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Dialysis for Chronic Kidney Failure
A Review

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IMPORTANCE More than 3.5 million people worldwide and 540 000 individuals in the US receive maintenance hemodialysis or peritoneal dialysis for the treatment of chronic kidney failure. The 5-year survival rate is approximately 40% after initiation of maintenance dialysis.

OBSERVATIONS Hemodialysis and peritoneal dialysis remove metabolic waste and excess body water and rebalance electrolytes to sustain life. There is no recommended estimated glomerular filtration rate (eGFR) threshold for initiating dialysis, and patient-clinician shared decision-making should help determine when to initiate dialysis. Persistent signs and symptoms of uremia (eg, nausea, fatigue) and volume overload (eg, dyspnea, peripheral edema), worsening eGFR, metabolic acidosis, and hyperkalemia inform the timing of therapy initiation. A randomized clinical trial reported no mortality benefit to starting dialysis at higher eGFR (10-14 mL/min/1.73 m^2) vs lower eGFR (5-7 mL/min/1.73 m^2) levels. Observational data suggested no differences in 5-year mortality with use of hemodialysis vs peritoneal dialysis. Cardiovascular (eg, arrhythmias, cardiac arrest) and infection-related complications of maintenance dialysis are common. In the US, hemodialysis catheter–related bloodstream infections occur at a rate of 1.1 to 5.5 episodes per 1000 catheter-days and affect approximately 50% of patients within 6 months of catheter placement. Peritonitis occurs at a rate of 0.26 episodes per patient-year and affects about 30% of individuals in the first year of peritoneal dialysis therapy. Chronic kidney failure–related systemic complications, such as anemia, hyperphosphatemia, hypocalcemia, and hypertension, often require pharmacologic treatment. Hypotension during dialysis, refractory symptoms (eg, muscle cramps, itching), and malfunction of dialysis access can interfere with delivery of dialysis.

CONCLUSIONS AND RELEVANCE In 2021, more than 540 000 patients in the US received maintenance hemodialysis or peritoneal dialysis for treatment of chronic kidney failure. Five-year survival rate after initiation of maintenance dialysis is approximately 40%, and the mortality rate is similar with hemodialysis and peritoneal dialysis. Decisions about dialysis initiation timing and modality are influenced by patient symptoms, laboratory trajectories, patient preferences, and therapy cost and availability and should include shared decision-making.

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Kidney failure, defined by a glomerular filtration rate (GFR) of less than 15 mL/min/1.73 m^2, can be treated with kidney transplant, hemodialysis, peritoneal dialysis, or supportive care. More than 3.5 million people with chronic kidney failure worldwide receive maintenance dialysis,[1] with 90% receiving hemodialysis.[2] However, dialysis is resource-intensive and more than half of individuals with kidney failure worldwide do not have access to dialysis.[2]

Patients receiving maintenance dialysis for chronic kidney failure have a high mortality rate, with 5-year survival of less than 50% after dialysis initiation in the US.[3] Cardiovascular complications are the leading cause of death, with 40% of deaths attributed to arrhythmia or cardiac arrest.[3] Systemic complications of chronic kidney failure include anemia, hypertension, and mineral bone disorders, such as hyperphosphatemia and hyperparathyroidism. Dialysis treatment–related complications, such as vascular access dysfunction, infections, and hemodynamic instability during dialysis, are common and may cause distressing symptoms, including cramping, post-dialysis fatigue, and poor quality of life.[4]

This review summarizes current evidence regarding pathophysiology, diagnosis, and management of dialysis-dependent chronic kidney failure.

Methods

PubMed, Embase, Scopus, the Cochrane Database of Systematic Reviews, and the CENTRAL Clinical Trial Registry were searched for English-language articles describing meta-analyses, systematic reviews, and guidelines published between January 1, 2013,

and April 18, 2024, and randomized clinical trials (RCTs) published between January 1, 2019, and April 18, 2024. A total of 3363 articles were identified. A review of society guideline recommendations yielded 9 additional guidelines. The authors selected 110 articles for inclusion, including 33 meta-analyses or systematic reviews, 20 RCTs, 6 prospective studies, 5 cohort or observational studies, 11 review articles, 6 registry reports, and 29 guidelines, scientific statements, or expert consensus documents.

Discussion/Observations

Systemic Complications of Dialysis-Dependent Chronic Kidney Failure

Dialysis-dependent chronic kidney failure has multiple systemic complications, including anemia, mineral metabolism abnormalities, and hypertension. Anemia is caused by decreased erythropoietin production, disordered iron homeostasis, and coagulation dysfunction.[5] Mineral metabolism disturbances, including decreased active vitamin D production, hyperphosphatemia, and hypocalcemia, contribute to secondary hyperparathyroidism and kidney osteodystrophy, defined as alterations in bone morphology associated with chronic kidney disease (CKD), which are associated with increased rates of fracture and cardiovascular disease.[6] Hypertension results from increased salt sensitivity and volume expansion, increased activity of renin-angiotensin-aldosterone and sympathetic nervous systems, increased arterial stiffness, and endothelial cell dysfunction.[7] Hypertension, inflammation, and altered levels of 1,25-dihydroxyvitamin D, parathyroid hormone (PTH), and uremic toxins contribute to cardiovascular complications, such as arterial vascular calcification, heart failure, arrhythmias, and sudden cardiac death.[7] Changes in innate and adaptive immunity in patients with chronic kidney failure are associated with an increased risk of infection.[8]

Clinical Presentation

Chronic kidney failure typically presents with signs and symptoms of uremia that include nausea (33%-46%),[9] poor appetite (48%-56%),[9] metallic taste (25%-27%),[10] shortness of breath (11%-55%),[11] fatigue (60%-97%),[12] pruritus (41%-54%),[9] cognitive impairment (70%),[13] and, rarely, seizures and coma. Depression (23%-28%)[9] and anxiety (12%-52%)[11] are common among patients with kidney failure. On physical examination, patients may have signs of fluid overload (eg, peripheral edema and hypertension), a pericardial friction rub, reduced muscle strength, asterixis, and/or xerosis.

When to Initiate Dialysis

There is no specific threshold of estimated GFR (eGFR) or other laboratory value (eg, potassium, bicarbonate, phosphorus) at which dialysis should be initiated (**Box**).[14-16] A study that randomized 828 patients to early hemodialysis (eGFR, 10-14 mL/min/1.73 m^2) vs late hemodialysis (eGFR, 5-7 mL/min/1.73 m^2) reported no difference in mortality after a median follow-up of 3.6 years (37.6% vs 36.6%; HR, 1.04 [95% CI, 0.83-1.30]).[17] Severe hyperkalemia and/or metabolic acidosis can lead to life-threatening arrhythmias and, if refractory to medical management (ie, oral potassium binder and bicarbonate supplementation), may necessitate dialysis.[14] Uremic signs and symptoms and laboratory trajectories (eg, rate of eGFR decline) typically inform dialysis initiation decision-making. Calculated scores, such as the 4-variable Kidney Failure Risk Equation (KFRE, which includes age, sex, eGFR, and urinary albumin to creatinine ratio) can assist decision-making. The KFRE is associated with 2- and 5-year probability of treated kidney failure (dialysis or transplant) and demonstrated excellent 2-year discrimination for kidney failure development (c statistic, 0.90 [95% CI, 0.89-0.92]) among 721 357 people with CKD stages 3-5.[18]

Box. Commonly Asked Questions About Dialysis-Dependent Chronic Kidney Failure

When should dialysis be initiated for people with advanced chronic kidney disease?

There is no recommended estimated glomerular filtration rate (eGFR) threshold for initiation of dialysis. Persistent signs and symptoms of uremia and volume overload, such as nausea, fatigue, dyspnea, and peripheral edema, that are refractory to medical therapies and worsening eGFR, metabolic acidosis, and hyperkalemia inform the timing of dialysis initiation.

What are the most common dialysis treatment–related complications?

Catheter-related bloodstream infections and peritonitis are the most common infectious complications of hemodialysis and peritoneal dialysis, respectively. Common noninfectious complications of hemodialysis include muscle cramps, itching, fatigue, hypotension during dialysis, and arrhythmia. Common noninfectious complications of peritoneal dialysis include abdominal and back pain; catheter leak, migration, and kinking; and metabolic disturbances, such as hyperglycemia.

How should clinicians care for patients receiving maintenance dialysis?

Clinicians should avoid prescribing nephrotoxic agents, such as nonsteroidal anti-inflammatory agents and iodinated contrast media (unless medically necessary), for patients undergoing dialysis who have residual kidney function (defined as production of >1-2 cups of urine per day). For patients receiving maintenance dialysis, clinicians should dose-adjust certain medications, such as some antimicrobials, antihyperglycemic agents, and gabapentin.

Hemodialysis

With hemodialysis, concentration gradients cause solute (eg, urea) diffusion from blood to dialysate (ie, dialysis solution) and bicarbonate from dialysate to blood. Ultrafiltration, defined as fluid removal, can be performed concurrently with or separately from hemodialysis. Hemodiafiltration is a form of hemodialysis that uses diffusive and convective (ie, pressure gradient–induced solute drag) clearance, removing more middle molecular–weight solutes, such as β-2 microglobulin, than standard hemodialysis. Commonly used in Europe and Japan, hemodiafiltration is not currently used in the US outpatient setting. In an RCT of 1360 patients with kidney failure randomized to either hemodiafiltration or conventional hemodialysis, all-cause mortality occurred in 17.3% of patients receiving hemodiafiltration vs 21.9% receiving conventional hemodialysis (HR, 0.77 [95% CI, 0.65-0.93]) at a median follow-up of 30 months.[19]

Standard hemodialysis can be performed in a dialysis clinic or at home. When performed at a dialysis clinic, hemodialysis typically occurs 3 times weekly for approximately 4 hours per treatment.

At some clinics, shorter, more frequent or longer, overnight treatments can be delivered. Home hemodialysis in the US consists most often of short, daily treatments (~2-3 hours, 4-6 days/week) but can be prescribed as less frequent, longer treatments (~5-7 hours, 3-6 days/week). Most home hemodialysis machines can be transported, enabling therapy during travel. Patients using home hemodialysis often have partners at home who help with treatment, but this is not required. No large RCTs have shown survival differences between home and in-center hemodialysis.[15,20] Small RCTs have reported that more intensive hemodialysis, defined as more frequent and/or longer treatments, decreased systolic blood pressure (SBP) and left ventricular hypertrophy, compared with less frequent and/or shorter treatments, but longer and more frequent treatments may increase vascular access complications (ie, dysfunction requiring repair)[21-23] (**Figures 1** and **2**; **Table 1**).[24-26]

Peritoneal Dialysis

With peritoneal dialysis, typically a glucose-based dialysis solution is instilled in the abdomen. Transperitoneal membrane diffusive and osmotic forces facilitate toxin removal, ultrafiltration (fluid removal), and electrolyte homeostasis. The degree of solute exchange depends on gradient magnitudes, peritoneal membrane characteristics, and peritoneal surface area in contact with dialysate.[27] Patients perform peritoneal dialysis at home via machine-automated exchanges or manual exchanges, which use gravity instead of a machine to instill and drain fluid. Continuous ambulatory peritoneal dialysis (CAPD) typically consists of 4 to 6 manual exchanges per day, whereas automated peritoneal dialysis (APD) uses a machine (cycler) to instill and drain fluid, often at night. CAPD is more cost-effective and more commonly used in low-resource settings outside the US.[28] As residual kidney function declines and/or the peritoneal membrane scleroses (ie, becomes scarred), patients using nocturnal APD often add daytime exchanges to increase dialysis dose and avoid additional time attached to a machine[29] (Figures 1 and 2; Table 1).

Modality Selection

Based on 17 observational studies (113 578 patients), no clear survival difference was demonstrated between initiating hemodialysis vs peritoneal dialysis.[30] Some patients may transition between hemodialysis and peritoneal dialysis due to preference or changes in clinical status, such as worsening heart failure, dialysis access dysfunction, or severe peritonitis. For patients deemed eligible, dialysis can be temporary and serves as a bridge to kidney transplantation. Patient education and shared decision-making among clinicians, patients, and their caregivers is important when selecting dialysis modality and type and should include patient preferences and goals, therapy availability, clinical and socioeconomic factors, and cost.[31] Lifestyle considerations also influence modality selection. Home dialysis allows for more flexible dialysis treatment times and does not involve traveling to a dialysis clinic, but requires substantial home equipment and supplies. In-center hemodialysis requires traveling to a dialysis clinic multiple times per week at an assigned treatment time, but occurs in a controlled and monitored environment.

Access to predialysis nephrology care and the urgency of the need to initiate dialysis affect the selection of dialysis modality (ie, peritoneal or hemodialysis). Approximately one-third of US patients with kidney failure had no predialysis nephrology care,[3] and most of these patients initiated therapy with hemodialysis because it can be administered immediately following central venous catheter placement. However, "urgent-start" peritoneal dialysis can be initiated 2 days after peritoneal catheter placement and has comparable mortality to a traditional peritoneal dialysis initiation (>2 weeks after catheter placement).[32] Regional policies are relevant to modality selection. Hong Kong policies require a peritoneal dialysis–first approach, with more than 70% peritoneal dialysis uptake.[33] In contrast, only 14% of patients in the US who initiated dialysis in 2021 received home-based therapy (13% peritoneal dialysis, 1% home hemodialysis).[3]

Dialysis Access

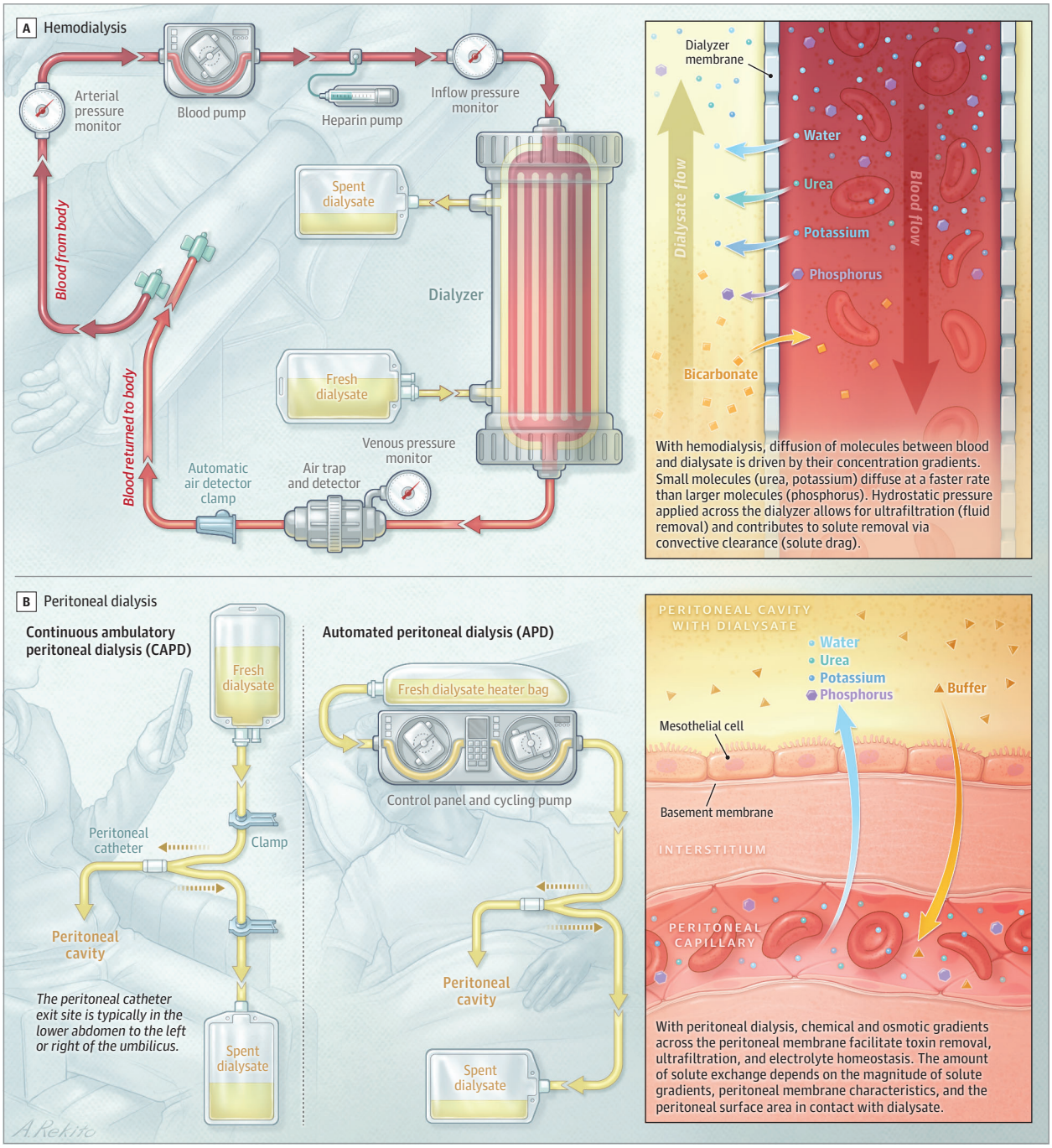
In hemodialysis, an arteriovenous (AV) fistula, AV graft, or a tunneled central venous catheter provides bloodstream access.[34,35] An AV fistula directly connects a vein and artery. An AV graft connects a vein and artery via graft material (synthetic or biologic). Most AV accesses are located in the arm; leg and chest grafts can be considered if arm vasculature is unsuitable.[35] Most AV grafts can be used 3 to 6 weeks after placement.[35] AV fistulas take 8 to 12 weeks to mature[35] and more than 40% require additional procedures (eg, angioplasty, stent placement) before use.[36] Hemodialysis central venous catheters are double lumen and are usually placed in the internal jugular vein, although femoral, transhepatic, and translumbar catheters can be alternatives.[35] In a 62-study systematic review (586 337 patients), tunneled central venous catheters were associated with higher infection risk (relative risk [RR], 1.49-2.12), hospitalization (RR, 1.51-1.68), and mortality (RR, 1.38-1.53) vs AV access (absolute rates unavailable).[37] However, based on the 2023 United States Renal Data System Annual Data Report, 82% of patients in the US used a tunneled catheter at hemodialysis initiation.[3]

Infectious Complications

For patients receiving hemodialysis (**Table 2**),[38-47] catheter-related bloodstream infections are common (1.1-5.5 episodes/1000 catheter-days).[35] In a study of 472 patients undergoing hemodialysis, 54% experienced a catheter-related bloodstream infection within 6 months of placement of their first tunneled dialysis catheter.[48] Initial management of suspected bacteremia requires blood culture collection and treatment with empirical intravenous gram-positive and gram-negative antibiotics, such as vancomycin or ceftazidime.[35] Catheter exchange, typically over a guidewire, following an episode of bacteremia can help prevent recurrence.[35] Preventive measures include infection control practices, such as use of a mask and sterile gloves with dressing changes and exit site care, antiseptic-coated catheter hub devices, antibiotic catheter lock solutions, and avoidance of showering and swimming.[35]

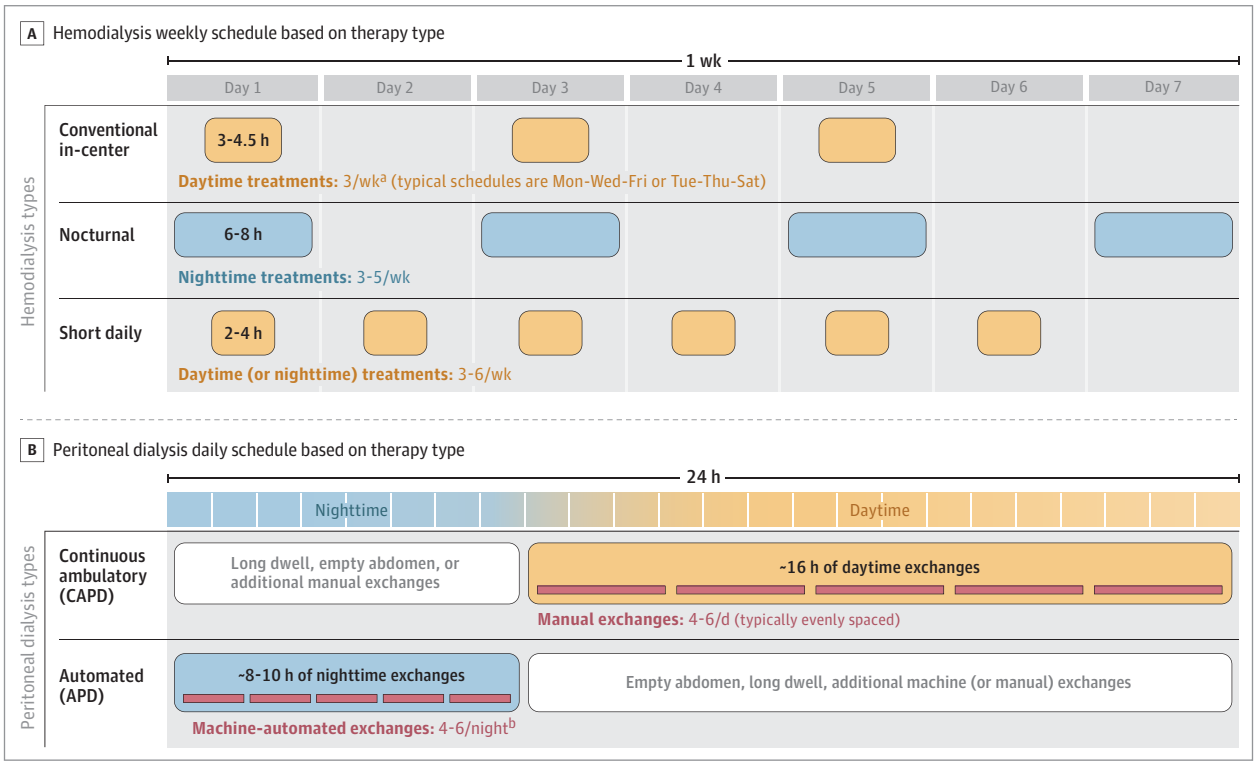
For patients receiving peritoneal dialysis (Table 2), peritonitis occurs commonly (0.26 and 0.30 episodes/patient-year in the US and worldwide, respectively).[49,50] In a study of 1677 patients receiving peritoneal dialysis, 28% experienced peritonitis in their first year of therapy.[51] Peritonitis typically presents with abdominal pain and/or cloudy effluent fluid and is diagnosed with peritoneal fluid cell count differential and culture. Presence of at least 2 of the following conditions indicates peritonitis: (1) abdominal pain or cloudy effluent, (2) effluent white blood cell count more than 100 per mL or more than 50% polymorph mononuclear leukocytes,

Figure 1. How Hemodialysis and Peritoneal Dialysis Work



During hemodialysis (A), blood goes from the patient to the machine, passing through a circuit. The circuit consists of a blood pump, dialyzer, and safety features, including pressure and flow monitors and an air detector. In the dialyzer, blood runs countercurrent to dialysate solution, and solutes diffuse from the blood to the dialysate (eg, urea) and from the dialysate to the blood (eg, bicarbonate). Smaller molecular-weight solutes (eg, urea) diffuse quickly, and larger molecules (eg, phosphate and protein-bound uremic toxins) diffuse slowly or not at all. Ultrafiltration (ie, fluid removal) is achieved by applying hydrostatic pressure across the dialyzer. Peritoneal dialysis (B) is performed by manually instilling and draining dialytic fluid (continuous ambulatory peritoneal dialysis) or by using a machine (cycler) to instill and drain fluid (automated peritoneal dialysis). Peritoneal dialysis fluid is typically glucose-based, with higher glucose concentrations enhancing ultrafiltration. During a peritoneal dialysis "exchange," the filling and dwelling phases generate chemical and osmotic gradients necessary for the toxin and excess fluid removal that occurs during the draining phase. Transperitoneal membrane diffusive and osmotic forces facilitate toxin removal, ultrafiltration, and electrolyte homeostasis. The degree of exchange depends on gradient magnitudes and the peritoneal membrane surface area in contact with dialysate.

Figure 2. Hemodialysis and Peritoneal Dialysis Prescription Profiles for Chronic Kidney Failure



Schematic representation of the most common prescription profiles of hemodialysis (A) and peritoneal dialysis (B) for the treatment of chronic kidney failure. When initiating dialysis, patients may begin with either more intensive or less intensive schedules, depending on factors such as residual kidney function, urgency of uremic toxin and fluid removal, and severity of metabolic derangements. If patients choose to discontinue dialysis, they may transition to less intensive schedules prior to fully discontinuing therapy.

[a]If additional fluid, solute, or toxin removal is required, a fourth treatment can be added on another day not typically scheduled for treatment (based on clinic availability).

[b]If additional fluid, solute, or toxin removal is required, exchanges can be modified or extra exchanges can be added when the patient has an empty abdomen or during a long dwell.

and (3) positive effluent culture.[52] Treatment includes empirical intraperitoneal antibiotics (gram-positive and gram-negative coverage) modified based on culture results.[52,53] The most common organisms are streptococcal and staphylococcal species and *Escherichia coli*.[52,53] Fungal and *Pseudomonas aeruginosa* peritonitis and peritonitis not resolving after 5 days necessitate catheter removal.[52] Peritoneal dialysis catheter infections limited to the catheter exit site can be treated with oral therapies, such as cefalexin, but catheter tunnel infections, defined as erythema, swelling, and tenderness along the catheter tunnel, require catheter removal in addition to antibiotics tailored to culture results.[52,54]

Noninfectious Complications of Dialysis

Common noninfectious complications of hemodialysis (Table 2) include muscle cramps (53% [95% CI, 43%-62%])[10] and headache (30% [95% CI, 24%-37%]).[10] Hemorrhage (14-91 per million treatments)[55] can occur during dialysis due to needle dislodgement, catheter misconnection, AV access rupture, or inadvertent catheter removal. Allergic reactions during hemodialysis occur infrequently (21-170 per million treatments)[55] and may be precipitated by the hemodialysis membrane or sterilizing agents, disinfectants, and medications (eg, heparin, iron).[55]

Volume-related complications with hemodialysis are common. In a meta-analysis (8 studies, 14 883 patients), hypotension during dialysis (ie, intradialytic hypotension), defined as a decrease in SBP to less than 90 mm Hg, occurred in 4% to 17% of hemodialysis treatments.[56] In a 1409-patient study, intradialytic hypotension, even when asymptomatic, was associated with increased 2-year mortality (adjusted odds ratio [OR], 1.56 [95% CI, 1.05-2.31]) (absolute rates unavailable).[57] Insufficient ultrafiltration and high weight gains (defined on an individual basis) contribute to hypertension, left ventricular hypertrophy, and heart failure.[58]

With peritoneal dialysis (Table 2), hemodynamic instability is uncommon, but 80% of patients receiving peritoneal dialysis have hypertension.[59] Prescribing low-sodium diets and diuretics, customizing the length of time the dialysis solution is left in the abdomen (ie, dwell times), and using higher-tonicity glucose-based peritoneal dialysis solutions or icodextrin, a slow-resorbing glucose polymer, can enhance ultrafiltration.[59] Patients with diabetes using glucose-based peritoneal dialysis solutions require close glycemic monitoring because glucose can be absorbed from the dialysis solution into the blood.[59] Approximately 10% of patients experience peritoneal catheter flow complications (eg, migration or kinks) and about 6% develop catheter leaks.[60] Per the International Society for Peritoneal Dialysis guidelines, constipation prevention with a stool softener (docusate) and laxative (senna) enhances bowel motility, improving solute exchange and catheter function.[61]

Table 1. Dialysis Therapies for Chronic Kidney Failure

	Hemodialysis	Peritoneal dialysis
Type and location	Conventional in-center	CAPD
	Nocturnal in-center or at home	APD
	Short daily in-center or at home	All PD performed at home
	(See Figure 1A for exemplar prescriptions)	(See Figure 1B for exemplar prescriptions)
Dialysis access	AV access (fistula or graft)	PD catheter
	Tunneled central venous catheter	
Dialysis solution (dialysate)	Sodium: 137 (134-140 mmol/L)	Sodium: 132 (130-137 mmol/L)
	Potassium: 2 (1-4 mEq/L)	Potassium: 0 (0-2 mEq/L)
	Chloride: 105 (87-120 mEq/L)	Chloride: 96 (95-96 mmol/L)
	Calcium: 2.5 (2-3 mEq/L)	Calcium: 1.25 (1.25-1.75 mmol/L)
	Bicarbonate: 37 (32-40 mEq/L)	Lactate: 40 (30-40 mmol/L)
	Magnesium: 0.5 (0.5-1.0 mEq/L)	Magnesium: 0.5 (0.25-0.75 mmol/L)
	Dextrose: 100 (0-200 mg/dL)	Dextrose: 1.5% (76 mmol/L), 2.5% (126 mmol/L), 4.25% (214 mmol/L), and/or icodextrin 7.5% (high molecular weight glucose polymer)
Volume-related parameters	Pre- and post-HD treatment weights	Daily weights
	Estimated dry weight (weight with no excess fluid)	Estimated dry weight (weight with no excess fluid)
	Interdialytic weight gain (gain between treatments)	Ultrafiltration volume (amount of fluid removed)
	Ultrafiltration volume (amount of fluid removed)	BP (at least weekly)
	Ultrafiltration rate (speed of fluid removal)	
	Pre-, intra- (~every 15 min), and post-HD BPs	
Outcomes across modalities	No 5-y mortality difference (HD vs PD at dialysis initiation [propensity-matched observational data])[87]	No 5-y mortality difference (HD vs PD at dialysis initiation [propensity-matched observational data])[87]
	No adverse cardiovascular event difference (HD vs PD at dialysis initiation [meta-analysis of observational data])[88]	No adverse cardiovascular event difference (HD vs PD at dialysis initiation [meta-analysis of observational data])[88]
Outcomes across select types of therapy	Nocturnal 6/wk (vs in-center 3/wk) may improve BP and LVH (small RCTs)[21,23]	CAPD (vs APD) with more time for work and family and lower rates of peritonitis, but no difference in ultrafiltration (small RCT)[89]
	Short daily 6/wk (vs in-center 3/wk) may improve survival and LVH mass (small RCT)[22]	
Lifestyle considerations	In-center	More schedule flexibility[a]
	Rigid treatment schedules	Less frequent (1-3/quarter) travel to a clinic[a]
	Monitored environment with trained personnel	Unrestricted mobility for CAPD (no machine)
	Less burdensome for caregivers	Less restrictive diet for potassium and phosphorus (not sodium)[a]
	No medicalization of the home	Requires home medical equipment/supplies
	Home	Therapy delivery by caregiver and/or patient[b]
	More schedule flexibility[a]	Potential for caregiver burnout
	Less frequent (~1/mo) travel to a clinic[a]	
	Less restrictive diet for potassium and phosphorus (not sodium)[a]	
	Requires home medical equipment/supplies	
	Therapy delivery by caregiver and/or patient	
	Potential for caregiver burnout	

Abbreviations: APD, automated peritoneal dialysis; AV, arteriovenous; BP, blood pressure; CAPD, continuous ambulatory peritoneal dialysis; HD, hemodialysis; LVH, left ventricular hypertrophy; PD, peritoneal dialysis; RCT, randomized controlled trial.

[a] Compared with in-center hemodialysis, administered 3 to 4 hours 3 times per week.

[b] Some regions have assisted PD, in which a technician or nurse comes to the home to assist with cycler connection and disconnection.

Management of Conditions Associated With Dialysis-Dependent Kidney Failure

Anemia

More than 85% of patients in the US receiving dialysis receive treatment for anemia. The Kidney Disease: Improving Global Outcomes (KDIGO) guidelines recommend starting intravenous iron and/or erythropoietin stimulating agent therapy if hemoglobin is less than 10 g/dL, maintaining hemoglobin 10 g/dL to 11.5 g/dL, and starting intravenous iron if transferrin saturation (TSAT) is less than 20% to 30%.[5] In an RCT of 2141 patients randomized to intravenous iron at high dose (400 mg/month, unless ferritin >700 ug/L or TSAT ≥40%) vs low dose (0-400 mg/month, with ferritin <200 µg/L or TSAT <20% triggering administration), 320 patients (29.3%) receiving high-dose iron vs 338 patients (32.2%) receiving low-dose iron experienced cardiovascular morbidity or death (HR, 0.85 [95% CI, 0.73-1.00]).[62] Hypoxia-inducible factor–prolyl hydroxylase domain inhibitors (HIF-PHIs), such as daprodustat, are newer but expensive anemia therapies that may be used in patients nonresponsive to epoetin.[63,64] HIF-PHIs activate the HIF oxygen-sensing pathway, stimulate endogenous erythropoietin production, and modulate iron metabolism.[63,64] There is no evidence-based hemoglobin threshold for blood transfusion in dialysis-dependent kidney failure. Clinicians should make transfusion decisions based on factors such as cardiac risk profile, active bleeding, and transplant eligibility, as transfusions can result in antibody production, rendering a patient "immunologically sensitized," and more likely to experience transplant rejection (Table 3).[65-75]

Table 2. Hemodialysis and Peritoneal Dialysis Treatment Complications

Complication	Description or diagnosis (frequency)[a]	Management[b]
Hemodialysis		
Infectious complications		
Catheter-related bacteremia	Clinical manifestations with ≥1 positive peripheral blood culture (dialysis circuit or vein) and no other apparent source, with positive catheter segment/hub/tip culture, with same isolated organism from periphery and catheter[32] 54% of catheter-based patients by 6 mo;[35] 1.1-5.5 episodes per catheter-day[32]	Stabilize hemodynamics Empirical intravenous antibiotics with gram-negative and gram-positive coverage (usually given with HD treatment); tailor to culture results Exchange catheter over a guidewire Remove catheter if *pseudomonas* or fungal in origin and/or concurrent tunnel infection, immediate removal if patient unstable
Exit site/catheter tunnel infections	Exit site: tenderness, hyperemia, and/or induration ≤2 cm from catheter exit site[32] Tunnel: tenderness, hyperemia, and/or induration along catheter tunnel[32] 0.3 to 8.3 exit site infections per 1000 tunneled catheter-days (absolute rates not reported)[32]	Exit site: empirical intravenous antibiotics with gram-positive coverage; tailor to culture results Tunnel: empirical intravenous antibiotics with gram-negative and gram-positive coverage; tailor to culture results Catheter exchange if not improving with antibiotics (exit site/tunnel) and create new tunnel (tunnel), immediate removal if patient unstable
Infection transmission[c]		
Respiratory pathogens	Infection prevention and control actions, including standard precautions Influenza and pneumococcal pneumonia vaccinations often given at dialysis clinic	Provide supportive care for acute illness Antivirals if indicated
Blood-borne pathogens	Hepatitis B and C testing annually at minimum,[90,91] HBsAg testing monthly if patient not immune, hepatitis B vaccination given at dialysis facility[91]	
Noninfectious complications		
Peridialytic symptoms	Muscle cramps (53%), itching (51%), restless legs (33%), headache (30%), nausea (28%), vomiting (14%), diarrhea (20%), dry mouth (43%), shortness of breath (38%), presyncope/dizziness (36%), sensation change in AV access arm (38%), postdialysis fatigue (70%)[10,92]	Treatment of symptoms (exemplar treatments below) Muscle cramps: slow or stop ultrafiltration, fluid bolus, optimize weight/hemodynamics, massage/stretch, correct electrolytes, intradialytic exercise Restless legs: treat anemia, intradialytic exercise, dopamine agonist, gabapentin
Arrhythmia	Bradyarrhythmias most common[93] Precipitants: electrolyte derangements, such as hyperkalemia, hypokalemia, and hypomagnesemia; fluid shifts; medications 19% (95% CI, 11%-33%) with at least 1 bradycardia/asystole event per year[93]	Cardiopulmonary resuscitation if indicated Acute treatment of electrolyte derangements Cardiology evaluation (pacemaker for bradycardia)
Intradialytic hypotension	Symptomatic drop in BP or a nadir intradialytic systolic BP <90 mm Hg[45] 4%-17% of treatments[43]	Slow or stop ultrafiltration Fluid bolus Place in Trendelenburg position Lower temperature of the dialysate
Dialyzer reactions	Type A: IgE-mediated, urticaria, bronchospasm, laryngeal edema, shock[42] Type B: complement activation, less intense symptoms (ie, chest pain, back pain)[42] Precipitants: dialyzer, disinfectants, medications (heparin, iron)[42] 21-170 reactions per million treatments[42]	Stabilize hemodynamics, provide supportive care (eg, epinephrine, fluids, antihistamine, steroid) Immediately stop treatment and do not return blood (Type A) For future dialysis treatments: change dialyzer type, pretreat with antihistamine, prerinse HD tubing with saline
AV access bleeding	Prolonged bleeding after needle removal; may indicate access dysfunction[32] Needle dislodgement can cause life-threatening bleeding within minutes[42] 14-91 needle dislodgements per million treatments[42]	Prolonged bleeding: evaluate with fistulogram Needle dislodgement: apply pressure, stabilize hemodynamics
Disequilibrium syndrome	Nausea/vomiting, encephalopathy, or seizures in setting of severe azotemia[42] Rapid decline in blood urea, blood-brain osmotic gradient, cerebral edema 8.5-33 episodes per million treatments[42]	Provide supportive care Hypertonic saline, mannitol Use CKRT vs intermittent HD if cerebral edema Reduce risk with shorter HD treatment, lower blood flow, and/or higher dialysate sodium
Calciphylaxis[d]	Vasculopathy resulting from calcium deposition in the arteriolar microvasculature of the deep dermis and subcutaneous adipose tissue Often presents as extremely painful violaceous to hyperpigmented plaques and nodules that evolve to necrosed, open wounds with high risk of infection; 1-y mortality rate: 45%-80%[94] Risk factors: obesity, diabetes, female sex, hyperPTH, warfarin, vitamin K and D deficiencies 3.5 cases per 1000 patient-years in hemodialysis (absolute rate not reported)[94]	Wound care, including surgical debridement Sodium thiosulfate Multimodal analgesia Hyperbaric oxygen

(continued)

Table 2. Hemodialysis and Peritoneal Dialysis Treatment Complications (continued)

Complication	Description or diagnosis (frequency)[a]	Management[b]
Peritoneal dialysis		
Infectious complications		
Peritonitis	Presence of ≥2 of the following: (1) abdominal pain or cloudy effluent, (2) effluent WBC >100 per mL or >50% PMLs, (3) positive effluent culture[39] 28% prevalence in first year of therapy;[38] 0.26 episodes per patient-year[36]	Empirical intraperitoneal antibiotics with gram-negative and gram-positive coverage; tailor to culture results Hospitalize if fever, septic, severe pain, or unable to perform PD at home Remove catheter if fungal or pseudomonas in origin or refractory (continues to meet diagnostic criteria after 5 d of therapy)
Exit site/catheter tunnel infections	Exit site: purulent discharge at catheter site[41] Tunnel: erythema, swelling, tenderness anywhere along catheter tunnel[41] 0.06-0.42 episodes per year (absolute rates not reported)[41]	Empirical oral antibiotic therapy with *staphylococcus aureus* coverage; tailor to culture results
Noninfectious complications		
Metabolic disturbances	Hypokalemia, hyperglycemia, metabolic syndrome[24,46] 55% of patients develop some type of glucose metabolism disturbance[95]	Oral potassium supplementation for hypokalemia Carbohydrate-sparing solutions (eg, icodextrin)
Peridialytic symptoms	Abdominal pain (during infusion or drainage), abdominal distension, back pain[24] 28% of patients have drain pain (ie, pain with drainage)[96]	Raise dialysate pH (infusion pain) Slow rate of dialysate infusion (infusion pain) Incompletely drain the fluid after a dwell (infusion and drain pain) Bowel regimen to prevent constipation (drain pain) Switch from APD to CAPD (drain pain) Decrease dialysate fill volume (back pain)
Catheter dysfunction	Leak, migration, kink, omentum wrapping, inadequate drainage[48] ~10% of catheters have flow complications; ~6% of patients have leaks[47]	Bowel regimen to prevent constipation Low-volume, supine exchanges with no daytime dwell of dialysis solution in the abdomen (leak) Exchange/remove catheter if no improvement with supportive measures
Intra-abdominal pressure sequelae	Fluid migration (eg, hydrothorax, scrotal/vulvar edema, hydrocele), hernia[24,48] 4%-10% of patients have hernia[97,98]	Low-volume, supine exchanges with no daytime dwell of dialysis solution in the abdomen VATS or pleurodesis (hydrothorax) Surgical repair (hernia)
Encapsulating peritoneal sclerosis	Progressive peritoneal fibrosis with long-term PD (>5 y), bowel encasement that can present as failing to thrive, intermittent SBO[99] 0.4%-8.9% of patients have EPS; 0.7-13.6 per 1000 patient-years[99]	Change to HD and permanently stop PD Tamoxifen ± steroids Surgical intervention for adhesions/obstruction

Abbreviations: APD, automated peritoneal dialysis; AV, arteriovenous; BP, blood pressure; CAPD, continuous ambulatory peritoneal dialysis; CKRT, continuous kidney replacement therapy; EPS, encapsulating peritoneal sclerosis; HBsAg, hepatitis B surface antigen; HD, hemodialysis; hyperPTH, hyperparathyroidism; IgE, immunoglobulin E; PD, peritoneal dialysis; PML, polymorphonuclear leukocytes; SBO, small bowel obstruction; VATS, video-assisted thoracic surgery; WBC, white blood cell count.

[a] Absolute rates are provided when available. Complications are listed in order of declining frequency.

[b] Acute management approaches most commonly used.

[c] Infection prevention and control practices may vary regionally and based on specific clinical scenarios.

[d] Not a complication of the dialysis treatment itself but occurs most commonly in the setting of hemodialysis-dependent chronic kidney failure.

Mineral and Bone Disorders

Management of mineral and bone disorders is important for reducing fracture risk, a common complication of kidney failure due to kidney impairment–related changes in bone turnover, mineralization, and volume. Hip fracture risk in patients receiving dialysis is approximately 6 times higher than the risk in the general population.[76] A meta-analysis (26 observational studies) of patients with dialysis-dependent kidney failure reported a 5-year mortality rate of 56% (95% CI, 41%-71%) after hip fracture and a 5-year mortality rate of 48.3% after spine fracture.[77] Dietary and pharmacologic strategies to regulate phosphorus, calcium, vitamin D, and intact parathyroid hormone (iPTH) are important components of management.[6] Dietary phosphorus reduction includes curtailing intake of dairy products; phosphorus-based preservatives, such as phosphoric acid; and phosphorus-containing beverages, such as colas.[6] Most patients, including 93% of US Medicare-insured patients receiving chronic dialysis in 2019, receive oral phosphorus binders, such as calcium acetate and sevelamer carbonate, to lower phosphorus levels toward the normal range.[6,78,79]

The KDIGO guidelines suggest that iPTH, measured quarterly, should be no more than 2 to 9 times the upper limit of normal to reduce fracture risk but rated the evidence quality as low.[6] Vitamin D analogs (eg, calcitriol) and calcimimetics (eg, cinacalcet) are titrated based on phosphorus, calcium, and iPTH levels.[6,80,81] The KDIGO guidelines recommend titrating vitamin D analogs, calcimimetics, calcium-containing phosphorus binders, and the calcium concentration of the hemodialysis solution to maintain calcium levels in the normal range for patients with CKD.[6] Parathyroidectomy may be considered for hyperparathyroidism refractory to medical management.[6,82] The KDIGO guidelines recommend bone mineral density testing (ie, with dual-energy x-ray absorptiometry) to assess fracture risk if results will change clinician treatment decisions[6] (Table 3).

Table 3. Medical Management of Selected Systemic Effects of Dialysis-Dependent Chronic Kidney Failure

Complications[a] and frequency	Targets of therapy/definition	Therapies[b]	Highest level of evidence for therapies[b]
Anemia: 85.6% (HD) and 77.3% (PD) with hemoglobin <12 g/dL[3]	Hemoglobin: 10.0-11.5 g/dL[5] Ferritin: 200-500 µg/L[5] Iron saturation: 20%-50%[5]	ESA	RCTs (HD): ESA with lower risk of blood transfusion vs placebo (low certainty)[100]
		Intravenous iron	RCT (HD): proactive high-dose iron strategy superior to reactive low-dose strategy for decreasing ESA dose and composite outcome of cardiovascular events or death (NNT = 33)[49] RCT (PD): Iron sucrose with higher mean hemoglobin (+1.3 ± −1.1 g/dL) vs no iron (+0.7 ± 1.1 g/dL) (mean difference, 0.6 g/dL), fewer transfusions, and less ESA dose escalation[101]
		Hypoxia-inducible factor stabilizers	RCT (HD): HIF stabilizer noninferior to ESA for increasing hemoglobin (AD = 0.2 ± 1.2 g/dL [95% CI, −0.02 to 0.5]); less hypertension but more hyperkalemia vs ESA[51]
Hypertension: 59%-83% (HD and PD)	Systolic blood pressure[61] Age <65 y: <130 mm Hg Age ≥65 y: 130-140 mm Hg	Ultrafiltration	RCT (HD): greater reduction in ambulatory SBP from baseline to 8 wk with dry weight probing via ultrafiltration (−13.5 mm Hg) vs control (−6.9 mm Hg); $P = .02$[66] RCT (PD): enhanced ultrafiltration with icodextrin vs glucose-containing solution (weighted mean difference, 448.5 mL/d [95% CI, 289.3-607.8])[102]; uncertain effect on BP[103]
		Dietary sodium restriction	RCTs (HD and PD): dietary sodium reduction to 1690 mg/d lowered SBP/DBP by −6.91/−3.91 mm Hg (95% CI, −8.82 to −4.99/−4.80 to −3.02) (high certainty)[64]
		Lower dialysate sodium	RCTs (HD): lower (vs higher) dialysate sodium lowered pre-HD mean arterial BP (mean difference, −3.58 mm Hg [95% CI, −5.46 to −1.69]) and post-HD mean arterial BP (mean difference, −3.26 mm Hg [95% CI, −1.70 to −4.82]) (moderate certainty)[65]
		β-blockers (non-dialyzable), renin-angiotensin system inhibitors	RCT (HD): similar 12-mo SBP reduction with atenolol (−21.4 ± 2.4 mm Hg) and lisinopril (−17.9 ± 2.6 mm Hg); P = NS; atenolol with fewer serious cardiovascular events (20 events/16 patients) vs lisinopril (43 events/28 patients), incidence rate ratio, 2.36 (95% CI, 1.36-4.23)[69]
		Calcium channel blockers	RCT (HD): lower risk of composite end point of mortality or cardiovascular event with amlodipine (19 events/123 patients, 15%) vs placebo (32 events/128 patients, 25%); $P = .03$[70]
		MRAs	RCTs (HD and PD): lower risk of cardiovascular mortality with MRAs (16 deaths) vs control (46 deaths); higher risk of gynecomastia (6.0-fold higher) and hyperkalemia (1.4-fold higher) with MRAs vs control[71]
CKD mineral bone disease[c]: 81.0% (HD) and 62.4% (PD) on vitamin D receptor agonist[104] 81.5% (HD) and 86.3% (PD) on phosphorus binder[104] 28.4% (HD) and 20.7% (PD) on calcimimetic[104]	Phosphorus: within normal limits[6] Calcium: within normal limits[6] iPTH: 2-9 × upper limit of normal (130-600 pg/mL)[6]	Phosphorus binders (eg, calcium acetate, sevelamer)	RCTs (HD and PD) lower all-cause death and hypercalcemia with sevelamer vs calcium-based binders (low certainty); no evidence that binders (of any type) vs placebo lower risk of cardiovascular death, MI, stroke, or fractures[54]
		Active vitamin D (eg, calcitriol, doxercalciferol)	RCTs (HD and PD): lower intact PTH levels with active vitamin D vs placebo (low certainty); more hyperphosphatemia and hypercalcemia vs placebo (low certainty); no evidence of improved fracture, overall survival, or cardiovascular survival[57]
		Calcimimetics (eg, cinacalcet HCl)	RCTs (HD and PD): lower intact PTH levels with calcimimetics vs placebo (high to moderate certainty); more hypocalcemia and nausea than placebo; no survival difference[56]
Hyperlipidemia: 30% (HD) and 45% (PD) with LDL >130 mg/dL[105]	Lipids: no population-specific targets[46,74]	No evidence-based therapy	RCTs (HD and PD): no cardiovascular or mortality benefit with statins (143 events/y per 1000 treated with statins) vs without statins (150 events/y per 1000 without statins) (moderate to high grade)[73]
Arrhythmia: 19% (95% CI, 11%-33%) with bradycardic/asystole event per year[93] 23.2% (HD) and 17.6% (PD) with atrial fibrillation[3]	Prevention	No evidence-based therapy	RCT (HD and PD): no cardiovascular benefit for ICD (5-y cumulative incidence of sudden cardiac death = 9.7% in ICD group vs 7.9% in control; $P = .55$); higher risk of infection with ICD[75]
Fatigue: 70% (95% CI, 64%-76%) HD and PD[10]	Symptom relief	CBT and/or stepped approach to pharmacotherapy	RCT (HD): modest improvement in FACIT-F fatigue score with CBT-based intervention vs control (adjusted mean group difference, 2.81 [95% CI, 0.86-4.75])[79]
Insomnia: 57% (95% CI, 52%-62%) HD and PD[10]	Symptom relief	No evidence-based therapy	RCT (HD): no clinically significant improvement in ISI score with CBT (−3.7) or trazadone (−4.2) vs placebo (−3.1)[106]
Pruritus: 51% (95% CI, 41%-60%) HD and PD[10]	Symptom relief	Difelikefalin	RCT (HD): improvement in WI-NRS score with difelikefalin (51.9%) vs placebo (30.9%), NNT = 4.8;[78,107] not currently approved for patients receiving PD
		Emollients/ good skin care	Expert opinion[77]

(continued)

Table 3. Medical Management of Selected Systemic Effects of Dialysis-Dependent Chronic Kidney Failure (continued)

Complications[a] and frequency	Targets of therapy/definition	Therapies[b]	Highest level of evidence for therapies[b]
Depression: 40% (95% CI, 32%-47%) HD and PD[10]	Symptom relief	Cognitive behavioral therapy	RCTs: improvement in BDI score with CBT vs usual care (AD, −6.1 [95% CI, −8.6 to −3.6]) (moderate certainty)[108]
		Sertraline (starting dose 25 mg/d up to a maximum dose of 200 mg/d)	RCT: improvement in QIDS-C score with sertraline (baseline, 10.9 ± 4.9; 12 wk, 5.9 ± 4.5) and CBT (baseline, 12.2 ± 5.1; 12 wk, 8.1 ± 5.1); 12-wk QIDS-C score lower with sertraline vs CBT (effect estimate, 1.84 [95% CI, −3.54 to −0.13])[80]
		Exercise	RCTs: improvement in BDI score with exercise vs control (mean difference, −7.61 [95% CI, −9.59 to −5.63]) (moderate certainty)[108]
		Relaxation techniques	RCTs: improvement in BDI score with relaxation techniques vs control (mean difference = −5.77 [95% CI, −8.76 to −2.78]) (moderate certainty)[108]
Malnutrition: 11.8% (HD) and 27.5% (PD) with albumin <3.5g/dL[109]	Protein intake 1.0-1.2 g/kg/d for stable nutritional status[85]	Protein supplements	RCTs (HD and PD): improvement in serum albumin with ONS vs control (mean difference, 1.44 g/dL [95% CI, 0.76-2.12]);[110] little evidence for lower hospitalization or mortality risks with ONS vs control[109]

Abbreviations: AD, absolute difference; BDI, Beck Depression Inventory; BP, blood pressure; CBT, cognitive behavioral therapy; CKD, chronic kidney disease; DBP, diastolic blood pressure; ESA, erythropoietin stimulating agents; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue scale; HD, hemodialysis; HIF, hypoxia-inducible factor; ICD, implantable cardioverter-defibrillator; iPTH, intact parathyroid hormone; ISI, Insomnia Severity Index; LDL, low-density lipoprotein; MI, myocardial infarction; MRA, mineralocorticoid receptor antagonist; NNT, number needed to treat; NS, nonsignificant; ONS, oral nutrition supplementation; PD, peritoneal dialysis; PTH, parathyroid hormone; QIDS-C, Quick Inventory of Depressive Symptomology-Clinician-Rated; RCT, randomized controlled trial; SBP, systolic blood pressure; WI-NRS, Worst Itching Intensity-Numerical Rating Scale.

[a] Complications listed by decreasing frequency, with approximate prevalence listed in parentheses.

[b] Citations were selected based on study size and publication date, with preference given to larger (>100 participants), more recent RCTs. Absolute differences and NNT are reported (when available) for select outcomes. When available, a meta-analysis/systematic review of relevant trials is cited and denoted by "RCTs" with the summative level of evidence provided (eg, low certainty) when reported.

[c] CKD mineral bone disease is defined as a systemic disorder of mineral and bone metabolism due to CKD manifested by either 1 or a combination of the following: (1) abnormalities of calcium, phosphorus, iPTH, or vitamin D metabolism; (2) abnormalities in bone turnover, mineralization, volume, linear growth, or strength; and (3) vascular or other soft tissue calcification.

Hypertension

Hypertension affects 59% to 83% of patients receiving hemodialysis.[83] Although prevalence of hypertension is thought to be similar among patients receiving peritoneal dialysis, data are lacking.[83,84] There is no evidence-based blood pressure (BP) target for people receiving maintenance dialysis. The International Society of Hypertension recommends a target SBP of less than 130 mm Hg for individuals aged younger than 65 years and less than 140 mm Hg for individuals aged 65 years and older.[85] Lowering BP reduces cardiovascular mortality. In a meta-analysis of 8 RCTs (1679 patients undergoing dialysis), 20% of patients receiving antihypertensives died of cardiovascular causes compared with 27% of control patients (RR, 0.71 [95% CI, 0.50-0.99]).[86] Home BP readings correlate more closely with mortality risk than in-clinic BPs. In a 150-patient study, in-center pre- and post-hemodialysis BP were not associated with mortality, whereas there was a nearly 50% higher death rate for a 22 mm Hg increment in SBP using ambulatory BPs (absolute data unavailable).[87] In patients with dialysis-dependent kidney failure, home BP measures should guide treatment.[7,58,83]

First-line hypertension treatment for patients undergoing dialysis includes dietary salt restriction,[88] use of a lower dialysate sodium concentration,[89] and ultrafiltration.[84,90-92] However, antihypertensive medications are often needed. β-blockers and renin-angiotensin system blockers are typically the first- and second-line medications, respectively.[83] An RCT of 200 patients receiving hemodialysis who had hypertension and left ventricular hypertrophy showed similar SBP reduction over 12 months with atenolol and lisinopril, but serious cardiac events, such as myocardial infarction, stroke, heart failure hospitalization, and cardiovascular death, occurred in 16 patients (16%) treated with atenolol (20 events) and 28 patients (28%) treated with lisinopril (43 events) (incidence rate ratio, 2.36 [95% CI, 1.36-4.23]).[93] Calcium channel blockers may be used as third-line antihypertensive agents.[94] Aldosterone antagonists, such as spironolactone or eplerenone, may be associated with lower mortality in patients with dialysis-dependent chronic kidney failure. A meta-analysis of RCTs and crossover RCTs that enrolled people with kidney failure requiring dialysis reported that aldosterone antagonists, compared with controls, reduced the risk of all-cause death (5.9% vs 13.1% in 9 studies of 1119 participants; RR, 0.45 [95% CI, 0.30-0.67]), and reduced the risk of death from cardiovascular disease (3.7% vs 10.1% in 6 studies of 908 participants; RR, 0.37 [95% CI, 0.22-0.64]).[95] However, most included studies had an unclear or high risk of bias.[95] Aldosterone antagonist use compared with control was associated with increased gynecomastia (3.1% vs 0.5%; RR, 5.95 [95% CI, 1.98-18.28]) and hyperkalemia (12.8% vs 9.1%; RR, 1.4 [95% CI, 0.72-2.78]).[95] There are no RCTs of diuretics in the dialysis population. Medication timing with hemodialysis is important because some antihypertensives are removed by dialysis (eg, metoprolol and lisinopril given before hemodialysis treatment). In addition, medications lowering BP too extensively can reduce ultrafiltration capacity. However, there is currently no evidence-based guidance about antihypertensive timing relative to the dialysis procedure[58,83] (Table 3).

Prevention of Cardiovascular Events

Guidelines recommend smoking cessation and diabetes and hypertension control for cardiovascular risk reduction in patients with dialysis-dependent kidney failure.[59] Statins and implantable cardioverter defibrillators (ICDs) are not effective primary cardiovascular event prevention strategies for patients receiving dialysis. An RCT of 2776 patients receiving hemodialysis who were randomized to rosuvastatin 10 mg per day or placebo with median follow-up of

3.8 years reported no difference in the composite end point of cardiovascular death, nonfatal myocardial infarction, and nonfatal stroke between rosuvastatin and placebo (HR, 0.96 [95% CI, 0.84-1.11]), despite a reduction in low-density lipoprotein from 100 to 57 mg/dL.[96] Initiation of statin therapy is not recommended for primary cardiovascular event prevention in patients with dialysis-dependent kidney failure regardless of cholesterol level.[59,97] For patients already prescribed a statin medication, general recommendations suggest continuing it.[98] In an RCT of 188 patients with heart failure treated with dialysis, the cumulative 5-year sudden cardiac death incidence was 9.7% (95% CI, 3.3-16.2) in the ICD group and 7.9% (95% CI, 1.7-14.0) in the control group (HR, 1.32 [95% CI, 0.53-3.29]) at median follow-up of 7 years.[99] Complications, such as infection and lead malfunction, occurred in 28% of patients with ICDs.[99] However, ICDs are recommended for secondary sudden cardiac death prevention in patients receiving dialysis[100] (Table 3).

Common Symptoms in People Receiving Dialysis

Patients with dialysis dependence experience multiple symptoms, including pruritus (51% [95% CI, 41%-60%]), concentration impairment (51% [95% CI, 30%-71%]), muscle cramping (53% [95% CI, 43%-62%]), insomnia (57% [95% CI, 52%-62%]), fatigue (70% [95% CI, 64%-76%]), and depressed mood (40% [95% CI, 32%-47%]).[10] First-line pruritus therapies include fragrance-free emollients (moisturizers) with high water content; oral antihistamines, such as loratadine; and topical analgesics, such as menthol, camphor, or phenol.[101] Difelikefalin, a selective κ opioid agonist, is a newer and more expensive medication. An RCT of 378 patients receiving hemodialysis who had moderate to severe pruritus were randomized to intravenous difelikefalin or placebo 3 times per week for 12 weeks. In the difelikefalin group, 51.9% had a decrease of 3 or more points in the 24-hour Worst Itching Intensity Numerical Rating Scale score (primary outcome) vs 30.9% in the placebo group (RR, 1.65 [95% CI, 1.26-2.14]).[102]

An RCT of 160 patients receiving hemodialysis who had fatigue, pain, or depression demonstrated that a stepped, individualized approach using telehealth-delivered cognitive behavioral therapy and/or relevant pharmacotherapy, such as antidepressants, modestly reduced fatigue measured by the Functional Assessment of Chronic Illness Therapy instrument (coprimary outcome; clinically important difference: ≥3 points) (mean difference, 2.81 [95% CI, 0.86-4.75]) vs control (mean difference, 0.65 [95% CI, −0.66 to 1.96]).[103] An RCT of 120 patients receiving hemodialysis who had depression reported that those randomized to sertraline, initiated at 25 mg per day and titrated to 200 mg per day as tolerated, had decreased Quick Inventory of Depressive Symptomology-Clinician-Rated depression scores at 12 weeks compared with those receiving cognitive behavioral therapy (effect estimate, −1.84 [95% CI, −3.54 to −0.13]; $P = .035$), although adverse events such as nausea and vomiting were more frequent in the sertraline group[104] (Table 3).

Prognosis

Mortality of patients receiving hemodialysis is highest in the 6 months after initiating dialysis. In a study of 86 886 patients receiving hemodialysis at a median follow-up of 1.2 years, 1939 deaths occurred in the first 120 days and 12 669 deaths occurred after 365 days of therapy (26.7 [95% CI,17.0-33.5] and 13.7 [95% CI, 5.2-19.9] deaths per 100 patient-years, respectively).[105] The most common causes of death in the US are cardiovascular-related (52.2%), infection (18.1%), and dialysis withdrawal (16.1%).[3] Mortality rates among patients receiving peritoneal and hemodialysis are similar over 3 to 5 years.[3] The leading causes of death among patients receiving peritoneal dialysis are cardiovascular complications (53%), dialysis withdrawal (18%), and infection (10%).[3]

A study that included 1412 and 1427 patients receiving hemodialysis and peritoneal dialysis, respectively, in the US measured the burden of kidney disease (eg, life interference, time spent, family burden) using the Kidney Disease Quality of Life instrument (higher scores indicate lower burden).[4] A low burden of kidney disease (burden score ≥75) was reported by 25% of patients receiving hemodialysis and 37% of patients receiving peritoneal dialysis. A high burden of kidney disease (burden score <25) was reported by 23% of patients receiving hemodialysis and 14% of patients receiving peritoneal dialysis.[4] This study also reported higher employment rates among patients receiving peritoneal vs hemodialysis among those aged 45 years and younger (39% vs 19%), 46 to 54 years (44% vs 23%), and 55 to 64 years (41% vs 17%).[4]

Dialysis Care Delivery in the US

In 1973, Medicare coverage was extended to individuals requiring maintenance dialysis regardless of age. Dialysis care in the US is delivered in clinics owned primarily by private (ie, nongovernment) organizations. Within each facility, an interdisciplinary care team composed of a nephrologist, nurse, patient care technician, social worker, and dietitian provide care. Nephrologists visit in-center hemodialysis patients at least once and up to 4 times monthly and see home-based patients monthly via telehealth or in clinic. Clinics typically use disease management protocols (eg, for anemia and bone mineral disease) to promote delivery of evidence-based, consistent care, which has population-level benefits. Recently KDIGO and Centers for Medicare & Medicaid Services endorsed strategies to promote more personalized care, such as using patient life goals to inform decisions about modality selection and dialysis prescriptions.[29,106,107]

Practical Considerations

Clinicians can help preserve residual kidney function (defined as >1-2 cups urine per day)[108] by avoiding nephrotoxic agents such as nonsteroidal anti-inflammatory drugs and intravenous iodinated contrast media (unless it is diagnostically essential). Dialysis does not reduce contrast-induced kidney injury.[108] Reduced dosing of medications, such as gabapentin, antimicrobials (eg, quinolones, cephalosporins, sulfamethoxazole, and trimethoprim), benzodiazepines, muscle relaxers (eg, baclofen), and diabetes medications (eg, insulin, sulfonylureas), is important to decrease medication-related harm among patients receiving dialysis. Although opiates are not recommended routinely, time-limited opiate therapy for severe pain may be appropriate. Hydromorphone and fentanyl (at the lowest effective doses) are preferred over morphine and codeine in patients with dialysis-dependent kidney failure because of adverse effects associated with the accumulation of morphine and codeine active metabolites.

Clinicians can also support patients with dialysis-dependent kidney failure by providing dietary and vaccination recommendations.

Dietary salt restriction of less than 2.3 g per day and fluid restrictions of 1 to 1.5 L per day are recommended for most patients receiving dialysis,[109] but the thresholds should be individualized based on degree of residual kidney function and interdialytic weight gains. Dietary potassium restriction, generally less than 3 g per day, is recommended for patients receiving hemodialysis when predialysis serum potassium levels are greater than 6 mEq/L.[109] Patients receiving peritoneal dialysis usually do not require dietary potassium restriction and many require potassium supplementation (often initiated when serum potassium <3.5 mEq/L) due to poor nutritional intake and dialysis and urinary potassium losses.[109] The recommended daily protein intake for individuals receiving dialysis is 1.0 to 1.2 g/kg/d (Table 3).[109] In addition to routine vaccinations recommended for the general population, patients undergoing dialysis should receive hepatitis B virus, pneumococcal, and COVID-19 vaccines, and those aged 60 years and older should receive the respiratory syncytial virus vaccine.[110] In the US, hepatitis B, influenza, and pneumococcal vaccines are administered routinely at outpatient dialysis clinics.

Limitations

This review has limitations. First, it is not a systematic review and the quality of evidence was not formally assessed. Second, articles may have been missed. Third, this review focused on dialysis-dependent chronic kidney failure and does not apply to dialysis-dependent acute kidney injury. Fourth, this review does not cover all aspects of dialysis-dependent chronic kidney failure.

Conclusions

In 2021, more than 540 000 patients in the US received maintenance hemodialysis or peritoneal dialysis for treatment of chronic kidney failure. Five-year survival after initiation of maintenance dialysis is approximately 40%, and the mortality rate is similar with hemodialysis and peritoneal dialysis use. Decisions about dialysis initiation timing and modality are influenced by patient symptoms, eGFR, laboratory trajectories, and dialysis cost and availability and should involve a shared decision-making process.

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