpatient mortality associated with diagnosis, and 50% are dead at 5 years [1].

The benefits of ACEi and mineralocorticoid receptor antagonists in relation to heart failure prognosis are just as important in patients with concomitant CKD. (Angiotensin II receptor blockers (ARBs) in patients intolerant of ACEi).

The risks/benefits of temporarily holding or continuing these therapeutic agents during inter-current illness are different in patients with both heart failure and CKD compared to patients with CKD alone.

PERMISSIBLE RISES IN CREATININE WITH ACEi / ARB

Because of the need to reach adequate ACEi dosing to see a prognostic benefit in heart failure,
'a Cr increase of up to 50% above baseline, or 266µmol/L, or eGFR <25 mL/min/1.73 m2, whichever is the smaller'
is acceptable in patients with concomitant CKD and heart failure [3]. ***This is a larger increase than that which is considered acceptable for patients without heart failure.***

MANAGEMENT OF INDIVIDUALS WITH CKD AND HEART FAILURE

Patient education is an integral part of overall management

Lifestyle changes; exercise, weight loss and smoking cessation should be advised

ACEi/ARB Therapy:

- Check renal function prior to initiation of therapy
- Stop concomitant nephrotoxic drugs e.g. NSAIDS
- Recheck 1-2 weeks after initiation and 1-2 weeks after final dose titration
- Recheck renal function four monthly thereafter

- **Maximal** doses of ACE inhibitors or ARBs (unless contraindicated)
- ACEi/ARBs should not be held if BP low unless significant symptomatic hypotension.
- If Cr >200µmol/L, eGFR < 25 ml/min or K+ >5.5mmol/L, seek specialist help.
- Additional antihypertensive therapy may be required.

Monitor K+ :

- A rise in potassium of up to ≤ 5.5 mmol/L is acceptable.
- Stop potassium supplements or potassium sparing drugs (e.g. amiloride) if high potassium an issue.
- Consider low dose Sodium Bicarbonate (max 500mg BD PO) if patient is acidotic actual venous bicarbonate <22.
- Consider increasing loop diuretic if patient experiencing symptoms of overload.

Treat dyslipidaemia (serum cholesterol, LDL cholesterol and serum triglycerides to targets)

Aspirin therapy if indicated (2^{o} prevention)

Ensure prescribing is consistent with CKD

Sick day guidance: Consider holding ACEi and seek early medical attention.

References

1. National Heart Failure Audit 2014-15. NICOR. https://www.ucl.ac.uk/nicor/audits/heartfailure/documents/annualreports/annual_report_2014_15_v2
2. Bakris GL, Weir MR. Angiotensin-converting enzyme inhibitor-associated elevations in serum creatinine. Arch Intern Med (2000);160:685–93.
3. 2016 ESC Guidelines for the treatment and management of acute and chronic heart failure. European Heart Journal (2016); 37:2129–2200

Frailty and Chronic Kidney Disease (CKD)

Endorsed by Medicine for The Elderly department, Imperial College NHS Healthcare Trust

Management of CKD in the context of frailty requires a holistic approach

Kidney Ageing

Kidney function (GFR) declines with age:
- ~0.8 mL/min/year after 35 years old
- up to 2mL/min/year after 70 years old

- eGFR >30mL/min in the absence of acute illness, proteinuria or uncontrolled HTN is unlikely to progress to end-stage kidney disease

Focus of Care in Frail Patients

- Should be patient and outcome centred
- View CKD in the context of an individual's comorbidities and personal priorities
- Renal replacement therapy (RRT) may not improve quality of life – focus on symptom control may be more appropriate
- Advance care planning should be a priority

MANAGEMENT OF FRAIL PATIENTS WITH CKD

Identify frailty and screen for cognitive impairment
- Consider calculating EFI score (https://doi.org/10.1093/ageing/afw039)
- Consider screening cognition using GPCOG (http://gpcog.com.au/)

Medications
- Frail patients are more susceptible to harm from medications
- Refer to "Drugs and CKD" page

Blood pressure (BP) or HbA1c targets - individualise to patient:
- Be wary of falls risk – check postural BPs
- Higher BP targets are appropriate eg. systolic BP 130-159 mmHg / diastolic BP 70-89 mmHg
- Be wary of hypoglycaemia risk with insulin and oral hypoglycaemic agents
- Higher HbA1c targets are appropriate eg. 58-68 mmol/mol

Diet – avoid protein restriction / aggressive salt restriction

Monitoring of renal function
- If renal replacement therapy (RRT) is considered - refer to page 3
- If RRT is unlikely to improve quality of life, tailor frequency to clinical need

In event of sudden eGFR decline exclude common causes:
- UTIs
- obstructive uropathy
- Medications (eg. anti-hypertensives, NSAIDs)

Consider nephrology advice if:
- Unexplained and sustained decline in renal function / new nephrotic range proteinuria
- Refractory and symptomatic anaemia (<100g/L) in advanced CKD (stages 3b – 5)

may require intravenous iron +/- erythropoietin supplementation

Further advice

Specialty advice is available to North West London primary care services:
- ICHC-tr.ckdadvice@nhs.net (nephrology consultant advice)
- ICHC-tr.adviceelderlymedicine-imperial@nhs.net (consultant geriatrician advice)

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