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Review

CHRONIC KIDNEY DISEASE - PERIDIALYSIS PERIOD: PREDIALYSIS, DIALYSIS PREPARATION, AND INITIAL DIALYSIS PRESCRIPTION

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Summary

Two periods adjacent to starting dialysis are called "chronic kidney disease - peridialysis." The predialysis period is of varying duration, while the dialysis period lasts up to 3 months after the first dialysis session. During the peridialysis period of chronic kidney disease, complications, mortality, and treatment costs increase significantly. The rate of glomerular filtration rapidly decreases, which requires intensive treatment. Management of the peridialysis period is a challenging clinical problem. This review aims to acquaint all working with patients with chronic kidney disease with the novelties published in the medical literature in recent years about the principle of work in patients with glomerular filtration below 15 ml/min per 1.73 m².

Keywords: chronic kidney disease, chronic kidney disease - peridialysis period, anemia, end-stage kidney disease, replacement treatment

Introduction

Nearly 850 million people have chronic kidney disease (CKD), and it is the sixth leading cause of death [1]. There are 700,000 CKD patients in Bulgaria. Of these, 13.90% have advanced kidney disease. According to data from the National Statistical Institute (NSI) and the National Center for Public Health and Analyses of the Ministry of Health for 2018, 1.4% of mortality in the country is from urogenital diseases, and in 2019, this percentage increased by 1.7% [1]. The increase in CKD is also attributable to the increasing frequency of risk factors in the population. CKD increases the risk of cardiovascular and cerebrovascular diseases and mortality risk [2]. Many patients progress to end-stage renal disease (ESKD), necessitating renal replacement therapy or transplantation. Furthermore, CKD affects multiple systems and organs, leading to complications, e.g., hypertension, mineral and bone disorders, anemia, and water-electrolyte and acid-base balance disorders [3, 4], all requiring significant medical resources. CKD is an important public

health problem. Over the past 30 years, many clinical practice guidelines for CKD have been developed. There are currently few publications on managing patients in predialysis and initial dialysis treatment. Improving the treatment of patients in the peridialysis period is vital to improve the survival and quality of life of these patients. In 2015, the Peridialysis Project: The Influence of Predialysis Factors on the Initial Course of Dialysis (Predialysis), sponsored by Herlev Hospital, was launched – 1 400 patients from 15 hospitals in Northern Europe and the Baltics are being followed up to 2020. In 2022, guidelines for conducting CKD-peridialysis were published for the first time in China.

Definition of CKD-peridialysis

CKD-peridialysis was defined as when the patient's estimated glomerular filtration rate (eGFR) fell below 15 ml/min per 1.73 m² to 3 months after starting dialysis. Therefore, it includes two stages: predialysis and initial dialysis. The total duration of the two stages can be different - 1 to 2 years, the more extended period being the predialysis phase in CKD G5 [5]. Most patients with end-stage renal disease/ ESKD/ are elderly due to the increasing age of the general and dialysis population [3, 6-8]. In the past, the leading etiological causes of end-stage renal failure were glomerulonephritis, hypertensive kidney damage, polycystic kidney disease, diabetic nephropathy, etc. More recently, the proportion of ESKD patients with diabetic nephropathy has increased with age and dietary changes in the population [5]. The share of patients with scheduled dialysis remains low [6-12]. Worldwide, in different years, renal replacement therapy (RRT) is started urgently in about 50-80% of cases. In St. Anna University Hospital's dialysis department, patients who had begun emergency hemodialysis treatment without being monitored before were followed for 12 years (2009-2020). The highest number was observed in 2014 – 53.62% of all dialysis patients, and the lowest – in 2018 - 25.4% [12]. Due to the listed features in peridialysis patients, improving the individual treatment approach is necessary.

Control of CKD peridialysis.

Predialysis is a transition for patients to ESKD. Most patients have a range of symptoms, syndromes, and complications associated with CKD. At this stage, the overall assessment of the disease, regular monitoring, and timely treatment are of particular importance. In addition, patients should be educated about the disease, compliance with a hygienic dietary regime, types of RRT, and preventing deterioration of kidney function. GFR was estimated using the CKD-EPI-2021 formula based on serum creatinine. The degree of eGFR decline directly determines the risk of rapid progression to ESKD. An annual decline in eGFR levels by ≥5 ml/min per 1.73 m² or macroalbuminuria (urinary albumin to creatinine ratio >300 mg/g) indicates rapid progression of CKD [13, 14]. A recent study showed considerable individual variation between eGFR slopes (ml/min per 1.73 m²/year) [15]. It is recommended that all predialysis patients with CKD stage G5 be evaluated every two months to detect those patients who progress more rapidly than those who move more slowly or do not progress [13, 14].

Management of blood pressure (BP)

Measuring BP is critical. Office BP, home BP, and ambulatory BP are used. BP was measured according to the recommended procedures for preparing and correcting the BP measurement technique. The correct measurements to diagnose and treat elevated BP are taken and accurately documented. BP readings must be accurate to be accurately averaged. Indications are provided to patients [16-19]. It is crucial to appreciate the so-called "nightfall". BP measurements should not be taken on a limb with an arteriovenous fistula (AVF) or arteriovenous graft (AVG)[16]. PB should be measured at each visit. The daily average should also be calculated from 2 home BP recordings [5].

Management of volume loading

Management of volume loading and assessment of cardiac function – BP, presence of pulmonary/ congestive/wet rales or venous filling of jugular veins, degree of edema, and weight change should be assessed [20, 21]. Troponin and, if possible, N-terminal pro-B-type natriuretic peptide (NT-proBNP) are monitored [20-22]. Imaging diagnostics are performed - chest x-ray, echocardiography, and, if possible, bioelectrical impedance analysis [20, 22]. Volumes should be assessed at initial diagnosis and every month in

patients without volume overload. Total body water and extracellular volume can be measured by bioimpedance [5]. Measurement of troponin is recommended in patients with heart failure (HF), as well as in the suspected diagnosis of acute myocardial infarction, as well as to assess the prognosis in patients with acute HF [20-22]. The diagnostic thresholds of BNP and NT-proBNP should be increased depending on the stage of CKD [23]. NT-proBNP has better diagnostic sensitivity and specificity than BNP in patients with CKD [24]. In patients with an unstable disease or heart failure and those requiring drug dose adjustment, NT-proBNP should be measured every two weeks. In stable patients, NT-proBNP should be measured monthly or every two months[20-22].

Management of Electrolyte and Acid-Base Balance Disturbances

Serum potassium, sodium, chloride, and HCO3 are examined to determine hyperkalemia (plasma potassium level>5.0 mmol/L) [25]. In CKD patients on peridialysis, hyperkalemia is the most common electrolyte disturbance. A recent meta-analysis with individual human data found an unfavorable prognosis even when baseline potassium was in the upper reference limit. Hyperkalemia at extreme potassium levels of 6.5 mmol/l is a clinical emergency that can be life-threatening [26]. Milder hyperkalemia (5.5 mmol/l) warrants a review of contributing factors [27]. Medications that lead to hyperkalemia are potassium-sparing diuretics, renin-angiotensin-aldosterone system (RAASI) inhibitors, aldosterone antagonists, trimethoprim-containing medications, and nonsteroidal anti-inflammatory drugs. A patient's age is a risk factor for hyperkalemia, with the incidence of hyperkalemia doubling every decade over 40 years of age. In patients with eGFR<30 ml/min per 1.73 m², hyperkalemia is detected 20 times more often and increases 4-5 times in patients with diabetes, HF, and peripheral arterial disease [28]. As GFR progressively decreases, the prevalence and severity of metabolic acidosis increase. It is necessary to measure HCO_3^- every 2-3 months [27]. Regardless of whether the patient uses RAASI, a patient's serum electrolytes should always be measured at the first visit and each subsequent visit. When starting dialysis, electrolytes are measured monthly. If RAASI is started, serum potassium is rechecked after 1-2 weeks. In the presence of hyperkalemia, all factors that may cause it should be reviewed, including errors in diet or medication intake. After pseudohyperkalemia is ruled out, hyperkalemia is treated immediately, serum potassium is checked every 24-48 hours, and treatment is adjusted accordingly for potassium. In patients with diabetic kidney disease (DKD), serum potassium should be measured monthly. Patients treated with RAASI may require more frequent testing [5]. If hyperkalemia is suspected, an electrocardiogram is necessary. With characteristic changes in the electrocardiogram, treatment can be started even before the result of the serum potassium level is obtained [27].

Management of Mineral and Bone Disorders

Serum calcium – total and ionized, phosphorus, intact parathyroid hormone (iPTH), alkaline phosphatase (ALP), and serum 25 (OH) D levels are investigated [29]. High ALP levels are strongly associated with early death in dialysis patients [30]. ALP results can help monitor non-dialysis and dialysis patients [31]. Dynamic bone disease is not always associated with negative results from antiresorptive medications. There is no evidence of benefit, and there is no "damage" data. However, this does not mean that there is no harm [32]. Bone mineral density and markers of bone metabolic exchange are investigated. If necessary, a bone biopsy is ordered[29]. Indicators of vascular calcification include coronary artery calcification, heart valves, abdominal aorta, etc. [29]. The following are periodically tested: Calcium and Phosphorus every 1-3 months; iPTH at 3-6 months, ALP at 12 months/in the case of elevated iPTH levels, testing is recommended every six months; 25 (OH) D – by baseline and intervention decision making; vascular calcification – at 1 to 3 months. There is a specific difference in mineral and bone disorders in CKD patients with end-stage renal disease on dialysis (ESRD-5D) for different age groups. Such a difference was found in follow-up patients in Hungary and Pleven-Bulgaria [33].

Energy intake management and anthropometric measurements included calculating body mass index, skinfold thickness measurement, upper arm circumference, and

dietary intake. Biochemical studies include serum albumin, transferrin, albumin, and serum cholesterol. Patients can be grouped into three groups: A (well-nourished), B (slightly to moderately malnourished), and C (severely malnourished). Subjective comprehensive nutritional assessment should be assessed every two months [34, 35](Table 1).

Management of anemia

Hemoglobin (Hb), reticulocyte count, iron metabolic status/serum ferritin (SF), serum iron, total iron-binding capacity, and transferrin saturation were measured periodically [36, 37]. In cases where patients take ESA, a functional deficit may be missed if only transferrin and ferritin saturation are examined. Therefore, the content of Hb in reticulocytes should be determined. Changes in the percentage of hypochromic erythrocytes are superior to other iron test parameters in detecting functional iron deficiency [38]. To identify the causes of anemia, it is also necessary to measure the serum level of folic acid and vitamin B_{12}, perform a fecal test for occult bleeding, and, if necessary, a bone marrow examination to rule out anaemia due to hematological disease. Hemoglobin tests should be performed monthly, and iron metabolism should be monitored every two months in patients with CKD G5. According to the patient's clinical condition, the frequency of examinations and examinations can be adjusted [36, 37].

Management of patients with diabetes.

Glucose levels (fasting and 2-hour plasma glucose) and glycated hemoglobin are tested [5]. Continuous glucose monitoring can be used when possible [39, 40]. In patients with unstable blood sugar, a 7-point profile is examined - before three meals, two hours after three meals, and in the evening before going to bed. In patients with stable blood sugar, fasting blood sugar should be monitored once or twice weekly, and a 7-point profile blood glucose measurement should be performed once a month. In patients with Diabetic Kidney Disease/DKD/ glycated hemoglobin is examined every month, and in patients without DKD – every three months.

Patient Education

Patients with CKD are at an increased risk of cardiovascular disease and mortality than patients without CKD. Individual risks vary across age and ethnic groups [2]. Patient education is widely recognized as an essential component of CKD care. There are severe deficits in patient awareness of CKD, including those at the highest risk of progression to ESCD [41, 42]. Approximately half of the National Health and Nutrition Examination Survey (NHANES) participants at moderate or high risk were unaware of their kidney disease and the extent of the disease. The reasons for this are limited educational incentives and fear of inciting stress for the patient. Multidisciplinary group approaches, including family and media

Table 1. Subjective comprehensive nutritional assessment scale [5]

Item	Grade A (well nourished)	Grade B (mild-to-moderate malnutrition)	Grade C (severe malnutrition)
Recent weight change	None/Increased	Less than 5% reduction	More than a 5% reduction
Diet change	None	Decrease	No food/low-energy liquid die
Gastrointestinal symptoms	None/decreased appetite	Mild nausea, vomiting	Mild nausea, vomiting
Change in mobility	None/decreased	Ambulatory	Bedridden
Stress response	None/low	Moderate	Heigh
Muscle wasting	None	Mild	Severe
Triceps skinfold thickness (mm)	Normal (> -8)	Mild decrease (6.5–8)	Severe decrease (<6.5)
Ankle edema	None	Mild	Severe

education and awareness of CKD, should be most effectively focused on patients with eGFR <30ml/min per 1.73 m². Training should start from CKD G4. Patients should know kidney structure and function, the main clinical manifestations of CKD, its prevention and treatment, and indicators of kidney function. Patients should be informed about the types of renal replacement therapy, indications and contraindications for the type of therapy, vascular access, operative methods, and precautions for kidney transplantation, peritoneal dialysis (PD), and hemodialysis at home or in a center. The patient's family and medical staff should also be educated [43, 44] on diet, lifestyle, and vascular protection of the upper extremities in patients with CKD [45] and avoiding catheters at the start of dialysis [46]. Participation of caregivers is also essential in vascular access planning [47]. Patients should be followed up every 1-2 months [5].

Preparation for dialysis

For patients who have chosen dialysis treatment, the initiation of dialysis is determined by uremic signs and symptoms, alkaline-metabolic balance and volume control disorders, the presence of metabolic encephalopathy, or protein energy loss from HF, etc. A decision made in this way is better than one based on serum creatinine or eGFR levels alone [43, 44]. Early dialysis does not reduce treatment costs and mortality [48]. The most common symptoms of advanced kidney failure are fatigue, pain, nausea and vomiting, itching, anxiety, depression, and cognitive impairment. Patients classify symptoms as impairing their quality of life [49]. The main goal of renal replacement treatment is to reduce mortality. Considering life quality should be noticed. The presence of one or more of the following uremic clinical signs is an indication for initiation of urgent dialysis treatment: signs and symptoms, including neurological signs and symptoms caused by uremia, pericarditis, anorexia, severe acid-base imbalance or electrolyte imbalance, unexplained weight loss, persistent and prolonged itching, and bleeding; volume overload or hypertension that cannot be controlled by medication [43, 44]. The achievement of euvolemia is a big challenge in treating patients with CKD and ESKD. Progressive malnutrition is untreatable. Other causes of anorexia, nausea/vomiting, pruritus, drowsiness, difficulty concentrating, fatigue, low energy, and pain not associated with uremia should be corrected before deciding to start dialysis. Other reasons that may exhibit such clinical findings must be adjusted before starting dialysis. Not only eGFR is a determining factor for the time of initiation of dialysis treatment. Careful clinic and paraclinical follow-up are required when eGFR is <15 ml/min per 1.73 m². At eGFR levels of 10-24 ml/min per 1.73 m², the likelihood of starting dialysis increases over time. Patients with CKD were followed in a US health system in Northern California. Among those with an eGFR of 10 to 13 ml/min per 1.73 m², the 1-year odds of starting dialysis increased by 5.3% compared to patients with higher eGFR values [50]. In the last 20 years, internationally, the eGFR level of patients initiating intermittent dialysis has been influenced by various factors: system level, physician level, and patient level [51]. The Initiating Dialysis Early and Late (IDEAL) study [52] found no systematic clinical benefit of starting dialysis earlier versus later. Dialysis treatment is appropriate when eGFR decreases <10 ml/min per 1.73 m². In countries such as Canada, initiation of dialysis treatment occurs when eGFR falls below 5 ml/min per 1.73 m² [52, 53]. According to current standards of care, when eGFR is between 5 and 10 ml/min per 1.73 m², patients can start dialysis treatment, and when eGFR falls below 5 ml/min per 1.73 m², dialysis must start treatment [54].

Dialysis Mode

When choosing a dialysis regimen, a patient-oriented approach should be adopted. The attending physician should fully assess the patient's disease state and consider their wishes. Dialysis regimens should be selected with local medical resources and affordability, reimbursement policy for health insurance, and available facilities [43, 44]. Most commonly, patients report improved quality of life. In a survey of 180 US patients with advanced CKD making modality choices, nearly half of dialysis patients stated that the decision to undergo hemodialysis was essentially not their choice. Lack of choice was reported by only 3% of PD patients [54]. Contraindications for PD are occlusion of the peritoneal cavity and loss of peritoneal function. Anuria is not a

contraindication to PD. In patients who have chosen hemodialysis, it is necessary to establish vascular access and vascular protection of the upper extremities. Patients should be instructed on how to preserve the vessels of the selected arm for arteriovenous fistula (AVF). Unnecessary venipuncture and blood tests should be avoided. The dorsal veins of the arm should be punctured when collecting blood for investigations. Before and after AVF creation, patients should do arm exercises. Treatment for upper extremity skin lesions is required [45, 55, 56].

Vascular access time: If the patient chooses hemodialysis as a renal replacement therapy, it takes up to 6 months. The first choice for vascular access is the AVF with preoperative ultrasound mapping of the vessels, which provides a morphological and functional assessment of the peripheral arteries and veins [57]. If it is necessary to put AVG as vascular access to HD, this should be done 3-6 weeks before the start of HD. Patients with significant uremic symptoms and very difficult to control with conservative treatment should be made as early as possible vascular access for HD-AVF or arteriovenous graft (AVG) [45]. AVF and AVG require maturation and interventions in some patients [58]. After successfully ripening, AVF has fewer interventions [59]. Initial catheter dependence in the US [60] and Europe is uncommon, particularly in older adults. Due to late targeting and urgency for dialysis in many Western countries, over 60% start HD with a catheter. In the United States, the creation of AVF against AVG is associated with a more considerable dependence on the catheter at three months (82.8% vs. 41.2%) and lower dependence at 12 months (14.2% vs. 15.8%) and at 36 months (8.2% vs. 15.0%) [61, 62]. In patients who chose PD, planned implantation of an abdominal catheter was performed two weeks before starting PD. If urgent PD is to be activated, the peritoneal catheter can be implanted 24-48 hours before starting PD. Shifting should be reduced to prevent tunnel leakage and/or compaction. There are three methods of placing an abdominal peritoneal catheter: direct visual surgical incision, laparoscopic, and percutaneous "blind" catheterization. Laparoscopic catheterization is performed in patients with a history of abdominal surgery or a floating previous catheter[62].

Initial management of dialysis

Screening for predialysis infections and bleeding and coagulation testing should be performed. Serological tests for hepatitis B and C, HIV, and syphilis are performed before initial dialysis or upon referral to another dialysis facility to determine the dialysis treatment area and hemodialysis machine [63]. Bleeding and coagulation parameters include platelets, count, measurement of prothrombin time, partial thromboplastin time, and antithrombin activity. Anticoagulants for dialysis should be selected based on the results of the parameters listed above [63]. Before the patient begins dialysis, a dialysis regimen must be selected and vascular access established, i.e., planned initiation of hemodialysis. The aim is to reduce catheter use at the start of HD and prevent related complications. Unplanned initiation is called the initiation of dialysis when there is still no vascular access, and the patient needs to be hospitalized, or if the selected dialysis regimen cannot be implemented. In clinical practice, it is accepted that more than 70% of patients should start dialysis by planning, and currently, about 50% to 80% of patients worldwide start with a catheter because planning does not begin early enough. The European renal best practice guidelines indicate that the risk of renal failure and mortality in renal disease can guide early decision-making and allow more timely preparation for renal replacement therapy [64]. Emergency initiation of hemodialysis is started immediately on vital indications in patients with life-threatening conditions and is activated in patients with uremia, severe hyperkalemia, hypertension, or HF (due to volume overload), in which control with medication alone is impossible.

Among hemodialysis patients with significant residual renal function /RKF/, intermittent hemodialysis is a safe treatment regimen that preserves RKF to a greater extent. Patients with the lowest RKF should start the complete regimen, as they have a higher mortality risk in the first year of dialysis [65, 66]. Patients with RKF of eGFR ≥5 ml/min per 1.73 m², daily urine volume ≥600 ml, and good clinical condition can undergo dialysis for 4 hours 2-3 times/week. Nevertheless, RKF should be monitored monthly, and if renal function declines progressively, the frequency and duration of dialysis should

be gradually increased. Patients with eGFR < 5%) who have difficulty maintaining dry weight, have poor BP control or frequent intradialytic hypotension, have severe refractory hyperphosphatemia, or have severe metabolic acidosis and/or hyperkalemia should undergo mandatory HD 3 times per week for 4 hours, and if necessary - more hours and/or frequency per week. It is recommended initially to carry out short-term „daily" hemodialysis 3-6 times a week with a duration of 2.0 - 2.5 hours. Dialysis frequency or duration should be increased in patients who gain weight (body weight > 5%), have difficulty maintaining dry weight, have poor BP control or frequent IDH, and have severe hyperphosphatemia or severe metabolic acidosis and/ or hyperkalemia. Additional indications for intensification of dialysis include preserving opportunities for work or education.

Dialysis membranes with good biocompatibility should be used for high-flux hemodialysis and low-flux treatment. High-flux dialysis increases toxin removal but does not improve survival in intermittent hemodialysis patients compared with low-flux hemodialysis. It is currently unclear whether hemodiafiltration improves outcomes [66]. A randomized clinical trial (RCT) showed a clear survival benefit of hemodiafiltration, but the study groups were not well balanced because hemodiafiltration patients were younger with a lower comorbid Charlson index and less frequent central venous catheters [67]. Two large RCTs comparing high-flux hemodialysis and high-volume hemodiafiltration are now underway. They need to clarify whether hemodiafiltration is associated with lower mortality and better affects the quality of life [67, 68]. Each dialysis facility can choose low- or high-flow dialysis by reassessing the benefit of reducing cardiovascular death against treatment costs and affordability. During the first 3-5 hemodialysis sessions, patients are prone to dialysis disequilibrium syndrome /DDS/. Measures to prevent its development are crucial. A slow lowering of the urea concentration in the blood is recommended, which requires a gradual increase in the dialysis dose - this is the so-called induced dialysis [43, 44]. The duration of the initial dialysis session should be up to 2.5 hours. The duration of the dialysis sessions is gradually increased until the conventional duration is reached. The blood flow rate during the first hemodialysis should be 150-200 ml/min. During subsequent sessions, the blood flow rate gradually increases to 4 times the patient's body weight. A higher blood flow (about 400 ml/min) is used in the United States. This achievement of a higher dialysis dose (urea clearance index [Kt/V] of about 1.31-1.72, as in the hemodialysis study) did not improve outcomes [68]. Extending the time to 7 hours 3 times per week with lower dialysate blood flow improved survival among European HD patients [69, 70]. To reduce the risk of DDS, a small dialyzer surface area (1.3-1.5 m^2) is used for initial dialysis, and a larger area for dialysis maintenance to ensure adequate dialysis. The flow rate should be reduced if DDS occurs during the first dialysis sessions. Dialysate Na, K, and calcium concentrations are individualized according to patient volume, BP control, and the patient's serum sodium, potassium, and calcium. Dialysis potassium concentrations below 2 mmol/l are not recommended. A dialysis temperature of 36.5 C is suitable but can be individualized according to the patient's needs. At a lower dialysis temperature, intradialytic hypotension decreases. Ultrafiltration (UF) - volume and rate are determined according to the patient's condition, cardiopulmonary function, diuresis, and BP. Dry weight should be achieved gradually over 1-3 months. Currently, the recommendation in US patients is not to exceed a UF rate of <13 ml/kg/h [71]. Higher UF during hemodialysis was associated with more frequent intradialysis hypotension, sudden cardiac arrest, and mortality. Their frequency is increased to avoid DDS during the initial dialysis sessions. The main anticoagulants during hemodialysis are unfractionated heparin (UF heparin) and low molecular weight heparin (LMW heparin). Heparin-induced thrombocytopenia type II occurs less frequently with low molecular weight heparin than with UF heparin. LMW heparin has several advantages besides cost. New anticoagulants have emerged in recent years, each with unique advantages and disadvantages. In maintenance hemodialysis patients with an increased risk of bleeding, dialysis without heparin or regional anticoagulation can be undertaken [72]. UF heparin should be used in patients who are at risk of coagulation disorders, do not have significant disorders of lipid metabolism or impaired bone metabolism, and have a plasma antithrombin activity III above

50%, and a normal or slightly increased platelet count, prothrombin time, and thromboplastin time values. LMW heparin is recommended in patients with antithrombin activity greater than 50%, near-normal platelet count, severe abnormal fat and bone metabolism, prolonged partial thromboplastin time and prothrombin time, and potential risk of bleeding. Dialysis without anticoagulant is recommended in patients with clinically significant coagulation disorders, significant bleeding tendency, or significantly prolonged plasma partial thromboplastin and prothrombin times. Daily administration of antiplatelet agents is used in patients at higher risk of cardiovascular disease due to other primary diseases, such as diabetic nephropathy and hypertensive renal injury, but with normal or elevated platelet counts and normal or hyperactive platelet function [63]. Dial dialysis is considered adequate if the patient achieves and maintains a good clinical condition during dialysis treatment. Dialysis adequacy was measured using Kt/V and urea reduction URR [43, 44, 63]. It is necessary to achieve a volumetric balance. Acid-base, electrolyte and calcium-phosphorus metabolism, nutritional and anthropometric measurements should be within acceptable limits. Dialysis is considered insufficient in the presence of nausea, vomiting, insomnia, and restless legs syndrome. Clinical manifestations of water and sodium retention are hypertension, weight change, edema, and HF. In these cases, bioelectrical impedance is measured if possible, but this methodology has limited efficacy in improving clinical outcomes [73, 74]. Although effective clearance of uremic toxins helps improve a patient's quality of life and better prognosis, the Kt/V value does not predict the survival rate at a value of 1.2. Achieving Kt/V ≥1.2 and a urea reduction factor ≥65% is recommended. Ideally, single pool Kt/V values ≥1.4 and urea reduction factor ≥70% will be achieved. Can include β2-microglobulin in the quality control of hemodialysis treatment - a reduction of at least ≥30% and ideally ≥50%. During initial dialysis, individualized goals for the above parameters should be determined according to the patient's condition [2, 43, 63]. It must be recognized that the urea clearance provided by current dialysis methods approaches the theoretical limits with available blood flows and membrane areas. Many modern researchers are studying other solutes that are less efficiently cleared than urea by dialysis but probably contribute more to the complaints of hemodialysis patients. Various methods are currently being developed to increase the clearance of urea-free solutions. Future clinical studies are needed to evaluate the clearance of "medium molecules" or "uraemic toxins". Sequential dialysis is recommended in patients who fail to control sodium levels with a salt-free diet, have a higher serum sodium concentration before dialysis, or are thirsty after dialysis [63]. One observation reported that the routine use of sodium profiling to prevent intradialytic hypotension (IDH) has higher total and cardiovascular mortality [75] and should be used cautiously. It is necessary to individualize the concentration of sodium in the dialysate. If necessary, slow, continuous UF can remove excess sodium and water from the patient to achieve an acceptable patient weight. These options are also suitable for patients who have HF or insufficient RAAS/sympathetic reactivity, who cannot control their dry weight, and for intradialysis hypotension [63].

According to recent data, PD is used in about 11% of people with kidney failure. Data published in the second Global Kidney Health Atlas commissioned by the International Society of Nephrology (ISN) reveals the disparity in providing renal replacement therapy (via different modalities). A study of PA in 160 countries shows that 30 countries do not provide PA, especially in Africa and low-income countries. Average exchange volumes are insufficient in 28% of countries. Most countries do not measure patient-reported PD outcomes[76]. In PD patients, the condition of the peritoneum should be evaluated as a result of previous abdominal operations, hernias, or digestive system diseases [77]. Good nutrition that maintains serum albumin is important [78]. The risk factor for mortality increases with progressively lower serum albumin. In patients followed for six months, those who increased their serum albumin by 0.3 g/dL were at a lower risk of all-cause mortality and cardiovascular and infectious-cause death. There was a higher mortality in cases of reduction of serum albumin by >0.2 g/dl, confirmed over five years [79]. Depending on the characteristics of the patient's peritoneal

transport, urea Kt/V and creatinine clearance, nutritional status, CKF, and RKF, the different dialysis regimens for prolonged ambulatory PD (CAPD) are selected. CAPD is currently used in most PD patients. Automated PD (APD) has some advantages: reduced risk of complications related to increased intra-abdominal pressure, lower incidence of peritonitis, and better quality of life. APD is divided into four modes: intermittent PD, continuous cyclic PD, nocturnal intermittent PD, and (iv) tidal PD. The appropriate regimen is selected individually for each patient. A neutral pH should be used for the peritoneal dialysate. Low-glucose solutions can be used to protect CKF and peritoneal function. In PD patients with insufficient peritoneal UF and problems with normal volume maintenance, once-daily icodextrin peritoneal dialysate can be used with a prolonged stay. The dialysis regimen (CAPD or APD) is determined after a comprehensive assessment of the patient and the patient's wishes and lifestyle. The glucose concentration in the dialysate is determined depending on the patient's condition. The initial dialysis dose is determined according to the patient's RKF. Dialysis should be started with peritoneal dialysate containing 1.5% glucose and then gradually increased depending on CKD. Nevertheless, once the initial decision to prescribe dialysis is made, patients should be monitored closely for changes in PD volume, UF, and volume status. If other methods cannot correct volume overload, the glucose concentration in the peritoneal dialysate should be increased. In recent years, dialysis doses in CAPD have been 6-10 liters per day [77]. Large dialysis doses are recommended for patients with a large body surface [5]. RKF should be determined for all PD patients. PD should achieve and maintain clinical euvolemia, taking into account CKF as well as its preservation. Patients with good RKF can start dialysis with a lower dialysis dose or a shorter dialysis stay. It is necessary to improve CKF monitoring and, if necessary, adjust the dialysis prescription. Treatment goals should be encouraged by modifying the individually prescribed dialysis dose in response to the patient's clinical symptoms, RKF, laboratory parameters, solute clearance, volume, and nutritional status. Kt/V and creatinine clearance rate should be assessed when the patient is clinically stable. The first assessment is performed one month after starting dialysis and then every three months. Patients with peritonitis should be evaluated four weeks after resolution of the condition. Fluid balance is essential to improve patient outcomes. Volume loading, uremic symptoms, and malnutrition may be observed, and if goals are not met, the PD regimen and dose of PD should be adjusted [53]. Peritoneal transport characteristics should be assessed periodically. Peritoneal equilibration tests (PET) are used to assess peritoneal transport characteristics. There are two methods of conducting PET: the standard and the modified method. The latter used 4.25% (instead of 2.5%) glucose peritoneal dialysate to assess peritoneal UF function. PETs should be performed 2-4 weeks after PD implantation to measure the patient's baseline. PET should then be repeated every six months. If changes in peritoneal function are suspected, PET is performed as soon as possible. Patients with peritonitis should have PETs 1 month after control of inflammation [5]. Dialysis dwell time can be shortened in patients with high transport capacity, or APD can be adopted. CAPD or APD is an appropriate treatment method for patients with average transport capacity. In patients with low transport capacity, the dialysis dose should be increased; correspondingly, a larger dose of ADP should be administered. In patients with low transport capacity, the dialysis dose should be increased, or a higher dose of ADP therapy should be administered. Dynamic observations of PETs help to make timely corrections and achieve dialysis adequacy [5]. The PD dose should be increased for patients with uremic symptoms even when the minimum target is reached. Anuric patients may not achieve adequately standardized Kt/V with PD. The first choice for this type of patient should be an intermittent 24-hour PD regimen. The goal is for the patient to achieve an optimal dialysis weight without volume-dependent hypertension, HF, pulmonary edema, serous effusion, interstitial retention, or peripheral edema. If this cannot be achieved, the patient undergoes temporary or permanent hemodialysis treatment.

Conclusion

This review is based on current publications and recommendations that indicate the need for research in various aspects of CKD. Given the high frequency and socio-medical importance of CKD, this review represents a modern and professional approach to treating patients with CKD and may help improve the quality of life of CKD patients in the peridialysis period.

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