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Chronic Kidney Disease

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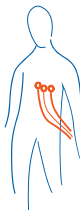

DEFINITION AND EPIDEMIOLOGY

Chronic kidney disease (CKD) is defined as persistent, progressive, and irreversible loss of renal function. The spectrum of CKD includes earlier stages of kidney damage (characterized by proteinuria, electrolyte abnormalities, and elevated serum creatinine) that represent a decrease in the glomerular filtration rate (GFR) and extends to complete loss of kidney function—that is, kidney failure or end-stage renal disease (ESRD). Markers of kidney damage or GFR less than 60 mL/min/1.73 m^2 must be present to meet the diagnostic criteria of CKD. In addition, these must be present and persistent for at least 3 months to differentiate CKD from acute kidney injury. According to the Kidney Disease: Improving Global Outcomes (KDIGO) 2012 clinical practice guideline, CKD is classified based on the underlying cause of kidney disease, GFR category, and degree of albuminuria. There are six GFR categories, ranging from normal or high (G1, ≥90 mL/min/1.73 m^2) to kidney failure (G5, <15 mL/min/1.73 m^2), and three albuminuria categories based on severity (Table 32-1).

CKD is a worldwide public health problem of increasing magnitude; in the United States, CKD is estimated to affect 20 million people. Although some have mildly decreased GFR with mild to moderate albuminuria (Fig. 32-1), many people with CKD progress to ESRD and require dialysis or kidney transplantation. The rate of new ESRD patients in the United States has been relatively stable since 2000; however, it was 4% lower (357 per million population) in 2011, as reported by the United States Renal Data System (USRDS) in 2013 (E-Fig. 32-1). Trends in overall prevalence of ESRD suggest a continuing increase in the numbers of patients requiring care, although in 2011 the increase was only 3.4%—the lowest in 30 years (E-Fig. 32-2). Care of the ESRD patient is costly, accounting for $34 billion (6.3%) of the U.S. Medicare budget in 2011. In addition to concern about progression to ESRD, decreased GFR and proteinuria have each been recognized as independent risk factors for cardiovascular disease and death. Therefore, diagnosis of CKD confers risk not only for progressive loss of kidney function but also for decreased survival.

TABLE 32-1 CATEGORIES OF GLOMERULAR FILTRATION RATE AND ALBUMINURIA IN CHRONIC KIDNEY DISEASE

CATEGORY	GFR (mL/min/1.73 m^2)	TERMS
G1*	≥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	<15	Kidney failure

CATEGORY	AER (mg/24 hr)	ACR (mg/g)	ACR (mg/mmol)	Terms
A1	<30	<30	<3	Normal to mildly increased
A2	30-300	30-300	3-30	Moderately increased
A3	>300	>300	>30	Severely increased

Modified from Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group: KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease, Kid Intl Suppl 3:1–150, 2013.

ACR, Albumin-to-creatine ratio; AER, albumin excretion rate; GFR, glomerular filtration rate.

*G1 and G2 alone, without other evidence of kidney damage, do not meet the criteria for chronic kidney disease.

The most common causes of ESRD are diabetes mellitus (45%), hypertension (28%), glomerulonephritis (6-7%), and cystic or congenital conditions (2-3%). During the evaluation of CKD, every attempt should be made to arrive at the specific cause of kidney disease. Renal biopsy is the most specific approach to definitive diagnosis; it also can guide treatment and help to determine suitability for kidney transplantation. However, the procedure has potential complications, and clinical and imaging information may be sufficient to provide a conclusive diagnosis.

PATHOLOGY

After renal injury, surviving nephrons must adjust by increasing their filtration and excretion rates to ensure adequate solute, water, and acid-base balances. Patients with CKD are vulnerable to edema formation and severe volume overload, hyperkalemia, hyponatremia, and azotemia. Initially, sodium balance is maintained by increasing fractional excretion of sodium by the nephrons. Acid excretion is maintained until late stages of CKD (when the GFR falls to less than 30 mL/minute) by increased tubular ammonia synthesis, which provides an adequate buffer for hydrogen in the distal nephron. Later, a significant decrease in distal bicarbonate regeneration results in hyperchloremic metabolic acidosis. Further nephron loss leads to retention of organic ions such as sulfates, which results in an anion gap metabolic acidosis. There is active research to determine whether metabolic acidosis is itself a contributor to progression of CKD and whether its correction by base supplementation is a potential treatment.

Once GFR has decreased below a critical level, CKD tends to progress to ESRD, regardless of the initial insult. Figure 32-2 shows how risk factors may interact with pathophysiologic