Chronic Kidney Disease (CKD)

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Definition

- Defined by **structural** or **functional** abnormalities of the kidney for **3 months** or longer, with or without decreased glomerular filtration rate (GFR).
- Normal GFR **is ≥90 mL/min/1.73 m2**.
- Presence of **albuminuria** or **proteinuria** is associated with increased risk of death or complications in patients with CKD

Definition

- The National Kidney Foundation has established the following stages of CKD:
  - **Stage I:**
    - Kidney damage (proteinuria, cyst formation, etc.) with normal or increased GFR
  - **Stage II:**
    - Kidney damage with mild decrease in GFR (GFR 60–89 mL/min/1.73 m2)
  - **Stage III:**
    - Moderate decrease in GFR (GFR 30–59 mL/min/1.73 m2)
    - **stage IIIa** (GFR 45–60 mL/min/1.73 m2)
    - **stage IIIb** (GFR 30–45 mL/min/1.73 m2)
  - **Stage IV:**
    - Severe decrease in GFR (GFR 15–29 mL/min/1.73 m2)
  - **Stage V:**
    - Kidney failure (GFR 15 mL/min/1.73 m2 or dialysis)

Stages of CKD

Guide to Frequency of Monitoring (number of times per year) by GFR and Albuminuria Category				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30-300 mg/g 3-30 mg/mmol	>300 mg/g >30 mg/mmol
GFR categories (ml/min/ 1.73 m^2) Description and range	G1	Normal or high	≥90	1 if CKD	1	2
	G2	Mildly decreased	60-89	1 if CKD	1	2
	G3a	Mildly to moderately decreased	45-59	1	2	3
	G3b	Moderately to severely decreased	30-44	2	3	3
	G4	Severely decreased	15-29	3	3	4+
	G5	Kidney failure	<15	4+	4+	4+

Epidemiology

- Many patients with CKD progress to ESRD
- **Prevalence increases with age**
- Estimated ESRD prevalence in the United States in 2019 was over 808,000, with an annual incidence of greater than 110,000

Etiology

- Diabetes (~40%)
- Hypertension (~25%)
- Glomerulonephritis (~10%)
- Genetic or congenital (e.g., polycystic kidney disease;~3%)
- Urologic (~2%)

Clinical Presentation

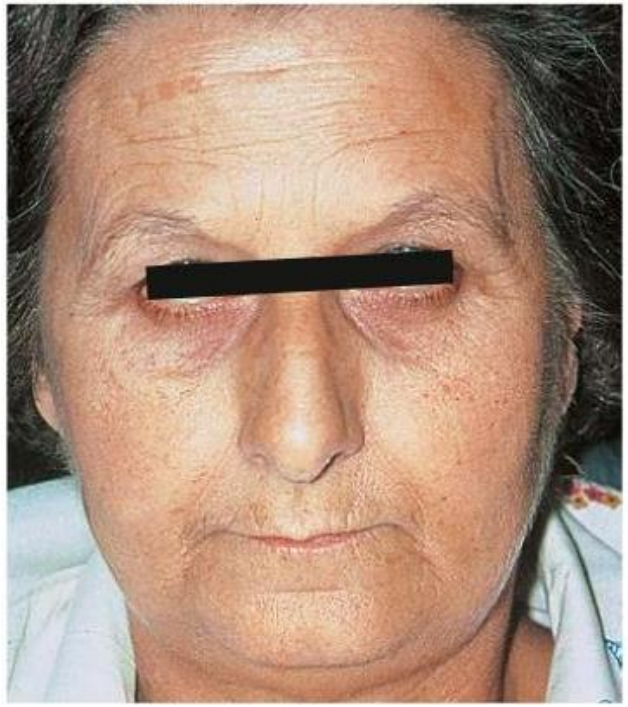
- Usually **asymptomatic** until the late stages of renal failure
- Onset of symptoms is usual indication for initiation of dialysis

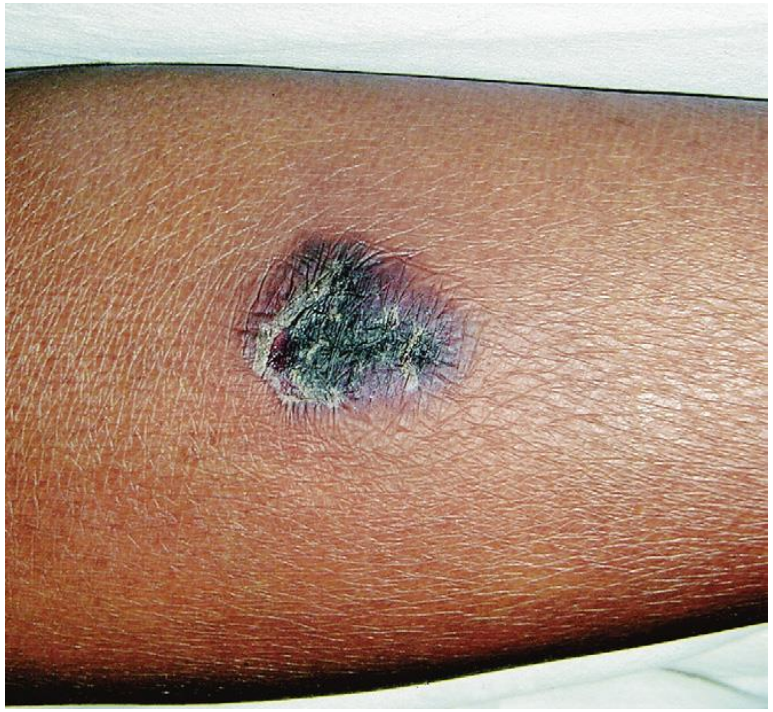
- **Early symptoms:**
  - anorexia, nausea, lethargy, fatigue
- **Late symptoms:**
  - pruritis, mental status changes due t encephalopathy, volume overload, chest pain from pericarditis, neuropathy

Clinical Presentation

- Physical examination findings:
  - **Asterixis** (indicative of encephalopathy)
  - **Pericardial friction rub**
  - Signs of **volume overload**
  - **Uremic fetor**: Foul-smelling breath similar to urine or fish
  - **Pallor**
  - **Calciphylaxis**: Calcification of arterioles seen in patients with ESRD (not just CKD), Also called (**calcific uremic arteriolopathy**).

Clinical Presentation





Clinical Presentation

- Metabolic abnormalities often seen:
  - **Anemia**
  - **Secondary** and **tertiary hyperparathyroidism** (associated with hypocalcemia, hyperphosphatemia, and metabolic bone disease)
  - **Acidosis**
  - **Hyperkalemia**
  - **Volume overload**

Diagnosis

- Diagnose by **estimated** or **actual GFR**, **not serum creatinine (Cr) levels**
- Normal GFR is usually greater than 90 mL/min in women and greater than 100 mL/min in men
- **CKD is underdiagnosed if serum Cr is used as sole measure**
- Need to use GFR estimation equations formula is preferred for estimating GFR.
- Chronic Kidney Disease Epidemiology Collaboration (**CKD-EPI**) equation improves GFR estimation compared with (**MDRD**) equation in those with GFR above 60 mL/min/1.73 m2

Diagnosis

- **Cockcroft-Gault equation** is an alternative:

$$\frac{(140 - \text{age}) \times \text{lean body weight (kg)}}{\text{Serum Cr (mg/dL)} \times 72}$$

- For GFR in women, multiply equation by 0.85

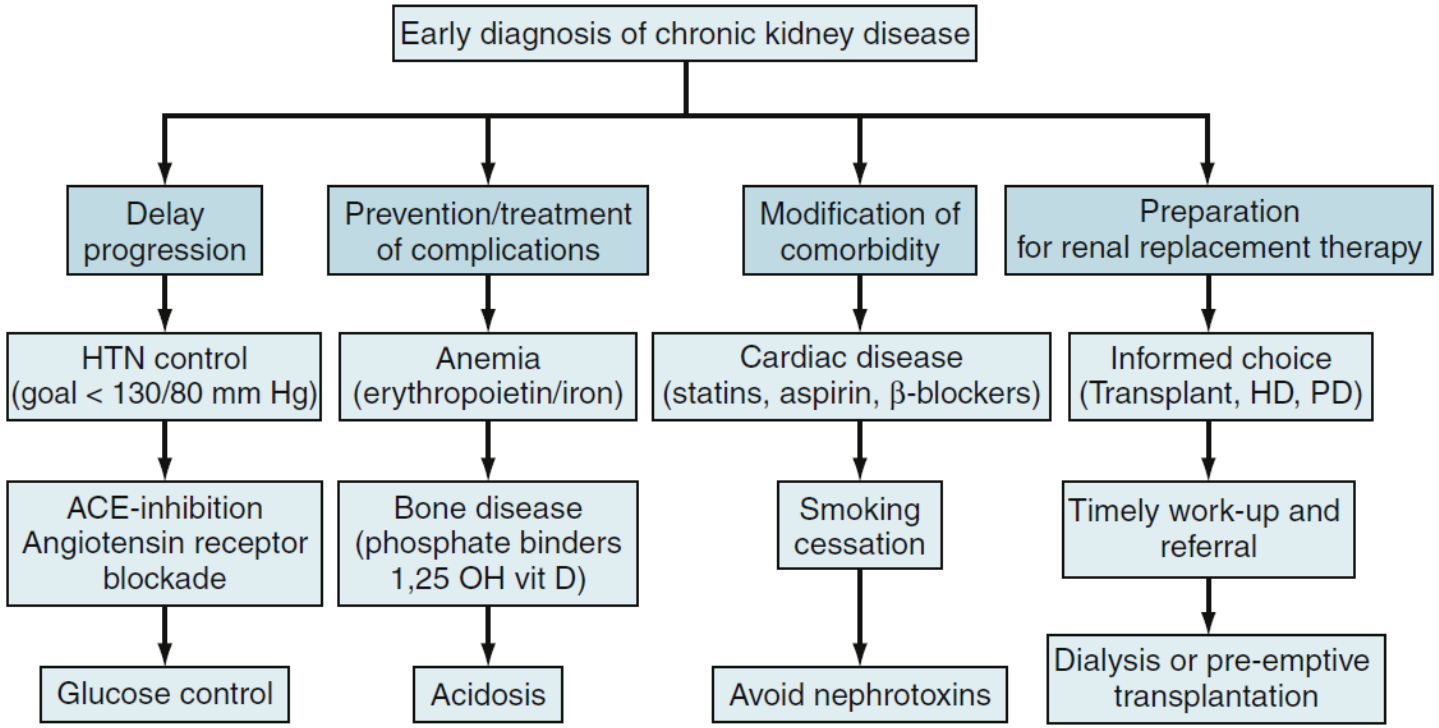
Diagnosis

- **Other features that indicate CKD:**
  - Evidence that low GFR is long-standing (more than one measure over longer than 3 months)
  - Small kidneys on renal ultrasound (normal kidney size is 10 to 12 cm; kidneys are smaller in women)
  - Presence of manifestations of CKD: anemia, secondary hyperparathyroidism
- **Should rule out reversible causes in any patient with renal insufficiency**
  - Obstruction and prerenal causes
  - Treatable glomerular disease
  - Atherosclerotic renal vascular disease

Management

- Early recognition of CKD
- Delay progression of CKD
- Prevent and treat complications of CKD
- Avoid additional insults
- Avoid volume depletion
- Avoid iatrogenic complications from medications
- Renal replacement therapy (RRT)

Management


Early diagnosis of chronic kidney disease
Delay progression
Prevention/treatment of complications
Modification of comorbidity
Preparation for renal replacement therapy
HTN control (goal < 130/80 mm Hg)
Anemia (erythropoietin/iron)
Cardiac disease (statins, aspirin, β-blockers)
Informed choice (Transplant, HD, PD)
ACE-inhibition Angiotensin receptor blockade
Bone disease (phosphate binders 1,25 OH vit D)
Smoking cessation
Timely work-up and referral
Glucose control
Acidosis
Avoid nephrotoxins
Dialysis or pre-emptive transplantation

Management

- **Early recognition of CKD**
  - Early referral to nephrologist shown to improve outcomes
  - Consider nephrology referral for:
    - Unexplained proteinuria or hematuria suggestive of glomerulonephritis
    - Rapid decline in GFR (>5 mL/min/1.73 m2 per year)
    - All patients with GFR less than 30 mL/min/1.73 m2
    - Allows for early intervention

Management

- **Delay progression of CKD:**
  - Management of hypertension
    - Hypertension is a very important risk factor for acceleration in decline in GFR
    - Adequate control of blood pressure reduces rate of decline in GFR
    - Further reduction in blood pressure below 130/80 mm Hg (125/75 mm Hg) may have added benefit in patients, especially those with proteinuria
    - ACE inhibitors or ARBs should be first line, given their independent benefits in slowing progression of renal disease

Management

- **Delay progression of CKD:**
  - Management of glucose in patients with diabetes mellitus and CKD
    - Tight control of patient's blood glucose may slow progression of diabetic nephropathy
    - Goal hemoglobin A1c (Hgb A1c) is 6%
  - Modify other cardiovascular risk factors (e.g., tobacco use, hypercholesterolemia)
  - Avoid nephrotoxins and use renally cleared drugs with caution

Management

- **Delay progression of CKD:**
  - Angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs)
    - Mechanism: Decrease intraglomerular pressure and hyperfiltration
    - Problem: May lead to elevation of serum creatinine and potassium
    - Creatinine rise is 30% or less: Can continue therapy as there is long-term benefit in preservation of GFR
    - If potassium is elevated (goal to maintain ACE inhibitor or ARB therapy)
      - Exclude renal artery stenosis
      - Dietary potassium restriction (major culprits include bananas, cantaloupe, oranges, potatoes, tomatoes)
      - Use of potassium-depleting diuretic (thiazide type or loop diuretic)
      - Elimination of potassium-sparing diuretics (triamterene, spironolactone, or eplerenone)
      - Consider ß-blocker dose reduction (unless essential for other reasons)

Management

- **Delay progression of CKD:;**
  - SGLT2 inhibitors:
    - Reduce the risk of adverse outcomes in patients with CKD with DM
    - reduced albuminuria by 30% to 50%
    - interfere with the major mechanism of proteinuric CKD progression (i.e., glomerular hypertension and hyperfiltration)
    - Approved for patients with type II DM and CKD
    - Ongoing trials for CKD patients without diabetes
  - Non-dihydropyridine calcium channel blockers (NDHP):
    - diltiazem and verapamil, slow the progression of type 2 diabetic nephropathy with overt proteinuria almost to a similar extent as observed with ACE-I.

Management

- **Delay progression of CKD:**
  - Dietary protein restriction
    - Mechanism: In theory, reduced protein intake decreases intraglomerular pressure and metabolic demands on kidney
    - Conflicting efficacy data from trials
    - Recommendation (largely opinion-based): Maximum dietary restriction for a patient with CKD would be 0.7 g of protein/kg of body weight/day; many would suggest that 1 g of protein/kg of body weight/day would be more appropriate
    - If patient is placed on protein-restricted diet, must
    - have close follow-up of nutritional status to avoid malnutrition

Management

- **Prevent and treat complications of CKD**
  - Anemia, metabolic bone disease, acidosis, and volume overload
    - Recent studies suggest increased risk of cardiovascular events (especially stroke) with normalization of hemoglobin (>13 g/dL)
    - Consider iron repletion in all patients and start erythropoiesis-stimulating agents if hemoglobin is below 9 g/dL
  - Other endocrine complications
    - Decreased GFR leads to prolonged half-life of insulin Patients with progressive renal failure need a downward titration of insulin and sulfonylurea dosing to avoid hypoglycemia

Management

- **Avoid additional insults**
  - Radiocontrast
    - Risk of acute renal failure 20% to 90%
    - Patients with diabetes at highest risk
    - Choose alternative imaging modality if possible
  - Gadolinium-based contrast agent contraindicated in those with estimated GFR less than 30 due to risk of nephrogenic systemic fibrosis (NSF)
    - if its use is essential in this high-risk group, use a low dose of a macrocyclic (more stable) agent (gadoteridol)
  - If radiocontrast use unavoidable:
    - Ensure adequate hydration with isotonic saline or sodium bicarbonate
    - Minimize contrast volume
    - Utilize nonionic contrast
    - N-Acetylcysteine 600 mg twice a day for 24 hours before procedure and 48 hours following procedure may reduce incidence of acute renal failure in high-risk groups (Recent studies found it ineffective)

Management

- **Avoid volume depletion**
  - Tolerated poorly in this patient population
  - May lead to worsening of CKD secondary to acute tubular necrosis
  - Low threshold for IV fluids for hydration
- **Avoid iatrogenic complications from medications**
  - Adjust dose and interval of all renally metabolized medications

Management

- **Renal replacement therapy - Renal transplantation**
  - Preferred treatment of ESRD
  - Every patient with ESRD should be considered a candidate for transplantation until proven otherwise
  - Refer to transplantation center for evaluation when GFR 30 mL/min or less
  - Patients can be listed for deceased donor transplant when GFR less than 20 mL/min
  - Treatment goal, for suitable candidate, is to receive a transplant before need for dialysis
  - Prognosis: The 5-year survival is 80% for deceased donor, 85% for living unrelated donor, and 90% for living related donor

Management

- **Renal replacement therapy - Dialysis**
  - 90% of patients are candidates for either hemodialysis (HD) or peritoneal dialysis (PD)
  - If therapy prescribed and monitored correctly, HD equals PD in effectiveness
  - Dialysis initiation: Usually based on combination of GFR level and presence of early symptoms of kidney failure
    - Diabetics: Estimated GFR less than 15 mL/min/1.73 m2
    - Nondiabetics: Estimated GFR less than 10 mL/min/1.73 m2

Management

- **Renal replacement therapy – Dialysis**
  - Absolute dialysis indications (ideal goal is to avoid these manifestations)
    - Uremic encephalopathy
    - Uremic pericarditis
    - Volume overload not responsive to diuretics
    - Hyperkalemia despite medical management
    - Acidosis despite medical management
  - Prognosis for dialysis patients is poor in general Median 5-year survival: 33% (1 in 3 dialysis patients will survive for 5 years after starting dialysis)
  - Most common cause of death: Heart disease (usually sudden cardiac death), followed by infection Patients who start dialysis with a catheter have the worst prognosis.

Evidence-Based Strategies to Slow the Progression of Kidney Disease	
Risk Factor	**Treatment Goals and Recommended Agents**
Overweight	Maintain a healthy weight (BMI 20–25 kg/m2)
Diet	Lower or maintain salt intake to <90 mmol/day (equivalent to <2 g sodium/day or <5 g sodium chloride/day) Low protein intake: 0.8 g/kg/day in adults with diabetes or without diabetes and CKD (G4–G5), with appropriate education
Smoking	Smoking cessation
Exercise	Encourage 30–60 min of aerobic exercise at least 5 times/wk
Proteinuria/albuminuria	Monitoring and follow up; treatment with ACE inhibitors/ARBs, with proteinuria >300 mg/24h
Blood pressure	<130/80 mm Hg (diabetes or proteinuric CKD),a <140/80 mm Hg (nondiabetic or nonproteinuric CKD)
Diabetes	HbA1c <7% and use of newer agents (i.e., SGLT2 inhibitors may yield significant benefits for patients with CKD stages 1–4 with regard to CV and kidney outcomes)
Dyslipidemia Metabolic acidosis	Use of lipid-lowering medications Bicarbonate supplementation with levels <20 mEq/L
Other metabolic risk factors (elevated uric acid)	Insufficient evidence to support or refute the use of agents for hyperuricemia


Thank You