Chronic Kidney Disease

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Case Presentations

56 year old Mr K admitted to the Emergency Department with one day onset of confusion. He has 10 year history of hypertension treated with Enalapril and HCTZ.

No previous vascular disease.

No important surgical history

No important family history

No other drug or over the counter or recreational drug use.

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On examination

Patient appears acutely ill with rapid acidotic type breathing and confusion (time and place).

BP 164/92 mm Hg , Heart rate 95 sinus rhythm, Temp Normal, Sats 90% on room air.

Slight pallor noted with pitting oedema

JVP raised 6 cm above sternal angle

S1 S2 S4 crackles both bases of lungs

Abdo slight bulging of flanks, ascites could not be ruled out

Lab results

Na 136 Cl 110 HCO3 15 urea 33.4 sCreat 1200 K^+ 6.4

Hb 7.6 MCV 82 Pl 233

Ca 1.0 Phos 2.0

Urine 2+ protein, no RBC or casts

What next?

Case presentation

62 year old Mrs E

Routine HT follow up at GP practice

Lab results show urea 12.2 sCreat 134 eGFR 44 K+ 5.1

Urine trace protein only

What next?

CKD definition

Chronic kidney disease is defined as the presence of an abnormality in kidney structure or function persisting for more than 3 months.

This includes 1 or more of the following:

(1) GFR less than 60 mL/min/1.73 m2;

(2) albuminuria (ie, urine albumin 30 mg per 24 hours or urine albumin-to-creatinine ratio [ACR] 30 mg/g);

(3) abnormalities in urine sediment, histology, or imaging suggestive of kidney damage;

(4) renal tubular disorders;

(5) history of kidney transplantation.

CKD definition

If the duration of kidney disease is unclear, repeat assessments should be performed to distinguish CKD from

- **acute kidney injury** (change in kidney function occurring within 2-7 days) and
- **acute kidney disease** (kidney damage or decreased kidney function present for 3 months).

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Epidemiology

10% of world population

Causes vary by region

Globally hypertension and diabetes mot common causes

Work Up

Staging: sCreat and UACR

Determine cause

Identify poor prognostic factors

Imaging: renal ultrasound

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Figure 2. Definition and Prognosis of Chronic Kidney Disease by GFR and Albuminuria Categories, KDIGO 2012

				Persistent albuminuria categories, description, and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g	30-300 mg/g	>300 mg/g
GFR categories, description, and range (mL/min/1.73 m^2)	G1	Normal or high	≥90			
	G2	Mildly decreased	60-89			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	<15			

GFR indicates glomerular filtration rate; KDIGO, Kidney Disease Improving Global Outcomes. Categories are grouped by risk of progression, which includes chronic kidney disease progression, defined by a decline in GFR category (accompanied by a ≥25% decrease in estimated GFR from baseline) or sustained decline in estimated GFR greater than 5 mL/min/1.73 m^2 per year. Green indicates low risk (if no other markers of kidney disease and no CKD); yellow, moderately increased risk; orange: high risk; and red, very high risk. Reproduced with permission from *Kidney International Supplements*.[5]

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Staging of CKD by CGA (cause, eGFR, and ACR)

Determine cause with clinical history, physical examination, and other studies

- Diabetes
- Hypertension
- Autoimmune disease
- Nephrotoxin exposure
- Chronic infection
- Malignancy
- Urinary obstruction
- Genetic or familial kidney disease
- Kidney imaging (eg, ultrasound)[a]
- Urine studies (eg, urinalysis and urine microscopy)[a]

Determine eGFR category

G1	≥90 mL/min/1.73 m^2
G2	60-89 mL/min/1.73 m^2
G3a	45-59 mL/min/1.73 m^2
G3b	30-44 mL/min/1.73 m^2
G4	15-29 mL/min/1.73 m^2
G5	<15 mL/min/1.73 m^2

Determine albuminuria category

A1	ACR <30 mg/g
A2	ACR 30-300 mg/g
A3	ACR >300 mg/g

Identification of poor prognostic factors

- Rapidly progressive CKD
- Uncontrolled hypertension
- Severe electrolyte abnormalities
- Structural abnormality
- Hereditary kidney disease
- Hematuria or sterile pyuria
- Recurrent or severe nephrolithiasis
- High 2-year end-stage kidney disease risk score[b]
- Nephrotic syndrome

JAMA. 2019;322(13):1294-1304. doi:10.1001/jama.2019.14745

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eGFR

Modification of Diet in Renal Disease equation

Chronic Kidney Disease Epidemiology Collaboration equation

Table 3. **Classification of CKD Based on the Presence or Absence of Systemic Disease and the Kidney Location of Pathologic Findings***

Diseases	*Examples of Systemic Diseases Affecting the Kidney*	*Examples of Primary Kidney Diseases (Absence of Systemic Disease)*
Glomerular	Diabetes, systemic autoimmune diseases, systemic infections (bacterial endocarditis, hepatitis B and C, HIV), drugs, neoplasia (including amyloidosis)	Diffuse, focal, or crescentic proliferative glomerulonephritis; focal and segmental glomerulosclerosis; membranous nephropathy; minimal change disease
Tubulointerstitial	Systemic infections, autoimmune, sarcoidosis, drugs, urate, environmental toxins (lead, aristolochic acid), neoplasia (myeloma)	Urinary tract infections, stones, obstruction
Vascular	Atherosclerosis, hypertension, ischemia, cholesterol emboli, systemic vasculitis, thrombotic microangiopathy, systemic sclerosis	ANCA-associated renal limited vasculitis, fibromuscular dysplasia
Cystic and congenital	Polycystic kidney disease, the Alport syndrome, Fabry disease	Renal dysplasia, medullary cystic disease, podocytopathies

Chronic Kidney Disease. In The Clinic. Annals of Internal Medicine 2015

Box. Clinical, Sociodemographic, and Genetic Risk Factors for Chronic Kidney Disease

Clinical

Diabetes

Hypertension

Autoimmune diseases

Systemic infections (eg, HIV, hepatitis B virus, hepatitis C virus)

Nephrotoxic medications (eg, nonsteroidal anti-inflammatory drugs, herbal remedies, lithium)

Recurrent urinary tract infections

Kidney stones

Urinary tract obstruction

Malignancy

Obesity

Reduced kidney mass (eg, nephrectomy, low birth weight)

History of acute kidney injury

Smoking

Intravenous drug use (eg, heroin, cocaine)

Family history of kidney disease

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Sociodemographic

Age >60 years

Nonwhite race

Low income

Low education

Genetic

APOL1 risk alleles

Sickle cell trait and disease

Polycystic kidney disease

Alport syndrome

Congenital anomalies of the kidney and urinary tract

Other familial causes

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Cardiovascular risk

Lancet 2021; 398: 786–802
Published Online June 24, 2021 https://doi.org/10.1016/ S0140-6736(21)00519-5

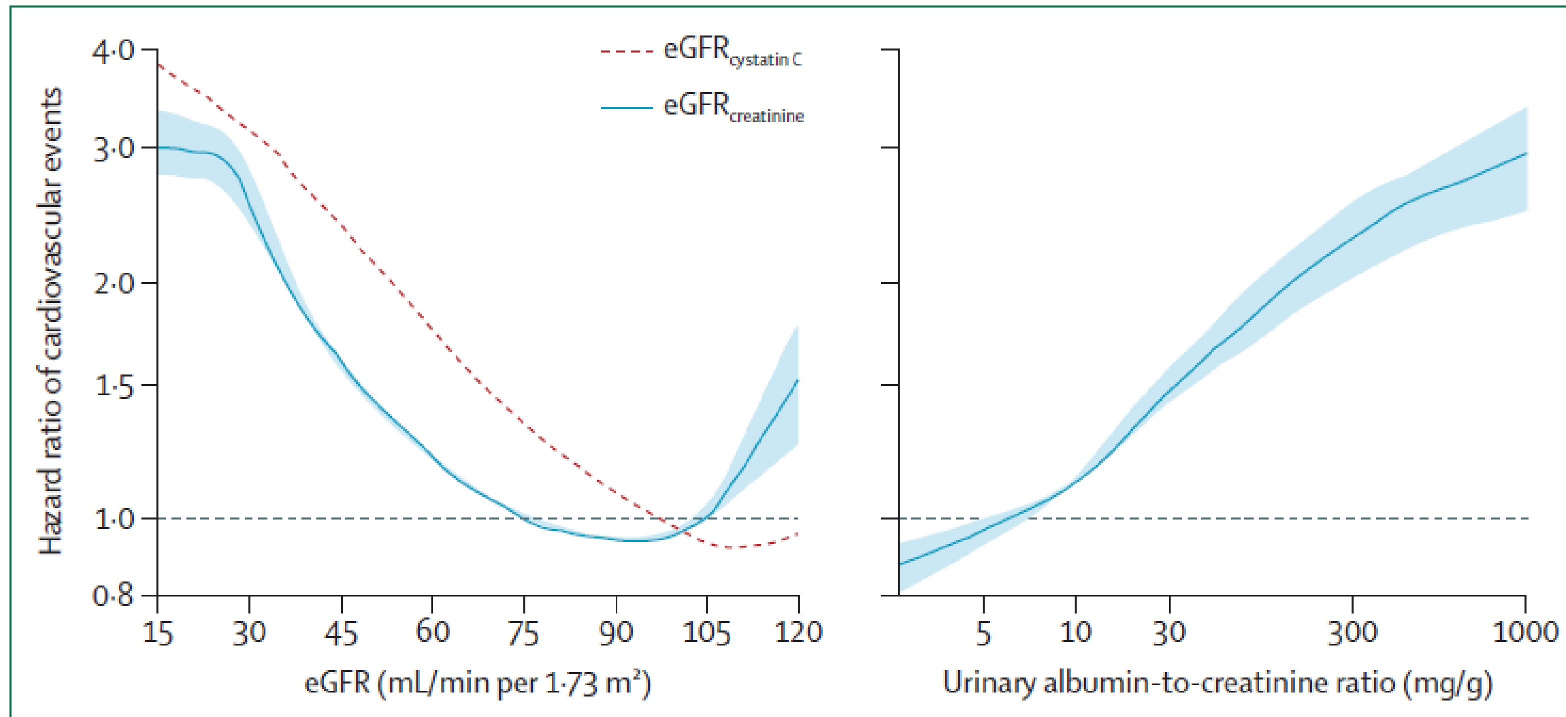

Figure 3: Association of eGFR and albuminuria with hazard ratio of cardiovascular events

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Which drugs and other agents cause acute kidney injury in patients with CKD?

NSAIDS

Contrast

Antibiotics

Tenofovir

Herbal Meds

Phosphate based bowel meds

Treatment and limiting progression

1. Treatment to prevent progression
2. HT and glucose management
3. Anemia rx
4. Fluid management
5. K/Phos/Ca management
6. Refer when needed

What do we want to achieve?

Lancet 2021; 398: 786–802
Published Online June 24, 2021 https://doi.org/10.1016/ S0140-6736(21)00519-5

Improved tubular structure, integrity, and function
(decreased sodium and glucose reabsorption and tubular energy expenditure)
- Dietary sodium restriction
- Glucose-lowering drugs
- SGLT2 inhibitors

Low-protein diet, weight loss, SGLT2 inhibitors

Low-salt diet, blood pressure-lowering agents

Vasoconstriction

Afferent arteriole

M

M

↓GFR
↓Hyper-filtration

↓Intraglomerular pressure

Tubulo-glomerular feedback

Distal tubule

Proximal tube

M

M

Efferent arteriole

Vasodilation

RAAS modulators

Reduction in intraglomerular pressure
(modulation of tubuloglomerular feedback, afferent and efferent arteriole tone, and distal sodium and chlorine delivery)
- Plant-dominant low protein diet
- Acidosis mitigation therapy
- SGLT2 inhibitors
- RAAS blockade

Decreased inflammation and interstitial fibrosis
(modulation of mesangial cell and signal transduction)
- Plant-dominant, low protein diet
- Mineralocorticoid receptor antagonists
- Disease-specific therapies

↓ Reduction effect

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What nondrug therapies should clinicians recommend?

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- Plant dominant low protein diets
- Nutrient focused diets (low Na, low Phos, Low K)
- Physical activity (150min/w)
- Weight reduction
- Smoking cessation
- Dietary Sodium restriction

Which drugs can slow progression?

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- RAAS blockade
- SGLT2 inhibitors (MD and non DM)
- Non steroidal MRA (DM)
- Tovaptan (PKD)
- Rituximab (primary membranous nephropathy)
- Steroids for Ig A nephropathy

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SGLT2 inhibitors: diabetes and non diabetes

CREDENCE
DAPA-CKD
Cardiovascular death

CREDENCE
DAPA-CKD
All-cause death

EMPEROR-reduced no-DM
EMPEROR-reduced DM
DAPA-HF no-DM
DAPA-HF DM
CREDENCE
DAPA-CKD
Cardiovascular death or hospitalization for heart failure

CREDENCE
DAPA-CKD DM
DAPA-CKD No-DM
DAPA-CKD
Primary combined kidney endpoint

0 0.2 0.4 0.6 0.8 1.0
Hazard ratio vs. placebo

DM and non-DM patients
Non-DM patients
DM patients

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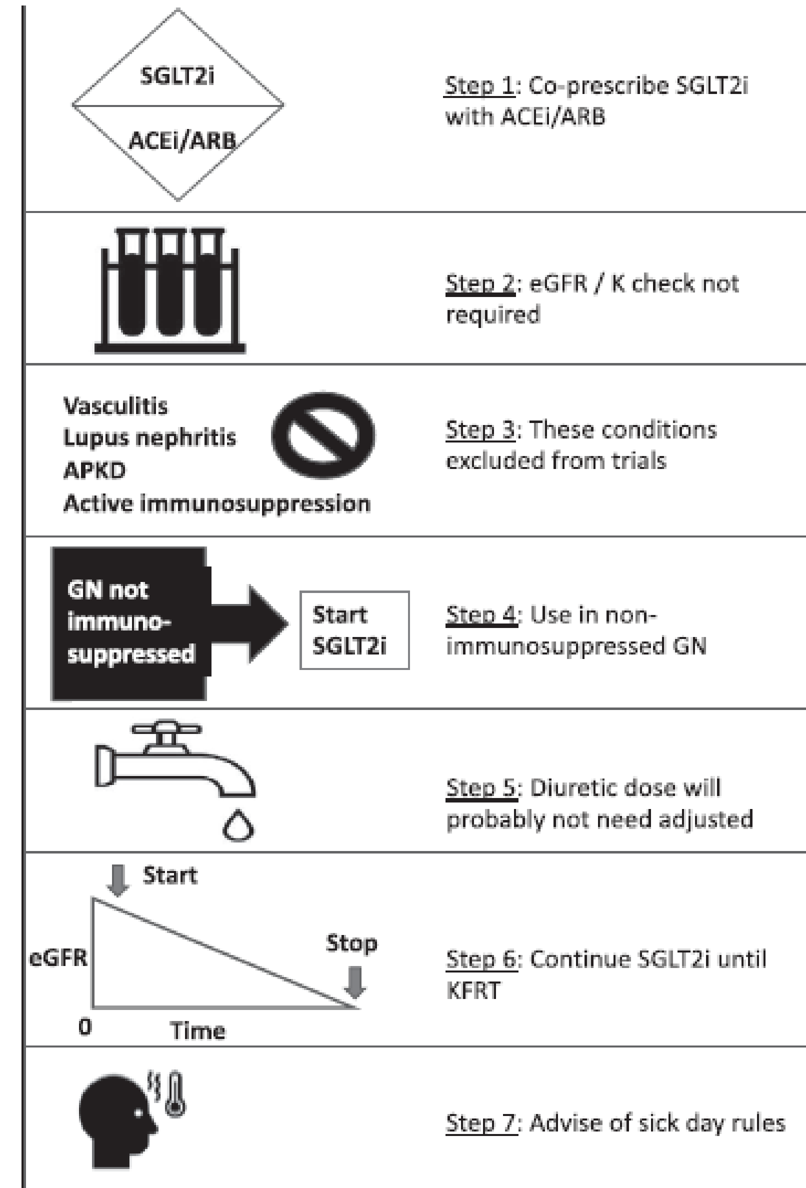
Clin Kidney J. 2020 Oct; 13(5): 728–733.
Published online 2020 Oct 9. doi: 10.1093/ckj/sfaa198

7 steps for SGLT2 use

Curr Opin Nephrol Hypertens 2022, 31:272–277
DOI:10.1097/MNH.0000000000000786



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Other strategies to treat uraemia and symptoms and slow progression

Lancet 2021; 398: 786–802
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- Sodium Bicarbonate and veverimer for acidosis
- Potassium binders (Kayexalate and zirconium)
- Sodium and volume management
- Symptom management (insomnia, pruritus)
- Anemia management (chk Fe/folate/B12 aim below 11.5 Hb) EPO sc
- Prevention of infection (Hep C , Covid)

How should clinicians manage metabolic complications?

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Hyper kalemia (level > 6 mmol/l)

Sodium Polystyrene Sulfonate (Kayexalate)

- Older agent, developed in the 1960s
- 15 g 1-4 times daily (constipation, sorbitol, colonic necrosis)

Newer Potassium binders

- Patiromer (Veltassa)
- Zirconium Cyclosillicate (Lokelma)

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Hyperphosphatemia, secondary hyper parathyroidism

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Restrict phosphate in diet

> 1.7 mmol/l consider binder

Binders : Ca based (Ca carbonate, Ca acetate)
non Ca (sevelamer (Renvela), Lanthanum (Fosrenol)

Chk Vit D level, Calciferol (D3) 50-300 000IU per week (or in dly doses)

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Metabolic acidosis (HCO3 < 22 mmol/l)

Soda bic 0.5-1 mEq/kg

Tabs have 11.9 mEq per 1000 mg tab

Baking soda 60 mEq/teaspoon

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Reducing cardiovascular risk

Statin therapy

BP therapy : Target Systolic < 120 mm Hg (KDIGO)

Glucose therapy

What are the indications for renal replacement therapy?

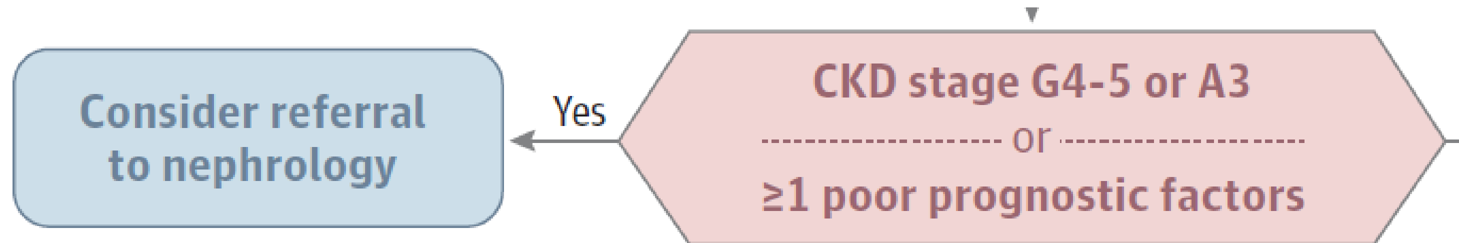
Common indications to initiate dialysis are

- volume overload unresponsive to diuretics,
- pericarditis,
- uremic encephalopathy,
- major bleeding secondary to uremic platelets,
- hypertension that does not respond to treatment
- hyperkalemia and metabolic acidosis that cannot be managed medically
- progressive “uremic” symptoms, such as fatigue, nausea and vomiting,

loss of appetite, evidence of malnutrition, and insomnia, are also indications for initiation of renal replacement therapy

When to refer?

eGFR < 30



UACR > 300mg/g

HT/K/Phos you can`t manage

Identification of poor prognostic factors

- Rapidly progressive CKD
- Uncontrolled hypertension
- Severe electrolyte abnormalities
- Structural abnormality
- Hereditary kidney disease
- Hematuria or sterile pyuria
- Recurrent or severe nephrolithiasis
- High 2-year end-stage kidney disease risk score[b]
- Nephrotic syndrome

Case presentation

62 year old Mrs E

Routine HT follow up at GP practice

Lab results show urea 12.2 sCreat 134 eGFR 44 K+ 5.1

Urine trace protein only

What next?

Evaluation

Clinical evaluation

Staging of CKD by CGA (cause, eGFR, and ACR)

Determine cause with clinical history, physical examination, and other studies

- Diabetes
- Hypertension
- Autoimmune disease
- Nephrotoxin exposure
- Chronic infection
- Malignancy
- Urinary obstruction
- Genetic or familial kidney disease
- Kidney imaging (eg, ultrasound)[a]
- Urine studies (eg, urinalysis and urine microscopy)[a]

Determine eGFR category

Category	eGFR
G1	≥90 mL/min/1.73 m^2
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G5	<15 mL/min/1.73 m^2

Determine albuminuria category

Category	ACR
A1	ACR <30 mg/g
A2	ACR 30-300 mg/g
A3	ACR >300 mg/g

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Evaluation

Other evidence of HT end organ damage?

Cardiovascular risk assessment

UACR to stage

Renal ultrasound

Treatment

BP treatment, lower targets, ACEI or ARB

Consider addition of SGLT2

Avoid nephrotoxic drugs

Monitor serum K+

6 monthly to annual monitoring of Creat, Ca, Phos, Hb

Keep referral criteria in mind: don’t refer too early but also not too late!