# CKD Overview: Clinical Approach & Classification

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March 2026

## CKD Overview: Clinical Approach & Classification

### Learning Objectives

By the end of this handout, students should be able to: 1. Define chronic kidney disease using KDIGO staging and risk classification 2. Distinguish true hypertensive nephropathy from other causes of CKD 3. Identify diagnostic pitfalls in CKD etiology determination 4. Apply evidence-based approaches to CKD diagnosis and initial management 5. Recognize special populations at diagnostic risk (African Americans, genetic disease carriers)

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### What Is Chronic Kidney Disease?

**CKD Definition (KDIGO 2024):** Abnormalities of kidney structure or function for ≥3 months with health implications. Diagnosed by: - eGFR <60 mL/min/1.73m² (kidney function), OR - Persistent albuminuria/proteinuria (kidney damage), OR - Abnormal kidney imaging/histology

**Key Point:** CKD is NOT a single disease—it's a syndrome with multiple etiologies requiring specific diagnosis.

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### KDIGO CKD Staging System

| G Stage | eGFR Range | Term | Clinical Significance |
|---|---|---|---|
| G1 | ≥90 | Normal/High | Normal function (abnormal kidney markers define CKD) |
| G2 | 60-89 | Mildly Decreased | Mild function loss |

| G Stage | eGFR Range | Term | Clinical Significance |
|---|---|---|---|
| G3a | 45-59 | Mildly-Moderately Decreased | Increased screening for complications |
| G3b | 30-44 | Moderately-Severely Decreased | Increased risk, medication dosing considerations |
| G4 | 15-29 | Severely Decreased | Major complications common; prepare for RRT |
| G5 | <15 | Kidney Failure | Symptomatic; RRT needed or withheld |

**Albuminuria Classification (KDIGO)**

| A Stage | UACR Range | Risk Stratification |
|---|---|---|
| A1 | <30 mg/g | Normal-mildly elevated |
| A2 | 30-300 mg/g | Moderately elevated |
| A3 | >300 mg/g | Severely elevated |

**Color-Coded Risk:** Green (low) ☐ Yellow (moderate) ☐ Orange (high) ☐ Red (very high) based on eGFR + albuminuria combination.

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## The Challenge: "Hypertensive Nephropathy"

### The Problem

Hypertensive nephropathy is the **second-leading reported cause of CKD**, yet recent evidence reveals fundamental diagnostic flaws:

**Key Statistics:** - Clinical diagnostic criteria achieve only **13% sensitivity** (miss 87% of true cases) - **70% of African Americans** with suspected hypertensive nephropathy actually have APOL1-associated genetic disease - **7-fold geographic variation** in diagnosis rates between European countries with similar hypertension prevalence - **Inverse correlation** between population hypertension burden and diagnosed hypertensive kidney disease—higher hypertension prevalence = fewer diagnoses

### Why This Diagnosis Is Problematic

1. **No pathognomonic findings:** Kidney biopsy cannot definitively prove hypertensive etiology
2. **Diagnosis by exclusion:** Default label when other causes can't be identified
3. **Genetic misclassification:** APOL1 variants explain >50% of "hypertensive" cases in African Americans
4. **Risk of therapeutic failure:** Genetic disease and primary nephritis don't respond as well to standard antihypertensive therapy

### Clinical Criteria for "True" Hypertensive Nephropathy

If considering this diagnosis, require: - ☐ Long-standing severe hypertension (usually >10 years at high levels: 195/126 mmHg median) - ☐ Minimal proteinuria early in course (suggests not primary glomerulonephritis) - ☐ Proportional vascular changes throughout the body - ☐ **Exclusion of genetic causes** via genetic testing - ☐ Absence of features suggesting primary kidney disease

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## Identifying the True Cause of CKD

### Step 1: Clinical History & Risk Factors

| History Element | Suspect Diagnosis |
|---|---|
| Diabetes × years, proteinuria, retinopathy | Diabetic kidney disease |
| Hematuria, flank pain, positive family history | Polycystic kidney disease |
| Sudden AKI, progressive CKD over weeks/months | Primary glomerulonephritis, vasculitis |
| Prolonged NSAID use, multiple myeloma | Acute tubular necrosis, cast nephropathy |
| Systemic symptoms (rash, arthralgias, fever) | Autoimmune disease, vasculitis, infection |
| African American ethnicity | Consider APOL1 testing early |
| Deafness, ocular abnormalities, family history | Alport syndrome (COL4A mutation) |

### Step 2: Laboratory Findings

**Proteinuria Pattern:** - <1g/day, no blood: more consistent with hypertensive damage or early CKD - >1g/day: suggests primary glomerular disease - Predominantly albumin: RAAS dysfunction (diabetes, hypertension) - Non-selective: glomerulonephritis

**Urinalysis:** - **RBC casts** = glomerulonephritis (not hypertensive damage) - **WBC casts** = interstitial inflammation - **Pyuria without infection** = vasculitis or interstitial disease

**Serologies:** - ANA, ANCA, anti-GBM, complement levels - Immunoglobulin levels (if proteinuria >3g/day)

### Step 3: Genetic Testing (Increasingly Important)

**APOL1 Testing** (for African Americans with suspected hypertensive nephropathy): - 13% of African Americans carry two risk alleles - Associated with 7-10× increased ESKD risk - High-risk genotypes show reduced responsiveness to standard antihypertensives

**Other Genetic Tests Consider:** - COL4A mutations (Alport syndrome) — 62% previously misdiagnosed as hypertensive - UMOD variants (chronic interstitial disease) - PKD1/PKD2 (obvious if imaging done, but screen early)

**Current Guidelines:** KDIGO 2024 recommends genetic testing for most CKD patients to establish causation.

### Step 4: Kidney Biopsy (Selective Use)

**Consider Biopsy If:** - Rapid CKD progression (eGFR decline >5 mL/min/1.73m²/year) - Significant proteinuria (>1g/day) with atypical features - Systemic disease suspected - Diagnostic uncertainty affecting management

**Avoid Biopsy If:** - Very advanced CKD (eGFR <15) unless considering immunosuppression - Clinical diagnosis clear (diabetic kidney disease with retinopathy) - Patient unwilling/unable to tolerate procedure

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## Clinical Pearls

### Pearl 1: The "Diagnostic Convenience" Problem

Many CKD cases labeled "hypertensive nephropathy" actually represent: - Primary kidney disease with secondary hypertension - Genetic nephropathies (APOL1, COL4A) - True idiopathic CKD (honest acknowledgment of diagnostic uncertainty)

**Clinical Action:** Avoid defaulting to hypertensive nephropathy without positive evidence.

### Pearl 2: Ethnic Disparities in Diagnosis

African Americans receive hypertensive nephropathy diagnosis 2× more often than whites with identical clinical presentations. This reflects: - Diagnostic bias (not just APOL1 genetics) - Less comprehensive workup in underserved populations - Delayed specialist referral - Missing genetic testing opportunities

**Clinical Action:** Ensure equitable, comprehensive diagnostic evaluation regardless of ethnicity.

### Pearl 3: Geographic Variation Reflects Practice, Not Biology

7-fold variations in hypertensive nephropathy diagnosis between European countries with similar populations suggest: - Diagnostic convention varies by region - Biopsy rates higher in regions with lower hypertensive nephropathy labels - Some regions classify uncertain cases as "unknown etiology" (more honest)

**Clinical Action:** When diagnosis uncertain, acknowledge it rather than default to hypertensive nephropathy.

### Pearl 4: eGFR Decline Rate Matters

- **Stable:** <1 mL/min/1.73m²/year ☐ reassure, follow closely
- **Moderate:** 1-3 mL/min/1.73m²/year ☐ standard CKD progression

- **Rapid:** >5 mL/min/1.73m²/year ☐ investigate urgently; consider biopsy
- **Very rapid:** >10 mL/min/1.73m²/year ☐ possible AKI, vasculitis, or acute GN

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## CKD Diagnosis: A Systematic Approach

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┌─ CKD Suspected (eGFR <60 or albuminuria)
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├──→ Step 1: Confirm diagnosis
│    └─ Verify eGFR (repeat if new)
│    └─ Quantify albuminuria (UACR preferred)
│    └─ Assess duration (need ≥3 months)
│
├──→ Step 2: Determine etiology
│    └─ Diabetes + retinopathy = DKD (usually)
│    └─ RBC/WBC casts = GN (biopsy indicated)
│    └─ African American + progressive = APOL1 test
│    └─ Family history of kidney disease = genetic screen
│    └─ Systemic symptoms = autoimmune workup
│    └─ None of above = comprehensive evaluation
│
├──→ Step 3: Assess cardiovascular risk
│    └─ BP, proteinuria, albuminuria guide intensity
│
├──→ Step 4: Initiate cardioprotective therapy
│    └─ RAAS blocker (if albuminuria/HTN)
│    └─ SGLT2 inhibitor (regardless of diabetes)
│    └─ Consider GLP-1 RA if diabetic
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└──→ Step 5: Monitor & adjust
     └─ Labs: K⁺, Cr at 2 weeks, then q3–6 months
     └─ Track eGFR slope
     └─ Repeat albuminuria annually
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## Practice Questions

**Question 1:** A 58-year-old African American man presents with CKD stage 3b (eGFR 38), blood pressure 148/92, no albuminuria, and no diabetes. His nephrologist says he has "hypertensive nephropathy." What is the most appropriate next step?

A) Start lisinopril and accept the diagnosis
B) Perform APOL1 genetic testing
C) Order kidney ultrasound to rule out polycystic kidney disease
D) Refer for kidney biopsy

**Answer: B** — APOL1 testing should be standard in African Americans with suspected hypertensive nephropathy. Genetic disease explains ~70% of such cases and won't respond as well to stan-

dard therapy.

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**Question 2:** A 45-year-old White woman with 12-year history of hypertension (currently on 3 antihypertensives) presents with CKD stage 4 (eGFR 18), hypertension, and 2.8g/day proteinuria. Urinalysis shows no cells or casts. What is the diagnostic likelihood of true hypertensive nephropathy?

A) Very high (>80%)
B) Moderate (50-60%)
C) Low (20-30%)
D) Very low (<10%)

**Answer: C** — While she has long-standing hypertension and advanced CKD, the significant proteinuria (2.8g/day) makes primary glomerular disease likely. Clinical criteria alone achieve only 13% sensitivity; biopsy would clarify diagnosis.

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**Question 3:** You are evaluating a 62-year-old man with type 2 diabetes, eGFR 52, UACR 45 mg/g (microalbuminuria), and hypertension. He has no diabetic retinopathy. What is your approach to determining he has diabetic kidney disease?

A) Accept diabetic kidney disease diagnosis based on diabetes + albuminuria
B) Obtain kidney ultrasound to rule out other causes
C) Perform renal biopsy to confirm glomerular pathology
D) Order genetic testing to exclude hereditary kidney disease

**Answer: A** — Type 2 diabetes + albuminuria + absence of retinopathy still supports diabetic kidney disease diagnosis in ~95% of cases. Biopsy/genetic testing not routinely needed unless atypical features present (rapidly progressive decline, hematuria, systemic symptoms).

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## Summary Table: CKD Etiology Clues

| Clinical Feature | Points Away from HTN | Suggested Diagnosis |
|---|---|---|
| Age <40 | — | Consider genetic (PKD, Alport, IgA) |
| RBC or WBC casts | Strong | Primary/secondary glomerulonephritis |
| Hematuria + proteinuria | Strong | Glomerulonephritis, Alport, vasculitis |
| Proteinuria >3g/day | Moderate | Primary nephrotic syndrome |
| Family history kidney disease | Moderate | Genetic disease, autoimmune familial form |
| Systemic symptoms | Strong | Vasculitis, lupus, infection-related |
| Rapid eGFR decline (>5/year) | Strong | AKI component, active GN, vasculitis |

| Clinical Feature | Points Away from HTN | Suggested Diagnosis |
|---|---|---|
| African American ethnicity | Moderate | APOL1-associated disease |
| Normal BP with CKD | Strong | Non-hypertensive etiology |

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## See Also

### Related Student Handouts

- CKD Complications
- CKD Nutrition and Dietary Management
- Diabetic Kidney Disease
- Hypertension Management
- Nephritic and Nephrotic Syndromes

### Clinical Content (01-Clinical-Medicine/Nephrology)

- CKD Hub - Full Clinical Reference
- Hypertension Hub
- Essential Renal Laboratory Tests

### Atomic Notes (ZK)

- CKD Classification and Global Standards

### Butler-COM Resources

- Butler COM - Nephrology Deep Dive

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## Additional Resources

- Full Evidence Review: Hypertensive Nephropathy Diagnostic Reckoning
- KDIGO 2024 CKD Clinical Practice Guideline
- Genetic Testing in CKD: Updated Approach

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*This handout emphasizes diagnostic precision and recognition that "hypertensive nephropathy" represents a diagnosis of exclusion, not a positive diagnosis. Modern practice should move toward defining CKD etiology through positive evidence rather than clinical assumption.*

## Clinical Resources

- Clinical Review: Comprehensive Nsaid Ckd Report — Comprehensive clinical review with PubMed references
- Clinical Review: Ckd Sacubitril Review — Comprehensive clinical review with PubMed references

- Clinical Review: Hypocalcemia Management Severe Ckd Clinical Report — Comprehensive clinical review with PubMed references
- Clinical Review: Ckd Protein Restriction Report — Comprehensive clinical review with PubMed references
- Clinical Review: Ckd — Comprehensive clinical review with PubMed references
- Clinical Review: Protein Restriction In Ckd Evidence Review — Comprehensive clinical review with PubMed references
- Clinical Review: Ckd Mbd Comprehensive Review — Comprehensive clinical review with PubMed references
- Clinical Review: Ckd Staging Classification Review — Comprehensive clinical review with PubMed references
- Clinical Review: Hypertesnive Nephropathy Cause Of Ckd — Comprehensive clinical review with PubMed references
- Clinical Review: Sglt2i Ckd Notes — Comprehensive clinical review with PubMed references