Chronic Kidney Disease: Overview

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Abstract

Chronic kidney disease (CKD) is a condition characterized by gradual loss of kidney function over time. The major role of the kidney is excretion of water-soluble waste products. Meanwhile, the kidneys respond continually to changes in blood volume as well as osmolality, and adjust the levels of water, electrolyte, and acid-base balance by selectively excreting or reabsorbing them. In addition, the kidneys are main site of production for a number of hormones, chiefly renin and erythropoietin. Millions of adults have CKD and others who have diabetes, hypertension, and family history of renal failure are at high risk. Glomerular filtration rate is the best estimate of kidney function, combining with proteinuria is used for staging of CKD. Patients with CKD may develop complications like cardiovascular disease, anemia, mineral and bone disorders, and nervous system diseases. Those who develop kidney failure require dialysis or kidney transplantation. The cost of treatment for this growing epidemic represents an enormous burden on healthcare systems worldwide. In this chapter, we will overview definition, epidemiology, cost, and outcomes of CKD. The detailed diagnosis and treatment will be discussed in the following chapters.

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1.1 Introduction

Chronic kidney disease (CKD) has become a global public health problem with an increasing prevalence and high mortality [1]. Owing to the growing elderly population and the increasing prevalence of hypertension and diabetes as well as the improving treatment strategies, the prevalence of CKD will inevitably continue to increase in the near future. Glomerular filtration rate (GFR) and albuminuria are proposed as the best indicators of kidney function, with low GFR and increased albuminuria being associated with a high risk of kidney failure requiring renal replacement therapy and of cardiovascular disease, anemia, mineral and bone disorder, and other complications. On account of the significant development of CKD definitions by the Kidney Disease: Improving Global Outcomes (KDIGO), the recognition of CKD has greatly improved in the last few years [2]. Increased awareness of and uniform classification criteria for CKD have led to greater focus on the development of methods to slow CKD progression,

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increased emphasis on the early recognition and prevention of complications associated with CKD, and better understanding of the economic burden of CKD and accompanying illnesses. Despite the progress, therapies and clinical trials on which to base recommendations remain remarkably limited.

1.2 Definition

CKD is defined as abnormalities of kidney structure or function, present for >3 months [3]. Table 1.1 summarizes the criteria for CKD, either of which should be present for >3 months.

1.3 Staging

The KDIGO 2012 Clinical Practice Guideline suggested that CKD could be classified according to cause, GFR category, and albuminuria category (CGA) [3].

Assign causes based on observed or presumed pathological–anatomical findings within the kidney and presence or absence of systemic disease.

Assign GFR categories as shown in Table 1.2.

Assign albuminuria categories as shown in Table 1.3.

Alternatively, protein or urinary reagent strip results can be substituted (Table 1.4).

1.4 Causes and Risk Factors

Diabetes and hypertension are the leading causes of CKD in all industrialized countries and several underdeveloped countries. However, glomerulonephritis and unknown causes are more common in Asian and Sub-Saharan African countries. Table 1.5 lists the risk factors for CKD [1–3].

In China, the current leading causes of CKD are glomerular disease, diabetic kidney disease, and hypertension. IgA nephropathy is one of the most common glomerular diseases.

Table 1.1 Criteria for CKD (either of the following should be present for >3 months)

- Albuminuria (AER ≥30 mg/24 h; ACR ≥30 mg/g [≥3 mg/mmol])
- Urinary sediment abnormality
- Electrolyte and other abnormalities due to tubular disorders
- Abnormalities detected by histology
- Structural abnormalities detected by imaging
- History of kidney transplantation
- GFR <60 mL/min/1.73 m^2

CKD chronic kidney disease, *AER* albumin excretion rate, *ACR* albumin-to-creatinine ratio, *GFR* glomerular filtration rate (Reproduced with permission from Elsevier [3])

Table 1.2 GFR categories in CKD

GFR category	GFR (mL/min/1.73 m^2)	Terms
G1	≥90	Normal/high
G2	60–89	Mildly decreased (relative to young adult level)
G3a	45–59	Mildly to moderately decreased
G3b	30–44	Moderately to severely decreased
G4	15–29	Severely decreased
G5	<15	Kidney failure

GFR glomerular filtration rate, *CKD* chronic kidney disease

Table 1.3 Albuminuria categories in CKD

Category	AER (mg/24 h)	ACR (mg/mmol)	ACR (mg/g)	Terms
A1	<30	<3	<30	Normal to mildly increased
A2	30–300	3–30	30–300	Moderately increased (relative to young adult level)
A3	>300	>30	>300	Severely increased (including nephrotic syndrome)

AER albumin excretion rate, *ACR* albumin-to-creatinine ratio

Table 1.4 Categories of proteinuria in CKD

Category	PER (mg/24 h)	PCR (mg/mmol)	PCR (mg/g)	Protein reagent strip
A1	<150	<15	<150	Negative to trace
A2	150–500	15–50	150–500	Trace to positive
A3	>500	>50	>500	Positive or greater

CKD chronic kidney disease, *PER* protein excretion rate, *PCR* protein-to-creatinine ratio

Table 1.5 Risk factors for CKD

Clinical factors	• Diabetes • Hypertension • Autoimmune disease • Systemic infection • Urinary tract infection • Urinary stones • Lower urinary tract obstruction • Urolithiasis • Family history of CKD • Recovery from acute kidney injury • Kidney mass reduction • Exposure to certain drugs • Low birth weight
Sociodemographic factors	• Older age • Race • Exposure to certain chemical and environmental conditions • Low income/education

CKD chronic kidney disease (Reproduced with permission from Elsevier [3])

These differences among countries are primarily related to disease burden shifting from infections toward chronic lifestyle-related diseases, increased life expectancy, and decreased birth rates in industrialized countries. In contrast, infectious diseases continue to be prevalent in less developed countries secondary to poor sanitation, lack of safe water, and high concentrations of disease-transmitting vectors. Furthermore, environmental pollution, pesticides, analgesic abuse, herbal medications, and use of unregulated food additives contribute to the burden of CKD in underdeveloped countries.

Rapid urbanization and globalization have accelerated the transition and led to an overlap in disease burden in Latin American and South Asian countries, with continued high prevalence of infectious diseases and increasing prevalence and severity of lifestyle-related diseases, such as diabetes, hypertension, and obesity.

1.5 Prevalence

Approximately 10% of the population is affected by CKD worldwide, with millions annually dying because of lack of access to affordable treatment [1]. In China, the adjusted prevalence rate of estimated GFR (eGFR) <60 mL/min/1.73 m^2 and albuminuria is 1.7% and 9.4%, respectively. The overall prevalence rate of CKD is approximately 10.8%; therefore, 119.5 million patients are estimated to have CKD in China [4].

CKD can affect individuals of any race. In particular, African American, American Indians, Hispanics, and individuals of South Asian origin (Bangladesh, India, Sri Lanka, or Pakistan) have a high risk of CKD. The prevalence of CKD is high in the northern (16.9%) and southwest (18.3%) regions of China compared with that in other regions. In rural areas of China, the prevalence of albuminuria positively correlates with the level of local economic development.

Although CKD can occur at any age, it becomes more common with increasing age and in the female gender. It has been known for decades that eGFR declines in parallel with age. The mean age of 9614 patients presenting with stage 3 CKD in India and 1185 patients in China is 51.0 and 63.6 years, respectively. It is estimated that one in five males and one in four females among individuals aged 65–74 years worldwide have CKD. The prevalence rate of CKD in the Chinese females population increases from 7.4% among those aged 18–39 years to 18.0% and 24.2% among those aged 60–69 and 70 years, respectively. Relative increases in the prevalence of CKD with age are equally striking in the USA, Canadian, and European populations despite between-country differences in the absolute prevalence. Moreover, it is estimated that the number of CKD cases will disproportionately increase in China, where the elderly population is

growing. This effect will be further magnified if the trends of increasing prevalence of diabetes and hypertension persist, competing cardiovascular diseases- and stroke-caused deaths are reduced and access to treatment improves.

When CKD finally progresses to kidney failure, renal replacement therapy becomes essential for patients' survival. However, the current treatment situation is appalling. Over two million patients worldwide presently undergo dialysis or transplantation, yet this number may only represent 10% of those who actually require treatment to live. The majority of these patients receiving therapy for kidney failure reside in only five countries, namely the USA, Japan, Germany, Brazil, and Italy, which represent only 12% of the global population. More than 80% of all patients receiving therapy for kidney failure are from affluent countries, with the remaining 20% being treated in approximately 100 developing countries, which constitute over 50% of the global population. The point prevalence of patients with kidney failure on maintenance dialysis (including hemodialysis and peritoneal dialysis) in 2008 was estimated to be 71.9 per million population in mainland China, with an annual increase in the prevalence rate of 52.9%, and reached 2584, 1106, and 1870 per million population in 2010 in Taiwan, Hong Kong, and the USA, respectively. Approximately 90% of patients with kidney failure on dialysis in China underwent hemodialysis at the end of 2012, meaning that 270,000 patients underwent hemodialysis compared with just 30,000 patients on peritoneal dialysis [1, 4, 5–7].

CKD resulted in 956,000 deaths in 2013. According to the 2010 Global Burden of Disease Study, the rank of CKD in the list of causes of total number of deaths worldwide rose from 27th in 1990 to 18th in 2010, with such movement of ranking up the list being second only to that for human immunodeficiency virus (HIV) infection and acquired immune deficiency syndrome (AIDS). The overall increase in years of life lost due to premature mortality caused by CKD is 82%, being only behind HIV infection and AIDS (396%) and diabetes mellitus (93%). The raw annual mortality in patients on maintenance hemodialysis in Beijing, China, was 76.8 per 1000 patient-years in 2010, which was relatively low compared with 236.3 per 1000 patient-years in 2009 in the USA. The three leading causes of death in patients on hemodialysis in China are cardiovascular disease (31.0%), stroke (20.3%), and infection (19.9%).

Despite the high prevalence, screening individuals without risk factors or symptoms for CKD is not recommended. Current recommendations suggest screening those with structural diseases of the renal tract, hypertension, cardiovascular disease, diabetes, autoimmune diseases with potential for kidney involvement, family history of kidney disease, marked obesity, and age >60 years during routine primary health encounters. Despite screening for CKD in individuals with diabetes is cost-effective, it remains unclear whether screening for CKD in the general population is cost-effective.

1.6 Costs

The cost of treatment for this dramatically growing epidemic represents an enormous burden on healthcare systems worldwide. Patients with kidney failure require dialysis or transplantation, which are exceedingly costly and consume a sizeable portion of the health budget.

In low- and middle-income countries, treatment with dialysis or transplantation imposes a huge financial burden upon most patients who require it. In another 112 countries, long-term dialysis is unaffordable for many patients, resulting in death due to untreated kidney failure in over one million individuals.

CKD was defined as a major chronic disease by the Chinese government and enrolled in three basic medical insurance systems in China. The economy will lose US$558 billion over the next decade owing to effects on death and disability attributable to heart and kidney diseases [7, 8].

An extreme example is in Uruguay, the annual cost of dialysis is close to 30% of the National Resources Fund's budget for specialized therapies.

The high cost of long-term dialysis for an increasing number of patients is also a problem

even in high-income countries. Kidney failure is a major cost driver among patients and their families as well as taxpayers.

In the USA, the treatment for CKD is likely to exceed $48 billion per year. Less than 1% of the covered population consumes 6.7% of the total Medicare budget for treatment for kidney failure.

CKD costs more than breast, lung, colon, and skin cancers combined in England, recently reported by NHS Kidney Care.

Treatment for all current and new cases of kidney failure up to 2020 will cost about $12 billion in Australia.

1.7 Diagnosis

The diagnosis of CKD includes the evaluation of chronicity, causes, GFR, albuminuria, and progression [6].

1.7.1 Evaluation of Chronicity

For individuals with kidney damage or GFR <60 mL/min/1.73 m^2 (Table 1.1), reviewing their history and past measurements is necessary to determine the course of kidney disease.

CKD is confirmed if the course exceeds 3 months; otherwise, not confirmed. Tests should be accordingly repeated to differentiate CKD, acute kidney disease, or both.

1.7.2 Evaluation of Causes

Review family and personal history, environmental and social factors, and medications, and perform physical examination, lab and imaging measurements to determine the causes of CKD and establish a pathological diagnosis.

1.7.3 Evaluation of GFR

It is recommended to use serum creatinine (SCr)-based GFR-estimating equation for initial assessment.

Table 1.6 Sources of error in GFR estimation using creatinine

Source of error	Example
Non-steady state	AKI
SCr difference	
• Creatinine generation	• Race/ethnicity • Extremes of muscle mass • Extremes of body size • Diet and nutritional status High-protein diet Creatine supplements • Muscle-wasting diseases • Ingestion of cooked meat
• Tubular secretion of creatinine	• Decrease by drug-induced inhibition Trimethoprim Cimetidine Fenofibrate
• Extrarenal elimination of creatinine	• Dialysis • Inhibition of gut creatininase by antibiotics • Large volume loss of extracellular fluid
Higher GFR	Measurement error in SCr and GFR
Interference with creatinine assay	• Spectral interferences (bilirubin, some drugs) • Chemical interferences (glucose, ketones)

AKI acute kidney injury, *SCr* serum creatinine, *GFR* glomerular filtration rate

Use SCr-based GFR-estimating equation (2009 Chronic Kidney Disease Epidemiology Collaboration [CKD-EPI] creatinine equation) instead of SCr concentration alone although $eGFR_{creat}$ might be less accurate in some clinical settings (Table 1.6).

Furthermore, the performance of additional tests (cystatin C) for confirmation is suggested when SCr-based eGFR is less accurate.

To confirm CKD, cystatin C should be measured in adults with $eGFR_{creat}$ of 45–59 mL/min/1.73 m^2 but without kidney damage markers.

CKD is confirmed if eGFRcys or eGFRcreat–cys is also <60 mL/min/1.73 m^2. Otherwise, CKD is not confirmed if eGFRcys or eGFRcreat–cys is ≥60 mL/min/1.73 m^2.

Similarly, use cystatin C-based GFR-estimating equations (2012 CKD-EPI cystatin C and 2012 CKD-EPI creatinine–cystatin C equations) rather than cystatin C concentration alone. Sometimes, eGFRcys and eGFRcreat–cys are also less accurate in clinical settings (Table 1.7).

Table 1.7 Sources of error in GFR estimation using cystatin C

Source of error	Example
Non-steady state	AKI
Serum cystatin C difference	
• Cystatin C generation	• Race/ethnicity • Thyroid function disorders • Corticosteroid administration • Other hypothesized factors (diabetes, adiposity)
• Tubular secretion of creatinine	None identified
• Extrarenal elimination of creatinine	Severe decrease in GFR
Higher GFR	• Biological variability in non-GFR determinants relative to GFR • Measurement error in serum cystatin C and GFR
Interference with cystatin C assay	Heterophilic antibodies

AKI acute kidney injury, *GFR* glomerular filtration rate

It is necessary to measure GFR using exogenous filtration markers when more accurate ascertainment of GFR will affect treatment decisions. The strengths and limitations of clearance methods and filtration markers for clearance measurements are summarized in Table 1.8.

1.7.4 Evaluation of Albuminuria

For initial proteinuria testing, the following measurements are suggested using early morning urine sample (in descending order): urinary albumin-to-creatinine ratio (ACR), urinary protein-to-creatinine ratio, reagent strip urinalysis for total protein with automated reading, and reagent strip urinalysis for total protein with manual reading.

The high biological variation and other physiological and pathological causes affect the accuracy of albuminuria (Table 1.9), repeat testing is required to confirm albuminuria. It is more accurate to measure the albumin excretion rate or total protein excretion rate in a timed urine sample.

Urinary albumin or protein may be analyzed using fresh samples, stored at 4 °C within 1 week, or stored at −70 °C for longer periods. However, freezing at −20 °C may result in the loss of measurable albumin. Stored samples should be allowed to attain room temperature and thoroughly mixed prior to analysis.

Non-albumin proteinuria could be detected using assays for specific urinary proteins, such as monoclonal heavy or light chains (known as "Bence Jones" proteins) and α1-microglobulin.

1.7.5 Evaluation of Progression

GFR and albuminuria should be assessed at least annually in individuals with CKD. Moreover, assess GFR and albuminuria more often in individuals at a higher risk of progression and/or in cases in which measurement will affect therapeutic decisions. However, GFR are commonly fluctuated slightly and not necessarily indicative of progression.

Accelerated CKD progression is defined as a drop in GFR ≥25% from baseline, a decline in GFR category, and a sustained decrease in GFR >5 mL/min/1.73 m^2 per year.

Take the following steps to determine the rate of CKD progression: perform a minimum of three GFR estimations over a period of not less than 90 days; for individuals with a new finding of reduced GFR, review the current management, repeat GFR estimation within 2 weeks to exclude causes of acute deterioration in GFR (e.g., AKI or initiation of renin–angiotensin system [RAS] antagonist therapy), and consider referral to a specialist.

CKD patients are at increased risk of progression to end-stage kidney disease if posed with either of accelerated progression conditions.

1.8 Management Principles

The management of CKD begins by providing patient education and offering information tailored to the cause, severity, and associated complications of CKD and the risk of progression [6]. Encourage patients to perform exercise, loss weight, and stop smoking. Offer dietary advice about salt intake, potassium, calorie, and phosphate appropriate to the severity of CKD (Table 1.10).

Table 1.8 Strengths and limitations of GFR measurement methods and markers

Approach	Strengths	Limitations
Methods		
Urinary clearance		
Bladder catheter and continuous intravenous infusion of marker	• Gold standard method	• Invasive
Spontaneous bladder emptying	• Patient comfort • Less invasive	• Possibility of incomplete bladder emptying • Low flow rates in individuals with low GFR levels
Bolus administration of marker	• Shorter duration	• Rapidly declining plasma levels at high GFR levels • Longer equilibration time in extracellular volume expansion
24-h urine collection		• Cumbersome • Prone to error
Plasma clearance	• No urine collection required • With potential for increased precision	• Overestimation of GFR in extracellular volume expansion • Inaccurate values with one-sample technique, particularly at lower GFR levels • Longer plasma sampling duration required at low GFR levels
Nuclear imaging	• No urine collection or repeated blood sampling required	• Less accurate
Markers		
Inulin	• Gold standard • No side effects	• Expensive • Difficult to dissolve and maintain in solution • Short supply
Creatinine	• Endogenous marker, no need for administration • Assay available in all clinical laboratories	• Section can vary among and within individuals
Iothalamate	• Inexpensive • Long half life	• Probable tubular secretion • Requirement for storage, administration, and disposal of radioactive substances when using ^{125}I as tracer • Requirement for expensive assay when using nonradioactive iothalamate • Cannot be used in patients with allergies to iodine
Iohexol	• Nonradioactive • Inexpensive • Sensitive assay allows for low dose	• Possible tubular reabsorption or protein binding • Requirement for expensive assay when using low doses • Cannot be used in patients with allergies to iodine • Nephrotoxicity and risk of allergic reactions at high doses
EDTA	• Widely available in Europe	• Probable tubular reabsorption • Requirement for storage, administration, and disposal of radioactive substances when using ^{51}Cr as tracer
DTPA	• Widely available in the USA • New, sensitive, and easy-to-use assay for gadolinium	• Requirement for storage, administration, and disposal of radioactive substances when using ^{99m}Tc as tracer • Requires standardization for ^{99m}Tc • Dissociation and protein binding of ^{99m}Tc • Concern for NSF when using gadolinium as tracer

GFR glomerular filtration rate, *EDTA* ethylenediaminetetraacetic acid, *DPTA* diethylenetriamine pentaacetic acid, *NSF* nephrogenic systemic fibrosis

For individuals with CKD, aim to maintain the blood pressure below 140 (target range, 120–139 mmHg)/90 mmHg. For those with diabetes and ACR ≥70 mg/mmol, aim to maintain the blood pressure below 130 mmHg (target range, 120–129 mmHg)/80 mmHg.

RAS antagonist should be administered to individuals with CKD under the following conditions:

Table 1.9 Factors affecting urinary albumin-to-creatinine ratio

Factors	Examples of effect
Preanalytical factors	
Transient elevation in albuminuria	• Menstrual blood contamination • Symptomatic urinary tract infection • Exercise • Upright posture (orthostatic proteinuria) • Other conditions that increase vascular permeability (e.g., septicemia)
Intraindividual variability	• Intrinsic biological variability • Genetic variability
Preanalytical storage conditions	Albumin degradation prior to analysis
Nonrenal causes of variability in creatinine excretion	• Age (lower in children and older people) • Race • Muscle mass • Gender (lower in women)
Change in creatinine excretion	Non-steady state creatinine concentration (acute kidney injury)
Analytical factors	
Antigen excess (prozone) effect	Samples with very high albumin concentrations may be falsely reported as low or normal using some assays

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(1) diabetes and an ACR ≥3 mg/mmol (ACR category A2 or A3) and (2) hypertension and an ACR ≥30 mg/mmol (ACR category A3) or ACR ≥70 mg/mmol (irrespective of hypertension or cardiovascular disease). However, the evidence supporting these criteria in individuals aged >70 years is limited. Do not administer a combination of RAS antagonists to individuals with CKD.

Serum potassium concentrations and estimate GFR should be measured before starting RAS antagonist therapy. Repeat tests between 1 and 2 weeks after starting RAS antagonist therapy and after each dose increase. Do not routinely administer RAS antagonist to individuals if pretreatment serum potassium concentration is >5.0 mmol/L. When hyperkalemia precludes the use of RAS antagonists, assessment, and treatment of factors promoting hyperkalemia should be undertaken, then recheck the serum potassium

Table 1.10 Dietary and lifestyle modification for patients with CKD

Salt intake	• Lower salt intake to <90 mmol (<2 g) of sodium per day (corresponding to 5 g of sodium chloride) in adults, unless contraindicated • Restrict sodium intake in children with CKD who have hypertension (systolic and/or diastolic blood pressure >95th percentile) or prehypertension (systolic and/or diastolic blood pressure >90th percentile and <95th percentile), following the age-based recommended daily intake • Supply free water and sodium to children with CKD and polyuria to avoid chronic intravascular depletion and to promote optimal growth
Protein intake	• Lower protein intake to 0.8 g/kg/day in adults with or without diabetes and GFR <30 mL/min/1.73 m^2 (G4–G5) • Avoid high protein intake (>1.3 g/kg/day) in adults with CKD at risk of progression
Hyperuricemia	Despite the relationship between hyperuricemia and incidence of CKD, there is insufficient evidence supporting or refuting the use of agents to lower serum uric acid concentrations in individuals with CKD and either symptomatic or asymptomatic hyperuricemia in order to delay CKD
Lifestyle	• Encourage patients with CKD to perform physical activity compatible with their cardiovascular health and tolerance (aiming for at least 30 min five times per week) • Achieve a healthy weight (BMI 20–25, according to country-specific demographics) • Stop smoking
Additional dietary advice	Provide expert dietary advice and information in the context of an education program tailored to the severity of CKD and the need to intervene on salt, phosphate, potassium, and protein intake, when indicated

CKD chronic kidney disease, *GFR* glomerular filtration rate, *BMI* body mass index

concentration. Stop RAS antagonist therapy if the serum potassium concentration increases to ≥6.0 mmol/L and discontinue other drugs known to promote hyperkalemia.

Following the introduction of RAS antagonists or an increase in their dose, do not modify the dose if either the GFR decrease from pretreatment baseline is <25% or the SCr increase from baseline is <30%. If there is a <25% decrease in eGFR or 30% increase in SCr from baseline after starting RAS antagonist therapy or increasing the dose of RAS antagonists, repeat the test in 1–2 weeks. Do not modify the dose of RAS antagonists if the change in eGFR or SCr is <25% or <30%, respectively. If the change in eGFR or SCr is ≥25% or ≥30%, respectively, investigate other causes of deterioration in renal function, such as concurrent medication or volume depletion. If no other causes of deterioration in renal function are identified, stop the RAS antagonist therapy or reduce to previous tolerated dose and add an alternative antihypertensive medication, if required.

For CKD patients with diabetes, the target hemoglobin A1c (HbA1c) level is approximately 7.0% (53 mmol/mol) in order to prevent or delay the progression of diabetic kidney disease. This HbA1c target is not suitable for patients at risk of hypoglycemia. The target HbA1c level should be extended above 7.0% in individuals with limited life expectancy, comorbidities or at risk of hypoglycemia. For patients with CKD who have diabetes, glycemic control should be accompanied by multifactorial intervention strategies including blood pressure control and cardiovascular risk care. Use of RAS antagonists, statins, and antiplatelet therapy are recommended if clinically indicated.

For the prevention and treatment of cardiovascular diseases and several complications including anemia, bone conditions, and metabolic acidosis, see Part II.

When assessing CKD progression, extrapolate the current rate of decline in GFR, and take this into account when planning intervention strategies, particularly if it suggests that patients might require renal replacement therapy throughout their lifetime.

Patients with features summarized in Table 1.11 should normally be referred to a specialist for assessment.

Provide patients with stage 5 CKD with information on treatment options for renal replacement therapy. Treatment options include transplantation and dialysis (hemodialysis and peritoneal dialysis). Table 1.12 shows the timing for the initiation of renal replacement therapy.

Table 1.11 When to refer

GFR <30 mL/min/1.73 m^2 (GFR category G4 or G5), with or without diabetes
ACR ≥70 mg/mmol, unless known to be due to diabetes and already appropriately treated
ACR ≥30 mg/mmol (ACR category A3), together with hematuria
Sustained decrease in GFR ≥25%, and a change in GFR category or sustained decrease in GFR ≥15 mL/min/1.73 m^2 within 12 months
Hypertension that remains poorly controlled despite the use of at least four antihypertensive drugs at therapeutic doses
Known or suspected rare or genetic causes of CKD
Suspected renal artery stenosis

GFR glomerular filtration rate, *ACR* albumin-to-creatinine ratio, *CKD* chronic kidney disease (Reproduced with permission from Elsevier [3])

Table 1.12 Timing for the initiation of renal replacement therapy

Initiation of dialysis	• Symptoms or signs attributable to kidney failure (e.g., serositis, acid-base or electrolyte abnormalities, pruritus) • Inability to control volume status or blood pressure • Cognitive impairment or progressive deterioration in nutritional status refractory to dietary intervention • This often but not invariably occurs in the GFR range of 5–10 mL/min/1.73 m^2
Initiation of transplantation with living donor	GFR is <20 mL/min/1.73 m^2 with evidence of progressive and irreversible CKD over the preceding 6–12 months

GFR glomerular filtration rate, *CKD* chronic kidney disease

Key Messages

- KDIGO defined CKD as kidney abnormalities or GFR <60 mL/min/1.73 m^2 for 3 months or longer and classified CKD based on CGA.
- Lifestyle-related diseases, including diabetes, hypertension, and obesity, and glomerular disease are the major causes of and risk factors for CKD.
- The incidence and prevalence of CKD substantially differ across countries and regions. The number of patients with CKD is expected to continuously increase worldwide. Low levels of economic development have been strongly associated with reduced availability of renal replacement therapy.
- The cost of treatment with dialysis or kidney transplantation for kidney failure represents an enormous burden on healthcare systems in both developed and developing countries.
- Evaluate chronicity, causes, GFR, and albuminuria to confirm the diagnosis of CKD.
- General approaches to CKD management include patient education (e.g., lifestyle modification), treatment of primary diseases (e.g., hypertension, diabetes), prevention and treatment of complications (e.g., cardiovascular diseases, anemia), and renal replacement therapy.

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