Chronic Kidney Disease

Previously referred to as chronic renal failure, chronic kidney disease (CKD) is a progressive, irreversible loss of kidney function resulting in reduced filtration, build-up of toxins and fluid, and electrolyte imbalances. Chronic kidney disease is defined based on the presence of either kidney damage or decreased kidney function for three or more months, irrespective of cause. Continued decline in kidney function (e.g. progression of CKD) will lead to end-stage renal disease (ESRD), in which the kidneys no longer function and dialysis or transplant becomes necessary (Fatehi et al., 2024).

Definition

The Kidney Disease: Improving Global Outcomes (KDIGO) workgroup defines CKD as either of the following for ***at least three months*** (KDIGO, 2024):

- Estimated glomerular filtration rate (eGRF) less than 60 mL/min/1.73 m^2

OR

- Markers of kidney damage (one or more)
  - Albuminuria
    - Albumin-to-creatinine ratio (ACR) greater than or equal to 30 mg/g (3mg/mmol)
  - Urine sediment abnormalities
  - Persistent hematuria
  - Electrolyte and other abnormalities due to tubular disorders
  - Abnormalities detected by histology
  - Structural abnormalities detected by imaging
  - History of kidney transplantation

Classification of CKD

CKD is classified based on **C**ause, **G**FR category (G1-G5), and **A**lbuminuria category (A1-A30) abbreviated as CGA. The cause of CKD is based on the presence or absence of systemic disease and the location within the kidney of pathologic-anatomic findings (KDIGO, 2024). GFR reflects total filtration in all functioning nephrons.

To assess GFR, the KDIGO (2024) recommends using a creatinine-based estimated GFR rate (eGFRcr). However, if serum cystatin C is available, the GFR category should be estimated using a combination of the two to improve the accuracy of the estimation.

Glomerular Filtration Rate (GFR) Categories (KDIGO, 2024)		
GFR category	**GFR (mL/min/1.73m^2)**	**Terms**
G1	Greater than or equal to 90	Normal or high
G2	60-89	Mildly decreased
G3a	45-59	Mildly to moderately decreased
G3b	30-44	Moderately to severely decreased
G4	15-29	Severely decreased
G5	Less than 15	Kidney Failure

Protein filtered from the blood is typically reabsorbed in the nephron tubules with minimal amounts excreted in the urine. In CKD, glomerular permeability increases allowing protein to cross back into the

urine. Since albumin is the primary protein in the urine of people with CKD, elevated urine albumin is a marker for glomerular disease (Vaidya et al., 2024).

Albuminuria Categories in CKD (KDIGO, 2024)				
	Albumin Excretion Rate (AER)	**Urine Albumin (mg)-to-Creatinine (g) Ratio (ACR) (Approximate equivalent)**		
Category	(mg/24 hours)	(mg/mmol)	(mg/g)	Terms
A1	Less than 30	Less than 3	Less than 30	Normal to mildly increased
A2	30-300	3-30	30-300	Moderately increased
A3	Greater than 300	Greater than 30	Greater than 300	Severely increased

Most Common Causes & Risk Factors

CKD: Common Causes and Risk Factors (Banasik, 2022)	
Diabetes	Smoking
Hypertension	Increasing Age
Glomerular diseases	Hyperlipidemia
Cystic Kidney Disease	Gender: more common in males than females
Crush injury	Obesity
Toxins and medications (e.g., ibuprofen, aspirin, contrast dyes)	Race: higher risk in Black, Hispanic, Pacific Islander, and Native American populations
Chronic autoimmunue disorders (e.g., systemic lupus erythematosus, scleroderma, amyloidosis) and congenital kidney conditions (renal agenesis, aplastic kidneys)	Family history of kidney disease and cardiovascular disease
Renal malignancy	Personal history of Acute Kidney Injury (AKI)
Infection (recurrent pyelonephritis, renal tuberculosis)	

Signs and Symptoms

Signs and symptoms will vary based on the stage of disease. Many patients are asymptomatic until CKD is advanced.

- Nausea, vomiting
- Dependent edema
- Poor appetite, anorexia
- Dry, itchy skin
- Weakness, fatigue, malaise
- Decreased urine output, urinary frequency, blood in urine
- Shortness of breath
- Bone/joint pain

Diagnosis

Laboratory Tests: Important to establish cause and to stage the disease.

- Chemistry: sodium, potassium, calcium, chloride, phosphorus, bicarbonate, glucose, pH
- Albumin
- Blood urea nitrogen (BUN) and creatinine
- Complete blood count
- Parathyroid hormone, calcitriol
- Additional tests to rule out glomerular disease, viral infection, or hematologic disorders as clinically indicated (anti-PLA2R, ANCA, anti-GBM antibodies, serum-free light chains, serum and protein electrophoresis/immunofixation)
- Genetic testing
- Urine:
    - Urinalysis to detect albuminuria, proteinuria, hematuria,
    - Urine sediment examination
    - Urine albumin-to-creatinine ratio
    - Urine protein electrophoreisis

Imaging

- Ultrasonography of the kidney and perirenal structures – to detect kidney tissue damage, kidney stones, urinary tract obstruction or other abnormalities
- Computed tomography (CT) scan – detects structural abnormalities of kidneys, ureters, bladder
- Renal angiography – examines the blood vessels
- If radiocontrast is necessary for imaging, the following recommendations are provided by KDIGO (2024):
    - Use low-osmolality and iso-osmolarity contrast media.
    - Use the minimum dose of radiocontrast to achieve the diagnostic study.
    - Withdraw non-essential potentially nephrotoxic agents before and 48 hours after the procedure.
    - Avoid dehydration in those not undergoing dialysis and have eGFR less than 30 mL/min/1.73m^2 or AKI and receiving intravenous contrast.
    - Measure GFR 48-96 hours after the procedure.
    - Avoid gadolinium-containing contrast media in GFR less than 15 mL/min/1.73m^2.

Diagnostic Procedures

- Electrocardiography (ECG) to assess for arrhythmias related to electrolyte imbalance
- Kidney biopsy (ultrasound guided) to evaluate for malignancy in suspicious lesions and determine etiology of nephrotic syndrome, acute nephritic syndrome, unexplained AKI

Treatment & Management (KDIGO, 2024)

The following measures aim to treat the reversible causes of kidney disease, slow its progression, and treat complications.

- Control blood pressure; target systolic blood pressure of less than 120 mmHg, if tolerated
    - Consider less intense target in those that are frail, at high risk for falls, have limited life expectancy, or have symptomatic postural hypotension.
- Evidence-based pharmacologic treatments that delay the progression of CKD (KDIGO, 2024)

    - Renin-angiotensin-system inhibitors (RASi) are beneficial in decreasing blood pressure, reducing mortality in heart failure, decreasing proteinuria, and slowing progressive loss of kidney function in patients with CKD and include:
        - Angiotensin-coverting enzyme inhibitors (ACEi) and
        - Angiotensin II receptor blockers (ARB)
    - Initiate therapy with a RASi in patients with CKD, with and without diabetes and with moderately to severely increased albuminuria
    - Avoid combination of ACEi, ARB, and direct renin inhibitors in those with CKD with and without diabetes
    - Initiate therapy with SGLT2i in patients with type 2 diabetes, CKD, and an eGFR greater than or equal to 20 mL/min per 1.73 m^2
    - Initiate therapy with an SGLT2i in CKD patients without diabetes if the patient has
        - eGFR greater than or equal to 20 mL/min per 1.73 m^2 with ACR greater than or equal to 200 mg/g
        - eGFR 20 to 45 mL/min per 1.73 m^2 with ACR less than 200 mg/g
        - heart failure (regardless of albuminuria)
- Initiate therapy with a mineralocorticoid receptor antagonist (MRA) in patients with type 2 diabetes, an eGFR greater than 25 mL/min per 1.73 m^2, normal serum potassium concentration, and albuminuria (greater than 30 mg/g) despite maximum tolerated dose of a RASi
- Manage diabetes (KDIGO, 2024).
    - Individualized target hemoglobin A1c from less than 6.5 to less than 8% in patients with CKD not treated with dialysis with goal to avoid hypoglycemia
    - Accuracy of hemoglobin A1C may decline in those being treated with dialysis
- Measure hemoglobin to monitor for anemia. Assess for iron deficiency anemia and treat with iron supplementation accordingly.
- Monitor serum potassium level. Potassium-sparing medications, dietary intake, insulin deficiency, and metabolic acidosis can increase the risk of hyperkalemia in patients with CKD.
- Encourage smoking cessation.
- Encourage weight reduction.
- Encourage moderate intensity physical activity for at least 150-minutes/week if tolerated
- Temporarily discontinue nephrotoxic and renally excreted medications if GFR less than 60 mL/min/1.73m^2 and increased risk of AKI (KDIGO, 2024; Norton et al., 2017a) such as non-steroidal anti-inflammatory drugs (NSAIDS), diuretics, metformin, lithium, digoxin, quinolones, B-lactam antibiotics, sulfonamides. Adjust drug doses for the level of GFR. Examples of common drugs requiring renal dose adjustments include allopurinol, lithium, acyclovir, gabapentin, rivaroxaban (Xarelto), cephalexin, Bactrim, amoxicillin, and levofloxacin. Metformin is contraindicated in patients with an eGFR below 30 mL/min/1.73 m^2.
- Refer to specialty kidney care services.

Diet

- Adaptation of a healthy and diverse diet with higher consumption of plant-based food compared to animal-based foods.
- Restrict salt intake (KDIGO, 2024).
    - Goal is less than 90 mmol (2 grams/day), unless contraindicated.
- Modify protein intake (KDIGO, 2024).
    - Maintain protein intake of 0.8 grams/kg body weight per day.

    - Avoid high protein intake (greater than 1.3 g/kg/day) in adults with CKD at risk of progression.
- Avoid foods high in potassium, phosphorus, and sodium.
- Restrict fluid intake based on urine production.
- Weight loss counseling in those with obesity and CKD.
- Older adults with frailty and sarcopenia may require higher protein and calorie targets.

Renal Replacement Therapy (RRT) (Vaidya et al., 2024)

Hemodialysis

- In patients with CKD, an optimal eGFR in the absence of symptomatic kidney disease has not been established.
- Initiate in patients with CKD when one or more of the following are present (KDIGO, 2024):
    - Signs or symptoms of kidney failure (neurological signs and symptoms attributable to uremia, pericarditis, anorexia, medically resistant acid-base or electrolyte abnormalities, intractable pruritus, or serositis)
    - Inability to control volume status or blood pressure
    - Progressive decrease in nutritional status unresponsive to dietary intervention
- Consider planning for dialysis access and/or kidney transplantation in adults when GFR is less than 15-20 mL/min/1.73m^2 or risk for renal replacement therapy (RRT) is greater than 40% over 2 years.
- Dialysis machine is used to filter waste products from the blood three or more times a week; diffusion efficacy depends on the dialysate solution.
- Hemodialysis can be performed at in-center locations or at home.
- Vascular access required
    - Arteriovenous fistula: an artificial connection between an artery and vein diverting blood to the vein; preferred access method
    - Arteriovenous graft: second option if fistula cannot be created
    - In an emergency, temporary vascular access may be obtained in a central vein (e.g., internal jugular) however these are associated with inadequate dialysis, increased infection rates, clotting, and inflammation.

Peritoneal dialysis

- The peritoneal membrane is used as a semipermeable filter, replacing the kidneys. A dialysis solution (osmotic agent) is infused into the abdominal cavity through a percutaneous catheter. Through diffusion, waste products are pulled from the blood in the peritoneal capillaries into the dialysate. Following the prescribed dwell time, the solution is drained through the catheter.
- Efficacy is based on:
    - Concentration gradient
    - Size of the solute
    - Permeability of the peritoneal membrane
- Restrict potassium intake.
- Replace amino acids.
- Increase dietary proteins.
- Monitor glucose closely; insulin may be added to dialysis solution.

Kidney transplant (Chadban et al., 2020)

- All patients with CKD G4-G5 who are expected to reach end-stage kidney disease, in the absence of a systemic end-stage disease (multiple myeloma, advanced extrarenal amyloidosis, decompensated cirrhosis, severe irreversible obstructive or restrictive lung disease, or severe uncorrectable cardiac disease) should be informed of, educated about, and considered for kidney transplantation regardless of socioeconomic status, sex, gender identity, or race/ethnicity.
- Refer candidates at least 6 to 12 months before anticipated dialysis and those on dialysis when medically stable and kidney failure deemed irreversible.
- Renal transplant is associated with the best quality of life and survival. Pretransplant evaluation is extensive and varies from facility to facility.

Conservative Management (KDIGO, 2024)

- Option for people who choose not to pursue RRT
- Advance care planning and end-of-life care
- Include protocols for dietary restrictions, symptom and pain management, psychological care, spiritual care, culturally sensitive care, and bereavement support.

References

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