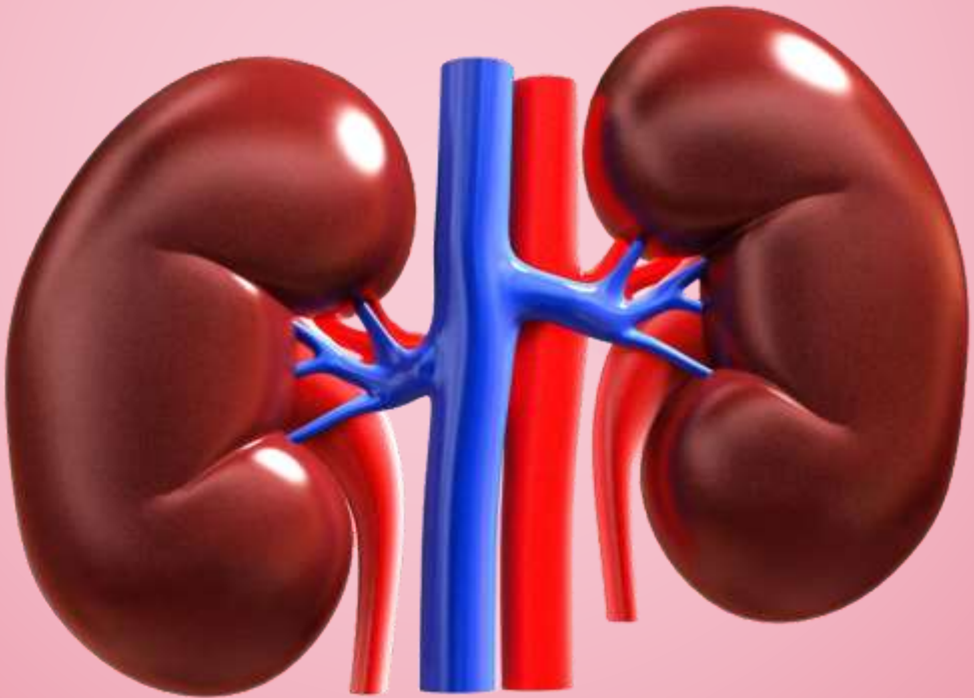
Module on End-Stage Renal Disease (ESRD)

Module II



TREATMENT OPTIONS FOR ESRD (DIALYSIS VS. TRANSPLANTATION)

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I. TREATMENT STRATEGIES FOR ESRD

Management of end-stage renal disease (ESRD) involves a multifaceted approach aimed at addressing both the underlying causes and associated complications. Initiatives to slow disease progression include treating hypertension and proteinuria, with specific blood pressure targets and the use of ACE inhibitors or ARBs for diabetic patients with proteinuria. Additionally, interventions focus on tight glycemic control, cardiovascular risk reduction, and lifestyle modifications such as smoking cessation and dietary restrictions. Addressing chronic metabolic acidosis, dyslipidemia, volume overload, anemia, hyperphosphatemia, and hypocalcemia are essential aspects of ESRD management. Long-term renal replacement therapy (RRT), including hemodialysis, peritoneal dialysis (PD), or kidney transplantation, may be necessary for uremic manifestations.[1]

Furthermore, the management regimen includes interventions such as erythropoiesis-stimulating agents for anemia, phosphate binders and dietary phosphate restriction for hyperphosphatemia, and supplementation with vitamin D analogs for hypocalcemia and hyperparathyroidism. Lifestyle modifications, including adherence to low-salt and renal diets, along with protein restriction, play a crucial role in managing the disease burden and improving outcomes for individuals with ESRD.[1]

1. WHEN SHOULD PATIENT WITH CKD BE REFERRED TO A NEPHROLOGIST?

The National Kidney Foundation Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines recommend referring a patient with chronic kidney disease (CKD) to a nephrologist when their glomerular filtration rate (GFR) drops below 30 mL per minute per 1.73 m^2. A more proactive approach suggests initiating a referral when the GFR falls below 60 mL per minute per 1.73 m^2. Additionally, if a patient experiences a rapidly declining GFR, with or without the presence of hematuria or proteinuria, a consultation is advisable even if the GFR is above 60 mL per minute per 1.73 m^2.[2]

Late referrals to nephrologists are common in the United States and are generally defined as situations where patient management could have been significantly enhanced by earlier involvement of the nephrology team. Typically, late referral is considered when a patient is referred to a nephrologist less than three months before the initiation of dialysis therapy. Early referrals offer numerous benefits, including the opportunity for patients and their families to participate in educational sessions about CKD and receive individualized counseling from a multidisciplinary kidney care team, which may include a nurse practitioner, physician, dietitian, and social worker.[2]

These early interventions are crucial in helping patients and families navigate the complexities of CKD, its complications, and the transition to ESRD. They facilitate informed decisions regarding dialysis modalities, timely placement of dialysis access, and even preemptive kidney transplants. Early referrals also contribute to non-emergent dialysis initiation, lower morbidity, improved rehabilitation outcomes, shorter and less frequent hospital stays, reduced healthcare costs, and better survival rates. With aggressive intervention, many CKD patients can stabilize their condition or even improve their CKD stage.[2]

The National Kidney Foundation classifies CKD into stages 1 through 5, and unfortunately, many patients with ESRD are often threatened with dialysis by primary care providers or family members as a means of encouraging compliance with treatment plans. This well-meaning but counterproductive approach can instill fear of dialysis, leading to patients with stage 5 CKD delaying or outright refusing RRT for extended periods, sometimes over a year.[2]

Ironically, advancements in managing CKD stage 5 comorbidities, such as anemia, hypertension, metabolic acidosis, and secondary hyperparathyroidism with hyperphosphatemia, have improved patients' quality of life so significantly that they may question the necessity of dialysis. With diligent management, patients can avoid symptoms like fatigue, weakness, cognitive impairment, severe itching, chronic heart failure, shortness of breath, and difficulties with daily activities. Many can continue to lead active lives, engaging in physical activities and daily tasks without significant limitations, even with a GFR below 15 mL per minute.[2]

2. INDICATIONS FOR RRT

ESRD is diagnosed only after a thorough investigation that rules out all reversible causes of renal failure. A comprehensive work-up involves a detailed medical history, physical examination, and various laboratory tests, including renal ultrasound, chest X-ray, and advanced imaging studies like CT scans or MRIs when necessary. Reviewing previous medical records is essential to ensure a complete understanding of the patient's condition.[2]

According to the National Kidney Foundation's KDOQI guidelines, CKD is defined by kidney damage lasting for three months or more, characterized by structural or functional abnormalities, with or without a decreased GFR. Indications for RRT, such as hemodialysis, are considered when the GFR falls below 15 mL per minute per 1.73 m^2, or when specific complications arise, including:[2]

- Intractable extracellular fluid volume overload
- Hyperkalemia
- Hyperphosphatemia
- Hypercalcemia or hypocalcemia
- Metabolic acidosis
- Anemia
- Neurological dysfunction (e.g., neuropathy, encephalopathy)
- Pleuritis or pericarditis
- Unexplained decline in functioning or well-being
- Gastrointestinal dysfunction (e.g., nausea, vomiting, diarrhea, gastroduodenitis)
- Weight loss or evidence of malnutrition
- Hypertension

Once the diagnosis of ESRD is confirmed, the selection of the most suitable mode of RRT becomes crucial. Patients and their families must be thoroughly informed about the various options available, as RRT is a life-saving treatment for individuals with ESRD who would otherwise succumb to uremic complications. Due to the complexity and emotional impact of these discussions, they are best conducted by the nephrology team, who can dedicate the necessary time and expertise to ensure patients and families fully understand their options and make informed decisions.[2]

3. OPTIONS FOR RRT FOR ESRD

Patients with ESRD have several treatment options available to them, each with its own benefits and considerations:[2]

3.1 Kidney Transplantation

- Deceased donor
- Living donor

3.2 Peritoneal Dialysis (PD)

- Continuous ambulatory PD (CAPD)
- Continuous cycler PD (CCPD)
- Nocturnal intermittent PD (NIPD)
- NIPD-wet day
- Tidal PD

3.3 Hemodialysis

- Conventional: Typically conducted in a dialysis center for 3 to 5 hours, 3 times per week.
    - In-center hemodialysis
    - Home hemodialysis
    - Nocturnal home hemodialysis
    - Nocturnal in-center hemodialysis
- Daily home hemodialysis (Day or Nocturnal)
- Day or nocturnal 8–10-hour hemodialysis

Ongoing demonstration projects are exploring variations of these renal replacement therapies to improve outcomes, aiming to reduce morbidity, mortality, and hospitalization days associated with ESRD.[2]

The goals of RRT include prolonging life, alleviating symptoms of uremia, restoring the patient to their previous lifestyle and activities of daily living, maintaining a positive nitrogen balance and adequate energy intake, minimizing patient inconvenience, and maximizing quality of life. Each treatment modality is tailored to meet these objectives while considering the individual patient's needs and preferences.[2]

II. RENAL TRANSPLANTATION (RT)

RT stands as the optimal treatment for select patients grappling with ESRD, offering a substantial enhancement in quality of life and a reduction in long-term dialysis-related mortality. However, the effectiveness of transplantation is hampered by the glaring gap between the increasing demand for organs and the inadequate supply. Strategies to expand the organ donor pool have been implemented, including the utilization of living donor kidneys in various transplant schemes, transplantation across HLA and ABO boundaries, and the acceptance of extended criteria allografts. Despite advancements, chronic graft loss after the first year remains a significant challenge, compounded by the surgical complexities of operating on recipients with multiple comorbidities and employing allografts with intricate vascular anatomy.[3]

The history of RT underscores a journey marked by notable milestones and challenges. From the pioneering attempts in the early 20th century, such as Mathieu Jaboulay's pig and goat kidney transplants, to the breakthroughs in the mid-20th century with the introduction of immunosuppressive agents, RT has evolved into a viable treatment option for ESRD. In the United Kingdom, where over 6000 patients await kidney transplants, deceased and live donor operations continue to be vital lifelines for patients on the waiting list. Despite the considerable progress, challenges persist, necessitating ongoing advancements in transplantation techniques and organ procurement strategies.[3]

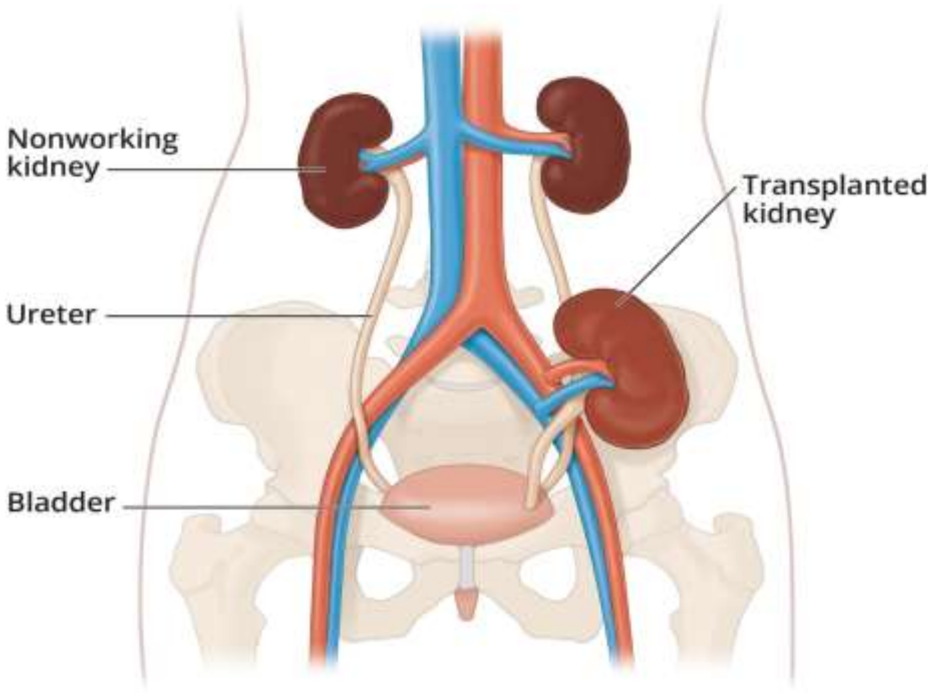

Figure 1. Kidney Transplant[4]

Successful RT hinges not only on surgical expertise but also on meticulous recipient assessment and immunosuppressive management. Recipients undergo thorough evaluations to ascertain transplant feasibility and identify potential complications. Immunological compatibility between donor and recipient, determined by blood group and HLA tissue typing, plays a crucial role in graft outcomes. Living donation, offering superior outcomes and preemptive transplantation opportunities, has emerged as a preferred option, supported by altruistic donation and paired exchange programs to expand the donor pool.[3]

Immunosuppression regimens, tailored to mitigate acute rejection and minimize long-term complications, are central to transplant success. Induction agents administered during anesthesia induction, followed by maintenance therapy comprising calcineurin inhibitors, anti-proliferative agents, and steroids, aim to prevent rejection and preserve graft function. Donor nephrectomy techniques have evolved towards minimally invasive approaches, enhancing donor safety and recovery. Despite these advancements, ongoing research and collaboration are imperative to address the persistent challenges and improve outcomes in RT for patients with ESRD.[3]

III. DIALYSIS

Dialysis is a medical procedure used to remove waste products and excess fluid from the blood when the kidneys are no longer able to perform these functions effectively. This treatment is essential for individuals with ESRD, a severe condition where the kidneys fail to function adequately. There are two main types of dialysis: hemodialysis and PD.[5]

1. HEMODIALYSIS

Hemodialysis works by using a dialyzer, or artificial kidney, to filter waste products and excess fluid from the blood. The process involves the following steps:[5]

- **Blood Flow:** Heparinized blood is pumped from the patient's body through a dialyzer at flow rates of 300 to 500 mL per minute.
- **Dialysate Flow:** A dialysis solution, or dialysate, flows in the opposite direction at rates of 500 to 800 mL per minute to maximize the removal of waste products.
- **Diffusion and Filtration:** The dialyzer facilitates the diffusion of solutes between the blood and dialysate. Waste products like urea are removed from the blood, and essential buffers are replenished. This process achieves a 65 to 70 percent reduction in blood urea nitrogen concentration during a typical three to four-hour session.
- **Fluid Removal:** Adjusting the transmembrane pressure across the dialyzer allows precise control over fluid removal from the plasma into the dialysate.

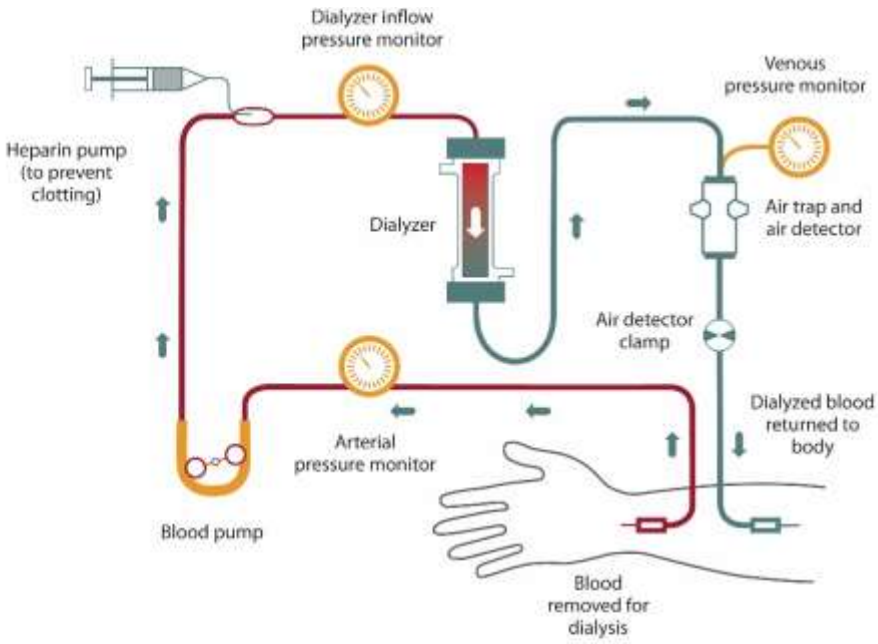

Figure 2. Schematic illustration of hemodialysis circuit[6]

1.1 Composition of Dialysate

The dialysate composition is crucial for effective hemodialysis:[5]

- **Bicarbonate:** Replaces acetate as the buffer to avoid complications and improve patient comfort.
- **Potassium:** Typically set at 2.0 mmol per liter, with net potassium loss depending on the patient's predialysis potassium levels.
- **Calcium:** Often at 1.25 mmol per liter to prevent hypercalcemia, which is a common complication with higher calcium concentrations.
- **Sodium:** Approximately 140 mmol per liter to reduce the risk of hypotension, cramping, nausea, vomiting, fatigue, and dizziness during treatment. Sodium modeling, which involves starting with a higher sodium concentration and gradually lowering it, can help manage osmolar shifts and reduce dialysis-related symptoms.
- **Glucose:** Included at 200 mg per deciliter to maintain blood glucose levels and prevent drops in blood insulin during treatment.

1.2 Water Purification

Water used for dialysate must be meticulously purified to prevent contamination and adverse reactions. This is typically achieved through reverse osmosis, which removes over 90 percent of dissolved ions and microbiologic contaminants. Despite these measures, occasional pyrogenic reactions can occur, emphasizing the need for stringent monitoring and maintenance of water-treatment systems.[5]

2. PERITONEAL DIALYSIS (PD)

PD is a well-established treatment method for managing end-stage renal failure (ESRF). The development of this therapy required extensive research and innovation over more than a century. A significant milestone was achieved in 1959 when Maxwell and colleagues introduced a simplified method of intermittent peritoneal irrigation using a single disposable catheter and commercially prepared dialysis solutions. The subsequent introduction of a permanent, indwelling silicone-rubber catheter with Dacron cuffs marked another important advancement. Despite these developments, intermittent PD initially played a limited role in ESRF treatment. This changed with Popovich and colleagues' introduction of the "portable/wearable equilibration" technique, which evolved into the widely accepted CAPD. By the end of 1997, approximately 120,000 patients worldwide were undergoing PD, constituting about 15% of all dialysis patients globally.[7]

2.1 Process of PD

In PD, solute and fluid exchange occurs between the blood in the peritoneal capillaries and the dialysis solution in the peritoneal cavity. This exchange happens across the peritoneal membrane, which includes the vascular wall, interstitium, and mesothelium. The movement of solutes follows the physical laws of diffusion and convective transport, while fluid shifts occur due to osmosis, driven by the addition of osmotic agents in the dialysis solutions.[7]

2.2 Key Components and Factors

- **Peritoneal Blood Flow:** The blood flow through the peritoneal capillaries is crucial for the exchange process but cannot be directly manipulated.[7]
- **Peritoneal Membrane:** This highly vascular membrane facilitates solute and fluid exchange. Its permeability influences the effectiveness of the dialysis.[7]
- **Dialysis Solution Flow Rate and Volume:** These are adjustable factors that can be optimized to maximize solute and fluid removal. Various techniques and regimens have been developed to enhance transport characteristics.[7]

2.3 Solute Movement and Membrane Permeability

- **Diffusion and Convection:** Solutes move according to diffusion and convective transport principles, influenced by the permeability of the peritoneal membrane.[7]
- **Osmosis:** Fluid shifts occur due to osmotic gradients created by osmotic agents in the dialysis solutions.[7]

The peritoneal membrane is not a perfect semipermeable membrane and tends to be more permeable than the synthetic membranes used in hemodialysis. The effectiveness of the membrane in transporting solutes can be assessed using the peritoneal equilibration test, which measures the rate of movement of small molecules such as creatinine and glucose across the membrane.[7]

2.4 Peritoneal Equilibration Test

This test helps classify the peritoneal membrane's transporter status based on the rate of small molecule movement:[7]

- **High Transporter Status:** Indicates a highly permeable membrane with rapid solute transport but limited ability to maintain an osmotic gradient for prolonged fluid removal.
- **Low Transporter Status:** Indicates a less permeable membrane with slower solute transport but better capacity for long-term ultrafiltration.

IV. COMPARISON OF DIALYSIS AND RT FOR ESRD

Patient survival after RT demonstrates marked improvements compared to hemodialysis or PD. However, the perceived benefits of transplantation may be influenced by patient selection, as individuals with severe comorbidities may not qualify for transplantation and thus remain in the dialysis group. Comparative studies have suggested that including high-risk patients in the dialysis group may bias outcomes in favor of transplantation.[8]

Analysis of survival outcomes, adjusting for significant variables related to mortality, has shown that RT recipients generally experience better survival rates than hemodialysis patients, particularly among diabetic populations. When adjusted for comorbid factors, overall survival is significantly higher in RT recipients compared to hemodialysis patients. However, the choice of treatment modality did not significantly impact mortality when considering factors such as age, heart disease, cancer, and smoking habits in non-diabetic patients.[8]

In non-diabetic patients, survival rates adjusted for age and comorbid conditions were similar between RT recipients and hemodialysis patients. Conversely, in diabetic patients, treatment modality significantly affected mortality, with RT recipients demonstrating substantially higher five-year adjusted survival rates compared to hemodialysis patients.[8]

Furthermore, analyses focusing on ESRD patients without comorbid risk factors at the start of dialysis revealed no significant differences in survival between hemodialysis patients and RT recipients over a ten-year period.[8]

These findings are consistent with previous studies, which have also demonstrated comparable survival outcomes between dialysis and RT after accounting for pretreatment risk factors. Notably, diabetic RT recipients have shown markedly lower long-term mortality risks compared to diabetic dialysis patients.[8]

Quality of life measures indicate that transplant recipients generally experience higher levels of life satisfaction and psychosocial well-being compared to dialysis patients. Successful RTs have been associated with significant improvements in psychosocial well-being, although physical activity levels may not increase significantly. Additionally, RT recipients are more likely to be able to work compared to dialysis patients, though economic productivity may not differ significantly between the two groups.[8]

In summary, evidence suggests that RT offers superior survival and quality of life outcomes compared to dialysis, particularly among diabetic patients. However, treatment modality should be carefully evaluated for each patient based on individual demographics and comorbid conditions.[8]

V. CRITERIA FOR SELECTION OF ESRD TREATMENT MODALITIES

The treatment of ESRD necessitates careful consideration of various factors to determine the most suitable RRT modality. The primary options – hemodialysis, PD, and RT – each offer unique advantages and challenges. Optimal decision-making requires an individualized approach that prioritizes long-term physical and psychological well-being, as well as integration into family and society.[8]

1. FACTORS INFLUENCING TREATMENT MODALITY SELECTION

1.1 Demographic and Comorbid Factors

When selecting the appropriate treatment modality for ESRD patients, it's crucial to consider demographic factors and comorbid conditions. Among these, diabetes, cardiovascular disease, and older age pose significant risks for mortality in ESRD patients. Each of these patient groups presents unique characteristics and considerations, which warrant independent analysis.[8]

Diabetes patients

In diabetic patients with ESRD, mortality rates are notably higher compared to non-diabetic counterparts, particularly among those undergoing dialysis. Our analysis of 531 patients on hemodialysis, adjusting for age and comorbidity, revealed a 2.39 times greater risk of death for diabetic patients ($P < 0.0001$). However, survival rates after RT are currently similar between diabetic and non-diabetic patients.[8]

RT emerges as the optimal choice for diabetic patients, provided careful consideration of post-transplantation risks. Significant predictors of mortality include preexisting ischemic heart disease, stroke, and peripheral vascular disease. Notably, patients with ischemic heart disease pre-transplantation exhibit lower survival rates, emphasizing the importance of comprehensive vascular evaluation before transplantation.[8]

For diabetic transplant candidates, aged over 35 or presenting clinical evidence of arterial disease, an extensive vascular assessment is imperative, including stress thallium myocardial imaging and coronary arteriography if indicated. Coronary revascularization should be strongly considered in patients with coronary artery disease before transplantation.[8]

Combined pancreas-kidney transplantation (PKT), particularly simultaneous pancreas and kidney transplantation from a single cadaveric donor, offers superior glycemic control and improved quality of life. However, the procedure entails greater morbidity, including cardiovascular and urologic complications, and has been associated with high mortality rates in some reports. Consequently, PKT is typically restricted to young patients with few diabetic complications and no coronary artery disease.[8]

Despite RT being the preferred treatment for diabetic ESRD patients, many are placed on dialysis while awaiting transplantation or as their sole therapy. The choice between dialysis modalities remains contentious. CAPD has been proposed as the initial therapeutic option due to advantages such as avoiding vascular access problems, better blood pressure control, and greater independence, especially for older diabetic patients. However, survival outcomes between CAPD and hemodialysis patients have varied across studies.[8]

Diabetic patients experience high mortality rates and poor quality of life, even in the predialysis phase, with cardiovascular disease being a leading cause of death. Prevention of cardiovascular disease is paramount in enhancing survival among diabetic ESRD patients. Individualized therapy before, during, and after kidney transplantation, coupled with meticulous management of hypertension, obesity, and hyperlipidemia, can mitigate the progression of macrovascular disease and improve long-term survival prospects.[8]

PATIENTS WITH CARDIOVASCULAR DISEASE

Cardiovascular disease is prevalent among patients undergoing long-term dialysis, contributing to nearly 50% of overall mortality in this population. It serves as a robust predictor of mortality in individuals with ESRD.[8]

Managing dialysis in patients with a history of congestive heart failure, cardiomegaly, or ischemic heart disease poses significant challenges. In hemodialysis, intradialytic hypotension can lead to complications such as arrhythmias, myocardial ischemia, mesenteric ischemia, and exacerbation of retinopathy. Notably, type II diabetic patients experiencing frequent intradialytic hypotensive episodes are at a substantially elevated risk of myocardial infarction death.[8]

Several studies have demonstrated successful PD outcomes in patients with severe heart failure. PD offers advantages such as improved hemodynamic control, reduced acute hypokalemia, and better anemia management. Additionally, it has been suggested that PD may contribute to the reduction of left ventricular mass, potentially improving cardiac function compared to hemodialysis.[8]

In patients with severe cardiovascular instability, PD or continuous cyclic PD (CCPD) should be prioritized as the treatment modality. However, if hemodialysis is necessary, measures such as using bicarbonate dialysate buffer, correcting anemia with erythropoietin, and enhancing cardiovascular performance through various strategies like increasing dialysate calcium concentration and maintaining cool temperature dialysate can be employed.[8]

Evaluation for arteriosclerotic heart disease is considered mandatory before RT, even in patients who may not be transplant candidates. The correction of coronary lesions, either through percutaneous transluminal coronary angioplasty (PTCA) or coronary artery bypass grafting (CABG), should be strongly considered. CABG is generally preferred over PTCA due to its lower risk of subsequent cardiac events.[8]

All dialysis patients, irrespective of transplant candidacy, should undergo comprehensive evaluation for arteriosclerotic heart disease, ensuring equitable treatment standards with non-uremic subjects. This underscores the importance of personalized care and meticulous consideration of cardiovascular health in dialysis management.[8]

ELDERLY PATIENTS

The elderly population requiring dialysis is steadily increasing, with a significant proportion undergoing in-center hemodialysis. Despite complex medical and psychosocial conditions, survival rates and quality of life among elderly dialysis patients are generally acceptable, although outcomes vary across studies.[8]

Dialysis should not be withheld from elderly patients if there's potential for meaningful life extension, but it shouldn't be used solely to prolong the dying process. Absolute contraindications to dialysis include advanced malignancy, irreversible dementia, and severe cardiopulmonary diseases.[8]

Comparative survival between hemodialysis and PD in the elderly remains underexplored, but most studies suggest similar survival rates between the two modalities. Elderly patients often face vascular access challenges, with polytetrafluoroethylene (PTFE) grafts commonly used when endogenous arteriovenous (AV) fistulas are not feasible.[8]

Hemodialysis in elderly patients is associated with more intradialytic complications, particularly hypotension, which may necessitate treatment interruptions. RT has become a viable option for elderly patients with ESRD, with improved patient selection and transplant outcomes. However, transplantation should be carefully considered and individualized based on risk factors such as coronary artery disease.[8]

PATIENT PREFERENCE AND PSYCHOSOCIAL FACTORS

Patient preference and psychosocial factors significantly influence the choice of RRT. Preferences should be discussed with patients, but nephrologists must also provide guidance. Motivated patients with resources may benefit from home hemodialysis, associated with improved survival and quality of life. Psychological stability is crucial for home-based modalities like CAPD or home hemodialysis. Having a living-related donor is preferable for transplantation. In-center hemodialysis is common for patients lacking support or living far from treatment centers.[8]

NON-MEDICAL FACTORS

The choice of RRT is influenced by non-medical factors such as cultural, legal, and economic considerations. Transplant rates vary globally due to factors like organ availability and cultural attitudes. In dialysis, hemodialysis is more common worldwide, but CAPD/CCPD is prevalent in certain countries like the UK and Australia. Non-medical factors like reimbursement, training, resource availability, and cultural norms impact modality selection. However, training and knowledge of the nephrology team are crucial in modality decisions. Centers offering both hemodialysis and CAPD/CCPD, along with transplantation services, provide comprehensive care. Physicians should be trained in all modalities to optimize patient care. Both hemodialysis and PD are valuable options, each with its own benefits and challenges. Choosing the right modality and optimizing treatment can improve outcomes and enhance quality of life for ESRD patients.[8]

VI. REFERENCES

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Notes

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